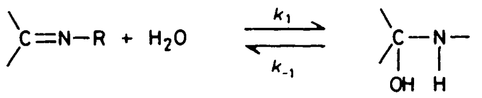
Kinetics of Hydrolysis of Some *N'*-(4-Substituted Benzylidene)salicylohydrazides

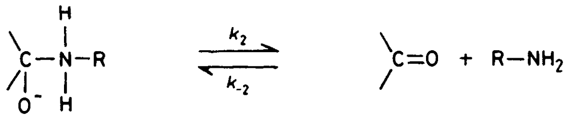
Yassien M. Temerk,* Mostafa M. Kamal, and Mohamed E. Ahmed
Chemistry Department, Faculty of Science, Assiut University, Assiut, Egypt

The rates of hydrolysis of a series of substituted benzylidenesalicylohydrazide derivatives in 40% (v/v) ethanol–buffer mixture have been investigated by differential pulse polarography. The hydrolysis is catalysed by H^+ and its rate follows strictly first-order kinetics. The rate constant decreases with increasing pH up to around pH 3.9, beyond which no measurable reaction was observed; here the protonation of imine begins to be significantly incomplete. The attack of water on the protonated substrate is considered to be the rate-determining step. The effects of pH, molecular structure, and temperature on the reaction rate and the activation energy are reported. Thermodynamic parameters ($\Delta G^‡$, $\Delta H^‡$, and $\Delta S^‡$) for the hydrolysis are discussed.

The mechanism of hydrolysis of simple azomethines derived from aliphatic or aromatic amines has been studied extensively.[1–10] It has been suggested that the hydrolysis proceeds through equations (i) and (ii), with step (i) rate-determining at neutral and alkaline pH and step (ii) rate-determining at acidic pH. However, no information is available concerning the hydrolysis of azomethines derived from acid hydrazides. We report here a study of the mechanism of hydrolysis of some substituted benzylidenesalicylohydrazides in acidic buffer solution containing ethanol (40% v/v). The effects of pH, polar substituents, and temperature were investigated.



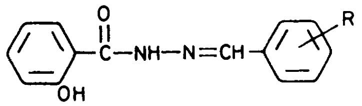
(i)



(ii)

Experimental

Materials.—Arylmethylenesalicylohydrazides (I) were prepared and purified by the conventional method.[11] The purity of the compounds was checked by elemental analysis and m.p. determination. Stock 0.01M-solutions were prepared in absolute ethanol. The modified universal buffer series of Britton and Robinson [12] was used as both supporting electrolyte and hydrolysis medium. The pH values were checked using a digital Radiometer PHM 64 pH meter, accurate to within ±0.005 unit.



(I) a; R = H
b; R = 4-OH
c; R = 4-NMe$_2$
d; R = 4-OMe
e; R = 4-NO$_2$
f; R = 3-NO$_2$
g; R = 2-NO$_2$

Instrumentation.—Differential pulse polarograms were obtained with a Princetone Applied Research (PAR) 174 A Polarographic Analyzer equipped with PAR 172 Drop Timer and Electrode Assembly. Polarograms were recorded with an advanced X-Y recorder (Hewlett Packard 7045 A). A thermostatted Metrohm cell with a three-electrode system was used. All measurements were performed in the temperature range 7—35 (±0.05) °C, with the aid of a HAAK KT 33 thermostat. The solution was deaerated by passing through it a slow stream of pure nitrogen for 45 min; the inert atmosphere was maintained during the measurements by passing nitrogen over the solution.

Rate Measurements.—The universal buffer solution (20 ml) containing ethanol (40% v/v) was placed in the electrolysis cell, and deaerated with nitrogen. After 45 min temperature equilibration the required volume of benzylidenesalicylohydrazide solution was added rapidly.

The differential pulse peak (the reduction peak corresponding to C=N reduction) was recorded under the conditions described in the preceding section. The decay of this peak was recorded at appropriate time intervals. The hydrolysis products do not exhibit any reduction current in the range of the reduction potential of the benzylidenesalicylohydrazide derivatives.

The variation of the peak height (μA) with time (min) was replotted as log i_p *vs.* time. A good linear correlation was obtained in each case, which indicates that the hydrolysis follows strictly first-order kinetics. For every run, the rate constant was obtained from the slope of the least-squares-refined linear plot. The reported rate constant is the mean for four replicate runs. Activation parameters were obtained from Arrhenius plots and the appropriate ancillary equations. The disappearance of the compounds under investigation was followed to 60—80% completion.

Results and Discussion

The hydrolysis of benzylidenesalicylohydrazide and its derivatives in 40% (v/v) ethanol–buffer mixtures is considered as a first-order reaction. The disappearance of hydrazide in acidic medium (pH 2.25—3.9) is strictly first-order (Figure 1). The rate constant increases gradually on decreasing the pH. However, no measurable hydrolysis was observed in slightly acidic and neutral media up to pH 7.2.

The rate constant, activation energy, and other thermodynamic parameters for the hydrolysis (Table 1) predict a significant variation with change of [H^+]; this is characteristic of hydrolysis reactions catalysed by [H^+].[13] This idea is supported by the linear variation of the rate constant with [H^+]. Such behaviour is observed under conditions in which the substrate exists as free base and can suffer attack by

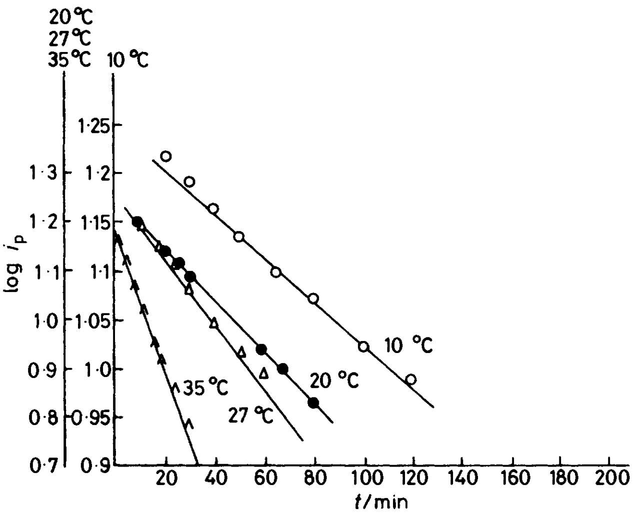


Figure 1. First-order plots of log i_p against t at pH 2.51 for hydrolytic decomposition of (Ia) (5×10^{-5}M) at various temperatures

Table 1. Specific rate constant, activation energies, and thermodynamic parameters of activation for the hydrolytic decomposition of the hydrazide (Ia) at various pH values

pH	$10^{-4}k$/ min^{-1}	$E_a^‡$ / kcal mol^{-1}	$-\Delta G^‡$ / kcal mol^{-1}	$\Delta H^‡$ / kcal mol^{-1}	$-\Delta S^‡$ / cal mol^{-1} K^{-1}
2.25	210 ± 10	10.50 ±0.10	19.49	9.83	32.96
2.51	120 ± 5	14.15 ±0.08	19.83	13.48	21.67
3.10	43.5 ± 3	15.50 ±0.21	20.43	14.83	19.11
3.90	13.5 ± 3	18.20 ±0.22	21.00	17.53	11.84

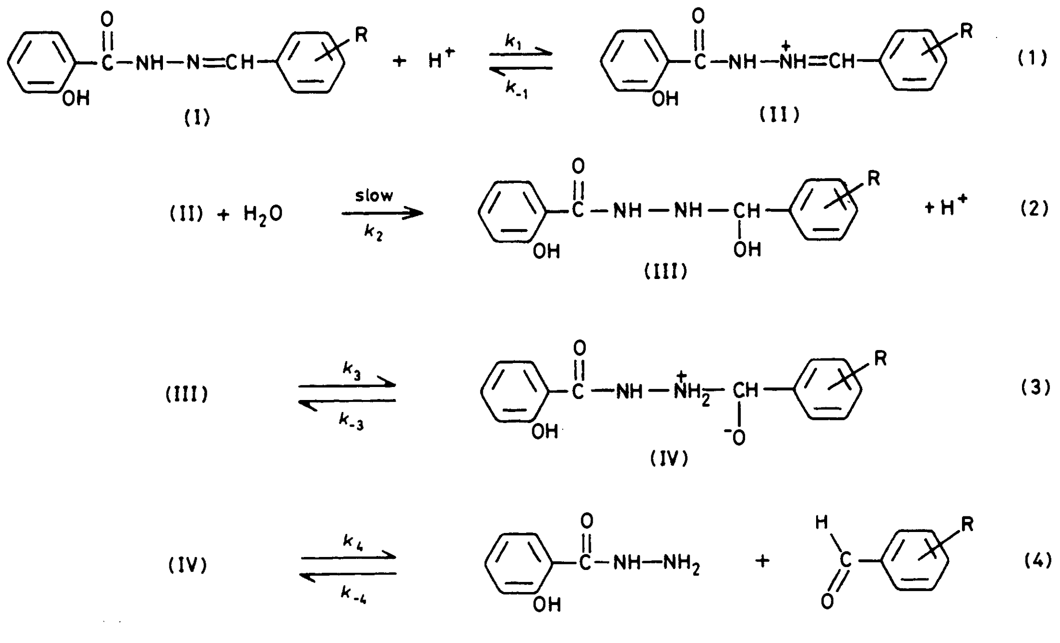
proton;[13,14] thus the mechanism shown in the Scheme is suggested.

The rate-determining step is considered to be attack of water on the protonated hydrazide [step (2)]. This is supported by the finding that the observed rate constant increases with increasing electron-donating power in the benzylidene moiety.[15] The intermediate (IV) [step (3)] must undergo at least one proton transfer before its decomposition to products, and such a proton transfer is expected to be fast.[9] According to the above mechanism, the rate follows the first-order equation $-d[(II)]/dt = k_1[(II)]$.

Table 2 shows that both the rate of hydrolysis and the activation energy are largely dependent on molecular structure. The following order parallels the increase in rate and decrease in the energy of activation: 4-NMe$_2$ > 4-OH > 4-OMe > 4-H > 3-NO$_2$ > 4-NO$_2$ > 2-NO$_2$. This behaviour can be explained in the light of the aforementioned mechanism.

Table 2. Specific rate constant, activation energies, and thermodynamic parameters of activation for the hydrolytic decomposition of hydrazides (I) (5×10^{-4}M) at pH 2.51

Structure	10^{-4}k/ min^{-1}	$E_a^‡$ / kcal mol^{-1}	$-\Delta G^‡$ / kcal mol^{-1}	$\Delta H^‡$ / kcal mol^{-1}	$-\Delta S^‡$ / cal mol^{-2} K^{-1}
(Ic)	175 ± 8	11.5 ±0.14	19.63	10.83	30.03
(Ib)	169 ± 9	12.7 ±0.14	19.50	12.03	25.49
(Id)	135 ± 8	13.4 ±0.21	19.77	12.98	24.88
(Ia)	120 ± 5	14.15 ±0.08	19.83	13.48	21.67
(If)	26 ± 2	16.3 ±0.22	20.70	15.63	71.30
(Ie)	22 ± 1	17.0 ±0.24	20.70	16.33	14.91
(Ig)	17 ± 1	20.1 ±0.30	20.98	19.40	5.39



Scheme.

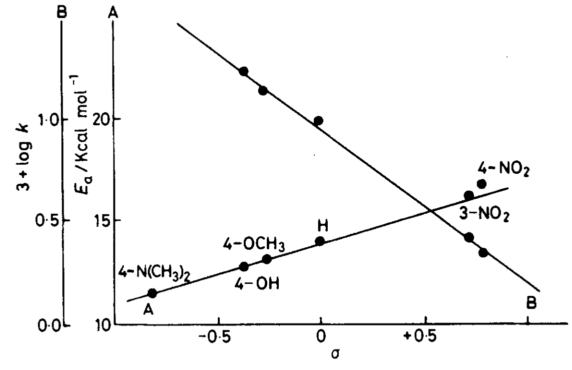


Figure 2. Variation of rate constant and activation energy for the hydrolytic decomposition of hydrazide derivatives (I) with Hammett constant

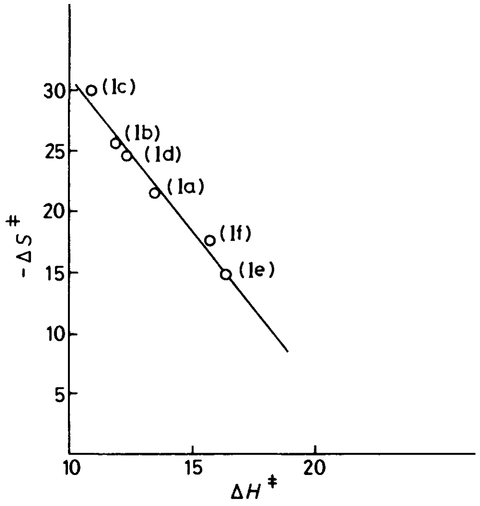


Figure 3. Linear variation of $\Delta H^‡$ with $\Delta S^‡$ for the hydrolytic decomposition of hydrazides (I) at pH 2.51

Increase in the electron-donating character of the substituent increases the electron density on the nitrogen atom of the azomethine linkage, which in turn causes a shift in the equilibrium of step (1) in the forward direction. This increases k_1 and is reflected in a net increase in the reaction rate constant. On the other hand, in the case of the nitro derivatives the rate constant is decreased by delocalization of the electron density on the nitrogen atom, whereas the value of $E_a^‡$ is increased.

The foregoing discussion is supported by the linear relationship obtained on plotting log k or $E_a^‡$ as a function of the Hammett σ constant (Figure 2). It is evident that the rate constant is strongly dependent on the type of mesomeric interaction of the substituent.

The plot of $-\log k_{obs}$ *vs.* σ is linear, with ρ^+ 0.87. Since attack of water molecules on protonated substrates yields ρ^+ values near unity,[16] this value supports the foregoing mechanism and confirms the suggestion that step (2) is rate-determining.

Thermodynamic parameters of activation ($\Delta G^‡$, $\Delta H^‡$, and $\Delta S^‡$) for the hydrolysis of the hydrazide (Ia) at different pH values and for all compounds investigated at pH 2.51 are given in Tables 1 and 2. The data show that increases in both [H$^+$] and the electron-donating power of the substituent will enhance the hydrolysis; consequently, values $\Delta G^‡$ and $\Delta H^‡$ are expected to decrease in the same direction.

The high $-\Delta S^‡$ value for (Ic) (R = NMe$_2$) may indicate a less random distribution of solvent molecules around the transition state. This is explained on the basis that the higher donating power of the NMe$_2$ group would favour charge localization, and the activated complex would therefore be less randomly linked to solvent molecules. On the other hand compounds with R = NO$_2$ would have more random distribution of solvent molecules around the activated state. This behaviour is in agreement with the direction of change of the rate constant and $E_a^‡$ values. The plot of $\Delta H^‡$ as a function of $-\Delta S^‡$ is a straight line (Figure 3), of slope (isoequilibrium temperature) 320 K. This should be taken to indicate that there is only one mechanism of hydrolysis for the investigated compounds.[17]

References

1 E. J. Pozionet, D. N. Kramer, B. W. Fromm, and W. A. Mosher, *J. Org. Chem.*, 1961, **26**, 423.
2 B. M. Anderson and W. P. Jencks, *J. Am. Chem. Soc.*, 1960, **82**, 1773.
3 R. Wolfenden and W. P. Jencks, *J. Am. Chem. Soc.*, 1961, **83**, 2763.
4 E. H. Cordes and W. P. Jencks, *J. Am. Chem. Soc.*, 1962, **84**, 832.
5 E. H. Cordes and W. P. Jencks, *J. Am. Chem. Soc.*, 1962, **84**, 4319.
6 A. V. Willi, *Helv. Chim. Acta*, 1956, **39**, 1193.
7 R. L. Reeves, *J. Am. Chem. Soc.*, 1962, **84**, 3332.
8 J. Archila, H. Bull, C. Lagenaur, and E. H. Cordes, *J. Org. Chem.*, 1971, **36**, 1345.
9 D. Pites, G. Favini, and D. Grasso, *J. Chem. Soc., Perkin Trans. 2*, 1974, 1595.
10 J. J. Charette and E. De Hoffmann, *J. Org. Chem.*, 1979, **44**, 2256.
11 G. Sturve and Radenhouseu, *J. Prakt. Chem.*, 1895, **52**, 170.
12 H. T. S. Britton, ' Hydrogen Ions,' vol. 1, 2nd edn., Chapman and Hall, London, 1952, p. 262.
13 A. C. Dash, B. Dash, and M. Patra, *Indian J. Chem.*, 1980, **19B**, 492.
14 R. K. Chaturvedi and E. H. Cordes, *J. Am. Chem. Soc.*, 1967, **89**, 1230.
15 E. H. Cordes and W. P. Jencks, *J. Am. Chem. Soc.*, 1963, **85**, 2843.
16 K. Kochier, W. Sandstrom, and E. H. Cordes, *J. Am. Chem. Soc.*, 1964, **86**, 2413.
17 J. E. Leffer, *J. Org. Chem.*, 1955, **20**, 1202.

Received 13*th December* 1982; *Paper* 2/2074