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Note

syn and *anti* oxime isomers of an *aldehydo* sugar derivative

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Wolfrom *et al.*[1] obtained from *aldehydo*-D-glucose pentaacetate an oxime, that on acetylation produced two D-glucose oxime hexaacetates having m.p. 79° and 119.5°, respectively. The lower melting compound was very unstable and changed spontaneously into the higher melting isomer. These compounds were presumed to be the acyclic *syn* and *anti* D-glucose oxime hexaacetates. To a third D-glucose oxime hexaacetate[1–3], m.p. 109–110° (m.p. 113–115°, ref. 1), obtained from D-glucose oxime and which unlike the isomer of m.p. 119.5° was not converted into D-gluconic acid nitrile pentaacetate, has been assigned a cyclic structure.

Mild acetylation of *aldehydo*-D-galactose oxime pentaacetate yielded an acyclic D-galactose oxime hexaacetate, m.p. 145–6°. To a second D-galactose oxime hexaacetate, m.p. 129–30°, obtained by acetylation of D-galactose oxime, and which is not convertible to the former isomer, was assigned a cyclic structure[4]. The structures of the acyclic and cyclic oximes isomers mentioned earlier have been confirmed by *O*-acetyl and *N*-acetyl determination[5].

3-*O*-Benzyl-2,4-*O*-ethylidene-*aldehydo*-D-erythrose, prepared from its methylphenylhydrazone with nitrous acid, or by oxidation of 3-*O*-benzyl-2,4-*O*-ethylidene-D-erythritol, has been characterized by its oxime[6] (**1**), needles melting at 61–63°. We have observed now that recrystallization of **1** from boiling benzene (Norit) produced very thin needles, m.p. 147–48° (**2**). A mixture of **1** and **2** melted at 64–120° and could not be separated or distinguished from the pure compounds by t.l.c.

Compound **2** analyzed as the oxime, and is dextrorotatory, whereas the parent compound is levorotatory. I.r. absorption bands at 3550, 3308 (OH); and 1640 cm^{-1} (weak, C=N) in the spectra of both **1** and **2** suggested them to be *syn-anti* oxime isomers. N.m.r. analysis confirmed this assumption, and identified the low melting oxime **1** as the *syn*, and the higher melting oxime **2** as the *anti* geometrical isomers.

The n.m.r. analysis of both **1** and **2** showed very similar spectra: signals of aromatic protons at τ 2.70 (**1**) and τ 2.63 (**2**), and practically identical spectra from τ 5.00 upfield. In the spectrum of **2**, a broad doublet of H-2 at τ 5.00 ($J_{1,2}$ 8 Hz) was resolved into a sharp doublet when decoupled from H-1 (CH=N, see later). A one proton quartet of $>CH\text{-}CH_3$ at τ 5.23 (J_{H,CH_3} 5 Hz) resolved into a singlet when decoupled from the adjacent methyl protons (τ 8.67), a two-proton singlet at τ 5.45,

a proton multiplet at τ 5.86, and a two-proton doublet at τ 6.50 ($J_{3,4}$ 8 Hz) were assigned to the benzyl-methylene protons, H-3 and H-4, respectively. This part of the spectrum showed the chemical shifts of all the protons of the oximes **1** and **2** but those of H-1 and =NO–H.

Phillips[7] has determined the chemical shifts of the CH=N protons of the mixture of the two geometric isomers of aldoximes, and, on theoretical grounds, he assigned the signals at the lower field to the *syn* isomer. Study of the n.m.r. spectra of the *syn* and of the *anti p*-chlorobenzaldoxime isomers[8] (whose structure has been established by crystallographic studies[9]) confirmed the assignment made by Phillips to the CH=N protons of the isomeric aldoximes.

Kleinspehn *et al.*[10] have shown that owing to spin coupling the signals of the =NO–H protons of aliphatic aldoximes are not split, and that the protons of the *syn* isomers absorb at a higher field than do the *anti* isomers.

In the n.m.r. spectra of the oximes under study, a singlet in each of the isomers, at τ 0.98 (**1**) and τ 0.88 (**2**), which disappeared after treatment with D_2O, was assigned to the =NO–H proton, the only exchangeable proton of the oximes.

A one-proton doublet at τ 2.55 ($J_{1,2}$ 6 Hz), a field below that of the aromatic protons of **1**, was assigned to H-1. A one-proton doublet τ 3.22 ($J_{1,2}$ 8 Hz) of **2**, in the field above that of the aromatic protons, was assigned to H-1. The doublet of H-1 of **2** was resolved into a singlet when decoupled from H-2.

The magnitude of the difference $\tau_{OH} - \tau_{CH=N}$ of the oxime isomers has been suggested as a criterion for assigning aldoxime configuration[11], the smaller difference being characteristic for the *syn* and the greater for the *anti* isomer. Under our experimental conditions $\tau_{OH} - \tau_{CH=N}$ for **1** and **2** were 82 and 146 Hz, respectively.

EXPERIMENTAL

General methods. — The experimental methods have been described earlier[6]. Optical rotations were measured with a Perkin–Elmer Model 141 polarimeter. I.r. spectra were recorded with a Perkin–Elmer grating spectrometer Model 337, and n.m.r. spectra with a Varian T-60 NMR spectrometer in chloroform-*d* (tetramethylsilane as internal reference).

syn-*3-O-Benzyl-2,4-O-ethylidene*-D-*erythrose oxime*[6] (**1**). — The oxime was prepared as described earlier and crystallized from chloroform and cyclohexane without warming; $[\alpha]_D^{23}$ −8.31° (*c* 3.02, chloroform) differs from that reported earlier[6] (−5.9°), the variance being attributed to the better performance of the polarimeter used here; $\nu_{max}^{chloroform}$ 3550, 3308 (OH); 1640 cm^{-1} (C=N); n.m.r. data: τ 0.98 (singlet, 1 proton, =NO–H), 2.55 (doublet, 1 proton, $J_{1,2}$ 6 Hz, H-1), 2.70 (singlet, 5 aromatic protons), 5.05 (doublet, 1 proton, $J_{1,2}$ 6 Hz, H-2), 5.30 (quartet, 1 proton, J_{H,CH_3} 5 Hz, CH–CH_3), 5.46 (singlet, 2 benzyl methylene protons), 5.86 (multiplet, 1 proton, H-3), 6.50 (doublet, 2 protons, H-4), 8.67 (doublet, 3 protons, $J_{CH_3,H}$ 5 Hz, > CH–CH_3).

anti-*3-O-Benzyl-2,4-O-ethylidene*-D-*erythrose oxime* (**2**). — This isomer can be

obtained from **1** by recrystallization from benzene (Norit A, acid washed) or by several recrystallizations from benzene without charcoal treatment. The isomer can also be obtained directly from the *aldehydo* sugar when prepared in hot aqueous ethanol, R_F 0.42 in 1:1 ethyl acetate–cyclohexane, $[\alpha]_D^{23}$ +59.35° (*c* 1.39, chloroform); i.r. data: $\nu_{max}^{chloroform}$ 3550, 3308 (OH); 1640 cm^{-1} (C=N); n.m.r. data: τ 0.88 (singlet, 1 proton, =NO–H), 2.63 (singlet, 5 aromatic protons), 3.22 (doublet, 1 proton, $J_{1,2}$ 8 Hz, H-1), 5.00 (doublet, 1 proton, $J_{1,2}$ 8 Hz, H-2), 5.23 (quartet, 1 proton, J_{H,CH_3} 5 Hz, > CH–CH_3), 5.45 (singlet, 2 benzyl methylene protons), 5.86 (multiplet, 1 proton, H-3), 6.50 (doublet, 2 protons, H-4), 8.67 (doublet, 3 protons, CH–CH_3).

Anal. Calc. for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found: C, 61,95; H, 6.63; N, 5.78.

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