Versatile route to 2,6-dideoxyamino sugars from non-sugar materials: Syntheses of vicenisamine and kedarosamine

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A new strategy for the synthesis of 2,6-dideoxyamino sugars from non-sugar starting materials has been developed. The key reaction in this strategy is the acid-catalyzed intramolecular cyclization, by which a nitrogen functional group is introduced with simultaneous control of vicinal chiral centers. The synthesis of two kinds of 2,6-dideoxyamino sugars, D-vicenisamine and L-kedarosamine, by this strategy is described.

Amino sugars, especially deoxyamino sugars, are found in various clinically important antibiotics such as antimicrobial macrolides and anthracycline antitumor antibiotics.[1] The sugar moieties of those antibiotics are essential for exerting biological activity in most cases; however, the more detailed functions of such sugars have yet to be evaluated.[2]

Vicenistatin, an antitumor antibiotic isolated from *Streptomyces* sp. HC-34, is unique in its structure, which includes a 20-membered macrocyclic lactam aglycone and an amino sugar, vicenisamine, as shown in Fig. 1.[3,4] Recently the whole 20-membered macrolactam ring skeleton was successfully synthesized and the absolute configuration was verified.[5] More recently, we have isolated a new congener, vicenistatin M, having a neutral sugar, D-mycarose, and have shown that it has no cytotoxicity.[6] This strongly suggests that the vicenisamine amino sugar plays an important role in exerting the cytotoxicity of vicenistatin.

We envisaged that modification of the sugar part of vicenistatin may serve as a tool for investigating the significance of the amino sugar and the structure–activity relationship. To this end, a versatile synthetic method for vicenisamine and modified amino sugars was most desirable. Particularly, we were interested in developing a synthetic route for amino sugars from non-sugar materials.

Our prime targets were vicenisamine and kedarosamine. The latter is an homologous stereoisomer of the former and is a component of the antitumor antibiotic kedarcidin's chromophore[7–9] and that of the antifungal macrolide A82548A.[10]

In this paper we describe a novel synthesis of methyl D-vicenisaminide **1** and methyl L-kedarosaminide **2** *via* the same strategy. Methyl D-vicenisaminide[11] and methyl L-kedarosaminide[12–14] were previously synthesized by different approaches.

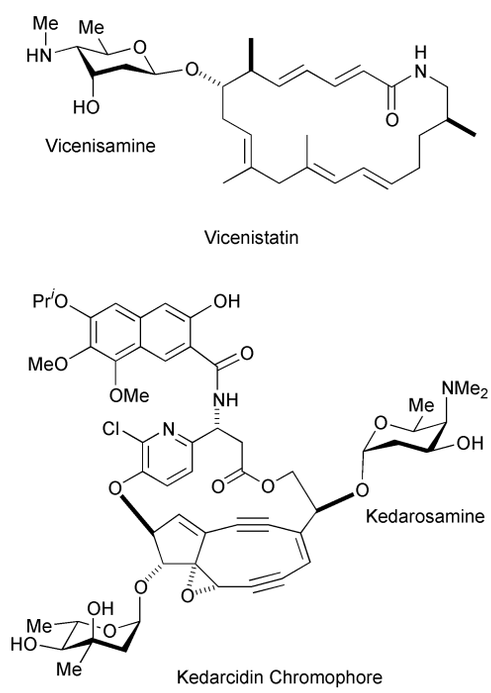
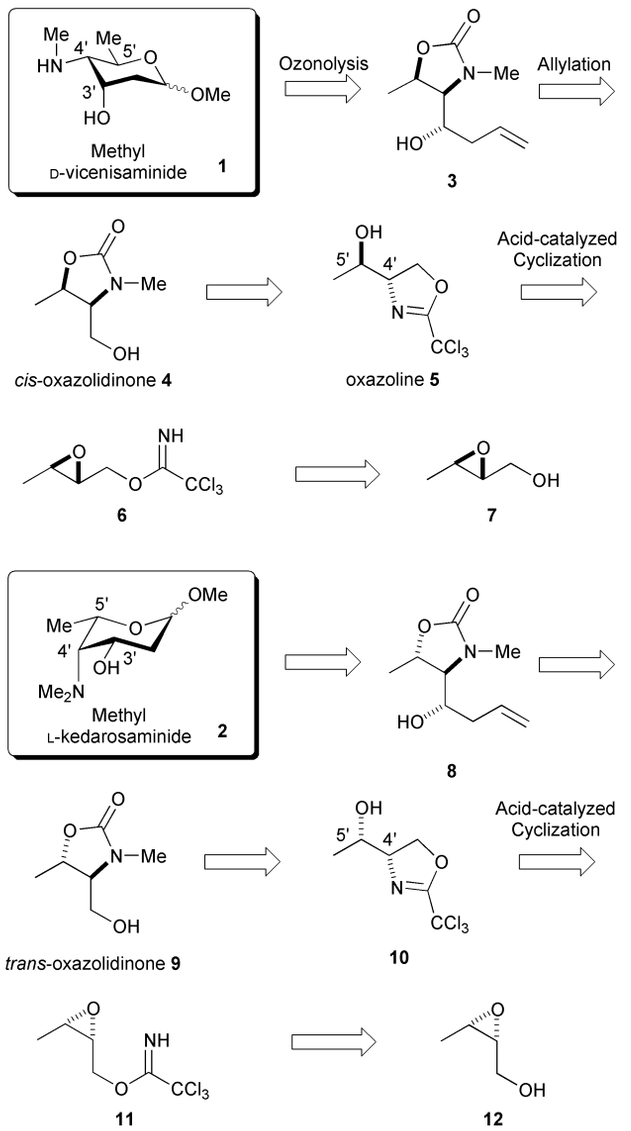


Fig. 1 Structure of vicenistatin and kedarcidin chromophore.

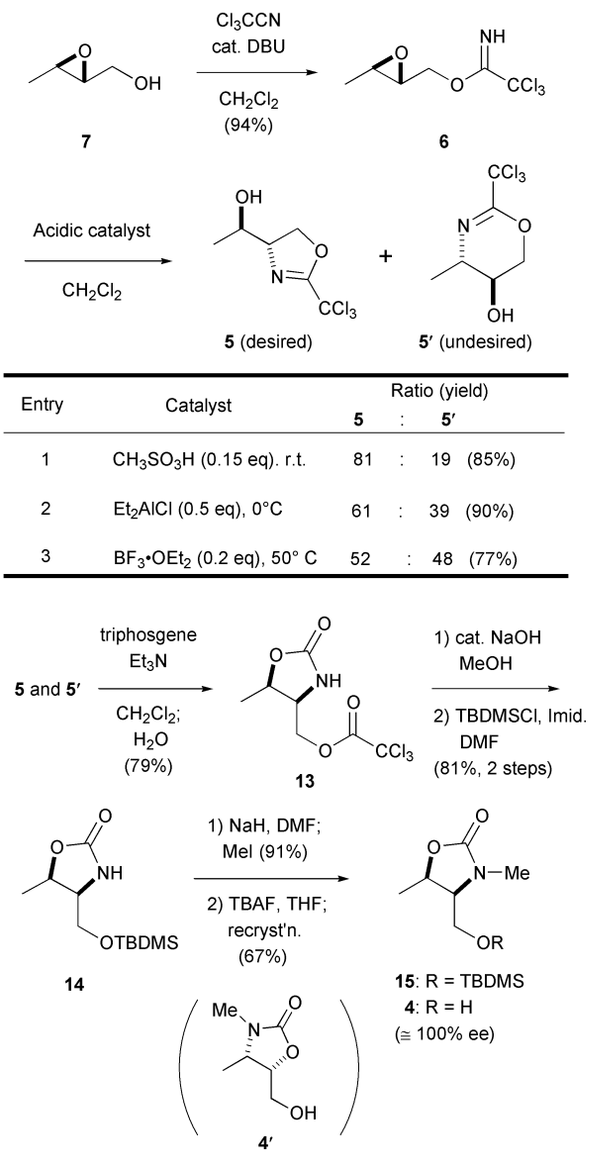
Results and discussion

Our general strategy for the construction of vicenisamine and kedarosamine is based on the retrosynthetic analysis shown in Scheme 1. Methyl vicenisaminide **1** was anticipated to be synthesized by oxidative cleavage of the side chain of **3**, followed by hydrolysis and acidic treatment. The side chain of the oxazolidinone **3** could be introduced by diastereoselective allylation of the intermediary aldehyde derived from chiral oxazolidinone alcohol **4**. The latter was supposed to be equivalent to the oxazoline **5**. The key transformation was to control the stereochemistry of nitrogen introduction, *i.e.*, an acid-catalyzed intramolecular cyclization[15–17] of epoxytrichloroacetimidate **6** should give rise to the oxazoline **5**. Evidently both enantiomers of the starting chiral *trans*-epoxy alcohol **7** are easily obtained by Sharpless asymmetric epoxidation.[18] Methyl kedarosaminide **2** should also be obtained according to this strategy by employing *cis*-epoxy alcohol **12**[18] as a starting material.

The first key manipulation of our work was the acid-catalyzed intramolecular cyclization, by which a nitrogen functional group was introduced with simultaneous control of vicinal chiral centers, and subsequent transformation to an important intermediate **4** as shown in Scheme 2. At first, *trans*-epoxy alcohol **7**[18] was easily converted into epoxytri-



Scheme 1 Retrosynthetic analysis of vicenisamine and kedarosamine.



Entry	Catalyst	Ratio (yield) 5 : 5′
1	CH_3SO_3H (0.15 eq). r.t.	81 : 19 (85%)
2	Et_2AlCl (0.5 eq), 0°C	61 : 39 (90%)
3	$BF_3{\cdot}OEt_2$ (0.2 eq), 50° C	52 : 48 (77%)

Scheme 2 Introduction of nitrogen functional group.

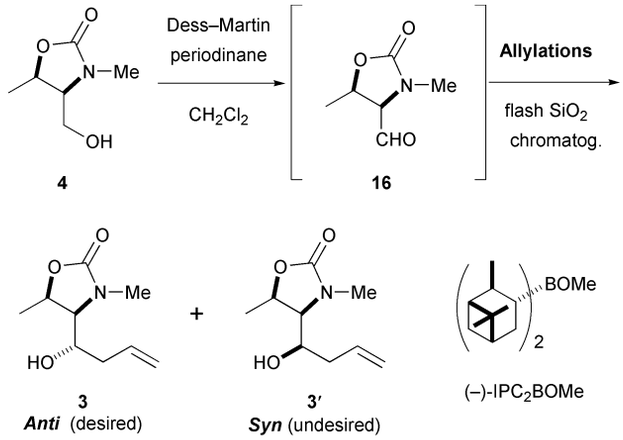
chloroacetimidate **6**, which was subsequently subjected to acidic rearrangement with several kinds of catalyst as reported by Schmidt[16] and Hatakeyama.[17] The course of the reaction to form either the five-membered ring (5-*exo*-cyclization) or six-membered ring (6-*endo*-cyclization) is known to be controlled by the structure of the starting epoxide, and occasionally, also by the catalysts as well.[15–17] In the case of our substrate **6**, methanesulfonic acid afforded the desired 5-*exo*-cyclization product **5** in good yield. The ratio of the oxazoline **5** to the dihydrooxazine **5′** was found to be 81 to 19 by ^{1}H NMR analysis, but unfortunately, the desired oxazoline **5** was inseparable from the minor isomer **5′**.

The mixture of these isomers was treated with triphosgene and triethylamine, by which the intermediary imidatonium ion was gradually hydrolyzed with water to the oxazolidinone **13**. The trichloroacetyl group of compound **13** was replaced by a *tert*-butyldimethylsilyl (TBDMS) group, and a methyl group was introduced on the nitrogen of oxazolidinone **14** to give **15**. The silyl protecting group of **15** was removed by treatment with tetrabutylammonium fluoride (TBAF). The resulting alcohol **4** was able to be favorably separated from the isomer **4′** by recrystallization. Enantiomeric purity of **4** was determined to be almost 100% ee by the ^{1}H NMR analysis of the corresponding methoxy(trifluoromethyl)phenylacetate (MTPA) ester.

The next stage was the diastereoselective allylation to construct the (1′*S*) alcohol group, as shown in Scheme 3. The aldehyde **16**, which was obtained by Dess–Martin oxidation of **4**, was subjected to allylation conditions without purification. Originally diastereoselective allylation using chiral auxiliary was supposed to be the most reliable way to obtain significant diastereoselectivity. Brown's diisopinocamphenylborane, $(IPC)_2B$, was examined as the chiral auxiliary, since it was known to have been applied to a variety of aldehydes and the stereochemical outcome of the reaction was predictable.[19] The attempted allylation reaction, however, led to almost the same results with low and undesired diastereoselectivity† (*anti*-**3**: *syn*-**3′** = 15 : 85, 79% yield in 2 steps) regardless of whether (+)- or (−)-$(IPC)_2B$ was employed. Similarly, almost complete *syn*-selectivity was observed in the case of achiral allyltin reagent. We thus turned our attention to higher selectivity under the achiral conditions, especially focusing on the indium-promoted allylation. An advantage of the latter conditions was that the reaction could be carried out in an aqueous medium;[20] in other words, extraction of the intermediary polar aldehyde **16** from the quenching aqueous medium was not necessary.

This one-pot oxidation–allylation procedure allowed us to obtain homoallyl alcohol **3′** in good yield (71%, 2 steps). Although, the resulting alcohol was the undesired stereoisomer

† The stereochemistry of the resulting alcohols was respectively determined after their conversion into the corresponding hexopyranosides *vide infra.*

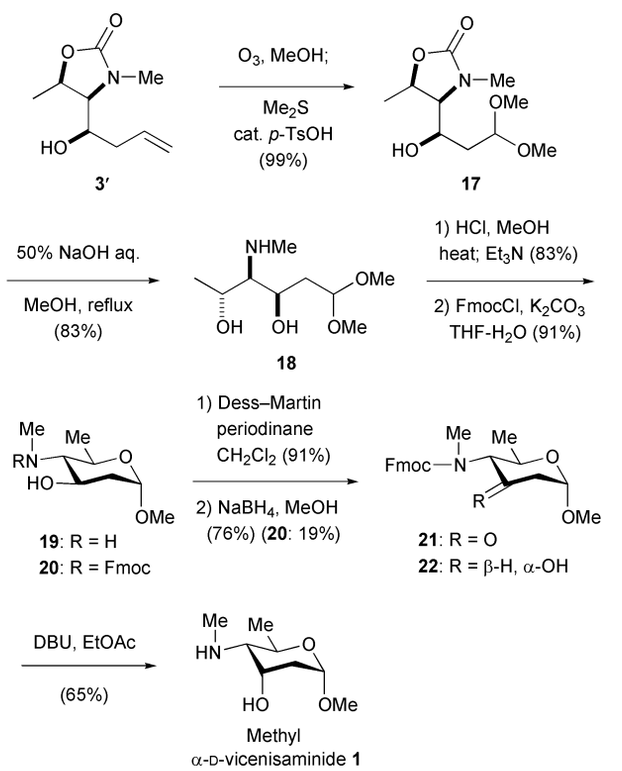


Entry	Conditions	Yield (%, 2 steps) *anti*	*syn*
1	**(–)**-$(IPC)_2BOMe$, AllylMgBr Et_2O-THF	12	67
2	**(+)**-$(IPC)_2BOMe$, AllylMgBr Et_2O-THF	12	67
3	$BF_3{\bullet}OEt_2$, $AllylSnBu^n{}_3$ CH_2Cl_2	trace	58
4	Indium, AllylBr ***H_2O***	trace	71

Scheme 3 Selectivity of allylation-1.

3′ just as anticipated, its stereochemistry was actually inverted at a later stage, *vide infra*.

Ozonolysis of the terminal olefin of **3′** in MeOH, followed by work-up with dimethyl sulfide and a catalytic amount of toluene-*p*-sulfonic acid (*p*-TsOH), quantitatively yielded dimethyl acetal **17** (Scheme 4). Alkaline hydrolysis of the oxazolidinone

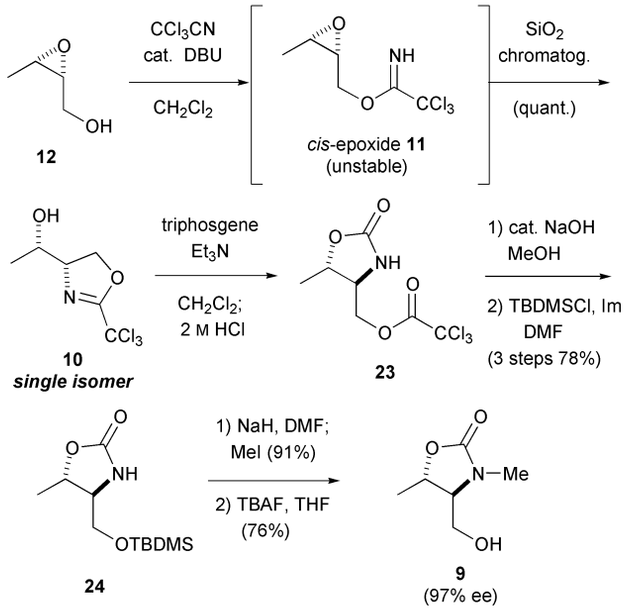


Scheme 4 Synthesis of methyl vicenisaminide.

ring in **17** liberated free amino alcohol **18**, which was subsequently cyclized to hexopyranoside in HCl–MeOH, producing mainly an α-anomer **19**. The free amino group of **19** was then protected by an Fmoc (fluoren-9-ylmethoxycarbonyl) group to give **20**. The stereochemistry at C-3 of **20** was inverted by the reduction of the corresponding ketone **21** by $NaBH_4$ to give diastereoisomeric alcohols **22**. Finally, the Fmoc proctective group of **22** was removed by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[21] to give methyl α-D-vicenisaminide **1**. A portion of **1** was transformed into the β-anomer by heating in HCl–MeOH. The spectroscopic properties of the β-anomer were confirmed to be identical with those of the naturally derived product.

Next, the synthesis of kedarosamine was pursued starting from the *cis*-epoxy alcohol **12**.[18] We were interested in the cyclization reaction of *cis*-epoxytrichloroacetimidate **11** in comparison with its *trans*-counterpart **6**. Although racemic *cis*-isomer had previously been reported, its reactivity was not discussed in detail.[15]

It was unexpectedly found that the *cis*-isomer **11** was significantly more reactive than the *trans*-isomer **6**. In fact, exothermic cyclization spontaneously took place during its purification by silica gel chromatography to quantitatively give the desired *threo*-oxazoline **10** as a single isomer in 2 steps (Scheme 5). Subsequently the oxazoline **10** was transformed



Scheme 5 Synthesis of *trans*-oxazolidinone from *cis*-epoxy alcohol.

into oxazolidinone **24** *via* **23** in 3 steps. It should also be noted that there was a marked difference in reactivity between *threo*-oxazoline **10** and *erythro*-isomer **5**, that is, acidic conditions (2 M HCl) were required for the reaction of *threo*-oxazoline **10**, whereas *erythro*-isomer **5** was easily converted into the oxazolidinone **13** under neutral aqueous conditions. These results may probably be due to different steric repulsion between the methyl group and a hydrogen in the imidatonium ions as illustrated in Fig. 2.

The oxazolidinone **24** was subsequently converted into alcohol **9** by the same reaction as described for the vicenisamine synthesis. Repeated recrystallization of **9** raised its enantiomeric purity up to 97% ee.

Dess–Martin oxidation of **9** cleanly afforded *threo*-aldehyde **25**, which was further subjected to an allylation reaction. A different trend of reactivity was observed in this case from that of *erythro*-aldehyde **16** as depicted in Scheme 6. In every case, relatively low to moderate yields were attained, probably because of the instability of **25**. The second concern was the diastereoselectivity. Almost no diastereoselectivity was observed in the case of using an achiral reagent, and the desired *anti*-isomer was obtained with a moderate selectivity (*anti*-**8** : *syn*-**8′** = 75 : 25; 53% yield in 2 steps) by the use of (−)-$(IPC)_2B$. On the other hand, when (+)-$(IPC)_2B$ was employed,

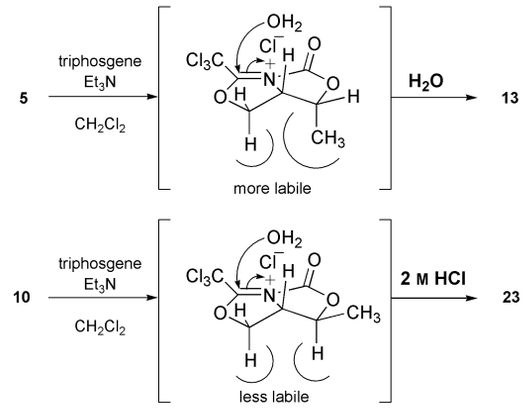
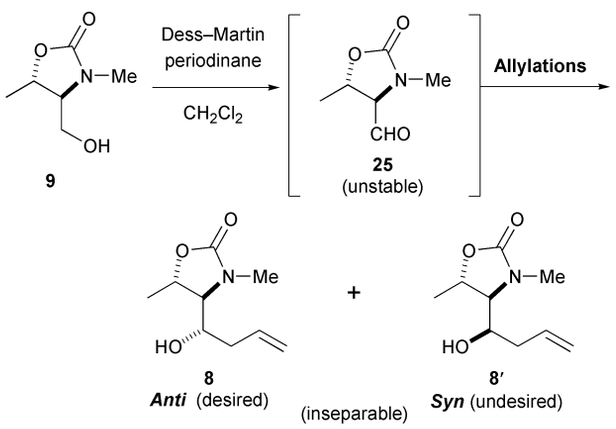


Fig. 2 Lability of intermediary imidatonium ions to hydrolytic conditions.



Entry	Reagents	*anti* : *syn*	Yield (%, 2 steps)
1	AllylBr, In	33 : 67	40
2	$AllylSnBu_3$, $BF_3{\cdot}Et_2O$	43 : 57	26
3	$AllylB\{(+)\text{-}IPC\}_2$	3 : 97	55
4	$AllylB\{(-)\text{-}IPC\}_2$	75 : 25	53

Scheme 6 Selectivity of allylation-2.

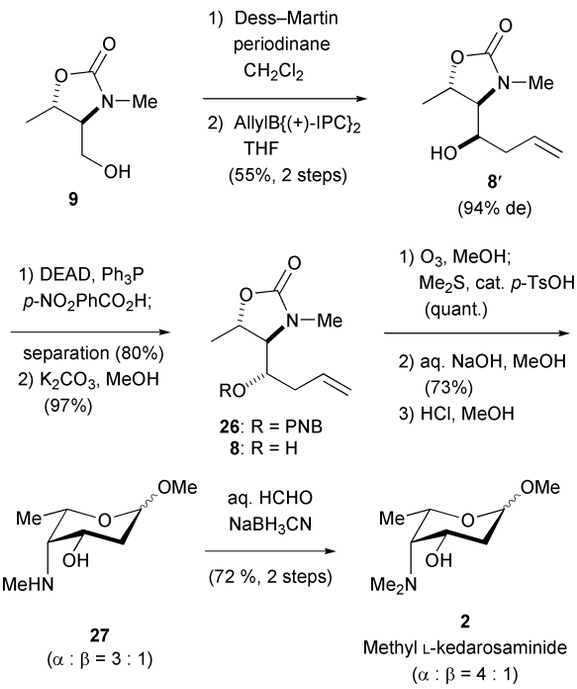
the reaction led to high *syn*-selectivity (**8** : **8′** = 3 : 97; 55% yield in 2 steps).

It seems relevant here to discuss the stereochemical differences of the allylations of **16** and **25**. Steric repulsion by the *cis*-methyl group in the *erythro*-aldehyde **16** appeared to be responsible for the result that the undesired diastereomer **3′** was obtained as a major isomer regardless of the conditions. On the other hand, the stereochemistry of allylation from the *threo*-aldehyde **25** was mainly dependent on the chirality of the auxiliary employed.

The allylation products from **25** were transformed into the corresponding *p*-nitrobenzoates, which were fortunately chromatographically separable. Furthermore, the undesired compound **8′** could be converted into **8** by Mitsunobu inversion and hydrolysis of the resulting *p*-nitrobenzoate **26**.

Thus the obtained compound **8** was transformed into hexopyranoside **27** by the same sequential transformations as in the vicenisamine synthesis, *i.e.*, ozonolysis, hydrolysis and subsequent cyclization. Finally, *N*-methylation was carried out to yield methyl L-kedarosaminide **2** as a mixture of anomers (α : β = 4 : 1) as shown in Scheme 7. Its spectroscopic data were identical with those described in the literature.[8]

In order to develop a more convenient route to the target amino sugars, we attempted simple conversion of *erythro*-oxazolidinone **4** into *threo*-isomer **9**, but with little success. Previously, Masamune and Sharpless and co-workers had reported efficient conversion of acetonide-protected 2,3-



Scheme 7 Synthesis of methyl kedarosaminide.

erythro-aldoses into 2,3-*threo*-aldoses by treatment with K_2CO_3 in MeOH.[22] Accordingly, the *erythro*-aldehyde **16** was subjected to a similar epimerization. Unfortunately, however, decomposition or complex reaction was observed in this case, mainly because of the unstable nature of *threo*-aldehyde **25**.

In conclusion, we have successfully synthesized D-vicenisamine and L-kedarosamine as their methyl hexopyranosides, showing our synthetic strategy for 2,6-dideoxyamino sugars using easily accessible non-sugar starting materials to be versatile.

Experimental

All mps are uncorrected. NMR spectra were recorded on a JEOL LA-300, or a Bruker DRX-500 spectrometer. ^1H NMR and ^{13}C NMR chemical shifts were reported in δ-values based on internal tetramethylsilane (TMS) ($\delta_H = 0$), or solvent signal ($CDCl_3$ $\delta_C = 77.0$; CD_3OD $\delta_H = 4.78$, $\delta_C = 49.0$) as reference. IR spectra were recorded on a Horiba FT-710 Fourier-transform infrared spectrometer. Optical rotations were measured on a JASCO DIP-360 polarimeter. $[\alpha]_D$-Values are given in units of 10^{-1} deg cm^2 g^{-1}. Mass spectra were measured on a JEOL AX-505HA mass spectrometer. Silica gel column chromatography was carried out with Merck Kieselgel 60, Art. Nr. 7734, and flash silica gel column chromatography was carried out with Merck Kieselgel 60, Art. Nr. 9385.

(2*R*,3*R*)-2,3-Epoxybutyl trichloroacetimidate 6

To an ice-cooled solution of (2*R*,3*R*)-2,3-epoxybutan-1-ol[18] **7** (420 mg, 4.77 mmol) and trichloroacetonitrile (550 mm^3, 5.49 mmol) in CH_2Cl_2 (6 cm^3) was added dropwise DBU (82 mm^3, 0.55 mmol) and the mixture was stirred at rt for 1 h. The solvent was removed *in vacuo*, and the residue was purified by silica gel chromatography (hexane–EtOAc, 5 : 1 to 4 : 1) to afford **6** (1.04 g, 94%) (Found: C, 30.86; H, 3.63; N, 5.76. Calc. for $C_6H_8Cl_3NO_2$: C, 31.00; H, 3.47; N, 6.02%); $[\alpha]_D^{28}$ +31.7 (*c* 1.04, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3344, 1668, 1331, 1300, 1084, 1022, 1001, 989, 830, 800 and 647; δ_H (300 MHz; $CDCl_3$) 1.37 (d, *J* 5.1 Hz, 3H), 3.01–3.11 (m, 2H), 4.23 (dd, *J* 5.6, 12.2 Hz, 1H) and 4.56 (dd, *J* 2.9, 12.2 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 17.2, 52.3, 55.9, 69.0, 91.0 and 162.6.

(4*S*)-4-[(1′*R*)-1′-Hydroxyethyl]-2-trichloromethyl-4,5-dihydrooxazole 5

To a solution of **6** (1.69 g, 7.27 mmol) in dry CH_2Cl_2 (72 cm^3) was added methanesulfonic acid (71 mm^3, 1.09 mmol) and the mixture was stirred at rt for 2 h. To the mixture was added saturated aq. $NaHCO_3$ and the CH_2Cl_2 layer was separated. The organic layer was washed with saturated aq. $NaHCO_3$, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by silica gel chromatography (hexane–EtOAc, 5 : 1 to 1 : 2) to afford a mixture of **5** and **5′** (1.44 g, 85%; **5** : **5′** = 81 : 19 by ^{1}H NMR), which was used for the next reaction without further purification; ν_{max} (neat)/cm^{-1} 3388, 1662, 1238, 1028, 991, 843, 823, 795 and 665; δ_H (300 MHz; $CDCl_3$) 1.22 (d, *J* 6.6 Hz, 3H), 4.14–4.20 (m, 1H), 4.32 (dt, *J* 3.7, 9.2 Hz, 1H) and 4.65 (dd, *J* 3.5, 9.1 Hz, 2H); δ_C (75 MHz; $CDCl_3$) 19.1, 67.6, 71.6, 72.3, 86.4 and 164.0.

(4*S*,5*R*)-5-Methyl-4-(trichloroacetoxymethyl)oxazolidin-2-one 13

To an ice-cooled solution of a mixture of **5** and **5′** (75.0 g, 323 mmol) and triethylamine (58.5 cm^3, 419 mmol) in dry CH_2Cl_2 (1520 cm^3) was added triphosgene (38.3 g, 129 mmol) in portions, and the mixture was stirred at rt for 3 h. The reaction mixture was poured into saturated aq. NH_4Cl (1600 cm^3) at 0 °C and stirred for 10 h. The organic layer was separated, and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic extract was dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by silica gel chromatography (hexane–EtOAc, 3 : 1 to 1 : 50) to afford **13** (70.1 g, 79%), which was contaminated with a corresponding isomer derived from **5′** (Found: C, 30.67; H, 3.11; N, 4.82. Calc. for $C_7H_8Cl_3NO_4$: C, 30.41; H, 2.92; N, 5.07%); $[a]_D^{28}$ −18.4 (*c* 4.76, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3284, 1766, 1751, 1389, 1377, 1238, 1097, 991, 850, 828 and 678; δ_H (300 MHz; $CDCl_3$) 1.49 (d, *J* 6.6 Hz, 3H), 4.10–4.13 (m, 1H), 4.33 (dd, *J* 6.3, 11.5 Hz, 1H), 4.53 (dd, *J* 4.9, 11.5 Hz, 1H), 4.92 (dq, *J* 6.8, 7.8 Hz, 1H) and 6.38 (br s, 1H); δ_C (75 MHz; $CDCl_3$) 14.5, 53.5, 66.1, 75.1, 89.0, 159.8 and 161.4.

(4*S*,5*R*)-4-*tert*-Butyldimethylsiloxymethyl-5-methyloxazolidin-2-one 14

To a solution of **13** (1.04 g, 3.75 mmol) in dry MeOH (9 cm^3) was added powdered NaOH (37.5 mg, 0.94 mmol) and the mixture was stirred at rt for 0.5 h and concentrated *in vacuo*. To an ice-cooled solution of the residue and imidazole (765 mg, 11.2 mmol) in dry dimethylformamide (DMF) (8 cm^3) was added TBDMSCl (1.13 g, 7.50 mmol) and the mixture was stirred for 0.5 h. To the reaction mixture was added crushed ice and the mixture was stirred for 20 min before being extracted twice with Et_2O, and the combined organic extract was washed successively with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by silica gel chromatography (hexane–EtOAc, 3 : 1 to 1 : 3) to afford **14** (747 mg, 81% in 2 steps), which was contaminated with a corresponding isomer derived from **5′** (Found: C, 53.58; H, 9.53; N, 5.41. Calc. for $C_{11}H_{23}NO_3Si$: C, 53.84; H, 9.45; N, 5.71%); $[a]_D^{26}$ −27 (*c* 1.04, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3282, 1751, 1471, 1389, 1254, 1227, 1138, 1099, 837, 775 and 665; δ_H (300 MHz; $CDCl_3$) 0.07 (s, 6H), 0.89 (s, 9H), 1.40 (d, *J* 6.6 Hz, 3H), 3.61 (dd, *J* 6.8, 10.2 Hz, 1H), 3.67 (dd, *J* 4.9, 10.2 Hz, 1H), 3.76–3.84 (m, 1H) and 4.81 (dq, *J* 6.6, 7.6 Hz, 1H).

(4*S*,5*R*)-4-*tert*-Butyldimethylsiloxymethyl-3,5-dimethyloxazolidin-2-one 15

Sodium hydride (1.42 g, ≈60% dispersion in mineral oil; 35.5 mmol) was washed with dry hexane, and was then suspended in dry DMF (65 cm^3). To the ice-cooled suspension was added dropwise a solution of **14** (4.26 g, 17.4 mmol) in dry DMF (40 cm^3). The mixture was warmed to rt, and stirred for 0.5 h. To the reaction mixture was added dropwise methyl iodide (3.3 cm^3, 53 mmol) at 0 °C, and the mixture was warmed to rt and stirred for 0.5 h. The reaction was quenched by the addition of cold water and saturated aq. NH_4Cl at 0 °C. The mixture was extracted five times with Et_2O, and the combined extract was washed successively with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by silica gel chromatography (hexane–EtOAc, 3 : 1 to 1 : 3) to afford **15** (4.11 g, 91%), which was contaminated with a corresponding isomer derived from **5′** (Found: C, 55.48; H, 9.93; N, 5.41. Calc. for $C_{12}H_{25}NO_3Si$: C, 55.56; H, 9.71; N, 5.40%); $[a]_D^{22}$ −1.6 (*c* 1.06, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1753, 1431, 1400, 1255, 1132, 1088 and 837; δ_H (300 MHz; $CDCl_3$) 0.08 (s, 6H), 0.89 (s, 9H), 1.43 (d, *J* 6.6 Hz, 3H), 2.88 (s, 3H), 3.59 (m, 1H), 3.72 (dd, *J* 3.9, 11.0 Hz, 1H), 3.78 (dd, *J* 4.6, 11.0 Hz, 1H) and 4.68 (dq, *J* 6.6, 7.8 Hz, 1H); δ_C (75 MHz; $CDCl_3$) −5.7, 14.6, 17.8, 25.6, 29.6, 58.9, 61.2, 72.7 and 158.6.

(4*S*,5*R*)-4-Hydroxymethyl-3,5-dimethyloxazolidin-2-one 4

To a solution of **15** (41.2 g, 159 mmol) in dry THF (1060 cm^3) was added dropwise TBAF (1.0 M solution in THF; 167 cm^3, 167 mmol) at 0 °C, and the mixture was stirred at rt for 0.5 h. The solvent was removed *in vacuo*, and the residue was purified by silica gel chromatography ($CHCl_3$–MeOH, 100 : 1 to 5 : 1) to afford a mixture of **4** and **4′** (22.6 g, 98%). Recrystallization from EtOAc and hexane (30 : 1) gave pure **4** (15.4 g, 67%, almost 100% ee by ^{1}H NMR analysis of the corresponding Mosher ester) (Found: C, 49.56; H, 7.81; N, 9.64. Calc. for $C_6H_{11}NO_3$: C, 49.65; H, 7.64; N, 9.65%); mp 72.7–76.0 °C; $[a]_D^{17}$ −17 (*c* 1.07, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3629, 3420, 1743, 1435, 1406, 1234, 1072 and 1045; δ_H (300 MHz; $CDCl_3$) 1.47 (d, *J* 6.6 Hz, 3H), 2.92 (s, 3 H), 3.65 (m, 1H), 3.82 (m, 2H), 4.73 (dq, *J* 6.6, 7.8 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 14.6, 29.5, 58.3, 61.1, 73.2 and 158.9.

(4*S*,5*R*)-4-[(1′*R*)-1′-Hydroxybut-3′-enyl]-3,5-dimethyloxazolidin-2-one 3′

To a solution of **4** (4.07 g, 28.0 mmol) in dry CH_2Cl_2 (140 cm^3) was added Dess–Martin periodinane (16.0 g, 42.5 mmol) at 0 °C. The mixture was stirred for 0.5 h at rt, treated with 10% aq. $Na_2S_2O_3$, and then CH_2Cl_2 was removed *in vacuo.* To the residual aqueous suspension were added indium powder (4.83 g, 42.0 mmol) and allyl bromide (4.85 cm^3, 56.0 mmol). After sonication for several minutes, the mixture was stirred for 23 h at rt. To complete the reaction, additional amounts of indium (1.60 g, 13.9 mmol) and allyl bromide (2.50 cm^3, 28.9 mmol) were necessary. To the mixture was added EtOAc and the mixture was stirred for 2 h. After filtration through a pad of Celite, the layers were separated. The aqueous layer was extracted seven times with EtOAc, and the combined organic layer was dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash silica gel chromatography (hexane–EtOAc 3 : 1 to 1 : 5) to afford **3′** (3.71 g, 71% in 2 steps) as a white solid (Found: C, 58.23; H, 8.44; N, 7.44. Calc. for $C_9H_{15}NO_3$: C, 58.36; H, 8.16; N, 7.56%); mp 64.3–66.5 °C; $[a]_D^{22}$ −27 (*c* 1.13, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3359, 1716, 1670, 1645, 1408, 1294, 1234, 1068, 1032, 1011, 933, 850, 766 and 675; δ_H (300 MHz; $CDCl_3$) 1.48 (d, *J* 6.6 Hz, 3H), 2.37 (t, *J* 6.8 Hz, 2H), 3.04 (s, 3H), 3.57 (dd, *J* 3.7, 7.6 Hz, 1H), 3.87 (dt, *J* 3.7, 6.8 Hz, 1H), 4.68 (dq, *J* 6.6, 7.6 Hz, 1H), 5.17–5.24 (m, 2H) and 5.81 (ddt, *J* 7.1, 10.5, 16.6 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 14.8, 32.2, 39.7, 63.0, 68.9, 73.8, 118.4, 133.8 and 158.9.

(4*S*,5*R*)-4-[(1′*R*)-1′-Hydroxy-3′,3′-dimethoxypropyl]-3,5-dimethyloxazolidin-2-one 17

Ozone was introduced into a solution of **3′** (238 mg, 7.92 mmol) in MeOH (18 cm^3) at −78 °C until the color of the solution became slightly pale blue. Excess of ozone was purged

with a stream of argon. To the mixture were added sequentially dimethyl sulfide (2.0 cm^3, 27.2 mmol) and *p*-TsOH monohydrate (30 mg, 0.174 mmol) at −78 °C. The bath was removed and the solution was allowed to warm gradually to rt with stirring for 18 h. After the addition of $NaHCO_3$ powder to the mixture, the whole was concentrated *in vacuo*. The residue was mixed with EtOAc, and the resulting suspension was filtered through a pad of Celite, and then the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography (hexane–EtOAc, 1 : 1 to 0 : 1) to afford **17** (297 mg, 99%) (Found: C, 51.46; H, 8.49; N, 5.76. Calc. for $C_{10}H_{19}NO_5$: C, 51.49; H, 8.21; N, 6.00%); $[\alpha]_D^{24}$ −24 (*c* 1.02, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3438, 1734, 1442, 1392, 1230, 1122, 1082 and 1047; δ_H (300 MHz; $CDCl_3$) 1.48 (d, *J* 6.6 Hz, 3H), 1.74 (ddd, *J* 2.0, 4.4, 14.1 Hz, 1H), 1.97 (ddd, *J* 5.6, 10.3, 14.1 Hz, 1H), 2.99 (s, 3H), 3.40 (s, 3H), 3.42 (s, 3H), 3.53 (dd, *J* 4.0, 7.7 Hz, 1H), 4.09 (m, 1H), 4.57 (dd, *J* 4.6, 5.1 Hz, 1H) and 4.65 (dq, *J* 6.6, 7.3 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 15.1, 32.0, 37.3, 54.0, 54.6, 63.9, 66.6, 73.4, 104.2 and 159.0.

(2*R*,3*R*,4*R*)-6,6-Dimethoxy-3-(methylamino)hexane-2,4-diol 18

A solution of **17** (1.51 g, 6.49 mmol) in MeOH (18 cm^3) and 50% aq. NaOH (12 cm^3) was refluxed for 3 h. The reaction mixture was cooled, and concentrated *in vacuo*. The residue was dissolved in a minimum amount of water and extracted four times with EtOAc. The combined organic extract was dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by silica gel chromatography ($CHCl_3$–MeOH, 20 : 1 to 5 : 1) to afford **18** (1.11 g, 83%) (Found: C, 51.88; H, 10.34; N, 6.52. Calc. for $C_9H_{21}NO_4$: C, 52.15; H, 10.21; N, 6.76%); $[\alpha]_D^{24}$ −3.3 (*c* 1.06, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3356, 1448, 1423, 1383, 1124 and 1053; δ_H (300 MHz; $CDCl_3$) 1.26 (d, *J* 6.6 Hz, 3H), 1.74 (ddd, *J* 2.9, 6.1, 14.1 Hz, 1H), 1.98 (ddd, *J* 4.9, 9.8, 14.1 Hz, 1H), 2.17 (dd, *J* 2.7, 4.2 Hz, 1H), 2.50 (s, 3H), 3.36 (s, 6H), 4.01 (dq, *J* 4.1, 6.6 Hz, 1H), 4.11 (dt, *J* 2.7, 9.8 Hz, 1H) and 4.60 (dd, *J* 5.1, 5.9 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 19.9, 35.5, 37.5, 53.5, 53.7, 63.8, 67.1, 67.3 and 103.6.

Methyl 2,4,6-trideoxy-4-methylamino-α-D-*arabino*-hexopyranoside 19

To an HCl–MeOH solution, which had been prepared by adding AcCl (1.80 cm^3, 25.3 mmol) to ice-cooled dry MeOH (18 cm^3), was added a solution of **18** (633 mg, 3.05 mmol) in dry MeOH (18 cm^3) at 0 °C and the reaction mixture was refluxed for 2 h. After the addition of Et_3N (4 cm^3, 28.7 mmol) at 0 °C, the mixture was concentrated *in vacuo*. The residue was purified by repeated flash silica gel chromatography (EtOAc–MeOH, 20 : 1 to 10 : 1) to afford **19** (443 mg, 83%) (Found: C, 54.66; H, 9.85; N, 7.69. Calc. for $C_8H_{17}NO_3$: C, 54.84; H, 9.78; N, 7.99%); $[\alpha]_D^{19}$ +123 (*c* 1.05, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3354, 1446, 1379, 1126, 1105, 972, 908 and 756; δ_H (300 MHz; $CDCl_3$) 1.30 (d, *J* 6.3 Hz, 3H), 1.66 (ddd, *J* 3.7, 11.2, 12.7 Hz, 1H), 2.06 (t, *J* 9.9 Hz, 1H), 2.19 (dd, *J* 5.1, 12.7 Hz, 1H), 2.48 (s, 3H), 3.31 (s, 3H), 3.70 (dq, *J* 6.3, 9.8 Hz, 1H), 3.81 (ddd, *J* 5.1, 9.8, 11.5 Hz, 1H) and 4.75 (d, *J* 3.4 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 18.6, 33.1, 37.8, 54.7, 65.5, 66.9, 67.8 and 98.6.

Methyl 2,4,6-trideoxy-4-[(fluoren-9-ylmethoxycarbonyl)methylamino]-α-D-*arabino*-hexopyranoside 20

To a solution of **19** (70 mg, 0.40 mmol) in THF (1.8 cm^3)–water (0.9 cm^3) were added sequentially potassium carbonate (341 mg, 2.47 mmol) and FmocCl (297 mg, 1.15 mmol) at 0 °C and the mixture was stirred for 0.5 h. Water was added to the mixture and the organic layer was separated. The aqueous layer was extracted twice with Et_2O. The combined organic layers were dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash silica gel chromatography (hexane–EtOAc, 2 : 1 to 1 : 5) to afford **20** (145 mg, 91%), which was used for the next reaction without further purification; $[\alpha]_D^{28}$ +47 (*c* 1.13, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3587, 3438, 1689, 1450, 1311, 1149, 1126 and 978; δ_H (300 MHz; $CDCl_3$) 0.91, 1.14 (d, *J* 6.0 Hz, 3H), 1.52, 1.73 (ddd, *J* 3.4, 9.5, 12.9 Hz, 1H), 2.16, 2.22 (dd *J* 4.7, 12.9 Hz, 1H), 2.74, 2.76 (s, 3H), 3.26, 3.28 (s, 3H), 3.68–4.00 (m, 2H), 4.26 (t, *J* 6.3 Hz, 1H), 4.52, 4.62 (d, *J* 6.4, 2H), 4.72 (dd, *J* 3.2, 12.9 Hz, 1H), 7.32 (t, *J* 7.3 Hz, 2H), 7.40 (t, *J* 7.3 Hz, 2H), 7.60 (d, *J* 6.6 Hz, 2H), 7.77 (d, *J* 7.3 Hz, 2H); δ_C (75 MHz; $CDCl_3$) 17.5, 17.6, 28.3, 38.5, 39.0, 47.1, 54.6, 62.6, 63.2, 63.9, 64.3, 67.2, 77.2, 98.2, 98.4, 119.8, 124.8, 127.0, 127.5, 141.2, 143.8, 144.0 and 157.0.

Methyl 2,4,6-trideoxy-4-[(fluoren-9-ylmethoxycarbonyl)methylamino]-α-D-*erythro*-hexopyranosid-3-ulose 21

To a solution of **20** (611 mg, 1.59 mmol) in dry CH_2Cl_2 (25 cm^3) was added Dess–Martin periodinane (1.33 g, 3.14 mmol) at 0 °C. The mixture was stirred for 1 h at rt. To the mixture were added 10% aq. $Na_2S_2O_3$ and saturated aq. $NaHCO_3$, and the mixture was extracted three times with Et_2O. The organic layers were dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by silica gel chromatography (hexane–EtOAc, 5 : 1 to 1 : 1) to afford **21** (555 mg, 91%) {HRFAB-MS (NBA matrix) *m*/*z* 396.1772 $[(M + H)^+$. Calc. for $C_{23}H_{26}NO_5$: *m*/*z*, 396.1811]}; $[\alpha]_D^{28}$ +43 (*c* 1.16, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1732, 1697, 1450, 1402, 1300, 1244, 1169, 1130, 1045, 759 and 743; δ_H (300 MHz; $CDCl_3$) 1.11, 1.33 (d, *J* 6.1 Hz, 3H), 2.54, 2.72 (d, *J* 4.4 Hz, 1H), 2.61, 2.66 (d, *J* 1.4 Hz, 1H), 2.77, 2.85 (s, 3H), 3.33, 3.38 (s, 3H), 4.20–4.31 (m, 2H), 4.41, 4.49 (d, *J* 6.8 Hz, 2H), 4.46–4.55 (m, 1H), 4.95, 5.00 (t, *J* 2.95 Hz, and d, *J* 3.9 Hz, 1H) and 7.26–7.75 (m, 8H); δ_C (75 MHz; $CDCl_3$) 18.4, 18.7, 46.0, 46.3, 47.2, 54.7, 65.8, 67.0, 67.5, 67.9, 77.2, 98.8, 119.7, 124.4, 124.8, 126.8, 127.4, 141.1, 143.5, 143.7, 155.9, 156.8, 200.1 and 200.6.

Methyl 2,4,6-trideoxy-4-[(fluoren-9-ylmethoxycarbonyl)methylamino]-α-D-*ribo*-hexopyranoside 22

To a solution of **21** (511 mg, 1.29 mmol) in MeOH (30 cm^3) was added $NaBH_4$ (103 mg, 2.72 mmol) at −15 °C, and the mixture was stirred for 5 min. To the mixture was added saturated aq. NH_4Cl, and MeOH was removed *in vacuo*. The residue was dissolved in a minimum amount of water and extracted twice with Et_2O. The combined organic layer was dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash silica gel chromatography (hexane–EtOAc, 5 : 1 to 1 : 1) to afford **22** (391 mg, 76%) {HRFAB-MS (NBA matrix) *m*/*z* 398.1945 $[(M + H)^+$. Calc. for $C_{23}H_{28}NO_5$: *m*/*z*, 398.1967]}; $[\alpha]_D^{29}$ +124 (*c* 1.19, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3510, 1695, 1450, 1317, 1122, 1097 and 1049; δ_H (300 MHz; $CDCl_3$) 1.03 (d, *J* 6.1 Hz, 3H), 1.22 (d, *J* 6.3 Hz, 3H), 1.60 (dt, *J* 3.3, 14.4 Hz, 1H), 1.90 (dd, *J* 2.7, 14.4 Hz, 1H), 1.94–2.08 (m, 1H), 2.91 (s, 3H), 3.01 (s, 3H), 3.25 (dd, *J* 2.1, 10.5 Hz, 1H), 3.35 (s, 3H), 3.41 (s, 3H), 3.52–3.61 (m, 1H), 3.91 (d, *J* 9.8 Hz, 1H), 4.08 (m, 1H), 4.20–4.28 (m, 2H), 4.41 (s, 1H), 4.43 (d, *J* 1.0 Hz, 1H), 4.57 (dq, *J* 5.4, 6.8 Hz, 2H), 4.72 (d, *J* 3.2 Hz, 1H), 4.81 (d, *J* 2.2 Hz, 1H) and 7.28–7.78 (m, 8H); δ_C (75 MHz; $CDCl_3$) 18.1, 31.0, 31.3, 36.3, 36.5, 47.3, 55.2, 59.3, 60.4, 60.6, 66.7, 67.4, 69.0, 77.2, 98.6, 98.8, 119.7, 119.9, 124.5, 125.0, 127.0, 127.6, 141.3, 144.0, 156.2 and 157.0; further elution with hexane–EtOAc (1 : 5) gave **20** (98 mg, 19%).

Methyl 2,4,6-trideoxy-4-methylamino-α-D-*ribo*-hexopyranoside (methyl α-D-vicenisaminide) 1

To a solution of **22** (236 mg, 0.61 mmol) in EtOAc (34 cm^3) was added DBU (138 cm^3, 0.92 mmol), and the mixture was stirred for 0.5 h at rt. The solvent was removed *in vacuo* and the residue was purified by silica gel chromatography (16 g, $CHCl_3$–MeOH–water, 20 : 1 : 0 to 65 : 25 : 4) to afford **1** (70 mg, 65%) {HRFAB-MS (glycerol matrix) *m*/*z* 176.1273 $[(M + H)^+$. Calc. for $C_8H_{18}NO_3$: *m*/*z*, 176.1287]}; $[\alpha]_D^{26}$ +30 (*c* 0.23, $CHCl_3$); δ_H (300

MHz; $CDCl_3$) 1.32 (d, *J* 6.1 Hz, 3H, H_3-6), 1.85 (ddd, *J* 3.4, 3.7, 14.6 Hz, 1H, H-2_{ax}), 2.09 (dd, *J* 2.9, 10.0 Hz, 1H, H-4), 2.15 (ddd, *J* 1.0, 2.4, 14.6 Hz, 1H, H-2_{eq}), 2.44 (s, 3H, NMe), 3.37 (s, 3H, OMe), 3.71 (dq, *J* 6.2, 10.0 Hz, 1H, H-5), 4.07 (dd, *J* 3.2 Hz, 1H, H-3) and 4.77 (d, *J* 3.4 Hz, 1H, H-1); δ_C (75 MHz; $CDCl_3$) 18.6, 33.7, 35.2, 55.1, 62.8, 63.7, 64.0 and 98.4.

This was partly transformed into the β-anomer (methyl β-D-vicenisaminide) by heating in HCl–MeOH, and it was confirmed that its spectroscopic data (^{1}H, ^{13}C NMR) as the hydrochloride salt were identical with those described in ref. 3. Specific rotation and spectroscopic properties in the NH free form were identical with those of the naturally derived product; $[\alpha]_D^{23}$ −3.6 (NH free, *c* 0.52, MeOH) [natural origin: $[\alpha]_D^{22}$ −5.4 (NH free, *c* 0.46, MeOH)]; δ_H (300 MHz; CD_3OD) 1.16 (d, *J* 6.3 Hz, 3H, H_3-6), 1.45 (ddd, *J* 2.9, 9.5, 13.4 Hz, 1H, H-2_{ax}), 1.88 (ddd, *J* 2.2, 3.9, 13.4 Hz, 1H, H-2_{eq}), 2.07 (dd, *J* 3.2, 9.5 Hz, 1H, H-4), 2.30 (s, 3H, NMe), 3.32 (s, 3H, OMe), 3.59 (dq, *J* 6.3, 9.5 Hz, 1H, H-5), 4.10 (q, *J* 3.2 Hz, 1H, H-3) and 4.58 (dd, *J* 2.2, 9.5 Hz, 1H, H-1); δ_C (75 MHz; CD_3OD) 19.3, 33.7, 39.3, 56.6, 64.2, 65.5, 71.0 and 100.4; HRFAB-MS (glycerol matrix) *m*/*z* 176.1269 [(M + H)$^+$. Calc. for $C_8H_{18}NO_3$: *m*/*z*, 176.1287].

(4*S*)-4-[(1′*S*)-1′-Hydroxyethyl]-2-trichloromethyl-4,5-dihydrooxazole 10

To an ice-cooled solution of (2*R*,3*S*)-2,3-epoxybutan-1-ol[18] **12** (7.96 g, 90.3 mmol) and trichloroacetonitrile (10.9 cm^3, 108 mmol) in CH_2Cl_2 (200 cm^3) was added DBU (1.41 cm^3, 9.03 mmol, 10 mol%). After stirring for 15 min, the reaction mixture was evaporated to dryness. The residue was subjected to silica gel column chromatography (hexane–EtOAc, 7 : 3) to afford, through a spontaneous epoxide opening, **10** (20.9 g, quant.) as a colorless oil (Found: C, 30.70; H, 3.67; N, 5.84. Calc. for $C_6H_8Cl_3NO_2$: C, 31.00; H, 3.47; N, 6.02%); δ_H (300 MHz; $CDCl_3$) 1.28 (d, *J* 6.4 Hz, 3H), 2.49 (br s, 1 H), 3.86 (br quin, *J* 6.1 Hz, 1H), 4.32 (ddd, *J* 5.6, 8.3, 9.8 Hz, 1H), 4.46 (t, *J* 8.31 Hz, 1H) and 4.67 (dd, *J* 8.5, 9.8 Hz, 1H).

(4*S*,5*S*)-4-*tert*-Butyldimethylsiloxymethyl-5-methyloxazolidin-2-one 24

To an ice-cooled solution of **10** (15.3 g, 65.8 mmol) and triethylamine (11.9 cm^3, 85.5 mmol) in CH_2Cl_2 (330 cm^3) was added triphosgene (7.81 g, 26.3 mmol). After stirring of the mixture for 2 h at rt, 2 M HCl (100 cm^3) was added and stirring was continued for 30 min at rt, and then the resulting mixture was concentrated *in vacuo*. To a solution of the residue in MeOH (130 cm^3) was added NaOH (3.95 g, 98.7 mmol) and the mixture was stirred for 30 min at rt. After filtration through a small pad of Celite, the filtrate was evaporated to give a crude alcohol.

To an ice-cooled mixture of the crude alcohol and imidazole (13.4 g, 197 mmol) in DMF (130 cm^3) was added TBDMSCl (24.8 g, 165 mmol) and the resulting mixture was stirred for 2 h at rt. The reaction was quenched with water, and the mixture was extracted three times with Et_2O. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane–EtOAc, 4 : 1 to 7 : 3) to afford **24** (12.6 g, 78%, 3 steps) as a colorless oil (Found: C, 53.67; H, 9.57; N, 5.44. Calc. for $C_{11}H_{23}NO_3Si$: C, 53.84; H, 9.45; N, 5.71%); $[\alpha]_D^{24}$ −29.9 (*c* 1.1, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 1755, 1725, 1529, 1434, 1268 and 1241; δ_H (300 MHz; $CDCl_3$) 0.06 (s, 6H), 0.89 (s, 9H), 1.44 (d, *J* 6.4 Hz, 3H), 3.48 (q, *J* 5.3 Hz, 1H), 3.54–3.67 (m, 2H), 4.45 (quin, *J* 6.3 Hz, 1H) and 6.15–6.31 (br s, 1H); δ_C (75 MHz; $CDCl_3$) −5.5 , 18.1, 20.7, 25.7, 60.5, 64.5, 76.1 and 159.4.

(4*S*,5*S*)-4-Hydroxymethyl-3,5-dimethyloxazolidin-2-one 9

Sodium hydride (3.08 g, ≈60% dispersion in mineral oil; 77.1 mmol) was washed with dry hexane and suspended in dry DMF (260 cm^3). To the suspension was added dropwise the oxazolidinone **24** (12.6 g, 51.4 mmol) as a solution in dry DMF (20 cm^3) at 0 °C and the mixture was stirred for 90 min at rt. The mixture was recooled to 0 °C, and then methyl iodide (8.0 cm^3, 128 mmol) was added. The resulting mixture was stirred for 2 h at rt. The reaction mixture was recooled, quenched with saturated aq. NH_4Cl, and extracted three times with Et_2O. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane–EtOAc, 4 : 1 to 7 : 3) to afford an intermediary TBDMS ether (11.5 g, 86%) as a colorless oil (Found: C, 55.44; H, 9.91; N, 5.30. Calc. for $C_{12}H_{25}NO_3Si$: C, 55.56; H, 9.71; N, 5.40%); δ_H (300 MHz; $CDCl_3$) 0.08 (s, 6H), 0.89 (s, 9H), 1.40 (d, *J* 6.3 Hz, 3H), 2.87 (s, 3H), 3.29 (ddd, *J* 1.2, 4.6, 5.3 Hz, 1H), 3.70 (dd, *J* 1.2, 5.3 Hz, 2H) and 4.35 (quin, *J* 6.1 Hz, 1H); δ_C (75 MHz; $CDCl_3$) −5.7, 18.1, 18.0, 20.6, 25.6, 29.3, 62.3, 65.2 and 72.7.

To an ice-cooled solution of the TBDMS ether (711 mg, 2.74 mmol) in THF (13.7 cm^3) was added TBAF (3.02 cm^3, 1.0 M solution in THF; 3.02 mmol). After stirring for 30 min at rt, the mixture was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (EtOAc) to afford **9** (301 mg, 76%, ≈86% ee by ^{1}H NMR analysis of the corresponding Mosher ester) as a white solid. After recrystallization from EtOAc twice, enantiomeric purity was raised to ≈97% ee (Found: C, 49.92; H, 7.85; N, 9.62. Calc. for $C_6H_{11}NO_3Si$: C, 49.65; H, 7.64; N, 9.65%); mp 91.0–92.2 °C; $[\alpha]_D^{24}$ −41.4 (*c* 1.0, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3629, 3421, 1743, 1437, 1408, 1387, 1250, 1072 and 1039; δ_H (300 MHz; $CDCl_3$) 1.43 (d, *J* 6.3 Hz, 3H), 2.46–2.77 (br s, 1H), 2.89 (s, 3H), 3.29 (dt, *J* 6.1, 3.9 Hz, 1H), 3.62–3.73 (m, 1H), 3.82 (dt, *J* 11.5, 4.9 Hz, 1H) and 4.96 (quin, *J* 6.3 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 20.4, 29.3, 60.5, 65.5, 72.6 and 158.5.

(4*S*,5*S*)-4-[(1′*R*)-1′-Hydroxybut-3′-enyl]-3,5-dimethyloxazolidin-2-one 8′

To an ice-cooled solution of **9** (2.26 g, 15.6 mmol) in dry CH_2Cl_2 (52 cm^3) was added Dess–Martin periodinane (9.88 g, 23.4 mmol), and the mixture was stirred for 10 min at the same temperature and for 30 min at rt. The reaction was quenched with 10% aq. $Na_2S_2O_3$, and the mixture was extracted exhaustively with $CHCl_3$. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residual crude aldehyde **25** was used for the next reaction without purification.

To a solution of (+)-*B*-methoxydiisopinocamphenylborane (IPC_2BOMe) (14.8 g, 46.8 mmol) in freshly distilled THF (52 cm^3) was added dropwise allylmagnesium bromide (39.0 cm^3, ≈1 M solution in Et_2O; 39.0 mmol) under argon at −78 °C and the mixture was stirred for 30 min at the same temperature and for 1 h at rt. The mixture was recooled to −78 °C, a solution of the crude aldehyde **25** in THF (5 cm^3) was added dropwise, and the resulting mixture was stirred for 2 h at −78 °C and for 3 h at −25 °C. The reaction was quenched with saturated aq. NH_4Cl, and the mixture was extracted three times with EtOAc. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (hexane–EtOAc, 3 : 2 to 2 : 3) to afford **8′** (1.58 g, 55% in 2 steps, 94% de) as a white solid (Found: C, 58.52; H, 8.01; N, 7.49. Calc. for $C_9H_{15}NO_3$: C, 58.36; H, 8.16; N, 7.56%); mp 58.8–59.2 °C; $[\alpha]_D^{24}$ −37.4 (*c* 1.01, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3388, 2981, 2902, 1754, 1708, 1411 and 1371; δ_H (300 MHz; $CDCl_3$) 1.40 (d, *J* 6.3 Hz, 3H), 2.09–2.23 (m, 1H), 2.24–2.35 (m, 1H), 2.77 (br d, *J* 3.9 Hz, 1H), 2.90 (s, 3H), 3.33 (t, *J* 4.9 Hz, 1H), 3.83 (br sex, *J* 5.1 Hz, 1H), 4.45 (dt, *J* 11.0, 6.3 Hz, 1H), 5.18 (d, 6.6 Hz, 1H), 5.23 (s, 1H) and 5.74–5.92 (m, 1H); δ_C (75 MHz; $CDCl_3$) 21.5, 31.1, 36.5, 67.3, 70.5, 71.8, 119.3, 133.3 and 158.1.

(4*S*,5*S*)-3,5-Dimethyl-4-[(1′*S*)-1′-(*p*-nitrobenzoyl)but-3′-enyl] oxazolidin-2-one 26

To an ice-cooled solution of **8′** (886 mg, 4.78 mmol), triphenylphosphine (1.88 g, 7.18 mmol) and *p*-nitrobenzoic acid (1.20 g, 7.18 mmol) in dry THF (25 cm^3) was added dropwise diethyl azodicarboxylate (DEAD) (1.13 cm^3, 7.18 mmol) under argon and the mixture was stirred for 10 h at rt. The reaction was quenched with saturated aq. $NaHCO_3$, and the mixture was extracted three times with EtOAc. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. Crystalline by-product (diethylhydrazine-1,2-dicarboxylate) was removed by recrystallization from EtOAc. The filtrate was concentrated to dryness and the residue was purified by flash silica gel column chromatography (hexane–EtOAc, 4 : 1 to 2 : 1) to afford **26** (1.28 g, 80%, 100% de) as a colorless syrup (Found: C, 57.18; H, 5.60; N, 8.15. Calc. for $C_{16}H_{18}N_2O_6$: C, 57.48; H, 5.43; N, 8.34%); $[\alpha]_D^{24}$ −0.2 (*c* 1.00, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 1749, 1531, 1348 and 1101; δ_H (300 MHz; $CDCl_3$) 1.50 (d, *J* 6.3 Hz, 3H), 2.37–2.62 (m, 2H), 2.92 (s, 3H), 3.51 (dd, *J* 1.7, 4.1 Hz, 1H), 4.75 (d quin, *J* 4.4, 6.3 Hz, 1H), 5.12–5.26 (m, 2H), 5.50 (ddd, *J* 1.5, 6.1, 7.8 Hz, 1H), 5.71–5.86 (m, 1H), 8.12–8.19 (br d, *J* 9.0 Hz, 2H) and 8.27–8.33 (br d, *J* 8.8 Hz, 2H); δ_C (75 MHz; $CDCl_3$) 21.7, 29.6, 34.3, 65.8, 70.3, 70.7, 119.7, 123.7, 130.8, 131.5, 134.5, 150.7, 157.3 and 163.8.

(4*S*,5*S*)-4-[(1′*S*)-1′-Hydroxybut-3′-enyl]-3,5-dimethyloxazolidin-2-one 8

To an ice-cooled solution of **26** (1.02 g, 3.06 mmol) in THF (4 cm^3) and MeOH (6 cm^3) was added potassium carbonate (12.7 mg, 9.18×10^{-2} mmol, 3 mol%) and the mixture was stirred for 90 min at rt. After filtration through a pad of Celite, the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane–EtOAc, 7 : 3 to 2 : 1) afforded **8** (548 mg, 97%) as a white solid (Found: C, 58.47; H, 8.23; N, 7.56. Calc. for $C_9H_{15}NO_3$: C, 58.36; H, 8.16; N, 7.56%); mp 81.2–82.0 °C; $[\alpha]_D^{23}$ −41.1 (*c* 1.01, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3448, 2976, 2911, 1749, 1720, 1483, 1444, 1413 and 1157; δ_H (300 MHz; $CDCl_3$) 1.40 (d, *J* 6.4 Hz, 3H), 2.09–2.32 (m, 2H), 2.83 (s, 3H), 3.23 (dd, *J* 1.7, 5.1 Hz, 1H), 3.32–3.39 (m, 1H), 3.92 (br t, *J* 5.9 Hz, 1H), 4.62 (quin, *J* 6.1 Hz, 1H), 5.14 (s, 1H), 5.18 (d, 4.1 Hz, 1H) and 5.76–5.92 (m, 1H); δ_C (75 MHz; $CDCl_3$) 21.6, 29.2, 36.6, 67.2, 67.8, 70.1, 118.5, 133.7 and 158.5.

Methyl 2,4,6-trideoxy-4-methylamino-L-*lyxo*-hexopyranoside (methyl *N*-demethyl-L-kedarosaminide) 27

Ozone was introduced into a solution of **8** (341 mg, 1.84 mmol) in MeOH (20 cm^3) at −78 °C until the color of the solution became slightly pale blue. Excess of ozone was purged with a stream of argon. To the mixture were added sequentially dimethyl sulfide (2.7 cm^3, 36.9 mmol) and *p*-TsOH monohydrate (31.7 mg, 0.184 mmol, 10 mol%) at −78 °C. The bath was removed and the solution was allowed to warm gradually to rt with stirring for 18 h. After the addition of $NaHCO_3$ powder to the mixture, the whole was concentrated *in vacuo*. The residue was suspended with EtOAc, the suspension was filtered through a pad of Celite, and the solvent was removed *in vacuo*. The residue was purified by silica gel column chromatography (hexane–EtOAc, 1 : 4 to 1 : 9) to afford a dimethyl acetal (432 mg, quant.) as a colorless oil (Found: C, 51.64; H, 8.29; N, 5.84. Calc. for $C_{10}H_{19}NO_5$: C, 51.49; H, 8.21; N, 6.00%); $[\alpha]_D^{23}$ −27.9 (*c* 1.10, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3012, 2935, 1743, 1437, 1234 and 1122; δ_H (300 MHz; $CDCl_3$) 1.40 (d, *J* 6.8 Hz, 3H), 1.60–1.80 (m, 2H), 2.93 (s, 3H), 3.22 (dd, *J* 2.2, 5.5 Hz, 1H), 3.28 (d, *J* 1.9 Hz, 1H), 3.40 (s, 3H), 3.42 (s, 3H), 4.03 (br dd, *J* 2.0, 10.6 Hz, 1H), 4.44 (quin, *J* 5.6 Hz, 1H) and 4.61 (t, 5.3 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 21.6, 29.8, 34.4, 54.0, 54.5, 65.7, 68.4, 70.5, 103.7 and 158.3.

A solution of the resulting dimethyl acetal (234 mg, 1.00 mmol) in MeOH (3.5 cm^3) and 10% aq. NaOH (2 cm^3) was refluxed for 3 h. The reaction mixture was cooled, and concentrated *in vacuo*. The residue was dissolved in a minimum amount of water and extracted five times with EtOAc. The combined organic layer was dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (EtOAc–MeOH, 10 : 1 to 7 : 3) to afford an amino alcohol (151 mg, 73%) as a pale yellow syrup (Found: C, 51.85; H, 10.26; N, 6.63. Calc. for $C_9H_{21}NO_4$: C, 52.15; H, 10.21; N, 6.76%); $[\alpha]_D^{22}$ +12.3 (*c* 1.31, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3479, 3006, 2969, 2937, 1456, 1415, 1375, 1124 and 1080; δ_H (300 MHz; $CDCl_3$) 1.24 (d, *J* 6.6 Hz, 3H), 1.71–1.93 (m, 2H), 2.18 (br t, *J* 3.2 Hz, 1H), 2.53 (s, 3H), 3.37 (s, 3H), 3.38 (s, 3H), 3.82–4.13 (m, 5H) and 4.62 (t, *J* 5.9 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 20.7, 35.8, 36.7, 53.3, 53.6, 66.0, 67.4, 68.3 and 103.6.

To an HCl–MeOH solution, which had been prepared by adding AcCl (365 mm^3, 5.13 mmol) to ice-cooled dry MeOH (7.3 cm^3), was added a solution of the amino alcohol (151 mg, 0.730 mmol) in dry MeOH (1 cm^3) at rt and the reaction mixture was refluxed for 90 min. After cooling, 1 M NaOH was added to the mixture, and the resulting mixture was concentrated *in vacuo*. The residual aqueous layer was extracted five times with EtOAc. The combined organic layer was dried ($MgSO_4$), and concentrated *in vacuo* to afford **27** (112 mg, 88%, α : β ≈ 3 : 1) as a pale yellow syrup, which was used without purification.

Methyl 2,4,6-trideoxy-4-dimethylamino-L-*lyxo*-hexopyranoside (methyl L-kedarosaminide) 2

To a solution of **27** (112 mg, 0.639 mmol) in acetonitrile (2 cm^3)–aq. formaldehyde (274 mm^3, 35% aq. solution; 3.20 mmol) was added sodium cyanoborohydride (121 mg, 1.92 mmol) at rt and the reaction mixture was stirred for 15 min, neutralized with acetic acid, and concentrated *in vacuo*. The residue was dissolved in a minimum amount of 1 M NaOH and extracted five times with EtOAc. The combined organic layer was dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (EtOAc–MeOH, 10 : 1) to afford methyl L-kedarosaminide **2** (100 mg, 82%) as a pale yellow syrup, which was a mixture of isomers (α : β ≈ 4 : 1) {HRFAB-MS (NBA matrix) *m/z* 190.1464 [$(M + H)^+$. Calc. for $C_9H_{20}NO_3$: *m/z*, 190.1443]}; its spectroscopic data shown below were identical with those described in ref. 8.

α-Anomer: δ_H (500 MHz; $CDCl_3$) 1.43 (d, *J* 7.0 Hz, 3H, H_3-6), 1.78 (ddd, *J* 3.9, 10.3, 13.7 Hz, 1H, H-2_{ax}), 1.91 (ddd, *J* 2.7, 5.7, 13.7 Hz, 1H, H-2_{eq}), 2.51 (dd, *J* 3.3, 5.2 Hz, 1H, H-4), 2.62 (s, 6H, NMe_2), 3.33 (s, 3H, OMe), 3.96 (dt, *J* 5.5, 10.3 Hz, 1H, H-3), 4.13 (dq, *J* 3.2, 7.0 Hz, 1H, H-5) and 4.82 (br t, *J* 3.2 Hz, 1H, H-1); δ_C (125 MHz; $CDCl_3$) 17.9 (C-6), 35.5 (C-2), 44.8 (NMe_2), 44.8 (NMe_2), 54.8 (OMe), 63.4 (C-3), 63.9 (C-4), 67.6 (C-5) and 97.9 (C-1).

β-Anomer: δ_H (500 MHz; $CDCl_3$) 1.48 (d, *J* 6.9 Hz, 3H, H_3-6), 1.63 (ddd, *J* 9.0, 11.3, 13.1 Hz, 1H, H-2_{ax}), 2.05 (ddd, *J* 2.6, 5.8, 13.2 Hz, 1H, H-2_{eq}), 2.48 (dd, *J* 2.8, 5.4 Hz, 1H, H-4), 2.66 (s, 6H, NMe_2), 3.49 (s, 3H, OMe), 3.71 (dq, *J* 3.0, 6.9 Hz, 1H, H-3), 3.75 (dt, *J* 5.7, 11.1 Hz, 1H, H-5) and 4.37 (dd, *J* 2.7, 9.0 Hz, 1H, H-1); δ_C (125 MHz; $CDCl_3$) 18.5 (C-6), 37.1 (C-2), 44.9 (NMe_2), 44.9 (NMe_2), 56.2 (OMe), 63.2 (C-3), 65.8 (C-4), 72.5 (C-5) and 101.5 (C-1).

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