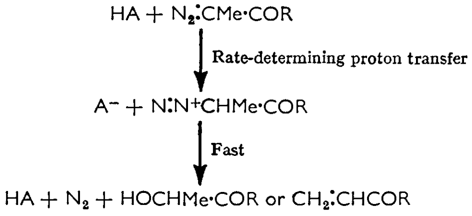
Kinetic Isotope Effects and Aliphatic Diazo-compounds. Part I. General Acid Catalysis and the Brønsted Coefficients

By **W. J. Albery,* A. N. Campbell-Crawford,** and **K. S. Hobbs,** Physical Chemistry Laboratory, Oxford

The acid-catalysed decompositions of 3-diazobutan-2-one and of ethyl diazopropionate show general acid catalysis. Data are reported for both compounds for a series of carboxylic acids and for H_3O^+ as catalysts. The Brønsted coefficient is 0·61 for 3-diazobutan-2-one and 0·59 for ethyl diazopropionate. The difference in the u.v. spectra between diazo-ketones and diazo-esters is also discussed.

THE acid-catalysed decomposition of 3-diazobutan-2-one or ethyl diazopropionate takes place according to the A–S_E2 mechanism[1,2] as shown in Scheme 1, where R = Me for the diazobutanone and OEt for the ester. In contrast to ethyl diazoacetate, the first proton-transfer step for both compounds is rate-determining. Both 3-diazobutan-2-one and ethyl diazopropionate are decomposed by general acid catalysis and the overall solvent isotope effect, k_{D_2O}/k_{H_2O} is[1] *ca.* 0·40 for both compared[3,4] with 3·1 for ethyl diazoacetate.



SCHEME 1

This series of papers reports (1) measurements of rate constants for catalysis by H_3O^+ and carboxylic acids for 3-diazobutan-2-one and ethyl diazopropionate; (2) measurements of rate constants and isotope effects in relatively concentrated buffer solutions; (3) measurements of the solvent isotope effect for catalysis by L_3O^+ in mixtures of H_2O and D_2O for both diazo-compounds;

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[1] H. Dahn, H. Gold, M. Ballenegger, J. Lenoir, G. Diderich, and R. Malherbe, *Helv. Chim. Acta*, 1968, **51**, 2065.

[2] H. Dahn and M. Ballenegger, *Helv. Chim. Acta*, 1969, **52**, 2417.

[3] P. Gross, H. Steiner, and F. Krauss, *Trans. Faraday Soc.*, 1938, **34**, 351.

[4] W. J. Albery and M. H. Davies, *Trans. Faraday Soc.*, 1969, **65**, 1066.

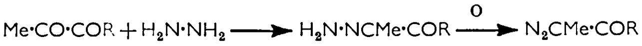
(4) measurements of the solvent isotope effect in mixtures of H_2O and D_2O for the reaction of AcOH with the diazo-ester and for the reaction of $C_5H_5N^+H$ with the diazobutanone; and (5) measurements of the secondary isotope effect for the reaction of $CD_3{\cdot}CO_2H$ with the diazobutanone. The results first show that the second step can become partially rate-determining, secondly allow deductions to be made about the nature and symmetry of the transition states, thirdly, provide confirmation of the theory and treatment of isotope effects in terms of fractionation factor theory,[5,6] and, fourthly, are discussed in terms of the Marcus theory of proton transfer.[7]

EXPERIMENTAL

Materials and Solutions.—All water was doubly distilled; the second distillation was from a $KMnO_4$ solution in an all-glass still. All reagents were AnalaR and were used without further purification except for glycollic and cyanoacetic acids, for which samples of technical grade were recystallised from ether and benzene respectively. The purity of the carboxylic acids was tested by titration with NaOH and by their ^1H n.m.r. spectra. The results of the titration were in all cases within 0·5% of those expected for the pure acid; the ^1H n.m.r. spectrum of each acid showed that other proton signals were <1% of those due to the acid.

To make up buffer solutions a 0·050M solution of NaA was prepared by titrating 0·10M-NaOH and 0·10M-HA, with a Radiometer Titrator TTT 1C set to give an end point at pH 7. The ionic strength of the buffer solutions was adjusted to 0·050M by addition of $NaClO_4$.

Diazo-compounds.—The diazo-compounds were prepared by oxidation of the hydrazone as shown in Scheme 2, where R = Me or OEt.



$$Me{\cdot}CO{\cdot}COR + H_2N{\cdot}NH_2 \longrightarrow H_2N{\cdot}NCMe{\cdot}COR \xrightarrow{O} N_2CMe{\cdot}COR$$

SCHEME 2

Following previous procedures[8,9] the hydrazone was isolated and the oxidising agent used was silver oxide. However it was more convenient and better yields were obtained if the hydrazone was not isolated and if nickel peroxide[10] was used as the oxidising agent. Biacetyl (for the diazobutanone) or ethyl pyruvate (for diazo-ester) (10 ml) were cooled to −20 °C in a wide test tube in a Dewar flask containing acetone and solid CO_2. A slight excess of hydrazine hydrate (6 ml for the diazobutanone, 4·5 ml for the ester) and water (2—3 ml) were added dropwise during 15 min at −20 °C. The mixture was then allowed to reach room temperature, whereupon the clear yellow liquid was added to ether (100 ml). The aqueous phase was removed by addition of a large quantity of anhydrous Na_2SO_4. NiO_2 (25 g) was slowly added to the slurry and after addition was complete the solution was left to stand for 1 h. It was filtered off and dried (Na_2SO_4), and the ether removed on a water-bath. The remaining yellow solution was distilled at 12—13 mmHg and 30—32 °C to give the diazo-compound (*ca.* 4 ml).

The purity of the compounds were tested by manometric measurements of the N_2 evolved in acid solution (typical results were 97—99% pure) and by ^1H n.m.r.; signals due to other protons were <1% of those due to the diazo-compounds. All ^1H n.m.r. spectra were obtained on a Varian A60A 60 MHz spectrometer with the sample at 40 °C.

Kinetic Measurements.—The reactions were followed spectrophotometrically with a Cary 14 double-beam instrument to measure the decrease in optical density with time at 287 nm for 3-diazobutan-2-one and at 263 nm for ethyl diazopropionate. The reaction solution was thermostatted by the optical cell being contained in a copper block through which water thermostatted to 25·00 ± 0·05 °C was circulated at 20 ml s^{-1}. The water was also circulated through the walls of the optical compartment of the spectrometer. The temperature of the thermostat tank was measured by a Beckmann thermometer which had been calibrated against a thermometer calibrated at the National Physical Laboratory. The instrument room was thermostatted to 23·5 ± 0·5 °C. The temperature difference between the reaction solution in the spectrometer and the water in the thermostat tank was measured with a copper–constantan thermocouple and a Pye differential photocell amplifier to be less than 0·05 °C.

The reaction was initiated by first allowing the acid solution to reach thermal equilibrium in the instrument; thermocouple experiments showed that this was achieved after 1 h. Then a drop of aqueous 0·05M solution of 3-diazobutan-2-one or ethyl diazopropionate was added and mixed. The initial optical density was chosen to be >2 to allow further time (*ca.* 15 min) for the re-establishment of thermal equilibrium before readings were taken. The data of optical density and time were punched on paper tape by a Solartron Data Logger; at least 250 points were collected for each run. The data tapes were processed directly, by use of a least-mean-squares treatment, on an Elliott 903 computer.

RESULTS AND DISCUSSION

Product Determination.—The ^1H n.m.r. spectrum of the products obtained from decomposing a 1M solution of 3-diazobutan-2-one has exactly the same peaks as the spectrum of a known mixture of $CH_2{:}CHCOMe$ and HO·CHMe·COMe. From the relative size of the COMe peaks we estimate the percentage of the olefin was 25 ± 5%. The ratio of the products was the same whether the diazo-ketone was decomposed with $HClO_4$ or AcOH. A similar comparison of the ^1H n.m.r. spectrum of the products from ethyl diazopropionate and from $HO{\cdot}CHMe{\cdot}CO_2Et$ and $CH_2{:}CH{\cdot}CO_2Et$ showed that the major product was ethyl lactate with some of the olefin; there were also significant amounts of other unidentified products. During the course of our work Dahn and Ballenegger[2] published the results of their thorough investigation of the product ratios; they had used not only ^1H n.m.r. but also colorimetry, polarography, iodometric titration, and g.l.c. Our results are in good agreement with theirs;

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[5] V. Gold, *Trans. Faraday Soc.*, 1960, **56**, 255.

[6] A. J. Kresge, *Pure. Appl. Chem.*, 1964, **8**, 243.

[7] R. A. Marcus, *J. Phys. Chem.*, 1968, **72**, 891.

[8] O. Diels and K. Pflaner, *Ber.*, 1915, **48**, 229.

[9] H. Morrison, S. Danishefsky, and P. Yates, *J. Org. Chem.*, 1961, **26**, 2617.

[10] K. Nakagawa, H. Onone, and K. Minami, *Chem. Comm.*, 1966, 730.

they also found that the product ratio was independent of the acid catalyst.

Catalysis by H_3O^+.—Figure 1 shows typical first-order plots for 3-diazobutan-2-one and ethyl diazopropionate. Figure 2 shows the dependence of the first-order rate constant for the diazo-ketone on $[H_3O^+]$. In these experiments no additional salt was added since the ionic strength was small enough for the activity coefficient ratio to be close to 1. For the diazo-ester the reaction rate is faster and so the reaction could be followed to higher pH; the results are shown in Figure 3. For comparison with the carboxylic acids a series of experiments were also carried out at an ionic strength of $\mu = 0{\cdot}050$M. The results are in Table 1. The ratio of the rate constants for $\mu = 0{\cdot}05$M and $\mu =$ *ca.* 10^{-3}M is *ca.* 1·05 for each compound and this is a reasonable value for a salt effect for a reaction where there is no change of charge.

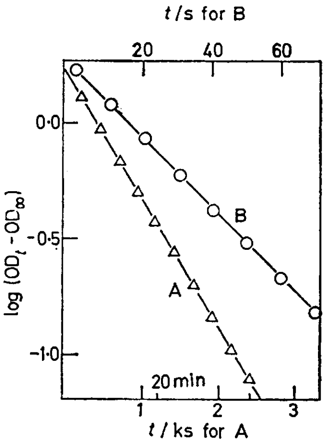


FIGURE 1 Typical first-order plots for A, 3-diazobutan-2-one in 1·9mM-$HClO_4$ and B, ethyl diazopropionate in 1·0mM-$HClO_4$

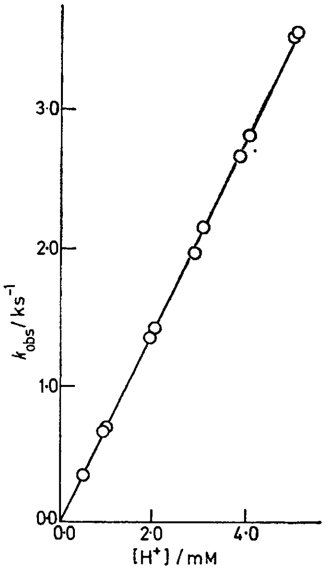


FIGURE 2 Variation of observed first-order rate constant for 3-diazobutan-2-one with $[H_3O^+]$ in solutions of $HClO_4$

TABLE 1

Rate constants for catalysis by H_3O^+

	3-Diazobutan-2-one	Ethyl diazopropionate	
	$\mu = 0{\cdot}050$M	$\mu = 10^{-3}$M	$\mu = 0{\cdot}05$M
	k_{H^+}/l mol^{-1} s^{-1}	k_{H^+}/l mol^{-1} s^{-1}	k_{H^+}/l mol^{-1} s^{-1}
	0·740	19·0	20·5
	0·737	19·2	21·0
	0·735	18·8	20·6
	0·742	19·5	20·6
		19·2	
Mean	0·738 ± 0·002	19·2 ± 0·2	20·4 ± 0·2

From Figure 2 for 3-diazobutan-2-one, $\mu =$ *ca.* 10^{-3}M, $k = 0{\cdot}710 \pm 0{\cdot}003$ l mol^{-1} s^{-1}.

The ester decomposes 28 times more rapidly than the ketone. This may be connected with the greater development in the ketone of the delocalised π system (Scheme 3). Restricted rotation about the C·C bond causes broadening and splitting of the ^{1}H n.m.r. spectra of diazo-ketones and diazo-esters [11] through the sluggish interconversion of the two isomers (1) and (2). The ^{1}H n.m.r. spectrum of 3-diazobutan-2-one at 40 °C has one sharp and one broad CH_3 peak; ethyl diazopropionate, like ethyl diazoacetate, does not show any

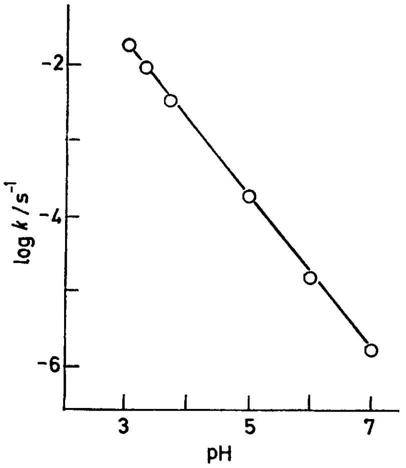
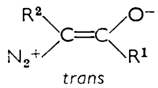


FIGURE 3 Variation of observed first-order rate constant for ethyl diazopropionate with pH; the line has a gradient of unity

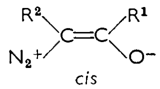
$$N^{-}{:}N^{+}{:}CR^{2}COR^{1} \longleftrightarrow N\vdots N^{+}CR^{2}{:}C(O^{-})R^{1}$$

SCHEME 3



trans

(1)



cis

(2)

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[11] F. Kaplan and G. K. Meloy, *J. Amer. Chem. Soc.*, 1966, **88**, 950.

broadening at this temperature. However at lower temperatures (−20 to −40 °C) the diazoacetate spectrum does broaden and split[11] into distinct signals from the two isomers. The same behaviour is observed for 3-diazobutan-2-one which has a coalescence temperature of 20 °C.[12]

An interesting difference between diazo-ketones and diazo-esters is their u.v. spectra. The diazo-ketones generally have a double-peaked u.v. absorption band;[13-15] the relative intensity of the two peaks can be varied by changing the solvent and there is usually an isosbestic point. Figure 4 shows that 3-diazobutan-2-one follows this pattern; ethyl diazopropionate on the other hand, like ethyl diazoacetate, has a single maximum ($\lambda_{max.}$ 263 nm in H_2O), which, like that of ethyl diazoacetate,[16] changes only slightly with change of solvent. The isosbestic point for the ketones suggests an equilibrium involving two isomers or tautomers. Explanations involving keto–enol or diazo–isodiazo-tautomerism have been considered[13] but as shown in Table 2 the results for 3-diazobutan-2-one confirm the conclusion[15] that explanations of this sort are unlikely. It has been suggested[15] that the double-peaked spectra are caused by the *cis*- and *trans*-isomers found by ^1H n.m.r. The rate of interconversion of the isomers is irrelevant on the time-scale of u.v. spectroscopy, but the equilibrium proportions are important. They are given in Table 2. This explanation also does not seem too convincing. Further, while the u.v. spectra change with solvent, Kaplan and Meloy found that the proportion of *cis*-isomer of $N_2CH{\cdot}COMe$ was the same to within 2% in neat diazo-ketone, in $CDCl_3$, and in acetone. Thus at the moment there seems to be no satisfactory explanation of these spectra except possibly for the solvation of the diazo-ketone in two different forms.[14]

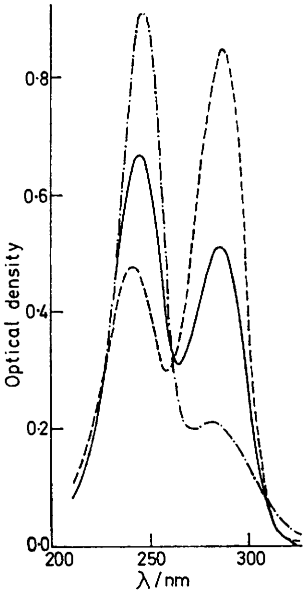

FIGURE 4 The u.v. spectra of 3-diazobutan-2-one in various solvents; - - - - H_2O, —— MeOH, and – · – · – Et_2O

TABLE 2

U.v. spectra of diazo-compounds

Compound	U.v. spectrum	Ref.	Tautomeric explanations (I)	(II)	(III)	(IV)	% *cis*-Isomer	Ref.
$N_2CH{\cdot}CO_2Et$	Single	13	×	√	×	√	54	11
$N_2CH{\cdot}CO{\cdot}Bu^t$	Double	13	×	√	×	√	>99	11
$N_2CMe{\cdot}COMe$	Double	This work	√	×	√	×	80	12

(I) $N_2CR{\cdot}CO{\cdot}CH{<} \rightleftharpoons N_2CR{\cdot}COH{:}C{<}$ (II) $N_2CH{\cdot}COR \rightleftharpoons N_2C{:}COHR$ (III) $N_2CR{\cdot}COCH{<} \rightleftharpoons HN_2^+CR{\cdot}CO^-{:}C{<}$

(IV) $N_2CH{\cdot}COR \rightleftharpoons HN_2^+C{:}CO^-R$

Catalysis by R^2CO_2H.—In the buffer solutions the observed rate constant is the sum of two terms [equation (1)]. Let h be defined by equation (2). Since the ionic

$$k_{obs} = k_{H^+}[H_3{}^+O] + k_{HA}[HA] \quad (1)$$

$$h = [H_3O^+] = K[HA]/[A^-] \quad (2)$$

strength μ was kept constant the activity coefficients can be included in k_{H^+}, k_{HA}, and K; these constants then refer to an ionic strength of 0·050M.

Now the buffer solutions are made up from standard

$$c = [H_3O^+] + [HA] \quad (3)$$

$$c' = [Na^+] = [A^-] - [H_3O^+] \quad (4)$$

solutions of HA and NaA so that we know c and c' [equations (3) and (4)]. Substitution in equation (2) gives a quadratic equation (5) for h. Equation (1) is

$$h^2 + h(c' + K) - Kc = 0 \quad (5)$$

rearranged to give (6). The calculation of h depends on

$$k_{obs}/h = k_{H^+} - k_{HA} + k_{HA}(c/h) \quad (6)$$

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[12] C. Wentrup and H. Dahn, *Helv. Chim. Acta*, 1970, **53**, 1637.

[13] F. A. Miller and W. B. White, *J. Amer. Chem. Soc.*, 1957, **79**, 5974.

[14] E. Fahr, *Chem. Ber.*, 1959, **92**, 398.

[15] C. Pecile, A. Foffani, and S. Ghersetti, *Tetrahedron*, 1964, **20**, 823.

[16] E. A. Moelwyn-Hughes and P. Johnson, *Trans. Faraday Soc.*, 1941, **37**, 282.

the value of K. From data[17] on the dissociation of acetic acid in salt solutions we write, for all the carboxylic acids at $\mu = 0{\cdot}050\text{M}$, $K/K_0 = 1{\cdot}47$, where K_0 is the dissociation constant of the acid at infinite dilution. Values of K_0 were taken from a recent compilation.[18]

The value of k_{HA} determined from the gradient of a plot of the data according to equation (4) will be somewhat sensitive to the value of K used in equation (2). From equation (5) we obtain equation (7), because in

$$\frac{\ln h}{\partial \ln K} = \frac{K(c/h - 1)}{c' + K + 2h} \simeq \frac{1 - h/c}{1 + h/[\text{A}^-]} \simeq 1 - h/c \quad (7)$$

our experiments $h/[\text{A}^-]$ is usually less than 0·1. If k_{HA} is determined between $(c/h)_1$ and $(c/h)_2$ then we obtain equation (8).

$$\frac{\partial \ln k_{\text{HA}}}{\partial \ln K} \simeq -\frac{(k_{\text{H}^+}/k_{\text{HA}} - 1)}{(c/h)_1(c/h)_2} = -\varepsilon \quad (8)$$

Values of ε are considerably <1 so that the determination of k_{HA} is not vitiated by small uncertainties in the value of K. The advantage of the procedure described here is that there is no restriction on the composition of the buffer solutions; their composition may be chosen to give a convenient rate of reaction and to avoid large concentrations of either HA or A^-.

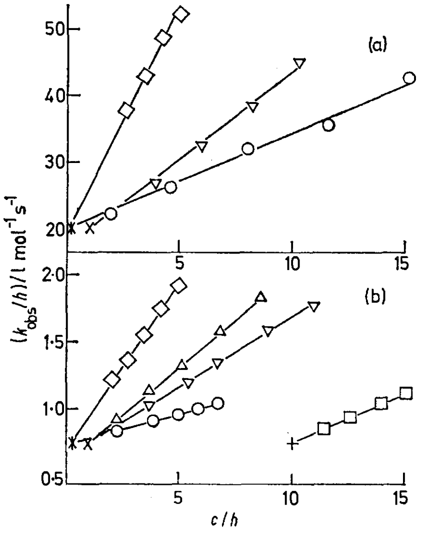

FIGURE 5 Plots of equation (6) for (a) ethyl diazopropionate and (b) 3-diazobutan-2-one. Acids: dichloroacetic plotted as 10x, □; cyanoacetic, △; monochloroacetic, ▽; glycollic plotted as x/10, ◇; acetic plotted as x/10, ○. The point (k_{H^+}, 1) plotted as x/10, ✳; plotted directly ×; plotted as 10x, +

Figure 5 shows plots of equation (6) for the diazo-compounds. Good straight lines are obtained which pass through the point (k_{H^+}, 1·0) as required by equation (6). Values of k_{HA} found from the gradients are given in Table 3, together with values of ε from equation (5). Figure 6 shows Brønsted plots for both compounds. The rate constants used are those at $\mu = 0{\cdot}050\text{M}$ while

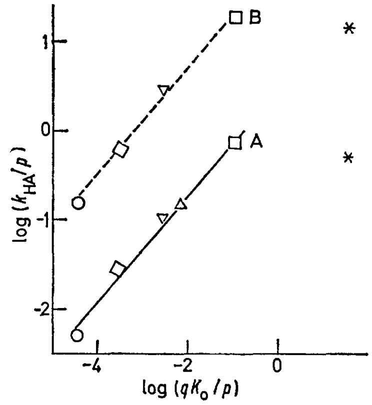

FIGURE 5 Brønsted plots for A, 3-diazobutan-2-one and B, ethyl diazopropionate according to equation (9); symbols for acids as in Figure 5; ✳, H_3O^+

the values of K_0[18] were those at infinite dilution. Statistical factors were used as in equation (9), where for

$$\log(k_{\text{HA}}/p) = \alpha_{\text{B}} \log(qK_0/p) + \text{constant} \quad (9)$$

$\text{R}^2\text{CO}_2\text{H}$ $p = 1$ and $q = 2$, and for H_3O^+ $p = 3$ and $q = 2$. The carboxylic acids gave the following values

TABLE 3

Rate constants for catalysis by $\text{R}^2\text{CO}_2\text{H}$ at $\mu = 0{\cdot}050\text{M}$

	3-Diazobutan-2-one		Ethyl diazopropionate	
Acid	$\frac{10^3 k_{\text{HA}}}{\text{l mol}^{-1}\text{ s}^{-1}}$	ε	$\frac{k_{\text{HA}}}{\text{l mol}^{-1}\text{ s}^{-1}}$	ε
AcOH	5·0 ± 0·2	0·05	0·147 ± 0·007	0·05
$\text{HO}{\cdot}\text{CH}_2{\cdot}\text{CO}_2\text{H}$	24·3 ± 0·5	0·03	0·65 ± 0·50	0·02
$\text{CH}_2\text{Cl}{\cdot}\text{CO}_2\text{H}$	103 ± 1	0·17	2·88 ± 0·08	0·15
$\text{NC}{\cdot}\text{CH}_2{\cdot}\text{CO}_2\text{H}$	141 ± 1	0·26		
$\text{CHCl}_2{\cdot}\text{CO}_2\text{H}$	730 ± 20	0·01	17·0 ± 1·5	0·16

of α_{B}: 0·61 ± 0·03 for 3-diazobutan-2-one and 0·59 ± 0·04 for ethyl diazopropionate. For both compounds the point for H_3O^+ lies well below the extrapolated line for the carboxylic acids. This behaviour is found for many A-$S_{\text{E}}2$ reactions.[19] Discussion of the values of α and the points for H_3O^+ is left to Part VI.

Finally, some of the values for the rate constants for 3-diazobutan-2-one are compared with those of Dahn and Ballenegger[2] in Table 4. Our results are *ca.* 20% higher. The reason for this discrepancy is not clear. It is significantly higher than the deviation in the means of either group. One possibility is a systematic error in the estimation of catalyst concentrations. In our case titrations of acid solutions carried out against different standard solutions of NaOH were always in good agree-

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[17] H. S. Harned and B. B. Owen, 'The Physical Chemistry of Electrolytic Solutions,' Reinhold, New York, 1958, p. 676.

[18] G. Kortüm, W. Vogel, and K. Andrussow, 'Dissociation Constants of Organic Acids in Aqueous Solution,' Butterworths, London, 1961.

[19] J. M. Williams and M. M. Kreevoy, *Adv. Phys. Org. Chem.*, 1968, **6**, 63.

ment. The fact that the point (k_{H^+}, 1) lies on each line in Figure 5 also suggests that there was no gross error in making up solutions. Another possibility is a systematic error in the temperature; our thermostatting arrangements are described in the Experimental section.

TABLE 4

Comparison of rate constants for 3-diazobutan-2-one

	Dahn and Ballenegger [2]		This work	
Catalyst	$\frac{k}{\mathrm{l\ mol^{-1}\ s^{-1}}}$	$\frac{\mu}{\mathrm{M}}$	$\frac{k}{\mathrm{l\ mol^{-1}\ s^{-1}}}$	$\frac{\mu}{\mathrm{M}}$
H_3O^+	0·58	0·010	0·68	$\sim 10^{-3}$
H_3O^+	0·65	0·076	0·74	0·050
$CHCl_2{\cdot}CO_2H$	0·59	0·076	0·73	0·050

We make one more observation on the data in Table 4. One can calculate the salt effect on the H_3O^+ reaction according to equation [20] (10) where, since all the ions are

$$\log k_2 = \log k_{2,0} + s\mu \qquad (10)$$

singly charged, μ is the same as the salt concentration. The values of s obtained by Dahn and Ballenegger [2] were 0·76 and in this work 0·33. Values of s for the reaction of diazoacetone [21] in $NaClO_4$ and in $HClO_4$ are 0·48 and 0·36 and for ethyl diazoacetate in $NaClO_4$ and KCl are 0·30 and 0·20 respectively.[22]

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[2/446 *Received, 28th February*, 1972]

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[20] R. P. Bell, 'Acid–Base Catalysis,' Oxford Univ. Press, 1941, p. 34.

[21] C. E. McCauley and C. V. King, *J. Amer. Chem. Soc.*, 1952, **74**, 6221.

[22] W. J. Albery, J. E. C. Hutchins, R. M. Hyde, and R. H. Johnson, *J. Chem. Soc.* (*B*), 1968, 219.