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# 3-AMINO-2,3-DIDEOXY-D-*ERYTHRO*-FURANOSE DERIVATIVES

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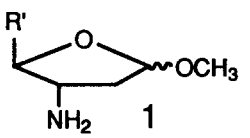
Abstract D-xylose has been converted into methyl 3-nitro-2,3-dideoxy-D-*erythro*-furanoside and several analogs which are modified at the 5-position (5-O-benzoyl, 5-O-trimethylacetyl, the uronic acid and methyl uronate ester). These nitro sugars were conveniently hydrogenated to the corresponding amino sugars 1A-1E. The utility of the trimethylacetyl protecting group has been demonstrated for this sequence of reactions.

Introduction: Amino sugars are widely distributed in nature[1], often as a unit of an antibiotic molecule[1,2] or a polymer.[3] The occurrence, chemistry and synthesis of amino sugars have been reviewed.[4] A large majority of the known examples are hexose derivatives and belong to the pyranose series.[5,6] Such amino sugars have been synthesized by a variety of methods[1-5] including azide displacement of a mesylate or tosylate followed by reduction[7], direct replacement of a trifluoromethanesulfonyl group with ammonia,[8] reduction of oximes[9,10] and nitro sugars.[10]. We have prepared nitro furanose **6** by oxidation of oxime **5**. Hyrogenation (Pd-C, acetic acid, 1-2 torr, 20 °C) of 2,3-dideoxy-3-nitrofuranoses derived from **6** has given amino furanoses **1A-1E.**. This route has not been widely exploited because of the difficulties in synthesizing furanose nitro sugars. Recent syntheses[14] of nitro sugars from non-carbohydrate precursors may make this route to amino sugars more attractive. The 3-oximino furanose derivatives from which **IA-IE** could be made by direct reduction are unreported.



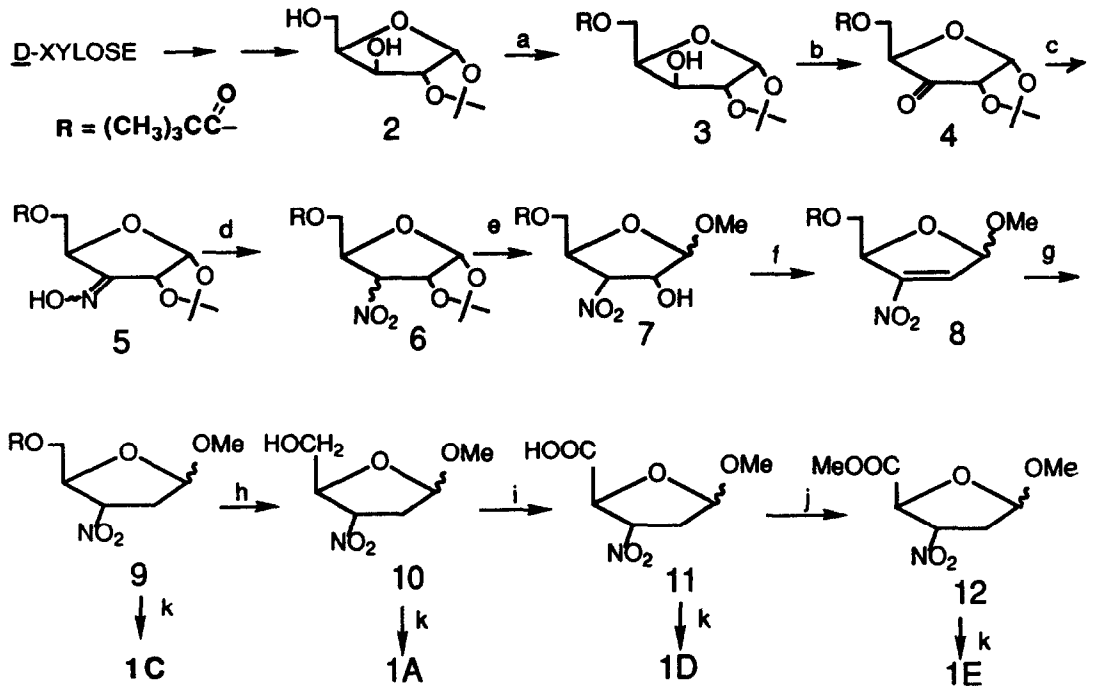

1

R' = A $-CH_2OH$ B $-CH_2OCOPh$ C $-CH_2OCOC(CH_3)_3$
D $-COOH$ E $-COOCH_3$

Discussion: The conversion of D-xylose into methyl 2,3-dideoxy-3-D-pentofuranoside, **10**, was carried through the sequence shown in Scheme I. This synthesis follows the published method[11] with the exception exception that the primary alcohol function at C-5 was previously protected by a benzoyl group, but in the revised procedure it is protected with the trimethylacetyl (pivaloyl) group. This alternate method of protection gives equivalent yields of mono-substitution (**D-xylose** → **2**) with less di-substitution, in contrast to benzoylation which usually gave about 5-10% of the troublesome dibenzoate.[9,11] The deprotection, **9**→ **10**, is more convenient and gives more consistent yields. The individual steps are described (experimental section).

The conversion of oxime **5** to nitro compound **6** is a key step in this sequence to amino sugars **1A - 1E**. The trifluoroperoxyacetic acid oxidations (yields of 85-95%) were according to the method developed by Nakagawa and coworkers[12] as originated by Emmons and Pagano.[14] The peroxy acid was prepared (caution[15])

SCHEME 1




Notes. a) $(CH_3)_3CCOCl$, Py, –10 °C. b) PDC, $CH_2Cl_2$, $Ac_2O$. b) $NH_2OH{\cdot}HCl$, Py, AcOH, 20 °C. d) 90% $H_2O_2$, ($CH_3CN$, $Na_2HPO_4$, urea). e) Anhyd. $CH_3OH$, Dowex-50W-X8. f) 1. MsCl/THF. 2. $NEt_3$. g) $NaBH_4$. h) $CH_3OH/NaOCH_3$, 20 °C. i) $RuCl_3{\cdot}3H_2O$, 2.2% equ., $NaIO_4$, $CCl_4$:$CH_3CN$:$H_2O$. j) $CH_3OH$, DCC, DMAP. k) $H_2$-(Pd-C), $CH_3OH$, AcOH.

from trifluoroacetic anhydride and 90% hydrogen peroxide[15] (acetonitrile solvent, 0 °C). The nitro ester **6** could be prepared from the starting material **2** as an approximate 5:2 mixture of *xylo* and *ribo* isomers after flash chromotography[16] in an overall yield of 77% without purification of intermediates **3** and **5**. Also the conversion of **6** (mixture of isomers) to **10** could be carried out without purification of intermediates **7**, **8** and **9** in an overall crude yield of 61%. The crude product was separated by chromatography to give a 25% yield of the pure β-anomer (**10**), 10% of pure α-anomer and 26% of a mixture of α and β anomers. Thus this mixture of α and β anomers of **10**, which could be used as such in the next step, was produced in an overall yield of 46% from the starting material **2**. This compares with an overall yield of 15-20% previously reported[13] for the similar sequence using protection of the primary alcohol by the benzoyl group instead of the trimethylacetyl group. Oxidation of the primary alcohol **10** (both α and β anomers) to the known acid[13] **11** was accomplished by a variation of the Sharpless oxidation[18] as previously described[11] in yields of 80-85% on a two-gram or less scale; ten-gram or larger scale oxidations gave poorer yields.

The nitro compounds **9, 10, 11,** and **12** were hydrogenated (10% Pd-C, methanol). The reaction was relatively slow unless acetic acid was added, in which case the acetate salts of the amines **1A, 1C,** and **1E** were isolated directly in good yields. These salts were readily crystallizable; but evaporation of their solutions resulted in partial loss of acetic acid with resulting difficulties in purification. Short exposure of acetates **1B** and **1C** in methanol solution to basic ion exchange resin gave the free amines; but longer resin treatment resulted in loss of the protecting benzoyl or trimethylacetyl groups to give **1A** as the free amine. The 5-O-benzoyl analog of **9** was also reduced to give the 3-amino-5-O-benzoyl derivative **1B**. Oxime **5** was directly hydrogenated (Raney Ni) to give the known[7] methyl 3-amino-3-deoxy-1,2-O-isopropylidine-α-D-ribofuranoside (**13**). Several of the nitro to amine reductions were accomplished with equal facility by use of the hydrazine-Pd·C method[19] usually reserved for aromatic nitro compounds.

Experimental. Melting points were taken in capillaries and are uncorrected. The NMR spectra were determined on a Varian 400 MHz FT super conducting instrument in $CDCl_3$ and recorded in ppm δ downfield from tetramethylsilane (TMS) unless otherwise noted. Coupling constants are reported in hertz (Hz) and splitting pattern abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet, m, unresolved multiplet; br, broad. Infrared spectra were taken on a Perkin Elmer Series 1600 FTIR instrument; intensity abbreviations: s, strong; m, medium; w, weak; br, broad. Optical rotations were taken at 20 °C on a Rudolf Autopol III polarimeter with the sample in a 10-cm, thermostated cell with permanent windows. Reactions were routinely followed by silica gel, thin layer chromatography (TLC, Analtech, GF, 250 μm). TLC plates were developed with 7% phosphomolybdic acid solution followed by brief heating at 150 °C. The method of Still.[16] was used for rapid (flash) chromatography.
1,2-O-Isopropylidene-5-O-trimethylacetyl-α-D-xylofuranose **3**. To a stirred, cooled (ca 0 °C) solution of 1,2-O-isopropylidene-α-D-xylofuranose (**2**, 57.06 g, 300 mmol) in anhydrous pyridine (600 mL) was added trimethylacetyl chloride (38.36 g, 315 mmol) over a 25-min period followed by stirring for 4 h until the reaction was complete as shown by TLC. The mixture was stirred (1 hr) with ice (400 g) and water (800 g) and extracted with $CH_2Cl_2$. The organic layer was washed (sat. $NaHCO_3$, sat. NaCl, $H_2O$), dried ($MgSO_4$), evaporated and the residual oil flash chromatographed (silica gel, 1:1 EtOAc:hexane) to give **3** which solidified on storage and was recrystallized from ether-hexane; m.p. 44-45 °C, 75.4 g, 92%; $[\alpha]^{20}_D$ + 25.7° (c 1.83, $CH_2Cl_2$); IR (film): 3497 (br), 2980 (m), 1734 (s), 1165 (s), 788 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 5.92 (1 H, d, J = 3.6 Hz, H-1), 4.58 (1 H, d, J = 3/6 Hz. H-2), 4.56 (1 H, dd, J = 4.8, 8.0 Hz, H-5a), 4.21 (1 H, m, H-4), 4.14 (1 H, dd, J = 11.2, 4.8 Hz, H-5b), 4.04 (1 H, d, J = 2.0, H-3), 1.51, 1.32 (6 H, 2s, $Me_2C$), 1.22 (9 H, s, $Me_3C$); $^{13}C$ NMR (400 MHz, $CDCl_3$): δ 179.6, 111.8, 104.6, 84.9, 78.5, 74.3, 60.9, 38.9, 27.1, 26.8, 26.1. Anal. calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 56.59; H, 8.04. The dipivalate isolated by chromatography had the following NMR ($CDCl_3$): δ 5.93 (1 H, d, J = 3.6 Hz, H-1), 5.26 (1 H, d, J = 3.6 Hz, H-2), 4.53 (1 H, ddd, J = 6.8, 6.4, 2.8 Hz, H-4), 4.45 (1 H, d, J = 3.6 Hz, H-3), 4.25 (1 H, dd, J = 11.2, 6.4 Hz, H-5a), 4.19 (1 H, dd, J = 11.2, 6.8 Hz, H-5b), 1.53, 1.23 (6 H, 2 s, $(CH_3)_2C$), 1.26 (9 H, s, $(CH_3)_3C$), 1.23, -1.19 (9 H, 3 s, $C(CH_3)_3$).
1,2-O-Isopropylidine-5-O-trimethylacetyl-α-D-*erythro*-pent-3-ulofuranose, **4** A solution of 1,2-O-isopropylidene-5-O-trimethylacetyl-α-D-xylofuranose (**3**, 39.0 g in $CH_2Cl_2$, 50 mL) was added to a slurry of pyridinium dichromate (powdered PDC, 98%, 56.1 g), activated molecular sieve[20] (71 g, 3Å, powder) and acetic anhydride (29.3 g, 99% in $CH_2Cl_2$, 420 mL). The mixture turned black within 5 minutes and spontaneously refluxed. After the mixture cooled, it was stirred for (5 hr), cooled and it was diluted with ether (300 mL). The evaporated filtrate

(Celite-silica gel pad) was purified by flash chromatography[16] ($SiO_2$, 40:60 EtOAc/hexane) to give an oil (**4**, 34.7 g, 90% yield); $[\alpha]^{20}_D$ + 136° (C 3.3, $CH_2Cl_2$); IR (film): 2979 (m), 1778 (m), 1735 (s), 1385 (m), 1156 (s), 1095 (m), 1031 (m), 868 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 6.10 (1 H, d, J = 4.4 Hz, H-1), 4.57 (1 H, dt, J = 2.9, 1.0 Hz, H-4), 4.39 (1 H, dd, J = 14.7, 2.8 Hz, H-5a), 4.38 (1 H, s, H-5b), 4.23 (1 H, dd, J = 12.1, 3.1 Hz, H-2), 1.50 , 1.44 (6 H, 2 s, $(CH_3)_2C$), 1.18 (9 H, s, $(CH_3)_3C$), $^{13}C$ NMR ($CDCl_3$): δ 208.0, 177.6, 114.3, 103.2, 77.3, 76.3, 63.3, 38.6, 27.5, 27.1. Anal. calcd for $C_{13}H_{20}O_6$: C. 57.34; H, 7.40. Found: C, 57.15; H, 7.39.

1,2-O-Isopropylidene-5-O-trimethylacetyl-α-D-*erythro*-pent-3-ulofuranose Oxime **5**. This was prepared as described for the 5-O-benzoyl analog[13]. From 55.0 g of **4** was obtained a crude oil which on flash chromatography[16] ($SiO_2$, 40:60 EtOAc/hexane) gave **5** as a syrup (2:1 mixture of *syn* and *anti* isomers; 56.9 g, 98%), [a]$^{20}_D$ + 167°(c 1.55, $CH_2Cl_2$); IR (film) 3407 (br), 2977 (m), 1734 (s), 1714 (m), 1481 (m), 1381 (m), 1159 (s), 1082, (m), 1031, (m), 866 (w) cm-1; major component, $^1H$ NMR ($CDCl_3$): δ 8.50 (1 H, s, oxime OH), 6.02 (1 H, d, J = 4.3 Hz, H-1), 5.29 (1 H, d, J = 1.6 Hz, H-4), 5.03 (1 H, dd, J = 4.4, 1.1 Hz, H-2), 4.59 (1 H, dd, J = 11.7, 2.5 Hz, H-5a), 4.24 (1 H, dd, J = 11.8, 2.4 Hz, H-5b), 1.50, 1.45 (6 H, 2 s, $(CH_3)_2C$), 1.19 (9 H, s $(CH_3)_3C$); minor component, $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.58 (1 H, s, oxime OH), 5.99 (1 H, d, J = 4.3 Hz), 5.30 (1 H, d, J = 1.6 Hz), 5.00 (1 H, t, J = 2.1 Hz), 4.36 (1 H, dd, J = 11.9, 2.5 Hz, H-5a), 4.26 (1 H, dd, J = 12.0, 4.7 Hz, H-5b), 1.53, 1.45 (6 H, 2 s, $(CH_3)_2C$), 1.19 (9 H, s, $(CH_3)_3C$); major component, $^{13}C$ NMR ($CDCl_3$) δ 178.2 , 157.8, 114.2, 105.0, 78.4, 75.8, 64.0, 38.6, 27.3 (two C's), 27.1 (27.132); minor component, $^{13}C$ NMR ($CDCl_3$): δ 178.4, 156.8, 113.6, 104.7, 75.6, 73.5, 64.9, 38.7, 27.7, 27.4, 27.1 (27.083). Anal. calcd for $C_{13}H_{21}NO_6$: C, 54.35; H, 7.37; N, 4.88. Found C, 54.35; H, 7.25; N, 4.95.

3-Deoxy-1,2-O-isopropylidene-3-nitro-5-O-trimethylacetyl-D-ribo- and xylo-furanose **6**. This method[12] was previously described for the 5-O-benzoyl analogs.[11] Trifluoroacetic anhydride (58 g) was added dropwise to a solution of $H_2O_2$ (9.5 g, 90%, Caution![15]) in acetonitrile (75 mL) at 0 °C. After being stirred at 0 °C for 10 min., this solution was added via a glass pipet, dropwise with stirring at 0°C over a 30-min period, to a previously prepared solution of crude oxime **5** (8.0 g mixture of *syn* and *anti* isomers) in acetonitrile (150 mL) containing $Na_2HPO_4$ (39.5 g) and urea (3.3 g). The mixture was heated in an oil bath at 50-60 °C for 2 h and processed to give compound **6** (8.2 g, 98%) as a mixture of isomers (2.3:1.0). This oxidation was also done on a larger scale (Caution![15]) 53.2 g of the oxime gave the mixture of nitro compounds **6** (52.7 g, 94%, 2:1 isomer mixture after flash chromatography); major isomer: $^1H$ NMR ($CDCl_3$) δ 5.89 (1 H, d, J = 3.7 Hz, 5.08 (1 H, d, J = 3.7 Hz), 4.91 (1 H, td, J = 9.2, 3.7 Hz), 4.77 (1 H, dd, J = 9.2, 5.5 Hz), 4.47 (1 H, dd, J = l2.4, 3.7 Hz), 4.31 (1 H, dd, J = 12.4, 3.7 Hz), 1.56 (3 H, s), 1.37 (3 H, s), 1.20 (9 H, s); minor isomer, $^1H$ NMR ($CDCl_3$): δ 6.15 (1 H, d, J = 3.7 Hz), 5.08 (1 H, dd, J = 3.7, 1.8 Hz), 5.03 (1 H, d, J = 4.6 Hz), 4.69 (1 H, q, J = 5.5 Hz), 4.27 (1 H, br, s), 4.25 (1 H, d, J = 1.8 Hz), 1.59 (3 H, s), 1.54 (3 H, s), 1.21 (9 H, s). Major isomer: $^{13}C$ NMR ($CDCl_3$) δ 177.5, 113.7, 102.9, 88.7, 81.5, 76.7, 60.5, 38.6, 26.9, 26.8, 26.4; minor isomer, $^{13}C$ NMR ($CDCl_3$: δ 177.4, 1112.7, 105.6, 83.8, 78.9, 74.1, 61.7, 38.6, 26.9, 26.2, 25.9. Anal. Calcd for $C_{13}H_{21}NO_7$: C, 51.48, H, 6.98; N, 4.62. Found: C, 51.26; H, 6.93; N, 4.41.

Methyl 3-Deoxy-3-nitro-5-O-trimethylacetyl-D-pento-furanoside **7**. The crude mixture of ribo and xylo nitro compounds **6** (25.2 g) in methanol (1000 mL) was refluxed (24 h) with Dowex 50W-X8 acid ion exchange resin (18 g). Evaporation of the filtrate gave an oil (98 %) which upon flash chromatography followed by evaporation gave an oil (18.3 g, 80%). In another experiment, chromatography ($SiO_2$, 1:2 EtOAc/hexane) of the crude oil gave the major component: $^1H$ NMR ($CDCl_3$): δ 5.11 (1 H, dd, J = 7.6, 4.7 Hz), 5.00 (1 H, td, J = 7.5, 5.0 Hz), 4.93 (1 H, s), 4.61 (1 H, t, J = 5.5 Hz), 4.35 (1 H, dd, J = 11.7, 4.7 Hz), 4.27 (1 H, dd, J = 11.7, 5.3 Hz), 3.37

(3 H, s), 2.61 (1 H, d, J = 5.9 Hz, OH), 1.21 (9 H, s); $^{13}$ C NMR ($CDCl_3$ ): δ 178.4, 107.6, 86.2, 75.6, 75.5, 64.2, 55.2, 38.8, 27.0. Anal. calcd for $C_{11}H_{19}NO_7$: C, 47.65; H, 6.91; N, 5.05. Found: C, 47.81; H, 6.92; N, 4.79. The initial crude oil was used in the subsequent reaction. The enantiomer of **7** (R = H) has been made by a completely different route and its reduction reported[20]

Methyl 2,3-Didehydro-2,3-dideoxy-3-nitro-5-O-trimethylacetyl β-pentofuranoside **8β**. Methanesulfonyl chloride (5.61 g) was added at 0 °C over 5 min to a solution of isomeric mixture of β-pentofuranoside **7** (6.66 g) in dry THF (165 mL). Triethylamine (5.34 g) was added and the solution was stirred at 20-24 °C for 30 min. Water (75 mL) was added and the mixture was extracted (3 x 200 mL $Et_2O$); the extracts were dried ($MgSO_4$) and the concentrated residue was chromatographed ($SiO_2$, 25% EtOAc/hexane) to give pure **8β** (6.2 g, 99%); TLC $R_f$ = 0.60 ($SiO_2$, 1:1 EtOAc/hexane): $[\alpha]^{20}_D$ = -51.45° c 1.59, $CH_3OH$); IR (film): 2974 (m), 1734 (s), 1532 (s), 1482 (m), 1399 (m), 1326 (m), 1195 (w), 1158 (s), 1083 (m); $^1$H NMR ($CDCl_3$): δ 6.90 (1 H, t, J = 1.5 Hz), 5.77 (1 H, t, J = 1.3 Hz), 5.24 (1 H, m), 4.51 (1 H, dd, J = 12.2, 2.0 Hz), 4.45 (1 H, dq, J = 12.2, 3.6 Hz), 3.46 (3 H, s), 1.18 (9 H, s); $^{13}$C NMR ($CDCl_3$): δ 177.9, 151.7, 131.3, 106.2, 79.3, 63.3, 55.9, 38.8, 26.9.

Methyl 2,3-Didehydro-2,3-dideoxy-3-nitro-5-O-trimethylacetyl-α-pentofuranoside **8α**. The above procedure was applied to the isomeric mixture of methyl α-pentofuranosides **7** (4.4 g) to give the α-isomer of **8** (3.8 g, 92%), TLC $R_f$ = 0.72 ($SiO_2$, 1:1 EtOAc/hexane): IR (film): 2973 (m), 1732 (s), 1557 (s), 1482 (m), 1367 (m), 1285 (s), 1161 (s), 1113 (s), 1036 (s), 937 (m), 771 (m) cm$^{-1}$; $^1$H NMR ($CDCl_3$): δ 6.90 (1 H, t, J = 1.7 Hz), 5.88 (1 H, dd, J = 4.6, 1.1 Hz), 5.42 (1 H, dt, J = 4.5, 2.2 Hz), 4.47 (2 H, $AB_{degenerate}$, J = 12.5, 10.4 Hz), 3.48 (3 H, s), 1.16 (9 H, s); $^{13}$C NMR ($CDCl_3$): δ 177.5, 151.7, 131.4, 106.2, 79.4, 62.1, 55.1, 38.6, 26.9, Anal. calcd for $C_{11}H_{17}NO_6$: C, 50.96; H, 6.61; N, 5.40. Found: C, 51.04; H, 6.72; N, 5.54.

Methyl 2,3-Dideoxy-3-nitro-5-O-trimethylacetyl-β-D-*erythro*-pentofuranoside **9**. An absolute ethanol (30 mL) solution of sodium borohydride (0.85 g) was added over 20 min at 0 °C to **8β** (2.6 g) in absolute ethanol (10 mL). After warming (20 °C, 1 h) the reaction mixture was diluted with water (25 mL) and the mixture was acidified (4 mL, cold 3N HCl). Vacuum removal of the ethanol gave a residue which was extracted with ether and the extracts were washed (sat'd $NaHCO_3$, NaCl), dried ($MgSO_4$) and vacuum evaporated to give an oil which was chromatographed ($SiO_2$, 1:4 EtOAc/hexane) to give **9** (2.3 g, 88%): $[\alpha]^{20}_D$ = 75° (c 1.05, $CH_3OH$); IR (film): 2974 (m), 1734 (s), 1559 (s), 1369 (m), 1158 (s), 1050 (s), 957 (w), 878 (w), 769 cm$^{-1}$ (w); $^1$H NMR ($CDCl_3$): δ 5.22 (1 H, dd, J = 5.3, 1.5 Hz), 5.10 (1 H, dt, J = 7.5, 4.3 Hz), 4.70 (1 H, td, J = 7.0, 4.9 Hz), 4.28 (1 H, dd, J = 11.4, 5.5 Hz), 4.19 (1 H, dd, J = 11.4, 7.3 Hz), 3.35 (3 H, s), 2.84 (1 H, ddd, J = 14.0, 6.9, 5.3 Hz), 2.53 (1 H, ddd, J = 14.0, 8.0, 1.5 Hz), 1.23 (9 H, s); $^{13}$C NMR ($CDCl_3$): δ 177.8, 105.3, 85.9, 80.5, 64.4, 55.2, 38.7, 37.9, 27.0. Anal. calcd for $C_{11}H_{19}NO_6$: C, 50.57; H, 7.33, N, 5.36. Found: C, 50.99; H, 7.43; N, 5.30. The mesylation, elimination and reduction steps were also performed without isolation of intermediate **8**. The mixed isomers **7** (1.38 g) were treated with $MeSO_2Cl$, $Et_3N$ and $NaBH_4$ as indicated above. The final oil was chromatographed ($SiO_2$, 40 x 15 cm) to give **9** (1.0 g, 77% yield, as a 12:1 mixture of isomers).

Methyl 2,3-Dideoxy-3-nitro-β-D-*erythro*-pentofuranoside **10** Nitro ester **9** (0.58 g) in methanol was added to a solution of sodium methoxide (0.3 g Na in $CH_3OH$, 20 mL) and the mixture was stirred (6 hr, 20 °C) until methanolysis was complete (TLC analysis). After the mixture was stirred (1 hr) with $NH_4Cl$ (0.9 g crystals) it was diluted with ether, filtered and the residue from vacuum evaporation was chromatographed ($SiO_2$, EtOAc/hexane 20 → 35%) to give product **10** (0.35 g, 90%); $[\alpha]^{20}_D$ - 108.7° (c 1.1, $CH_3OH$; lit.[13] -102°, c 1.2, $CH_3OH$); IR (film) 3460 br, 2932 w, 1558 s, 1554 s, 1374 w, 1205 w, 1091 m, 1043 s, 951 w cm$^{-1}$; $^{13}$C NMR ($CDCl_3$): δ105.3, 85.1, 84.2, 63.6, 55.5, 37.6. The $^1$H NMR was as published.[11]

Methyl 3-Amino-5-O-benzoyl-2,3-dideoxy-β-D-ribofuranoside, 1B Acetate and Base. The general procedure ($H_2$, Pd·C, HOAc, $CH_3OH$) for most of the nitro sugar reductions follows. A solution ($CH_3OH$, 5 mL) containing acetic acid (0.04 mL) and methyl 2,3-dideoxy-5-O-benzoyl-3-nitro-β-D-ribofuranoside[11] (150 mg, **9**, R = benzoyl instead of pivaloyl)) was hydrogenated (1.0–1.5 torr, pre-reduced 10% Pd·C, 150 mg). Vacuum evaporation of the filtered mixture gave an oil which solidified on trituration with ether (**1B** acetate, 156 mg, 94%). This solid was recrystallized (ether-methanol or ethyl acetate), m.p. 112-114 °C, $[\alpha]^{20}_D$ -53.7° (c 1, MeOH). Anal. calcd for $C_{15}H_{21}NO_6$: C, 57.86; H, 6.80; N, 4.50. Found: C, 57.38; H, 6.81; N, 4.46. $^1$H NMR ($CDCl_3$): δ 8.07, 7.57, 7.45 (5 H, d, t, t, o, p, m-ArH), 5.05 (1 H, d, $J_{1,2\alpha}$ = 6.8 Hz, H-1), 4.46 (2 H, ddd, J ≈ 11.7, J = 4.7 Hz, H-5α,5β), 4.03 (1 H, q, $J_{3,2\alpha,2\beta}$ = 7.2, $J_{3,4}$ = 3 Hz, H-3), 3.31 (3 H, $OCH_3$), 3.00 (b, OH, $NH_2$), 2.31 ( H, dd, J = 9.6, 7.2 Hz, H-2α), 2.07 (3H, OAc), 1.93 (1 H, m, H-2β). A methanol solution of this acetate (0.885 g) was stirred with Amberlite RA-400 resin in $HO^-$ form for 20 sec and the solution immediately filtered. Vacuum evaporation gave the free amine **1B** (0.718 g), m.p. 42-44 °C; $^1$H NMR ($CDCl_3$): δ 8.09, 7.57, 7.46 (5 H, d, t, t, o, p, m-ArH), 5.04 (1 H, d, $J_{1,2\alpha}$ = 5.1 Hz, H-1), 4.51 (1 H, dd, $J_{5\alpha,5\beta}$ = 11.7, $J_{5\alpha,4}$ = 4.7 Hz, H-5α), 4.41 (1 H, $J_{5\beta,5\alpha}$) = 11.7, $J_{5\beta,4}$ = 5.6 Hz, H-5β), 3.96 (1 H, ddd, $J_{4,5\alpha}$ = 4.7, $J_{4,5\beta}$ = 5.6, $J_{4,3}$ = 6.8 Hz, H-4), 3.68 (1 H, ddd, $J_{3,4}$ = 6.8, $J_{3,2\alpha}$ = 9.3, $J_{3,2\beta}$ = 6.9 Hz, H-3), 3.32 (3 H, $OCH_3$), 2.27 (1 H, dd, $J_{2\beta,3}$ = 6.9, $J_{2\alpha-2\beta}$ = 12.6 Hz, H-2β), 1.85 (1 H, ddd, $J_{2\beta,2\alpha}$ = 12.6, $J_{1,2\alpha}$ = 5.1, $J_{2\alpha,3}$ = 9.3 Hz, H-2α), 1.32 (2 H, br, $NH_2$). This same crystalline amine **1B** with indistinguishable properties was also obtained by direct hydrogenation of the benzoyl nitro compound **1B** (165 mg, Pd·C catalyst in methanol but without added acetic acid, 24 h); 72% yield.

Methyl 3-Amino-2,3-dideoxy-β-D-ribofuranoside, 1A, By Methanolysis of the O-Benzoate 1B. The acetate salt of the O-benzoate **1B** (141 mg) was debenzoylated by stirring in methanol with Amberlite IRA-400, $HO^-$ form, for 4 hr. Vacuum evaporation of the filtrate gave an oil which was chromatographed (silica gel, eluted with 4:1, benzene: methanol) to give pure amine **1A**, 73 mg (90%) identical to the product obtained as follows: 3-nitro-β-furanoside **10** (710 mg) in $CH_3OH$ (40 mL) was hydrogenated in the presence of Pd· C (700 mg, 10%) in the absence of acetic acid. Filtration and vacuum evaporation gave an oil (502 mg, 86%); $^1$H NMR ($CDCl_3$) [$D_2O$]: δ 5.04 (1 H, d, $J_{1,2\alpha}$ = 5.3 Hz, H-1) [4.90], 3.82 (1 H, m, H-4) [3.63], 3.77 (1 H, dd, $J_{5\alpha,5\beta}$ = 12.0, $J_{5\alpha,4}$ = 3.4 Hz, H-5α) [3.55], 3.67 (1 H, m, H-3) [3.39], 3.65 (1 H, dd, $J_{5\alpha,5\beta}$ = 12.0, $J_{5\beta,4}$ = 3.9 Hz, H-5β) [3.21], 3.38 (3 H, s, $OCH_3$) [3.16], 2.27 (1 H, dd, $J_{2\alpha,2\beta}$ = 13.4, $J_{2\beta,3}$ = 7.4 Hz, H-2β) [2.10], 1.86 (1 H, ddd, $J_{2\beta,2\alpha}$ = 13.4, $J_{2\alpha,1}$ = 5.3, $J_{2\alpha,3}$ = 8.3 Hz, H-2α)[1.78], 1.68 (3 H, br, OH and $NH_2$); $^{13}$C NMR ($CDCl_3$, 100.6 MHz): δ 104.9 (C-1); 87.6 (C-4), 63.7 (C-5), 55.0 ($OCH_3$), 51.8 (C-3), 43.1 (C-2); $^{13}$C NMR ($D_2O$): δ 104.9 (C-1), 86.7 (C-4), 63.4 (C-5), 54.6 ($OCH_3$), 50.9 (C-3), 40.8 (C-2).

Methyl 3-Amino-2,3-dideoxy-α-D-ribofuranoside, α-Anomer of 1A, by Hydrazine-Pd·C Procedure[19]. An ethanol solution (14 mL) of the α-anomer of **10** (162 mg) and Pd·C (50 mg) was held at 70-75 °C while hydrazine hydrate (190 mg, 90%) was added. After 7 h, the cooled solution was filtered and vacuum evaporated to give the α-anomer of **1A** (125 mg, 92% yield) as an oil: $^1$H NMR ($CDCl_3$), δ 5.05 (1 H, dd, $J_{1,2\beta}$ = 5.2, $J_{1,2\alpha}$ = 1.6 Hz, H-1), 3.84 (1 H, ddd, $J_{4,5\alpha}$ = 3.7, $J_{4,5\beta}$ = 4.5, $J_{4,3}$ = 5.4 Hz, H-4), 3.78 (1 H, dd, $J_{5\alpha,5\beta}$ = 11.4, $J_{5\alpha,4}$ = 3.7 Hz, H-5α), 3.65 (1 H, dd, $J_{5\alpha,5\beta}$ = 11.4, $J_{5\beta,4}$ = 4.5 Hz, H-5β), 3.38 (3 H, s, $OCH_3$); 3.32 (1 H, ddd, $J_{3,2\beta}$ = 8.6, $J_{3,2\alpha}$ = 3.8, $J_{3,4}$ = 5.4 Hz, H-3), 2.31 (1 H, ddd, $J_{2\alpha,2\beta}$ = 13.6, $J_{2\beta,3}$ = 3.8, $J_{2\beta,1}$ = 5.2 Hz, H-2β), 1.86 (3 H, br, OH and $NH_2$); $^{13}$C NMR ($CDCl_3$): 105.2 (C-1), 86.2 (C-4), 63.1 (C-5), 54.9 ($OCH_3$), 52.6 (C-3), 42.9 (C-2); $^{13}$C NMR ($D_2O$): δ 105.2 (C-1), 85.6 (C-4), 61.6 (C-5), 54.7 52.6 (C-3), 42.9 (C-2); $^{13}$C NMR ($D_2O$): δ 105.2 (C-1), 85.6 (C-4), 61.6 (C-5), 54.7 ($OCH_3$), 51.0 (C-3), 40.4 (C-2).

Methyl 3-Amino-2,3-dideoxy-5-O-trimethylacetyl-β-D-ribofuranoside, 1C, Acetate and Base. 3-Nitro-5-trimethylacetyl ester **9** (112 mg) was hydrogenated (Pd-C, MeOH, HOAc) by the general procedure to give **1C** as the acetate (107 mg, 85% yield), m.p. 87-89 °C (microscope hot stage), $[\alpha]^{20}_D$ –49.4° (c, 1.23, MeOH): IR (KBr): 2974 (m), 1733 (s), 1031 (s), 939 (w), 646 (w) $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 5.05 (1 H, d, J = 4.9 Hz), 4.19 (2 H, dd, J = 4.9 Hz), 3.83 (1 H, q, J = 5.7 Hz), 3.55 (1 H, q, J = 7.2 Hz), 3.32 (3 H, s, $OCH_3$), 2.35 (3 H, br, $NH_3^+$), 2.20 (1 H, dd, J = 7.0, 12.9 Hz), 2.09 (3 H, s, OAc), 1.85 (1 H, ddd, J = 13, 9.2, 5.3 Hz), 1.23 (9 H, s); $^{13}C$ NMR ($CDCl_3$): δ 178.5, 176.8, 104.7, 83.0, 65.0, 54.8, 52.0 , 40.6, 38.8, 27.0, 22.2; Anal calcd for $C_{13}H_{25}NO_6$: C, 53.59; H, 8.65, N, 4.81. Found: C, 52.76; H, 8.23; N, 4.78. On attempted repeated recrystallizations,this sample lost the acetate signal and gave an oil with an $^1H$ NMR ($CDCl_3$) corresponding with the free base: δ 4.95 ( 1 H, d, J = 4.9 Hz), 4.19 (2 H, dd, J = 5.6 Hz), 3.81 ( 1 H, q, J = 9.3 Hz), 3.32 (3 H, s), 2.23 (1 H, dd, J = 12.8, 7.0 Hz), 1.82 (1 H, ddd, J = 14.3, 9.3, 5.1 Hz), 1.44 (2 H, br, $NH_2$), 1.23 (9 H, s). IR (KBr): 3362 (br), 2960 (br), 1732 (s), 1481 (s), 1367 (w), 1286 (s), 1162 (s), 1102 (w), 954 (w), 859 (w), 770 (w) $cm^{-1}$. Anal. calcd for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06. Found: C, 57.23; H, 9.15; N, 4.88.

Methyl 3-Amino-2,3-dideoxy-β-D-ribofuranosiduronic acid, 1D, Acetate and Amino Acid. The nitrouronic acid **11**[11] (81 mg) was hydrogenated according to the general procedure (Pd-C, MeOH, HOAc) to give a solid which was recrystallized (MeOH/$Et_2O$) to give **1D** as the acetate (55 mg, 80%) m.p. 72-73 °C. Attempted crystallization gave a new solid which lacked the acetate NMR signal; m.p. ca 250 °C dec. on rapid heating, but melted above 310 °C when heated slowly. We interpret the m.p. and spectra to mean that **1C** exists in the zwitterion form; IR (KBr): 3423 (br), 3000, 2934, following peaks sharp and strong, 1648, 1603, 1539, 1402, 1372, 1309, 1108, 1071, 1047, 960, 848, 775, 662, 609 $cm^{-1}$; $^1H$ NMR ($D_2O$): δ 5.06 (1 H, d, J = 5.2 Hz), 4.23 (1 H, d, J = 4.4 Hz), 4.03 (1 H, q, J = 6.3 Hz), 3.22 (3 H, s, $OCH_3$), 2.21 (1 H, dd, J = 14.0, 6 Hz), 2.06 (1 H, td, J = 14.0, 6.4 Hz). Anal. calcd for: $C_6H_{11}NO_4$: C, 44.72; H, 6.88; N, 8.69; Found: C, 43.92; H, 7.06; N, 8.66.

Hydrogenation of Methyl 2,3-Dideoxy-3-nitro-β-D-ribofuranosiduronic Acid Methyl Ester **12**. The hydrogenation of **12** by the general procedure (Pd-C, $CH_3OH$, HOAc) in an attempt to obtain **1E** gave a solid which did not melt below 300 °C. Attempted purification by crystallization led to loss of the acetate signal but still gave a high melting product with IR and $^1H$ NMR which resembled but were different from those of the amino acid **1D**.

3-Amino-5-O-benzoyl-3-deoxy-1,2-O-isopropylidene-α-D-ribofuranose, **13**. 5-O-Benzoyl-1,2-O-isopropylidene-α-D-erythro-pent-3-ulofuranose oxime[11] (240 mg) was hydrogenated using W-2 Raney nickel catalyst (1.5 g) at 300 psi at 75° in ethanol (5 mL) for 3 h. Vacuum evaporation of the filtered reduction mixture gave an oil (191 mg). Flash chromatography removed 15% unreduced oxime and separated the mixture of isomers. The major product was the previously reported[7] ribo isomer (120 mg); NMR ($CDCl_3$): δ 5.83 (1 H, d, J = 4 Hz, H-1), 4.64 (1 H, dd, $J_1$ = 12.4, $J_2$ = 2.2 Hz, H-5), 4.46-4.55 (2 H, m, H-5 and H-2), 3.94-4.00 (1 H, m, H-4), 3.11 (1 H, dd, $J_1$ = 9.7, $J_2$ = 5 Hz, H-3), 1.56, 1.36 (2 H, 2 s, isopropyl).

3-Amino-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-allofuranose[8], **14**. 3-Deoxy-1,2:5,6-di-O-isopropylidene-3-nitro-α-D-allofuranose[12] (1.0 g, m.p. 112-113 °C) was hydrogenated (Pd-C, $CH_3OH$) to give the corresponding amine (**14**, 0.81 g, 90%) as an oil which solidifed and was crystallized from hexane-ether, m.p. 90-92 °C (lit.95-96 °C[7], 92-93°C[8]. The NMR was not previously reported; NMR ($CDCl_3$): δ 5.76 (1 H, d, $J_1$ = 3.7 Hz, H-1), 4.57 (1 H, dd, $J_1$ = 4.4, $J_2$ = 3.7 Hz, H-2), 4.13 (1 H, dd, $J_1$,$J_2$ = 5.7 Hz, H-6), 4.09 (1 H, dd, $J_1$ = 8.1, $J_2$ = 6.3 Hz, H-5), 4.02 (1 H, dd, $J_1$ = 7.5, $J_2$ = 5.9 Hz, H-6'), 3.62 (1 H, dd, $J_1$ = 9.2, $J_2$ = 6.5 Hz, H-4), 3.14 (1 H, dd, $J_1$ = 9.1, $J_2$ = 4.9, H-3), 1.47, 1.44, 1.34 (12, H 3s, 2 isopropyl).

Methyl 3-Amino-3-deoxy-β-D-ribofuranoside. **15**. The major isomer of **7** (presumably the β-anomer, 1.20 g) was reduced by the general procedure (Pd-C, $CH_3OH$, $CH_3COOH$) to give a crude amine acetate (1.09 g). This crude product was hydrolyzed (10% NaOH, 12 hr, 20°). Thorough extraction ($CH_2Cl_2$) followed by drying ($MgSO_4$) and vacuum evaporation gave an oil which was chromatographed[16]. The major fraction (0.49 g) which solidified on storage was crystallized from hexane, to give a product which corresponded in $^1H$ NMR and melting point 107-108 °C to the literature values[9,21] (108-110°, 107-109 °C) for the β-anomer.

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15. Although purchased previously[11] 90% $H_2O_2$ was no longer commercially available. For these experiments it was prepared by careful removal of the calculated amount of water from 70% $H_2O_2$ by vacuum distillation (20-30 mm) in all glass apparatus with 10-cm long Vigreaux column, vacuum fraction cutter, and 50-cm flask heated by an electrically controlled oil bath, all behind a safety shield. A maximum of 20 mL of 70% hydrogen peroxide was charged to the flask at any one time. The oil bath temperature was not allowed to exceed 55 °C. The water was removed at a maximum take off temperature of 35 °C until the calculated amount of $H_2O$ had been trapped at -60 °C and weighed to give residual 90% $H_2O_2$. The oil bath was lowered and the flask cooled before the vacuum was released and the flask removed. Attemptred oxidations with 70% $H_2O_2$ or with peroxy benzoic acid were unsuccessful.
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