Mesoionic Compounds. Part III.[1,2] Acid-catalysed Hydrolysis and Protonation Behaviour of 4,5-Diphenylisosydnone

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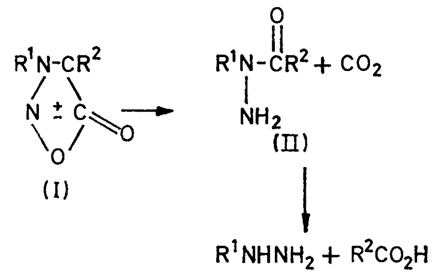
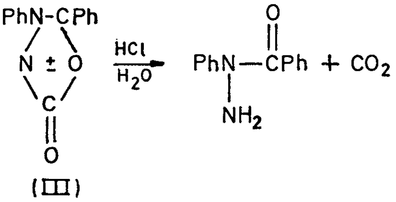
The hydrolysis of 4,5-diphenylisosydnone has been studied in aqueous solutions of mineral acids. For perchloric, sulphuric, and hydrobromic acids, plots of the first-order rate coefficient k_1 against [H+] show maxima which are caused by extensive protonation of the substrate. The protonation behaviour of 4,5-diphenylisosydnone has been studied and correlates better with the amide acidity function, H_A, than with H_0.

3-ARYL- or -ALKYL-SYDNONES (I; R^1 = alkyl or aryl, R^2 = H) hydrolyse in the presence of hydrochloric acid to form the corresponding hydrazine, formic acid, and carbon dioxide.[3,4] Baker and Ollis[5] suggested the mechanism of hydrolysis shown in Scheme 1. The formation of acylhydrazide intermediates has been confirmed by their isolation in several cases, *e.g.* of 1-phenylacetohydrazide (II; R^1 = Ph, R^2 = Me) from the hydrolysis of 4-methyl-3-phenylsydnone.[6] The mechanisms of hydrolysis of 3-alkyl- and -aryl-sydnones in strong acids have been studied in some detail.[1,2] The *N*-acylhydrazide 1-phenylbenzohydrazide (II; R^1 = R^2 = Ph) formed in the hydrolysis of 3,4-diphenylsydnone is stable in acid solution and so the hydrolysis stops at this stage.



SCHEME 1

Hashimoto and Ohta have reported that the analogous 4,5-diphenylisosydnone (III) also hydrolyses in hydrochloric acid to 1-phenylbenzohydrazide and carbon dioxide[7] (Scheme 2).



SCHEME 2

No kinetic study of the hydrolyses of isosydnones has previously been reported. In order to provide evidence of the mechanism of decomposition of such compounds in the presence of acids, we have examined both the effect of added acids and salts at relatively high electrolyte strength on the rate of hydrolysis of 4,5-diphenylisosydnone, and also the protonation behaviour of this compound in sulphuric acid.

EXPERIMENTAL

Materials.—4,5-Diphenylisosydnone was prepared by the action of phosgene on *N*-benzoyl-*N*-phenylhydrazine hydrochloride[7] and after recrystallization from benzene had m.p. 163° (col. plates) (lit.,[7,8] 162, 160°).

Acid-catalysed Hydrolyses.—The acids used were of analytical reagent quality. Their concentrations were determined by titration with standard alkali. Sodium chloride was a recrystallized commercial sample. It was dehydrated at *ca.* 150° and kept in a vacuum at this temperature for 24 h with a diffusion pump. Anhydrous sodium chloride, sodium bromide, and sodium hydrogen sulphate were prepared similarly.

Kinetic Measurements.—The rates of hydrolysis were determined spectrophotometrically by following the decrease in the characteristic absorption (297 nm) of the isosydnone.

Procedure.—4,5-Diphenylisosydnone (10 μl of stock solution in dioxan; $6\cdot0 \times 10^{-3}$M) was added to the reaction solution containing acid (3·0 ml) thermostatted to ±0·03 °C in a stoppered cell. The cell contents were shaken rapidly and readings of optical density (*D*) taken at intervals.

TABLE 1

Hydrolysis of 4,5-diphenylisosydnone in water and at 40·0 °C unless otherwise indicated

(a) At constant ionic strength					
$[HClO_4]$/M	1·00	2·00	3·00	4·00	5·00
$[NaClO_4]$/M	4·00	3·00	2·00	1·00	
10^3k_1/min^{-1}	1·29	2·67	3·32	3·68	3·68
10^3k_2/l mol^{-1} min^{-1}	1·29	1·34	1·11	0·92	0·74
[HBr]/M	1·00	2·00	3·00	4·00	5·00
[NaBr]/M	4·00	3·00	2·00	1·00	
10^3k_1/min^{-1}	3·59	5·62	8·45	10·4	14·5
10^3k_2/l mol^{-1} min^{-1}	3·59	2·81	2·82	2·60	2·90
$[H_2SO_4]$/M	1·00	2·00	3·00	4·00	5·00
$[NaHSO_4]$/M	4·00	3·00	2·00	1·00	
10^3k_1/min^{-1}	6·45	9·76	11·5	12·0	12·5
10^3k_2/l mol^{-1} min^{-1}	6·45	4·88	3·84	3·00	2·50
(b) At different temperatures					
T/°C	29·9	40·0	50·1	60·1	69·2
10^3k_1/min^{-1} (2·00M-$HClO_4$)	0·78	2·76	9·90	28·6	67·3
10^3k_1/min^{-1} (2·00M-$NaClO_4$)	0·10	0·65	2·76	7·35	25·3

Values of the first-order rate coefficients were determined graphically from the plot of log $(D_t - D_\infty)$ against time and are shown in Table 1 and Figures 1 and 2.

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[1] Part I, S. Aziz, A. F. Cockerill, and J. G. Tillett, *J. Chem. Soc.* (*B*), 1970, 416.

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[3] J. C. Earl and A. W. Mackney, *J. Chem. Soc.*, 1925, 899.

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[5] W. Baker and W. D. Ollis, *Quart. Rev.*, 1957, **11**, 15.

[6] S. A. Zotova and V. G. Zashunskii, *Zhur. org. Khim.*, 1967, **3**, 942.

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[8] A. R. McCarthy, W. D. Ollis, A. N. M. Barnes, L. E. Sutton, and C. Ainsworth, *J. Chem. Soc.* (*B*), 1969, 1185.

Influence of Temperature.—The entropies ($\Delta S^‡$) and enthalpies ($\Delta H^‡$) were calculated from the equation $k = (\boldsymbol{k}T/h)\exp(\Delta S^‡/R)\exp(-\Delta H/RT)$ by a least-squares procedure. The values obtained for the acid-catalysed hydrolysis of 4,5-diphenylisosydnone (2·00M-HClO$_4$) [Table 1(b)], were $\Delta S^‡ = -8{\cdot}6 \pm 1{\cdot}1$ cal mol^{-1} K^{-1} [based on k_{obs}(2M-HClO$_4$) − k_{obs}(2M-NaClO$_4$) and calculated at 40°]; $\Delta H^‡ = 22{\cdot}6 \pm 0{\cdot}4$ kcal mol^{-1}.

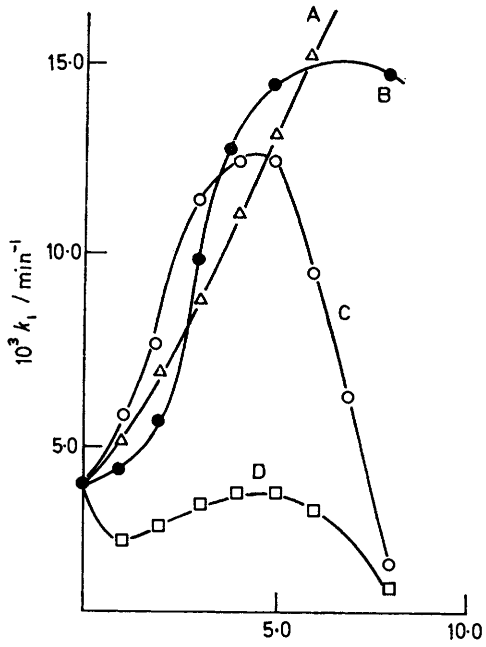

FIGURE 1 Effect of added acids **on the rate of hydrolysis** of 4,5-diphenylisosydnone at 40°: A, HCl; B, HBr; **C, H$_2$SO$_4$**; D, HClO$_4$

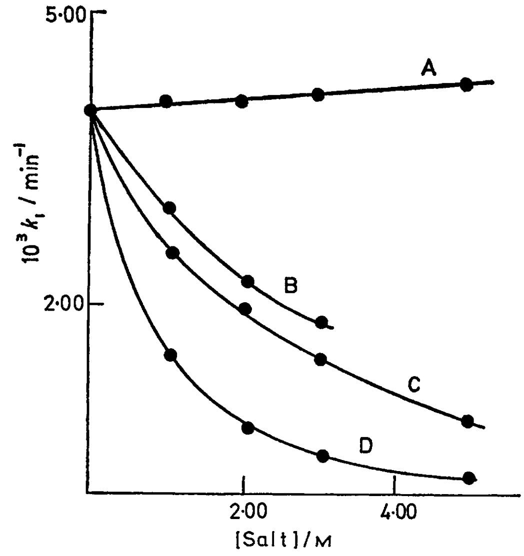

FIGURE 2 Effect of added salts on the neutral hydrolysis of 4,5-diphenylisosydnone at 40°: A, NaHSO$_4$; B, NaCl; C, NaBr; D, NaClO$_4$

Protonation Equilibria.—The absorbances at a number of wavelengths between 200 and 400 nm were recorded for various concentrations of sulphuric acid at a constant concentration of 4,5-diphenylisosydnone. Measurements were carried out on a Unicam SP 500 spectrophotometer thermostatted at 25 ± 0·2 °C. The protonation equilibria in perchloric acid could not be accurately studied because of the small differences between the spectra of the substrate and its conjugate acid. The ionization ratio I (= [BH$^+$]/[B]) was determined from absorbance measurements at 225 nm from equation (1) where D_{B} is the absorption of the unprotonated form, D_{BH^+} is the corresponding value of the completely protonated form, and D is the value in a solution of intermediate acidity (Table 2).

$$\log I = \log[(D - D_{\text{BH}^+})/(D_{\text{B}} - D)] \qquad (1)$$

The ionization ratios so obtained (Table 3) were fitted by a least-squares method to equations (2)—(4).

TABLE 2

Protonation data for 4,5-diphenylisosydnone

[H$_2$SO$_4$]/M		3·00	4·00	6·00	7·00
D_{225}	0·590	0·563	0·560	0·496	0·449
log I		−0·98	−0·93	−0·30	−0·02
H_0		−1·37	−1·84	−2·57	−3·27
H_{A}		−1·24	−1·60	−2·20	−2·48
[H$_2$SO$_4$]/M	8·00	9·00	10·0	12·0	
D_{225}	0·396	0·363	0·347	0·304	
log I	0·32	0·59	0·75		
H_0	−3·86	−4·38	−4·92		
H_{A}	−2·75	−3·02	−3·32		

TABLE 3

pK Values for 4,5-diphenylisosydnone

Method	Slope	pK
Equation (2)	0·55 ± 0·03	−3·33 ± 0·29
Equation (3)	0·94 ± 0·07	−2·49 ± 0·36
Equation (4)	0·46 *	−2·18 *

* Graphically.

DISCUSSION

Rate Dependence on Acidity.—The first-order rate coefficients for the hydrolysis of 4,5-diphenylisosydnone at various acidities in different mineral acids are plotted against acid concentration in Figure 1. The complex kinetic behaviour is quite unlike that observed for the hydrolysis of 3-aryl- or -alkyl-sydnones [1,2] or for 3,4-diphenylsydnone.[9] The most striking feature of the acid–rate profile is the occurrence of rate maxima with perchloric, sulphuric, and hydrobromic acid. An additional peculiarity is that the acid–rate profile for perchloric acid goes through a minimum. Rate maxima can arise in two main ways, either because of extensive protonation of a basic substrate as in the hydrolysis of amides [10] or hydroxamic acids,[11] or from the superposition of a specific salt effect on an acid-catalysed reaction (often accompanied by a considerable effect on a concurrent neutral reaction) such as observed in the

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[9] A. J. Buglass and J. G. Tillett, unpublished results.

[10] J. T. Edward, H. P. Huthinson, and S. C. R. Meacock, *J. Chem. Soc.*, 1955, 2520; J. T. Edward and S. C. R. Meacock, *ibid.*, 1957, 2000, 2007.

[11] A. J. Buglass, K. Hudson, and J. G. Tillett, *J. Chem. Soc.* (*B*), 1971, 123.

hydrolysis of some sulphites,[12] phosphates,[13] phosphinates,[14] and carboxylates.[15]

Evidence bearing on the cause of the observed rate maxima can be obtained from a study of the effect of added acids under conditions of constant ionic strength. In mixtures of hydrobromic acid and sodium bromide at constant bromide ion concentration (5·00M) [Table 1(a)], the rate of hydrolysis increases approximately linearly with acid concentration. In mixtures of perchloric acid and sodium perchlorate [Table 1(a)] and sulphuric acid and sodium hydrogen sulphate [Table 1(a)] at the same ionic strength, however, the rate of hydrolysis at first increases linearly with increase in acid concentration but then reaches a maximum. If the rate maximum were due to the superposition of a specific salt effect on an acid-catalysed reaction it should disappear under such conditions. Similar behaviour to that observed with the two stronger acids was also observed in the hydrolysis of hydroxamic acids under conditions of constant ionic strength [11] and is characteristic of extensive conversion of the substrate into its conjugate acid. To provide unambiguous confirmation of this conclusion the protonation behaviour of 4,5-diphenylisosydnone was studied in concentrated sulphuric acid solution.

Protonation Behaviour.—To avoid the necessity of developing unique scales of acidity for different types of substrate we have chosen to analyse the protonation data in terms of the H_0 acidity scale according to equation (2) where M is a measure of the protonation

$$\log I = M(\text{p}K - H_0) \qquad (2)$$

behaviour of substrate B relative to Hammett bases (primary aromatic amines) used for the determination of H_0 (if $M = 1$, B is a Hammett base). A plot of $\log I$ *versus* H_0 gives a straight line of slope (0·55) considerably less than unity [Table 3]. Slopes (M) of similar magnitude have been observed for the protonation of amides,[16] sulphoxides,[17] acetates,[18] and hydroxamic acids.[11] Because diphenylisosydnone does not behave like a simple Hammett base, the pK obtained represents the H_0 value for half-protonation and does not correspond to a thermodynamic pK_a.[19]

It is also informative to analyse the ionization data in terms of the amide acidity function, H_A [20] [equation (3)].

$$\log I = cH_A + d \qquad (3)$$

The slope ($c = 0{\cdot}94$) of the plot of $\log I$ against H_A [Table 3] is close to unity, is similar in magnitude to that observed for the protonation of hydroxamic acids [11] (0·94—1·02), and suggests that the protonation behaviour of isosydnones is similar to that of amides and related compounds. The value of $-d/c$ (H_A value for half-protonation) should represent the thermodynamic pK value and is less negative than the apparent value based on equation (2).

An alternative method of determining pK values is to use the linear free energy approach of Bunnett and Olsen [21] [equation (4)].

$$\log I + H_0 = \phi(H_0 + \log[\text{H}^+]) + \text{p}K_{\text{BH}^+} \qquad (4)$$

Provided the plot of the left-hand side of equation (4) *versus* ($H_0 + \log[\text{H}^+]$) is linear, thermodynamic quantities can be calculated because the intercept of the plot represents the pK_{BH^+} value referred to infinite dilution in water as the standard state. The slope (ϕ) is a measure of the susceptibility of the equilibrium to changing acid concentration. The value of the pK determined in this way [Table 3] is less negative than that based on the H_A scale [equation (3)]. This is consistent with the suggestion that the H_A scale should be shifted *ca.* 0·3 H_A units towards less negative values [20] and would bring the pK values determined by the two methods into close agreement.

The ϕ value for 4,5-diphenylisosydnone (0·46) is of similar magnitude to those observed for amides [21] (0·42—0·55), sulphoxides [17] (0·4—0·6), and hydroxamic acids [11] (0·51—0·57), so that all four classes of compound show similar protonation behaviour.

Pre-equilibrium Protonation.—The value of the kinetic solvent isotope effect, $k_1(\text{D}_2\text{O})/k_1(\text{H}_2\text{O}) = 1{\cdot}44$, for the hydrolysis of 4,5-diphenylisosydnone in perchloric acid solution at an acidity (2·00M) too low to give substantial protonation is characteristic of reactions which proceed by a rapid pre-equilibrium proton transfer.[22]

At the present time there is no direct evidence as to whether initial protonation of isosydnones occurs on nitrogen or on oxygen. Studies on the acid-catalysed hydrolysis of alkyl- and aryl-sydnones have assumed protonation on nitrogen (N-2) of the sydnone ring.[1,2,23] Olah and his co-workers have recently shown, however, that the protonation of 3-phenylsydnone in $\text{FSO}_3\text{H–SbF}_3$ solution occurs exclusively on the carbonyl oxygen atom.[24] It is possible, however, that whilst the *O*-protonated form is thermodynamically more stable, attack of water occurs mainly at the *N*-protonated

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[12] J. G. Tillett, *J. Chem. Soc.*, 1960, 5138; C. A. Bunton and G. Schwerin, *J. Org. Chem.*, 1966, **31**, 842.

[13] *Cf.* C. A. Bunton and S. J. Farber, *J. Org. Chem.*, 1969, **34**, 3396.

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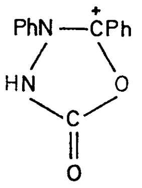
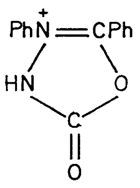
[24] G. A. Olah, D. P. Kelly, and N. Swein, *J. Amer. Chem. Soc.*, 1970, **92**, 3133.

form. This situation is similar to that observed in the controversial case of the hydrolysis of amides for which conflicting evidence abounds.[25] We have assumed, as did earlier workers,[7] that the acid-catalysed hydrolysis of diphenylisosydnone proceeds through the *N*-protonated conjugate acid (IV) which is resonance stabilised, *e.g.* as in (V).

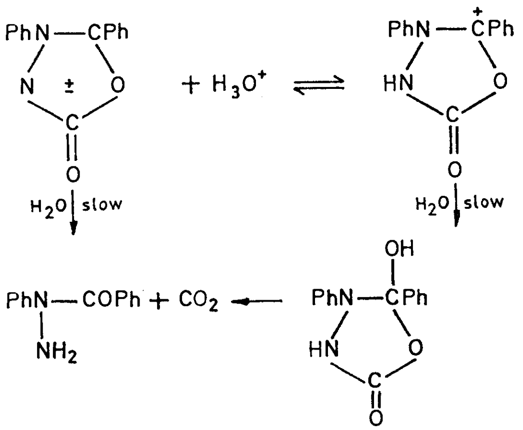


(IV)



(V)

Mechanism of Hydrolysis.—Detailed interpretation of the kinetic behaviour shown in Figure 1 is complicated by the presence of a neutral reaction which is strongly susceptible to salt effects as shown in Figure 2. It can be seen that sodium chloride, sodium bromide, and sodium perchlorate exert a very large negative salt effect whereas sodium hydrogen sulphate causes only a slight increase in rate which might be due to a small amount of acid catalysis resulting from dissociation of the hydrogen sulphate ion. The order of the effect of catalysing acids on the overall rate of hydrolysis at 1·00M-acid, HCl > HBr > $HClO_4$, fits exactly the inverse order of negative salt effects, $NaClO_4$ > NaBr > NaCl, on the neutral rate. The negative salt effect exerted on the neutral rate by perchlorate ion is initially so large that it outweighs the positive acid catalysis at low perchloric acid concentration and so the overall rate of hydrolysis is reduced. Eventually a point is reached (at *ca.* 1·00M-acid) where the two effects balance and a rate minimum is observed (Figure 1). At higher acidities acid catalysis dominates and the rate begins to increase. The subsequent rate maximum arises because above *ca.* 5·00M-perchloric acid diphenylisosydnone is almost completely protonated and any further small increase in the concentration of the conjugate acid brought about by increasing acidity is more than offset by the decreasing availability of water required for a bimolecular rate-determining step. One possible reaction sequence for the neutral and acid-catalysed pathways is shown in Scheme 3. The magnitude of the entropy of activation (—8·6 cal mol^{-1} K^{-1}) for the acid-catalysed reaction in the low acidity region is also consistent with an *A*-2 mechanism.[26] A plot of the Bunnett–Olsen kinetic linear free energy relationship[27] for moderate or strongly basic substrates of $\log k_1 - \log([SH^+]/[S])$ against $(H_0 + \log[H^+])$ gave a good straight line of slope, ϕ, 0·90. This relatively high value which is similar to those observed for hydroxamic acids[11] (0·84—1·1) suggests that water has some additional role in the rate-limiting step as well as that of a nucleophile.



Scheme 3

We thank the S.R.C. for a studentship (to A. J. B.).

[3/687 *Received, 2nd April,* 1973]

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[25] *Cf.* C. O'Connor, *Quart. Rev.*, 1970, **24**, 553; R. Huisgen and H. Brade, *Chem. Rev.*, 1957, **90**, 1432; M. Liler, *Chem. Comm.*, 1971, 115; *J. Chem. Soc.* (*B*), 1971, 334; R. B. Martin, *J.C.S. Chem. Comm.*, 1972, 793; C. R. Smith and K. Yates, *Canad. J. Chem.*, 1972, **50**, 771.

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