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Note

Effect of calcium ion on rearrangement of aldos-2-uloses to aldonic acids

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It was earlier shown[1] that, in alkali, 2-anthraquinonesulfonic acid oxidizes D-glucose to D-*arabino*-hexos-2-ulose. Calcium and barium ions were found to promote the rearrangement of the intermediate aldosulose to D-mannonic acid. Other D-aldoses have now been oxidized under similar conditions. Based on the results obtained, a general theory for the calcium (or barium)-ion-catalyzed rearrangement of aldos-2-uloses is presented.

RESULTS AND DISCUSSION

Calcium ion enhanced the formation of one of the epimeric, rearrangement products of all of the aldos-2-uloses studied, except for tetros-2-ulose (see Table I).

TABLE I

FORMATION OF ALDONIC ACIDS (%) FROM D-ALDOSES ON TREATMENT WITH 4mM SODIUM 2-ANTHRAQUINONESULFONATE IN 10mM SODIUM HYDROXIDE IN THE ABSENCE AND PRESENCE OF 10mM CALCIUM CHLORIDE, AT 50°

Sugar	*Product*	*Without $CaCl_2$*	*10mM $CaCl_2$*	*10mM $CaCl_2$ in 3:2 (w/w) 1,4-dioxane–water*
Glyceraldehyde	glyceric acid	84	92	87
Erythrose	erythronic acid	27	29	22
	threonic acid	33	34	34
Arabinose or	arabinonic acid	25	11	2
ribose	ribonic acid	3	18	35
Xylose	lyxonic acid	13	71	42
	xylonic acid	4	3	5
Allose	allonic acid	5	13	22
	altronic acid	34	4	<1
Galactose	galactonic acid	23	2	<1
	talonic acid	2	40	63
Glucose or	gluconic acid	5	3	8
mannose	mannonic acid	9	57	57
Cellobiose	cellobionic acid	2	1	
	glucosylmannonic acid	2	48	
Maltose	glucosylmannonic acid	3	92	
	maltobionic acid	3	<1	

In the former cases, the favored aldonic acids had HO-2 and HO-3 *cis* in the Fischer projection formula, which indicated the existence of an intermediate complex between calcium ion and O-2 and HO-3 of the aldos-2-uloses.

The yield of the favored aldonic acid naturally depends on the degree of complexation of the aldos-2-ulose and the rate of rearrangement of the complex, relative to that of the other, competing reactions, which proceed through the uncomplexed form of the aldos-2-ulose (see Eq. *1*).

$$x/(1-x) = \frac{k_c}{k} K_c[Ca^{2+}] = K[Ca^{2+}], \qquad (1)$$

where x, k_c/k, and K_c respectively denote the molar yield of the rearrangement product, and the constants for the relative rate of rearrangement and for the complex-formation. Eq. *1* was strictly obeyed in the oxidation of maltose, where up to 95% of 4-*O*-D-glucosyl-D-mannonic acid was obtained (see Fig. 1). The value of K was conspicuously high in relation to the strength of other types of complexes of sugars with calcium ion[2].

Unlike maltosone, the other aldos-2-uloses obviously appear in significant proportions as conformers incapable of forming the complex with calcium ion, and therefore their rearrangement did not obey Eq. *1*, and the yields of their rearrangement products were lower. However, the magnitude of K remained roughly constant, as deduced from the great influence of low concentrations of calcium ion (<2mM) in the oxidation of cellobiose and glucose[1].

The increased conversion of glyceraldehyde into glyceric acid indicated that calcium ion can form a complex with the acyclic forms of aldos-2-uloses. However, the rearrangement through the acyclic form cannot be important for higher aldos-2-uloses, as shown by the inefficiency of calcium ion in the oxidation of erythrose.

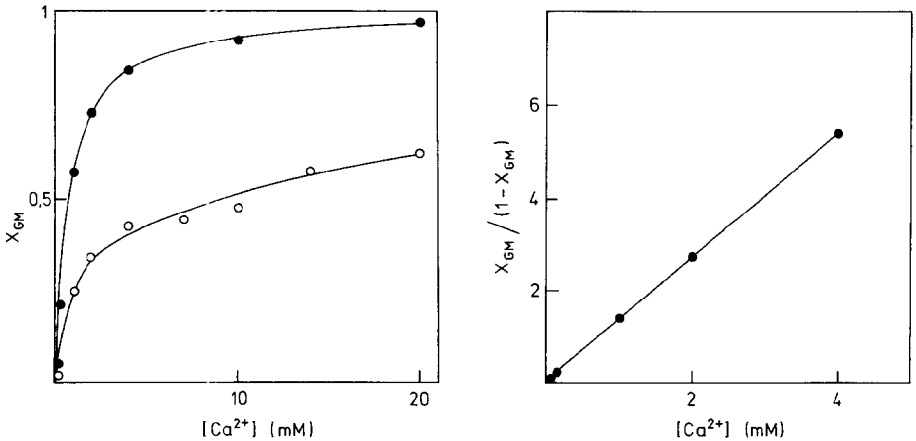

Fig. 1. Effect of calcium-ion concentration on the formation of glucosylmannonic acid from cellobiose (○) and maltose (●) in 10mM sodium hydroxide containing 4mM sodium 2-anthraquinonesulfonate, at 50°.

This is not surprising, as the aldos-2-uloses (like aldoses[3,4]) most probably exist as the aldo-pyranoses or -furanoses, because of the high tendency of aldehydes to form hemiacetals[5].

Because calcium ion had practically no effect in the oxidation of erythrose, the 2-ketoaldofuranoses may be excluded as the possible ligands in the intermediate complex. This can be explained by the relatively large, dihedral angle between O-2 and HO-3 (~30–60°) in the furanose structure.

The strong influence of calcium ion in the oxidation of cellobiose, glucose, maltose, mannose, and xylose is readily understood, because the $^4C_1$(D) conformations of the corresponding aldos-2-uloses, having no axial substituents, have a favorable dihedral angle (~0°) for complex-formation. The same is true for D-galactose, even though the favored conformation ($^4C_1$) has one axial hydroxyl group. Instead, the dihedral angle of the more-stable conformation ($^4C_1$) of D-*ribo*-hexos-2-ulose (~90°) is too large for complex-formation, which explains the smaller effect of calcium ion in the oxidation of allose. The probabilities of the presence of the $^4C_1$ and $^1C_4$ conformers of D-*erythro*-pentos-2-ulose are of the same order, and this was reflected by the relatively small influence of calcium ion on the rearrangement, in this case. It is also noteworthy that the proportion of furanoses generally tends to be high when the pyranose forms are equally stable[3,6].

Calcium ion can also catalyze the rearrangement of those α-dicarbonyl compounds that lack the vicinal hydroxyl group[7,8], but, in the case of aldos-2-uloses, the similar effect is probably compensated for by a simultaneous increase in the rate of the other, competing reactions that are initiated by enolization[7,9–11]. It must also be emphasized that the catalytic effect of calcium ion is much higher when the complex between O-2 and HO-3 is formed; *e.g.*, for maltosone, it is ~100 times that for glyoxal[8].

One interesting phenomenon not yet mentioned was the enhancement of the rearrangement in an organic solvent–water mixture in the case of those aldos-2-uloses which, otherwise, were least influenced by calcium ion. The solvent can change both the ratio of the conformers and the stability of the intermediate complex.

EXPERIMENTAL

The oxidations were conducted in pre-thermostated, de-aerated solutions under a nitrogen atmosphere. The initial concentrations of the sugar, sodium 2-anthraquinonesulfonate, and sodium hydroxide were 1, 4, and 10mM, respectively. After the treatment (for at least 3 h at 50°), the acidic reaction-products were isolated by ion-exchange[1].

The oxidation products of the monosaccharides were per-*O*-(trimethylsilyl)ated after their conversion into ammonium salts, and analyzed by g.l.c. on an OV-101 fused-silica, capillary column[12,13].

The mixture of oxidation products of the disaccharides (1–5 mg) was treated

with trifluoroacetic acid (50 μL, 5 min) in order to lactonize the glucosylhexonic acids. Pyridine (0.5 mL) and trifluorobis(trimethylsilyl)acetamide (0.4 mL) containing 5% of chlorotrimethylsilane were added, and the mixture was shaken for a moment. The per-*O*-(trimethylsilyl)ation was accomplished in less than 10 min.

The per-*O*-(trimethylsilyl)ated glucosylhexonolactones were analyzed by g.l.c. on an OV-1701 fused-silica, capillary column (25 m × 0.32 mm i.d.). The oven temperature was held for 2 min at 100°, raised at a rate of 20°/min to 250°, and held for 10 min at 250°. The injection port and manifold were kept at 280°. The flow-rate of hydrogen carrier-gas was 2.5 mL/min. The retention times of the trimethylsilyl derivatives of maltobiono-, cellobiono- (used also as the internal standard in the oxidation of maltose), 4-*O*-β-D-glucopyranosyl-D-mannono-, 4-*O*-α-D-glucopyranosyl-D-mannono-, and lactobiono-lactones (the internal standard in the oxidation of cellobiose) were 15.45, 15.60, 15.96, 16.06, and 16.10 min, respectively.

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