Pergamon

Tetrahedron: *Asymmetry* 12 (2001) 1573–1577

TETRAHEDRON: *ASYMMETRY*

Synthesis and epimerization of 10-*N*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl)-(11a*S*)-pyrrolo[2,1-*c*][1,4]benzodiazepin-5,11-dione

Driss Bouhlal,[a] Patrick Martin,[b,*] Mohamed Massoui,[a] Guy Nowogrocki,[c] Serge Pilard,[b] Pierre Villa[b] and Gérard Goethals[b]

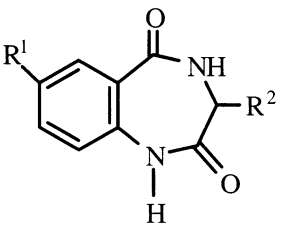
[a]*Laboratoire de Chimie des Agroressources, Faculté des Sciences, Université Ibn Tofaïl, Kénitra, Maroc*
[b]*Laboratoire des Glucides, Université de Picardie Jules Verne, 33 rue Saint Leu, F-80039 Amiens, France*
[c]*Laboratoire de Cristallochimie et Physicochimie du Solide, ENSC Lille, F-59652 Villeneuve d'Ascq, France*

Received 13 April 2001; accepted 19 June 2001

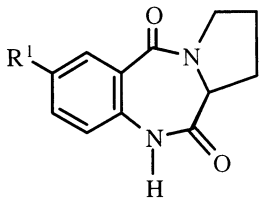
Abstract—The reaction of the 1,2:3,4-di-*O*-isopropylidene-6-*O*-tosyl-α-D-galactopyranose **2** with (11a*S*)-pyrrolo[2,1-*c*][1,4]benzodiazepin-5,11-dione **1**, prepared from L-proline and isatoic anhydride, gave two products which were previously reported as conformational isomers. In this work, an X-ray crystallographic study showed these to be the diastereomeric pair (11a*S*)- and (11a*R*)-10-*N*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl)-pyrrolo[2,1-*c*][1,4]benzodiazepin-5,11-diones as a consequence of C(11a) epimerization in the benzodiazepine moiety during glycosylation under basic reaction conditions. The hydrosolubility of the deprotected products were compared with those of the analogous benzodiazepine derivatives.

1. Introduction

The effects of both 1,4-benzodiazepin-2,5-diones (**A**) and pyrrolo[2,1-*c*][1,4]benzodiazepin-5,11-diones (**B**) on the nervous system are abundantly described in the literature;[1–4] moreover CpIIbIIIa antagonist,[5] antitumoral and antibiotic activities[6–12] are observed with these compounds but their very low hydrosolubility can restrict their applications.



A



B

In a recent work,[13] we attached glucopyranosyl and xylityl groups to N(1) of benzodiazepine systems of type **A** to increase the water solubility and to confer amphiphilic properties. The ^{13}C NMR spectra of the acetal protected glycoderivatives and corresponding deacetalized compounds showed split signals, whereas related unsubstituted benzodiazepines showed single signals. This phenomenon was interpreted as the consequence of a low N(1) conformer interconversion for the glycoderivatives (Fig. 1, Su = acetal protected and deprotected polyhydroxylated groups), while benzodiazepines (**A**) show coalescence to form a single resonance.

A similar interpretation was applied to the analogous glycobenzodiazepines of type **B**. The interpretations previously reported[14] have now been superceded following the isolation and full characterization, including NMR and X-ray analysis, of the diastereoisomers obtained from condensation of the chiral (11a*S*)-pyrrolo[2,1-*c*][1,4]benzodiazepin-5,11-dione **1** with the diacetonegalactose tosylate **2**.[15] In addition, we compared the hydrosolubility of deprotected glycosylated products to those of analogous benzodiazepine **1** derivatives.

2. Results and discussion

The (11a*S*)-pyrrolo[2,1-*c*][1,4]benzodiazepin-5,11-dione **1**, obtained from reaction of L-proline and isatoic anhy-

* Corresponding author. E-mail: patrick.martin@u-picardie.fr

0957-4166/01/$ - see front matter
PII: S0957-4166(01)00282-8

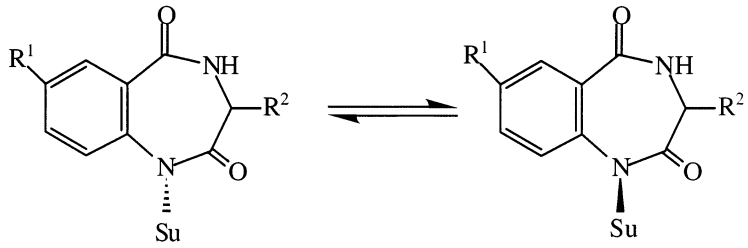


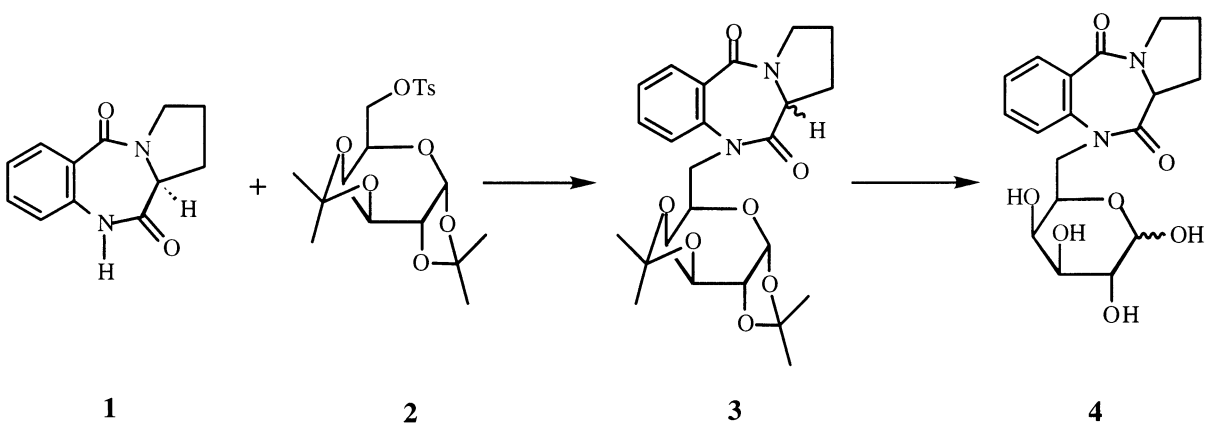
Figure 1. Conformational isomerism in benzodiazepine derivatives.

dride according to the method of Kamal,[9] was condensed with 6-*O*-tosyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose **2** in DMF at 130°C, in the presence of K_2CO_3 and Bu_4NBr, as previously described[14] (Scheme 1), to obtain 10-*N*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl)-pyrrolo[2,1-*c*]-[1,4]benzodiazepin-5,11-diones **3** in 60% yield after flash silica gel chromatography, which appeared at first to be a pure product by TLC. However, the ^{13}C NMR spectrum in Me_2SO-d_6 at room temperature shows split signals for the product **3** but no splitting is seen for the benzodiazepine **1**. Also, no coalescence was observed in the ^{13}C NMR spectrum of **3** when the temperature increased from 25 to 80°C; this indicates either very slow interconversion of the N(10) isomer or the presence of an alternative isomer in the mixture. Careful silica gel chromatography of **3** allowed the separation of the isomers **3a** and **3b**. Therefore, the split signals observed for **3** were in fact the result of a single signal observed for each of the diastereoisomers **3a** and **3b** spectra. Moreover, **3a** and **3b** have different optical rotations, and an X-ray crystallographic study (Table 1) indicates that **3a** forms orthorhombic crystal with absolute (*R*) configuration at C(11a) (Fig. 2), whereas **3b** forms monoclinic crystal with (*S*) absolute configuration (Fig. 3).

Table 1. Crystallographic data for compounds **3a** and **3b** at room temperature

Compound	**3a**	**3b**
Space group	$P2_12_12_1$	$P2_1$
Crystal size (mm^3)	$0.35\times0.30\times0.25$	$0.30\times0.25\times0.20$
a (Å)	9.466(3)	9.157(2)
b (Å)	10.549(3)	9.840(2)
c (Å)	23.824(7)	13.489(3)
α (°)	90.0	90.0
β (°)	90.0	101.91(1)
γ (°)	90.0	90.0
V ($Å^3$)	2379(1)	1189.3(4)
Z	4	2
Linear abs coeff (μ mm^{-1})	0.094	0.094
D_{calcd} (g cm^{-3})	1.30	1.28
θ limits (°)	2–23.4	2–23.3
hkl limits	−10, 10; −11, 11; −26, 26	−10, 10; −10, 10; −14, 14
Number of data collected	12623	7366
Number of intensities $I>2\sigma(I)$	2343	2426
R_1	0.0430	0.0430
wR_2	0.0826	0.1037
Goodness of fit	0.971	0.802
Number of variables	317	316

These results suggest that during the condensation step, the chiral benzodiazepine **1** and/or the condensed product undergoes racemization at C(11a) catalysed by K_2CO_3. This was verified by submitting both compounds **1** and **3a** to the same conditions as used in the condensation step; then optical rotation values for the recovered products were much lower (Table 2) than those initially observed for **1** and **3a**, respectively. Moreover the ^{13}C NMR spectrum of the recovered product from **3a** showed a split signal in accordance with the isomeric mixture **3**.



1 **2** **3** **4**

Scheme 1. Synthesis of the 10-*N*-(6-deoxy-D-galactopyranos-6-yl)-pyrrolo[2,1-*c*][1,4]benzodiazepin-5,11-diones **4**.

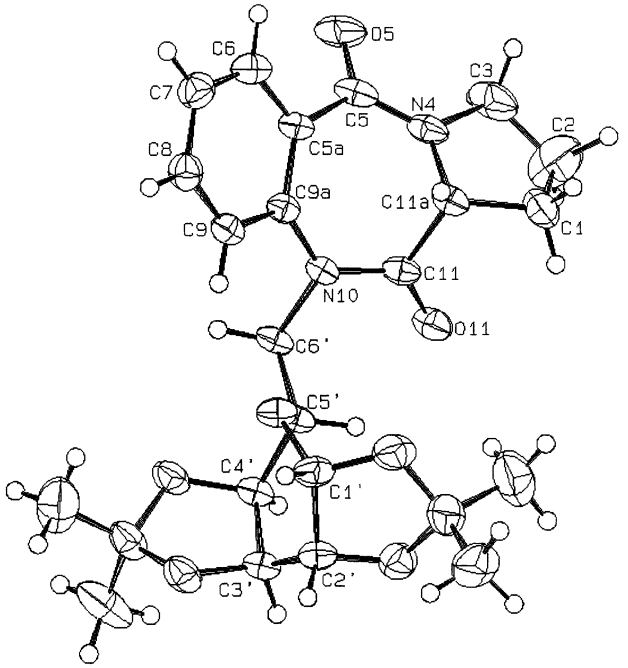


Figure 2. X-Ray crystal structure of **3a**.

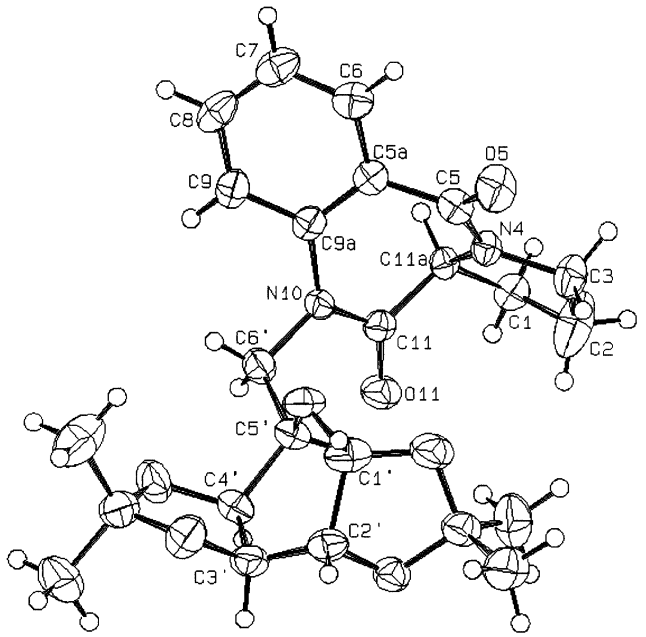


Figure 3. X-Ray crystal structure of **3b**.

Table 2. Optical rotation variation of **1** and **3a** ($CHCl_3$, 25°C) after treatment with K_2CO_3 (0.5 equiv.) in DMF at 130°C

Compound	**1**	**3a**
t_0	500	−152
t_0+72 h	21	−16

Compounds **3a** and **3b** were deprotected with 9:1 CF_3COOH–H_2O to obtain the corresponding 10-*N*-(6-deoxy-D-galactopyranos-6-yl)-pyrrolo[2,1-*c*][1,4]-benzodiazepin-5,11-diones **4a** and **4b** in 76 and 72% yield, respectively. During this reaction the configuration at C(11a) is preserved (no split signals were observed in the ^{13}C NMR).

A hydrosolubility study showed that the galactopyranosyl group increases the water solubility (Sw) more than 500 times relative to the benzodiazepine **1** (0.2×10^{-3} mol L^{-1} for **1** and $115–120\times10^{-3}$ mol L^{-1} for **4a** and **4b**, at 25°C). Similar effects were observed with analogous glycobenzodiazepines.[14] However, the results shown in Table 3 indicate that the hydrosolubility is also affected by differences in structure of the hydrophilic moiety, since in spite of the presence of four OH groups in all the glycoderivatives compared, the glucopyranosyl forms show the highest Sw value. Hydrosolubility in the other compounds is reduced, presumably due to both the steric hindrance of the hydrophobic moiety near a *cis* OH group and the competitive intramolecular hydrogen bonds between neighbouring *cis* OH groups, which reduce the intermolecular hydrogen bonding with water molecules.

3. Experimental

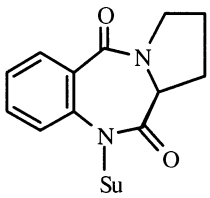
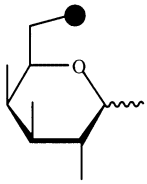
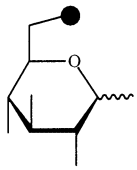
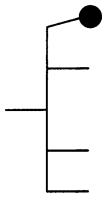
3.1. General methods

Melting points were determined on an electrothermal automatic apparatus, and are uncorrected. Optical rotations, for solutions in $CHCl_3$ or MeOH, were measured with a digital polarimeter JASCO model DIP-370 using a sodium lamp at 25°C. For deprotected compounds, optical rotations were measured after 72 h at equilibrium in MeOH. Infrared spectra were recorded on a Perkin–Elmer 1750 IR Fourier Transform spectrophotometer using KBr pellets. NMR spectra were recorded with a Bruker WB-300 instrument for solutions in $CDCl_3$, Me_2SO-d_6 and C_5D_5N (internal Me_4Si). All compounds were characterized by acquisition of ^1H, ^{13}C, DEPT, ^1H–^1H COSY and ^1H–^{13}C correlated experiments. Mass spectra were obtained by positive ESI-MS using a Micromass Q-TOF hybrid quadrupole/time-of-flight instrument (Micromass UK Ltd). Elemental analyses were performed by the Laboratoire de Chimie Organique de l'Université de Champagne (Reims, France). Analytical TLC was performed on Merck aluminium backed silica gel (Silica Gel F254). Column chromatography was performed on silica gel (60 mesh, Matrex) by gradient elution with hexane–acetone.

3.2. X-Ray diffraction

The X-ray diffraction measurements were performed on an AXS Bruker diffractometer with a CCD detector (λMo Kα = 0.71069 Å, graphite monochromator, T = 294 K, ω scans). Absorption correction was not necessary. Structure solution was obtained by direct methods (SHELXS-97). Refinement by SHELXL-97 program. Hydrogen atoms were refined in a constrained geometry and their thermal parameters were assigned 1.2 times the value of the atom they were bound to.

Table 3. Water solubility (Sw, 10^{-3} mol L^{-1}) of benzodiazepine derivatives at 25°C

		Su			
					
	H				
Sw	0.18^{14}	115	**4a**	180^{14}	31^{14}
		120	**4b**		

3.3. Water solubility (Sw)

Water solubility (Sw) was determined by stirring excess compound in water for 3 h at 50°C and then leaving it for 2 days at 25°C. Solubility values were obtained from the difference between initial compound weight and the residue recovered on a glass filter. Using this process, none of the compounds were hydrolyzed.

3.4. Procedure for condensation step

To a solution of pyrrolo[2,1-*c*][1,4]benzodiazepin-5,11-dione **1** (1.5 g, 6.9 mmol), K_2CO_3 (0.5 g, 3.6 mmol) and Bu_4NBr (0.2 g, 0.6 mmol) in DMF (100 mL), at 130°C, was added 1,2:3,4-di-*O*-isopropylidene-6-*O*-tosyl-α-D-galactopyranose **2** (2.9 g, 6.9 mmol). When no more starting material was detected by TLC, the mixture was concentrated under reduced pressure. The residue was extracted with Et_2O–H_2O. The organic phase was separated, washed with water (twice), dried (Na_2SO_4) and concentrated under diminished pressure. The crude product was purified by column chromatography on 100 g of silica gel using 9:1 hexane–acetone to give the product **3** in 60% yield (1.9 g, 4.1 mmol), which appeared pure on TLC control; mp = 140°C; $[\alpha]_D^{25}$ = +43.2 (*c* 1.0, $CHCl_3$). A larger chromatographic column (200 g of silica gel for 1.7 g of **3**) was used with a hexane–acetone gradient of 19:1–10:1 to initially give **3a** as a white crystalline solid (0.83 g, 39% overall), followed by **3b** as a white crystalline solid (0.80 g, 38% overall).

3a: mp 173°C; $[\alpha]_D^{25} = -152.5$ (*c* 0.9, $CHCl_3$); υ_{max} (KBr) 1677.5, 1640.0 cm^{-1} (C=O); δ_H ($CDCl_3$, 300 MHz) 7.88 (dd, 1H, $J_{6,7}$ = 7.8 Hz, $J_{6,8}$ = 1.6 Hz, H-6), 7.77 (dd, 1H, $J_{8,9}$ = 8.3 Hz, $J_{7,9}$ = 0.9 Hz, H-9), 7.50 (dd, 1H, H-8), 7.27 (dd, 1H, $J_{7,8}$ = 8.1 Hz, H-7), 5.58 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 4.62 (dd, 1H, $J_{2,3}$ = 7.9 Hz, $J_{3,4}$ = 2.3 Hz, H-3), 4.43 (dt, 1H, $J_{5,6a}$ = 8.9 Hz, $J_{4,5} = J_{5,6b}$ = 2.5 Hz, H-5), 4.32 (dd, 1H, H-2), 4.26 (dd, 1H, H-4), 4.10 (dd, 1H, $J_{11a,2a}$ = 8.0 Hz, $J_{11a,2b}$ = 1.6 Hz, H-11a), 4.09 (dd, 1H, $J_{6a,6b}$ = 14.6 Hz, $J_{5,6b}$ = 2.9 Hz, H-6b), 3.82 (m, 1H, H-3b), 3.79 (dd, 1H, H-6a), 3.54 (m, 1H, H-3a), 2.66 (m, 1H, H-1b), 2.12 (m, 1H, H-2b), 2.00 (m, 1H, H-2a), 1.96 (m, 1H, H-1a), 1.45–1.31 (4s, 12H, CMe_2); δ_C ($CDCl_3$, 75.5 MHz) 169.6 (C-11), 165.6 (C-5), 140.9 (C-9a), 132.5 (C-8), 130.6 (C-5a), 130.2 (C-6), 126.0 (C-7), 124.7 (C-9), 109.8, 109.3 (*C*Me_2), 96.8 (C-1), 72.2 (C-4), 71.3 (C-3), 70.9 (C-2), 65.5 (C-5), 57.5 (C-11a), 52.2 (C-6), 47.0 (C-3a), 27.0 (C-1a), 26.4–24.7 (C*Me*$_2$), 24.3 (C-2a). ESI-MS; $[M+H]^+$: *m*/*z* 459, $[M+Na]^+$: *m*/*z* 481. HR-MS; $[M+H]^+$, found 459.2151, $C_{24}H_{31}N_2O_7$ requires 459.2131. Anal. calcd for $C_{24}H_{30}N_2O_7$ (458.50): C, 62.87; H, 6.59; N, 6.11; found: C, 62.60; H, 6.49; N, 6.02%.

3b: mp 182°C; $[\alpha]_D^{25}$ = +199.6 (*c* 1.2, $CHCl_3$); υ_{max} (KBr) 1677.7, 1641.4 cm^{-1} (C=O); δ_H ($CDCl_3$, 300 MHz) 7.88 (dd, 1H, $J_{6,7}$ = 7.8 Hz, $J_{6,8}$ = 1.7 Hz, H-6), 7.46 (dd, 1H, $J_{7,8}$ = 7.6 Hz, $J_{8,9}$ = 8.0 Hz, H-8), 7.25 (dd, 1H, H-7), 7.22 (d, 1H, H-9), 5.26 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1), 4.51 (dd, 1H, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 7.9 Hz, H-3), 4.48 (dd, 1H, $J_{6a,6b}$ = 13.6 Hz, $J_{5,6b}$ = 3.4 Hz, H-6b), 4.15 (dd, 1H, H-2), 4.11 (dd, 1H, $J_{4,5}$ = 1.7 Hz, H-4), 4.10 (m, 1H, H-5), 4.02 (dd, 1H, $J_{11a,1a}$ = 6.1 Hz, $J_{11a,1b}$ = 2.1 Hz, H-11a), 3.81 (m, 1H, H-3b), 3.72 (dd, 1H, $J_{5,6a}$ = 9.0 Hz, H-6a), 3.49 (m, 1H, H-3a), 2.66 (m, 1H, H-1b), 2.04 (m, 1H, H-2b), 1.96 (m, 2H, H-1a, H-2a), 1.51–1.30 (4s, 12H, CMe_2); δ_C ($CDCl_3$, 75.5 MHz) 170.1 (C-11), 165.4 (C-5), 141.2 (C-9a), 132.1 (C-8), 131.5 (C-5a), 130.3 (C-6), 126.1 (C-7), 123.7 (C-9), 109.8, 108.8 (*C*Me_2), 96.6 (C-1), 71.7 (C-4), 71.4 (C-3), 70.6 (C-2), 65.5 (C-5), 57.7 (C-11a), 50.2 (C-6), 46.6 (C-3a), 26.9 (C-1a), 26.2–4.9 (C*Me*$_2$), 24.1 (C-2a). ESI-MS; $[M+H]^+$: *m*/*z* 459, $[M+Na]^+$: *m*/*z* 481. HR-MS; $[M+H]^+$, found 459.2119, $C_{24}H_{31}N_2O_7$ requires 459.2131. Anal. calcd for $C_{24}H_{30}N_2O_7$ (458.50): C, 62.87; H, 6.59; N, 6.11; found: C, 62.71; H, 6.64; N, 6.20%.

3.5. General procedure for deprotection of 3a and 3b

Compounds **3a** and **3b** (0.5 g, 1.1 mmol) were each added to a stirred solution of 9:1 CF_3COOH–H_2O (5 mL) at 20°C. After 1 h, the solution was concentrated to dryness under diminished pressure. The crude product, in each case, was purified by column chromatography using 1:7 hexane–acetone and the resulting

solid recrystallized in Et_2O to give **4a** as a white crystalline solid (0.31 g, 0.84 mmol, 76%, $\alpha/\beta = 9:11$) and **4b** as a white crystalline solid (0.30 g, 0.80 mmol, in 74%, $\alpha/\beta = 2:3$).

4a: $\alpha/\beta = 9:11$; mp 89°C; $[\alpha]_D^{25}$ −175.6 (*c* 0.9, 72 h, MeOH); υ_{max} (KBr) 3396 cm^{-1} (O-H, large), 1676.6, 1620.3 cm^{-1} (C=O). ESI-MS; $[M+H]^+$: *m/z* 379, $[M+Na]^+$: *m/z* 401. HR-MS; $[M+Na]^+$, found 401.1292, $C_{18}H_{22}N_2O_7Na$ requires 401.1325. Anal. calcd for $C_{18}H_{22}N_2O_7$ (378.38): C, 57.14; H, 5.86; N, 7.40; found: C, 57.21; H, 5.91; N, 7.51%. **4a** β anomer; δ_H (C_5D_5N, 300 MHz) 8.19 (d, 1H, $J_{8,9} = 8.1$ Hz, H-9), 8.10 (dd, 1H, $J_{6,7} = 7.7$ Hz, $J_{6,8} = 1.7$ Hz, H-6), 7.35 (ddd, 1H, $J_{7,8} = 7.8$ Hz, H-8), 7.20 (masked by C_5D_5N), 5.04 (d, 1H, $J_{1,2} = 7.7$ Hz, H-1), 4.70 (m, 1H, H-6b), 4.48 (dd, 1H, $J_{2,3} = 9.4$ Hz, H-2), 4.38 (m, 1H, $J_{6a,6b} = 11.4$ Hz, H-6a), 4.35 (m, 1H, H-5), 4.31 (d, 1H, $J_{3,4} = 3.3$ Hz, H-4), 4.07 (dd, 1H, H-3), 3.94 (dd, 1H, $J_{3a,11a} = 6.9$ Hz, $J_{3b,11a} = 13.1$ Hz, H-11a), 3.78 (m, 1H, H-3b), 3.49 (m, 1H, H-3a), 2.62 (m, 1H, H-1b), 2.00 (m, 1H, H-1a), 1.72 (m, 2H, H-2); δ_C (C_5D_5N, 75.5 MHz) 170.0 (C-11), 165.8 (C-5), 141.0 (C-9a), 132.3 (C-8), 130.1 (C-6), 126.0 (C-7), 99.5 (C-1), 75.2 (C-3), 73.9 (C-2), 72.5 (C-5), 70.9 (C-4), 57.7 (C-11a), 52.4 (C-6), 46.8 (C-3), 26.9 (C-1), 24.0 (C-2).

4b: $\alpha/\beta = 2:3$; mp 75.2°C; $[\alpha]_D^{25}$ 234.4 (*c* 0.9, 72 h, MeOH); υ_{max} (KBr) 3392 cm^{-1} (O-H, large), 1676.6, 1617.1 cm^{-1} (C=O). ESI-MS; $[M+H]^+$: *m/z* 379, $[M+Na]^+$: *m/z* 401. HR-MS; $[M+Na]^+$, found 401.1296, $C_{18}H_{22}N_2O_7Na$ requires 401.1325. Anal. calcd for $C_{18}H_{22}N_2O_7$ (378.38): C, 57.14; H, 5.86; N, 7.40; found: C, 57.19; H, 5.83; N, 7.35%. **4b** β anomer; δ_H (C_5D_5N, 300 MHz) 8.01 (dd, 1H, $J_{6,7} = 7.7$ Hz, $J_{6,8} = 1.6$ Hz, H-6), 7.45 (d, 1H, $J_{8,9} = 7.4$ Hz, H-9), 7.34 (ddd, 1H, $J_{7,8} = 7.5$ Hz, H-8), 7.20 (dd, masked by C_5D_5N, H-7), 5.04 (m, 1H, H-6b), 4.91 (d, 1H, $J_{1,2} = 7.7$ Hz, H-1), 4.29 (m, 1H, H-6a), 4.26 (t, 1H, $J_{2,3} = 8.0$ Hz, H-2), 4.22 (t, 1H, $J_{3,4} = 3.3$ Hz, H-4), 4.18 (m, 1H, H-5), 4.03 (m, 1H, H-11a), 3.95 (dd, 1H, H-3), 3.73 (m, 1H, H-3b), 3.50 (m, 1H, H-3a), 2.68 (m, 1H, H-1b), 2.02 (m, 2H, H-2), 1.80 (m, 2H, H-1a); δ_C (C_5D_5N, 75.5 MHz) 170.2 (C-11), 166.6 (C-5), 141.7 (C-9a), 132.2 (C-8), 129.8 (C-6), 125.8 (C-7), 99.5 (C-1), 75.1 (C-3), 73.8 (C-2), 73.6 (C-5), 70.6 (C-4), 58.0 (C-11a), 50.9 (C-6), 46.7 (C-3), 26.9 (C-1), 24.1 (C-2).

References

1. Wright, W.; Brabander, H.; Greenblatt, E.; Day, I.; Hardy, R. *J. Med. Chem.* **1978**, *21*, 1087.
2. Kamal, A.; Venugopal Rao, N. *Chem. Commun.* **1996**, 385.
3. Puvvada, M.; Forrow, S.; Hartley, J.; Stephenson, P.; Gibson, I.; Jenkins, T.; Thurston, D. *Biochemistry* **1997**, *36*, 2478.
4. Wagner, J.; Wagner, M. L.; Hening, W. A. *Ann. Pharmacol.* **1998**, *32*, 680.
5. Blackburn, B.; Lee, A.; Baier, M.; Kohl, B.; Olivero, A.; Matamoros, R.; Robarge, K.; McDowell, R. *J. Med. Chem.* **1997**, *40*, 717.
6. Thurston, D.; Bose, D.; Howard, P.; Jenkins, T.; Leoni, A.; Baraldi, P.; Guitto, A.; Cacciari, B.; Kelland, L.; Foloppe, M. P.; Rault, S. *J. Med. Chem.* **1999**, *42*, 1951.
7. Baraldi, P.; Cacciari, B.; Guitto, A.; Leoni, A.; Romagnoli, R.; Spalluto, G.; Mongelli, N.; Howard, P.; Thurston, D.; Bianchi, N.; Gambari, R. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3019.
8. Thurston, D.; Subhas Bose, D. *Chem. Rev.* **1994**, *94*, 433.
9. Kamal, A.; Praveen Reddy, B.; Narayan Reddy, B. *Tetrahedron Lett.* **1996**, *37*, 6803.
10. Jones, G.; Davey, C.; Jenkins, T.; Kamal, A.; Kneale, G.; Neidle, S.; Webster, G.; Thurston, D. *Anti Cancer Drug Design* **1990**, *5*, 249.
11. Kamal, A.; Damayanthi, Y.; Narayan Reddy, B.; Lakminarayana, B.; Praveen Reddy, B. *Chem. Commun.* **1997**, 1015.
12. Hurley, L.; Reck, T.; Thurston, D.; Langley, D.; Holden, K.; Hertzberg, R.; Hoover, J.; Gallagher, G.; Faucette, L.; Mong, S.; Johnson, R. *Chem. Res. Toxicol.* **1998**, *1*, 258.
13. Bouhlal, D.; Godé, P.; Goethals, G.; Massoui, M.; Villa, P.; Martin, P. *Carbohydr. Res.* **2000**, *329*, 207.
14. Bouhlal, D.; Godé, P.; Goethals, G.; Massoui, M.; Villa, P.; Martin, P. *Heterocycles* **2001**, *55*, 303.
15. Goueth, P.; Ramiz, A.; Ronco, G.; Mackenzie, G.; Villa, P. *Carbohydr. Res.* **1995**, *266*, 171.