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DEHYDRATIVE RING-CLOSURE OF 3-SUBSTITUTED 2-QUINOXALINONES TO GIVE FUSED AND NONFUSED PYRAZOLOQUINOXALINES*

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ABSTRACT

Reaction of L-ascorbic acid with *o*-phenylenediamine and arylhydrazines afforded 3-(1-arylhydrazono-L-*threo*-2,3,4-trihydroxybutyl)-2-quinoxalinones (**1–6**). Whereas compounds **1–6** reacted with alkali to give 1-aryl-3-(L-*threo*-glycerol-1-yl)-flavazoles, the corresponding acetates (**7**) underwent deacetylation and rearrangement to 3-[1-aryl-5-(hydroxymethyl)pyrazol-3-yl]-2-quinoxalinones (**20–24**). Compounds **20–24** were also prepared from **1–5** by treatment with hot hydroxylamine hydrochloride. The action of boiling acetic anhydride on **1–5** or **7** afforded colorless products identified as the pyrazole acetates (**15–19**), which could also be obtained by the acetylation of compounds **20–24**. Deacetylation of **15** gave **20**. Oxidation of **20** with potassium permanganate gave the 5-carboxylic acid **26**. The i.r., n.m.r., and mass spectra of some of these compounds are discussed.

INTRODUCTION

As many carbohydrate derivatives of nitrogen heterocycles are therapeutically active agents[2,3], our attention was drawn towards the synthesis of nitrogen heterocycles from carbohydrate precursors[1,4–7]. Dicarbonyl compounds are generally excellent precursors for heterocyclic compounds *via* their reactions with hydrazines or diamines. Saccharides, as polyhydroxyalkyl-aldehydes or -ketones, have similar reactivity, and could be changed into heterocycles[8,9] either directly or through transformation into their dicarbonyl derivatives, namely, aldos-2-uloses (osones). In its oxidized form, L-ascorbic acid possesses greater reactivity than osones, because of the presence of an extra carboxyl group adjacent to the *vic*-dicarbonyl groups. Recently, the reaction of mono- and bis-hydrazones of dehydro-L-ascorbic acid has been investigated[1,5,6], and a variety of heterocycles prepared. The reaction of dehydro-L-ascorbic acid with *o*-phenylenediamine gave a variety of products[9], and that

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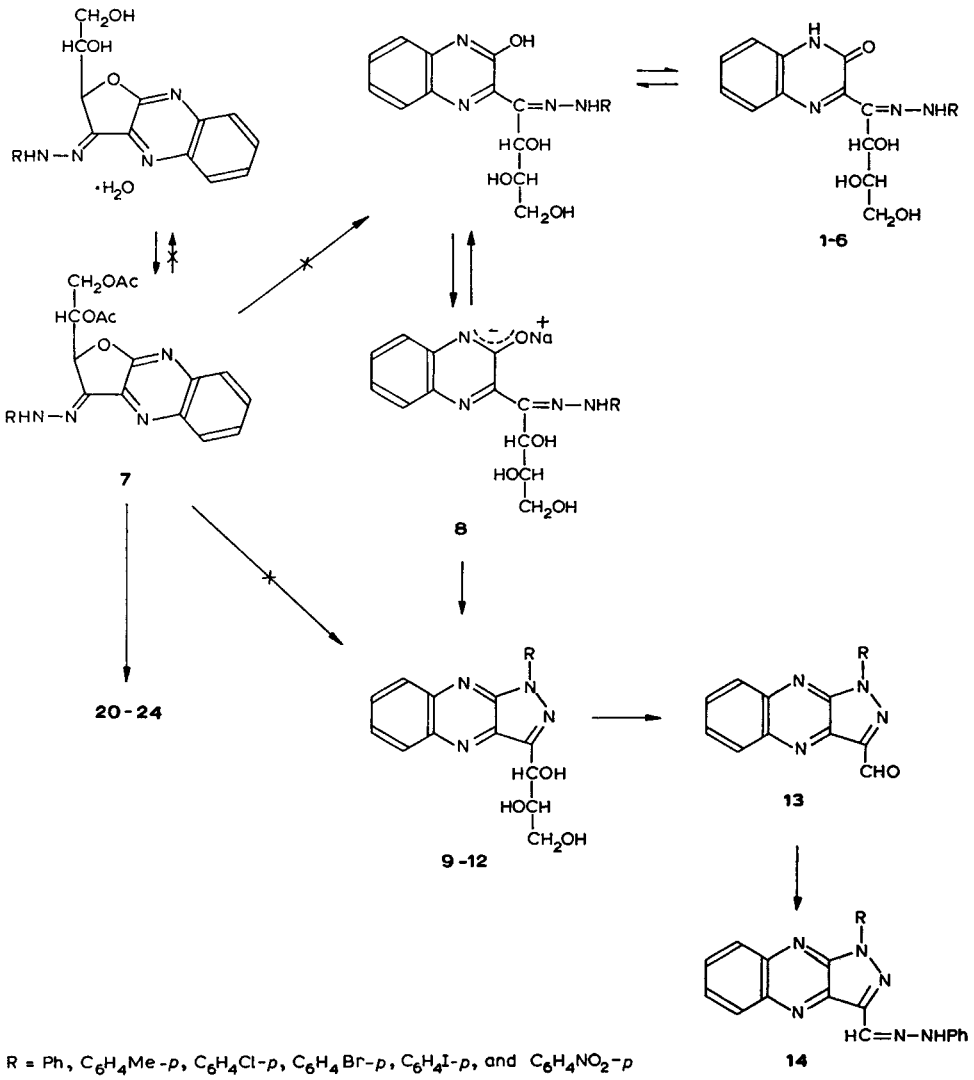
resulting from the condensation of one molar equivalent with C-1 and C-2 is claimed to react with phenylhydrazine to give 2,2′-anhydro-[2-hydroxy-3-(1-phenylhydrazono-L-*threo*-2,3,4-trihydroxybutyl)quinoxaline] which, supposedly, upon acetylation, gives 2,2′-anhydro-[2-hydroxy-3-(1-phenylhydrazono-L-*threo*-3,4-diacetoxy-2-hydroxybutyl)quinoxaline][10] (**7**). We have extended this sequence of reactions to a variety of arylhydrazines. The synthesis of **1–7** and their transformation into other heterocyclic compounds under the influence of acids or alkalis constitute the objectives of this publication. Two types of pyrazole were prepared during this investigation, namely, pyrazoles fused to the quinoxaline ring, and pyrazoles attached by a C-3–C-3′ linkage to quinoxaline.

DISCUSSION AND RESULTS

The condensation of L-ascorbic acid with *o*-phenylenediamine gives various products that depend upon the reaction conditions and the ratio of the reactants. One of these reaction products has a free 3-carbonyl group capable of further reaction with an arylhydrazine. Thus, allowing L-*threo*-2,3-hexodiulosono-1,4-lactone, obtained by the oxidation of L-ascorbic acid with *p*-benzoquinone, to react with one molar equivalent of *o*-phenylenediamine, followed by reaction of the product with an arylhydrazine, gives 3-(1-arylhydrazono-L-*threo*-2,3,4-trihydroxybutyl)-2-quinoxalinones (**1–6**). The same products are obtained by allowing a 1:1:2 mixture of L-ascorbic acid, *o*-phenylenediamine, and an arylhydrazine to react together (making use of the oxidizing property of arylhydrazines). Derivatives of types **1–6** possessing *p*-tolyl, *p*-chlorophenyl, *p*-bromophenyl, *p*-iodophenyl, and *p*-nitrophenyl substituents have been prepared, and crystallized from ethanol as red crystals. Their elemental analyses agreed with those calculated for the open-chain structures **1–6** (or its hydrated, anhydro form). Their presence in the open-chain structure was shown by the results of periodate oxidation of **1** as well as by the infrared (i.r.) spectra, which showed the presence of bands at 1665–1660 cm^{-1}, in addition to the hydroxyl absorption at 3430–3360 cm^{-1}.

1-Phenylflavazoles of monosaccharides were first prepared by Ohle and coworkers[11–14], and the series was later extended to oligosaccharides[15]. The reaction is general for reducing sugars not substituted on O-2 and O-3, and involves the action of *o*-phenylenediamine and phenylhydrazine on them. The reaction proceeds through the formation of an arylhydrazono group on C-3 of a sugar moiety attached to a quinoxaline, which undergoes ring closure to the flavazole. This prerequisite intermediate in flavazole synthesis could be 3-(1-phenylhydrazono-L-*threo*-2,3,4-trihydroxybutyl)-2-quinoxaline[10] which, on treatment with alkali, gave 3-(L-*threo*-glycerol-1-yl)-1-phenylflavazole. We have extended this reaction to a variety of arylhydrazones (**2–6**), and have studied their possible rearrangement under the action of alkali. The rearrangement proceeds with boiling, dilute, aqueous sodium hydroxide solution during 1 h, whereas a more concentrated solution of the alkali causes fission of the polyhydroxyalkyl chain. On the other hand, dissolution of **1** in alkali, followed



Scheme 1

immediately by acidification, regenerates the starting material. Under similar conditions, L-*threo*-2,3-hexodiulosono-1,4-lactone 2,3-bis(2-arylhydrazones) could not be regenerated on dissolution in alkali, but rearranged to 1-aryl-3-(L-*threo*-glycerol-1-yl)-4,5-pyrazoledione 4-(2-arylhydrazones) *via* a carboxylate intermediate, where the cyclization of the carboxyl group with the 3-hydrazone is facile, compared with the intermediate **8** (which could be readily transformed into **1**, rather than being cyclized to **9**). This rearrangement appears to be general for L-ascorbic acid derivatives, and, besides use for comparison with the pyrazoles to be described, it provides an inexpensive and simple route to flavazoles that could be obtained from L-galactose

or L-talose. These flavazoles **9–12** are readily crystallizable derivatives having a yellow color that distinguishes them from their (red) starting derivatives. Moreover, bands in the carbonyl-frequency region in the i.r. spectra of their precursors disappear, and their hydroxyl absorption appears at 3400–3300 cm^{-1}. Periodate oxidation of one mole of 1-(*p*-chlorophenyl)-3-(L-*threo*-glycerol-1-yl)flavazole (**10**) led to the consumption of two moles of oxidant per mole, with the separation of 1-(*p*-chlorophenyl)-3-formylflavazole (**13**). The latter showed, in its i.r. spectrum, an aldehydic group at 1700 cm^{-1}.

An approach to oligosaccharide sequencing as a model study for oligosaccharide analysis by mass spectrometry was reported by Johnson *et al.*[16], who used the 1-phenylflavazole peracetates because of the unsuitability of free sugars in mass-spectrometric studies. We have investigated the mass spectra (see Fig. 1) of 1-aryl-3-(L-*threo*-glycerol-1-yl)flavazoles (**10–12**), compounds labelled at N-1 by *p*-chloro-, *p*-bromo-, and *p*-iodo-phenyl substituents (see Table I). The difference in the natural-abundance ratio of the isotopes of the three halogen atoms helps in educing the probable structures for some of the fragments by comparison of the three spectra. Homologies within the spectra clearly show that similar bond-cleavage occurs in **10–12**; ions from which the halogen was lost appear at the same values of *m/e* in all three spectra. Molecular-ion peaks were observed at *m/e* 414, 416, and 462, respectively, in the spectra of the *p*-bromo- (**11**) and *p*-iodo-phenyl (**12**) derivatives, whereas that of the *p*-chlorophenyl derivative (**10**) (expected at *m/e* 370, 372) was not seen. The data given in Table I indicate the presence of the usual series of ions arising by elimination processes involving the sugar moiety attached to the nitrogen heterocycle. The principal route of fragmentation for all three spectra is rupture of the C-1′–C-2′ bond (of the sugar moiety), giving the group of ions corresponding to B + 29 (base peak of **10**), B + 30 (base peak of **11** and **12**), and B + 31; these ions frequently appear in the mass spectra of nucleosides[17]. The formation of the B + 31 ion from the molecular ion from **11** and **12** was confirmed by the presence of the corresponding metastable ions. Complete loss of the sugar moiety gives rise to B, B + 1, and B + 2 ions. Loss of the halogen, and cleavage in the sugar portion, gave a second series of minor ions, and loss of both the halogen and the side chain gave an ion at *m/e* 245, which was the second-largest peak in all three spectra. Other minor fragmentations appear to involve the heterocyclic ring, *p*-halogenated phenylinium ions, and fragments derived from the side chain.

Acetylation of **1** with acetic anhydride in pyridine afforded the di-*O*-acetyl derivative[10] **7**. Attempted acetylation of the red **1**, or further acetylation of **7**, with boiling acetic anhydride gave, not the *N*-acetyl-di-*O*-acetyl derivative expected, but a colorless product formulated as $C_{20}H_{16}N_4O_3$ and assigned structure **15**. Extending this reaction to the red *p*-tolyl, *p*-chlorophenyl, *p*-bromophenyl, and *p*-iodophenyl derivatives **2–5** also afforded colorless products, formulated as $C_{14}H_{11}N_4O_3R$ (indicating the generality of the reaction) and assigned structures **16–19**. The proposed structures were based on the following evidence: their i.r. spectra had a band at 1745–1720 cm^{-1} assigned to the acetyl groups, in addition to a band at 1660 cm^{-1}

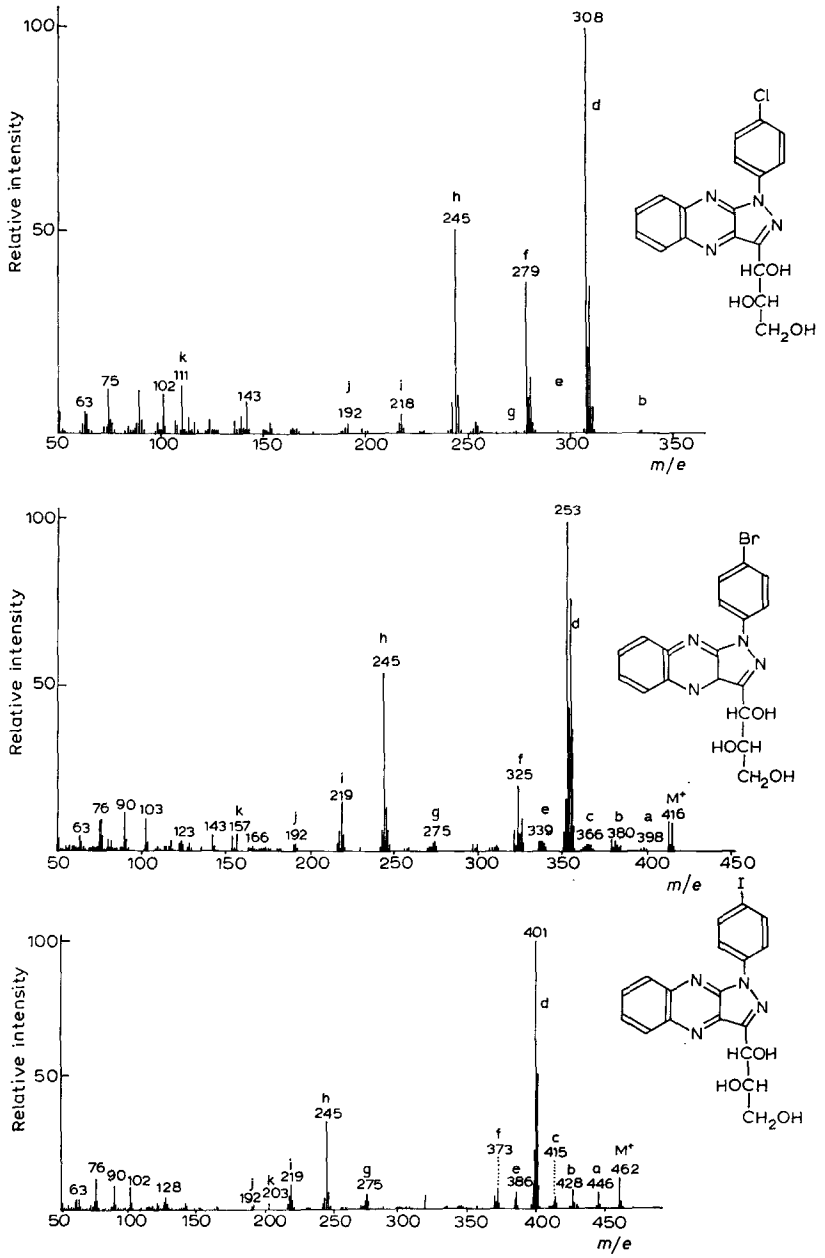
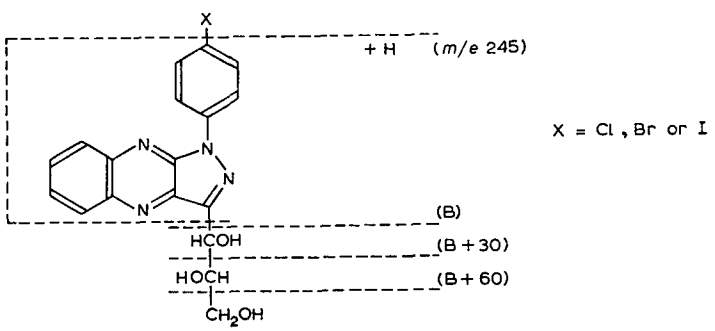


Fig. 1. The mass spectra of 1-(*p*-chlorophenyl)-3-(L-*threo*-glycerol-1-yl)flavazole (**10**) (top curve), 1-(*p*-bromophenyl)-3-(L-*threo*-glycerol-1-yl)flavazole (**11**) (middle curve), and 3-(L-*threo*-glycerol-1-yl)-1-(*p*-iodophenyl)flavazole (**12**) (bottom curve).

TABLE I

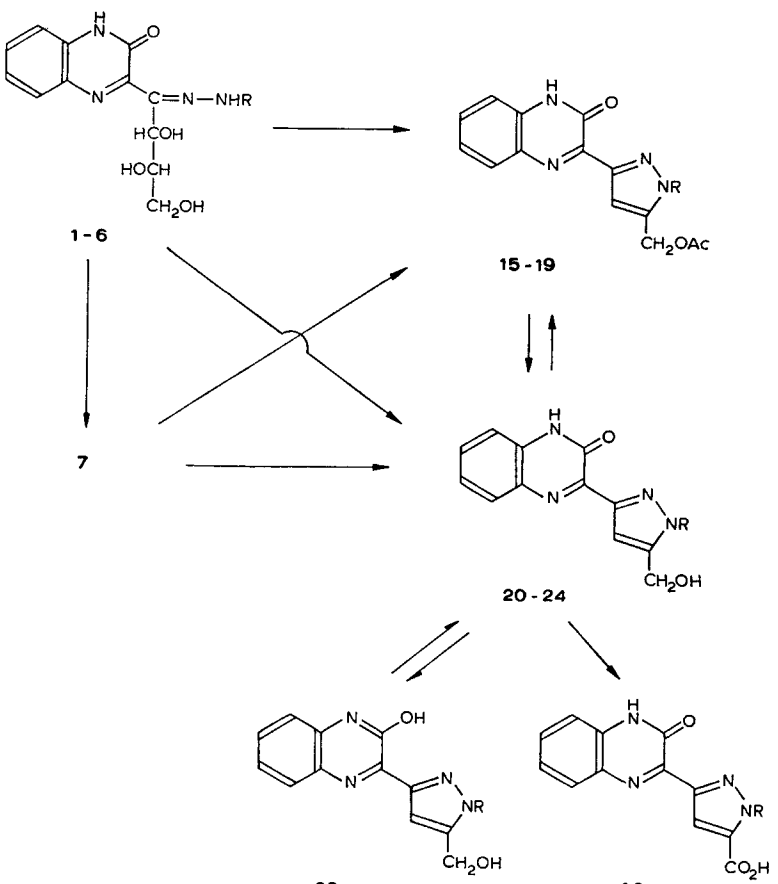
SELECTED IONS IN THE MASS SPECTRA OF 1-ARYL-3-(L-*threo*-GLYCEROL-1-YL)FLAVAZOLES (**10–12**)

Ion	**10**	**11**	**12**
M		414 (8), 416 (8)	462 (11)
M − O		398, 400	446 (6)
M − H_2O		398, 396 (1)	
M-CH_2OH		383 (2), 385 (2)	431 (2)
M-H_2O − O	336, 338	380 (4), 382 (4)	428 (7)
M-CH_2OH − O	320, 322	367 (2), 369 (1)	415 (4)
M-CH_2OH − OH		366 (3), 368 (2)	414 (3)
M-CH_2OH-OH − 2H		364 (2), 366 (3)	412 (1)
M-CH_2OH-H_2O − 2H or M − 3OH		363 (1), 365 (2)	411 (1)
B + 31		354 (43), 356 (37)	402 (50)
B + 30	309 (22), 311 (7)	353 (100), 355 (76)	401 (100)
B + 29	308 (100), 310 (36)	352 (15), 354 (43)	400 (22)
B + 31 − O		338 (3), 340 (3)	386 (7)
B + 31 − OH		337 (3), 339 (4)	385 (4)
B + 2		325 (20), 327 (11)	373 (8)
B + 1	280 (9), 282 (3)	324 (2), 326 (5)	372 (2)
B	279 (38), 281 (14)	323 (6), 325 (20)	371 (5)
B + 31 − halogen	275	275 (4)	275 (6)
B + 30 − halogen	274	274 (3)	274 (4)
B + 29 − halogen	273	273 (2)	273 (2)
B + 1 − halogen	245 (50)	245 (54)	245 (33)



assigned to the OCN groups. The n.m.r. spectra of **16** and **18** showed a three-proton singlet at δ 2.08 (CH_3 of the acetyl group). Two-proton singlets appeared at δ 5.00 and 5.12, respectively, corresponding to a methylene group not adjacent to a carbon atom bearing protons. A multiplet appeared at δ 7.20–8.08 due to the aromatic protons. A broad and exchangeable singlet appeared in the spectrum of **18** at δ 11.43, due to the NH proton. An extra singlet was shown by **16** at δ 2.28, due to the methyl of the *p*-tolyl group. Deacetylation of **15** afforded a product identical with the known 2-hydroxy-3-[5-(hydroxymethyl)-1-phenylpyrazol-3-yl]quinoxaline (**25**), obtained by the action of hydroxylamine hydrochloride on **1**. Moreover, oxidation of the de-

acetylated product **20** with potassium permanganate gave the carboxylic acid[10] **26**, which showed in its i.r. spectrum a band at 1720 cm^{-1} (COO), in addition to the 1660 cm^{-1} (OCN) band which is present in the spectrum of its precursor. Extension of the reaction with hydroxylamine hydrochloride to the *p*-tolyl, *p*-chlorophenyl, *p*-bromophenyl, and *p*-iodophenyl derivatives **2–5** afforded **21–24** as colorless, crystalline compounds, although their two-step synthesis from compounds of the type of **1** by treatment with boiling acetic anhydride and then deacetylation is more convenient and gives higher yields. Their i.r. spectra showed a band at 1670–1660 cm^{-1} (OCN). The n.m.r. spectrum of **21** showed at δ 2.20 a singlet of three-proton intensity, due to the methyl protons of the *p*-tolyl group, in addition to a two-proton singlet at δ 5.00 due to the hydroxymethylene group. The aromatic protons appeared as two multiplets, at δ 7.16–7.52 and 7.89–8.20. Acetylation of **20–24** with acetic anhydride in pyridine gave the monoacetyl derivatives **15–19**, identical with those obtained by the action of boiling acetic anhydride on compounds **1–5**. This confirmed



R = Ph, C_6H_4Me-*p*, C_6H_4Cl-*p*, C_6H_4Br-*p*, and C_6H_4I-*p*

Scheme 2

the structure assigned, and indicates that, during the reaction of **1–5** with acetic anhydride, closure of the pyrazole ring takes place by elimination of two molecules of water per molecule (in its open chain structures **1–5**). Interestingly, similar pyrazole formation occurred[18–20] on boiling sugar arylosazones with acetic anhydride, although dehydro-L-ascorbic acid arylosazones did not undergo this reaction, despite great structural similarity to **1**. Elimination of acetic acid also occurs readily from phenylhydrazones of acetylated aldoses[21–23], for example, D-glucose and D-mannose derivatives, which are induced to lose acetic acid by heating in ethanol, giving 3,4,5,6-tetra-*O*-acetyl-1,2-dideoxy-1-phenylazo-D-*arabino*-hex-1-enitol. Moreover, the mechanism of formation of anhydro-osazones suggested by Simon and coworkers[24], and the explanation of their stereospecificity proffered by El Khadem[25], indicated the presence of 2-ene intermediates during their reactions; such could also be a possible intermediate in pyrazole formation of this kind. On the basis of the i.r. spectra of compounds **15–26** (which showed OCN bands), they were formulated as 2-quinoxalinone derivatives rather than as the tautomeric 2-quinoxalinols **25**, although both tautomers could be present in equilibrium. The mass spectra of **21**, **16**, and **18** showed molecular ions, which are the base peaks; loss of CO from M^+ to give ions at *m/e* 304,346, and 410,412, respectively, plus loss of the hydroxyl group in **21**, and acetyl groups in **16** and **18** as well. Loss of the substituents from the phenyl ring also occurs, as well as loss of the quinoxaline ring and the hydroxymethylene or the acetoxymethylene group from M^+, to give ions corresponding to the pyrazole ring at *m/e* 157 for **21** and **16**, and at 220 and 222 for **18**.

EXPERIMENTAL

General methods. — Melting points were determined with a Kofler-block apparatus and are uncorrected. I.r. spectra were recorded with a Unicam SP200 spectrometer, and n.m.r. spectra (for solutions in pyridine-d_5 or chloroform-*d*), with a Jeol-100 spectrometer, with tetramethylsilane as the standard. Chemical shifts are given on the δ scale. Mass spectra were recorded with an A.E.I. MS902 instrument; intensities are given in parentheses, as percentages of the base peak. Microanalyses were performed in the Chemistry Department, Faculty of Science, Cairo University, Cairo, Egypt.

*3-(1-Arylhydrazono-*L-threo-*2,3,4-trihydroxybutyl-2-quinoxalinones* (**1–6**). — (*a*) A mixture of L-ascorbic acid (17.6 g, 0.1 mole) and *p*-benzoquinone (10.8 g, 0.1 mole) in ethanol (150 ml) was stirred for 90 min at room temperature. The resulting, homogeneous, dark-yellow solution was treated with a solution of *o*-phenylenediamine (10.8 g, 0.1 mole) in methanol (100 ml) and water (500 ml), and then heated until boiling. The arylhydrazine (0.1 mole) in ethanol (50 ml) was added, and the mixture was boiled for 5–10 min, whereupon red, crystalline products separated out. They were recrystallized from ethanol as red needles (see Table II).

(*b*) A suspension of L-ascorbic acid (17.6 g, 0.1 mole) in water (400 ml) and ethanol (250 ml) was treated with *o*-phenylenediamine (10.8 g, 0.1 mole), the aryl-

TABLE II

MICROANALYTICAL AND SPECTRAL DATA FOR 3-(1-ARYLHYDRAZONO-L-*threo*-2,3,4-TRIHYDROXYBUTYL)-2-QUINOXALINONES

Compound No.	*R*	*Yield (%)*	*M.p. (degrees)*	*Molecular formula*	*Calculated (%)*			*Found (%)*			ν_{max}^{Nujol} (cm^{-1})		
					C	*H*	*N*	*C*	*H*	*N*			
2	C_6H_4Me-*p*	75	206–207	$C_{19}H_{20}N_4O_4$	61.9	5.5	15.2	62.0	5.5	15.3	1615	1665	3400
3	C_6H_4Cl-*p*	80	208	$C_{18}H_{17}ClN_4O_4$	55.6	4.4	14.4	55.9	4.4	14.3	1640	1660	3400
4	C_6H_4Br-*p*	75	215	$C_{18}H_{17}BrN_4O_4$	49.9	4.0	12.9	50.1	4.3	13.0	1635	1650	3430
5	C_6H_4I-*p*	75	218	$C_{18}H_{17}IN_4O_4$	45.0	3.6	11.7	44.7	3.2	11.5	1635	1665	3360
6	$C_6H_4NO_2$-*p*	65	217	$C_{18}H_{17}N_5O_6$	54.1	4.3	17.5	54.1	4.5	17.1	1645	1665	3400

TABLE III

MICROANALYTICAL AND SPECTRAL DATA FOR 1-ARYL-3-(L-*threo*-GLYCEROL-1-YL)FLAVAZOLES AND THEIR DERIVATIVES

Compound No.	*R*	*Yield (%)*	*M.p. (degrees)*	*Molecular formula*	*Calculated (%)*			*Found (%)*			ν_{max}^{Nujol} (cm^{-1})
					C	*H*	*N*	*C*	*H*	*N*	
9	C_6H_4Me-*p*	70	192–193	$C_{19}H_{18}N_4O_3$	65.1	5.2	16.0	64.9	5.5	15.6	3400
10	C_6H_4Cl-*p*	75	211	$C_{18}H_{15}ClN_4O_3$	58.3	4.1	15.1	58.5	4.3	14.8	3400
11	C_6H_4Br-*p*	80	220	$C_{18}H_{15}BrN_4O_3$	52.1	3.6	13.5	52.0	3.8	13.4	3300
12	C_6H_4I-*p*	65	223–225	$C_{18}H_{15}IN_4O_3$	46.8	3.3	12.1	46.7	3.5	12.4	3350
13	C_6H_4Cl-*p*	95	219–220	$C_{16}H_9ClN_4O$	62.2	2.9	18.2	61.9	2.9	18.0	1700
14	C_6H_4Cl-*p*	95	228–229	$C_{22}H_{15}ClN_6$	66.3	3.8	21.1	66.7	3.5	21.0	

TABLE IV

MICROANALYTICAL AND SPECTRAL DATA FOR 3-[5-(ACETOXYMETHYL)-1-ARYLPYRAZOL-3-YL]-2-QUINOXALINONES

Compound No.	*R*	*Yield (%)*	*M.p. (degrees)*	*Molecular formula*	*Calculated (%)*			*Found (%)*			ν_{max}^{Nujol} (cm^{-1})		
					C	*H*	*N*	*C*	*H*	*N*			
15	Ph	90	249–250[a]	$C_{20}H_{16}N_4O_3$	66.7	4.5	15.6	66.6	4.6	15.9	1620	1660	1720
16[b]	C_6H_4Me-*p*	90	240–241	$C_{21}H_{18}N_4O_3$	67.4	4.9	15.0	67.3	5.2	15.4	1615	1660	1745
17	C_6H_4Cl-*p*	70	233–234	$C_{20}H_{15}ClN_4O_3$	60.8	3.8	14.2	60.5	4.2	13.9	1620	1660	1740
18[c]	C_6H_4Br-*p*	95	260–262	$C_{20}H_{15}BrN_4O_3$	54.6	3.4	12.7	54.7	3.3	12.5	1620	1660	1730
19	C_6H_4I-*p*	85	255	$C_{20}H_{15}IN_4O_3$	49.4	3.1	11.5	49.2	3.5	11.8	1620	1660	1720

[a]Lit.[10] m.p. 244°. [b]N.m.r.-spectral data in $CDCl_3$: δ 2.08 (s, $COCH_3$), 2.28 (s, CH_3), 5.00 (s, CH_2), and 7.20–8.08 (m, Ar and = CH). [c]N.m.r.-spectral data in $CDCl_3$: δ 2.08 (s, $COCH_3$), 5.12 (s, CH_2), and 7.20–8.08 (m, Ar and = CH).

TABLE V

MICROANALYTICAL AND SPECTRAL DATA FOR 3-[1-ARYL-5-(HYDROXYMETHYL)PYRAZOL-3-YL]-2-QUINOXALINONES

Compound No.	*R*	*Yield (%)*	*M.p. (degrees)*	*Molecular formula*	*Calculated (%)*			*Found (%)*			ν_{max}^{Nujol} (cm^{-1})		
					C	*H*	*N*	*C*	*H*	*N*			
20	Ph	60	250–252[a]									1660	3500
21[b]	C_6H_4Me-*p*	65	288	$C_{19}H_{16}N_4O_2$	68.7	4.9	16.9	68.8	5.1	16.5	1610	1660	3450
22	C_6H_4Cl-*p*	70	290	$C_{18}H_{13}ClN_4O_2$	61.3	3.7	15.9	61.0	4.1	15.6	1620	1670	3500
23	C_6H_4Br-*p*	75	278–280	$C_{18}H_{13}BrN_4O_2$	54.4	3.3	14.1	54.0	3.1	13.8	1645	1670	3400
24	C_6H_4I-*p*	60	288–290	$C_{18}H_{13}IN_4O_2$	48.7	3.0	12.6	48.5	3.2	12.2	1640	1665	3400

[a]Lit.[10] m.p. 255°. [b]N.m.r.-spectral data in C_5D_5N: δ 2.20 (s, CH_3), 5.00 (s, CH_2), and 7.16–7.52 and 7.89–8.20 (m, Ar and = CH).

hydrazine (0.2 mole), and acetic acid (15 ml). The mixture was refluxed for 1 h, whereupon red, crystalline products separated out that were identical with those obtained by method *a*.

1-Aryl-3-(L-threo-*glycerol-1-yl)flavazoles* (**9–12**). — A suspension of compound **2–5** in 0.01M sodium hydroxide (25 ml) and 1-butanol (2 ml) was boiled under reflux for 60–90 min. The mixture was then cooled, the suspension filtered, the solid washed with water, and the yellow product recrystallized from ethanol (see Table III).

1-Aryl-3-formylflavazoles (**13**). — A suspension of compound **10** (0.5 g) in water was stirred with the calculated amount of sodium metaperiodate for 24 h. The mixture was filtered and the solid was washed with water, and recrystallized from ethanol (see Table III).

3-(Arylhydrazones) (**14**) *of 1-aryl-3-formylflavazoles.* — A solution of **13** (0.1 g) in ethanol (20 ml) was boiled under reflux for 15 min with phenylhydrazine (0.1 g). The product was crystallized from ethanol (see Table III).

3-[5-(Acetoxymethyl)-1-arylpyrazol-3-yl]-2-quinoxalinones (**15–19**). — (*a*) A solution of **20–24** (0.1 g) in pyridine (5 ml) was treated with acetic anhydride (1 ml), and the mixture was kept for 24 h at room temperature. It was poured into ice-cold water, and the product that solidified was recrystallized from ethanol (see Table IV).

(*b*) A solution of compound **1–5** (0.2 g) in acetic anhydride (5–10 ml) was boiled under reflux for 15 min, and the mixture was cooled, and poured onto crushed ice. The product crystallized from ethanol in colorless needles, identical with those obtained by method *a*.

3-[1-Aryl-5-(hydroxymethyl)pyrazol-3-yl]-2-quinoxalinones (**20–24**). — (*a*) A mixture of compound **1–5** (0.1 g), hydroxylamine hydrochloride (0.2 g), and ethanol (5 ml) was boiled under reflux for 8–10 h. The solution was concentrated, and the product obtained on cooling was recrystallized from ethanol to give colorless crystals (see Table V).

(*b*) A solution of acetates **7** (0.1 g) and sodium hydroxide (0.1 g) in 1 : 1 water–ethanol (10 ml) was boiled under reflux for 4 h. The mixture was cooled, acidified with acetic acid, allowed to crystallize, and the product recrystallized from methanol as colorless needles identical with those obtained by method *a*.

Oxidation of **20** *with potassium permanganate.* — Compound **20** (0.3 g) in water (25 ml) containing sodium hydroxide (0.2 g) was titrated with 0.2M potassium permanganate solution until the violet color remained. The solution was acidified, and the product was recrystallized from ethanol, to yield 3-(5-carboxy-1-phenyl-pyrazol-3-yl)-2-quinoxalinone (**26**); m.p. 249–250° (lit.[10] m.p. 246°).

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