The Acidities of Weak Acids. Part II.[1] Some Acetophenones

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The acidities of a series of *para*-substituted acetophenones have been measured at 298 K using solutions of tetramethylammonium hydroxide (0.011 M) in water containing varying amounts of dimethyl sulphoxide. The pK_a values correlate well with the Hammett σ constants and also with the previously determined, hydroxide-catalysed detritiation rate constants although there are signs of curvature in both pK_a–σ and pK_a–lg$k^{\mathrm{T}}_{\mathrm{OH^-}}$ relationships.

ALTHOUGH the acidities of β-diketones have been the subject of extensive study [2,3] considerably less attention has been paid to the much weaker ketones. This is so despite the fact that as long ago as 1932 Conant and Wheland [4] chose acetophenone as their reference compound, ascribing to it a pK_a of 20. At about the same time McEwen,[5] using methanol (pK_a 16) as a standard, obtained a value of 19 in ether. Since then many qualitative observations concerning ease of metallation have been reported but only very recently have more quantitative values of acetophenone acidities become available. Thus Zook and his co-workers [6] reported a pK_a of 19·1 for acetophenone itself in polyether solvents using 4-nitrodiphenylamine (pK_a 15·9) as standard. This can be compared with a value of 22·5, relative to fluorene (pK_a 20·5) in dimethyl sulphoxide as solvent.[7]

In addition to pK_a determinations the large accelerations in the rates of ionisation of weak acids in highly basic media [8] have made possible the extension of the Brönsted relationship to much weaker acids and this in turn has enabled estimates of the acidities of some of the more fundamentally important organic compounds, *e.g.* toluene, to be made. Rate–equilibria correlations for a series of fluorenes and some polyarylmethanes have already been reported.[9–12]

Although the process of ionisation in the acetophenones is accompanied by spectral changes in the absorption spectra the extinction coefficients for the anions are very low. The customary methods of acidity determination [13] for acids of this strength, such as the competitive and acidity function approach, are not therefore applicable. This is so for many types of carbon acids and we have therefore developed a new method [1,14] well suited to these circumstances, and which is employed in the present study.

EXPERIMENTAL

Materials.—The acetophenones were obtained commercially, solids being purified by recrystallisation from ethanol–water and liquids by distillation under reduced pressure. In the case of *p*-chloro-, *p*-methyl-, and acetophenone itself further purification was effected by preparative g.l.c. using a Varian Autoprep 705 containing a 10 ft column made up of 10% Bentone 34–10% silicone on 72—85 mesh Celite and operating at 160—180°.

The 'standard' carbon acids used in this work were

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methyldeoxybenzoin and 9-t-butylfluorene. The preparation of the former has been described [15] as well as that of the tritium-labelled form.[16] 9-t-Butylfluorene was prepared as in the literature [17] and tritium incorporated into the C-9 position by an hydroxide-catalysed exchange procedure using tritiated water.[16]

Reagent grade dimethyl sulphoxide was purified by distillation under reduced pressure in the presence of nitrogen and stored over 4A molecular sieves. G.l.c. analysis showed $<0{\cdot}1$ wt. % water.

Stock tetramethylammonium hydroxide solutions were made up at frequent intervals by addition of the solid pentahydrate to freshly distilled deionised water. The highly basic media comprising dimethyl sulphoxide, water, and tetramethylammonium hydroxide were made up by weight, the hydroxide ion concentration being 0·0110M.

Acidity Determination.—The method used to determine the acidities of the acetophenones is the same as that employed for the diphenylamine and aniline-type indicators and has been described in detail.[1] It is based on following the rates of detritiation of a 'standard' carbon acid in a series of different H_- solutions and then repeating the procedure in the presence of a known concentration of an acid whose pK_a needs to be calculated. In the case of acetophenone itself the $[R_2^-]:[R_2H]$ ratio was varied widely (0·1—5) in order to see whether the variation of $\lg\{[R_2^-]/[R_2H]\}$ with H_- was linear with a slope of unity. To a good approximation this was found to be so, the slope being $0{\cdot}95 \pm 0{\cdot}05$. The behaviour of acetophenone in this respect is therefore very similar to the anilines and diphenylamines used to set up the H_- scale of Dolman and Stewart.[18] The uncertainty in any of the pK_a values ($\pm 0{\cdot}1$—$0{\cdot}2$) is slightly higher than was the case for the previously studied anilines and diphenylamines.[1]

RESULTS AND DISCUSSION

The value of $21{\cdot}5_5$ for the pK_a of acetophenone lies between those reported in the early work [4,5] and the recently determined value of 22·5 in dimethyl sulphoxide.[7] Whether it represents anything more than the fact that in a $DMSO–H_2O–OH^-(0{\cdot}011M)$ medium of H_- $21{\cdot}5_5$ acetophenone is 50% ionised will only become clear if the ideals of the acidity function concept [19] are known to be obeyed by the nitrogen indicators used to set up the H_- scale and if the acetophenones respond to basicity changes in a similar manner to those indicators. In the case of acetophenone itself we have found that this second requirement holds and for the first also there seems to be ground for optimism. Thus both primary and secondary amines describe the same H_- scale [18] and this is not very different from that in which a series of fluorene-type indicators were employed.[20] Removal of the uncertainty [13,21] concerning the acidity of 9-phenylfluorene, one of the most frequently used of anchor acids, would help in this respect. The recent work of Arnett and his co-workers [22] showing that the heats of deprotonation in dimethyl sulphoxide correlate well with the pK_a values referred to the aqueous state also strongly supports the validity of the acidity function approach.

Acidities and detritiation rate constants for some acetophenones at 298 K

Substituent	pK_a in $DMSO–H_2O$ mixtures	$10^4 k^T_{OH^-}$ ($l\ mol^{-1}\ s^{-1}$) in H_2O [30]
(1) *p*-Me_2N	$22{\cdot}60 \pm 0{\cdot}3$	6·95 [a]
(2) *p*-Bu^t	$22{\cdot}0_5 \pm 0{\cdot}1_5$	(32) [b]
(3) *p*-MeO	$22{\cdot}00 \pm 0{\cdot}1$	24·7
(4) *p*-Me	$21{\cdot}8_5 \pm 0{\cdot}1_5$	35·5
(5) H	$21{\cdot}5_5 \pm 0{\cdot}2$	54·0
(6) *p*-Cl	$20{\cdot}4_5 \pm 0{\cdot}1$	90·0
(7) *p*-Br	$20{\cdot}40 \pm 0{\cdot}1$	91·0
(8) *p*-CN	$18{\cdot}40 \pm 0{\cdot}2$	237

[a] Previously unpublished. [b] Interpolated from the data of ref. 30 assuming a σ value of $-0{\cdot}20$.

The small (1 p*K*) difference between our value for the pK_a of acetophenone and that reported by Bordwell [7] suggests, in contrast to nitromethane [23] ($\Delta pK = pK_{(DMSO)} - pK_{H_2O}$ *ca.* 5), that specific solvation and hydrogen bonding effects are not important factors. The differential effect of dimethyl sulphoxide on the strengths of the benzoic acids has been shown to be three times greater than the differential action of water [24] and by a factor of 1·4 for a series of phenols.[25] For several types of carbon acids the value may still be closer to unity, a necessary prerequisite for the successful operation of the acidity function concept.

The effect of substituents on the acidities of the acetophenones is illustrated in Figure 1, the pK_a–σ relationship taking the form of a curve. In principle there is no reason why one should observe a linear relationship as it seems most unlikely that the value of ρ should remain exactly constant for a series of solutions varying in composition from 60 to >90 mol % dimethyl sulphoxide. The variation of ρ with $DMSO–H_2O$ composition has not been studied for an equilibrium process involving carbon acids. However in a kinetic investigation [26] on the isomerisation of allylbenzenes ρ varied from 3·38 to 3·54 as the DMSO content of the medium was increased from 74·5 to 90·6 mol %.

Curvature similar to that observed in the present work has been found for some substituted 9-phenylfluorenes [27] and was ascribed to the difficulty which the 9-phenyl groups have in attaining coplanarity with the fluorene nucleus in the carbanion as a result of steric interactions with the C-1 and C-8 hydrogen atoms. On closer scrutiny the results for a series of 2-substituted fluorenes [28]

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(pK_a values cover a similar range to the acetophenones studied here, varying from 17·96 for the nitro- to 22·36 for the methoxy-compound) can also be interpreted in terms of a curved plot.

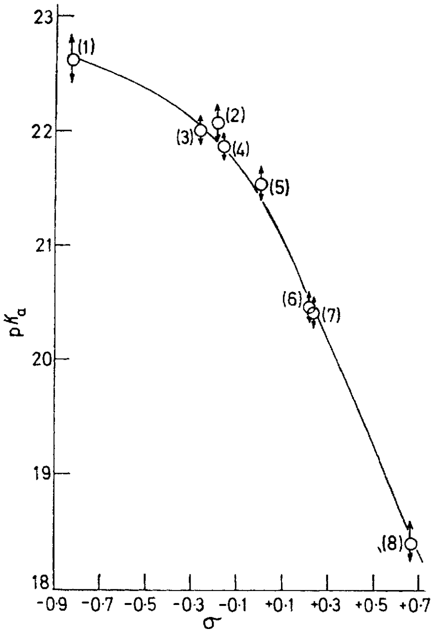

FIGURE 1 Plot of acetophenone pK_a values against Hammett substituent constants σ; see Table for key

If one neglects the points for the *p*-dimethylamino- and *p*-methoxy-substituents, the remainder form a linear relationship with a slope (ρ) of 4·6, similar to that reported for the diphenylamine indicators[18] (4·1) and somewhat lower than the value of *ca.* 7 witnessed for the 2-substituted fluorenes.[28] It can also be compared with a value of 5 for substitution in the diphenylmethane series[29] and one of at least 7 and probably closer to 10 for the toluenes.[18,29]

The rates of ionisation of the substituted acetophenones have previously been studied in aqueous hydroxide solutions.[30] The reaction constant had a value of unity so that despite the differences in the solvent systems used for the equilibrium and kinetic studies it is clear that the transition state involves a carbanion in which the charge is only partially developed.

Although a previous report[6] mentions that for some dialkyl and alkyl aryl ketones the equilibrium acidities did not parallel the rates of ionisation we find that the acetophenone pK_a values correlate well with the hydroxide-catalysed rates of detritiation (Figure 2) although there are again distinct signs of curvature in the plot. Several studies[8,31] of the rates of ionisation of carbon acids in highly basic media have shown that the weaker the acid the more receptive is the rate to increasing solution basicity. Consequently the relative values of the detritiation rate constants will be a function of medium composition and it seems preferable to refer these to purely aqueous conditions and, if possible, extrapolate the pK_a values to the same standard state.

If the points for the *p*-dimethylamino- and *p*-methoxy-substituents are neglected once again then the remainder form a fairly good linear relationship with a slope of 0·20 ± 0·02. This is a very low value but not much different to those obtained for other weak carbon acids; *e.g.* for a number of di- and tri-arylmethanes,[12] considerably weaker than the acetophenones studied here, the value is 0·31 and for some fluorene-type hydrocarbons having pK_a values in the range 15—24 the value is 0·37.[11]

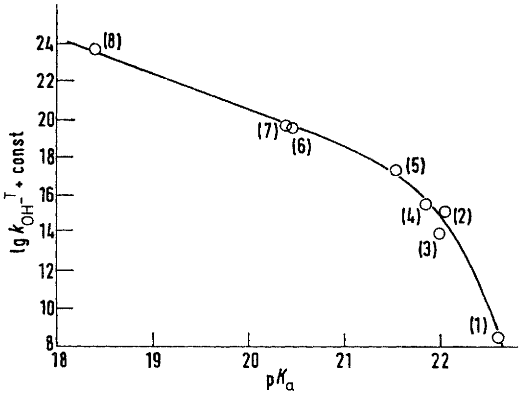

FIGURE 2 Brönsted plot of acetophenone pK_a values against the logarithm of the hydroxide-catalysed detritiation rate constants ($k_{OH^-}^T$); see Table for key

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