Note

The reaction of potassium thiolacetate with 2^1,5-di-*O*-*p*-tolylsulfonyl-"α"-D-isosaccharin*

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Several years ago, the configuration at C-4 of "α"-D-isosaccharin[1] (**1**), a 3-deoxy-2-*C*-(hydroxymethyl)-pentono-1,4-lactone, was known to be D-*glycero*[2], but the configuration at C-2 had not been established. At that time, an attempt was made to determine by chemical means whether the lactone has the D-*erythro* or the D-*threo* configuration. The proposed route consisted of *p*-toluenesulfonylation of **1** to give the 2^1,5-di-*O*-*p*-tolylsulfonyl derivative (**2**), which it was supposed, would be converted into the corresponding 2^1,5-di-*S*-acetyl-2^1,5-dithio derivative of **1** by reaction with potassium thiolacetate. The two *S*-acetyl groups were to be removed, to give 2^1,5-dithio-"α"-D-isosaccharin. Inspection of Dreiding molecular models revealed that oxidation of this dithiol derivative would only produce an intramolecular disulfide bond were the configuration of "α"-D-isosaccharin to be D-*erythro*. The formation of a disulfide bond from the D-*threo* isomer, in which the two CH_2SH groups would be on opposite sides of the lactone ring, is sterically impossible; in this way, a choice between the two configurations was to be made. However, while these experiments were in progress, the configuration of "α"-D-isosaccharin was established unequivocally as D-*erythro* (**1**) by X-ray diffraction methods[3]. Nonetheless, a chemical proof was thought to be of interest and this work was continued. As a result, it was observed that the configuration at C-2 of "α"-D-isosaccharin could not be established by the proposed route. The displacement reaction of 2^1,5-di-*O*-*p*-tolylsulfonyl-"α"-D-isosaccharin with potassium thiolacetate took an unexpected course to give a new anhydro lactone, the structure of which is the subject of this communication.

Di-*p*-toluenesulfonylation of **1** in pyridine solution gave a product to which structure **2** was assigned. A band at 1785 cm^{-1} in the i.r. spectrum showed the presence of a γ-lactone ring, and a four-proton multiplet at δ 4.17 p.p.m. in the p.m.r. spectrum could only be assigned to the protons at C-2^1 and C-5 of **2**. The fact that these four protons had the same chemical shift indicated that sulfonylation had occurred at the two primary hydroxyl groups, as was to be expected. A solution of

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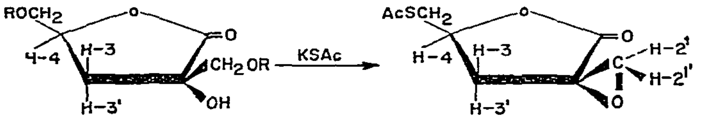
compound **2** and potassium thiolacetate in ethanol was heated, and a crystalline product (*A*) was isolated from the reaction mixture in 25% yield.

Elemental analysis and high-resolution mass spectrometry of *A* showed that both *p*-tolylsulfonyl groups had been displaced from **2**, but that only one thiolacetate group had entered the molecule; the i.r. spectrum of the product had bands at 1802 and 1745 cm^{-1} that were assigned to the γ-lactone and the thiolacetate group, respectively*. Based on these data and mechanistic considerations, the most reasonable structure for *A* is **3**, which would be formed from **2** by intermolecular displacement of the 5-*p*-tolylsulfonyloxy group by thiolacetate ion and intramolecular displacement of the 2^1-*p*-tolylsulfonyloxy group by the 2-hydroxyl group. Structure **3** is supported by the p.m.r. data. At 60 and 100 MHz, the spectra were very complicated, but, at 220 MHz, the spectrum was amenable to first-order analysis. In chloroform-*d*, the obvious features of the spectrum were a three-proton singlet at δ 2.12 p.p.m. (CH_3COS), a doublet of doublets of doublets at δ 5.19 (H-4), and an AB quartet, $J_{2^1,2^{1'}}$ 12.0 Hz at δ 2.16 (H-$2^{1'}$) and δ 3.31 p.p.m. (H-2^1). The four protons remaining could be grouped into pairs based on unequal, geminal coupling-constants. Only one of these protons was strongly coupled to H-4, and this result was confirmed by spin-decoupling experiments. The dihedral angle, H-4–C–C–H-3′ = 0°, which was measured from Dreiding molecular models, indicated that, of the protons in **3**, H-3′ should be the most strongly coupled to H-4. On this basis, the resonance at δ 3.15 p.p.m. ($J_{3',4}$ 7.5 Hz, $J_{3,3'}$ 11.0 Hz) was assigned to H-3′. Thus, the resonance at δ 2.68 ($J_{3,4}$ 1.5 Hz, $J_{3,3'}$ 11.0 Hz) was assigned to H-3, and the two protons remaining, δ 2.79, a doublet, J_{gem} 13.0 Hz and δ 2.95, a doublet of doublets, J_{gem} 13.0 Hz, coupled to H-4, J 4.5 Hz, were those attached to C-5. The p.m.r. spectrum was also recorded for solutions in benzene-d_6, and the aromatic-induced solvent-shifts aided in the analysis. For comparison, chemical shifts of **3** are given in Table I for the two solvents.



1 R = H
2 R = $SO_2-C_6H_4-Me$-*p*

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In the high-resolution mass spectrum, the product gave principal ions at $C_8H_{10}O_4S$ (M), (M-C_2H_2O), (M-CH_3S), (M-$C_2H_4O_2$), (M-C_2H_3OS), and (M-C_3H_5OS), consistent with structure **3**.

EXPERIMENTAL

N.m.r. spectra were recorded for solutions in chloroform-*d*, with tetramethylsilane as the internal reference standard. Abbreviations used are d, doublet; m, mul-

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*The frequency of the thiolacetate absorption is higher than expected. The reason for this is not clear.

tiplet; q, quartet; s, singlet; t, triplet. All solutions were evaporated under diminished pressure in a rotary evaporator.

TABLE I

P.M.R. PARAMETERS FOR 5-*S*-ACETYL-2,2^1-ANHYDRO-3-DEOXY-5-THIO-D-*erythro*-PENTONO-1,4-LACTONE (3)

Solvent	*Chemical shift (δ, p.p.m.)*							
	H-2^1	*H-2*$^{1\prime}$	*H-3*	*H-3'*	*H-4*	*CH*$_3$	*H-5*	*H-5'*
Chloroform-*d*	3.31	2.16	2.68	3.15	5.19	2.12	2.79	2.95
Benzene-d_6	2.80	1.24	2.40	2.69	4.10	1.57	2.02[a]	1.93[a]

[a] These assignments assume that the *J* values are the same in both solvents.

*3-Deoxy-2-*C*-(hydroxymethyl)-di-*O*-*p*-tolylsulfonyl-*D-erythro*-pentono-1,4-lactone* (2). — To a solution of 8.1 g (50 mmoles) of lactone **1** in 40 ml of pyridine was added a cold solution of 23.8 g (125 mmoles) of *p*-toluenesulfonyl chloride in 60 ml of pyridine, and the solution was kept overnight at room temperature; it was then cooled to 0°, and water (5 ml) was added. After 1 h, the solution was evaporated, and the residue was dissolved in chloroform. The solution was successively washed with M hydrochloric acid and water, dried (anhydrous sodium sulfate), and evaporated. The product **2** (13.4 g, 57%) was crystallized from chloroform–petroleum ether; m.p. 109–110°. An analytical sample was obtained by recrystallization from the same solvent mixture; m.p. 110–111°, $[\alpha]_D^{25}$ +36.0° (*c* 1.0, chloroform); p.m.r. data: δ 2.18, d (*J* 3.5 Hz, 1 H, H-3); δ 2.32, d (*J* 2 Hz, 1 H, H-3'); δ 2.43, s (6 H, aromatic CH_3); δ 3.58, s (1 H, OH); δ 4.17, m (4 H, CH_2OTs); δ 4.83, m (1 H, H-4); δ 7.36 and δ 7.80 p.p.m. (AB quartet, *J* 8.0 Hz, 8 H, aromatic protons): ν_{max}^{Nujol} 1785 (γ-lactone), 1174, 985, 848, and 812 cm^{-1}.

Anal. Calc. for $C_{20}H_{22}O_9S_2$: C, 51.1; H, 4.7; S, 13.6. Found: C, 51.0; H, 4.7; S, 13.7.

*5-*S*-Acetyl-2,2^1-anhydro-3-deoxy-5-thio-*D-erythro*-pentono-1,4-lactone* (3). — Compound **2** (5.0 g) and potassium thiolacetate (5.0 g) in abs. ethanol (125 ml) were boiled for 4.5 h under reflux. The mixture was cooled, and the solids were filtered off and washed with ethanol. The filtrates were combined and evaporated, the residue was dissolved in chloroform, and the solution was washed with three 50-ml portions of water, dried (anhydrous sodium sulfate), and concentrated to ~35 ml. Petroleum ether was added to turbidity, and, after 18 h, the crystalline product (0.49 g, 23%) was filtered off (filtrate *B*), and washed with petroleum ether; m.p. 146–147°. An analytical sample of **3** was recrystallized from methanol–petroleum ether; it had m.p. 148–149°, $[\alpha]_D^{25}$ +6.0° (*c* 1.0, chloroform); ν_{max}^{KBr} 1802 (γ-lactone) and 1745 cm^{-1} (CH_3COS).

Anal. Calc. for $C_8H_{10}O_4S$: C, 47.5; H, 5.0; S, 15.9; mol. wt., 202.0300. Found: C, 47.6; H, 5.0; S, 16.1; mol. wt., 202.0319 (by high-resolution mass spectrometry).

T.l.c. showed that the filtrate *B* contained a complex mixture of products. The residue could not be induced to crystallize, and this material was not investigated further.

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