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Note

A simple synthesis of 4,6-di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enono-1,5-lactone*

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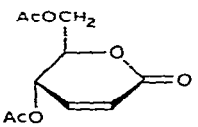
As part of a program concerned with the cycloaddition reactions of unsaturated carbohydrates, we became interested in synthesizing both the title compound (**1**) and, therefrom, such protected derivatives as **2** for use as potential dienophiles. In addition, lactone **1** is of recent interest, because of its structural similarity to a series of antimicrobial 2*H*-pyran-2-ones, including a 4-*O*-acetyl-6,7-anhydro-2,3,8-trideoxy-oct-2-enono-1,5-lactone[1,2] (asperlin, **3**). We desired to prepare substantial quantities of **1**, and therefore needed a short, simple, and inexpensive synthesis. Lactone **1** has been obtained[3] as a by-product in the $PdCl_2$-catalyzed oxidation of 3,4,6-tri-*O*-acetyl-1,2-dideoxy-D-*arabino*-hex-1-enitol (**4**) and by methyl sulfoxide–pyridine–sulfur trioxide mediated oxidation of **5**, obtained by way of the glycosyl halide. A simple, two-step synthesis of **1** from **4** that is amenable to scale-up is here reported.



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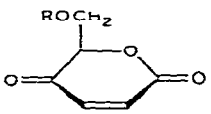

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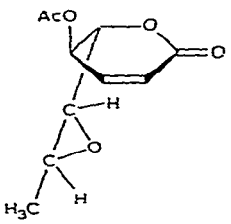

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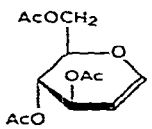

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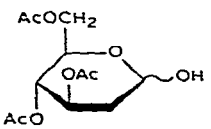

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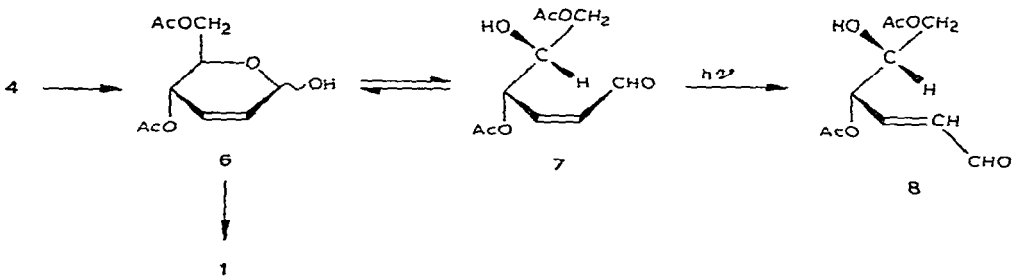
*Contribution No. 2982 from the Department.

Hydration of **4** in boiling water is well known to afford[4,5] hemiacetal **6**. Fraser-Reid and Radatus demonstrated[5] that **6** is in equilibrium with the hydroxy aldehyde **7**, and that **7** is photochemically isomerized to **8**. In addition, the relative amounts of **7** increase with increase in the duration of the hydration reaction; our t.l.c. and ^{1}H-n.m.r. evidence is in complete agreement with these findings, and suggests that **6** would not be a practical precursor to **1**. However, we have found that, if **6** is prepared (and handled) in the dark, employing a reflux period of <20 min, oxidation with a suitable oxidant does afford **1** in good yield. When crude **6** is treated with pyridinium chlorochromate, using sodium acetate as a buffer, in dichloromethane, lactone **1** is readily isolated in 48% yield after column chromatography. The i.r.-, ^{1}H-n.m.r.-, and ^{13}C-n.m.r.-spectral data (see Experimental section) of **1** were consistent with literature reports[1,3]. The overall yield of **1** is only 30%, but the simplicity and directness render this a viable method for its preparation.



EXPERIMENTAL

General methods. — Optical rotations were determined with a Perkin–Elmer 241 MC polarimeter. U.v. spectra were recorded with a Cary 17 spectrophotometer. Infrared spectra were recorded with a Nicolet 7199 FT-IR spectrometer. ^{1}H-N.m.r. spectra were recorded, for solutions in chloroform-*d*, with a Varian EM-390 or HR-220 spectrometer, and are referenced to internal tetramethylsilane. ^{13}C-N.m.r. spectra were recorded with a Bruker WH-90 instrument, and are referenced to internal tetramethylsilane. Liquid chromatography was performed in a Waters Prep LC/System 500 instrument.

4,6-Di-O-acetyl-2,3-dideoxy-D-erythro-*hex-2-enopyranose* (**6**). — A suspension of **4** (Aldrich; 30.0 g, 110.2 mmol) in distilled water (600 mL; pH 5.8) was boiled under reflux for 20 min. The resulting solution was cooled in ice–water, and extracted several times with dichloromethane. The extracts were combined, successively washed with saturated sodium hydrogencarbonate and water, dried (magnesium sulfate), and evaporated, to give crude **6** as a light-yellow syrup (16.0 g; 63%). Thin-layer chromatography revealed the presence of one minor and two major components; ν_{max}^{neat} 3420 and 1705 cm^{-1}.

4,6-Di-O-acetyl-2,3-dideoxy-D-erythro-*hex-2-enono-1,5-lactone* (**1**). — A solution of crude **6** (15.78 g, 68.5 mmol) in dichloromethane (340 mL) was treated with

anhydrous sodium acetate (17.1 g, 208 mmol) and pyridinium chlorochromate (51.3 g, 240 mmol), and the resulting mixture was mechanically stirred for 24 h at room temperature. Ether was added, the suspension was filtered through Celite, and the solvents were evaporated under diminished pressure. Chromatography on silica gel with ether afforded **1** (7.49 g, 48%) as a colorless oil: b.p. (kugelrohr) 155–160°/1 mm Hg; $[\alpha]_D$ +122° (*c* 1.31, $CHCl_3$); λ_{max}^{EtOH} 258 nm (ε 283); ν_{max}^{neat} 1740 (broad, C=O absorption) and 1225 cm^{-1}; ^{1}H-n.m.r. (220 MHz): δ 2.06 (s, 3 H, acetate), 2.10 (s, 3 H, acetate), 4.11 (A of ABC, 1 H, H-6, *J* 3.5 and 12 Hz), 4.27 (B of ABC, 1 H, H-6′, *J* 4.5 and 12 Hz), 4.59 (ddd, 1 H, H-5, *J* 3.5, 4.5, and 7.5 Hz), 5.45 (ddd, 1 H, H-4, *J* 1.5, 3.0, and 7.5 Hz), 6.01 (dd, 1 H, H-2, *J* 1.5 and 10 Hz), and 6.67 (dd, 1 H, H-3, *J* 3.0 and 10 Hz); ^{13}C-n.m.r.: δ 170.2 (C=O, acetate), 169.7 (C=O, acetate), 161.2 (C-1), 143.4 (C-3), 122.4 (C-2), 77.5 (C-5), 63.6 (C-4), 62.3 (C-6), and 20.6 (CH_3, acetate).

Anal. Calc. for $C_{10}H_{12}O_6$: C, 52.63; H, 5.30. Found: C, 52.71; H, 5.35.

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