

A NEW SYNTHETIC APPROACH TO L-2,3-O-ISOPROPYLIDENE-C₃ CHIRONS

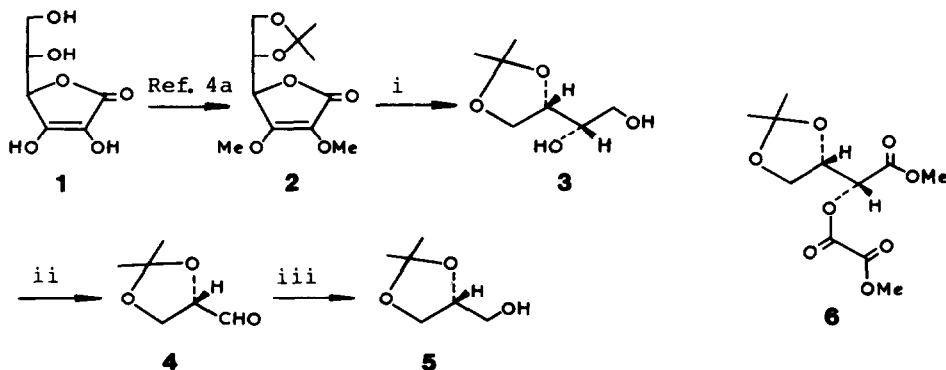
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Abstract. - Starting from L-ascorbic acid the preparation of L-(S)-glyceraldehyde and L-(R)-glycerol acetonides, and 1,2-O-isopropylidene-L-threitol is described.

The chiron approach to the synthesis of natural products is limited by the availability of simple, highly functionalized C₃ and C₄ chiral building blocks.¹ In this letter we report a new and simple synthesis of the useful 1,2-O-isopropylidene-L-threitol,² 3, L-(S)-glyceraldehyde and L-(R)-glycerol acetonides,³ 4 and 5, starting from L-ascorbic acid,⁴ 1.

Jung and Shaw^{4a} described the ozonolysis, followed by dimethyl sulfide treatment, of 2 (see Scheme) giving "high yields of the ester oxalate 6, but when further transformations of 6 proved difficult, this route was abandoned". We have now reinvestigated this process, modifying it and found that the ozonolysis of 2 followed by lithium aluminium hydride reduction of the crude reaction mixture gives compound 3² in 60% overall yield.⁵ This method compares favourably in terms of simplicity and yields with the synthesis of 3 starting from (2R,3R)-dimethyl tartrate.²



Scheme. i: O₃, CH₂Cl₂, -78°C, 15 min; then, evaporation, LAH, THF, 0°C → r.t. overnight. ii: Pb(OAc)₄, CH₂Cl₂, K₂CO₃. iii: NaBH₄, EtOH.

Lead (IV) acetate cleavage of **3** according to the procedure of Dumont and Pfander⁶ gave **4** (80% yield) [b.p.: 43–46°C (13 mm Hg); $[\alpha]_{\text{D}}^{25}$ -63.0° (benzene, c 8). Lit.⁷ $[\alpha]_{\text{D}}^{25}$ -67.9° (benzene, c 8)].⁸

Reduction of **4** with sodium borohydride in ethanol⁹ gave **5** (90% yield) [oil, $[\alpha]^{25}$ -11.2° (MeOH, c 2.6). Lit.⁹ $[\alpha]^{25}$ -10.7° (MeOH, c 1.55)].¹⁰

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References and notes

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4. Alternative methods for the synthesis of **3** and **4** starting from **1** have been previously described: a) M. E. Jung and T. J. Shaw, *J. Am. Chem. Soc.*, **1980**, *102*, 6304; b) S. Takano, H. Numata, and K. Ogasawara, *Heterocycles*, **1982**, *19*, 327; c) C. Hubschwerlen, *Synthesis*, **1986**, 962.
5. In a typical experiment 3.4 g (0.013 mol) of **2**, dissolved in 150 ml of dry CH₂Cl₂ and cooled at -78°C, were ozonized for 15 min. After the flask was flushed with argon, the solvent was evaporated and the oily residue dissolved in dry THF (50 ml) and treated with 2 g (0.05 mol) of LAH at 0°C. The mixture was stirred at room temperature overnight and treated with 2 ml of H₂O, 2 ml of NaOH (15% w/v) and 6 ml of H₂O, filtered and evaporated. Flash-chromatography (silica gel, EtOAc) yielded **3** (60%): oil, $[\alpha]_{\text{D}}^{25}$ +3.5° (MeOH, c 1.8) [Lit.² $[\alpha]_{\text{D}}^{25}$ +3.9° (MeOH, c 1.4)]; IR (film): 3500–3200 cm⁻¹; ¹H NMR (90 MHz, CDCl₃) δ: 4.20–3.55 (6H, m), 2.85 (2H, br s, two OH), 1.45 (3H, s), 1.35 (3H, s); identical in all respects with the described compound.²
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8. IR (film): 1740, 1380 cm⁻¹; ¹H NMR (90 MHz, CDCl₃) δ: 9.70 (1H, d, J = 1.5 Hz), 4.50–3.95 (3H, m), 1.45 (3H, s), 1.40 (3H, s).
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10. IR (film): 3500–3200 cm⁻¹; ¹H NMR (90 MHz, CDCl₃) δ: 4.40–3.55 (5H, m), 2.50 (1H, br s, OH), 1.45 (3H, s), 1.40 (3H, s); identical to the described data.^{4a}

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