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PREPARATION AND REACTIONS OF SOME 1-AMINO-1-DEOXYHEPTITOLS

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In their studies on the condensation of nitromethane with hexoses, Sowden and Fischer[1] reduced 1-deoxy-1-nitro-D-*glycero*-D-*gulo*-heptitol with hydrogen and Raney nickel, and isolated 1-amino-1-deoxy-D-*glycero*-D-*gulo*-heptitol (**1**) as the crystalline *p*-toluenesulfonate. Later, Sowden and Schaffer[2] reduced 1-deoxy-1-nitro-D-*glycero*-D-*galacto*-heptitol similarly, and isolated 1-amino-1-deoxy-D-*glycero*-D-*galacto*-heptitol (**2**) as the crystalline oxalate. More recently, McDonald[3] obtained a crystalline *N*-acetyl derivative of **2** after reducing the nitro compound in the presence of a palladium-on-carbon catalyst. Apparently, no other 1-aminoheptitols have been described previously, and neither the free bases nor the hydrochlorides have been obtained crystalline.

We have reduced D-*glycero*-D-*gulo*-heptose oxime[4] with hydrogen and platinum oxide to **1**, which was isolated as the crystalline hydrochloride. The reduction of 1-deoxy-1-nitro-D-*glycero*-D-*galacto*-heptitol[2] with hydrogen and platinum oxide gave **2**, also isolated as its crystalline hydrochloride; removal of the hydrogen chloride by standard methods afforded crystalline **2**. This base was further characterized through its crystalline *N*-salicylidene derivative, as well as through the known *N*-acetyl derivative[3]. The reduction of 1-deoxy-1-nitro-D-*glycero*-L-*manno*-heptitol[5] with hydrogen and platinum oxide gave 1-amino-1-deoxy-D-*glycero*-L-*manno*-heptitol (**3**), also isolated as its crystalline hydrochloride.

The deamination of **2** with nitrous acid gave three products that could be readily separated on a column of Dowex 50W-X8 (Ba^{2+}). One of these was identified as perseitol (**4**; D-*glycero*-D-*galacto*-heptitol ≡ L-*glycero*-D-*manno*-heptitol), formed by replacement of the amino group by a hydroxyl group. The other two had mobilities on paper chromatograms that suggested that they might be anhydroheptitols, and the composition of one that crystallized (m.p. 162–163°) confirmed this speculation. Since the formation of an anhydroheptitol by deamination might involve an epoxide at C-1 and C-2, and its migration to C-2 and C-3, then 2,6-anhydro-D-*glycero*-D-*galacto*-heptitol would be one possible product; Sowden *et. al.*[6] have, however, described this compound (m.p. 142–144°), and it is obviously different from ours. So

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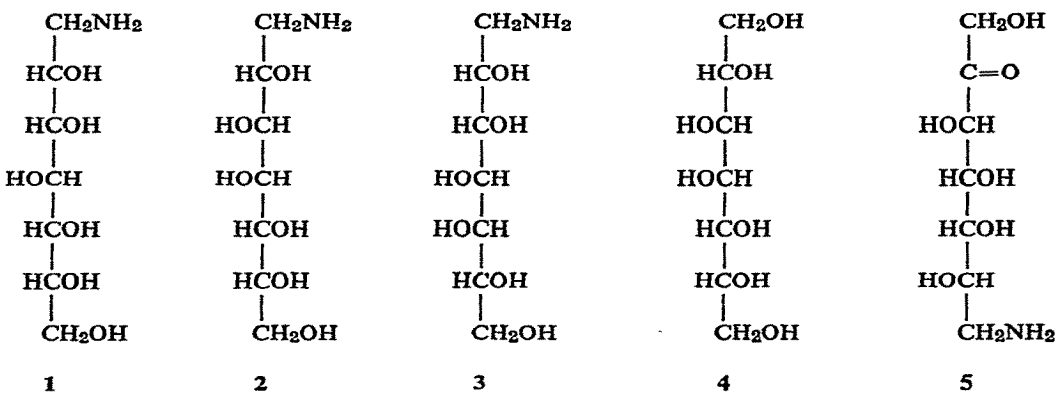
also are the two other anhydroheptitols known, namely, 2,6-anhydro-D-*glycero*-D-*gulo*-heptitol (m.p. 204–205°) and 2,6-anhydro-D-*glycero*-L-*manno*-heptitol (hemihydrate, m.p. 121–122°), described by Coxon and Fletcher[7]. Similar deamination of **1** with nitrous acid gave three substances that, from paper-chromatographic evidence only, are believed to be the expected *meso-glycero-gulo*-heptitol and two anhydroheptitols.

McDonald[3] has recently prepared 7-acetamido-7-deoxy-L-*galacto*-heptulose by the action of *Acetobacter suboxydans* on 1-acetamido-1-deoxy-D-*glycero*-D-*galacto*-heptitol (the *N*-acetyl derivative of **2**). Unaware of this work, we started our studies of the action of *A. suboxydans* on the unacetylated aminoheptitols **1**, **2**, and **3**. As would be expected from the Bertrand rule, as modified by Hann *et. al.*[8], both **1** and **2** were oxidized, whereas growth of the *A. suboxydans* in the medium containing **3** was not detected. The product from **2**, presumably 7-amino-7-deoxy-L-*galacto*-heptulose (**5**), has been obtained in crystalline form and will be further described at a later date. These 7-amino-7-deoxyheptuloses, when spotted on paper and sprayed with the orcinol–hydrochloric acid reagent and then heated, give a reddish orange color, in contrast to the blue or greenish blue colors characteristic of the corresponding heptuloses themselves.



EXPERIMENTAL

1-Amino-1-deoxy-D-glycero-D-gulo-*heptitol* (**1**) *hydrochloride*.—D-*glycero*-D-*gulo*-Heptose oxime was prepared by the following modification of the method described by Hockett and Chandler[4]. Anhydrous sodium carbonate (14.0 g; 0.13 mole) was added to a stirred solution of hydroxylamine hydrochloride (14.0 g; 0.20 mole) in 250 ml of absolute ethyl alcohol at 50–60°. A vigorous reaction ensued; this subsided in *ca.* 25 min. D-*glycero*-D-*gulo*-Heptose[9] (21.0 g; 0.10 mole) was added, and the mixture stirred for 45 min at 70–80° under reflux. The hot mixture was rapidly filtered and the solid was washed on the funnel with ethyl alcohol (100 ml). The combined filtrate and washings were concentrated *in vacuo* to a colorless syrup (28.0 g) consisting

of the heptose oxime, apparently contaminated with hydroxylamine hydrochloride. This crude syrup was dissolved in 3:1(v/v) ethyl alcohol–water (200 ml), acetic acid (50 ml) and platinum oxide (0.2 g) were added, and the mixture was shaken with hydrogen at atmospheric pressure for 48 h. The catalyst was removed by filtration, and the solution concentrated *in vacuo* to a syrup that was dissolved in water (100 ml). This solution was passed down a column (3 × 27 cm) of Amberlite IR-120 (H^+) ion-exchange resin. The column was then washed with water (750 ml), and eluted with 3N ammonia (1 l). The eluate was concentrated *in vacuo* to a syrup (17.9 g) that was dissolved in water (100 ml) and acidified with 2N hydrochloric acid (30 ml). The yellow solution was decolorized (Darco X), filtered, and concentrated to a mobile syrup to which pyridine (25 ml) was added. The solution was cooled, nucleated with crystals of the hydrochloride (obtained in a preliminary experiment), and kept for 4 days at − 10°. The resulting small prisms were filtered off, washed successively with cold pyridine, ethyl alcohol, and ether, and dried at 40° *in vacuo*; 12.7 g (51%, based on the D-*glycero*-D-*gulo*-heptose), m.p. 114–115°. Recrystallization was difficult, but was effected by dissolving the hydrochloride (12.7 g) in water (8 ml), adding pyridine (80 ml), and keeping the solution for 48 h at − 10°. The m.p. of the material thus obtained varied from 113–115° to 117–118° with different preparations. The compound appeared to crystallize initially as a pyridine solvate; spears, m.p. 92–94°. A sample having m.p. 113–115° and $[\alpha]_D^{20} - 4.7°$ (*c* 1.1, water) was analyzed.

Anal. Calc. for $C_7H_{18}ClNO_6$: C, 33.94; H, 7.33; Cl, 14.31; N, 5.66. Found: C, 34.17; H, 7.05; Cl, 14.31; N, 5.71.

1-Amino-1-deoxy-D-glycero-D-galacto-*heptitol* (**2**) *hydrochloride.* — To a solution of 1-deoxy-1-nitro-D-*glycero*-D-*galacto*-heptitol[2] (6.0 g; 0.025 mole) in water (200 ml) were added acetic acid (5 ml) and platinum oxide (0.2 g). The mixture was reduced overnight with hydrogen at atmospheric pressure. The catalyst was removed by filtration, and the theoretical volume of hydrochloric acid (12.5 ml of 2N) was added to the filtrate. Evaporation of the solution yielded the hydrochloride of **2** (5.9 g; 96%) as clusters of tiny needles; after two recrystallizations from 2:1 (v/v) ethyl alcohol–water (4 ml/g), m.p. 184–185°, $[\alpha]_D^{20}$ −5.9° (*c* 1.0, water).

Anal. Calc. for $C_7H_{18}ClNO_6$: C, 33.94; H, 7.33; Cl, 14.31; N, 5.66. Found: C, 34.20; H, 7.30; Cl, 14.05; N, 5.57.

1-Amino-1-deoxy-D-glycero-D-galacto-*heptitol* (**2**). — A sample (5 g) of the hydrochloride of **2** was dissolved in water (100 ml) and the solution passed down a column (3 × 27 cm) of Amberlite IR-120 (H^+) ion-exchange resin. The column was washed with water (500 ml), and then eluted with 3N ammonia (500 ml). Concentration of the eluate gave an almost quantitative yield of **2** which, on recrystallization from 2:1 (v/v) ethyl alcohol–water, separated as fine needles; m.p. 181–184°, $[\alpha]_D^{20} + 0.7°$ (*c* 2.0, water).

Anal. Calc. for $C_7H_{17}NO_6$: C, 39.81; H, 8.11; N, 6.63. Found: C, 39.86; H, 8.24; N, 6.56.

1-Deoxy-1-(salicylidenamino)-D-glycero-D-galacto-*heptitol.* — To a solution of **2** (0.20 g) and sodium acetate trihydrate (0.22 g; 2 mol. equiv.) in water

(4 ml) was added a solution of salicylaldehyde (0.20 g; 2 mol. equiv.) in methanol (12 ml). Yellow prisms soon crystallized from the solution while it was kept for 3 h in the dark. The product was filtered off, and successively washed with 3:1 (v/v) methanol–water (20 ml) and ether; yield, 0.24 g (94%). After recrystallization from hot water (40 ml) by the addition of methanol (20 ml), it had m.p. 228–229°.

Anal. Calc. for $C_{14}H_{21}NO_7$: C, 53.33; H, 6.71; N, 4.44. Found: C, 53.46; H, 6.48; N, 4.32.

1-Acetamido-1-deoxy-D-glycero-D-galacto-*heptitol.* — A portion (5.0 g) of the hydrochloride of **2** was converted into the free base as described above, and the ammoniacal eluate was evaporated *in vacuo* to a crystalline residue. To this were added acetic anhydride (5 ml) and methanol (50 ml), and the mixture was heated for 30 min on a steam bath. Cooling and filtration gave the title compound (4.5 g; 88%). After recrystallization from 2:1 (v/v) ethyl alcohol–water (10 ml/g), the compound (very small prisms) had m.p. 199–200° and $[\alpha]_D^{20}$ −16.5 ± 1.5° (*c* 1.1, water), in good agreement with the lit. values[3] of 200° and −15.5°, respectively. Analyses for carbon, hydrogen, and nitrogen confirmed its composition.

1-Amino-1-deoxy-D-glycero-L-manno-*heptitol* (**3**) *hydrochloride.* — 1-Deoxy-1-nitro-D-*glycero*-L-*manno*-heptitol monohydrate (6.5 g)[5] was reduced to the amino compound as described for **2**, and the resulting hydrochloride was recrystallized, in clusters of small plates from aqueous pyridine as described for the hydrochloride of **2**, giving 4.0 g (64%) of product which showed no evidence of forming a solvate with pyridine; m.p. 150–152°, and $[\alpha]_D^{20}$ −3.5° (*c* 1.1, water).

Anal. Calc. for $C_7H_{18}ClNO_6$: C, 33.94; H, 7.33; Cl, 14.31; N, 5.66. Found: C, 33.91; H, 7.05; Cl, 14.43; N, 5.50.

Deamination of 1-amino-1-deoxy-D-glycero-D-galacto-*heptitol* (**2**) *hydrochloride.* — The hydrochloride of **2** (1.24 g; 0.005 mole) was dissolved in a solution of acetic acid (3 ml) in water (25 ml). Sodium nitrite (1.03 g; 0.015 mole) was added with stirring, and the solution was kept overnight at room temperature. After deionization with Amberlite IR-120 (H^+) and Duolite A-4 (OH^-) resins, the solution was concentrated to a syrup. This was dissolved in water (10 ml), the solution was transferred to the top of a column (2.5 × 68 cm) of Dowex 50W-X8 (Ba^{2+}) resin, and elution was conducted with water. The eluate was collected in 4-ml fractions.

Fractions 33–50 contained a substance having the mobility of perseitol on paper chromatograms. The combined fractions were evaporated to a crystalline residue that was recrystallized twice from aqueous ethyl alcohol, to give 60 mg of product, m.p. 186–187° alone, m.p. 187–188° when mixed with authentic **4**.

Fractions 22–28 contained a substance having a mobility slightly less than that of rhamnose in 3:1:1 butyl alcohol–ethyl alcohol–water. These fractions were combined, and evaporated to a syrup which soon crystallized; recrystallization from aqueous ethyl alcohol yielded 30 mg of a compound having m.p. 162–163° and the composition of an anhydroheptitol.

Anal. Calc. for $C_7H_{14}O_6$: C, 43.29; H, 7.27. Found: C, 43.43; H, 7.06.

Fractions 12–18 contained a substance having practically the same R_F value as

the crystalline product isolated from fractions 22–28, but it has thus far resisted all attempts at crystallization; it is presumed to be a second anhydroheptitol.

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SUMMARY

The hydrochlorides of 1-amino-1-deoxy-D-*glycero*-D-*gulo*-heptitol (**1**), 1-amino-1-deoxy-D-*glycero*-D-*galacto*-heptitol (**2**), and 1-amino-1-deoxy-D-*glycero*-L-*manno*-heptitol (**3**), as well as the free aminoheptitol **2**, have been obtained in crystalline form. Deamination of **2** with nitrous acid yielded three products: perseitol (**4**) and two compounds that appear to be anhydroheptitols. Deamination of **3** gave similar results. In agreement with the accepted rule, compounds **1** and **2** were oxidized by *Acetobacter suboxydans*, whereas compound **3** was not. The oxidation product from **2**, presumably 7-amino-7-deoxy-L-*galacto*-heptulose (**5**), has been obtained crystalline.

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