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Note

Derivatives from D-ascorbic acid*

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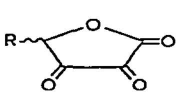
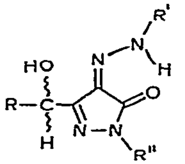
The structural features existing in the 4-substituted 2,3-dioxobutyro-1,4-lactones (**A**) promise their synthetic utility for the preparation of nitrogen heterocyclic compounds, *via* their mono-[2–8] and bis-(hydrazones)[9–15], as well as *via* their reaction with *ortho*-diamines[16–19] whereby various types of heterocyclic compounds may be prepared. Ring opening of the corresponding 2,3-bis(arylhydrazones) provides access to the synthesis of pyrazolediones[9–13] (**B**) *via* cyclization of the resulting carboxyl group with the 3-hydrazono group on basic treatment.

Controlled reaction of arylhydrazines with 2,3-dioxobutyro-1,4-lactone allowed the synthesis of mono(arylhydrazones) which, on brief reaction with another type of hydrazine, give mixed bis(hydrazones) that, in turn, provide access to the preparation of compounds having various substituents on the ring. Another way of achieving introduction of substituents on the ring is by variation of substituents on C-4 of 2,3-dioxobutyro-1,4-lactone. In view of these considerations, various compounds have been prepared by reaction of the parent compound (**A**, R = H) to afford derivatives having a hydroxymethylene group as the side chain; the latter group resulted from the opening of the lactone ring. Derivatives of **A** having a 1,2-dihydroxyethyl or 1,2,3-trihydroxypropyl group afforded the corresponding derivatives of **B** bearing substituents having the D-*erythro*- and L-*threo*-trihydroxypropyl, and



A



B

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[*] Heterocycles from Carbohydrate Precursors, Part XVIII. For Part XVII, see ref. 1.

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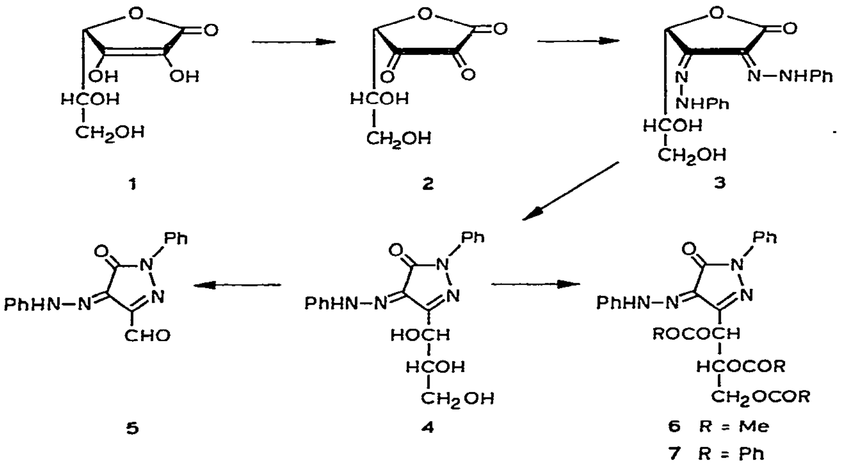
D-*arabino*- and L-*xylo*-tetrahydroxybutyl, side-chains, respectively. To the best of our knowledge, such a derivative having the D-*threo*-trihydroxypropyl side-chain, which could be prepared from the D analog of L-ascorbic acid (vitamin C), is unknown.

For the preparation of the D-*threo* analog, the starting material, namely, D-ascorbic acid (**1**), needed for this study was prepared by cyanohydrin synthesis[21] from D-*threo*-pentos-2-ulose (D-xylosone); on oxidation, the product gave D-*threo*-2,3-hexodiulosono-1,4-lactone (**2**), and this reacted with phenylhydrazine to give the corresponding bis(hydrazone), namely, D-*threo*-2,3-hexodiulosono-1,4-lactone 2,3-bis(phenylhydrazone) (**3**). Dissolution of **3** in alkali, followed by acidification, afforded 3-(D-*threo*-glycerol-1-yl)-1-phenyl-4,5-pyrazoledione 4-(phenylhydrazone) (**4**), whose structure was deduced from the mode of formation, as well as from its combustion analysis, which agreed with the molecular formula $C_{18}H_{18}N_4O_4$, and its infrared (i.r.) spectrum, which showed one band in the carbonyl frequency region at 1660 cm^{-1} due to the OCN group, instead of that at 1745 cm^{-1} appearing in the spectrum of its precursor **3** (due to the lactone group). Moreover, periodate oxidation of **4** gave an aldehyde identical with that obtained from its analogs, and formulated as 3-formyl-1-phenyl-4,5-pyrazoledione 4-(phenylhydrazone) (**5**). Acetylation of **4** with acetic anhydride in pyridine afforded a yellow-orange product whose elemental analysis agreed with the molecular formula $C_{24}H_{24}N_4O_7$, indicating the presence of three acetyl groups, and that showed in its i.r. spectrum a band at 1750 cm^{-1} due to the OAc groups, in addition to the OCN band at 1660 cm^{-1}. Therefore, it is formulated as 1-phenyl-3-(1,2,3-tri-*O*-acetyl-D-*threo*-glycerol-1-yl)-4,5-pyrazoledione 4-(phenylhydrazone) (**6**). Benzoylation of **4** with benzoyl chloride in pyridine afforded 1-phenyl-3-(1,2,3-tri-*O*-benzoyl-D-*threo*-glycerol-1-yl)-4,5-pyrazoledione 4-(phenylhydrazone) (**7**), whose i.r. spectrum showed the OBz and OCN groups at 1720 and 1660 cm^{-1}, respectively.



EXPERIMENTAL

General methods. — Melting points were determined on a Kofler-block apparatus and are uncorrected. I.r. spectra were recorded with a Unicam SP-200 spectrophotometer. Microanalyses were performed in the Chemistry Department, Faculty of Science, Cairo University, Cairo, Egypt.

D-threo-*2,3-Hexodiulosono-1,4-lactone 2,3-bis(phenylhydrazone)* (**3**). — D-Xylose was transformed into D-xylosone which, on application of the cyanohydrin reaction, afforded **1**; oxidation of **1** then gave **2**. Treatment of an aqueous solution of **2** (1.3 g) with phenylhydrazine (2.5 g) and a few drops of acetic acid, followed by heating for 1 h on a boiling-water bath, afforded a red precipitate (yield 60%) that was purified by repeated precipitation from aqueous ethanol; ν_{max}^{Nujol} 1745 cm^{-1} (COO).

From the mother liquor, a trace of compound **5** was separated.

*3-(*D-threo-*Glycerol-1-yl)-1-phenyl-4,5-pyrazoledione 4-(phenylhydrazone)* (**4**).— A suspension of compound **3** (1 g) in M sodium hydroxide solution (50 mL) was heated until all of the bis(hydrazone) had dissolved. The hot solution was then carefully made neutral with acetic acid, whereupon a yellow-orange product was immediately precipitated; this was filtered off, washed with water, dried (yield 80%), and recrystallized from ethanol, to give orange needles, m.p. 208–210°; ν_{max}^{Nujol} 3450 (OH) and 1660 cm^{-1} (OCN).

Anal. Calc. for $C_{18}H_{18}N_4O_4$: C, 61.0; H, 5.1; N, 15.8. Found: C, 61.0; H, 4.7; N, 15.7.

Periodate oxidation of compound **4**. — A suspension of compound **4** in water was subjected to the action of an aqueous solution of sodium metaperiodate, and the reaction mixture was processed as usual, affording yellow-orange needles, m.p. 140°, unchanged on admixture with an authentic sample of 3-formyl-1-phenyl-4,5-pyrazoledione 4-(phenylhydrazone) (**5**) prepared from other analogs[14,15].

*1-Phenyl-3-(1,2,3-tri-O-acetyl-*D-threo-*glycerol-1-yl)-4,5-pyrazoledione 4-(phenylhydrazone)* (**6**). — A solution of compound **4** (50 mg) in dry pyridine (2 mL) was treated with acetic anhydride (1 mL), and the mixture was kept overnight at room temperature. The excess of acetic anhydride was hydrolyzed with cold water, the mixture was evaporated, and then toluene was added and re-evaporated, to give an orange syrup that crystallized from ethanol in yellow-orange needles (yield 90%), m.p. 129–130°; ν_{max}^{KBr} 1750 (OAc) and 1660 cm^{-1} (OCN).

Anal. Calc. for $C_{24}H_{24}N_4O_7$: C, 60.0; H, 5.0; N, 11.7. Found: C, 60.1; H, 5.4; N, 11.3.

*1-Phenyl-3-(1,2,3-tri-O-benzoyl-*D-threo-*glycerol-1-yl)-4,5-pyrazoledione 4-(phenylhydrazone)* (**7**). — A stirred solution of compound **4** (50 mg) in dry pyridine (2 mL) was treated with benzoyl chloride (0.5 mL), and the mixture was kept overnight at room temperature, poured onto crushed ice, and the product filtered off, washed with water, and dried. It was recrystallized from ethanol, to give orange crystals (yield 85%), m.p. 155–157°; ν_{max}^{KBr} 1720 (OBz) and 1660 cm^{-1} (OCN).

Anal. Calc. for $C_{39}H_{30}N_4O_7$: C, 70.3; H, 4.5; N, 8.4. Found: C, 70.4; H, 4.7; N, 8.6.

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