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Hydroxylated Pyrrolidines. Synthesis of 1,4-Dideoxy-1,4-Imino-L-lyxitol, 1,4,5-Trideoxy-1,4-imino-D- and -L-*lyxo*-hexitol, 2,3,6-Trideoxy-3,6-imino-D-*glycero*-L-*altro*- and -D-*glycero*-L-*galacto*-octitols, and of a Chiral Potential Precursor of Carbapenem Systems

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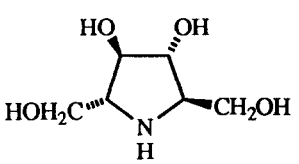
Abstract: Enantiospecific syntheses are reported for the title pyrrolidines, from carbohydrate precursors. An intermediate in one of the routes, ethyl 2,3,6-trideoxy-3,6-imino-4,5:7,8-di-*O*-isopropylidene-D-*glycero*-L-*altro*-octonate (23), could be converted in two steps into a β-lactam.

There has been considerable interest in recent years in the chemistry and biochemistry of hydroxylated pyrrolidines, piperidines, pyrrolizidines, and indolizidines, triggered by the isolation of such compounds from natural sources[1] and the recognition that they and related synthetic analogues can act as specific and potent inhibitors of glycosidases.[2] This inhibitory activity has potential application in a number of areas of agricultural and medicinal significance, which is perhaps most notably shown by the anti-HIV activity displayed by some compounds of this type.[3]

A number of compounds in the pyrrolidine subgroup display interesting bioactivity, as for example the inhibition of glucosidases, including the α-glucosidase I of glycoprotein processing,[4] by the dihydroxymethyl-dihydroxypyrrolidine **1**,[5] and the inhibition of yeast α-glucosidase[6] by 1,4-dideoxy-1,4-imino-D-arabinitol (**2**).[7]



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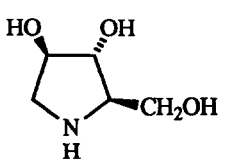

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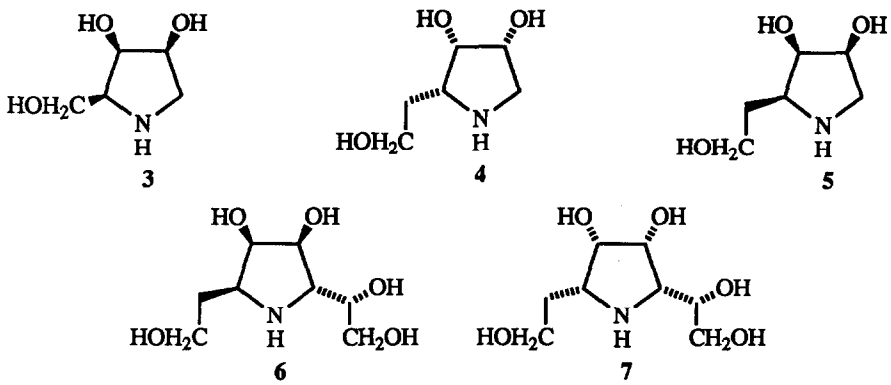
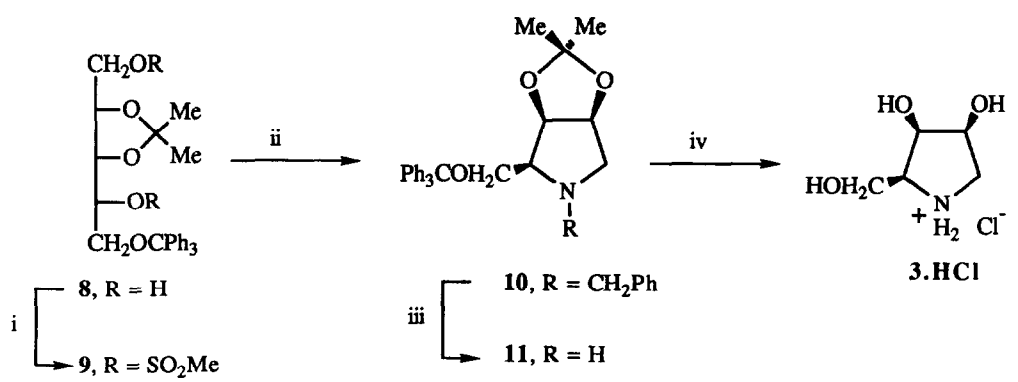
This latter compound is one of the structurally-simple 1,4-dideoxy-1,4-iminopentitols, and syntheses have been reported for the 1,4-dideoxy-1,4-imino-derivatives of D-xylitol,[7,8] L-xylitol,[8,9] D-arabinitol (**2**),[10,11] L-arabinitol,[7,10] D-ribitol,[12] L-ribitol,[13,14] and D-lyxitol.[13,15] In this paper we describe a route to 1,4-dideoxy-

1,4-imino-L-lyxitol (**3**), and also syntheses of the related iminohexitols **4** and **5** and the imino-octitols **6** and **7**. We also show that an intermediate in the synthesis of **6** can be employed to prepare a β-lactam with the carbapenam skeleton.



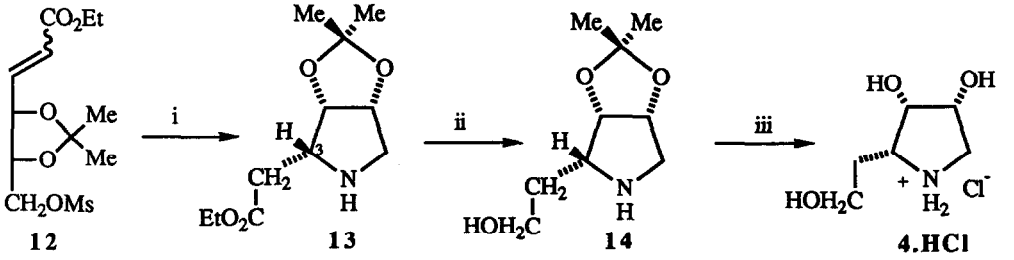
Pyrrolidine **3** could be obtained in four steps (Scheme 1) from 2,3-*O*-isopropylidene-5-*O*-trityl-D-ribitol (**8**),[16] easily prepared from D-ribose in three steps. Addition of **8** to excess methanesulfonyl chloride in pyridine containing *p*-dimethylaminopyridine (DMAP) gave the dimesylate **9** in high yield, which on treatment with benzylamine at 80°C smoothly gave the pyrrolidine **10**, in which the all-*cis* arrangement of substituents was strongly supported by the significant coupling (4.8 Hz) observed between H-3 and H-4. Hydrogenolysis of the *N*-benzyl group in ethanol was not accompanied by significant detritylation, and the resultant secondary amine **11** could be deprotected with acid to give **3**, isolated as its crystalline hydrochloride, and with n.m.r. data in excellent agreement with that reported for the enantiomer.[15,17]



Scheme 1. i, excess MsCl, C_5H_5N, DMAP; ii, $PhCH_2NH_2$, 80°; iii, H_2, Pd/C, EtOH; iv, TFA-H_2O

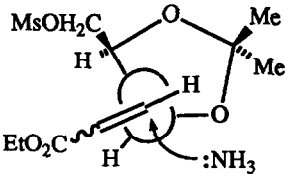
During the course of our studies, other workers have reported a synthesis of **3** along similar lines, but involving a greater number of steps,[18] and an alternative approach from non-carbohydrate precursors, involving a nitroaldol condensation, has also been reported recently.[19]

For the syntheses of the trideoxy-iminoalditols **4** - **7**, we employed a method for the stereoselective synthesis of hydroxylated pyrrolidines which involves conjugate addition of ammonia to an α,β–unsaturated ester, followed by intramolecular cyclization, and which has been the subject of a previous brief report from this laboratory.[20] Thus (Scheme 2), when the enoate **12**,[21] obtained as an 8:3 mixture of *Z*- and *E*-isomers by Wittig reaction of 2.3-*O*-isopropylidene-D-erythrose in refluxing dichloromethane, followed by mesylation,[20] was treated with ethanolic ammonia at room temperature for 4 days, the pyrrolidine **13** was obtained as a 9:1 mixture with its C-3 epimer.[20] Reduction of **13** and its epimer with $LiAlH_4$ gave the D-*lyxo*-iminohexitol **14**, separable by chromatography from its stereoisomer. Deprotection of the acetonide with aqueous trifluoroacetic acid (TFA) then gave 1,4,5-trideoxy-1,4-imino-D-*lyxo*-hexitol (**4**), isolated as its crystalline hydrochloride.



Scheme 2. i, NH_3, EtOH, 4 days; ii, $LiAlH_4$; iii, TFA-H_2O, then HCl, EtOH, Et_2O

The *threo*-selectivity in the conjugate addition has precedent,[22] and can best be rationalized[20] in terms of reaction through the Cornforth-type model **15**; alternative transition-state models, such as a Felkin-type[22] would have prohibitive steric interactions, particularly for the *Z*-isomer of **12**.

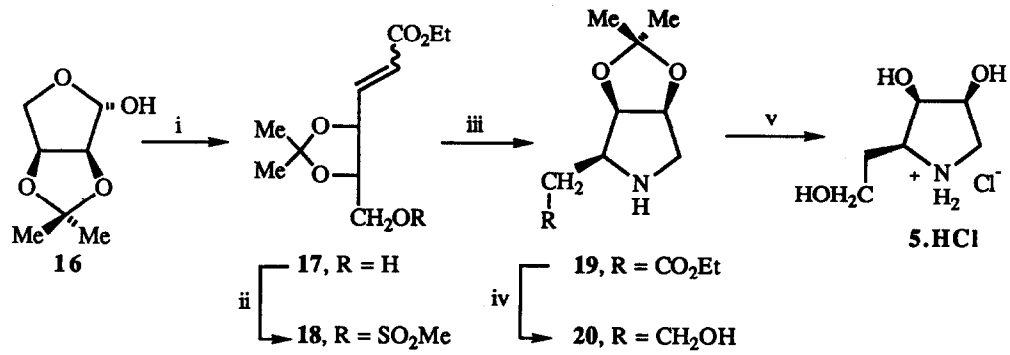


15

During the course of our work, Jager and Hummer reported an alternative route to **4** involving introduction of chirality by asymmetric oxidation and cyclization by haloamidation.[23]

The enantiomer **5** was prepared analogously (Scheme 3). Thus 2,3-*O*-isopropylidene-L-erythrose **16**, prepared by periodate cleavage of 3,4-*O*-isopropylidene-L-arabinopyranose[24] was converted by Wittig reaction[21] in dichloromethane at reflux to alkene **17** (87%) (*Z* : *E*, 8 : 3), and hence to the corresponding mesylates **18**. Treatment with ammonia to give **19**, again as a 9:1 mixture with the diastereomer, reduction to **20** and deprotection gave 1,4,5-trideoxy-1,4-imino-L-*lyxo*-hexitol hydrochloride **5.HCl**.

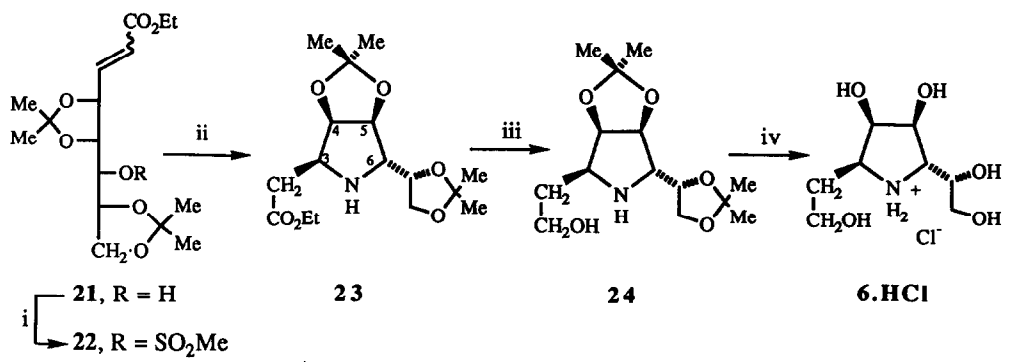
Similar methods could also be used to prepare stereoselectively a 2,5-disubstituted pyrrolidine, as illustrated by the sequence of reactons in Scheme 4. The enoate **21** can be prepared with high *trans*-stereoselectivity by Wittig reaction of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose,[25] and could be converted



Scheme 3. i, $Ph_3PCH{=}CO_2Et$, CH_2Cl_2,reflux; ii, MsCl, C_5H_5N; iii, NH_3,EtOH; iv, $LiAlH_4$; v, TFA-H_2O, then HCl, EtOH, Et_2O

in high yield to the mesylate **22**. Treatment of this with ethanolic ammonia for several days led to the formation of the pyrrolidine **23**, as a 9:1 mixture with its inseparable C-3 epimer (79% combined yield).

The stereochemistry of **23** was strongly supported by n.m.r. data. The ^{1}H-spectrum of **23** showed $J_{3,4}$ as 4.4 Hz and $J_{5,6}$ as very small (0.9 Hz), as would be anticipated in compounds of this type if the relative stereochemistry is as indicated.[21,26] Additionally, in the ^{13}C-spectrum, the signals for C-2 (δ 34.5) and the acetal carbon of the 4,5-*O*-isopropylidene group (δ 111.5) were shielded relative to the equivalent signals from the minor isomer (δ 38.5 and 114.5 respectively), as would be expected given the steric compression in the major 3,4-*cis*-isomer **23**.[27]

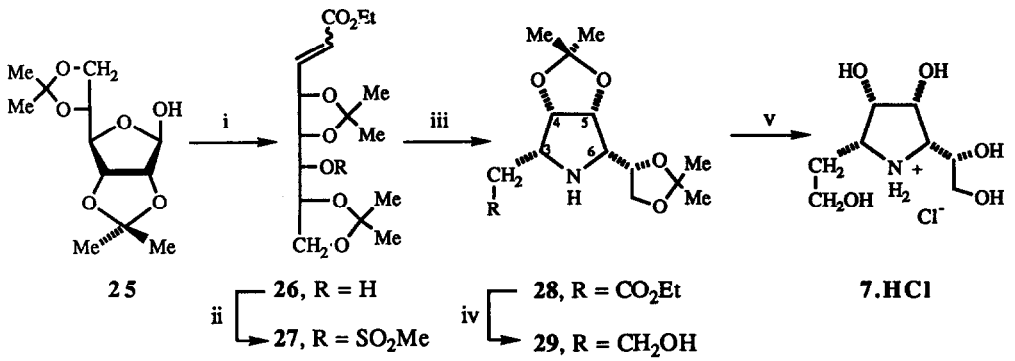


Scheme 4. i, MsCl, C_5H_5N; ii, NH_3,EtOH; iii, $LiAlH_4$; iv, TFA-H_2O, then HCl, EtOH

Reduction of **23** with lithium aluminium hydride gave, after chromatography, the solid iminoalditol **24** (77%), which could be deprotected with aqueous TFA to give 2,3,6-trideoxy-3,6-imino-D-*glycero*-L-*altro*-octitol **6**, isolated as its crystalline hydrochloride.

We were also interested in investigating the extent to which the procedure of Michael addition-cyclization could be used to prepare pyrrolidines with more severe steric congestion around the ring. To this end, the sequence of reactions in Scheme 5 was carried out. Wittig reaction of 2,3:5,6-di-*O*-isopropylidene-D-allofuranose **25**[28] with carboethoxymethylene triphenylphosphorane led to the alkenes **26**. In this *allo*-configured

series, there was a considerable tendency for the initially-formed products **26** to undergo intramolecular cyclization to tetrahydrofuran derivatives. This could be suppressed, however, by carrying out the reaction at room temperature in CH_2Cl_2 in the presence of 3 mole equivalents of benzoic acid, although a long reaction time was necessary.[29] Under these conditions, the enoate **26** was produced as a 7:3 mixture of *E*- and *Z*- isomers. Other workers have discussed the effect of sugar configuration on *E/Z*- ratios in Wittig reactions with stabilized phosphoranes,[30] and based on their findings a greater proportion of *Z*-isomer might have been expected in reactions of **25**. We did however find considerable variations in *E/Z*- ratio under other conditions which also produced tetrahydrofuran byproducts.



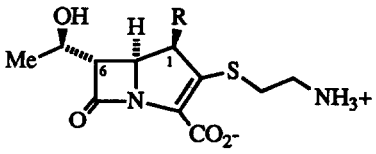
Scheme 5. i, $Ph_3P{=}CHCO_2Et$, $PhCO_2H$, CH_2Cl_2, RT, 14 days; ii, MsCl, C_5H_5N; iii, NH_3,EtOH; iv, $LiAlH_4$; v, TFA-H_2O, then HCl, EtOH, Et_2O

The alkene **26** could be converted in high yield to mesylate **27** with the same isomer ratio. Treatment of **27** with ammonia in ethanol for several days led to the formation of pyrrolidine **28** as a mixture (ca. 7:1) with its C-3 epimer. The formulation of the major product as the D-*glycero*-L-*galacto*- product **28** was supported by the observation, in the ^{1}H-n.m.r. spectrum, of significant values for both $J_{3,4}$ and $J_{5,6}$ (4.12 and 4.36 Hz respectively), and once again, in the ^{13}C-spectrum, C-2 for the major isomer was shielded as compared with the equivalent signal for the minor component. Thus this approach can indeed be used to make a pyrrolidine with an all-*cis*- substitution pattern, although the modest yield (~40%) obtained may well reflect the strain in the transition state for cyclization in this case. The stereochemistry at C-3, however, continues to be controlled by the *threo*-selective conjugate addition of ammonia to the enoate.

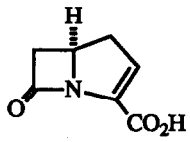
Reduction to the alcohol **29** and final deprotection to the iminooctitol hydrochloride **7.HCl** was carried out as in the previous series.

Evaluation of the iminoalditols **3** - **7** against glycosidases will be reported elsewhere, but none of these compounds showed more than low levels of inhibition of the replication of HIV-1.

The discovery of the carbapenem family of β-lactam antibiotics, such as thienamycin **30**, has led to considerable activity directed towards their total synthesis,[31] and carbohydrate-based routes have been reported to thienamycin[32] and to the structurally-simple carbapenem SQ 27860 **31**, lacking the C-6 side-chain.[33] Further, interesting bioactivity has been found for 1-substituted carbapenems, such as 1β-methyl thienamycin **32**[34] and the 1β-methoxy compound **33**.[35]



30, R = H
32, R = Me



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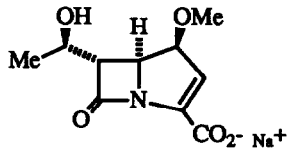

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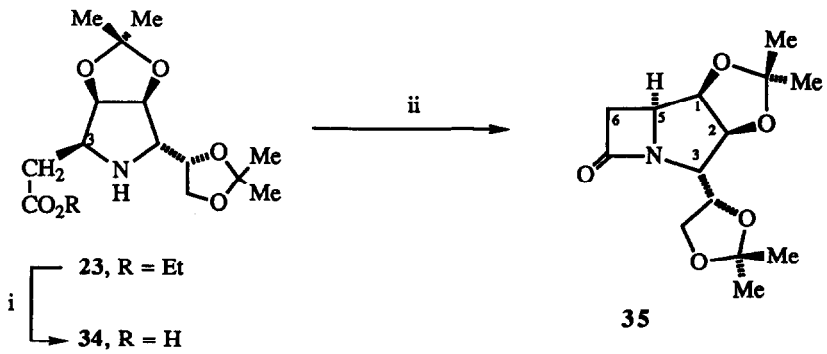
It seemed to us that cyclization of the ester **23** could give access to the carbapenam skeleton with the correct absolute stereochemistry, and with functionality already present at C-1 (carbapenem numbering). Thus basic hydrolysis of **23**, as a 9:1 mixture with its C-3 epimer,was carried out to give the aminoacid **34** (Scheme 6), still containing ~10% of the epimer. On treatment with 2,2'-dipyridyl disulfide and triphenyl phosphine[33,36] in refluxing acetonitrile, this aminoacid underwent cyclization to the β-lactam **35**, isolated as a solid in 62% yield after chromatography. The structure and stereochemistry of **35** was fully supported by spectroscopic data; in particular, the ^{1}H-n.m.r. spectrum was well resolved, and the signal for H-5 showed couplings of *ca.* 5 Hz to both H-1 and H-6$_\alpha$, whilst H-2 appeared as a broad doublet, with no measureable coupling to H-3.



Scheme 6. i, K_2CO_3, MeOH, H_2O; ii, Ph_3P, $(PyS)_2$, MeCN, Δ

EXPERIMENTAL

IR spectra were recorded on Perkin-Elmer 157G or 580 instruments. Mass spectrometry was performed using an updated M.S. 9, and VG ZAB-E high resolution EI/CI/FAB instruments. NMR spectra were recorded on Bruker WP 200SY and WH 400 spectrometers using deuteriochloroform as solvent unless otherwise stated. *J* values are given in Hz. Specific rotations were measured at room temperature using a Bendix-NPL 143D automatic polarimeter (path length 1 cm); units for $[\alpha]_D$-values are 10^{-1} deg cm^2 g^{-1}. Melting points were determined in capillaries and are uncorrected. Adsorption chromatography was carried out using Kiesegel H type 60 (Merck) or Sorbsil C60 (SL 1330). For TLC, precoated aluminium-backed plates [Kieselgel HF 254 type 60 (Merck)] were used. Light petroleum refers to material of b.p. 40-60° C. Organic extracts were dried with anhydrous sodium sulfate.

2,3-*O*-isopropylidene-5-*O*-trityl-D-ribitol (8)[16] - 2,3-*O*-isopropylidene-5-*O*-trityl-D-ribofuranose (5.0 g) in ethanol (100 cm^3) was added with stirring to $NaBH_4$ (0.85 g) in ethanol (50 cm^3). After 2 hours, ammonium chloride was added, the mixture was filtered and evaporated, and the residue was chromatographed on silica, with toluene-ether (1:1) as eluent to give the diol **8** (4,88 g, 96%) as white crystals, m.p. 156°C, $[\alpha]_D$ +12.8 (*c* 0.93, $CHCl_3$); δ_H (200 MHz) 1.3 (6H, s, CMe_2), 3.28 (1H, dd, *J* 9.7 and 6.7, 5_a-H), 3.3 (2H, br. s, OH), 3.46 (1H, dd, $J_{5,4}$ 2.9, 5_b-H), 3.80 (3H, m), 4.12 (1H, dd, *J* 9.5 and 5.7, 1_b-H), 4.32 (1H, m, 4-H), 7.3 (15H, m, CPh_3); δ_C (50 MHz) 25.2 and 27.7 (C*Me*$_2$), 60.7 and 65.2 (C-1 and C-5), 69.0, 76.8, 87.0 (*C*Ph_3), 108.4 (*C*Me_2), 127.1, 127.8, 128.5, 143.8.

2,3-*O*-isopropylidene-1,4-di-*O*-methanesulfonyl-5-*O*-trityl-D-ribitol (9)- A solution of diol **8** (4.88 g) in pyridine (30 cm^3) was added dropwise over 30 min to a stirred solution of methanesulfonyl chloride (4.1 cm^3) and DMAP (0.5 g) in pyridine (10 cm^3). After 2 hours the mixture was evaporated and the residue was partitioned between chloroform and water. The dried organic layers were evaporated and the residue was chromatographed on silica with toluene-chloroform (6:1) as eluent to give dimesylate **9** (5.58 g, 84%) as colourless crystals, m.p. 156°C, $[\alpha]_D$ -17.5 (*c* 1.08, $CHCl_3$); δ_H (200 MHz) 1.37 and 1.45 (each 3H, s, CMe_2), 2.90 and 3.05 (each 3H, s, SO_2Me), 3.35 (1H, dd, *J* 11.3 and 4.9, 5_a-H), 3.58 (1H, dd, *J* 11.3 and 2.7, 5_b-H), 4.34 (1H, m), 4.4-4.6 (3H, m), 4.92 (1H, m, 4-H), 7.3 (15H, m, CPh_3); δ_C (50 MHz) 25.26 and 27.38 (C*Me*$_2$), 37.32 and 39.18 (SO_2Me), 62.86 (C-1), 68.11 (C-5), 74.22, 74.90, 78.51 (C-2,-3,-4), 87.37 (*C*Ph_3), 109.5 (*C*Me_2), 127.3, 127.9, 128.5, 142.9; *m/z* 590 (M^+) (Found: C, 58.8; H, 5.9; S, 10.9. $C_{29}H_{34}O_9S_2$ requires C, 59.0; H, 5.9; S, 10.8%).

***N*-Benzyl-1,4-dideoxy-1,4-imino-2,3-di-*O*-isopropylidene-5-*O*-trityl-L-lyxitol (10)**- Dimesylate **9** (2.38 g) and benzylamine (12 cm^3) were stirred together at 70-80°C for 4 days, the reaction being monitored by t.l.c. Excess benzylamine was removed under vacuum,and the residue was partitioned between brine and chloroform. The washed, dried organic layer was evaporated and the residue was chromatographed on silica, with light petroleum - ethyl acetate as eluent to give the pyrrolidine **10** (1.3g, 64%), as a syrup, $[\alpha]_D$ +50.1 (*c* 1.67, $CHCl_3$); δ_H (200 MHz) 1.30 and 1.40 (each 3H, s, CMe_2), 2.00 (1H,dd, J_{gem} 11.2, $J_{1\beta,2}$ 4.6, 1_β-H), 2.41 (1H, m, 4-H), 2.97 (1H, d, *J* 10.9, 1_α-H), 3.11 (1H, d, *J* 13.6, CH_2Ph), 3.31 (1H, dd, *J* 9.5 and 5.4, 5_a-H), 3.67 (1H, dd, *J* 9.5 and 6.1, 5_b-H), 4.08 (1H, d, *J* 13.6, CH_2Ph), 4.54 (1H, dd, $J_{1\beta,2}$ 4.6, $J_{2,3}$ 6.4, 2-H), 4.70 (1H dd, $J_{2,3}$ 6.4, $J_{3,4}$ 4.8, 3-H), 7.3 (20H, m); δ_C (50 MHz) 26.0 and 26.3 (C*Me*$_2$), 57.8, 59.7, 62.3 (3 x CH_2), 67.6, 78.1,-81.1 (3 x CH), 87.0 (*C*Ph_3), 111.1 (*C*Me_2); *m/z* 490 $(M\text{-}Me)^+$, 262 $(M\text{-}Tr)^+$, 232 $(M\text{-}CH_2OTr)^+$. [Found: MH^+ (f.a.b.) 506.26950. Calc. for $C_{34}H_{36}NO_3$, 506.26950].

1,4-Dideoxy-1,4-imino-2,3-di-*O*-isopropylidene-5-*O*-trityl-L-lyxitol (11)- The *N*-benzyl compound **10** (1.25 g) in ethanol (50 cm^3) was hydrogenated at 1 atm over Pd/C (5%, 0.5 g) for 6 hours. The mixture was filtered through celite and evaporated. Chromatography on silica, with ethyl acetate - light petroleum (7:3) as eluent gave amine **11** (0.68 g, 66%), as a white solid, m.p. 120°C, $[\alpha]_D$ +33.8 (*c* 0.65, $CHCl_3$); δ_H (200 MHz) 1.30 and 1,37 (each 3H, s, CMe_2), 1.8 (1H, br. s,,NH), 2.62 (1H, dd, $J_{1\beta,2}$ 3.2, J_{gem} 13.1, 1_β-H), 2.87 (1H, dt, $J_{3,4}$ ~3.5, $J_{4,5a}$~$J_{4,5b}$~6.5, 4-H), 3.08 (1H, d, J_{gem} 13.1, 1_α-H), 3.27 (1H, dd, *J* 9.1 and 6.3, 5_a-H), 3.42 (1H, dd, *J*9.2 and 6.5, 5_b-H), 4.66 (2H, m, 2-H, 3-H), 7.4 (15H, m, CPh_3); δ_C (50 MHz) 24.1 and 25.7 C*Me*$_2$), 53.0 (C-1), 61.8 (C-5), 63.6 (C-4), 81.1 and 81.5 (C-2, C-3), 86.6 (*C*Ph_3), 110.4 (*C*Me_2),

126.8, 127.6, 128.8, 144.1; *m/z* 415 (M^+), 400 (M^+-Me), 142 (M^+-CH_2OTr). [Found: (M^+-Me), 400.18809; Calc. for $C_{26}H_{26}NO_3$, 400.1905].

1,4-Dideoxy-1,4-imino-L-lyxitol hydrochloride (3.HCl)- The protected compound **11** (82 mg) was stirred for 24 h in aqueous trifluoroacetic acid (1:1, 30 cm^3). The solvent was evaporated and residual trifluoroacetic acid was neutralized with aqueous NaOH. The solution was filtered and applied to a column of Amberlite IR 120 (H^+ form), which was elutedwith water and then with aqueous ammonia (0.5 M) Acidification of the free base in aqueous solution to pH 4 with dil. HCl afforded after freeze-drying 1,4-dideoxy-1,4-imino-L-lyxitol hydrochloride (**3.HCl**) (30 mg, 90%), m.p. 141°C (dec.), $[\alpha]_D$ -17.2 (*c* 0.4, water) [lit.[18] m.p. 155-157°C, $[\alpha]_D$ -18.3 (*c* 0.6, water)]; δ_H (200 MHz, D_2O) 3.16 (1H, dd, *J* 12.1 and 7.1, 1_a-H), 3.49 (1H, dd, *J* 12.1 and 7.3, 1_b-H), 3.69 (1H, m, 4-H), 3.84 (1H, dd, *J* 11.9 and 8.1, 5_a-H), 3.95 (1H, dd, *J* 11.9 and 5.1, 5_b-H), 4.30 (1H, t, J 4.1, 3-H), 4.45 (1H, dt, $J_{1a,2}$~$J_{1b,2}$~7.3, $J_{2,3}$ 4.1, 2-H); δ_C (50 MHz, D_2O) 47.04 (C-1) 57.46 (C-5), 63.30 (C-4), 69.78 and 69.86 (C-2, C-3); *m/z* (f.a.b.) 134 (MH^+), 102 ($M-CH_2OH)^+$. (Found: MH^+ 134.0817. Calc. for $C_5H_{12}NO_3$ 134.0817).

1,4,5-Trideoxy-1,4-imino-2,3-*O*-isopropylidene-D-*lyxo*-hexitol (14). - To a solution of the ester (**13**) and its epimer[20] (500 mg) in THF (25 cm^3), at 0°C, was added a suspension of lithium aluminium hydride (325 mg) in THF (25 cm^3). After warming to room temperature the reaction was stirred for 2 days. The sequential addition at 0°C, with intervals of 10 minutes, of water (0.33 cm^3), 15% sodium hydroxide (0.33 cm^3) and water (0.99 cm^3) gave a granular solid. After drying, the residue after evaporation was chromatographed on silica eluting with methanol - ethyl acetate (1:20, then 3:20) to give a solid product. Recrystallization from ethyl acetate - hexane afforded the pyrrolidine **14** (223mg, 55%) , m.p. 95-6°C, $[\alpha]_D$ -39.45 (*c* 1.09, $CHCl_3$); υ_{max} 3180 cm^{-1} (OH and NH); δ_H (200MHz) 1.27 and 1.41 (each 3H, s, C*Me*$_2$), 1.82 (2H, m, 5-H_2), 2.57 (1H, dd, $J_{1\beta,2}$ 3.8, J_{gem} 13.4, 1_β-H), 2.72 (1H, ddd, $J_{3,4}$ 4.0, $J_{4,5a}$ 5.1, $J_{4,5b}$ 8.7, 4-H), 3.04 (1H, d, 1_α-H), 3.30 (2H, br. s, NH, OH), 3.74 (2H, m, 6-H_2), 4.51 (1H, dd, $J_{2,3}$ 5.5, 3-H), 4.64 (1H, dd, 2-H); δ_C (50MHz) 23.8 and 25.7 (C*Me*$_2$), 31.0 (6-C), 53.2 (1-C), 61.2 (5-C), 62.7 (4-C), 81.4 and 82.1 (2-C & 3-C), 110.4 (*C*Me$_2$); *m/z* 188 (*M*H^+, 5%), 187 (*M*$^+$, 14%), 172 (*M*$^+$-Me, 19%).(Found C, 57.7; H, 9.3; N, 7.3. $C_9H_{17}NO_3$ requires C, 57.7; H, 9.2; N, 7.5%).

1,4,5-Trideoxy-1,4-imino-D-*lyxo*-hexitol hydrochloride (4.HCl). - The acetonide (**14**) (258mg) in 80% aqueous trifluoroacetic acid (10cm^3) was left to stand overnight. Evaporation gave the free pyrrolidine, which on trituration with ethanolic hydrogen chloride and ether gave the triol hydrochloride **4.HCl** (214mg, 87%), m.p. 135-8°C, $[\alpha]_D$ -4.4 (*c* 0.46 in H_2O) {lit.[23] m.p. 137-8°C, $[\alpha]_D$ -7.0 (*c* 0.193, MeOH)}; υ_{max} 3360 cm^{-1} (NH, OH); δ_H (200MHz, D_2O) 1.86 (2H, m, 5-H_2), 2.95 (1H, dd, $J_{1\beta,2}$ 8.1, J_{gem} 12.0, 1_β-H), 3.36 (1H, dd, $J_{1\alpha,2}$ 8.2, 1_α-H), 3.53 (3H, m, 4-H, 6-H_2), 4.05 (1H, t, $J_{2,3}$=$J_{3,4}$ 3.7, 3-H), 4.33 (1H, dt, 2-H); δ_C (50MHz, D_2O) 28.4 (5-C), 46.7 (1-C), 58.1 (6-C), 59.8 (4-C), 69.7 (3-C), 70.3 (2-C); m/z 147 (*M*$^+$, 3%). (Found: *M*$^+$, 147.09133. Calc. for $C_6H_{13}NO_3$, 147.0895).

2,3-*O*-Isopropylidene-L-erythrose (16).- L-Arabinose (10 g), *p*-toluenesulphonic acid (150 mg) and 2,2-dimethoxypropane (27 cm^3) were stirred in dimethylformamide (130 cm^3) for 1.5h. After neutralization, with solid sodium carbonate, and evaporation, the residue was partitioned between water (120 cm^3) and light petroleum (60 cm^3)[24]. Sodium periodate (35.6 g) was added to the aqueous layer and the mixture stirred for 2h, when solid sodium carbonate was added and the slurry was stirred for 1h. Extraction with ethyl acetate gave a

residue on evaporation which was extracted with dichloromethane.The residue from this was purified by column chromatography, with ether-light petroleum (1:3) as eluent, to give 2,3-*O*-isopropylidene-L-erythrose **16** (5.79g, 55%) (α:β-isomers, 4:21), m.p. 24 - 26°C, $[\alpha]_D$ +66.3 (*c* 2.7, $CHCl_3$) {lit.[37] m.p. 30-32.5°C, $[\alpha]_D$ +83.2 (*c* 4.36, EtOAc)}; υ_{max} (film) 3420 cm^{-1} (OH); δ_H (200MHz) signals for β–isomer :- 1.26 and 1.44 (each 3H, s, C*Me*$_2$), 3.60 (1H, d, $J_{1,OH}$ 2.6, 1-OH), 3.90 - 4.10 (2H, m, 4-H_2), 4.53 (1H, d, $J_{2,3}$ 5.9, 2-H), 4.80 (1H, ddd, $J_{3,4a}$ 0.6, $J_{3,4b}$ 3.2, 3-H), 5.37 (1H, d, 1-H); δ_C (50MHz) signals for β-isomer:- 24.7 and 26.2 (C*Me*$_2$), 71.9 (4-C), 79.9 (3-C), 85.2 (2-C), 101.7 (1-C), 112.3 (*C*Me$_2$); signals for α-isomer:- 24.8 and 25.9 (C*Me*$_2$), 67.6 (4-C), 78.3, 79.6, 97.4 (1-C).

(*E*)- and (*Z*)- Ethyl 2,3-dideoxy-4,5-*O*-isopropylidene-6-*O*-methanesulphonyl-L-*erythro*-hex-2-enonate (18) .- The (*E*) and (*Z*)-alkenes **17** (5.2g) were treated as for the (*E*)-isomer of the enantiomer[20] to give the (*E*) and (*Z*) mesylates **18** (6.43g, 92%) as an oil (*E*:*Z*-isomers, 3:8), $[\alpha]_D$ -95.7 (*c* 1.42, $CHCl_3$); spectroscopic data for the (*E*)-isomer was as previously reported for the enantiomer;[20] signals for *Z*-isomer; δ_H (200 MHz) 1.30 (3H, t, OCH_2Me), 1.40 and 1.52 (each 3H, s, C*Me*$_2$), 3.03 (3H,s, OMs) 4.0-4.3 (4H, m) 4.74 (1H, ddd, $J_{5,6a}$ 3.2, $J_{5,6b}$ 6.5, $J_{4,5}$ 7.3, 5-H), 5.62 (1H, ddd, $J_{2,4}$ 1.8, $J_{3,4}$ 6.7, 4-H), 5.97 (1H, dd, $J_{2,3}$ 11.5, 2-H), 6.33 (1H, dd, 3-H); δ_C (50MHz) 14.1 (OCH_2Me) 24.7 and 27.3 (C*Me*$_2$) 37.5 (SO_2Me) 60.6, 68.5, 74.5, 75.6, 122.3 (2-C), 145.1 (3-C), 165.4 (1-C) [Found: (M^+-Me), 293.06721. Calc. for $C_{11}H_{17}O_7S$ 293.06950].

Ethyl 1,4,5-trideoxy-3,6-imino-4,5-*O*-isopropylidene-L-*arabino*-hexonate (19)- Treatment of mesylate **18** (4.16 g) as described for the enantiomer[20] gave the pyrrolidine **19** (1.85 g, 52%) as a 9:1 mixture with the L-*ribo*-epimer, m.p. 28-30°C, $[\alpha]_D$ +46.2 (*c* 0.85, $CHCl_3$), with spectroscopic data as for the enantiomer.[20]

1,4,5-Trideoxy-1,4-imino-2,3-*O*-isopropylidene-L-*lyxo*-hexitol (20).- Reduction of the ester **19** (0.5 g) as for the enantiomer (see above) gave the alcohol **20** (0.22 g, 55%), m.p. 95-97°C, $[\alpha]_D$ + 38.8 (*c* 1.03, $CHCl_3$), with spectroscopic data as for the enantiomer.

1,4,5-Trideoxy-1,4-imino-L-*lyxo*-hexitol hydrochloride (5.HCl).- The acetonide (**20**) (192 mg) was treated as described above for the enantiomer to give the triol hydrochloride **5.HCl** (144 mg, 77%), m.p. 138-140°C, $[\alpha]_D$ +4.8 (*c* 1.04 in H_2O), with spectroscopic data as for the enantiomer above (Found: C,39.1; H, 7.6; N, 7.5, Cl, 19.0. $C_6H_{13}NO_3$.HCl requires C, 39.2; H, 7.7; N,7.6; Cl, 19.3%. Found: M^+ 147.0920. Calc. for $C_6H_{13}NO_3$, 147.0895).

(*E*)-Ethyl 2,3-dideoxy-4,5:7,8-di-*O*-isopropylidene-6-*O*-methanesulphonyl-D-manno-oct-2-enonate (22)- To methanesulphonyl chloride (4.23 cm^3) and pyridine (20 cm^3) at 0°C, was added the alkene **21** (6g) in dichloromethane (70 cm^3) over 20 minutes. The reaction mixture was stirred at room temperature for 18h. Careful addition of water (3 cm^3) was followed by partitioning between dichloromethane (50 cm^3) and water (50 cm^3). Evaporation of the washed, dried organic layer and column chromatography eluting with ether - toluene (1:9) gave the *mesylate* **22** (6.7g, 90%), $[\alpha]_D$ +19.64 (*c* 1.12, $CHCl_3$); υ_{max} (KBr) 1720 (C=O), 1655 (C=C), 1360 and 1040 cm^{-1} (OSO_2); δ_H (200 MHz) 1.27 (3H, t, *J* 7.1, CH_2CH_3), 1.34, 1.39, 1.42 and 1.53 (each 3H, s, C*Me*$_2$), 3.08 (3H, s, SO_2Me), 3.90 - 4.20 (3H, m, 7H, 8-H_2), 4.17 (2H, q, CH_2CH_3), 4.36 (1H, dd, *J* 6.3 and 7.6, 5-H), 4.61 (1H, t, *J* ~7, 6-H), 4.79 (1H, dt, $J_{2,4}$ 1.6, $J_{3,4}$ 6.3, 4-H), 6.07 (1H, dd, $J_{2,3}$

15.6, 2-H), 6.98 (1H, dd, 3-H); δ_C (50 MHz) 14.1 ($CH_2\underline{C}H_3$), 25.2, 25.5, 25.9 and 27.3 ($C\underline{M}e_2$), 39.1 (S-CH_3), 60.5 ($\underline{C}H_2CH_3$), 66.9 (8-C), 74.7, 76.4, 77.8 and 79.3 (4-C - 7-C), 109.5 and 110.4 ($\underline{C}Me_2$), 124.6 (2-C), 142.1 (3-C), 165.4 (1-C); *m/z* 393 (M^+-Me).

Ethyl 2,3,6-trideoxy-3,6-imino-4,5:7,8-di-*O*-isopropylidene-D-*glycero*-L-*altro*-octonate (23) and the-D-*glycero*-L-*allo*- epimer.- The mesylate **22** (6g) was dissolved in ethanol (120cm^3) and the solution saturated with ammonia. After stirring for 14 days the reaction mixture was evaporated. Column chromatography on silica eluting with ether - methanol (98:2) gave the *pyrrolidine* **23** and its epimer (3.8g, 79%) (L-*altro*: L-*allo*, 9:1) as an amorphous solid, $[\alpha]_D$ +0.1 (*c* 1.7, $CHCl_3$); υ_{max} 3330 (NH), 1730 cm^{-1} (C=O); δ_H (400MHz) signals for L-*altro* -epimer:- 1.21 (3H, t, *J* 7.16, $CH_2\underline{C}H_3$), 1.26, 1.29, 1.38 and 1.42 (each 3H, s, $C\underline{M}e_2$), 2.27 (1H, br. s, NH), 2.53 (1H, dd, $J_{2a,3}$ 6.9, J_{gem} 16.4, 2_a-H), 2.60 (1H, dd, $J_{2b,3}$ 7.0, 2_b-H), 3.11 (1H, br. d, $J_{6,7}$ 5.8, 6-H), 3.57 (1H, dt, $J_{3,4}$ 4.4, 3-H), 3.77 (1H, dt, 7-H), 3.96 - 4.06 (2H, m, 8-H_2), 4.10 (2H, dq, $\underline{C}H_2CH_3$), 4.45 (1H, dd, $J_{5,6}$ 0.9, $J_{4,5}$ 5.8, 5-H), 4.63 (1H, dd, 4-H); signals for L-*allo* -epimer:- 1.209 (3H, t, *J* 7.10, $CH_2\underline{C}H_3$), 2.44 (1H, dd, $J_{2a,3}$ 8.9, J_{gem} 16.4, 2_a-H), 2.69 (1H, dd, $J_{2b,3}$ 4.1, 2_b-H); δ_C (50MHz) signals for L-*altro* -isomer:- 14.08 ($CH_2\underline{C}H_3$), 24.3, 25.4, 26.0 and 26.4 ($C\underline{M}e_2$), 34.5 (2-C), 57.7 (3-C), 60.3 ($\underline{C}H_2CH_3$), 65.7 (6-C), 66.7 (8-C), 75.8 (7-C), 81.8 and 84.0 (4-C, 5-C), 109.4 ($\underline{C}Me_2$ sidechain), 111.5 ($\underline{C}Me_2$), 171.9 (1-C); signals for L-*allo* -isomer:- 25.2, 26.6, 27.4 and 29.6 ($C\underline{M}e_2$), 38.5 (2-C), 60.0 (3-C), 66.2 (7-C), 66.4 (8-C), 77.9 (6-C), 81.4 and 84.2 (4-C & 5-C), 114.2 ($\underline{C}Me_2$); m/z (F.A.B.) : 330 ($\underline{M}H^+$, 100%). (Found: $\underline{M}H^+$, 330.1917. Calc. for $C_{16}H_{28}NO_6$, 330.1917).

2,3,6-Trideoxy-3,6-imino-4,5:7,8-di-*O*-isopropylidene-D-*glycero*-L-*altro*-octitol (24)- Lithium aluminium hydride (225 mg) in THF (25 cm^3) was slowly added over 10 minutes to a solution of the pyrrolidine **23** and its epimer (500 mg) in THF (25 cm^3) at 0°C. After warming to room temperature the reaction mixture was stirred for 2 days. At 0°C were added water (0.2 cm^3), aqueous sodium hydroxide (15%, 0.2 cm^3) and water (0.6 cm^3) to give granular aluminium salts. Column chromatography of the dried organic layers, with ethyl acetate-methanol (9:1) as eluent, gave the amino alcohol **24** (336mg, 77%), m.p. 41-3°C, $[\alpha]_D$ -13.6 (*c* 1.11, $CHCl_3$); υ_{max} 3400 (NH), 3230 cm^{-1}(OH); δ_H (200MHz) 1.32, 1.34, 1.42 and 1.47 (each 3H, s, $C\underline{M}e_2$), 1.60 - 1.80 (2H, m, 2-H_2), 3.02 (2H, br. s, NH, OH), 3.15 (1H, d, *J* 4.9), 3.34 (1H, ddd, $J_{3,4}$ 4.1, $J_{2a,3}$ 5.6, $J_{2b,3}$ 9.8, 3-H), 3.7 - 3.9 (3H, m), 4.0- 4.2 (2H, m), 4.55 (1H, dd, $J_{5,6}$ 1.0, $J_{4,5}$ 5.7, 5-H), 4.63 (1H, dd, 4-H); δ_C (50MHz) 24.2, 25.4, 26.1 and 26.3 ($C\underline{M}e_2$), 31.8 (2-C), 61.1 (3-C), 61.5 (1-C), 65.6 (6-C), 66.8 (8-C), 76.1 (7-C), 83.0 (4-C), 84.2 (5-C), 109.4 and 111.5 ($\underline{C}Me_2$); *m/z* 272 (M^+-Me). [Found: C, 58.0; H, 8.7; N, 4.7. $C_{14}H_{25}NO_5$ requires C, 58.3; H, 8.3; N, 4.3%. Found: (M^+-Me), 272.14725. Calc. for $C_{13}H_{22}NO_5$, 272.14980].

2,3,6-Trideoxy-3,6-imino-D-*glycero*-L-*altro*-octitol hydrochloride (6.HCl).- The diacetonide **24** (250mg) was dissolved in 80% aqueous trifluoroacetic acid (10 cm^3) at 0°C. After stirring at room temperature for 2 days the solution was evaporated under reduced pressure and flushed with water. The aqueous solution was washed with ether, then evaporated to dryness. The free amine residue was triturated with ethanolic hydrogen chloride and ether to give **6.HCl** (162 mg, 76%), m.p. 150-151°C, $[\alpha]_D$ -29.5 (*c* 0.48, H_2O); υ_{max} 3350 cm^{-1} (OH, NH); δ_H (200MHz,D_2O) 1.90 - 2.20 (2H, m, 2-H_2), 3.52 (1H, dd, $J_{6,7}$ 4.5, $J_{5,6}$ 9.0, 6-H), 3.60 - 3.80 (5H, m, 1-H_2, 3-H, 8-H_2), 3.97 (1H, q, $J_{6,7}$=$J_{7,8a}$=$J_{7,8b}$ 4.4, 7-H), 4.24 (1H, m, 4-H), 4.31 (1H, dd, $J_{4,5}$ 3.6, 5-H); δ_C (50MHz, D_2O) 28.5 (2-C), 58.0 (1-C), 59.5 (3-C), 61.8 (6-C), 63.1 (8-C), 68.1 (7-C), 70.5 (4-

C), 72,3 (5-C).(Found: C, 38.8; H, 7.4; N, 5.6; Cl, 14.4. $C_8H_{17}NO_5.HCl.0.25H_2O$ requires C, 38.7; H, 7.5; N, 5.6; Cl, 14.3%).

Ethyl 2,3-dideoxy-4,5:7,8-di-*O*-isopropylidene-D-*allo*-oct-2-enonate (26).- 2,3:5,6-Di-*O*-isopropylidene-α-D-allofuranose (**25**) (3.7 g), carboethoxymethylene triphenylphosphorane (5.45 g) and benzoic acid (5.2 g) in dichloromethane (85 cm^3) were stirred at room temperature for 14 days. After evaporation *in vacuo* the residue was partitioned between ether (50 cm^3) and saturated sodium hydrogen carbonate (2 x 50 cm^3). The dried organic layers were evaporated and purified by column chromatography on silica eluting with ether - toluene (1:9) to give the (*E*) and (*Z*)-alkenes **26** (4.53g, 96%) (*E*:*Z*-isomers, 7:3), *m/z* 315 (M^+-Me). [Found: (M^+-Me), 315.14360. $C_{15}H_{23}O_7$ requires *m/z* 315.14438]. A small sample was separated by further chromatography into the two isomers.

E-isomer:- $[\alpha]_D$+11.9 (*c* 0.9, $CHCl_3$); υ_{max} 1715 (C=O), 1655 cm^{-1} (C=C); δ_H (200MHz) 1.31 (3H, t, *J* 7.13Hz, CH_2CH_3), 1.35 (6H, s, CMe_2), 1.42, 1.54(each 3H, s, CMe_2), 2.25 (1H, br. s, OH), 3.80 - 4.40 (7H, m, 5-H - 8-H_2, CH_2CH_3), 4.87 (1H, ddd, $J_{2,4}$ 1.6, $J_{3,4}$ 4.8, $J_{4,5}$ 6.4, 4-H), 6.15 (1H, dd, $J_{2,3}$ 15.6, 2-H), 7.08 (1H, dd, 3-H); δ_C (50MHz) 14.1 (OCH_2Me), 26.2, 26.4, 27.3 and 27.5 (CMe_2), 60.4 (CH_2Me), 63.2 (8-C), 67.9, 76.2, 76.9, 77.7, 108.6 & 109.6 (CMe_2), 122.4 (2-C), 143.1 (3-C), 166.2 (1-C).

Z-isomer:-$[\alpha]_D$+102.4 (*c* 0.85, $CHCl_3$); δ_H (200MHz) 1.30 (3H, t, *J* 7.13, CH_2CH_3), 1.33, 1.34, 1.42 and 1.50 (each 3H, s, CMe_2), 2.70 (1H, d, *J* 2.0, OH), 3.91 (1H, ddd, *J* 8.2, 2.5, 2.0, 6-H), 4.0-4.1 (2H, m), 4.19 (2H, q, CH_2CH_3), 4.20 (1H, m), 4.31 (1H, dt, *J* 3.0 and 7.0), 5.70 (1H, ddd, $J_{2,4}$ 1.5, $J_{4,5}$ 6.5, $J_{3,4}$ 8.1Hz, 4-H), 6.00 (1H, dd, $J_{2,3}$ 11.6, 2-H), 6.29 (1H, dd, 3-H); δ_C (50MHz) 14.1 (CH_2CH_3), 25.2, 25.3, 26.3 and 27.8 (CMe_2), 60.8 (CH_2CH_3), 63.8 (8-C), 68.7, 74.4, 76.4 and 78.8 (4-C - 7-C), 108.7 and 109.4 (CMe_2), 122.5 (2-C), 144.7 (3-C), 166.3 (1-C).

Ethyl 2,3-dideoxy-4,5:7,8-di-*O*-isopropylidene-6-*O*-methanesulphonyl-D-*allo*-oct-2-enonate (27).- To a solution of methanesulphonyl chloride (2.8 cm^3) and pyridine (2.9 cm^3) in dichloromethane (40 cm^3) at 0°C, was added the (*E*) and (*Z*)-alkenes **26** (4 g) in dichloromethane (30 cm^3) over 30 minutes. After warming to room temperature the reaction mixture was stirred for 48 h. The reaction mixture was partitioned between water (80 cm^3) and dichloromethane (80 cm^3) and washed with 1M hydrochloric acid, saturated sodium hydrogen carbonate and water. The dried organic layers were evaporated and the residue purified by column chromatography eluting with ether-toluene (1:4) to give mesylate **27** (4.38g, 88%) (*E*:*Z*-isomers, 7:3) as a syrup, $[\alpha]_D$ for *E*-isomer +5.0 (*c* 1.00, $CHCl_3$); $[\alpha]_D$ for *Z*-isomer +114.5 (*c* 1.47, $CHCl_3$); υ_{max} 1715 (C=O), 1655 (C=C), 1370 and 1050 cm^{-1} (OSO_2); δ_H (200MHz) signals for *E*-isomer :- 1.30 (3H, t, *J* 7.10Hz, CH_2Me), 1.33 (6H, s, 2 x CMe_2), 1.45 and 1.53 (3H, s, CMe_2), 3.10 (3H, s, SMe), 3.90 - 4.30 (3H, m), 4.23 (2H, q, CH_2Me), 4.53 (1H, dd, *J* 3.5 and 7.2, 5-H), 4.70 (2H, m, 4-H, 6-H), 6.15 (1H, dd, $J_{2,3}$ 15.6 $J_{2,4}$ 1.6, 2-H), 6.96 (1H, dd, $J_{3,4}$ 6.0, 3-H); signals for Z-isomer :- 1.32 (3H, t, *J* 7.1Hz, CH_2Me), 1.36, 1.39, 1.45 and 1.54 (each 3H, s, CMe_2), 3.10 (3H, s, SCH_3), 4.0-4.3(5H, m), 4.80 (2H, m), 5.70 (1H, ddd, $J_{2,4}$ 1.9, $J_{3,4}$ 6.6, $J_{4,5}$ 8.3, 4-H), 6.06 (1H, dd, $J_{2,3}$ 11.5Hz, 2-H), 6.35 (1H, dd, 3-H); δ_C (50MHz) signals for *E*-isomer :- 14.1 (CH_2Me), 24.80, 24.85, 26.2 and 27.1 (CMe_2), 38.8 (SMe), 60.5 (CH_2Me), 65.6 (8-C), 74.3, 76.0, 77.8 and 78.8 (4-C - 7-C), 109.3 and 109.5 (CMe_2), 124.0 (2-C), 142.0 (3-C), 165.5 (1-C); signals for Z-isomer :- 23.7, 24.8, 26.0 and 26.5 (CMe_2), 38.8 (SMe), 60.8 (CH_2Me), 65.3 (8-C), 74.3, 74.5, 78.5 and 80.3 (4-C - 7-C), 109.3 and 109.4 (CMe_2), 122.7 (2-C), 144.8 (3-C); *m/z* 393 (M^+-Me); *m/z* (F.A.B.) 409 (MH^+, 14%), 393 (M^+-Me, 15%). (Found: (MH^+), 409.1474. Calc. for $C_{17}H_{29}O_9S$, 409.1532).

Ethyl 2,3,6-trideoxy-3,6-imino-4,5:7,8-di-*O*-isopropylidene-D-*glycero*-L-*galacto*-octonate (28) and the D-*glycero*-L-*talo*-isomer - A solution of the (*E*) and (*Z*)-mesylates **27** (1.82 g) in ethanol (35 cm^3) saturated with ammonia was stirred at room temperature for 14 days. Column chromatography of the residue eluting with ether gave the pyrrolidine **28** and its C-3 epimer (508 mg, 38%) (L-*galacto*: L-*talo* ratio 7:1) as a low melting solid, $[\alpha]_D$ +2.5 (*c* 1.20, $CHCl_3$); υ_{max} 3350 (NH), 1730 cm^{-1} (C=O); δ_H (200MHz) signals for L-*galacto* -isomer :- 1.20 (3H, t, *J* 7.20, CH_2Me), 1.23, 1.30, 1.37 and 1.40 (each 3H, s, CMe_2), 2.25 (1H, br. s, NH), 2.63 (2H, d, $J_{2,3}$ 6.8, 2-H_2), 2.76 (1H, dd, $J_{5,6}$ 4.31, $J_{6,7}$ 8.2, 6-H), 3.15 (1H, dt, $J_{3,4}$ 4.1, 3-H), 3.66 (1H, m, 8_a-H), 4.00 - 4.20 (2H, m, 7-H, 8_b-H), 4.09 (2H, q, CH_2Me), 4.45 (1H, dd, $J_{4,5}$ 5.8, 4-H), 4.58 (1H,dd, 5-H); signals for L-*talo* -isomer :- 2.36 (1H, dd, *J* 1.3 and 7.5); δ_C (50MHz) signals for the L-*galacto* isomer :-14.1 (CH_2Me), 24.4, 25.4, 25.6 and 26.8 (CMe_2), 33.8 (2-C), 57.9 (3-C), 60.3 (CH_2Me), 65.0 (6-C), 67.0 (8-C), 76.4 (7-C), 80.7 (4-C), 81.4 (5-C), 109.2 and 111.5 (CMe_2), 172.0 (1-C); signals for the L-*talo* isomer :- 24.3 and 26.2 (CMe_2), 37.1 (2-C), 60.0 (3-C), 60.9 (CH_2Me), 63.7 (6-C), 67.5 (8-C), 76.2 (7-C), 85.5 (5-C); *m/z* (F.A.B.) 659 $(2M+H)^+$, 330 (MH^+). (Found: MH^+, 330.1917. Calc. for $C_{16}H_{28}NO_6$ 330.1917).

2,3,6-Trideoxy-3,6-imino-4,5:7,8-di*O*-isopropylidene-D-*glycero*-L-*galacto*-octitol (29) - To a solution, of the ester **28** and its epimer (300 mg) in THF (15 cm^3), at 0°C, was added lithium aluminium hydride (135 mg) in THF (15 cm^3) over 10 minutes. After stirring at room temperature for 48 h the reaction was worked up to give granular aluminium salts, and the residue after evaporation was chromatographed, eluting with ethyl acetate - methanol (9:1) to yield the amino alcohol **29** (127 mg, 48%), m.p. 99-101°C, $[\alpha]_D$ +12.9 (*c* 0.54, $CHCl_3$); υ_{max} 3400 - 3240 cm^{-1} (OH, NH); δ_H (200MHz) 1.29, 1.38, 1.43 and 1.44 (each 3H, s, CMe_2), 1.80 - 1.95 (2H, m, 2-H_2), 2.68 (2H, br. s, NH and OH), 2.77 (1H, dd, $J_{5,6}$ 4.1, $J_{6,7}$ 7.8, 6-H), 2.91 (1H, ddd, $J_{3,4}$ 3.7, $J_{2a,3}$ 6.5, $J_{2b,3}$ 7.2, 3-H), 3.65 - 3.90 (3H, m), 4.10 - 4.25 (2H, m), 4.51 (1H, dd, $J_{4,5}$ 5.6, 5-H), 4.58 (1H, dd, 4-H) δ_C (50MHz) 24.1, 25.48, 25.53 and 26.7 (CMe_2), 31.4 (2-C), 60.7 (3-C), 60.8 (1-C), 65.4 (6-C), (67.2 (8-C), 76.0 (7-C), 81.3 (4-C), 82.4 (5-C), 109.3 and 111.2 (CMe_2); *m/z* 272 (M^+-Me). [Found: (M^+-Me), 272.15052. Calc. for $C_{13}H_{22}NO_5$ 272.14980. Found C, 58.0; H, 7.5; N, 5.0. $C_{14}H_{25}NO_5$ requires C, 58.5; H, 8.7; N, 4.9%].

2,3,6-Trideoxy-3,6-imino-D-*glycero*-L-*galacto*-octitol hydrochloride (7.HCl) -Deprotection, in 80% aqueous trifluoroacetic acid (7 cm^3), of the acetonide **29**(164 mg) gave after evaporation the free amine as an oil. Crystallization from ethanolic hydrogen chloride - ether gave the hydrochloride **7.HCl** (89 mg, 64%) as a very hygroscopic solid , $[\alpha]_D$ -13.6 (*c* 0.51, H_2O); δ_H (200MHz, D_2O) 1.80 - 2.30 (2H, m, 2-H_2), 3.50 - 3.80 (6H, m), 4.05 (1H, m), 4.30 - 4.50 (2H, m); δ_C (50MHz, D_2O) 28.6 (2-C), 58.1 (3-C), 58.3 (1-C), 61.3 (6-C), 62.9 (8-C), 67.1 (7-C), 69.4 and 70.1 (4-C and 5-C).

2,3,6-Trideoxy-3,6-imino-4,5:7,8-di-*O*-isopropylidene-D-*glycero*-L-*altro*-octonic acid (34) and the-D-*glycero*-L-*allo*- epimer.- To ester **23** and its epimer (500 mg) in methanol (15cm^3) and water (5 cm^3) was added potassium carbonate (0.53 g). After stirring at room temperature for 2 days, the methanol was removed *in vacuo*. The solution was neutralized with dilute hydrochloric acid, saturated with sodium chloride and extracted with ethyl acetate. Evaporation gave the amino acid and its C-3 epimer (324 mg, 71%) (L-*altro*: L-*allo*, 9:1), m.p. 78 - 80°C, $[\alpha]_D$ +11.9 (*c* 1.01, $CHCl_3$); δ_H (200MHz) signals for L-*altro* acid :- 1.32, 1.37, 1.48 and 1.53 (each 3H, s, CMe_2), 2.70 (2H, br. s, 2-H_2), 3.52 (1H, d, *J* 5.5, 6-H), 3.9 (2H, m), 4.0 - 4.3 (2H,

m), 4.56 (1H, d, *J* 5.8, 5-H), 4.74 (1H, br. t, *J*~5, 4-H), 8.35 (2H, br. s, NH & CO_2H) ; signals for L-*allo* acid :- 3.70 (1H, m), 4.35 (1H, m); δ_C (50MHz) signals for L-*altro* acid :- 24.2, 25.0, 25.6 and 26.4 (C*Me*$_2$), 33.4 (2-C), 57.9 (3-C), 64.9 (6-C), 66.5 (8-C), 74.4 (7-C), 80.6 (5-C), 82.4 (4-C), 110.0 and 112.3 (*C*Me$_2$), 174.9 (1-C); signals for L-*allo* acid :- 25.2, and 27.2 (C*Me*$_2$), 60.5, 65.3, 66.1, 75.1, 77.2, 83.1, 114.8 (*C*Me$_2$); *m/z* 301 (M^+, 1%), 286 (M^+-Me), 9%). [Found: (M^+-Me), 286.12941. Calc. for $C_{13}H_{20}NO_6$ 286.12906].

(2*S*,3*S*,4*R*,5*S*)-3,4-isopropylidenedioxy-2-[(*R*)-2,2-dimethyldioxolan-4-yl]-1-azabicyclo-[3.2.0]-heptan-7-one (35).- The amino acid **34** and its epimer (50 mg) , 2,2'-dipyridyl disulfide (44 mg) and triphenylphosphine (52 mg) in acetonitrile (17cm^3) were heated under reflux for 18h. Evaporation *in vacuo*, followed by column chromatography on silica with 5% ether in dichloromethane as eluant gave the β-lactam **35** (29 mg, 62%), m.p. 74-76°C, $[\alpha]_D$ +56.7 (*c* 0.74, $CHCl_3$); υ_{max} 1765 cm^{-1} (β-lactam); δ_H (400MHz) (carbapenam numbering) 1.31, 1.32, 1.37 and 1.45 (each 3H, s, C*Me*$_2$), 3.12 (1H, dd, $J_{5,6\alpha}$ 5.15, J_{gem} 15.3, 6$_\alpha$-H), 3.23 (1H, dd, $J_{5,6\beta}$ 2.2, 6β-H), 3.76 (1H, t, *J*~ 7.8, 3"$_a$-H), 3.82 (1H, dt, $J_{1,5}$~ $J_{5,6\alpha}$~5, 5-H), 3.86 (1H, m, 3-H), 4.03 (1H, dd, $J_{3',3"b}$ 6.5, J_{gem} 8.2, 3"$_b$-H), 4.22 (1H, ddd, $J_{3,3'}$ 2.3, $J_{3',3"a}$ 7.5, 3'-H), 4.78 (1H, t, $J_{1,2}$~ $J_{1,5}$~ 5.0, 1-H), 4.97 (1H, br. d, $J_{1,2}$ 5.3, 2-H); δ_C (50MHz) 24.2, 25.3, 26.0 and 26.2 (C*Me*$_2$), 38.8 (6-C), 56.1 (5-C), 64.2 (3-C), 66.6 (3"-C), 76.1 (3'-C), 79.4 (1-C), 89.5 (2-C), 109.3 and 112.9 (*C*Me$_2$), 175.6 (7-C); *m/z* 283 (M^+, 0.2%), 268 (M^+-Me), 7%). [Found: (M^+-Me), 268.11888. Calc. for $C_{13}H_{18}NO_5$, 268.11850].

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