Vitamin C and isovitamin C derived chemistry. 2. Synthesis of some enantiomerically pure 4,5,6-trihydroxylated norleucines

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A sequence leading to enantiomerically pure 4,5,6-trihydroxylated norleucines 23-25, their 5,6-O-isopropylidene derivatives 17a,b and 20, and lactones 19a,b and 22 from relatively inexpensive carbohydrate precursors is described. 5,6-O-Isopropylidene-L-gulono-, D-mannono-, and D-galactono-1,4-lactones (2a,b and 7b) react readily with 2 equiv of mesyl chloride in pyridine at 0 °C to produce hex-2-eno-1,4-lactone 1-Mesylates 11a,b and 12, which are then treated with sodium azide in DMF to generate the configurationally C-2-inverted azides 15a,b and 16. Hydrogenation thereof, in the presence of triethylamine, gives the 5,6-O-isopropylidenedenic title compounds 17a,b and 20, which are hydrolyzed in boiling water to give amino acids 23-25 and are converted into lactones 19a,b and 22 by treatment with dilute hydrochloric acid under reflux. The lactones are optimally produced directly from 15a,b and 16 by hydrogenation in the presence of acid.

The ascorbic acids 1a,b represent inexpensive industrially produced bulk chemicals whose potential as a source of chiral carbon compounds has been little exploited.1 A recent2 publication describes their transformation into chirally defined butenolides 3a,b via Hanessian-type deoxygenations of their reduced 5,6-O-isopropylidene acetals 2a,b (Scheme I). Continuation of these studies required the development of more efficient ways for preparing 3a,b from 2a,b in larger quantities. Olefins are known to arise via the reductive elimination of vic-ditosylates and -dimesylates3 (tosyl = p-tolysulfonyl; mesyl = methylsulfonyl). Attention was directed therefore toward converting 2a,b and subsequently 7b into 4a,b and 9c. Conventional mesylations, however, were found to proceed beyond the production of 4a,b and 9c, to give instead, 2-mesylated hex-2-eno-1,4-lactones 5a,b and 8 cleanly and efficiently. The present report describes some aspects of these reactions, the resultant products, and their subsequent conversion into enantiomerically pure trihydroxylated norleucine analogues 23-25.

Results and Discussion

Mesylation Studies. Treatment of 2a in ice-cold pyridine with 2 equiv of mesyl chloride produced a crystalline product in excellent yield. NMR spectroscopy revealed the presence of one mesyl group at 3.3 ppm and a vinyl doublet at 7.15 ppm (J = 2 Hz). In conjunction with analytical data, it was assigned structure 5a. Examination of the crude product mixtures (NMR; TLC) failed to reveal the presence of 4a. The comparable reaction of 2a with 1 equiv of mesyl chloride produced 6a regioselectively in high yield; its structure was supported by spectral evidence. This showed a doublet (J = 5 Hz) at 5.59 ppm for the proton geminal to the mesylate. Mono-mesylation of 2a would be expected to occur preferentially at the C-2 rather than at the C-3 OH in view of the former’s greater acidity and accessibility. Subsequent treatment of 6a with mesyl chloride in pyridine led to 5a, most likely through the intermediacy of the dimesylate 4a. Similar treatment of acetal 2b with 2 equiv of mesyl chloride proceeded less cleanly to produce 45% of 5b as the main product. Monomesylate 6b resulted on treatment of 2b with 1 equiv of mesyl chloride. No improvement in the overall yield of 5b was noted when 6b was allowed to...
react with additional mesyl chloride. The butenolide was also obtained by the reaction of 6b with phosphorus oxychloride in pyridine. Compound 5b was obtained optimally (55%) by subjecting 2b in pyridine to the successive action of 1 equiv of mesyl chloride and phosphorus oxychloride in a one-pot sequence (Scheme II).

The L-threo and D-erythro isomers 5a,b differ spectrally, featuring vinylic doublets at 7.15 vs. 7.29 ppm and H-4 protons with coupling constants amounted to 3.5 and 7 Hz, respectively. Compound 5a showed broader H-5 and H-6 multiplets and less separation between the methyl signals of the isopropylidene group.

Compounds 5a,b must clearly have arisen by way of the trans elimination of MesOH from 4a,b. It was, therefore, of interest to examine the feasibility of exploiting comparable cis eliminations as a way of generating related 2-0-substituted 1,4-lactones 2-mesylates. The synthesis of 7b was therefore undertaken. Molar scale catalytic oxidation of D-galactose (aqueous NaOH, pH 9.5, Pd-C; 0.5 h; 55 °C) provided aqueous solutions of sodium D-galactonate, which were further characterized by analysis and spectral evidence. Dimesylate 2a,b was then isolated as a syrup by extraction with ether.

Scheme IIIa

**Figure 1.** I-IIIa,b: R is compatibly functionalized one, two, or three-carbon fragment; Y = Ac, Bu, Bz, Ts; X = NHAc, OAc, OBz, OBn, Br, OTs; (a) -HOY, (b) catalytic reduction.

Selective cis elimination of the coproduct 9c would then account for the observed presence of 8 (Scheme III).

Compounds 5a,b and 8 were further characterized by their conversion to the deprotected diols 10a-c by acid hydrolysis in propan-2-ol solution.
tions transformed 5b and 8 into 11b and 12. NMR spectroscopy showed 1H 14C 17C 16 Hz. The isopropylidene methyl group signals were spaced further apart in the D-arabino compound 11b than in the corresponding L-xypo derivative 11a (Table I). Compounds 5a and 8 and also their reduction products 11a and 12 constitute enantiomeric pairs.

The modes of formation of 5a,b and 8 from 4a,b and 9c merit additional comment. Whereas 5a,b must have ensued from the trans elimination of methanesulfonic acid from 4a,b, the generation of 8 via an apparent cis elimination from 9c is less evident. We suggested recently that the cis elimination of formate ester intermediate 13 to 14 may have involved a six-center transition state promoted by the carboxyl- and iodo-enhanced acidity of H(2)2 (Scheme IV). An E1 mechanism had been proposed earlier for a related cis elimination.25 The possibility of 7b having undergone C-2 epimerization prior to elimination was considered unlikely since NMR-monitored control experiments demonstrated the monomesylates 6a,b, 11a,b, and 12 to be resistant toward pyridine-induced deprotonation at C-2. These results, however, did not rule out the possibility of pyridine eliciting the deprotonation and consequential enolization of dimesylates 4a,b and 9c, thus leading to intermediates 1Va,b and V. The subsequent expulsion of the C-3 mesylate would then give 5a,b and 8 (Scheme V). Such an E1 mechanism would obviate the need of invoking cis and trans elimination pathways and would reduce the issue to one of minor differences in the kinetic acidity of the proton on C-2. The process would derive its impetus from the relief of nonbonded interactions between substituents at C-2, C-3, and C-4 and would be accelerated sterically (Scheme V).

The synthetic potential of 5a,b and 8 differs fundamentally from that of their congener depicted in Figure 1. Whereas all the sterecontrolled reductions had given rise to products featuring their C-2 and C-4 substituents in a cis relationship, the nucleophilic displacement of the C-2 mesylate fragments encountered in reduction products 11a,b and 12 would lead to structures having their substituents in a trans geometry. To test the concept in a scheme for constructing D- or L-amino acid derivatives, the preparation of enantiomerically pure 4,5,6-trihydroxylated norleucines 23-25 was undertaken. Carbohydrates have previously been applied in the elaboration of chiral a-amino acids such as the bleomycin component L-erythro-β-hydroxystatidin16 (A) and (+)-furanomycin15 (B).

Catalytic reduction (10% Pd-C, 1 equiv of triethylamine, 75% EtOH, 50 lbs/in.2) of 15a yielded 86% of solid

![Scheme IV](image)

![Scheme V](image)

Synthesis of 23-25. Compound 11a was treated therefore with sodium azide in DMF at room temperature to give 90% of the pure azido derivative 15a. Its structural assignment was based on the earlier described elucidation of the geometry of 3-deoxy 2,4-disubstituted 1,4-lactones.18 These studies had shown the sum of the ring proton vicinal coupling constants to be greater for the cis isomers than for their trans counterparts. The differences have been ascribed to the change of an axial-axial interaction to an equatorial-equatorial one on going from the cis to the trans isomers. Compound 15a revealed 1H 14C 17C 16 Hz being in agreement with its proposed C-2-C-4 trans geometry. Similar azide displacements on mesylates 11b and 12 led to the NMR-supported structures 15b and 16. In contrast with 15a and 16, the methyl signals of the isopropylidene group of 15b showed a clearly defined separation (Table I).
material. The broad IR absorption maxima at 3500-2500 and 1600 cm\(^{-1}\) characterized the product as an amino acid zwitterion. In conjunction with NMR data, showing the presence of an isopropylidene group, it was assigned structure 17a. The retention of the original configuration at C-2 was substantiated by the NMR spectrum of the (2,4-dinitrophenyl)amino compound 18a. This was obtained by treatment of 17a with 2,4-dinitrofluorobenzene-K\(_2\)CO\(_3\) in DMF and subsequent acidification with aqueous HCl. The product was characterized as the (2,4-dinitrophenyl)amino compound 18a. This was obtained by treatment of 17a with 2,4-dinitrofluorobenzene-K\(_2\)CO\(_3\) in DMF and subsequent acidification with aqueous HCl. The product was characterized as the (2,4-dinitrophenyl)amino compound 18a. This was obtained by treatment of 17a with 2,4-dinitrofluorobenzene-K\(_2\)CO\(_3\) in DMF and subsequent acidification with aqueous HCl. The product was characterized as the (2,4-dinitrophenyl)amino compound 18a. This was obtained by treatment of 17a with 2,4-dinitrofluorobenzene-K\(_2\)CO\(_3\) in DMF and subsequent acidification with aqueous HCl. The product was characterized as the (2,4-dinitrophenyl)amino compound 18a. This was obtained by treatment of 17a with 2,4-dinitrofluorobenzene-K\(_2\)CO\(_3\) in DMF and subsequent acidification with aqueous HCl. The product was characterized as the (2,4-dinitrophenyl)amino compound 18a. This was obtained by treatment of 17a with 2,4-dinitrofluorobenzene-K\(_2\)CO\(_3\) in DMF and subsequent acidification with aqueous HCl. The product was characterized as the (2,4-dinitrophenyl)amino compound 18a.

The amino acid 17a was crystallized from methanol. Its NMR spectrum was rather complex due to the additional NH-CH coupling. The H-3 and H-3' absorption pattern is also influenced strongly by the solvent used: in CDCl\(_3\) a 16-peak multiplet was observed, as in all other 3-deoxy-2,4-disubstituted 1,4-lactones studied, but in Me\(_2\)SO-\(d_6\) both protons coincided to simplify the signal to that of a doublet of doublets (J\(_{2,3}\) = 9.5 Hz, J\(_{3,4}\) = 6 Hz). These data suggest a 2,4-trans geometry for the substituents on 18a and hence also for the ones on 17a. The amino acid 17a gave the corresponding deprotected 1,4-lactone 19a on treatment with aqueous HCl. The product was characterized spectroscopically, showing \(\gamma\)-lactone absorption at 1800 cm\(^{-1}\) (infrared) and the absence of an isopropylidene acetal fragment (NMR). Catalytic reductions of 15b and 16 in the manner described for 15a yielded amino acids 17b and 20, which were characterized as the (2,4-dinitrophenyl)amino analogues 18b and 21. They also underwent acid-catalyzed deprotection and lactonization to give 19b and 22. Lactones 19a,b and 22 were best obtained directly from 15a,b and 16 by catalytic hydrogenation under acidic conditions (Scheme VI).

The action of boiling water transformed partially protected 17a,b and 20 into the free amino acids 23-25. Since these were difficult to handle, they were derivatized and purified as their copper(II) salts. Compound 19b has been reported\(^\text{19}\) previously in a sequence for the preparation of the antipode of naturally occurring muscarine through the assumed intermediacy of structure 24.

### Concluding Remarks

Compounds 23-25 may be viewed as 4,5,6-tri-hydroxylated norleucines or as 3-deoxyhexosaminic acids; formally they represent terminally \(sp^2\)-carbon-linked alanine and glyceral units. Hexosaminic acids have been obtained by way of the C-1 oxidation of aldosesamines\(^\text{16}\) and by the Strecker homologation of the lower aldoses.\(^\text{21}\) 2-Acetamido-2-deoxy-D-mannono-1,4-lactone has been obtained by way of the C-2 epimerization of D-glucosaminic acid.\(^\text{16}\) Of the 3-deoxyhexosaminic acids, only 24 has been reported previously via a non-carbohydrate approach.\(^\text{19}\) The present route for preparing 23-25 exploits aldono-1,4-lactone chemistry throughout. Whereas carbohydrate-based schemes for constructing chiral carbon compounds have almost invariably been predicated on furanoside and pyranoside transformations,\(^\text{22}\) concepts centering on aldono-1,4-lactones have attracted surprisingly little attention. Their potential in synthesis stems from the following. Aldono-1,4-lactones and their lactols constitute interconvertible synthetic equivalents. Generous amounts of starting lactones can be prepared by the catalytic oxidation of the corresponding aldoses; L-gulono- and D-mannono-1,4-lactones are obtained from the Pd-catalyzed reduction of the plentiful ascorbic acids 1a,b.\(^\text{2}\) The presence at C-1 of a carbonyl group rather than a conformational stability of the \(\gamma\)-lactone rings makes them


added dropwise over 0.5 h to a cooled (-10 °C), stirred solution of (4S,5R)-5a. Mesyl chloride (26.4 g, 0.23 mol) was added dropwise over 15 min to a stirred, cooled (-10 °C) solution of (2S,4S,5R)-lla,b and ultimately the D-amino acids cis and trans (4S,5S)-5a and (4S,5R)-5b produces (2S,4S,5S)- and (2S,4S,5R)- D-amino acids.

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Tables 1. Relevant 1H NMR Data of 2,4-Disubstituted γ-Lactones

 attrative substrates for the restructuring of mono-saccharides by way of relatively straightforward processes. In practice, aldono-1,4-lactones are highly crystalline and easily manipulated substances, readily identified by NMR spectroscopy. These aspects are borne out by the aldono-1,4-lactone-based syntheses of 23-25 via easily handled solid lactone intermediates derived from inexpensive bulk chemicals. The concept is an efficient one in giving access to both D- and L- amino acid derivatives whose C-2 stereochemistry is laid down by the original C-4 configuration of the unsaturated mesylates 5a,b and 8. Reduction of (4S,5S)-5a and (4S,5R)-5b produces (2S,4S,5S)- and (2S,4S,5R)-5a,b and ultimately the D-amino acids (2R,4S,5S)-23 and (2R,4S,5R)-24. The l-amino acid (2S,4S,5R)-25 originates via the parallel elaboration of reduction product (2R,4S,5R)-12 obtained from (4R,5R)-8.

Experimental Section

General Methods. Microanalytical data were supplied by H. Eding. Proton NMR spectra were recorded on a Hitachi Perkin-Elmer R24B spectrometer, Me4Si as internal standard. Optical rotations were determined on an optical activity AA-10 polarimeter. Melting points (recorded on a Fischer-Johns block) are uncorrected. Column chromatography was carried out on silica gel (Merck, Kieselgel 60) and thin-layer chromatography (TLC) on aluminum sheets precoated with silica gel (Merck, Art. 5554).

3-Deoxy-5,6-O-isopropylidene-2-O-mesy1-1-threo-hex-2-enono-1,4-lactone (5a). Mesityl chloride (2.29 g, 0.02 mol) was added dropwise over 0.5 h to a stirred, cooled (-10 °C) solution of acetal 2a (4.3 g, 0.02 mol) in pyridine (64 mL). The reaction was allowed to proceed for a further 5 h at 0 °C wherein ice-water (300 mL) was added and the mixture stirred at room temperature for 0.5 h. The precipitated crude product was collected by filtration, washed successively with water (300 mL), methanol (75 mL), and ether (50 mL), and recrystallized from methanol to yield title product 5a: 22.5 g (81%); mp 121-122 °C; [α]D +41° (c 1.81, CHCl3); 1H NMR (CDCl3) δ 1.33 (s, 3 H), 1.38 (s, 3 H), 3.34 (s, 3 H), 3.6-4.6 (m, 3 H), 5.10 (d, J = 3.5 and 1.75 Hz, 1 H), 7.14 (d, J = 1.75 Hz, 1 H). Anal. Calcd for C15H18O5: C, 43.6; H, 5.2. 1H NMR (CDCl3) δ 1.33 (s, 3 H), 1.38 (s, 3 H), 3.34 (s, 3 H), 3.6-4.6 (m, 3 H), 5.10 (d, J = 3.5 and 1.75 Hz, 1 H), 7.14 (d, J = 1.75 Hz, 1 H). Anal. Calcd for C15H18O5: C, 43.6; H, 5.2.

5,6-O-isopropylidene-2-O-mesy1-1,4-lactone (6a). Mesityl chloride (2.29 g, 0.02 mol) was added dropwise over 0.5 h to a stirred, cooled (-10 °C) solution of acetal 2a (4.3 g, 0.02 mol) in pyridine (10 mL), maintaining the temperature below -5 °C. The reaction was then allowed to proceed at 0 °C for 1 h, after which water (80 mL) was added. The precipitated crude product was collected by filtration, washed successively with water, propan-2-ol, and ether, and then triturated with propan-2-ol to give compound 6a: 4.55 g (76%); mp 185-186.5 °C; [α]D +31° (c 1.81, CHCl3); 1H NMR (D2O) δ 1.34 (s, 3 H), 1.38 (s, 3 H), 3.32 (s, 3 H), 4.3-4.7 (m, 6 H), 5.59 (d, J = 4.5 Hz, 1 H). Anal. Calcd for C15H18O5: C, 40.54; H, 5.44. Found: C, 40.5; H, 5.4.

3-Deoxy-5,6-O-isopropylidene-2-O-mesy1-d-erythro-hex-2-enono-1,4-lactone (5b). Mesityl chloride (7.22 g, 0.063 mol) was added dropwise over 15 min to a stirred, cooled (-10 °C) solution of 5,6-O-isopropylidene-2-O-mesy1-1,4-lactone [2b; 12.0 g, 0.055 mol] in pyridine (35 mL) and the resultant mixture allowed to react at 0 °C for 1.25 h. The mixture was then recooled to -10 °C, treated dropwise over 15 minutes with phosphorus oxychloride (9.63 g, 0.063 mol), and then allowed to proceed at 0 °C for 3 h. Ice-water (165 mL) was added to the mixture, and after being kept at room temperature for 0.5 h the crude product was collected by filtration and washed successively with water (165 mL),
methanol (55 mL), and ether (35 mL). Recrystallization of this material [9.43 g (62%)] from methanol gave title product 15b: 3.25 g (65%); mp 12.5 and 1.1 Hz, 1.35 (s, 3 H), 1.32 (s, 3 H),

2.30 (dt, J = 12 and 10 Hz, 1 H), 2.86 (dd, J = 6, 9, and 12 Hz, 1 H), 3.25 (s, 3 H), 3.7-4.4 (m, 3 H), 4.61 (dd, J = 4, 6, and 9 Hz, 1 H), 5.06 (dd, J = 6, 9, and 12 Hz, 1 H). Anal. Caled for C₉H₁₃N₃O₄: C, 47.9; H, 5.7.

3-Deoxy-5,6-0-isopropylidene-2-O-mesylo-arabino-hexono-1,4-lactone (11b). Hydrogenation (5h) of the unsaturated mesylate 5b (6.22 g, 0.022 mol), in the presence of palladium charcoal (10%, 0.3 g), in the same manner as described above, followed by trituration of the crude product (6.25 g, 100%) with methanol (20 mL) at 0 °C for 1 h gave pure 11b: 5.10 g (82%); mp 142-143.5 °C; [α]D₂₀ = -46°; [α]D₁₀ = -49° (c 0.66, CHCl₃); 'H NMR (CDCl₃) δ 1.32 (s, 3 H), 1.36 (s, 3 H), 2.30 (dt, J = 12 and 10 Hz, 1 H), 2.86 (dd, J = 6, 9, and 12 Hz, 1 H), 3.25 (s, 3 H), 3.7-4.4 (m, 3 H), 4.57 (dt, J = 9.5 and 5.5 Hz, 1 H), 5.59 (dd, J = 9 and 10 Hz, 1 H). Anal. Caled for C₈H₁₀N₃O₄: C, 42.5; H, 5.7. Found: C, 42.3; H, 5.8.

3-Deoxy-5,6-0-isopropylidene-2-O-mesylo-xylo-hexono-1,4-lactone (12). Compound 12 was prepared as described for 11a in 75% yield: mp 110-114 °C; [α]D₂₀ = +154° (c 1.06, MeOH); 'H NMR (CDCl₃) δ 1.32 (s, 3 H), 1.36 (s, 3 H), 2.30 (dt, J = 12 and 10 Hz, 1 H), 2.86 (dd, J = 6, 9, and 12 Hz, 1 H). Anal. Caled for C₉H₁₃N₃O₄: C, 47.9; H, 5.7.

2-Azido-2,3-dideoxy-5,6-0-isopropylidene-L-lyxo-hexono-1,4-lactone (15a). A solution of saturated mesylate 11a (2.90 g, 0.01 mol) in DMP (10 mL) was treated with sodium azide (10 g, 0.158 mol) and allowed to stir at room temperature for 18 h. The mixture was filtered to give a residue (500 mg) which was washed with water (1 × 20; 5 × 10 mL). The washed, dried (MgSO₄) ethereal layer was evaporated in vacuo to give an oil that crystallized on standing. Trituration of the crude product (2.08 g (91%)) with ice-cold diisopropyl ether (4 mL) gave pure azide 15a: 1.75 g (77%); mp 62-63.5 °C; [α]D₂₀ = +198° (c 0.97, MeOH); 'H NMR (CDCl₃) δ 1.35 (s, 3 H), 2.22 (dt, J = 13.5 and 9.5 Hz, 1 H), 2.66 (dd, J = 13.5, 8.5, and 3 Hz, 1 H), 3.94 (dd, J = 8.5 and 7 Hz, 1 H), 4.07 (dd, J = 8.5 and 7 Hz, 1 H), 4.16 (dd, J = 7 and 2 Hz, 1 H), 4.51 (dd, J = 9.5 and 6 Hz, 1 H), 4.55 (dd, J = 9.5, 3, and 2 Hz, 1 H). IR (KBr) νmax 2100 (N₃), 1790 cm⁻¹ (C=O). Anal. Caled for C₉H₁₅N₃O₄: C, 47.57; H, 5.77, N, 18.49. Found: C, 47.9; H, 5.75; N, 18.4.

Azide 15a was also obtained (65% yield) from compound 5a in a one-pot sequence, without prior isolation of intermediate 11a (vide infra).

2-Azido-2,3-dideoxy-5,6-0-isopropylidene-D-ribo-hexono-1,4-lactone (15b). Treatment of mesylate 12 as described above for 11a gave azide 15b: 4.17 g (73%); mp 60-61.5 °C; [α]D₂₀ = +134° (c 1.06, MeOH); 'H NMR (CDCl₃) δ 1.32 (s, 3 H), 1.45 (s, 3 H), 2.17 (dt, J = 13.5 and 8.5 Hz, 1 H), 2.51 (dd, J = 8.5, 3.5, and 1.5 Hz, 1 H), 3.75 (dd, J = 8.5 and 5.5 Hz, 1 H), 1.41 (dd, J = 8.5 and 7.5 Hz, 1 H), 4.26 (dd, J = 7.5 and 5.5, and 1 Hz, 4.59 (dt, J = 8.5 and 7 Hz, 1 H), 4.48 (dd, J = 8.5 and 3.5 Hz, 1 H), 5.42 (dd, J = 8.5 and 7 Hz, 1 H). Anal. Caled for C₉H₁₄N₃O₄: C, 56.4 (C-2), 65.7 (C-6), 75.7 (C-4), 78.0 (C-5), 110.4 (CMEO₃), 173.05 (C-1); (IR (KBr) νmax 2100 (N₃), 1790 cm⁻¹ (C=O). Anal. Caled for C₇H₁₀N₂O₄: C, 47.57; H, 5.77; N, 18.49. Found: C, 47.9; H, 5.75; N, 18.4.

Azide 15b was also obtained (72% yield) from 5b, without isolation of intermediate compound 11b (vide infra).

2-Azido-2,3-dideoxy-5,6-0-isopropylidene-D-lyxo-hexono-1,4-lactone (16). The crude product from 15b was treated with sodium azide (5.0, 0.077 mol) in DMP (50 mL) with stirring for 24 h. The crude product was filtered and washed with water (5 × 10 mL). The washed, dried (MgSO₄) ethereal layer was evaporated in vacuo to give an oil that crystallized on standing. Trituration of the crude product (6.25 g) with ice-cold diisopropyl ether (4 mL) gave pure azide 16: 2.10 g (77%); mp 150-155 °C; [α]D₂₀ = -141° (c 0.97, MeOH); 'H NMR (CDCl₃) δ 1.32 (s, 3 H), 1.35 (s, 3 H), 1.38 (s, 3 H), 1.45 (s, 3 H), 2.18 (dd, J = 8.5 and 7 Hz, 1 H), 2.92 (dt, J = 8.5 and 7 Hz, 1 H), 4.16 (dd, J = 9.5 and 5.5 Hz, 1 H), 4.54 (dd, J = 9.5 and 3 Hz, 1 H). Anal. Caled for C₉H₁₄N₃O₄: C, 56.4 (C-2), 65.7 (C-6), 75.7 (C-4), 78.0 (C-5), 110.4 (CMEO₃), 173.05 (C-1); (IR (KBr) νmax 2100 (N₃), 1790 cm⁻¹ (C=O). Anal. Caled for C₇H₁₀N₂O₄: C, 47.57; H, 5.77; N, 18.49. Found: C, 47.9; H, 5.75; N, 18.4.
palladized charcoal (10%, 3.0 g) in ethanol-water (3:1, 240 mL) containing triethylamine (8.4 mL, 1 equiv) was hydrogenated overnight at 50 psi. The catalyst was removed by filtration and washed with ethanol-water (3:1) and water. The combined filtrate and washings were evaporated in vacuo, and ethanol was distilled in vacuo from the residue, which was then purified by chromatography with ether to give the crude product 17a, 10.66 g (84%). Recrystallization from 1,4-dioxane-H2O (1:91) gave pure 17a: mp 190–192 °C; [a]D +14.5° (c 1.85, H2O); 1H NMR (D2O) δ 1.36 (s, 3 H), 1.43 (s, 3 H), 1.88 (dt, J = 15.5 and 9 H, 1 H), 2.10 (dd, J = 3, 5.5, and 15.5 H, 1 H), 3.7–4.2 (2, 5.5, and 9 H, 1 H), 4.6 (d, J = 4.5 Hz, 2 H), 4.65 (s, 6 H).

2-Amino-2,3-dideoxy-5,6-O-isopropylidene-D-ribo-hexonic Acid [5,6-O-Isopropylidene-D(3R,S),6R,6-trihydroxy-L-norleucine] (17b). Azide 15b (10.5 g, 0.046 mol) was reduced in the manner described for 15a. The crude product (8.24 g (81%)) was recrystallized from 1,4-dioxane-water (1:91) to give 17b as needles: mp 202.5–203.5 °C; [a]D +153° (c 1.13, H2O); 1H NMR (D2O) δ 1.35 (s, 3 H), 1.43 (s, 3 H), 1.92 (dt, J = 15.5 and 9 H, 1 H), 2.18 (dd, J = 3, 5.5, and 15.5 H, 1 H), 3.6–4.15 (5 H), 4.6 (d, J = 4.5 Hz, 2 H), 4.98 (td, J = 9.5 and 8 H, 1 H), 7.20 (d, J = 9 Hz, 1 H), 8.80 (d, J = 8 Hz, 1 H), 8.82 (d, J = 3 Hz, 1 H). Anal. Found: C, 49.1; H, 4.7; N, 11.3.

2-Amino-2,3-dideoxy-5,6-O-isopropylidene-L-lyxo-hexono-1,4-lactone Hydrochloride (19a). A suspension of azide 15a (1.136 g, 0.005 mol) in ethanol (18 mL) and 2 M HCl (6 mL) was hydrogenated overnight at 50 psi, in the presence of palladized charcoal (10%, 0.5 g). The catalyst was removed by filtration, and concentration of the filtrate in vacuo, followed by recrystallization of the residue with propan-2-ol (6 mL), afforded 19a [0.867 g (88%)], recrystallization of which from methanol gave analytically pure material: mp 184–186 °C; [a]D +65° (c 1.13, H2O); 1H NMR (D2O) δ 2.75 (ddd, J = 8, 10.5, and 14 Hz, 1 H), 2.86 (ddd, J = 3.5, 9, and 14 Hz, 1 H), 3.7–4.1 (m, 3 H), 4.65 (dd, J = 9 and 10.5 Hz, 1 H), 4.8 (s, 5 H), 5.09 (ddd, J = 3, 5.5, and 8 Hz, 1 H); IR (KBr) νmax 3700–2500 (OH, NH₃+); 1750–1595 cm⁻¹ (CO₂). Anal. Calcld for C₉H₁₇NO₅Cl₂: C, 46.7; H, 6.12; N, 7.09. Found: C, 36.8; H, 6.0; N, 6.9.

2-Amino-2,3-dideoxy-5,6-O-isopropylidene-L-lyxo-hexono-1,4-lactone Hydrochloride (19b). A solution of compound 17b (0.552 g, 0.025 mol) in 1 M HCl (5 mL) was heated under reflux, with stirring, for 0.5 h. The mixture was evaporated to dryness in vacuo and the residue triturated with propan-2-ol (2 mL) to afford compound 19b [0.402 g (81%)], recrystallization of which from ethanol-water gave analytical purity: mp 185–188 °C; [a]D +65° (c 0.79, H2O); 1H NMR (D2O) δ 2.62 (ddd, J = 8.5, 10.5, and 14 Hz, 1 H), 2.88 (ddd, J = 2.5, 9.5, and 14 Hz, 1 H), 3.79 (d, J = 5.5 Hz, 1 H), 3.80 (d, J = 6.5 Hz, 1 H), 3.9–4.3 (m, 1 H), 4.62 (ddd, J = 9.5 and 10.5 Hz, 1 H), 4.7 (s, 5 H), 5.34 (ddd, J = 2.5, 3.5, and 8.5 Hz, 1 H). Anal. Found: C, 36.4; H, 6.0; N, 7.0.

2-Amino-2,3-dideoxy-5,6-O-isopropylidene-L-lyxo-hexono-1,4-lactone Hydrochloride (20). Compound 20 was prepared in the manner described for compounds 19a or 19b, in comparable yield: mp 196–198 °C; [a]D +66° (c 0.70, H2O); 1H NMR (D2O) δ 2.76 (ddd, J = 14, 10.5, and 8 Hz, 1 H) 2.87 (ddd, J = 14, 9, and 3.5 Hz, 1 H), 3.7–4.1 (m, 3 H), 4.65 (dd, J = 10.5 and 9 Hz, 1 H), 4.8 (s, 5 H) 6.09 (ddd, J = 8.5, 3.5, and 2 Hz, 1 H). Anal. Found: C, 36.65; H, 6.1; N, 6.95.

2-Amino-2,3-dideoxy-5,6-O-isopropylidene-ribitol (21). Treatment of compound 17b in the above manner gave the product: mp 116 mg (55%); mp 210–214 °C; 1H NMR crude acid (D2O) δ 2.01 (t, J = 4.5 Hz, 2 H), 3.4–3.9 (m, 5 H), 4.65 (s, 6 H). Anal. Found: C, 34.8; H, 5.7; N, 6.8.

2-Amino-2,3-dideoxy-5,6-O-isopropylidene-ribitol (22). Compound 20 in an analogous manner gave the product: 96 mg (46%); mp 210–216 °C; 1H NMR crude acid (D2O) δ 1.85 (dd, J = 9.5 Hz, 2 H), 3.5–4.0 (m, 5 H), 4.75 (s, 8 H). Anal. Found: C, 34.1; H, 5.0; N, 6.5.