Deuterium Solvent Isotope Effects in Methanol Solution. Part II.[1] The General Acid-catalysed Reaction of Cyanoketen Dimethyl Acetal with Solvent

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The kinetics of the acid-catalysed reaction of cyanoketen dimethyl acetal in methanol solution, involving addition of solvent to the olefinic double bond of the substrate, have been studied by spectrophotometry at 24·8 °C. Catalysis by dilute strong mineral acid (hydrochloric acid) and by dichloroacetic acid were observed. The dependence of the rate constant on concentration of hydrochloric acid is linear in the presence of, but not strictly linear in the absence of, added electrolyte in swamping concentration, which suggests the operation of a significant salt effect. For reactions in methanolic dichloroacetic acid–sodium dichloroacetate buffers, the results at high buffer concentrations point to a significant amount of association between acid and anion. This conclusion is compatible with molecular weight determinations by vapour-pressure osmometry. The kinetic results are analogous to those previously obtained for the acid-catalysed hydrolysis of cyanoketen dimethyl acetal in aqueous solution. A common mechanism with a rate-limiting proton attachment to the olefinic double bond is indicated. Small amounts of residual water in the solvent do not greatly complicate the kinetic analysis.

The hydrochloric acid-catalysed reaction has also been studied in mixtures of MeOH and MeOD. The theory of the solvent isotope effect appropriate to this type of solvent system and reaction is developed and applied, again pointing to a close similarity to the solvent isotope effect of the reaction in aqueous solution. It is shown that the study of the solvent isotope effect in alcoholic solutions offers a convenient alternative procedure to the use of buffers for the investigation of general acid catalysis.

THE reaction of cyanoketen dimethyl acetal in and with water, according to equation (1), has been shown to be

$$H_2O + (MeO)_2C{:}CHCN \longrightarrow MeO_2C{\cdot}CH_2CN + MeOH \quad (1)$$

subject to general acid catalysis.[2] A range of aliphatic carboxylic acids are effective catalysts, with a Brønsted exponent $\alpha_A = 0{\cdot}62$. Hydrogen ions are also catalytic but their reactivity, though high, falls short of that

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[1] Part I, V. Gold and S. Grist, *J. Chem. Soc.* (*B*), 1971, 1665.

[2] V. Gold and D. C. A. Waterman, *J. Chem. Soc.* (*B*), 1968, 839.

predicted from the Brønsted catalysis law. In deuterium oxide as solvent the catalytic constants of the carboxylic acids are reduced by a factor of *ca.* 5·3. The catalytic constant of hydrogen ions is correspondingly reduced by a factor of *ca.* 3·0. In mixtures of H_2O and D_2O the catalytic constant of the hydrogen ion shows the dependence on the atom fraction of deuterium which is expected for a reaction in which the rate-limiting step is proton (or deuteron) transfer to the substrate [3] and in which the parameter α of the solvent isotope effect theory has a value in the range 0·5—0·65. The parameter α can be regarded as the Brønsted exponent for *proton* transfer from the series of isotopic hydrogen ions H_3O^+, H_2DO^+, and HD_2O^+. The fact that the range of α-values consistent with the results [2] straddles the value of α_A suggests that either of these values, α or α_A, can equally be admitted as evidence for incomplete proton transfer in the transition state or, in other terms, for a reaction mechanism with proton transfer to the substrate as the rate-limiting step. It is not essential to this argument to maintain that α and α_A must inevitably be identical,[4,5] nor that either provides a quantitative measure of the degree of proton transfer in the transition state.[6] The realisation that the catalysis law is only approximate [7] must in any case caution us against such generalisations.

The above experimental facts together build up a strong case for a mechanism in which the first and rate-limiting step can roughly be represented by equation (2). For related systems (ortho-esters [8,9] and acetals [10])

$$\mathrm{HA + (MeO)_2C{:}CHCN \xrightarrow{1} (MeO)_2\overset{+}{C}{\cdot}CH_2CN + A^-} \qquad (2)$$

there is evidence that proton transfer to a substrate may be synchronous with rupture of a C–O bond. However, these cases are not truly comparable, in that the receptor site of the transferred proton is an oxygen atom of the substrate molecule. In the case of keten acetals the proton transfer takes place to a carbon atom, as is confirmed, for the closely related system 2-dichloromethylene-1,3-dioxolan,[6] by the isotopic composition of the CH_2 group of the product, when the reaction is carried out in a mixture of H_2O and D_2O. By writing equation (2) we do not thereby dismiss the possibility that the proton transfer in (2) may be synchronous with nucleophilic attack by water on the adjoining carbon atom. This mechanistic variant appears to us to be indistinguishable on the basis of existing experimental evidence.

The conclusion, that experiments with strong acid as catalyst, in H_2O–D_2O mixtures, suffice to establish proton transfer in the rate-limiting step of a reaction, is interesting in that it suggests a method of studying general acid catalysis in systems where the use of buffers may not be practicable. An extension of this principle to other hydroxylic solvent systems would be particularly valuable since the sparing solubility of organic compounds in water often makes the use of alcohols as solvents a convenient alternative. On the other hand, from an electrochemical point of view, alcohols are less simple solvents since ionic association and other intermolecular and interionic interactions assume a greater importance and are less well understood. For this reason, the use of buffer solutions in the study of catalysis in alcohol solutions is not straightforward.

Early work on acid catalysis in methanol solution (or other alcohol solutions) gives virtually no guidance on the possibility of observing general acid catalysis. Bell's re-interpretation [11] of Goldschmidt's results on esterifications [12] shows that they are all consistent with specific hydrogen ion catalysis. The observation of kinetics which are of second order with respect to carboxylic acid for the esterification of these acids in alcohol solution [13] was put forward as *prima facie* evidence for catalysis by undissociated acid, but the conclusion requires reconsideration.

The decomposition of diazo-compounds in alcohols,[14] especially of diphenyldiazomethane in ethanol, is catalysed by a wide variety of carboxylic acids. The accepted mechanism involves proton transfer in a kinetically significant step. The solvent isotope effect,[15] whereby the rate is decreased in EtOD, for catalysis by toluene-*p*-sulphonic acid (a strong acid) is one of the most persuasive of the early experimental results in favour of such a mechanism. This work was not extended to mixtures of EtOH and EtOD.

This type of substrate and reaction was not selected for the present work mainly as a result of the observation [16] that the decomposition of 9-diazofluorene in aqueous solution was much less straightforward than in non-aqueous media. Because of this complication, the kinetic establishment of general acid catalysis and its characteristics in aqueous solution, with which we wished to compare the behaviour of an alcohol solvent system, seemed more difficult for this reaction than for the reaction chosen. In addition, it is known that there are subtle complications in the product-forming steps of the decomposition of diazo-compounds although, on current

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

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

[5] V. Gold, *Adv. Phys. Org. Chem.*, 1969, **7**, 259.

[6] V. Gold and D. C. A. Waterman, *J. Chem. Soc.* (*B*), 1968, 849.

[7] M. Eigen, *Angew. Chem. Internat. Edn.*, 1964, **3**, 1.

[8] J. G. Fullington and E. H. Cordes, *J. Org. Chem.*, 1964, **29**, 970; E. H. Cordes, *Progr. Phys. Org. Chem.*, 1967, **4**, 1.

[9] C. A. Bunton and R. H. De Wolfe, *J. Org. Chem.*, 1965, **30**, 1371.

[10] E. Anderson and B. Capon, *J. Chem. Soc.* (*B*), 1969, 1033.

[11] R. P. Bell, ' Acid–Base Catalysis,' Oxford Univ. Press, 1941, pp. 56–57, 100.

[12] H. Goldschmidt and P. Dahll, *Z. phys. Chem.*, 1925, **114**, 1; 1925, **117**, 312; 1927, **129**, 223.

[13] A. C. Rolfe and C. N. Hinshelwood, *Trans. Faraday Soc.*, 1934, **30**, 935; C. N. Hinshelwood and A. R. Legard, *J. Chem. Soc.*, 1935, 587.

[14] For a comprehensive review and references, see R. A. More O'Ferrall, *Adv. Phys. Org. Chem.*, 1967, **5**, 331.

[15] J. D. Roberts and C. M. Regan, *J. Amer. Chem. Soc.*, 1952, **74**, 3695.

[16] D. C. A. Waterman, Ph.D. Thesis, London, 1967.

interpretations, these do not apply to the rate-limiting process.[14]

The present investigation has accordingly concentrated on a reaction for which general acid catalysis is thoroughly established in aqueous solution and for which an analogous mechanism could reasonably be expected to apply in methanol, the alcohol most closely related to water. The study is concerned with the demonstration of general acid catalysis by use of buffer solutions, in the manner usually adopted for rigorous investigations in aqueous solution, and the application of the kinetic solvent isotope effect (mixtures of MeOH and MeOD) to the same problem. The reaction of a keten acetal was expected to be particularly suitable for the detection of catalysis by an acid other than the hydrogen ion since, in aqueous solution, the latter is less reactive than the catalysis law predicts.[2]

The transfer of the kinetic study of the reaction of a substrate with the solvent to a different solvent necessarily involves not only a 'medium effect' (whatever extended meaning we attach to this term) but also a change in the nature of the chemical reaction and, in the present case, of the actual product. The overall reaction is now described by equation (3). As for the aqueous reaction, the nature of the reaction product[17] requires a proton transfer to the olefinic portion of the

$$(\mathrm{MeO})_2\mathrm{C{:}CHCN} + \mathrm{MeOH} \longrightarrow (\mathrm{MeO})_3\mathrm{C{\cdot}CH_2CN} \quad (3)$$

substrate. The observation of general acid catalysis, now reported, again points to reaction (2) as the rate-limiting step, *i.e.*, the same process as in the reaction in aqueous solution.

EXPERIMENTAL

Methanol and methan[$^2H_1$]ol were dried and distilled as before.[1] In preliminary work the solvent was dried with magnesium and iodine.[18] This method is more efficient in removing water but had to be abandoned since it introduced a basic impurity at a level (up to 5×10^{-4}M) which was disturbingly high in view of the low concentrations of catalysing acid used.[19] The possibility of hydrogen exchange ruled out subsequent treatment of the dried alcohol with an involatile acid[18] and most of the usual efficient drying methods. With the exception of the experiments on the effect of added water (Table 1), all kinetic results therefore relate to solvent dried with calcium sulphate. Solutions were made up and transferred to spectrophotometer cells inside a dry-box.

Cyanoketen dimethyl acetal was prepared by McElvain and Schroeder's method.[17] The progress of its reaction with solvent (at 24·8 °C throughout) was followed spectrophotometrically (Unicam SP 800 or SP 500) at a wavelength close to its absorption maximum at 230 nm ($\varepsilon_{\max.}$ = 16,000) where the absorption of the ortho-ester formed according to equation (3) is small by comparison (ε = 77).

The production of the ortho-ester under conditions closely similar to those of the kinetic experiments was confirmed by isolation and comparison of i.r. and n.m.r. spectra with those of an authentic sample of ortho-ester prepared by the normal route.[20] For this product isolation a concentrated solution of the keten acetal in dry methanol was slowly injected into a stirred dry methanolic solution of hydrogen chloride (0·01M) or of dichloroacetic acid–sodium dichloroacetate at such a rate as to prevent a large build-up of reactant concentration. After completion of the reaction, excess of acid was destroyed by addition of calcium carbonate, the solution was filtered, and the solvent was then distilled off. No n.m.r. resonance due to a $CHCl_2$ grouping was detectable for the product isolated from the experiment with dichloroacetate buffer, implying that if any of the primary reaction product should be that of addition of dichloroacetic acid to the double bond, this must rapidly be solvolysed to ortho-ester.

Before a kinetic run, a stoppered spectrophotometer cell containing catalyst solution was allowed to attain thermal equilibrium in the thermostatted cell compartment of the spectrophotometer. It was then briefly opened for 1 μl of a methanol stock solution of the substrate to be injected from a Hamilton syringe, closed, vigorously shaken, and quickly replaced.

Under the conditions of the kinetic experiments the substrate concentration (*ca.* 10^{-4}M) is less than that of the residual water in the dried solvent. The isolation experiment therefore does not establish that the first product formed in these runs is the ortho-ester and not its hydrolysis product, methyl cyanoacetate. Further evidence on this

TABLE 1

Effect of water on rate of reaction of cyanoketen dimethyl acetal with solvent

A. H_2O in MeOH; [HCl] = $1{\cdot}93 \times 10^{-3}$M

$10^4[H_2O]$/M [a]	$10^4 k_{obs}$/s^{-1}	k_2/l mol^{-1} s^{-1} [b]	$10^4[MeOH_2^+]$/M [c]	k_M/l mol^{-1} s^{-1} [d]
133 [e]	271	14·0	18·22	14·9
317	242	12·5	16·91	14·3
506	224	11·6	15·74	14·2
689	205	10·6	14·76	13·9
872	191	9·9	13·89	13·8
1061	185	9·6	13·09	14·1
1244	171	8·9	12·40	13·8
1428	167	8·7	11·77	14·2
1617	158	8·2	11·19	14·1

B. L_2O in MeOL; $[LCl]_{stoich}$ = $7{\cdot}75 \times 10^{-4}$M; hydroxylic deuterium content = 97%

$10^4[D_2O]$/M [a]	$10^4 k_{obs}$/s^{-1}	k_2/l mol^{-1} s^{-1} [b]	$10^4[MeOL_2^+]$/M [c]	k_{MD}/l mol^{-1} s^{-1} [f]
110 [g]	46·8	6·04	7·39	6·34
110 [g]	45·7	5·90	7·39	6·19
110 [g]	44·5	5·74	7·39	6·03
275	41·5	5·35	6·90	6·02
445	38·7	4·99	6·46	5·99
610	37·2	4·80	6·08	6·11
775	34·8	4·49	5·75	6·05
975	34·0	4·39	5·44	6·25
1110	32·5	4·19	5·17	6·28

[a] Stoicheiometric total water concentration. [b] $k_2 = k_{obs}/[HCl]_{stoich}$ or $k_2 = k_{obs}/[LCl]_{stoich}$. [c] Calc. from equation (5), with K_4 = 4·5 l mol^{-1}. [d] $k_M = k_{obs}/[MeOH_2^+]$. [e] Residual water concentration, estimated by Karl–Fischer titration and by hydrolysis of ortho-ester. [f] $k_{MD} = k_{obs}/[MeOL_2^+]$. [g] Residual water concentration, estimated by hydrolysis of ortho-ester.

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[17] S. M. McElvain and J. P. Schroeder, *J. Amer. Chem. Soc.*, 1949, **71**, 40.

[18] H. Lund and J. Bjerrum, *Ber.*, 1931, **64**, 210.

[19] See also H. Goldschmidt and P. Dahll, *Z. phys. Chem.*, 1924, **108**, 121.

[20] S. M. McElvain and J. P. Schroeder, *J. Amer. Chem. Soc.*, 1949, **71**, 40.

point is provided by experiments on the hydrolysis of the ortho-ester (see below).

The reactions strictly obeyed first-order kinetics, rate constants evaluated from the observations on a single experiment having standard deviations of the order of 0·3—0·4%. The reproducibility of replicate runs was ±2%, the wider error limits being possibly due to slight variations in water content. Tables 1—5 summarise the rate constants (all at 24·8 °C).

TABLE 2

Dependence of reaction velocity on concentration of hydrogen chloride (without added salts)

10^3[HCl]/M	10^2k_{obs}/s^{-1}	k_2/l mol^{-1} s^{-1}
0·137	0·155	11·3
0·161	0·186	11·6
0·251	0·268	10·7
0·371	0·472	12·7
0·440	0·550	12·5
0·539	0·712	13·2
0·551	0·700	12·7
0·634	0·800	12·6
0·801	1·07	13·3
0·825	1·11	13·4
0·836	1·10	13·1
1·058	1·41	13·3
1·208	1·63	13·5
1·238	1·63	13·2
1·543	2·10	13·6
1·769	2·42	13·7
2·652	3·78	14·3
4·15	6·23	15·0
5·11	7·64	15·0
6·84	10·9	15·9
8·29	13·1	15·8

TABLE 3

Dependence of reaction velocity on concentration of hydrogen chloride in presence of sodium perchlorate (total ionic strength = 0·117M)

10^3[HCl]/M	10^2k_{obs}/s^{-1}	10^2k/l mol^{-1} s^{-1} *
1·437	2·76	19·2
1·968	3·97	20·1
2·60	4·97	19·1
3·33	6·37	19·1
3·64	7·20	19·8
3·86	7·68	19·9
5·10	9·63	18·9
5·97	11·2	18·8
6·86	13·4	19·5
7·73	14·4	18·6
8·29	15·9	19·2
8·82	17·0	19·3
9·47	18·4	19·4
10·14	20·1	19·8

* The best value of k_2 obtained from the regression of k_{obs} upon [HCl] is 19·3 ± 0·3 l mol^{-1} s^{-1}.

Catalysis by Hydrochloric Acid.—The dependence of the rate constant on the concentration of hydrogen chloride was examined for solutions containing hydrogen chloride as the only added solute besides the substrate (Table 2) and for solutions containing a swamping concentration of sodium perchlorate (total ionic strength = 0·117M) (Table 3). In the latter case, the observed rate constant was proportional to the acid concentration, and the second-order rate coefficients ($k_2 = k_{obs}$/[HCl]) showed no significant trend over the concentration range 0·00014—0·01M. On the other hand, in the experiments with hydrogen chloride alone, the value of k_2 was smaller and increased with acid concentration. The two sets of observations suggest the presence of a positive electrolyte effect on the reaction rate. The equilibrium constant for dissociation of un-ionised and associated forms of hydrogen chloride into free ions, derived from conductivity measurements,[21] predicts almost complete dissociation at [HCl] = *ca.* 10^{-3}M. This is in the range where the concentration-dependence of the second-order rate constant is very marked, so that it does not seem probable that a dissociation equilibrium can be held responsible for this concentration-dependence.

TABLE 4

Deuterium solvent isotope effect on hydrogen chloride-catalysed reaction

n	10^3[LCl]/M	10^3k_{obs}/s^{-1}	k_2/s^{-1}
0·0	0·3712	0·472	12·72
0·0	0·4401	0·550	12·50
0·0	0·5385	0·712	13·22
0·0	0·5510	0·700	12·70
0·0	0·6342	0·800	12·62
0·0	0·8006	1·068	13·34
0·0	0·8247	1·108	13·44
0·0	0·8355	1·109	13·13
0·0809	0·5662	0·713	12·59
0·0809	0·6920	0·886	12·79
0·0809	0·8177	1·041	12·73
0·0948	0·9436	1·216	12·89
0·1365	0·5621	0·714	12·71
0·1365	0·7026	0·873	12·43
0·1580	0·5662	0·692	12·22
0·1580	0·6920	0·861	12·45
0·1580	0·9436	1·181	12·52
0·2006	0·4216	0·512	12·14
0·2006	0·5621	0·688	12·24
0·2006	0·7026	0·836	11·90
0·2388	0·5662	0·682	12·04
0·2388	0·6920	0·833	12·03
0·2388	0·9436	1·158	12·27
0·2584	0·4216	0·493	11·70
0·2584	0·5621	0·676	12·02
0·2584	0·7026	0·828	11·79
0·3217	0·5662	0·636	11·23
0·3217	0·6920	0·775	11·20
0·3217	0·8177	0·954	11·67
0·3217	0·9436	1·114	11·81
0·4120	0·9436	1·062	11·26
0·4124	0·8177	0·928	11·34
0·4127	0·6920	0·759	10·96
0·4130	0·5662	0·636	11·23
0·4930	0·9436	0·986	10·45
0·4933	0·8177	0·866	10·59
0·4937	0·6920	0·722	10·43
0·4940	0·5662	0·587	10·36
0·5866	0·6920	0·699	10·10
0·5870	0·5662	0·587	10·36
0·6767	0·9436	0·887	9·40
0·6776	0·6920	0·649	9·39
0·6780	0·5662	0·507	8·95
0·7546	0·9436	0·822	8·71
0·7553	0·8177	0·691	8·45
0·7560	0·6920	0·574	8·29
0·7566	0·5662	0·481	8·50
0·8563	0·9436	0·699	7·41
0·8573	0·8177	0·594	7·27
0·8581	0·6920	0·506	7·31
0·8591	0·5662	0·410	7·24
0·9629	0·9436	0·545	5·77
0·9639	0·8177	0·456	5·58
0·9649	0·6920	0·368	5·32
0·9659	0·5662	0·304	5·37
0·9669	0·4404	0·235	5·34
0·9686	0·5621	0·317	5·64
0·9691	0·6323	0·337	5·33
0·9696	0·7026	0·366	5·21

[21] T. Shedlovsky and R. L. Kay, *J. phys. Chem.*, 1956, **60**, 151.

TABLE 5

Kinetic experiments in dichloroacetic acid-sodium dichloroacetate buffer solutions (ionic strength $= 0{\cdot}1$M)

A. $[HA]/[A^-] = 0{\cdot}921$

10^3[HA]/M	10^4k_{obs}/s^{-1}
0·78	1·64
1·72	2·59
2·16	3·44
3·03	4·14
3·64	4·40
5·44	6·54
5·52	6·72
6·53	7·80
6·65	7·89
7·08	8·19
8·83	9·85
8·99	9·99
9·56	10·60
12·07	12·9
12·59	13·4
15·36	15·5
16·21	16·3
20·30	19·5

B. $[HA]/[A^-] = 0{\cdot}409$

10^3[HA]/M	10^4k_{obs}/s^{-1}
1·09	1·63
4·09	4·40
6·67	6·86
9·64	9·14
12·08	10·8
15·54	12·9

C. $[HA]/[A^-] = 1{\cdot}80$

10^3[HA]/M	10^4k_{obs}/s^{-1}
2·27	4·44
4·43	6·64
4·45	6·86
6·60	9·83
8·52	10·8
8·79	11·5
12·53	15·7
15·29	18·0
16·82	19·1
20·61	22·6
21·52	23·2
24·28	24·9

The fact that the dependence of reaction velocity on catalyst concentration is not strictly linear in the absence of swamping electrolyte creates a problem for the comparison of rate constants for hydrochloric acid catalysis in isotopically different solvents (Table 4). These experiments could not all be performed at exactly the same concentration of acid, nor was it practicable to make a detailed examination of the acidity-dependence of the rate constants for every isotopic solvent composition used. Two separate methods of treating the data were tried in an attempt to overcome the difficulty and, in addition, the measurements were restricted to a limited range of catalyst concentrations (4×10^{-4}—$1{\cdot}0 \times 10^{-3}$M) over which the second-order rate constant increases by only *ca.* 7%. In the first method all rate constants, for runs within this range of catalyst concentrations, were used without modification, and the scatter of the points was accepted as a feature of the least-squares analysis which is compensated by the large number (58) of data. In the second method a small percentage correction was applied to all second-order rate constants to relate them to a uniform acid concentration of 7×10^{-4}M. The correction was deduced from the best curve drawn through the values of k_2 as a function of [HCl] in light water, and was assumed to apply also to the partially deuteriated media. This procedure leads to a small, but not spectacular, reduction in the residual error of the least-squares polynomial regression of k_2 upon n. Because of possible objections to the manner of the correction, the results are here presented according to the first method. Since the correction by the second method does not eliminate the scatter of the points we suspect that variable ingress of moisture or basic impurity in the solvent have not entirely been eliminated.

Catalysis by Dichloroacetic Acid.—Dichloroacetic acid–dichloroacetate buffer stock solutions were prepared by neutralisation of 0·1M-sodium methoxide with dichloroacetic acid and addition of an excess of acid. The solutions were periodically checked by titration and found to be stable if stored at −40 °C. For kinetic experiments the buffer stock solutions were diluted by weight with 0·1M-sodium perchlorate solution so as to maintain a constant ionic strength of 0·1M. Because of light absorption by buffer at 230 nm the formation of product was in this case followed spectrophotometrically at slightly longer wavelengths, as close to the absorption maximum of reactant as possible. Sets of experiments were carried out at varying acid concentration for three different buffer ratios (Table 5).

Hydrolysis of Methyl Orthocyanoacetate.—This reaction was studied with a view to its use as a technique for estimating water in methanol. The extinction coefficient of methyl cyanoacetate at 230 nm (ε 16) is less than that of the ortho-ester (ε 77). Since both these values are very much smaller than that for the substrate, the observed infinity readings in the reaction of cyanoketen dimethyl acetal do not allow us to deduce whether the formation of ester or ortho-ester is being followed. However, by use of higher concentrations of ortho-ester than were present in the reactions of the keten acetal, it is possible to observe the decrease in absorption which accompanies the hydrolysis of ortho-ester to methyl cyanoacetate in methanol containing water in quite low concentration. Over a limited concentration range (with $[H_2O] <$ [ortho-ester]) it was found that the decrease in optical density is independent of the concentration of ortho-ester and increased by small amounts of added water. If we assume that the hydrolysis is stoicheiometrically complete, it is possible to calculate from this decrease, for methanol solutions without added water, the residual concentration of water not removed by drying. The result thus obtained (*ca.* 0·014M) for ordinary methanol agreed to within ±20% with the titrimetric estimation of water by the Karl–Fischer method. This kinetic analysis method, which is more economical in the amount of solvent required, was therefore used for estimating the concentration of water in MeOD. The reaction is not instantaneous and requires the presence of acid (*ca.* 10^{-3}M-HCl) as catalyst.

Molecular-weight Determinations.—The effective molecular weight of dichloroacetic acid in methanol solutions of its sodium salt was determined at 35 °C by use of a Perkin-Elmer–Hitachi model 115 vapour-pressure osmometer. Acetanilide was used as standard solute; the calibration is expressible as 9134 scale units of resistance/(mol kg^{-1}). The acid solutions were prepared by addition of standard amounts of dichloroacetic acid to standardised solutions of sodium methoxide. Results are in Table 6.

TABLE 6

Vapour-pressure osmometry on solutions of sodium dichloroacetate–dichloroacetic acid in methanol at 35 °C

A. [NaA] = 0

[HA]/(mol kg^{-1})	5·75	11·49	17·24	22·99	28·74	45·98
ΔR *	55·5	111·0	154·8	211·6	260·0	407·6
ΔR_0 †	52·5	104·9	157·5	210·0	262·5	420·0
i ‡	1·06	1·06	0·98	1·01	0·99	0·97

B. [NaA] = 15·46 molal

[HA]/(mol kg^{-1})	10·21	15·34	20·48	25·61	30·74	35·88
ΔR *	84·5	132·5	176·5	215·5	254·5	303·5
ΔR_0 †	93·3	140·1	187·1	233·9	280·8	327·7
i ‡	0·91	0·95	0·94	0·92	0·91	0·93

* ΔR = (scale reading of osmometer) − (scale reading of osmometer in absence of added acid). † ΔR_0 = value of ΔR expected from stoicheiometric concentration of acid and calibration of osmometer with acetanilide (1 mol kg^{-1} ≡ 9134 scale units). ‡ $i = \Delta R/\Delta R_0$.

DISCUSSION

Effect of Water on Reaction Velocity.—The results in Table 1 indicate that added water has a pronounced effect on the rate. Since the methanol used in the kinetic studies contained an appreciable residual concentration of water, this introduces a complication into the kinetic analysis which must be clarified at the outset. It might be thought that this difficulty could have been completely avoided by more efficient drying methods but we found that such methods had other disadvantages and either introduced basic impurities or caused some hydrogen exchange and hence loss of deuterium from MeOD.

The presence of water in the solvent raises the question whether reaction (3) is indeed the process under investigation or whether this is, entirely or in part, the direct hydrolysis of the keten acetal to ester [reaction (1)]. To the extent that all measurements relate to media of approximately constant water content, and hence presumably to the formation of the same product or mixture of products, the question does not seem important. Further, we have already concluded that proton transfer, as formulated in equation (2), is involved in the rate-limiting step, so that any assistance from the interaction of a water molecule with the incipient carbonium centre is probably of similar importance as the corresponding interaction of a methanol molecule. Since the ortho-ester is hydrolysed in wet methanol, the ultimate product must be methyl cyanoacetate. The fact that this hydrolysis is relatively slow makes it more probable that the primary product of the reaction of cyanoketen dimethyl acetal with slightly wet methanol is the ortho-ester, but the argument is not conclusive.

A different question is whether the proton solvated by methanol ($MeOH_2^+$) is the only effective catalyst in the slightly wet methanol used or whether hydrated protons (H_3O^+) must also be considered. Over the narrow solvent composition range with which we are concerned, it seems unnecessary to seek an even finer distinction between hydrogen ions (of either kind) according to their further solvation by water or methanol.[22]

All these problems can more or less be circumvented by a short extrapolation of all rate measurements to zero water concentration. From Table 1 it is possible to deduce that the residual amount of water present in dried methanol depresses the reaction velocity for MeOH and MeOD by a very similar factor, close to unity (1·05—1·06), from the rate in anhydrous solvent. Accordingly, *relative* rate measurements taken in solvent dried by our method are good approximations to *relative* rate constants in perfectly dry methanol.

The same conclusion follows from a more detailed analysis where we explicitly allow for the reaction (4). The equilibrium constant (K_4) of this reaction is reasonably well known for methanol containing only a small amount of water. A variety of experimental determinations [19,23] all indicate a value of K_4, defined without

$$MeOH_2^+ + H_2O \rightleftharpoons H_3O^+ + MeOH \qquad (4)$$

inclusion of the solvent concentration according to equation (5) and in molarity concentration units, close to 4·5.

$$K_4 = [H_3O^+]/([MeOH_2^+][H_2O]) \qquad (5)$$

If we admit the possibility of catalysis by both H_3O^+ and $MeOH_2^+$ (catalytic coefficients k_W and k_M), the observed first-order rate constant should be given by equations (6) and (7). Equation (5) allows us to calculate the

$$k_{obs} = k_M[MeOH_2^+] + k_W[H_3O^+] \qquad (6)$$

$$= (k_M - k_W)[MeOH_2^+] + k_W[H^+]_{Total} \qquad (7)$$

concentrations of $MeOH_2^+$ and H_3O^+ as a function of acid and water concentration. According to equation (7) k_{obs} should be proportional to $[MeOH_2^+]$ at a fixed stoicheiometric hydrogen ion concentration. A test of equation (7) on this basis is shown in Figure 1. The lines through the points indicate the absence of a significant intercept and hence a negligible contribution from H_3O^+-catalysis to the reaction rate. This conclusion again implies that for the experiments without deliberately added water (for which the concentration of H_3O^+ is very small compared with that of $MeOH_2^+$) the stoicheiometric second-order rate constant differs only very slightly from the catalytic constant for the $MeOH_2^+$ ion. Although it is not known what precise value of K_4 should be taken for the deuteriated solvent systems, the fact that the error caused by presence of the aqueous hydrogen ion is so slight allows us to regard all rates in methanolic solvents dried by the same standard procedure as reliable relative to each other. In other words, the ratios $(k_{obs})_D/(k_{obs})_H$ are taken to be indistinguishable from $(k_M)_D/(k_M)_H$ at the level of accuracy of our work.

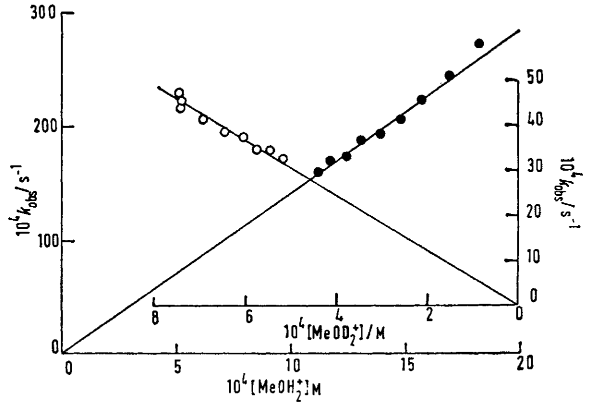

FIGURE 1 Effect of water concentration on rate: dependence of observed rate constant on calculated concentration of $MeOH_2^+$ (or $MeOD_2^+$)

When allowance is made for the concentration of methanol, the value of K_4 implies that the $MeOH_2^+$ ion in methanol is a much stronger acid than H_3O^+ in methanol. The large difference in the catalytic constants of these species is thus intelligible.

Catalysis by Hydrochloric Acid in Light Solvent.—The reaction is catalysed by hydrogen chloride but, in the absence of other added electrolyte, the second-order rate constant increases with acid concentration (Table 2).

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[22] C. F. Wells, *Discuss. Faraday Soc.*, 1960, **29**, 231.

[23] H. Goldschmidt and A. Thuesen, *Z. phys. Chem.*, 1912, **81**, 30; L. Thomas and E. Marum, *ibid.*, 1929, **143**, 191; L. S. Guss and I. M. Kolthoff, *J. Amer. Chem. Soc.*, 1940, **62**, 1494.

In the presence of a swamping concentration of sodium perchlorate, so as to maintain the ionic strength at 0·117M, this drift of the second-order rate constants is not observed and the value of the constant is significantly higher (Table 3). Both these findings suggest that the reaction is subject to a small positive electrolyte effect. In the absence of acid the rate is immeasurably small.

Catalysis by Dichloroacetic Acid in Light Solvent.—The reaction can also be catalysed by dichloroacetic acid–sodium dichloroacetate buffer solutions (Table 5). At low concentrations of acid the observed rate constant increases linearly with the concentration of dichloroacetic acid. The slope is the same for different buffer ratios, indicating that there is no effect due to the dichloroacetate ion. There is a finite intercept, corresponding to the extrapolated rate constant at zero concentration, the magnitude of which depends on the buffer ratio. Since there is no measurable reaction in the absence of catalyst, these results suggest general acid catalysis by two species in these solutions, according to equations (8) and (9). In those equations the first term of the right-hand side should correspond to the intercept and k_{HA} to the slope in

$$k_{obs} = k_H[H^+] + k_{HA}[HA] \qquad (8)$$

$$= k_H K'_{HA}[HA]/[A^-] + k_{HA}[HA] \qquad (9)$$

a series of experiments at constant buffer ratio and varying concentration of HA. In equation (9) K'_{HA} is the concentration quotient $[H^+][A^-]/[HA]$.

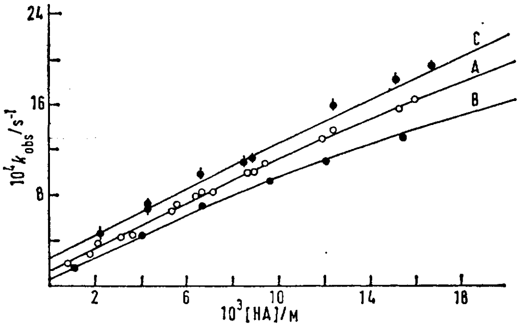

FIGURE 2 Catalysis by dichloroacetic acid–sodium dichloroacetate buffers (experimental points with calculated curves, see text). Buffer ratios for curves A, B, and C are given in Table 5.

Buffer Interactions.—Although the dependence of rate constant on buffer concentration is satisfactorily linear at low concentrations, a definite curvature, concave to the concentration axis, is noticeable when the graphs are extended to higher concentration (Figure 2). This behaviour is most marked for the block of experiments with the lowest buffer ratio, $[HA]/[A^-] = 0{\cdot}409$. The effect is reminiscent of the hydrolysis of cyanoketen dimethyl acetal where a similar reduction of the catalytic activity of certain carboxylic acids at high concentrations of acid or sodium carboxylate was ascribed to dimerisation and association, according to equations (10) and (11),[2] the species $(HA)_2$ and HA_2^- being assumed to have negligible catalytic effect.

$$2HA \rightleftharpoons (HA)_2 \qquad (10)$$

$$HA + A^- \rightleftharpoons HA_2^- \qquad (11)$$

For the reaction in water this phenomenon is not noticed with dichloroacetic acid, but only becomes prominent with appreciably weaker carboxylic acids. The effect is pronounced with aqueous acetic acid and Gold and Waterman used a curve-fitting approach to obtain values of the equilibrium constants (concentration quotients) of the reactions of equations (10) and (11) (called K_d and K_{ass}, respectively) from rate data,[2] on the assumption that the species $(HA)_2$ and HA_2^- are catalytically inactive. The same approach has been used in the present study for methanolic dichloroacetic acid. The best fit for all kinetic data in Table 5 is obtained for the following numerical values: $k_{HA} = 0{\cdot}106$ l mol^{-1} s^{-1}; $k_H K'_{HA} = 1{\cdot}3 \times 10^{-4}$ s^{-1}; $K_{ass} = 8{\cdot}2$ l mol^{-1} l; $K_d = 0{\cdot}28$ l mol^{-1}. The solid curves in Figure 2 are calculated with these parameters. The product $k_H K'_{HA}$, defining the intercept, can be resolved into its factors. The value of k_H at an ionic strength of 0·1M is, according to the data in Tables 2 and 3, *ca.* 18 l mol^{-1} s^{-1}, giving $K'_{HA} = 7 \times 10^{-6}$ mol l^{-1}. This value may be compared with an approximate estimate based on old literature data. Combining a conductimetric value of the dissociation constant at very low concentration [24] with the observation that 0·1M-lithium chloride, added as swamping electrolyte, increases the value of K'_{HA} of several carboxylic acids in methanol by the same factor,[25] we are led to a value of *ca.* 4×10^{-6} mol l^{-1} for K'_{HA} in 0·1M-lithium chloride. Since this type of salt effect may be somewhat specific, the value of K'_{HA} in 0·1M-sodium perchlorate, the swamping electrolyte used in our kinetic experiments with dichloroacetic acid, could slightly differ from this estimate. The approximate agreement of the two very differently deduced values indicate that the ' acidic species ' formed on ionisation of a carboxylic acid in methanol has a concentration reasonably predictable from simple equilibria and a catalytic effect closely similar to that of hydrogen chloride in solution. The simplest conclusion from these findings is that in both cases the same ' acidic species ' is formed, and that this is the solvated hydrogen ion.

Comparison of the values of K_{ass} and K_d for dichloroacetic acid in methanol with the values for aqueous acids suggests that reactions (10) and (11) both assume greater importance in methanol, but that K_{ass} is increased relative to K_d. If the effects of the non-linear dependence of k_{obs} upon buffer concentration are correctly described in these terms, and are not due to some unrecognised mechanistic complication, then the consequences of reactions (10) and (11) should also appear as irregularities in colligative properties of the buffer solutions. This prediction appears to be borne out by determinations of the molecular weight of dichloroacetic acid in methanol solutions containing sodium dichloro-

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[24] H. Goldschmidt and F. Aas, *Z. phys. Chem.*, 1924, **112**, 423.
[25] M. Kilpatrick, *J. Amer. Chem. Soc.*, 1953, **75**, 584 and following papers.

acetate as additional solute (Table 6). These measurements were performed by vapour-pressure osmometry and, since the lowest practicable temperature on our equipment proved to be 35 °C, they do not relate to exactly the same conditions as the kinetic measurements. A significant effect was observable only at a concentration of sodium dichloroacetate which was near the upper limit for the instrument. Table 6 compares the observed reading of the osmometer, for various additions of dichloroacetic acid to a solution containing 0·0155 molal sodium dichloroacetate, with that expected in the absence of association. Because of the association, the effective molecular weight appears to be *ca.* 10% larger than when dichloroacetic acid is added to methanol by itself. This is the order of magnitude required by the values of K_d and K_{ass} deduced from the analysis of the rate data, according to the following approximate treatment.

It follows from equations (10) and (11) that the concentration of free acid ([HA]) should be reduced below the stoicheiometric concentration ($[HA]_{stoich}$), in accordance with equation (12). It follows that the ratio i of the observed vapour pressure lowering to the expected one, is given by equation (13). Inserting the previously deduced value of K_d one finds that the effect of dimerisation should cause a *ca.* 1% change in i at the highest concentration of acid used in the osmometry experiments and would therefore escape detection. The product $K_{ass}[A^-]$ has the value 0·10, whence i = *ca.* 0·9. The results of these vapour-pressure osmometry measurements are thus compatible with the conclusions reached from the rate studies, but the vapour-pressure osmometry technique proved insufficiently accurate to extend these conclusions.

$$[HA] = [HA]_{stoich} - K_d[HA]^2 - K_{ass}[HA][A^-] \quad (12)$$

$$\begin{aligned}[HA]/[HA]_{stoich} &= i \\ &= (1 + K_d[HA] + K_{ass}[A^-])^{-1} \quad (13)\end{aligned}$$

The occurrence of association and dimerisation will not only diminish the effective concentration of the catalysing acid HA but, by virtue of the consequent effect on the ratio [HA]/[A⁻], the concentration of hydrogen ion should now depend on the concentration of buffer even when the buffer ratio is kept constant. Because the contribution of the hydrogen ion-catalysed reaction is small under the conditions of our experiments, this complication was not noticeable. However, according to our experiments in aqueous solution, the effects of dimerisation and/or association become more marked with weaker acids. Indeed, they were not observed at all with aqueous dichloroacetic acid. It must accordingly be expected that precise kinetic or thermodynamic experiments with buffers of weaker acids (acetic acid, for example) in methanol solution, would be severely complicated by these effects.

Comparison of Catalytic Coefficients.—Although a consideration of the effects of traces of water and of interaction between the constituents of the buffer have to be taken into account for the detailed description of the catalysis phenomena, the evaluation of the catalytic coefficients of hydrogen ion and dichloroacetic acid does not seriously depend on this analysis. These second-order rate constants are accordingly known more reliably; their values at an ionic strength of 0·1M, maintained by addition of sodium perchlorate, are $k_H = 18$, $k_{HA} = 0{\cdot}11$ l mol⁻¹ s⁻¹. The corresponding rounded values for the reaction in aqueous solution (at I 0·1M, with potassium chloride) are $k_H = 27$, $k_{HA} = 23$ l mol⁻¹ s⁻¹. It is noteworthy that, whereas the solvent change produces only a very small effect on the catalytic effect of solvated hydrogen ions, the catalytic coefficient of dichloroacetic acid in methanol is approximately 200 times smaller than in water. This fits with the idea that the incipient charge separation, which accompanies the formation of the transition state for catalysis by dichloroacetic acid, is energetically more favourable in the more polar solvent water. On the other hand, proton transfer from the solvated hydrogen ion is a charge-conserving reaction and thus less sensitive to solvent changes. The relative reactivities of hydrogen ion and dichloroacetic acid in methanol appear less 'anomalous' than the corresponding values in water, where the hydrogen ion is much less reactive than one would predict from its strength as an acid. However, this low reactivity of the hydrogen ion made the detection of general catalysis in water very easy. On the other hand, in methanol solution the catalytic effect of the weaker carboxylic acids is not detectable, and dichloroacetic acid, a much stronger acid than is usually chosen for studies of general acid catalysis, was therefore used in the present work. If our explanation of the solvent effect on the catalysis by dichloroacetic acid in terms of charge separation is correct, then it would follow that, where it is possible, the use of cation acids might have advantages in studies of general acid catalysis in non-aqueous solvents.

Solvent Isotope Effect for Catalysis by Methanolic Hydrogen Ion.—The theory of the deuterium solvent isotope effect for a reaction involving rate-limiting proton and deuteron transfer from the aqueous hydrogen ion to the substrate, according to equation (14), has recently been reviewed.[5] If equation (14) is an adequate representation of the process, so that no other hydrogen nucleus (such as those in the secondary solvation shell of the hydrogen ion) need be included, the dependence of the second-order rate constant on the isotopic composition of the solvent (deuterium atom fraction n) is expressed[3,26] in equation (15). If equation (14) is

$$L_3O^+ + S \longrightarrow \overbrace{(L_2O \cdots L \cdots S)}^{+}{}^{\ddagger} \longrightarrow L_2O + LS^+ \quad (14)$$

$$\frac{k_n}{k_H} = \frac{(1 - n + nl^{1-\alpha})^2(1 - n + nl^{1+2\alpha}k_D/k_H)}{(1 - n + nl)^3} \quad (15)$$

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

inadequate, expression (15) will be found to be unsatisfactory, a situation which can formally be remedied [27] by the postulation of 'transfer' effects. The parameter α can be regarded as the exponent in an expression equivalent to the Brønsted catalysis law, relating the reactivity of isotopic hydrogen ions to their acid strengths.[3] Equation (15) successfully predicts the deuterium solvent isotope effect on the hydrolysis of cyanoketen dimethyl acetal in aqueous solution [2] without the need of involving a transfer contribution. The required value of α lies in the range 0·5—0·65 and agrees (or coincides) with the value of the Brønsted exponent for catalysis by carboxylic acids.[2] The ratio of rate constants at the two extremes of the isotopic composition range, k_D/k_H, is 0·33.

The reaction model on which equation (15) is based can readily be adapted to the reaction in methanol. On the assumption that the methanolic hydrogen ion has the formula $MeOH_2^+$, equation (16) can be written

$$MeOL_2^+ + S \longrightarrow \overbrace{(MeLO \cdots L \cdots S)}^{+}{}^{\ddagger} \longrightarrow MeOL + LS^+ \qquad (16)$$

$$\frac{k_n}{k_H} = \frac{(1 - n + nl_M^{1-\alpha})(1 - n + nl_M^{1+\alpha}k_D/k_H)}{(1 - n + nl_M)^2} \qquad (17)$$

as the analogue of (14), and the corresponding expression for the solvent isotope effect is (17). Equations (15) and (17) differ only in the numerical values of some exponents. These changes reflect differences in molecular symmetry between L_3O^+ and $MeOL_2^+$, between L_2O and MeOL, and between the transition states of the two reactions.

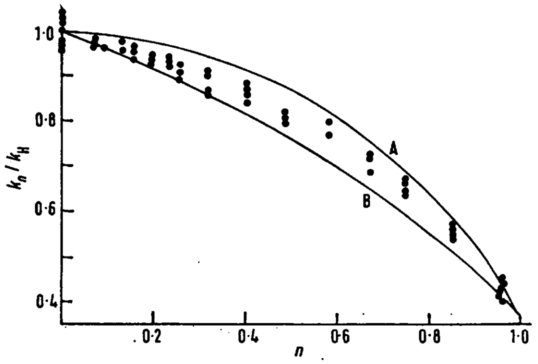

FIGURE 3 Deuterium solvent isotope effect for catalysis by hydrochloric acid; curves calculated from equation (17), with α = 1 and α = 0 (A and B respectively)

Figures 3 and 4 illustrate the fit of equation (17) to the experimental data. In Figure 3 the curves drawn in correspond to values of α of 0 (curve A) and 1 (curve B) respectively. The experimental points are seen to scatter within the area bounded by these curves, suggesting that α has an intermediate value. The extremes of the two curves have been fixed by an objective extrapolation of the polynomial expression (25) which represents the best least-squares fit of all experimental values of k_2 to a third-order polynomial (18) in n, the inclusion of higher powers not being statistically significant.

$$k_2/\text{l mol}^{-1}\,\text{s}^{-1} = 13{\cdot}023 - 4{\cdot}932n + 3{\cdot}885n^2 - 7{\cdot}085n^3 \qquad (18)$$

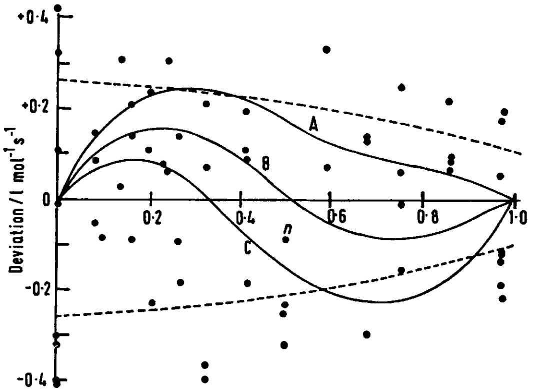

FIGURE 4 Deuterium solvent isotope effect for catalysis by hydrochloric acid; experimental points and curves, calculated from equation (17), with α = 0·7, 0·6, and 0·5 (curves A, B, and C respectively) expressed as deviations from equation (18)

Figure 4 gives a more searching test of equation (17). A series of curves of k_n/k_H as a function of n were computed according to equation (17) with different values of α between 0 and 1. It is found that values of α outside the range 0·5—0·7 give a poor fit to the polynomial (18), but that curves calculated with α-values between 0·5 and 0·7 are compatible with the experimental data. In Figure 4 these calculated curves are plotted as deviation functions from the polynomial (18) and the experimental points are similarly inserted as deviations from the polynomial (18). It is seen that α = *ca.* 0·6, practically the same value as found for the reaction in water,[2] gives the best fit.

TABLE 7

Fit of equation (17) to experimental values of k_n/k_H (using k_D/k_H = 0·376 and a range of α-values)

α	r *	δr †
0	0·040	0·002
0·10	0·035	0·002
0·20	0·030	0·002
0·30	0·026	0·002
0·40	0·021	0·001
0·45	0·019	0·001
0·50	0·017	0·001
0·55	0·016	0·001
0·60	0·016	0·001
0·65	0·016	0·001
0·70	0·017	0·001
0·75	0·019	0·001
0·80	0·021	0·001
0·90	0·027	0·002
1·00	0·036	0·002

* $r = 0{\cdot}6745\left[\sum_{i=1}^{N} d_i^2/(N-1)\right]^{1/2}$ where $d_i = [k_n(\text{calc.}) - k_n(\text{obs.})]/k_n(\text{obs.})$. † $\delta r = 0{\cdot}4769r/N^{1/2}$.

Table 7 illustrates the same point in numerical form. Values of the probable fractional error r and of δr (the

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[27] V. Gold, *Trans. Faraday Soc.*, 1968, **64**, 2143.

probable error of r) are tabulated for the fit to the experimental values of k_n/k_H of equation (17) with a range of α-values and k_D/k_H as given by equation (18). The value of r is at a minimum near $\alpha = 0{\cdot}62$, but the size of δr indicates that the best value of α is less precisely defined and likely to lie somewhere in the range 0·48—0·72. The calculation of r (defined in the footnote to Table 7) is based on the assumption that the percentage precision, rather than the absolute precision, is likely to be the same over the isotopic composition range.

According to equation (18) the value of k_D/k_H in methanol is 0·38, as compared with 0·33 in water.[2]

To the extent that the isotopic α or the Brønsted exponent for catalysis by different weak acids is an indication of mechanism, we may infer that proton transfer to the substrate is a similar process in the two solvents. We also tentatively conclude that the very different ratio of rate constants for hydrogen ion and dichloroacetic acid as catalysts in the two solvents does not imply a marked difference in transition-state structure (or degree of proton transfer), but rather arises from the chemical (and electrical) difference between these acids and the consequent differentiating solvent effect on their reactions with an electrically neutral substrate. Because of the difficulty of using carboxylic acid buffers in methanol for the purpose of establishing general acid catalysis, the study of catalysis by strong acid in MeOH–MeOD mixtures offers a practicable alternative. Similar considerations are likely to apply to other alcohols as solvents.

Formal Consequences of Breakdown of Rule of Geometric Mean.—The derivation of equation (17), like that of equation (15), assumes the validity of the rule of the geometric mean.[28] In the methanol system the only species to be considered is the hydrogen ion $MeOL_2^+$. The equilibrium constant K_{disp} for the disproportionation (19) is therefore implicitly taken to have the

$$MeOH_2^+ + MeOD_2^+ \rightleftharpoons 2MeOHD^+ \qquad (19)$$

statistical value of 4. At the present stage of refinement of theory and experimental data it does not seem timely to pursue in detail the consequences of departures from the rule of the geometric mean. We merely state the salient formal results if the consequences of a breakdown of the rule are included on the lines of a treatment previously developed for solutions of hydrogen ions in water.[29]

The generalised expression for the solvent isotope effect on an equilibrium (20) in terms of fractionation factors ϕ is, with assumption of the rule of the geometric mean, given by equation (21). Assigning the equilibrium

$$LS + MeOL \rightleftharpoons S^- + MeOL_2^+ \qquad (20)$$

$$\frac{K_H}{K_n} = \frac{1 - n + n\phi_{LS}}{(1 - n + nl_M)^2} \qquad (21)$$

constant K_{disp} to reaction (19) and defining the parameter F by equation (22), we obtain the more general result (23). It is worth noting that, because LS is a

$$F = [MeOD_2^+]/]MeOH_2^+] \qquad (22)$$

$$\frac{K_H}{K_n} = \frac{1 - n + n\phi_{LS}}{(1 - n)^2[1 + (K_{disp}F)^{\frac{1}{2}} + F]} \qquad (23)$$

monohydric solute in a monohydric solvent, its isotopic equilibrium with the solvent is unaffected by the value of K_{disp} and ϕ_{LS} is invariant with isotopic composition of the solvent. On the other hand, the fractionation factor l_M for the species $MeOL_2^+$ depends on n according to equation (24).

$$l_M = \frac{2F + (FK_{disp})^{\frac{1}{2}}}{2 + (FK_{disp})^{\frac{1}{2}}} \cdot \frac{1 - n}{n} \qquad (24)$$

The limiting value K_H/K_D is given by (25)

$$\frac{K_H}{K_D} = K_{disp}\phi_{LS}/4(l_M)_0^2$$
$$= \phi_{LS}/(l_M)_0(l_M)_1 \qquad (25)$$

where $(l_M)_0$ and $(l_M)_1$ are the values of l_M for the isotopic abundances $n = 0$ and $n = 1$ respectively.

Table 8 illustrates the effects of assuming different non-statistical values for K_{disp}. $(l_M)_{rel}$ expresses the dependence of l_M on n according to equation (26).

$$l_M = (l_M)_0 \times (l_M)_{rel} \qquad (26)$$

TABLE 8

Calculated consequences of non-statistical disproportionation equilibrium for $MeOHD^+$

	$K_{disp} = 3{\cdot}5$		$K_{disp} = 3{\cdot}7$		$K_{disp} = 3{\cdot}9$	
n	% Dev	$(l_M)_{rel}$	% Dev	$(l_M)_{rel}$	% Dev	$(l_M)_{rel}$
0·0	0·0	1·00	0·0	1·00	0·0	1·00
0·2	0·26	1·019	0·15	1·011	0·05	1·003
0·4	1·22	1·042	0·69	1·024	0·22	1·007
0·6	3·32	1·069	1·88	1·039	0·60	1·012
0·8	7·25	1·102	4·12	1·057	1·30	1·018
1·0	14·29	1·143	8·11	1·081	2·56	1·026

The column labelled % Dev gives the percentage deviation of calculated ratios K_n/K_H from the corresponding ratios evaluated with $K_{disp} = 4$. The calculated deviations are larger than for corresponding effects for aqueous solutions, where the isotopic disproportionation of both water and hydroxonium ions results in some cancellation of the effects.

[1/865 *Received, May 27th*, 1971]

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[28] J. Bigeleisen, *J. Chem. Phys.*, 1955, **23**, 2264.
[29] V. Gold, *Trans. Faraday Soc.*, 1968, **64**, 2770.