

AN UNSATURATED KETOHEXOSE AND DERIVED HEXENETETROLS

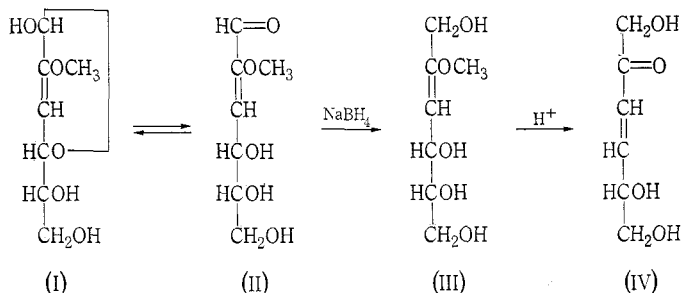
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[Manuscript received March 17, 1966]

Summary

The unsaturated ketose, 3,4-dideoxy-D-glycero-hex-trans-3-enulose, was prepared from 3-deoxy-2-O-methyl-β-D-erythro-hex-2-enofuranose by reduction with sodium borohydride followed by an allylic rearrangement under mild acid conditions. Further reduction of the ketose with sodium borohydride yielded *erythro*- and *D-threo*-hex-trans-3-ene-1,2,5,6-tetrols. The 1,2:5,6 di-O-isopropylidene derivatives of the tetrols were also prepared. The main evidence for the *trans* configuration of the double bonds of these five compounds is that they have a large value for $J_{3,4}$ (15.4 – 16.4 c/s).

Although many unsaturated sugars have now been reported¹ no simple α,β-unsaturated ketose was known.² The unsaturated ketose (IV)[†] was prepared by the reduction with sodium borohydride of a solution of the unsaturated aldose (I), followed by a mild acid treatment. The compound actually reduced was no doubt the aldehydo sugar (II), formed in the mutarotation of (I). The acid treatment caused an allylic rearrangement³ involving the hydroxyl group at C4, to give a hemiacetal which hydrolysed to the unsaturated ketone (IV).



That the product was an α,β-unsaturated carbonyl compound was shown by its ultraviolet and infrared spectra (λ_{max} 225 mμ and a strong band at 1705 cm⁻¹ with a medium one at 1645 cm⁻¹). Thin-layer chromatography of the ketose, and gas chromatography of its pertrimethylsilyl derivative, showed only one component,

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† A preliminary account of some of this work has been given.²

¹ Ferrier, R. J., *Adv. Carbohydr. Chem.*, 1965, **20**, 67.

² Anet, E. F. L. J., *Carbohydr. Res.*, 1965, **1**, 95.

³ Stiles, M., and Longroy, A., *Tetrahedron Lett.*, 1961, 337.

probably the *trans* isomer (as indicated by the presence of a band at 975 cm^{-1} in its infrared spectrum).

The proton magnetic resonance spectrum confirmed the general structure of the ketose as (IV) and in, particular, the *trans* configuration at the double bond (Fig. 1). The p.m.r. spectrum was similar to that reported⁴ for the *trans* form of

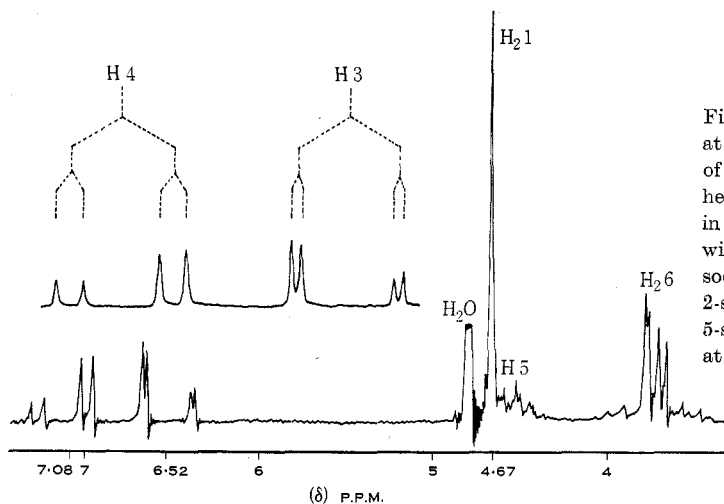
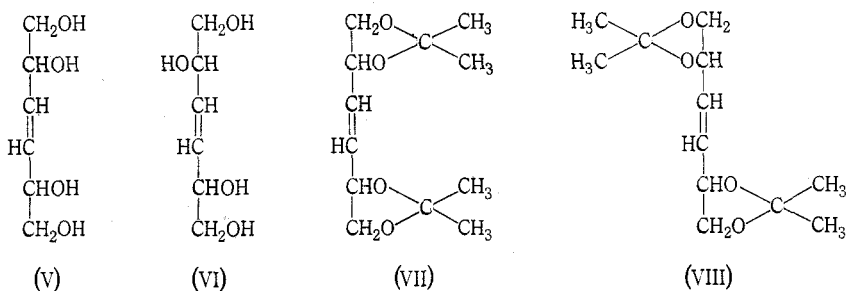


Fig. 1.—P.m.r. spectrum at 60 Mc/s of 3,4-dideoxy-D-glycero-hex-*trans*-3-enulose (IV) in deuterium oxide with internal sodium 2,2-dimethyl-2-silapentane 5-sulphonate at $\delta\ 0.00$ p.p.m.

3,4-dideoxy-D-glycero-hex-3-enulose, the aldehyde from (IV), except that the signal of H 1 had double the intensity and was shifted upfield. For both compounds the coupling constants for H 3 and H 4 were similar ($J_{3,4}$ 16.4 and 16.0 c/s) and in the range for *trans*-olefinic protons (J 11–18 c/s).⁵ The *cis* isomers of 3,4-dideoxyhex-3-enosuloses gave much lower values (10.4 c/s) for $J_{3,4}$.^{4,6} If any of the *cis* isomer was present, the proportion was too small to be detected by p.m.r. spectroscopy.



The hexenetetrols (V) and (VI) were formed by the reduction with sodium borohydride of the ketose (IV), the hex-*trans*-3-ene-*erythro*-1,2,5,6-tetrol (V) being

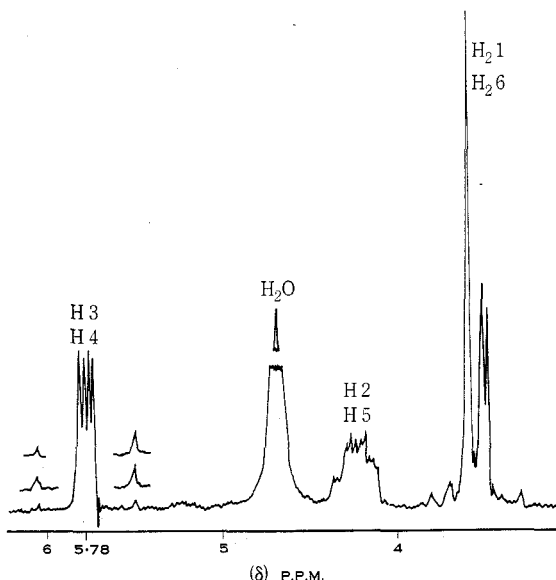
⁴ Anet, E. F. L. J., *Aust. J. Chem.*, 1962, **15**, 503.

⁵ Jackman, L. M., "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry." (Pergamon Press: London 1959.)

⁶ Anet, E. F. L. J., *Aust. J. Chem.*, 1965, **18**, 837.

obtained directly from the mixture by fractional crystallization.* The residues from the mother liquors were converted to the di-*O*-isopropylidene derivatives, which yielded the known *D*-*threo* isomer (VIII).^{7,8} The *D*-*threo*-tetrol (VI) was prepared by hydrolysis of the isopropylidene groups of (VIII) and was identical with that recently synthesized by another method by Tipson and Cohen.⁸ The more soluble *erythro*-di-*O*-isopropylidene derivative (VII) was prepared from the pure *erythro* tetrol (V). The *erythro* and *D*-*threo* isomers of each pair (V–VI) and (VII–VIII) were not distinguished by thin-layer or gas chromatographic methods. However, the

Fig. 2.—P.m.r. spectrum at 60 Mc/s of hex-*trans*-3-ene-*erythro*-1,2,5,6-tetrol (V) in deuterium oxide with internal sodium 2,2-dimethyl-2-silapentane 5-sulphonate at δ 0.00 p.p.m.



infrared spectra of the tetrols showed marked differences. The C=C band (1650 cm^{-1}) was only seen in the spectrum of the *D*-*threo* isomer (VI), while many sharp bands were present only in that of the *erythro* isomer.

The p.m.r. spectra of (V–VIII) all showed a similar sextet for H3 and H4 at δ 5.78 ($J_{3,4}$ 15.4 c/s for (V) and (VI), and 15.5 c/s for (VII) and (VIII)), confirming the *trans* configuration at the double bonds. From the signal of H3 and H4, calculations⁹ showed that $J_{2,3} = J_{4,5} = 6.1\text{ c/s}$; $J_{3,5} = J_{2,4} = -1.2\text{ c/s}$; and $J_{2,5} \approx 0$. With these compounds the p.m.r. spectra of the *erythro* and *threo* isomers were barely distinguishable. The p.m.r. spectrum of (V) is shown in Figure 2.

EXPERIMENTAL

(a) General

Melting points were corrected. The microanalyses were carried out by the Australian Micro-analytical Service, Melbourne, and the nuclear magnetic resonance spectra were obtained on a Varian A60 spectrometer by Mr P. J. Collins of the Division of Coal Research, CSIRO.

* The tetrol which crystallized out from the mixture was incorrectly assigned the *D*-*threo* configuration in the preliminary communication.²

⁷ Haines, A. H., *Chem. Ind.*, 1964, 1991.

⁸ Tipson, S. R., and Cohen, A., *Carbohydr. Res.*, 1965, **1**, 338.

⁹ Grant, D. M., and Hirst, R., *J. chem. Phys.*, 1963, **38**, 470.

(b) *3,4-Dideoxy-D-glycero-hex-trans-3-enulose (IV)*

An aqueous solution (200 ml) of 3-deoxy-2-*O*-methyl- β -D-erythro-hex-2-enofuranose⁶ (I) (26 g) was added gradually (5 min) to a solution of sodium borohydride (3 g) in water (100 ml). The solution warmed up to 40° and was allowed to stand overnight. Excess reagent was destroyed with acetone and the sodium ions were removed with a sulphonated polystyrene resin (hydrogen form). The solution was concentrated and repeatedly treated with methanol to remove the borates. The residue (24 g) was a nearly colourless *syrup*, $[\alpha]_D^{25} -18.8^\circ$ (c, 1 in water), $\lambda_{\max}(\text{H}_2\text{O})$ 225 m μ (ϵ 7000), a strong band at 1705 cm⁻¹ with medium bands at 1645 and 975 cm⁻¹ (Found: C, 49.0; H, 7.0. C₆H₁₀O₄ requires C, 49.3; H, 6.9%). The p.m.r. spectrum is shown in Figure 1. The unsaturated ketose gave a single spot on thin-layer chromatograms¹⁰ and the gas chromatograph of its pertrimethylsilyl derivative showed only one component.¹¹

(c) *Hex-3-ene-1,2,5,6-tetrols*

An aqueous solution (100 ml) of the unsaturated ketose (IV) (22 g) was added to a solution of sodium borohydride (3 g) in water (100 ml). The reaction mixture only warmed up slightly and was allowed to stand overnight. Excess reagent was destroyed with acetone and the sodium ions were removed with a sulphonated polystyrene resin (hydrogen form). The borate present was removed by repeated distillations with methanol. The residue (21.8 g), a clear syrup, was a mixture of (V) and (VI).

(i) *Hex-trans-3-ene-erythro-1,2,5,6-tetrol (V)*

The mixed tetrols above were triturated with warm acetone (30 ml), filtered, and washed with acetone (10 ml). The filtrate and washing contained mainly the D-*threo* isomer. The crystals (9 g), m.p. c. 80°, were recrystallized twice from ethanol and then from water to yield the pure *erythro* tetrol (V), m.p. 114–114.5°, $[\alpha]_D^{25}$ between 0° and -0.05° (c, 2 in water) (Found: C, 48.5; H, 8.1. C₆H₁₂O₄ requires C, 48.6; H, 8.2%). The tetrol (V) showed the following absorption bands: $\lambda_{\max}(\text{H}_2\text{O})$ 189 m μ (ϵ 9400) and, as a 1% disk in KCl, sharp medium to strong bands at 741, 850, 935, 970, 1001, 1078, 1115, 1245, 1282, 1345 cm⁻¹ as well as the intense broad band due to O-H stretch at c. 3200 cm⁻¹. The p.m.r. spectrum is shown in Figure 2.

(ii) *1,2:5,6-Di-O-isopropylidenehex-trans-3-ene-erythro-1,2,5,6-tetrol (VI)*

The pure tetrol (V) (2 g) in dry acetone (100 ml) containing sulphuric acid (0.3 ml) was stirred for 18 hr with anhydrous copper sulphate (4 g). The solution was filtered, neutralized with anhydrous sodium carbonate, filtered, and stirred overnight with more sodium carbonate. The solvent was evaporated off and the residue was extracted with warm pentane. On cooling, the extract yielded the di-*O*-isopropylidene derivative (VII) (2.3 g). The product was recrystallized from methanol twice, m.p. 70–71°, $[\alpha]_D^{25} < +0.1^\circ$ (c, 1 in CHCl₃), and it readily decolorized aqueous permanganate solution (Found: C, 63.0; H, 9.0. C₁₂H₂₀O₄ requires C, 63.2; H, 8.8%). The p.m.r. spectrum showed the following peaks of correct intensity: singlets at δ 1.37 (two CH₃) and δ 1.40 (two CH₃), quartets at δ 3.58 (H 1a and H 6a) and δ 4.08 (H 1b and H 6b), a multiplet at δ c. 4.50 (H 2 and H 5), and a sextet at δ 5.79 (H 3 and H 4), all from internal tetramethylsilane at δ 0.0 p.p.m. in carbon tetrachloride ($J_{3,4}$ 15.5 c/s). The infrared spectrum showed the two bands at 1368 and 1377 cm⁻¹ typical of isopropylidene groups, but no absorption bands near 1650 cm⁻¹.

(iii) *1,2:5,6-Di-O-isopropylidenehex-trans-3-ene-D-threo-1,2,5,6-tetrol (VIII)*

The crude D-*threo* tetrol from (i) above was diluted with anhydrous acetone (1000 ml) containing sulphuric acid (3 ml) and the mixture was stirred with anhydrous copper sulphate (40 g) for 20 hr. The filtered solution was neutralized with anhydrous sodium carbonate, filtered, and refluxed for 1 hr with more sodium carbonate and decolorizing charcoal. After filtration and evaporation of the solvent, the residue was crystallized from pentane and then three times from ether to yield the di-*O*-isopropylidene derivative (VIII), m.p. 82°, $[\alpha]_D^{25} +57.8^\circ$ (c, 1 in CHCl₃)

¹⁰ Wolfrom, M. L., Patin, D. L., and Lederkremer, R. M., *Chem. Ind.*, 1964, 1065.

¹¹ Sweeley, C. C., Bentley, R., Makita, M., and Wells, W. W., *J. Am. chem. Soc.*, 1963, **85**, 2497.

(Found: C, 63.0; H, 9.0. $C_{12}H_{20}O_4$ requires C, 63.2; H, 8.8%). The p.m.r. spectrum was barely distinguishable from that of the *erythro* isomer (VII). These properties agree with those reported earlier^{6,7} and furthermore the infrared spectrum of this sample was identical with that obtained by Tipson and Cohen.⁸

(iv) *Hex-trans-3-ene-D-threo-1,2,5,6-tetrol* (VI)

The pure di-*O*-isopropylidene derivative (VIII) (1 g) was heated at 50° for 30 min in 0.05N hydrochloric acid in 50% aqueous methanol (6 ml). The cooled solution was diluted with water and neutralized with a strong-base resin (carbonate form), filtered, and concentrated. The *residue* was crystallized from ethanol yielding the pure *D-threo* tetrol (VI), m.p. 64–65°, $[\alpha]_D^{25} -14.6^\circ$ (c, 0.5 in water) (Found: C, 48.6; H, 8.3. $C_6H_{12}O_4$ requires C, 48.6; H, 8.2%). The p.m.r. spectrum was barely distinguishable from that of the *erythro* isomer shown in Figure 2. These properties agree with those reported recently by Tipson and Cohen and the infrared spectrum was identical with that obtained by them.¹²

ACKNOWLEDGMENT

The author is indebted to Mr D. Gallimore for technical assistance.

¹² Tipson, S. R., private communication.