The Acidities of Weak Acids. Part I. A New Method for determining pK_a Values in the Range 12—24 [1]

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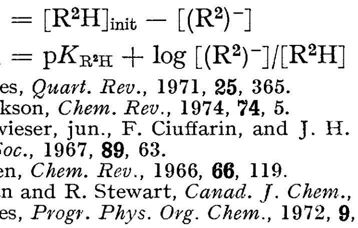
A kinetic method of determining weak acidities, based on following the rates of detritiation of a ' standard ' carbon acid in a series of dimethyl sulphoxide–water solutions containing a fixed concentration of hydroxide ions, both in the presence and absence of a second acid, is reported. The method, which has been established by redetermining the acidities of some diphenylamine and aniline-type indicators is well suited to studying acids (pK_a values in the range 12—24) whose absorption spectra do not undergo significant change on ionisation.

APART from the need to quantify the stability of anions there are several good reasons for determining the acidities of weak acids. For carbon acids in particular there is an increasing awareness of the possible applications of carbanions in chemical syntheses.[2] In addition many compounds form planar anions on ionisation so that the theoretical pK_a values can be calculated; [3] comparison with experimental findings could therefore lead to advances in theory. Thirdly, the equilibrium data, taken in conjunction with the rates of ionisation, provide a great deal of additional information,[4] *e.g.* on the rates of recombination of the ions. Finally a knowledge of the influence of solvent on acidity can lead to a better appreciation of solvent–solute interactions.[5]

Because the acidities of organic compounds vary from those that are stronger than the mineral acids to compounds such as methane, the acidity of which is virtually undetectable, a large number of methods [6,7] have been employed for measuring pK_a values. These vary from the classical methods of the physical chemists to the more qualitative observations of the organic chemists. For acids with pK_a values in the range 10—30 two methods, the competitive [8] and acidity function approach [9] are the most widely used although both have serious limitations. Thus the former gives a relative pK_a value and is restricted in terms of the range of acidities that can be measured whereas in the latter method the necessary assumptions concerning activity coefficient behaviour may not always be valid. Consequently we have devised a new kinetic method which has some features common to both these methods but does away with some of the limitations.

The method is based on the ability of dimethyl sulphoxide to increase the basicity of an aqueous hydroxide ion solution (by >14 H_- units) [10] and consequently the rates of many hydroxide-catalysed reactions.[11] The procedure entails following the rates of detritiation of a ' standard ' carbon acid in a series of dimethyl sulphoxide–water solutions containing a fixed concentration of hydroxide ion. The same reaction is then studied in the presence of a second acid, the pK_a of which is to be determined, and which is appreciably ionised under these conditions. The presence of this acid brings about a decrease in the hydroxide ion concentration and therefore in the rate of detritiation of the ' standard ' acid. This rate decrease can be related to the concentration of the anion $(R^2)^-$ formed and hence the true concentration of R^2H determined (see Scheme). The relevant equations (1)—(3) follow.



$$R^1T + OH^- \xrightarrow{k_1^T} (R^1)^- + HTO$$

$$\begin{array}{l} R^1T + OH^- \xrightarrow{k_2^T} (R^1)^- + HTO \\ \qquad\; + \\ \quad\; R^2H \\ \qquad \updownarrow \\ (R^2)^- + H_2O \end{array}$$

SCHEME

$$[(R^2)^-] = \Delta[OH^-] = [OH^-]\{1 - k_2^T/k_1^T\} \qquad (1)$$

$$[R^2H] = [R^2H]_{init} - [(R^2)^-] \qquad (2)$$

$$H_- = pK_{R^2H} + \log [(R^2)^-]/[R^2H] \qquad (3)$$

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[1] Preliminary communication, D. W. Earls, J. R. Jones, T. G. Rumney, and A. F. Cockerill, *J. Amer. Chem. Soc.*, 1974, **96**, 575.

[2] D. C. Ayres, 'Carbanions in Synthesis,' Oldbourne, London, 1966.

[3] A. Streitwieser, jun., ' Molecular Orbital Theory for Organic Chemists,' Wiley, New York, 1961, p. 414.

[4] J. R. Jones, ' The Ionisation of Carbon Acids,' Academic Press, London, 1973, ch. 8.

[5] ' Solute-Solvent Interactions,' eds. J. F. Coetzee and C. D. Ritchie, Dekker, New York, 1969.

[6] J. R. Jones, *Quart. Rev.*, 1971, **25**, 365.

[7] R. C. Cookson, *Chem. Rev.*, 1974, **74**, 5.

[8] A. Streitwieser, jun., F. Ciuffarin, and J. H. Hammons, *J. Amer. Chem. Soc.*, 1967, **89**, 63.

[9] K. Bowden, *Chem. Rev.*, 1966, **66**, 119.

[10] D. Dolman and R. Stewart, *Canad. J. Chem.*, 1967, **45**, 911.

[11] J. R. Jones, *Progr. Phys. Org. Chem.*, 1972, **9**, 241.

The successful operation of the method is subject to the conditions that (1) the equilibrium between the acid whose pK_a is to be determined and the hydroxide ion is established before the rate of detritiation is studied, (2) the anion $(R^2)^-$ does not catalyse this reaction, and (3) the second-order rate constant $k^T/[OH^-]$ in a particular dimethyl sulphoxide–water system is indeed constant. Its general validity has been tested by redetermining the pK_a values of several nitrogen indicators the majority of which had been used by Dolman and Stewart[10] in setting up their H_- scale in DMSO–OH^-–H_2O.

EXPERIMENTAL

Materials.—The diphenylamines and anilines were obtained commercially and purified before use. The ' standard ' carbon acids employed were 9-t-butylfluorene. fluorene, and methyldeoxybenzoin. They were labelled with tritium by a homogeneous exchange reaction[12] using HTO (5 mCi ml^{-1}).

Reagent grade dimethyl sulphoxide was dried over freshly prepared calcium oxide for 12 h before being fractionally distilled under reduced pressure in the presence of nitrogen. It was subsequently stored over 4A molecular sieves; g.l.c. analysis showed the water content to be $<0·1$ wt %. Stock tetramethylammonium hydroxide solutions were prepared by addition of the solid pentahydrate to freshly distilled deionised water and standardised against potassium hydrogen phthalate. The highly basic media consisting of dimethyl sulphoxide, water, and tetramethylammonium hydroxide were made up by weight, the hydroxide solution being added to give a concentration of 0·011M.

Procedure.—Preliminary investigations showed that during the course of a detritiation experiment a side-reaction occurred to an unacceptable extent. This was probably due to the presence of oxygen and in order to overcome this difficulty vigorous degassing of the solutions was necessary. For this reason the apparatus shown in Figure 1 was constructed.

In a typical experiment an accurately known weight of the acid whose pK_a was to be determined was placed in tube B along with a trace of the labelled ' standard ' carbon acid. The H_- medium (7 ml) was placed in tube A and the cell assembled as shown. The apparatus was evacuated at D and then, by manipulation of taps E and F, flushed with nitrogen which had previously been passed over a BASF R311 catalyst to remove traces of oxygen and anhydrous magnesium perchlorate to remove water. Tubes A and B were then cooled in liquid nitrogen and the apparatus was evacuated. The contents were then allowed to melt at room temperature with consequent degassing, before being reflushed with nitrogen. The degassing procedure was repeated before the apparatus was thermostatted at 25°. After equilibration the apparatus was inverted and thoroughly shaken to allow mixing of the contents.

A slight positive pressure of nitrogen was introduced through tap E and whilst still in the inverted position tap F was gently opened so as to fill a microcell (path length 0·1 mm) that had been attached at D. Tap F was closed, the microcell removed, and the u.v. spectrum of the solution repeatedly monitored over the course of the detritiation experiment. No spectral changes were observed during this time interval. On returning to the upright position the apparatus (with the reaction solution in tube A and a substantial flow of nitrogen passing over the surface) was divided at joint G. Portions (0·5 ml) were then withdrawn at appropriate intervals and the detritiation reaction quenched by injecting them into tubes containing water (10 ml) and scintillator (10 ml) (3·4 g l^{-1} of 2,5-diphenyloxazole in toluene). After shaking and allowing to settle most of the toluene layer was pipetted off and dried (Na_2SO_4) prior to analysing samples (5 ml) for the tritium content. Runs in the absence of a second acid were performed in a similar manner. It was customary to follow reactions to $>80\%$ completion. No departures from first-order kinetics were observed and rate coefficients were reproducible to within $\pm 2\%$.

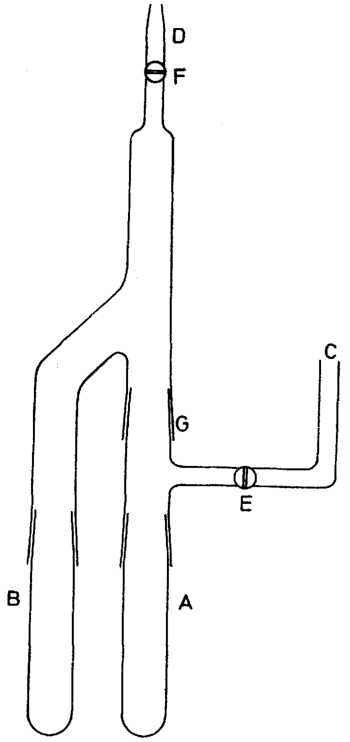

FIGURE 1 Apparatus for measuring acidities

A Typical pK_a *Calculation.*—For 3-chlorodiphenylamine (0·00711M) a solution (mole % dimethyl sulphoxide = 82·70) of H_- 20·90 was employed; the hydroxide ion concentration was 0·01095M. [9-^{3}H]Fluorene was the 'standard ' carbon acid employed and the values of k_1^T and k_2^T were $31·6 \times 10^{-4}$ and $22·4 \times 10^{-4}$ s^{-1}, respectively. The new hydroxide ion concentration is therefore $0·01095 \times 22·4/31·6 = 0·007760$M and $[(R^2)^-] = 0·01095 - 0·007760 = 0·00319$M and $[R^2H] = 0·00711 - 0·00319 = 0·00392$M. The H_- value of the solution is now $20·90 - \{\log [OH^-]_1 - \log [OH^-]_2\} = 20·75$. The p$K_a$ of 3-chlorodiphenylamine is therefore $20·75 - \log\{[(R^2)^-]/[R^2H]\} = 20·84$. Four other experiments gave values of 20·71, 20·66, 20·62, and 20·76, average $20·72 \pm 0·06$.

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[12] J. R. Jones and R. Stewart, *J. Chem. Soc.* (*B*), 1970, 194.

RESULTS AND DISCUSSION

The pK_a values (Table) for the four diphenylamine and four aniline-type indicators, when compared with the literature values, show good agreement with differences in excess of 0·3 pK units being observed only for 2,3,5,6-tetrachloroaniline and 4-nitro-2,6-dichloroaniline.

Acidities of some indicator acids in dimethyl sulphoxide–water mixtures

Compound	pK_a	Literature value
4-Methyldiphenylamine	22·83 ± 0·06	22·95 [10]
Diphenylamine	22·53 ± 0·11	22·44 [10]
3-Chlorodiphenylamine	20·70 ± 0·05	20·73 [10]
2,3,5,6-Tetrachloroaniline	19·61 ± 0·06	19·22 [10]
2-Nitrodiphenylamine	17·96 ± 0·06	17·91 [10]
2-Nitro-4-chloroaniline	17·33 ± 0·01	17·08,[10] 17·22,[a] 17·13 [b]
4-Nitro-2,6-dichloroaniline	15·87 ± 0·01	15·55 [a]
4-Nitro-2,5-dichloroaniline	16·16 ± 0·04	16·05 [a]

[a] R. Stewart and J. P. O'Donnell, *Canad. J. Chem.*, 1964, **42**, 1681. [b] Recalculated (in note *a*) data of C. H. Langford and R. L. Burwell, jun., *J. Amer. Chem. Soc.*, 1960, **82**, 1503.

In the majority of the other cases the agreement is within ±0·1 pK unit. Other findings offer further support for the method's general validity. Thus there is no observable trend in the pK_a values as the concentration of the acid is varied, as would be expected if, in addition to hydroxide ion, the anion $(R^2)^-$ catalysed the reaction. This will probably always be the case as long as the negative charge on the carbanion is extensively delocalised. The observation of good first-order kinetic plots as well as the monitored spectral changes confirm that the equilibrium between acid (R^2H) and hydroxide ion is rapidly established.

The need for the second-order rate constant $k^T/[OH^-]$ at any given DMSO–H_2O composition to be effectively constant has been tested for all three of the 'standard' carbon acids employed, methyldeoxybenzoin (54, 62, and 70 mole % DMSO), fluorene (70 and 81 mole % DMSO), and 9-t-butylfluorene (86, 91, and 96 mole % DMSO). The results for the last compound are given in Figure 2. This necessary requirement is met by all three compounds with the exception of 9-t-butylfluorene in the 96 mole % DMSO medium, where the concentration of water is at its lowest. It is reasonable to suppose that in changing the hydroxide ion concentration five-fold the extent of solvation is altered and this would be consistent with the observation that $k_{OH^-}{}^T$ increases with increasing hydroxide ion concentration. At lower mole % DMSO solutions there is presumably sufficient water present to prevent this problem arising. This observation therefore places a lower limit, corresponding to H_- between 23 and 24, to the acidities that can be determined by this method using solutions of DMSO–OH^-–H_2O.

The first six indicators in the Table were used to establish Dolman and Stewart's [10] H_- scale and our results provide indirect evidence in favour of its validity. They also draw attention to the advantages of having a second analytical method of determining the ratio $[(R^2)^-]/[R^2H]$ as difficulties in interpreting changes in u.v. absorption spectra are frequently encountered in this kind of work.[13,14] In fact many carbon and other kinds of acids do not exhibit such a spectrum or alternatively exhibit a spectrum that does not undergo significant change on ionisation. This method seems to be well suited to the study of such compounds.

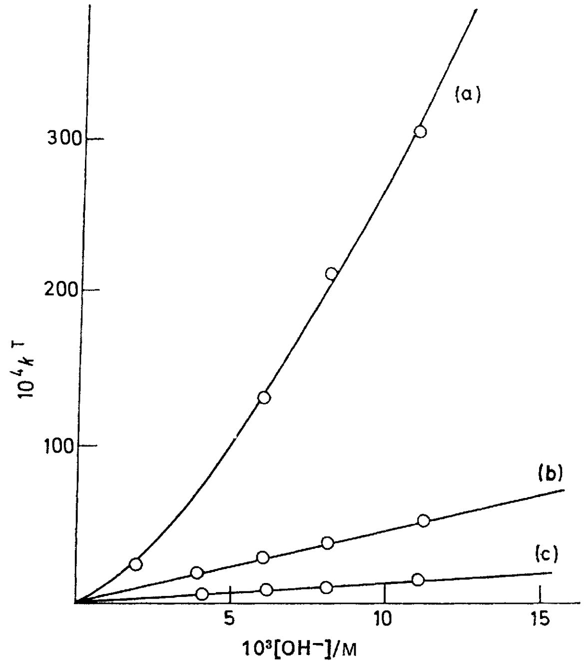

FIGURE 2 Dependence of detritiation rate constant for [9-^{3}H]-9-t-butylfluorene on hydroxide ion concentration for different dimethyl sulphoxide–water compositions: (a) 96 mole % DMSO; (b) 91 mole %; (c) 86 mole %

The method also offers another advantage over the customary spectrophotometric method where one of the requirements of an indicator is that the ratio $\log\{[(R^2)^-]/[R^2H]\}$ when plotted against H_- should be linear with a slope of unity. In other words any particular indicator can only be safely used over a maximum of two H_- units. However the slopes of the $\log k^T$ against H_- plots are much lower, varying from 0·49 for methyldeoxybenzoin [15] to 0·74 for 9-t-butylfluorene; [16] for fluorene the value is 0·56 [16] so that these compounds can each be used to cover 3—4 H_- units. Relatively few compounds are therefore necessary in order to cover a wide H_- range.

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