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Note

Acid-catalysed re-arrangement of 2,4-*O*-ethylidene-D-erythrose

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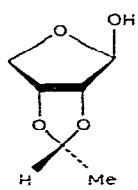
Treatment of the title compound with dilute, aqueous acid generally produces D-erythrose, but the formation of *endo*-2,3-*O*-ethylidene-β-D-erythrofuranose (**1**) has also been reported[1,2]. On treatment of 2,4-*O*-ethylidene-D-erythrose with boiling 0.125M sulphuric acid, three products were detected by t.l.c. in addition to D-erythrose. These products were isolated and identified as **1**, its *exo*-isomer (**2**), and *exo*-1,2-*O*-ethylidene-α-D-erythrofuranose (**3**). Of the rearrangement products **1**–**3**, **1** preponderated during the first 15 min, but **2** preponderated after 45 min.



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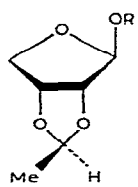
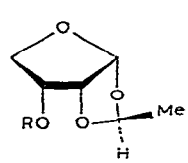


2 R = H
2a R = Ac



3 R = H
3a R = Ac

Compound **1** was identified by means of literature data[1,3], whereas the structures **2** and **3** were established by comparing ^{1}H-n.m.r. (see Table I) and m.s. data.

The weak coupling, $J_{1,2}$ <0.5 Hz, in the ^{1}H-n.m.r. spectrum ($CDCl_3$) of **2** accords with a β configuration[4], and since H-1 resonated 0.8 p.p.m. further downfield in the corresponding acetate **2a**, the *O*-ethylidene group is 2,3. The ethylidene methine proton of **2** is deshielded[3,5,6] in relation to that of **1**, and **2** is thus the *exo*-methyl isomer of **1**. A comparison of aromatic solvent-induced shifts[3] (C_6D_6 relative to $CDCl_3$) for the acetate **2a** showed that both the ethylidene methyl and methine protons were shielded similarly (0.11 and 0.10 p.p.m., respectively). This observation is also consistent with the *exo*-methyl assignment for **2**.

Similarly, comparison of the benzene-induced solvent shifts for **3a** established that **3** has an *exo*-methyl configuration at the acetal carbon. The *O*-ethylidene group in this case is 1,2, since, on acetylation of **3**, the signal for H-3 shifted 0.8 p.p.m.

TABLE I

^{1}H-N.M.R. DATA (100 MHz) FOR ETHYLIDENE DERIVATIVES OF D-ERYTHROSE

Compound (solvent)	**1** *$CDCl_3$*	**2** *$CDCl_3$*	**2a** *$CDCl_3$*	**2a** *C_6D_6*	**3** *$CDCl_3$*	**3a** *$CDCl_3$*	**3a** *C_6D_6*
Chemical shifts (p.p.m.)							
H-1	5.46d[a]	5.43d[a]	6.20s	6.41s	5.76d	5.77d	5.45d
H-2	4.59d	4.33d	4.63d	4.25–4.55m	4.50dd	4.76dd	4.37dd
H-3	4.73dt	4.84m	4.88m	4.25–4.55m	4.15m	4.98ddd	5.15ddd
H-4*endo*	4.06d	4.02dd	4.03dd	3.88d	3.48t	3.75dd	3.55dd
H-4*exo*	4.06d	4.08dd	4.13dd	3.77d	4.07t	4.17dd	3.74dd
OR, OH	2.89d	2.88d	2.05s	1.57s	2.95b	2.12s	1.65s
MeC*H* (q)	5.00	5.18	5.21	5.11	5.38	5.33	5.19
*Me*CH (d)	1.38	1.31	1.33	1.22	1.37	1.37	1.22
Coupling constants J (Hz)[b]							
$J_{1,OH}$	2.5	2.5					
$J_{1,2}$	<0.5	<0.5	<0.5	<0.5	4.0	4.0	3.7
$J_{2,3}$	6.0	6.0	5.5		6.0	6.0	6.0
$J_{3,4endo}$	2.0	3.5	1.5	<0.5	7.5	7.5	7.0
$J_{3,4exo}$	2.0	1.5	3.5	3.1	7.5	8.5	8.1
$J_{4(exo),4(endo)}$		10.0	10.0	10.5	7.5	9.0	9.3

[a]Coupled to OH. [b]*J* 4.6–5.0 Hz for ethylidene methine and methyl protons are excluded.

downfield. The value (4.0 Hz) of $J_{1,2}$ accords with an α configuration[+], as expected on steric grounds.

The *erythro* configuration of **1–3** was established by acid hydrolysis of each compound, which yielded D-erythrose, identified[7] by g.l.c.–m.s. (after reduction and acetylation). It has been suggested[8] that the *endo* isomer **1** is the product of kinetic control. The observation made here that the amount of the *exo* form **2** increased with time in the reaction mixture (see Experimental) confirms this suggestion.

EXPERIMENTAL

The general methods described earlier[9] were used with the following modifications. T.l.c. was performed on silica gel with ethyl acetate–light petroleum (b.p. 60–70°) *A*, 1:1; *B*, 2:3; and detection (as green spots) with ethanolic *p*-anisaldehyde–sulphuric acid at 120°. Acetylation of **2** and **3** was performed essentially as described in ref. 9. Sugar analysis[7] was effected by g.l.c. at 190° on a Varian 2700 instrument equipped with a column containing 3% of OV-225 on Gas Chrom Q (100–120 mesh). ^{1}H-N.m.r. spectra were recorded with a Varian HA-100D instrument with spin decoupling.

Acid hydrolysis of 2,4-O-ethylidene-D-erythrose. — (*a*) A 2% solution of 2,4-*O*-ethylidene-D-erythrose was hydrolysed[9,10] in 0.125M sulphuric acid at reflux temperature. The reaction was monitored by t.l.c. (solvent *A*). During the first 15 min, of the rearrangement products formed (**1–3**), **1** preponderated; at the end of the reaction (45 min), except for D-erythrose, **2** was the most abundant.

(*b*) D-Erythrose (75.0 g), obtained by acid hydrolysis of 2,4-*O*-ethylidene-D-erythrose as described above, was dissolved in 0.3M acetate buffer of pH 4.5 (2 litres) and the solution was boiled under reflux for 45 h under nitrogen*. The reaction mixture was then extracted with ethyl acetate and the extract was dried with sodium sulphate. After filtration and evaporation of the solvent, the residue (9.2 g) was applied to a column (6 × 100 cm) of Sephadex LH-20, and the first main fraction (collected by elution with water) contained **1–3**. This fraction (2.33 g) was eluted from a column of silica gel with solvent *A*. Three main fractions were collected, according to t.l.c. analysis. Compound **2** (783 mg) was eluted in the first fraction, and **1** (245 mg) crystallised from the next fraction. The third fraction (93 mg), containing **3**, was further purified by elution from silica gel with solvent *B*, to give a chromatographically pure product (22 mg).

endo-2,3-*O*-Ethylidene-β-D-erythrofuranose (**1**) had m.p. 64–65° (from heptane), $[\alpha]_D$ −118° (*c* 0.3, benzene), R_F 0.41 (solvent *A*); lit[1]. m.p. 66–67°, $[\alpha]_D^{25}$ −116° (*c* 1, benzene).

exo-2,3-*O*-Ethylidene-β-D-erythrofuranose (**2**) was amorphous and had $[\alpha]_D$ −99° (*c* 0.5, benzene), R_F 0.50 (solvent *A*). Mass spectrum: *m/z* 145 (0.6%, M − H^+), 131 (4), 102 (13), 85 (17), 73 (7), 71 (22), 69 (5), 59 (5), 57 (42), 56 (27), 55 (24), 47 (17), 45 (100), 44 (17), and 43 (94).

Anal. Calc. for $C_6H_9O_4$ (M − H^+): *m/z* 145.050. Found: *m/z* 145.048.

The acetate (**2a**) of **2** was amorphous. Mass spectrum: *m/z* 173 (0.6%, M − M^+), 145 (5), 129(7), 101 (18), 99 (8), 85 (6), 71 (6), 69 (22), 57 (8), 55 (7), 45 (23), 44 (6), and 43 (100).

exo-1,2-*O*-Ethylidene-α-D-erythrofuranose (**3**) was amorphous and had $[\alpha]_D$ +30° (*c* 0.4, benzene), R_F 0.29 (solvent *A*). Mass spectrum: *m/z* 145 (2%, M − H^+), 131 (9), 102 (6), 101 (6), 86 (7), 85 (19), 84 (6), 83 (13), 73 (7), 71 (23), 69 (14), 57 (21), 56 (12), 55 (14), 47 (9), 45 (69), 44 (40), and 43 (100).

Anal. Calc. for $C_6H_9O_4$ (M − H^+): 145.050. Found: *m/z* 145.049.

The acetate (**3a**) of **3** was amorphous. Mass spectrum: *m/z* 187 (0.6%, M − H^+), 173 (9), 127 (5), 85 (13), 71 (7), 57 (11), 55 (5), 45 (15), 44 (7), and 43 (100). The n.m.r. data for **1–3** are given in Table I.

Acid hydrolysis of **1–3**. — Compounds **1–3** were hydrolysed separately as 2% solutions in 0.25M sulphuric acid at 96° for 4 h. After neutralisation of the hydrolysate with barium carbonate, subsequent reduction ($NaBH_4$), and acetylation (Ac_2O/pyridine), only erythritol tetra-acetate was detected by g.l.c.–m.s.

*These are the conditions previously[11] used to obtain aromatic compounds from D-erythrose.

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REFERENCES

1 J. W. VAN CLEVE AND C. E. RIST, *Carbohydr. Res.*, 4 (1967) 82–90.
2 C. E. BALLOU, *J. Am. Chem. Soc.*, 82 (1960) 2585–2588.
3 K. D. CARLSON, C. R. SMITH, JR., AND I. A. WOLFF, *Carbohydr. Res.*, 13 (1970) 403–415, and references cited therein.
4 J. D. STEVENS AND H. G. FLETCHER, JR., *J. Org. Chem.*, 33 (1968) 1799–1805.
5 W. E. WILLY, G. BINSCH, AND E. L. ELIEL, *J. Am. Chem. Soc.*, 92 (1970) 5394–5402.
6 W. E. DICK, JR., AND D. WEISLEDER, *Carbohydr. Res.*, 39 (1975) 87–96.
7 J. S. SAWARDEKER, J. H. SLONEKER, AND A. JEANNES, *Anal. Chem.*, 37 (1965) 1602–1604.
8 K. D. CARLSON, C. R. SMITH, JR., AND I. A. WOLFF, *Carbohydr. Res.*, 13 (1970) 391–402.
9 R. ANDERSSON, O. THEANDER, AND E. WESTERLUND, *Carbohydr. Res.*, 61 (1978) 501–509.
10 R. SCHAFFER, *J. Am. Chem. Soc.*, 81 (1959) 2838–2842.
11 O. THEANDER AND E. WESTERLUND, *Acta Chem. Scand. B.*, in press.