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Salt Effects on the Intramolecular Cannizzaro Reaction of Phenylglyoxal. Specific Acceleration by Calcium Ion

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Synopsis. Effects of added salts on the rate of alkaline rearrangement of phenylglyoxal to mandelic acid were examined in aqueous solution at 30 °C. The reaction showed positive salt effects. Specific acceleration was found with some metal ions, the efficiency decreasing in the order $Ca^{2+} > Tl^{+} > Sr^{2+} > Ba^{2+}$.

The intramolecular Cannizzaro reaction of α-keto aldehydes in alkaline solutions to give α-hydroxy carboxylate ions has long been known and established to proceed through a 1,2-hydride shift.[1–4] The reaction has recently attracted renewed interest in relation to a formally similar reaction catalyzed by the glyoxalase system,[5–9] which involves zinc ion as a constituent essential for the enzymatic activity.[10] Enzyme-model reactions were found to be affected only very slightly by added magnesium ion in aqueous solutions.[7,8b] In the course of the studies on some model reactions of glyoxalase I involving metal ion catalysis,[11,12] we have found that Ca^{2+} and some other metal ions effectively accelerate the alkaline rearrangement of phenylglyoxal to mandelic acid (an intramolecular Cannizzaro reaction). The present communication describes results of the studies on such metal ion catalyses.

Experimental

Phenylglyoxal hydrate was prepared according to the literature.[11,13] Inorganic salts of reagent grade were used without further purification. Glass-distilled water was used throughout the work.

The Cannizzaro reaction was initiated by addition of 0.03 cm^3 of an aqueous stock solution of phenylglyoxal (typically 7×10^{-3} M (1 M=1 mol dm^{-3})) into 3 cm^3 of an alkaline solution which had been equilibrated at 30 ± 0.1 °C in a stoppered quartz cuvette. Reactions were monitored by following the decrease in UV absorption of phenylglyoxal at 250 nm on a Shimadzu UV 200 spectrophotometer. Pseudo-first-order plots were linear over 3 lifetimes for all the runs.

Results and Discussion

At a constant ionic strength of 0.10 maintained with added KCl, the rates are dependent on [NaOH] in accord with Scheme I as reported previously:[5] $k_1=1.5\times10^{-4}\ s^{-1}$ and $k_2K_2=5.7\times10^{-2}\ M^{-1}\ s^{-1}$ using an assumed value of $K_1=250\ M^{-1}$.[5]

With the alkaline concentration and ionic strength maintained at [NaOH]=0.01 M and $\mu=0.10$, respectively, the effects of different salts on the rate were examined. The results are summarized in Table 1. While the alkali metal ions and anions show virtually no specific effect, Ca^{2+}, Tl^{+}, Sr^{2+}, and Ba^{2+} accelerate the reaction significantly. Of the various cations examined, Ca^{2+} is the most effective, showing a 13-fold acceleration at its concentration of 0.01 M.

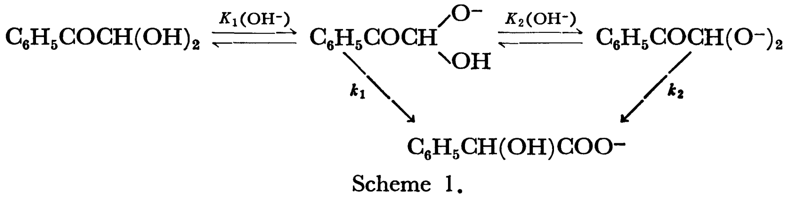
Table 1. Effects of added salts on the rate of rearrangement of phenylglyoxal[a)]

Salt	$10^4\ k_{obsd}/s^{-1}$
KCl	6.10
KNO_3	6.20
NaCl	6.15
$KCl+CaCl_2$[b)]	81.3
$KCl+SrCl_2$[b)]	16.4
$KCl+BaCl_2$[b)]	11.1
KNO_3+TlNO_3[b)]	21.4

a) [NaOH]=0.01 M, $\mu=0.10$, 30 °C. b) The concentration of a second salt was 0.01 M.

When [NaOH] was kept constant at 0.01 M, the rate increased linearly with [$CaCl_2$] as is shown in Fig. 1. The slope is greater at lower ionic strength: 0.71 $M^{-1}\ s^{-1}$ at $\mu=0.10$ and 0.44 $M^{-1}\ s^{-1}$ at $\mu=0.50$. The effect of Ca^{2+} is thus largely dependent on the ionic strength. Figure 2 illustrates some details of such a dependence of the Ca^{2+} catalysis on μ. As is apparent from Fig. 2, the salt effect is positive in the absence of Ca^{2+} but is negative in the presence of Ca^{2+} ([$CaCl_2$]=0.001 M). In effect, the apparent catalytic efficiency of Ca^{2+} is the greater, the smaller the ionic strength. Addition of Ca^{2+} at a concentration as low as 10^{-3} M accelerates the reaction nearly 5-fold at the extrapolated zero ionic strength while it enhances the rate only by a factor less than 1.2 at ionic strengths greater than 0.5.

The marked catalytic effects of non-transition metal ions like Ca^{2+} found here may closely be related to the earlier observations of Pfeil *et al.*[14] They found that TlOH, $Ba(OH)_2$, and $Sr(OH)_2$ are much better catalysts for the benzilic acid rearrangement than alkali metal hydroxides in aqueous dioxane. They have not examined effects of $Ca(OH)_2$.[15] A univalent ion Tl^{+} also significantly accelerates the present reaction. Since the benzilic acid rearrangement takes place essentially in the same way as does the present



Scheme 1.

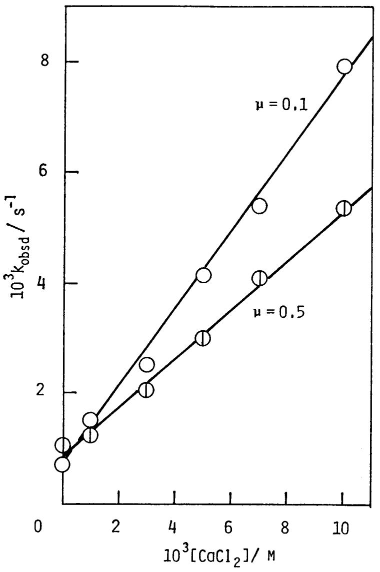


Fig. 1. Effects of [$CaCl_2$] on the rate of rearrangement of phenylglyoxal in alkaline solution ([NaOH] = 0.01 M) at $\mu = 0.10$ (○) and $\mu = 0.50$ (⦶). Ionic strength was adjusted with KCl.

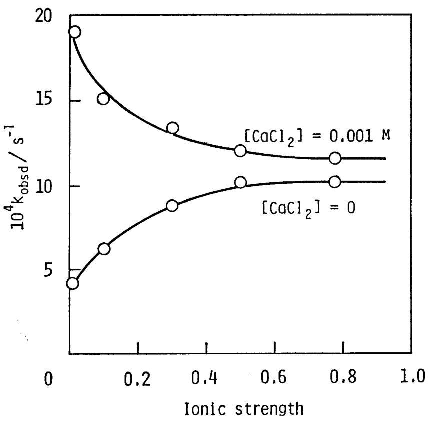
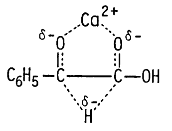


Fig. 2. Effects of ionic strength on the rate of rearrangement of phenylglyoxal in alkaline solution ([NaOH] = 0.01 M) in the absence and in the presence of Ca^{2+} ([$CaCl_2$] = 0.001 M) at 30 °C. Ionic strength was increased by the addition of KCl.

reaction,[17] the mechanisms of these catalytic actions of metal ions must be similar to each other.

The observed positive salt effect on the rearrangement of phenylglyoxal is not unexpected for a reaction of charged species.[4] The specific effects of Ca^{2+} may be accounted for by its influence either on the equilibrium constants, K_1 and/or K_2, or on the rate constants, k_1 and/or k_2. In any case, the transition state for the hydride shift must be stabilized by the formation of a Ca^{2+} chelate. Added potassium ion may compete with Ca^{2+} to interact with the ionized phenylglyoxal hydrate, thus greatly interfering with the transition-state chelation of Ca^{2+}. This would be a possible reason for the negative salt effects on the Ca^{2+} ion-catalyzed rearrangement. Stability constants for some metal chelations are also known to depend strongly on the ionic strength.[18]



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