[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

Glycofuranosides and Thioglycofuranosides. IV. Direct Formation of Dimethyl Acetal and Preparation of α-Ethylfuranoside from *l*-Rhamnose Ethylmercaptal

BY JOHN W. GREEN[1] AND EUGENE PACSU

In the previous articles of this series[2] the preparation of glycofuranosides from the mercaptals of glucose, galactose and *l*-arabinose was described. In each case the thioethyl groups were eliminated from the sugar with the formation of a <1–4> ring linked by oxygen.

l-Rhamnose ethylmercaptal has been treated similarly with mercuric chloride in neutral alcoholic solutions. In ethyl alcohol the reaction runs in the expected manner and the product is a negatively rotating sirup. From this sirup a small yield of pure crystalline α-ethyl *l*-rhamnofuranoside was obtained. These crystals have a specific rotation of −95.5° in water solution, similar in magnitude (but necessarily opposite in sign) to the value for α-methyl-*d*-mannofuranoside.[3] The crystals melt at 54–56° and are very hygroscopic.

Similarly, from the reaction carried out in methyl alcohol solution, a negatively rotating sirup is obtained. From this sirup a small amount of crystalline material is isolated very easily, and this product is not a furanoside. The specific rotation in water solution is 10.2° and the melting point is 123–124°. The crystals are not hygroscopic. The carbon–hydrogen analysis agrees perfectly with the empirical formula of a dimethyl acetal. The small rotation is also typical of an open-chain derivative.

This is the first observed case where an acetal of a sugar has been formed without blocking some[4] or all[5] of the hydroxyl groups. It has been believed that the mechanism of the mercaptal–mercuric chloride reaction was always an initial ring closure to a thiofuranoside,[2a] then subsequent secondary changes to a glycofuranoside, a glycopyranoside or the free sugar, depending on the experimental conditions. Here is a definite case where the expected ring closure does not occur. The greater amount of the ethyl rhamnofuranoside sirup has not been obtained crystalline so it cannot be said that there is no ethyl acetal present. However, the isolation of some ethyl rhamnofuranoside shows that ring closure does occur, at least in part, when rhamnose ethylmercaptal reacts with mercuric chloride in neutral ethyl alcohol solution.

On the other hand, the greater part of the mother liquor from the dimethyl acetal has not been crystallized and so it cannot be said definitely that the acetal is the only product. The similarity in rotation of the two reaction sirups would lead to the assumption that in both cases the rhamnofuranoside is formed and in one case at least the acetal also.

The conception of the acetal as an intermediate in the glycofuranoside formation seems unlikely and the acetal is probably formed as a by-product. An intermediate product in the acetal reaction would necessarily have to be the mixed acetal, with one methoxyl and one thioethyl group. This brings up the possibility of glycofuranoside formation from the mixed acetal, which might explain why none of the sugars (except glucose) form the thiofuranosides.

The mother liquors of these two new compounds will be investigated further.

Experimental

Preparation of α-Ethyl *l*-Rhamnofuranoside.—A mixture of 10.8 g. of *l*-rhamnose ethyl mercaptal, 22 g. of mercuric chloride (2 moles), 12 g. of yellow mercuric oxide and 6 g. of drierite was shaken with 80 cc. of absolute ethyl alcohol at 25° for four hours. The mixture was filtered, the filtrate treated with 5 cc. of pyridine and kept at 0° for two hours. The pyridine–mercuric chloride was filtered and the solution evaporated to a sirup *in vacuo* at 40°. The substance was dissolved in a little cold water, the solution filtered and neutralized to phenolphthalein, with a few drops of sodium hydroxide solution, then evaporated *in vacuo* at 40°. The resulting sirup was evaporated successively from methyl alcohol and ethyl acetate solutions. The sirupy residue rotated −53° in water solution and after two months in the ice box changed to a semi-solid mass which melted at room temperature.

From 20 cc. of dry ethyl acetate solution, diluted with dry ether to a slight turbidity at 0°, 200 mg. of crystals rotating −71° in water solution was deposited. After three recrystallizations from 5 cc. of dry ether diluted

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[1] Research Assistant on Special Funds from the Rockefeller Foundation.

[2] (a) Green and Pacsu, THIS JOURNAL, **59**, 1205 (1937); (b) Green and Pacsu, *ibid.*, **59**, 2569 (1937); (c) Green and Pacsu, *ibid.*, **60**, 2056 (1938).

[3] Haworth and Porter, *J. Chem. Soc.*, 649 (1930).

[4] Wolfrom, Tanghe, George and Waisbrot, THIS JOURNAL, **60**, 132 (1938).

[5] (a) Wolfrom and Waisbrot, *ibid.*, **60**, 854 (1938); (b) Montgomery, Hann and Hudson, *ibid.*, **59**, 1124 (1937); Campbell and Link, *J. Biol. Chem.*, **122**, 635 (1938).

with petroleum ether (b. p. 30–60°), a pure product was obtained in the form of long stout needles: yield 50 mg., m. p. 54–56°, $[\alpha]^{20}_{D}$ 95.5° (0.0330 g. of substance, 3 cc. of water solution, 2-dm. semi-micro tube, 2.10° rotation to the left). The crystals were very hygroscopic and did not reduce Fehling's solution. Before analysis the substance was kept over phosphorus pentoxide in a desiccator for three days.

Anal. Calcd. for $C_8H_{16}O_5$: C, 50.0; H, 8.33. Found: C, 49.4; H, 8.6.

Preparation of *l*-Rhamnose Dimethyl Acetal.—A mixture of 5.4 g. of *l*-rhamnose ethylmercaptal, 10.8 g. of mercuric chloride (2 moles), 5 g. of yellow mercuric oxide and 3 g. of drierite was shaken in 60 cc. of absolute methyl alcohol at 25° for four hours, and worked up as in the above experiment. The sirup, rotating −35° in water solution, on evaporation from ethyl acetate solution became partly crystalline.

From a solution of 15 cc. of dry ethyl acetate in *the ice box* 300 mg. of crystals was deposited, and after one recrystallization from 15 cc. of dry ethyl acetate at 0°, 200 mg. of pure crystals was obtained: yield 5%; m. p. 123–124°; $[\alpha]^{20}_{D}$ 10.2° (0.1070 g. substance, 3 cc. of solution, 2-dm. semi-micro tube, rotation 0.73° to the right). The crystals are long fine needles, are not hygroscopic and do not reduce Fehling's solution. They are easily hydrolyzed by 0.01 *N* hydrochloric acid at 100° in a few minutes.

Anal. Calcd. for $C_8H_{18}O_6$: C, 45.7; H, 8.57. Found: C, 45.8; H, 8.5.

Summary

α-Ethyl *l*-rhamnofuranoside has been isolated in crystalline form from the reaction of ethyl mercaptal with mercuric chloride in neutral ethyl alcoholic solution. The pure crystals have a specific rotation of −95.5° in water solution and melt at 54–56°. They are hygroscopic and do not reduce Fehling's solution.

l-Rhamnose dimethyl acetal has been isolated in crystalline form by a similar reaction of the ethyl mercaptal in methyl alcohol. The pure crystals have a specific rotation of 10.2° in water solution and melt at 123–124°. This is the first observed case of direct formation of an acetal from a sugar without blocking the hydroxyl groups to prevent glycoside formation.

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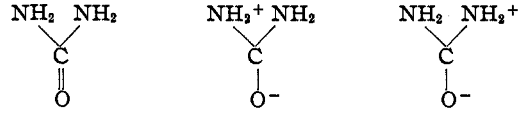
The Influence of Substances on the Optical Rotation of Gelatin. VII. Rotatory Dispersion of Gelatin in Urea Solutions[1]

BY D. C. CARPENTER AND F. E. LOVELACE

The rotatory dispersion of gelatin–sodium halide systems follows a single-term Drude equation $[\alpha]_\lambda = k/(\lambda^2 - \lambda_0^2)$ in which λ_0 is the position of an absorption band at 2200 Å. The effect of the halides of sodium on the rotatory dispersion constant of gelatin has been shown[2] to follow a linear equation with reference to salt concentration at 40°, and at 0.5° to be the result of two effects, one linear with respect to salt concentration and the other related to salt concentration by the equation

$$a/(1 - a) = e^{kC}/K^k$$

In connection with the foregoing studies of the optical behavior of protein ions in the presence of highly ionized inorganic salts, it appeared that similar studies with an optically inactive organic dipole ion would be desirable. From measurements of the dielectric constant of urea solutions[3] it has been inferred that urea exists in solution as the dipole ion $..{}^+NH_3C(=NH)O^-$. The dielectric constant data, however, may be accounted for by the resonance formula



as well as the zwitter ion formula. It is common knowledge that the presence of urea brings about the "denaturation" of many proteins. Only recently have the effects of urea on proteins been followed in the ultracentrifuge. Watson, Arrhenius and Williams[4] reported that the molecular weight of zein was not affected by urea. Williams and Watson[5] believe that the action of urea on egg albumin is that of dissociation, the molecular weight of the pieces being of the order of one-half that of the original protein molecule. On dialyzing out the urea from their solutions about

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[1] Approved by the Director of the New York State Experiment Station for publication as Journal Paper No. 275.

[2] Carpenter and Lovelace, THIS JOURNAL, **57**, 2342 (1935); **58**, 2438 (1936); **59**, 2213 (1937); Carpenter, *Cold Spring Harbor Symposia*, **6**, in press (1938).

[3] Devoto, *Atti soc. ital. progresso. sci.*, **19**, 2, 167 (1931).

[4] Watson, Arrhenius and Willams, *Nature*, **137**, 322 (1936).

[5] Williams and Watson, *ibid.*, **139**, 506 (1937).