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Note

An unexpected formation of 2,3-*O*-isopropylidene-β-L-erythrofuranosyl 2,3-*O*-isopropylidene-β-L-erythrofuranoside from 2,3-*O*-isopropylidene-L-erythrose

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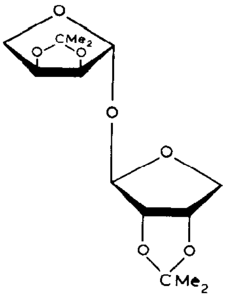
2,3-*O*-Isopropylidene-L-erythrose is a free-flowing, colorless liquid, which has been prepared from 6-deoxy-L-mannose[1], D-gulono-1,4-lactone[2], and D-ribono-1,4-lactone[3]. In 1968, a sample of 2,3-*O*-isopropylidene-L-erythrose[2] was stored in the dark. Slowly, the liquid became more viscous, and began to crystallize in the 1970's. Recent examination of this substance revealed that the monosaccharide had condensed with itself to form the disaccharide, 2,3-*O*-isopropylidene-β-L-erythrofuranosyl 2,3-*O*-isopropylidene-β-L-erythrofuranoside (**1**), an unusual occurrence in carbohydrate chemistry.



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The crystals of **1** were isolated simply by trituration with water and filtration, and the thoroughly dried needles were then characterized. The properties of this new substance clearly proved that it was the disaccharide derivative. The elemental analysis and molecular weight determinations provided direct proof. The rapid mobility on t.l.c. plates compared to 2,3-*O*-isopropylidene-L-erythrose suggested that there was no free hydroxyl group, and this was verified by n.m.r. and i.r. spectroscopy. The i.r. spectra also showed that there was no peak for a carbonyl group either. The ^{1}H-n.m.r. spectrum exhibited very sharp peaks for the expected

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disaccharide structure. Especially significant were the sharp singlets for the anomeric proton and isopropylidene protons, and the sharp doublet for H-2, which indicated that there was only one anomeric form. The singlet at δ 5.22 and the doublet at δ 4.43 confirmed that the configuration was β for both L-erythrose units.

It is difficult to explain how this "spontaneous" formation of the disaccharide occurred. However, this is not the first unintentional synthesis of a nonreducing disaccharide, nor is this the first report of a tetrose–tetrose nonreducing structure. Several years ago, van Cleve reported that a change in the extraction process for 2,3-*O*-ethylidene-D-erythrose, which had been prepared from periodate-oxidized starch, caused the formation of 2,3-*O*-ethylidene-β-D-erythrofuranosyl 2,3-*O*-ethylidene-β-D-erythrofuranoside[4]. Refluxing benzene had been used in place of chloroform to extract the sugar derivative from an acidic, aqueous medium. In a separate experiment, it was shown that the disaccharide would form in boiling benzene containing some *p*-toluenesulfonic acid[4]. This experiment was now repeated with 2,3-*O*-isopropylidene-L-erythrose, and a 35% yield of **1** was obtained.

The formation of small proportions of disaccharides under acidic conditions is well-known[5], and it affords possible explanations of what caused the formation of **1** during storage of 2,3-*O*-isopropylidene-L-erythrose. The glass surface of the storage flask could have provided a catalytic surface, or perhaps a trace of acid could have been generated in a step prior to distillation and been carried over. Also, the storage flask was the source of material for several experiments, and it could have become contaminated with an as yet unknown catalyst. Experiments are underway to investigate this phenomenon further.

EXPERIMENTAL

General methods. — Melting points were determined with a Kofler micro hot-stage and correspond to corrected values. Optical rotations were measured with a Perkin–Elmer 141 polarimeter. I.r. spectra were recorded with a Perkin–Elmer Model 21 spectrohotometer, and ^{1}H-n.m.r. spectra with an IBM 250 AF spectrometer for a solution in (^{2}H)chloroform and tetramethylsilane as the internal reference. T.l.c. was performed on 0.25-mm layers of Silica gel HF (E. Merck, Darmstadt); the chloroform used contained 0.75% ethanol. Evaporations were performed on a rotary evaporator under reduced pressure at 35°. The elemental analysis was performed by the Spang Microanalytical Laboratory, Eagle Harbor, Michigan.

*Isolation and characterization of 2,3-*O*-isopropylidene-β-L-erythrofuranosyl 2,3-*O*-isopropylidene-β-L-erythrofuranoside* (**1**). — The crystalline substance (~0.5 ±0.1 g), which had slowly formed from the oil during storage over 17 years, was triturated with water and kept this way for several days with occasional trituration. The crystals were filtered off, air-dried, then dried under vacuum for 5 days, and finally dried for 18 h under high vacuum in the presence of P_2O_5 in a drying pistol at 64°. The white, feathery needles weighed 533 mg, m.p. 117–118°, $[\alpha]_D^{26}$ +221° (*c*

2.07, ethyl acetate); t.l.c. (99:1, v/v, chloroform–methanol) R_F 0.43 (R_F 0.19 for 2,3-*O*-isopropylidene-L-erythrose); ^{1}H-n.m.r.: δ 5.22 (s, 2 H, H-1), 4.73 (dd, 2 H, H-3), 4.43 (d, 2 H, H-2), 3.95 (d, 2 H, $J_{4,4'}$ 10.4 Hz, H-4'), 3.80 (dd, 2 H, H-4), 1.39 and 1.24 (both s, 12 H, 2 × 2 *gem*-Me_3). I.r. spectra were recorded for a KBr pellet and for a film deposited on an NaCl plate with dichloromethane as the solvent. There were no peaks corresponding to either the hydroxyl or the carbonyl groups; ν_{max} 1382 (*gem*-dimethyl), 1165, 1108, 1075, and 1052 cm^{-1} (C–O–C, dioxolane ring).

Anal. Calc. for $C_{14}H_{22}O_7$: C, 55.62; H, 7.34; mol. wt. 302. Found: C, 55.37; H, 7.44; mol. wt. (Rast[6]), 306 ±20.

Synthesis of **1** *from 2,3-O-isopropylidene-*L*-erythrose in hot benzene.* — A mixture of 2,3-*O*-isopropylidene-L-erythrose (400 mg), benzene (dried over Na ribbon, 160 mL), and *p*-toluenesulfonic acid monohydrate (100 mg) was heated under reflux for 18 h. A Dean–Stark trap was used to remove water and the reaction mixture was protected from external moisture. The dark solution was cooled to room temperature and washed with saturated $NaHCO_3$ solution (2 × 50 mL), filtered through a cone of anhydrous $MgSO_4$, and evaporated. The residue was dissolved in 1:1 (v/v) methanol–chloroform, treated with Norit A, filtered, and evaporated to dryness. Crystals formed, which were dissolved in a minimal amount of warm methanol, and the solution brought to turbidity with water. After the initial crystallization, additional crystals were obtained by further intermittent dropwise addition of water. The crystals were filtered off, washed, and dried as described above. Two crops (132 mg, 35% yield) were obtained, which were identical to **1** described above as determined by m.p., t.l.c., and i.r. spectroscopy.

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