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## Note

# 5,6-*O*-Benzylidene derivatives of dehydro-L-ascorbic acid and dehydro-D-isoascorbic acid osazones

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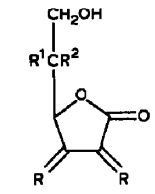
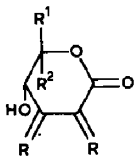
The structure of dehydro-L-ascorbic acid phenylosazone has been a subject[1–6] of controversy. Structures possessing γ- (**1**) and δ-lactone (**2**) rings have been proposed and **1** is the presently accepted structure. The azohydrazino structure, 2,3-dideoxy-3-phenylazo-2-phenylhydrazino-L-*threo*-hex-2-enono-1,4-lactone[4] (**3**), was proposed for the hydrazone residues, but the bishydrazono structure **1** has been confirmed[3]. The structure of the phenylosazone of dehydro-D-isoascorbic acid, which could be **4** or **5**, has received little attention. A study of benzylidene acetals of the dehydroascorbic acid osazones has now provided confirmation of the size of the lactone ring.

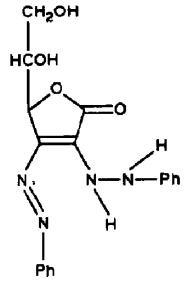


**1** $R^1 = H, R^2 = OH$
**4** $R^1 = OH, R^2 = H$



**2** $R^1 = H, R^2 = CH_2OH$
**5** $R^1 = CH_2OH, R^2 = H$

R = N—NH—Ph



**3**

Dehydro-L-ascorbic acid phenylosazone was assumed by Roberts[4] to be the azohydrazine **3**, and the structure **7** was assigned to the benzylidene derivative on the basis of its identity with the product obtained by the condensation of phenylhydrazine with 5,6-*O*-benzylidene-L-*threo*-2,3-hexodiulosono-1,4-lactone 2-phenylhydrazone. I.r. spectra cannot be used reliably to confirm the size of the lactone

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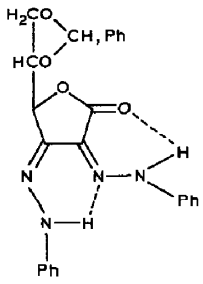
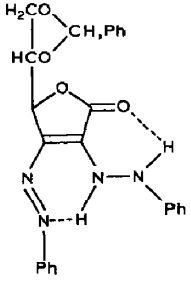
ring in this type of compound since a change in the geometry of the hydrazone residues may dramatically change the frequency of the carbonyl lactone.

When the osazone of dehydro-L-ascorbic acid was treated with benzaldehyde–zinc chloride, a product was obtained in high yield which was identical to that of Roberts and has been shown to have the structure **6**. The i.r. spectrum of **6** contained bands at 1730 (COO) and 3220 $cm^{-1}$ (NH), the former suggesting a 1,5-lactone structure. The $^1$H-n.m.r. data for **6** and its rearranged product **8** indicated that **6** was a γ-lactone. Thus, the $^1$H-n.m.r. spectrum of **6** contained, *inter alia,* signals at δ 5.15 (d, $J_{4,5}$ 4.5 Hz, H-4), 5.80 and 5.92 (2 s, 1 H, diastereoisomeric PhC*H*), and 10.83 and 11.80 (2 s, 2 NH) indicative of the structure assigned.

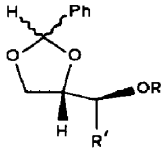
Rearrangement[7] of **6** by treatment with alkali in aqueous acetone afforded 3-(2,3-*O*-benzylidene-L-*threo*-glycerol-1-yl)-1-phenyl-4,5-pyrazoledione 4-phenylhydrazone (**8**). The rearrangement was confirmed by the i.r. spectrum of **8**, which indicated the presence of OCN and hydroxyl groups. The $^1$H-n.m.r. spectrum of **8** contained, *inter alia,* signals at δ 3.2 and 13.7 (OH and NH), 5.85 and 6.03 (diastereoisomeric PhC*H*), and 4.5 (d, H-4; *cf.* δ 5.15 for **6**). Acetylation of **8** gave a mono-acetate **9**. Since only the chemical shift of the signal for H-4 was markedly affected in the conversions **6**→**8** and **8**→**9**, **6** must have a 1,4-lactone structure.



**6**

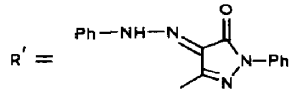


**7**



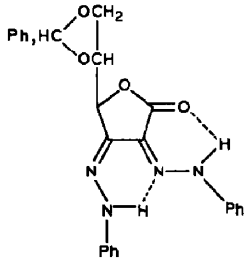
**8** R = H

**9** R = Ac

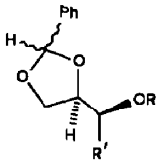


Benzylidenation of dehydro-D-isoascorbic acid phenylosazone [**4**, D-*erythro*-2,3-hexodiulosono-1,4-lactone 2,3-bis(phenylhydrazone)] afforded the 5,6-*O*-benzylidene derivative **10** (85%), which had i.r. bands at 1745 (COO) and 3240 $cm^{-1}$ (NH). The $^1$H-n.m.r. spectrum of **10** contained, *inter alia,* signals at δ 5.33 and 5.43 (2 d, $J_{4,5}$ 3.0 Hz, H-4) reflecting the different anisotropic effects of the phenyl group of the benzylidene acetal on H-4 of the diastereoisomers. This effect does not occur in **6** indicating that H-4 in the L derivative is remote from the phenyl group of the benzylidene acetal. There were also signals at δ 5.83 and 5.94 for diastereoisomeric PhC*H*, and at 10.83, 10.93, 11.7, and 11.87 (4 s, 2 H, 2 NH) reflecting the anisotropic effect on NH of the phenyl group of the diastereoisomeric benzylidene acetals.

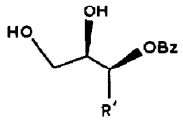
Base-catalysed rearrangement of **10** afforded 3-(2,3-*O*-benzylidene-D-*erythro*-glycerol-1-yl)-1-phenyl-4,5-pyrazoledione 4-phenylhydrazone (**11**). Acid hydrolysis of the benzoate (**12**) of **11** cleaved the acetal ring to give **13**. The i.r. spectrum of **13** indicated the absence of a lactone ring and those of **11–13** contained a band at ~1660 $cm^{-1}$ for an OCN group. The $^1$H-n.m.r. spectra showed that the deshielding effect of the lactone ring on H-4 in **10** had disappeared on conversion into **11**, and reappeared on benzoylation (→**12**), indicating the involvement of position 4 in **10** in the lactone ring.



**10**



**11** R = H
**12** R = Bz



**13**

Thus, the benzylidene acetals of the phenylosazones of dehydro-L-ascorbic acid and its D-*erythro* analogue are γ-lactones, since there is no indication of rearrangement of the lactone ring under the conditions of benzylidenation.

## EXPERIMENTAL

*General.* — Melting points were determined with a Kofler block or a "Meltemp" apparatus and are uncorrected. I.r. spectra were recorded with Unicam SP 200 and 1025 spectrophotometers. $^1$H-N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal $Me_4Si$) with Varian XL–100-15, EM-390, and Jeol-100 spectrometers. Microanalyses were performed in the Chemistry Department, Cairo University.

*5,6-O-Benzylidene-*L-threo-*2,3-hexodiulosono-1,4-lactone 2,3-bis(phenylhydrazone)* (**6**). — A mixture of powdered, fused zinc chloride (4.0 g) and dry benzaldehyde (20 mL) was vigorously stirred for 15–20 min, and then with **1** (2.0 g) for 30 min. The mixture was poured onto crushed ice (1 kg), the product was collected, and a solution in methanol was poured onto crushed ice. This process was repeated four times. The final product (92%) was collected, washed with water and then methanol, dried, and recrystallised from chloroform–methanol to give red crystals of **6**, m.p. 207–208° (lit.[4] m.p. 206–207°); $\nu_{max}^{KBr}$ 1730 (COO) and 3220 $cm^{-1}$ (NH). $^1$H-N.m.r. data: δ 4.4 (m, 3 H, H-5,6,6′), 5.15 (d, 1 H, $J_{4,5}$ 4.5 Hz, H-4), 5.80 and 5.93 (2 s, 1 H, PhC*H*), 7.4 (m, 15 H, 3 Ph), and 10.83 and 11.8 (2 s, 2 H, 2 NH).

*Anal.* Calc. for $C_{25}H_{22}N_4O_4$: C, 67.9; H, 5.0; N, 12.7. Found: C, 67.6; H, 4.8; N, 12.9.

*3-(2,3-O-Benzylidene-*L*-threo-glycerol-1-yl)-1-phenyl-4,5-pyrazoledione 4-phenylhydrazone* (**8**). — A solution of **6** (1.0 g) in acetone (100 mL) was stirred at 70–80° with 2M potassium hydroxide (200 mL) for 6 h, and then kept overnight at room temperature. The resulting solution was cooled to 5°, and glacial acetic acid was added to pH 7 keeping the temperature at <10°. The product (91%) was collected immediately, washed with water and then cold ethanol, dried, and recrystallised from acetone–ethanol to give **8** as orange needles, m.p. 175–176°; $\nu_{max}^{KBr}$ 1665 (OCN) and 3450 $cm^{-1}$ (OH). $^1$H-N.m.r. data: $\delta$ 3.2 (bs, 1 H, OH), 4.25 (m, H-3,3'), 4.8 (m, 2 H, H-1,2), 5.85 and 6.03 (2 s, 1 H, PhC*H*), 7.3 and 7.9 (m and q, 15 H, 3 Ph), and 13.7 (bs, 1 H, NH).

*Anal.* Calc. for $C_{25}H_{22}N_4O_4$: C, 67.9; H, 5.0; N, 12.7. Found: C, 68.0; H, 5.4; N, 12.8.

*3-(1-O-Acetyl-2,3-O-benzylidene-*L*-threo-glycerol-1-yl)-1-phenyl-4,5-pyrazoledione 4-phenylhydrazone* (**9**). — Conventional treatment of **8** (0.3 g) with dry pyridine (4 mL) and acetic anhydride (3 mL), with recrystallisation of the product (90%) from acetone–ethanol, gave **9** as orange needles, m.p. 183–186°; $\nu_{max}^{KBr}$ 1590 (C=N), 1660 (OCN), and 1745 $cm^{-1}$ (OAc). $^1$H-N.m.r. data: $\delta$ 2.16 and 2.19 (2 s, 3 H, COMe), 4.2 (m, 2 H, H-3,3'), 5.0 (m, 1 H, H-2), 5.86 and 6.02 (2 s, 1 H, PhC*H*), 6.23 and 6.30 (2 d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 7.4 and 7.9 (m and q, 15 H, 3 Ph), and 13.7 (bs, 1 H, NH).

*Anal.* Calc. for $C_{27}H_{24}N_4O_5$: C, 66.9; H, 5.0; N, 11.6. Found: C, 66.9; H, 5.2; N, 11.9.

*5,6-O-Benzylidene-*D*-erythro-2,3-hexodiulosono-1,4-lactone 2,3-bis(phenylhydrazone)* (**10**). — The osazone **4** was treated as for **1** to yield crude **10** (85%). Recrystallisation from chloroform–methanol gave red needles, m.p. 226–229°; $\nu_{max}^{KBr}$ 1745 (COO) and 3240 $cm^{-1}$ (NH). $^1$H-N.m.r. data: $\delta$ 4.1 and 4.3 (2 q, 2 H, $J_{6,6'}$ 10.5, $J_{5,6'}$ 6.8, $J_{5,6}$ 5.3 Hz, H-6,6'), 4.7 (m, 1 H, H-5), 5.33 and 5.43 (2 d, 1 H, $J_{4,5}$ 3.0 Hz, H-4), 5.83 and 5.93 (2 s, 1 H, PhC*H*), 7.2 (m, 15 H, 3 Ph), 10.83 and 10.93 (2 s, 1 H, NH), and 11.77 and 11.86 (2 s, 1 H, NH).

*Anal.* Calc. for $C_{25}H_{22}N_4O_4$: C, 67.9; H, 5.0; N, 12.7. Found: C, 68.0; H, 5.2; N, 12.5.

*3-(2,3-O-Benzylidene-*D*-erythro-glycerol-1-yl)-1-phenyl-4,5-pyrazoledione 4-phenylhydrazone* (**11**). — Treatment of **10** as described for **6** yielded crude **11** (89%). Recrystallisation from acetone–ethanol gave orange needles, m.p. 196–198°; $\nu_{max}^{KBr}$ 1660 (OCN) and 3500 $cm^{-1}$ (OH). $^1$H-N.m.r. data: $\delta$ 2.9 (bs, 1 H, OH), 4.2 (m, 2 H, H-3,3'), 4.7 (m, 1 H, H-2), 5.06 and 5.20 (2 d, 1 H, $J_{1,2}$ 5.3 Hz, H-1), 5.77 and 6.06 (2 s, 1 H, PhC*H*), 7.3 and 7.9 (m and q, 15 H, 3 Ph), and 13.7 (bs, 1 H, NH).

*Anal.* Calc. for $C_{25}H_{22}N_4O_4$: C, 67.9; H, 5.0; N, 12.7. Found: C, 67.9; H, 5.2; N, 12.3.

*3-(1-O-Benzoyl-2,3-O-benzylidene-*D*-erythro-glycerol-1-yl)-1-phenyl-4,5-*

*pyrazoledione 4-phenylhydrazone* (**12**). — Conventional treatment of **11** (0.4 g) with dry pyridine (5 mL) and benzoyl chloride (2 mL), with recrystallisation of the product (78%) from acetone–ethanol, gave **12** as orange needles, m.p. 182–184°; $\nu_{max}^{KBr}$ 1590 (C=N), 1665 (OCN), and 1720 (OBz). $^1$H-N.m.r. data: $\delta$ 4.4 and 4.5 (2 q, 2 H, $J_{3,3'}$ 11.5, $J_{2,3'}$ 8.0, $J_{2,3}$ 5.0 Hz, H-3,3'), 5.0 (m, 1 H, H-2), 5.83 and 6.03 (2 s, 1 H, PhC*H*), 6.53 and 6.63 (2 d, 1 H, $J_{1,2}$ 5.3 Hz, H-1), 7.3 and 8.0 (2 m, 20 H, 4 Ph), and 13.7 (bs, 1 H, NH).

*Anal.* Calc. for $C_{32}H_{26}N_4O_5$: C, 70.3; H, 4.8; N, 10.3. Found: C, 70.5; H, 5.1; N, 10.7.

*3-(1-O-Benzoyl-*D-erythro-*glycerol-1-yl)-1-phenyl-4,5-pyrazoledione4-phenylhydrazone* (**13**). — (*a*) A solution of **12** (0.2 g) was treated[8] with aqueous 90% trifluoroacetic acid (4 mL) for 15 min at room temperature. The mixture was diluted with cold water, and the product (97%) was collected, washed with water and then ethanol, dried, and recrystallised from ethanol to give **13** as orange needles, m.p. 192–194°.

(*b*) A suspension of **12** (0.2 g) in water (5 mL) and aqueous 75% acetic acid (25 mL) was boiled under reflux until dissolution was complete and then kept for 24 h at room temperature. The mixture was diluted with cold water, and the product (74%) was collected, washed with water and then ethanol, dried, and recrystallised from ethanol to give **13** as orange needles, m.p. 192–194° alone or in admixture with the product from (*a*).

*Anal.* Calc. for $C_{25}H_{22}N_4O_5$: C, 65.5; H, 4.8; N, 12.2. Found: C, 65.5; H, 5.0; N, 12.6.

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