Carbohydrate Research, 127 (1984) 327–330
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Note

Alkali-catalyzed rearrangement of glyoxal and 3-deoxy-D-*erythro*-hexos-2-ulose

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(Received October 15th, 1983; accepted for publication, November 7th, 1983)

Although α-dicarbonyl structures are formed in carbohydrates in many elimination and oxidation reactions, little is known about the kinetics of rearrangement of these intermediates. Instead, the rearrangement of many other α-dicarbonyl compounds, including benzil[1], phenylglyoxal[2], and glyoxal[3], has been studied. Carbohydrates, however, form intramolecular hemiacetals, and this capability can make their behavior quite different. Herein, the kinetics of rearrangement of 3-deoxy-D-*erythro*-hexos-2-ulose (**1**), in addition to the effect of solvent on the rearrangement of glyoxal (**2**), are discussed.

RESULTS

Rearrangement of glyoxal (**2**). — The rearrangement of **2** was earlier found to be second-order with respect to hydroxyl ion, and largely affected by the ionic strength of the reaction medium[3]. It was proposed that, in the rate-determining step, hydroxyl ion attacks the hydrated and singly ionized **2**.

In ethanol–water, the rearrangement of **2** was markedly retarded, probably because the hydration of **2** was suppressed by the formation of hemiacetals with ethanol (see Fig. 1). In 1,4-dioxane–water, the degree of ionization of **2** was exceptionally high (as deduced from an instantaneous drop in pH after addition of **2**), and was accompanied by an increased rate of rearrangement.

No accurate values for the rate constants were calculated, as the disappearance of **2** was influenced to some extent by the composition of the stock solutions and by the mixing procedure.

Rearrangement of **1**. — In accordance with the literature[4], the volatile, per(trimethylsilyl)ated reaction products of **1** were comprised almost exclusively of 3-deoxyhexonic acids (>95%). However, the absolute yield of these rearrangement products was lower (~80 and 70 mol-% in 0.01 and M sodium hydroxide, respectively), which indicated the existence of some competing reaction, although of minor importance.

0008-6215/84/$ 03.00

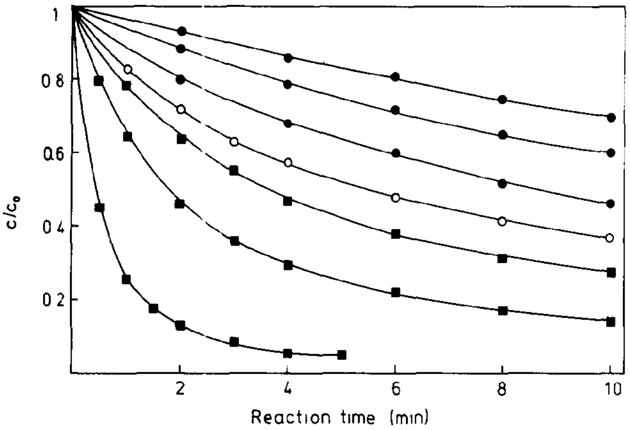

Fig. 1. Disappearance of 5mM glyoxal (**2**) in 5mM sodium hydroxide in 70, 44, and 21% (w/w) ethanol–water, and 26, 51, and 76% (w/w) 1,4-dioxane–water, reading down, at 25°.

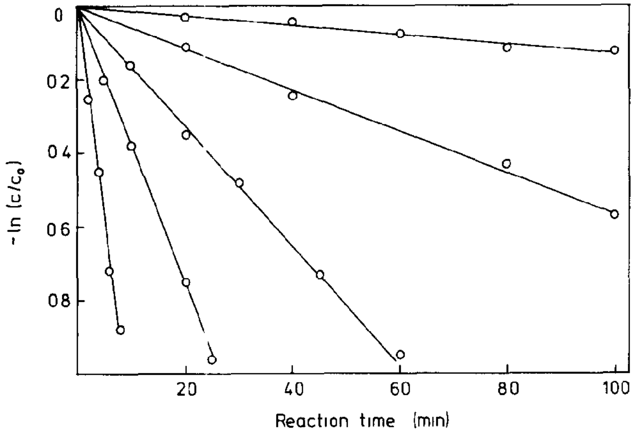

Fig. 2. Disappearance of 1.5mM compound **1** at pOH 4, 3, 2, 1, and 0, reading clockwise, at 25°.

Expectedly, the disappearance of **1** followed *pseudo*-first-order kinetics, according to Eq. *1* (see Fig. 2).

$$\ln (c/c_0) = -k.t \tag{1}$$

The reaction medium had a very limited influence on the disappearance of **1** (compared with **2**), and this was obviously related to its low degree of hydration. The rate of disappearance was slightly increased both in ethanol–water and 1,4-dioxane–water (see Table I). Increasing ionic strength (μ <1) accelerated the reaction, roughly according to Eq. *2*.

$$\log (k/k_0) = 0.08 \sqrt{\mu} \tag{2}$$

TABLE I

EFFECT OF SOLVENT ON THE RATE OF DISAPPEARANCE OF **1** IN 0.1M SODIUM HYDROXIDE AT 25°

Solvent	*Non-aqueous % (w/w)*	$k.10^3$ (s^{-1})
Ethanol	0	0.52
	16	0.55
	34	0.60
	54	0.65
1,4-Dioxane	21	0.68
	41	0.80
	61	1.25

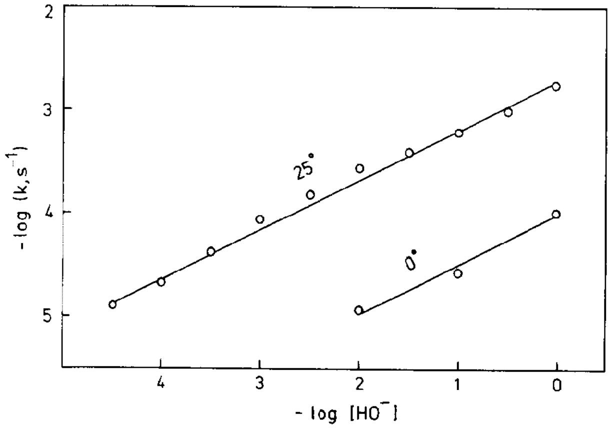

Fig. 3. Effect of hydroxyl-ion concentration on the rate of disappearance of **1** at 0 and 25°.

The disappearance of **1** was approximately proportional to the square root of the hydroxyl-ion concentration (see Fig. 3). For comparison, it may be mentioned that the rearrangement of both benzil[1] and phenylglyoxal[2] have proved to be first-order, and that of glyoxal[3] second-order, with respect to hydroxyl ion.

The activation energies of the rearrangement of **1** and **2** were of the same order [82 and 76 (ref. 3) kJ.mol^{-1}, respectively], whereas the absolute values of the rate constant of **1** were significantly lower.

EXPERIMENTAL

Disappearance of glyoxal (**2**). — To a thermostated solution of 5mM sodium hydroxide (100 mL) was added 2M glyoxal (250 μL) under vigorous stirring. The pH of the solution was monitored, and the consumption of **2** was calculated as the consumption of alkali (from the decrease in pH).

Preparation of **1**. — Compound **1** was prepared from D-glucose by the method of Madson and Feather[5], and stored, as an ~0.1M solution in methanol, in a refrigerator. To determine the concentration and purity of the stock solution, 0.1M D-gluconic acid (internal standard; 0.5 mL), 30% hydrogen peroxide (30 μL), and M ammonia (2 mL) were added in a 0.5-mL sample. The mixture was kept for 30 min at room temperaure, and then evaporated to dryness. The per(trimethylsilyl)ated acids were analyzed by g.l.c.[6,7]. The proportion of 2-deoxy-D-*erythro*-pentonic acid was ~95% of the reaction products.

Reaction products of **1**. — To a de-aerated solution of sodium hydroxide (0.01–1M, 10 mL) was added a mixture of **1** and D-gluconic acid (0.05M each, 0.5 mL) under a nitrogen atmosphere. To complete the reaction, the solution was kept overnight at room temperature, and then the acidic reaction-products were converted into their ammonium salts, and these analyzed by g.l.c. as their per(trimethylsilyl) derivatives[6,7].

Disappearance of **1**. — The solutions having pH 9.5–11 were mixtures of M sodium hydrogencarbonate and 0.5M sodium carbonate. Other alkali solutions were prepared from sodium hydroxide and sodium chloride (to provide a constant ionic strength, usually $\mu = 1$).

After thermostating, 0.1M compound **1** (150 μL) was added to alkali solution (10 mL) under vigorous stirring. To monitor the reaction, a 250-μL sample of the solution was added to a test tube containing 2M sulfuric acid (5 mL). The tube was stoppered tightly, and shaken. After all of the samples had been taken, the tubes were heated for 60 min at 80° to convert the unreacted **1** into 5-(hydroxymethyl)-2-furaldehyde. The tubes were cooled to room temperature in a water bath, the absorbances of the solutions were measured at 283 nm, and the disappearance rate-constant was calculated according to Eq. *1*.

ACKNOWLEDGMENT

Thanks are expressed to Professor Eero Sjöström for valuable suggestions during the preparation of the manuscript.

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