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2,3,4,5-TETRAACETYLADONITOL AND 1-CHLORO-1-DESOXY-2,3,4,5-TETRAACETYLADONITOL

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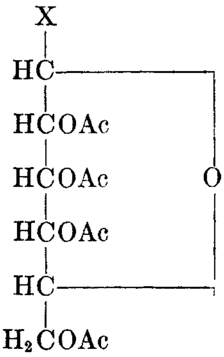
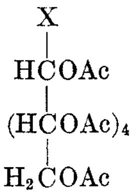
In 1870, Colley (1) prepared acetochloroglucose, the first aceto-halogen sugar by acetylating glucose with acetyl chloride. Since that time many aceto-halogen sugars have been made and have found application in the synthesis of glycosides by the Koenigs-Knorr reaction (2). It is now generally known that, with few exceptions (3, 4, 5) sugar acetates or aceto-halogen sugars prepared by direct acetylation have the lactol or cyclic hemiacetal structure (formula I).



where X = halogen or acetoxy group

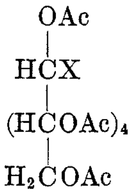
I

The acyclic or aldehydo sugar acetates have been prepared, in the main, by indirect methods. For example, Wolfrom (6) prepared the acyclic aldehydo glucose pentaacetate by hydrolysis of the acetylated glucose ethylmercaptal with mercuric chloride in the presence of cadmium carbonate. The same compound was obtained by Cook and Major (7) upon catalytic reduction of pentaacetylgluconyl chloride. Halogenation of the aldehydo sugar acetates was effected by Wolfrom and his co-workers (8, 9, 10, 11), who found that treatment of the acyclic sugar acetates with acyl halides produced acyl halide-carbonyl addition compounds (formulas II and III).



$$\begin{array}{c} X \\ | \\ HCOAc \\ | \\ (HCOAc)_4 \\ | \\ H_2COAc \end{array}$$

II



$$\begin{array}{c} OAc \\ | \\ HCX \\ | \\ (HCOAc)_4 \\ | \\ H_2COAc \end{array}$$

III

X = halogen

In the light of the work already done in the field of aceto-halogen sugars and in view of their importance in sugar chemistry it is remarkable that almost nothing is known of related sugar alcohols. When, during the course of an investigation in these laboratories some years ago, it became necessary to prepare an acetylated sugar alcohol with a halogen on carbon 1, it was noted that there was an almost complete absence of such compounds in the literature. A dichlorohydrin of mannitol tetraacetate melting at 128–130° was reported by Griner (12), and another dichlorohydrin of mannitol tetraacetate melting at 214° was obtained by Fischer and Armstrong (13). A dulcitol chlorohydrin pentaacetate was also reported by Bouchardat (14) who made it by refluxing dulcitol with 6–8 moles of acetyl chloride. In all these compounds, the positions of the halogens were undefined.

In the present study, it was decided to prepare 1-chloro-1-desoxy-2,3,4,5-tetraacetyladonitol by reducing *aldehydo*-tetraacetyl-D-ribose (15) to adonitol and then halogenating it with an appropriate chlorinating agent. Accordingly, *aldehydo*-tetraacetyl-D-ribose was treated with hydrogen at low pressure and room temperature in the presence of platinum oxide, but no reduction took place. With Raney nickel under the same conditions, however, the reduction went smoothly to give the desired 2,3,4,5-tetraacetyladonitol in the form of soft white needles melting at 55–57°. The ease of reduction is noteworthy, since Gardner (16) in attempting to reduce *aldehydo*-D-glucose and *aldehydo*-D-galactose pentaacetates to sorbitol and dulcitol pentaacetates respectively experienced considerable difficulty, and was ultimately unsuccessful. He found for example, that manganese dioxide on kieselguhr, and platinum oxide in various solvents and at high temperatures and pressures would not effect reduction. With the use of nickel catalyst on kieselguhr or Raney nickel at temperatures between 150–165° and pressures of 1800 lbs. he obtained reduction and simultaneously, partial deacetylation.

Tetraacetyladonitol is the second acetylated adonitol to be reported. The pentaacetyl derivative was obtained as a non-crystallizable syrup by direct acetylation of the alcohol (17, 18).

Halogenation of the tetraacetyladonitol was effected with thionyl chloride, phosphorus pentachloride, and titanium tetrachloride. Phosphorus trichloride was tried unsuccessfully. The desired 1-chloro-1-desoxy-2,3,4,5-tetraacetyladonitol was obtained as a clear, colorless, viscous liquid which partially solidified on standing. In addition to the desired product, a small quantity of a white crystalline material, m.p. 134–134.5° was obtained in every instance. The analysis:—C, 47.8; H, 6.3; Cl, 10.5; acetyl, 49.8 corresponds reasonably to the empirical formula $C_{14}H_{21}ClO_8$ (theory: C, 48.0; H, 6.0; Cl, 10.1; acetyl, 48.7). A sample of this material on standing in a capped amber bottle for about four years has partially liquefied and possesses a strong odor of acetic acid.

ACKNOWLEDGMENT

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EXPERIMENTAL

All melting points are corrected and boiling points uncorrected.

2,3,4,5-Tetraacetyladonitol. Thirty grams of *aldehydo*-tetraacetyl-D-ribose dissolved in approximately 100 cc. of purified dioxane was reduced with hydrogen in the presence of Raney nickel catalyst. The reduction was carried out at 30 lbs. pressure and at room temperature, though on several occasions it was found advisable to apply mild heat (50°) to ensure complete reduction. When the theoretical quantity of hydrogen had been taken up, the reaction mixture was filtered and the dioxane was removed under vacuum to yield 28.5 g. (95%) of a syrup which gave no test with Shaffer-Hartmann solution. The syrup was heated with petroleum ether, and on cooling, long, fine white needles appeared. The crystalline product was dissolved in ethanol, treated with Norit, filtered, and evaporated on a steam-bath. The syrupy residue on standing in the refrigerator crystallized in long soft needles melting at 55–57°. The product was soluble in water and the common organic solvents.

Anal. Calc'd for $C_{13}H_{20}O_9 \cdot \frac{1}{2} H_2O$: Acetyl, 52.3. Found: Acetyl, 52.1.
$[\alpha]_D^{24} - 7.4°$, *c*, 5% in water

1-Chloro-1-desoxy-2,3,4,5-tetraacetyladonitol. (A) *With thionyl chloride.* Tetraacetyladonitol was warmed on the steam-bath with an excess of thionyl chloride for several minutes. The thionyl chloride was then removed under vacuum and the residue was distilled to yield a clear, colorless, viscous distillate, b.p. 150° at 0.6–0.7 mm. On standing, a slight precipitate appeared in the distillate. The precipitate, like the distillate, was insoluble in water. To effect a separation, the mixture was dissolved in a little hot methanol. On cooling, a microcrystalline solid appeared. The precipitate was filtered off and the filtrate was concentrated under vacuum to a clear syrup. The syrup was distilled, b.p. 134–136° at 0.2 mm., n_D^{26}, 1.450; $[\alpha]_D$ insignificant in methanol, chloroform, dioxane, acetone, and ethyl acetate.

Anal. Calc'd for $C_{13}H_{19}ClO_8$: C, 46.0; H, 5.6; Cl, 10.2.
Found: C, 45.9; H, 5.8; Cl, 10.3.

The precipitate on recrystallization from methanol was obtained as white rhomboids, m.p. 134–134.5°.

(B) *With phosphorus pentachloride.* Eighty-five grams of the adonitol tetraacetate dissolved in dry chloroform was treated with phosphorus pentachloride portionwise. A vigorous reaction took place with the evolution of hydrogen chloride. When the further addition of phosphorus pentachloride failed to yield a strong effervescence of hydrogen chloride, the reaction was considered complete. A total of 56 g. of phosphorus pentachloride (slightly in excess of the theoretical quantity) was required. The chloroform solution was then washed with ice-water, sodium bicarbonate solution, and finally more ice-water. The neutral chloroform layer was then dried over anhydrous sodium sulfate, filtered, and the chloroform removed under vacuum. The oily residue was distilled; b.p. 146–150° at 0.4–0.5 mm., n_D^{26} 1.451; yield 65.5 g. On standing, the clear distillate yielded a slight precipitate. Separation was effected as previously described and on recrystallization from methanol the solid melted at 134–135° and proved to be identical with the rhomboids reported above.

(C) *With titanium tetrachloride.* Five grams of adonitol tetraacetate dissolved in 35 g. of dry chloroform was treated with 3 g. of titanium tetrachloride in 12 g. of dry chloroform. Heat was evolved and a yellow precipitate appeared which dissolved on shaking. The reaction mixture was heated in a water-bath under reflux for 3 hours. After cooling, the chloroform solution was washed and dried as before and the chloroform was removed under vacuum. The residual syrup promptly showed signs of precipitation. It was therefore separated from the solid in the usual manner before distillation. The solid, on recrystallization, melted at 133.5–134.5°. The distillate was the desired adonityl chloride.

SUMMARY

This report concerns the preparation of 2,3,4,5-tetraacetyladonitol by the catalytic reduction of the corresponding *aldehydo*-tetraacetyl-D-ribose and the preparation of 1-chloro-1-desoxy-2,3,4,5-tetraacetyladonitol by chlorination of the adonitol.

NUTLEY, N. J.

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