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## Note

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# Cyclic oxalic and phthalic esters of D-glucose[*]

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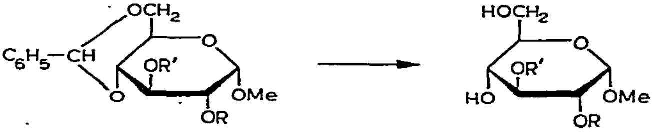
Cyclic derivatives have been extensively employed in carbohydrate chemistry to selectively block two hydroxyl groups in a glycose residue. The derivatives most generally used fall into three classes: (a) acetals, which are formed by condensation with aldehydes or ketones, and are stable to alkali, but sensitive to acid; (b) boric esters, which are sensitive to both acid and alkali; (c) carbonates formed from phosgene, which are hydrolyzed by alkali. Since the reaction of phosgene with vicinal hydroxyl groups produces 5-membered rings (the cyclic carbonates), this imposes steric restrictions on the use of this reagent. It seems possible that the steric problem could be resolved, and the cyclic ester class extended by the use of dicarboxylic acid chlorides. As shown in the present study, methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**1**) was treated with oxalyl chloride to give the corresponding 2,3-oxalic ester **2**. Hydrogenolysis yielded methyl 2,3-*O*-oxalyl-α-D-glucopyranoside (**4**). Preliminary experiments with other dicarboxylic acid chlorides, such as phthaloyl chloride, indicated that other cyclic esters (**3**) could be prepared similarly. In addition to its potential usefulness as a protective group, the oxalyl derivative may have a special application, as oxalic acid has been used in the pyrolysis of glycerol to allyl alcohol[2]. The oxalic esters reported here are high-melting crystalline solids that evolve gas at their decomposition points. Conceivably, these derivatives could be used to introduce double bonds into glycose chains.



**1** R = R' = H
**2** R,R' = —CO—CO—
**3** R,R' = —CO—$C_6H_4$—CO—(*o*)

**4** R,R' = —CO—CO—
**5** R = R' = H
**6** R,R' = —CO—$C_6H_4$—CO—(*o*)

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[*] This study was performed in partial fulfillment of the requirements for the Ph.D. degree from the University of Wisconsin; Ph.D. Thesis, 1947 (S.R.). A preliminary report was presented[1].
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## EXPERIMENTAL

*General.* — Melting points are uncorrected. Elemental analyses were performed by W. Saschek (Univ. of Chicago) and Microtech Laboratories (Illinois).

*Methyl 4,6-O-benzylidene-2,3-O-oxalyl-α-D-glucopyranoside* (**2**). — Carefully dried methyl 4,6-*O*-benzylidene-α-D-glucopyranoside[3] (**1**, 10.0 g) was dissolved in anhydrous pyridine (22.8 ml) in a three-necked flask protected from the atmosphere and equipped with a thermometer, stirrer, and dropping funnel. Precautions were taken to avoid moisture, *i.e.*, the apparatus was assembled while hot. The solution was vigorously stirred at 0° while a solution containing 3.2 ml of oxalyl chloride (Eastman Kodak, redistilled) in pure, anhydrous chloroform (50 ml )was added as rapidly as possible while maintaining the temperature below 5°. Following addition of the acid chloride solution, the mixture was allowed to stand in the ice-bath. In periods ranging from 2–12 h, white crystals appeared. The reaction product was rapidly filtered off and washed with anhydrous chloroform. The yield at this point was variable, ranging from 2.6 to 7.5 g. From 0.2 to 0.5 g of second crop material could be isolated from the filtrate after washing the chloroform layer, drying, and concentrating. Recrystallization of the first crop material was effected first from anhydrous chloroform, and then from reagent grade acetone. The final, neutral product, white long needles, was obtained in a maximum yield of 40%, dec. 274–276° with the evolution of gas (presumably $CO_2$) to give a clear, colorless liquid.

*Anal.* Calc. for $C_{16}H_{16}O_8$: C, 57.14; H, 4.78; MeO, 9.23; saponif. equiv., 2.00; oxalic acid, 1.00; mol. wt. 336. Found: C, 57.15, 57.02; H, 4.90, 4.78; MeO, 9.51, 9.42; saponif. equiv. 1.99; oxalic acid, 1.02 mol; mol. wt. 337, 352 (ebulliometric, in ethyl acetate and acetone), 343 (Rast, camphor).

Mild alkaline hydrolysis with 10mM NaOH in acetone for 2 h at room temp., gave the starting material, methyl 4,6-benzylidene-α-D-glucopyranoside in better than 90% yield.

*Methyl 2,3-O-oxalyl-α-D-glucopyranoside* (**4**). — The benzylidene derivative **2** (3.5 g) was dissolved in purified ethyl acetate (120 ml), and hydrogenated in the presence of conc. hydrochloric acid (3 drops), glacial acetic acid (40 ml), and freshly prepared palladium black (0.6 g) at atmospheric pressure. After 2 h, hydrogen consumption ceased, slightly more than the calculated quantity being taken up. Filtration of the mixture, followed by concentration of the filtrate gave 2.2 g of crystals, m.p. 187–189°. The crude product was recrystallized either from ethyl acetate, or by adding petroleum ether to a solution in *p*-dioxane, giving 2.0 g of pure, neutral product consisting of long, hexagonal prisms, m.p. 194–196°; compound **4** was insoluble in nonpolar organic solvents, but was soluble in water, *p*-dioxane, and acetone.

*Anal.* Calc. for $C_9H_{12}O_8$: C, 43.53; H, 4.88; MeO, 12.50; saponif. equiv. 2.00; mol. wt. 248. Found: C, 43.65; H, 5.16; MeO, 12.63; saponif. equiv., 1.94; mol. wt., 220 (Rast, camphor).

Alkaline hydrolysis of **4** gave methyl α-D-glucopyranoside (**5**) and condensation with benzaldehyde **2**; compound **4** (0.10 g) was shaken with purified benzaldehyde (0.16 ml) in the presence of fused, anhydrous zinc chloride (0.05 g). After 3 h, the oily mass had solidified, and was triturated with ice water and petroleum ether. After drying in a desiccator, the product (0.10 g), m.p. 238–242°, was purified by recrystallization from anhydrous chloroform, giving the desired product which showed no depression of the m.p. when mixed with **2**.

*Methyl 4,6-O-benzylidene-2,3-O-phthaloyl-α-D-glucopyranoside* (**3**). — A solution of **1** (6.0 g) in anhydrous pyridine (10 ml) and anhydrous chloroform (50 ml) was cooled to 0° and treated with a slight excess (3.12 ml, 1.02 mol) of phthaloyl chloride in anhydrous chloroform (50 ml). When the reaction was conducted as described with oxalyl chloride, the product was obtained in ~60% yield. However, yields up to about 90% were obtained when the reaction products were continuously removed from the reaction mixture. The two ice-cold chloroform solutions (one containing the benzylidene derivative and pyridine, the other containing phthaloyl chloride) were added at identical rates to the top of a 92-cm glass rod which was continuously rotated in order to mix the two solutions. The reaction mixture was collected at the bottom of the rod in a flask immersed in ice. The entire apparatus was carefully protected from the atmosphere with drying tubes; the glass rod was contained within a glass tube of large diameter so that the solutions were confined to the rod. Following mixing of the reactants either in a flask, or on the glass rod, the resulting solution was stored for 1 day at 0° and for an additional day at room temperature. The mixture was concentrated in a vacuum to a syrup, which was dissolved in ethyl acetate (100 ml). The solution was washed with ice-cold solutions of dilute sulfuric acid, saturated sodium hydrogencarbonate, and finally with ice water. After being dried (sodium sulfate), the solution was concentrated, yielding **3** as a white, amorphous solid (microscopic, very small round particles), m.p. 226–229°, which was purified by adding ether to a solution in chloroform, ethyl acetate, or acetone, m.p. 229–235°. Attempts to obtain crystals from a large variety of solvents were unsuccessful. Compound **3** was soluble in boiling ethanol and cold toluene, pyridine, dichloromethane, acetone, benzene, *p*-dioxane, ethyl acetate, chloroform, and most of the glycols; and insoluble in cold alcohol, water, ether, and petroleum ether.

*Anal.* Calc. for $C_{22}H_{20}O_8$: C, 64.04; H, 4.89; saponif. equiv., 2.00; mol. wt., 412. Found: C, 64.13; H, 5.08; saponif. equiv., 2.04; mol. wt., 422 (Rast, 5% borneol).

*Methyl 2,3-O-phthaloyl-α-D-glucopyranoside* (**6**). — This compound was obtained by reductive cleavage. Compound **3** (3.0 g) was dissolved in ethyl acetate (100 ml) and reduced with hydrogen at atmospheric pressure in the presence of glacial acetic acid (10 ml), 5% hydrochloric acid (2 drops), and freshly prepared 5% palladium–Norit (2 g). After 2.5 h the hydrogen uptake had declined to a very low rate; 18% more hydrogen was taken up than the calculated value. The mixture was filtered, and the filtrate concentrated in a vacuum. A quantitative yield of an amorphous solid, dec. 235°, was isolated. The product was purified by precipitation from an acetone solution with anhydrous ether. It was soluble in ethanol, methanol, acetone, hot butanol, and amyl alcohol, moderately soluble in *p*-dioxane, and insoluble in chloroform, ether, and toluene. It was too insoluble in the usual solvents used for the Rast method to obtain a mol. wt. by this procedure.

*Anal.* Calc. for $C_{15}H_{16}O_8$: C, 55.54; H, 4.97; saponif. equiv., 2.00. Found: C, 55.23; H, 5.26; saponif. equiv. 2.09.

## ACKNOWLEDGMENTS

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## REFERENCES

1 S. Roseman and K. P. Link, *Abstr. Pap. Am. Chem. Soc. Meet.*, 118 (1950) R7.
2 Shell Chemical Corporation, *Allyl Alcohol*, Shell Chemical Corporation Technical Publication, (1946) SC: 32–46.
3 K. Freudenberg, H. Toepffer, and C. C. Anderson, *Ber.*, 61 (1928) 1750–1760.