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4-ALKOXYCARBONYLOXAZOLES AS β-HYDROXY-α-AMINO ACID SYNTHONS: EFFICIENT, STEREOSELECTIVE SYNTHESES OF 3-AMINO-2,3,6-TRIDEOXYHEXOSES AND A HYDROXY AMINO ACID MOIETY OF AI-77-B †,1

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Abstract: 5-Substituted 4-alkoxycarbonyloxazoles **13a-c** have been easily prepared by direct C-acylation of isocyanoacetic esters with O-protected α-hydroxycarboxylic acids **12a-c** by use of diphenyl phosphorazidate (DPPA). Acid treatment of the oxazole derivatives **13a-c** affords 5-substituted 3-aminotetronic acids **14a-c**, which are stereoselectively hydrogenated to give 5-substituted 2-amino-3-hydroxy-1,4-lactones **15a**, **16b**, and so on. From the L-lyxo-1,4-lactone **15a**, three 3-amino-2,3,6-trideoxyhexoses, L-daunosamine (**7**), L-vancosamine (**8**), and D-ristosamine (**9**) have been conveniently prepared by use of the Wittig homologation. Similar treatment of the D-ribo-1,4-lactone **16b** has produced a hydroxy amino acid moiety **A** of AI-77-B (**11**) as its protected form **10**.

Introduction

4-Alkoxycarbonyloxazoles **1** have been revealed[2] to be useful synthons for β-hydroxy-α-amino acids **2**:

1 **2**

4-Alkoxycarbonyloxazoles **1** are easily obtained by direct C-acylation of isocyanoacetic esters with carboxylic acids.[3] When O-protected α-hydroxycarboxylic acids **3** are used, the corresponding oxazole derivatives **4** are obtained in good yields. Diphenyl phosphorazidate (DPPA, $(PhO)_2P(O)N_3$) or diethyl phosphorocyanidate (DEPC, $(EtO)_2P(O)CN$) together with base has proved to be useful coupling reagents in the oxazole synthesis. When optically active carboxylic acids **3** are used, DPPA causes no or little, if any,

† Dedicated to Professor W. David Ollis on the occasion of his 65th birthday and retirement from Sheffield University.

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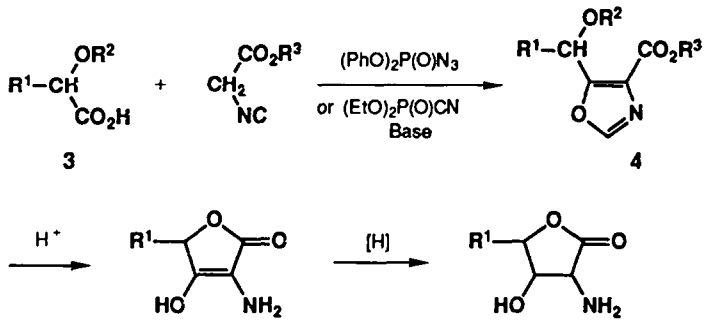
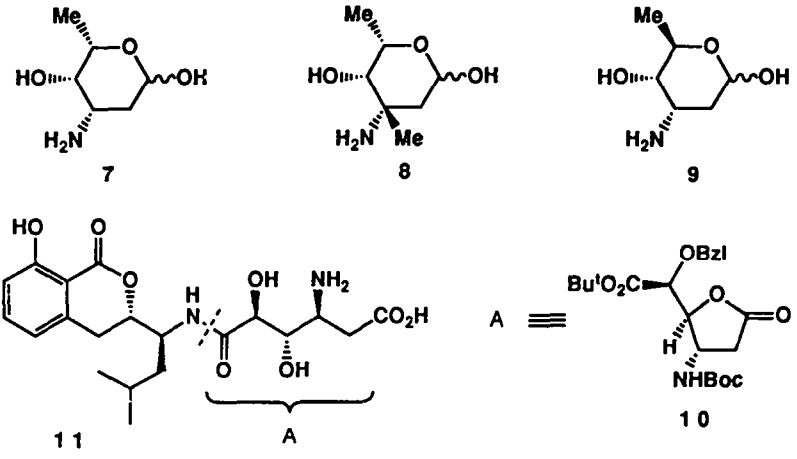
racemization at the chiral center[4] while DEPC causes a little racemization. The oxazole ring of **4** is easily cleaved under acidic conditions to give 5-substituted 3-aminotetronic acids **5**, amino reductones, when O-protective groups are susceptible to acids. Hydrogenation of **5** or congeners gives 5-substituted 2-amino-3-hydroxy-1,4-lactones **6**, β-hydroxy-α-amino acid equivalents, as shown in Scheme 1. The lactones **6** have revealed to be quite useful starting materials for the construction of various natural products including amino sugars and amino acids.[2]



Scheme 1.

We now disclose here the detail of the efficient and stereoselective preparation of the lactones **6** utilizing the reaction in Scheme 1, which has been successfully applied to the stereoselective syntheses of 3-amino-2,3,6-trideoxyhexoses,[5] i.e., L-daunosamine (**7**),[6] L-vancosamine (**8**),[7] and D-ristosamine (**9**),[8] and the protected form **10** of a hydroxy amino acid moiety **A** of Al-77-B (**11**) a gastroprotective substance from *Bacillus pumilus* Al-77.[9, 10]



5-Substituted 3-Aminotetronic Acids

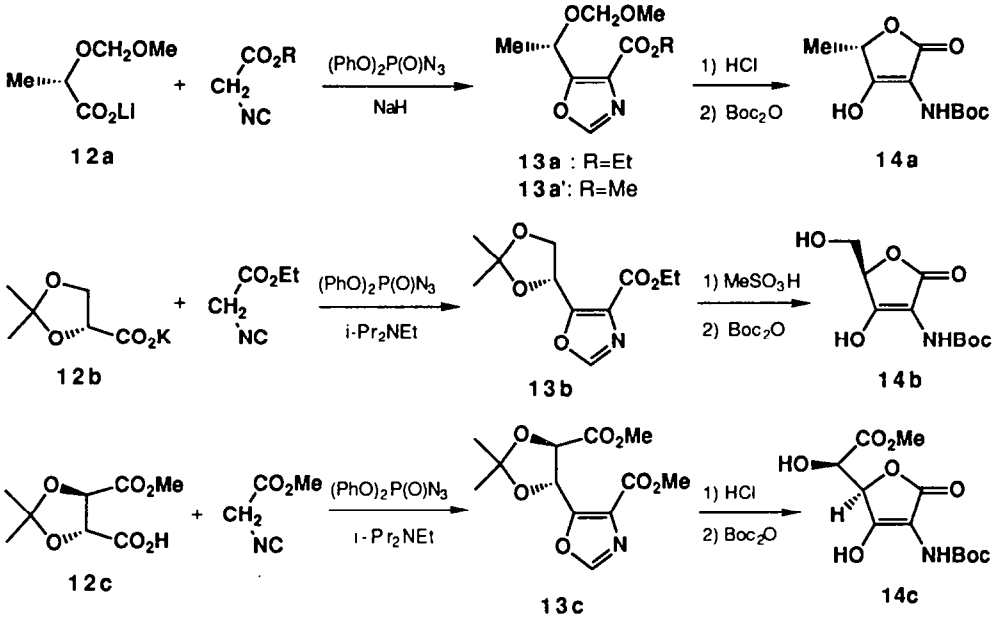
We prepared 5-substituted 3-aminotetronic acids **5** as their N-tert-butoxycarbonyl (Boc) derivatives **14** since **5** were very susceptible to air.

The lithium salt **12a** of (S)-(O-methoxymethyl)lactic acid, the starting acid for the preparation of **14a**, was prepared from ethyl (S)-lactate in 90 % yield by methoxymethylation followed by hydrolysis

with aqueous lithium hydroxide. After activation of the carboxylate function of **12a** with DPPA, treatment with sodium salt of ethyl isocyanoacetate afforded the oxazole derivative **13a** in 69 % yield. Analogously, the corresponding methyl ester **13a'** was obtained in 70 % yield by use of methyl isocyanoacetate. The configurational homogeneity of **13a** and **13a'** was ascertained by their ^{1}H-NMR spectra using the chiral shift reagent, Eu(facam)$_3$. The oxazole ring was quantitatively cleaved with 10 % hydrogen chloride in methanol to give 3-amino-5-methyltetronic acid (**5**, R^1 = Me) as its hydrochloride, which was converted to the Boc derivative **14a** with di-tert-butyl dicarbonate (Boc_2O) in 92 % yield, as shown in Scheme 2.

Analogously, the potassium salt **12b** of (R)-(O,O'-isopropylidene)glyceric acid was condensed with ethyl isocyanoacetate by use of DPPA in the presence of diisopropylethylamine. The oxazole derivative **13b** obtained quantitatively was treated with 10 % hydrogen chloride in methanol, then Boc_2O. The desired aminotetronic acid derivative **14b** was produced, but the yield was rather low (46 %) because of the formation of another product, 3-tert-butoxycarbonylamino-4-hydroxy-2-pyrone (29 % yield). However, replacement of hydrogen chloride in methanol with methanesulfonic acid followed by treatment with Boc_2O afforded the Boc-tetronic acid **14b** in 63 % yield. The pyrone derivative was formed in only 2 % yield in this case.

The tartaric acid derivative **12c** also underwent the analogous C-acylation of methyl isocyanoacetate with DPPA and diisopropylethylamine. The resulting oxazole **13c** produced in 79 % yield was converted to the aminotetronic acid **14c** in 71 % yield by the successive treatment with 10 % hydrogen chloride in methanol and Boc_2O.

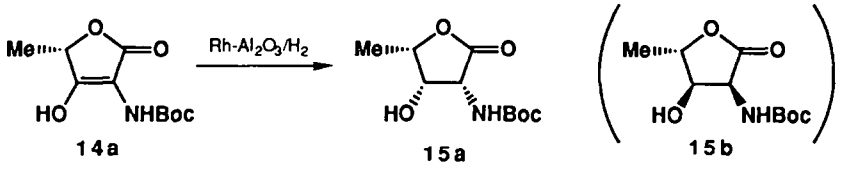


Scheme 2.

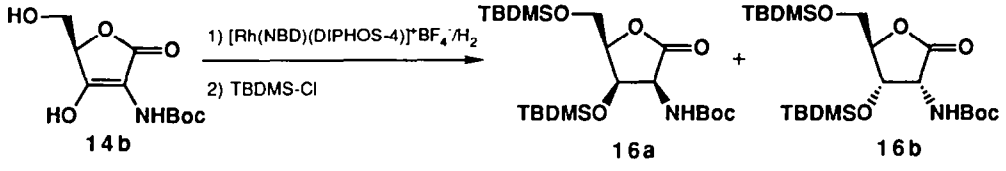
5-Substituted 2-Amino-3-hydroxy-1,4-lactones

If the hydrogenation of the carbon-carbon double bond in the aminotetronic acids **14a-c** obtained as above would be possible in a stereoselective manner, the 1,4-lactones suitable for the preparation of chiral amino sugars and amino acids would be formed.

The first trial of the catalytic hydrogenation of the tetronic acid **14a** by use of Adams' platinum oxide or 5 % rhodium carbon in ethyl acetate at ambient temperature under a medium pressure (~ 6.5 atmospheric pressure) resulted in the recovery of the starting material. However, the use of 5 % rhodium-alumina at 6.5 atmospheric pressure afforded the L-lyxo-1,4-lactone **15a** as a hydrogenation product in 59 % yield though the reaction time was rather long (96 h). Increase of the pressure to 36 atmospheric pressure shortened the reaction time to 68 h together with the increase of the yield of the lactone **15a** to 86 %. The definitive result was obtained when the catalytic hydrogenation over 5 % rhodium-alumina was carried out in ethyl acetate at 120 atmospheric pressure and ambient temperature for 24 h. The lyxo-1,4-lactone **15a** was obtained in 91 % yield as a sole product. None of the diastereoisomer **15b** could be found in the reaction mixture. This complete stereoselectivity of the hydrogenation would be due to the presence of the α-methyl function in **14a**, which would completely block the attack of hydrogen from the α-face of the carbon-carbon double bond. Thus, the absolute stereochemistry of the hydrogenation product could be assigned as shown in **15a**, and unambiguously determined by the conversion of **15a** to L-daunosamine (**7**) as later described.



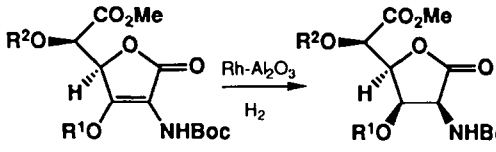
Next, our attention was turned to the hydroxy directed homogeneous hydrogenation[11] of **14b** utilizing its primary hydroxyl function as a directing handle. After several trials we found that the stereoselective hydrogenation smoothly proceeded by use of the cationic rhodium catalyst, [Rh(NBD)(DIPHOS-4)]$^+$ BF_4^- (20 mole %),[12] in methylene chloride at 130 atmospheric pressure and ambient temperature, giving, after treatment with tert-butyldimethylchlorosilane (TBDMS-Cl), the D-ribo isomer **16b** in 86 % yield in preference to the D-lyxo isomer **16a** (~ 91 : 9).



Results on the catalytic hydrogenation of the tetronic acid **14c** and its O-protected derivatives **18**, **20**, and **22** are summarized in Table 1. Since hydrogen will attack from the less hindered α-side of the molecule in the hydrogenation over rhodium-alumina, the stereochemistry of the products could be assigned from the product ratio. Thus, the major isomers were assigned as the D-lyxo isomers (**17a**, **19a**, and **21a**) while the minor isomers were assigned as the D-ribo isomers (**17b**, **19b**, and **21b**). In the hydrogenation of the acetate **22**, the starting material was found to be decomposed.

Furthermore, the α-hydroxy methyl ester **18** was converted to the glycol **24** in 93 % yield by the selective reduction with lithium aluminum hydride. The reason for the chemoselectivity of this reduction

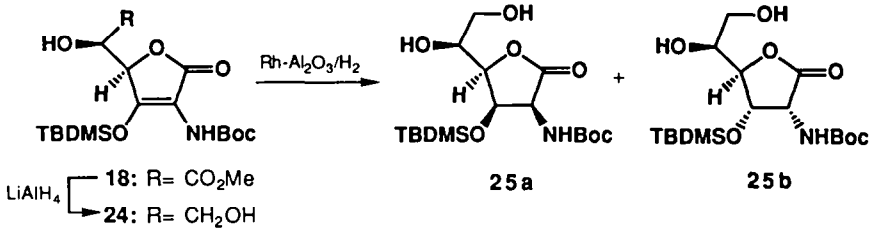
Table 1.



			R_1	R_2
14c	**17a**	**17b**	H	H
18	**19a**	**19b**	TBDMS	H
20	**21a**	**21b**	H	$HO(i\text{-}Pr)_2SiOSi(i\text{-}Pr)_2$
22	**23a**	**23b**	H	AcO

starting compd No.	reaction solvent	reaction conditions	yield(%) of D-lyxo	D-ribo
14c	AcOEt	90atm, rt, 49h	26	2
18	AcOEt	140atm, rt, 70h	50	3
18	AcOEt:EtOH(1:1)	90atm, rt, 72h	34	34
20	AcOEt	100atm, rt, 90h	60	—
22	AcOEt	100atm, rt, 94h	decomposed	

will be as follows: lithium aluminum hydride will first react with the secondary α-hydroxyl group of **18**, then the preferential reduction of the methyl ester function will occur by the formed α-alkoxy aluminum hydride. Catalytic hydrogenation of the glycol over 5 % rhodium-alumina took a longer time to give the D-lyxo isomer **25a** in 46 % yield and the D-ribo isomer **25b** in 10 % yield.



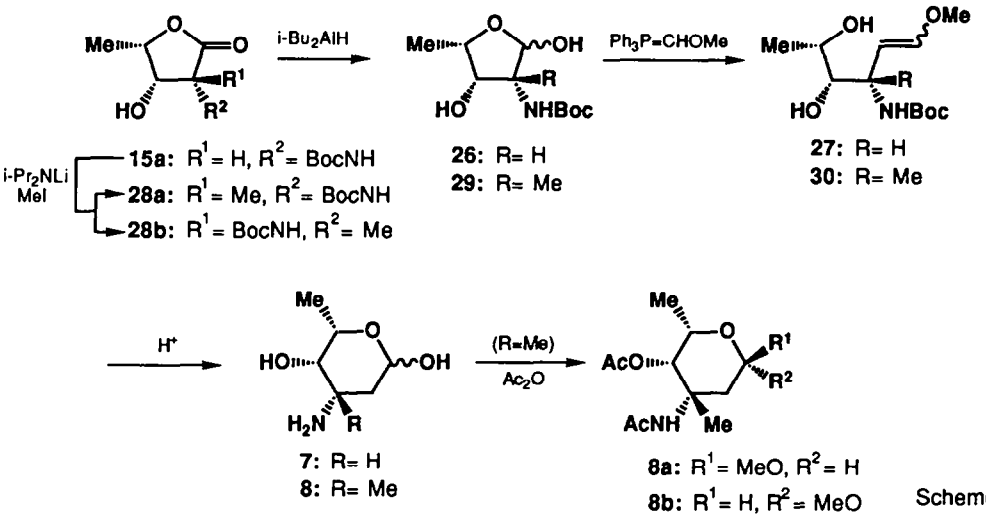
Since various 5-substituted 2-amino-3-hydroxy-1,4-lactones were now available in their lyxo and/or ribo forms, their conversion to 3-amino-2,3,6-trideoxyhexoses and a hydroxy amino acid moiety of Al-77-B was developed.

L-Daunosamine

L-Daunosamine (**7**, 3-amino-2,3,6-trideoxy-L-lyxo-hexose) is the carbohydrate constituent of the important anthracycline antitumor agents, daunorubicin (daunomycin), adriamycin, and their congeners. Because of the medicinal importance of L-daunosamine (**7**), numerous preparative methods have been developed.[5,13]

We have also achieved[6] an efficient synthesis of **7** by use of the L-lyxo-1,4-lactone **15a** prepared as above in ca. 50 % overall yield from ethyl (S)-lactate. Reduction of the lactone carbonyl group of **15a** was carried out with diisobutylaluminum hydride (DIBAL), giving the lactol **26** in 80 % yield. Introduction of

the required C_1-unit was achieved by the Wittig reaction of **26** with methoxymethylenetriphenylphosphorane. The resulting methyl enol ether **27** obtained in 64 % yield was treated with hydrochloric acid in tetrahydrofuran to produce the hydrochloride of L-daunosamine (**7**) in 90 % yield. Thus, L-daunosamine could be synthesized efficiently and stereoselectively from readily available ethyl (S)-lactate in 9 steps with a good overall yield of 24 %.



Scheme 3.

L-Vancosamine

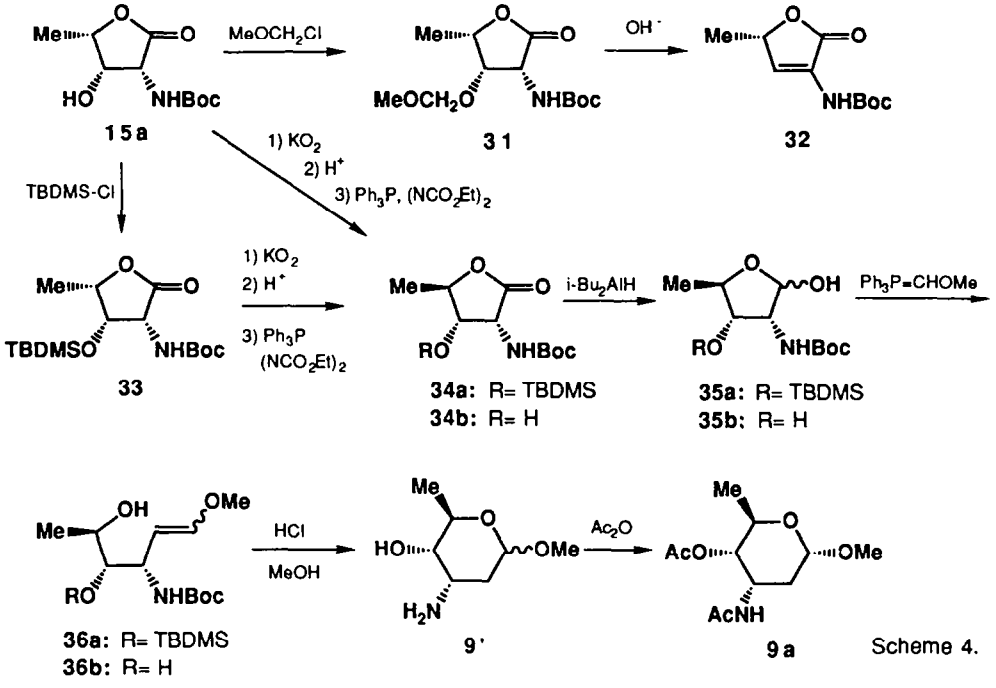
L-Vancosamine (**8**, 3-amino-2,3,6-trideoxy-3-C-methyl-L-lyxo-hexose) is a carbohydrate component of the antibiotics vancomycin[14] and sporaviridin.[15] Since L-vancosamine is the C-3 methyl analogue of L-daunosamine, we again utilized the L-lyxo-1,4-lactone **15a** as the starting material for the synthesis of **8**,[7] as shown in Scheme 3. Introduction of the extra methyl group to **15a** was easily carried out by treatment of lithium diisopropylamide, then methyl iodide. The methylation preferentially occurred from the less hindered β-side of the molecule giving the β-C-methyl lactone **28a** as the major product together with its isomer **28b** in 69 % yield (96 : 4). Reduction of this mixture with DIBAL, followed by the purification of the crude product on a silica gel column afforded the pure lactol **29** in 73 % yield. The Wittig reaction with methoxymethylenetriphenylphosphorane analogous to the daunosamine synthesis afforded the methyl enol ether **30** in 59 % yield. Treatment of **30** with hydrochloric acid in tetrahydrofuran effectively used for the construction of L-daunosamine molecule was not suitable for the construction of L-vancosamine. After several futile attempts, we found that hydrofluoric acid was effective to prepare L-vancosamine (**8**). Successive treatment of **30** with hydrofluoric acid in methanol, triethylamine, and acetic anhydride in pyridine afforded an anomeric mixture of methyl N,O-diacetyl-L-vancosaminides (**8a** and **8b**).

D-Ristosamine

The analogous sequence of reactions from the L-lyxo-1,4-lactone **15a** established a new preparative route to D-ristosamine (**9**), the enantiomer of the carbohydrate component of the antibiotic ristomycin (ristocetin) as its N,O-diacetyl methyl glycosides,[8] as shown in Scheme 4. The required operation for the

construction of D-ristosamine is the inversion of the 5-methyl group of the L-lyxo-1,4-lactone **15a**. Thus, the lactone **15a** was converted to the corresponding O-methoxymethyl derivative **31**. Various attempts to open the lactone ring of **31** by alkaline treatment unexpectedly afforded the elimination product **32** in almost quantitative yield. On the contrary, the TBDMS derivative **33** smoothly underwent the ring opening by treatment with potassium superoxide and 18-crown-6. After neutralization, the Mitsunobu reaction with a mixture of triphenylphosphine and diethyl azodicarboxylate afforded the desired D-ribo-1,4-lactone **34a** in 54 % yield from **33**. Treatment of **34a** with DIBAL, then methoxymethylene-triphenylphosphorane afforded the methyl enol ether **36a** in 42 % yield via **35a**. Final construction of D-ristosamine (**9**) as its N,O-diacetyl methyl glycoside **9a** was accomplished in 61 % yield by treatment of **36a** with hydrogen chloride in methanol, then acetic anhydride in pyridine.

Alternatively, the D-ristosamine derivative **9a** was prepared in a more efficient way without protection of the hydroxyl group of **15a**. Hydrolysis of **15a** with potassium superoxide and 18-crown-6, acidification to pH 4, followed by the Mitsunobu reaction as described above afforded an inseparable mixture of the D-ribo-1,4-lactone **34b** and diethyl hydrazinedicarboxylate in a ratio of 1.3 : 1. Reduction of this mixture with DIBAL gave the pure lactol **35b** in 71 % yield from **15a** after chromatographic purification. Analogous sequential treatment with the Wittig reagent, methanolic hydrogen chloride, and acetic anhydride in pyridine as described above furnished the D-ristosamine derivative **9a** in 23 % yield.



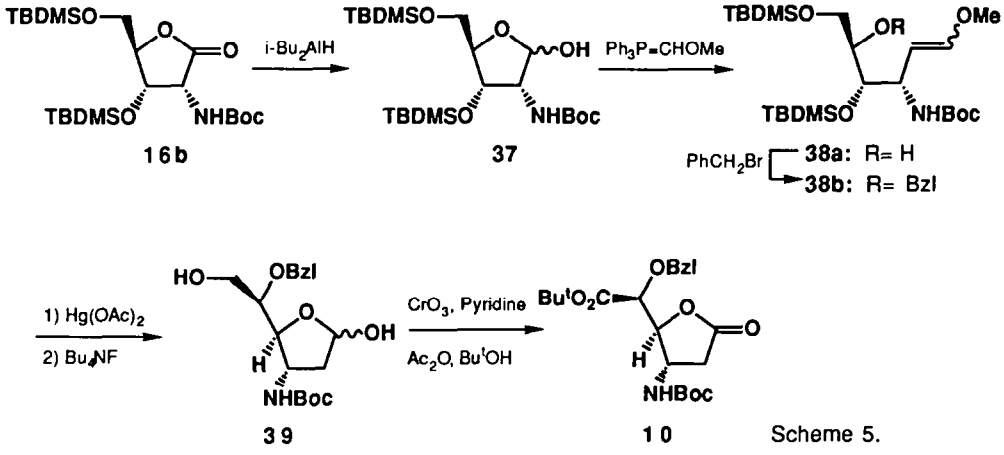
Scheme 4.

A Hydroxy Amino Acid Moiety of Al-77-B

Al-77-B (**11**) is a gastroprotective substance isolated from a culture broth of *Bacillus pumilus* Al-77.[17] We have already accomplised[10] the total synthesis of this structurally unique and medicinally interesting compound. In another synthetic approach to **11**, the D-ribo-1,4-lactone **16b** was thought to be

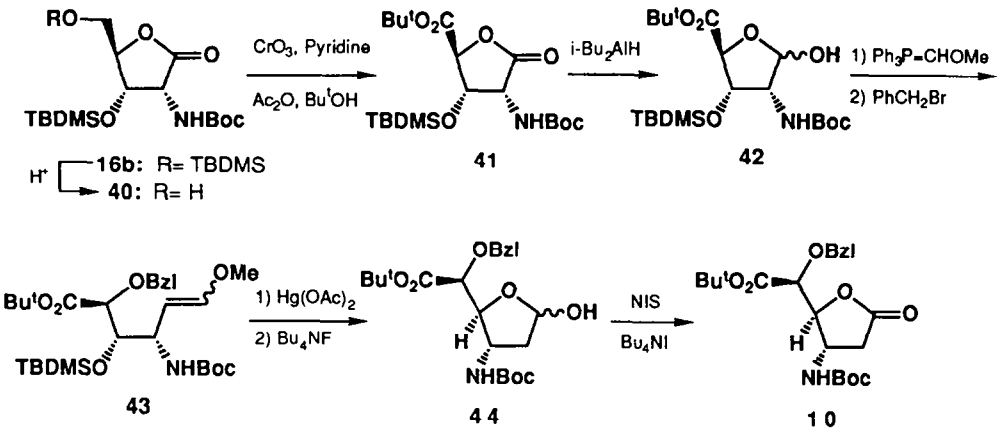
a suitable starting material for the construction of the eastern hydroxy amino acid moiety **A** of Al-77-B.[9,18] Our strategy was quite similar to those for the construction of 3-amino-2,3,6-trideoxyhexoses described earlier.

The D-ribo-1,4-lactone **16b** was first reduced with DIBAL to give the lactol **37** in 96 % yield. The Wittig homologation with methoxymethylenetriphenylphosphorane smoothly proceeded to give the methyl enol ether **38a** in almost quantitative yield. The secondary hydroxyl function of the Wittig product **38a** was protected with the benzyl group to give the benzyl ether **38b** in 42 % yield. Successive treatment of **38b** with mercuric acetate[19] and tetra-n-butylammonium fluoride afforded the benzyl lactol **39** in 73 % yield. Although the air oxidation of **39** over platinum catalyst[20] was fruitless to oxidize the primary alcoholic function, oxidation under Corey's conditions[21] using chromic acid-pyridine-acetic anhydride-tert-butanol afforded the desired lactone **10**, the protected form of a hydroxy amino acid moiety **A** of Al-77-B (**11**), in 30 % yield.



Scheme 5.

Further improvements were made to prepare **10** from **16b**, as shown in Scheme 6. Selective removal of one of the TBDMS groups of **16b** was achieved with aqueous acetic acid in tetrahydrofuran to give the monohydroxy compound **40** in 79 % yield. Oxidation of **40** under the above Corey's conditions[21] afforded the tert-butyl ester **41** in 70 % yield. The following sequence of the reactions was done quite similarly as described above. The lactone function of **41** was selectively reduced with DIBAL to give the lactol **42** in 52 % yield, which was subjected to the Wittig homologation followed by benzylation. The methyl enol ether **43** obtained in 72 % yield was treated successively with mercuric acetate[19] and tetra-n-butylammonium fluoride to furnish the lactol **44** in 98 % yield. Oxidation of the lactol **44** with N-iodosuccinimide-tetra-n-butylammonium iodide[22] quantitatively afforded the desired lactone **10**. This alternative route to **10** takes much longer steps from **16b** than the first route, but gives much better overall yields of 21 %.



Scheme 6.

Conclusion

The above series of experiments have well established the efficient use of 4-alkoxycarbonyloxazoles as β-hydroxy-α-amino acid synthons. The synthetic procedures described here will promise a convenient entry to various physiologically active compounds having hydroxy amino acid moieties from suitable oxazole derivatives.[23]

EXPERIMENTAL

Melting points were uncorrected. IR spectra were recorded on JASCO IRA-2 or IRA-180 spectrometers. NMR spectra were recorded on JEOL PMX-60, FX-100, or GX-400 spectrometers in $CDCl_3$ solution using tetramethylsilane as an internal standard (unless otherwise stated) (s, singlet; d, doublet; t, triplet; m, multiplet; b, broad). Optical rotations were determined on a JASCO DIP-140 automatic polarimeter. Analytical TLC was performed on a silica gel plate (E. Merck Art 5715). Column chromatography was carried out on silica gel BW-200 or BW-820MH (Fuji Davison Co.) by use of a low-pressure technique.

Ethyl (S)-(O-Methoxymethyl)lactate. To a cooled (-5°C), stirred solution of ethyl (S)-lactate (23.6 g, 0.2 M) in CH_2Cl_2 (70 ml) was added dropwise diisopropylethylamine (139.4 ml, 0.8 M) below -5°C under an atmosphere of argon and the solution was stirred for 1 h. Chloromethyl methyl ether (30.38 ml, 0.4 M) was added dropwise below 0°C, and the solution was stirred at 0°C for 2 h and at ambient temperature for 22 h. After dilution with CH_2Cl_2 (700 ml), the whole was washed with 10 % aqueous citric acid, water, and saturated brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by distillation (57°C, 6 mmHg) to give 29.26 g (90.3 %) of ethyl (S)-(O-methoxymethyl)lactate as a colorless oil, $[\alpha]_D^{26.5}$ -79.3° (c 1, MeOH). IR (film) : 2950, 1745, 1450, 1380, 1200, 1025 cm^{-1}. ^1H NMR δ : 1.26 (3H, t, J = 7 Hz), 1.41 (3H, d, J = 7 Hz), 3.37 (3H, s), 4.19 (3H, q, J = 7 Hz), 4.67 (2H, s). Anal. Calcd for $C_7H_{14}O_4$: C, 51.84 ; H, 8.70. Found : C, 51.61 ; H, 8.96.

Lithium salt 12a of (S)-(O-Methoxymethyl)lactic Acid. To a cooled (-5°C), stirred solution of ethyl (S)-(O-methoxymethyl)lactate (14 g, 86.4 mmol) in THF (150 ml) was added dropwise 0.864 N aqueous LiOH (100 ml), and the solution was stirred at -5°C for 1 h and at ambient temperature for 1 h. After removal of the solvent, the residue was diluted with EtOH-benzene (1 : 1, 50 ml).

Concentration in vacuo as an azeotropic mixture (dilution followed by concentration was repeated five times) afforded 12.1 g (100 %) of the Li carboxylate **12a** as a colorless solid.

Ethyl (S)-5-(1-Methoxymethoxy)ethyl-4-oxazolecarboxylate (13a). To a cooled (-5°C), stirred solution of **12a** (420 mg, 3 mmol) in DMF (4.5 ml) was added dropwise diphenyl phosphorazidate (DPPA) (920 mg, 3.34 mmol) in DMF (3 ml) under an atmosphere of argon. After the mixture was stirred for 6 h, a solution of the carbanion (prepared from ethyl isocyanoacetate (654 mg, 6.6 mmol) and 60 % NaH (217 mg, 5.4 mmol) in DMF (8 ml) at -10°C) was added dropwise. The solution was stirred at 0 °C for 2 h and at ambient temperature for 22 h. After dilution with EtOAc-benzene (1 : 1, 300 ml), the whole was washed with water and saturated brine, dried over Na_2SO_4, and concentrated in vacuo. Chromatographic purification (BW-200, 40 g, EtOAc-hexane = 1 : 1) of the residue provided 475 mg (69 %) of **13a** as a pale yellow oil. $[\alpha]_D^{25}$ -22.6° (c 1, MeOH). IR (film) : 3130, 1730, 1610, 1520, 1380, 1295, 1040, 650 cm^{-1}. ^1H NMR δ : 1.45 (3H, d, J = 7 Hz), 1.52 (3H, t, J = 7 Hz), 3.35 (3H, s), 4.42 (2H, q, J = 7 Hz), 4.59 (2H, s), 5.60 (1H, q, J = 7 Hz), 7.90 (1H, s). Anal. Calcd for $C_{10}H_{15}NO_5$: C, 52.40 ; H, 6.60 ; N, 6.11. Found : C, 52.29 ; H, 6.57 ; N, 6.11. The configurational homogeneity of **13a** was ascertained by the ^1H NMR spectral study using chiral shift reagent, Eu(facam)$_3$.

Methyl (S)-5-(1-Methoxymethoxy)ethyl-4-oxazolecarboxylate (13a'). By a similar procedure to **13a**, hydrolysis of methoxymethyl (S)-(O-methoxymethyl)lactate (prepared by treatment of (S)-lactic acid with chloromethyl methyl ether as in the preparation of the corresponding ethyl ester), followed by C-acylation of methyl isocyanoacetate using DPPA gave **13a'** in 70 % yield. $[\alpha]_D^{21}$ -21.93° (c 1, MeOH). IR (film) : 3120, 1725, 1610, 1520, 1205, 1110, 1060, 650 cm^{-1}. ^1H NMR δ : 1.60 (3H, d, J = 7 Hz), 3.38 (3H, s), 3.98 (3H, s), 4.65 (2H, s), 5.60 (1H, q, J = 7 Hz), 7.96 (1H, s). Anal. Calcd for $C_9H_{13}NO_5$; C, 50.23 ; H, 6.09 ; N, 6.51. Found : C, 50.39 ; H, 6.38 ; N, 6.44.

Ethyl 5-((1R)-1,2-Isopropylidenedioxy)ethyl-4-oxazolecarboxylate (13b). The potassium salt **12b** of O,O'-isopropylidene-(R)-glyceric acid (11.04 g, 60 mmol) prepared from D-mannitol via four steps[24] was dissolved in DMF (60 ml) under an atmosphere of argon, and to this was added dropwise ethyl isocyanoacetate (10.18 g, 90 mmol) in DMF (60 ml). The mixture was chilled in an ice-methanol bath (-10°C) and DPPA (21.25 g, 77 mmol) was added. After the mixture was kept at the same temperature for 15 min, a solution of diisopropylethylamine (17.06 g, 132 mmol) in DMF (60 ml) was added dropwise below 0°C over 1 h. The mixture was stirred at 0°C for 2 h and then at ambient temperature for 24 h. The mixture was diluted with benzene-EtOAc (1 : 1, 1.4 L), washed with 10 % aqueous citric acid, water, saturated aqueous $NaHCO_3$, water, and saturated brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by flash chromatography (BW-200, 250 g, benzene-EtOAc = 3 : 1) provided 14.4 g (99.9 %) of **13b** as a pale yellow oil, $[\alpha]_D^{24}$ +6.41° (c 1.2, CH_2Cl_2). IR (film) : 3400, 3120, 1730, 1715, 1610, 1515, 1375, 645 cm^{-1}. ^1H NMR δ : 1.40 (3H, t, J = 7 Hz), 1.46 (3H, s), 1.54 (3H, s), 4.15 (1H, dd, J = 7 Hz, 10 Hz), 4.30 (1H, t, J = 7 Hz), 4.39 (2H, q, J = 7 Hz), 5.81 (1H, t, J = 7 Hz), 7.93 (1H, s). Anal. Calcd for $C_{11}H_{15}NO_5$: C, 54.77 ; H, 6.27 ; N, 5.81. Found : C, 54.63 ; H, 6.30 ; N, 6.03. The configurational homogeneity of **13b** was ascertained by ^1H NMR spectral study using the chiral shift reagent, Eu(facam)$_3$.

Methyl (2R,3R)-2,3-Isopropylidenedioxy-3-(4-methoxycarbonyloxazolyl)-propionate (13c). To a stirred solution of methyl hydrogen (2R,3R)-2,3-O,O'-isopropylidenetartrate (**12c**) (490 mg, 2.4 mmol) in DMF (2 ml) was added methyl isocyanoacetate (476 mg, 4.8 mmol) in DMF (2 ml) followed by DPPA (779 mg, 2.6 mmol) in DMF (2 ml). After addition of diisopropylethylamine

(682 mg, 5.3 mmol) in DMF (2 ml), the mixture was stirred at 0°C for 2 h, then at ambient temperature for 20 h. The work-up as described above afforded a yellow oil, which was purified by column chromatography (BW-200, 45 g, benzene-EtOAc = 3 : 1) to give the oxazole **13c** (539 mg, 79 %) as a slightly yellow oil. $[\alpha]_D^{25}$ -20.6° (c 1, MeOH) (lit.[4] -27.6° (c 1, MeOH)). IR (film) : 3125, 3000, 2950, 1760 - 1730, 1620, 1510, 1440, 650 cm^{-1}. ^1H NMR δ : 1.66 (6H, s), 3.88 (3H, s), 4.03 (3H, s), 4.83 (1H, d, J = 8 Hz), 6.03 (1H, d, J = 8 Hz), 8.08 (1H, s). The configurational homogeneity of **13c** proved to be more than 90 % e.e. by ^1H-NMR spectral study using Eu(facam)$_3$.

(S)-3-tert-Butoxycarbonylamino-5-methyltetronic Acid (14a).[25] A solution of the (S)-oxazole **13a** (700 mg, 3.25 mmol) in 10 % HCl-MeOH (35 ml) was stirred at ambient temperature for 20 h. Volatiles were removed in vacuo, and the residue was concentrated in vacuo as an azeotropic mixture after being added EtOH-benzene (1 : 1, 30 ml x 3) to give 588 mg of the amino reductone as a yellow amorphous solid, which was directly used in the next step without further purification. To a cooled (0°C), stirred solution of the above material (588 mg, 3.55 mmol) in water (8 ml) was added $NaHCO_3$ (895 mg, 10.65 mmol), followed by Boc_2O (929 mg, 4.26 mmol) in dioxane (8 ml). The mixture was stirred at 0°C for 1 h and then at ambient temperature for 6 h. After dilution with saturated aqueous $NaHCO_3$ (100 ml), the whole was washed twice with EtOAc (each 100 ml), acidified with 10 % aqueous citric acid, and extracted three times with EtOAc (each 100 ml). The combined organic phase was washed with water and saturated brine, and dried over Na_2SO_4. Concentration in vacuo gave 684 mg (92 %) of **14a** as pale yellow crystals, mp 115 - 116°C. $[\alpha]_D^{20.5}$ -15.05° (c 1, MeOH). IR (KBr): 3400, 2980, 1750, 1690, 1520, 1370, 1350, 1330, 1160 cm^{-1}. ^1H NMR δ : 1.43 (3H, d, J = 7 Hz,), 1.48 (9H, s), 4.77 (1H, q, J = 7 Hz), 6.37 (1H, bs), 11.30 (1H, s). Anal. Calcd for $C_{10}H_{15}NO_5$: C, 52.39 ; H, 6.60 ; N, 6.11. Found : C, 52, 44 ; H, 6.55 ; N, 5.87.

(R)-3-tert-Butoxycarbonylamino-5-hydroxymethyltetronic Acid (14b). a) To a cooled (0°C), stirred solution of the oxazole **13b** (482 mg, 2 mmol) in EtOH-water (5 ml - 0.5 ml) was added dropwise methanesulfonic acid (1.46 ml, 20 mmol). After being stirred at ambient temperature for 4 h, the reaction mixture was diluted and decanted twice with Et_2O. Volatiles were removed in vacuo, and the residue was dissolved in saturated aqueous K_2CO_3 (4 ml). Boc_2O (502 mg, 2.3 mmol) in dioxane (2 ml) was added at 0°C. After being stirred at ambient temperature for 13 h, the mixture was diluted with EtOAc and washed with water. The aqueous layer was acidified with citric acid, and extrated twice with EtOAc. The combined organic extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by flash chromatography (BW-200, 30 g, CH_2Cl_2-EtOH = 10 : 1) provided 308 mg (63 %) of **14b** as colorless crystals, mp 137 - 139°C (dec.). $[\alpha]_D^{24}$ +31.3° (c 1, MeOH). IR (KBr) : 3430, 2980, 1740, 1680, 1660, 1535, 1160, 1050 cm^{-1}. ^1H NMR δ : 1.50 (9H, s), 3.10 (1H, b, disappeared with D_2O), 3.83 (1H, dd, J = 4 Hz, 13 Hz), 4.10 (1H, dd, J = 3 Hz, 13 Hz), 4.80 (1H, dd, J = 3 Hz, 4 Hz), 6.92 (1H, b, disappeared with D_2O), 11.50 (1H, bs, disappeared with D_2O). Anal. Calcd for $C_{10}H_{15}NO_6$: C, 48.98 ; H, 6.16 ; N, 5.71. Found : C, 49.23 ; H, 6.38 ; N, 5.49.

3-tert-Butoxycarbonylamino-4-hydroxy-2-pyrone (10 mg, 2 %) was also obtained as colorless crystals, mp 112 - 115°C. IR (KBr) : 3380, 2900, 1725, 1690, 1650, 1500, 1310 cm^{-1}. ^1H NMR δ : 1.54 (9H, s), 6.13 (1H, d, J = 6 Hz), 7.18 (1H, b, disappeared with D_2O), 7.21 (1H, d, J = 6 Hz), 12.11 (1H, s, disappeared with D_2O). Anal. Calcd for $C_{10}H_{13}NO_5$: C, 52.87; H, 5.77; N, 6.16. Found : C, 52.67; 5.76; N, 6 07.

b) A solution of the oxazole **13b** (2.63 g, 10.9 mmol) in 10 % HCl-MeOH (90 ml) was stirred at ambient temperature for 15 h, and treated as in the synthesis of **14a**. The amino reductone (2.866 g) obtained as a yellow oil was dissolved in water (32 ml). $NaHCO_3$ (2.747 g, 32.7 mmol) and then Boc_2O (2.855 g, 13.1 mmol) in dioxane (32 ml) was added. The mixture was stirred at 0°C for 1 h, then at ambient temperature for 19 h. Analogous work-up as in the synthesis of **14a** gave a yellow oil, which was purified by column chromatography (BW-200, 40 g, CH_2Cl_2-MeOH = 20 : 1) to give 1.212 g (46 %) of **14b** and 0.709 g (29 %) of the pyrone derivative.

(5R)-3-tert-Butoxycarbonylamino-5-((1R)-1-hydroxy-1-methoxycarbonylmethyl)tetronic Acid (14c). A solution of the oxazole **13c** (3.4 g, 11.9 mmol) in 10 % HCl-MeOH (60 ml) was stirred at ambient temperature for 24 h. After concentration, MeOH-benzene (1 : 1, 40 ml) was added and removed in vacuo. This work-up was repeated several times. The crude, slightly yellow, amorphous solid (3.08 g) thus obtained was dissolved in water (20 ml). After adjustment of pH of the solution to ca. 8 with $NaHCO_3$ (4.77 g, 47.6 mmol) while ice-cooling, Boc_2O (5.19 g, 23.8 mmol) in dioxane (20 ml) was added, and the mixture was stirred at room temperature for 22 h. The mixture was diluted with water (100 ml) and extracted with EtOAc (100 ml). The aqueous layer was acidified to pH 3 with 1N hydrochloric acid, and extracted three times with EtOAc (each 80 ml). The combined organic extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo to give a brown oil. Purification by column chromatography (BW-820MH, 60 g, $CHCl_3$-MeOH = 30 : 1) afforded 2.59 g (71 %) of the tetronic acid **14c**, mp 153 - 154°C (dec., CH_2Cl_2-hexane). $[\alpha]_D^{24}$ +113.4° (c 0.83, MeOH). IR (KBr) : 3450, 3300, 2975, 1750, 1740, 1690, 1665, 1540, 1375, 1340 cm^{-1}. ^1H NMR δ : 1.50 (9H, s), 3.18 (1H, bd, J = 7 Hz, disappeared with D_2O), 3.90 (3H, s), 4.56 (1H, dd, J = 2.7 Hz, J = 2 Hz after addition of D_2O), 5.06 (1H, d, J = 2 Hz), 6.56 (1H, bs), 11.4 (1H, bs, disappeared with D_2O). Anal. Calcd for $C_{12}H_{17}NO_8$: C, 47.53 ; H, 5.65 ; N, 4.62. Found : C, 47.50 ; H, 5.48 ; N, 4.42. Mass m/z : 303 (M^+), 247, 229, 203, 108.

tert-Butyldimethylsilyl (5R)-3-tert-Butoxycarbonylamino-5-((1R)-1-hydroxy-1-methoxycarbonylmethyl)tetronate (18). A mixture of the tetronic acid **14c** (2.0 g, 6.59 mmol), imidazole (1.3 g, 19.8 mmol), and TBDMS-Cl (2.0 g, 13.2 mmol) in DMF (6.5 ml) was stirred at room temperature for 12 h. The mixture was poured into Et_2O (300 ml), successively washed with water, saturated aqueous $NaHCO_3$, water, and saturated brine, and dried over $MgSO_4$. Concentration in vacuo followed by purification over silica gel (BW-200, 50 g, EtOAc-hexane = 3 : 2) afforded 2.5 g (91 %) of the teronate **18** as colorless crystals, mp 84 - 87°C (Et_2O-hexane). $[\alpha]_D^{22}$ +139.5° (c 1.09, MeOH). IR (KBr) : 3375, 2925, 1760, 1700, 1670, 1530, 1360, 1280, 1160 cm^{-1}. ^1H NMR δ : 0.03 (3H, s), 0.10 (3H, s), 0.85 (9H, s), 1.50 (9H, s), 3.85 (3H, s), 4.62 (1H, d, J = 2 Hz), 5.25 (1H, d, J = 2 Hz), 6.60 (1H, bs). Anal. Calcd for $C_{18}H_{31}NO_8Si$: C, 51.78 ; H, 7.48 ; N, 3.35. Found : C, 51.89 ; H, 7.41 ; N, 3.38.

Reaction of 14c with 1,1,3,3-Tetraisopropyl-1,3-dichlorodisiloxane. Formation of 20. A mixture of the tetronic acid **14c** (100 mg, 0.33 mmol), imidazole (90 mg, 1.32 mmol), and 1,1,3,3-tetraisopropyl-1,3-dichlorodisiloxane (114 mg, 0.36 mmol) in DMF (1 ml) was stirred at ambient temperature for 5 h. Imidazole (22.5 mg, 0.33 mmol) and 1,1,3,3-tetraisopropyl-1,3-dichlorodisiloxane (52 mg, 0.17 mmol) was added, and the mixture was stirred at ambient temperature for 17 h. After addition of Et_2O (50 ml), the mixture was washed with saturated aqueous $NaHCO_3$ and saturated brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by preparative TLC (Merck

Art 5717, 2 mm thickness plate x 2, $CHCl_3$-MeOH = 10 : 1), then column chromatography (BW-820MH, 28 g, Et_2O-hexane = 1 : 1) to give 124 mg (67 %) of **20** as a colorless oil, $[\alpha]_D^{22}$ +85.1° (c 0.53, MeOH). IR (film) : 3500, 3300, 1770, 1700, 1680, 1540 cm^{-1}. ^1H NMR δ : 1.00, 1.04 (28H, s), 1.48 (9H, s), 3.80 (3H, s), 4.80 (1H, d, J = 2 Hz), 5.14 (1H, d, J = 2 Hz), 6.46 (1H, bs), 11.2 - 11.6 (1H, b, disappeared with D_2O). Anal. Calcd for $C_{24}H_{44}NO_{10}Si_2$: C, 51.22 ; H, 7.88 ; N, 2.49. Found : C, 51.58 ; H, 8.01 ; N, 2.26.

(5R)-3-tert-Butoxycarbonylamino-5-((1R)-1-acetoxy-1-methoxycarbonylmethyl)tetronic Acid (22). A mixture of the tetronic acid **14c** (450 mg, 1.48 mmol), acetic anhydride (1.4 ml, 14.8 mmol), and pyridine (1.5 ml) was stirred at room temperature for 30 h. After addition of MeOH (5 ml), the mixture was concentrated in vacuo. The residue was dissolved in EtOAc (200 ml), and successively washed with 10 % aqueous citric acid, water, and saturated brine. The solution was dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification of the residue by column chromatography (BW-200, 30 g, $CHCl_3$-MeOH = 20 : 1) afforded **22** as a colorless solid (462 mg) together with a yellow oil (41 mg). The latter was further purified by preparative TLC (Merck Art 5744, 0.5 mm thickness x 1, $CHCl_3$-MeOH = 10 : 1) to give a further crop (30 mg) of **22**. The total yield of **22** was 492 mg (96 %), mp 163 - 166°C (dec., EtOAc-hexane). $[\alpha]_D^{26}$ +3.38° (c 0.57, MeOH). IR (KBr) : 3350, 2975 - 2925, 1760, 1740, 1700, 1660, 1530, 1210 cm^{-1}. ^1H NMR δ : 1.50 (9H, s), 2.16 (3H, s), 3.84 (3H, s), 5.28 (1H, d, J = 2 Hz), 5.52 (1H, d, J = 2 Hz), 6.46 (1H, bs). Mass m/z : 345 (M^+), 245, 230, 229, 153.

tert-Butyldimethylsilyl (5R)-3-tert-Butoxycarbonylamino-5-((1R)-1,2-dihydroxy)ethyltetronate (24). To a stirred solution of the tetronic acid **18** (1.0 g, 2.4 mmol) in THF was added dropwise a solution of 1 M $LiAlH_4$ in THF (4.8 ml, 4.8 mmol) with external ice-cooling. After 15 min, acetone (5 ml) was added. The pH of the solution was adjusted to 5 with 10 % aqueous K_2SO_4. After addition of $MgSO_4$, the mixture was stirred for 1 h and filtered. The filtrate was concentrated in vacuo to give 867 mg (93 %) of **24** as a yellow amorphous solid. IR (film) : 3450-3300, 1770, 1705, 1540 cm^{-1}. ^1H NMR δ : 0.07 (6H, s), 0.90 (9H, s), 1.50 (9H, s), 3.60-4.23 (5H, b), 4.73 (1H, bs), 6.50 (1H, bs). The amorphous solid of **24** could be purified by column chromatography, but colorless crystals obtained were not dissolved in almost any organic solvents.

2-tert-Butoxycarbonylamino-2,5-dideoxy-L-lyxo-1,4-lactone (15a). The tetronic acid **14a** (115 mg, 0.5 mmol) was dissolved in dry EtOAc (8 ml) and stirred under an initial hydrogen pressure of 120 atmospheric pressure in the presence of 5 % Rh - alumina (115 mg) at ambient temperature for 36 h. The catalyst was filtered and the filtrate was concentrated in vacuo. After dilution with EtOAc (100 ml), the whole was washed with saturated aqueous $NaHCO_3$ (80 ml). The aqueous layer was extracted twice with EtOAc (each 70 ml). The combined organic phase was washed with water and saturated brine, dried over Na_2SO_4, and concentrated in vacuo to give 105 mg (91 %) of **15a** as colorless crystals, mp 133.5 - 134.5°C. $[\alpha]_D^{21}$ -47.7° (c 1, MeOH). IR (KBr) : 3400, 1780, 1750, 1500, 1365, 1160 cm^{-1}. ^1H NMR δ : 1.47 (3H, d, J = 6 Hz), 1.48 (9H, s), 2.40 (1H, bs), 4.42 (1H, dd, J = 3 Hz, 6 Hz), 4.49 (1H, t, J = 6 Hz), 4.58 (1H, dq, J = 3 Hz, 6 Hz), 5.15 (1H, bs). Anal. Calcd for $C_{10}H_{17}NO_5$: C, 51.94 ; H, 7.41 ; N, 6.06. Found : C, 51.71 ; H, 7.44 ; N, 6.31.

[Rh(NBD)(DIPHOS-4)]$^+$BF$_4^-$.[12c,26] The catalyst was prepared and used under an argon atmosphere. Extreme care was taken to exclude air from the solvents. To a stirred suspension of $[Rh(NBD)Cl]_2$ (2.6 g) in methanol (80 ml) was added 1,4-bis(diphenylphosphino)butane (DIPHOS-4)

(3.13 g) by portions at ambient temperature. The mixture was stirred for 2 h, and then DIPHOS-4 (3.13 g) was added by portions. After the mixture was stirred for 30 min, insoluble precipitates were filtered under an argon atmosphere. A solution of $NaBF_4$ (57.2 g) in water (340 ml) was added dropwise to the filtrate at room temperature over 30 min. The rhodium complex was precipitated as orange solids. The precipitates were filtered, washed with water, and dried. This gave 12 g of the catalyst.

2-tert-Butoxycarbonylamino-3,5-bis-O-tert-butyldimethylsilyl-2-deoxy-D-ribo- and D-lyxo-1,4-lactones (16b and 16a). In an autoclave, which was dried and flushed with argon, were placed the unsaturated lactone **14b** (5.3 g, 0.021 M) and $[Rh(NBD)(DIPHOS)\text{-}4]^+BF_4^-$ (2.89 g, 4.08 mmol). Anhydrous CH_2Cl_2 (210 ml) distilled from CaH_2 under argon was added. The autoclave was pressure-flushed with hydrogen (3 times) and the mixture was pressurized to 130 atmospheric pressure of hydrogen. The lactone **14b** was reduced at 130 atmospheric pressure and ambient temperature for 20 h. After evaporation of the solvent in vacuo, chromatographic purification (BW-200, 70 g, EtOAc-hexane = 5 : 1) of the residue gave 4.9 g as a mixture of the saturated lactones, which was used in the nest step without further purification. TBDMS-Cl (17.9 g, 0.119 mol) and imidazole (9.4 g, 0.138 mol) was added to a stirred solution of the mixture (4.9 g) in DMF (10 ml). The reaction mixture was stirred at ambient temperature for 30 h. After dilution with benzene-EtOAc (1 : 1, 800 ml), the whole was washed with 10 % aqueous citric acid, water, saturated aqueous $NaHCO_3$, water, and saturated brine, and concentrated in vacuo. Purification of the residue by flash chromatography (BW-200, 400 g, hexane-Et_2O = 5 : 1) provided 8.82 g (86 %) of the desired isomer **16b** together with 0.867 g (8.4 %) of the minor isomer **16a**.

The D-ribo-1,4-lactone **16b**, colorless crystals, mp 96 - 98°C (petroleum ether). $[\alpha]_D^{27}$ - 8.57° (c 1, CH_2Cl_2). IR (nujol) : 3450, 2950, 1780, 1730, 1500, 1460, 1365, 1255, 1105 cm^{-1}. ^1H NMR δ : 0.09 (6H, s), 0.10 (6H, s), 0.89 (9H, s), 0.90 (9H, s), 1.45 (9H, s), 3.81 (2H, d, J = 3.5 Hz), 4.31 (1H, t, J = 3.5 Hz), 4.43 (1H, d, J =5.5 Hz), 4.79 (1H, dd, J = 5.5 Hz, 8.9 Hz), 4.91 (1H, d, J = 8.8 Hz). Anal. Calcd for $C_{22}H_{45}NO_6Si_2$: C, 55.54 ; H, 9.53 ; N, 2.94. Found : C, 54.87 ; H, 9.41 ; N, 2.94.

The D-lyxo-1,4-lactone **16a**, a colorless oil. $[\alpha]_D^{27}$ +37.8° (c 0.96, CH_2Cl_2). IR (film) : 3420, 2950, 1780, 1710, 1500, 1245 cm^{-1}. ^1H NMR δ : 0.08 (6H, s), 0.09 (6H, s), 0.90 (18H, s), 1.46 (9H, s), 3.86 (1H, dd, J = 5.9 Hz, 11.2 Hz), 3.89 (1H, dd, J = 6 Hz, 11.2 Hz), 4.39 (1H, dt, J = 5.8 Hz, 2.7 Hz), 4.52 (1H, dd, J = 2.7 Hz, 4.4 Hz), 4.58 (1H, dd, J = 4.4 Hz, 7.6 Hz), 5.09 (1H, d, J = 7.6 Hz). Anal. Calcd for $C_{22}H_{45}NO_6Si_2$: C, 55.54 ; H, 9.53 ; N, 2.94. Found C, 55.12 ; H, 9.31 ; N, 2.89.

2-tert-Butoxycarbonylamino-2-deoxy-5-methoxycarbonyl-L-1,4-lactones (17a and 17b). Catalytic hydrogenation of **14c** (800 mg, 2.64 mmol) was carried out as described in the hydrogenation of **14a** by use of 5 % Rh-alumina (1.6 g) suspended in EtOAc (30 ml) at 90 atmospheric pressure and ambient temperature for 49 h. The catalyst was filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (BW-820 MH, 75 g, $CHCl_3$-EtOH = 30 : 1 → 10 : 1) to give 14 mg (2%) of **17b** (Rf 0.58 in $CHCl_3$-EtOH = 10 : 1) and 213 mg (26 %) of **17a** (Rf 0.46 in $CHCl_3$-EtOH = 10 : 1).

The D-lyxo lactone **17a**, a colorless oil. IR (film) : 3425 - 3350, 1790, 1730, 1700, 1510, 1360 cm^{-1}. ^1H NMR δ : 1.48 (9H, s), 3.88 (s), 3.88 - 4.08 (b) (4H, 1H disappeared with D_2O), 4.32 - 4.88 (m), 4.72 (bs) (5H, disappeared with D_2O), 5.40 (1H, bd, J = 8 Hz).

The D-ribo lactone **17b**, a colorless solid. IR (film) : 3350, 1790, 1730, 1700, 1530 - 1510, 1360 cm^{-1}. ^1H NMR δ : 1.44 (9H, s), 3.20 - 3.60 (1H, b), 3.84 (3H, s), 4.18 (1H, bs), 4.36 - 4.88 (4H, m), 5.26 (1H, bd, J = 8 Hz).

2-tert-Butoxycarbonylamino-3-O-tert-butyldimethylsilyl-2-deoxy-5-methoxycarbonyl-L-1,4-lactones (19a and 19b). a) Catalytic hydrogenation of **18** (852 mg, 2.04 mmol) was carried out in EtOAc (30 ml) by use of 5 % Rh-alumina (1.6 g) at 140 atmospheric pressure and ambient temperature for 36 h. Filtration followed by concentration of the filtrate gave a slightly yellow oil (800 mg), which was again hydrogenated over 5 % Rh-alumina (1.7 g) at the same conditions as above. The same work-up as described in the formation of **17**, followed by column chromatography (BW-820MH, 70 g, benzene-hexane-EtOAc = 5 : 1 : 1) gave 26 mg (3 %) of **19b** and 430 mg (50 %) of **19a**.

The D-lyxo lactone **19a**, colorless crystals, mp 123 - 124°C. $[\alpha]_D^{21}$ +48.2° (c 1, MeOH). IR (KBr) : 3500, 3450 cm^{-1}. ^1H NMR δ : 0.12, 0.14 (6H, s, s), 0.90 (9H, s), 1.46 (9H, s), 3.30 (1H, bs, disappeared with D_2O), 3.80 (3H, s), 4.40-4.64 (4H, m), 5.04-5.24 (1H, b). Anal. Calcd for $C_{18}H_{33}NO_8Si$: C, 51.43; H, 7.93; N, 3.34. Found : C, 51.45; H, 8.04; N, 3.14.

The D-ribo lactone **19b**, a colorless oil. IR (film): 3450, 3350, 1795, 1720-1680, 1510 cm^{-1}. ^1H-NMR δ : 0.12 (6H, s), 0.88 (9H, s), 1.46 (9H, s), 3.56 (1H, bs, disappeared with D_2O), 3.80 (3H, s), 3.98-4.58 (4H, m), 5.08-5.60 (1H, bs).

b) Rh-alumina hydrogenation of **18** (174 mg) in EtOAc-EtOH (1 : 1) was analogously carried out at 90 atmospheric pressure for 72 h. The work-up as above afforded 81 mg (34 %) of **19a** and 81 mg (34 %) of **19b**.

Catalytic Hydrogenation of 20. Formation of 21a. Prepared as described in the synthesis of **15a** from **20** at 100 atmospheric pressure for 90 h. The usual work-up, followed by column chromatography (BW-820MH, 20 g, EtOAc-hexane = 1 : 3) provided 210 mg (60 %) of **21a** as a colorless oil. IR (film) : 3450-3350, 2925, 1780, 1740-1680, 1510 cm^{-1}. ^1H-NMR δ : 1.02 (d, J = 2 Hz), 1.04 (d, J = 2 Hz) (28H), 1.46 (9H, s), 3.20-3.48 (1H, b, disappeared with D_2O), 3.80 (3H, s), 4.40-4.68 (3H, M), 4.88 (1H, d, J = 8 Hz).

2-tert-Butoxycarbonylamino-3-O-tert-butyldimethylsilyl-(5S)-hydroxymethyl-1,4-lactones (25a and 25b). Prepared as described in the synthesis of **15a** from crude **24** (860 mg, 2.2 mmol) at 40 - 100 atmospheric pressure and ambient temperature for 3 days. The usual work-up, followed by column chromatography (BW-200, 50 g, hexane-EtOAc = 4 : 3) provided 394 mg (46 %) of the D-lyxo lactone **25a**, 88.5 mg (10 %) of the D-ribo lactone **25b**, and 112.5 mg (13 %) of the recovered starting material **24**.

The D-lyxo lactone **25a**, a colorless oil. IR (film) : 3450-3350, 1780, 1700, 1510 cm^{-1}. ^1H NMR δ : 0.13 (6H, s), 0.90 (9H, s), 1.45 (9H, s), 3.73 (3H, b), 4.00-4.83 (5H, b), 5.47 (1H, b).

The D-ribo lactone **25b**, a colorless oil. IR (film) : 3450-3350, 1790, 1705, 1510 cm^{-1}. ^1H NMR δ : 0.12, 0.14 (6H, s,s), 0.88 (9H, s), 1.46 (9H, s), 3.80 (2H, m), 4.10 (1H, bd), 4.20-4.88 (3H, b), 5.16 (1H, b).

2-tert-Butoxycarbonylamino-2,5-dideoxy-L-lyxo-pentose (26). To a cooled (-73 °C), stirred solution of the L-lyxo lactone **15a** (462 mg, 2 mmol) in CH_2Cl_2 (18 ml) was added dropwise 1M solution of DIBAL in toluene (7 ml) below -70°C under an atmosphere of argon, and the reaction mixture was kept for 6 h under this condition. After quenching of the reaction mixture with 10 % aqueous citric acid, the mixture was allowed to warm to ambient temperature, concentrated, and diluted with water.

The whole was extracted four times with EtOAc (each 100 ml). The EtOAc extracts were washed with water and saturated brine, dried over Na_2SO_4, and removed in vacuo. Purification of the residue by flash chromatography (BW-200, 100 g, EtOAc-hexane = 2 : 1) followed by recrystallization from EtOAc-hexane gave 373 mg (80.0 %) of **26** as colorless crystals, mp 84 - 85°C. $[\alpha]_D^{24.5}$ +17.5° (soon after being dissolved)→ -41.3° (equil. c 1, MeOH). IR (KBr) : 3400, 2950, 1700, 1500, 1365, 1160 cm^{-1}. ^1H NMR δ : 1.50 (3H, d, J = 6 Hz), 1.50 (9H, s), 2.80 (2H, bs, disappeared with D_2O), 4.15 (3H, m), 5.30 (2H, bs, disappeared with D_2O). Anal. Calcd for $C_{10}H_{19}NO_5$: C, 51.49 ; H, 8.21 ; N, 6.01. Found : C, 51.30 ; H, 7.80 ; N, 6.01.

1,2-Anhydro-3-tert-butoxycarbonylamino-3,6-dideoxy-1-O-methyl-L-lyxo-hexitol (27). To a cooled (-15°C), stirred suspension of triphenyl methoxymethyl phosphonium chloride (1.435 g, 4.189 mmol) in toluene (2 ml) was added dropwise a suspension of potassium tert-butoxide (458 mg, 4.084 mmol) in glyme-toluene (each 1.5 ml) under an atmosphere of argon. After the mixture was stirred for 10 min, the L-lactol **26** (244 mg, 1.047 mmol) in glyme-toluene (each 1.5 ml) was added dropwise to this dark red solution below -10 °C. The mixture was stirred at -10 °C for 30 min and then at ambient temperature for 1 h. After quenching of the reaction mixture with 10 % aqueous citric acid, the aqueous phase was extracted four times with EtOAc (each 50 ml). The EtOAc extracts were dried over Na_2SO_4 and removed in vacuo. Purification of the residue by flash chromatography (BW-200, 30 g, EtOAc-hexane = 1 : 1) provided 174 mg (64 %) of **27** as a colorless oil, $[\alpha]_D^{24.5}$ -10.2° (c 1.17, MeOH). IR (film) : 3420, 2950, 1685, 1650, 1490, 1370, 1160, 1043 cm^{-1}. ^1H NMR δ : 1.20 (3H, d, J = 6 Hz), 1.43 (9H, s), 3.30 (2H, b, disappeared with D_2O), 3.30 (1H, q, J = 6 Hz), 3.50 (1.5H, s), 3.60 (1.5H, s), 4.10 (1H, q, J = 7 Hz, 13 Hz), 4.40 (1H, m) 4.70 (1H, dd, J = 7 Hz), 5.10 (1H, b, disappeared with D_2O), 5.95 (0.5H, d, J = 5 Hz), 6.40 (0.5H, d, J = 15 Hz). Anal. Calcd for $C_{12}H_{23}NO_5$: C, 55.16 ; H, 8.87 ; N, 5.36. Found : C, 55.27 ; H, 8.95 ; N, 4.90.

3-Amino-2,3,6-trideoxy-L-lyxo-hexose (L-Daunosamine) (7) Hydrochloride. To a stirred solution of the methyl enol ether **27** (30 mg, 0.115 mmol) in THF (0.5 ml) was added 20 % aqueous HCl-THF (1 : 1.7, 2 ml) and the solution was stirred at 40 - 50°C for 10 h. After removal of the solvent, the residue was diluted with EtOH-benzene (1 : 1, each 20 ml) and concentrated in vacuo. This work-up was repeated five times. The residue was diluted with acetone, and the resulting precipitates were filtered under an atmosphere of argon to give 19 mg (90 %) of the hydrochloride of **7** as colorless crystals, mp 165 -166° (dec.). $[\alpha]_D^{27}$ -68.8° (equil. c 1, 0.1N HCl). IR (KBr) : 3360, 3120, 1596, 1502, 1409, 1340, 1270, 1195, 1125, 1070, 1020, 990, 960 cm^{-1}. ^1H NMR ($Me_3Si(CH_2)_3SO_3Na/D_2O$), mixture of α- and β-daunosamine δ: 1.23 (3H, dx2, J = 6 Hz), 1.95 (2H, m), 3.40 - 3.90 (3H, m), 4.05 (1H, m). ^{13}C NMR (TPS/D_2O) δ: 15.157, 16.765 (C-6), 28.706 (C-2), 47.957 (C-3), 67.160 (C-5), 67.404 (C-4), 96.695 (C-1). The synthetic sample was completely identical with L-daunosamine hydrochloride, mp 167.5°C (dec.), $[\alpha]_D^{27}$ -69.9° (equil. c 1, 0.1 NHCl), prepared from natural daunorubicin by acidic hydrolysis.

2-tert-Butoxycarbonylamino-2,5-dideoxy-2-C-methyl-L-lyxo-1,4-lactones (28a and 28b) . To a cooled (-76°C), stirred solution of lithium diisopropylamide (6.6 mmol) in THF (24 ml) was added dropwise the L-lyxo lactone **15a** (468 mg, 2 mmol) in THF (2 ml) under an atmosphere of argon. After the mixture was stirred at -76° for 40 min, methyl iodide (149 μl, 2.4 mmol) was added. The mixture was stirred at -76°C for 2 h and then -50 - -60°C for 4 h. After quenching of the reaction mixture with 10 % aqueous citric acid (20 ml), the whole was extracted three times with EtOAc (each 70

ml). The EtOAc extracts were washed with saturated brine, dried over Na_2SO_4, and removed in vacuo. Purification of the residue by flash chromatography (BW-200, 100 g, EtOAc-hexane = 1 : 1) provided 339 mg (69.2 %) of the C-methylated lactones **28a** and **28b** (96 : 4) as a colorless oil, $[\alpha]_D^{20.5}$ -59.8° (c 0.73, MeOH). IR (film) : 3400, 2980, 1775, 1690, 1500, 1440, 1380, 1368 cm^{-1}. ^1H NMR δ : 1.48 (3H, s), 1.48 (3H, d, J = 6 Hz), 1.50 (9H, s), 3.50 (1H, bs), 4.30 (1H, d, J = 4 Hz), 4.70 (1H, dd, J = 4 Hz, 6 Hz), 5.40 (1H, s). Anal. Calcd for $C_{11}H_{19}NO_5$: C, 53.87 ; H, 7.81 ; N, 5.71. Found : C, 53.52 ; H, 7.57 ; N, 5.64.

2-tert-Butoxycarbonylamino-2,5-dideoxy-2-C-methyl-L-lyxo-pentose (29). Prepared in a similar manner as described in the synthesis of **26** from the C-methylated lactones **28a** and **28b** (307 mg, 1.25 mmol), 1.758 M solution of DIBAL in toluene (2.28 ml, 4 mmol), and CH_2C_{12} (10 ml). After the usual work-up, chromatographic purification provided 224 mg (72.5 %) of the title compound **29** as a colorless oil, $[\alpha]_D^{20.5}$ -11.7° (equil. c 0.59, MeOH). IR (film) : 3420, 2980, 1705, 1495, 1445, 1370, 1170 cm^{-1}. ^1H NMR δ : 1.40 (3H, d, J = 6 Hz), 1.40 (3H, s), 1.45 (9H, s), 3.25 (1H, d, J = 8 Hz, disappeared with D_2O), 3.90 (1H, d, J = 4 Hz), 4.30 (1H, d of q, J = 3 Hz, 6 Hz), 4.60 (1H, bd, J = 6 Hz, disappeared with D_2O), 5.08 (1H, d, J = 6 Hz), 5.53 (1H, bs, disappeared with D_2O). Anal. Calcd for $C_{11}H_{21}NO_5$: C, 53.43 ; H, 8.56 ; N, 5.66. Found : C, 53.15 ; H, 8.49 ; N, 5.30.

1,2-Anhydro-3-tert-butoxycarbonylamino-3,6-dideoxy-1-methyl-3-C-methyl-L-lyxo-hexitol (30). Prepared in a similar manner as described in the synthesis of **27** from the C-methylated lactol **29** (124 mg, 0.5 mmol), triphenyl methoxymethyl phosphonium chloride (873 mg, 2.55 mmol), potassium tert-butoxide (281 mg, 2.5 mmol) and glyme (6 ml). After the usual work-up, chromatographic purification (BW-200, 48 g, EtOAc-hexane = 1 : 1) provided 81 mg (59 %) of the title compound **27** as a colorless oil. IR (film) : 3400, 2980, 2950, 1690, 1510, 1450, 1390, 1100, 910 cm^{-1}. ^1H NMR δ : 1.25 (3H, d, J = 6 Hz), 1.45 (9H, s), 1.55 (3H, s), 3.20 (1H, b, disappeared with D_2O), 3.40 (1H, dd, J = 3 Hz, 7 Hz), 3.65 (3H, s), 4.00 (1H, b, disappeared with D_2O), 4.40 (1H, d, J = 7 Hz), 5.93 (1H, d, J = 7 Hz), 6.20 (1H, bs, disappeared with D_2O). Anal. Calcd for $C_{13}H_{25}NO_5$: C, 56.71 ; H, 9.15 ; N, 5.09. Found : C, 56.21 ; H, 8.89 ; N, 4.73.

Methyl N,O-Diacetyl-α and β-L-vancosaminides (8a and 8b). To a stirred solution of the methyl enol ether **30** (100 mg, 0.364 mmol) in MeOH (6 ml) was added dropwise 46 % hydrofluoric acid-MeOH (1 : 5, 2 ml) at 0°C. After the mixture was stirred at ambient temperature for 18 h, Et_3N (1 ml) was added, followed by the addition of acetic anhydride (2 ml) - pyridine (3 ml). The mixture was stirred at room temperature for 15 h. Volatiles were removed in vacuo, and purification of the residue by chromatography (BW-200, 20 g, toluene-EtOAc-EtOH = 15 : 5 : 3) followed by preparative TLC (Merck Art 5744, 0.5 mm thickness x 1, toluene-EtOAc-EtOH = 15 : 5 : 3 → CH_2Cl_2-EtOH = 20 : 1) gave 30 mg (33 %) of the α-methyl glycoside **8a** together with 3 mg (3 %) of the β-methyl glycoside **8b**.

8a, mp 163 - 165°C, $[\alpha]_D^{25.5}$ -209.5° (c 0.1, MeOH). IR (KBr) : 3600 - 3200, 3300, 2950, 1730, 1655, 1550, 1440, 1375, 1240, 1125 cm^{-1}. ^1H NMR δ : 1.14 (3H, d, J = 6 Hz), 1.73 (3H, s), 1.87 (3H, s), 1.90 - 2.40 (2H, m), 2.18 (3H, s), 3.32 (3H, s), 4.11 (1H, q, J = 6 Hz), 4.79 (1H, dd, J = 4 Hz), 4.91 (1H, s), 5.59 (1H, s); identified with the sample from natural sporaviridin.[15]

8b, mp 115 - 119 °C. IR (KBr) : 3600 - 3100, 3300, 2920, 1735, 1650, 1550, 1445, 1375, 1300, 1240, 1160, 1080 cm^{-1}. ^1H NMR δ : 1.20 (3H, d, J = 6 Hz), 1.63 (3H, s), 1.89 (3H, s), 2.19 (3H, s) 1.50 - 2.40 (2H, m), 3.50 (3H, s), 3.88 (1H, q, J = 6 Hz), 4.52 (1H, dd, J = 2.5 Hz, 10 Hz), 5.00 (1H, s), 5.49 (1H, s). The spectra were identical with those of **8b** from natural sporaviridin.[15]

3-tert-Butoxycarbonylamino-2,5-dideoxy-3-O-methoxymethyl-L-lyxo-1,4-lactone (31). To an ice-cooled, stirred solution of **15a** (231 mg, 1 mmol) in CH_2Cl_2 (2 ml) was added diisopropylethylamine (780 μl, 4.5 mmol) under argon. After 10 min, chloromethyl methyl ether (171 μl, 2.25 mmol) was added. The mixture was stirred at ambient temperature for 40 h. CH_2Cl_2 (80 ml) was added, and the mixture was washed with 10 % aqueous citric acid, water, and saturated brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography (BW-200, 30 g, CH_2Cl_2-MeOH = 30 : 1) to give 152 mg (55 %) of **31** as colorless crystals, mp 97-99°C. $[\alpha]_D^{21}$ -44.4 ° (c 1, MeOH). IR (KBr) : 2950, 1785, 1710, 1500, 1370, 1160 cm^{-1}. ^1H NMR δ : 1.48 (9H, s), 1.49 (3H, d, J = 6 Hz), 3.40 (3H, s), 4.10 (1H, q, J = 6 Hz), 4.30-4.90 (2H, m), 4.69 (2H, s), 5.20 (1H, bd, disappeared with D_2O). Anal. Calcd for $C_{12}H_{21}NO_6$: C, 52.35; H, 7.69; N, 5.09. Found : C, 52.52; H, 7.61; N, 5.21.

2-tert-Butoxycarbonylamino-4-hydroxy-2-pentenoic Acid 1,4-Lactone (32). To a solution of the methoxymethyl lactone **31** (55 mg, 0.2 mmol) in MeOH or DMF (2 ml) was slowly added an aqueous alkaline solution (2N NaOH, 1 N Cs_2CO_3, or 1N LiOH ; 150 μl) at -10°C with stirring. After 10 min, 50 μl of the aqueous alkaline solution was added. The mixture was stirred for 40 min, acidified with 1N HCl (200 μl), and extracted with EtOAc. The aqueous layer was salted out, and extracted with EtOAc. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography (BW-200, 5 g, EtOAc-hexane = 1 : 1) to give 37-40 mg (86-94 %) of **32**, mp 110-115°C. $[\alpha]_D^{21}$ -1.29° (c 1, MeOH). IR (KBr) : 3300, 2980, 1760, 1725, 1665, 1525, 1160. ^1H NMR δ : 1.42 (3H, d, J = 6 Hz), 1.49 (9H, s), 5.15 (1H, dq, J = 2 Hz, 6 Hz), 6.80 (1H, bs, disappeared with D_2O), 7.08 (1H, d, J = 2 Hz). Anal. Calcd for $C_{10}H_{15}NO_4$: C, 56.33; H, 7.09; N, 6.57. Found.: C, 56.06; H, 7.31; N, 6.15.

2-tert-Butoxycarbonylamino-3-O-tert-butyldimethylsilyl-2,5-dideoxy-L-lyxo-1,4-lactone (33). A mixture of the L-lyxo lactone **15a** (1.155 g, 5 mmol), TBDMS-Cl (1.507 g, 10 mmol), and imidazole (885 mg, 13 mmol) in DMF (2 ml) was stirred at ambient temperature for 48 h. After dilution with EtOAc (200 ml), the mixture was washed with water, and saturated brine, dried over Na_2SO_4, and concentrated in vacuo. Chromatographic purification (BW-200, 40 g, Et_2O-hexane = 3 :1) of the residue provided 1.688 g (97 %) of **33** as a colorless oil, $[\alpha]_D^{21}$ -64.3° (c 0.22, MeOH). IR (film) : 3350, 2920, 1785, 1710, 1510, 1250, 1060, 840 cm^{-1}. ^1H NMR δ : 0.09 (6H, s), 0.93 (9H, s), 1.47 (3H, d, J = 6 Hz), 1.49 (9H, s), 4.30 - 4.80 (3H, m), 5.00 (1H, bs, disappeared with D_2O). Anal. Calcd for $C_{16}H_{31}NO_5Si$: C, 55.62 ; H, 9.04 ; N, 4.05. Found : C, 55.43 ; H, 9.17 ; N, 4.16.

2-tert-Butoxycarbonylamino-3-O-tert-butyldimethylsilyl-2,5-dideoxy-D-ribo-1,4-lactone (34a). The L-lyxo lactone **33** (174 mg, 0.5 mmol) was dissolved in THF-MeOH-water (4 : 1 : 1, 6 ml) and the mixture was cooled in an ice-methanol bath. Potassium superoxide (107 mg, 1.5 mmol) followed by 18-crown-6 (40 mg, 0.15 mmol) was added at 0°C by portions. After being stirred at ambient temperature for 3 h, the reaction mixture was poured into ice-water (25 ml). The mixture was acidified to pH 4 with 1N HCl, and extracted three times with Et_2O (each 35 ml). The combined Et_2O extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo to give 174 mg (95.3 %) of the hydroxy carboxylic acid as a colorless oil (IR (film) : 3400, 2900, 1720, 1705, 1490, 1365 cm^{-1}), which was used in the next step without further purification. To a cooled (0°C), stirred solution of the hydroxy carboxylic acid (174 mg) in THF (3 ml) was added slowly triphenylphosphine (138 mg, 0.524 mmol) followed by diethyl azodicarboxylate (83 μl, 0.52 mmol) under an atmosphere of argon.

After being stirred for 15 h, the whole was extracted twice with EtOAc (each 50 ml). The EtOAc solution was washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo. Chromatographic purification (BW-200, 30 g, Et_2O-hexane = 1 : 2) of the residue gave 89 mg (54 % from **33**) of **34a** as a colorless oil, $[\alpha]_D^{23}$ -17.0° (c = 0.28, MeOH). IR (film) : 3330, 2930, 1785, 1710, 1520, 1250, 1070 cm^{-1}. ^1H NMR δ : 0.09 (6H, s), 0.92 (9H, s), 1.46 (3H, d, J = 6 Hz), 1.48 (9H, s), 4.10 - 4.80 (3H, m), 5.10 (1H, bs). Anal. Calcd for $C_{16}H_{31}NO_5Si$: C, 55.62 ; H, 9.04 ; N, 4.05. Found : C, 55.51 ; H, 9.31 ; N, 4.27.

2-tert-Butoxycarbonylamino-2,5-dideoxy-D-ribo-1,4-lactone (34b). Prepared in a similar manner as described in the synthesis of **34a** from the L-lyxo lactone **15a** (924 mg, 4 mmol), potassium superoxide (856 mg, 12 mmol), 18-crown-6 (320 mg, 1.2 mmol), and THF-MeOH-water (32 ml - 8 ml - 8 ml). After acidification to pH 4 followed by evaporation in vacuo as an azeotropic mixture, the resulting solid was treated with triphenylphosphine (1.18 g, 4.48 mmol), diethyl azodicarboxylate (280 μl, 1.78 mmol), and THF (28 ml) at 0°C under an atmosphere of argon. After the usual work-up, chromatographic purification provided an inseparable mixture (1.353 g) of the D-ribo lactone **34b** and diethyl hydrazinedicarboxylate in a ratio of 1.3 : 1, which was used in the next step without further purification.

2-tert-Butoxycarbonylamino-3-O-tert-butyldimethylsilyl-2,5-dideoxy-D-ribo-pentose (35a). Prepared in a similar manner as described in the synthesis of **26** from the D-ribo lactone **34a** (218 mg, 0.632 mmol), 1.758 M solution of DIBAL in toluene (0.79 ml, 1.39 mmol), and CH_2Cl_2 (6 ml). After the usual work-up, chromatographic purification provided 180 mg (82 %) of **35a** as a colorless oil. $[\alpha]_D^{22}$ +5.08° (equil., c 0.1, MeOH). IR (film) : 3430, 2920, 1705, 1500, 1215, 1060, 840 cm^{-1}. ^1H NMR δ : 0.09 (6H, s), 0.92 (9H, s), 1.21 (3H, d, J = 6 Hz) 1.47 (9H, s), 3.90 - 4.30 (4H, m, 1H, disappeared with D_2O), 5.30 (1H, b, disappeared with D_2O), 5.30 (1H, b). Anal. Calcd for $C_{16}H_{33}NO_5Si$: C, 55.30 ; H, 9.57 ; N, 4.03. Found : C, 55.01 ; H, 9.43 ; N, 4.31.

2-tert-Butoxycarbonylamino-2,5-dideoxy-D-ribo-pentose (35b). Prepared in a similar manner as described in the synthesis of **26** from a mixture of the D-ribo lactone **34b** and diethyl hydrazinedicarboxylate in a ratio of 1.3 : 1 (1.35 g), 1.758 M solution of DIBAL in toluene (16.33 ml, 28.66 mmol), and CH_2Cl_2 (40 ml). After the usual work-up, chromatographic purification (BW-200, 40 g, EtOAc-hexane = 1 : 1) provided 662 mg (71 % from **15a**) of **35b** as colorless crystals, mp 89 - 91°C. $[\alpha]_D^{20}$ +18.67° → -11.65° (equil., c 1, MeOH). IR (KBr) : 3400, 2950, 1700, 1500, 1365, 1160 cm^{-1}. ^1H NMR δ : 1.32 (3H, d, J = 7 Hz), 1.47 (9H, s), 4.08 (4H, m), 5.20 (2H, m), 5.60 (1H, bd). Anal. Calcd for $C_{10}H_{19}NO_5$: C, 51.49 ; H, 8.21 ; N, 6.01. Found : C, 51.39 ; H, 7.98 ; N, 6.12.

1,2-Anhydro-3-tert-butoxycarbonylamino-4-O-tert-butyldimethylsilyl-3,6-dideoxy-1-O-methyl-D-ribo-hexitol (36a). Prepared in a similar manner as described in the synthesis of **27** from the D-ribo lactol **35a** (78 mg, 0.225 mmol), triphenyl methoxymethyl phosphonium chloride (331 mg, 0.966 mmol), and potassium tert-butoxide (108 mg, 0.944 mmol) in glyme (3 ml). After the usual work-up, chromatographic purification (BW-200, 30 g, EtOAc-hexane = 1 : 3) provided 43 mg (51 %) of **36a** as a colorless oil. IR (film) : 3350, 2950, 1690, 1650, 1490, 1460, 1250, 840 cm^{-1}. ^1H NMR δ : 0.09 (6H, s), 0.93 (9H, s), 1.21 (3H, d, J = 6 Hz), 1.46 (9H, s), 2,70 (1H, bs), 3.57 (2.7H, s), 3.62 (0.3H, s), 3.80 - 4.20 (3H, m), 4.80 (0.9H, d, J = 13 Hz), 4.89 (0.1H, d, J = 7 Hz), 5.20 (1H, bd), 6.60 (0.9H, d, J = 13 Hz), 6.60 (0.1H, d, J = 7 Hz).

1,2-Anhydro-3-tert-butoxycarbonylamino-3,6-dideoxy-1-O-methyl-D-ribo-hexitol (36b). Prepared in a similar manner as described in the synthesis of **27** from the D-ribo lactol **35b** (127 mg, 0.545 mmol), triphenyl methoxymethyl phosphonium chloride (750 mg, 2.18 mmol), potassium tert-butoxide (239 mg, 2.12 mmol), and glyme-toluene (3 ml - 4.5 ml). After the usual work-up, chromatographic purification (BW-200, 30 g, EtOAc-hexane = 1 : 1) provided 68 mg (48 %) of **36b** as a colorless oil. IR (film) : 3410, 2930, 1690, 1645, 1375, 1160 cm^{-1}. ^1H NMR δ : 1.26 (3H, d, J = 6.5 Hz), 1.49 (9H, s), 3.58 (1H, s), 3.67 (2H, s), 4.20 (1H, m), 4.52 (1H, m), 4.30 - 4.70 (2H, b), 4.90 (1H, m), 5.49 (1H, b), 6.10 (0.3H, d, J = 7 Hz), 6.60 (0.7H, d, J = 13 Hz).

Methyl N,O-Diacetyl-α-D-ristosaminide (9a). a) To a stirred solution of the methyl enol ether **36a** (25 mg, 0.067 mmol) in MeOH (1 ml) was added dropwise 5 % HCl-MeOH (1.5 ml). The mixture was stirred at room temperature for 5 h and then at 40 ° for 15 h. Volatiles were removed in vacuo, and the resulting residue was diluted EtOH-benzene (1 : 1) and concentrated in vacuo. This work-up was repeated three times. To this residue was added acetic anhydride (0.8 ml) and pyridine (0.5 ml). After being stirred at room temperature for 36 h, the whole was extracted twice with EtOAc (each 25 ml). The combined EtOAc extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by preparative TLC (Merck Art 5715, toluene-EtOH = 5 : 1) followed by recrystallization from petroleum ether provided 10 mg (61 %) of **9a** as colorless crystals, mp 50 - 52°C. $[\alpha]_D^{23}$ +127.6° (c 0.30, $CHCl_3$). IR (KBr) : 3425, 2940, 1735, 1675, 1515, 1370, 1235, 1055 cm^{-1}. ^1H NMR δ : 1.21 (3H, d, J = 7 Hz), 1.80 - 2.10 (2H, m), 2.00 (3H, s), 2.02 (3H, s), 3.42 (3H, s), 3.97 (1H, dq, J = 7 Hz, 10 Hz), 4.55 (1H, m), 4.63 (1H, m), 4.76 (1H, d, J = 4 Hz), 6.75 (1H, bd). High - resolution MS m/z : calcd for $C_{11}N_{18}NO_5$ (M-H) : 244.11849. Found : 244.11911. Calcd for $C_{11}H_{20}NO_5$(M + H) : 246.13414. Found : 246.13695. The structure of **9a** was confirmed by comparsion of the corresponding L-isomer.[27]

b) The analogous treatment of the methyl enol ether **36b** (65 mg, 0.25 mmol) with 5% HCl-MeOH, acetic anhydride-pyridine, followed by purification on preparative TLC provided 29 mg (48 %) of **9a**.

2-tert-Butoxycarbonylamino-3,5-bis-O-tert-butyldimethylsilyl-2-deoxy-D-ribo-pentose (37). Prepared in a similar manner as described in the synthesis of **26** from the lactone **16b** (540 mg, 1.137 mmol), 1.5 M solution of DIBAL in toluene (1.44 ml, 2.16 mmol), and CH_2Cl_2 (10 ml). After the usual work-up, chromatographic purification (BW-200, 30 g, Et_2O-hexane = 1: 2) provided 522 mg (96.3 %) of **37** as a colorless oil. $[\alpha]_D^{18}$ -4.84 ° (equil., c 1, MeOH); IR (film) : 3400, 2930, 1700, 1500, 1460, 1020 cm^{-1}. ^1H NMR δ : 0.06 (6H, s), 0.11 (6H, s), 0.93 (18H, s), 1.46 (9H, s), 3.40 - 4.00 (4H, m), 4.10 (1H, dd, J = 4 Hz, 10 Hz), 4.42 (1H, dd, J = 5 Hz, 10 Hz), 5.21 (1H, d, J = 4 Hz), 5.29 (1H, d, J = 4 Hz). Anal. Calcd for $C_{22}H_{47}NO_6Si_2$: C, 55.31 ; H, 9.91 ; N, 2.93. Found : C, 55.34 ; H, 9.88 ; N, 2.90.

1,2-Anhydro-3-tert-butoxycarbonylamino-4,6-bis-O-tert-butyldimethylsilyl-3-deoxy-1-O-methyl-D-ribo-hexitol (38a). Prepared in a similar manner as described in the synthesis of **27** from the lactol **37** (184 mg, 0.387 mmol), triphenyl methoxymethyl phosphonium chloride (694 mg, 2.03 mmol), potassium tert-butoxide (222 mg, 1.97 mmol) and glyme-toluene (4 ml - 5 ml). After the usual work-up, chromatographic purification (BW-200, 30 g, EtOAc-hexane = 1 : 3) provided 192 mg (98.3 %) of the methyl enol ether **38a** as a pale yellow oil. IR (film) : 3400, 2940, 1690, 1650, 1490, 1250 cm^{-1}. ^1H NMR δ : 0.01 (12H, s), 0.93 (18H, s), 1.43 (9H, s), 2.40 (1H,

s), 3.52 (2.5H, s), 3.61 (0.5H, s), 3.80 - 4.50 (5H, m), 4.70 - 5.00 (1H, dx2, J = 5 Hz, 13 Hz), 4.80 (1H, b), 6.00 (0.2H, d, J = 5 Hz), 6.55 (0.8H, d, J = 13 Hz).

1,2-Anhydro-5-O-benzyl-3-tert-butoxycarbonylamino-4,6-bis-O-tert-butyldimethylsilyl-3-deoxy-1-O-methyl-D-ribo-hexitol (38b). To a stirred solution of the methyl enol ether **38a** (700 mg, 1.386 mmol) obtained above in THF (3 ml) was added in one portion 50 % NaH (108 mg, 2.24 mmol) at room temperature. After the mixture was stirred for 2 h, benzyl bromide (266 μl, 2.24 mmol) was added at 0 °C . The reaction mixture was stirred at room temperature for 15 h. After quenching of the mixture with ice-water, the whole was extracted three times with EtOAc (each 50 ml). The combined organic extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo. Chromatographic purification (BW-200, 50 g, hexane-ether = 5 : 1) of the residue provided 350 mg (42 %) of **38b** as a colorless oil. IR (film) : 3400, 2900, 1700, 1650, 1480, 1250, 1090, 770 cm^{-1}. ^1H NMR δ : 0.09 (12H, s), 0.93 (18H, s), 1.43 (9H, s), 3.50 - 3.53 (3H, sx2), 3.60 - 4.10 (2H, m), 4.50 (2H, s), 4.10 - 4.70 (3H, m), 4.70 (1H, b), 4.90 (1H, m), 6.40 - 6.50 (1H, dx2, J = 6 Hz, 12 Hz), 7.28 (5H, s).

5-O-Benzyl-3-tert-butoxycarbonylamino-2,3-dideoxy-5-hydroxymethyl-D-ribo-pentose (39). To a stirred solution of the methyl enol ether **38b** (305 mg, 0.513 mmol) in THF-H_2O (6 ml : 0.6 ml) was added mercuric acetate (490 mg, 1.54 mmol). The mixture was stirred at ambient temperature for 3 h. Saturated aqueous KI (6 ml) was added dropwise with ice-cooling. The mixture was extracted with ether. The ether extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo. The residue (295 mg) was dissolved in THF (8 ml), and treated with tetra-n-butylammonium fluoride (335 mg, 1.28 mmol) at ambient temperature for 18 h. The mixture was diluted with water, and extracted with EtOAc. The EtOAc extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo. The residual oil was purified by column chromatography (BW-200, 40 g, EtOAc-hexane = 1 : 1) to give 132 mg (73 %) of **39** as colorless crystals, mp 145 - 148.5°C. IR (KBr) : 3350, 2950, 1680, 1535, 1370, 700 cm^{-1}. ^1H NMR δ : 1.43 (9H, s), 1.90 - 2.20 (2H, m), 3.40 - 4.30 (7H, m), 4.60 (2H, s), 5.40 (1H, bd, J = 8 Hz), 5.50 (1H, bd, J = 4 Hz), 7.30 (5H, s).

2-tert-Butoxycarbonylamino-3-O-tert-butyldimethylsilyl-2-deoxy-D-ribo-1,4-lactone (40). The bis-TBDMS ether **16b** (3.77 g, 7.93 mmol) was dissolved in AcOH-water-THF (65 ml : 35 ml : 15 ml), and the mixture was stirred at 30 °C for 15 h. Volatiles were removed in vacuo, and the residue was taken up with EtOAc. The whole was washed with saturated aqueous $NaHCO_3$, water, and saturated brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by chromatography (BW-820MH, 200 g, EtOAc-hexane = 1 : 1) gave 2.25 g (79 %) of **42** as a colorless oil. IR (film) : 3450, 2950, 1780, 1700, 1510, 1250, 1110 cm^{-1}. ^1H NMR δ : 0.10 (6H, s), 0.91 (9H, s), 1.49 (9H, s), 3.40 (1H, bs), 3.92 (2H, d, J = 3 Hz), 4.30 - 5.00 (3H, m), 5.10 (1H, b).

5-tert-Butoxycarbonyl-2-tert-butoxycarbonylamino-3-O-tert-butyldimethylsilyl-2-deoxy-D-ribo-1,4-lactone (41). Chromium (VI) oxide (76 mg, 0.72 mmol) and pyridine (116 μl, 1.44 mmol) in CH_2Cl_2-DMF (4 : 1, 2 ml) was stirred for 15 min at 23°C. The lactone **40** (65 mg, 0.18 mmol) in CH_2Cl_2-DMF (4 : 1, 1 ml) was added, followed by the addition of acetic anhydride (136 μl, 1.44 mmol) and tert-butyl alcohol (339 μl, 3.6 mmol). The mixture was stirred at ambient temperature for 20 h. EtOH (0.5 ml) was added, and the mixture was stirred for an additional 15 min and diluted with EtOAc (20 ml). The resulting mixture was filtered with gentle suction through a sintered glass funnel packed with silica gel by use of ethyl acetate, with a layer of anhydrous Na_2SO_4 on the top. Elution

with EtOAc, removal of the solvent in vacuo, and column chromatography (BW-820 MH, 15 g, Et_2O-hexane = 1 : 1) yielded 54 mg (70 %) of **41** as a colorless oil. IR (film) : 3300, 2900, 1805, 1745, 1710, 1510, 1255 cm^{-1}. ^1H NMR δ : 0.30 (6H, s), 0.92 (9H, s), 1.45 (9H, s), 1.50 (9H, s), 4.40 - 4.70 (3H, m), 4.94 (1H, b).

tert-Butyl (2S,3S,4R)-4-tert-Butoxycarbonylamino-3-tert-butyldimethylsilyloxy-5-hydroxy-2-tetrahydrofurancarboxylate (42). To a cooled (-73°C), stirred solution of the lactone **41** (545 mg, 1.265 mmol) in toluene (12 ml) was added dropwise 1.5 M solution of DIBAL in toluene (1.1 ml, 1.645 mmol) below -70°C under an atmosphere of argon. After the mixture was stirred for 3 h, 1.5 M solution of DIBAL in toluene (0.5 ml, 0.75 mmol) was added below -70°C, and the mixture was stirred for 1 h under this condition. After quenching of the reaction mixture with 10 % aqueous citric acid, the whole was extracted three times with EtOAc. The combined organic extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on silica gel (BW-200, 50 g, ether-hexane = 3 : 2) to give 285 mg (52 %) of **42** as a colorless oil. IR (film) : 3400, 2900, 1740, 1700, 1370, 1250 cm^{-1}. ^1H NMR δ : 0.16 (6H, s), 0.92 (9H, s), 1.46 (9H, s), 1.49 (9H, s), 3.45 (1H, d, J = 10 Hz), 4.00 (1H, m), 4.30 (1H, d, J = 4 Hz), 4.52 (1H, s), 5.02 (1H, bd), 5.35 (1H, dd, J = 6 Hz, 10 Hz).

tert-Butyl (2S,3S,4S)-2-Benzyl-4-tert-butoxycarbonylamino-3-tert-butyldimethylsilyloxy-6-methoxy-5-hexenoate (43). Prepared in a similar manner as described in the synthesis of **27** from the lactol **42** (220 mg, 0.508 mmol), triphenyl methoxymethyl phosphonium chloride (435 mg, 1.27 mmol), potassium tert-butoxide (137 mg, 1.22 mmol) in glyme-toluene (5 ml - 5 ml). After the usual work-up, chromatographic purification provided 211 mg (90 %) of the methyl enol ether as a pale yellow oil, which was submitted to the next benzylation because of its unstability.

To a cooled (0 °C), stirred solution of the methyl enol ether (61 mg, 0.132 mmol) in DMF (0.2 ml) was added in one portion 50 % NaH (10 mg, 0.199 mmol). After the mixture was stirred for 30 min, benzyl bromide (24 µl, 0.199 mmol) was added at 0°C. The reaction mixture was stirred at 0°C for 30 min and then at ambient temperature for 8 h. After quenching of the mixture with water, the whole was extracted three times with EtOAc (each 30 ml). The EtOAc extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by flash chromatography (BW-200, 30 g, ether-hexane = 1 : 1) provided 58 mg (80 %) of **43** as a pale yellow oil. ^1H NMR δ : 0.10 (6H, s), 0.95 (9H, s), 1.41 (9H, s), 1.49 (9H, s), 3.50 (2H, s), 3.60 (1H, s), 3.80 - 4.90 (4H, m), 4.60 (2H, s), 5.20 (1H, b), 6.10 - 6.80 (1H, m), 7.25 (5H, s).

5-O-Benzyl-5-tert-butoxycarbonyl-3-tert-butoxycarbonylamino-2,3-dideoxy-D-ribo-pentose (44). To a stirred solution of **43** (78 mg, 0.14 mmol) in THF-water (1 ml - 0.1 ml) was added mercuric acetate (135 mg, 0.425 mol) at ambient temperature. After the mixture was stirred for 1 h, saturated aqueous KI (0.3 ml) was added to the mixture. The solution was stirred at room temperature for 5 min, and was extracted three times with Et_2O (each 20 ml). The combined organic extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo. Tetra-n-butylammonium fluoride (82 mg, 0.31 mmol) was added in one portion to a stirred solution of the resulting residue in THF (2 ml) at room temperature and the solution was stirred for 18 h. The reaction mixture was diluted with water (20 ml) and extracted three times with EtOAc (each 30 ml). The combined organic phase was washed with saturated brine, dried over Na_2SO_4, and concentrated in vacuo. Chromatographic purification (BW-200, 20 g, hexane-EtOAc = 2 : 1) of the residue provided 59 mg (98 %) of **44** as a pale

yellow oil. ^{1}H NMR δ : 1.42 (9H, s), 1.53 (9H, s), 2.00 - 3.00 (2H, m), 3.20 (1H, b), 4.05 - 4.70 (3H, m), 4.70 (2H, s), 4.80 (1H, b), 5.35 (1H, b), 7.30 (5H, s).

5-O-Benxyl-5-tert-butoxycarbonyl-3-tert-butoxycarbonylamino-2,3-dideoxy-D-ribo-1,4-lactone (10). a) To a stirred solution of N-iodosuccinimide (43 mg, 0.19 mmol), tetra-n-butylammonium iodide (14 mg, 0.038 mmol) in CH_2Cl_2 (0.7 ml) was added the lactol **44** (8 mg, 0.019 mmol) in CH_2Cl_2 (0.3 ml) under an atmosphere of argon, and the solution was stirred at ambient temperature for 3 h. Saturated aqueous $Na_2S_2O_3$ (2 ml) was added and the mixture was stirred for 5 min. After dilution with CH_2Cl_2 (50 ml), the whole was washed with water and saturated brine, and concentrated in vacuo. Chromatographic purification (BW-200, 10 g, hexane-EtOAc = 3 : 1) of the residue provided 8 mg (quantitative) of **10** as colorless crystals, mp 170 - 171°C. IR (nujor) : 3370, 1775, 1735, 1690, 1520, 1270, 730 cm^{-1}. ^{1}H NMR δ : 1.42 (9H, s) 1.50 (9H, s), 2.40 (1H, dd, J = 4 Hz, 16 Hz), 2.98 (1H, dd, J = 8 Hz, 16 Hz), 4.05 - 4.60 (3H, m), 4.65 (2H, s), 4.80 (1H, b), 7.30 (5H, s).

b) Prepared in a similar manner as described in the synthesis of **41** with chromium (VI) oxide (63 mg, 0.6 mmol), pyridine (97 μl, 1.2 mmol), the lactol **39** (30 mg, 0.085 mmol), acetic anhydride (76 μl, 0.8 mmol), tert-butyl alcohol (189 μl, 2 mmol), and CH_2Cl_2-DMF (4 :1, 3 ml). After the usual work-up, chromatographic purification provided 11 mg (30 %) of **10** as colorless crystals.

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