The combined chloroform extracts were extracted with dilute hydrochloric acid, the acid aqueous extract was evaporated *in vacuo* and the residue was extracted with absolute alcohol. The alcoholic solution on evaporation left a residue of 518.8 mg. of the crystalline hydrochloride of the basic cleavage product, the purity of which was demonstrated by analysis; yield 97.4%. The recrystallization of this material is effected by dissolving in a minimum amount of absolute alcohol, adding an excess of dioxane and allowing to stand.

From the alkaline liquor after chloroform extraction, a further quantity of 25.3 mg. of acidic cleavage product was obtained by neutralizing and concentrating to a small volume; total yield 561 mg. or 93.1% of the theoretical. Fine white needles are obtained on recrystallization from hot water.

TABLE I

ANALYSES

| | C | H | N | S | Cl |
|---|---|---|---|---|---|
| I. Dried for anal. in vac. over $P_2O_5$ at 100° | | | | | |
| Calcd. for $C_6H_9N_3SO_3$ | 35.44 | 4.46 | 20.68 | 15.78 | ... |
| Found Not recryst. | 35.34 | 4.03 | ... | 15.88 | ... |
| Found Water recryst. | 35.36 | 4.60 | 20.53[a] | 16.01 | ... |
| II. Dried for anal. in vac. over $P_2O_5$ | | | | | |
| Calcd. for $C_6H_9NSO \cdot HCl$ | 40.09 | 5.61 | 7.80 | 17.85 | 19.74 |
| Found | 39.80[b] | 5.89[b] | 7.81[c,d] | 17.85[c] | 19.48[c] |

[a] Kjeldahl. [b] Not recryst.; dried at 55°. [c] Recryst. from alcohol–dioxane and dried at room temp. [d] Dumas.

In another experiment 203 mg. of vitamin hydrochloride was allowed to react at *p*H 5.0 in a sealed tube at room temperature with a solution containing by analysis 231.9 mg. of sodium bisulfite. After standing for forty-eight hours the solution was made alkaline with baryta and the precipitate so formed was suspended in water, decomposed with hydrochloric acid and excess sulfite determined iodimetrically. The sulfite consumed was 74.5 mg. or 116%. Blank experiments accounted for the excess above one mole equivalent as due to losses of sulfur dioxide by atmospheric oxidation and volatilization. The reaction products were isolated as indicated above.

We are grateful to Miss Marion Ammerman for physiological assays, to Dr. H. T. Clarke and Dr. Oskar Wintersteiner for microchemical facilities, to Mr. W. J. Saschek for performance of the microanalyses and to the Carnegie Corporation for a grant of funds through the Carnegie Institution of Washington.

## Summary

Vitamin $B_1$ is split quantitatively at room temperature by sulfite at *p*H 5 into two products having the compositions $C_6H_9N_3SO_3$ (I) and $C_6H_9NSO$ (II), respectively.

I is a sparingly soluble acidic product.

II is a chloroform soluble base which has been isolated in the form of a crystalline hydrochloride.

NEW YORK CITY RECEIVED DECEMBER 11, 1934

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[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

# The Configuration and the Mechanism of Hydrolysis of the Maltose Derivatives with Orthoester Structure

BY EUGENE PACSU

Several years ago Freudenberg and Ivers[1] prepared a new acetochloromaltose from octaacetylmaltose using an ether solution of dry hydrogen chloride. From the methyl alcoholic suspension of this halogeno derivative, on treatment with pyridine, Freudenberg and co-workers[2] obtained a new heptaacetylmethylmaltoside. Both of these maltose derivatives were later recognized by Freudenberg,[3] as possessing "orthoester" structures. It has been suggested by Haworth[4] that formation of such orthoester derivatives may occur "whenever, as in the β-mannose, -lyxose, and -rhamnose series, adjacent hydroxyl groups congregate in clusters on the same side of the six-atom ring." Since no congestion of hydroxyl groups is prevalent in maltose, it appears that two adjacent hydroxyl groups on the same side of the plane are sufficient for the formation of orthoester derivatives. If this be true, then Freudenberg's maltose derivatives must have α-configurations, since β-maltose is so constituted that each hydroxyl group occupies a *trans* position with respect to its neighbor. Hydrolysis experiments with very dilute hydrochloric acid on the "γ"-monoacetylmethylmaltoside[2,3] (I) confirm this. Two consecutive reactions were found to take place, when the hydrogen-ion concentration of the solution corresponded to *p*H 4 (Table I).

The first reaction, strongly catalyzed by hydrogen ions, was so rapid that it was completed in less than two minutes. During this time the original specific rotation of $[\alpha]_D^{23}$ 103.7° increased

(1) Freudenberg and Ivers, *Ber.*, **55**, 929 (1922).

(2) Freudenberg, v. Hochstetter and Engels, *ibid.*, **58**, 666 (1925).

(3) Freudenberg, *Naturwiss.*, **18**, 393 (1930); Freudenberg and Scholz, *Ber.*, **63**, 1969 (1930).

(4) Haworth, "Rapports sur les Hydrates de Carbone," Xième Conférence de l'Union Internationale de Chimie, Liége, 1930.

TABLE I

HYDROLYSIS OF "γ"-MONOACETYLMETHYLMALTOSIDE (I) AT 23° BY DILUTE HYDROCHLORIC ACID; *p*H = 4; 0.2457 G./25 CC.; 2-DM. TUBE

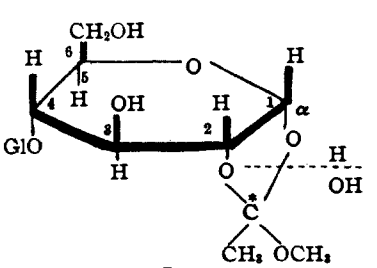
| Time, min. | $\alpha_D$ | $K = \frac{1}{t}\log\frac{\alpha_\infty - \alpha_0}{\alpha_\infty - \alpha}$ |
|---|---|---|
| 0 | +2.04° ($[\alpha]_D^{23}$ 103.7°) | ... |
| 1.25 | 2.55° ($[\alpha]_D^{23}$ 134.6°) | ... |
| 0 | $\alpha_0$ = 2.55° | ... |
| 4 | .53 | [0.0047] |
| 8 | .49 | .0078 |
| 13 | .43 | .0098 |
| 18 | .40 | .0093 |
| 28 | .34 | .0092 |
| 38 | .27 | .0103 |
| 48 | .24 | .0095 |
| 58 | .20 | .0102 |
| 120 | .11 | .0101 |
| 300 | $\alpha_\infty$ = 2.08° ($[\alpha]_D^{23}$ 109.8°) | mean: .0095 |

TABLE II

HYDROLYSIS OF "γ"-MONOACETYLMETHYLMALTOSIDE (I) AT 23° BY DILUTE HYDROCHLORIC ACID; *p*H = 4.8; 0.3696 G./25 CC.; 2-DM. TUBE

| Time, min. | $\alpha_D$ | $K = \frac{1}{t}\log\frac{\alpha_\infty - \alpha_0}{\alpha_\infty - \alpha}$ |
|---|---|---|
| 0 | $\alpha_0$ = 3.15° ($[\alpha]_D^{23}$ 106.5) | .. |
| 1 | .20 | [0.047] |
| 1.75 | .24 | .0515 |
| 2 | .26 | .0565 |
| 3 | .30 | .0542 |
| 5 | .37 | .0532 |
| 6 | .40 | .0532 |
| 7 | .44 | .0575 |
| 8.5 | .46 | .0530 |
| 10 | .50 | .0567 |
| 12 | .54 | .0605 |
| 14 | .56 | .0590 |
| 16 | .58 | .0614 |
| 18 | .60 | [ .066] |
| 20 | .61 | [ .069] |
| 22 | .62 | .. |
| 24 | $\alpha_\infty$ = 3.63° ($[\alpha]_D^{23}$ 127.4°) | mean: .0560 |
| On addition of alkali | 3.10° ($[\alpha]_D^{23}$ 108.8°) | |

to $[\alpha]_D^{23}$ 134.6°. The latter figure represents the specific rotation of the 2-monoacetyl-α-maltose formed during this process by the opening up of the orthoester ring along the dotted line (I) and




I

immediate loss of methyl alcohol from the orthoacetyl group at position 2. The second reaction, only very slightly catalyzed by hydrogen ions, corresponded to the *downward* mutarotation of the 2-monoacetyl-α-maltose formed; its rate at 23°, $K$ = 0.0095, is comparable with the rate of the mutarotation of maltose, which in pure water at 20° has the value of $K$ = 0.0072.[5]

When the hydrogen-ion concentration, in a second experiment (Table II), was decreased to *p*H 4.8, the rate of the first reaction was found to be measurable, and the mean value of $K$ = 0.0560 was only slightly influenced by the mutarotation of the liberated 2-monoacetyl-α-maltose proceeding in the opposite direction. At the end of the first reaction, the rate accelerating effect of added alkali eliminated the slow *downward* mutarotation of the 2-monoacetyl-α-maltose formed, the equilibrium value being attained at once. From these experiments two conclusions can be drawn: first, that Freudenberg's new maltose derivatives possess α-configuration; second, that hydrolysis of these orthoesters occurs between the central carbon atom and that oxygen atom of the orthoester ring which is linked to carbon atom 1. This process is accompanied by instantaneous loss of methyl alcohol from the orthoacetyl group liberated at position 2, and by the slow downward mutarotation of the 2-monoacetyl-α-maltose so formed. In similar experiments on "γ"-monoacetylmethylrhamnoside and its dimethyl derivative, Haworth and co-workers[6] found that the first reaction is the hydrolysis of the methoxyl group of the orthoester ring, followed by the rupture of the same ring, and mutarotation to α-, and β-forms in equilibrium.

## Summary

1. From the hydrolysis studies of Freudenberg's "γ"-monoacetylmethylmaltoside in very slightly acid solutions it has been concluded that the compound and its acetyl and chloroacetyl derivatives possess α-configuration at carbon atom 1.

2. The hydrolysis occurs between the central carbon atom and that oxygen atom of the orthoester ring which is linked to carbon atom 1, followed by the immediate loss of methyl alcohol from the orthoacetyl group liberated at carbon atom 2, and by the downward mutarotation of the 2-monoacetyl-α-maltose so formed.

PRINCETON, N. J. RECEIVED DECEMBER 13, 1934

(5) Osaka, *Z. physik. Chem.*, **35**, 661 (1900).

(6) Haworth, Hirst and Samuels, *J. Chem. Soc.*, 2861 (1931).