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Note

Regioselective hydrazonation at C-2 of dehydroascorbic acid*

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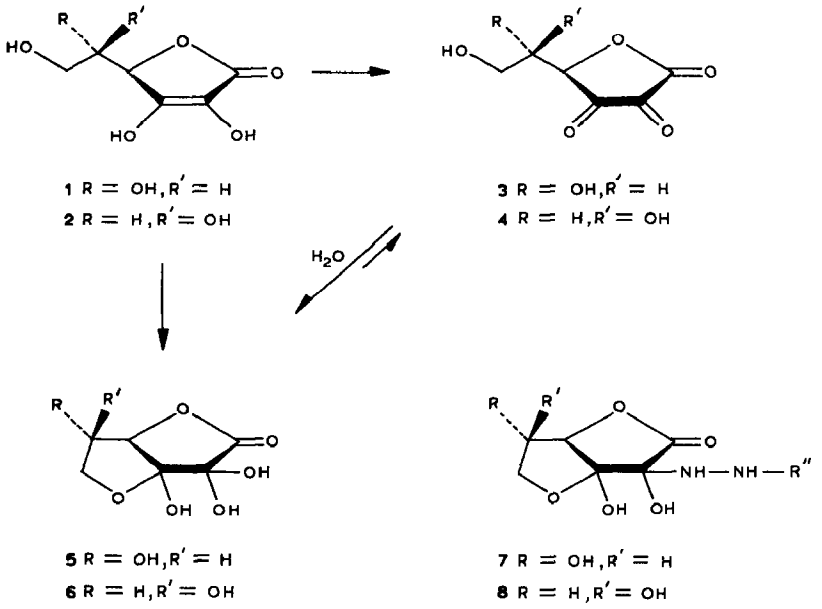
2-Arylhydrazones of dehydro-L-ascorbic acid (**3**, L-*threo*-2,3-hexodiulosono-1,4-lactone) and its analogues are potential precursors for the synthesis of heterocyclic compounds[2] and a facile method for their synthesis is required. The first synthesis[3] of dehydro-L-ascorbic acid 2-phenylhydrazone was multi-stage; subsequently, the reaction of **3** with 1-acetyl-2-phenylhydrazine was used[4,5], but the yield was low. El Ashry and co-workers[6–8] synthesised the *p*-substituted phenylhydrazones of **3** by the controlled reaction of **5** or the D-*erythro* analogue **6** in aqueous



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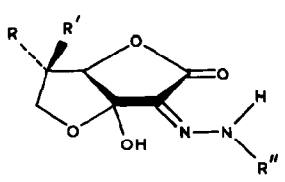
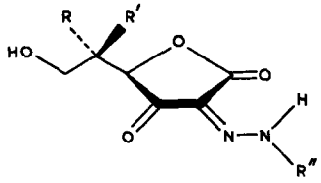
solution with the corresponding hydrazine. Similarly, the phenylhydrazone of **6** but not that of **5** could be prepared[9]. Hvoslef and Pedersen[10] prepared the *p*-bromophenylhydrazone of **5** by using *N,N*-dimethylacetamide as the reaction solvent, and Pedersen[11] detected the formation of the phenyl-, *p*-bromophenyl-, and *p*-nitrophenyl-hydrazones of **5** in *N,N*-dimethylformamide.

We now report that the regioselective formation of arylhydrazones at position 2 of dehydro-L-ascorbic acid can be effected with an acetone arylhydrazone in an aqueous medium. The reaction was applied for the synthesis of the phenylhydrazone and *p*-substituted analogues, and was also applied to dehydro-D-isoascorbic acid (**4**). Acetone arylhydrazones are easily prepared and the acetone liberated does not interfere with the isolation of the product.

Although the C-2 carbonyl of dehydroascorbic acids is the most reactive, the regioselective hydrazonation was enhanced by the existence of **3** and **4** mainly in the bicyclic forms **5** and **6**, respectively. The preponderance of the bicyclic form immediately after the oxidation of **1** has been confirmed[12–14]. However, in spite of the anticipated formation[11] of the intermediates **7** and **8** from the reaction of the corresponding C-2 of **5** or **6**, the products isolated were the monocyclic compounds **11** and **12** and not **9** and **10**, respectively. This finding was supported by the results of Hvoslef[10,15] on the X-ray crystallography of the *p*-bromophenylhydrazone **11b**. The disruption of the furanoid ring follows the introduction of the hydrazone residue at C-2 which induces π-electron delocalisation in the system.



9 R = OH, R′ = H
10 R = H, R′ = OH



11 R = OH, R′ = H
12 R = H, R′ = OH

a R″ = C_6H_5
b R″ = 4-Br-C_6H_4
c R″ = 4-Cl-C_6H_4

The structures of the monoarylhydrazones were confirmed by comparison with authentic compounds prepared by other methods. The monohydrazones had i.r. bands for carbonyl at 1690 (C-3 carbonyl) and 1760 cm^{-1} (lactone carbonyl).

EXPERIMENTAL

General methods. — Melting points were determined with a "Meltemp" apparatus and i.r. spectra with a Pye Unicam SP 1025 spectrometer.

2-Arylhydrazones. — (*a*) L-threo-*2,3-Hexodiulosono-1,4-lactone* (**1**). A stirred

solution of **1** (1.76 g, 0.01 mol) in water (25 mL) was treated with iodine till a permanent pale-yellow colour appeared. The acetone arylhydrazone (0.01 mol) was added, and the mixture was heated for 2 min at 60° and then kept overnight at room temperature. The products were collected, washed with water and then ethanol, and recrystallised from ethanol to afford bright-yellow crystals of **11a** (88%), m.p. 166–169° (lit.[5] m.p. 167–170°); **11b** (62%), m.p. 206–208° (lit.[10] m.p. 208°, lit.[7] m.p. 220–221°); **11c** (57%), m.p. 199–202° (lit.[7] m.p. 203–204°).

(*b*) D-erythro-*2,3-Hexodiulosono-1,4-lactone*. Use of the conditions in (*a*), but with **2**, gave **12a** (75%), m.p. 191–193° (lit.[9] m.p. 194–195°); **12b** (68%), m.p. 206–208° (lit.[6] m.p. 213–214°); **12c** (70%), m.p. 195–197° (lit.[6] m.p. 198–199°).

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