# Kinetics and Mechanism of Base-catalysed Hydrolysis of Phthalimide

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The kinetics of base-catalysed hydrolysis of phthalimide were studied at 1.02M ionic strength in alkaline medium. The data were found to be well fitted with a series first-order consecutive reaction mechanism. The sodium hydroxide concentration dependence of the reaction was found in accordance with $k_{1obs} = B_1 + B_2[OH^-]$ and $k_{2obs} = C_1 + C_2[OH^-]$ where $k_{1obs}$ and $k_{2obs}$ are rate constants corresponding to general reaction scheme $A \xrightarrow{k_{1obs}} B \xrightarrow{k_{2obs}} X$ where A, B, and X stand for phthalimide, phthalamic acid, and ammonia, respectively. The hydrolysis was studied in the temperature range of 60—95 °C. The activation parameters corresponding to first and second consecutive steps of the reaction are: $\triangle H_I^* = 19.9 \pm 0.3$ kcal mol$^{-1}$, $\triangle S_I^* = -21.2 \pm 0.8$ cal K$^{-1}$ mol$^{-1}$; $E_{aI} = 20.6 \pm 0.3$ kcal mol$^{-1}$, $\ln A_I = 19.99 \pm 0.75$ s$^{-1}$, and $\triangle H_{II}^* = 10.0 \pm 0.5$ kcal mol$^{-1}$; $\triangle S_{II}^* = -50.9 \pm 1.32$ cal K$^{-1}$ mol$^{-1}$, $E_{aII} = 10.7 \pm 0.5$ kcal mol$^{-1}$, $\ln A_{II} = 6.02 \pm 1.31$ s$^{-1}$.

BENDER *et. al.*[1] have studied acid hydrolysis of phthalimide and phthalamic acid with a view to investigating the intramolecular catalysis of the reaction. They observed that the hydrolysis of phthalimide is a one-step first-order reaction. A polarographic study of base-catalysed hydrolysis of phthalimide in an aqueous ethanol solution was carried out by Tirouflet and Trouit[2] where the kinetics were found to be simple first-order. Bruylants *et al.*[3] have studied the first-stage of hydrolysis of phthalamide in alkaline medium where phthalimide is first formed and is further hydrolysed to phthalamic acid. In continuation of our work on the consecutive nature of the hydrolysis of imides and related compounds[4,5], we now report on the kinetics and mechanism of alkaline hydrolysis of phthalimide.

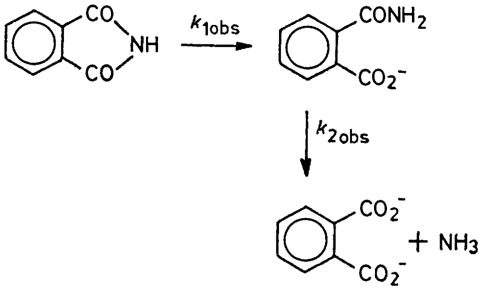
## EXPERIMENTAL

Phthalimide (B.D.H.) was recrystallized from ethanol[6] before use; a solution was prepared in 0.02M-NaOH solution just before the start of the reaction. There was no detectable hydrolysis of phthalimide in 0.02M-NaOH at 30 °C. All the other chemicals used were of reagent grade. Nessler's reagent was prepared as described by Vogel.[7]

*Kinetic Measurements.*—The solutions of phthalimide, sodium hydroxide, and sodium nitrate (for adjustment of ionic strength) were taken in a two-necked flask which was thermostatted at the experimental temperature. The flask was fitted with a double-surface condenser to check evaporation. The ammonia evolved with the progress of the reaction was swept out by a current of nitrogen gas and was absorbed in hydrochloric acid. The absorbed ammonia was estimated by Nessler's reagent spectrophotometrically[8] at 450 nm using a Bausch and Lomb Spectronic-20 instrument. The rate constants given in the paper are the mean of the two independent observations.

## RESULTS AND DISCUSSION

The evolution of ammonia during the hydrolysis of phthalimide was observed not to follow a simple one-step first-order kinetic path. Thus, initially, the rate of ammonia evolution was slow: it then increased before decreasing towards the end of the reaction. This indicates a two step reaction given by equation (1). The concentration of ammonia ($X$) is given by equation[9] (2) as a function of $k_{1obs}$, $k_{2obs}$, and time '$t$'.



(1)

$A_0$ Is the initial concentration of phthalimide. In equation (2), $k_{1obs}$ and $k_{2obs}$ are interchangeable without any effect on the solution of the equation, but since the imide bond is more easily hydrolysed than the amide bond, $k_{1obs}$ has been considered to be greater than $k_{2obs}$.

$$X = A_0\left[1 + \frac{1}{(k_{1obs} - k_{2obs})}\,(k_{2obs}e^{-k_{1obs}t} - k_{1obs}e^{-k_{2obs}t})\right] \quad (2)$$

The results of the rate constants calculated by the method described earlier[5] are summarized in Table 1. The rate constant ($k_f'$), for the second step when the imide concentration is reduced to less than 1%, may be calculated by using equation (3). Here $B_0$ and $X_0$ are the concentrations of phthalamic acid and ammonia at time $t_0$ (255 min for the kinetic run shown by Table 1). These results are given in the last column of Table 1 and are comparable with $k_{2obs}$ obtained from equation (2).

$$k_f' = \frac{1}{t_t - t_0}\ln\frac{B_0}{(B_0 - (X_t - X_0)} \quad (3)$$

The dependence of hydrolysis on the sodium hydroxide concentration was studied at ionic strength of 1.02M adjusted by sodium nitrate. The rate constants $k_{1obs}$ and $k_{2obs}$ were found to increase with increase in the concentration of sodium hydroxide. The results are

TABLE 1

Comparison of rate constants evaluated for typical kinetic run [a]

| Time<br>min | $10^4X_{obs}$<br>M | $10^4A$ [b] calcd<br>M | $10^3k$ [c] 1obs<br>min$^{-1}$ | $10^3k_f$ [d]<br>min$^{-1}$ | $10^3k_f$ [e]<br>min$^{-1}$ |
|---|---|---|---|---|---|
| 60 | 8.65 | 31.42 | 19.29 | 1.508 | |
| 90 | 16.10 | 17.49 | 19.37 | 1.951 | |
| 120 | 21.55 | 11.61 | 17.94 | 2.023 | |
| 150 | 27.85 | 7.19 | 17.55 | 2.176 | |
| 180 | 34.80 | 4.13 | 17.70 | 2.376 | |
| 212 | 43.10 | 2.01 | 18.42 | 2.660 | |
| 255 | 49.65 | 1.07 | 17.79 | 2.691 | |
| 319 | 60.75 | 0.30 | 18.20 | 2.932 | 3.990 |
| 377 | 68.30 | 0.10 | 18.26 | 3.047 | 3.900 |
| 437 | 74.75 | 0.03 | 18.37 | 3.149 | 3.913 |

[a] Conditions: 0.01M-phthalimide, 0.52M-NaOH, 0.1M-$KNO_3$, 95 °C. [b] Calculated from $k_{1obs}$ and $k_{2obs}$ obtained from the method described in this paper. [b] $A_{calcd} = A_0e^{-k_{1obs}t}$. [c] Calculated from the method described in this paper; $dk_f = \frac{1}{t}\ln\left(\frac{A_0}{A_0 - X_t}\right)$. [e] Calculated from equation $k_f' = \left(\frac{1}{(t_t - t_0)}\ln\frac{B_0}{B_0 - (X_t - X_0)}\right)$ with $10^4B_0 = 49.28$M, $t_0 =$ 255 min, $10^4X_0 = 49.65$M.

TABLE 2

Linear parameters

| Reaction | $10^3B_1(C_1)$<br>min$^{-1}$ | $10^3B_2(C_2)$<br>l mol$^{-1}$ min$^{-1}$ | $10^4$<br>R.m.s.[a] |
|---|---|---|---|
| $A \xrightarrow{k_{1obs}} B$ | 2.44 ± 0.48 [b] | 8.56 ± 0.70 [b] | 3.030 |
| $B \xrightarrow{k_{2obs}} X$ | (0.87 ± 0.18) | (3.54 ± 0.26) | (1.111) |

[a] Root-mean-square deviation between observed and calculated values. [b] Error limits are standard deviations.

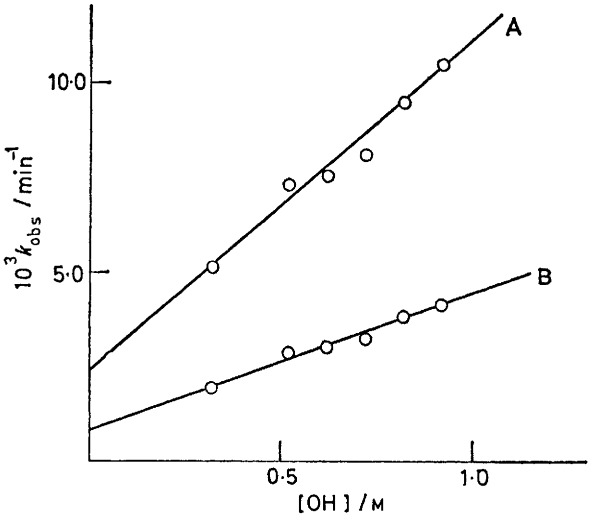
shown in Figure 1. The data were found to be well fitted by the empirical equations (4) and (5).

$$k_{1obs} = B_1 + B_2[OH^-] \qquad (4)$$

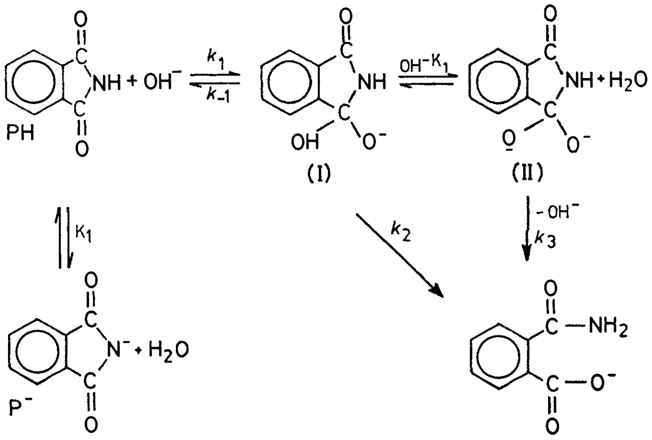
$$k_{2obs} = C_1 + C_2[OH^-] \qquad (5)$$

The linear adjustable parameters, $B_1$, $B_2$, $C_1$, and $C_2$ were determined by the least-squares technique, and are summarized in Table 2.

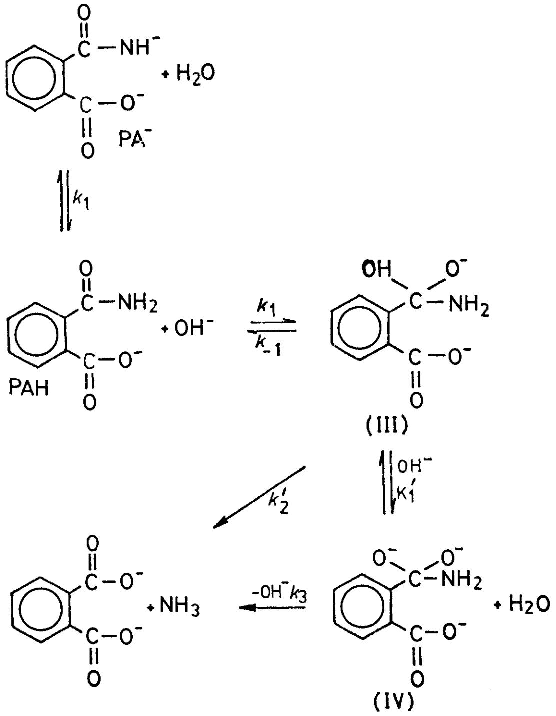
Temperature dependence of hydrolysis was studied within the range 66—95 °C. The various activation parameters were evaluated using Arrhenius and Eyring equations [10] by the least-squares technique. The results are summarized in Table 3.



Effect of concentration of sodium hydroxide on pseudo-first-order rate constants for hydrolysis of phthalimide at 85 °C; $A = k_{1obs}$, $B = k_{2obs}$



SCHEME 1



SCHEME 2

TABLE 3

Activation parameters

| Reaction | $\Delta H^*$<br>kcal mol$^{-1}$ | $E_a$<br>kcal mol$^{-1}$ | $\ln A$<br>s$^{-1}$ | $-\Delta S^*$<br>cal K$^{-1}$ mol$^{-1}$ | $10^4$<br>R.m.s.[a] |
|---|---|---|---|---|---|
| $A \xrightarrow{k_{1obs}} B$ | 19.9<br>±0.3 [b] | 20.6<br>±0.3 [b] | 19.99<br>±0.75 [b] | 21.2<br>±0.8 [b] | 5.193 |
| $B \xrightarrow{k_{2obs}} X$ | 10.0<br>±0.5 | 10.7<br>±0.5 | 5.02<br>±1.31 | 50.9<br>±1.3 | 2.192 |

[a] Root-mean-square deviation between observed and calculated values. [b] Error limits are standard deviations.

The dependence of the hydrolysis of phthalimide on hydroxide ion concentration indicates that the rate of production of phthalamic acid and ammonia is followed by the decomposition of a tetrahedral addition intermediate in two parallel kinetic paths, one of which is catalysed by hydroxide ion. Thus the probable mechanism consistent with the observed results is shown in Schemes 1 and 2.

By applying a steady-state approximation for reactive intermediates (I) and (III), the following kinetic equations have been derived on the basis of the above mechanisms.

$$k_{1\mathrm{obs}} = \frac{k_1[\mathrm{OH^-}]}{1 + K_\mathrm{i}[\mathrm{OH^-}]} \times \frac{k_2 + k_3\,K_\mathrm{I}\,[\mathrm{OH^-}]}{k_{-1} + k_2 + k_3K_\mathrm{I}[\mathrm{OH^-}]} \qquad (8)$$

$$k_{2\mathrm{obs}} = \frac{k_1'[\mathrm{OH^-}]}{1 + K_\mathrm{i}[\mathrm{OH^-}]} \times \frac{k_2' + k_3'K_\mathrm{i}'[\mathrm{OH^-}]}{k_{-1}' + k_2' + k_3'K_\mathrm{I}[\mathrm{OH^-}]} \qquad (9)$$

Where $K_\mathrm{i} = \frac{K_\mathrm{a}}{K_\mathrm{w}}$ and $K_\mathrm{i}' = \frac{K_\mathrm{a}'}{K_\mathrm{w}}$ with $K_\mathrm{a} = \frac{[\mathrm{P^-}][\mathrm{H^+}]}{[\mathrm{PH}]}$
$K_\mathrm{a}' = \frac{[\mathrm{PA^-}][\mathrm{H^+}]}{[\mathrm{PAH}]}$ and $K_\mathrm{w} = [\mathrm{H^+}][\mathrm{OH^-}]$

The conditions that $(k_{-1} + k_2) \gg k_3K_1[\mathrm{OH^-}]$ and $(k_{-1} + k_2') \gg k_3'\ K_\mathrm{I}'[\mathrm{OH^-}]$ reduce equations (8) and (9) to equations (10) and (11).

$$k_{1\mathrm{obs}} = \frac{k_1[\mathrm{OH^-}]}{1 + K_\mathrm{i}[\mathrm{OH^-}]} \times \frac{k_2 + k_3K_\mathrm{I}[\mathrm{OH^-}]}{k_{-1} + k_2} \qquad (10)$$

$$k_{2\mathrm{obs}} = \frac{k_1'[\mathrm{OH}]}{1 + K_\mathrm{i}[\mathrm{OH^-}]} \times \frac{k_2' + k_3'K_\mathrm{I}'[\mathrm{OH^-}]}{k_{-1}' + k_2'} \qquad (11)$$

These equations are further reduced to equations (12) and (13) provided $1 \ll K_\mathrm{i}[\mathrm{OH^-}]$ and $K_\mathrm{i}'[\mathrm{OH}]$ respectively, which is to be expected because of the acidic nature of phthalimide.

$$k_{1\mathrm{obs}} = \frac{k_1k_2}{K_\mathrm{i}(k_{-1} + k_2)} + \frac{k_1k_3K_\mathrm{I}[\mathrm{OH}]}{k_\mathrm{i}(k_{-1} + k_2)} \qquad (12)$$

$$k_{2\mathrm{obs}} = \frac{k_1'k_2'}{K_\mathrm{i}'(k_{-1}' + k_2')} + \frac{k_1'k_3'K_\mathrm{I}'[\mathrm{OH^-}]}{K_\mathrm{i}'(k_{-1}' + k_2'} \qquad (13)$$

The equations (12) and (13) are similar to those of (4) and (5) with $B_1 = k_1k_2/K_\mathrm{i}\ \ (k_{-1} + k_2)$, $B_2 = k_1\ \ k_3K_\mathrm{i}\ (k_{-1} + k_2)$, $C_1 = k_1'k_2'/K_\mathrm{i}'(k_{-1}' + k_2')$ and $C_2 = k_1'k_3'$-$K_\mathrm{I}'(k_{-1}' + k_2')$. The mechanism shown by Scheme 2 is similar to that found in a separate study of hydrolysis of phthalamic acid.[11]

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