

The Hydrolysis Kinetics of Glucono- δ -lactone in Solutions without Anion Catalysis and a Systematical Error in Weakly Buffered pH-static Kinetics

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The hydrolysis of glucono- δ -lactone has been investigated by a pH-static method in the pH-range from 4.5 to 8.5. Kinetic measurements have been made in pure water or in very dilute buffer solutions to avoid anion catalysis. The rate constants for water and hydroxide ion catalysis have been determined to $k_{\text{H}_2\text{O}} = 4.59 \times 10^{-5} \text{ s}^{-1}$ and $k_{\text{OH}^-} = 2.76 \times 10^3 \text{ s}^{-1} \text{ l mol}^{-1}$, at 25 °C.

The temperature dependency has been investigated, and the activation energies of the water and hydroxide ion catalyzed reactions have been determined to $E_{\text{H}_2\text{O}}/R = 7360 \text{ K}^{-1}$ and $E_{\text{OH}^-}/R = 8880 \text{ K}^{-1}$.

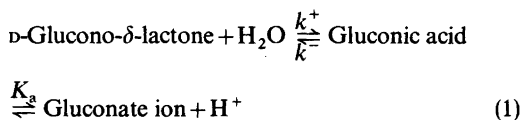
In solutions with very low buffer capacity too high initial rates were observed. These are shown to be caused by pH-gradients in the solution due to insufficient stirring. A model describing the effect has been set up, and correct reaction rates are shown to be obtained after sufficient time. Furthermore, it is shown that the mixing time for the added base must be several orders of magnitude lower than the half-life of the reaction, thus introducing uncertainties in kinetic constants determined from initial slopes in weakly buffered solutions.

In the electrochemical oxidation of glucose on Pt, the δ -lactone of gluconic acid has been shown to be a primary reaction product.^{1,2}

To investigate the role of the lactone and gluconic acid as possible inhibitors of the glucose oxidation or as sources of further oxidation steps, a detailed knowledge of the kinetics of the hydrolysis of glucono- δ -lactone in different ionic media is necessary.

Several authors have investigated the hydrolysis

of the lactone^{3–7} and have shown the reaction scheme to be as given in eqn. (1).



Mitchell and Duke⁵ have shown the interconversion of the δ -lactone to the γ -lactone to be insignificant in the pH-range investigated in the present work.

The kinetics of the hydrolysis has been investigated by polarimetric^{3,5,6} colorimetric⁴ and pH-static methods³ and the results obtained show large discrepancies. An explanation of most of the discrepancies was given by Pocker and Green⁶ who carefully investigated the role of the buffer system used. They showed the reaction to be general acid-base catalyzed, an effect previous workers did not take into account, and determined the catalytic constants for a variety of acid-base pairs. The constants for H_3O^+ , H_2O and OH^- were determined by measuring the rate constants at a constant ionic strength of 0.5 mol l^{-1} with different buffer concentrations and then extrapolated to zero buffer concentration.

An inherent drawback of this method is that the activity coefficients of H_3O^+ and OH^- are needed in order to determine the actual concentrations.

At present no appropriate theoretical method to do this is known except for very dilute solutions.

One way of avoiding the influence of the buffer system is to determine the kinetic constants pH-

statically in pure water or in an inert supporting electrolyte.

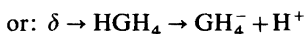
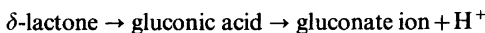
In the present work the hydrolysis constants for glucono- δ -lactone have been determined by a pH-static method in pure water or with very low buffer concentrations (4×10^{-3} M) in the pH range from 4.5 to 8.5, which has allowed the catalytic constants for water and OH^- to be determined. Special care has been taken to avoid the influence from the low buffering capacity.

The activation energy. In spite of its biological importance most of the measurements of the hydrolysis of the lactone have been made at ambient temperature and very few attempts have been made to determine the activation energy. Sawyer and Bagger³ have determined the activation energy at pH=4 in the temperature range from 20 to 25 °C and Pocker and Green⁶ have determined it at pH=4.4 in the range from 20 to 45 °C using data extrapolated to zero buffer concentration.

In the present work rate constants determined pH-statically in the temperature range from 25 to 37 °C at different pH values have been used to determine the activation energy of both the water catalyzed and the hydroxide ion catalyzed hydrolysis of glucono- δ -lactone.

THEORY

In the pH-static experiment the total amount of base used to neutralize the protons formed in the overall reaction:



is measured.

Reversible first order kinetics of reaction (1) leads to

$$\ln \frac{c_\delta - c_{\delta,\infty}}{c_\delta^0 - c_{\delta,\infty}} = (k_+ + k_-)t$$

The amount of hydroxide ions added per liter at the time t is

$$[\text{OH}^-]_t = c_{\text{GH}_4^-}$$

The mass balance

$$c_\delta^0 - c_\delta = c_{\text{GH}_4^-} + c_{\text{HGH}_4}$$

gives by the use of

$$c_{\text{HGH}_4} = \frac{a_{\text{H}^+}}{K_a} \cdot \gamma \cdot c_{\text{GH}_4^-} = A[\text{OH}^-]_t$$

$$c_\delta^0 - c_\delta = (1 + A)[\text{OH}^-]_t$$

and

$$\frac{c_\delta - c_{\delta,\infty}}{c_\delta^0 - c_{\delta,\infty}} = \frac{[\text{OH}^-]_\infty - [\text{OH}^-]_t}{[\text{OH}^-]_\infty} \quad (2)$$

which leads to the final integrated rate expression (3), where

$$\ln([\text{OH}^-]_\infty - [\text{OH}^-]_t) = -k't + \ln[\text{OH}^-]_\infty \quad (3)$$

$$k' = (k_{\text{H}} + c_{\text{H}^+} + k_{\text{OH}} - c_{\text{OH}^-} + k_{\text{H}_2\text{O}})[1 + K_\delta^{-1} / (1 + K_a/c_{\text{H}^+})]$$

THE TEMPERATURE DEPENDENCY

In the pH-range where only water and hydroxyl ion catalysis takes place the rate constant is

$$k' = k_{\text{H}_2\text{O}} + k_{\text{OH}} - c_{\text{OH}^-} = k_1 + k_2$$

In a temperature range which is small compared to the absolute temperature the following approximation can be used:⁸

$$\ln k' \cong \ln(k_\infty^0 + k_2^0) + \frac{k_1^0 \cdot \frac{E_1^*}{R} + k_2^0 \cdot \frac{E_2^*}{R}}{k_1^0 + k_2^0} \cdot \Delta \frac{1}{T}$$

This shows that the energy of activation E^*/R found by a plot of $\ln k'$ vs. T^{-1} is a mean value of the activation energies of the two parallel reactions

$$\frac{E^*}{R} = \frac{k_1^0 \frac{E_1^*}{R} + k_2^0 \frac{E_2^*}{R}}{k_1^0 + k_2^0} \quad (4)$$

EXPERIMENTAL

In the experiments a RADIOMETER pH-stat (TTT2 + ABU13 + REA300), was used, and the thermostated (150 ml) reaction vessel was deaerated with nitrogen. To avoid leakage from the burette tip in the long time runs (up to 900 min) the glass tip of the burette was drawn to a capillary and bent so the tip ended just above the surface of the solution.

The D-glucono- δ -lactone obtained from Merck, Darmstadt, melted at 151–153 °C and was used without further purification. All other chemicals were analytical grade, also from Merck.

To keep the volume changes negligible the lactone concentration was *ca.* $2 \times 10^{-2} \text{ mol l}^{-1}$ and 1 mol l^{-1} NaOH was used as titrant. In the initial runs the $[\text{OH}^-]_t$ vs. time curve showed steps due to pH changes caused by the addition of base [the base is not added continuously but in small portions (10^{-2} ml)]. To diminish this effect a small amount of phosphate buffer ($4 \times 10^{-3} \text{ M}$) was added to the solution. This buffer concentration is so low that the influence on the rate constant is insignificant at $\text{pH} \geq 7$ and less than 5% at $\text{pH} = 6.25$.

After addition of buffer the $[\text{OH}^-]_t$ vs. time curves became smooth, but a slight curvature of the $\log([\text{OH}^-]_t - [\text{OH}^-]_\infty)$ vs. time curve remained as can be seen in Fig. 1. This curvature is due to a difference in the mean pH of the solution and the pH measured by the glass electrode and is caused by an insufficient dilution and mixing of the added base. This effect is treated in detail in the appendix, where the correct slope is shown to be obtained after sufficient time. Increased stirring did remove the curvature and thus shows the effect to be solely caused by the inhomogeneity of the solution. At

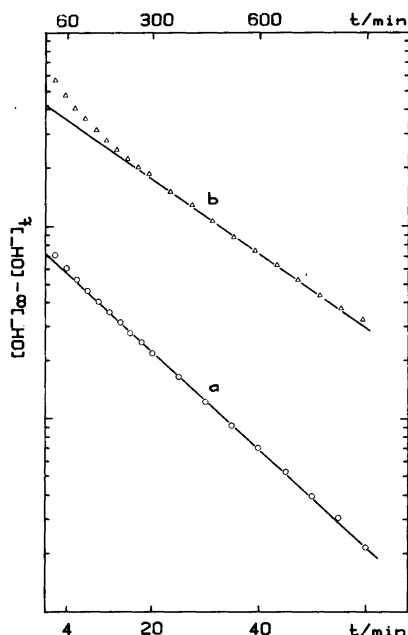


Fig. 1. Plot of $\log([\text{OH}^-]_\infty - [\text{OH}^-]_t)$ vs. time. a: 0.0117 M lactone in 0.004 M phosphate buffer, $\text{pH} = 7.5$, $t = 25^\circ\text{C}$. b: 0.0147 M lactone in pure water, $\text{pH} = 4.5$, $t = 25^\circ\text{C}$.

these high stirring rates however, excessive splashing took place. A little lower stirring rate was therefore used and the rate constants were determined from the straight portion of the curve.

At $\text{pH} = 4.5$ and 4.75 the rate constant is so low that even the small amount of buffer, which was used at the higher pH values would cause significant error. Fortunately, at these pH values the buffer capacity of water and the gluconic acid–gluconate pair is sufficient to give reasonably straight lines as can be seen in Fig. 1b.

RESULTS AND DISCUSSION

Rate constants determined in the pH-range from 4.5 to 8.5 at 25°C are shown in Fig. 2.

Eqn. 3 in the form

$$k' = (k_{\text{H}_2\text{O}} + k_{\text{OH}^-} \times 10^{\text{pH}-14}) [1 + K_\delta^{-1} / (1 + K_a / 10^{-\text{pH}})]$$

is fitted to the experimental points with $K_\delta = 3.68^*$ and $K_a = 2.40 \times 10^{-4} \text{ l mol}^{-1}$ and substituting activities with concentrations in those very diluted solutions ($\gamma_\pm \approx 0.998$).

The best values found are

$$k_{\text{H}_2\text{O}} = 4.59 \times 10^{-5} \text{ s}^{-1} \text{ and } k_{\text{OH}^-} = 2.76 \times 10^3 \text{ s}^{-1} \text{ l mol}^{-1}$$

* To determine the value of $K_\delta = a_{\text{HGH}_4} / a_\delta$, we have used the value of $K_L = a_{\text{HGH}_4} / (a_\delta + a_\gamma) = 1.53^7$ determined by Skibsted and Kilde⁷ and the value of $K_{\delta,\gamma} = a_\delta / a_\gamma = 0.712$ determined by Mitchell and Duke.⁵

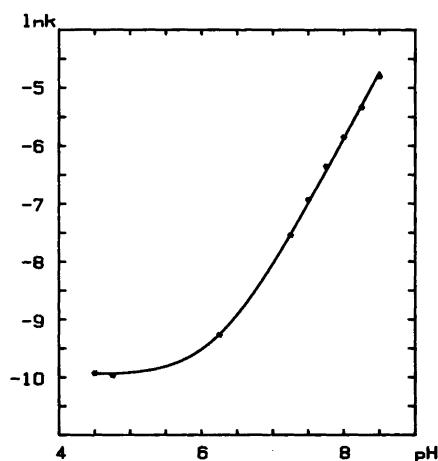


Fig. 2. Hydrolysis of glucono- δ -lactone. pH-dependence of the rate constant. *, experimental values; -, values computed with $k_{\text{H}_2\text{O}} = 4.59 \times 10^{-5} \text{ s}^{-1}$ and $k_{\text{OH}^-} = 2.76 \times 10^3 \text{ s}^{-1} \text{ l mol}^{-1}$.

and the k' vs. pH curve calculated from these values is also shown in Fig. 2.

The value of $k_{\text{H}_2\text{O}} = 4.59 \times 10^{-5} \text{ s}^{-1}$ is very close to the value of $k_{\text{H}_2\text{O}} = 4.3 \times 10^{-5} \text{ s}^{-1}$ determined by Pocker and Green and lower than the values determined by other workers in cases where anion catalysis or pH-stat errors might have influenced the results. The value of $k_{\text{OH}^-} = 2.76 \times 10^3 \text{ s}^{-1} \text{ l mol}^{-1}$, however, differs from the value of $k_{\text{OH}^-} = 1.9 \times 10^3 \text{ s}^{-1} \text{ l mol}^{-1}$ determined by Pocker and Green, and the difference is larger than the experimental uncertainties of the constants presented in this paper. One reason for this discrepancy might be that the values determined by Pocker and Green are obtained by extrapolation to infinite dilution from ionic strengths where the theoretical expressions used for activity coefficients are inadequate.

The values determined by Jermyn⁴ and Mitchell and Duke⁵ ($4 \times 10^3 \text{ s}^{-1} \text{ l mol}^{-1}$) may be expected to be larger than the values presented here as they are determined in buffers, where anion catalysis is present.

At pH = 6.25, 7.24 and 7.75 the rate constants were determined as function of temperature in the range from 25°C to 37°C, and the results are shown in Fig. 3.

The plots of $\log k$ vs. T^{-1} are seen to give straight lines and the apparent activation energies are found to be $E^*/R = 7360$, 8500 and 8840 K^{-1} at pH = 6.25, 7.25, and 7.75. The use of eqn. (4) then gives the following activation energies of the water catalyzed and the hydroxide ion catalyzed reactions:

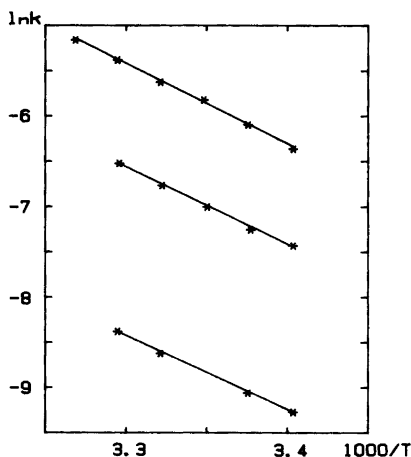


Fig. 3. Temperature dependence of the rate constants at pH = 6.25 (upper curve), pH = 7.25 and pH = 7.75 (lower curve).

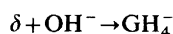
$$E_{\text{H}_2\text{O}}^*/R = 7360 \text{ and } E_{\text{OH}^-}^*/R = 8880 \text{ K}^{-1}.$$

The $E_{\text{H}_2\text{O}}^* = 61.1 \text{ kJ mol}^{-1}$ ($= 14.6 \text{ kcal mol}^{-1}$) value is in fair agreement with activation energies of $15.3 \text{ kcal mol}^{-1}$ determined by Sawyer and Bagger³ at pH = 4.0 and 14 kcal mol^{-1} determined by Pocker and Green⁶ at pH = 4.44.

APPENDIX

A systematical error in weakly buffered pH static kinetics. As many reactions studied by pH static technique are general acid-base catalyzed it is often necessary to work in slightly buffered medium to prevent the catalytic effect of the buffer system. To avoid an appreciable dilution the solution added to maintain pH at the preset value normally has a pH far from that of the reaction medium. Therefore, gradients in pH will be present at the burette outlet and the reaction will be accelerated in this region. In the following the influence of the finite mixing time on the observed overall reaction rate will be analyzed and it will be shown that this effect explains the deviations from a linear $\log c$ versus t relationship observed in the present work.

Consider the reaction



with the rate expression

$$\frac{dc_\delta}{dt} = -k_{\text{H}_2\text{O}}c_\delta - k_{\text{OH}^-}c_{\text{OH}^-}c_\delta$$

in a volume V_0 of a solution with the preset OH^- concentration \bar{c}_{OH^-} containing a buffer system HA/A^- with concentrations c_{HA}^0 and $c_{\text{A}^-}^0$.

Let ΔV_j be the volume of NaOH solution, with concentration $c_{\text{OH}^-}^0$, added from the pH stat burette in the time interval $t_j/t_j + \Delta t_j$ to compensate for the OH^- consumption of the reaction. After the addition this volume will be diluted with bulk solution and to the time t it will be contained in the volume V_j . Initially when the OH^- concentration is large compared to the buffer concentration the mixing is a simple dilution process and c_{OH^-} is determined by:

$$\begin{aligned} c_{\text{OH}^-} &= \frac{c_{\text{OH}^-}^0 \Delta V_j - c_{\text{HA}}^0 (V_j - \Delta V_j)}{V_j} \\ &\simeq c_{\text{OH}^-}^0 \frac{\Delta V_j}{V_j} \end{aligned} \quad (\text{A1})$$

After a certain time τ the base added is neutralized by the buffer and the concentration drops rapidly to the preset value, \bar{c}_{OH^-} . As c_{OH^-} is large compared to c_{OH^-} during the mixing period, the increased rate of the base catalyzed hydrolysis of glucono-lactone in the volume element V_j is given by

$$\frac{dn_{\delta,j}}{dt} = -V_j k_{\text{OH}^-} c_{\text{OH}^-} c_{\delta} \quad (\text{A2})$$

or combined with eqn. (A1)

$$\frac{dn_{\delta,j}}{dt} = -k_{\text{OH}^-} c_{\text{OH}^-}^{\circ} c_{\delta} \Delta V_j \quad (\text{A3})$$

This rate is independent of details in the mixing process, and the overall rate increase due to gradients in pH is only depending on the amount of base added in the mixing period τ . As τ must be small compared to the half time of the reaction, the overall reaction rate can be considered constant and the volume added in the time period τ is

$$V_{\varepsilon} = -\tau \frac{V_o}{c_{\text{OH}^-}^{\circ}} \frac{dc_{\delta}}{dt} \quad (\text{A4})$$

where V_o is the total reaction volume. The overall rate increase can therefore be written as:

$$\frac{dn_{\delta}}{dt} = -k_{\text{OH}^-} V_o \tau \frac{d\bar{c}_{\delta}}{dt} \quad (\text{A5})$$

and the reaction rate observed is:

$$\frac{d\bar{c}_{\delta}}{dt} = -k' \bar{c}_{\delta} + k_{\text{OH}^-} \tau \frac{d\bar{c}_{\delta}}{dt} \quad (\text{A6})$$

where $k' \bar{c}_{\delta}$ is the ideal contribution. Integrating (A6) yields the observed concentration vs. time relation.

$$\ln \frac{\bar{c}_{\delta}}{c_{\delta}^{\circ}} + k_{\text{OH}^-} \tau (c_{\delta}^{\circ} - \bar{c}_{\delta}) = -k' t \quad (\text{A7})$$

where the term linear in \bar{c}_{δ} is the deviation from ideal behavior caused by the finite mixing time.

In Fig. 4 eqn. (A7) is compared to an experimental curve. Reasonable agreement is obtained although the linear behaviour is observed somewhat earlier than predicted by the model. This is probably

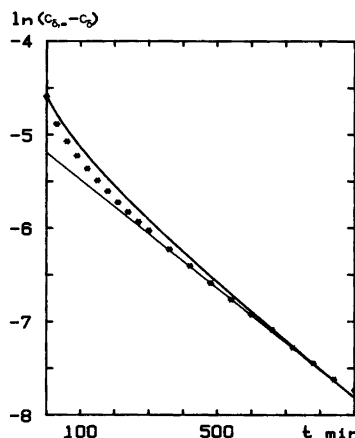


Fig. 4. Deviations from first order kinetics introduced by insufficient stirring. *, experimental values determined at pH=4.5 and $t=25^{\circ}\text{C}$; -, values calculated from eqn. (A7) with $k_{\text{OH}^-} \tau = 59$, $k_{\text{H}_2\text{O}} + k_{\text{OH}^-} c_{\text{OH}^-} = 4.91 \times 10^{-5}$ and $\Delta_{\delta}^{\circ} = 0.0102$ M.

due to a decrease in mixing time caused by an increase in buffer capacity when gluconic acid is formed, which reduces the volume necessary to neutralize the base added. It is noted that a mixing time of only 0.02 s being six orders of magnitude smaller than the half time of the reaction may cause an appreciable deviation from linear behaviour. Therefore, great attention should be paid to the mixing efficiency and rate constants should not be determined from initial slopes in this kind of work.

$$t_{\frac{1}{2}} \gg \frac{k_{\text{OH}^-} \tau (c_{\delta}^{\circ} - \bar{c}_{\delta})}{k'} \sim \frac{k_{\text{OH}^-} \tau c_{\delta}^{\circ}}{k'} \quad (\text{A8})$$

may be of value in the planning of experiments and in the control of experimental results.

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