and chloride) and the two structures for α-methylacetylcholine iodide contain bond length and bond angle differences which are large enough to affect the rigid-geometry maps (see section IV). However, it is not clear because of the crudeness of some of the X-ray determinations whether the surprisingly large differences found in some of the cases are actually correct. It seems desirable, therefore, that more precise data be obtained for these and similar molecules. If the differences do turn out to be real, it is clear that straightforward averaging to obtain a "standard" structure, which neglects particulars of chain substitution, crystal packing, and other possible chemical differences is not valid and further investigation of these interactions will be required.

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Equilibrium Acidities of Carbon Acids. VI. Establishment of an Absolute Scale of Acidities in Dimethyl Sulfoxide Solution[1]

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Abstract: An accurate spectrophotometric method of determining relative equilibrium acidities of carbon acids in DMSO has been developed. The pK scale in DMSO has been anchored by comparisons of values obtained by the spectrophotometric method with those obtained potentiometrically in the 8 to 11 pK range. As a result, the pK of fluorene, formerly arbitrarily taken as 20.5, has been raised to an absolute value of 22.6. The pK's of other carbon acids previously reported, including nitromethane, acetophenone, acetone, phenylacetylene, dimethyl sulfone, acetonitrile, and the corresponding indicator pK's must also be raised. The pK's have been found to be correlated with heats of deprotonation in DMSO by potassium dimsyl, and evidence is presented to show that pK measurements in DMSO are free from ion association effects. Data are presented which indicate a pK of 35.1 for DMSO. In the methane carbon acids, CH_3EWG, the order of acidities is $NO_2 \gg CH_3CO >$ CN, CH_3SO_2. The differences amount to 12.2 and 6.8 kcal/mol, respectively, which are believed to be of a comparable magnitude to gas-phase substituent effects. Carbon acids wherein the charge on the anion resides mainly on oxygen, such as ketones and nitroalkanes, are found to be weaker acids in DMSO than in water by 5.5 to 9.6 pK units. On the other hand, carbon acids wherein the charge on the anion is delocalized over a large hydrocarbon matrix, such as in the anion derived from 9-cyanofluorene, are stronger acids in DMSO than in water. Factors that may contribute to this reversal are discussed. The scale of pK's for 9-substituted fluorenes in DMSO is shown to be expanded when compared to the earlier pK scale determined by the H_- method. A rationale is presented. The apparent relative acidities of fluorenes and phenylacetylene differ by 6 and 11 pK units, respectively, for cyclohexylamine (CHA) vs. DMSO solvents and benzene vs. DMSO solvents. Similarly, in benzene, acetophenone is a stronger acid than fluorene by ca. 6 pK units, whereas in DMSO acetophenone is a weaker acid by 3.2 pK units. These differences result from ion association effects that occur in solvents of low dielectric constant (benzene, ether, CHA, etc.) causing relative acidities to be dependent on the reference base, as well as the solvent. This is not true in strongly dissociating solvents of high dielectric constant, such as DMSO. A list of 13 indicators covering the pK range 8.3 to 30.6 in DMSO is presented.

Equilibrium acidities of weak (i.e., p$K \geq 15$) carbon acids have been measured by a variety of methods[3] in a variety of solvents including ether,[4a] benzene,[4b] diglyme,[5] cyclohexylamine (CHA),[6] mixtures of dimethyl sulfoxide (DMSO) with ethanol, methanol, or water,[7,8,9] and pure DMSO.[10] We have chosen DMSO for our studies because it allows accurate measurements to be made spectrophotometrically for many different types of carbon acids over a wide range of pK (ca. 30 pK units) with apparently little or no interference from ion association effects.[1] Furthermore, measurements have been made in this medium by potentiometric,[10,11] spectrophotometric,[11] and conductometric methods,[11] which provide a basis for anchoring our pK measurements on an absolute scale. In our previous studies we chose the pK 20.5 for fluorene, determined potentiometrically,[10] as our reference standard.[1] Our measurements, using the indicator method, have now been extended down into the pK range 5 to 15. Comparison with absolute measurements made in this region[10,11] has shown, however, that the pK's we reported earlier,[1] based on fluorene at pK = 20.5 as a reference standard, are about 2 pK units too low. A revised listing of pK's in DMSO covering the range 8 to 31 will be presented, and comparisons with results in the gas phase and in other solvent systems will be made.

Results and Discussion

General Description of the Method. The method which we have adopted consists essentially in relating the acidity of two acids by titrating a solution of one acid, containing a known concentration of its colored anion, with a solution of a second acid, the anion of which is either colorless or absorbs at a different wavelength. The concentration of the colored anion is measured spectrophotometrically after each addition of the second acid, and the equilibrium position is calculated from this and the known concentrations of the two acid solutions. The method requires that the pK of one of the acids be known, and, for accurate results, that the two acids do not differ from one another by more than 2 pK units. Precautions must be taken to keep the solutions out of contact with the atmosphere since the strongly basic anions present react rapidly with oxygen.

In a previous paper we have described how a series of indicators less acidic than fluorene were overlapped using various types of carbon acids forming colorless anions, including ketones, sulfones, phenylacetylene, nitriles, and sulfoxides.[1b] A similar procedure has now been used for carbon acids more acidic than fluorene. As a result it is now possible to measure the acidities of carbon acids that are more acidic than fluorene by as much as 15 pK units. Development of a reliable series of indicators to be used for compounds forming colorless anions and a series of standard acids to be used for compounds with colored anions in this region is still underway. Indicators that have been related to fluorene (with an assumed pK of 20.5) include 4-nitroaniline, 18.9; 4-chloro-2-nitroaniline, 16.8; 9-phenylfluorene, 15.8; 9-phenylthiofluorene, 13.3; 9-phenylsulfonylfluorene, 9.4_5; 9-carboxymethylfluorene, 8.2; 9-benzoylfluorene, 8.0; 9-cyanofluorene, 6.2. The absorbance observed for the hydrocarbon indicator anions was stable in every instance over long periods of time (minutes or even hours). This was true also for the anion derived from 4-chloro-2-nitroaniline, but not for that derived from 4-nitroaniline (NAH). For the latter the absorbance slowly dropped from the maximum value in the presence of excess NAH, indicating that a reaction of some sort was occurring. This indicator is no longer used.

One of the important features of the method now in use is that the concentration of the base solution ($DMSO^-K^+$/DMSO) is determined internally as a part of each run. This is done by titrating the base solution with a known indicator acid (HIn) solution until the maximum absorption is reached. The concentration of In^- at maximum absorbance then gives an accurate measure of the base concentration in the cell at the time measurements are being made. This preliminary standardization of the base also serves to convert the highly reactive dimsyl anion completely to the indicator anion. These anions are less basic and much more sterically hindered than the dimsyl anion. As a consequence they generally effect rapid deprotonation of the carbon acids, but are less prone to participate in condensation reactions with other reactive functions in the carbon acids.

Table I. Summary of Equilibrium Acidities in DMSO Obtained by Indicator and Potentiometric Methods

Compd	pK[a]	pK[b]	ΔpK	Ref[c]
Fluorene	(20.5)	20.5	(0.0)	10a
9-Methylfluorene	20.2	19.7	+0.5	10a
4-Chloro-2-nitroaniline	16.8	15.1	+1.7	10c
9-Phenylfluorene	15.8	16.4	−0.6	10b
Nitromethane	15.1	15.9	−0.8	10a
Nitroethane	14.6	13.9	+0.7	10c
Malononitrile	9.0	11.0	−2.0	10b
9-Carboxymethylfluorene	8.2_5	10.3	−2.1	10b
9-Cyanofluorene	6.2	8.4	−2.2	10d
Benzoic acid	8.7[d]	11.0	−2.3	10c, 11
p-Chlorobenzoic acid	8.1	10.1	−2.0	10c
p-Nitrobenzoic acid	6.9[e]	8.9	−2.0	10c, 11
3,5-Dinitrobenzoic acid	5.2	7.4	−2.2	11
Salicylic acid	4.7	6.8	−2.1	11

[a] Indicator method. [b] Potentiometric method. [c] References for the absolute measurements. [d] Average of 11 runs with four different indicators. [e] Average of five runs with a single indicator.

The pK's determined with a given set of solutions are usually reproducible to within ±0.05 pK unit. Measurements for the same compound by a different investigator with freshly prepared solutions are generally within ±0.1 pK unit.

One problem encountered is that the anions for a sizable number of weak acids are unstable. For these, one point titrations can often be obtained if the anions are stable for a minute or more, but these determinations are, of course, less accurate. It is difficult at present to judge the accuracy of the measurements over the whole 25 pK range that we have worked to date. Our present interests are mainly with comparisons made over more limited pK ranges, however, and for this purpose we believe that the values are generally valid to within ±0.1 pK unit.

Anchoring of the p*K* Scale in DMSO. One important advantage of DMSO as a solvent for acidity measurements is that its relatively high dielectric constant (49 to 20°) makes possible measurements by potentiometric and conductometric methods, as well as by spectrophotometric methods. A number of accurate direct measurements for acids in the pK range 3–12 have been made by these methods, which provide an absolute base for our scale. A comparison of our results with those obtained by potentiometric methods is given in Table I.

Examination of Table I shows that agreement between results obtained by the spectrophotometric indicator method and by the potentiometric method is poor in the 14 to 20.5 pK region, but is good in the 7 to 11 pK region, *if an adjustment factor of ca. 2.1 pK units is applied.*[12]

The standard deviations in our titrations with various benzoic acids were usually ca. ±0.1 pK unit, and the pK values tended to decrease during a run as additional acid was added. This is to be contrasted with measurements made with carbon acids, where standard deviations are seldom worse than ±0.05 pK unit, and where no consistent trends are observed during a run. Kolthoff and Chantooni have shown that the benzoic acids and their anions combine to form complexes in DMSO ("homoconjugation"), and that the apparent pK varies appreciably, depending on the relative concentrations of undissociated acid and salt present.[11] Complications of this type should be minimized at the low concentrations at which we are working (ca. 10^{-2}

M), but may account for the lower precision in these runs. In any event, the average values we obtain for various benzoic acids agree reasonably well with those of Ritchie[10c] and Kolthoff[11b] once our values are adjusted to a 2.1 p*K* higher scale (Table I).

Additional confidence in the absolute values obtained by adjusting the values in Table I upward by 2.1 p*K* units is gained by the reasonably good agreement obtained between the adjusted values for nitromethane (pK = 17.2) and nitroethane (pK = 16.7) and those reported in DMSO relative to thymol blue (pK = 15.3) as an indicator.[13] Our values for CH_3NO_2 and $MeCH_2NO_2$ are 0.25 and 0.29 p*K* units higher, respectively, than those reported;[13] our value for $EtCH_2NO_2$ is 0.30 unit higher, and that for Me_2CHNO_2 is 0.71 unit higher.[14] Except for the latter value, there appears to be a constant difference of ca. 0.3 p*K* unit in the two sets of values. It is possible that the standard indicator thymol blue may have a p*K* of 15.6, rather than 15.3, since Kolthoff, who made the original assignment, gives it a value of *about* 15.3.[11a]

It is clear from the results in Table I that the p*K* of fluorene, which was previously taken as a standard, needs to be adjusted upward by ca. 2.1 p*K* units to fit it on an absolute scale. All previously reported p*K*'s will have to be similarly adjusted. It seems best to anchor our scale on the carbon acids 9-cyanofluorene, 9-carboxymethylfluorene, and malononitrile, which appear to respond well in both the indicator and potentiometric methods, and where homoconjunction problems are absent.

Ion Association Effects and Correlation of p*K*'s with Heats of Deprotonation. Evidence from a variety of sources indicates that at low concentrations (ca. 10^{-2} *M*) and with potassium ion as the counterion, salts of carbon acids in DMSO exist essentially as fully dissociated ions.[15] Conductivity measurements of inorganic and organic salts of strong acids have shown them to be completely dissociated in DMSO at least up to concentrations of 10^{-3} *M*.[15g] Furthermore, similar measurements have shown that even dimsyl-potassium behaves as a strong 1:1 electrolyte in DMSO up to a concentration of at least 0.01 *M*.[15f] Also, Arnett has found no concentration dependence in heats of deprotonation of carbon acids by 0.1 *M* K^+DMSYL^-, and has shown that heats of solution of fluorene in 0.1 *M* K^+DMSYL^-, in 0.05 *M* K^+DMSYL^-, and in 0.05 *M* K^+DMSYL^- with 0.05 *M* dibenzo-18-crown-6 ether, a strong K^+ complexer, were all the same within experimental error.[15e] In our work the fact that carbon acids of widely different structure can be related using the same hydrocarbon (or other type) indicators (see Table V) also supports this view. In addition, we find that the observed p*K*'s do not vary appreciably during a titration as the $[HA]/[A^-]$ ratio changes, or when the concentration of the indicator anion (i.e., the base) is varied by a factor of as much as tenfold. Finally, a plot of p*K*'s in DMSO for a wide variety of weak acids, numbering over 30, against heats of deprotonation[16] gives a good linear correlation. If the p*K* measurements were subject to ion association effects, the equilibrium position would depend on the degree of association of *both* K^+In^- and K^+A^- in the equilibrium,

$$K^+In^- + HA \rightleftarrows K^+A^- + HIn$$

Since no HIn or K^+In^- is present in the measurements of the heats of deprotonation, the linear correlation of p*K* and ΔH_D indicates that these species are not affecting the p*K*'s. Note also that the concentrations are much higher in the solutions Arnett is using for ΔH_D measurements than in our work. His evidence for the absence of ion association, together with the p*K* vs. ΔH_D correlation, constitutes strong evidence, then, for the absence of ion association at the low concentrations used for the p*K* measurements.

Table II. Absolute Equilibrium Acidities of Carbon Acids in Dimethyl Sulfoxide

Carbon acid[a]	p*K*[b]	Carbon acid[a]	p*K*[b]
9-Cyanofluorene	8.3[c]	Isopropyl phenyl ketone	26.3
9-Carboxymethylfluorene	10.3_5[d]	Acetone	26.5
Malononitrile	11.1	Diethyl ketone	27.1
Nitroethane	16.7	9-Phenylxanthene	27.9[h]
Nitromethane	17.2	Phenylacetylene	28.8
9-Phenylfluorene	17.9[e]	Benzyl methyl sulfoxide	29.0
9-Methylfluorene	22.3	Methyl phenyl sulfone	29.0
Fluorene	22.6[f]	Diphenylyldiphenylmethane	29.4[i]
Dibenzyl sulfone	23.9_5	Triphenylmethane	30.6[j]
Ethyl phenyl ketone	24.4	Dimethyl sulfone	31.1
Acetophenone	24.7	Acetonitrile	31.3
1,3,3-Triphenylpropene	25.6[g]		

[a] Abbreviations are given for compounds used as indicators. [b] Adjusted from previous values[1] or those given in Table I by addition of 2.1 p*K* units; for p*K*'s measured with TPH and less acidic indicators a further correction of +0.2 p*K* unit has been added (see Experimental Section). The p*K* values have *not* been statistically corrected. [c] 9-CN-FH. [d] 9-CO_2Me-FH. [e] 9-Ph-FH. [f] FH. [g] TPH. [h] 9-Ph-XH. [i] DDH. [j] TH.

From the discussion presented earlier it is apparent that the p*K*'s given in our preliminary accounts[1] need to be adjusted upward by 2.1 p*K* units to place them on an absolute scale. Acidities adjusted by addition of 2.1 to the p*K*'s reported earlier,[1b,c] and for compounds in Table I, are given in Table II.

Our data suggest that the presently accepted p*K* value for DMSO of 33, which is based on H_- extrapolations[9b] and on an estimate made from kinetic acidities,[17] is too low. The p*K* intercept at $\Delta H_D = 0$ is 37, corresponding to an acid as weak as DMSO. Ritchie and Uschold reported an equilibrium constant of 1.6×10^4 for the reaction of dimsyl ion with triphenylmethane (TH) in DMSO.[18] Repetition of this experiment gave an equilibrium constant of 3.0×10^4. Using our p*K* value of 30.6 for TH (Table II) gives a calculated p*K* for DMSO of 35.1.

Comparison with Gas-Phase Acidities and with Gas-Phase Substituent Effects. The ionic dissociation of acids in solvents such as DMSO is, of course, enormously favored over ionic dissociation in the gas phase. An appreciation of the magnitude of solvent effects can be gained by comparing $\Delta H°$ for ionization of hydrogen chloride in the gas phase (+333 kcal/mol) with $\Delta H°$ for ionization in water (−16 kcal/mol).[19] Compared to these differences the effect of solvent variation is small. For example, the solvation enthalpies for chloride ion in H_2O, DMSO, and MeOH are 86.8, 81.7, and 84.9 kcal/mol, respectively, and the corresponding values for perchlorate ion are 57, 61.8, and 58.1 kcal/mol.[20] In view of the extremely large stabilization of anions afforded by solvation one would expect substituent effects to be leveled in solution, relative to the gas phase. This is observed for substituent effects on acidities of aliphatic carboxylic acids,[21] and for substituent effects that are transmitted across an aromatic ring, as in four-substituted pyridinium ions,[22] meta- and para-substituted benzoic acids,[23] and meta- and para-substituted phenols.[24] In these instances the charge is more or less localized at the acidic site. For extensively delocalized ions such as resonance-stabilized carbanions, aryl cations, and polyaromatic radical anions, however, relative substituent effects appear to be almost as large in solution as in the gas phase.[1e,25] This suggests that the relative equilibrium acidities of the methane carbon acids, CH_3EWG, in DMSO give a reasonably good index of relative intrinsic EWG substituent effects, as judged by gas-phase acidities.[1e] In accord with this idea we find that the order of EWG effects, $NO_2 > CH_3CO > CN$, is the same as that reported by Bohme,[26] and that the differences are large (12.2 and 6.8 kcal/mol, respectively). On the other hand, Bohme finds the order $CH_3CN > CH_3SO_2CH_3$, whereas we find these acids to be of the same strength; Kebarle finds the order $CH_3CN > CH_3COCH_3$ in the gas phase,[27] which is opposite to the order that we observe in DMSO and to that reported by Bohme.[26]

Table II shows the acidifying effects on methane carbon acids to be $NO_2 \gg CH_3CO \gg CH_3SO_2$, CN, with the nitro group being 9 pK units more effective than the aceto group, and the latter being 5 pK units more effective than the methylsulfonyl or cyano groups. Preliminary evidence indicates that these differences, which amount to ca. 12 and 7 kcal/mol, respectively, are associated primarily with the relative abilities of these groups to stabilize the negative charge in the CH_2EWG^- anions by resonance effects.[28,29]

Comparisons with Acidities in Water. Anchoring of the pK scale in DMSO allows direct comparisons to be made between acidities of weak acids in DMSO and in water. These are the only two solvents for which extensive equilibrium data free of ion association effects are at present available. We will find that the solvents complement one another in dissociating ability, oxygen acids generally being more acidic in water and hydrocarbon acids generally being more acidic in DMSO. The properties of the solvent that determine the position of the equilibrium,

$$\text{H-A} + \text{solvent} \rightleftarrows \text{solvent}{\cdot}\text{H}^+ + \text{A}^-$$

upon which the relative acidities depend, include: (a) hydrogen bonding ability, (b) basicity, (c) bulk dielectric constant, (d) dipole moment, (e) polarizability, and (f) structural organization.

Water acts as a strong hydrogen bond acceptor and also as a strong hydrogen bond donor, whereas DMSO acts as a strong hydrogen bond acceptor but only a very weak donor. The weak hydrogen bond donor properties of DMSO make it relatively poor at stabilizing anions wherein the charge is localized, and acids producing such anions are generally much more acidic in water than in DMSO. Examples include oxygen acids, such as phenols and carboxylic acids, which are 6 to 7 pK units more acidic in water than DMSO,[10c,11,32] and also carbon acids, such as ketones and nitroalkanes, in which the negative charge in the anion resides largely on oxygen. The pK's of acetophenone and acetone are much too high to be measured in water, but reasonable estimates have been made on the basis of kinetic acidities by an extrapolation, using the Bronsted relationship, from ketonic substrates upon which direct measurements can be made.[33] Using the estimates of pK 19.2 for acetophenone and 20 for acetone thus obtained,[33] and data in Table II, gives ΔpK's of 5.6 and 6.5, respectively, for the acidities in DMSO vs. water. Similarly, a comparison of literature data for pK's of nitromethane, nitroethane, and nitrocyclohexane in water with those in DMSO[14] (Table II) gives ΔpK's of 7.0, 8.0, and 9.6, respectively.

Kolthoff has concluded that DMSO in DMSO is more basic than water in water by about 1.5 ± 0.5 pK units,[11a] and we can expect HA to have a greater acidity in DMSO by about this amount. This effect is balanced, however, by the somewhat higher dielectric constant of water (80 vs. 49 at 20°). A simple calculation based on electrostatic effects using the Born equation indicates that this difference should lead to a higher acidity in water than in DMSO by ca. 1 pK unit.[34]

The larger dipole moment of DMSO (3.9 D vs. 1.8 D for water) and its larger size and polarizability ($n^{20}\text{D}$ is 1.478 vs. 1.333 for water) should make it superior to water in stabilizing molecules and ions through dipole and induced dipole interactions (i.e., through van der Waals attractive forces). These attractive forces depend, of course, on the shape, as well as the size, of the interacting molecules. For large molecules and ions van der Waals attractions may become a decisive factor in determining the acidity. Grunwald and Price have shown that the acidity of picric acid, relative to that of acetic acid, is increased by ca. 100-fold in changing from water to ethanol solvent. (The absolute acidities are decreased by ca. 5 pK units by this solvent change.) They have suggested that increased stabilization of the large, highly delocalized picrate ion by (London) dispersion forces in ethanol is largely responsible for this change.[35] A similar effect is noted for acidities in water vs. DMSO for the series phenol, 4-nitrophenol, 2,6-dinitrophenol, and 2,4,6-trinitrophenol. Here the ΔpK's change from 6.5 to 3.8 to 1.3 to ca. −1.3.[11a] DMSO is slightly larger than EtOH and more polarizable. The progressive drop in ΔpK (DMSO-H_2O) in this series can likewise be rationalized by assuming a progressive increased stabilization of the anion by dispersion forces as the degree of delocalization increases, with DMSO having much greater dispersion attractions than does water.

If hydrogen bonding to large, highly delocalized carbanions is weak and stabilization of such anions by induced dipole interactions is strong, as seems likely, these carbon acids should be substantially *stronger* in DMSO than in water. Ritchie has explained the 5.5-6.5 pK unit lower acidities of fluoradene, 9-cyanofluorene, and 9-carbomethoxyfluorene in MeOH vs. DMSO in this way.[10d] Unfortunately, there is very little information available as yet with respect to acidities of hydrocarbons in pure water. Since acidities of phenols, carboxylic acids, nitroalkanes, and the like are higher in water than in MeOH by 4 to 5 pK units, presumably due primarily to the better hydrogen bonding properties of water, hydrocarbon acids might also be substantially more acidic in water than in methanol. This view is supported by the fact that we find 9-cyanofluorene to have a pK in 50% (v/v) MeOH-H_2O (70 mol % water) of 11.2,[36] as compared to 14.2 in pure methanol.[10d] Its pK is probably lower still in pure water, but it seems unlikely that it will be as low as the value of 8.3 observed in DMSO.

Comparison with Equilibrium Acidities Determined by H_- Techniques. Extensive investigations have been undertaken to establish an H_- scale in strongly basic aqueous media in order to determine relative acidities of weak acids "anchored in water".[37] Judging from the near constancy of the derived pK values in different solutions for a variety of diphenylamines, a satisfactory H_- scale appears to have been established for nitrogen acids,[37,38] but carbon acids and oxygen acids behave poorly by this criterion.[38c] Doubts have been raised about the validity of H_- scale even for nitrogen acids, however.[10d] Furthermore, Kreevoy has pointed out that there is a systematic deviation of H_- functions from ideal behavior, and has concluded that it seems unlikely that H_- functions can be used to give accurate pK's when the structure of the acid varies appreciably from the structure of the indicators used to establish the scale.[39]

The difficulties inherent in the H_- method can perhaps be brought out by comparisons of acidities measured or expected in pure water and in pure DMSO with those observed in water-DMSO mixtures by the H_- method. In the previous section we saw that acids forming anions that are strong hydrogen bond acceptors (e.g., phenols, nitroalkanes,

Table III. Comparison of p*K*'s of Weak Acids in Pure DMSO with p*K*'s in DMSO–H_2O, DMSO–EtOH, DMSO–MeOH, as Determined by the H_- Method

Acid	p*K*-(DMSO)[a]	p*K*-(DMSO–H_2O)[c]	p*K*-(DMSO–EtOH)[c]	p*K*-(DMSO–MeOH)[c]
4-Chloro-2-nitroaniline	18.9	17.1[d]		
4-Nitroaniline	21.0	18.9[d]		
Diphenylamine	23.5[b]	22.4[d]		
3-Chloroaniline	26.7[b]	25.6[d]		
9-Cyanofluorene	8.3		11.41	
9-Carbomethoxyfluorene	10.3		12.88	
9-Phenylfluorene	17.9	(18.59)	18.59	18.1
2-Bromofluorene	~20.0	20.6	21.0	20.5
9-Benzylfluorene		21.2		
9-Methylfluorene	22.3	21.8		
Fluorene	22.6	22.1		
7*H*-Benzo[*b*]fluorene	22.9			<19.5
9-*tert*-Butylfluorene	24.3_5	23.4		
9-Phenylxanthene	27.9			24.2

[a] Data from this laboratory unless otherwise noted. [b] Reference 11c. [c] Data summarized in ref 7b unless otherwise noted. [d] Reference 38b.

etc.) are much more acidic in water than in DMSO, whereas acids forming anions wherein the charge is delocalized primarily to carbon atoms (e.g., hydrocarbon acids) are less acidic in water than in DMSO. For a series of acids of the first type the effect of adding DMSO to water in order to ascend the H_- scale will be to decrease the acidity relative to that expected in pure water. In other words, the p*K*'s registered in the high H_- region will be higher than would be expected in pure water. (The p*K*'s of acids of this type may be as much as 5.5–9.5 units higher in DMSO than in water.) The result is to expand the p*K* scale relative to that expected in pure water. For a series of acids of the second type the effect of adding DMSO to water in order to ascend the H_- scale will be to increase the acidity over that expected in pure water; the result will be to contract the p*K* scale relative to that expected in pure water or that expected in pure DMSO.

Anilines and diphenylamines are probably examples of acids of the first type since one would expect $ArNH^-$ and $ArAr'N^-$ anions to be strong hydrogen bond acceptors. These compounds have been studied over an H_- range of 12 to 26.[38] Data in DMSO are not available as yet for compounds in the low H_- region,[40] but the anilines listed in the top part of Table III show the expected behavior. In the medium (water-like) H_- region the p*K*'s are substantially lower than in DMSO, and in the high H_- region, where the concentration of DMSO is high, the p*K*'s are much closer to those in pure DMSO.

The substituted fluorenes listed in the bottom part of Table III are examples of acids of the second type. In the low H_- region the p*K*'s are higher than those in pure DMSO and as the H_- scale is ascended the values approach those in DMSO. (The values in pure water would be expected to be substantially higher.) The H_- scale is therefore compressed relative to the p*K* scale observed in pure DMSO, or that expected in pure water.

We conclude from these examples that p*K* measurements obtained by the H_- method in mixed solvents can never give a p*K* scale identical with that expected for pure water, although in the lower H_- region they may approach this ideal.

Comparison with Equilibrium Acidities in Solvents of Low Dielectric Constant. Semiquantitative measurements of equilibrium acidities of a variety of hydrocarbons and of a few other types of weak acids were made in the 1930's in ether and in benzene in the classical studies of Conant, Wheland, and McEwen.[4] Additional, more accurate measurements of this type have been made for a variety of ketones in polyether solvents (glyme and diglyme).[5] Extensive quantitative measurements relating the acidities of a variety of hydrocarbons have been made in cyclohexylamine (CHA).[6] The ion-pair p*K* of 22.7 assigned to fluorene in CHA using cesium cyclohexylamide[41] is essentially identical with the absolute p*K* assigned to fluorene (Table II) in DMSO (22.6). This is purely fortuitous. Streitwieser adopted the p*K* of 18.5 found for 9-phenylfluorene (9-Ph-FH) in aqueous sulfolane (by the H_- technique) as an arbitrary reference standard. There is no reason to believe, however, that 9-Ph-FH has a p*K* of 18.5 in CHA. In fact, judging from the relative dielectric constants of CHA ($\epsilon \simeq 6$), sulfolane ($\epsilon^{30°} = 44$), water ($\epsilon^{20°} = 80$), and DMSO ($\epsilon^{20°} = 49$), the p*K* of 9-Ph-FH in CHA, if it could be measured free of ion pairing, would be 15 to 20 p*K* units higher than in sulfolane-water or DMSO.[34] On the other hand, the greater basicity of CHA than sulfolane-water or DMSO would tend to cause greater dissociation.[42]

Acetophenone has been assigned a p*K* of 19 on the McEwen scale (indene as a reference indicator and benzene or ether as a solvent with methanol as a "reference standard"). A p*K* of 19.1 has been assigned in diglyme by relating acetophenone to 2-nitrodiphenylamine indicator[5] (water as a "reference standard"). A p*K* of 19.2 has been estimated in water from kinetic acidities.[33] The closeness of these values is a remarkable coincidence. For reasons just given we can expect acetophenone in benzene to be dissociated to a lesser extent than in water or DMSO by many powers of ten. No significance should therefore be attached to either the apparent "agreement" of the McEwen and Bell p*K*'s, or the fact that the p*K* on the McEwen scale is about 4.5 p*K* units lower than our "absolute" p*K* in DMSO (24.7). The apparent acidity in diglyme would no doubt be different from that in benzene if the measurements were made against the same reference base. It is of interest to note that the apparent acidity of acetophenone on the McEwen scale is *greater* than that of fluorene by 6 p*K* units, whereas in DMSO acetophenone is found to be *less* acidic than fluorene by over 3 p*K* units. It would appear that in benzene (or ether[4a]) the equilibrium,

$$M^+In^- + PhCOCH_3 \rightleftarrows M^+[PhCOCH_2]^- + HIn$$

is shifted to the right by the greater stability of the enolate salt aggregate, $M^+[PhCOCH_2]^-$, as compared to the indicator salt aggregate, M^+In^-.

As has been pointed out several times previously,[9b,10d] there is remarkably little difference in the apparent relative p*K*'s of a series of hydrocarbon indicators (Δp*K*'s) as determined in benzene, CHA, or DMSO (Table IV), despite the marked differences in the nature of the solvents. This is at first sight surprising since in the solvents of low dielectric constant, benzene and CHA, salts exist as ion aggregates. (In CHA there is spectroscopic evidence for ion pairing.[41]) The position of the equilibrium,

$$M^+B^- + H\text{-}A \rightleftarrows M^+A^- + H\text{-}B$$

from which the apparent p*K* is obtained, is determined to an appreciable extent in such instances by the nature of the ion pairs, M^+B^- and M^+A^-, and their state of aggregation. In other words, we can expect these measurements to follow the general rule that "*in a solvent where ions are associated* *the apparent relative acidities of two acids will depend upon the base used for comparison*".[43] The explanation for the small difference in Δp*K*'s in the solvents of low dielectric constant and DMSO lies in the similarity in structure of the hydrocarbons used. The measurements in CHA were made by equilibrating pairs of hydrocarbons of similar structure. Evidently, under these circumstances, the degree of ion association for M^+B^- and M^+A^- does not differ greatly, and the positions of equilibria in CHA give a reasonably good measure of the relative acidities of HA and HB, as judged by the measurements in DMSO where ion association is not a problem. The situation changes dramatically, however, when two acids, HA and HB, differing appreciably in structure are compared. Now the ion aggregates, M^+A^- and M^+B^-, will differ appreciably in stability, and the apparent p*K* will change markedly for solvents of low dielectric constant with a change in solvent. For example, whereas in ether phenylacetylene has an apparent acidity close to that of the hydrocarbon indicator 9-phenylfluorene,[4] in CHA its acidity is close to that of fluorene.[44] This apparent 5 p*K* unit greater acidity of phenylacetylene in ether than in CHA has been attributed to tighter ion pairing in ether than in CHA.[44] The p*K* of phenylacetylene in DMSO, where ion association should not be a factor,[45] is 28.8 (Table II). The p*K* of phenylacetylene in DMSO is about 6 units higher than its apparent p*K* in CHA and about 11 units higher than its apparent p*K* in ether.[1c]

In view of the common practice of presenting tables of "p*K*'s" of carbon acids or of p*K*'s of carbon acids "relative to water" in textbooks,[46] it needs to be emphasized that the p*K*'s in benzene (McEwen scale), or in CHA, or those in the composite MSAD scale of Cram[47] *have no absolute meaning, and that the relative values given may be highly dependent on the reference base and the solvent.*[43]

General Conclusion. It is apparent from the above discussion that DMSO is a solvent wherein equilibrium acidities of weak acids, free of problems of ion association, can be measured over a range of about 30 powers of ten. The acidity studies in DMSO therefore complement those that have been made in water, and extend the range upward by 20 p*K* units. We believe that DMSO is destined to achieve an importance as a solvent for quantitative work in organic chemistry comparable to that of water in inorganic chemistry.

Experimental Section

Nuclear magnetic resonance (NMR) spectra were obtained on a Varian T-60 spectrometer in deuteriochloroform. Melting points are reported uncorrected and were determined using either a Fischer-Johns melting point apparatus or a Thomas Hoover Unimelt capillary melting point apparatus. Vapor-phase chromatography (VPC) analyses were performed using a Varian 5750 Research Chromatograph. Preparative VPC was done on an Aerograph Autoprep A-700.

Manipulations. Because of the sensitivity of carbanions to oxygen and water extreme care was taken to work under an inert atmosphere of dry, purified nitrogen. Apparatus and nonvolatile samples were degassed repeatedly by evacuating to less than 50 μ and purging with dry nitrogen (see nitrogen below). Liquids were transferred by reaching through the bore of a three-way stopcock with the needle of a degassed, gas-tight syringe or a short length of small diameter Teflon tubing. A stream of nitrogen through the side opening of the stopcock protected the liquid from air. When Teflon tubing was used, a positive pressure of nitrogen on the reservoir was used to pump the liquid out through the tubing.

Nitrogen. Prepurified nitrogen (Matheson Gas Products) was further purified by passing over molecular sieves (Linde) and Ridox oxygen scavenger (Fisher Scientific Co.).

Dimethyl Sulfoxide. DMSO, 3 pints (Mallinckrodt Analytical Reagent grade, 0.2% water), was dried for several days over activated Linde 4A molecular sieves. The dried DMSO was transferred with a positive pressure of nitrogen, through Teflon tubing to a magnetically stirred 2-l. flask equipped with a 25-cm Vigreux column connected to a Friedrich type condenser with receiver, all of which has been degassed as previously described. After charging with DMSO, the system was again evacuated until the DMSO no longer bubbled. Several crystals of triphenylmethane (ca. 10 mg) and several grams of commercial sodium amide were added to the distillation pot. The red color of triphenylmethide and the odor of ammonia were immediately observed. If the red color was not visible or did not persist more sodium amide was added. The distillation system was immediately evacuated (cautiously) and the evolving ammonia was collected in a liquid nitrogen trap. After the evolution of ammonia ceased, the DMSO was distilled at 35-40°C under a manifold pressure of 0.5 to 0.1 mm. A forerun of 150 ml was discarded before the main fraction was collected in a degassed 1-l. flask. The temperature of the water bath used to heat the pot was kept below 50°C. Water circulated from a constant temperature bath was used to maintain both the condenser and receiver at just over 18°C (DMSO freezes at 18°C). The receiver, when filled with 1 l. of clear colorless distillate, was capped with a three-way stopcock in a ₸ inner joint. The capped flask was again evacuated until the DMSO stopped bubbling and was purged with nitrogen. The DMSO was stored in this receiver and removed as needed by syringe as described above.

Table IV. Equilibrium Acidities for Hydrocarbon Indicators in Benzene, Cyclohexylamine (CHA), and DMSO Relative to Fluorene

Hydrocarbon	Δp*K* $(C_6H_6)^a$	$(CHA)^b$	$(DMSO)^c$
9-Phenylfluorene	−4	−4.2	−5.0
4,5-Methylenephenanthrene		−0.1	−0.5
9-Methylfluorene		0.0	−0.6
Fluorene	(0.0)	(0.0)	(0.0)
Benzo[*b*]fluorene		0.5	0.5
1,3,3-Triphenylpropene		3.9	3.0
9-Phenylxanthene	4	5.8	5.3
Diphenylyldiphenylmethane	6	7.5	6.5
Triphenylmethane	8	8.8	7.7
Diphenylmethane	10	9.4	9.6

[a] Based on fluorene, p*K* = 25; not statistically corrected (ref 4). [b] Based on fluorene, p*K* = 22.7; statistically corrected (data from A. Streitwieser, Jr., E. Ciuffarin, and J. H. Hammons, *J. Am. Chem. Soc.*, 89, 63 (1967)). [c] Based on fluorene, p*K* = 22.6; statistically corrected.

Potassium Dimsyl.[48] Under a flow of nitrogen 2-5 ml of commercial potassium hydride dispersed in mineral oil (Ventron Corp., 25-35% KH) was syringed into a degassed, 100-ml reservoir containing a glass-coated stirring bar. The reservoir was sealed with a 6-mm bore stopcock, above which was a side-arm stopcock for nitrogen flush. The mineral oil was removed by 3-5 successive washings with ca. 10 ml of dry pentane. The hydride-oil-pentane mixture was stirred vigorously and the hydride was allowed to settle with each wash. After most of the final wash of pentane had been syringed out the remainder was evaporated under vacuum. About 50 ml of dry distilled DMSO (above) was added to the hydride through a Teflon tube under a positive pressure of nitrogen. To control frothing the reservoir was gently swirled or shaken by hand. Only a mild evolution of heat was observed. The hydrogen formed was completely removed under vacuum and the reservoir was purged with nitrogen as usual. The potassium dimsyl solutions prepared in this way were clear and almost colorless (pale yellow or pale green). To stabilize the solution, triphenylmethane (<1 mg) dissolved in a few drops of dry DMSO was added. The resulting pink solution was protected from light by covering the reservoir with aluminum foil. The solutions prepared were 0.1-0.5 *M* in potassium dimsyl and gave linear Beer's law plots for the indicator triphenylmethane to ca. 70% titration (see p*K* measurement below).

Indicators. To be considered as an indicator a compound must meet the following requirements: (1) it must obey Beer's law on treatment with potassium dimsyl in DMSO, (2) its anion must ab-

Table V. Indicators for p*K* Measurements in DMSO

Indicator	Abbrev	p*K*	Mp, °C	Lit. mp, °C
Triphenylmethane[a]	TH	30.6	114–115[b]	115[49]
Diphenylyldiphenylmethane	DDH	29.4	112[b,d]	112–113[50]
9-Phenylxanthene	9-Ph-XH	27.9	145[b]	145[51]
9-(3-Chlorophenyl)xanthene	9-(3-Cl-Ph)-XH	26.6	111–112[e]	
1,3,3-Triphenylpropene	TPH	25.6	95–96[e]	95–97[52]
9-*tert*-Butylfluorene	9-*t*-Bu-FH	24.3_5	101.5–102[f]	101.5[53]
Fluorene[a]	FH	22.6	114–115[c]	116[54]
4-Chloro-2-nitroaniline[a]	CNAH	18.9	93–94[b]	92–93[55]
9-Phenylfluorene	9-Ph-FH	17.9	146[b]	145[56]
9-Phenylthiofluorene	9-PhS-FH	15.4	48–49[b]	48–49[57]
9-Phenylsulfonylfluorene	$9-PhSO_2-FH$	11.5_5	181.5–182.5[b]	182–183[57]
9-Carbomethoxyfluorene	$9-CO_2Me-FH$	10.3_5	65–66[f]	64–65[53]
9-Cyanofluorene	9-CN-FH	8.3	150.5–151.5[g]	151–152[58]

[a] Commercial sample from Aldrich Chemical Co. [b] Purified by recrystallization from 95% ethanol to a constant mp. [c] Purified by sublimation under reduced pressure followed by recrystallization from 95% ethanol to a constant melting point. [d] Granular crystals formed by slow evaporation of the solvent; cooling of more concentrated hot solutions produced needles, mp 102° (see below). [e] Purified by column chromatography (see below) followed by recrystallization from 95% ethanol to a constant mp. [f] Purified by recrystallization from methanol to a constant mp. [g] Purified by recrystallization from 95% ethanol under N_2 to a constant mp.

sorb in a region of the visible spectrum where other species in the experiment are transparent, (3) its anion must be stable for at least 20 min in the presence of $DMSO\text{-}K^+DMSYL^-$, (4) its anion must be stable in the presence of excess indicator, and (5) the indicator-indicator anion solution must give a stable acid-base equilibration with the acid being measured. In addition, in order to obtain an accurate equilibrium measurement, the p*K* of the indicator must be within ca. 2 units of the p*K* of the acid being measured. Any acid meeting these conditions can be used as an indicator. Acids of unknown p*K* having visibly absorbing anions and meeting these conditions were used as their own indicators by measuring against acids of known p*K* having colorless anions.

The compounds presently being used as indicators are listed in Table V.

All of the indicators listed in Table V have been found to be reasonably stable when protected from light, air, and moisture. If stored for extended periods of time, however, they should be recrystallized just prior to use.

4-Diphenylyldiphenylmethane (DDH). DDH was prepared by the reduction of 4-diphenylyldiphenylcarbinol (DDOH). DDOH was prepared by adding 200 ml of 0.5 *M* ethereal solution of biphenylmagnesium bromide (Matheson Coleman and Bell) to 36.4 g (0.2 mol) of dry benzophenone under nitrogen. After standing for 24 hr at room temperature the mixture was quenched with cold aqueous NH_4Cl. Separation, drying (Na_2SO_4), and evaporation of organic layer left the carbinol as a yellow oil which solidified upon standing. The crude solid was triturated with cold methanol and the solids were collected. Chromatography on silica gel with hexane as eluent furnished pure DDOH but was unnecessary for the preparation of DDH. DDH was prepared by vigorously stirring 2 g of DDOH (pure or crude) with 30 ml of refluxing 98% formic acid and 0.2 g of sodium formate until the red color initially formed had disappeared. Dilution with water precipitated the crude DDH which was collected by filtration and recrystallized from 95% ethanol.

Two crystalline forms could be produced depending upon the conditions of crystallization. Slow cooling of hot, concentrated ethanolic DDH solutions produced white needles, mp 102°. Evaporation of ethanolic solutions at room temperature gave colorless granules, mp 112°. The two forms could be interconverted by crystallization under the appropriate conditions: lit.[50] mp 112–113°.

9-Phenylxanthene (PXH). PXH was prepared by reduction of 9-hydroxy-9-phenylxanthene. This alcohol was prepared by the method of Ullman and Engi[51] from phenylmagnesium bromide and xanthone. The alcohol, 5 g, was quantitatively hydrogenolized by treatment with 0.2 g of 5% Pd/C in 250 ml of ethanol under 50 psi of hydrogen. Recrystallization from 95% ethanol gave pure 9-phenylxanthene as white needles: mp 145° (lit.[50] mp 145°).

9-(3-Chlorophenyl)xanthene (9-(3-Cl-Ph)-XH). 9-(3-Cl-Ph)-XH was prepared by the same general scheme employed for 9-phenylxanthene. 3-Chlorophenylmagnesium chloride was prepared by normal Grignard procedures under nitrogen from 9.72 g (0.4 mol) of magnesium turnings and 29.4 g (0.2 mol) of *m*-dichlorobenzene in 100 ml of dry THF. A small crystal of iodine and warming of the reaction mixture were required to initiate the reaction. The mixture was refluxed an additional 2.5 hr after addition of the halide solution was complete. The Grignard reagent was transfered by syringe to the addition funnel on a dried nitrogen filled flask containing 75 ml of dry THF and 19.6 g (0.1 mol) of freshly sublimed xanthone. The Grignard solution was added rapidly dropwise to the ketone. The suspension formed was diluted with an additional 50 ml of dry THF and stirred at room temperature for 7 hr. It was then quenched with aqueous ammonium chloride and extracted with ether. The ethereal phase was washed, dried ($MgSO_4$), and condensed to yield 36 g of crude brown solid. The crude solid was partially purified by chromatography on silica gel eluting first with carbon tetrachloride then with benzene. The second component eluted, R_f 0.42 silica gel-benzene, was 16.9 g of off-white solid whose spectra fit the expected 9-(3-chlorophenyl)-9-hydroxyxanthene: ir (Nujol) 3400; NMR ($CDCl_3$) δ 2.63 (1 *H*, s), 6.9–7.6 (12 *H*, m). The alcohol, still showing minor amounts of two impurities by TLC, was used without further purification.

The 16.9 g of alcohol was reduced by refluxing in 175 ml of freshly distilled 98% formic acid containing ca. 0.5 g of sodium formate until the initially formed red color had disappeared. The 9-(3-chlorophenyl)xanthene was precipitated by cooling the acid solution in an ice bath, and collected by filtration. After drying under vacuum for several days 15.1 g of yellow solid remained. The solid was purified by chromatography on silica gel with hexane–0 to 3% dichloromethane eluent. The 12.6 g of white solid was recrystallized from 95% ethanol to yield 10.5 g of needle shaped crystals: mp 111–112°; NMR ($CDCl_3$) δ 5.16 (1 *H*, s), 6.9–7.2 (12 *H*, m).

Anal. Calcd for $C_{19}H_{13}ClO$: C, 77.95; H, 4.48. Found: C, 77.90; H, 4.28.

1,3,3-Triphenylpropene (TPH). 1,3,3-Triphenylpropan-1-one was prepared by the method of Shildneck.[59] The ketone was reduced quantitatively to 1,3,3-triphenylpropan-1-ol by treatment overnight with excess $NaBH_4$ in ethanol. The alcohol was then dehydrated to 1,3,3-triphenylpropene by dissolving 10.9 g of crude alcohol in 50 ml of acetic anhydride, and 150 ml of acetic acid containing 20 drops of H_2SO_4. The mixture was warmed for 3 hr, refluxed 0.5 hr, then diluted with 500 ml of water and extracted with ether. The ethereal phase was washed, dried ($MgSO_4$), and concentrated to yield 9.7 g of white solid. The solid was purified by column chromatography on silica gel with hexane eluent, followed by recrystallization from 95% ethanol. White needle shaped crystals were obtained: mp 95.5–96.5° (lit.[52] mp 95–97°).

9-*tert*-Butylfluorene (9-*t*-Bu-FH). 9-*tert*-Butylfluorene was prepared by the method of Anet.[53] Repeated crystallization from methanol gave white needles: mp 101.5–102.5° (lit.[53] mp 101.5°).

9-Phenylfluorene (9-Ph-FH). 9-Phenylfluorene was prepared by the method of Ullman and Wursternberger.[56] It was recrystallized from 95% ethanol: mp 146° (lit.[56] mp 145°).

9-Phenylthiofluorene (9-PhS-FH). 9-Phenylthiofluorene was prepared by the method of Bavin.[57] Repeated recrystallization from 95% ethanol gave colorless plates: mp 48–49° (lit.[57] mp 48–49°).

9-Phenylsulfonylfluorene ($9-PhSO_2-FH$). 9-Phenylthiofluorene was oxidized by stirring overnight at room temperature with 2.2 equiv of *m*-chloroperoxybenzoic acid in dichloromethane. The organic mixture was then washed with sodium bisulfite, sodium bicarbonate, and brine, dried ($MgSO_4$), and concentrated. The crude solid was purified by recrystallizing from 95% ethanol to give colorless prisms: mp 181.5–182.5° (lit.[57] mp 182–183°).

9-Carbomethoxyfluorene (9-CO_2Me-FH). 9-Carbomethoxyfluorene was prepared by two methods.

(a) 9-Fluorenecarboxylic acid was prepared by the method of Burtner and Cusic,[60] and converted to its methyl ester by the method of Anet and Bavin.[53] The product was purified by chromatography on silica gel with CCl_4 as eluent, followed by two crystallizations from methanol: mp 65–66° (lit.[53] mp 64–65°).

(b) Sodium hydride, 2.2 g of 50% oil dispersion (45 mmol), was washed three times with pentane under nitrogen in a round-bottom flask. Reagent DMSO, 25 ml, was added. To this stirred mixture in a cold-water bath 5 g (30 mmol) of fluorene was cautiously added in portions. After stirring for 10 min at room temperature 12 ml (140 mmol) of dimethyl carbonate was added slowly (1 hr). The deep red solution was then quenched in cold, dilute HCl and extracted with ether. The crude orange product was recrystallized from methanol to yield 4 g (59%) of orange crystals: mp 64.9–65.2°. The color was removed by short-path distillation and the sample was further purified as in (a).

9-Cyanofluorene (9-CN-FH). 9-Formylfluorene was prepared as by method (b) above except that ethyl formate was substituted for dimethyl carbonate. Vigorous foaming was observed upon addition of the ethyl formate. The crude aldehyde was converted to the nitrile by the method of Wislicenus and Russ.[58] Repeated recrystallization from 95% ethanol under nitrogen gave long white needles: mp 150.5–151.5° (lit.[58] mp 151–152°).

Acids. Nitromethane and Nitroethane. Samples of these compounds were donated by Commercial Solvents Corp. and were 99.99 and 99.92% pure by VPC, respectively.

Benzoic Acids. All of the benzoic acids used were commercially available (Aldrich Chemical Co.) and were recrystallized from water or ethanol–water. The melting points determined in sealed capillary tubes were: benzoic acid 121.5–122° (lit.[61] mp 121.4°); 4-chlorobenzoic acid 238.5–240° (lit.[62] mp 236–237°); 4-nitrobenzoic acid 236–237° (lit.[63] mp 238°); 3,5-dinitrobenzoic acid 203.5–205.5° (lit.[64] mp 204°); salicylic acid 156–158° (lit.[65] mp 159°).

Acetone, 3-Pentanone, Isobutyrophenone, Malononitrile, Phenylacetylene, and Diphenylmethane. Commercial samples of these compounds were distilled through a short Vigreux column, and analyzed for purity by VPC.

Acetonitrile. A sample (J. T. Baker) was distilled from P_2O_5 and stored over molecular sieves. It was found to be greater than 99.9% pure by VPC analysis.

Acetophenone and Propiophenone. Commercial samples (Aldrich Chemical Co.) were purified by preparative VPC on a 10 ft, 10% Carbowax 20M on Chromosorb W-AW-dmcs column at 185–190 and 200°, respectively. The collected samples were then evaporatively distilled at 105° (30 mm) and 60° (0.3 mm), respectively.

Dibenzyl Sulfone and Phenyl Methyl Sulfone. Samples on hand were recrystallized from ethanol and/or hexane to give nice white crystalline solids: mp 86.5–87.5 and 150–151°, respectively (lit.[66] mp 88 and 151°, respectively).

Dimethyl Sulfone. A sample (Crown Zellerbach) was recrystallized from 95% ethanol to give white needles: mp 108–109° (lit.[67] mp 109°).

Benzyl Methyl Sulfoxide. Benzyl methyl sulfoxide was prepared by the method of Bordwell and Pitt.[68] Recrystallization from ethanol–water or hexane gave white needles: mp 54° (lit.[69] mp 54°).

Benzo[*b*]fluorene. A commercial sample (K&K Laboratories Inc.) was purified first by column chromatography on silica gel with benzene as eluent. The lime green compound obtained was then twice sublimed very slowly at 115° (0.2 mm). A pearly white solid was obtained: mp 208–209° (lit.[52] mp 208.5–209.5°).

9-Methylfluorene. 9-Methylfluorene was prepared by the method of Badger.[70] Short-path distillation followed by repeated recrystallization from methanol gave white needles: mp 45–46° (lit.[70] mp 45–46°).

9-Benzoylfluorene. Commercial *n*-butyllithium (0.028 mol) was added to a solution of fluorene (4.15 g, 0.025 mol) in 50 ml of dry THF under a nitrogen atmosphere. The resulting solution of 9-fluorenyllithium was transferred by gas tight syringe to a flask containing 10 g of dry, degassed ethyl benzoate. The mixture was stirred for 30 min, then diluted with benzene and aqueous $NaHCO_3$. Isolation, drying (Na_2SO_4), and evaporation of the benzene layer left a mixture of ethyl benzoate and 9-benzoylfluorene. Removal of the ester by evaporation in vacuo left the 9-benzoylfluorene as a yellow oily solid. Three recrystallizations from methanol furnished pure 9-benzoylfluorene as pale yellow needles: mp 135.5–136.5° (lit.[71] mp 135°).

2-Bromofluorene and 4,5-Methylenephenanthrene. Commercial samples (Aldrich Chemical Co.) were recrystallized from 95% ethanol to give white crystalline compounds: mp 110–111 and 114.5–115.5°, respectively (lit. mp 110–111.5[72] and 114–115°,[73] respectively).

4-Nitroaniline. A commercial sample (Aldrich Chemical Co.) was recrystallized from H_2O to give pale yellow needles: mp 147–148° (lit.[74] mp 148°).

Indicator and Acid Reservoirs. Reservoirs for solid samples consisted of two parts. The lower half was a flat-bottomed chamber of 10–25-ml capacity having a ₸ inner joint on top. The upper half was a ₸ outer joint sealed with a three-way stopcock. Reservoirs for liquid samples were one-piece 10–25-ml chambers sealed with a three-way stopcock.

p*K* Cells. Determinations of p*K* were made in standard 1-cm Pyrex spectrophotometric cuvettes closed on top with a three-way stopcock.

Syringes. Hamilton gas tight syringes fitted with 10–12 in needles were used.

Weights. All weights were recorded to ±0.0001 g using a Mettler H10 balance.

Spectrophotometer. Absorbance was measured with a Cary 15 Spectrophotometer.

Calculations. Calculation of p*K* was done on a Wang 700 calculator using a program written by Dr. J. E. Bartmess.

p*K* Measurement. Solutions of the solid acids and indicators were prepared in the reservoirs described above by weighing ca. 100 mg of compound into the tared, dried lower portion. The reservoir was then assembled and degassed in the usual manner. The reservoir with contents was then weighed and the desired amount of DMSO was added by syringe (usually 10–25 ml). The exact amount of DMSO was determined gravimetrically. Solutions of liquid samples were prepared by first assembling, degassing, and taring the liquid reservoirs (above). The liquid sample was then placed in a vial sealed with a rubber stopper having a three-way stopcock. The vial with the sample inside was degassed by several rapid vacuum–nitrogen cycles. A small amount ca. 100 mg of the degassed liquid was transferred by syringe to the tared, nitrogen purged reservoir. The reservoir with contents was then weighed and DMSO was added as for solid samples.

The p*K* measurement was begun by degassing and taring the spectrophotometric cell (above). The exact amounts of all solution added to the cell were determined gravimetrically. The cell was first charged with ca. 2.5 ml of DMSO and weighed. A small amount, 0.02–0.1 g, of the stock potassium dimsyl solution was then added and the cell again weighed. A wavelength was then chosen such that when an amount of indicator in excess of the amount of potassium dimsyl present was added the absorbance would be ca. 1.5 units. The cell was then placed in the spectrophotometer and the absorbance adjusted to zero. The appropriate indicator solution was then added in small aliquots such that several points (at least three) could be obtained with less total indicator added than potassium dimsyl present and the weight and absorbance for each point recorded. Since the indicator was always at least several powers of ten more acidic than potassium dimsyl it could be assumed to be quantitatively deprotonated, and plotting the absorbance versus indicator concentration produced Beer's law plots, the slope of which gave the extinction coefficient for the indicator anion at the chosen wavelength. The correlation coefficient for the Beer's law plot was generally between 0.9999 and 0.999999. An excess of indicator solution was then added (1.5- to 5-fold), and after several minutes to equilibrate the absorbance was recorded. From the absorbance with excess indicator present, the known concentration of the indicator, and the experimentally determined extinction coefficient, the total amount of indicator and indicator anion present in the cell could be determined. Several aliquots of the acid to be measured were then added and the weights and absorbances recorded. From the change in the absorbance the equilibrium constant between indicator and acid could be calculated for each aliquot of acid added. From the equilibrium constant and the known p*K* of the indicator or acid the p*K* of the other was calculated for each aliquot of acid. For the several values generated within a run the pK generally varied by less than 0.05 units and often less than 0.01 unit. The reproducibility between runs, often with new solutions, and different indicators by different experimenters was generally better than 0.1 unit.

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