

THE QUANTITATIVE STUDY OF VERY WEAK BASES

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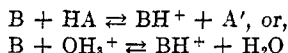
There are large groups of organic compounds for which basic properties have been demonstrated, but whose base strength is so small that its quantitative measurement is impossible within the limits of the classical field for the investigation of electrolytes, the dilute aqueous solution. Among these, the oxygen bases are of especial interest both in theory and in practice.

Thus the discovery by Collie and Tickle in 1899 of the salt-forming properties of the oxygen compound, dimethylpyrone, has led to a development by which the basicity of oxygen has become an important and recognized principle of organic chemistry (1). And the investigation by Hantzsch in 1908 (2, 3) of the properties of sulfuric acid as an electrolytic solvent demonstrated that nearly all oxygen compounds can act as bases provided only that the medium in which they are dissolved is of sufficiently high acidity. Yet quantitative progress has been so slow that only one determination of the base strength of an organic oxygen compound, that of dimethylpyrone by Walden in 1902 (4), had been published until very recently.

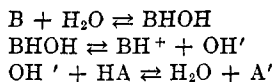
Such a discrepancy between qualitative and quantitative information is always distressing; it is particularly so in this case because of the important problems which wait upon the quantitative data. It is, for instance, a widely held hypothesis that catalysis by acids depends upon the addition of hydrogen ion to the substrate, which is to say upon basic properties in the substrate. In the light of Brönsted's relation between the catalytic effect of an acid or base and its strength (5), and of the evidence, presented at this meeting by myself and Pfluger, and to be published shortly, of a close relation between the strength of a carboxylic

acid and the rate of addition of the corresponding methyl ester to a tertiary amine, a knowledge of the strength of acids and bases becomes of the greatest importance for the interpretation of reaction velocities. It seems indeed quite possible that the base strength of the substrate will be found to have an importance in an acid catalyzed reaction equal to that of the acid strength of the catalyst.

The first requirement for a quantitative study is a numerical definition of the quantity, base strength, in question. This necessitates some limitation of the field. In the ordinary parlance of organic chemistry a base is a substance like aniline, whose electrically neutral molecule is capable of adding a hydrogen ion to form a positive ion. This reaction it is convenient to call the ionization of the base. The extent of ionization increases with increasing acidity of the medium in which the base is placed, and with increasing strength of the base. Whether the ionization of a base, B, takes place by direct transfer of a hydrogen ion from an acidic substance



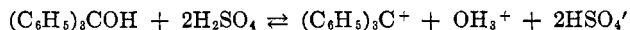
or whether it proceeds through intermediate steps to the same result, as has frequently been assumed,



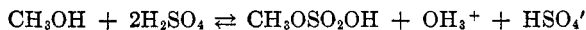
can have no significance for measurements which depend upon equilibrium states (6). The studies of Brønsted on catalysis by bases (5, 7) do however make the direct reaction much the more probable.

Cryoscopic and conductivity studies have shown that the typical organic acids, esters, ketones, aldehydes, and ethers, as well as the amines and amides, act as bases in this sense when they are dissolved in 100 per cent sulfuric acid (2, 3). Such substances I have referred to as simple bases (8). For hydroxy compounds direct evidence of a simple basic ionization is lacking, because these give much larger freezing point depressions in sulfuric acid

than do simple monoacid bases. Hantzsch's interpretation (2) is the reaction



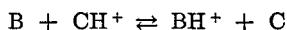
in the case of triphenylcarbinol derivatives, and



in the case of simple aliphatic alcohols. The available evidence is, however, hardly sufficient to justify the assignment of different ionization mechanisms and osmotic factors to the two groups of substances. α, β -Unsaturated ketones containing more than one ethylene group have a similarly complex ionization in sulfuric acid (9, 3). It is clear that the strengths of these pseudo bases measured by complex ionization reactions are incommensurable with those of simple bases.

If, moreover, following Brönsted (10) and Lowry (11) we extend the definition of the word "base" to include all molecules and ions which can add a hydrogen ion, we find that the relative strength of two bases, one neutral and the other charged, say aniline and acetate ion, is greatly affected by a change in medium, whereas the relative strength of two bases of the same electrical type is not (12, 13).

The base strength discussed in what follows pertains therefore exclusively to simple, electrically neutral, monoacid bases. For its quantitative measurement we must ultimately depend in every case upon the determination of concentrations. In particular the only experimental measure of the relative strength of two bases, B and C, is the position of equilibrium in the reaction



which is to say, the value of the concentration ratio

$$\frac{C_{\text{B}} \cdot C_{\text{CH}^+}}{C_{\text{BH}^+} \cdot C_{\text{C}}}$$

So long as we remain within a medium of constant properties so that the law of equilibrium in terms of concentrations is applicable, the relative strength of two bases, B and D, follows directly

if the relative strengths of the pairs, B and C, and C and D, are known. Since, further, we measure only relative strengths, we shall have to fix arbitrarily the strength of some one base in order to obtain a numerical scale.

All this gives measures of relative strength only for one particular medium, that in which the comparison is made. The crucial question for the present inquiry is whether these will also be valid measures for other media; for instance, whether the relative strength of two very weak bases in glacial acetic acid or in a 75 per cent sulfuric acid-water mixture is the same as it is in water, in which the ionization is too small for direct measurement. To this no complete answer can yet be given. The rule that the relative strengths of a series of bases of the same electrical type are independent of the medium is certainly a valuable first approximation. As such its validity has been amply demonstrated (14), even for so extreme a case as that represented by a transfer from water to benzene as a solvent (15). As an exact rule, it has been found applicable within the precision of the most careful colorimetric measurements for certain ranges of medium variation. This will be referred to later in this paper. Beyond this its limits of precision and range are not definitely established and require demonstration in every case of its application (40).

The rule may be given a certain theoretical background in terms of considerations first suggested by Bjerrum and Larsson (16). The quantity

$$K' = \frac{a_B a_{H^+}}{a_{BH^+}}$$

where the a 's are activities (referred for all media to one common standard of reference rather than to infinite dilution in each solvent), is a universally valid but not directly determinable inverse measure of the strength of the base B. The concentration equilibrium ratio for two bases is related to these constants by the equation

$$\frac{C_B C_{CH^+}}{C_{BH^+} C_C} = \frac{K'_B}{K'_C} \times \frac{f_{BH^+} f_C}{f_B f_{CH^+}}$$

where the f 's are activity coefficients. Only to the extent that the f ratio in this equation is constant will the relative strength of the two bases be independent of medium variations. Each f , being a measure of the deviation of the solute from ideality, is a function of the energy of interaction of the molecules of the solute with those of the medium. For the ion of an organic base, which is a large molecule bearing a localized charge and quite different from the spherically symmetrical ion of the Debye-Hückel theory, this interaction energy is the sum of two terms of coordinate importance and relative independence, one representing the energy due to the charge, the other that due to the rest of the molecule. Because of the logarithmic relation between the activity coefficient and the energy, we may therefore write

$$f_{\text{BH}^+} = f_{\text{BH}^+}^e f_{\text{BH}^+}^u$$

where $f_{\text{BH}^+}^e$ is a function of charge and of what may be called the effective diameter of the atom bearing the charge, but not of any other properties of the ion; and $f_{\text{BH}^+}^u$ is a function of dipole interactions and van der Waals forces which are of nearly the same magnitude in the ion as in the neutral base (17). We may therefore set

$$f_{\text{BH}^+}^u = f_{\text{B}}, f_{\text{CH}^+}^u = f_{\text{C}}$$

and

$$\frac{C_{\text{B}}C_{\text{CH}^+}}{C_{\text{BH}^+}C_{\text{C}}} = \frac{K'_{\text{B}}}{K'_{\text{C}}} \times \frac{f_{\text{BH}^+}^e}{f_{\text{CH}^+}^e}$$

The ratio $f_{\text{BH}^+}^e/f_{\text{CH}^+}^e$ should be very nearly one for organic bases, since the charge is the same and the diameter of the oxygen or nitrogen atom carrying the charge is nearly the same for the two bases.

The first advance in the direction of the use of media of acidity higher than is attainable in dilute aqueous solutions was made by Conant and Hall (18) with acetic acid as a solvent. Electro-metric, indicator, and catalytic studies were made in this solvent, and the whole scale was found to be shifted toward the acid side when compared with aqueous solutions. The important observa-

tion was made that the relative strengths of those bases which can be measured both in the aqueous and in the acetic acid systems is unaltered by the shift from the one to the other within the precision of the measurements. The extrapolation of the rule that there is no shift to bases which cannot be directly measured in both media is therefore a safe one. Among the very weak bases thus studied anisalacetophenone (19) and a group of triphenylcarbinols (20) are especially notable.

This most important step still does not carry us far enough toward the acid side for a general attack on the base strength of oxygen compounds. The obvious extension to the use of stronger acids is important and desirable, although its utility for the present purpose is likely to be limited. Thus formic acid is a more acid solvent than acetic acid, but it is also relatively basic (21, 22). The resultant large solvent ionization masks the ionization of the weaker bases, and severely restricts the range of base strengths accessible to investigation in it. As for inert solvents, which are very weakly basic without being strongly acidic, these are rarely if ever satisfactory solvents for electrolytes. This is not merely an inconvenience but a difficulty in principle. The more widely we depart for the measurement of base strengths from the hydroxylic, good salt solvent, high dielectric constant type of solvent in which the most important applications are likely to be made, the greater becomes the danger of error due to a shift in relative base strength.

A medium whose acidity varies continuously from that of water to that of sulfuric acid and which is liable to no such objections is obtained by mixing the two liquids in varying proportions. Against these advantages we must set one real and one apparent disadvantage. The apparent disadvantage is the fact that these solutions are neither ideal nor dilute. We find, however, that no shift in relative strength of a series of bases results from those changes in medium properties which accompany the variation of the proportion of acid and water. The apparent disadvantage translates itself therefore into an opening out of this field of concentrated solutions to quantitative investigation, not only for the determination of base strength, but for reaction velocity

and solubility studies. The real disadvantage is the fact that the mixtures are so heavily buffered that no reasonable addition of base can change significantly any property of the solution as a whole. We cannot therefore rely upon a measurement of the conductivity or acidity of the solution but must use some specific property of the base, recognizable and measurable in the mixture, and altered by conversion of base to ion in a recognizable and measurable fashion.

One such property is that of light absorption. The loss or gain of a hydrogen ion by an organic acid or base, its ionization, seems to be accompanied by a change in light absorption in every case in which there is absorption at all (23). When the neutral molecule or the ion is colored, this results in appearance or disappearance of color when ionization takes place or in a large change in color quality or intensity. When the absorption is in the ultraviolet the fact is less obvious but apparently just as general (24 to 31). Whether or not the reason for the difference in color between neutral molecule and ion is a change in structure capable of representation by our usual symbols is unimportant for the present purpose so long as the difference exists. Even if molecule or ion is present as a mixture of tautomers in mobile equilibrium, the color is still a valid measure of degree of ionization, as was long ago demonstrated by A. A. Noyes (32). In so far as acids are concerned, it is now well-established that no tautomeric equilibrium is concerned in the ionization and that the acid may be represented by one single structural formula, the ion by another (33, 34).

The first attempt to base some sort of a quantitative measure of the strength of very weak bases upon the difference in color between base and ion was that of Baeyer and Villiger in 1902 (35). They dissolved the base in a mixture of acetic and sulfuric acids, and measured its strength by the volume of 75 per cent aqueous ethyl alcohol required to destroy the color of the solution. The same method and closely similar ones (36) have been much used, more largely however for pseudo bases of the triphenylcarbinol and dibenzalacetone types than for simple bases. Ziegler and Boye (37) found however that very serious error may arise from

the fact that the amount of basic solvent required for decolorization is just as much a function of the color intensity of the ionized form as it is of the base strength. They suggest the measurement of base strength by the quantity of basic solvent required to reduce the color intensity not to zero but to a definite fraction of that possessed by the completely ionized substance. This certainly rates the bases in the proper order, but does not lead to the quantitative measure of base strength as it has here been defined.

With the development of precise methods for the colorimetric study of indicators, it has become possible to determine the relative strength of two simple bases which possess indicator properties and are not too widely separated in strength by the colorimetric determination of the degrees of ionization of both in a suitable acid-water mixture (8). There are some complications arising from the fact that ionization is a sufficient but not a necessary condition for color change, and the results have to be corrected for the change in light absorption due to the change in the nature of the medium necessary to obtain the reference colors of base and ion. The correction seems to be quite satisfactory in most cases and the overall precision of the comparison is about ± 4 per cent.

By this method a number of nitrogen and oxygen bases ranging in strength from *p*-nitroaniline, which is appreciably ionized in water, to trinitroaniline, which is incompletely ionized in sulfuric acid, have been studied by myself and Deyrup (8) with the result that constancy of relative strength has been thoroughly verified. That is, it was found that the relative strength of any two bases is the same for the whole range of sulfuric acid-water mixtures in which they can be directly compared. It was likewise found to be the same for mixtures of perchloric acid and water and for solutions in anhydrous formic acid. Unpublished work by myself and Paul shows that the same values are obtained for a number of these indicators in mixtures of hydrochloric and of nitric acids with water.

It is impossible by this or any other method to compare directly the strengths of two bases when these differ so widely that the

ionization of the one becomes appreciable only in media of acidity so high that the ionization of the other is practically complete. Such bases may however be compared by an indirect or step method which uses a series of bases intermediate in strength between the two extremes to be compared and sufficient in number to make possible direct comparison between successive members of the series. In this way numerical values were obtained for all of the bases studied, using the strength of *p*-nitroaniline in aqueous solution as a natural reference point. The determination of the strength of any simple monoacid base which has indicator or halochromic properties by comparison with this series has therefore become a simple matter.

Where no visible color change accompanies the ionization, some other criterion must be found for the determination of the ionization ratio. One possibility which is now being investigated at Columbia University uses the change in ultra-violet absorption which accompanies ionization; in effect it extends the colorimetric method from the visible to the ultra-violet.

Among the other optical methods which suggest themselves is one of limited applicability for which some data is already available. Baker (38) has shown that the large change in rotation observed when camphor is dissolved in sulfuric acid is at least partly the result of salt formation.

A method of quite a different sort depends upon the behavior of the solubility of organic oxygen compounds in mixtures of strong acids with water. In unpublished work in this laboratory Deyrup found that this increases very sharply within a narrow range of acid concentration and in a way which strongly suggests that conversion of the base to the ion in the range of acidities there attained is responsible for the increase in solubility. Quantitative studies by Dr. Chapman show that in many instances the course of the increase agrees with this assumption, and that solubility measurements in sulfuric acid-water mixtures may be used for the determination of base strength.

Equivalent in principle to the determination of base strength by solubility is its determination by distribution. The possibility of measuring the distribution of organic compounds between

sulfuric acid–water mixtures and ligroin has been demonstrated by Baker and his coworkers (39), and the method has been used by them for the qualitative study of the basicity of benzaldehyde, acetophenone, ethyl benzoate, and other oxygen compounds. It should be especially valuable with bases whose solubility as neutral molecules is large in the acid–water mixtures, or where the appearance of new phases, bisulfates of the organic base, complicate the solubility method.

SUMMARY

It is shown that several methods are available for the translation of the existing qualitative knowledge that the typical organic ketone, aldehyde, ester, acid, or ether is a base into a quantitative knowledge of its basic strength.

REFERENCES

- (1) HENRICH: *Theorien der organischen Chemie*, Chapter 18. Fried. Vieweg und Sohn, Braunschweig, Germany (1921).
- (2) HANTZSCH: *Z. physik. Chem.* **61**, 257 (1908); **65**, 41 (1908).
- (3) HAMMETT AND DEYRUP: *J. Am. Chem. Soc.* **55**, 1900 (1933).
- (4) WALDEN: *Ber.* **34**, 4185 (1902).
- (5) BRÖNSTED AND PEDERSEN: *Z. physik. Chem.* **108**, 185 (1924).
See the review by Kilpatrick and Kilpatrick: *Chem. Rev.* **10**, 213 (1932).
- (6) HAMMETT: *Solutions of Electrolytes*, p. 96. New York (1929).
- (7) BRÖNSTED: *Chem. Rev.* **5**, 231 (1928).
- (8) HAMMETT AND DEYRUP: *J. Am. Chem. Soc.* **54**, 2721 (1932).
- (9) HANTZSCH: *Ber.* **B55**, 953 (1922).
- (10) BRÖNSTED: *Rec. trav. chim.* **42**, 718 (1923).
- (11) LOWRY: *Chemistry & Industry* **42**, 43 (1923).
- (12) BRÖNSTED: *J. Chem. Soc.* **119**, 574 (1921); *J. Phys. Chem.* **30**, 777 (1926); *Ber.* **61**, 2049 (1928).
- (13) HAMMETT: *J. Am. Chem. Soc.* **50**, 2666 (1928).
- (14) Reviewed in reference 8.
- (15) LA MER AND DOWNES: *J. Am. Chem. Soc.* **55**, 1840 (1933).
- (16) LARSSON: *Dissertation*, Lund, 1924; *Z. physik. Chem.* **127**, 238 (1927).
BJERRUM AND LARSSON: *Z. physik. Chem.* **127**, 378 (1927).
See also HAMMETT: Reference 13; HALFORD: *J. Am. Chem. Soc.* **53**, 2939 (1931).
- (17) SMALLWOOD: *J. Am. Chem. Soc.* **54**, 3048 (1932).
- (18) CONANT AND HALL: *J. Am. Chem. Soc.* **49**, 3047, 3062 (1927).
- (19) HALL: *J. Am. Chem. Soc.* **52**, 5115 (1930).
- (20) CONANT AND WERNER: *J. Am. Chem. Soc.* **52**, 4436 (1930).
- (21) HAMMETT AND DIETZ: *J. Am. Chem. Soc.* **52**, 4795 (1930).

- (22) HAMMETT AND DEYRUP: J. Am. Chem. Soc. **54**, 4239 (1932).
- (23) v. HALBAN: Z. Elektrochem. **30**, 601 (1924).
- (24) BALY AND EWBANK: J. Chem. Soc. **87**, 1345 (1905).
- (25) WRIGHT: J. Chem. Soc. **103**, 528 (1913).
- (26) BIELECKI AND HENRI: Ber. **46**, 1304 (1913).
- (27) HANTZSCH: Ber. **46**, 3570 (1913).
- (28) HENRI: Ber. **46**, 3650 (1913).
- (29) HANTZSCH: Z. physik. Chem. **86**, 624 (1914).
- (30) SCHAEFER: Z. anorg. allgem. Chem. **97**, 285 (1916); **98**, 70, 77 (1916).
- (31) LEY AND ARENDT: Z. physik. Chem. **B4**, 234 (1929).
- (32) NOYES: J. Am. Chem. Soc. **32**, 815 (1910).
See also BJERRUM: Sammlung Chem. and chem.-techn. Vorträge **21**, 59 (1915).
- (33) v. HALBAN AND EBERT: Z. physik. Chem. **112**, 359 (1924).
- (34) HANTZSCH: Ber. **B60**, 1933 (1927).
- (35) BAEYER AND VILLIGER: Ber. **35**, 1189 (1902).
- (36) STOBBE: Ann. **370**, 93 (1909).
STOBBE AND HAERTEL: Ann. **370**, 99 (1909).
STOBBE AND SEYDEL: Ann. **370**, 129 (1909).
- (37) ZIEGLER AND BOYE: Ann. **458**, 229 (1927).
- (38) BAKER: J. Chem. Soc. **1932**, 2917.
- (39) BAKER: J. Chem. Soc. **1931**, 307; **1932**, 1226.
BAKER AND HEY: J. Chem. Soc. **1932**, 2917.
- (40) HALFORD: J. Am. Chem. Soc. **55**, 2272 (1933).