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1-Methyl(or phenyl)-5-(penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)pyrazoles from the reactions of 3,4,5,6,7-penta-*O*-acetyl-1,2-dideoxy-1-nitro-D-*galacto*-hept-1-enitol with aldehyde methyl(or phenyl)hydrazones

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ABSTRACT

The title hept-1-enitol (**2**) reacted with aldehyde methyl(or phenyl)hydrazones in refluxing methanol or butyl acetate to give 1-methyl(or phenyl)-5-(penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)pyrazoles in good (for 1-methylpyrazoles) or moderate yields (for 1-phenylpyrazoles). The *O*-deacetylated products were obtained in high yields. A Michael-type adduct was obtained for the reactions of **2** with *p*-tolualdehyde and *p*-nitrobenzaldehyde methylhydrazones, and its role as an intermediate was proved by conversion into the pyrazole derivative under the conditions of the above reactions. Only for the reaction with formaldehyde phenylhydrazone was the observed regioselectivity abnormal. The structures proposed were confirmed by spectral data.

INTRODUCTION

Our interest in the synthesis of analogues of natural *C*-nucleosides from hexose derivatives led to a study of the reactions of hexose aryl- or methyl-hydrazones with nitroalkenes[1,2] and cyclodehydration[3] of the pentitol-1-yl chain at C-3 of the resulting pyrazole derivatives. A new type of pyrazole *C*-nucleoside with the sugar moiety at C-5 of the heterocycle should be accessible by interchanging the functionality of the reagents. We now report their formation by the reaction of aldehyde methyl- or phenyl-hydrazones with 3,4,5,6,7-penta-*O*-acetyl-1,2-dideoxy-1-nitro-D-*galacto*-hept-1-enitol (**2**). The olefin **2** and other sugar nitroalkenes have been used[4,5] in 1,3-dipolar cycloaddition reactions with diazoalkanes in order to obtain nitropyrazoline derivatives.

RESULTS AND DISCUSSION

The reactions of the hydrazones of aromatic aldehydes **1a–d** and **5a–d** with **2** were performed in refluxing methanol. Monitoring by t.l.c. indicated that the reactions were complete within 5–24 h, except for those of **5a–b** and **5d**, which led only to decomposition products even after reaction for 8 days under nitrogen. The hydrazones of aliphatic

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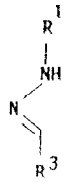
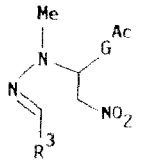
aldehydes **7**–**10**, prepared *in situ*, were each reacted with **2** in boiling butyl acetate under nitrogen for 8 h.

The unique, or for **1b** and **1d** the major, product of the reaction was a pyrazole derivative (**4a**–**d**, **6**, and **11**–**14**) that lacked the nitro group, in agreement with observations[1,2] for reagents with interchanged functionality, and the yields (64–81%) of the 1-methylpyrazoles obtained were greater than those (37–45%) of the 1-phenylpyrazoles.

The observed regioselectivity was "normal" in all of the reactions except that of formaldehyde phenylhydrazone (**8**). Only in two reactions (with **1b** and **1d**) was an intermediate compound [**3b** (7%), and **3d**] detected and isolated; **3d** formed a 1:1 mixture with **4d** that, on *O*-deacetylation, afforded exclusively the pyrazole **15d**, acetylation of which yielded pure **4d**. The intermediates **3b** and **3d** are Michael-type adducts



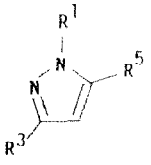


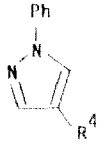
	R^1	R^3
1a–d	Me	Ar
5a–d	Ph	Ar
7	Ph	^{i}Pr
8	Ph	H
9	Me	Me
10	Me	^{i}Pr

2

3b,d R^3 = Ar

	R^3
a	Ph
b	$-C_6H_4$-*p*-Me
c	$-C_6H_4$-*p*-OMe
d	$-C_6H_4$-*p*-NO_2

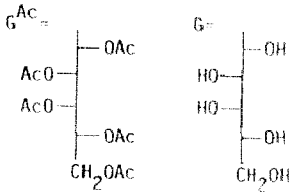




	R^1	R^3	R^5
4a–d	Me	Ar	G^{Ac}
6	Ph	$-C_6H_4$-*p*-OMe	G^{Ac}
11	Ph	^{i}Pr	G^{Ac}
13	Me	Me	G^{Ac}
14	Me	^{i}Pr	G^{Ac}
15a–d	Me	Ar	G
16	Ph	$-C_6H_4$-*p*-OMe	G
17	Ph	^{i}Pr	G
19	Me	Me	G
20	Me	^{i}Pr	G

12 R^4 = G^{Ac}

18 R^4 = G



that result from the nucleophilic attack of the sp^3 N of the hydrazone on the nitro-olefin system, and prove that the mechanism for this type of cyclisation is stepwise[1] and not concerted[6].

Conventional treatment of the foregoing pyrazole derivatives with methanolic sodium methoxide gave the *O*-deacetylated compounds **15**–**20** in high yields (80–95%) except for **15d**, which was obtained from the crude mixture of **3d** and **4d** in a yield of 40%.

The elemental analyses of the new compounds accorded with the structures proposed, which were confirmed by their physical properties. The arylpyrazoles **4a–d**, **6**, **11**, and **12** showed one u.v. band in the range 239–317 nm, and the alkylpyrazoles **13** and **14** absorbed at 222–224 nm, as do structurally related pyrazoles[7]. The i.r. spectra showed the expected bands (see Experimental) and the absence of bands assignable to a nitro group except for **4d** and **15d**. In contrast, the Michael adduct **3b** showed the two expected strong bands at 1555 and 1370 cm^{-1}.

The ^{1}H-n.m.r. data for the pyrazole derivatives are summarised in Tables I and II. For the penta-acetates **4a–d**, **6**, and **11**–**14**, the protons of the pentitol-1-yl moiety resonated in the range δ 3.8–6.1 and appeared in the order of increasing field H-1′ < H-2′ ~ H-3′ < H-4′ < H-5′a,5′b (for **4a–d**, and **12**–**14**), or H-1′ < H-3′ < H-4′ < H-2′ < H-5′a,5′b (for **6** and **11**). The upfield shift of the H-2′ resonance may be attributed to shielding by the 1-phenyl group. Such shielding is not possible in **12** due to the greater distance between the phenyl group and the side chain. The *J* values for the pentitol-1-yl moiety could be measured only for **6**, **11**, and **14**, and indicated that the chain adopted a planar zigzag conformation in solution as in the crystals of **4a** (ref. 8) and **12** (ref. 9). The unique pyrazole proton present in all of the acetylated derivatives, except **12**, resonated at δ 5.99–6.62 (s) in a range typical[10] of H-4 and not of H-5, thus showing that the regioselectivity was "normal". The signals of the pyrazole protons for **12** appeared at δ 7.62 and 7.87, and were assigned to H-3 and H-5, respectively, on the basis of antecedents[10], thus demonstrating the reverse regioselectivity. The same relationship occurred for the signals of the pyrazole protons of the *O*-deacetylated compounds **15a–d** and **16**–**20**; only **18** showed two signals at δ 7.80 and 8.41 attributable to H-3 and H-5, respectively, but the other compounds gave only one signal at δ 6.11–7.15, assigned to H-4.

The ^{13}C-n.m.r. spectra of the pyrazole derivatives (Table III) confirmed the reverse regioselectivity. Thus, the pyrazole carbons resonated in the order of decreasing field C-3 > C-5 > C-4, as established[11], but the signals of C-3 (δ 139.4 and 140.6, respectively) of the reversed compounds **12** and **18** were shifted upfield due to the lack of any substituent[11,12] (*cf.* the δ values 147.1–159.6 and 145.5–158.0 for the acetylated and *O*-deacetylated 3-substituted compounds, respectively). A similar upfield shift was observed for the C-5 resonances in **12** and **18** as compared with those of the respective related compounds. The signal for C-4 in **12** and **18** was shifted downfield correspondingly in comparison with those in the other compounds. An additional proof of the reverse orientation in the reaction leading to **12** was that the δ values for the resonances of the phenyl *ortho*-carbons in **12** and **18** were much lower than those in the "normal"

TABLE I

^{1}H-N.m.r. data (200 MHz, $CDCl_3$, internal Me_4Si) for **4a**, **d**, **6**, and **11**–**14**

Compound	*Chemical shifts (δ in p.p.m.)*															
	H-1′	*H-2′*	*H-3′*	*H-4′*	*H-5′a*	*H-5′b*	*AcO*					*R*^{1}	*H-3*	*H-4*	*H-5*	*Other*
4a	6.07d	←——5.5m——→		5.34ddd	4.25dd	3.86dd	1.99s	2.01s	2.03s	2.07s	2.11s	3.99s		6.51s		7.2–7.8m
4b	6.07d	←——5.5m——→		5.33ddd	4.24dd	3.85dd	1.98s	2.01s	2.02s	2.07s	2.10s	3.97s	–	6.49s		2.35s 7.17d 7.61d
4c	6.07d	←——5.5m——→		5.34ddd	4.25dd	3.87dd	1.99s	2.01s	2.03s	2.07s	2.10s	3.97s		6.46s	–	3.82s 6.91d 7.66d
4d	6.07d	←——5.5m——→		5.33ddd	4.27dd	3.87dd	1.99s	2.02s	2.06s	2.07s	2.13s	4.02s	–	6.62s		7.89d 8.24d
6	6.00d	5.04dd	5.40dd	5.23ddd	4.18dd	3.79dd	1.93s	1.94s	1.95s	1.99s	2.14s	7.5–7.7m		6.55s	–	3.83s 6.91d 7.72d
11	5.98d	4.94dd	5.38dd	5.24ddd	4.18dd	3.78dd	1.93s	1.94s	1.95s	2.00s	2.14s	7.4–7.6m	–	6.13s	–	1.25d 2.99hp
12	6.07d	←——5.5m——→		5.30ddd	4.26dd	3.85dd	2.01s	2.03s	2.06s	2.08s	2.09s	7.2–7.7m	7.62s	–	7.87s	–
13	6.01d	←——5.5m——→		5.28ddd	4.27dd	3.87dd	2.00s	2.03s	2.05s	2.06s	2.08s	3.86s	–	6.00s		2.19s
14	5.99d	5.36dd	5.45dd	5.28ddd	4.23dd	3.85dd	1.96s	2.00s	2.03s(6H)		2.07s	3.84s		5.99s		1.18d 2.87hp

	Coupling constants (J in Hz)							
	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'a}$	$J_{4',5'b}$	$J_{5'a,5'b}$	J_{CH_2} (*Ac*)	*J*(*iPr*)
4a	4.4			5.2	7.2	11.6		
4b	4.4			5.0	7.5	11.7	8.0	
4c	4.4			5.4	7.2	11.5	8.9	
4d	2.1			5.1	7.3	11.6	8.9	
6	2.5	9.7	2.2	5.2	7.6	11.6	8.9	
11	2.4	9.9	2.1	5.0	7.5	11.6		7.0
12	3.1			5.1	7.3	11.5		
13				5.3	7.7	11.9		
14	3.9	9.3	2.1	5.1	7.3	11.5		6.9

TABLE II

^{1}H-N.m.r. data (200 MHz, $(CD_3)_2SO$, internal Me_4Si) for **15–20**

Compound	*Chemical shifts (δ, p.p.m.)*														
	H-1′	*H-2′*	*H-3′*	*H-4′*	*H-5′a*	*H-5′b*	*HO-1′*	*HO-2′,3′,4′*			*HO-5′*	*R*[1]	*H-3*	*H-4*	*H-5*	*Other*
15a	5.14	3.78	3.68	3.88	←3.55→		←5.3–4.3→					3.98		6.78	–	7.3–7.9
15b	5.10	3.77	3.67	3.89	←3.55→		←5.3 4.3→					3.96		6.73		2.42
15c	5.10	3.76	3.66	3.88	←3.54→		5.24	4.77	4.44	4.37	4.62	3.95	–	6.69	–	7.29, 7.73 3.88
15d	5.14	3.78	3.68	3.88	←3.55→		5.37	4.84	4.46	4.39	4.63	4.03	–	6.98	–	7.06, 7.77 8.11, 8.37
16	5.00	3.75	3.64	3.88	←3.54→		5.27	4.99	4.32	4.30	4.59	7.5–7.8	–	7.15	–	3.91
17	4.92	3.63	3.54	3.81	←3.48→		←4.0 3.5→					7.4–7.6		6.60		7.12, 7.87 1.31, 3.01
18	5.01	←3.66→		3.86	←3.54→		←5.2–4.3→					7.3–8.0	7.80	–	8.41	–
19	5.01	3.68	3.61	3.84	←3.52→		←5.2–4.3→					3.81	–	6.11	–	2.20
20	5.02	3.69	3.61	3.85	←3.52→		5.12	4.64	4.39	4.35	4.60	3.84		6.17	–	1.27, 2.91

	Coupling constants (J in Hz)									
	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{1',OH}$	$J_{2',OH}$	$J_{3',OH}$	$J_{4',OH}$	$J_{5',OH}$	$J_{o,m}$ (*Ar*)	J(*iPr*)
15a	1.2	8.3	~0							
15b	1.4	9.4	0.8						8.2	
15c	~0	9.8	~0	7.3	7.5	7.5	6.4	5.5	8.8	
15d	1.6	9.3	1.0	7.3	7.5	7.6	6.3	5.5	8.9	
16	1.5	9.0	1.2	7.3	7.5	7.6	6.6	5.3	8.9	
17	1.1	9.0	1.1						7.0	
18	~0									
19	1.2	9.3	~0							
20	1.3	9.2	1.1	7.5	7.6	7.3	6.2	5.6		6.9

TABLE III

^{13}C-N.m.r. data (50.3 MHz, internal Me_4Si) (δ in p.p.m.) for **4a**–**d**[a], **6**[a], **11**–**14**[a], and **15**–**20**[b]

Compound	*C-3*	*C-4*	*C-5*	*C-1′,4′*		*C-5′*	R^1					R^3				
							Me	*Ph (i)*	(o)	(m)	(p)	*Alk.*	*Ar(i)*	(o)	(m)	(p)
4a	150.2	102.9	138.1	68.1 67.5	68.0 65.0	61.6	37.0						132.7	125.2	128.4	127.5
4b	150.3	102.8	138.0	68.2 67.5	68.1 65.0	61.6	37.0					21.2	129.9	125.1	129.1	137.3
4c	150.2	102.5	138.0	68.1 67.5	68.0 65.0	61.6	37.0					55.1	125.6	126.5	113.8	159.2
4d	147.9	103.8	139.0	68.1 67.5	67.9 64.8	61.6	37.4						138.8[c]	125.6	123.9	146.9
6	151.5	102.9	139.3	68.0 67.5	67.7 65.3	61.8		139.1[c]	126.3[d]	128.8	129.1	55.2	125.4	126.8[d]	113.9	159.5
11	159.6	103.0	138.2	68.2 67.6	67.7 65.4	62.0		139.2[c]	126.2	128.6	129.2	27.8(CH) 20.6(Me) 20.5(Me)				
12[e]	139.4	118.5	125.6	69.7 67.6	68.1 65.4	61.9		139.5	119.0	126.7	129.3					
13	147.1	105.2	137.1	68.2 67.4	67.9 64.8	61.5	36.4					13.0				
14	158.1	102.4	137.0	68.3 67.6	68.0 64.9	61.7	36.6					27.5(CH) 22.8(Me) 22.7(Me)				
15a	148.7	102.5	146.9	72.2 69.6	70.1 64.6	63.3	37.5						133.9	129.2[c]	125.3	127.8
15b	148.6	102.1	146.7	72.1 69.6	70.1 64.5	63.3	37.4					21.2	136.9	129.7[c]	125.2	131.1
15c	148.2	101.5	146.3	71.8 69.3	69.8 64.2	62.9	37.0					55.2	126.3	126.3	114.2	158.7
15d	147.6	103.9	140.3	72.1 69.5	70.0 64.6	63.2	37.9						140.0	125.9[d]	124.6[f]	146.6

16	150.2	103.7	147.3	72.2 69.4	70.0 63.2	63.2		139.9	125.0	129.2	127.7	55.3	126.0	126.6	114.3	159.2
17	158.0	103.8	146.0	72.2 69.4	69.9 62.8	63.1		140.1	124.8	129.0	127.2	27.5(CH) 22.9(Me)				
18[e]	140.6	127.4	126.7[c]	73.5 70.0	70.6 65.3	63.4		140.3	118.7	130.3	126.1[c]					
19	145.7[c]	104.6	145.5[c]	72.2 69.6	70.1 64.4	63.2	36.8					13.6				
20	156.4	101.8	145.5	72.3 69.7	70.2 64.4	63.4	36.9					27.6(CH) 23.4(Me)				

[a] In $CDCl_3$. [b] In $(CD_3)_2SO$. [c,d] These assignments may be interchanged. [e] Sugar residue at C-4.

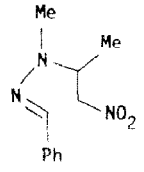
products **6**, **11**, **16**, and **17**, due[11] to the coplanarity of both rings in the latter compounds.

The ^{1}H- and ^{13}C-n.m.r. spectra (Tables IV and V) of the intermediates **3b** and **3d** accorded with the structures proposed. The most downfield ^{1}H signals (dd at δ 5.78 and 5.69, respectively) of the 3,4,5,6,7-penta-*O*-acetyl-1,2-dideoxy-1-nitroheptitol-2-yl chains were assigned to H-3; the diastereotopic protons H-1a and H-1b appeared (as dd) at δ 4.64 and 4.38 for **3b**, and at 4.72 and 4.41 for **3d**. The other pair of diastereotopic protons H-7a,7b gave a similar pattern of signals (see Table IV). The signal of H-2 for **3d** was shifted downfield in comparison with that for **3b**, due to deshielding by the *p*-nitrobenzaldehyde hydrazone moiety. The *N*-methyl proton signal (δ 2.92 and 3.02 for **3b** and **3d**, respectively) was shifted upfield by $\sim$ 1.0 p.p.m. in comparison with the corresponding signals for **4b** and **4d**. The azomethine proton gave signals (bs) at δ 7.27 (**3b**) or 7.24 (**3d**). In the ^{13}C-n.m.r. spectra, the most characteristic signals were those of C-1 ($\delta \sim 75$) and C-7 ($\delta \sim 62$), assigned on the basis of the APT spectra[13], the *N*-methyl carbons (δ 38.2 and 38.6 for **3b** and **3d**, respectively), and the azomethine carbon (δ 134.6 and 130.2), assigned also with the aid of the APT spectra.

The mass spectra of **4a–d**, **6**, and **11**–**14** confirmed the structures proposed. The most significant fragmentations involved the penta-*O*-acetylpentitol-1-yl chain. With the exception of **12**, the peak for M$^+$ was intense, and was the base peak for **4c** and **6**. The base peak for **4a** and **4d** was AcOH$^+$, and, for the remainder of the compounds, (B$^+$ + 30), where B connotes the pyrazole ring with the rest of substituents, and 30 corresponds to a protonated formyl group in agreement with data for other polyacetoxyalkyl heterocycles[14].

In order to obtain more information about the mechanism of these reactions, benzaldehyde methylhydrazone and 1-nitropropene were reacted to give a mixture of the Michael adduct **21** and the pyrazole derivative **22**. Transformation of **21** → **22** under the conditions of the reaction established **21** as an intermediate. These results differed from those obtained[15] for the reactions of aldehyde phenylhydrazones with nitroalkenes, probably due to the different conditions used. The isolation of **21** and the analogous intermediates **3b** and **3d** supports the first step of the mechanism proposed by Snider *et al.*[15], but the lack of a nitro group on the pyrazole ring of **22** and the other pyrazole derivatives described here is incompatible with the remaining steps, and may be explained by an alternative scheme[1].

In order to explain the abnormal regioselectivity observed for the reaction of **2** with formaldehyde phenylhydrazone (**8**), which gave **12**, it is proposed tentatively (Scheme 1) that nucleophilic addition of the azomethine carbon atom of the hydrazone



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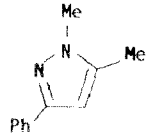

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TABLE IV

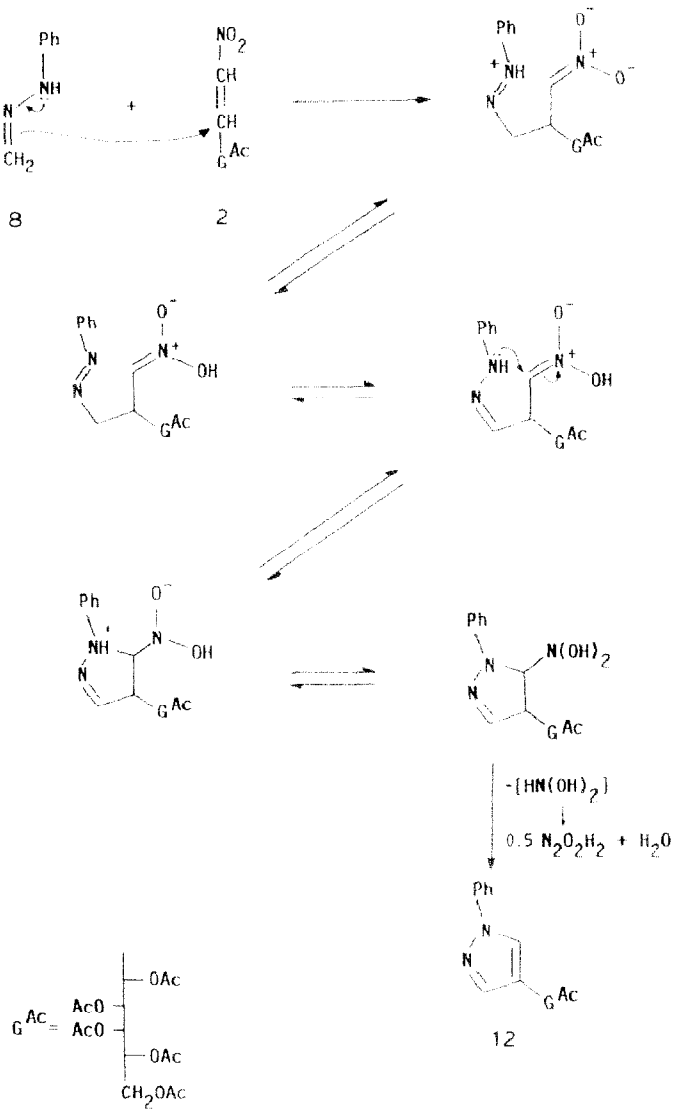
^{1}H-N.m.r. data (200 MHz, $CDCl_3$, internal Me_4Si) for **3b** and **3d**

Compound	*Chemical shifts (δ in p.p.m.)*														
	H-1	*H-1'*	*H-2*	*H-3*	*H-4*	*H-5,6*	*H-7a*	*H-7b*	*HC=N*	*N-Me*	p-*R*-C_6H_4		*OAc*		
3b	4.64	4.38	3.95	5.78	5.49	5.20–5.26	4.28	3.79	7.27	2.92	2.36	7.16 7.48	2.00 2.12	2.01 2.17	2.08
3d	4.72	4.41	4.10	5.69	5.40	5.19–5.28	4.26	3.78	7.24	3.02		7.67 8.20	2.00 2.14	2.01 2.18	2.07
	Coupling constants (J in Hz)														
	$J_{1,1'}$	$J_{1,2}$	$J_{1',2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{6,7a}$	$J_{6,7b}$	$J_{7a,7b}$		$J_{o,m}$				
3b	13.0	6.8	5.4	9.5	1.3	9.7	4.7	6.6	11.6		8.0				
3d	13.0	8.2	4.7	9.2	1.5	9.8	4.8	6.7	11.4		8.8				

TABLE V

^{13}C-N.m.r. data (50.3 MHz, $CDCl_3$, internal Me_4Si) (δ in p.p.m.) for **3b** and **3d**

Compound	*C-1*	*C-2/6*		*C-7*	*N-Me*	*HC=N*	p-*R*-C_6H_4				*OAc*			
							Me	(i)	(o,m)	(p)	*Me*		*C=O*	
3b	74.9	69.5 67.6 64.2	67.7 67.1	62.2	38.2	134.6	21.2	133.3	129.2 125.7	138.0	20.8 20.7 20.5	20.7 20.6	171.0 170.6 169.0	170.8 170.4
3d	75.1	69.0 67.5 64.2	67.5 66.9	62.0	38.6	130.4		142.2	125.6 124.0	146.6	20.6 20.5 20.3	20.5 20.4	171.0 170.3 169.1	170.7 169.8



Scheme 1. Possible origin of the abnormal regioselectivity observed in the reaction of **2** with formaldehyde phenylhydrazone (**8**).

to the nitro-olefin is followed by proton migration, cyclisation by nucleophilic attack of the amine nitrogen on the nitronic acid group to give a zwitterion, tautomerisation of which gives a dihydroxylamine derivative, and loss of hyponitrous acid and water to give the final product **12**.

EXPERIMENTAL

General methods. — Solvents were evaporated *in vacuo* at < 45°. Melting points were determined with a Büchi apparatus and are uncorrected. Optical rotations were

measured with a Perkin–Elmer 241 MC polarimeter. T.l.c. was performed on Silica Gel HF_{254} (Merck), and detection with u.v. light and/or by charring with sulphuric acid. Flash chromatography was conducted on Silica Gel 60 (Merck, 63–200 μm). I.r. spectra were recorded for KBr discs with a Perkin–Elmer 299 spectrophotometer and u.v. spectra with a Perkin–Elmer 545 spectrophotometer. N.m.r. spectra (internal Me_4Si) were recorded with a Varian XL-200 spectrometer; $J_{H,H}$ values were measured directly from the spectra, and assignments for ^1H were confirmed by deuteration and/or double-resonance experiments and, for ^{13}C, from APT spectra[13]. E.i.-mass spectra (70 eV) were recorded with a Kratos MS-80RFA instrument operated at an ionising current of 100 μA, an accelerating voltage of 4 kV, and a resolution of 1000 (10% valley definition).

*Reactions of 3,4,5,6,7-penta-*O*-acetyl-1,2-dideoxy-1-nitro-*D*-galacto-hept-1-enitol* (**2**) *with methyl- or phenyl-hydrazones of aromatic aldehydes.* — The hydrazone (**1a–d**, **5a–d**, 4.4 mmol) was added to a suspension of **2** (1.73 g, 4.0 mmol) in methanol (20 mL), the mixture was boiled under reflux, and the reaction was monitored by t.l.c. After the time stated, the solvent was evaporated, the residue was extracted with ether, the extract was dried ($MgSO_4$) and concentrated, and the residue was purified by column chromatography (3:2 ether–hexane, or a gradient of ether–hexane). For some reactions, the treatment with ether before the chromatography was not necessary.

The following results were obtained.

Hydrazone (*g*)	*Time of reflux* (*h*)	*Products and yields* (*g*, %)	
1a (0.59)	8		**4a** (1.33, 64)
1b (0.65)	5	**3b** (0.16, 7) and	**4b** (1.45, 68)
1c (0.86)	8		**4c** (1.78, 81)
1d (0.79)	24	**3d** + **4d** (1.20)[a]	
5a (0.86)	192[b]	decomposition	
5b (0.92)	192[b]	decomposition	
5c (0.99)	8[b]		**6** (0.93, 37)
5d (1.00)	192[b]	decomposition	

[a] 1:1 mixture (from the intensities of the signals of the *N*-methyl protons in the n.m.r. spectrum). [b] Under nitrogen.

The following compounds were prepared, for which the n.m.r. data are given in Tables I and III–V.

1-Methyl-5-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-3-phenylpyrazole (**4a**), m.p. 109–110°, $[\alpha]_D^{25}$ +69° (*c* 1, chloroform); λ_{max}^{MeOH} 251.5 nm (ε 7800); ν_{max} 1750 cm^{-1} (ester C=O). Mass spectrum: *m/z* 60 (100%), 187 (64, $[B + 30]^+$), 518 (34, M^+), 519 (10, $[M + 1]^+$) (Found: C, 57.68; H, 6.01; N, 5.38. $C_{25}H_{30}N_2O_{10}$ calc.: C, 57.91; H, 5.83; N, 5.40%).

p-Tolualdehyde *N*-methyl-*N*-(3,4,5,6,7-penta-*O*-acetyl-1,2-dideoxy-1-nitro-D-*galacto*-heptitol-2-yl)hydrazone (**3b**), eluted first (ether–hexane gradient), m.p. 93–95°, $[\alpha]_D^{25}$ −45° (*c* 1, chloroform); ν_{max} 1750 (ester C=O), 1555 and 1370 cm^{-1} (NO_2). Mass

spectrum: *m/z* 581 (< 1%, M^+) (Found: C, 53.69; H, 6.05; N, 6.85. $C_{26}H_{35}N_3O_{12}$ calc.: C, 53.70; H, 6.07; N, 7.22%); and 1-methyl-5-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-3-(*p*-tolyl)pyrazole (**4b**), eluted second, m.p. 92–93°, $[\alpha]_D^{25}$ + 72° (*c* 1, chloroform); λ_{max}^{MeOH} 255.5 nm (ε 11 900); ν_{max} 1745 cm^{-1} (ester C=O). Mass spectrum: *m/z* 201 (100%, $[B + 30]^+$), 532 (84, M^+), 533 (25, $[M + 1]^+$) (Found: C, 58.42; H, 6.22; N, 5.27. $C_{26}H_{32}N_2O_{10}$ calc.: C, 58.64; H, 6.06; N, 5.26%).

3-(*p*-Methoxyphenyl)-1-methyl-5-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)pyrazole (**4c**), m.p. 119–120°, $[\alpha]_D^{25}$ + 74° (*c* 1, chloroform); λ_{max}^{MeOH} 261.5 nm (ε 21 600); ν_{max} 1745 cm^{-1} (ester C=O). Mass spectrum: *m/z* 548 (100%, M^+), 217 (69, $[B + 30]^+$), 549 (30, $[M + 1]^+$) (Found: C, 56.70; H, 5.89; N, 5.03. $C_{26}H_{32}N_2O_{11}$ calc.: C, 56.93; H, 5.88; N, 5.11%).

p-Nitrobenzaldehyde *N*-methyl-*N*-(3,4,5,6,7-penta-*O*-acetyl-1,2-dideoxy-1-nitro-D-*galacto*-heptitol-2-yl)hydrazone (**3d**) [mass spectrum: *m/z* 612 (< 1%, M^+)] and 1-methyl-3-(*p*-nitrophenyl)-5-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)pyrazole (**4d**), obtained as a 1:1 mixture (n.m.r. data), which was treated with methanolic sodium methoxide as described below, to give 1-methyl-3-(*p*-nitrophenyl)-5-(D-*galacto*-pentitol-1-yl)pyrazole (**15d**, 0.56 g, 40%), m.p. 243–244°, $[\alpha]_D^{25}$ + 14° (*c* 1, pyridine) (Found: C, 50.81; H, 5.46; N, 11.81. $C_{15}H_{19}N_3O_7$ calc.: C, 50.99; H, 5.42; N, 11.89%). Acetylation of **15d** (0.100 g, 0.28 mmol) with acetic anhydride (1 mL) in pyridine (1 mL) for 48 h at 0° afforded **4d** (0.13 g, 81%), m.p. 92–94° (from ether–hexane), $[\alpha]_D^{25}$ + 76° (*c* 1, chloroform); λ_{max}^{MeOH} 316.5 nm (ε 14 400); ν_{max} 1745 (ester C=O), 1515 and 1370 cm^{-1} (NO_2). Mass spectrum: *m/z* 60 (100%), 232 (51, $[B + 30]^+$), 563 (29, M^+) (Found: C, 53.02; H, 5.15; N, 7.38. $C_{25}H_{29}N_3O_{12}$ calc.: C, 53.28; H, 5.19; N, 7.46%).

3-(*p*-Methoxyphenyl)-5-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)-1-phenylpyrazole (**6**), m.p. 99–101°, $[\alpha]_D^{25}$ + 16° (*c* 1, chloroform); λ_{max}^{MeOH} 270 nm (ε 13 600); ν_{max} 1750 cm^{-1} (ester C=O). Mass spectrum: *m/z* 610 (100%, M^+), 279 (81, $[B + 30]^+$), 611 (35, $[M + 1]^+$) (Found: C, 60.77; H, 5.49; N, 4.45. $C_{31}H_{34}N_2O_{11}$ calc.: C, 60.98; H, 5.61; N, 4.59%).

3-Isopropyl-5-(1,2,3,4,5-penta-O-*acetyl*-D-galacto-*pentitol-1-yl)-1-phenylpyrazole* (**11**). — Isobutyraldehyde (0.46 mL, 5 mmol) was added to a solution of phenylhydrazine (0.49 mL, 5 mmol) in butyl acetate (3 mL), and the mixture was stirred for 10 min at 0°, then for 1 h at room temperature. This solution of isobutyraldehyde phenylhydrazone (**7**) was treated with a solution of **2** (1.73 g, 4 mmol) in butyl acetate (20 mL), and the mixture was boiled to reflux under nitrogen. The reaction was monitored by t.l.c. (3:1 ether–hexane). After 8 h, the solvent was evaporated and the residue was purified by column chromatography (ether–hexane gradient) to give **11** (0.90 g, 42%), m.p. 104–105°, $[\alpha]_D^{25}$ +12° (*c* 1, chloroform); λ_{max}^{MeOH} 239 nm (ε 8800); ν_{max} 1750 cm^{-1} (ester C=O). Mass spectrum: *m/z* 215 (100%, $[B + 30]^+$), 546 (45, M^+), 547 (14, $[M + 1]^+$) (Found: C, 59.17; H, 6.27; N, 5.00. $C_{25}H_{34}N_2O_{10}$ calc.: C, 59.33; H, 6.27; N, 5.13%).

4-(1,2,3,4,5-Penta-O-*acetyl*-D-galacto-*pentitol-1-yl)-1-phenylpyrazole* (**12**). — Aqueous 37% formaldehyde (0.38 mL, 5 mmol) and anhydrous sodium sulphate (1 g) were added to a solution of phenylhydrazine (0.49 mL, 5 mmol) in butyl acetate (3 mL).

The mixture was stirred for 10 min at 0°, then for 1 h at room temperature, and extracted with butyl acetate (2 × 1 mL). The combined extracts that contained the formaldehyde phenylhydrazone (**8**) were treated with a solution of **2** (1.73 g, 4 mmol) in the same solvent (20 mL). The mixture was boiled under reflux under nitrogen and the reaction was monitored by t.l.c. (3:1 ether–hexane). After 8 h, the mixture was boiled with activated charcoal, filtered, and concentrated. The syrupy residue was purified by column chromatography (3:2 ether–hexane) to yield **12** (0.91 g, 45%), m.p. 154–155°, $[\alpha]_D^{25}$ + 50° (*c* 1, chloroform); λ_{max}^{MeOH} 245 nm (ε 14 200); ν_{max} 1740 cm^{-1} (ester C=O). Mass spectrum: *m/z* 173 (100%, $[B + 30]^+$), 504 (1, M^+) (Found: C, 56.96; H, 5.49; N, 5.53. $C_{24}H_{28}N_2O_{10}$ calc.: C, 57.14; H, 5.59; N, 5.55%).

*1,3-Dimethyl-5-(1,2,3,4,5-penta-*O*-acetyl-*D*-galacto-pentitol-1-yl)pyrazole* (**13**). — Acetaldehyde (0.28 mL, 5 mmol) was added with stirring to a solution of methylhydrazine (0.25 mL, 5 mmol) in butyl acetate (3 mL) at 0°. The mixture was stirred for 10 min at 0°, then for 1 h at room temperature, and to the resulting suspension of acetaldehyde methylhydrazone (**9**) was added a solution of **2** (1.73 g, 4 mmol) in butyl acetate (20 mL). The mixture was boiled under reflux under nitrogen until t.l.c. (3:1 ether–hexane) indicated no further reaction (8 h). The solution was then concentrated and kept at 0° to give several crops of product (1.48 g, 81%), m.p. 129–130°. Recrystallisation from ether–hexane afforded **13** (1.28 g, 70%), m.p. 132–133°, $[\alpha]_D^{25}$ + 52° (*c* 1, chloroform); λ_{max}^{MeOH} 224 nm (ε 3300); ν_{max} 1750 cm^{-1} (ester C=O). Mass spectrum: *m/z* 125 (100%, $[B + 30]^+$), 456 (8, M^+) (Found: C, 52.42; H, 6.16; N, 6.24. $C_{20}H_{28}N_2O_{10}$ calc.: C, 52.63; H, 6.18; N, 6.14%).

*3-Isopropyl-1-methyl-5-(1,2,3,4,5-penta-*O*-acetyl-*D*-galacto-pentitol-1-yl)pyrazole* (**14**). — Isobutyraldehyde (0.36 mL, 5 mmol) was added to a solution of methylhydrazine (0.26 mL, 5 mmol) in butyl acetate (3 mL) at 0°, and the mixture was stirred for 10 min at 0°, then for 1 h at room temperature. To the resulting solution of isobutyraldehyde methylhydrazone (**10**) was added a solution of **2** (1.73 g, 4 mmol) in butyl acetate (20 mL), and the mixture was boiled under reflux under nitrogen until t.l.c. (3:1 ether–hexane) indicated no further reaction (8 h). The mixture was heated with activated charcoal, filtered, and concentrated to a syrup, which was purified by column chromatography (2:1 ether–hexane) to yield **14** (1.45 g, 75%), m.p. 77–78°, $[\alpha]_D^{25}$ + 49° (*c* 1, chloroform); λ_{max}^{MeOH} 222 nm (ε 5400); ν_{max} 1750 cm^{-1} (ester C=O). Mass spectrum: *m/z* 153 (100%, $[B + 30]^+$), 484 (59, M^+), 485 (14, $[M + 1]^+$) (Found: C, 54.31; H, 6.62; N, 5.73. $C_{22}H_{32}N_2O_{10}$ calc.: C, 54.54; H, 6.66; N, 5.78%).

Deacetylation of **4a–d**, **6**, *and* **11–14**. — A few drops of methanolic 2M sodium methoxide were added to a solution of the appropriate 5-(1,2,3,4,5-penta-*O*-acetyl-D-*galacto*-pentitol-1-yl)pyrazole derivative (0.20 g) (or of the mixture of **3d** and **4d**, as indicated for **15d** below) in dry methanol (10 mL) at room temperature. After 1 h, the mixture was neutralised with IR-120 (H^+) resin and filtered, the resin was washed with methanol (5 mL), and the combined filtrate and washings were concentrated to give the crystalline deacetylated product.

The following compounds were prepared in this manner. The n.m.r. data are given in Tables II and III.

1-Methyl-5-(D-*galacto*-pentitol-1-yl)-3-phenylpyrazole (**15a**; 0.11 g, 92%), m.p. 150–152°, $[\alpha]_D^{25}$ +18° (*c* 1, pyridine) (Found: C, 58.32; H, 6.48; N, 8.99. $C_{15}H_{20}N_2O_5$ calc.: C, 58.43; H, 6.54; N, 9.09%).

1-Methyl-5-(D-*galacto*-pentitol-1-yl)-3-(*p*-tolyl)pyrazole (**15b**; 0.105 g, 87%), m.p. 165–167°, $[\alpha]_D^{25}$ +15° (*c* 1, pyridine) (Found: C, 59.55; H, 6.91; N, 8.50. $C_{16}H_{22}N_2O_5$ calc.: C, 59.61; H, 6.88; N, 8.69%).

3-(*p*-Methoxyphenyl)-1-methyl-5-(D-*galacto*-pentitol-1-yl)pyrazole (**15c**; 0.12 g, 95%), m.p. 141–142°, $[\alpha]_D^{25}$ +14° (*c* 1, pyridine) (Found: C, 56.59; H, 6.52; N, 8.22. $C_{16}H_{22}N_2O_6$ calc.: C, 56.80; H, 6.55; N, 8.28%).

1-Methyl-3-(*p*-nitrophenyl)-5-(D-*galacto*-pentitol-1-yl)pyrazole (**15d**; 0.56 g, 40%; from 1.20 g of the mixture of **3d** and **4d** described above), m.p. 243–244°, $[\alpha]_D^{25}$ +14° (*c* 1, pyridine) (Found: C, 50.81; H, 5.46; N, 11.81. $C_{15}H_{19}N_3O_7$ calc.: C, 50.99; H, 5.42; N, 11.89%).

3-(*p*-Methoxyphenyl)-5-(D-*galacto*-pentitol-1-yl)-1-phenylpyrazole (**16**; 0.125 g, 95%), m.p. 155–156°, $[\alpha]_D^{25}$ −12° (*c* 1, pyridine) (Found: C, 62.96; H, 6.00; N, 6.97. $C_{21}H_{24}N_2O_6$ calc.: C, 62.99; H, 6.04; N, 7.00%).

3-Isopropyl-5-(D-*galacto*-pentitol-1-yl)-1-phenylpyrazole (**17**; 0.10 g, 80%), m.p. 159–160°, $[\alpha]_D^{25}$ −1° (*c* 1, pyridine) (Found: C, 60.81; H, 7.23; N, 8.30. $C_{18}H_{24}N_2O_5$ calc.: C, 60.70; H, 7.19; N, 8.33%).

4-(D-*galacto*-Pentitol-1-yl)-1-phenylpyrazole (**18**; 0.11 g, 98%), m.p. 166–168°, $[\alpha]_D^{25}$ +11° (*c* 1, pyridine) (Found: C, 57.02; H, 6.16; N, 9.45. $C_{14}H_{18}N_2O_5$ calc.: C, 57.13; H, 6.16; N, 9.52%).

1,3-Dimethyl-5-(D-*galacto*-pentitol-1-yl)pyrazole (**19**; 0.10 g, 93%), m.p. 149–150°, $[\alpha]_D^{25}$ +4° (*c* 1, pyridine) (Found: C, 48.90; H, 7.35; N, 11.32. $C_{10}H_{18}N_2O_5$ calc.: C, 48.77; H, 7.37; N, 11.38%).

3-Isopropyl-1-methyl-5-(D-*galacto*-pentitol-1-yl)pyrazole (**20**; 0.10 g, 89%), m.p. 145–146°, $[\alpha]_D^{25}$ +8.5° (*c* 1, pyridine) (Found: C, 52.28; H, 8.15; N, 10.23. $C_{13}H_{24}N_2O_5$ calc.: C, 52.54; H, 8.08; N, 10.21%).

Benzaldehyde N-methyl-N-(1-methyl-2-nitroethyl)hydrazone (**21**) *and 1,5-dimethyl-3-phenylpyrazole* (**22**). — 1-Nitropropene (0.87 g, 10 mmol) was added to a solution of benzaldehyde methylhydrazone (**1a**; 1.34 g, 10 mmol) in methanol (10 mL), and the mixture was kept at room temperature for 1 h. The solvent was then evaporated and the residue was purified by column chromatography (ether–hexane, 2:3) to give, first, **21** (1.28 g, 58%), m.p. 55–56°, ν_{max} 1550 and 1380 cm^{-1} (NO_2) (Found: C, 59.62; H, 6.90; N, 18.91. $C_{11}H_{15}N_3O_2$ calc.: C, 59.71; H, 6.83; N, 18.99%).

Eluted second was **22** (0.55 g, 32%), m.p. 37–38°; lit.[16] m.p. 36°.

Monitoring of a methanolic solution of **21** by t.l.c. showed its quantitative transformation into **22**. This process was catalysed by acids (H_2SO_4 or HOAc).

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