Stereoselective Syntheses of Nitropyrazolines by 1,3-Dipolar Cycloaddition of Diazoalkanes to Sugar Nitro Olefins

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

Department of Organic and Pharmaceutical Chemistry, Faculty of Pharmacy, University of Seville, 41071-Seville, Spain

Received October 13, 1987

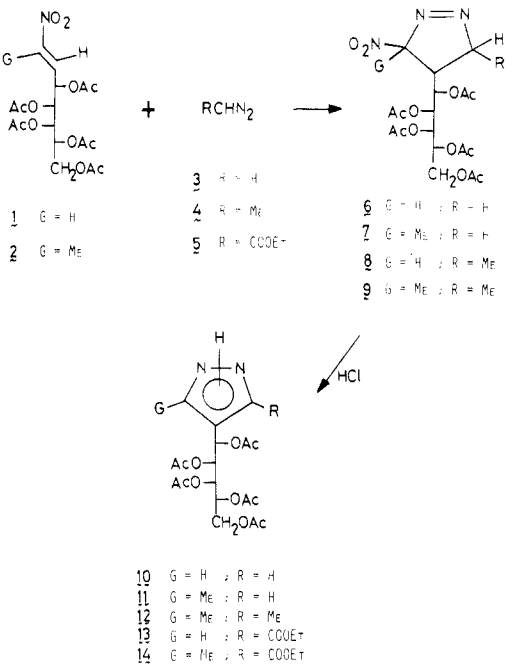
The reaction of (*E*)-3,4,5,6,7-penta-*O*-acetyl-1,2-dideoxy-1-*C*-nitro-D-*galacto*-hept-1-enitol (**1**) and of the new nitro olefin (*E*)-4,5,6,7,8-penta-*O*-acetyl-1,2,3-trideoxy-2-*C*-nitro-D-*galacto*-oct-2-enitol (**2**) with diazoalkanes gives a series of 4-(D-*galacto*-pentaacetoxypentyl)-3-nitropyrazolines which are further aromatized to 4-(D-*galacto*-pentaacetoxypentyl)pyrazoles. The presence of the sugar chain joined to one of the olefinic carbons makes the reaction highly stereoselective, and one single stereoisomer is obtained in each case.

The mechanism and the direction of addition of diazoalkanes to activated olefins has been extensively studied.[1-4] However, the antecedents about the use of nitro olefins as dipolarophiles are more scarce,[5-7] and to our knowledge, no report exists about the additions to sugar nitro olefins.[8] Since these can be of interest in the syntheses of acyclic sugar *C*-nucleosides and other sugar derivatives, we examined the conditions and the regio- and stereospecificity of the reactions.

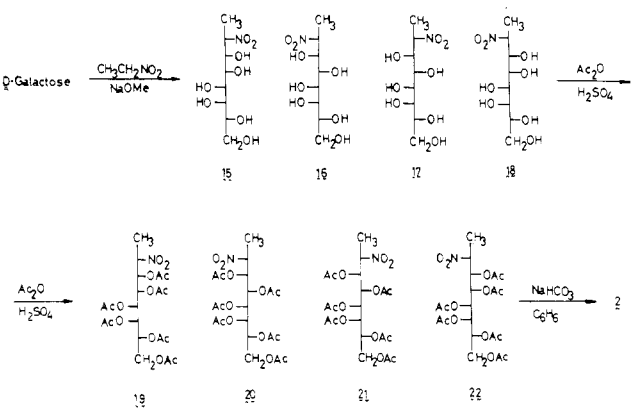
The syntheses of (pentaacetoxypentyl)pyrazoles **10–14** with the sugar nitro olefins 1 and **2** as dipolarophiles were performed according to Scheme I. Initially, the cycloadditions gave the pyrazolines **6–9**, which were aromatized to the pyrazoles.

The nitro olefin **1** was prepared by the method described by Sowden and Strobach.[9] We have now assigned the stereochemistry *E* to this nitro olefin on the basis of the big value (13.5 Hz) of its $J_{1,2}$.[10] The new nitro olefin **2** was prepared by a similar procedure from D-galactose and nitroethane. In the course of the preparation of **1** the two expected epimeric nitro alcohols were isolated, but the reaction with nitroethane did not afford the four possible stereoisomers **15–18** (Scheme II). On the contrary, the isolated crystalline solid was a mixture of only two compounds (60:40 ratio) as was demonstrated by their ^1H and ^{13}C NMR spectra and by those of their hexaacetates. From the mixture of hexaacetates we have prepared the nitro olefin **2**, and one single diastereomer was isolated in 96% yield. The stereochemistry of **2** is tentatively assigned on the basis of its NMR data. Thus, the chemical shift of the olefinic proton (6.73 ppm) is closer to the expected value for the *E* configuration (6.91) than to that expected for the *Z* configuration (6.29).[11] In addition, the allylic coupling constant, $J_{1,3}$ = 1.13 Hz, is also indicative of the *E* configuration.[9] The favored conformation in solution must be the one pointed out in **2** (*E*), in which H-3 and H-4 have an anti disposition ($J_{3,4}$ = 8.8 Hz) and the H-4 is eclipsed with the ethylenic bond. In this conformation the (*si*, *si*) face of the nitro olefin is sterically hindered by the sugar chain.

Scheme I



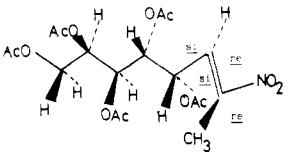
Scheme II



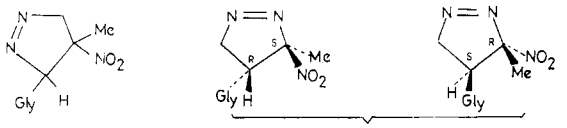
The addition of diazomethane to (*E*)-4,5,6,7,8-penta-*O*-acetyl-1,2,3-trideoxy-2-*C*-nitro-D-*galacto*-oct-2-enitol (**2**) yields a mixture (quantitative) of the two possible regioisomers **7** and **7′** in the 9:1 ratio, as was determined by ^{13}C NMR spectroscopy. The ^1H NMR spectrum showed

(1) Huisgen, R. *Angew. Chem.* **1963**, *75*, 604–637, 742–754.
(2) Firestone, R. A. *J. Org. Chem.* **1968**, *33*, 2285–2290.
(3) Huisgen, R. *J. Org. Chem.* **1968**, *33*, 2291–2297.
(4) Bastide, J.; El Gandhour, N.; Henri-Rousseau, O. *Tetrahedron Lett.* **1972**, 4225–4228; *Bull. Soc. Chim. Fr.* **1973**, 2290–2293.
(5) Parham, W. E.; Bleasdale, J. L. *J. Am. Chem. Soc.* **1950**, *72*, 3843–3846.
(6) Parham, W. E.; Hasek, W. R. *J. Am. Chem. Soc.* **1954**, *76*, 799–801.
(7) Parham, W. E.; Braxton, H. G.; O'Connor, P. R. *J. Org. Chem.* **1961**, *26*, 1805–1807.
(8) After the submission of this manuscript a paper on this subject has been published by: Baer, H. H.; Gilron, I. *Carbohydr. Res.* **1987**, *164*, 486–492.
(9) Sowden, J. C.; Strobach, D. R. *J. Am. Chem. Soc.* **1960**, *82*, 954–955.
(10) Bovey, F. A. *Nuclear Magnetic Resonance Spectroscopy*; Academic: New York, 1970.
(11) Pretsch, E.; Clerc, T.; Seibl, J.; Simon, W. In *Tables of Spectral Data for Structure Determination of Organic Compounds*: Boschke, F. L., Fresenius, W., Huber, J. F. K., Pungor, E., Rechnitz, G. A., Simon, W., West, Th. S., Eds.; Springer-Verlag: 1983; p H215.

0022-3263/88/1953-5648$01.50/0



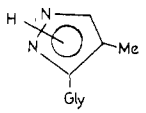
2 (E)



7′ 7

that the major product was **7**. Thus, the signal for the methyl group on C-3 appeared as a singlet at 1.87 ppm, and the H-5a, H-5b, and H-4 formed the characteristic ABX system. Although the absolute stereochemistry on C-3 and C-4 has not been determined, the configuration of the pyrazoline may be *E*, like in the parent nitro olefin. Furthermore, because the ^{13}C NMR spectrum showed exclusively two types of signals assigned to the two regioisomers, we believe that only one of the diastereomers **7** was obtained, which could be the 3*S*,4*R* originated by addition of diazomethane to the less hindered (*re*, *re*) face of the nitro olefin.

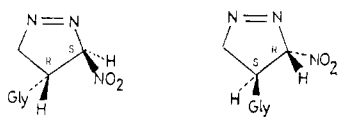
The aromatization of the mixture of pyrazolines **7** and **7′**, prompted by HCl, gave a mixture of the two pyrazoles **11** and **11′**, as was shown by its ^1H NMR spectrum. The



11′

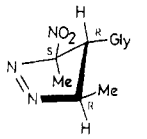
major product **11** was isolated, in 85% yield, by fractional crystallization. The pyrazole structure is in agreement with its ^1H NMR spectrum. Thus, the methyl group on C-3(5) gave a singlet at 2.39 ppm, shifted downfield from the position of the methyl signal in the pyrazoline spectrum, as could be expected; the N–H appeared as a broad singlet at 7.51 ppm. H-1′ originated a double doublet at 5.95 ppm ($J_{1',5}$ = 1.1, $J_{1',2'}$ = 2.4 Hz). The ^{13}C NMR spectrum also confirmed this structure.

The addition of diazomethane to (*E*)-3,4,5,6,7-penta-*O*-acetyl-1,2-dideoxy-1-*C*-nitro-D-*galacto*-hept-1-enitol (**1**) took place readily in dioxane at 0 °C. A crystalline solid was isolated, in 86% yield, and identified as 3-nitro-4-(D-*galacto*-penta-*O*-acetylpentitol-1-yl)-1-pyrazoline (**6**) on the basis of its ^1H and ^{13}C NMR spectra. In this case only one of the two regioisomers was detected, which appeared to be the 3*S*,4*R* diastereomer. The aromatization of **6** gave a syrup that could not be crystallized. Its ^1H NMR spectrum suggested the pyrazole structure **10**.



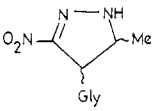
6 GLY = D-GALACTO CHAIN

The cycloaddition reaction of **2** with diazoethane at 0 °C, in dioxane, gave the pyrazoline **9** in quantitative yield. The other possible regioisomer was not formed. Since the reaction is a concerted syn addition, compound **9** could be a mixture of four stereoisomers. However, the ^1H and ^{13}C NMR spectra suggested that the solid obtained was a pure compound. As in the case of compounds **6** and **7**, the attack by the less hindered face of the nitro olefin controlled the stereochemistry of C-3 and C-4 to produce the 3*S*,4*R* diastereomer. The observed value of $J_{4,5}$ (7.86 Hz) indicated an anti arrangement of these protons, in agreement with a 5*R* configuration in the ^4E conformation of the heterocycle. Treatment of **9** with HCl gave a syrupy compound to which the pyrazole structure **12** was assigned on the basis of its ^{13}C NMR spectrum that showed the signal of C-3(5) at 143.36 ppm while C-4 appeared at 113.36 ppm. The ^1H NMR spectrum also confirmed the proposed structure.



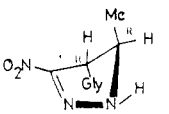
9

When diazoethane reacted with the nitro olefin **1**, the pyrazoline **8′** was obtained, in 82% yield, as a single regioisomer. The 2-pyrazoline structure is deduced from



8′

the ^1H NMR spectrum that showed the NH signal at 7.14 ppm and a doublet signal for the methyl group on C-5 (1.21 ppm, J = 6.50 Hz). The ^{13}C NMR spectrum showed the signal of a quaternary carbon at 151.29 ppm, assigned to C-3, and two signals of tertiary carbons at 64.48 and 49.12 ppm, assigned to C-5 and C-4, respectively. Compound **8′** was also a single stereoisomer. As in the preceding cases, we have tentatively assigned the 4*R*,5*R* configuration because the attack of diazoethane must take place on the less hindered face of the nitro olefin and the trans arrangement of the substituents on C-4 and C-5 is thermodynamically favored. The value (4.0 Hz) of $J_{4,5}$ indicates the pre-



8′

ponderance of the ^5E conformation. This conformation must be the most stable because of its lack of gauche interactions between the bulky substituents on C-4 and C-5 and also its lack of cis-1,3 interactions. Treatment of **8′** with HCl gave the pyrazole **12** already obtained from the pyrazoline **7**.

When **1** was treated with ethyl diazoacetate the 2-pyrazoline could not be isolated. Instead, by a comparatively slow reaction, a complex mixture of products was formed. Following chromatography on silica gel, 3(5)-(Ethoxycarbonyl)-4-(D-*galacto*-1,2,3,4,5-penta-*O*-acetylpentitol-1-yl)pyrazole (**13**) was obtained, in 37% yield, as a crystalline solid. The ^1H NMR spectrum of this substance only showed one pyrazole ring proton due to H-3(5) at 7.7 ppm. The protons of the pentaacetoxypentyl chain originated a simple first-order pattern which could be completely assigned to demonstrate the *P* conformation, generally observed for acyclic sugar derivatives having the D-*galacto* configuration.[12,13]

(12) Blanc-Muesser, M.; Defaye, J.; Horton, D. *Carbohydr. Res.* **1980**, *87*, 71–86.
(13) Román, E.; Galbis, J. A.; Arévalo, M. A. *Carbohydr. Res.* **1983**, *116*, 255–262.

From the reaction of **2** with ethyl diazoacetate, the pyrazole **14** was isolated as a white solid in 44% yield. The ^{1}H NMR spectrum registered for **14** showed similar characteristics to that of **13**; but a singlet signal at 2.35 ppm, assigned to the methyl group on C-3(5), is shown instead of the aromatic CH signal. The ^{13}C NMR spectrum gave signals for the pyrazole ring carbons at 144.83, 135.81, and 116.62 ppm (C-3, C-5, and C-4).

The success of the reactions described for the nitro olefin **1** contrasts with results concerning the cycloaddition of diazoalkanes to 1-nitro-2-phenylethene, reported by Parham and Bleasdale.[5] Their postulate for the necessary absence of a hyrogen on the carbon holding the nitro group appears to be nonessential.

Experimental Section

General Methods. All melting points were taken on a Electrothermal melting point apparatus and are uncorrected. IR spectra were measured with an Perkin-Elmer 1310 spectrophotometer. Fourier transform NMR spectra (in $CDCl_3$ and DMSO-d_6) were measured at 80 MHz on a Bruker WP-80-SY spectrometer with Me_4Si as the internal standard. Chemical shifts are given in δ, in ppm downfield from internal Me_4Si, and coupling constants are given in hertz. TLC was performed on precoated glass plates (0.25 mm) coated with silica gel 60F-254 (Merck); components were detected by spraying the plates with 10% sulfuric acid, with subsequent heating, and by UV light. Paper chromatography was carried out by ascending technique on Whatman No. 1 filter paper with the following mobile phases: (a) butan-1-ol–pyridine–water (1:1:1); (b) butan-1-ol–acetone–water (2:7:1). Compounds were detected with alkaline silver nitrate. Solutions were dried with magnesium sulfate and evaporated under diminished pressure below 50 °C.

1,2-Dideoxy-2-*C*-nitrooctitols. To a stirred suspension of D-galactose (25 g, 140 mmol) in absolute methanol and nitroethane (140 mL, 150 mmol) was added a cold solution containing sodium (6.5 g) in absolute methanol (150 mL). After being stirred (24 h), the mixture was treated with an excess of Dowex-50 resin and was evaporated to give a syrup that was crystallized from ethanol (96%) to afford a mixture of two octitols (in a ratio of 6:4 by ^{1}H NMR spectra): yield, 8.5 g (24%); mp 166–168 °C; IR (KBr) ν_{max} 3350 (OH), 1550 cm^{-1} (NO_2); ^{1}H NMR (major product; DMSO-d_6) 1.37 (d, 3, $J_{1,2}$ = 6.6 Hz, C_1H), 3.30–3.80 (m, 6, C_4H to C_8H), 4.26 (dd, 1, $J_{3,4}$ = 9.7 Hz, C_3H), 4.84 (m, 1, $J_{2,3}$ = 2.9 Hz, C_2H); ^{13}C NMR (DMSO) 15.51 (C_1), 63.31 (C_8), 68.36–70.33 (C_4 to C_7), 72.40 (C_3), 84.04 (C_2); ^{1}H NMR (minor product; DMSO-d_6) 1.47 (d, 3, $J_{1,2}$ = 6.8 Hz, C_1H), 3.30–3.80 (m, 7, C_3H to C_8H), 4.84 (m, 1, $J_{2,3}$ = 9.3 Hz, C_2H); ^{13}C NMR (DMSO-d_6) 10.05 (C_1), 63.31 (C_8), 68.36–70.31 (C_4 to C_7), 71.56 (C_3), 84.51 (C_2). Anal. Calcd for $C_8H_{17}O_8N$: C, 37.65; H, 6.66; N, 5.49. Found: C, 37.90; H, 6.78; N, 5.60.

3,4,5,6,7,8-Hexa-*O*-acetyl-1,2-dideoxy-2-*C*-nitrooctitols. The solution of the nitro alcohols described about (1.3 g, 5.09 mmol) in acetic anhydride (10 mL) was treated with one drop of concentrated sulfuric acid, and the acetylation mixture was poured onto ice and water. The resulting solid was recrystallized from ethanol to afford a mixture of hexaacetates, in an overall yield of 96%, which could be separated by fractional crystallization. The minor product was recrystallized from ethanol to give 820 mg (33%): mp 110–111 °C; IR (KBr) ν_{max} 1740 (C=O), 1555 cm^{-1} (NO_2); ^{1}H NMR ($CDCl_3$) 1.54 (d, 3, $J_{1,2}$ = 6.8 Hz, C_1H), 2.07 (s, 15, OAc), 3.80 (dd, 1, $J_{8',7}$ = 7.1 Hz, $C_{8'}$H), 4.26 (dd, 1, $J_{8,7}$ = 5.19, $J_{8,8'}$ = −11.57 Hz, C_8H), 4.47 (m, 1, $J_{2,3}$ = 3.1 Hz, C_2H), 5.11 (m, 1, C_7H), 5.19 (dd, 1, $J_{6,7}$ = 6.98 Hz, C_6H), 5.24 (dd, 1, $J_{5,6}$ = 2.2 Hz, C_5H), 5.46 (dd, 1, $J_{4,5}$ = 10.00 Hz, C_4H), 5.53 (dd, 1, $J_{3,4}$ = 3.0 Hz, C_3H); ^{13}C NMR ($CDCl_3$) 12.84 (C_1), 20.54 (OAc), 62.12 (C_8), 66.75–68.39 (C_4 to C_7), 69.67 (C_3), 81.06 (C_2), 169.77 (OAc). The major product was also recrystallized from ethanol to give 1.29 g (52%): mp 121–123 °C; ^{1}H NMR ($CDCl_3$) 1.57 (d, 3, $J_{1,2}$ = 6.9 Hz, C_1H), 2.07 (s, 15, OAc), 3.80 (dd, 1, $J_{8',7}$ = 7.1 Hz, $C_{8'}$H), 4.27 (dd, 1, $J_{8,7}$ = 5.19, $J_{8,8'}$ = −11.57 Hz, C_8H), 4.81 (m, 1, $J_{2,3}$ = 5.2 Hz, C_2H), 5.10–5.53 (m, 5, C_3H to C_7H); ^{13}C NMR ($CDCl_3$) 15.20 (C_1), 20.54 (OAc), 62.28 (C_8), 66.75–68.39 (C_4 to C_7), 70.56 (C_3), 81.83 (C_2), 169.77 (OAc). Anal. Calcd for $C_{20}H_{29}O_{14}N$: C, 47.34; H, 5.72; N, 2.76. Found: C, 47.05; H, 5.83; N, 2.58.

4,5,6,7,8-Penta-*O*-acetyl-1,2,3-trideoxy-2-*C*-nitro-D-*galacto*-oct-2-enitol (2). A solution of the hexaacetates mixture (3 g, 5.9 mmol) in dry benzene (25 mL) was refluxed (2.5 h) with sodium hydrogen carbonate (15 g). The mixture was cooled, filtered, and evaporated to give a crystalline residue, which on recrystallization from ethanol gave the acetylated nitro olefin **2** (2.38 g, 90%, mp 143–145 °C): IR (KBr) ν_{max} 1550 (NO_2), 1660 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) 2.10 (s, 15, OAc), 2.30 (d, 3, $J_{1,3}$ = 1.13 Hz, C_1H), 3.85 (dd, 1, $J_{7,8'}$ = 7.12, $J_{8,8'}$ = −11.5 Hz, $C_{8'}$H), 4.28 (dd, 1, $J_{7,8}$ = 5.2 Hz, C_8H), 5.20–5.54 (m, 3, C_5H to C_7H), 5.57 (dd, 1, $J_{4,5}$ = 2.8 Hz, C_4H), 6.73 (m, 1, $J_{3,4}$ = 8.9 Hz, C_3H); ^{13}C NMR ($CDCl_3$) 13.21 (C_1), 20.38 (OAc), 61.92 (C_8), 67.40–69.04 (C_4 to C_7), 127.32 (C_3), 151.05 (C_2), 169.41 (OAc). Anal. Calcd for $C_{18}H_{25}O_{12}N$: C, 48.32; H, 5.59; N, 3.13. Found: C, 48.50; H, 5.44; N, 2.99.

3-Methyl-3-nitro-4-(D-*galacto*-penta-*O*-acetylpentitol-1-yl)-1-pyrazoline (7) and 4-Methyl-4-nitro-3-(D-*galacto*-penta-*O*-acetylpentitol-1-yl)-1-pyrazoline (7′). A solution of **2** (60 mg, 0.13 mmol) in dioxane (5 mL) was cooled to 0 °C, and to it was added a solution of diazomethane (13 mg, 0.3 mmol) in ether (5 mL). The resulting solution was stored (0 °C; 1 h) and was evaporated to dryness, leaving a white solid that was recrystallized from methanol, affording a 9:1 mixture of **7** and **7′**: R_f 0.45 (ether–hexane, 3:1); yield 65 mg (quantitative); mp 129–131 °C; IR (KBr) ν_{max} 1745 (C=O), 1560 (N=N), 1545 (NO_2) cm^{-1}; ^{1}H NMR [of **7**] ($CDCl_3$) 1.86 (s, 3, Me), 2.00–2.10 (s, 15, OAc), 2.93 (m, 1, C_4H), 3.78 (dd, 1, $J_{4',5''}$ = 7.3, $J_{5',5''}$ = −11.7 Hz, $C_{5''}$H), 4.31 (dd, 1, $J_{4',5'}$ = 4.8 Hz, $C_{5'}$H), 4.63 (dd, 1, $J_{4,5b}$ = 7.0, $J_{5a,5b}$ = −18.3 Hz, C_{5b}H), 4.86 (dd, 1, $J_{4,5a}$ = 8.7 Hz, C_{5a}H), 5.04–5.35 (m, 4, $C_{1'}$H to $C_{4'}$H); ^{13}C NMR ($CDCl_3$) 16.75 (Me), 20.45 (OAc), 44.59 (C_4), 62.15 ($C_{5'}$), 66.95–69.68 ($C_{1'}$ to $C_{4'}$), 78.77 (C_5), 122.91 (C_3), 169.77 (OAc); ^{1}H NMR [of **7′**] ($CDCl_3$) 1.55 (s, 3, Me), 2.00–2.10 (s, 15, OAc), 2.93 (m, 1, C_4H), 3.78 (dd, 1, $J_{4',5''}$ = 7.3, $J_{5',5''}$ = −11.7 Hz, $C_{5''}$H), 4.31 (dd, 1, $J_{4',5'}$ = 4.8 Hz, $C_{5'}$H) 5.04–5.35 ($C_{1'}$H to $C_{4'}$H); ^{13}C NMR ($CDCl_3$) 14.64 (Me), 20.16 (OAc), 44.59 (C_4), 62.16 ($C_{5'}$), 66.94–69.68 ($C_{1'}$ to $C_{4'}$), 77.60 (C_5), 121.13 (C_3), 169.68 (OAc). Anal. Calcd for $C_{19}H_{27}O_{12}N_3$: C, 46.62; H, 5.52; N, 8.59. Found: C, 46.90; H, 5.57; N, 8.63.

3(5)-Methyl-4-(D-*galacto*-penta-*O*-acetylpentitol-1-yl)-pyrazole (11). The aromatization was performed by passing a stream of hydrogen chloride through the mixture of **7** and **7′** (2 g, 4 mmol) in dioxane (20 mL). Evaporation of the solvent provided an amorphous tautomeric mixture containing two isomers (**11** and **11′**) in the ratio of 9:1, as determined by the intensities of the methyl signals at δ 2.39 (**11**) and 2.61 (**11′**) in the ^{1}H NMR spectrum. The major product **11** was isolated by fractional crystallization as a white solid (85%, mp 98–100 °C): IR (KBr) ν_{max} 3510 (NH), 1750 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) 2.05 (s, 15, OAc), 2.39 (s, 3, Me), 3.85 (dd, 1, $J_{4',5''}$ = 7.1 Hz, $C_{5''}$H), 4.25 (dd, 1, $J_{4',5'}$ = 5.0, $J_{5',5''}$ = −11.6 Hz, $C_{5'}$H), 5.20–5.50 (m, 3, $C_{2'}$H to $C_{4'}$H), 5.95 (dd, 1, $J_{1',2'}$ = 2.4, $J_{1',3}$ = 1.2 Hz, $C_{1'}$H), 6.50 (br s, 1, NH), 7.51 (s, 1, C_3H); ^{13}C NMR ($CDCl_3$) 10.31 (Me), 20.44 (OAc), 61.99 ($C_{5'}$), 65.72–70.04 ($C_{1'}$ to $C_{4'}$), 114.23 (C_4), 134.17 (C_5), 141.26 (C_3), 169.60 (OAc). Anal. Calcd for $C_{19}H_{26}O_{10}N_2 \cdot {}^1/_2H_2O$: C, 50.55; H, 5.98; N, 6.21. Found: C, 50.35; H, 6.03; N, 6.30.

Compound **8′** (475 mg, 1 mmol), by the method described for **12**, after recrystallization from methanol, also gave **11** (322 mg, 74%, mp 98–100 °C).

3-Nitro-4-(D-*galacto*-penta-*O*-acetylpentitol-1-yl)-1-pyrazoline (6). A solution of **1** (870 mg, 2 mmol) in dioxane (5 mL) underwent diazomethane cycloaddition under the same conditions used in the preparation of **7** to give **6** as a solid that was recrystallized from methanol: mp 171–173 °C; yield, 819 mg (86%); IR (KBr) ν_{max} 1745 (C=O), 1560 (N=N), 1550 cm^{-1} (NO_2); ^{1}H NMR ($CDCl_3$) 2.10 (s, 15, OAc), 2.73 (m, 1, C_4H), 3.80 (dd, 1, $J_{5',5''}$ = −11.8, $J_{4',5''}$ = 7.1 Hz, $C_{5''}$H), 4.29 (dd, 1, $J_{4',5'}$ = 4.8 Hz, $c_{5'}$H), 4.55 (dd, 1, $J_{4,5b}$ = 7.4, $J_{5a,5b}$ = −18.2 Hz, C_{5b}H), 5.08 (dd, 1, $J_{4,5a}$ = 9.1 Hz, C_{5a}H), 5.10–5.30 (m, 4, $C_{1'}$H to $C_{4'}$H), 6.56 (m, 1, $J_{3,4}$ = 7.1, $J_{3,5}$ = 3.03 Hz, C_3H); ^{13}C NMR ($CDCl_3$) 20.42 (Me), 40.04 (C_4), 62.06 ($C_{5'}$), 67.10–69.28 ($C_{1'}$ to $C_{4'}$), 80.98 (C_5), 117.56 (C_3), 170.19 (OAc). Anal. Calcd for $C_{18}H_{25}O_{12}N_3$: C, 45.47; H, 5.26; N, 8.84. Found: C, 45.07; H, 5.35; N, 8.80.

4-(D-*galacto*-Penta-*O*-acetylpentitol-1-yl)pyrazole (10). Treatment of **6** (475 mg, 1 mmol) with hydrogen chloride under the same conditions used in the preparation of **11** led to **10** as

a syrup (218 mg, 51%) that did not crystallize: IR ν_{max} 3530 (NH), 1760 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) 2.1 (s, 15, OAc), 3.85 (dd, 1, $J_{4',5''}$ = 7.0 Hz, $C_{5''}H$), 4.24 (dd, 1, $J_{4',5'}$ = 4.8, $J_{5',5''}$ = −11.6 Hz, $C_{5'}H$), 5.36 (m, 3, $C_{2'}H$ to $C_{4'}H$), 5.99 (d, 1, $C_{1'}H$), 7.1 (br s, 3, NH and C_3H); ^{13}C NMR ($CDCl_3$) 20.47 (OAc), 62.03 ($C_{5'}$), 66.02–70.21 ($C_{1'}$ to $C_{4'}$), 113.78 (C_4), 134.52 ($C_{3(5)}$), 169.60 (OAc). Anal. Calcd for $C_{18}H_{24}O_{10}N_2$: C, 50.46; H, 5.72; N, 6.54. Found: C, 50.32; H, 6.01; N, 6.78.

3,5-Dimethyl-3-nitro-4-(D-*galacto*-penta-*O*-acetylpentitol-1-yl)-1-pyrazoline (9). Treatment of nitro olefin **2** (1.23 g, 2.7 mmol) with diazoethane (0.30 g, 5.3 mmol) at 0 °C for 48 h gave a residue, which was shown by TLC to contain one compound. Recrystallization from ethanol (96%) gave **9** (1.32 g, 95%, mp 120–122 °C): R_f 0.42 (ether–hexane, 3:1); IR (KBr) ν_{max} 1560 (N=N), 1550 cm^{-1} (NO_2); ^1H NMR ($CDCl_3$) 1.55 (d, 3, $J_{Me,5}$ = 7.12 Hz, Me), 1.77 (s, 3, Me), 2.01 (s, 15, OAc), 2.46 (dd, 1, $J_{4,5}$ = 7.89, $J_{4,1'}$ = 9.78 Hz, C_4H), 3.73 (dd, 1, $J_{4',5''}$ = 7.19, $J_{5',5''}$ = −11.71 Hz, $C_{5''}H$), 4.21 (dd, 1, $J_{4',5'}$ = 4.8 Hz, $C_{5'}H$), 4.43 (dd, 1, C_5H), 5.00–5.09 (m, 3, $C_{2'}H$) to $C_{4'}H$), 5.22 (dd, 1, $J_{1',2'}$ = 1.6 Hz, $C_{1'}H$); ^{13}C NMR ($CDCl_3$) 16.68 (Me), 18.49 (Me), 20.47 (OAc), 47.70 (C_4), 61.94 ($C_{5'}$), 67.78–68.74 ($C_{1'}$ to $C_{4'}$), 88.12 (C_5), 123.72 (C_3), 170.00 (OAc). Anal. Calcd for $C_{20}H_{29}O_{12}N_3$: C, 47.71; H, 5.76; N, 8.35. Found: C, 47.66; H, 5.92; N, 8.29.

3,5-Dimethyl-4-(D-*galacto*-penta-*O*-acetylpentitol-1-yl)-pyrazole (12). Dry hydrogen chloride was bubbled through a solution of **9** (1 g, 2 mmol) in chloroform (10 mL). TLC indicated the rapid formation of the pyrazole **12** as the only product with R_f 0.70 (chloroform–methanol, 1:2). The solvent was evaporated to dryness, leaving a syrup (0.752 g, 83%) that did not crystallize: IR ν_{max} 3520 (NH), 1745 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) 2.05 (s, 15, OAc), 2.45 (s, 6, Me), 3.83 (dd, 1, $J_{4',5''}$ = 7.1 Hz, $C_{5''}H$), 4.26 (dd, 1, $J_{4',5'}$ = 4.9, $J_{5',5''}$ = −11.7 Hz, $C_{5'}H$), 5.14–5.47 (m, 3, $C_{2'}H$ to $C_{4'}H$), 5.95 (d, 1, $J_{1',2'}$ = 3.7 Hz, $C_{1'}H$), 10.0 (br s, 1, NH); ^{13}C NMR ($CDCl_3$) 10.08 (Me), 20.35 (OAc), 61.81 ($C_{5'}$), 65.20–69.18 ($C_{1'}$ to $C_{4'}$), 113.36 (C_4), 143.37 ($C_{3(5)}$), 169.44 (OAc). Anal. Calcd for $C_{20}H_{28}O_{10}N_2$: C, 52.63; H, 6.14; N, 6.14. Found: C, 52.35; H, 5.98; N, 6.29.

5-Methyl-3-nitro-4-(D-*galacto*-penta-*O*-acetylpentitol-1-yl)-2-pyrazoline (8'). A solution of **1** (2.4 g, 4.7 mmol) in dioxane (50 mL) was added dropwise to a solution of diazoethane (0.60 g, 10.81 mmol) in ether (30 mL). After 48 h at room temperature TLC showed complete conversion to **8'**. Evaporation of the solvent gave a syrup that was crystallized from ethanol (96%) to afford a yellow solid with R_f 0.40 (ether–hexane, 5:1), (2.18 g, 82%, mp 148–150 °C): IR (KBr) ν_{max} 3400 (NH), 1750 (C=O), 1570 cm^{-1} (NO_2); ^1H NMR ($CDCl_3$) 1.21 (d, 3, $J_{Me,5}$ = 6.50, Me), 2.08 (s, 15, OAc), 3.47 (dd, 1, $J_{4,5}$ = 4.0, $J_{4,1'}$ = 8.4 Hz, C_4H), 3.81 (dd, 1, $J_{4',5''}$ = 7.2 Hz, $C_{5''}H$), 4.29 (m, 2, $J_{4',5'}$ = 4.9, $J_{5',5''}$ = −11.6 Hz, $C_{5'}H$, C_5H), 5.14–5.44 (m, 4, $C_{1'}H$ to $C_{4'}H$), 7.15 (br s, 1, NH); ^{13}C NMR ($CDCl_3$) 20.60 (OAc), 20.67 (Me), 49.12 (C_4), 62.18 ($C_{5'}$), 64.48 (C_5), 67.87–68.36 ($C_{1'}$ to $C_{4'}$), 151.29 (C_3), 170.15 (OAc). Anal. Calcd for $C_{19}H_{27}O_{12}N_3$: C, 46.62; H, 5.52;, N, 8.59. Found: C, 46.82; H, 5.70; N, 8.42.

3(5)-Methyl-5(3)-(ethoxycarbonyl)-4-(D-*galacto*-penta-*O*-acetylpentitol-1-yl)pyrazole (14). A solution of **2** (1.8 g, 1.79 mmol) and ethyl diazoacetate (1 g, 8.83 mmol) in methylene chloride (30 mL) was heated under reflux (72 h). Evaporation of the solvent left a syrup that was dried by repeated coevaporation of residual solvent with cyclohexanol to give **14** (0.4 g, 44%) as a white solid, which was recrystallized from methanol (mp 170–172 °C): IR (KBr) ν_{max} 3450 (NH), 1730 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) 1.44 (t, 3, J_{Me,CH_2} = 7.2 Hz, Et), 2.06 (s, 15, OAc), 2.36 (s, 3, Me), 3.86 (dd, 1, $J_{5'',4'}$ = 7.36, $J_{5',5''}$ = −11.52 Hz, $C_{5''}H$), 4.30 (dd, 1, $J_{4',5'}$ = 4.9 Hz, $C_{5'}H$), 4.4 (q, 2, Et), 5.32 (m, 1, $J_{3',4'}$ = 3.2 Hz, $C_{4'}H$), 5.53–5.61 (m, 2, $C_{2'}H$, $C_{3'}H$), 6.58 (d, 1, $J_{1',2'}$ = 2.6 Hz, $C_{1'}H$), 8.7 (br s, 1, NH); ^{13}C NMR ($CDCl_3$) 12.32 (Et), 14.27 (Me), 20.61 (OAc), 61.33 (Et), 62.32 ($C_{5'}$), 67.11–70.34 ($C_{1'}$ to $C_{4'}$), 116.62 (C_4), 135.81 (C_5), 144.83 (C_3), 160.47 (CO_2Et), 169.86 (OAc). Anal. Calcd for $C_{22}H_{30}O_{12}N_2$: C, 51.56; H, 5.86; N, 5.47. Found: C, 51.32; H, 5.99; N, 5.25.

3(5)-(Ethoxycarbonyl)-4-(D-*galacto*-penta-*O*-acetylpentitol-1-yl)pyrazole (13). The nitro olefin **1** (2 g, 4.61 mmol) was treated with ethyl diazoacetate (1 g, 8.83 mmol) in methylene chloride (30 mL). Isolation of the product as described for **14** gave **13** (925 mg, 37%, mp 76–78 °C): R_f 0.15 (ether–hexane 3:1); IR (KBr) ν_{max} 3530 (NH), 1745 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) 1.53 (t, 3, J_{Me,CH_2} = 7.1 Hz, Et), 2.04 (s, 15, OAc), 3.90 (dd, 1, $J_{5'',4'}$ = 7.62, $J_{5',5''}$ = −11.46 Hz, $C_{5''}H$), 4.12 (q, 2, Et), 4.31 (dd, 1, $J_{4',5'}$ = 5.07 Hz, $C_{5'}H$), 5.34 (m, 1, $C_{4'}H$), 5.52 (dd, 1, $J_{3',4'}$ = 1.9 Hz, $C_{3'}H$), 5.69 (dd, 1, $J_{2',3'}$ = 10.1 Hz, $C_{2'}H$), 6.53 (d, 1, $J_{1',2'}$ = 2.22 Hz, $C_{1'}H$), 7.71 (br s, 1, $C_{3(5)}H$); ^{13}C NMR ($CDCl_3$) 14.13 (Me), 20.41 (OAc), 61.15 (Et), 62.14 ($C_{5'}$), 66.22–69.22 ($C_{1'}$ to $C_{4'}$), 119.97 (C_4), 133.03 ($C_{3(5)}$), 136.33 ($C_{5(3)}$), 160.87 (CO_2Et), 169.64 (OAc). Anal. Calcd for $C_{21}H_{28}O_{12}N_2$: C, 50.40; H, 5.60; N, 5.60. Found: C, 50.55; H, 5.99; N, 5.81.

Acknowledgment. We thank Professor P. H. Gross for assistance with the typescript and the Consejeria de Educación y Ciencia of the Junta de Andalucia (España) for financial support.

Registry No. **1**, 37093-75-7; **2**, 115797-84-7; **6**, 115797-89-2; **7**, 115797-85-8; **7'**, 115797-86-9; **8'**, 115797-88-1; **9**, 115797-91-6; **10**, 115797-90-5; **11**, 115797-87-0; **11'**, 115826-88-5; **12**, 115797-92-7; **13**, 115797-94-9; **14**, 115797-93-8; $H_3CCHOH(CHOH)_6H$, 115888-64-7; $H_3CCHNO_2(CHOAc)_6H$, 115797-83-6; D-galactose, 59-23-4; nitroethane, 79-24-3; diazomethane, 334-88-3; diazoethane, 1117-96-0; ethyl diazoacetate, 623-73-4.