Carbohydrate Research, 253 (1994) 307–316
Elsevier Science B.V., Amsterdam

Note

Preparation of 1-bromo-1-nitro-D-*galacto*(and -D-*manno*)-hept-1-enitols and their 1,3-dipolar cycloaddition reactions with diazoalkanes

Manuel Mancera, Enrique Rodríguez, Isaac Roffé and Juan A. Galbis *

Department of Organic and Pharmaceutical Chemistry, University of Seville, 41071 Seville (Spain)

(Received November 3rd, 1992; accepted July 16th, 1993)

In preceding articles[1,2], we have described stereoselective syntheses of nitropyrazolines by 1,3-dipolar cycloaddition of diazoalkanes to sugar nitro-olefins having the D-*galacto* and D-*manno* configurations. We now report the preparation of two new sugar nitro-olefins (**5** and **6**) bearing bromine as another functional group attached to the α-position, and their reactions with diazoalkanes.

These compounds were prepared from (*E*)-3,4,5,6,7-penta-*O*-acetyl-1,2-dideoxy-1-*C*-nitro-D-*galacto*(and -D-*manno*)-hept-1-enitol (**1** and **2**)[3,4] by bromination and dehydrobromination of the resultant *vic*-dibromides. The addition of bromine to nitro-olefins in nonpolar solvents can be the result of a competition between Ad_E2 and Ad_E3 mechanisms[5]. Both are stereospecific reactions and only two of the four possible isomers are formed. Thus, in the bromination of **1** and **2**, crystalline solids were isolated, in high yields, and identified as mixtures of the two diastereomeric 1,2-dibromo-1,2-dideoxy-2-*C*-nitroheptitols (**3**,**3′**, 85 : 15 ratio; and **4**,**4′**, 94 : 6 ratio), which could not be resolved chromatographically. The 1,2-elimination of hydrogen bromide from the mixture of dibromides gave the bromonitro-olefins **5** and **6**. The conditions employed must promote a *syn*-elimination[5] to give the *Z*-olefins. This configuration is in agreement with previous results on this reaction[6] and could be inferred from the chemical shifts of the olefinic protons (7.33 and 7.44 ppm).

The favored conformation of **5**, in solution, must be similar to that shown for other sugar olefins having D-*galacto*[1,7] and D-*manno*[2] configurations previously described, in which H-2 and H-3 have an *anti* disposition ($J_{2,3}$ 7.9 Hz), H-3 is eclipsed with the ethylenic bond, and no 1,3-parallel interactions exist among the acetoxyl groups (Fig. 1). In this conformation, the 1*si*,2*re* face of the nitro-olefin is sterically hindered by the sugar chain. A similar conformation is also proposed for

* Corresponding author.

SSDI 0008-6215(93)E0274-5

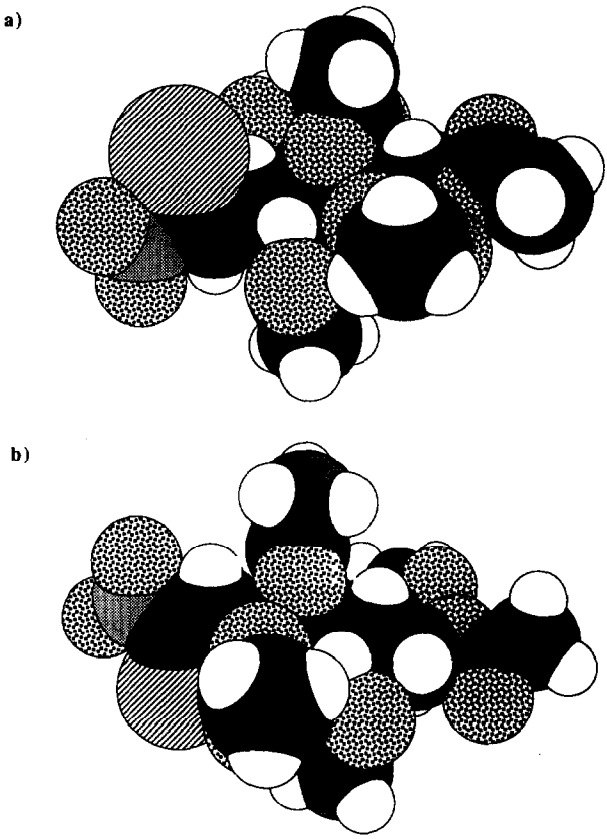


Fig. 1. Space filling model of the favored conformation of **5**: a) 1*si*,2*re* face; b) 1*re*,2*si* face.

6, but, in this case, the sugar chain has the D-*manno* configuration and the 1*re*,2*si* face is sterically hindered (Fig. 2).

The cycloaddition of diazomethane or diazoethane to **5**, in 1,4-dioxane at 0°C, gave the bromonitropyrazolines **7** and **8**, respectively, in high yields. As in the reactions[1] between (*E*)-4,5,6,7,8-penta-*O*-acetyl-1,2,3-trideoxy-2-*C*-nitro-D-*galacto*-oct-2-enitol and diazoalkanes, the stereochemistry of C-3,4 must be governed by the addition of the dipole to the less hindered face of the bromonitro-olefin (1*re*,2*si*) to give the 3*R*,4*S* diastereomers. This diastereofacial selectivity is in agreement with our preceding results[1], where the structure of the adduct (**9**) was demonstrated by X-ray diffraction[8], and has been also observed in Diels–Alder[9,10] and 1,3-dipolar[7] cycloaddition reactions involving α,β-unsaturated aldonic esters. The coupling constants $J_{4,5a}$ and $J_{4,5b}$ observed for **7** (7.9 and 7.8 Hz) are indicative of dihedral angles close to +30° and −30° for these protons[11], in agreement with a ^4E conformation of the pyrazoline ring. The configuration of C-5 of the pyrazoline **8** was tentatively assigned as 5*R*, in accordance with precedents in the preparation of **9**[1,8]. The value of $J_{4,5}$ (7.5 Hz) is in agreement with a flattened E_4 conformation (dihedral angle[11] $\phi_{4,5} = -143°$).

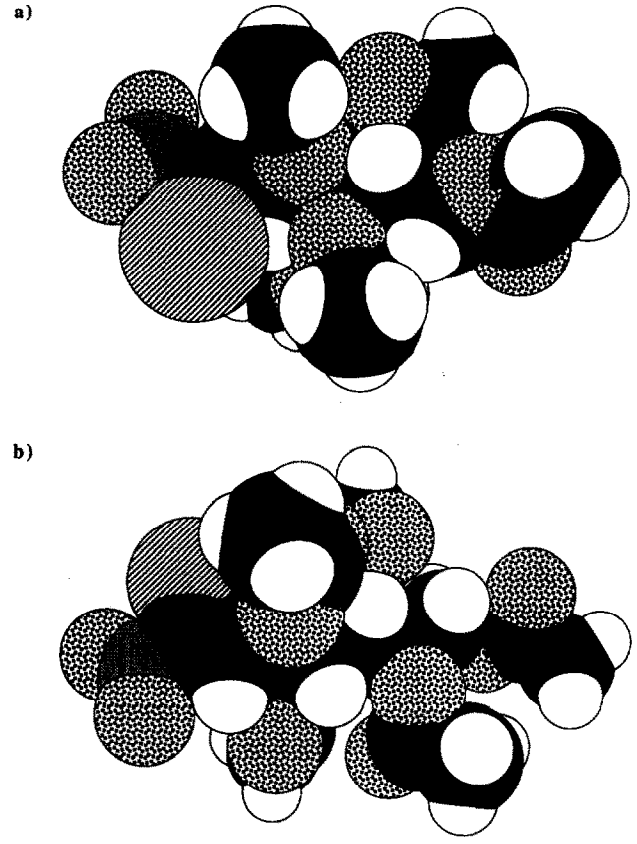
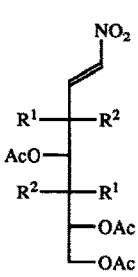
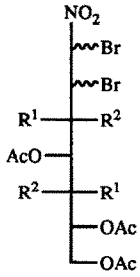


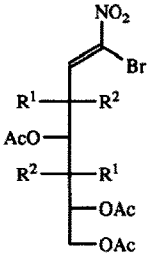
Fig. 2. Space filling model of the favored conformation of **6**: a) 1*re*,2*si* face; b) 1*si*,2*re* face.



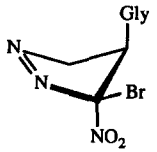
1 R^1= H, R^2= OAc
2 R^1= OAc, R^2= H



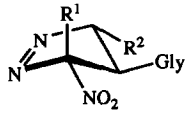
3 (3') R^1= H, R^2= OAc
4 (4') R^1= OAc, R^2= H



5 R^1= H, R^2= OAc
6 R^1= OAc, R^2= H

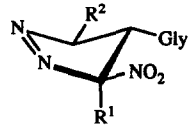


7



8 R^1= Br, R^2= Me
9 R^1= Me, R^2= Me

Gly: penta-*O*-acetyl-D-*galacto*-pentitol-1-yl



10 R^1= Br, R^2= Me
11 R^1= Me, R^2= Me

Gly: penta-*O*-acetyl-D-*manno*-pentitol-1-yl

The aromatisation of **7** and **8** could follow a different course depending upon the conditions employed[12]. In the presence of base, loss of the less basic bromide ion resulted in the formation of the nitropyrazoles. However, the preferential elimination of nitrous acid in acidic media resulted in the formation of the bromopyrazoles. Treatment of **7** and **8** with sodium hydrogen carbonate gave, in high yields, the nitropyrazoles **12** and **13**, respectively, whose structures were proved by NMR data. When the aromatisation was promoted by hydrogen chloride, the crystalline bromopyrazoles **18** (30%) and **19** (40%) were obtained.

The reaction of **5** with ethyl diazoacetate was very slow and gave a complex mixture of products, column chromatography of which gave the syrupy nitropyrazole **14** (52%).

When diazomethane reacted with **6** in 1,4-dioxane at 0°C, the bromonitropyrazoline could not be isolated. Even when the reaction was carried out under nitrogen at −50°C, a mixture of the two pyrazoles **15** and **20** (3:1 by NMR) was the only product that could be obtained. However, the addition of diazoethane to the olefin **6** yielded the 1-pyrazoline **10**. The attack must also take place on the less hindered face of the nitro-olefin (1*si*,2*re*) to give the 3*R*,4*S* stereomer. The value of $J_{4,5}$ (7.5 Hz) is also compatible with a 5*S* configuration and a flattened ^4E conformation. This structure is similar to that observed for **11**, which was obtained in the reaction of (*E*)-4,5,6,7,8-penta-*O*-acetyl-1,2,3-trideoxy-2-*C*-nitro-D-*manno*-oct-2-enitol with diazoethane, and whose structure was demonstrated by X-ray diffraction[2]. The aromatisation of **10** with sodium hydrogen carbonate gave a crystalline product (73%) having the nitropyrazole structure **16**.

Treatment of **6** with ethyl diazoacetate led to the pyrazoles **17** and **21** accompanied by several by-products. The two substances could be separated by column chromatography. The major product was identified, by elemental analysis, IR, ^{1}H and ^{13}C NMR spectroscopy, as the nitropyrazole **17** (45%). Unfortunately, we have been unable to isolate the bromopyrazole **21** as an analytically pure syrup. Small but significant amounts of **17** always contaminated the bromopyrazole, as determined by NMR.

EXPERIMENTAL

General methods.—Unless stated otherwise, these were as described[2]. NMR spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si), using a Bruker

AC-200 P or Bruker AMX-500 spectrometer. All reactions were monitored by TLC.

3,4,5,6,7-Penta-O-*acetyl-1,2-dibromo-1,2-dideoxy-1*-C-*nitro*-D-threo-L-gulo(talo)-*heptitols* (**3** *and* **3'**).—To a stirred cold solution of **1** (2.08 g, 4.80 mmol) in CH_2Cl_2 (15 mL) was added dropwise a solution of Br_2 (0.77 g, 4.80 mmol) in CH_2Cl_2 (10 mL). After stirring for 24 h at 0°C, the solution was evaporated to a syrup that crystallised from EtOH to afford a mixture (2.30 g, 81%) of the two dibromides (**3** and **3'**, ratio 85:15); mp 78–80°C; R_f 0.52 (3:1 CCl_4–EtOAc); ν_{max} 1740 (CO) and 1560 cm^{-1} (NO_2). NMR data: major product, ^1H, δ 2.03–2.14 (5 s, 15 H, 5 OAc), 3.83 (dd, 1 H, $J_{6,7b}$ 7.8, $J_{7a,7b}$ −11.7 Hz, H-7b), 4.30 (dd, 1 H, $J_{6,7a}$ 5.0 Hz, H-7a), 4.89 (dd, 1 H, $J_{2,3}$ 5.9 Hz, H-2), 5.20–5.70 (m, 4 H, H-3/6), 6.38 (d, 1 H, $J_{1,2}$ 9.3 Hz, H-1); ^{13}C, δ 20.40 (OAc), 46.60 (C-2), 61.90 (C-7), 67.40-67.70 (C-4/6), 68.30 (C-3), 77.00 (C-1), 169.80 (OAc); minor product, ^1H, δ 2.03–2.14 (5 s, 15 H, 5 OAc), 3.83 (dd, 1 H, $J_{6,7b}$ 7.8, $J_{7a,7b}$ −11.7 Hz, H-7b), 4.30 (dd, 1 H, $J_{6,7a}$ 5.0 Hz, H-7a), 5.20–5.70 (m, 5 H, H-2/6), 6.05 (d, 1 H, $J_{1,2}$ 10.3 Hz, H-1); ^{13}C, δ 20.30 (OAc), 50.30 (C-2), 61.90 (C-7), 67.60–67.90 (C-4/6), 69.69 (C-3), 75.90 (C-1), 169.90 (OAc). Anal. Calcd for $C_{17}H_{23}Br_2NO_{12}$: C, 34.42; H, 3.91; N, 2.36. Found: C, 34.51; H, 3.80; N, 2.14.

3,4,5,6,7-Penta-O-*acetyl-1,2-dibromo-1,2-dideoxy-1*-C-*nitro*-D-erythro-L-allo(manno)-*heptitols* (**4** *and* **4'**).—The procedure described above was used with **2** (0.50 g, 1.15 mmol) to give a mixture (0.60 g, 88%) of the two dibromides (**4** and **4'**, ratio 94:6); mp 158–160°C (from EtOH); R_f 0.50 (3:1 CCl_4–EtOAc); ν_{max} 1755 (CO) and 1560 cm^{-1} (NO_2). NMR data: major product, ^1H, δ 2.06–2.16 (5 s, 15 H, 5 OAc), 4.11 (dd, 1 H, $J_{6,7b}$ 2.9, $J_{7a,7b}$ −13.0 Hz, H-7b), 4.24 (dd, 1 H, $J_{6,7a}$ 4.4 Hz, H-7a), 4.91 (dd, 1 H, $J_{2,3}$ 4.8 Hz, H-2), 5.02 (m, 1 H, $J_{5,6}$ 9.0 Hz, H-6), 5.46 (dd, 1 H, $J_{4,5}$ 1.9 Hz, H-5), 5.54 (dd, 1 H, H-3), 5.66 (dd, 1 H, $J_{3,4}$ 7.5 Hz, H-4), 6.05 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1); ^{13}C, δ 20.60 (OAc), 48.60 (C-2), 61.60 (C-7), 67.60 (C-6), 68.30 (C-5), 69.40 (C-4), 69.80 (C-3), 79.10 (C-1), 169.60 (OAc); minor product, ^1H, δ 2.08–2.21 (5 s, 15 H, 5 OAc), 4.11 (dd, 1 H, $J_{6,7b}$ 2.9, $J_{7a,7b}$ −13.0 Hz, H-7b), 4.24 (dd, 1 H, $J_{6,7a}$ 4.4 Hz, H-7a), 5.02–5.66 (m, 5 H, H-2/6), 5.83 (d, 1 H, $J_{1,2}$ 11.1 Hz, H-1); ^{13}C, δ 20.60 (OAc), 49.70 (C-2), 61.60 (C-7), 67.10 (C-6), 68.90 (C-5), 69.40 (C-4), 69.80 (C-3), 78.30 (C-1), 169.60 (OAc). Anal. Calcd for $C_{17}H_{23}Br_2NO_{12}$: C, 34.42; H, 3.91; N, 2.36. Found: C, 34.27; H, 3.98; N, 2.16.

(Z)-3,4,5,6,7-Penta-O-*acetyl-1*-C-*bromo-1,2-dideoxy-1*-C-*nitro*-D-galacto-*hept-1-enitol* (**5**).—*Method A*: To a solution of the mixture of dibromides (**3** and **3'**) (50 mg, 0.08 mmol) in acetone (5 mL) was added pyridine (0.2 mL). After 3 h under reflux, the solution was evaporated to a syrupy residue and poured into water. The mixture was extracted with CH_2Cl_2, and the extract was succesively washed with aq HCl, water, aq $NaHCO_3$, and water, dried (Na_2SO_4), and evaporated to a syrup that crystallised by addition of EtOH. Recrystallisation from EtOH afforded **5** (25.9 mg, 60%); mp 112–114°C.

Method B: To a stirred cold solution of **1** (2.08 g, 4.80 mmol) in CH_2Cl_2 (15 mL) was added dropwise a solution of Br_2 (0.77 g, 4.80 mmol) in CH_2Cl_2 (10 mL).

After stirring for 24 h, a suspension of Ag_2CO_3 (8.00 g, 29.01 mmol) in MeCN (44 mL) was added and the mixture was stirred for 2 h more at room temperature. The solid was filtered off and the solution was concentrated to dryness. The solid residue was recrystallised from EtOH to give **5** (1.96 g, 79%); mp 112–114°C; $[\alpha]_D$ −6° (*c* 0.5, CH_2Cl_2); ν_{max} 1755 (CO) and 1550 cm^{-1} (NO_2). NMR data: ^1H, δ 2.03–2.14 (5 s, 15 H, 5 OAc), 3.86 (dd, 1 H, $J_{6,7b}$ 7.0, $J_{7a,7b}$ −11.6 Hz, H-7b), 4.30 (dd, 1 H, $J_{6,7a}$ 5.0 Hz, H-7a), 5.20–5.47 (m, 3 H, H-4/6), 5.60 (dd, 1 H, $J_{3,4}$ 2.0 Hz, H-3), 7.33 (d, 1 H, $J_{2,3}$ 7.9 Hz, H-2); ^{13}C, δ 20.50 (OAc), 62.00 (C-7), 67.90 (C-5/6), 68.50 (C-4), 69.80 (C-3), 132.80 (C-2), 133.70 (C-1), 169.60 (OAc). Anal. Calcd for $C_{17}H_{22}BrNO_{12}$: C, 39.86; H, 4.33; N, 2.73. Found: C, 39.95; H, 4.42; N, 2.89.

*(Z)-3,4,5,6,7-Penta-*O*-acetyl-1-C-bromo-1,2-dideoxy-1-C-nitro-*D*-manno-hept-1-enitol* (**6**).—It was prepared from **2** (0.60 g, 1.38 mmol) as described above for **5**. The solid residue was recrystallised from EtOH to give **6** (0.50 g, 70%); mp 83–85°C; $[\alpha]_D$ + 42° (*c* 0.5, pyridine); ν_{max} 1770 (CO) and 1550 cm^{-1} (NO_2). NMR data: ^1H, δ 2.06–2.12 (5 s, 15 H, 5 OAc), 4.07 (dd, 1 H, $J_{6,7b}$ 4.4, $J_{7a,7b}$ −11.6 Hz, H-7b), 4.25 (dd, 1 H, $J_{6,7a}$ 3.0 Hz, H-7a), 5.00–5.70 (m, 4 H, H-3/6), 7.44 (d, 1 H, $J_{2,3}$ 6.7 Hz, H-2); ^{13}C, δ 20.50 (OAc), 61.80 (C-7), 67.30 (C-6), 68.00 (C-5), 69.00 (C-4), 69.40 (C-3), 133.00 (C-2), 134.40 (C-1), 169.70 (OAc). Anal. Calcd for $C_{17}H_{22}BrNO_{12}$: C, 39.86; H, 4.33; N, 2.73. Found: C, 40.02; H, 4.26; N, 3.01.

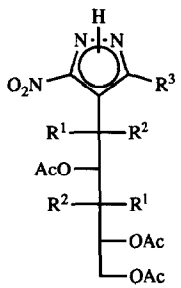
*(3R,4S)-3-Bromo-3-nitro-4-(penta-*O*-acetyl-*D*-galacto-pentitol-1-yl)-1-pyrazoline* (**7**).—A solution of **5** (0.50 g, 0.98 mmol) in 1,4-dioxane (5 mL) was cooled to 0°C and a solution of diazomethane (102 mg, 2.43 mmol) in ether (10 mL) was added to it. The resulting solution was stirred for 6 h at 0°C, and evaporated to dryness, leaving a white solid that was recrystallised from MeOH to give **7** (0.51 g, 94%); mp 116–118°C; $[\alpha]_D$ + 14° (*c* 0.5, CH_2Cl_2); R_f 0.70 (5:1 ether–hexane); ν_{max} 1760 (CO), 1565 (N=N), and 1550 cm^{-1} (NO_2). NMR data: ^1H, δ 2.00–2.09 (5 s, 15 H, 5 OAc), 3.23 (dd, 1 H, $J_{4,1'}$ 8.6 Hz, H-4), 3.82 (dd, 1 H, $J_{4',5'b}$ 7.4, $J_{5'a,5'b}$ −11.8 Hz, H-5′b), 4.29 (dd, 1 H, $J_{4',5'a}$ 5.2 Hz, H-5′a), 4.44 (dd, 1 H, $J_{4,5b}$ 7.8, $J_{5a,5b}$ −18.3 Hz, H-5b), 5.00 (dd, 1 H, $J_{4,5a}$ 7.9 Hz, H-5a), 5.09–5.42 (m, 3 H, H-2′/4′), 5.51 (dd, 1 H, $J_{1',2'}$ 1.2 Hz, H-1′); ^{13}C, δ 20.60 (OAc), 43.80 (C-4), 62.10 (C-5′), 68.00 (C-4′), 68.30 (C-3′), 68.80 (C-2′), 70.50 (C-1′), 79.30 (C-5), 120.30 (C-3), 170.20 (OAc). Anal. Calcd for $C_{18}H_{24}BrN_3O_{12}$: C, 39.00; H, 4.36; N, 7.58. Found: C, 38.69; H, 4.29; N, 7.67.

*(3R,4S,5R)-3-Bromo-5-methyl-3-nitro-4-(penta-*O*-acetyl-*D*-galacto-pentitol-1-yl)-1-pyrazoline* (**8**).—To a solution of **5** (0.5 g, 0.98 mmol) in 1,4-dioxane (5 mL) at 0°C was added dropwise a solution of diazoethane (110 mg, 1.96 mmol) in ether (5 mL). The mixture was stirred for 48 h at 0°C, then concentrated, and the residue was crystallised from MeOH to give **8** (0.45 g, 82%); mp 100–102°C; $[\alpha]_D$ + 9° (*c* 0.5, CH_2Cl_2); R_f 0.70 (5:1 ether–hexane); ν_{max} 1750 (CO) and 1550 cm^{-1} (NO_2). NMR data: ^1H, δ 1.65 (d, 3 H, $J_{Me,5}$ 7.2 Hz, Me), 2.01–2.17 (5 s, 15 H, 5 OAc), 2.70 (dd, 1 H, $J_{4,5}$ 7.5, $J_{4,1'}$ 10.0 Hz, H-4), 3.81 (dd, 1 H, $J_{4',5'b}$ 7.0, $J_{5'a,5'b}$ −11.4 Hz, H-5′b), 4.28 (dd, 1 H, $J_{4',5'a}$ 5.1 Hz, H-5′a), 4.58 (dq, 1 H, H-5), 5.07–5.22 (m, 3 H, H-2′/4′), 5.57 (dd, 1 H, H-1′); ^{13}C, δ 17.70 (Me), 20.50 (OAc), 49.40 (C-4),

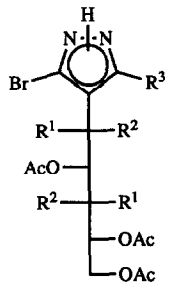
61.90 (C-5′), 67.80 (C-4′), 68.00 (C-3′), 68.60 (C-2′), 71.20 (C-1′), 88.30 (C-5), 120.20 (C-3), 169.90 (OAc). Anal. Calcd for $C_{19}H_{26}BrN_3O_{12}$: C, 40.15; H, 4.61; N, 7.39. Found: C, 40.24; H, 4.67; N, 7.28.

*(3*R*,4*R*,5*S*)-3-Bromo-5-methyl-3-nitro-4-(penta-*O*-acetyl-*D*-manno-pentitol-1-yl)-1-pyrazoline* (**10**).—Treatment of **6** (500 mg, 0.98 mmol) with diazoethane (110 mg, 1.96 mmol) as in the preparation of **8**, and recrystallisation of the product from EtOH gave **10** (0.48 g, 87%); mp 128–130°C; $[\alpha]_D$ −27° (*c* 1, CH_2Cl_2); R_f 0.64 (7:1 ether–hexane); ν_{max} 1750 (CO) and 1550 cm^{-1} (NO_2); NMR data: ^1H, δ 1.70 (d, 3 H, $J_{Me,5}$ 7.2 Hz, Me), 2.07–2.11 (5 s, 15 H, 5 OAc), 3.12 (t, 1 H, $J_{4,5} = J_{4,1'} = 7.5$ Hz, H-4), 4.14–4.21 (m, 2 H, H-5′a/5′b), 4.53 (t, 1 H, H-5), 4.90–5.37 (m, 3 H, H-2′/4′), 5.58 (dd, 1 H, $J_{1',2'}$ 4.08 Hz, H-1′); ^{13}C, δ 17.40 (Me), 20.50 (OAc), 49.50 (C-4), 61.17 (C-5′), 67.30 (C-4′), 68.40 (C-3′), 69.30 (C-2′), 72.30 (C-1′), 87.80 (C-5), 120.90 (C-3), 169.60 (OAc). Anal. Calcd for $C_{19}H_{26}BrN_3O_{12}$: C, 40.15; H, 4.61; N, 7.39. Found: C, 40.28; H, 4.75; N, 7.23.

*3(5)-Nitro-4-(penta-*O*-acetyl-*D*-galacto-pentitol-1-yl)pyrazole* (**12**).—To a solution of **7** (0.5 g, 0.90 mmol) in CH_2Cl_2 (15 mL) was added aq 5% $NaHCO_3$ (50 mL) and the mixture was stirred at room temperature for 24 h. The CH_2Cl_2 solution was separated, washed with water, dried with anhyd Na_2SO_4 and $MgSO_4$, and evaporated to dryness, leaving **12** (0.35 g, 81%); mp 201–202°C (from MeOH); $[\alpha]_D$ + 18° (*c* 0.5, CH_2Cl_2); λ_{max} 235 nm (ϵ_{mM} 3.81); ν_{max} 3380 (NH), 1760 (CO), and 1540 cm^{-1} (NO_2). NMR data: ^1H, δ 2.03–2.19 (5 s, 15 H, 5 OAc), 3.89 (dd, 1 H, $J_{4',5'b}$ 7.8, $J_{5'a,5'b}$ −11.9 Hz, H-5′b), 4.34 (dd, 1 H, $J_{4',5'a}$ 4.9 Hz, H-5′a), 5.29–5.56 (m, 3 H, H-2′/4′), 6.47 (s, 1 H, $J_{1',2'}$ 0.7 Hz, H-1′), 7.77 (s, 1 H, NH); ^{13}C, δ 20.20–20.40 (OAc), 62.10 (C-5′), 65.40 (C-4′), 68.00 (C-2′/3′), 68.50 (C-1′), 115.30 (C-4), 131.40 [C-5(3)], 152.30 [C-3(5)], 170.00 (OAc). Anal. Calcd for $C_{18}H_{23}N_3O_{12}$: C, 45.67; H, 4.90; N, 8.88. Found: C, 45.91; H, 5.09; N, 8.81.



12 R^1= H, R^2= OAc, R^3= H
13 R^1= H, R^2= OAc, R^3= Me
14 R^1= H, R^2= OAc, R^3= CO_2Et
15 R^1= OAc, R^2= H, R^3= H
16 R^1= OAc, R^2= H, R^3= Me
17 R^1= OAc, R^2= H, R^3= CO_2Et



18 R^1= H, R^2= OAc, R^3= H
19 R^1= H, R^2= OAc, R^3= Me
20 R^1= OAc, R^2= H, R^3= H
21 R^1= OAc, R^2= H, R^3= CO_2Et

*5(3)-Methyl-3(5)-nitro-4-(penta-*O*-acetyl-*D*-galacto-pentitol-1-yl)pyrazole* (**13**).—Treatment of **8** (0.50 g, 0.88 mmol) with $NaHCO_3$ under the conditions used in the preparation of **12** led to **13** as a syrup (175 mg, 41%) that did not crystallise; $[\alpha]_D$ + 15° (*c* 0.5, CH_2Cl_2); R_f 0.35 (5:1 EtOAc–hexane); λ_{max} 237 nm (ϵ_{mM} 3.89); ν_{max} 3280 (NH), 1760 (CO), and 1540 cm^{-1} (NO_2). NMR data: ^1H, δ 2.03–2.13 (5 s, 15 H, 5 OAc), 2.41 (s, 3 H, Me), 3.86 (dd, 1 H, $J_{4',5'b}$ 7.9, $J_{5'a,5'b}$ −11.9 Hz, H-5′b), 4.31 (dd, 1 H, $J_{4',5'a}$ 4.8 Hz, H-5′a), 5.20–5.55 (m, 3 H, H-2′/4′), 6.51 (d, 1 H, $J_{1',2'}$ 1.4 Hz, H-1′); ^{13}C, δ 10.40 (Me), 20.40–20.50 (OAc), 62.20 (C-5′), 65.50 (C-4′), 67.40 (C-3′), 68.00 (C-2′), 69.90 (C-1′), 114.20 (C-4), 134.6 [C-5(3)], 151.00 [C-3(5)], 170.20 (OAc). Anal. Calcd for $C_{19}H_{25}N_3O_{12}$: C, 46.82; H, 5.17; N, 8.62. Found: C, 47.02 H, 4.98; N, 8.59.

*3(5)-Bromo-5(3)-methyl-4-(penta-*O*-acetyl-*D*-galacto-pentitol-1-yl)pyrazole* (**19**).—A stream of HCl was passed through a solution of **8** (2 g, 3.52 mmol) in 1,4-dioxane (25 mL). Evaporation of the solvent gave a solid which was recrystallised from MeOH to give **19** (0.55 g, 30%); mp 92–94°C; $[\alpha]_D$ + 16° (*c* 0.5, CH_2Cl_2); R_f 0.40 (3:1 EtOAc–hexane); λ_{max} 234 nm (ϵ_{mM} 3.68); ν_{max} 3300 (NH) and 1750 cm^{-1} (CO). NMR. data: ^1H, δ 1.85–2.05 (5 s, 15 H, 5 OAc), 2.71 (s, 3 H, Me), 3.80 (dd, 1 H, $J_{4',5'b}$ 7.0, $J_{5'a,5'b}$ −11.6 Hz, H-5′b), 4.22 (dd, 1 H, $J_{4',5'a}$ 4.6 Hz, H-5′a), 4.94–5.67 (m, 3 H, H-2′/4′), 5.67 (d, 1 H, $J_{1',2'}$ 2.7 Hz, H-1′); ^{13}C, δ 11.00 (Me), 20.30–20.60 (OAc), 62.00 (C-5′), 65.90 (C-4′), 68.00 (C-3′), 68.60 (C-2′), 70.10 (C-1′), 124.20 (C-4), 130.90 [C-5(3)], 144.70 [C-3(5)], 170.00 (OAc). Anal. Calcd for $C_{19}H_{25}BrN_2O_{10}$: C, 43.78; H, 4.83; N, 5.37. Found: C, 44.09; H, 4.73; N, 5.45.

*3(5)-Bromo-4-(penta-*O*-acetyl-*D*-galacto-pentitol-1-yl)pyrazole* (**18**).—Treatment of **7** (2 g, 3.61 mmol) with HCl under the conditions used in the preparation of **19** led to **18** contaminated by a small proportion of the nitropyrazole. Evaporation of the solvent and column chromatography (1:2 EtOAc–hexane) of the syrupy residue afforded the bromopyrazole **18** (0.73 g, 40%) as a crystalline solid. Recrystallised from MeOH, **18** had mp 186–188°C; $[\alpha]_D$ + 21° (*c* 0.5, CH_2Cl_2); R_f 0.44 (5:1 EtOAc–hexane); λ_{max} 232 nm (ϵ_{mM} 3.42); ν_{max} 3350 (NH) and 1760 cm^{-1} (CO). NMR data: ^1H, δ 2.09–2.12 (5 s, 15 H, 5 OAc), 3.87 (dd, 1 H, $J_{4',5'b}$ 7.3 $J_{5'a,5'b}$ −11.5 Hz, H-5′b), 4.29 (dd, 1 H, $J_{4',5'a}$ 4.9 Hz, H-5′a), 5.23–5.44 (m, 3 H, H-2′/4′), 5.98 (d, 1 H, $J_{1',2'}$ 1.5 Hz, H-1′), 7.49 (s, 1 H, NH); ^{13}C, δ 20.40 (OAc), 62.10 (C-5′), 65.80 (C-4′), 68.10 (C-3′), 68.40 (C-2′), 69.60 (C-1′), 116.50 (C-4), 129.90 [C-5(3)], 144.90 [C-3(5)], 170.10 (OAc). Anal. Calcd for $C_{18}H_{23}BrN_2O_{10}$: C, 42.62; H, 4.57; N, 5.52. Found: C, 42.56; H, 4.65; N, 5.66.

*5(3)-Ethoxycarbonyl-3(5)-nitro-4-(penta-*O*-acetyl-*D*-galacto-pentitol-1-yl)pyrazole* (**14**).—A solution of **5** (2.0 g, 3.9 mmol) and ethyl diazoacetate (0.9 mL, 8.62 mmol) in CH_2Cl_2 (20 mL) was heated under reflux (6 days), then concentrated. Column chromatography of the residue afforded **14** as syrup (1.10 g, 52%); R_f 0.15 (5:1 ether–hexane); $[\alpha]_D$ + 21° (*c* 0.5, CH_2Cl_2); λ_{max} 232 nm (ϵ_{mM} 2.03); ν_{max} 3350 (NH), 1750 (CO), and 1550 cm^{-1} (NO_2). NMR data: ^1H, δ 1.46 (t, 3 H, $J_{Me,CH}$ 7.0 Hz, CH_3CH_2), 2.02–2.12 (5 s, 15 H, 5 OAc), 3.90 (dd, 1 H, $J_{4',5'b}$ 7.5, $J_{5'a,5'b}$ −11.6

Hz, H-5'b), 4.24 (q, 2 H, CH_3CH_2), 4.27 (dd, 1 H, $J_{4',5'a}$ 5.2 Hz, H-5'a), 5.35–5.65 (m, 3 H, H-2'/4'), 6.54 (d, 1 H, $J_{1',2'}$ 2.6 Hz, H-1'); ^{13}C, δ 13.70 (Et), 20.20 (OAc), 61.80 (Et), 62.40 (C-5'), 65.10 (C-4'), 67.80 (C-3'), 67.90 (C-2'), 69.40 (C-1'), 113.40 (C-4), 132.70 [C-5(3)], 154.60 [C-3(5)], 157.30 (CO_2Et), 169.60 (OAc). Anal. Calcd for $C_{21}H_{27}N_3O_{14}$: C, 46.24; H, 4.99; N, 7.70. Found: C, 46.00; H, 5.18; N, 7.53.

*3(5)-Nitro-4-(penta-*O*-acetyl-*D*-manno-pentitol-1-yl)pyrazole* (**15**) *and 3(5)-bromo-4-(penta-*O*-acetyl-*D*-manno-pentitol-1-yl)pyrazole* (**20**).—A solution of **6** (1.49 mg, 2.91 mmol) in 1,4-dioxane (5 mL) was treated with diazomethane (0.10 g, 2.38 mmol) as described in the preparation of **7**. Evaporation of the solvent gave a solid that was recrystallised from EtOH to afford a mixture (1.1 g) of **15** (R_f 0.18, 10:1 ether–hexane) and **20** (R_f 0.25). NMR data: **15**, ^1H, δ 1.90–2.15 (5 s, 15 H, OAc), 4.14 (dd, 1 H, $J_{4',5'b}$ 4.1, $J_{5'a,5'b}$ −12.5 Hz, H-5'b), 4.25 (dd, 1 H, $J_{4',5'a}$ 2.7 Hz, H-5'a), 5.10–5.20 (m, 1 H, H-4'), 5.60 (dd, 1 H, $J_{2',3'}$ 2.2, $J_{3',4'}$ 9.2 Hz, H-3'), 5.74 (m, 1 H, H-2'), 6.27 (d, 1 H, $J_{1',2'}$ 8.9 Hz, H-1'), 7.99 (s, 1 H, NH): ^{13}C, δ 20.37–20.80 (OAc), 61.86 (C-5'), 63.34 (C-4'), 67.33 (C-3'), 67.92 (C-2'), 69.95 (C-1'), 113.43 (C-4), 133.05 [C-5(3)], 153.44 [C-3(5)], 169.50–170.66 (OAc); **20**, ^1H, δ 1.90–2.16 (5 s, 15 H, 5 OAc), 4.10 (dd, 1 H, $J_{4',5'b}$ 4.1, $J_{5'a,5'b}$ −12.5 Hz, H-5'b), 4.23 (dd, 1 H, $J_{4',5'a}$ 2.7 Hz, H-5'a), 5.10–5.20 (m, 1 H, H-4'), 5.57 (dd, 1 H, $J_{2',3'}$ 2.2, $J_{3',4'}$ 9.0 Hz, H-3'), 5.74 (m, 1 H, H-2'), 5.77 (d, 1 H, $J_{1',2'}$ 8.6 Hz, H-1'), 7.74 (s, 1 H, NH); ^{13}C, δ 20.37–20.80 (OAc), 61.86 (C-5'), 64.45 (C-4'), 67.33 (C-3'), 67.92 (C-2'), 69.95 (C-1'), 116.49 (C-4), 131.04 [C-5(3)], 153.44 [C-3(5)], 169.50–170.66 (OAc).

*5(3)-Methyl-3(5)-nitro-4-(penta-*O*-acetyl-*D*-manno-pentitol-1-yl)pyrazole* (**16**).—A solution of **10** (0.80 g, 1.41 mmol) in CH_2Cl_2 (15 mL) was treated as described above in the preparation of **12**, to give **16** (0.50 g, 73%); mp 122–124°C; $[\alpha]_D$ + 83° (*c* 1, CH_2Cl_2); R_f 0.31 (7:1 ether–hexane); λ_{max} 238 nm (ϵ_{mM} 3.82); ν_{max} 3280 (NH), 1760 (CO), and 1540 cm^{-1} (NO_2); NMR data ^1H, δ 1.80–2.18 (5 s, 15 H, 5 OAc), 2.49 (s, 3 H, Me), 4.15 (dd, 1 H, $J_{4',5'b}$ 4.9, $J_{5'a,5'b}$ −12.5 Hz, H-5'b), 4.25 (dd, 1 H, $J_{4',5'a}$ 2.7 Hz, H-5'a), 5.10–5.20 (m, 1 H, H-4'), 5.60 (dd, 1 H, $J_{2',3'}$ 1.8, $J_{3',4'}$ 9.4 Hz, H-3'), 5.90 (dd, 1 H, $J_{1',2'}$ 10.4 Hz, H-2'), 6.15 (d, 1 H, H-1'); ^{13}C, δ 10.46 (Me), 20.11–20.65 (OAc), 61.98 (C-5'), 62.50 (C-4'), 67.18 (C-3'), 67.76 (C-2'), 68.74 (C-1'), 109.05 (C-4), 143.46 [C-5(3)], 154.10 [C-3(5)], 169.52–170.67 (OAc). Anal. Calcd for $C_{19}H_{25}N_3O_{12}$: C, 46.82; H, 5.17; N, 8.62. Found: C, 46.77; H, 5.35; N, 8.49.

*5(3)-Ethoxycarbonyl-3(5)-nitro-4-(penta-*O*-acetyl-*D*-manno-pentitol-1-yl)pyrazole* (**17**) *and 3(5)-bromo-5(3)-ethoxycarbonyl-4-(penta-*O*-acetyl-*D*-manno-pentitol-1-yl)pyrazole* (**21**).—A solution of **6** (1.0 g, 1.95 mmol) and ethyl diazoacetate (0.52 mL, 4.98 mmol) in CH_2Cl_2 (10 mL) was heated under reflux for 10 days, then concentrated, and cyclohexane was evaporated several times from the residue. Column chromatography (3:1 ether–hexane) of the syrupy residue afforded the major product **17** as a solid (475 mg, 45%); mp 58–60°C (from EtOH); $[\alpha]_D$ + 35° (*c* 1, CH_2Cl_2); R_f 0.33 (7:1 ether–hexane); λ_{max} 234 nm (ϵ_{mM} 2.04); ν_{max} 3350 (NH), 1750 (CO), and 1550 cm^{-1} (NO_2); NMR data: ^1H, δ 1.48 (t, 3 H, $J_{Me,CH}$ 7.2

Hz, CH_3CH_2), 1.83–2.18 (5 s, 15 H, 5 OAc), 4.14 (dd, 1 H, $J_{4',5'b}$ 5.0, $J_{5'a,5'b}$ −12.5 Hz, H-5'b), 4.26 (dd, 1 H, $J_{4',5'a}$ 2.7 Hz, H-5'a), 4.50 (q, 2 H, CH_3CH_2), 5.15–5.25 (m, 1 H, H-4'), 5.68 (dd, 1 H, $J_{2',3'}$ 1.8, $J_{3',4'}$ 9.5 Hz, H-3'), 6.14 (dd, 1 H, H-2'), 6.54 (d, 1 H, $J_{1',2'}$ 10.2 Hz, H-1'); ^{13}C, δ 14.09 (Et), 20.27–20.72 (OAc), 61.68 (Et), 62.08 (C-5'), 62.83 (C-4'), 67.74 (C-2'/3'), 69.31 (C-1'), 115.06 (C-4), 134.53 [C-5(3)], 154.90 [C-3(5)], 157.32 (CO_2Et), 169.86–170.78 (OAc). Anal. Calcd for $C_{21}H_{27}N_3O_{14}$: C, 46.24; H, 4.99; N, 7.70. Found: C, 46.21; H, 4.89; N, 7.40.

The minor product **21** was a syrup (120 mg, 11%); R_f 0.45 (7:1 ether–hexane); NMR data: ^1H, δ 1.48 (t, 3 H, $J_{Me,CH}$ 7.0 Hz, CH_3CH_2), 2.07 (5 s, 15 H, 5 OAc), 4.13 (dd, 1 H, $J_{4',5'b}$ 5.1, $J_{5'a,5'b}$ −12.5 Hz, H-5'b), 4.25 (dd, 1 H, $J_{4',5'a}$ 2.7 Hz, H-5'a), 4.47 (q, 2 H, CH_3CH_2), 5.12 (m, 1 H, H-4'), 5.65 (dd, 1 H, $J_{2',3'}$ 1.6, $J_{3',4'}$ 9.5 Hz, H-3'), 6.00 (dd, 1 H, H-2'), 6.08 (d, 1 H, $J_{1',2'}$ 10.3 Hz, H-1'); ^{13}C, δ 14.15 (Et), 20.21–20.73 (OAc), 62.12 (C-5'/Et), 63.12 (C-4'), 67.34 (C-3'), 67.92 (C-2'), 69.02 (C-1'), 118.63 (C-4), 133.70 [C-5(3)], 157.84 [C-3(5)/CO_2Et], 169.33–170.87 (OAc).

AKNOWLEDGMENT

We thank the C.I.C.Y.T. (Comisión Interministerial de Ciencia y Tecnología) for financial support (Grant MAT90-0779-C02-01).

REFERENCES

1 M. Mancera, E. Rodríguez, I. Roffé, and J.A. Galbis, *J. Org. Chem.*, 53 (1988) 5648–5651.
2 M. Mancera, E. Rodríguez, I. Roffé, J.A. Galbis, C.F. Conde, and A. Conde, *Carbohydr. Res.*, 210 (1991) 327–332.
3 J.C. Sowden and D.R. Strobach, *J. Am. Chem. Soc.*, 82 (1960) 954–955.
4 J.C. Sowden and R. Schaffer, *J. Am. Chem. Soc.*, 73 (1951) 4662–4664.
5 T.H. Lowry and K.S. Richardson, *Mechanism and Theory in Organic Chemistry*, 2nd ed., Harper and Row, New York, 1981, p. 520.
6 J.M.J. Tronchet, K. Deen Pallie, and F. Barbalat-Rey, *J. Carbohydr. Chem.*, 4 (1985) 29–52.
7 M. Mancera, E. Rodríguez, I. Roffé, and J.A. Galbis, *Carbohydr. Res.*, 210 (1991) 167–174.
8 C.F. Conde and A. Conde, *Acta Crystallogr., Sect. C*, 45 (1989) 1563–1565.
9 R. Casas, T. Parella, V. Branchadell, A. Oliva, R.M. Ortuño, and A. Guingant, *Tetrahedron*, 48 (1992) 2659–2680.
10 D. Horton, T. Machinami, Y. Takagi, C.W. Bergmann, and G.C. Christoph, *J. Chem. Soc., Chem. Commun.*, (1983) 1164–1166; D. Horton, T. Machinami, and Y. Takagi, *Carbohydr. Res.*, 121 (1983) 135–161.
11 C.A. Haasnoot, F.A.A.M. de Leeuw, and C. Altona, *Tetrahedron*, 36 (1980) 2783–2792.
12 W.E. Parham and J.L. Bleasdale, *J. Am. Chem. Soc.*, 73 (1951) 4664–4666.