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Note

New pentahydroxypentylpyrazoles from the reactions of D-mannose and D-galactose methylhydrazones with nitroalkenes*

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The reactions of D-galactose phenylhydrazone and nitroalkenes gave[1] 3-(D-*galacto*-pentitol-1-yl)pyrazole derivatives in moderate yields. These compounds have interest as intermediates in the synthesis of *C*-nucleosides[2]. We now report on the reaction of methylhydrazones of D-mannose (**1**) and D-galactose (**2**) with the nitroalkenes **3–6** in order to establish the validity of the method for the synthesis of *N*-alkylpentahydroxypentylpyrazoles. The yields (50–75%) of the 1-methylpyrazoles **7–12** obtained were greater than those[1] (8–59%) of the 1-arylpyrazoles. The reactions were performed at room temperature in 10:1 *N,N*-dimethylformamide–water and, as in the previous reactions[1], loss of the nitro group was observed. The structures of **7–12** were established as follows. Acetylation of **7–12** yielded the respective penta-acetates **13–18**, and periodate oxidation afforded the pyrazole-3-carbaldehydes **19–22** in good yields; **19** was prepared from **7** and **10**, and **22** from **9** and **12**. The consumption of periodate by **7–12** was consistent with the presence of pentahydroxypentyl groups. Reduction of **19** with $NaBH_4$ gave the carbinol **23**, and the pyrazole-3-carboxylic acids **24–26** were prepared from **19, 21,** and **22**, respectively, by oxidation with moist silver oxide.

The u.v. absorptions for **7–12** and **19–26** are summarised in Table I and are similar to those of other phenylpyrazole derivatives[3]. For some of the compounds (**22, 24, 25**), the bands show fine structure.

The compounds **7–26** had the appropriate i.r. absorptions: **7–12** and **23** at 3600–3000 cm^{-1} (HO), **13–18** at 1745–1735 cm^{-1} (Ac), **19–22** at 1690–1673 cm^{-1} (CHO), and **24–26** at 3600–2300 (HO) and 1720–1680 cm^{-1} (C=O). As in the previous series[1], a band at 1575–1530 cm^{-1} was assigned[2] to the pyrazole C=N, and one or two bands at 950–910 cm^{-1} to the pyrazole ring[4].

The ^{1}H-n.m.r. data for **7–26** are compiled in Table II. The high regioselectivity

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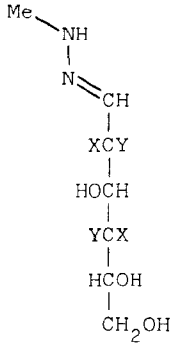
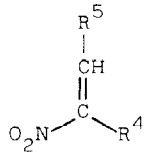


1 X = OH, Y = H

2 X = H, Y = OH

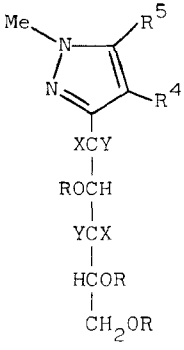


3 R^4 = H, R^5 = Ph

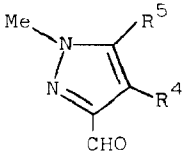
4 R^4 = Me, R^5 = Ph

5 R^4 = H, R^5 = *p*-tolyl

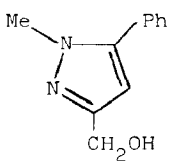
6 R^4 = Me, R^5 = *p*-tolyl



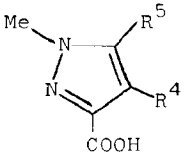
	R	X	Y	R^4	R^5
7	H	OH	H	H	Ph
8	H	OH	H	Me	Ph
9	H	OH	H	Me	*p*-tolyl
10	H	H	OH	H	Ph
11	H	H	OH	H	*p*-tolyl
12	H	H	OH	Me	*p*-tolyl
13	Ac	OAc	H	H	Ph
14	Ac	OAc	H	Me	Ph
15	Ac	OAc	H	Me	*p*-tolyl
16	Ac	H	OAc	H	Ph
17	Ac	H	OAc	H	*p*-tolyl
18	Ac	H	OAc	Me	*p*-tolyl



	R^4	R^5
19	H	Ph
20	Me	Ph
21	H	*p*-tolyl
22	Me	*p*-tolyl



23



	R^4	R^5
24	H	Ph
25	H	*p*-tolyl
26	Me	*p*-tolyl

TABLE I

U.V. ABSORPTION BANDS FOR COMPOUNDS **7–12** AND **19–26**

Compound	λ_{max} *(nm)*	ε *(L·mol^{-1})*	*Compound*	λ_{max} *(nm)*	ε *(L·mol^{-1})*
7[a]	240	15,000	**23**[a]	238	11,700
8[b]	242	11,100	**24**[a]	238	19,900
9[a]	244	10,270		240	20,900
10[a]	240	18,400		246	21,800
11[b]	244	19,900		252	22,100
12[a]	241	18,100		258	21,000
19[a]	236	20,400	**25**[a]	237	19,900
20[a]	237	21,900		241	21,200
21[a]	239	20,600		246	22,100
22[a]	237	21,500		252	22,500
	241	22,200		258	21,500
	246	22,600	**26**[a]	222	18,000
	252	22,700		238sh[c]	17,700
	258	21,500			

[a]In MeOH. [b]In EtOH. [c]Shoulder.

of the reactions leading to the (pentitol-1-yl)pyrazoles **7–12** is again shown by the δ value (6.18–6.94) for the resonance of the pyrazole proton in **7, 10, 11,** and their derivatives, which accords with the data reported[5] for H-4 in other 1-methylpyrazoles but not with those corresponding to H-5. The J values for alkyl protons of the polyol side-chain in compounds having the D-*manno* configuration (**7–9**, and **13–15**) indicate that H-1,2 and H-3,4 are *anti* and H-2,3 are *gauche*. The values of $J_{4,5}$ and $J_{4,5'}$ do not allow any conclusion on the conformation around the C-4–C-5 bond. Thus, **7–9** and **13–15** exist in solution preferentially in the planar zigzag conformation, as do similar D-*manno* compounds[6].

The ^{13}C-n.m.r. data for **7–9** are recorded in Table III. The assignments are based on bibliographic data for related compounds and APT spectra[7].

The proposed mechanism for the formation of 1-phenyl-3-(pentitol-1-yl)-pyrazoles from D-galactose phenylhydrazone and nitroalkenes[1] applies also to the 1-methyl-3-(pentitol-1-yl)pyrazoles reported here.

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) with the solvent systems indicated and detection with u.v. light or iodine vapor. I.r. spectra were recorded for KBr discs with a Perkin–Elmer 299 spectrophotometer. U.v. spectra were recorded with a Perkin–Elmer 545 spectrophotometer. N.m.r. spectra were recorded with a Varian XL-200 spectrometer; $J_{H,H}$ values were measured directly from the spectra and assignments

TABLE II

^{1}H-N.M.R. CHEMICAL SHIFTS (δ, P.P.M.)[a] AND COUPLING CONSTANTS (J, Hz) FOR COMPOUNDS 7–26 AT 200 MHz

Compound	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-5'*	*OH*	*OAc*	*N-Me*	*R*^{4}	*R*^{5}
7[b]	4.53dd $J_{1,2}$ 8.4 $J_{1,OH}$ 5.4	3.87dd[c] $J_{2,3}$ ~0 $J_{2,OH}$ 7.3	3.70dd[c] $J_{3,4}$ 8.4 $J_{3,OH}$ 7.0	3.55m $J_{4,5}$ 3.0 $J_{4,5'}$ 5.9 $J_{4,OH}$ 5.2	3.68m $J_{5,5'}$ 10.5 $J_{5,OH} = J_{5',OH} = 5.6$	3.44m	5.14d 1[d] 4.05d 2 4.25d 3 4.46d 4 4.35t 5		3.81s	6.33s	7.45–7.52m
8[b]	4.60dd $J_{1,2}$ 8.9 $J_{1,OH}$ 5.4	4.07dd $J_{2,3}$ 1.0 $J_{2,OH}$ 8.4	3.76dd[e] $J_{3,4}$ 8.1	3.54m $J_{4,5}$ 3.2 $J_{4,5'}$ 5.6 $J_{4,OH}$ 5.2	3.67m[e] $J_{5,5'}$ 10.2 $J_{5,OH} = J_{5',OH} = 5.5$	3.43dd[f]	4.87d 1 3.84d 2 4.12d 3 4.37d 4 4.27t 5		3.65s	1.96s	7.34–7.52m
9[b]	4.56dd $J_{1,2}$ 9.2 $J_{1,OH}$ 5.3	4.04dd $J_{2,3}$ 1.1 $J_{2,OH}$ 7.3	3.72m $J_{3,4}$ 8.2 $J_{3,OH}$ 7.4	3.45m $J_{4,5}$ 3.2 $J_{4,5'}$ 6.1 $J_{4,OH}$ 5.2	3.53m $J_{5,5'}$ 10.9 $J_{5,OH} = J_{5',OH} = 5.5$	3.38m	4.92d 1 3.87d 2 4.17d 3 4.43d 4 4.33t 5		3.63s	1.96s	2.37s 7.24d 7.33d *J* 8.3
10[b]	4.90d $J_{1,2}$ ~0 $J_{1,OH}$ 7.3	3.68dd $J_{2,3}$ 9.2	3.59dd $J_{3,4}$ ~0	3.79dd $J_{4,5}$ 6.5 $J_{4,5'}$ 6.6	3.50dd $J_{5,5'}$ 11.9	3.44dd	4.78d 1 4.19d 2[g] *J* 6.4 4.25d 3[g] *J* 7.4 4.27d 4[g] *J* 7.2 4.48t 5 *J* 5.6		3.81s	6.40s	7.40–7.60m
11[b]	4.91bs[h] $J_{1,2}$ 1.5	3.70dd $J_{2,3}$ 9.2	3.60dd $J_{3,4}$ 1.2	3.81m[e] $J_{4,5}$ 6.0 $J_{4,5'}$ 6.9	3.52dd $J_{5,5'}$ 10.9	3.46dd	4.1–4.8bm (5 H)		3.78s	6.35d *J* 1.2	2.36s 7.33d 7.41d *J* 8.3
12[b]	4.94d $J_{1,2}$ 1.8	3.75dd $J_{2,3}$ 8.6	3.61dd $J_{3,4}$ 1.2	3.81dd[e] $J_{4,5}$ 5.8 $J_{4,5'}$ 7.0	3.51dd $J_{5,5'}$ 11.0	3.45dd	3.5–5[i]		3.65s	1.96s	2.38s 7.27d 7.34d *J* 7.9
13[j]	5.88d $J_{1,2}$ 8.8	5.70dd $J_{2,3}$ 2.3	5.63dd $J_{3,4}$ 8.9	5.14ddd $J_{4,5}$ 2.8 $J_{4,5'}$ 5.1	4.25dd $J_{5,5'}$ 12.5	4.11dd		1.95s 2.06s 2.07s 2.09s 2.10s 1.88s	3.83s 3.69s	6.31s 2.07s[k]	7.40–7.43m 7.23–7.44m

14[j]	5.87d $J_{1,2}$ 9.7	5.79dd $J_{2,3}$ 1.9	5.67dd $J_{3,4}$ 9.2	5.14ddd $J_{4,5}$ 2.7 $J_{4,5'}$ 5.2	4.26dd $J_{5,5'}$ 12.4	4.11dd	1.88s 2.03s 2.07s 2.10s 2.14s	3.69s	2.07s[k]	7.23–7.44m
15[j]	5.87d $J_{1,2}$ 9.7	5.79dd $J_{2,3}$ 1.8	5.67dd $J_{3,4}$ 9.0	5.15ddd $J_{4,5}$ 2.7 $J_{4,5'}$ 5.2	4.27dd $J_{5,5'}$ 12.5	4.11dd	1.88s 2.03s 2.07s[l] 2.10s 2.15s	3.69s	2.07s[k,l]	2.14s 7.16d 7.26d J 8.2
16[j]	6.09d $J_{1,2}$ 2.4	5.58dd $J_{2,3}$ 9.6	5.51dd $J_{3,4}$ 1.9	5.32ddd $J_{4,5}$ 5.0 $J_{4,5'}$ 7.4	4.32dd $J_{5,5'}$ 11.6	3.92dd	2.02s 2.03s 2.07s 2.14s (6 H)	3.82s	6.22s	7.30–7.50m
17[j]	6.09d $J_{1,2}$ 2.4	5.57dd $J_{2,3}$ 9.5	5.51dd $J_{3,4}$ 1.8	5.31ddd $J_{4,5}$ 5.0 $J_{4,5'}$ 7.4	4.31dd $J_{5,5'}$ 11.6	3.91dd	2.02s 2.04s 2.07s 2.13s (6 H)	3.80s	6.18s	2.40s 7.24s
18[j]	6.13d $J_{1,2}$ 3.8	5.59dd $J_{2,3}$ 8.4	5.52dd $J_{3,4}$ 2.7	5.31ddd $J_{4,5}$ 4.8 $J_{4,5'}$ 7.2	4.29dd $J_{5,5'}$ 11.8	3.95dd	2.01s 2.03s 2.04s 2.05s 2.11s	3.68s	2.12s[k]	2.41s 7.15d 7.28d 7.28d J 8.2

Compound	*N-Me*	R^3	R^4	R^5	*Compound*	*N-Me*	R^3	R^4	R^5
19[j]	3.98s	9.99s	6.84s	7.30–7.50m	**23**[j]	3.86s	1.98s 4.72s	6.32s	7.43–7.47m
20[j]	3.85s	10.06s	2.23s	7.28–7.50m					
21[j]	3.97s	9.98s	6.81s	2.43s 7.31s	**24**[j]	4.00s	8.40s	6.94s	7.40–7.50m
					25[j]	3.98s	8.34s	6.89s	2.42s 7.30s
22[j]	3.84s	10.01s	2.23s	2.44s 7.20d 7.33d J 8.2	**26**[j]	3.83s	~7.3s[l]	2.22s	2.43s 7.19d 7.31d[l] J 8.4

[a]Me_4Si as internal reference. Assignments were confirmed by deuteration and/or double resonance experiments. [b]In $(CD_3)_2SO$. [c]Pseudotriplet with broad peaks. [d]Locant at the side chain. [e]Partially overlapped with the N-Me singlet. [f]Pseudoquintet partially overlapped with the H-4 multiplet. [g]These assignments may be interchanged. [h]This signal appears as a doublet in the spectrum of the deuterated sample. [i]Diffuse, broad, unresolved signal. [j]In $CDCl_3$. [k]This assignment may be interchanged with one of the AcO signals. [l]Overlapped signals.

TABLE III

^{13}C-N.M.R. CHEMICAL SHIFTS (δ, P.P.M.)[a], MULTIPLICITIES[b], AND ASSIGNMENTS FOR COMPOUNDS **7–9** IN $(CD_3)_2SO$

Carbon atom	*Compound*		
	7	**8**	**9**
Pyrazole 4-CH_3		8.4q	8.5q
Phenyl *para*-CH_3			20.7q
Pyrazole 1-CH_3	37.1q	36.7q	36.7q
C-5 of the alditol chain	63.5t	63.8t	63.9t
C-1, C-2, C-3, and C-4	67.5d	66.6d	66.7d
	69.4d	69.5d	69.6d
	71.0d	70.6d	70.7d
	71.3d	71.2d	71.3d
Pyrazole C-4	106.3d	111.9s	111.7s
Phenyl *para*-C	128.1d	128.0d	137.5s
Phenyl *ortho*-C	128.2d[c]	128.6d[c]	129.2d[d]
Phenyl *meta*-C	128.8d[c]	129.3d[c]	
Phenyl *ipso*-C	130.2s	129.9s	127.1s
Pyrazole C-5	143.1s	140.4s	140.3s
Pyrazole C-3	153.6s	150.8s	150.9s

[a]Internal Me_4Si. [b]From APT spectra. [c]Double intensity. [d]Quadruple intensity.

were confirmed by deuteration and/or double resonance experiments. The chemical shifts of ^{13}C resonances are relative to that of internal Me_4Si. The resonances were assigned from "off-resonance" spectra and the multiplicities from APT[7] spectra. Consumption of periodate was measured by a method based on the procedure of Fleury and Lange[8].

Preparation of 1-methyl-3-[D-galacto(D-manno)*-pentitol-1-yl]pyrazoles* (**7–12**). — A solution of D-mannose or D-galactose methylhydrazone[9] (**1** or **2**; 4.16 g, 20 mmol) in 10:1 *N,N*-dimethylformamide–water (20 mL) was added at room temperature to a solution of nitroalkene (**3–6**, 20 mmol) in the same solvent system (4 mL). The reaction at room temperature was monitored by t.l.c. (5:1 dichloromethane–methanol). Crystallisation of **7–12** took place during a few days. Each crude product was isolated in several crops and recrystallised from methanol.

The following amounts and conditions were used:

Hydrazone	*Nitroalkene (g)*	*Time (days)*	*Product*	*Yields of pure product (g, %)*
1[9]	**3**[10] (2.98)	4	**7**	3.10, 50
1	**4**[11] (3.26)	4	**8**	3.46, 54
1	**6**[11] (3.54)	4	**9**	3.60, 54
2[9]	**3** (2.98)	2	**10**	3.84, 62
2	**5**[a] (3.26)	2	**11**	4.62, 73
2	**6** (3.54)	2	**12**	5.05, 75

[a]Prepared from *p*-tolualdehyde and nitromethane, as described[10] for β-nitrostyrene, **5** had m.p. 102° (from ethanol).

The following compounds were prepared, for which the spectral data are given in Tables I–III.

1-Methyl-3-(D-*manno*-pentitol-1-yl)-5-phenylpyrazole (**7**), m.p. 150–151°, $[\alpha]_D^{25}$ −30° (*c* 1, pyridine); periodate consumption, 3.95 mol (Found: C, 58.40; H, 6.52; N, 9.23. $C_{15}H_{20}N_2O_5$ calc.: C, 58.44; H, 6.54; N, 9.09%).

1,4-Dimethyl-3-(D-*manno*-pentitol-1-yl)-5-phenylpyrazole (**8**), m.p. 184–185°, $[\alpha]_D^{28}$ −10° (*c* 1, pyridine); periodate consumption, 3.93 mol (Found: C, 59.39; H, 6.90; N, 8.80. $C_{16}H_{22}N_2O_5$ calc.: C, 59.61; H, 6.88; N, 8.69%).

1,4-Dimethyl-3-(D-*manno*-pentitol-1-yl)-5-(*p*-tolyl)pyrazole (**9**), m.p. 175–176°, $[\alpha]_D^{30}$ −8.5° (*c* 1, pyridine); periodate consumption, 4.07 mol (Found: C, 60.42; H, 7.05; N, 8.58. $C_{17}H_{24}N_2O_5$ calc.: C, 60.70; H, 7.19; N, 8.33%).

1-Methyl-3-(D-*galacto*-pentitol-1-yl)-5-phenylpyrazole (**10**), m.p. 185–186°, $[\alpha]_D^{23}$ +17° (*c* 1, pyridine); periodate consumption, 3.94 mol (Found: C, 58.37; H, 6.57; N, 9.09. $C_{15}H_{20}N_2O_5$ calc.: C, 58.43; H, 6.54; N, 9.09%).

1-Methyl-3-(D-*galacto*-pentitol-1-yl)-5-(*p*-tolyl)pyrazole (**11**), m.p. 182–184°, $[\alpha]_D^{23}$ +16.5° (*c* 1, pyridine); periodate consumption, 4.03 mol (Found: C, 59.35; H, 7.11; N, 8.89. $C_{16}H_{22}N_2O_5$ calc.: C, 59.61; H, 6.88; N, 8.69%).

1,4-Dimethyl-3-(D-*galacto*-pentitol-1-yl)-5-(*p*-tolyl)pyrazole (**12**), m.p. 158–160°, $[\alpha]_D^{23}$ +4° (*c* 1, pyridine); periodate consumption, 3.87 mol (Found: C, 60.42; H, 7.37; N, 8.18. $C_{17}H_{24}N_2O_5$ calc.: C, 60.70; H, 7.19; N, 8.33%).

Acetylation of **7–12**. — Compounds **7–12** (200 mg each) were each treated conventionally with pyridine (2 mL) and acetic anhydride (2 mL) for 48 h at 0°. After precipitation in ice–water, the crude products were recrystallised.

The following products were obtained, for which the ^{1}H-n.m.r. data are given in Table II.

Starting compound (mmol)	*Product*	*Recrystallised from*	*Yield (mg, %)*
7 (0.65)	**13**	ethanol	263 78
8 (0.62)	**14**	2:1 ethanol–water	222 67
9 (0.59)	**15**	methanol	260 80
10 (0.65)	**16**	3:1 ethanol–water	298 89
11 (0.62)	**17**	methanol	270 81
12 (0.59)	**18**	3:1 ethanol–water	260 80

1-Methyl-3-(D-*manno*-penta-acetoxypentyl)-5-phenylpyrazole (**13**), m.p. 131–132°, $[\alpha]_D^{25}$ +1.3° (*c* 1, chloroform) (Found: C, 57.52; H, 5.85; N, 5.42. $C_{25}H_{30}N_2O_{10}$ calc.: C, 57.91; H, 5.83; N, 5.40%).

1,4-Dimethyl-3-(D-*manno*-penta-acetoxypentyl)-5-phenylpyrazole (**14**), m.p. 105–107°, $[\alpha]_D^{25}$ +28° (*c* 1, chloroform) (Found: C, 58.89; H, 6.06; N, 5.33. $C_{26}H_{32}N_2O_{10}$ calc.: C, 58.64; H, 6.06; N, 5.26%).

1,4-Dimethyl-3-(D-*manno*-penta-acetoxypentyl)-5-(*p*-tolyl)pyrazole (**15**),

m.p. 107–108°, $[\alpha]_D^{30}$ +13.7° (*c* 1, dichloromethane) (Found: C, 59.57; H, 6.42; N, 4.98. $C_{27}H_{34}N_2O_{10}$ calc.: C, 59.33; H, 6.27; N, 5.13%).

1-Methyl-3-(D-*galacto*-penta-acetoxypentyl)-5-phenylpyrazole (**16**), m.p. 96–98°, $[\alpha]_D^{23}$ +46° (*c* 1, chloroform) (Found: C, 57.68; H, 5.98; N, 5.64. $C_{25}H_{30}N_2O_{10}$ calc.: C, 57.91; H, 5.83; N, 5.40%).

1-Methyl-3-(D-*galacto*-penta-acetoxypentyl)-5-(*p*-tolyl)pyrazole (**17**), m.p. 100–102°, $[\alpha]_D^{23}$ +6° (*c* 1, chloroform) (Found: C, 58.20; H, 6.03; N, 5.39. $C_{26}H_{32}N_2O_{10}$ calc.: C, 58.64; H, 6.06; N, 5.26%).

1,4-Dimethyl-3-(D-*galacto*-penta-acetoxypentyl)-5-(*p*-tolyl)pyrazole (**18**), m.p. 55–57°, $[\alpha]_D^{23}$ +49° (*c* 1, chloroform) (Found: C, 58.96; H, 6.30; N, 4.98. $C_{27}H_{34}N_2O_{10}$ calc.: C, 59.33; H, 6.27; N, 5.13%).

1-Methyl-5-phenylpyrazole-3-carbaldehyde (**19**). — A solution of **10** (1.00 g, 3.24 mmol) in 1:1 1,4-dioxane–water was treated at room temperature with a solution of sodium metaperiodate (2.62 g, 3% more than the stoichiometric amount) in water (160 mL). After 1 h, **19** (0.38 g) was collected and washed with cold water. The product was chromatographically homogeneous and had m.p. 107–108°, R_F 0.8 (35:1 dichloromethane–methanol). The filtrate was extracted with ether (4 × 50 mL), and the combined extracts were dried (Na_2SO_4) and concentrated to give more crude **19**, m.p. 102–103°, which was recrystallised from ether–hexane (combined yield: 0.56 g, 93%). For the n.m.r. data, see Tables I–II.

Anal. Calc. for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.04. Found: C, 70.55; H, 5.02; N, 15.11.

The aldehyde **19** (73%) was also obtained by periodate oxidation of **7**.

3-Hydroxymethyl-1-methyl-5-phenylpyrazole (**23**). — To a solution of **19** (0.48 g, 2.58 mmol) in ethanol (30 mL) was added a solution of sodium borohydride (50 mg) in water (4 mL). The mixture was kept for 1 h at room temperature, the excess of hydride was then decomposed with formic acid, the solution was concentrated, and the syrupy residue was dried by repeated distillation of methanol therefrom and then crystallised from methanol to yield **23** (0.36 g, 74%), m.p. 98–99°. For the spectral data, see Tables I and II.

Anal. Calc. for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.10; H, 6.38; N, 14.77.

1,4-Dimethyl-5-phenylpyrazole-3-carbaldehyde (**20**). — A solution of sodium metaperiodate (2.78 g, 5% more than the stoichiometric amount) in water (120 mL) was added at room temperature to a solution of **8** (1.00 g, 3.10 mmol) in water (100 mL). The mixture was stirred for 1 h with ether (50 mL), the ethereal layer was removed, and the aqueous phase was extracted with ether (3 × 40 mL). The combined organic layers were dried (Na_2SO_4) and concentrated, and the product (0.84 g), m.p. 59–61°, was recrystallised from ether–hexane to give **20** (0.76 g, 85%), m.p. 62–63°. For the spectral data, see Tables I and II.

Anal. Calc. for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 71.81; H, 5.94; N, 13.80.

1-Methyl-5-(p-tolyl)pyrazole-3-carbaldehyde (**21**). — To a solution of **11** (1.00

g, 3.10 mmol) in 1:1 1,4-dioxane–water was added a solution of sodium metaperiodate (2.74 g, 3% more than the stoichimetric amount) in water (150 mL) at room temperature. After 1 h, the product (0.57 g, 92%) was collected and washed with water, and proved to be chromatographically homogeneous (R_F 0.75, 35:1 dichloromethane–methanol) with m.p. 133–134°. Recrystallisation from ether–hexane afforded material (0.55 g, 89%) with m.p. 133–134°. For the spectral data, see Tables I and II.

Anal. Calc. for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 71.65; H, 5.97; N, 13.60.

1,4-Dimethyl-5-(p-tolyl)pyrazole-3-carbaldehyde (**22**). — A solution of sodium metaperiodate (2.62 g, 3% more than the stoichiometric amount) in water (150 mL) was added at room temperature to a solution of **12** (1.00 g, 2.97 mmol) in 1:1 1,4-dioxane–water (120 mL). The mixture was kept for 24 h at 0°, the crystalline product (0.37 g) was collected, the filtrate was extracted with ether (4 × 50 mL), and the combined extracts were dried (Na_2SO_4) and concentrated to an oil, which, on treatment with cold water, gave crystalline material (0.20 g); total yield, 0.57 g (90%) of chromatographically homogeneous product (R_F 0.75, 35:1 dichloromethane–methanol). Recrystallisation from ether–hexane gave **22** (0.53 g, 83%), m.p. 51–53°. For the spectral data, see Tables I and II.

Anal. Calc. for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59; N, 13.07. Found: C, 72.40; H, 6.42; N, 12.79.

The aldehyde **22** (87%) was also obtained by periodate oxidation of **9**.

1-Methylpyrazole-3-carboxylic acids (**24–26**). — A mixture of the aldehyde (**19**, **21**, or **22**; 1.5 mmol), aqueous silver nitrate (0.5 g, ~3 mmol, in 0.9 mL of water), and M NaOH (4.4 mL) was boiled under reflux for 45–60 min and then filtered hot. The insoluble material was washed with hot water (10–15 mL). The filtrate was acidified to pH 3–4 with nitric acid, and the crude product was collected and recrystallized from 1:1 ethanol–water.

The following compounds were prepared thus. For the spectral data, see Tables I and II.

1-Methyl-5-phenylpyrazole-3-carboxylic acid (**24**; 0.15 g, 50%), prepared from **19**, had m.p. 143–145°.

1-Methyl-5-(*p*-tolyl)pyrazole-3-carboxylic acid (**25**; 0.12 g, 36%), prepared from **21**, had m.p. 158–160° (Found: C, 66.67; H, 5.61; N, 13.20. $C_{12}H_{12}N_2O_2$ calc.: C, 66.65; H, 5.59; N, 12.95%).

1,4-Dimethyl-5-(*p*-tolyl)pyrazole-3-carboxylic acid (**26**; 0.13 g, 38%), prepared from **22**, had m.p. 183–184° (Found: C, 67.58; H, 6.25; N, 12.20. $C_{13}H_{14}N_2O_2$ calc.: C, 67.81; H, 6.13; N, 12.17%).

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