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TETRAHEDRON: *ASYMMETRY*

Chemoenzymatic syntheses of *N*-trifluoroacetyl-L-daunosamine, *N*-trifluoroacetyl-L-acosamine, *N*-benzoyl-D-acosamine, and *N*-benzoyl-D-ristosamine from an achiral precursor, methyl sorbate

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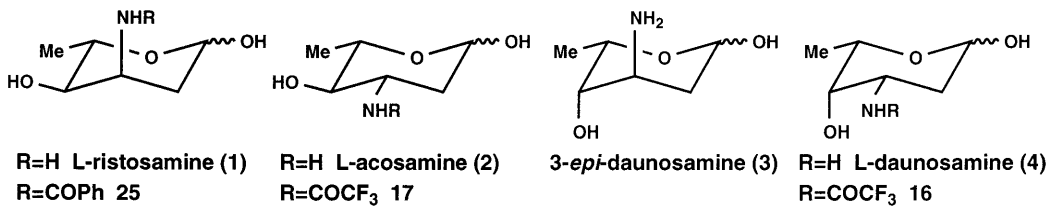
Abstract

A conjugated addition of benzylamine to methyl (4*R*,5*S*)-4,5-(isopropylidenedioxy)-(2*E*)-hexenoate **8a** followed by lactonization under acidic condition proceeds to the formal total syntheses of L-daunosamine **4** and L-acosamine **2**. On the other hand, direct conjugated addition of benzylamine to methyl (4*S*,5*S*)-4,5-epoxy-(2*E*)-hexenoate **5** and the subsequent intramolecular nucleophilic attack by the ester carbonyl group on the epoxy ring of the substrates leads to the formal total syntheses of D-acosamine **2** and D-ristosamine **1**.

1. Introduction

Three of the four diastereomers **1**–**4** of 3-amino-2,3,6-trideoxy-L-hexose are the naturally occurring amino sugars[1] (Scheme 1). The *ribo*-isomer, L-ristosamine **1**, is a component of the



Scheme 1.

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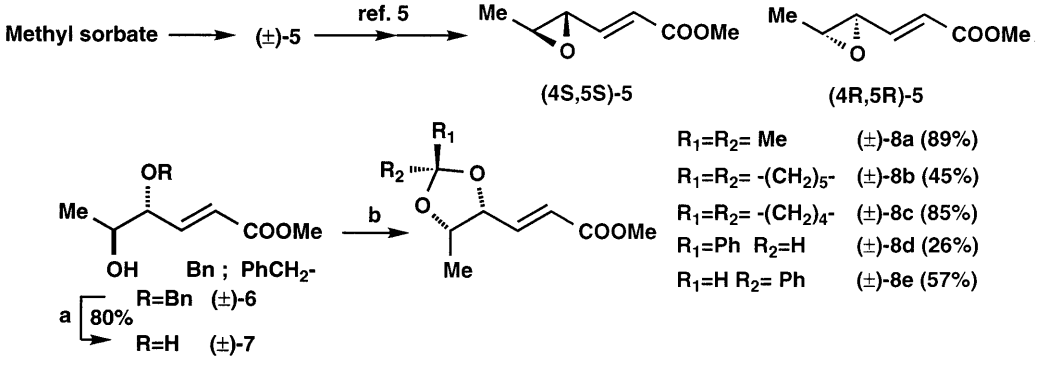
water-soluble glycoprotein ristomycin, which is a member of the vancomycin group of antibiotics.[1] Acosamine with the *arabino*-configuration have been found in both its L- and D-form. L-Acosame **2** was isolated from the antibiotic actinoidine and D-acosamine **2** was obtained from the basic antibiotic *N*-acetylsporaciridine.[1] While the *xylo*-isomer, 3-*epi*-L-daunosamine **3**, so far has not been found in nature, the *lyxo*-isomer, L-daunosamine **4**, is the glycosidic component of a number of important anthracycline antibiotics that exhibit impressive activity against a broad range of solid tumors and soft tissue sarcomas.[1] Changing L-daunosamine of adriamycin with its 4-epimer, L-acosamine **2** was reported to suppress the cardiotoxicity while retaining the anti-tumor activity.[2] Therefore, considerable interest has been shown in developing syntheses of enantiomerically pure L-daunosamine **4** and its analogues in order to provide sufficient material for pharmaceutical structure–activity studies.[3] Of several syntheses of L-daunosamine **4**, almost all of the chiral syntheses are based on conversion of natural carbohydrates such as D-mannose, L-rhamnose and D-glucose.[1] Approaches from non-carbohydrate precursors have also been reported; however, the known syntheses of **4** seem to be rather impractical.[4] We wish to report formal total syntheses of D-ristosamine **1**, L-acosamine **2**, D-acosamine **2**, and L-daunosamine **4**, starting from an achiral precursor, methyl sorbate, and employing enzymatic chiral induction and diastereoselective conjugated addition of benzylamine to the α,β-unsaturated ester.

2. Results and discussion

We reported the syntheses of the enantiomerically pure stereoisomers of *trans*-(4,5)-epoxy-2(*E*)-hexenoates (4*S*,5*S*)-**5** and (4*R*,5*R*)-**5** based on a chemoenzymatic method from an achiral precursor, methyl sorbate (Scheme 2).[5] For the syntheses of the target molecules from (4*S*,5*S*)-**5**, two synthetic routes are considered. One is the 1,4-addition of benzylamine to the α,β-unsaturated ester after epoxy ring opening of (4*S*,5*S*)-**5** by oxygen nucleophiles such as benzyl alcohol. The other is the direct 1,4-addition of benzylamine to the (4*S*,5*S*)-**5** and the subsequent regioselective cleavage of the epoxy ring by an intramolecular nucleophilic attack by the ester carbonyl group. At first, as a preliminary experiment of the former case, 1,4-addition of benzylamine to the olefinic moiety of the racemic **8a**–**e** derived from the reported benzyl ether (±)-**6**[5] was carried out. Treatment of (±)-**6** with $AlCl_3$ in the presence of *m*-xylene[5] gave a diol (±)-**7**, which was treated with 2,2-dimethoxypropane, cyclohexanone, cyclopentanone, and



Scheme 2. (a) $AlCl_3$, *m*-xylene/CH_2Cl_2; (b) $Me_2C(OMe)_2$/CSA for (±)-**8a**, cyclohexanone/*p*-TsOH·H_2O for (±)-**8b**, cyclopentanone/*p*-TsOH·H_2O for (±)-**8c**, benzaldehyde/*p*-TsOH·H_2O for (±)-**8d**,**e**

benzaldehyde in the presence of acid to afford the acetonide (±)-**8a** (89%), ketals (±)-**8b** (45%) and (±)-**8c** (85%), benzylidene acetals (±)-**8d** (26%) and (±)-**8e** (57%), respectively. The stereochemistry of the more polar benzylidene acetal (±)-**8e** was confirmed by difference nuclear Overhauser effect (NOE) spectra as shown in Fig. 1. The reaction of (±)-**8a–e** with benzylamine (2 equivalents) in the absence of solvent at room temperature afforded the 1,4-addition products, (±)-3,4-*syn*-**9a–e** and (±)-3,4-*anti*-**10a–e**, along with a small amount of starting materials **8a–e** as shown in Table 1. In the case of entries 1 and 2, the ratio of 3,4-*syn*-**9** and 3,4-*anti*-**10** were found to be 13.4:1 and 12.6:1, respectively. In order to determine the stereochemistry of the main product (±)-3,4-*syn*-**9a**, (±)-**9a** was converted into the known compound (±)-**11**. Hydrogenolysis of (±)-**9a** gave the 3-amino ester (±)-**12** (Scheme 3). Acetylation of (±)-**12** followed by treatment with 80% AcOH aqueous solution gave the (±)-*arabino*-3-acetoamino-γ-lactone **13**, which was converted into the known (±)-*arabino*-3-acetoamino-5-acetoxy-γ-lactone **11**.[6] The 3,4-*syn* stereochemistry of other (±)-**9b–e** was confirmed by the fact that treatment of (±)-**9b–e** with 2,2-dimethoxypropane in the presence of camphorsulfonic acid (CSA) afforded the above-mentioned (±)-**9a**. The stereochemistry of the minor product (±)-**10a** was confirmed to be 3,4-*anti* because optically active **10a** was chemically correlated to the known compound mentioned later in this text. From these conversion experiments, the relative configuration of the conjugated addition products (±)-**9a–e** was determined to be 3,4-*syn* and thence that of (±)-**10a–e** was confirmed to be 3,4-*anti*. The 3,4-*syn*-selective addition of a nucleophile to **8a** is explainable by a Felkin–Anh model[7] as depicted in Fig. 2.

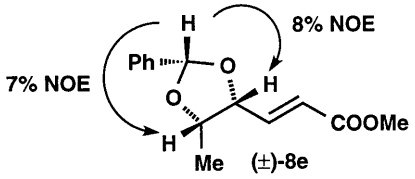
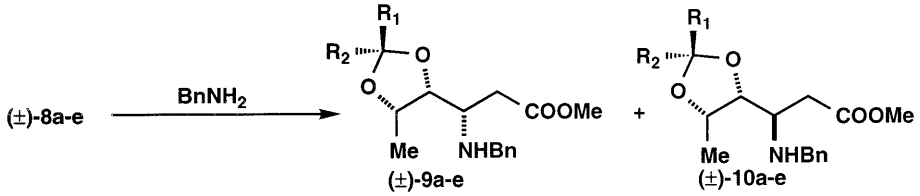
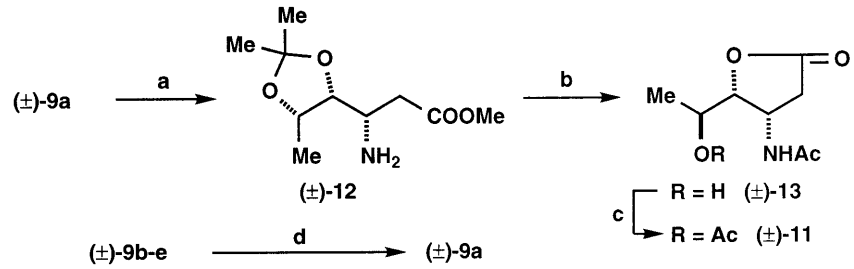


Figure 1.

Table 1



Entry			(±)-**9a–e**:(±)-**10a–e**	(±)-**9a–e** (%)	(±)-**10a–e** (%)
1	$R_1=R_2=Me$	(±)-**8a**	13.4:1	(±)-**9a** (67)	(±)-**10a** (5)
2	$R_1=R_2=-(CH_2)_5-$	(±)-**8b**	12.6:1	(±)-**9b** (63)	(±)-**10b** (5)
3	$R_1=R_2=-(CH_2)_4-$	(±)-**8c**	5.7:1	(±)-**9c** (57)	(±)-**10c** (10)
4	$R_1=Ph$, $R_2=H$	(±)-**8d**	5.1:1	(±)-**9d** (67)	(±)-**10d** (13)
5	$R_1=H$, $R_2=Ph$	(±)-**8e**	4:1	(±)-**9e** (52)	(±)-**10e** (13)



Scheme 3. (a) $H_2/Pd(OH)_2$–C; (b) (1) Ac_2O/pyridine, (2) 80% AcOH aq.; (c) Ac_2O/AcONa, reflux; (d) 40 equiv. $Me_2C(OMe)_2$/2 equiv. CSA/acetone, 90°C

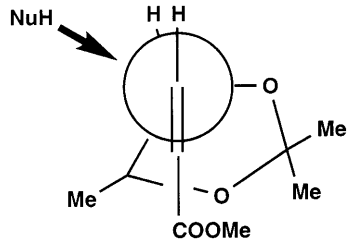
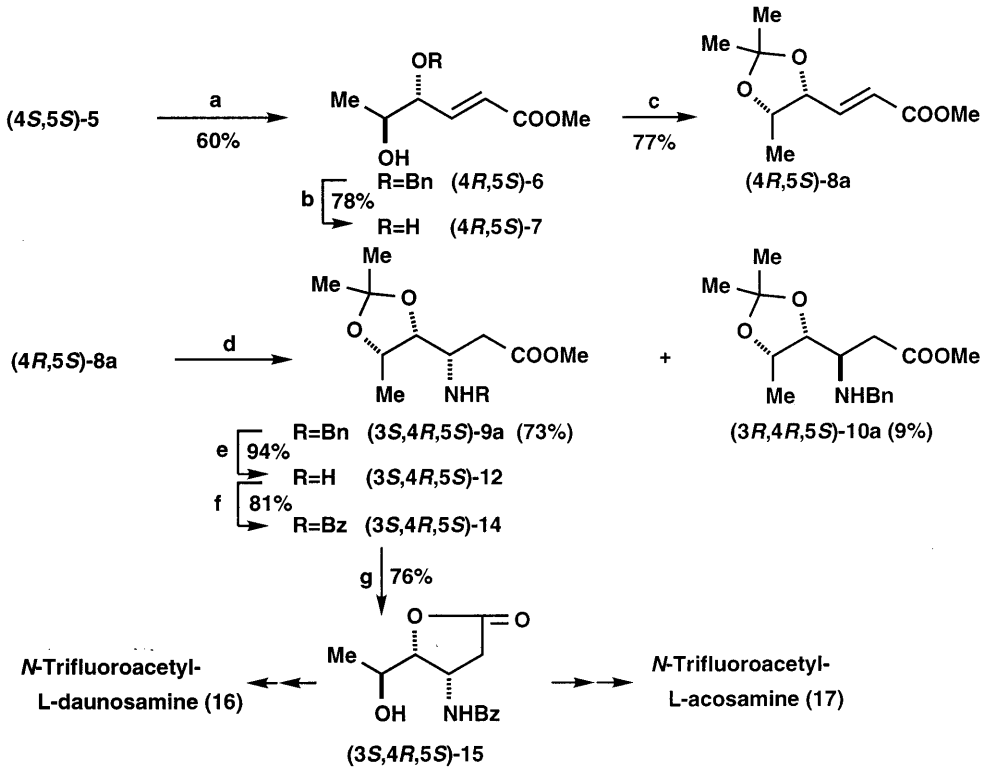


Figure 2.

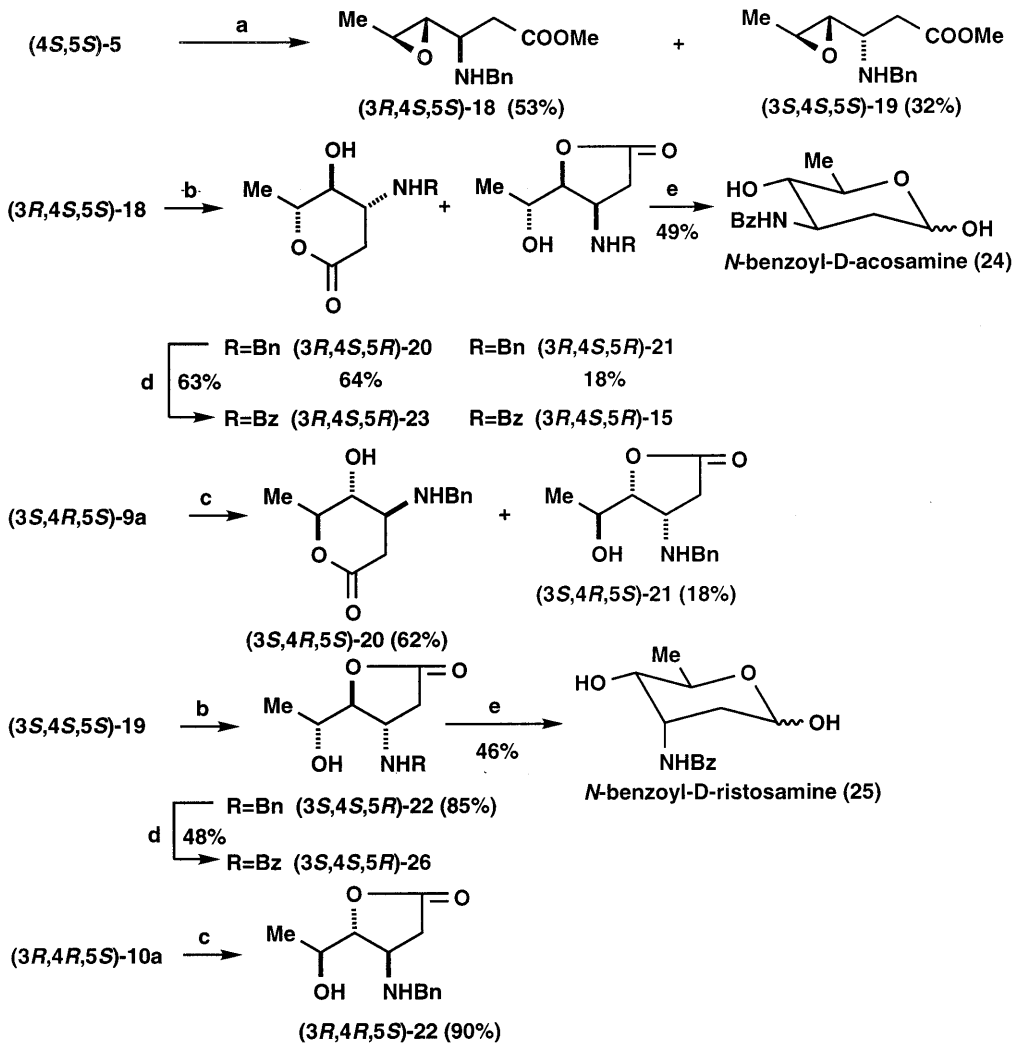
Then, the formal syntheses of L-acosamine **2** and L-daunosamine **4** from (4*S*,5*S*)-epoxy ester **5** are described. The reaction of (4*S*,5*S*)-**5** with benzyl alcohol in the presence of $BF_3{\cdot}Et_2O$ afforded (4*R*,5*S*)-**6**[5] {$[\alpha]_D$ −71.6 ($c=1.24$, $CHCl_3$)} as the main product, whose NMR spectra were identical with those of the reported[5] (±)-**6** (Scheme 4). Treatment of (4*R*,5*S*)-**6** with $AlCl_3$ in the presence of *m*-xylene[5] gave a diol (4*R*,5*S*)-**7** {$[\alpha]_D$ +16.7 ($c=0.86$, $CHCl_3$)}, which was subjected to acetonide formation to provide acetonide (4*R*,5*S*)-**8a** {$[\alpha]_D$ +0.49 ($c=3.67$, $CHCl_3$)}. The reaction of (4*R*,5*S*)-**8a** with benzylamine (2 equivalents) in the absence of solvent at room temperature afforded the 1,4-addition products, (3*S*,4*R*,5*S*)-**9a** {$[\alpha]_D$ +15.9 ($c=1.92$, $CHCl_3$)} and (3*R*,4*R*,5*S*)-**10a** {$[\alpha]_D$ −9.81 ($c=0.43$, $CHCl_3$)}. Hydrogenolysis of (+)-**9a** followed by treatment of the 3-amino ester (3*S*,4*R*,5*S*)-**12** {$[\alpha]_D$ −4.8 ($c=3.21$, $CHCl_3$)} with benzoyl chloride gave the 3-benzoylamino ester (3*S*,4*R*,5*S*)-**14** {$[\alpha]_D$ +9.3 ($c=2.84$, $CHCl_3$)}. Cleavage of the acetonide and the subsequent lactonization of **14** in aqueous 80% AcOH at reflux afforded the γ-lactone (3*S*,4*R*,5*S*)-**15**. Physical data {mp 139°C, $[\alpha]_D$ −47.3 ($c=0.77$, EtOH), IR and ^1H NMR} of the present γ-lactone **15** were identical with those {mp 155°C, $[\alpha]_D$ −43.2 ($c=1.1$, EtOH), IR and ^1H NMR} of the reported (3*S*,4*R*,5*S*)-**15**.[4] Therefore, the stereochemistries of (+)-**9a** and (−)-**10a** were determined to be (3*S*,4*R*,5*S*)-configuration and (3*R*,4*R*,5*S*)-configuration, respectively. As conversions of (3*S*,4*R*,5*S*)-**15** into *N*-trifluoroacetyl-L-daunosamine **16** and *N*-trifluoroacetyl-L-acosamine **17** have been reported,[4] chiral syntheses of the above-mentioned two amino sugar derivatives from an achiral precursor, methyl sorbate, could be achieved.

Next, the reaction of (4*S*,5*S*)-**5** with benzylamine (4 equivalents) at 40°C afforded the 1,4-addition products, (3*R*,4*S*,5*S*)-**18** {$[\alpha]_D$ −18.7 ($c=0.77$, $CHCl_3$)} and (3*S*,4*S*,5*S*)-**19** {$[\alpha]_D$ −21.1 ($c=0.6$, $CHCl_3$)} (Scheme 5). In order to determine the stereochemistry of the main product (−)-**18**, (−)-**18** was treated with CF_3SO_3H in CH_2Cl_2 at −20°C to give the δ-lactone **20** {$[\alpha]_D$ −49.2 ($c=0.47$, $CHCl_3$)} and γ-lactone **21** {$[\alpha]_D$ −51.5 ($c=0.71$, $CHCl_3$)}. For the purpose of comparison, the standard samples, δ-lactone (3*S*,4*R*,5*S*)-**20** {$[\alpha]_D$ +51.9 ($c=0.4$, $CHCl_3$)} and γ-lactone (3*S*,4*R*,5*S*)-**21** {$[\alpha]_D$ +45.3 ($c=0.23$, $CHCl_3$)}, were obtained by the treatment of the



Scheme 4. (a) BnOH, $BF_3{\cdot}Et_2O/CH_2Cl_2$, –20°C; (b) $AlCl_3$, *m*-xylene/CH_2Cl_2, 0°C; (c) $(MeO)_2CMe_2$, *p*-TsOH·H_2O/acetone, 0°C; (d) $BnNH_2$; (e) H_2, 20% $Pd(OH)_2$/MeOH; (f) BzCl/pyridine; (g) 80% AcOH, reflux

above-mentioned (3*S*,4*R*,5*S*)-**9a** with camphorsulfonic acid (CSA) in MeOH. The two δ-lactones were found to be enantiomeric because of identical spectrometric characteristics (IR and NMR) except for the sign of $[\alpha]_D$ of each enantiomer. Meanwhile, the two γ-lactones of (3*R*,4*S*,5*R*)-**21** and the standard sample (3*S*,4*R*,5*S*)-**21** were also found to be enantiomeric. Therefore, the stereochemistry of (–)-**18** was determined to be (3*R*,4*S*,5*S*). The stereochemistry of the minor product (–)-**19** was also determined to be (3*S*,4*S*,5*S*), because physical data {$[\alpha]_D$ +38.4 ($c=0.63$, $CHCl_3$)} of (+)-γ-lactone **22** derived from (–)-**19** were consistent with those {$[\alpha]_D$ –37.2 ($c=0.3$, $CHCl_3$)} of (–)-γ-lactone (3*R*,4*R*,5*S*)-**22** derived from the above-mentioned (3*R*,4*R*,5*S*)-**10a** except for the sign of $[\alpha]_D$ of each enantiomer. In the case of lactonization of (3,4)-*syn* **18**, an intramolecular nucleophilic attack by an ester carbonyl group in the C_5 position results in the formation of the δ-lactone **20**. Under these reaction conditions, the δ-lactone **20** comes to equilibrium with the γ-lactone **21**. Meanwhile, in the case of lactonization of (3,4)-*anti* **19**, an intramolecular nucleophilic attack by an ester carbonyl group in the C_5 position causes predominantly the formation of the δ-lactone, which was soon converted to the γ-lactone **22**. Hydrogenolysis of (3*R*,4*S*,5*R*)-**20** thus obtained followed by treatment with benzoyl chloride gave a mixture (63% yield) of δ-lactone **23** and γ-lactone **15**, which was reduced with diisobutylaluminum hydride (DIBAL) to the *N*-benzoyl-D-acosamine (3*R*,4*S*,5*R*)-**24** {$[\alpha]_D$ +13.1 ($c=0.6$, EtOH), mp 216–217°C}. The physical data (^1H and ^{13}C NMR) of the present **24** were identical with those (^1H and ^{13}C NMR) of the reported (3*R*,4*S*,5*R*)-**24**.[8] The (3*S*,4*S*,5*R*)-**22** was also converted into the *N*-benzoyl-D-ristosamine (3*S*,4*S*,5*R*)-**25** via (3*S*,4*S*,5*R*)-**26** {$[\alpha]_D$ –46.9 ($c=0.78$, THF} by the same way as for the conversion of **18** to **24**. The (3*S*,4*S*,5*R*)-**25** {$[\alpha]_D$



Scheme 5. (a) $BnNH_2$; (b) CF_3SO_3H/CH_2Cl_2, −20°C; (c) CSA/MeOH; (d) (1) H_2, 20% $Pd(OH)_2$–C/2 M HCl, (2) BzCl/pyridine; (e) $HAl(i\text{-}Bu)_2$/THF

+28.0 ($c=0.23$, EtOH), mp 131–133°C} thus obtained was consistent with the reported *N*-benzoyl-L-ristosamine (3*R*,4*R*,5*S*)-**25**[9] {$[\alpha]_D$ −12 ($c=1$, EtOH), mp 130–132°C} except for the sign of [α] of each enantiomer.

In conclusion, the syntheses of L-amino sugars such as L-daunosamine **4** and L-acosamine **2** and D-amino sugars such as D-acosamine **2** and D-ristosamine **1** were found to be distinguishable by changing the addition order of nucleophile against enantiomerically pure (4*S*,5*S*)-epoxy-(2*E*)-hexenoate **5**. Moreover, (4*R*,5*R*)-**5** could be applied in the above-mentioned reaction as a starting material and the syntheses of D-amino sugars such as D-daunosamine **4** and D-acosamine **2** and L-amino sugars such as L-acosamine **2** and L-ristosamine **1** could be achieved.

3. Experimental

3.1. General

All melting points were measured on a Yanaco MP-3S micro melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on JEOL AL 400 spectrometer in $CDCl_3$. Carbon substitution degrees were established by DEPT pulse sequence. The fast-atom-bombardment mass spectra (FAB MS) were obtained with JEOL JMS-DX 303 spectrometer. IR spectra were recorded a JASCO FT/IR-300 spectrometer. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. All evaporations were performed under reduced pressure. For column chromatography, silica gel (Kieselgel 60) was employed.

3.2. Methyl (4R*,5S*)-4,5-dihydroxy-2(E)-hexenoate (±)-7

To a well-stirred solution of $AlCl_3$ (4.26 g, 32 mmol) in CH_2Cl_2 (50 ml) at 0°C was added a solution of (±)-**6** (1.6 g, 6.4 mmol) in *m*-xylene (10 ml) and the whole mixture was stirred for 15 min at the same temperature. The reaction mixture was poured on ice and extracted with ether. The ether layer was washed with saturated brine and dried over $MgSO_4$. The ether layer was evaporated to give a crude residue, which was chromatographed on silica gel (50 g, *n*-hexane:AcOEt = 1:2) to give (±)-**7** (819 mg, 80%) as a colorless oil. IR (neat): 3410, 1709 cm^{-1}; NMR: δ 1.16 (3H, d, J = 7 Hz), 2.75, 3.12 (each 1H, br. s), 3.75 (3H, s), 3.96 (1H, br.), 4.31 (1H, br.), 6.13 (1H, dd, J = 2, 16 Hz), 6.96 (1H, dd, J = 5, 16 Hz). FAB MS m/z: 161 (M^++1).

3.3. Preparation of ketals (±)-8a–c from (±)-7, and acetals (±)-8d,e from (±)-7

(i) A solution of (±)-**7** (0.73 g, 4.4 mmol), CSA (0.1 g, 0.43 mmol), and 2,2-dimethoxypropane (9.58 g, 92 mmol) in acetone (5 ml) was stirred for 30 min. The reaction mixture was diluted with 7% aqueous $NaHCO_3$ and extracted with ether. The ether layer was washed with saturated brine and dried over $MgSO_4$. The ether layer was evaporated to give a crude residue, which was chromatographed on silica gel (30 g, *n*-hexane:AcOEt = 19:1) to give (±)-**8a** (812 mg, 89%) as a colorless oil. IR (neat): 1728 cm^{-1}; NMR: δ 1.16 (3H, d, J = 7 Hz), 1.38, 1.51 (each 3H, s), 3.76 (3H, s), 4.43 (1H, dq, J = 7, 7 Hz), 4.66 (1H, dt, J = 2, 7 Hz), 6.09 (1H, dd, J = 2, 16 Hz), 6.84 (1H, dd, J = 6, 16 Hz). Anal. found: C, 59.50; H, 8.23. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05%. FAB MS m/z: 201 (M^++1). (ii) A solution of (±)-**7** (5.8 g, 36.2 mmol), *p*-TsOH·H_2O (0.7 g, 3.68 mmol), and cyclohexanone (3.92 g, 40 mmol) in benzene (30 ml) was refluxed for 1 h by means of a Dean–Stark apparatus. The reaction mixture was diluted with saturated brine and extracted with ether. The ether layer was dried over $MgSO_4$ and evaporated to give a crude residue, which was chromatographed on silica gel (200 g) to afford (±)-**8b** (3.915 g, 45%) as a colorless oil from *n*-hexane:AcOEt = 19:1 eluate and starting material (±)-**7** (1.16 g, 20% recovery) from *n*-hexane:AcOEt = 1:1 eluate. (±)-**8b**: IR (neat): 1728 cm^{-1}; NMR: δ 1.16 (3H, d, J = 7 Hz), 1.37–1.45, 1.56–1.73 (10H, m), 3.75 (3H, s), 4.42 (1H, dq, J = 6, 6 Hz), 4.65 (1H, dt, J = 1.5, 6 Hz), 6.10 (1H, dd, J = 1.5, 16 Hz), 6.84 (1H, dd, J = 6, 16 Hz). Anal. found: C, 65.31; H, 8.56. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39%. FAB MS m/z: 241 (M^++1). (iii) A solution of (±)-**7** (0.69 g, 4.3 mmol), *p*-TsOH·H_2O (0.08 g, 0.42 mmol), and cyclopentanone (0.44 g, 5.2 mmol) in benzene (20 ml) was refluxed for 1 h by means of a Dean–Stark apparatus. The reaction mixture was worked up in the same way as for (ii) to afford (±)-**8c** (0.83 g, 85%) as a colorless oil. IR (neat): 1727

cm^{-1}; NMR: δ 1.17 (3H, d, $J=7$ Hz), 1.68–1.80, 1.88–2.00 (8H, m), 3.75 (3H, s), 4.31 (1H, dq, $J=6$, 6 Hz), 4.58 (1H, dt, $J=1.5$, 6 Hz), 6.08 (1H, dd, $J=1.5$, 16 Hz), 6.84 (1H, dd, $J=6$, 16 Hz). Anal. found: C, 63.35; H, 8.15. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02%. FAB MS m/z: 227 (M^++1). (iv) A solution of (±)-**7** (0.58 g, 3.6 mmol), p-TsOH·H_2O (0.07 g, 0.37 mmol), and benzaldehyde (0.45 g, 4.2 mmol) in benzene (10 ml) was refluxed for 1 h by means of a Dean–Stark apparatus. The reaction mixture was worked up in the same way as for (ii) to afford the less polar (±)-**8d** (0.233 g, 26%) as a colorless oil and the more polar (±)-**8e** (0.512 g, 57%) as a colorless oil. (±)-**8d**: IR (neat): 1724 cm^{-1}; NMR: δ 1.24 (3H, d, $J=6$ Hz), 3.77 (3H, s), 4.44 (1H, dq, $J=6$, 6 Hz), 4.81 (1H, dt, $J=2$, 6 Hz), 6.20 (1H, s), 6.20 (1H, dd, $J=2$, 16 Hz), 6.91 (1H, dd, $J=6$, 16 Hz), 7.33–7.47 (5H, m). Anal. found: C, 67.26; H, 6.50. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50%. FAB MS m/z: 249 (M^++1). (±)-**8e**: IR (neat): 1726 cm^{-1}; NMR: δ 1.28 (3H, d, $J=6$ Hz), 3.75 (3H, s), 4.46 (1H, dq, $J=6$, 6 Hz), 4.75 (1H, dt, $J=1.5$, 6 Hz), 5.85 (1H, s), 6.12 (1H, dd, $J=1.5$, 16 Hz), 6.84 (1H, dd, $J=6$, 16 Hz), 7.36–7.53 (5H, m). Anal. found: C, 68.02; H, 6.64. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50%. FAB MS m/z: 249 (M^++1).

*3.4. The reactions of ketals (±)-**8a–c** and benzylamine, and acetals (±)-**8d,e** and benzylamine*

(i) A mixture of (±)-**8a** (0.67 g, 3.3 mmol) and $BnNH_2$ (0.72 g, 6.7 mmol) was kept standing for 2 days at 30°C. The reaction mixture was directly chromatographed on silica gel (30 g) to afford starting material (±)-**8a** (0.107 g, 16% recovery) from n-hexane:AcOEt = 19:1 eluate, (±)-**10a** (0.051 g, 5%) as a colorless oil, and (±)-**9a** (0.689 g, 67%) as a colorless oil from n-hexane:AcOEt = 19:1 eluate in that order. (±)-**9a**: IR (neat): 3339, 1737 cm^{-1}; NMR: δ 1.26 (3H, d, $J=7$ Hz), 1.31, 1.45 (each 3H, s), 2.50 (2H, d, $J=6$ Hz), 3.18 (1H, dd, $J=6$, 12 Hz), 3.69 (3H, s), 3.78, 3.88 (each 1H, d, $J=13$ Hz), 4.10 (1H, t, $J=6$ Hz), 4.31 (1H, dq, $J=6$, 6 Hz), 7.22–7.36 (5H, m). FAB MS m/z: 308 (M^++1). (±)-**10a**: IR (neat): 3330, 1735 cm^{-1}; NMR: δ 1.24 (3H, d, $J=7$ Hz), 1.31, 1.41 (each 3H, s), 2.62 (1H, dd, $J=6$, 16 Hz), 2.75 (1H, dd, $J=4$, 16 Hz), 3.13 (1H, ddd, $J=4$, 6, 8 Hz), 3.69 (3H, s), 3.71, 3.85 (each 1H, d, $J=12$ Hz), 4.02 (1H, dd, $J=6$, 8 Hz), 4.38 (1H, dq, $J=7$, 7 Hz), 7.22–7.30 (5H, m). Anal. found: C, 66.22; H, 8.28; N, 4.53. Calcd for $C_{17}H_{25}NO_4$: C, 66.42; H, 8.20; N, 4.56%. FAB MS m/z: 308 (M^++1). (ii) A mixture of (±)-**8b** (0.49 g, 2 mmol) and $BnNH_2$ (0.44 g, 4.1 mmol) was kept standing for 2 days at 30°C. The reaction mixture was worked up in the same way as for (i) to give starting material (±)-**8b** (0.088 g, 18% recovery), (±)-**10b** (0.035 g, 5%) as a colorless oil, and (±)-**9b** (0.446 g, 63%) as a colorless oil. (±)-**9b**: IR (neat): 3338, 1738 cm^{-1}; NMR: δ 1.23 (3H, d, $J=6$ Hz), 1.33–1.66 (10H, m), 2.45 (1H, dd, $J=6$, 15 Hz), 2.49 (1H, dd, $J=5$, 15 Hz), 3.18 (1H, dt, $J=5$, 7 Hz), 3.69 (3H, s), 3.81, 3.90 (each 1H, d, $J=13$ Hz), 4.09 (1H, dd, $J=6$, 7 Hz), 4.29 (1H, dq, $J=6$, 6 Hz), 7.24–7.36 (5H, m). Anal. found: C, 68.86; H, 8.67; N, 3.92. Calcd for $C_{20}H_{29}NO_4$: C, 69.13; H, 8.41; N, 4.03%. FAB MS m/z: 348 (M^++1). (±)-**10b**: IR (neat): 3333, 1734 cm^{-1}; NMR: δ 1.21 (3H, d, $J=7$ Hz), 1.33–1.60 (10H, m), 2.64 (1H, dd, $J=6$, 16 Hz), 2.75 (1H, dd, $J=4$, 16 Hz), 3.13 (1H, dt, $J=4$, 6 Hz), 3.69 (3H, s), 3.70, 3.85 (each 1H, d, $J=13$ Hz), 3.98 (1H, dd, $J=6$, 8 Hz), 4.36 (1H, dq, $J=6$, 6 Hz), 7.21–7.32 (5H, m). Anal. found: C, 69.06; H, 8.51; N, 4.01. Calcd for $C_{20}H_{29}NO_4$: C, 69.13; H, 8.41; N, 4.03%. FAB MS m/z: 348 (M^++1). (iii) A mixture of (±)-**8c** (0.43 g, 1.9 mmol) and $BnNH_2$ (0.4 g, 3.7 mmol) was kept standing for 2 days at 30°C. The reaction mixture was worked up in the same way as for (i) to give starting material (±)-**8c** (0.138 g, 32% recovery), (±)-**10c** (0.063 g, 10%) as a colorless oil, and (±)-**9c** (0.361 g, 57%) as a colorless oil. (±)-**9c**: IR (neat): 3350, 1737 cm^{-1}; NMR: δ 1.25 (3H, d, $J=6$ Hz), 1.62–1.73, 1.82–1.89 (8H, m), 2.51 (2H, d, $J=6$ Hz), 3.17 (1H, dt, $J=6$, 6 Hz), 3.68 (3H, s), 3.78, 3.88 (each

1H, d, $J=13$ Hz), 4.00 (1H, t, $J=6$ Hz), 4.22 (1H, dq, $J=6$, 6 Hz), 7.22–7.35 (5H, m). Anal. found: C, 68.23; H, 8.53; N, 4.14. Calcd for $C_{19}H_{27}NO_4$: C, 68.44; H, 8.16; N, 4.20%. FAB MS m/z: 334 (M^++1). (±)-**10c**: IR (neat): 3330, 1735 cm^{-1}; NMR: δ 1.23 (3H, d, $J=7$ Hz), 1.63–1.71, 1.82–1.85 (8H, m), 2.58 (1H, dd, $J=7$, 16 Hz), 2.72 (1H, dd, $J=4$, 16 Hz), 3.12 (1H, dt, $J=4$, 7 Hz), 3.68 (3H, s), 3.72, 3.84 (each 1H, d, $J=13$ Hz), 3.95 (1H, dd, $J=6$, 7 Hz), 4.28 (1H, dq, $J=6$, 6 Hz), 7.21–7.32 (5H, m). Anal. found: C, 68.29; H, 8.65; N, 4.07. Calcd for $C_{19}H_{27}NO_4$: C, 68.44; H, 8.16; N, 4.20%. FAB MS m/z: 334 (M^++1). (iv) A mixture of (±)-**8d** (0.15 g, 0.6 mmol) and $BnNH_2$ (0.13 g, 1.2 mmol) was kept standing for 2 days at 30°C. The reaction mixture was worked up in the same way as for (i) to give starting material (±)-**8d** (0.015 g, 10% recovery), (±)-**10d** (0.028 g, 13%) as a colorless oil, and (±)-**9d** (0.144 g, 67%) as a colorless oil. (±)-**9d**: IR (neat): 3344, 1735 cm^{-1}; NMR: δ 1.34 (3H, d, $J=7$ Hz), 2.53 (1H, dd, $J=6$, 13 Hz), 2.57 (1H, dd, $J=6$, 13 Hz), 3.26 (1H, dt, $J=6$, 6 Hz), 3.68 (3H, s), 3.80, 3.90 (each 1H, d, $J=13$ Hz), 4.19 (1H, t, $J=6$ Hz), 4.41 (1H, dq, $J=6$, 6 Hz), 6.16 (1H, s), 7.22–7.44 (10H, m). Anal. found: C, 70.44; H, 7.16; N, 3.90. Calcd for $C_{21}H_{25}NO_4$: C, 70.96; H, 7.09; N, 3.94%. FAB MS m/z: 356 (M^++1). (±)-**10d**: IR (neat): 3328, 1732 cm^{-1}; NMR: δ 1.32 (3H, d, $J=6$ Hz), 2.69 (1H, dd, $J=6$, 16 Hz), 2.81 (1H, dd, $J=4$, 16 Hz), 3.23 (1H, ddd, $J=4$, 6, 9 Hz), 3.67 (3H, s), 3.72, 3.87 (each 1H, d, $J=12$ Hz), 4.06 (1H, dd, $J=6$, 9 Hz), 4.51 (1H, dq, $J=6$, 6 Hz), 6.05 (1H, s), 7.25–7.45 (10H, m). Anal. found: C, 70.45; H, 7.17; N, 3.69. Calcd for $C_{21}H_{25}NO_4$: C, 70.96; H, 7.09; N, 3.94%. FAB MS m/z: 356 (M^++1). (v) A mixture of (±)-**8e** (0.15 g, 0.6 mmol) and $BnNH_2$ (0.13 g, 1.2 mmol) was kept standing for 2 days at 30°C. The reaction mixture was worked up in the same way as for (i) to give starting material (±)-**8e** (0.024 g, 16% recovery), (±)-**10e** (0.028 g, 13%) as a colorless oil, and (±)-**9e** (0.112 g, 52%) as a colorless oil. (±)-**9e**: IR (neat): 3342, 1734 cm^{-1}; NMR: δ 1.42 (3H, d, $J=6$ Hz), 2.57 (2H, d, $J=6$ Hz), 3.27 (1H, dt, $J=6$, 6 Hz), 3.67 (3H, s), 3.76, 3.88 (each 1H, d, $J=12$ Hz), 4.19 (1H, t, $J=6$ Hz), 4.38 (1H, dq, $J=6$, 6 Hz), 5.79 (1H, s), 7.20–7.33, 7.47–7.50 (10H, m). Anal. found: C, 70.96; H, 7.23; N, 3.78. Calcd for $C_{21}H_{25}NO_4$: C, 70.96; H, 7.09; N, 3.94%. FAB MS m/z: 356 (M^++1). (±)-**10e**: IR (neat): 3332, 1732 cm^{-1}; NMR: δ 1.36 (3H, d, $J=7$ Hz), 2.65 (1H, dd, $J=5$, 16 Hz), 2.77 (1H, dd, $J=4$, 16 Hz), 3.25 (1H, ddd, $J=4$, 5, 8 Hz), 3.62 (3H, s), 3.73, 3.78 (each 1H, d, $J=13$ Hz), 4.13 (1H, dd, $J=7$, 8 Hz), 4.46 (1H, dq, $J=7$, 7 Hz), 5.75 (1H, s), 7.22–7.40, 7.45–7.47 (10H, m). Anal. found: C, 70.57; H, 7.18; N, 3.87. Calcd for $C_{21}H_{25}NO_4$: C, 70.96; H, 7.09; N, 3.94%. FAB MS m/z: 356 (M^++1).

3.5. Conversion of (±)-*9a* into (±)-arabino-*3-acetoamino-5-acetoxy-2,3,6-trideoxyaldonic acid γ-lactone* ***11***

(i) A solution of (±)-**9a** (0.5 g, 1.63 mmol) in MeOH (2 ml) was hydrogenated over 10% $Pd(OH)_2$–C (50 mg) at ambient temperature and pressure. After hydrogen absorption had ceased, the catalyst was filtered off and the filtrate was evaporated to give (±)-**12** (0.319 g, 90%) as a homogeneous oil. (±)-**12**: IR (neat): 1720 cm^{-1}; NMR: δ 1.28 (3H, d, $J=6$ Hz), 1.35, 1.48 (each 3H, s), 1.68 (2H, br. s), 2.35 (1H, dd, $J=9$, 16 Hz), 2.43 (1H, dd, $J=4$, 16 Hz), 3.28–3.33 (1H, m), 3.71 (3H, s), 3.87 (1H, dd, $J=6$, 6 Hz), 4.30 (1H, dq, $J=6$, 6 Hz). Anal. found: C, 54.83; H, 8.92; N, 6.25. Calcd for $C_{10}H_{19}NO_4$: C, 55.28; H, 8.82; N, 6.45%. (ii) A solution of (±)-**12** (0.5 g, 2.3 mmol) and Ac_2O (1.664 g 16.3 mmol) in pyridine (1 ml) was stirred for 3 days at room temperature. The reaction mixture was worked up by the usual procedure to give the corresponding acetate (0.417 g, 70%). A solution of the above-mentioned acetate (0.202 g, 0.78 mmol) in 80% aqueous AcOH (2 ml) was refluxed for 5 h. The reaction mixture was evaporated

to afford a residue, which was chromatographed on silica gel (10 g, *n*-hexane:AcOEt = 1:1) to give (±)-**13** (0.09 g, 62%) as a colorless oil. (±)-**13**: IR ($CHCl_3$): 1760, 1650 cm^{-1}; NMR: δ 1.32 (3H, d, J = 6 Hz), 2.07 (3H, s), 2.55 (1H, d, J = 17 Hz), 2.96 (1H, dd, J = 7, 17 Hz), 3.90 (1H, dq, J = 6, 8 Hz), 4.17 (1H, dd, J = 4, 8 Hz), 4.51 (1H, br. s), 4.77 (1H, ddd, J = 4, 6, 7 Hz), 7.48 (1H, d, J = 6 Hz). Anal. found: C, 51.58; H, 7.11; N, 7.20. Calcd for $C_8H_{13}NO_4$: C, 51.33; H, 7.00; N, 7.48%. (iii) A solution of (±)-**13** (0.054 g, 0.29 mmol) and AcONa (0.045 g, 0.54 mmol) in Ac_2O (1 ml) was stirred for 2 h at 120°C. The reaction mixture was worked up by the usual procedure to give (±)-**11** (0.023 g, 34%). Spectral data (IR and ^1H NMR) of (±)-**11** were consistent with the reported data.[6]

3.6. Conversion of (±)-9b–e into (±) 9a

(i) A solution of (±)-**9b** (0.1 g, 0.29 mmol), CSA (0.13 g, 0.56 mmol) and 2,2-dimethoxypropane (1.2 g, 11.5 mmol) in acetone (20 ml) was stirred for 12 h at 90°C. The reaction mixture was worked up in the same way as for the preparation of (±)-**9a** to give (±)-**9a** (0.054 g, 61%). NMR data of the present (±)-**9a** were identical with those of authentic (±)-**9a**. (ii) By applying method (i), (±)-**9c** (0.09 g, 0.27 mmol) was converted into **9a** (0.051 g, 61%). (iii) By applying method (i), (±)-**9d** (0.11 g, 0.31 mmol) was converted into **9a** (0.061 g, 64%). (iv) By applying method (i), (±)-**9e** (0.06 g, 0.17 mmol) was converted into **9a** (0.021 g, 38%).

3.7. Methyl (4R,5S)-4,5-(isopropylidenedioxy)-2(E)-hexenoate 8a

(i) To a solution of (4*S*,5*S*)-**5** (3.0 g, 21.1 mmol), BnOH (4.55 g, 42.1 mmol) in CH_2Cl_2 (30 ml) at −20°C was added $BF_3{\cdot}Et_2O$ (2.5 ml, 19.7 mmol) and the whole mixture was stirred for 3 h at −20°C. The reaction mixture was diluted with saturated brine and extracted with ether. The ether layer was dried over $MgSO_4$ and evaporated to give a residue, which was chromatographed on silica gel (100 g, *n*-hexane:AcOEt = 5:1) to give (4*R*,5*S*)-**6** (3.169 g, 60%) as a colorless oil. $[\alpha]_D^{23}$ −71.6 (c = 1.24, $CHCl_3$); IR and ^1H NMR data of (4*R*,5*S*)-**6** were identical with those of the reported (±)-**6**.[5] Anal. found: C, 67.07; H, 7.50. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25%. (ii) To a well-stirred solution of $AlCl_3$ (3.17 g, 23.7 mmol) in CH_2Cl_2 (20 ml) at 0°C was added a solution of (4*R*,5*S*)-**6** (1.19 g, 4.7 mmol) in *m*-xylene (5 ml) and the whole mixture was stirred for 30 min at the same temperature. The reaction mixture was worked up in the same way as for the preparation of (±)-**7** to afford (4*R*,5*S*)-**7** (0.594 g, 78%). $[\alpha]_D^{26}$ +16.7 (c = 0.86, $CHCl_3$); IR and ^1H NMR data of (4*R*,5*S*)-**7** were identical with those of the above-mentioned (±)-**7**. FAB MS m/z: 161 (M^++1). (iii) A solution of (4*R*,5*S*)-**7** (0.6 g, 3.7 mmol), *p*-TsOH (0.1 g, 0.53 mmol), and 2,2-dimethoxypropane (7.95 g, 75 mmol) in acetone (5 ml) was stirred for 30 min. The reaction mixture was worked up in the same way as for the preparation of (±)-**8a** to afford (4*R*,5*S*)-**8a** (0.577 g, 77%). $[\alpha]_D^{22}$ +0.49 (c = 3.67, $CHCl_3$); IR and ^1H NMR data of (4*R*,5*S*)-**8a** were identical with those of the above-mentioned (±)-**8a**. Anal. found: C, 59.53; H, 8.27. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05%.

3.8. Methyl (3S,4R,5S)-3-benzylamino-4,5-(isopropylidenedioxy)hexanoate 9a and methyl (3R,4R,5S)-3-benzylamino-4,5-(isopropylidenedioxy)hexanoate 10a

A mixture of (4*R*,5*S*)-**8a** (0.57 g, 2.8 mmol) and $BnNH_2$ (0.61 g, 5.7 mmol) was kept standing for 2 days at 30°C. The reaction mixture was directly chromatographed on silica gel (30 g) to

afford starting material (4*R*,5*S*)-**8a** (0.034 g, 6% recovery) from *n*-hexane:AcOEt = 19:1 eluate, (3*R*,4*R*,5*S*)-**10a** (0.079 g, 9%) as a colorless oil, and (3*S*,4*R*,5*S*)-**9a** (0.639 g, 73%) as a colorless oil from *n*-hexane:AcOEt = 19:1 eluate in that order. (3*S*,4*R*,5*S*)-**9a**: $[\alpha]_D^{21}$ +15.9 (c = 1.92, $CHCl_3$); IR and ^1H NMR data of (3*S*,4*R*,5*S*)-**9a** were identical with those of the above-mentioned (±)-**9a**. Anal. found: C, 66.16; H, 8.46; N, 4.65. Calcd for $C_{17}H_{25}NO_4$: C, 66.42; H, 8.20; N, 4.56%. FAB MS m/z: 308 (M^++1). (3*R*,4*R*,5*S*)-**10a**: $[\alpha]_D^{23}$ −9.8 (c = 0.43, $CHCl_3$); IR and ^1H NMR data of (3*S*,4*R*,5*S*)-**10a** were identical with those of the above-mentioned (±)-**10a**. Anal. found: C, 66.22; H, 8.28; N, 4.53. Calcd for $C_{17}H_{25}NO_4$: C, 66.42; H, 8.20; N, 4.56%. FAB MS m/z: 308 (M^++1).

*3.9. Conversion of methyl (3*S,*4*R,*5*S*)-3-benzylamino-4,5-(isopropylidenedioxy)hexanoate* ***9a*** *into (3*S,*4*R,*5*S*)-*arabino-*3-benzoylamino-2,3,6-trideoxyaldonic acid γ-lactone* ***15***

(i) A solution of (3*S*,4*R*,5*S*)-**9a** (0.48 g, 1.6 mmol) in MeOH (5 ml) was hydrogenated over 20% $Pd(OH)_2$–C (50 mg) at ordinary temperature and pressure. After hydrogen absorption had ceased, the catalyst was filtered off and the filtrate was evaporated to give (3*S*,4*R*,5*S*)-**12** (0.319 g, 94%) as a homogeneous oil. (3*S*,4*R*,5*S*)-**12**: $[\alpha]_D^{23}$ −4.8 (c = 3.21, $CHCl_3$); IR and ^1H NMR data of (3*S*,4*R*,5*S*)-**12** were identical with those of the above-mentioned (±)-**12**. (ii) A solution of (3*S*,4*R*,5*S*)-**12** (0.32 g, 1.5 mmol) and PhCOCl (0.31 g 2.2 mmol) in pyridine (1 ml) was stirred for 3 days at room temperature. The reaction mixture was diluted with 7% aqueous $NaHCO_3$ and extracted with ether. The organic layer was washed with saturated brine, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (10 g, *n*-hexane:AcOEt = 1:1) to give (3*S*,4*R*,5*S*)-**14** (0.383 g, 81%) as a colorless oil. (3*S*,4*R*,5*S*)-**14**: $[\alpha]_D^{21}$ +9.3 (c = 2.84, $CHCl_3$); IR ($CHCl_3$): 1760, 1650 cm^{-1}; NMR: δ 1.33 (3H, d, J = 6 Hz), 1.40, 1.57 (each 3H, s), 2.69 (1H, dd, J = 8, 16 Hz), 2.77 (1H, dd, J = 5, 16 Hz), 3.69 (3H, s), 4.33 (1H, dd, J = 2, 7 Hz), 4.47 (1H, dq, J = 6, 6 Hz), 4.50–4.54 (1H, m), 6.69 (1H, d, J = 8 Hz), 7.42–7.53 (3H, m), 7.75–7.78 (2H, m). Anal. found: C, 63.97; H, 7.29; N, 4.38. Calcd for $C_{17}H_{23}NO_5$: C, 63.53; H, 7.21; N, 4.36%. FAB MS m/z: 322 (M^++1). (iii) A solution of (3*S*,4*R*,5*S*)-**14** (0.28 g, 0.89 mmol) in 80% aqueous AcOH (5 ml) was refluxed for 4.5 h. The reaction mixture was condensed under reduced pressure and the residue was chromatographed on silica gel (10 g, *n*-hexane:AcOEt = 1:1) to give (3*S*,4*R*,5*S*)-**15** (0.165 g, 76%) as a colorless oil. Recrystallization of (3*S*,4*R*,5*S*)-**15** from CH_2Cl_2/Et_2O gave colorless prisms: mp 159°C; $[\alpha]_D^{19}$ −47.3 (c = 0.77, EtOH); IR ($CHCl_3$): 3600, 1740, 1640 cm^{-1}; NMR: δ 1.31 (3H, d, J = 6 Hz), 2.75 (1H, dd, J = 1, 18 Hz), 3.05 (1H, dd, J = 7, 18 Hz), 4.08 (1H, dq, J = 6, 6 Hz), 4.31 (1H, dd, J = 4, 6 Hz), 4.99–5.04 (1H, m), 7.44 (2H, t, J = 7 Hz), 7.54 (1H, t, J = 7 Hz), 7.86 (2H, d, J = 7 Hz), 8.12 (1H, br. s). Anal. found: C, 62.35; H, 6.18; N, 5.49. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62%. FAB MS m/z: 249 (M^++1). Physical data (mp, IR and ^1H NMR) of (3*S*,4*R*,5*S*)-**15** were identical with those {mp 155°C, $[\alpha]_D$ −43.2 (c = 1.1, EtOH)} of the reported (3*S*,4*R*,5*S*)-**15**.[4]

*3.10. Methyl (3*R,*4*S,*5*S*)-3-benzylamino-4,5-epoxyhexanoate* ***18*** *and methyl (3*S,*4*S,*5*S*)-3-benzylamino-4,5-epoxyhexanoate* ***19***

A mixture of (4*S*,5*S*)-**5** (1.17 g, 8.2 mmol) and $BnNH_2$ (3.53 g, 33 mmol) was kept standing for 2 days at 40°C. The reaction mixture was directly chromatographed on silica gel (120 g, *n*-hexane:AcOEt = 2:1) to afford (3*R*,4*S*,5*S*)-**18** (1.087 g, 53%) as a colorless oil and (3*S*,4*S*,5*S*)-**19** (0.656 g, 32%) as a colorless oil in eluate order. (3*R*,4*S*,5*S*)-**18**: $[\alpha]_D^{30}$ −18.7 (c = 0.77, $CHCl_3$);

IR (neat): 3329, 1736 cm^{-1}; NMR: δ 1.30 (3H, d, $J=5$ Hz), 2.50, 2.58 (1H, dd, $J=8$, 16 Hz), 2.76 (1H, dd, $J=2$, 6 Hz), 2.89 (1H, q, $J=7$ Hz), 2.89 (1H, dq, $J=2$, 5 Hz), 3.68 (3H, s), 3.84, 3.90 (each 1H, d, $J=13$ Hz), 7.21–7.34 (5H, m). Anal. found: C, 67.57; H, 7.91; N, 5.57. Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62%. FAB MS m/z: 250 (M^++1). (3*S*,4*S*,5*S*)-**19**: $[\alpha]_D^{29}$ −21.1 ($c=0.6$, $CHCl_3$); IR (neat): 3334, 1734 cm^{-1}; NMR: δ 1.24 (3H, d, $J=5$ Hz), 2.53 (1H, dd, $J=8$, 16 Hz), 2.62 (1H, dd, $J=2$, 7 Hz), 2.69 (1H, dd, $J=4$, 16 Hz), 2.75 (1H, ddd, $J=4$, 7, 8 Hz), 2.83 (1H, dq, $J=2$, 5 Hz), 3.68 (3H, s), 3.81, 3.86 (each 1H, d, $J=13$ Hz), 7.21–7.34 (5H, m). Anal. found: C, 67.56; H, 7.86; N, 5.50. Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62%. FAB MS m/z: 250 (M^++1).

*3.11. (3*R,*4*S,*5*R*)*-arabino-*3-Benzylamino-trideoxyaldonic acid δ-lactone* **20** *and (3*R,*4*S,*5*R*)*-arabino-*3-benzylamino-trideoxyaldonic acid γ-lactone* **21**

A solution of (3*R*,4*S*,5*S*)-**18** (0.42 g, 1.7 mmol) and CF_3SO_3H (0.3 ml, 3.4 mmol) in CH_2Cl_2 (40 ml) was stirred for 4 h at −20°C. The reaction mixture was diluted with 7% aqueous $NaHCO_3$ and extracted with ether. The organic layer was washed with saturated brine, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (20 g, *n*-hexane:AcOEt = 1:1) to give (3*R*,4*S*,5*R*)-**21** (0.071 g, 18%) from *n*-hexane:AcOEt = 2:1 eluate as a colorless oil and (3*R*,4*S*,5*R*)-**20** (0.253 g, 64%) from *n*-hexane:AcOEt = 1:1 eluate as a colorless oil. Recrystallization of the latter fraction from *n*-hexane/Et_2O gave colorless crystal (3*R*,4*S*,5*R*)-**20**. (3*R*,4*S*,5*R*)-**20**: mp 94–95°C; $[\alpha]_D^{28}$ −49.2 ($c=0.47$, $CHCl_3$); IR ($CHCl_3$): 3423, 3162, 1734 cm^{-1}; NMR: δ 1.45 (3H, d, $J=6$ Hz), 2.36 (1H, dd, $J=9$, 17 Hz), 2.93 (1H, dt, $J=6$, 9 Hz), 3.03 (1H, dd, $J=6$, 17 Hz), 3.28 (1H, t, $J=9$ Hz), 3.72, 3.88 (each 1H, d, $J=14$ Hz), 4.12 (1H, dq, $J=6$, 9 Hz), 7.26–7.36 (5H, m). FAB MS m/z: 236 (M^++1). HRMS (FAB^+ MS, matrix; *m*-nitrobenzyl alcohol (NBA)): calcd for $C_{13}H_{18}NO_3$ (M^++1) 236.1287; found 236.1284. (3*R*,4*S*,5*R*)-**21**: $[\alpha]_D^{25}$ −51.5 ($c=0.71$, $CHCl_3$); IR (neat): 3414, 3318, 1778 cm^{-1}; NMR: δ 1.33 (3H, d, $J=6$ Hz), 2.62 (1H, dd, $J=4$, 18 Hz), 2.71 (1H, dd, $J=7$, 18 Hz), 3.70 (1H, ddd, $J=4$, 6, 7 Hz), 3.70, 3.88 (each 1H, d, $J=13$ Hz), 3.99 (1H, dq, $J=6$, 8 Hz), 4.15 (1H, dd, $J=6$, 8 Hz), 7.26–7.37 (5H, m). FAB MS m/z: 236 (M^++1). HRMS (FAB^+ MS, matrix; NBA): calcd for $C_{13}H_{18}NO_3$ (M^++1) 236.1287; found 236.1307.

*3.12. (3*S,*4*R,*5*S*)*-arabino-*3-Benzylamino-trideoxyaldonic acid δ-lactone* **20** *and (3*S,*4*R,*5*S*)*-arabino-*3-benzylamino-trideoxyaldonic acid γ-lactone* **21**

A solution of (3*S*,4*R*,5*S*)-**9a** (0.16 g, 0.52 mmol) and CSA (0.24 g, 1.0 mmol) in MeOH (2 ml) was stirred for 2 days at room temperature. The reaction mixture was worked up in the same way as described in Section 3.11 to give (3*S*,4*R*,5*S*)-**21** (0.022 g, 18%) and (3*S*,4*R*,5*S*)-**20** (0.076 g, 62%). (3*S*,4*R*,5*S*)-**20**: $[\alpha]_D^{29}$ +51.9 ($c=0.40$, $CHCl_3$); ^1H NMR spectra of (3*S*,4*R*,5*S*)-**20** were identical with those of (3*R*,4*S*,5*R*)-**20**. FAB MS m/z: 236 (M^++1). (3*S*,4*R*,5*S*)-**21**: $[\alpha]_D^{24}$ +45.3 ($c=0.23$, $CHCl_3$); ^1H NMR spectra of (3*S*,4*R*,5*S*)-**21** were identical with those of (3*R*,4*S*,5*R*)-**21**. FAB MS m/z: 236 (M^++1).

*3.13. (3*S,*4*S,*5*R*)*-ribo-*3-Benzylamino-trideoxyaldonic acid γ-lactone* **22**

A solution of (3*S*,4*S*,5*S*)-**19** (0.37 g, 1.5 mmol) and CF_3SO_3H (0.27 ml, 3.0 mmol) in CH_2Cl_2 (40 ml) was stirred for 4 h at −20°C. The reaction mixture was diluted with 7% aqueous

$NaHCO_3$ and extracted with ether. The organic layer was washed with saturated brine, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (20 g, *n*-hexane:AcOEt = 1:1) to give (3*S*,4*S*,5*R*)-**22** (0.297 g, 85%) as a colorless oil. (3*S*,4*S*,5*R*)-**22**: $[\alpha]_D^{28}$ +38.4 ($c = 0.63$, $CHCl_3$); IR (KBr): 3405, 3127, 1765 cm^{-1}; NMR: δ 1.27 (3H, d, $J = 6$ Hz), 2.37 (1H, dd, $J = 5$, 18 Hz), 2.83 (1H, dd, $J = 8$, 18 Hz), 3.58 (1H, dt, $J = 5$, 8 Hz), 3.75, 3.81 (1H, d, $J = 13$ Hz), 3.97 (1H, dq, $J = 6$, 6 Hz), 4.06 (1H, t, $J = 5$ Hz), 7.27–7.37 (5H, m). Anal. found: C, 66.03; H, 7.52; N, 5.81. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95%. FAB MS *m*/*z*: 236 (M^++1).

3.14. (3R,4R,5S)-ribo-3-Benzylamino-trideoxyaldonic acid γ-lactone 22

A solution of (3*R*,4*R*,5*S*)-**10a** (0.04 g, 0.16 mmol) and CSA (0.06 g, 0.26 mmol) in MeOH (1 ml) was stirred for 12 h at room temperature. The reaction mixture was diluted with 7% aqueous $NaHCO_3$ and extracted with ether. The organic layer was washed with saturated brine, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (10 g, *n*-hexane:AcOEt = 1:1) to give (3*R*,4*R*,5*S*)-**22** (0.034 g, 90%) as a colorless oil. $[\alpha]_D^{23}$ −37.2 ($c = 0.3$, $CHCl_3$); ^1H NMR spectra of (3*R*,4*R*,5*S*)-**22** were identical with those of (3*S*,4*S*,5*R*)-**22**. FAB MS *m*/*z*: 236 (M^++1).

3.15. Conversion of (3R,4S,5R)-20 into N-benzoyl-D-acosamine 24

(i) A solution of (3*R*,4*S*,5*R*)-**20** (0.34 g, 1.4 mmol) in 2 M HCl (4 ml) was hydrogenated over 20% $Pd(OH)_2$–C (30 mg) at ordinary temperature and pressure. After hydrogen absorption had ceased, the catalyst was filtered off and the filtrate was treated with 7% aqueous $NaHCO_3$ and evaporated. A mixture of the residue and PhCOCl (0.4 g, 3.4 mmol) in pyridine (3 ml) was stirred for 12 h at room temperature. The reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated to give a residue, which was chromatographed on silica gel (10 g, *n*-hexane:AcOEt = 2:1) to give a mixture (0.227 g, 63%) of (3*R*,4*S*,5*R*)-**23** and (3*R*,4*S*,5*R*)-**15**. (ii) To a solution of the above-mentioned mixture (0.14 g, 0.56 mmol) in THF (3 ml) was added a 1.5 M solution of DIBAL (0.75 ml, 1.1 mmol) in toluene at −78°C, and the whole mixture was stirred for 1 h. MeOH (1.5 ml) was added to the reaction mixture at −50°C and the whole mixture was filtered off with the aid of Celite. The precipitate was washed with acetone. The washing was combined with the filtrate and the combined organic layer was evaporated to give a residue, which was chromatographed on silica gel (10 g, *n*-hexane:AcOEt = 1:1) to give *N*-benzoyl-D-acosamine **24** (0.069 g, 49%). Recrystallization of **24** from benzene afforded colorless crystal **24**. mp 216–217°C; $[\alpha]_D^{23}$ +13.1 ($c = 0.6$, EtOH); Anal. found: C, 62.49; H, 6.96; N, 5.14. Calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57%. IR (KBr): 3370, 3284, 1631, 1544 cm^{-1}; α-form: ^1H NMR (DMSO-d_6): δ 1.15 (3H, d, $J = 6$ Hz), 1.66 (1H, dt, $J = 3$, 13 Hz), 1.84 (1H, ddd, $J = 1$, 5, 13 Hz), 3.11 (1H, dt, $J = 6$, 10 Hz), 3.81 (1H, dq, $J = 6$, 9 Hz), 4.25 (1H, dddd, $J = 5$, 8, 9, 13 Hz), 4.85 (1H, d, $J = 6$ Hz), 5.10 (1H, ddd, $J = 1$, 3, 4 Hz), 6.15 (1H, d, $J = 4$ Hz), 7.43–7.54, 7.84–7.87 (5H, m), 8.10 (1H, d, $J = 8$ Hz). ^{13}C NMR (DMSO-d_6): δ 18.3, 36.9, 48.3, 67.6, 74.2, 89.8. β-form: ^1H NMR: δ 1.20 (3H, d, $J = 6$ Hz), 1.51 (1H, dt, $J = 10$, 13 Hz), 1.94 (1H, ddd, $J = 2$, 5, 13 Hz), 3.08 (1H, ddd, $J = 6$, 9, 10 Hz), 3.28 (1H, dq, $J = 6$, 10 Hz), 3.94 (1H, dddd, $J = 8$, 9, 10, 13 Hz), 4.71 (1H, ddd, $J = 2$, 6, 10 Hz), 4.85 (1H, d, $J = 6$ Hz), 6.51 (1H, d, $J = 4$ Hz), 7.43–7.54, 7.84–7.87 (5H, m), 8.23 (1H, d, $J = 8$ Hz). ^{13}C NMR (DMSO-d_6): δ 18.3, 38.91, 51.5, 72.8, 73.4, 93.5. Physical data (mp, IR and ^1H NMR) of **24** were identical with those (^1H NMR) of the reported **24**.[8]

3.16. Conversion of (3S,4S,5R)-22 into N-benzoyl-D-ristosamine 25

(i) A solution of (3*S*,4*S*,5*R*)-**22** (0.27 g, 1.14 mmol) in 2 M HCl (3 ml) was hydrogenated over 20% $Pd(OH)_2$–C (30 mg) at ordinary temperature and pressure. After hydrogen absorption had ceased, the catalyst was filtered off and the filtrate was treated with 7% aqueous $NaHCO_3$ and evaporated. A mixture of the residue and PhCOCl (0.36 g, 2.5 mmol) in pyridine (4 ml) was stirred for 12 h at room temperature. The reaction mixture was diluted with H_2O and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated to give a residue, which was chromatographed on silica gel (10 g, *n*-hexane:AcOEt = 1:1) to give (3*S*,4*S*,5*R*)-**26** (0.137 g, 48%). Recrystallization of **26** from AcOEt afforded colorless crystal **26**. mp 149°C; $[\alpha]_D^{26}$ –46.9 ($c = 0.78$, THF); IR (KBr): 3340, 1758, 1645, 1543 cm^{-1}; NMR: δ 1.39 (3H, d, $J = 7$ Hz), 2.64 (1H, dd, $J = 5$, 19 Hz), 4.04 (1H, dq, $J = 5$, 7 Hz), 4.31 (1H, dd, $J = 4$, 5 Hz), 4.83–4.89 (1H, m), 7.19 (1H, br. d, $J = 7$ Hz), 7.41–7.56, 7.79–7.82 (5H, m). Anal. found: C, 60.90; H, 6.37; N, 5.78. Calcd for $C_{13}H_{15}NO_4 \cdot 0.5H_2O$: C, 60.46; H, 6.24; N, 5.42%. FAB MS *m*/*z*: 250 (M^++1). (ii) To a solution of (3*S*,4*S*,5*R*)-**26** (0.08 g, 0.32 mmol) in THF (2 ml) was added a 1.5 M solution of DIBAL (0.45 ml, 0.68 mmol) in toluene at −78°C, and the whole mixture was stirred for 1 h. MeOH (1.5 ml) was added to the reaction mixture at −50°C and the whole mixture was filtered off with the aid of Celite. The precipitate was washed with acetone. The washing was combined with the filtrate and the combined organic layer was evaporated to give a residue, which was chromatographed on silica gel (10 g, *n*-hexane:AcOEt = 1:1) to give *N*-benzoyl-D-ristosamine **25** (0.037 g, 46%). Recrystallization of **25** from AcOEt afforded colorless crystal **25**. mp 131–133°C; $[\alpha]_D^{25}$ +28.0 ($c = 0.23$, EtOH); Anal. found: C, 61.70; H, 7.11; N, 5.11. Calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57%. IR (KBr): 3391, 3291, 1638, 1541 cm^{-1}; α-form: ^{1}H NMR (DMSO-d_6): δ 1.07 (3H, d, $J = 6$ Hz), 1.79 (1H, dd, $J = 5$, 13 Hz), 2.30 (1H, dd, $J = 9$, 13 Hz), 3.65 (1H, dq, $J = 5$, 6 Hz), 3.91 (1H, dt, $J = 4$, 5 Hz), 4.44 (1H, dddd, $J = 5$, 5, 8, 9 Hz), 4.63 (1H, m), 5.43 (1H, ddd, $J = 2$, 5, 5 Hz), 6.32 (1H, d, $J = 5$ Hz), 7.45–7.55, 7.75–7.87 (5H, m), 8.37 (1H, d, $J = 8$ Hz). ^{13}C NMR (DMSO-d_6): δ 17.9, 33.8, 46.8, 65.0, 71.3, 89.9. β-form: ^{1}H NMR (DMSO-d_6): δ 1.10 (3H, d, $J = 6$ Hz), 2.06 (2H, m), 3.70 (2H, m), 4.68 (1H, m), 5.42 (1H, m), 6.32 (1H, d, $J = 5$ Hz), 7.45–7.55, 7.75–7.87 (5H, m), 8.55 (1H, d, $J = 8$ Hz). ^{13}C NMR (DMSO-d_6): δ 18.6, 48.4, 69.6, 70.9, 91.2. Physical data (mp, IR and ^{1}H NMR) of **25** were identical with those (mp 130–132°C) of the reported **25**.[9]

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