Carbohydrate Research, 52 (1976) 79–86

SYNTHESIS OF GLYCOS-3-YL-α,γ-DIAMINO ACIDS. SYNTHESIS OF FOUR DIASTEREOMERIC SPIRO-3,4′-(*R* AND *S*)-3-DEOXY-1,2:5,6-DI-*O*-ISOPROPYLIDENE-α-D-*ribo*-HEXOFURANOSE)-3′-(*R* AND *S*)-ACETAMIDO-2′-PYRROLIDINONES

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(Received July 30th, 1975; accepted for publication in revised form, July 20th, 1976)

ABSTRACT

Treatment of (*Z*)-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-(methoxycarbonyl)-methylene-α-D-*ribo*-hexofuranose (**1**) with diazomethane in ether afforded the unstable Δ^1- and Δ^2-pyrazolines **2** and **2a**. High-pressure hydrogenation of the latter compounds over Raney nickel afforded a mixture of amines **3**, **5**, **7**, and **9** (in 80% yield), which were separated by chromatography. Acetylation of these compounds yielded the *N*-acetyl derivatives **4**, **6**, **8**, and **10**. X-Ray analysis of compounds **8** and **10** showed them to be spiro-3,4′-(*R*)-(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose)-3′-(*R*)-[and 3′-(*S*)]-acetamido-2′-pyrrolidinone, respectively. The structures of compounds **4** and **6** (determined by chemical means) were the corresponding spiro-3,4′-(*S*)-3′-(*R*)-acetamido-2′-pyrrolidinone and 3′-(*S*)-acetamido-2′-pyrrolidinone, respectively.

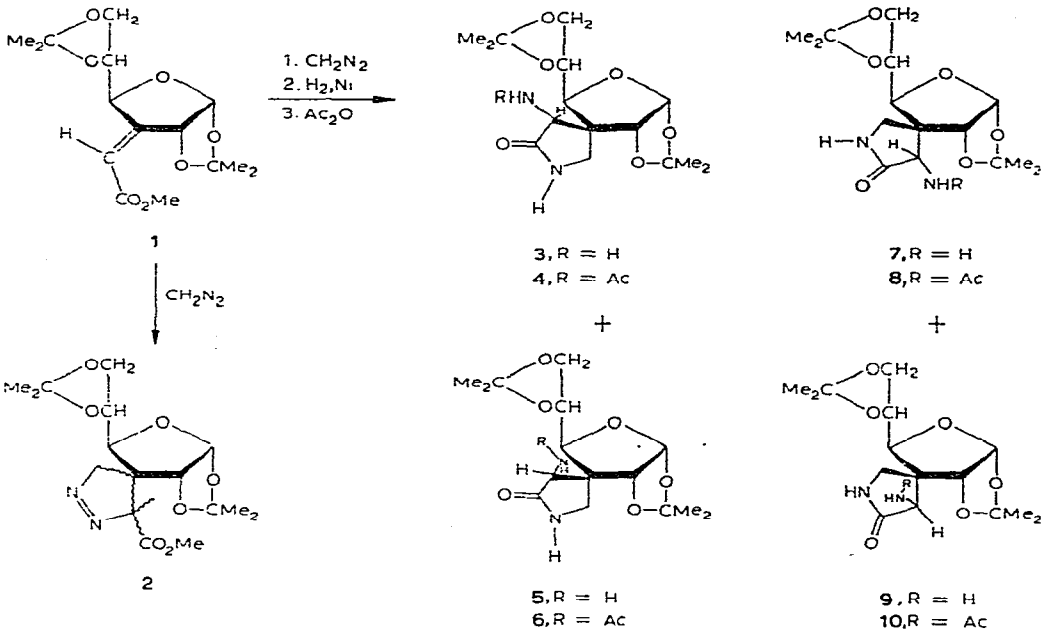
INTRODUCTION

In previous communications[1,2] we have reported a six-step synthesis of glycos-3-yl-α-amino acids and a ten-step synthesis of 3-deoxyglycos-3-yl-α-amino acids. Subsequently, we published a two-step synthesis of the latter compounds by application of the azlactone amino acid synthesis to a 3-ketose[3]. A serious disadvantage of the latter synthesis was the great difficulty encountered in removing the *N*-benzoyl protecting group. These investigations form part of our research programme dealing with syntheses of unusual and normal glycosyl amino acids that are related to the sugar moiety of the polyoxins[4], or in research directed towards the synthesis of *C*-glycosyl amino acids and *C*-nucleosides. In this communication we present a novel, facile route to glycosyl amino acids involving condensation of diazomethane with glycos-3-yl-α,β-unsaturated esters, followed by high-pressure hydrogenolysis of the resultant pyrazolines to afford glycos-3-yl-α,γ-diamino acids, which cyclized intramolecularly to form novel *ribo*-3,4′-spiro-2′-pyrrolidinones.

RESULTS AND DISCUSSION

When (*Z*)-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-(methoxycarbonyl)-methylene-α-D-*ribo*-hexofuranose[5] (**1**) was allowed to react with a slight excess of diazomethane in anhydrous ether for 8 h at 0–3°, a mixture of unstable pyrazolines

(**2** and **2a**) was formed. Column chromatography of the mixture on silica gel H with 4:1 benzene–ethyl acetate afforded mixtures of the Δ^1- and Δ^2-pyrazolines **2** and **2a**, respectively. These could be differentiated by infrared spectroscopy[6,7]. Δ^1-Pyrazolines have been shown to be the primary products of such reactions, although they may tautomerize to the more stable Δ^2-pyrazolines[6,8]. According to the interpretation of



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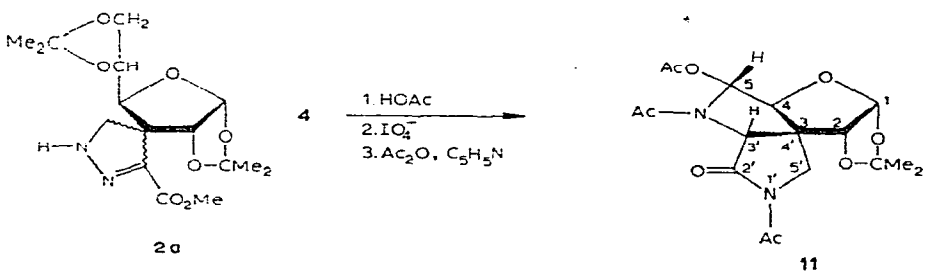
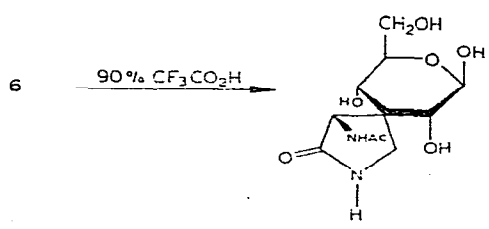


2a

11



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Huisgen[9], reactions of diazomethane with carbon–carbon bonds to form pyrazolines involve a concerted, *cis* cycloaddition process. With unhindered α,β-unsaturated esters, the carbon atom of the diazomethane adds to the double bond at the carbon atom β- to the methoxycarbonyl group. Thus, one might expect stereospecific addition of diazomethane, either from the α or β face of the carbon–carbon double bond, to afford a mixture of Δ^1-pyrazolines **2**. Attempts to determine whether attack of diazomethane occurred from both faces of **1** were unsuccessful because of the instability of product **2**. Product **2a** (possibly a mixture of spiro-Δ^2-pyrazolines) was crystalline. The i.r. spectrum of **2a** showed the presence of a C=N group (peak at 1548 cm^{-1}), thus indicating that the less stable Δ^1-pyrazoline might have tautomerized to the more stable Δ^2-pyrazoline **2a**.

It is noteworthy that Tronchet and coworkers[10] obtained spiro pyrazolines by treating 3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methylene-α-D-*ribo*-hexofuranose with diazomethane and found that the diazomethane added in a reverse manner to that observed by us.

Because the mixture of spiro pyrazolines **2** and **2a** was unstable, decomposing slowly at room temperature to yield intractable mixtures, the product was immediately hydrogenated at 2200 lb. in^{-2} in methanol over Raney nickel. Chromatography of the resultant mixture of carbohydrate amines in silica gel H, using 8:1 ethyl acetate–ethanol as developer, afforded four amines (**3**, **5**, **7** and **9**) in 80% yield. All four compounds exhibited strong infrared absorption at about 1700 cm^{-1}, thus indicating the presence of a 5-membered lactam ring. The lactams (pyrrolidinones) were presumed to be formed through intramolecular cyclization of the amine function with the ester group. The presence of the amino 2′-pyrrolidinones was confirmed by the p.m.r. spectra of the four compounds, which showed that methyl ester peaks were absent and two amino protons were present (resonating in the region τ 7.4 to 8.2), which exchanged rapidly with D_2O. In addition, there was one amide proton resonating in the region τ 2.4–2.9 which exchanged slowly with D_2O. Although the amino 2′-pyrrolidinones gave mass spectra (*m/e* 329) that agreed with their postulated structures, their chemical analyses were unsatisfactory. On conversion into their *N*-acetyl derivatives (**4**, **6**, **8**, and **10**), all afforded crystalline pyrrolidinones that gave elemental analyses in full agreement with the proposed structures. Because of the uncertainty of assigning structures to the four diastereoisomeric pyrrolidones from n.m.r. data, two of the pyrrolidinones (**8** and **10**) were analyzed* by X-ray crystallography[11]. Compound **8** was shown to be spiro-3,4′-(*R*)-(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose)-3′-(*R*)-acetamido-2′-pyrrolidinone and compound **10** was the diastereomeric spiro-3,4′-(*R*)-(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose)-3′-(*S*)-acetamido-2′-pyrrolidinone.

The additional two pyrrolidinones **4** and **6** must therefore be the remaining diastereoisomers formed by addition of diazomethane to the opposite face of the carbon–carbon double bond, followed by reduction. That is, the chirality of the spiro

*Performed by Dr J. Trotter of this department.

junction (C-3) of **4** and **6** should be *S* instead of *R* as in **8** and **10**. The assignment of chirality at C-3 of compounds **4** and **6** was accomplished by a sequence of reactions described by Yoshimura and co-workers[12]. When the glycosyl pyrrolidinones **4** and **6** were deacetonated at O-5–O-6, with subsequent periodate cleavage of the 5,6-diol, the corresponding 5-aldehydo glycosylpyrrolidinones were formed. The p.m.r. spectrum of the aldehydo pyrrolidinone derived from **6** exhibited an aldehyde hydrogen resonance at τ 0.07, whereas the aldehydo pyrrolidinone obtained from **4** showed no aldehyde proton, but an aminal was present. Acetylation of the aminal resulting from **4** afforded a triacetate **11**. The p.m.r. spectrum of the latter showed no coupling between H-4 and H-5, thus indicating that C-5 has the (*R*) configuration. Obviously, the C-5 aldehyde functionality of the periodate-cleaved product from **4** must have undergone intramolecular cyclization with the primary aminoacetyl group to yield the aminal acetate **11**. Thus, compound **4** must be spiro-3,4′-(*S*)-(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose)-3′-(*R*)-acetamido-2′-pyrrolidinone. The remaining diastereomeric pyrrolidinone **6** must, therefore, be spiro-3,4′-(*S*)-(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose)-3′-(*S*)-acetamido-2′-pyrrolidinone.

Interestingly, the rate of acid hydrolysis of the 5,6-*O*-isopropylidene group of compound **6** was about twenty times greater than that of compound **4**. This difference in chemical reactivity might be due to the fact that the basic acetamido group is nearer to the 5,6-*O*-isopropylidene group in compound **4** than in compound **6**, and this factor impedes protonation of the acetal group.

Surprisingly, under the conditions employed, the *E* isomer of compound **1** failed to react with diazomethane. From model studies of the *E* and *Z* unsaturated sugars **1**, it may be observed that the carbon–carbon double bond of the *Z* isomer should be more strained than that of the *E* isomer because of steric interaction of the methoxycarbonyl and 1,2-*O*-isopropylidene groups. Possibly, the greater steric strain in the carbon–carbon double bond of the *Z* than of the *E* isomer accounts for this difference in chemical reactivity of the two isomers.

The production of four diastereoisomers from the mixture of pyrazolines after reduction shows that diazomethane added from both faces of the sugar, This is the first instance, in our laboratory, of both α- and β-attack, and may indicate that a concerted, *cis* attack[9,13] is not operative. Possibly, as suggested by other workers[14,15], the terminal nitrogen atom of the diazomethane first adds to the methine carbon atom of the strained, exocyclic carbon–carbon double bond, with subsequent ring closure to yield the mixture of pyrazolines.

One of the *N*-acetylated spiro pyrrolidinones **6** was hydrolyzed to the free sugar with 80% trifluoroacetic acid in water. After prolonged hydrolysis at room temperature (48 h), both isopropylidene groups were removed, as indicated by p.m.r. and elemental analysis. Interestingly, the free sugar **12** was observed to be exclusively in the β-pyranose form according to its p.m.r. spectrum, which showed the anomeric proton resonance at τ 5.24 displaying a $J_{1,2}$ coupling constant of 8.0 Hz. This large

coupling is indicative of a *trans*-diaxial orientation between H-1 and H-2 on a pyranose ring.

EXPERIMENTAL

General methods. — I.r. spectra were recorded in chloroform solution with a Perkin–Elmer Model 337 spectrometer, and n.m.r. spectra were determined in chloroform-*d* solution with Me_4Si as the internal standard by using a Varian XL-100 spectrometer. Mass spectra were obtained with an HMS-9 spectrometer. Optical rotations were measured at room temperature with a Perkin–Elmer Model 141 automatic polarimeter. All melting points are corrected. Elemental analyses were performed by Mr. P. Borda, Microanalytical Laboratory, University of British Columbia, Vancouver.

Treatment of (Z)-*3-deoxy-1,2;5,6-di*-O-*isopropylidene-3*-C-(*methoxycarbonyl*)-*methylene*-α-D-ribo-*hexofuranose* (**1**) *with diazomethane to afford pyrazolines* **2** *and* **2a**. — To a solution of **1** (2.0 g) in 4 ml of purified diethyl ether at 0° was added a solution of diazomethane (0.42 g) in the same solvent (12 ml). The mixture was kept at 10° (or lower) for 8 h, and the ether was then removed under diminished pressure. The mixture of pyrazolines had to be kept under nitrogen at 0° as it was found to be unstable. An aliquot (450 mg) of this syrup was chromatographed on t.l.c.-grade silica gel (14 × 1.8 cm), with 4:1 benzene–ethyl acetate as developer, to afford the Δ^1-pyrazoline **2** (85 mg, 19%) having R_F 0.24, and the Δ^2-pyrazoline **2a** (255 mg, 56%) having R_F 0.28.

Product **2** was a syrup; $\nu_{max}^{CDCl_3}$ 1723 cm^{-1} (carbonyl); $\lambda_{max}^{Et_2O}$ 298 nm (ε 798); n.m.r. (benzene-d_6): τ 4.14 (d, 1, $J_{1,2}$ 3.0 Hz, H-1), 4.41–4.60 (m), 5.32 (d, 1, H-2), 5.62–6.80 (m), 6.38 (s, 3, CH_3 of methyl ester), and 8.38–8.80 (12, 4 CH_3); *m/e* 369.

Product **2a** crystallized from ether–hexane; m.p. 78–81°, $[\alpha]_D^{25}$ +147.9° (*c* 1, chloroform); $\nu_{max}^{CDCl_3}$ 3460 (NH), 1705 (C=O), and 1548 cm^{-1} (C=N); λ_{max} 291 nm (ε 1050); n.m.r. (benzene-d_6): τ 2.38 (s, 1, exchanges with D_2O), 3.72 (d, 1, $J_{1,2}$ 3.5 Hz, H-1), 5.32 (d, 1, H-2), 5.60–6.20 (m), 6.30 (s, 3, CH_3 of ester), and 8.48–8.80 (12, isopropylidene groups); *m/e* 369.

Hydrogenation of pyrazolines **2** *and* **2a** *to yield spiro-3,4'*-(S *and* R)-(*3-deoxy-1,2:5,6-di*-O-*isopropylidene*-α-D-ribo-*hexofuranose*)-*3'*-(R- *and* S)-*amino-2'-pyrrolidinones* **3**, **5**, **7**, *and* **9**. — The crude mixture of pyrazolines **2** and **2a** (1.6 g) in anhydrous methanol (40 ml) was hydrogenated with Raney nickel (50 mg) as catalyst for 8 h at 200 lb. in^{-2} and 75–80°. The catalyst was filtered off and the filtrate evaporated to afford a mixture of **3**, **5**, **7**, and **9** (1.6 g) as a yellow syrup. An aliquot of the product (1.4 g) was gradient-chromatographed on silica gel H (42 g, 22 × 2.5 cm) with ethyl acetate–ethanol as developer as follows: (*1*) 200 ml of 8:1 ethyl acetate–ethanol, (*2*) 200 ml of 7:1 mixture, (*3*) 200 ml of 5:1 mixture, (*4*) sufficient 3:1 mixture to elute off all components. Compound **3** [the spiro-3,4'-(*S*)-*ribo*-3'-(*R*)-aminopyrrolidinone) (220 mg, 16%, R_F 0.30), was crystallized from ethyl acetate–ethanol; m.p. 123–124°, $[\alpha]_D^{25}$ +50° (*c* 0.9, chloroform); $\nu_{max}^{CDCl_3}$ 1720 cm^{-1} (lactam); n.m.r. ($CDCl_3$): τ 2.79

(s, 1, exchanges with D_2O, lactam NH), 3.85 (d, 1, $J_{1,2}$ 3.6 Hz, H-1), 4.82–5.18 (m), 5.25 (d, 1, H-2), 5.40–5.91 (m), 5.98–6.48 (two doublets, AB system, 2, $J_{5'a,5'b}$ 12 Hz, H-5'a and H-5'b), 7.9 (s, 2, exchanges with D_2O, NH_2), and 8.17–8.60 (12, CH_3); *m/e* (M+1) 329.

Compound **5** [the spiro-3,4'-(*S*)-*ribo*-3'-(*S*)-aminopyrrolidinone] (450 mg, 32%, R_F 0.75) was a syrup, $[\alpha]_D^{25}$ +36.3° (*c* 1.0, chloroform); $\nu_{max}^{CDCl_3}$ 1730 cm^{-1} (lactam); n.m.r. ($CDCl_3$): τ 2.71 (s, 1, exchanges with D_2O, lactam NH), 4.38 (d, 1, $J_{1,2}$ 3.7 Hz, H-1), 5.27 (d, 1, H-2), 5.74–6.41 (m), 6.43–6.95 (two doublets, AB system, 2, $J_{5'a,5'b}$ 11.5 Hz, H-5'a and H-5'b), 7.71 (s, 2, exchanges with D_2O, NH_2), and 8.37–8.80 (12, CH_3); *m/e* (M+1) = 329.

Compound **7** [the spiro-3,4'-(*R*)-*ribo*-3'-(*R*)-aminopyrrolidinone] (185 mg, 14%, R_F 0.06) was a syrup, $[\alpha]_D^{25}$ +88.5° (*c* 1.6, chloroform); $\nu_{max}^{CDCl_3}$ 1710 cm^{-1} (lactam); n.m.r. ($CDCl_3$): τ 2.71 (s, 1, exchanges with D_2O, lactam NH), 4.38 (d, 1, $J_{1,2}$ 3.7 Hz, H-1), 5.27 (d, 1, H-2), 5.74–6.41 (m), 6.43–6.95 (two doublets, AB system, $J_{5'a,5'b}$ 11.5 Hz, H-5'a, H-5'b), 7.71 (s, 2, exchanges with D_2O, NH_2), and 8.37–8.80 (12, CH_3); *m/e* (M+1) 329, (M+2) 330.

Compound **9** [the spiro-3,4'-(*R*)-*ribo*-3'-(*S*)-aminopyrrolidinone] (250 mg, 18%, R_F 0.11) was a syrup, $[\alpha]_D^{25}$ +55.5° (*c* 1.0, chloroform); $\nu_{max}^{CDCl_3}$ 1720 cm^{-1} (lactam); n.m.r. ($CDCl_3$): τ 2.48 (s, 1, exchanges with D_2O, lactam NH), 4.16 (d, 1, $J_{1,2}$ 3.8 Hz, H-1), 5.35 (d, 1, H-2), 5.40–6.23 (m), 6.34–7.03 (two doublets, AB system, $J_{5'a,5'b}$ 11.3 Hz, H-5'a, H-5'b), 7.4–8.0 (s, 2, exchanges with D_2O, NH_2), and 8.28–8.62 (12, CH_3); *m/e* (M+1) 329, (M+2) 330. Attempted sublimation of **3**, **5**, **7**, and **9** gave decomposed products.

Conversion of amino pyrrolidinones into acetamido pyrrolidinones

Spiro-3,4'-(S)-(*3-deoxy-1,2:5,6-di*-O-*isopropylidene*-α-D-ribo-*hexofuranose*)-*3'*-(R)-*acetamido*-**2'**-*pyrrolidinone* (**4**). — To **3** (100 mg) in anhydrous methanol (1 ml) was added acetic anhydride (400 mg) and the mixture was kept for 48 h at room temperature. After the addition of xylene (2 × 1 ml), the solution was evaporated to dryness under vacuum, and the residue crystallized from ethyl–acetate–hexane; m.p. 213–215°, $[\alpha]_D^{25}$ −6.5° (*c* 3.6, chloroform); n.m.r. ($CDCl_3$): τ 3.48 (d, 1, exchanges with D_2O, $J_{NH,H-3'}$ 6.0 Hz, acetamido NH), 3.97 (s, 1, exchanges with D_2O, lactam NH), 4.18 (d, 1, $J_{1,2}$ 4.4 Hz, H-1), 5.01 (d, 1, H-2), 5.45 (d, becomes s in D_2O, H-3'), 5.52–6.22 (m), 6.29, 6.76 (two doublets, AB system, $J_{5'a,5'b}$ 12.1 Hz, H-5'a, H-5'b), 7.98 (s, 3, CH_3 of acetamido group), and 8.42–8.72 (12, CH_3).

Anal. Calc. for $C_{17}H_{26}N_2O_7$: C, 55.13; H, 7.08; N, 7.56. Found: C, 54.50; H, 6.90; N, 7.22.

Spiro-3,4'-(S)-ribo-*3'*-(S)-*acetamido*-**2'**-*pyrrolidinone* (**6**). — Compound **5** was acetylated to afford the acetamido pyrrolidinone **6** by the same procedure as already described, m.p. 217–219°, $[\alpha]_D^{25}$ +28.8° (*c* 1.0, chloroform); n.m.r. ($CDCl_3$): τ 2.36 (d, 1, exchanges with D_2O, $J_{NH,H-3'}$ 8.80 Hz, acetamido NH), 3.92 (s, 1, exchanges with D_2O, lactam NH), 4.34 (d, $J_{1,2}$ 3.1 Hz, H-1), 4.79 (d, becomes s in D_2O, H-3'), 5.18 (m, 1, $J_{4,5}$ 8.5 Hz, $J_{5,6a}$ 4.5 Hz, $J_{5,6b}$ 4.5 Hz, $J_{6a,6b}$ 8.6 Hz, H-6a), 6.13 (m, 1,

H-6b), 6.24 (d, 1, H-4), 6.32–6.50 (m), 7.97 (s, 3, CH_3 of acetamido group), and 8.40–8.79 (12, CH_3).

Anal. Calc. for $C_{17}H_{26}N_2O_7$: C, 55.13; H, 7.08; N, 7.56. Found: C, 55.03; H, 7.20; N, 7.26.

Spiro-3,4'-(R)-(*3-deoxy-1,2:5,6-di-*O-*isopropylidene-α-*D-ribo-*hexofuranose*)-*3'-*(R)-*acetamido-2'-pyrrolidinone* (**8**). — Compound **7** was acetylated to yield **8**, m.p. 261–263°, $[\alpha]_D^{25}$ +108.5° (*c* 0.6, chloroform); n.m.r. ($CDCl_3$): τ 2.66 (s, 1, exchanges with D_2O, lactam NH), 3.09 (d, 1, exchanges with D_2O, $J_{N\ H,H-3'}$ 8.9 Hz, acetamido NH), 4.21 (d, 1, $J_{1,2}$ 3.0 Hz, H-1), 4.76 (d, 1, becomes s in D_2O, H-3'), 5.31 (d, 1, H-2), 5.55–6.17 (m), 6.34, 7.07 (two doublets, AB system, $J_{5'a,5'b}$ 10.2 Hz, H-5'a, and H-5'b), 7.99 (s, 3, CH_3 of acetamido group), and 8.34–8.73 (12, CH_3).

Anal. Calc. for $C_{17}H_{26}N_2O_7$: C, 55.13; H, 7.08; N, 7.56. Found: C, 55.14; H, 7.16; N, 7.43.

Spiro-3,4'-(R)-(*3-deoxy-1,2:5,6-di-*O-*isopropylidene-α-*D-ribo-*hexofuranose*)-*3'-*(S)-*acetamido-2'-pyrrolidinone* (**10**). — Compound **9** was acetylated to afford **10**, m.p. 284–286°, $[\alpha]^{25}$ +98.3° (*c* 1.4, chloroform); n.m.r. ($CDCl_3$): τ 3.27 (s, 1, exchanges with D_2O, lactam NH), 3.78 (d, 1, exchanges with D_2O, $J_{N-H,H-3'}$ 10 Hz, acetamido NH), 4.34 (d, 1, $J_{1,2}$ 2.9 Hz, H-1), 4.67 (d, 1, becomes s in D_2O, H-3'), 5.45 (d, H-2), 5.65–6.37 (m), 6.61, 6.96 (two doublets, AB system, $J_{5'a,5'b}$ 10.9 Hz, H-5'a, H-5'b), 7.98 (s, 3, CH_3 of acetamido group), and 8.50–8.72 (12, CH_3).

Anal. Calc. for $C_{17}H_{26}N_2O_7$: C, 55.13; H, 7.08; N, 7.56. Found: C, 55.13; H, 7.15; N, 7.44.

Conversion of spiro pyrrolidinone 4 into aminal **11**. — A solution of pyrrolidinone **4** (100 mg) in 66% aqueous acetic acid (2 ml) was stirred for 72 h (reaction monitored by t.l.c.) at room temperature and then evaporated to dryness under diminished pressure to yield a syrup (95 mg). After the syrup had been oxidized with aqueous sodium periodate (56.55 mg, 0.25 mmol) at 0°, the solvent was removed by freeze-drying. The residue was extracted with ethyl acetate and the extract then evaporated under diminished pressure to a syrup (49 mg, 53%) that was a mixture of C-5 anomers. Acetylation of the mixture (150 mg) with acetic anhydride (600 mg) and pyridine (1 ml) required 4 days (as evidenced by t.l.c.). After removal of the acetic anhydride under diminished pressure, *p*-xylene (5 × 3 ml) was added to the residue and removed by evaporation under diminished pressure to afford a syrup (160 mg). Column chromatography of this syrup (silica gel H, 30 g, 8:1 ethyl acetate–ethanol) afforded the fully acetylated aminal **11** (80 mg, 42%), which was crystallized from ether–hexane; m.p. 156–157°, $[\alpha]_D^{25}$ +164 (*c* 0.5, chloroform); n.m.r. ($CDCl_3$): τ 3.61 (s, 1, H-5), 4.18 (d, 1, $J_{1,2}$ 3.6 Hz, H-1), 4.75 (s, 1, H-3'), 5.27 (d, 1, H-2), 5.47 (s, 1, H-4), 5.61–6.25 (two doublets, 2, AB system, $J_{5'a,5'b}$ 12.0 Hz, H-5'a and H-5'b), 7.54, 7.70, 8.06 (s, 9, CH_3 of acetate and of acetyl groups), and 8.47, 8.68 (s, 6, CH_3); *m/e* 382.4.

Anal. Calc. for $C_{17}H_{22}N_2O_8$: C, 53.40; H, 5.80; N, 7.33. Found: C, 53.53; H, 5.83; N, 7.09.

Conversion of pyrrolidinone **6** *into an aldehydo pyrrolidinone.* — A solution of

pyrrolidinone **6** was hydrolyzed with 66% aqueous acetic acid for 5.5 h (until the reaction was complete, as evidenced by t.l.c.). The hydrolyzed product (54 mg) was oxidized with sodium metaperiodate as already described to afford a product that crystallized from ethanol–hexane; m.p. 200–205°; n.m.r. ($CDCl_3$): τ 0.14 (s, 1, H-5 aldehyde), 1.81 (d, 1, exchanges with D_2O, $J_{N-H,H-3}$ 9.1 Hz, acetamido NH), 2.73 (s, 1, exchanges with D_2O, lactam NH), 4.21 (d, 1, $J_{1,2}$ 3.1 Hz, H-1), 4.25–6.58 (m), 5.29 (d, 1, H-2), 2.00 (s, 3, CH_3 of acetamido group), and 8.40–8.80 (6, CH_3); *m/e* 297 (M − 1).

Spiro-3,4'-(S)*-(3-deoxy-β-*D*-*ribo*-hexopyranose)-3'-*(S)*-acetamido-2'-pyrrolidinone* (**12**). — The spiro pyrrolidinone derivative **6** (30 mg) was hydrolyzed in 80% aqueous trifluoroacetic acid (1 ml) for 48 h at 25°. At this time the reaction was complete according to t.l.c. (5:1 ethyl acetate–ethanol). The solution was evaporated under diminished pressure to a syrup. Toluene was added and the solution was reconcentrated to a glass. To remove starting material, the product was passed through a column of charcoal (0.5 cm × 4 cm) with 10% aqueous methanol. The 10th to 30th ml of eluent contained the free sugar (10 mg). This sample was further purified by dissolving in pyridine (10 ml) and filtration to remove inorganic impurities. The pyridine solution was evaporated to a glass, which was dissolved in ethanol (1.0 ml) and hexanes were added to cause precipitation. The product was collected by centrifugation to yield **12** (7 mg, 30%); m.p. 141–145°, $[\alpha]_D^{25}$ +19.8° (*c* 0.4, ethanol); n.m.r. (Me_2SO-d_6): τ 2.11 (s, 1, lactam NH), 2.48 (d, 1, $J_{NH,3}$ 9.0 Hz, acetamido NH), 4.84 (d, 1, H-3'), 5.24 (d, 1, $J_{1,2}$ 8.0 Hz, H-1), 5.32 (broad s, 4, OH), 5.6–6.8 (complex, 7), and 7.76 (s, 3, CH_3 acetate).

Anal. Calc. for $C_{11}H_{18}N_2O_7$: C, 45.52; H, 6.25; N, 9.65. Found: C, 45.40; H, 6.35; N, 9.85.

ACKNOWLEDGMENT

The authors thank the National Research Council of Canada for financial support.

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