# Thermodynamic and Kinetic Acidities in Dimethyl Sulphoxide. Part 3.[1] Alcohols and Phenols

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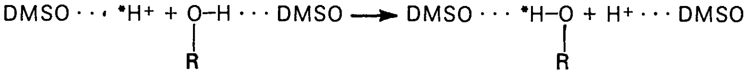
Proton transfer from and to the oxygen atom of a series of four alcohols (ROH) in anhydrous dimethyl sulphoxide was followed by dynamic n.m.r. spectroscopy under conditions of both acid (trifluoromethanesulphonic) and base (n-butylamine) catalysed exchange. A series of four phenols was also investigated in acidic conditions. Two kinetic processes were observed, one catalysed by the hydrogen ion DMSO $\cdots$ H$^+$ and the other by the conjugate alkoxide base. The results at 25 °C for alcohols are summarized by the equation, rate of hydroxylic proton exchange $= k_A[\text{DMSO}\cdots\text{H}^+] + k_2[\text{RO}^-]$, with $k_A$ 3.13 × $10^6$ and $k_2$ 1.36 × $10^{10}$ l mol$^{-1}$ s$^{-1}$ at 25 °C for EtOH. These rate constants, and the high p$K$ values (21.95 for EtOH) account for the slow exchange on the n.m.r. time scale over a wide range of pH (5.5—11.5), and thus for the successful use of DMSO as a solvent to observe O–H fission. This property arises not from the low rate constants in DMSO with respect to those in water or alcohols, but from the relatively smaller amounts of alkyloxonium and alkoxide ions. The rate constants $k_A$ and $k_2$ follow the order of decreasing acidities, and obey Hammett or Ingold–Taft relationships, $\rho^* = -0.227$ and $-0.289$ for alcohols; $\rho$ $-0.852$ for phenols. The $k_A$ values of phenols are consistent only with the concerted mechanism (i) which is also



$$\text{DMSO}\cdots{}^*\text{H}^+ + \underset{\displaystyle\text{R}}{\underset{|}{\text{O}}}\text{–H}\cdots\text{DMSO} \longrightarrow \text{DMSO}\cdots{}^*\text{H–}\underset{\displaystyle\text{R}}{\underset{|}{\text{O}}} + \text{H}^+\cdots\text{DMSO} \qquad \text{(i)}$$

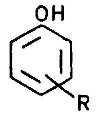
suggested for alcohols.

PROTON transfer reactions involving O–H bonds are known to be fast on the n.m.r. time scale, thus preventing O–H fission from being observed when alcohols or phenols contain traces of acids or bases. Strongly hydrogen bonding aprotic solvents [2,3] are used to slow down intermolecular exchanges and thus to observe such fissions. Dimethyl sulphoxide (DMSO) proved to be the most appropriate solvent in this connection.[4] Standard procedures use DMSO solutions to measure hydroxylic coupling constants of alcohols and polyols as an aid to conformational analysis of, for instance, cyclohexanols [5,6] and sugars.[7]

However, no information is available about proton transfer rates in such solutions. To our knowledge, kinetic measurements are at present restricted to methanol and ethanol using the alcohols themselves, or their aqueous mixtures, as solvents.[8-11] We have already pointed out [1] that the rates obtained in such media may not reflect the intrinsic reactivity of the acidic substrates on account of strong solvation of anions, the existence of various alcoholic hydrogen bonded polymers and the so-called abnormal proton conductivity phenomena. Moreover, the diversity of solvents prevents any reliable comparison between various substrates. All these facts prompted us to choose DMSO as a solvent not only to study proton transfers involving O–H bonds, but also N–H,[12] S–H,[1a] P$^+$–H,[13] and C≡CH [1b] bonds.

ROH

(1) R = Et
(2) R = PhCH$_2$
(3) R = HC≡CCH$_2$
(4) R = CCl$_3$CH$_2$



(5) R = 4-Bu$^t$
(6) R = H
(7) R = 3-Cl
(8) R = 4-NO$_2$

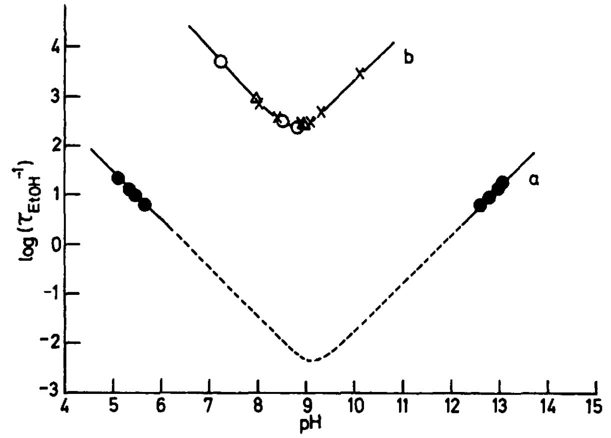


FIGURE 1 a, Plot of log($\tau^{-1}_{\text{EtOH}}$) in DMSO; solid lines correspond to the proton transfer rates being studied on the n.m.r. time scale and b, log($\tau^{-1}_{\text{MeOH}}$) in methanol from ref. 9

The present work is concerned with the transfer of a proton from and to a series of four alcohols, ethanol (1), benzyl (2), and propargyl alcohol (3), 2,2,2-trichloroethanol (4), and four phenols, 4-t-butyl- (5), unsubstituted (6), 3-chloro- (7) and 4-nitro-phenol (8).

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[1] (a) Part 1, J-J. Delpuech and D. Nicole, *J.C.S. Perkin II*, 1974, 1025; (b) Part 2, J. Chrisment and J.-J. Delpuech, *J.C.S. Perkin II*, 1977, 407.

[2] J. R. Holmes, D. Kivelson, and W. C. Drinkard, *J. Chem. Phys.*, 1962, **37**, 150.

[3] P. Laszlo, *Progr. NMR Spectroscopy*, 1967, **3**, 333.

[4] O. L. Chapman and R. W. King, *J. Amer. Chem. Soc.*, 1966, **86**, 2040.

[5] C. P. Rader, *J. Amer. Chem. Soc.*, 1966, **88**, 1713.

[6] J. J. Uebel and H. W. Goodwin, *J. Org. Chem.*, 1966, **31**, 2040.

[7] A. S. Perlin, *Canad. J. Chem.*, 1966, **44**, 539.

[8] Z. Luz, D. Gill, and S. Meiboom, *J. Chem. Phys.*, 1961, **34**, 375.

[9] E. Grunwald, C. F. Jumper, and S. Meiboom, *J. Amer. Chem. Soc.*, 1962, **84**, 4664.

[10] W. G. Paterson, *Canad. J. Chem.*, 1963, **41**, 714.

[11] W. G. Paterson and H. Spedding, *Canad. J. Chem.*, 1963, **41**, 243.

[12] B. Bianchin and J-J. Delpuech, *Bull. Soc. chim. France*, 1973, 34.

[13] J-J. Delpuech and D. Nicole, unpublished results.

Two different kinds of proton transfer are found in DMSO; they are demonstrated in a logarithmic plot of the reciprocal of the mean lifetime $\tau_{OH}$ of the hydroxylic protons against the pH of the solution (Figure 1a). Two straight lines with slopes +1 and −1 are obtained, of which only two small segments ranging over 0.5—0.8 pH unit are available on the n.m.r. time scale. These two pH ranges are so far from each other that, as with thiols,[1a] they may be studied independently. Kinetic laws supporting various reaction schemes are now described using variable pH and alcohol concentration.

## EXPERIMENTAL

Procedures used to purify DMSO and to prepare solutions have been described previously.[1] Alcohols (Fluka) were distilled in a Nester–Faust 60 cm spinning band column. Phenols (Fluka; puriss) were used without further purification. Basic solutions of alcohols and phenols were stable for several days. Acidic solutions of alcohols containing $10^{-5}$M-trifluoromethanesulphonic acid were stable for *ca.* 12 h, and solutions of phenols for several days. Spectrophotometric measurements were used to determine the pH of the DMSO solutions. Acidic solutions made use of $10^{-5}$M-2,4-dinitrophenol (molar absorptivity $\varepsilon$ $1.55 \times 10^5$ at 432 nm). The pH of basic solutions derived from a p*K* scale previously described,[1b] built from a series of overlapping indicators and anchored to the p*K* of 2,4-dinitroaniline (14.8), as determined by Ritchie and Uschold [14] by means of a reversible glass electrode standardized at pH 3. The p*K* of alcohols were taken as the pH of their solution in DMSO half-neutralized by methylsulphinylmethanide (dimsyl) anion.

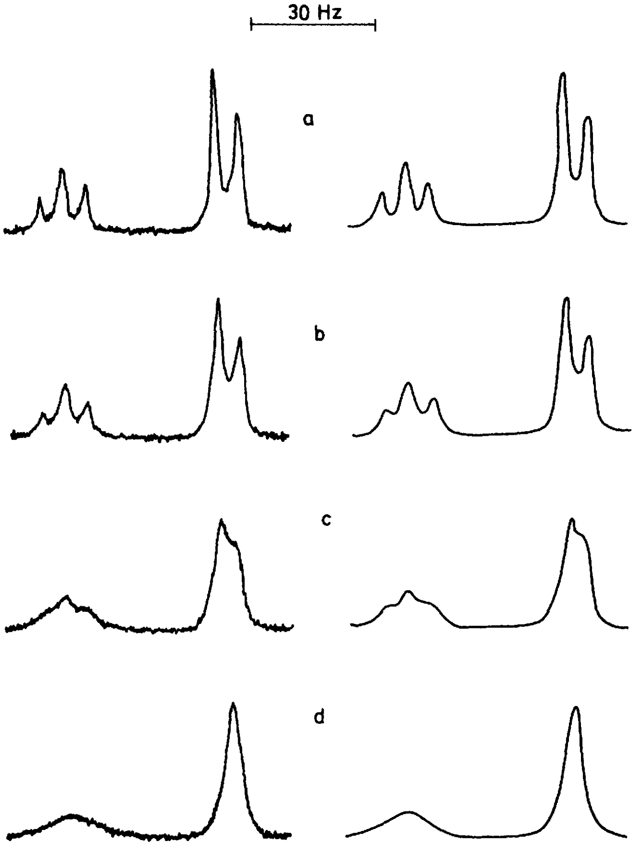

FIGURE 2 N.m.r. spectra of a 1.15M solution of benzyl alcohol in acidic DMSO. Experimental (right) and theoretical (left) curves, with $\tau_{OH}^{-1}$ = 0, 7.0; b, 10.5; c, 13.5; and d, 23.0 $s^{-1}$

N.m.r. spectra were taken with a JEOL C60-HL spectrometer at 60 MHz and 25 °C. Singlets and triplets were obtained for the hydroxylic protons of phenols and primary alcohols respectively. The triplets were not perfectly symmetrical and a second-order analysis ($AB_2$ type) was necessary to account for the observed lineshapes of both the hydroxy and methylene protons. Coalescence was brought about by addition of small quantities ($10^{-3}$—$10^{-5}$M) of either a strong acid (trifluoromethanesulphonic acid) or a strong base (diethyl- or n-butyl-amine). The mean lifetime $\tau_{OH}$ of the phenolic protons between two successive deprotonations was computed according to the formula $1/\tau_{OH} = \pi\Delta\nu$, where $\Delta\nu$ is the linewidth increase of the singlet due to chemical exchange. In the case of alcohols, the experimental curves (Figure 2) were analysed using the program EXCH14.[15] Theoretical curves were obtained from a Texas Instruments 980 A mini-computer and a recorder.

## RESULTS

*Measurements in Acidic Solutions.*—A thorough study was first carried out for benzyl alcohol. Coalescence was obtained for pH 5.2—6.3. Two methods were used in turn. In the first, the pH was measured by means of an indicator, 2,4-dinitrophenol (IH). The acidity of this indicator is high enough to provide the very small amount of protons ($10^{-5}$—$10^{-6}$M) necessary for coalescence. Table 1 shows the $\tau_{OH}^{-1}$ values using the four pH values and two alcohol concentrations.

TABLE 1

$[H^+]$ and $\tau_{OH}^{-1}$ values in acidic DMSO for various concentrations of benzylic alcohol using 2,4-dinitrophenol (IH) both as an acid and an indicator

| $[PhCH_2OH]$/M | $[IH]:[I^-]$ | $10^6[DMSO\cdots H^+]$/M | $\tau_{OH}^{-1}/s^{-1}$ |
|---|---|---|---|
| 0.386 | 0.087 | 0.549 | 2.0 |
| | 0.282 | 1.780 | 5.0 |
| | 0.562 | 3.545 | 11.0 |
| | 1.041 | 6.568 | 20.0 |
| 1.150 | 0.087 | 0.549 | 2.0 |
| | 0.428 | 2.700 | 5.0 |
| | 0.666 | 4.202 | 11.0 |
| | 1.000 | 6.310 | 19.0 |

One straight line is obtained, within experimental error (±5%), when plotting $\tau_{OH}^{-1}$ *versus* $[H^+]$ computed from the experimental $[IH]:[I^-]$ ratio and the p*K* of the indicator ($pK_{IH}$ 5.2 ± 0.15),[16] with slope $k_A = 2.96 \times 10^6$ l $mol^{-1}$ $s^{-1}$ at 25 °C. This graph provides evidence that protons are ***not*** transferred to the alcohol ROH from its conjugate oxonium ion $ROH_2^+$ according to equation (1). Moreover,

$$ROH + ROH_2^+ \longrightarrow ROH_2^+ + ROH \qquad (1)$$

the indicator itself may not be considered as the reactant since $\tau_{OH}^{-1}$ actually depends on the molar ratio $[IH]:[I^-]$

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[14] C. D. Ritchie and R. E. Uschold, *J. Amer. Chem. Soc.*, 1967, **89**, 1721; 1968, **90**, 2821.

[15] J-J. Delpuech and G. Serratrice, *Org. Magnetic Resonance*, 1972, **4**, 667.

[16] B. W. Clare, D. Cook, E. C. F. Ko, Y. C. Mac, and A. J. Parker, *J. Amer. Chem. Soc.*, 1966, **88**, 1910.

and not on the total concentration [I$^-$], or, alternatively [IH]. This point is made clear from the unchanged $\tau_{OH}^{-1}$ values for several DMSO solutions containing various indicator concentrations and the appropriate quantities of strong acid or base to bring them to the same pH. We are then left with two possibilities for the protonation of benzyl alcohol, involving either the hydronium $H_3O^+$ or the dimethylsulphoxonium DMSO $\cdots$ H$^+$ ion. These two species are in the equilibrium DMSO + $H_3O^+ \rightleftharpoons$ DMSO $\cdots$ H$^+$ + $H_2O$ where $K_{H_3O^+} = 2.2$ [17] or 2.13.[18]

For solutions containing *ca.* 0.03M water as an accompanying impurity, the molar ratio [DMSO $\cdots$ H$^+$] : [$H_3O^+$] is 73. In spite of this unfavourable ratio, protonation by hydronium ion might be predominant on account of the stronger basicity of DMSO with respect to that of water. This possibility was discarded by adding 0.1M-water and observing no variation of the n.m.r. spectra and of the pH. In the first instance, proton exchanges may be thought to arise from protonation of the alcohol by solvated protons [reaction (2)] followed by the reverse reaction (fast).

$$\text{ROH} + \text{DMSO} \cdots \text{H}^+ \xrightarrow{k_1} \text{ROH}_2^+ + \text{DMSO} \quad (2)$$

According to this view, chemical exchange would be twice as fast as the n.m.r. site exchange, $k_1 = 2k_A = 5.92 \times 10^6$ l mol$^{-1}$ s$^{-1}$ at 25 °C.

A more simple method used known quantities ($10^{-5}$—$10^{-6}$M) of trifluoromethanesulphonic acid, a strong acid completely dissociated in DMSO.[19] In these conditions, the amount of alkoxonium ion [$ROH_2^+$] is negligible with respect to that of solvated protons [DMSO $\cdots$ H$^+$], and $k_1$ may be computed as $k_1 = 2k_A = 2\tau_{OH}^{-1}/[CF_3SO_3H]$. The least squares rate constant is $4.32 \times 10^6$ l mol$^{-1}$ s$^{-1}$ at 25 °C, a value 25% lower than the previous one. The discrepancy may be accounted for by the uncertainty range ($\pm 0.15$) quoted [16] for the p$K$ of the indicator. The second $k_1$ value is therefore preferred to the first, with an uncertainty $< \pm 3\%$. The other alcohols were studied on similar lines.

There is no evidence for O–H fission in the spectrum of phenols. Proton transfers to phenols may however be studied because the OH singlet is much broadened even for very low concentrations ($10^{-4}$—$10^{-3}$M) of added trifluoromethanesulphonic acid. Rates of proton exchange are derived using relationship (3) due to Meiboom [20] (in which $\tau$ is replaced by $p\tau_{OH}$) where $p$ is the fractional population

$$\pi\Delta\nu = \delta^2 p^2 \tau_{OH}/(1 + \delta^2 p^2 \tau_{OH}^2) \quad (3)$$

of the less populated site, $\delta$ the chemical shift (in radian s$^{-1}$) between exchanging sites, and $\Delta\nu$ the line-broadening (Hz) of the unique dominant line being observed. Line-broadenings were found to be proportional to the concentration of acid $C_{H^+}$. This point may be accounted for by assuming the smaller site to be the solvated proton DMSO $\cdots$ H$^+$ and by considering either a slow transfer, in which case equation (4) applies, or a fast transfer with the rate equation (5). The

$$\pi\Delta\nu = \tau_{OH}^{-1} = k_A C_{H^+} \quad (4)$$

$$\pi\Delta\nu = \delta^2 p^2 \tau_{OH} = \delta^2 C_{H^+}/k_A[\text{phenol}]^2 \quad (5)$$

latter assumption must be rejected because $\Delta\nu$ was found to be independent of the phenol concentration. However equation (3) predicts a maximum, $(\Delta\nu)_{max.} = p\delta(\text{Hz}) \simeq 0.02$ Hz for 0.8M-phenol, with $p \simeq 10^{-4}$ and $\delta \simeq 240$ Hz, well below the experimentally observed (1—4 Hz). Additional experiments without phenol showed that the DMSO $\cdots$ H$^+$ line shifts from $\delta$ 13.75 to 8 when $C_{H^+}$ is decreased from 1.0 to 0.05M. This means that acidic protons are averaged on the n.m.r. time scale with those of the residual water at $\delta$ 3.3, thus increasing the $p$ and $\delta$ values to be introduced into equation (3): $p = (2[H_2O] + C_{H^+})/[\text{phenol}] \simeq 0.075$M, $\delta = 360$ Hz, and $(\Delta\nu)_{max.} \simeq 27$ Hz. When 0.8M-phenol was now added to such solutions, the O–H singlet at $\delta$ 9.36 was first broadened according to equation (4), when $C_{H^+} \simeq 10^{-4}$M (Figure 3), then vanished into the base line noise at coalescence ($C_{H^+} \simeq 10^{-3}$M), and appeared again as a sharp line, first upfield ($C_{H^+} \simeq 10^{-2}$M), and then downfield ($C_{H^+} \simeq 10^{-1}$M). The acidity range of interest for uncomplicated kinetic measurements thus corresponded to $C_{H^+}$ $10^{-4}$—$10^{-3}$M. Proton transfer to phenols must be traced to DMSO $\cdots$ H$^+$ only, as for alcohols, and not to $H_3O^+$, since the n.m.r. spectrum is not sensitive to massive additions of water (up

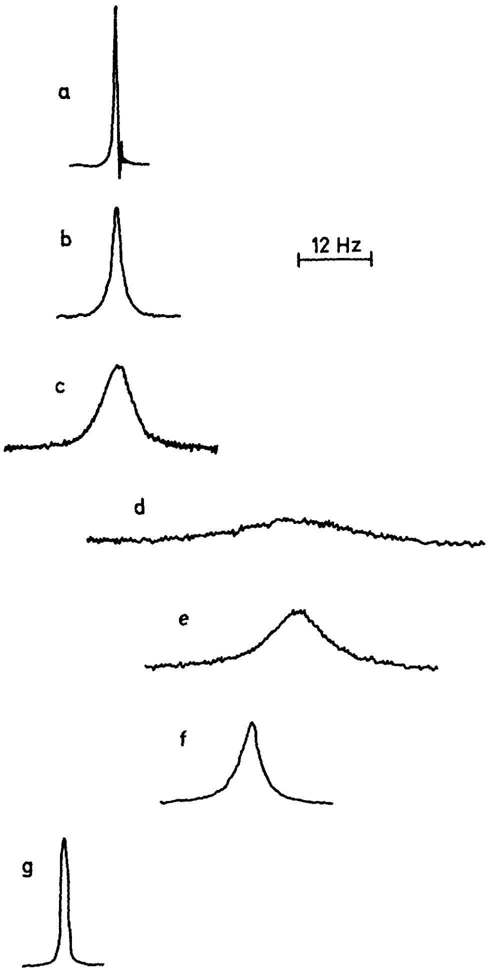

FIGURE 3 OH Linewidth of 0.8M-phenol in DMSO as a function of acidity: $C_{H^+}$ = a, 0; b, $4.3 \times 10^{-5}$; c, $1.1 \times 10^{-4}$; d, $10^{-3}$; e, $4 \times 10^{-3}$; f, $10^{-2}$; and g, $10^{-1}$

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[17] I. M. Kolthoff and T. B. Reddy, *Inorg. Chem.*, 1962, **1**, 189.

[18] R. L. Benoit and C. Buisson, *Inorg. Chim. Acta*, 1973, **7**, 256.

[19] R. L. Benoit and C. Buisson, *Electrochim. Acta*, 1973, **18**, 105.

[20] S. Meiboom, *J. Chem. Phys.*, 1961, **34**, 375.

to 0.2M). Results for the whole series of alcohols and phenols are reported in Tables 2 and 3.

TABLE 2

$[H^+]$/M and $\tau_{OH}^{-1}$ $s^{-1}$ values in acidic DMSO solutions of alcohols and phenols at 25 °C

| EtOH | | $PhCH_2OH$ | | $CH{\equiv}CCH_2OH$ | | $CCl_3CH_2OH$ | |
|---|---|---|---|---|---|---|---|
| $10^6[H^+]$ | $\tau_{OH}^{-1}$ | $10^6[H^+]$ | $\tau_{OH}^{-1}$ | $10^6[H^+]$ | $\tau_{OH}^{-1}$ | $10^6[H^+]$ | $\tau_{OH}^{-1}$ |
| 2.35 | 7.0 | 3.77 | 7.5 | 5.60 | 7.0 | 11.3 | 10.0 |
| 3.30 | 10.5 | 5.66 | 11.5 | 8.38 | 10.0 | 18.8 | 15.0 |
| 4.24 | 13.5 | 7.54 | 16.5 | 11.20 | 14.0 | 28.3 | 22.0 |
| 7.07 | 23.0 | 9.43 | 21.0 | 14.00 | 17.0 | 37.7 | 28.5 |
| $4\text{-}Bu^tC_6H_4OH$ | | PhOH | | $3\text{-}ClC_6H_4OH$ | | $4\text{-}NO_2C_6H_4OH$ | |
| 61 | 12.95 | 42.8 | 4.71 | 244 | 15.3 | 244 | 6.60 |
| 110 | 22.4 | 61.1 | 7.06 | 366 | 24.7 | 366 | 10.36 |
| 183 | 37.7 | 85.6 | 11.3 | 489 | 33.0 | 489 | 15.1 |
| 244 | 49.5 | 110 | 14.1 | 978 | 65.9 | 733 | 20.7 |

TABLE 3

p$K$ and rate constants $k_A$, $k_1$, $k_B$, and $k_2$ for alcohols and phenols in DMSO at 25 °C

| Substrate | p$K$ | $10^{-5}k_A$/ l $mol^{-1}$ $s^{-1}$ | $10^{-5}k_1$/ l $mol^{-1}$ $s^{-1}$ | $10^{12}k_A/s^{-1}$ | $10^{-9}k_2$/ l $mol^{-1}$ $s^{-1}$ |
|---|---|---|---|---|---|
| (1) | 21.95 | 31.3 | 62.6 | 1.52 | 13.6 |
| (2) | 21.30 | 21.6 | 43.2 | 4.24 | 8.47 |
| (3) | 19.85 | 12.2 | 24.4 | 8.47 | 0.60 |
| (4) | 18.60 | 7.75 | 15.5 | 510 | 2.03 |
| (5) | 16.43 | 2.04 | 4.08 | | |
| (6) | 16.0 | 1.26 | 2.52 | | |
| (7) | 14.7 | $0.67_2$ | $1.34_4$ | | |
| (8) | 11.0 | $0.28_8$ | $0.57_6$ | | |

*Measurements in Basic Solution.*—The n.m.r. method was restricted to alcohols since the phenolic singlet is not sensitive to the addition of base. This point suggests deprotonation involving the conjugate phenoxide or alkoxide ion according to equation (6) and not the dimsyl anion.

$$ROH + RO^- \xrightarrow{k_2} RO^- + ROH \qquad (6)$$

The p$K$ values of alcohols (1)—(4) were determined as the pH values at half neutralization, using, respectively, 4-nitroaniline, 2-nitrodiphenylamine, and 3-chlorodiphenylamine (twice) as indicators with p$K$ values all anchored to that of 2,4-dinitroaniline.[1b] The p$K$ values of phenols (5)—(7) were measured using 2,5-dichloro-4-nitroaniline (twice) and 2,4-dinitroaniline as indicators. The p$K$ of 4-nitrophenol was taken from Kolthoff.[21] These values may be compared with those from independent measurements in water p$K$ = 15.9(1), 15.05(2), 13.55(3), 12.24(4),[22] 10.25(5), 9.99(6), 9.02(7), and 7.15(8).[23] A constant difference, p$K$ (DMSO) − p$K$(water) = 6.12 ± 0.17 (excluding *p*-nitrophenol), was observed, very close to those obtained for acids of the same electrical type: toluene-α-thiol (6.0),[1a] nitromethane (5.7),[14] benzoic acid (5.8),[17,24] and acetic acid (6.7).[17]

The pH of solutions at coalescence range from 12.5 to 13.2 for ethanol, and from 10.3 to 11.1 for trichloroethanol. They were measured with two indicators, 6-bromo-2,4-dinitroaniline (p$K$ 13.4 from an overlap spectrophotometric comparison with 2,4-dinitroaniline) and 4-nitrophenol (p$K$ 11.0).[21] Small quantities ($10^{-3}$—$10^{-2}$M) of n-butylamine were used as a base to vary the pH. This base (B) does not contribute to the removal of hydroxylic protons. Such a reaction ($ROH + B \longrightarrow RO^- + HB^+$) would imply an independence of $\tau_{OH}^{-1}$ upon the alcohol concentration, in contrast with experiment. Moreover, using another base (diethylamine) leads to the same kinetic plots, as shown in Figure 4, yielding equal rate constants $k_B$ within ±2% (8.47 and 8.80 × $10^9$ l $mol^{-1}$ $s^{-1}$ at 25 °C).

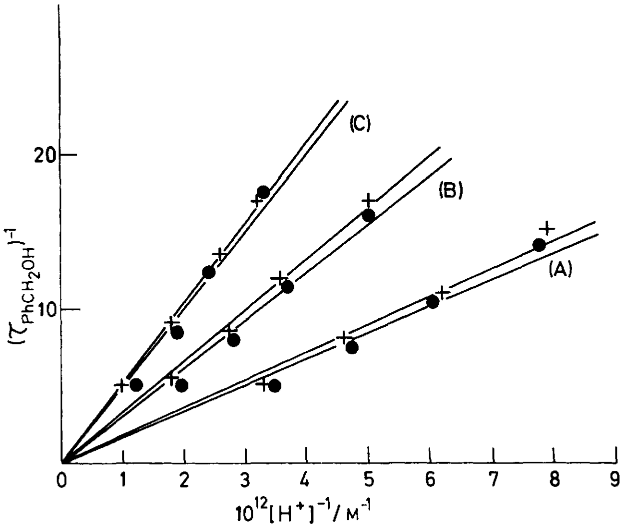

FIGURE 4 Plot of $(\tau_{PhCH_2OH})^{-1}$ *versus* $[H^+]^{-1}$ in basic DMSO, for $[PhCH_2OH]$ = 0.386 (A); 0.772 (B), and 1.15M (C), using either diethylamine (+) or n-butylamine (●) as base

Three sets of experiments using three different concentrations were performed with each alcohol. In each one, $\tau_{OH}^{-1}$ was measured at four pH, and plotted against $[H^+]^{-1}$, yielding a straight line of slope $p$ passing through the origin (Figure 4). These slopes $p$ are in turn proportional to the concentration of alcohol as shown in Figure 5. The least squares slopes of the straight lines of Figure 5 are reported in Table 3 as rate constants $k_B$. Rate constants $k_2$ of reaction

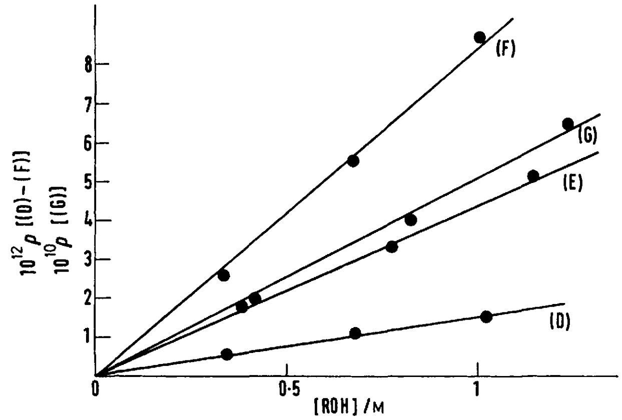

FIGURE 5 Plot of slopes $p$ of lines (A)—(C) (Figure 4) *versus* the concentration of ethanol (D), benzyl (E) and propargyl (F) alcohol, and 2,2,2-trichloroethanol (G)

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[21] I. M. Kolthoff, M. K. Chantooni, jun., and S. Bhowmik, *J. Amer. Chem. Soc.*, 1968, **90**, 23.

[22] P. Ballinger and F. A. Long, *J. Amer. Chem. Soc.*, 1960, **82**, 795.

[23] (*a*) G. Kortüm, W. Vogel, and K. Andrussow, ' Dissociation Constants of Organic Acids in Solution,' Butterworths, London, 1961; (*b*) R. W. Taft, in ' Proton-transfer Reactions,' eds. E. F. Caldin and V. Gold, Chapman and Hall, London, 1975, ch. 2.

[24] F. G. Brockman and M. Kilpatrick, *J. Amer. Chem. Soc.*, 1945, **56**, 1843.

(5) are obtained by dividing $k_B$ by the ionization constant $K_{ROH}$ of each alcohol.

## DISCUSSION

The complete kinetic law, including both equations (2) and (6) predicts a minimum $\tau_m^{-1}$ for the n.m.r. rate constant $\tau_{OH}^{-1}$ $\{\tau_m^{-1} = (2\ k_A k_B[\mathrm{ROH}])^{\frac{1}{2}}\}$ when $\mathrm{pH} = \mathrm{pH_m} = -\frac{1}{2}\log(k_B[\mathrm{ROH}]/k_A)$. Computed values for molar solutions of alcohols (1)—(4) are displayed in Table 4. If we compare our data for ethanol in DMSO with those of Grunwald [9] for methanol in pure methanol (Figure 1), $\mathrm{pH_m}$ values are very close in both media (9.15 and 8.80, respectively), but the rates $\tau_m^{-1}$ are larger in methanol by five orders of magnitude, $1.40 \times 10^2$ against $4.37 \times 10^{-3}$ s$^{-1}$. This dramatic fall accounts for the successful use of DMSO to observe OH fission by n.m.r. spectroscopy.

TABLE 4

$\sigma$ Values (Taft or Hammett), OH chemical shifts $\delta_{OH}$, minimum values $\tau_m^{-1}$ at 25 °C of the rate of proton exchange $\tau_{OH}^{-1}$ at pH = $\mathrm{pH_m}$, and values p$K$ of the conjugate acids of alcohols and phenols

| Substrate | $\sigma$ | $\delta_{OH}$ | $10^3\tau_m^{-1}$/s$^{-1}$ | $\mathrm{pH_m}$ | p$K$ of $\mathrm{ROH_2^+}$ In DMSO [a] | In $\mathrm{H_2O}$ [b] |
|---|---|---|---|---|---|---|
| (1) | 0 | 4.36 | 4.37 | 9.15 | −4.05 | −2.26 |
| (2) | 0.6 | 5.13 | 6.05 | 8.85 | −4.21 | −2.80 |
| (3) | 1.7 | 5.17 | 14.4 | 8.53 | −4.46 | −3.63 |
| (4) | 2.65 | 6.78 | 39.7 | 7.59 | −4.65 | −4.29 |
| (5) | −0.197 | 9.14 | | | −5.23 | −6.23 |
| (6) | 0 | 9.36 | | | −5.44 | −6.93 |
| (7) | 0.373 | 9.91 | | | −5.72 | −7.85 |
| (8) | 0.778 | 11.09 | | | −6.08 | −9.08 |

[a] From equation (8). [b] From equation (11).

Analysing the reasons for this fact, we notice that both acidic and basic overall rate constants are much smaller in DMSO ($k_A$ and $k_B = 3.13 \times 10^6$ l mol$^{-1}$ s$^{-1}$ and $1.52 \times 10^{-12}$ s$^{-1}$ against $8.79 \times 10^{10}$ l mol$^{-1}$ s$^{-1}$ and $2.25 \times 10^{-7}$ s$^{-1}$, respectively, at 25 °C). If we first examine basic solutions of alcohols, the first point deserving notice is the small influence of the solvent ($k_2 = 1.36 \times 10^{10}$ for EtOH in DMSO, against $1.85 \times 10^{10}$ for MeOH in methanol [9]). This result clearly demonstrates that it is not necessary to use hydrogen-bonded solvents to obtain fast proton transfers; successive fast proton switches along a Grotthuss chain are necessary in such solvents only because of strong solvation of the alkoxide anion hindering the approach of acid molecules. A second point is the large p$K$ decrease, *ca.* 6 (or 5) units on going from water (or methanol) to DMSO solutions, which accounts for the much longer lifetime of the hydroxy-protons in DMSO.

If we now examine the acidic rate constants of alcohols, the mechanism of proton transfer is not the same in DMSO as in methanol. In pure methanol,[9] proton transfer is mostly controlled by diffusion, and, in part, by the so-called mechanism of abnormal conductance of the hydrogen ion. A quite different situation prevails in DMSO solutions. This solvent is strongly hydrogen-bonded to alcohols,[3,25] thus preventing self-association of alcohol molecules. This point is made clear from the OH chemical shifts in DMSO (Table 4), which were found to be independent of alcohol concentration from 0.1 to 0.8M. Proton transfer may therefore be safely assumed to involve solvated monomeric alcohol molecules (and phenols as well). Overall rate constants $k_A$ are far from the diffusion controlled limit $k_D$, as it is observed in the case of methanol [9] for the transfer of one proton between two molecules of alcohol [equation (1)]. This transfer is not observed in DMSO, because reaction (2) predominates over (1), *i.e.*, $k_D[\mathrm{ROH_2^+}] \ll k_1[\mathrm{DMSO\cdots H^+}]$, or $[\mathrm{ROH_2^+}]:[\mathrm{DMSO\cdots H^+}] \ll 1.25 \times 10^{-3}$ for ethanol (taking $k_D = 5 \times 10^9$ l mol$^{-1}$ s$^{-1}$, computed for uncharged reactants of similar size [26] in DMSO of viscosity 0.019 8 poise).[27] The concentration ratio $[\mathrm{ROH_2^+}]:[\mathrm{DMSO\cdots H^+}]$ could be computed from the p$K$ of ethyloxonium ion in DMSO [p$K$($\mathrm{ROH_2^+}$)], if it were known. Conversely, the above inequality implies that this ratio is at most equal to $10^{-4}$, and that p$K$($\mathrm{ROH_2^+}$) < *ca.* −4 for molar solutions of ethanol. This inequality means in turn that the reverse reaction (7) is diffusion controlled, since

$$\mathrm{ROH_2^+ + DMSO \xrightarrow{k'_1} ROH + DMSO\cdots H^+} \quad (7)$$

$k'_1[\mathrm{DMSO}] > 10^4 k_1 \sim 6 \times 10^{10}$ s$^{-1}$. This result conversely suggests computing p$K$($\mathrm{ROH_2^+}$) from equation (8). This assumption leads to p$K$($\mathrm{EtOH_2^+}$) — 4.05 (in

$$K(\mathrm{ROH_2^+}) = k_D[\mathrm{DMSO}]/k_1 = 7.03 \times 10^{10}/k_1 \quad (8)$$

DMSO), as expected from our premises, and to a Brønsted relationship, where the $\alpha$-exponent is unity, for the computed p$K$ values of the other alkoxonium ions (Table 4).

If we turn now to structural effects, the rate constants $k_A$ or $k_1$ fall in the order predicted by simple polar inductive effects and the absence of steric hindrance, as shown by the close fit of the data to the $\rho^*$–$\sigma^*$ Ingold–Taft [28] relationship [$\log k_A = -0.227\ \sigma^* + 6.483$ (mean deviation $\delta\log k_A = 0.01$)]. With the above assumptions, this $\rho^*$ value applies to the p$K$ values of alkoxonium acids as well.

However, this interpretation is untenable when applied to phenols. Their conjugate acids are much more acidic than those of alcohols, as is clear from the few data presently available; *e.g.* the p$K$ values of ethyl- and phenyl-oxonium ions in water are −2.32 [29,30] and 6.74 [31] respectively, *i.e.*, a difference of −4.41. However the relevant rate constants $k_A$ differ only by about an

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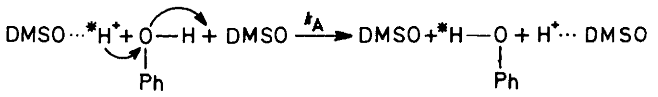
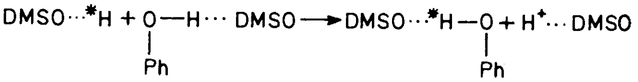
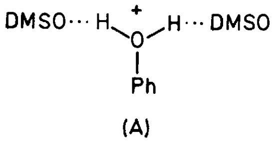
order of magnitude ($\Delta \log k_A$ — 1.40), instead of being nearly equal to $\Delta pK$ from the assumption of a Brønsted $\alpha$-exponent of unity. The argument is yet more convincing if this comparison is carried out within the series of phenols. The p$K$ values of phenyl- and *p*-nitrophenyl-oxonium ions are known in water, —6.74 [31] and —9.18 [32] respectively, from which we compute $\Delta pK$ — 2.44, $\Delta \log k_A$ — 0.640, and $\alpha = 0.262$ instead of 1. This inconsistency may alternatively be restated as follows. Rate constants $k_A$ obey a Hammett $\rho$–$\sigma$ relationship [$\log k_A = -0.852\sigma + 5.127$ (mean deviation $\delta \log k_A = 0.01$)], whose absolute $\rho$ value, $|\rho_{k_A}| = 0.852$, is much smaller than that from a similar relationship assumed for the p$K$ values of phenyloxonium ions, and roughly computed as $\rho_{PhOH_2^+} = -\Delta pK/(\sigma_{pNO_2C_6H_4OH} - \sigma_{PhOH}) = 3.08$. These two values would again lead to $\alpha = |\rho_{k_A}|/\rho_{PhOH_2^+} = 0.276$, instead of 1.

Moreover, the p$K_a$ values of the series of phenyloxonium ions in DMSO computed according to equation (8) seem highly unlikely when compared to experimentally measured values in water. Thus, the p$K$ difference for an acid in water and in DMSO has a large positive value contrasting with a small negative value observed for some diprotonated cations, such as diethylammonium ion.[21] A more convincing argument lies in the computed p$K$ difference between phenyl- and *p*-nitrophenyl-oxonium ions (—0.64) in contrast with the previously reported value in water (—2.44).


(9)


(10)

These inconsistencies prompt us to abandon, at least in the case of phenols, a mechanism where the conjugate acid $PhOH_2^+$ is an intermediate, and to envisage instead a concerted mechanism in which the two steps, protonation of phenol to its conjugate acid followed by a fast reverse deprotonation, occur simultaneously [reaction (9)]. A similar mechanism, involving the hydrated proton $H_3O^+$, had already been assumed by Grunwald and Puar [33] in aqueous solutions to account for proton transfer between phenol and water. The reaction is not actually termolecular since phenol is likely to be completely hydrogen-bonded to DMSO, so that reaction (9) should be rewritten as (10). This concerted mechanism is likely to overcome reaction (2); the measured rate constant $k_A$ is that from equation (10), and previously computed p$K(ROH_2^+)$ values are meaningless. In spite of a symmetrical transition state (A) increased basicity promotes faster proton transfer to phenols.


(A)

One may wonder which is the exact mechanism in the case of alcohols. Comparison with phenols may provide an answer. First, if we look at the various Hammett relationships, we notice that the $\rho$ values for the ionization of phenols ($\rho$ 2.113 in water,[34] or 3.094 in DMSO from our values, exluding *p*-nitrophenol) [28] are not widely different from the one previously computed for the ionization of phenyloxonium ions in water, ($\rho$ 3.08). We may therefore expect for the ionization of alkyloxonium acids a $\rho^*$ value close to the one observed for the ionization of alcohols, *i.e.* $\rho^*$ 1.27 in DMSO or 1.42 in water.[22] Unfortunately, the former value is unknown. However, if mechanism (2) is predominant, the relevant $\rho^*$ value has already been computed, $|\rho^*| = 0.227$, much smaller than 1.27. Another piece of evidence uses the Brønsted law. Such a relationship is expected for conjugate acids of phenols and alcohols, since a Hammett or Ingold–Taft correlation is observed for rate constants $k_A$ on the one hand, and is likely to hold for the ionization constants on the other. If phenols and alcohols obey the same mechanism, then the same Brønsted equation should hold for all of them. Using the three p$K$ values available, for ethyl,[29,30] phenyl,[31] and *p*-nitrophenyl [32] ions in water, the three corresponding points nicely fall on a straight line in a log $k_A$–p$K$ plot [equation (11)],

$$\log k_A = 0.299\,pK + 7.172 \qquad (11)$$
$$(\text{mean deviation } \delta \log k_A = 0.02)$$

again pointing to the existence of a unique concerted mechanism. Conversely, assuming the Brønsted equation (11) allows new p$K$ values of conjugate acids of the alcohols and phenols (1)—(8) in water to be computed (Table 4).

At last, we may carry out a brief comparison between transfers involving hydroxy- and mercapto-bonds. Both the acidic and basic rate constants of benzyl alcohol in

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DMSO are larger, as expected,[1a] than those of the analogous toluene-α-thiol, $k_A$ and $k_B = 2.16 \times 10^6$ and $8.47 \times 10^9$ l mol$^{-1}$ s$^{-1}$, against $2.35 \times 10^2$ and $2.62 \times 10^8$ l mol$^{-1}$ s$^{-1}$, at 25 °C, respectively. In both cases, the exchange involves the conjugate base of the substrate and the solvated proton in basic and acidic DMSO respectively; in the latter case, it is however impossible to decide between mechanisms (2) and (10) for the thiol.

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