Note

Cadmium D-*glycero*-D-*ido*-heptonate · cadmium chloride monohydrate: a convenient intermediate for isolating D-*glycero*-D-*ido*-heptonic acid*

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Heptonic acids, heptoses, and heptitols, derived from D-glucose, have many chemical and biological uses; hence, efficient methods for their synthesis are desirable. The preparation of sodium D-*glycero*-D-*gulo*-heptonate by the cyanohydrin synthesis has been developed commercially, and the salt is used in large quantities as a sequestering and cleaning agent. A syrupy residue from the preparation of this salt consists, in part, of sodium D-*glycero*-D-*ido*-heptonate. This syrup, available under the trade name** "Seqlene", provides a convenient source for the preparation of compounds having the D-*glycero*-D-*ido* configuration.

Our attempts to prepare sodium D-*glycero*-D-*ido*-heptonate and the corresponding lactone directly from "Seqlene" were unsuccessful. Attention was then directed to the separation of the cadmium salt of the acid by means of the double salt[1] with cadmium bromide, recommended by Richtmyer[2] for the separation of D-*glycero*-D-*ido*-heptonic acid in the cyanohydrin synthesis. We have found that the salt can be prepared directly from "Seqlene", and that it crystallizes readily. It was converted into the corresponding lactone by Richtmyer's method, *i.e.*, removal of the bromide ion as silver bromide, and of the cadmium ion as cadmium sulfide. This procedure is satisfactory for small preparations, but not for the large-scale production of the lactone.

In order to provide a simpler and less expensive method for preparing the lactone, we have now crystallized a new double salt of calcium D-*glycero*-D-*ido*-heptonate with cadmium chloride. This salt, although somewhat more soluble than the double salt with cadmium bromide, has the advantage of yielding hydrogen chloride, instead of hydrogen bromide, on removal of the cadmium ion. To prepare the lactone in quantity, the cadmium ion is removed by means of a cation-exchange resin, and the hydrogen chloride thus liberated is vaporized during concentration of the solution. The lactone crystallizes therefrom in good yield.

We have found that the cadmium bromide double salt is especially useful for the separation of the epimeric acids in the preparation of D-*glycero*-D-*gulo*-heptose-

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*Dedicated to Dr. Nelson K. Richtmyer in honor of his 70th birthday.

**"Seqlene" is a product of Pfanstiehl Laboratories, Inc., 1219 Glen Rock Avenue, Waukegan, Illinois, U. S. A.

1-^{14}C and D-*glycero*-D-*ido*-heptose-*1*-^{14}*C*. The procedures used were similar to those developed for other ^{14}C-labeled sugars[3].

The corresponding alditols, also, were prepared; they were obtained from the lactones by reduction with sodium borohydride[4]. Occasionally, the reductions yielded syrupy products that failed to crystallize. This difficulty is attributed to anhydro formation in the presence of the strongly acidic borate complex. By adjusting the pH of the reaction mixture to 5 with acetic acid, and distilling off the methyl borate *prior* to removal of the sodium ion, the alditols were obtained in good yield.

EXPERIMENTAL

Cadmium D-glycero-D-ido-*heptonate·cadmium chloride monohydrate* (**1**). — A solution of D-*glycero*-D-*ido*-heptono-1,4-lactone (**2**) (1 g) in water (10 ml) was treated with cadmium carbonate (0.5 g), heated and stirred for 2 h at 100°, and filtered. Anhydrous cadmium chloride (0.5 g) was dissolved in the filtrate, which was then saturated with ethanol. Compound **1** crystallized readily. By concentration of the mother liquor and addition of ethanol to incipent turbidity, an almost quantitative yield of **1** was obtained. To recrystallize the salt, it was dissolved in hot water (8 ml/g), and the solution was cooled, and treated with an equal volume of ethanol.

Anal. Calc. for $C_{14}H_{26}Cd_2Cl_2O_{16}\cdot H_2O$: C, 22.00; H, 3.70; Cd, 29.2. Found: C, 21.96; H, 3.74; Cd, 29.4.

The solubility of the new double salt is 8.1 g per 100 ml of water at 30°.

Double salts of D-glycero-D-ido-*heptonic acid from "Seqlene"*. — *A. Cadmium* D-glycero-D-ido-*heptonate·cadmium chloride monohydrate* (**1**). A solution of "Seqlene" (275 ml, containing 200 g of total solids) in water (2 liters) was passed through a column containing 1 liter of Amberlite IR-120 (H^+) cation-exchange resin (Rohm and Haas Co.). The effluent was stirred for 5 h at 100° with cadmium carbonate (74 g), and then treated with anhydrous cadmium chloride (80 g), and the suspension filtered through decolorizing carbon. The filtrate was concentrated *in vacuo* to about 1 liter, saturated with ethanol, and nucleated with the double salt **1**. Yield, 114 g (crude).

B. Cadmium D-glycero-D-ido-*heptonate.cadmium bromide monohydrate* (**3**). "Seqlene" (275 ml) was treated in the same way as in the preparation of **1**, except that cadmium bromide tetrahydrate (140 g) was substituted for cadmium chloride. The crude crystals of 3 weighed 180 g; after recrystallization from water and ethanol, the yield was 112 g.

D-glycero-D-ido-*Heptono-1,4-lactone* (**2**). — A solution of **1** (10 g) in water (200 ml) was passed through a column of Amberlite IR-120 (H^+) cation-exchange resin (35 ml). The effluent was evaporated *in vacuo* to a thick, almost colorless syrup, which was dissolved in 5 ml of methanol. The solution was re-evaporated, and the syrup was diluted with 10 ml of ethanol and the solution saturated with isopropyl alcohol. The lactone crystallized readily. By separating the crystals and re-concentrating the mother liquor, an almost quantitative yield of **2** was obtained.

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REFERENCES

1 E. M. Montgomery, N. K. Richtmyer, and C. S. Hudson, *J. Amer. Chem. Soc.*, 65 (1943) 1848 (footnote 17).

2 N. K. Richtmyer, *Methods Carbohyd. Chem.*, 1 (1962) 160.

3 H. S. Isbell, N. B. Holt, and H. L. Frush, *Methods Carbohyd. Chem.*, 1 (1962) 276; H. S. Isbell, H. L. Frush, and N. B. Holt, *J. Res. Nat. Bur. Stand.*, 53 (1954) 217, 325.

4 H. L. Frush and H. S. Isbell, *J. Amer. Chem. Soc.*, 78 (1956) 2844.