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Note

The acetolysis of D-galactose diethyl dithioacetal

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It has been stated in several reference books that acetolysis of aldose diethyl dithioacetals yields *aldehydo*-aldose peracetates as products [1–3]. The reference in each case is a paper by Pirie [4], who reported that acetolysis of 2,3,4,5,6-penta-*O*-acetyl-D-galactose diethyl dithioacetal (**3**, Scheme 1), in a mixture of acetic anhydride and concd sulfuric acid at 37 °C gave as the main product the acyclic heptaacetate of D-galactose (**4**). It was also claimed, but without experimental support, that the unblocked D-galactose diethyl dithioacetal (**1**) gave the same product. The present report demonstrates that the main product is not **4**, but 1,2,3,5,6-penta-*O*-acetyl-β-D-galactofuranose (**2**).

An approach was sought in this laboratory to find acetolysis conditions that may remove the thioethyl groups from acyclic diethyl dithioacetal aldoses without formation of the 1,1-diacetoxy derivatives, and possibly give the cyclic 1-*O*-acetoxy derivative in either the pyranose or furanose form. Under the acetolysis conditions employed (see Experimental section for details), including the original conditions of Pirie [4], 2,3,4,5,6-penta-*O*-acetyl-D-galactose diethyl dithioacetal (**3**) afforded crystalline 1,1,2,3,4,5,6-hepta-*O*-acetyl-*aldehydo*-D-galactose aldehydrol (**4**) as the main product. Although the composition of the mother liquors was not pursued, the values of the optical rotations (+34° to +39°) suggested that a good portion of the remaining syrups may be the cyclic pentacetates in the α configuration. The straight-chain heptaacetate **4** has a very low optical rotation (+4°). It is of some interest to note that another attempt to prepare **4** from an acetylated dithioacetal gave a mixture that the authors claimed was impossible to separate [5].

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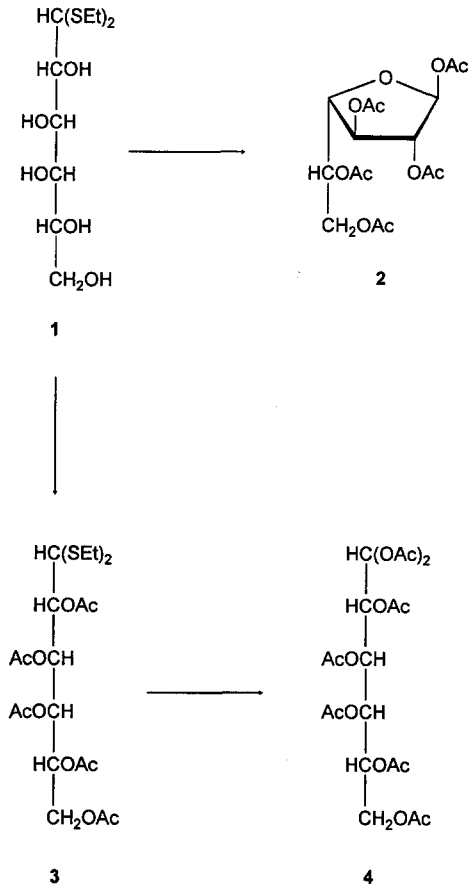

Scheme 1.

In contrast to the above results, acetolysis of D-galactose diethyl dithioacetal (**1**) under the various conditions studied yielded 1,2,3,5,6-penta-*O*-acetyl-β-D-galactofuranose (**2**) as the main product. Although there were some differences in the yields after only 24 h, after 3 days the yields were similar. There was no advantage to running the acetolysis for 6 days. A repeat of the acetolysis as described by Pirie also gave **2** rather than **4**.

Optical rotations obtained on the syrups after removal of the crystals showed values of +49° to +56°. These values are very close to that of α-D-galactofuranose pentaacetate. One of the reagents for acetylation and acetolysis (Reagent A) was originally devised as an isomerization reagent to convert β-acetates or anomeric mixtures of pyranoses into α anomers [6]. Use of Reagent A to acetylate D-galactose afforded an almost quantitative yield of 1,2,3,4,6-penta-*O*-acetyl-α-D-galactopyranose, an experiment that was performed to see if any furanose form of the sugar would result under the reaction conditions. When the above-mentioned syrups were treated with Reagent A,

additional crystalline **2** was obtained, suggesting that the main substance in the syrups was most probably the α product. Although the equilibrium tends to favor the β configuration with the furanose derivative, even in the pyranose series, D-allose also affords the β anomer [7].

A possible explanation for the preponderance of the furanose pentaacetates would be that one of the thioethyl groups would come off very fast with concomitant cyclization to give the ethyl thiofuranoside [8], which is then acetylated; finally, acetolysis of the thioglycoside would afford the α,β-furanose mixture.

1. Experimental

General methods and materials.—Melting points were determined on a Kofler hot stage and are corrected values. Optical rotations were obtained on a Perkin–Elmer Model 141 polarimeter. Evaporations were carried out on a rotary evaporator under reduced pressure and bath temperatures of 30–40 °C. All moist organic solutions were dried over anhyd Na_2SO_4. The activated charcoal used to removed colored contaminants was Darco G-60.

Acetolysis reagents.—Reagent A: acetic anhydride (13.7 mL), acetic acid (5.9 mL), and concd H_2SO_4 (0.46 mL); Reagent B: acetic anhydride (4 mL), acetic acid (40 mL), and concd H_2SO_4 (1.8 mL); Reagent C: acetic anhydride (20 mL) and concd H_2SO_4 (0.5 mL).

*Acetolysis of 2,3,4,5,6-penta-*O*-acetyl-*D*-galactose diethyl dithioacetal* (**3**).—Samples of **3** (2 g, 4 mmol) were acetolyzed separately with Reagents A and B for 3 days at room temperature. The reaction mixtures were poured into crushed ice and stirred for 1 h. The products were extracted several times with $CHCl_3$, and the extracts were combined and washed several times with H_2O, satd $NaHCO_3$ solution, then with H_2O again. Sometimes satd brine was required to help break an emulsion or as a final wash. After drying, the $CHCl_3$ was removed by evaporation, the syrup was dissolved in EtOH, and the solution was treated with activated charcoal. Following filtration, the volume of solvent was reduced to several mL by evaporation on a steam bath, then allowed to stand at room temperature, whereupon crystallization of **4** readily occurred as prismatic-like plates: mp 106–107 °C, $[\alpha]_D^{28}$ +4.0° (*c* 3.24, $CHCl_3$). Lit. [4,9] mp 106 °C, $[\alpha]_D$ +4° (*c* 3, $CHCl_3$). The yield obtained with Reagent A was 45%, and that with Reagent B was 64%.

The procedure described by Pirie [4] was repeated. The reagent was the same as Reagent C except that 1 mL of H_2SO_4 was used, the temperature was 37 °C, and the reaction was run for 1 day. The workup was the same as the above, and identical crystals of **4** were obtained in 59% yield.

Acetylation and acetolysis of D-*galactose diethyl dithioacetal* (**1**).—Samples of D-galactose diethyl dithioacetal (**1**) (1.14 g, 4 mmol) were separately treated with Reagents A and B for 1, 3, and 6 days at room temperature and worked up as described above. The product, 1,2,3,5,6-penta-*O*-acetyl-β-D-galactofuranose (**2**), was crystallized in each case from several mL of EtOH: mp 98–99 °C, $[\alpha]_D^{25}$ −41.9°(*c* 3.02, $CHCl_3$). Lit. [10] mp 98 °C, $[\alpha]_D^{20}$ −41.6° ($CHCl_3$). The yields obtained with Reagent A were

51% (1 day), 52% (3 days), and 58.5% (6 days). The yields obtained with Reagent B were 23% (1 day), 46% (3 days), and 47% (6 days).

Reagent C was only used in a three-day experiment and worked up the same as above. The yield of **2** was 44%.

The procedure described by Pirie [4] was repeated on **1** (1.14 g, 4 mmol). After the usual workup, **2** (592 mg, 38% yield) was crystallized, identical to the above samples. An additional 12 mg of crystals obtained from the mother liquor proved to be the heptaacetate **4**, mp 104–105 °C.

The syrups remaining after evaporation of the EtOH from some of the mother liquors were found to have $[\alpha]_D$ values in $CHCl_3$ of $+49°$ to $+56°$, indicative [11] that a main constituent was the α anomer of D-galactofuranose pentaacetate. These syrups were acetolyzed in one-half the amount of Reagent A for 3 days and worked up in the usual way. Additional **2** was isolated (mp 99–100 °C).

Acetylation of D-*galactose*.—The reaction and workup of D-galactose (721 mg, 4 mmol) was exactly as described above using Reagent A for 3 days at room temperature. Crystallization from EtOH gave 1.54 g (99%) of 1,2,3,4,6-penta-*O*-acetyl-α-D-galactopyranose: mp 96–97 °C, $[\alpha]_D^{28}$ $+106.8°$ (*c* 3.01, $CHCl_3$). Lit. [12] mp 96 °C, $[\alpha]_D^{20}$ $+106.7°$ (*c* 3, $CHCl_3$).

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