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The Strengths of Weak Bases in Aqueous Acid by Solvent Extraction and Gas Chromatography[1,2a]

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Further details are presented for the application and justification of a method[10] for determining the strengths of weak bases in aqueous strong acid by solvent extraction and g.l.c. analysis of the organic layer. It is shown that the method leads to a pK_a for the anisole oxonium ion within 0.04 pK unit of the value determined spectrophotometrically by the Hammett indicator method. Rough agreement is also found for several other compounds including tetrahydrothiophene, this being the first measurement of the pK_a of a sulfonium ion in aqueous solution. Anomalous solubility effects of the type discovered by Hammett and Chapman make the method inapplicable to nitrobenzene, benzoic acid and presumably numerous other weak bases. However, the solubility behavior of nitrobenzene and benzoic acid can easily be distinguished from simple protonation. Severe changes in the nature of the aqueous phase and organic phase are shown to have no influence on the basicity values of tetrahydrofuran and diethyl ether determined by this method. It is concluded on the basis of results in this paper and those to follow that this technique gives a true basicity measurement for most of the weak bases studied but that there are probably classes of compounds for which it may not be used.

Determination of the dissociation constants of oxonium ions is of considerable interest in that it allows the comparison of the influence of steric and electronic effects on oxygen with other basic atoms. Organic oxygen bases are for the most part much too weak to study in dilute aqueous acid but can be investigated by means of the elegant Hammett indicator method[3–5] provided they show suitable spectral properties which change on protonation. By this means we have measured the basicities of phenolic ethers[5] and shown them to respond rather differently to stereoelectronic influences from their aniline analogs. A more difficult, but in many respects more interesting, problem is that of the basicities of simple, aliphatic oxygen bases. Although this has been approached by many authors[6–8] through coördination of various acidic systems with ether oxygen, we know of no case which permits direct comparison of the results with the protonation equilibria of strong bases by direct translation to a standard state of infinite dilution in water such as is possible through the use of the $p\mathrm{H}-H_0$ scale. Examination of these sources and the work of many other authors too numerous to name here reveals that the order of basicity depends not only on the steric and electronic elements in the base but also those in the acid and in addition the nature of the medium. This gives added strength to the desirability of studying all bases, both weak and strong, on a single scale referred to a single standard state. The $p\mathrm{H}-H_0$ scale provides probably the broadest reactivity spectrum available at present, although its breadth by no means implies that it is either universal or absolute.

The problem of dealing with simple saturated oxygen bases is an analytical one since for the most part they lack suitable indicator properties. To our knowledge, saturated ketones[9] are so far the lone exception. In a recent communication[10] we presented a brief description of a method which combines solvent extraction with gas chromatography for the study of some classes of weak bases that do not have spectral indicator properties. It is the purpose of the present paper to give detailed evidence supporting the application of this technique to the basicities of saturated ethers and also to point out what we consider to be some of the limitations and hazards involved in the use of the method.

Our procedure involves determination of the distribution ratios of the weak base between an inert non-polar solvent and a series of increasingly strong acid solutions whose acidity may be expressed by the Hammett H_0 acidity function.[3,4] The change in distribution ratio with acidity may then be related, by means of a simple equation, to the dissociation constant of the oxonium ion. The distribution ratio is calculated from the disappearance of base from the non-aqueous phase which is analyzed for the base by means of gas chromatography. The major hazard that is involved in applying this method arises from the fact that the only measured quantity is the activity coefficient of the base and the results must be interpreted in such a way that the change in activity coefficient on increasing the strength of acid must be related unequivocally to protonation of the base and not to other unspecified factors[11] which may also produce large changes in activity coefficients as the acidity increases.

In this paper we shall justify our method and results by means of several independent checks: (a) by showing that the method *can* be used to give the correct pK_a's of several weak aromatic bases whose basicities have been well established by the

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(1) Stereoelectronic Effects in Organic Bases, VI; previous paper in this series, *J. Org. Chem.*, **27**, 111 (1962).

(2) (a) This investigation was supported by grants from the Public Health Service (A-3643 B.B.C.), National Institutes of Health and the National Science Foundation (N.S.F. G-14583). The Perkin-Elmer 21, Cary-14 and Beckman DU spectrophotometers used in conjunction with this research were also purchased with funds supplied by the same agencies. We are pleased to acknowledge our gratitude for this support. (b) The bulk of the work described here is taken from the thesis of Ching Yong Wu, presented to the University of Pittsburgh in the Spring of 1961 in partial fulfillment of the requirements for the Ph.D. degree.

(3) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter IX.

(4) M. A. Paul and F. A. Long, *Chem. Revs.*, **57**, 1 (1957).

(5) E. M. Arnett and C. Y. Wu, *J. Am. Chem. Soc.*, **82**, 5660 (1960).

(6) See for example: W. Gerrard and E. D. Macklen, *Chem. Revs.*, **59**, 1105 (1959).[7,8]

(7) F. G. A. Stone, *ibid.*, **58**, 101 (1958).

(8) S. Searles, E. F. Lutz and M. Tamres, *J. Am. Chem. Soc.*, **82**, 2932 (1960), and many previous articles by the same authors.

(9) H. J. Campbell and J. T. Edward, *Can. J. Chem.*, **38**, 2109 (1960).

(10) E. M. Arnett and C. Y. Wu, *J. Am. Chem. Soc.*, **82**, 4999 (1960).

(11) L. P. Hammett and R. P. Chapman, *ibid.*, **56**, 1282 (1934).

Hammett method, (b) by showing that other sources of activity coefficient change probably do not contribute in a way which would lead to their being misinterpreted as protonations. In the next two papers we will show that (c) the basicities of ethers measured by this method fall within a general region that is consistent with independent external evidence, (d) the pattern of variation of basicity of these ethers varies with their structure in a manner that is reasonable when the results are compared with the orders of base strength for the same compounds against other acids and (e) the basicity order is reasonable when the ethers are compared with analogous amines and phosphines.

We wish to make it plain to begin with that although these independent lines of evidence give powerful support to most of the pK_a's to be presented (and thereby to the validity of the method for selected cases) there is no reason to believe that the technique can be applied indiscriminately to all types of weak bases with success; indeed, because of the other activity coefficient effects[11] mentioned already, it will be completely inapplicable to certain classes of interesting compounds. Only further experimentation can delineate these limitations.

Description of the Method.—On the basis of the results of Deno and Perizzolo[12] one may expect that for the distribution of a rather weak organic base between a non-polar, inert solvent and aqueous strong acid solutions of increasing acidity there will be first a decrease in solubility of the base in the aqueous phase, relative to water, due to salting out.[13] From about 15% sulfuric acid to very strong acid the distribution ratio should then remain almost constant unless protonation occurs. If this does happen there should then be a sudden increase in solubility in the aqueous acid phase due to the formation of oxonium ions which are insoluble in the non-polar phase. The following analysis formalizes this approach and shows also that other factors are important.

Assuming that the base is unassociated in both layers[14–16] one may define a distribution ratio $K_D' = [B]_0/[B]_{aq}$ for the equilibrated base B between two mutually saturated immiscible layers: the organic phase in which its concentration is $[B]_0$ and the aqueous acid of low enough acidity so that the base is essentially unprotonated and in which its concentration is $[B]_{aq}$. Were it not for the salting out effect of the ions from the acid upon the activity of B in the aqueous layer, K_D' would be practically the same as K_D, the distribution constant for the base between mutually saturated organic layer and pure water.[17] As the acidity is increased so that some of the base in the aqueous layer becomes protonated, we may write the observed distribution ratio D in a solution of acidity h_0 as $D = [B]_0/([B]_{aq} + [BH^+])$. The dissociation constant of the conjugate acid in the aqueous layer[3,4] is $K_a = h_0[B]_{aq}/[BH^+]$ and combining this with the expression above for D gives

$$D = [B]_0/([B]_{aq} + h_0[B]_{aq}/K_a) \qquad (1)$$

Since we may replace $[B]_0$ with $K_D'[B]_{aq}$ we can cancel out $[B]_{aq}$ from all terms on the right side of eq. 1 to give $D = K_D'/(1 + h_0/K_a)$. Expressing this in a more useful linear form

$$D = K_D' - Dh_0/K_a \qquad (2)$$

gives us at once a method for the estimation of K_D' from the intercept of a plot of D *versus* Dh_0. The pK_a is best obtained from the logarithmic expression

$$H_0 = pK_a + \log [D/(K_D' - D)] \qquad (3)$$

since the slope of a plot of the logarithmic term on the right *versus* H_0 should be close to unity if the ether is behaving as a Brönsted base similar to a Hammett indicator. The slope thus provides a check on the results.

Values of D are easily obtained from the ether peaks of the gas chromatogram. The area of the ether peak relative to that of the solvent peak (allowing for suitable attenuation) is a direct measure of the ether concentration in the organic layer; this area is called A_s for the stock solution. After equilibrating a standard volume of stock solution with a suitable[18,22] volume of the aqueous acid, the relative area of the ether peak is A_0 and the stoichiometric concentration of ether remaining in the aqueous layer is taken to be directly proportional to $A_s - A_0$[19] so that $D = A_0/(A_s - A_0)$.

K_D' is the hypothetical distribution constant for free base between organic layer and aqueous acid in the region where appreciable protonation is occurring. Attempts to improve our results by inserting values of K_a from eq. 3 into eq. 2 and thence improved values for K_D' into eq. 3 show that eq. 3 is sufficiently insensitive to K_D' for this method of successive approximations to be of any value. Rewriting eq. 3 as $H_0 - pK_a = \log D - \log (K_D' - D)$ shows that if the base is quite insoluble in the aqueous phase so that K_D' is between 100 and 1000 one will need an acid of 2 to 3 H_0 units greater acidity than the pK_a of the compound to extract half of the base ($D = 1$) into the acidic layer. Therefore a very high acidity may be necessary to effect measurable extraction of a compound that is very insoluble in water even if it is quite a strong base unless a large excess of acid layer is used.[18,22]

Equation 3 also demands a unit slope for the plot of H_0 *versus* the logarithmic term provided that the activity coefficient ratio f_B/f_{BH^+} for the

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[12] N. C. Deno and C. Perizzolo, *J. Am. Chem. Soc.*, **79**, 1345 (1957).

[13] F. A. Long and W. F. McDevit, *Chem. Revs.*, **51**, 119 (1952).

[14] G. H. Morrison and H. Freiser, "Solvent Extraction in Analytical Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1957.

[15] L. C. Craig and D. Craig, "Technique of Organic Chemistry," Vol. III, Part I, ed. A. Weissberger, Interscience Pub., Inc., New York, N. Y., 1956, Chapter II.

[16] This is one reason why we have chosen ethers for our first study instead of alcohols, although the need for information about the latter is probably even more urgent. Associated systems may be handled[14,15] but are more complicated

[17] This situation is quite symmetrical to the problem of correcting spectral measurements for the medium effects of changing acid in the usual Hammett indicator method.[3–5]

[18] For most low molecular weight ethers, where K_D' is less than 50, equal quantities of organic and aqueous layers are used. For less soluble ethers ($K_D' = 50$ to several hundred) the volume of the aqueous phase must be two to five times that of the organic layer. D should be corrected by this same relative volume factor to give the true value for K_D'.

[19] For most ethers it is not feasible to measure directly the concentration of base in the acid layer. For anisole, however, this could be done spectrophotometrically and it was found in this case that the distribution ratio obtained in this way agreed within 1% with that obtained in the usual way—by difference.

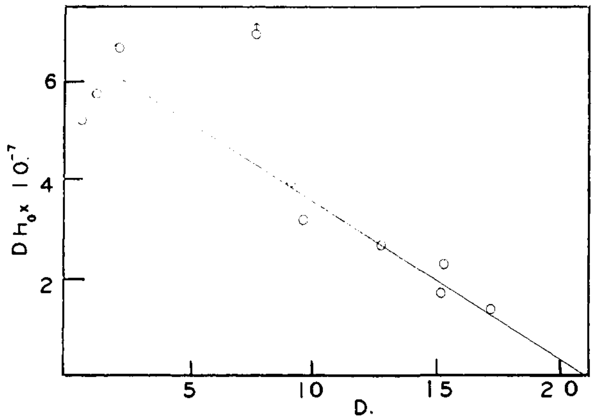

Fig. 1.—Estimation of K_D' of anisole.

extracted base exactly cancels the same ratio for the aromatic base used to construct the H_0 scale in that region of acidity. Table I presents a typical calculation of the pK_a of a base (anisole) by the gas chromatography–solvent extraction method. Figure 2 indicates that the slope of the logarithmic plot for this ether, whose structure is quite similar to that of Hammett's indicators, is indeed nearly unity (0.993 by least squares). The fact that this compound follows eq. 2 and 3 well and that it gives a pK_a which agrees within 0.04 pK_a unit (the usual experimental error for H_0 acidities[4,5]) with the value for its pK_a obtained by us previously[5] by the Hammett indicator method is a very powerful argument for the applicability of the general method and the strength of the underlying assumptions.

Table I

Solvent Extraction of Anisole[a]

% H_2SO_4	H_0[b]	D	$Dh_0 \times 10^{-8}$	$D/K_D' - D$	$\log \frac{D}{K_D' - D}$	pK_a[b]
72.17	−5.90	17.95	0.136	4.455	0.649	−6.55
73.21	−6.03	15.04	.162	2.524	.402	−6.43
74.30	−6.16	15.34	.222	2.710	.433	−6.58
75.30	−6.30	12.81	.256	1.564	.194	−6.49
76.84	−6.51	9.577	.310	0.8384	− .076	−6.43
77.57	−6.63	9.358	.399	.8038	− .095	−6.53
82.14	−7.29	4.029	.785	.2374	− .624	−6.67
83.08	−7.44	2.313	.638	.1238	− .907	−6.53
84.14	−7.60	1.419	.565	.07247	−1.140	−6.46
85.26	−7.77	0.872	.514	.04332	−1.1363	−6.41
					Average	−6.51

[a] From 3% (volume) solution of anisole in isoöctane at 0°. [b] All pK_a's and H_0 values presented in this and following papers are referred to the commonly used scale of Paul and Long.[4] See ref. 5 for comments on the accuracy of the H_0 scale.

We shall see in the papers to follow that logarithmic plots of eq. 3 for the saturated ethers also give good straight lines but that the slopes vary for the most part between 0.80 to 1.0. Here the structure of the base is so different from that of the Hammett indicator used to determine H_0 for the acidity range being covered that one could scarcely expect exact cancellation of the activity coefficient term. Long and Paul[20] have observed non-unit slopes for log k *versus* H_0 for the acid-catalyzed hydrolysis of epoxides where the base is quite similar in structure to the saturated ethers in the present study. Taft has also noted recently[21] that

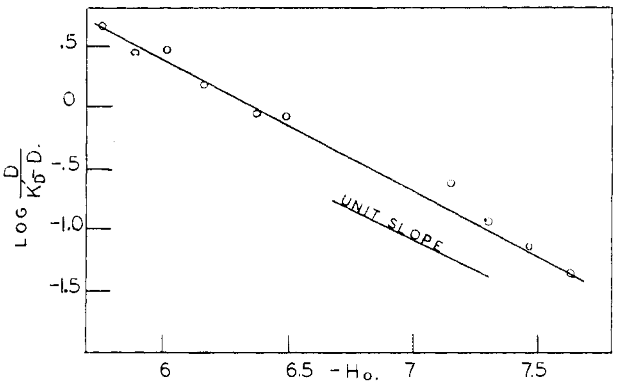

Fig. 2.—Determination of pK_A of anisole oxonium ion.

on close examination the activity coefficient terms for Hammett indicators of rather similar structure do not match perfectly. Therefore, our results are in reasonable agreement with the behavior predicted from eq. 3. Furthermore, since our data are based on an equilibrium, they indicate that considerable reserve should be used in the detailed mechanistic interpretation of transition states from non-unit log k *vs.* H_0 slopes observed in kinetic investigations. It should be clear that in cases where the conjugate acid of a base is undergoing unimolecular decomposition, a non-unit log k *vs.* H_0 slope can be produced by failure of the prior protonation equilibrium to meet the activity coefficient postulate as well as by departure of the mechanism from a strict A_1 pathway so that the slope of the final plot may be composite of both factors.

Application of the Solvent Extraction Method to Bases of Known pK_a.—Golumbic and Orchin[22] used a solvent extraction method similar to that described here but employed spectrophotometric analysis of the organic layer. They found that pK_a values for the strengths of a number of strong organic acids and bases agreed for the most part closely (within 0.2 pK_a unit) with well-established literature constants. Other workers[23–26] have used solvent extraction and spectrophotometry to study a few weak bases.

Hammett and Chapman[11] demonstrated clearly for some weak bases, for which the pK_a's of the conjugate acids had been established (nitrobenzene, *p*-dibenzoylbiphenyl and several benzoic acids) that there was a large and sudden tendency to be extracted from the solid phase into aqueous sulfuric acid solutions of increasing acidity long before the acid strength was sufficient to produce protonation. It is therefore by no means mandatory that because solvent extraction can be successfully applied to the determination of strong bases in dilute aqueous acid it can be used for weak bases in strong aqueous acid and one may expect that there will be some classes of compounds of the types tested by Hammett and Chapman that will not be

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(20) F. A. Long and M. A. Paul, *Chem. Revs.*, **57**, 935 (1957).

(21) R. W. Taft, Jr., *J. Am. Chem. Soc.*, **82**, 2965 (1960).

(22) C. Golumbic and M. Orchin, *ibid.*, **72**, 4145 (1950).

(23) P. A. Plattner, E. Heilbronner and S. Weber, *Helv. Chim. Acta*, **32**, 574 (1949).

(24) V. Gold and F. L. Tye, *J. Chem. Soc.*, 2181 (1952).

(25) N. C. Deno, P. T. Groves and G. Saines, *J. Am. Chem. Soc.*, **81**, 5790 (1959).

(26) D. A. McCaulay and A. P. Lien, *ibid.*, **73**, 2013 (1951).

amenable to the procedure. The fact that the solvent extraction–gas chromatography method works well for anisole even though it must be studied with strong acids where Hammett–Chapman effects should be serious, encourages confidence in applying the method to the saturated ethers which may be studied in more dilute acid.

Fehnel and Carmack[27] showed that sulfides, unlike ethers, absorb ultraviolet light in the 210–250 mμ region. It should therefore be possible to study sulfide analogs of the saturated ethers both as Hammett indicators and by solvent extraction. The results of Fehnel and Carmack suggested that tetrahydrothiophene would absorb at a sufficiently long wave length for treatment as a Hammett indicator and would be especially interesting by affording a comparison of the basic character of sulfur in contrast with ether oxygen in tetrahydrofuran which we have already reported.[10] Although the study of tetrahydrothiophene as an indicator is seriously weakened by a large blue shift as acidity increases and by the necessity of using a wave length on the side of a steep curve (at 210 mμ) the results when treated to correct for medium effects[5] yielded a good linear plot of slope 0.971 for log indicator ratio *versus* H_0 and a pK_a of -5.10 for the sulfonium ion. A parallel study of this compound by solvent extraction–gas chromatography gave a pK_a of -4.52 and a slope of 0.967. The failure of these results to match better may be attributed to the poor conditions for the indicator study. The fact that they agree this well indicates that there is probably no very large error in studying saturated sulfides (and also presumably ethers) by solvent extraction. To our knowledge this is the first measurement of the basicity of a sulfide in aqueous acid and we are extending the study to other related compounds.

Experiments using solvent extraction and spectrophotometric analysis of the organic layer gave agreement with established pK_a values within 0.3 pK_a unit[28] for the Hammett indicators 2,6-dinitro-4-methylaniline and 2,4-dichloro-6-nitroaniline as well as for *p*-methoxyacetophenone. Stewart and Yates[29] suggested that the basicity of the last compound was anomalously low because of strong hydrogen-bonding interactions with the solvent. The fact that solvent extraction can be applied to this compound and the others mentioned above in this section requires the conclusion that it is a valid method for some weak bases including some ethers, sulfides and ketones.

Nitrobenzene and Anomalous Solubility.—In the experiments of Hammett and Chapman to which we have already made reference[11] distribution was effected by employing the pure base as non-aqueous phase and many hours were required for the equilibration of phases. In order to be sure that their observations of anomalous solubility were not an experimental artifact which would not show up in our method, we tested the extraction behavior under our standard conditions using dilute solutions of the base in inert solvent and the short equilibration times possible with our apparatus.

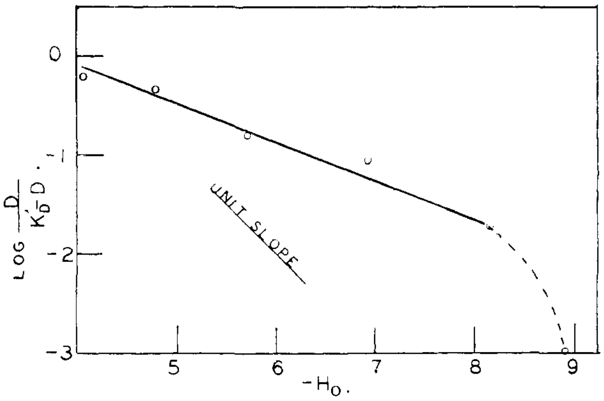

Fig. 3.—Extraction of nitrobenzene.

Nitrobenzene did indeed show a remarkable tendency to increase its solubility in the aqueous acid phase beginning at an H_0 of about -4 even though appreciable protonation only occurs at much greater acidities (pK_a -11.26).[30] However, when an attempt was made to fit the data from these experiments (Table II) to eq. 2 and 3, quite different behavior was found from that observed for the bases already described whose pK_a's from solvent extraction and indicator measurements agree. Failure of the data to conform in any orderly way to eq. 2 made the choice of a suitable K_D' difficult. When a line was drawn through the points that most nearly approached a straight line and the K_D' from this treatment was used for a plot following eq. 3 a straight line was obtained over a range of H_0 from -4 to about -8 but significantly the slope was 0.377 instead of close to unity (Fig. 3). Equation 3 shows that a poor choice of K_D' from eq. 2 would serve to shift the straight line along the H_0 scale but would have no effect on the slope. Beyond an H_0 of -8, where measurable protonation may be beginning,

TABLE II

EXTRACTION OF NITROBENZENE BY AQUEOUS SULFURIC ACID FROM A 1% SOLUTION IN CYCLOHEXANE[a]

% H_2SO_4	H_0	D	"log $(D/K_D' - D)$"[b]
18.4	0.78	29.59	
35.42	1.94	133.6	
48.84	3.12	42.42	
57.44	4.05	15.22	−0.2118
66.05	5.025	12.20	− .3579
73.83	5.97	5.76	− .7732
80.81	6.95	3.472	−1.022
89.72	8.15	0.7526	−1.717
95.9	8.88	0.039	−3.006

[a] Extraction at room temperature. Equal 10 ml. portions of organic and aqueous phases used. Six-foot column packed with LAC-3R-728 on Chromosorb-W eluted with helium at 84 ml./min. at 126°. [b] A plot of the data substituted in eq. 2 did not give a straight line. A rather arbitrary value for $K_D' = 40.0$ was chosen as the best estimate.

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(27) E. A. Fehnel and M. Carmack, *J. Am. Chem. Soc.*, **71**, 84 (1949).

(28) These were early experiments and are probably biased by the fact that equal volumes of organic and aqueous layers were used even though the compounds have K_D' values in excess of 50. We believe that use of a larger volume of aqueous layer would improve agreement.[18,22]

(29) R. Stewart and K. Yates, *J. Am. Chem. Soc.*, **80**, 6355 (1958).

(30) J. C. D. Brand, W. C. Horning and M. B. Thornley, *J. Chem. Soc.*, 1374 (1952).

our final point suggests that solubility is increasing even faster and that a slope of unity is being approached, or perhaps even a slope of 1.4 where protonation and the other effects are superimposed. We were unable to follow the curve further under the same experimental conditions because extraction into the final acid solution (96%, $H_0 = -8.88$) was nearly complete within experimental error.

To test the generality of this behavior for compounds showing the Hammett–Chapman effect, several tests were performed on the extraction of benzoic acid from cyclohexane with aqueous acid by means of spectrophotometry. A few trial experiments showed that this compound is increasingly salted out of the aqueous solution up to at least 57% sulfuric acid and following this its solubility in the aqueous layer sharply increases as it approaches protonation. The problem of dealing with this behavior coupled with that of correcting for varying degrees of association in the two phases and anomalous spectra[31] in the cyclohexane layer, forced us to abandon the investigation of this compound. These experiments with two compounds that show Hammett–Chapman anomalous solubility lead to the valuable conclusion that for them, at any rate, extraction behavior does not masquerade as protonation and would not lead to a false pK_a value.

Extraction of Tetrahydrofuran by Sulfuric and Phosphoric Acids.—It might still be argued that although nitrobenzene and benzoic acid do not show anomalous solubility which could be confused with protonation, the saturated ethers are in some way so different from these two compounds and from anisole and tetrahydrothiophene (which have been shown to give good results by the extraction technique) that the pK_a values to be quoted later are spurious results of anomalous solubility behavior. Strong evidence that this is not the case is provided by extraction of tetrahydrofuran which is sufficiently basic (pK_a in sulfuric acid $= -2.05$) so that it may be studied in aqueous phosphoric acid. This treatment gave a pK_a for the THF oxonium ion of -2.02.[32]

The difference in solvation and other activity factors between the 62% phosphoric acid and the 35% sulfuric acid solutions, in both of which the tetrahydrofuran is "half-protonated," must be considerable in view of the different amounts of "free" water available in the two media. This is supported by the difference in pK_a's observed for Hammett indicators in the two acids and also in our case by the fact that the slope of the logarithmic extraction plot for THF with phosphoric acid is 0.732 while with sulfuric acid solutions it is 0.920. This indicates that there is a greater difference between the activity coefficient ratio of THF and a Hammett indicator in phosphoric acid solutions than there is in sulfuric acid solutions. Downing and Pearson[33] have noted such large activity coefficient effects in strong phosphoric acid that they question the use of the H_0 function for this system.

TABLE III

EXTRACTION OF TETRAHYDROFURAN BY PHOSPHORIC ACID[a]

% H_3PO_4	H_0	D	$\log (D/K_D' - D)$[b]	pK_a[c,d]
0		1.90		
26.50	−0.10	1.96	1.369	−1.47
33.75	− .40	1.87	1.030	−1.43
39.90	− .69	1.75	0.766	−1.46
46.70	−1.07	1.38	.318	−1.39
50.80	−1.36	1.32	.259	−1.62
56.50	−1.78	0.969	− .0454	−1.73
59.20	−1.96	.866	− .134	−1.83
61.90	−2.09	.691	− .293	−1.80
64.25	−2.34	.618	− .3640	−1.98
67.75	−2.58	.487	− .504	−2.08

Corrected $pK_a = -2.02$[c]

[a] Extraction at room temperature from a 2% (volume) solution of THF in cyclohexane; equal volumes (5 ml.) of both phases agitated for 2 minutes; six-foot polyethylene glycol g.l.c. column at 60° eluted with helium. [b] $K_D' = 2.05$ obtained from plot following eq. 2. [c] From the data presented here an observed pK_a of -1.78 is obtained graphically. Data tabulated on p. 9 of ref. 4 show that for several indicators the pK_a in sulfuric acid is 0.24 unit lower than in phosphoric acid. Applying this correction gives the value presented above. [d] A trend in these figures is to be expected since the slope is not unity. There is therefore little value to taking an average of the figures in this column.

It seems highly unlikely that anomalous activity factors such as those that cause the Hammett–Chapman effect should be so similar in these very different acid systems that in both cases they would lead to such excellent agreement on a spurious value for the pK_a.

Experimental

Materials.—Anisole, tetrahydrofuran, tetrahydrothiophene and nitrobenzene were the best grade available from the Fisher Scientific Co. and were purified by standard methods until boiling point and refractive index matched literature values and until the (Perkin-Elmer-21) infrared spectrum was constant. They were then tested for homogeneity by gas chromatography. Benzoic acid was purified by repeated recrystallization followed by sublimation.

Cyclohexane (Matheson, Coleman and Bell) was purified for extraction by agitating with concentrated sulfuric acid containing 10% concd. nitric acid by means of a Fisher Vibrostirrer. This method of agitation is so effective that if a higher concentration of nitric acid is used a vigorous reaction giving off oxides of nitrogen ensues. The cyclohexane was then washed repeatedly with aqueous sodium carbonate and water, dried with Drierite and finally distilled from phosphorus pentoxide through a 45-inch helix-packed column.

Sulfuric and phosphoric acids were Baker and Adamson C.P. grade and were diluted with distilled water. The H_0-values were determined routinely by measurement of the density at 25°.[5] All of the phosphoric acid and many of the sulfuric acid solutions were checked independently by actual indicator H_0 measurements.

Isoöctane (Phillips pure grade) was agitated with aqueous potassium permanganate, washed with water, dried over Drierite and distilled. Fisher spectrograde carbon tetrachloride was used without further purification. None of the above solvents showed appreciable impurities by gas chromatography following the above treatment.

Extraction Technique.—Fresh stock solutions of the organic bases were prepared in the non-aqueous solvent. When the organic layer was to be analyzed by gas chromatography a 1–3% (by volume) solution of the base was used such as to give a solute peak of suitable area when a 50-μl.

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[31] The absorption peaks for both nitrobenzene (250 mμ) and benzoic acid (274 mμ) in cyclohexane show a considerable increase in absorbance when the cyclohexane is saturated with water. This may very well be another manifestation of specially strong interactions of these compounds with hydrogen-bonding solvents which also produces the Hammett–Chapman effect.

[32] Corrected for the difference between pK_a's of Hammett indicators in sulfuric and phosphoric acids[4]; see Table III.

[33] R. G. Downing and D. E. Pearson, *J. Am. Chem. Soc.*, **83**, 1718 (1961).

sample of stock solution was injected into the column at appropriate conditions. When ultraviolet analysis of the inert layer was to be used, the stock solution was prepared so as to give an optical density of 0.7 to 1.0 when 1-cm. quartz cells were used (Cary-14 or Beckman DU).

Extraction was performed in a special cylindrical 250 ml. separatory funnel with a Teflon tap at the bottom and a 45/50 standard taper joint at the top through which the dasher of a Fisher Vibrostirrer was inserted through a rubber diaphragm.

The container was designed to give optimum agitation with a minimum of loss through evaporation, splashing or poor separation of phases. Test experiments showed that with this apparatus equilibration can be reached within 15 seconds. Usually 1–2 minutes were allowed for equilibration. For compounds that are quite sensitive to acid it is clearly an advantage to have a means of basicity determination that requires such a short time of exposure to the acid. For compounds with fair water solubility equal 10-ml. aliquots of stock solution and acid were pipetted into the extraction container. Less soluble materials required a larger volume of acid.[18]

After complete separation of the phases, following equilibration, the aqueous phase was drained off and the organic layer passed through a Whatman No. 41 rapid filter paper to remove entrained droplets of aqueous phase. The organic phase was then usually stored in a small tightly stoppered bottle and refrigerated to prevent evaporation. It was then possible to perform all g.l.c. analyses within a short period of time under essentially constant conditions. In the cases of especially volatile or unstable compounds, to be described in later papers, g.l.c. analysis of the organic layer was performed immediately after extraction.

The extraction of anisole was performed using isoöctane at 0° to suppress sulfonation of the ether. This was accomplished by immersing the extraction apparatus and solutions in an ice slurry. We have demonstrated independently that the H_0 scale is not shifted appreciably on decreasing the temperature from 25° to 0°. Because of the insolubility of this ether in water, 25 ml. of the aqueous acid phase was used to each 5 ml. of organic phase. This factor of 5 cancels out of eq. 2 and 3, but must be applied to the apparent value of K_D'[21] to get the true value 105.

Gas Chromatography.—A Burrell K-2 Kromotog was employed using a 6-foot column and helium as carrier gas with a suitable flow rate (60–100 ml. per minute) to give good separation. The stationary phases were: for anisole, Apiezon-on firebrick; for tetrahydrofuran and tetrahydrothiophene, polyethylene glycol on Celite. Peak areas were determined with a model K1 Disk chart integrator fitted to the recorder of the Kromotog. Combined errors associated with sampling, agitation and gas chromatography were estimated from several identical runs using dioxane in cyclohexane as the organic phase when extracted with water. The high solubility of this ether in water should maximize many of the errors in procedure. The combined error was found to be 0.8% of the average relative peak area which is quite insignificant compared to error inherent in the H_0 acidity scale.

Tests of the Distribution Ratio.—Careful measurement of the volumes of aqueous and organic layers showed that they did not change during the equilibration process due to appreciable miscibility induced by the ether acting as cosolvent. No corrections of the concentrations are therefore needed from this source.

It is well known[4,34,35] that addition of salts to aqueous acid solutions has a pronounced effect on their strength as measured with H_0 indicators through effects on activity coefficients. In order to estimate any errors caused by a shifting of the acidity scale through the introduction of oxonium ions, we measured the H_0 of an acid solution before and after equilibration with a 1% solution of dioxane in cyclohexane using 2,4-dinitroaniline as indicator. The measured H_0 values were −4.23 and −4.20, respectively. The small change is in the direction to be expected from the results of Paul.[35] and Long and McIntyre.[34] although of too small a magnitude to influence our results and probably is not outside experimental error. Since dioxane[36] is the ether with the greatest water solubility of those we have studied and is completely protonated in acid of this strength, this should represent the limiting error from this source.

If decomposition of the ether in the acid phase occurs, the ether concentration in the organic layer $[B]_0$ will steadily diminish and give erroneous values for the distribution ratio that will be time variable. Reaction with acid was tested for by constancy of $[B]_0$ over longer agitation times. Only in the cases of the *t*-butyl[36] ethers did the concentration in the organic layer fail to become constant after 1-minute agitation of the two phases. Here the concentration of the ether in the organic layer at 15 seconds of agitation was estimated by back-extrapolation of a plot of the observed $[B]_0$ taken at a series of agitation times.

Of fundamental importance to the entire procedure is the constancy of the distribution ratio at any given acidity. If association occurs in either layer or some other complicating equilibrium is superimposed on the distribution equilibrium, the ratio of $[B]_0/[B]_{aq}$ will not be constant as the concentration of ether in the system is varied and the distribution law is invalid. A test of this is shown in Table IV.

TABLE IV

DISTRIBUTION RATIO FOR DIOXANE[33] BETWEEN CYCLOHEXANE AND WATER

Original concn. of dioxane in cyclohexane, %	$[B]_0/[B]_{aq}$
10.0	0.186
5.0	.237
2.5	.250
1.25	.232

The results show essential constancy of the ratio between 1–5% where all of our measurements were made. It is unlikely that the distribution ratio would depart seriously from constancy at lower concentrations.

The independence of the procedure from the nature of the organic layer (provided it is immiscible with the aqueous phase) is shown by the fact that the pK_a determined for diethyl ether[35] using carbon tetrachloride as organic layer is −3.48 in comparison with a value of −3.51 determined in the usual way with cyclohexane as non-polar solvent. This is despite the fact that the K_D' for diethyl ether in carbon tetrachloride is 14.2 as compared to 6.52 in cyclohexane.

It is difficult to assign a generally applicable estimate of the over-all error to the solvent extraction procedure. The fine agreement for estimates of the pK_a's of the oxonium ions of anisole, tetrahydrofuran and diethyl ether obtained from different systems suggests that in most of the cases the over-all error is probably no more than 0.10 pK unit and probably often approximates the 0.05 error of the H_0 scale. In our previous publication[10] we quoted errors based on least squares treatment of eq. 3 for several saturated ethers. We feel that these errors, in the neighborhood of 0.15 pK unit, are probably high since there is no way of assigning a different weight to points involving relatively larger errors at the beginning and end of the extraction run in comparison to the "best" points close to the pK_a which should have the greatest weight.

As the insolubility of the ether in the aqueous phase decreases and K_D' increases the error would be expected to increase. In the case of anisole this does not appear to have become important but we expect that there is enough difference from this source and from the possible intervention of small but varying contributions from Hammett–Chapman effects so that we do not feel it realistic to quote a single over-all error for the method.

Advantages of the Solvent Extraction–Gas Chromatography Method.—The main value of the present method is that it permits the study of certain classes of organic bases which have so far not yielded to other methods of investigation. Insofar as it is applicable, it compliments nicely the Hammett indicator method which is limited mostly to non-volatile aromatic compounds while the extraction–g.l.c. method is good for some volatile compounds lacking indicator properties.

The short time of exposure to the acid layer is a major advantage in the case of sensitive compounds. In cases where decomposition does occur it is furthermore usually apparent by the appearance of peaks corresponding to the products in the final chromatogram.

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(34) F. A. Long and D. McIntyre, *J. Am. Chem. Soc.*, **76**, 3243 (1954).

(35) M. A. Paul, *ibid.*, **76**, 3236 (1954).

(36) Conditions for g.l.c. analysis and extraction data will be presented in future papers. The technique is exactly the same as described here.

A suitable choice of conditions usually allows separation of the peak for the base under study from those of the solvent and any decomposition products and also from any other bases that are present. Thus, as will be shown in a future paper, it has been possible by this technique to measure simultaneously the basicities of *cis*- and *trans*-2,5-dimethyltetrahydrofuran even though they were not separated before the study. In principle, given the proper column, it would be possible to determine simultaneously the pK_a's of all the compounds described here and in future papers in one run with a series of acids.

When the organic layer is analyzed by spectrophotometry there is little advantage of this method over the usual Hammett indicator method and, as we have mentioned for nitrobenzene and benzoic acid, specific effects of water on the spectrum of the compound in the organic layer can make spectra uninterpretable. For compounds that do not suffer from this effect the use of solvent extraction and spectrophotometry in selected cases may be advantageous in that the spectrum of the compound in the organic layer does not show sensitivity to the complicated medium effects that are such a nuisance in the application of the Hammett indicator method to spectra in aqueous acid.[3-5,9,29]

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Base Strengths of Some Aliphatic Ethers in Aqueous Sulfuric Acid[1,2]

BY EDWARD M. ARNETT AND CHING YONG WU[3]

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The pK_a's for the oxonium ions of twelve saturated aliphatic ethers in aqueous sulfuric acid have been determined by the solvent extraction–g.l.c. method.[4,8] Validity is given to the method by comparing the results with independent estimates of the basicity range to be expected of saturated ethers. Comparison is also made with basicity data for some of these ethers in other non-aqueous systems and with results for analogous amines and phosphines. It is found that pK_a's for six methyl ethers correlate with Taft's σ^*-parameters, but that the other classes of ethers are sterically controlled. The results mainly support the predictions of previous theories[20,21] that oxygen bases are more sensitive to steric effects than their amine analogs, but indicate that in aqueous solution the important factor is steric hindrance to solvation and not B-strain. The matter of the basicities of ethers, alcohols and water is considered in the light of recent evidence.

In previous papers[4,5] we have described the importance and difficulty of measuring the pK_a's of aliphatic oxonium ions in aqueous strong acids. Although the basicities of alkyl phenyl ethers[5] might appear to provide a partial answer to the question of how alkyl groups influence the basicity of ether oxygen, the large contributions from steric inhibition of resonance observed in that series obscure the influences of other steric factors as well as the polar and solvation effects whose combined action may be expected to decide the base strengths of aliphatic ethers.

We shall present here our results for non-cyclic saturated ethers obtained by the method of solvent extraction–g.l.c.[4,8] In addition to comparing these results with those obtained by other workers for the same ethers with other acid systems and with basicities of comparable amines and phosphines, we shall consider the matter of the basicities of ethers *vis á vis* alcohols and water and the solvation of ethers. Further comments on these matters will be presented in a following paper on the basicities of saturated cyclic ethers.

Results

In Table I are the pK_a's of the oxonium ions of twelve selected aliphatic ethers and anisole[4,5,8] measured for the most part at room temperature by distribution between cyclohexane and aqueous sulfuric acid solutions. Although it is difficult to assign an error precisely to these results, it appears likely that most of the pK_a's are known to ± 0.10–0.20 pK_a unit.[4]

Although we have already[4] presented considerable evidence for the validity of this method for measuring the strengths of weak bases, it will be seen below that the data in Table I lend further support to the technique as it applies to ethers. However, in view of the hazards inherent in the method[4] and the fact that conflicting estimates in the literature for the strengths of other saturated weak bases often cover many powers of ten, we wish first to present several independent arguments that the data in Table I are of the right general order of magnitude.

TABLE I

DISSOCIATION CONSTANTS OF CONJUGATE ACIDS OF ALIPHATIC ETHERS[a]

Number	Ethers	pK_a	% H_2SO_4 at pK_a	K_D'[b]	Slope
1	Dimethyl	−3.83	54.4	0.435	0.81
2	Methyl ethyl	−3.82	54.2	1.65	.92
3	Methyl *n*-propyl	−3.79	54.0	9.0	.903
4	Methyl isopropyl	−3.47	51.0	4.85	.84
5	Diethyl	−3.59	52.3	6.52	.94
6	Methyl *n*-butyl	−3.50	51.3	35.0	.70
7	Methyl *t*-butyl	−2.89	45.2	12.3	.69
8	Ethyl *n*-butyl	−4.12	56.9	104	.97
9	Ethyl *t*-butyl	−2.84	44.8	41.0	1.03
10	Di-*n*-propyl	−4.40	59.5	93.0	1.14
11	Diisopropyl	−4.30	58.6	15.5	1.03
12	Di-*n*-butyl	−5.40	68.1	150	1.18
	Anisole	−6.54	78.2	105	1.028

[a] Each pK_a value is based on nine to twelve points covering a range of 2.5 to 4 H_0 units. [b] Using cyclohexane as solvent.

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(1) Stereoelectronic Effects in Organic Bases. VII; previous paper in this series, ref. 4.

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(3) The greater part of the work presented here is taken from the thesis of Ching Yong Wu presented to the Chemistry Department of the University of Pittsburgh in March, 1961, as partial fulfillment of the requirements for the Ph.D. degree.

(4) E. M. Arnett, C. Y. Wu, J. N. Anderson and R. D. Bushick *J. Am. Chem. Soc.*, **84**, 1674 (1962).

(5) E. M. Arnett and C. Y. Wu, *ibid.*, **82**, 5660 (1960).