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Note

Some aspects of the reaction products of dehydro-L-ascorbic acid with *o*-phenylenediamine and arylhydrazines*

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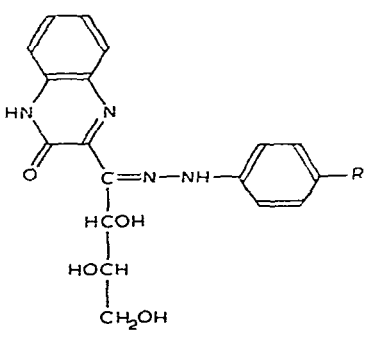
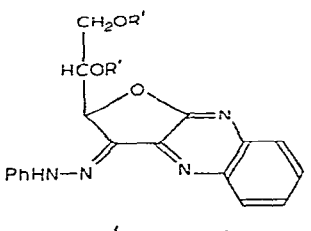
The reaction undergone by L-ascorbic acid (vitamin C), in its oxidized form, with *o*-phenylenediamine is of great potentiality in affording candidates for the synthesis of various heterocyclic compounds[1–7]. On reaction of the product with arylhydrazines, it afforded compounds[1,5] formulated in the acyclic[1] structure, namely, 3-(1-arylhydrazono-L-*threo*-2,3,4-trihydroxybutyl)-2-quinoxalinones (**1**), rather than the hydrated, cyclic structures[5], such as 2,2′-anhydro-[2-hydroxy-3-(1-phenylhydrazono-L-*threo*-2,3,4-trihydroxybutyl)quinoxaline] (**3**, R′ = H). The latter structure was based on the formation of its corresponding diacetyl derivative[5], namely, 2,2′-anhydro-[2-hydroxy-3-(1-phenylhydrazono-L-*threo*-3,4-diacetoxy-2-hydroxybutyl)quinoxaline] (**3**, R′ = Ac). When these compounds were acetylated under conditions slightly more vigorous than those used for formation of the diacetyl derivative **3** (R′ = Ac), they afforded[1,3] dianhydro derivatives formulated as 3-[5-(acetoxymethyl)-1-arylpyrazol-3-yl]-2-quinoxalinones. Accordingly, we decided to



1 R = H
2 R = NO_2

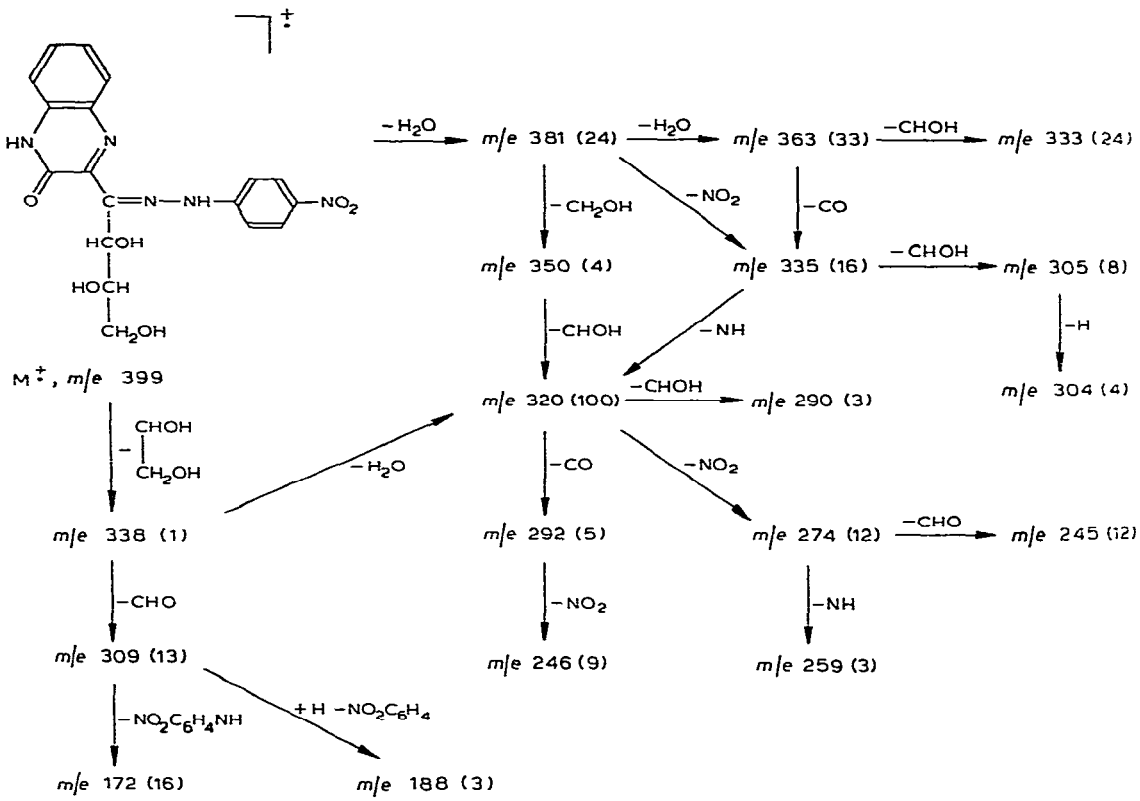


3 R′ = H or Ac

*Heterocycles from Carbohydrate Precursors. Part X. For Part IX. see R. S. Soliman, E. S. H. El Ashry, I. E. El Kholy, and Y. El Kilany, *Carbohydr. Res.*, 67 (1978) 179–188.

study the acetylation of a model compound having only one hydroxyl group, in order to ascertain whether the acetylation would afford the corresponding acetyl derivative, or whether the model compound would undergo anhydro-ring formation; elimination of two moles of water per mole, to form a pyrazolyl derivative would not be possible.

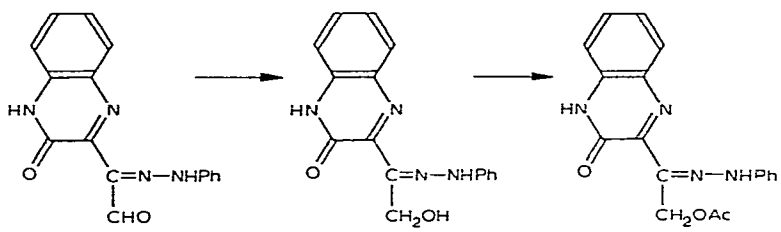
The acyclic structure given[1,2] for the products obtained from the reaction of dehydro-L-ascorbic acid with *o*-phenylenediamine and an arylhydrazine was based on their infrared spectra (which showed the presence of OCN bands, in addition to C=N bands), as well as periodate oxidation; additional evidence for the acyclic structure of **2** has now been obtained from a study of its mass spectrum. It showed a molecular-ion peak at *m/e* 399; however, its abundance was relatively small, especially with regard to the $M-H_2O$ peak at *m/e* 381, which might be taken as evidence for the hydrated, cyclic structure, but the mode of fragmentation agreed with the acyclic structure. Were the molecule to have the cyclic structure, the presence of peaks at *m/e* 335 and 292 due to the loss of CO from the ion at *m/e* 363 and 320, respectively, could not be explained; moreover, loss of the trihydroxybutyl side-chain was observed. Cleavage between C-3 and C-2 gave an ion at *m/e* 338 that lost CHO to give the ion at *m/e* 309. Similar cleavage, after the loss of H_2O, occurred at C-4–C-3.



Scheme 1 (Intensities are given, in parentheses, as percentages of the base peak.)

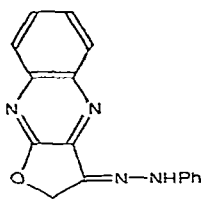
C-3–C-2, and C-2–C-1, to give ions at *m/e* 350, 320, and 290, respectively. That at *m/e* 320 loses CO or NO_2, to give ions at *m/e* 292 and 274, respectively. The base peak appeared at *m/e* 320; this may be due to the accumulation of various pathways of fragmentation, leading either to the same ion, or to other ions having the same *m/e*. Hydrogen transfer was also noted to accompany some of the fragmentations. Ions indicating the loss of $O_2NC_6H_4NH$ and $O_2NC_6H_4$, as well as the ions of some of the lost fragments, were also noted. The same type of fragmentation occurs with 6-chloro-3-[1-(*p*-nitrophenylhydrazono)-L-*threo*-2,3,4-trihydroxybutyl]-2-quinoxalinone[8], which shows the corresponding ions as pairs at higher masses, due to the chlorine atom.

To test the possibility of forming anhydro rings during the acetylation of such types of compound, we acetylated a model compound, 3-[2-hydroxy-1-(phenylhydrazono)ethyl]-2-quinoxalinone (**5**), prepared by reduction of the aldehyde **4** with sodium borohydride. Acetylation of **5** with acetic anhydride in pyridine, or with boiling acetic anhydride, surprisingly afforded the same (red) acetyl derivative **6**, formulated as 3-[2-acetoxy-1-(phenylhydrazono)ethyl]-2-quinoxalinone (**6**).



4 5 6

Three possible anhydro forms may be anticipated by the elimination of one molecule of water per molecule during such acetylations. (*a*) One of type **7**, where the elements of one molecule of water are eliminated from the quinoxalinol ring and the hydroxymethyl side chain; it cannot give an acetyl derivative. (*b*) The second type is an azoethylene derivative **8**, like that formed from the arylhydrazones of saccharide derivatives[9–12] *via* a 1,4-elimination process; in this particular case, it would not show the presence of any acetyl groups. (*c*) The third type could be formed by the elimination of one molecule of water from the quinoxalinol ring and the imino proton of the hydrazone residue (in alkaline solution), to afford the 3-(hydroxymethyl)-1-phenylflavazole (**9**); it would give the corresponding acetyl derivative **10**. Compound **9** was obtained by the action of alkali on **5**, and characterized by its yellow color and the absence of an OCN band from its infrared (i.r.) spectrum. Moreover, under the acetylating conditions used, **9** gave a monoacetyl derivative that was different from the monoacetyl derivative **6**. Similarly, benzoylation of **9** with benzoyl chloride in pyridine gave the monobenzoyl derivative **11**. The i.r. spectra of the compounds prepared are characteristic; both **5** and **6** showed an OCN band at 1665–1660 cm^{-1},



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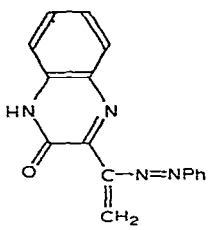

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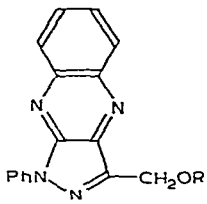

9 R = H
10 R = Ac
11 R = Bz

whereas the corresponding flavazoles **9–11** did not show such a band. The acetyl and benzoyl derivatives **7**, **10**, and **11** showed an ester band at 1730–1720 cm^{-1}.

In conclusion, the results of acetylation of the model compound **5** indicated that the anhydro derivative could not be formed during the reaction.

EXPERIMENTAL

General methods. — Melting points were determined with a Kofler-block apparatus and are uncorrected. I.r. spectra were recorded with a Unicam SP 200 spectrometer. Mass spectra were recorded with an A.E.I. MS 902 instrument. Microanalyses were performed in the Chemistry Department, Faculty of Science, Cairo University, Cairo, Egypt.

3-[2-Hydroxy-1-(phenylhydrazono)ethyl]-2-quinoxalinone (**5**). — A solution of compound **4** (0.5 g) in a mixture of *N*,*N*-dimethylformamide (15 mL) and methanol (10 mL) was treated with sodium borohydride (0.7 g). The mixture was stirred for 1 h at room temperature, kept for a further 4 h, and then diluted with water. The product (yield 70%) was recrystallized from ethanol, to give red needles, m.p. 228–230°: ν_{max}^{Nujol} 1665 (OCN) and 1600 cm^{-1}.

Anal. Calc. for $C_{16}H_{14}N_4O_2$: C, 65.3; H, 4.8; N, 19.0. Found: C, 65.2; H, 4.6; N, 19.3.

3-[2-Acetoxy-1-(phenylhydrazono)ethyl]-2-quinoxalinone (**6**). — (*a*) A solution of compound **5** (0.1 g) in pyridine (5 mL) was treated with acetic anhydride (2 mL): after 24 h, the mixture was poured onto crushed ice, and the product (yield 95%) that solidified was recrystallized from ethanol, to give orange-red needles, m.p. 225°: ν_{max}^{Nujol} 1730 (OAc), 1660 (OCN), and 1600 cm^{-1}.

Anal. Calc. for $C_{18}H_{16}N_4O_3$: C, 64.3; H, 4.8; N, 16.7. Found: C, 64.1; H, 4.6; N, 16.9.

(*b*) A suspension of compound **5** (0.1 g) in acetic anhydride (10 mL) was boiled under reflux for 30 min, and the mixture was processed as before. The crystalline product was identical with that obtained by method *a*.

3-(Hydroxymethyl)-1-phenylflavazole (**9**). — A suspension of compound **5** (0.3 g) in 0.01M sodium hydroxide (25 ml) and few drops of 1-butanol was boiled under

reflux for 1 h. The mixture was then cooled, and the crystalline product was filtered off, washed with water, and recrystallized from ethanol (yield 90%); m.p. 205°.

Anal. Calc. for $C_{16}H_{12}N_4O$: C, 69.6; H, 4.4; N, 20.3. Found: C, 69.8; H, 4.6; N, 20.7.

3-(Acetoxymethyl)-1-phenylflavazole (**10**). — A solution of compound **9** in pyridine was acetylated as for compound **20**. The product (yield 95%) was recrystallized from ethanol, to give yellow needles, m.p. 163–164°: ν_{max}^{Nujol} 1720 cm^{-1} (OAc).

Anal. Calc. for $C_{18}H_{14}N_4O_2$: C, 67.9; H, 4.4; N, 17.6. Found: C, 68.2; H, 4.5; N, 17.8.

3-(Benzoyloxymethyl)-1-phenylflavazole (**11**). — A solution of compound **9** (0.1 g) in pyridine (5 mL) was treated with benzoyl chloride (0.2 mL), and the mixture was kept for 24 h at room temperature. It was then poured onto crushed ice, and the solid product (yield 85%) was recrystallized from ethanol, to give yellow needles, m.p. 192°; ν_{max}^{Nujol} 1720 cm^{-1} (OBz).

Anal. Calc. for $C_{23}H_{16}N_4O_2$: C, 72.6; H, 4.2; N, 14.7. Found: C, 72.2; H, 4.5; N, 15.0.

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