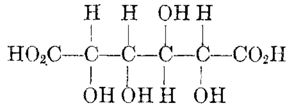
Notes A department for short papers of immediate interest.

Derivatives of D-Glucaric Acid[1]

EZRA L. TOTTON AND W. E. REID

Received September 17, 1956

A general reaction of the glycaric acids is the formation of diamides by treatment of these acids with primary aliphatic amines.[2] These diamides are very labile to alkaline hydrolysis. In efforts to find diamides of D-glucaric acid,



$$\begin{array}{ccccccccccc} & & \text{H} & & \text{H} & & \text{OH} & & \text{H} & & \\ & & | & & | & & | & & | & & \\ \text{HO}_2\text{C} & — & \text{C} & — & \text{C} & — & \text{C} & — & \text{C} & — & \text{CO}_2\text{H} \\ & & | & & | & & | & & | & & \\ & & \text{OH} & & \text{OH} & & \text{H} & & \text{OH} & & \end{array}$$

less easily hydrolyzed by alkali, some aromatic diamides of D-glucaric acid have been synthesized. These derivatives were less labile to alkali and could be acetylated in good yields without hydrolysis of the amide linkage. This note describes the preparation of *p*-D-glucarotoluidide, 4′,4″-dihydroxy-D-glucaranilide, *p*-D-glucarotoluidide tetraacetate, 4′,4″-diacetoxy-D-glucaranilide tetraacetate.

EXPERIMENTAL[3]

Potassium acid glucarate. There were placed in an evaporating dish of suitable size, 800 g. of starch and 6.4 liters of nitric acid of specific gravity 1.100. The mixture was evaporated over a low flame in a fume hood to a volume of about 2 liters. The cooled solution was filtered and allowed to remain at 0° for 12 hr. Oxalic acid which crystallized out was separated by filtration, and the solution diluted with 2.4 l. of water; the solution was heated to boiling and neutralized to litmus with a saturated solution of potassium carbonate. The dark red solution was acidified to a pH of 4.5 with glacial acetic acid and evaporated to a volume of 1.5 l. The concentrated solution, which contained some crystals, was shaken with 800 ml. of 1:1 acetic acid solution. The precipitated product was collected, washed with several 200-ml. portions of 1:1 acetic acid solution, and purified by crystallization from hot water. The yield was 225 g. When sucrose was used, a yield of 34% based on sucrose was obtained. Analysis by conversion to the silver salt gave a purity of 97%.

Lactone of D-*glucaric acid.* To 460 g. (2 moles) of potassium acid D-glucarate there was added 500 ml. of distilled water containing 122 ml. of concentrated sulfuric acid. The mixture was allowed to stand until solution was complete. The solution was concentrated to a thick sirup under reduced pressure. The sirup was stirred with 4 l. of 95% alcohol, the potassium acid sulfate was separated in a Büchner funnel by filtration, and the solution concentrated as before. More potassium acid sulfate was removed by filtration. The sirup was dissolved in 500 ml. of distilled water and the solution again concentrated under reduced pressure to a sirup. The sirup was heated for 3 hr. on a boiling water bath under reduced pressure. The product was a slightly reddish sirup.

p-D-*Glucarotoluidide* (I). To 348 g. (2 moles) of D-glucaric acid lactone in 2 l. of boiling absolute alcohol in a 5-l. round bottom flask, there was added 500 g. (4.6 moles) of *p*-toluidine dissolved in 500 ml. of boiling absolute alcohol. Precipitation started immediately, and the mixture was stirred rapidly. After the addition of the *p*-toluidine, the mixture was stirred and heated to boiling until the mixture had concentrated to such a point that considerable bumping took place. The time required was 6 hr. The product was collected in a Büchner funnel and the crystals triturated with two successive 500 ml. portions of hot absolute alcohol and filtered. The product weighed 493 g., which represented a yield of 63% based on the lactone of D-glucaric acid. A sample for analysis was purified by crystallization from dioxane. Two recrystallizations gave a pure product which melted at 228°C.

Anal. Calcd. for $C_{20}H_{24}N$: C, 62.10; H, 6.20; N, 7.21. Found: C, 62.00; H, 6.40; N, 7.50.

*4′,4″-Dihydroxy-*D-*glucaranilide* (II). The procedure for the preparation of di-*p*-toluidide of D-glucaric acid was used in the preparation of this compound. The product was purified by recrystallization from hot water. The pure product melted at 290° C.

Anal. Calcd. for $C_{18}H_{20}O_8N_2$: C, 55.09; H, 5.13. Found: C, 55.26; H, 5.07.

p-D-*Glucarotoluidide tetraacetate* (III). There was placed in a 2 liter beaker 393 g. (1.01 moles) of di-*p*-toluidide of D-glucaric acid. To this was added 826 g. of pyridine and 806 g. (8 moles) of acetic anhydride. The mixture became very warm; the *p*-toluidine dissolved. The solution was allowed to remain for 20 hr. at room temperature. The solution was poured slowly into 3 l. of ice cold water with rapid stirring. After the mixture had been stirred for 6 hr., the granular precipitate was collected, dissolved in 2 l. of hot acetone, treated with Norite, filtered, and sufficient distilled water added to precipitate the product. The product weighed 446 g., a yield of 79% based on the di-*p*-toluidide of D-glucaric acid. A pure sample melted at 215° C.

Anal. Calcd. for $C_{28}H_{32}O_{10}N_2$: C, 60.42; H, 5.77; N, 5.03. Found: C, 60.68; H, 5.89; N, 5.27.

4′,4″-Diacetoxy-D-glucaranilide tetraacetate (IV). This compound was prepared from the di-*p*-hydroxyanilide of D-glucaric acid by the procedure described for the acetylation of (I). The product was purified by crystallization from alcohol. It melted at 193–4° C.

Anal. Calcd. for $C_{30}H_{32}O_{14}N_2$: C, 55.58; H, 5.00. Found: C, 55.81; H, 5.14.

DEPARTMENT OF CHEMISTRY
NORTH CAROLINA COLLEGE AT DURHAM
DURHAM, N. C.

---

[1] This work was supported by a research grant AF33-(616)-409 from Wright Air Development Center.

[2] Dermer and King, *J. Org. Chem.*, **8**, 168 (1943).

[3] (a) All melting points were corrected: They were taken on a Fisher-Johns micro-hot stage.
(b) Analyses were performed by Micro-Tech Laboratories, Skokie, Ill.

Chlorosulfonylation of 7-Hydroxy-4-methyl-8-acetylcoumarin and Its Methyl Ether

J. R. MERCHANT AND R. C. SHAH

Received September 17, 1956

During the course of our investigations on the substitution reactions of benzopyrones, we had oc-