# **115.** *The Kinetics of the Alkaline Hydrolysis of Some γ-Lactones.*

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The rate of hydrolysis by aqueous sodium hydroxide of valerolactone, phthalide, and 5-aminophthalide has been determined at three temperatures by conductivity measurements, and that of butyrolactone at two temperatures. For valerolactone and phthalide, similar measurements have been carried out in ethanol–water mixtures. When $1/\sqrt{E}$ (or $E$) is plotted against log $PZ$, it is found that the data for all the reactions fall on a single straight line. A source of error in earlier measurements of the hydrolysis of phthalide and its derivatives is indicated.

THE alkaline hydrolysis of γ-lactones is difficult to measure by titration methods on account of its speed and sensitiveness to carbon dioxide, but it can be conveniently followed at high dilutions by conductivity measurements (cf. Caldin and Wolfenden, J., **1936**, 1239); the results obtained offer a convenient field for the analysis of the kinetics in terms of the $E$ and $PZ$ factors studied by Hinshelwood and his collaborators. Measurements have accordingly been made of the bimolecular reaction of sodium hydroxide with phthalide and valerolactone in water and ethanol–water mixtures; the alkaline hydrolysis of butyrolactone and 5-aminophthalide has also been measured in aqueous solution only. Except for butyrolactone, which is hydrolysed too rapidly at 25° for accurate measurement, the rates have been determined at 25°, 15°, and 0°.

## EXPERIMENTAL.

*Materials.*—Absolute alcohol was dried over freshly ignited lime and distilled. The alkali solution was made by dissolving pure sodium hydroxide in distilled water free from carbon dioxide; to remove any traces of carbonate, an amount of barium hydroxide equivalent to 1% of the sodium hydroxide was finally added. Butyrolactone was prepared by the method of Marvel and Birkhimer (*J. Amer. Chem. Soc.*, **1929**, **51**, 260), and valerolactone by that of Taylor and Close (*ibid.*, **1917**, **39**, 422); phthalide was obtained by recrystallising a commercial specimen (m. p. unchanged), and 5-aminophthalide by reduction of 5-nitrophthalide in alcoholic solution with ammonium sulphide (Teppema, *Rec. Trav. chim.*, **1923**, **42**, 30).

*Method.*—The weighed reactants were rapidly mixed without access to the atmosphere, and blown into the conductivity cell by a stream of air free from carbon dioxide; conductivity measurements could be begun about 5 minutes after the mixing of the reactants. The concentration of reactants ranged from 5 to 10 × $10^{-3}$ N; the conductivity cell had a capacity of *ca.* 20 c.c. and a cell constant of 0·455. It is necessary to deduce the velocity constant without knowledge of the time at which reaction effectively begins. For our present purposes the following expression is readily deduced for a bimolecular reaction between solutions of equivalent concentration

$$k = \frac{(R_2 - R_1)(R_\infty - R_0)R_\infty}{a(R_\infty - R_1)(R_\infty - R_2)(t_2 - t_1)R_0}$$

where $k$ is the velocity constant, $R_0$, $R_1$, $R_2$, and $R_\infty$ are the resistances of the reacting mixture at times $t = 0, t_1, t_2$, and infinity, respectively, and $a$ is the initial concentration of the reactants. $R_0$ was determined by independent measurements of the equivalent conductivity of sodium hydroxide when dissolved in the various solvents used over the concentration range used in the kinetic experiments. Conductivity measurements were continued until at least three-quarters of the lactone had been hydrolysed. $R_\infty$ was measured after the cell had been warmed, with precautions to prevent distillation, to accelerate completion of reaction. The absorption of carbon dioxide by the reaction mixture (although causing a deficiency in hydroxyl ion) affects the readings so as to produce a velocity constant increasing steadily as the reaction proceeds, as well as an abnormal value for $R_\infty$; it was therefore possible, by internal evidence as well as by blank experiments, to test the effectiveness with which carbon dioxide had been excluded.

*Results.*—The velocity constants, $k$ (in l. g.-mol.$^{-1}$ min.$^{-1}$), are recorded in Table I for four lactones under the headings of solvent composition and temperature. Every constant is the mean derived from at least three independent experiments.

TABLE I.

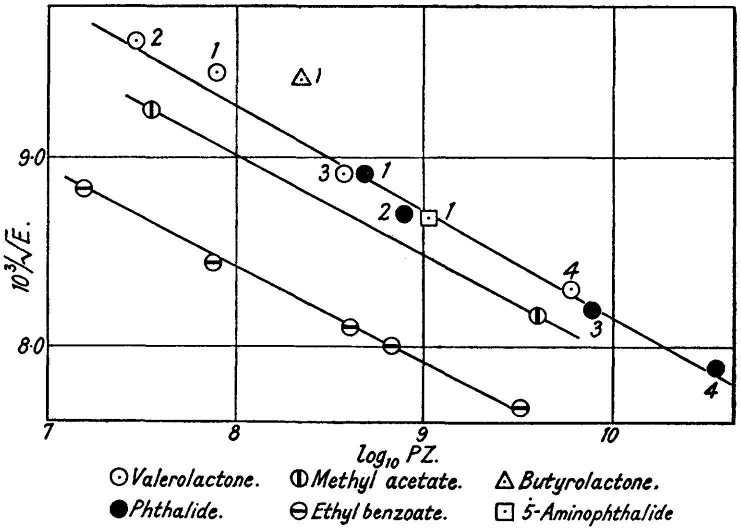
| Solvent. | *k*. $T = 0°$. | $T = 15°$. | $T = 25°$. | Solvent. | *k*. $T = 0°$. | $T = 15°$. | $T = 25°$. |
|---|---|---|---|---|---|---|---|
| | Valerolactone. | | | | Phthalide. | | |
| $H_2O$ ............ | 4·94 | 14·4 | 28·0 | $H_2O$ ............ | 2·35 | 7·78 | 16·4 |
| 21·5% EtOH... | 3·79 | 10·9 | 20·5 | 21·5% EtOH | 1·24 | 4·44 | 9·41 |
| 40% EtOH ... | 1·80 | 6·10 | 12·4 | 40% EtOH ... | 0·532 | 2·27 | 5·30 |
| 60% EtOH ... | 0·88 | 3·64 | 8·30 | 60% EtOH ... | 0·260 | 1·27 | 3·10 |
| | Butyrolactone. | | | | 5-Aminophthalide. | | |
| $H_2O$ ............ | 11·8 | 34·9 | — | $H_2O$ ............ | 1·36 | 4·90 | 10·6 |

After conversion of the velocity constants into terms of seconds, instead of minutes, values of the heat of activation *E* and of $\log_{10} PZ$ have been calculated; these are given in Table II.

TABLE II.

| Lactone. | Solvent. | *E*. | $\log_{10} PZ$. | Lactone. | Solvent. | *E*. | $\log_{10} PZ$. |
|---|---|---|---|---|---|---|---|
| Valerolactone | $H_2O$ | 11,200 | 7·89 | Phthalide | $H_2O$ | 12,600 | 8·68 |
| ,, | 21·5% EtOH | 10,800 | 7·46 | ,, | 21·5% EtOH | 13,200 | 8·89 |
| ,, | 40% EtOH | 12,600 | 8·57 | ,, | 40% EtOH | 14,900 | 9·89 |
| ,, | 60% EtOH | 14,500 | 9·78 | ,, | 60% EtOH | 16,100 | 10·54 |
| Butyrolactone | $H_2O$ | 11,300 * | 8·34 * | 5-Aminophthalide | $H_2O$ | 13,300 | 9·01 |

* The values for butyrolactone are necessarily less accurate than the rest. The heat of activation is much higher than that obtained by Caldin and Wolfenden. This is due to a regrettable miscalculation of their velocity constants at 25°; the recalculated value is approximately 70 (in minute units), in very fair agreement with the data given above.



*Solvents : 1 = water ; 2 = 21·5% ethanol ; 3 = 40% ethanol ; 4 = 60% ethanol.*

The figure shows the relationship between $10^3/\sqrt{E}$ and $\log_{10} PZ$ for our results; for purposes of comparison, similar data of Fairclough and Hinshelwood (J., 1937, 538) for the alkaline hydrolysis of methyl acetate and ethyl benzoate in various mixed solvents are shown on the same scale of co-ordinates.

## DISCUSSION.

The figure shows that the linear variation of $1/\sqrt{E}$ with log *PZ* is maintained not only with variation of medium but also with change of lactone. Such uniformity of behaviour is exceptional among the kinetic data that have so far been analysed in this way. It is also interesting to note that the two ester hydrolyses studied by Fairclough and Hinshelwood have $1/\sqrt{E}$ — log *PZ* lines of very nearly the same slope. It must be borne in mind that, as those authors have emphasised, a number of alternative functions of *E* (including its first power) will also vary linearly with log $PZ$ within the limits of experimental error.

A point of interest arises in connexion with the work of Tasman (*Rec. Trav. chim.*, 1927, **46**, 653), who made an extensive study of the alkaline hydrolysis (at a single temperature) of phthalide and a number of its derivatives. His velocity constants fell with the progress of the reaction, and he attributed this to the incompleteness of the conversion of lactone into hydroxy-acid anion, equilibrium being set up. As our own velocity constants showed no such drift, we examined the reversibility of the reaction by observing the change in conductivity of a freshly prepared N/100-solution of the sodium salt of α-hydroxy-*o*-toluic acid; its conductivity showed no change after 48 hours at 25°, and therefore it appears that the conversion of phthalide into the sodium salt is essentially irreversible. A more plausible explanation of the drift in Tasman's constants is to be found in the method by which he followed the course of reaction; he titrated the unused alkali with acid, using methyl-red as an indicator. In these circumstances, as soon as an appreciable quantity of lactone had been hydrolysed he was titrating a solution buffered over the range of the indicator; his titrations would over-estimate the amount of unused alkali and lead to abnormally low values of the velocity constant, which would decrease as the reaction proceeded. With a knowledge of the dissociation constants of the hydroxy-acids and the $p_{\text{H}}$ at which methyl-red changes colour, it would be possible to recalculate his results. We have done this roughly for phthalide itself (at 25°), using the dissociation constant given by Collan (*Z. physikal. Chem.*, 1892, **10**, 130) for α-hydroxy-*o*-toluic acid. The result is to change a velocity constant trending fairly steadily from 13·0 to 11·0 into a series of values fluctuating without any indication of systematic trend between 15·6 and 18·4.

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