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Note

Structure and reactions of 3-benzoyl-2-methyl-5-(D-*arabino*-tetrahydroxybutyl)pyrrole

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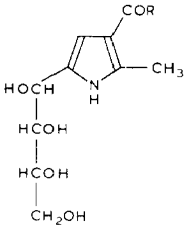
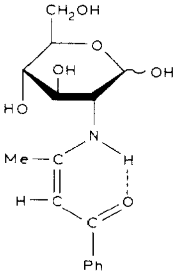
2-Amino-2-deoxy-D-glucose hydrochloride reacts with such β-dicarbonyl compounds[1-6] as 2,4-pentanedione or ethylacetoacetate to give pyrroles **1** or **2** respectively.

However, when 1-phenyl-1,3-butanedione was used[6], two products (**5** or **6**) could be obtained in the presence of triethylamine, formed through the keto-enamine intermediates **3** or **4**, respectively. The product formed in 74% yield was tentatively formulated as **5**.



1 R = CH_3
2 R = OEt



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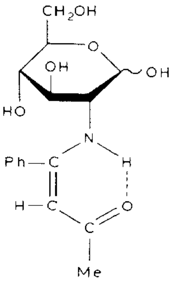

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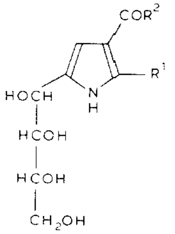

5 $R^1 = CH_3$, R^2 = Ph
6 R^1 = Ph, $R^2 = CH_3$

The reasons for this structural assignment are summarized as follows.

The ^1H-n.m.r. spectrum of **2** showed the methyl resonance at low field (2.85 p.p.m.) and likewise in its reaction products[7] (2.49–2.75 p.p.m.), thus resembling the hydrazone derivatives of **5** (resonance at 2.43–2.70), and much closer to a 2-CH_3 group attached to a pyrrole ring than an acetyl methyl group (~2.00 p.p.m.).

The ^{13}C-n.m.r. spectrum of 3-benzoyl-5-formyl-2-methylpyrrole 5-*p*-chlorobenzoylhydrazone (**8**), obtained by periodate oxidation of **5**, showed a signal at 12.90 p.p.m., which is closer to a 2-CH_3 group of a pyrrole ring than a methyl carbon atom of an acetyl group[7] (> 30 p.p.m.).

The mass-spectral fragmentation of the derived *p*-toluoylhydrazone **9** also confirmed structure **5** by the presence of fragments **10**, **11** and **12**.

When 3-benzoyl-2-methyl-5-(D-*arabino*-tetrahydroxybutyl)pyrrole (**5**) was heat-

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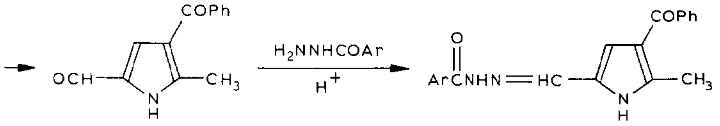

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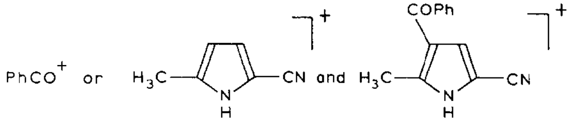
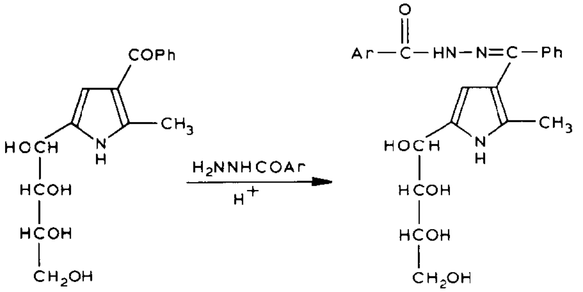
8 Ar = C_6H_4Cl-*p*

9 Ar = C_6H_4Me-*p*



10 11 12

m/*z* 105(22.9) *m*/*z* 210 (8.4)



5

	Ar		Ar
13	C_6H_5	17	C_6H_4Br-*p*
14	C_6H_4Cl-*o*	18	C_6H_4Me-*p*
15	C_6H_4Cl-*m*	19	$C_6H_4NO_2$-*p*
16	C_6H_4Cl-*p*	20	CH_2Ph

TABLE I

Analytical data of 5-acylhydrazones **13**, **15**, **17**, **19**, and **20**

Compound no.	*M.p.°*	*Yield (%)*	*Mol. formula*	*Analyses (%) Calc/found* C	H	N
13	133	72	$C_{23}H_{25}N_3O_5.2H_2O$	60.11	6.37	9.15
				59.98	6.31	8.97
15	140	75	$C_{23}H_{24}ClN_3O_5$	60.32	5.29	9.18
				60.00	5.18	8.88
17	145	79	$C_{23}H_{24}BrN_3O_5$	54.98	4.82	8.37
				54.84	4.60	8.00
19	142	68	$C_{23}H_{24}N_4O_7$	58.96	5.17	11.96
				58.90	5.30	11.70
20	215	28	$C_{24}H_{27}N_3O_5$	65.88	6.23	9.61
				65.68	6.40	9.80

ed under reflux with acylhydrazines (1 mol) in the presence of acetic acid, the corresponding acylhydrazones **13**–**20** were obtained.

Compounds **13**, **15**, **17**, **19** and **20** were crystalline, whereas **14**, **16** and **18** were amorphous.

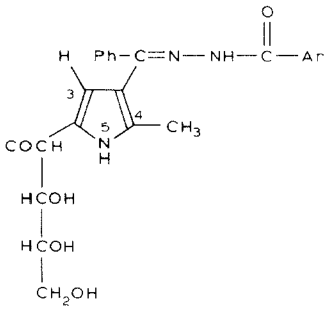
The i.r. spectra of the derived hydrazones showed bands at 3240–3360 (OH), 3020–3140 (NH), 1640–1680 (CONH), and 1590–1635 (C–N) cm^{-1}.

The electronic absorption spectra of the benzoylhydrazone **13** showed three maxima, at 210, 234 (sh), and 334 nm (log ε 4.37, 4.29, and 4.13), whreas the *m*-chlorobenzoylhydrazone (**15**) and *p*-nitrobenzoylhydrazone (**19**) derivatives showed only two maxima, at 238 (sh), 314 (sh) nm (log ε 4.41, 3.95), and 250, 318 (sh) nm (log ε 4.34, 4.00), respectively. The ^{1}H-n.m.r. spectra in CDCl$_3$–Me$_2$SO-d_6 of **15**, **17**, and **19** could be assigned conventionally (Table II).

Treatment of 3-benzoyl-5-(D-*arabino*-tetrahydroxybutyl)-2-methylpyrrole-3-acylhydrazones (**13**–**20**) with 1:1 acetic anhydride–pyridine afforded the corresponding acetates **21**–**28**.

TABLE II

^{1}H-N.m.r. spectra of 3-benzoyl-2-methyl-5-(D-*arabino*-tetrahydroxybutyl)pyrrole 3-acylhydrazones in CDCl$_3$-Me$_2$SO-d_6



Compound No.	*P.p.m.*					
	1-CH$_3$	H *of C-4 side-chain*	*H-3*	*Aryl*-H	*5-NH*	*NHCO*
15	2.43	3.50–5.17	6.20	7.00–8.00	8.85	10.37
17	2.47	3.35–5.30	6.37	7.00–8.00	8.75	10.40
19	2.70	3.65–5.50	6.53	7.40–8.60	9.20	10.41

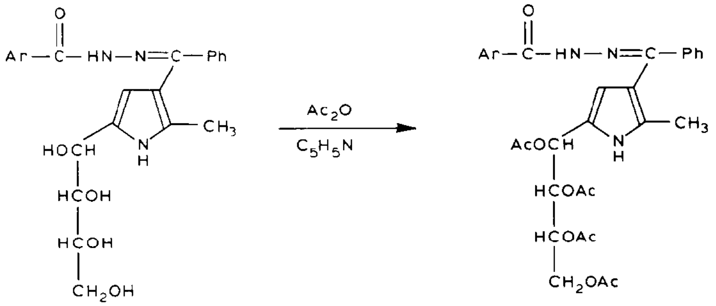
The i.r. spectra of **21**–**28** showed the NH band at 3300–3500, OAc at 1770–1780, amide 1660–1680, and C–N at 1600–1620 cm^{-1}, with disappearance of the OH band of the sugar residue of the parent hydrazones **13**–**20**. The electronic absorption spectrum of the acetylated benzoylhydrazone derivative **21** showed two absorption maxima, at 226 and 290 nm (log ε 4.49, and 4.43), whereas, the acetylated *o*-chlorobenzoylhydrazone derivative **22** showed the two maxima at 246 (sh) and 286 (sh) nm (log ε 4.19

and 4.01). The ^{1}H-n.m.r. spectra in $CDCl_3$ of 3-benzoyl-2-methyl-5-(D-*arabino*-tetra-*O*-acetyl-butyl)pyrrole 3-benzoylhydrazone (**21**) was assigned as shown in Table IV.

TABLE III

Analytical data for compounds **21**–**28**

Compound no.	*m.p.°*	*Yield (%)*	*M formula*	*Analyses (%) calc/found* C	H	N
21	129	57	$C_{31}H_{33}N_3O_9$	62.93	5.63	7.10
				63.00	5.70	7.30
22	122	33	$C_{31}H_{32}ClN_3O_9$	59.46	5.16	6.71
				59.70	5.30	6.70
23	95	44	$C_{31}H_{32}ClN_3O_9$	59.46	5.16	6.71
				59.30	5.10	6.50
24	140	37	$C_{31}H_{32}ClN_3O_9$	59.46	5.16	6.71
				59.30	5.00	6.30
25	139	31	$C_{31}H_{32}BrN_3O_9$	55.52	4.82	6.27
				55.80	5.00	6.00
26	90(d)	22	$C_{32}H_{35}N_3O_9$	63.45	5.84	6.94
				63.80	6.00	7.00
27	97(d)	32	$C_{31}H_{32}N_4O_{11}$	58.48	5.08	8.80
				58.41	4.89	8.69
28	85	30	$C_{32}H_{35}N_3O_9$	63.45	5.84	6.94
				63.50	5.90	6.80



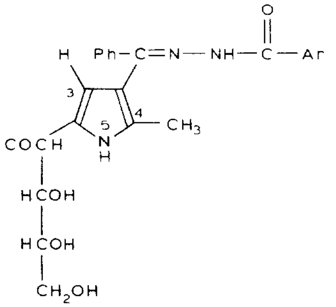
(13-20)

	Ar		Ar
21	C_6H_5	25	C_6H_4Br-*p*
22	C_6H_4Cl-*o*	26	C_6H_4Me-*p*
23	C_6H_4Cl-*m*	27	$C_6H_4NO_2$-*p*
24	C_6H_4Cl-*p*	28	CH_2Ph

TABLE IV

^{1}H-n.m.r. spectra of 3-benzoyl-2-methyl-5-(D-*arabino*-tetra-O-acetylbutyl)pyrrole 3-acylhydrazones (**21** and **25**) in CDCl$_3$

Compound no.	*P.p.m.*						
	CH$_3$CO	*1*-CH$_3$	H *of C-4 sidechain*	*H-3*	*Aryl*-H	*5-N*H	*NHCO*
21	1.92(s) 2.02(s) 2.15(s) 2.32(s)	2.52(s)	4.00–5.00(m)	6.20(s)	7.32–8.20(m)	8.70(s)	10.60(s)
25	1.87(s) 2.00(s) 2.07(s) 2.20(s)	2.47(s)	3.70–4.70(m)	6.27(s)	7.15–8.00(m)	8.77(m)	10.42(s)



EXPERIMENTAL

General methods. — Melting points were determined on a Kofler block and are uncorrected. I.r. and u.v. spectra were recorded respectively on Unicam SP 1025 and SP 1750 spectrometers. ^{1}H-N.m.r. spectra were recorded with Varian EM 360 L or XL 200 spectrometers. ^{13}C-N.m.r. spectra were recorded with Jeol JNM-FX 100 or XL 200 spectrometers. Mass spectra were recorded with a Kratos MS-30 instrument. Microanalyses were performed at the Faculty of Science, Cairo University, Cairo Egypt.

3-*Benzoyl-5-formyl-2-methylpyrrole 5*-p-*chlorobenzoylhydrazone* (**8**). — A solution of 3-benzoyl-2-methyl-5-pyrrolecarboxaldehyde[1] (3.0 g, 10 mmol) in EtOH (15 mL) containing AcOH (0.2 mL) was treated with *p*-chlorobenzoylhydrazine (2.4 g, 10 mmol) in EtOH (15 mL). The mixture was boiled under reflux (water bath) for 15 min. After cooling, the product **8** that separated out was filtered off, washed with EtOH and dried; yield 3.9 g (76%). It was crystallized from EtOH; m.p. 137°, $\nu_{\max}^{\mathrm{KBr}}$ 1610 (C–N), 1640 (CONH), 1670 (COPh) and 3360–3520 cm^{-1} (2NH); $\lambda_{\max}^{\mathrm{EtOH}}$ 242 and 330 nm (log ε

4.36 & 4.29), ^{1}H-n.m.r. (60 MHz, $CDCl_3$, Me_2SO-d_6): δ 2.60 (s, 3 H, CH_3), 6.57 (s, 1 H CH-pyrrole), 7.25–8.00 (m, 9 H, Ph and Ar), 8.13 (s, 1 H CH–N), 11.58 (s, 1 H, NH) and 11.84 (s, 1 H, NHCO)); ^{13}C-n.m.r. ($CDCl_3$–Me_2SO-d_6); δ 12.90 (C–CH_3), 116.20 (C–CH–N), 162.31 (C–CONH), 190.35 (C–COPh), 120.01, 124.81, 127.11, 127.82, 128.65, 130.33, 130.52, 131.80, 134.60, 139.51, 139.82 and 140.62 (remaining carbons of phenyl, aryl and pyrrole).

Anal. Calc. for $C_{20}H_{16}ClN_3O_2$: C, 65.66; H, 4.42; N, 11.49. Found: C, 66.00; H, 4.50; N, 11.40.

*3-Benzoyl-5-formyl-2-methylpyrrole 5-*p*-toluoylhydrazone* (**9**). — A solution of 3-benzoyl-2-methyl-5-pyrrolecarboxaldehyde (3.0 g, 10 mmol) in EtOH (15 mL) containing AcOH (0.2 mL) was treated with *p*-toluoylhydrazine (2.1 g, 10 mmol) in EtOH (15 mL). Processing as before gave the *p*-toluoylhydrazone derivative; yield 3.9 g (80%). Recrystallization from EtOH afforded needles, m.p. 148°; ν_{max}^{KBr} 1595 (C–N), 1630 (CONH), 1665 (COPh), and 3380–3520 cm^{-1} (2NH); λ_{max}^{EtOH} 246 and 334 nm (log ε 4.46 and 4.53); ^{1}H-n.m.r. (60 MHz, $CDCl_3$, Me_2SO-d_6): δ 2.40 (s, 3 H, *p*-CH_3), 2.60 (s, 3 H, CH_3), 6.78 (s, 1 H, CH-pyrrole), 7.25–8.06 (m, 9 H, Ph and Ar), 8.30, (s, 1 H, CH–N), 10.50 (s, 1 H, NH) and 11.15 (s, 1 H, NHCO); ^{13}C-n.m.r. ($CDCl_3$/Me_2SO-d_6): δ 13.58 (C–CH_3), 21.18 (C–*p*–CH_3), 116.37 (C–CH–N), 163.70 (C–CONH), 190.96 (C–COPh), 120.35, 125.96, 127.60, 128.07, 128.42, 128.89, 130.29, 131.05, 138.89, 140.24, 140.76, and 141.76 (remaining carbons of phenyl, aryl, and pyrrole); *m/z* 345 (27.80), 316 (1.13), 288 (0.71), 251 (0.06), 226 (0.92), 209 (20.99), 182 (0.60), 154 (2.62), 136 (13.56), 119 (100.00), 105 (22.90), 91 (54.42), 77 (19.77), 65 (17.21), 42 (6.09), and 30 (0.18).

Anal. Calc. for $C_{21}H_{19}N_3O_2.H_2O$: C, 69.39; H, 5.84; N, 11.56. Found: C, 69.50; H, 5.90; N, 11.89.

*3-Benzoyl-2-methyl-5-(*D-arabino*-tetrahydroxybutyl)pyrrole acylhydrazones* (**13**–**20**). — A solution of 3-benzoyl-2-methyl-5-(D-*arabino*-tetrahydroxybutyl)pyrrole[8] (10 mmol) in MeOH (15 mL) containing AcOH (0.2 mL) was treated with the required acylhydrazine (10 mmol) in MeOH (15 mL), and the mixture was refluxed (water bath) for 3 h. After cooling, the acylhydrazone derivative that separated out was filtered off, washed with MeOH, dried, and crystallized from MeOH in needles (Tables I and II).

*3-Benzoyl-2-methyl-5-(*D-arabino*-tetraacetoxybutyl)pyrrole acylhydrazones* (**21**–**28**). — A solution of 3-benzoyl-2-methyl-5-(D-*arabino*-tetrahydroxybutyl)pyrrole 3-benzoylhydrazone (10 mmol) in dry C_5H_5N (20 mL) was treated with Ac_2O (20 mL) for 48 h at 0°. The mixture was poured onto crushed ice and the crystalline solid was collected, washed thoroughly with water, dried, and then crystallized from MeOH (Tables III and IV).

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