Proton Transfers to and from Sulphur. Part I. Toluene-α-thiol in Dimethyl Sulphoxide

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Proton transfer from and to the sulphur atom of toluene-α-thiol in anhydrous dimethyl sulphoxide has been followed by n.m.r. spectroscopy under conditions of both acid (trifluoromethanesulphonic) and base (imidazole) catalysed exchange. The different mechanisms are discussed.

VERY little information is available about proton transfers to and from the sulphur atom of thiols. To our knowledge, only one publication[1] deals quantitatively with this problem applied to toluene-α-thiol. Two mechanisms (1) and (2) of transfer were found by adding either an acid or a base to the pure liquid thiol, in complete agreement with analogous conclusions from a detailed study of alcohols.[2,3] However, in the first

$$RSH + RSH_2^+ \xrightarrow{k_1} RSH_2^+ + RSH \qquad (1)$$

$$RSH + RS^- \xrightarrow{k_2} RS^- + RSH \qquad (2)$$

investigation[1] no pH measurement was reported, probably on account of the special nature of the medium (*i.e.* the pure thiol).

The present work is concerned with the transfer of a proton both from and to toluene-α-thiol using dimethyl sulphoxide (DMSO) as the solvent. In this medium no ion association occurs and data on the various p*K* values are readily available.

Two different kinds of proton transfer are found in DMSO by a logarithmic plot of the mean lifetime τ_{PhCH_2SH} of the acidic proton of $PhCH_2SH$ against the pH of the solution (Figure 1). Two straight lines with slopes ±1 are obtained, of which only two small segments ranging over 0·5—0·8 pH units may be examined

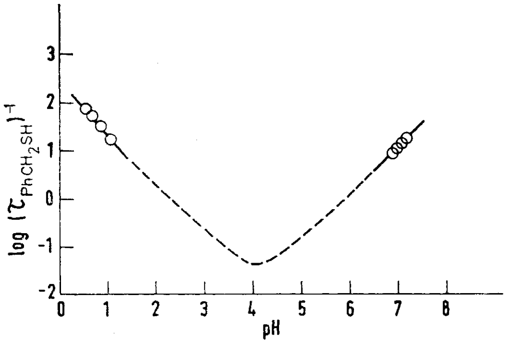

FIGURE 1 A plot of log $(\tau_{PhCH_2SH}^{-1})$ *versus* pH. The solid lines correspond to the proton transfer rates being studied on the n.m.r. time scale

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[1] M. Sheinblatt and Z. Luz, *J. Phys. Chem.*, 1962, **66**, 1535.

[2] Z. Luz, D. Gill, and S. Meiboom, *J. Chem. Phys.*, 1959, **30**, 1540.

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

on the n.m.r. time scale. These two pH ranges are so far from each other that they may be studied independently. In each case, we are concerned both with the pH of solutions and the pK of the thiol, and with proton transfer rates. Kinetic laws supporting various reaction schemes are established using variable pH and thiol concentration.

EXPERIMENTAL

Materials.—Dimethyl sulphoxide (Merck Uvasol) was left for 48 h on molecular sieves (Linde 3 Å), then distilled over calcium hydride under dry nitrogen at low pressure in an adiabatic fractionating column (1 m × 29 mm), with a reflux ratio of *ca.* 10, b.p. at 0·3 mmHg 27 °C. The water content of the purified solvent as found by Karl Fischer titration was $<5 \times 10^{-3}$M. Toluene-α-thiol, Bromocresol Green, imidazole, and trifluoromethanesulphonic acid were Fluka products, used without further purification. The nitroanilines were recrystallized from absolute ethanol. Methylsulphonylmethanide (dimsyl) anion (in DMSO) was prepared after Corey.[4]

Solutions.—Stock solutions of DMSO, containing the appropriate Hammett indicator and either trifluoromethanesulphonic acid or imidazole, were prepared in a glove box under purified argon. Stock solutions of toluene-α-thiol were freshly prepared before use. These solutions were mixed, and eventually diluted with pure DMSO, so as to obtain the desired concentrations. They were stable for *ca.* 48 h.

Spectrophotometric Measurements.—A Unicam SP 1800 spectrophotometer and a pair of 1 cm glass cells (Hellma 110-OS) with Teflon stoppers, were used for all measurements. The molar absorptivities of the yellow (ε^0 1·86 × 10^4 at 415 nm) and blue (ε^0 6·67 × 10^5 at 630 nm) forms of Bromocresol Green (1·7 × 10^{-5}M) were determined in solutions containing either CF_3SO_3H or dimsyl anion (10^{-3}M). The molar absorptivity (ε^0 1·5 × 10^3 at 400 nm) of the yellow form of *m*-nitroaniline was determined in pure DMSO. The ratio r of the two forms in an unknown solution was computed from its absorptivity ε or from the optical density D [$r = (\varepsilon^0 - \varepsilon)/\varepsilon = (D^0 - D)/D$]. If the p$K$ of the indicator (pK_I) is known, the value of the pH is then derived from pH = pK_I + log r.

N.m.r. Spectra.—N.m.r. spectra were taken with a Varian A-60 spectrometer at 60 MHz, or a JEOL PS-100 instrument at 100 MHz. The latter frequency was found to be necessary in order to study the methylene doublet of α-toluenethiol, which is partially obscured at 60 MHz by the ^{13}C satellites of DMSO. Theoretical curves (with and without exchange) were obtained from the IBM 370—165 computer [CNRS (CIRCE)] using program EXCH 14.[5]

RESULTS

Measurements in Acidic Solutions.—The DMSO solution was acidified [6] by adding CF_3SO_3H (AH) in concentrations up to 0·1M, so as to reach a pH close to unity for coalescence.

The pH scale. Using *m*-nitroaniline (Id_1H) as an indicator, we checked that the dissociation of AH is complete by plotting $-\log[AH]$ against $-\log([Id_1H_2^+]/[Id_1H])$. The plot is a straight line with a slope of unity (Figure 2) whose intercept yields p$K_{Id_1H_2^+}$ 0·87 at 25 °C, a value slightly different from that reported [7] (1·00).

Estimation of p$K_{PhCH_2SH_2^+}$. Adding the thiol does not change the experimental ratio: $[Id_1H_2^+]:[Id_1H]$. This fact demonstrates that toluene-α-thiol is an extremely weak base and $PhCH_2SH_2^+$ a strong acid whose pK cannot be measured on account of the levelling effect of basic DMSO. We have measured this pK in nitromethane using another Hammett indicator, 4-chloro-2-nitroaniline (Id_2H). The difference, $\Delta pK = pK_{Id_2H_2^+} - pK_{PhCH_2SH_2^+}$, is 2·62 in this solvent.

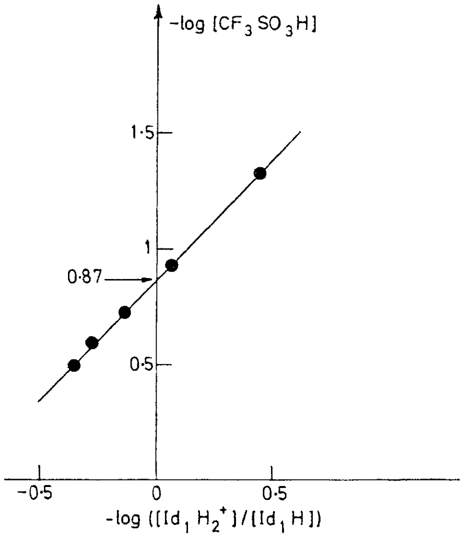

FIGURE 2 A logarithmic plot of the analytical concentration of CF_3SO_3H *versus* the ratio of the two forms of *m*-nitroaniline

Assuming ΔpK to be a constant, the unknown pK may be estimated if the pK of $Id_2H_2^+$ is itself known in DMSO. The latter is in turn estimated by the same method, on the basis of the known values [8, 9] of the difference $pK_{Id_2H_2^+} - pK_{Id_1H_2^+} = -3\cdot5$ in water the value of $pK_{Id_1H^+}$ being known (see above). The values $pK_{Id_2H_2^+} = -2\cdot63$ and $pK_{PhCH_2SH_2^+} = -5\cdot25$. This indirect value, although useful for discussion, is fortunately not needed to obtain rate constants.

Rate measurements. Rate measurements were based on the n.m.r. spectrum of the thiol [δ 2·70 (t, *J* 7·7 Hz)] and methylene [δ 3·71 (d, *J* 7·7 Hz)] protons of $PhCH_2SH$ (Figure 3). Dimethyl sulphoxide gives a strong signal at δ 2·50, overlapping with the triplet, and by a weak signal at δ *ca.* 13 (position depending on the acid concentration) for the solvated proton DMSO · · · H^+. This singlet also contains the small amount of the conjugate acid $PhCH_2SH_2^+$ ($<10^{-5}$M) and, eventually, of hydroxonium ion H_3O^+ (*ca.* 0·25% for DMSO containing 5 × 10^{-3}M-H_2O), rapidly exchanging with DMSO · · · H^+.

The doublet progressively broadens, then coalesces into a sharp line as a result of the chemical exchange of the SH

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

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protons, either with each other, or with DMSO · · · H^+. No distinction may be made between both types of exchange on the basis of the lineshape of the doublet, on account of the small [DMSO · · · H^+] : [RSH] ratio (*ca.* 0·1), and of a large chemical shift between the singlet and doublet, *i.e.* all exchanges are formally supposed to take place between like molecules of thiol. The doublet is actually asymmetric and the lineshape must be computed using a second order analysis and the density matrix formalism.[10,11] The method and the program EXCH 14 written for this purpose have been described previously.[5] A comparison of experimental and theoretical curves

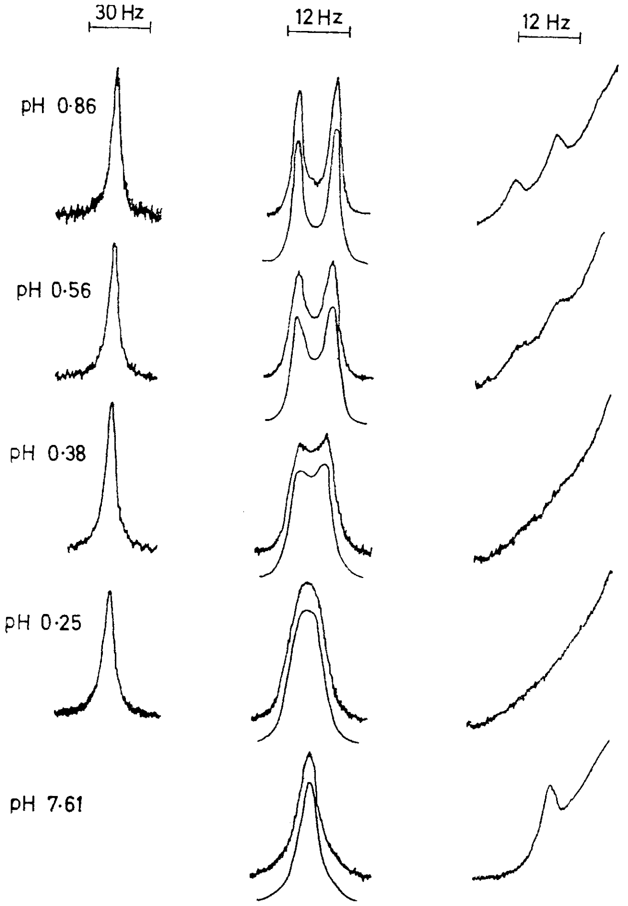


FIGURE 3 N.m.r. lineshapes as a function of the pH: singlet of DMSO · · · H^+ (left); doublet (middle), and triplet (obscured by the line of DMSO; right) of 0·34M-toluene-α-thiol at different pH values. Both experimental and theoretical curves are displayed for the doublet (above and below respectively). The intensity of the singlet actually increases from top to bottom as a consequence of a decreasing r.f. level

yields the mean lifetime τ_{PhCH_2SH} of a $PhCH_2SH$ molecule between two successive deprotonations. A pH range of 0·75 may be explored by this method with an accuracy of 1—5%.

Simultaneously, the triplet progressively broadens and shifts downfield, until it vanishes into the baseline noise; a similar phenomenon is observed for the singlet, but with an upfield shift. These changes probably reflect exchange between the thiol SH and solvated DMSO · · · H^+ protons [reaction (3)]. The triplet lineshape however is obscured by the neighbouring DMSO methyl resonance, and cannot be quantitatively exploited (Figure 3). The singlet broadens by the same quantity $\Delta\nu_S$ (from 0·4 to 6·3 Hz) at any pH (Figure 3), for a given concentration of thiol. It is possible to measure simultaneously τ_{PhCH_2SH} and $\tau_{H^+} = (\pi\Delta\nu_S)^{-1}$ for the smallest concentration of thiol, $[PhCH_2SH] = 0{\cdot}34$M. The ratio of these two values proves to be equal to the ratio $[CF_3SO_3H] : [PhCH_2SH]$ of the populations of the exchanging sites when the concentration of the acid is varied from 0·14 to 0·56M. This means that proton transfer should occur exclusively through reaction (3). An additional feature is that τ_{PhCH_2SH} is kept constant by addition of water to DMSO (up to 1·0M), while the ratios $\tau_{H^+} : \tau_{PhCH_2SH}$ and $([CF_3SO_3H] + 2[H_2O]) : [PhCH_2SH]$ remain equal. For the highest water concentration, the ratio $[DMSO \cdots H^+] : [H_3O^+] = K_{H_3O^+} : [H_2O]$ reaches a value of 2·2, if we adopt $K_{H_3O^+} = 2{\cdot}2$ in DMSO.[11] These facts seem to show that thiol protons exchange with H^+ at the same rate, whatever the solvating molecule (DMSO or H_2O), in sharp contrast with the large variations observed for alcohols.[2,12]

$$RSH + {}^*H^+ \cdots DMSO \xrightarrow{k_3} RSH^* + H \cdots DMSO \qquad (3)$$

Kinetic law. Three concentrations of toluene-α-thiol were used and, for each one, four concentrations of trifluoromethanesulphonic acid. The data of Table 1 effectively show $(\tau_{PhCH_2SH})^{-1}$ to be independent of the concentration of thiol. A plot of $(\tau_{PhCH_2SH})^{-1}$ against $[H^+]$ is linear (Figure 4) with a slope (k_3) of $1{\cdot}35 \times 10^2$ l mol^{-1} s^{-1} in accord with reaction (3) and equation (4) and not with reaction (1) and equation (5). A statistical factor of 1/2 is introduced since, in the envisaged protonation–deprotonation process, the second step is followed by a proton exchange with a probability of 1/2 only [reactions (6) and (7)]. These experiments therefore yield the rate constant

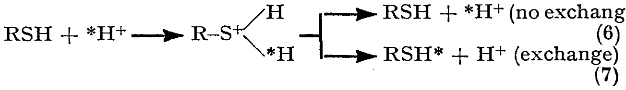
TABLE 1

$[H^+]$ and $(\tau_{PhCH_2SH})^{-1}$ values in acidic DMSO for various concentrations of toluene-α-thiol and trifluoromethanesulphonic acid

		$[CF_3SO_3H]$/M			
$[PhCH_2SH]$/M		0·0696	0·139	0·208	0·278
0·34	$[H^+]$/M	0·0745	0·135	0·195	0·254
	$(\tau_{PhCH_2SH})^{-1}$/s^{-1}	10	17	27	36
0·68	$[H^+]$/M	0·0826	0·148	0·199	0·254
	$(\tau_{PhCH_2SH})^{-1}$/s^{-1}	10	18	28	36
10·2	$[H^+]$/M	0·0843	0·145	0·216	0·266
	$(\tau_{PhCH_2SH})^{-1}$/s^{-1}	9	17	29	35

$$(\tau_{PhCH_2SH})^{-1} = k_3[H^+]/2 \qquad (4)$$

$$\tau_{PhCH_2SH} = k_1[RSH][H^+]/2K_{PhCH_2SH_2^+} \qquad (5)$$



$$RSH + {}^*H^+ \longrightarrow R\text{–}S^+\begin{matrix} H \\ {}^*H \end{matrix} \begin{cases} \longrightarrow RSH + {}^*H^+ \text{ (no exchange)} & (6) \\ \longrightarrow RSH^* + H^+ \text{ (exchange)} & (7) \end{cases}$$

of reaction (3) $k_3 = 2k = 2{\cdot}70 \times 10^2$ l mol^{-1} s^{-1} at 25 °C, and the rate constant for the reverse reaction, $k_{-3} = k_3/K_{PhCH_2SH_2^+} = 4{\cdot}80 \times 10^7$ l mol^{-1} s^{-1}. The uncertainties are of the order of ±5%.

Measurements in Basic Solutions.—Basic DMSO is obtained by addition of very small amounts (10^{-4}M) of a weak base, imidazole (Im). The pK of imidazole is 6·6

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[11] S. Alexander, *J. Chem. Phys.*, 1962, **37**, 967, 974.

[12] J. J. Delpuech and D. Nicole, unpublished results.

in DMSO using Bromocresol Green as indicator. As expected, this value is close to that obtained in water ($pK_{\mathrm{H_2O}}$ = 6·95 [9,13]). Bromocresol Green is a convenient indicator (pK = 7·3 [14]), in spite of its different electrical charge; as the ionic concentrations are very low (10^{-4}M), the activity coefficients are assumed to be unity.

Determination of $pK_{\mathrm{PhCH_2SH}}$. $pK_{\mathrm{PhCH_2SH}}$ is taken as the pH of a solution of toluene-α-thiol in DMSO half neutralized by dimsyl anion. This pH range demands a new indicator, Phenol Red (pK = 13·7 [15]). A value, $pK_{\mathrm{PhCH_2SH}}$ (DMSO) = 14·3, is thus obtained, which may be compared to an independent measurement in water, $pK_{\mathrm{PhCH_2SH}}$ (H_2O) = 8·3.[15] The difference, ΔpK = 6·0, is very close to those obtained for other acids of the same electrical type, phenol (6·4 [14,16,17]), nitromethane (5·7 [18,19]), benzoin (5·8 [20,21]), and acetic (6·7 [20]) acid.

Rate measurements. The same methods are used as for acidic solutions. However, the thiol triplet is observed to coalesce into a sharp line (Figure 3) without shifting, which is an indication of proton transfer between like molecules of thiol.

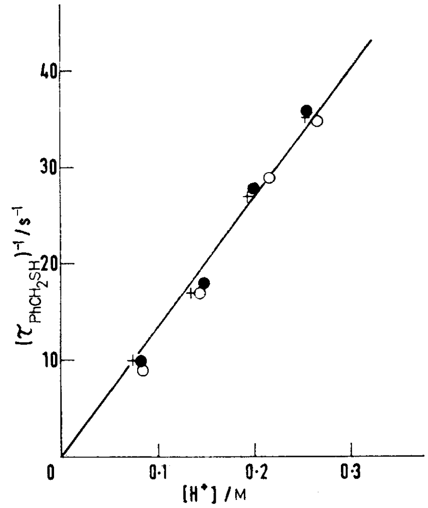

FIGURE 4 A plot of $(\tau_{\mathrm{PhCH_2SH}})^{-1}$ *versus* [H⁺] in acidic DMSO, for three concentrations: [PhCH₂SH] = 0·34 +; 0·68 ●; and 1·02M ○

Kinetic law. $(\tau_{\mathrm{PhCH_2SH}})^{-1}$ Rates were measured for three thiol concentrations and for four pH values in each case (Table 2). They fall along three straight lines A—C (Figure 5), one for each concentration, when they are plotted against 1/[H⁺]. A plot of the slopes 4·35, 7·60, and 12·2 × 10^{-7} l mol⁻¹ s⁻¹ of A—C against [RSH] again yields a straight line (Figure 6), as expected from equation (8).

$$(\tau_{\mathrm{PhCH_2SH}})^{-1} = k_2[\mathrm{RS^-}] = k_2K_{\mathrm{RSH}}[\mathrm{RSH}]/[\mathrm{H^+}] \quad (8)$$

The presence of the indicator (10^{-5}M) modifies the pH and therefore the transfer rate. However, we have checked that it does not contribute directly to the proton exchange by doubling its concentration; the new points obtained in this way fall exactly on the corresponding line A or B or C of Figure 5. A similar conclusion is drawn for imidazole. The exchange RSH + Im ⟶ RS⁻ + ImH⁺ is excluded. In this case, the points corresponding to an equal imidazole content should fall on horizontal parallel lines. This is not found.

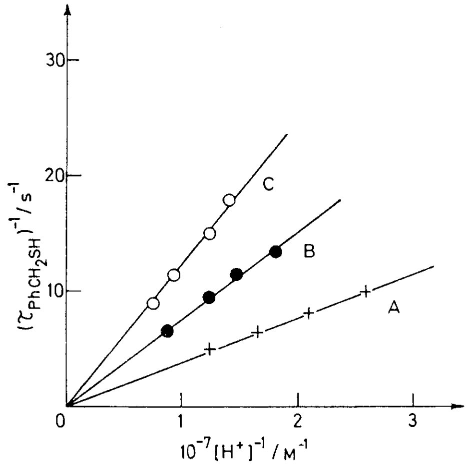

FIGURE 5 A plot of $(\tau_{\mathrm{PhCH_2SH}})^{-1}$ *versus* $[H^+]^{-1}$ in basic DMSO, for [PhCH₂SH] = A, 0·306; B, 0·612, and C, 0·918M

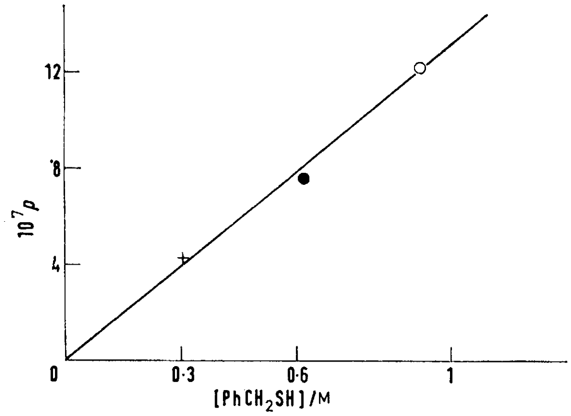

FIGURE 6 A plot of the slopes *p* of lines A—C (Figure 5) *versus* the concentration of toluene-α-thiol

TABLE 2

$[H^+]^{-1}$ and $(\tau_{\mathrm{PhCH_2SH}})^{-1}$ values in basic DMSO for various concentrations of toluene-α-thiol and imidazole (ImH)

		10^4[ImH]/M			
[PhCH₂SH]/M		1·48	2·22	2·96	3·70
0·306	$10^{-7}[H^+]^{-1}/M^{-1}$	1·23	1·66	2·10	2·60
	$(\tau_{\mathrm{PhCH_2SH}})^{-1}/s^{-1}$	5·0	6·5	8·0	10·0
0·612	$10^{-7}[H^+]^{-1}/M^{-1}$	0·87	1·23	1·47	1·80
	$(\tau_{\mathrm{PhCH_2SH}})^{-1}/s^{-1}$	6·6	9·5	11·5	13·5
0·918	$10^{-7}[H^+]^{-1}/M^{-1}$	0·74	0·93	1·23	1·39
	$(\tau_{\mathrm{PhCH_2SH}})^{-1}/s^{-1}$	9·0	11·5	15	17

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Finally, deprotonation of toluene-α-thiol by the dimsyl anion may be discarded because ^{13}C satellite lines of DMSO are not broadened when the doublet coalesces.

We may therefore conclude that in basic DMSO the transfer of the thiol proton is uniquely promoted by its conjugate base $PhCH_2S^-$, with a rate constant $k_2 = 2\cdot62 \times 10^8$ l mol^{-1} s^{-1} at 25 °C.

DISCUSSION

The complete kinetic law is written as (9) for DMSO

$$(\tau_{\mathrm{PhCH_2SH}})^{-1} = 1\cdot31 \times 10^{-6}/[\mathrm{H}^+] + 2\cdot70 \times 10^{2}[\mathrm{H}^+] \quad (9)$$

containing one mole of toluene-α-thiol. This law predicts a minimum for the proton transfer rate, $(\tau_{\mathrm{PhCH_2SH}})^{-1} = 0\cdot038$ s^{-1} at pH $= 4\cdot16$, which is very slow on the n.m.r. time scale (Figure 1), but still very fast for normal chemistry.

Interesting comparisons could be made with proton transfers on other atoms, in particular on the oxygen atom of alcohols.[2,3] Unfortunately the data in the literature are uncertain because they use the pure alcohol. This is a poor choice, since transfer mechanisms and rates may differ widely from one solvent to another. For example, transfers on toluene-α-thiol are described by reactions (1) and (2) in the pure liquid, and by (3) and (2) in DMSO.

Studies are therefore under way on benzyl alcohol in DMSO. Let us however compare the transfer reaction between RXH (X = O or S) and the hydroxonium ion H_3O^+ [reaction (10)]. $k_4 = 10^8$ and 10^6 l mol^{-1} s^{-1} for R = Me or Et, and X = O and $2\cdot70 \times 10^2$ l mol^{-1} s^{-1} for R = $PhCH_2$ and X = S. The comparison

$$\mathrm{RXH} + \mathrm{H_3O^+} \xrightarrow{k_4} \mathrm{RXH_2^+} + \mathrm{H_2O} \quad (10)$$

is not made for analogous substrates, nor in the same solvent (pure methanol and DMSO respectively). However, we may anticipate the conclusion that transfer rates for acidic alcohols are several orders of magnitude (10^4—10^6) higher than those for the corresponding thiols. This is in complete agreement with qualitative predictions that may be derived from the theory of hard and soft bases;[22,23] the hydrogen ion is hard and reacts more easily with a hard base such as ROH than with a soft base such as RSH.

Studies in basic medium show similar rate constants for reaction (2; X for S): $k_2 = 2\cdot62 \times 10^8$ l mol^{-1} s^{-1} for R = $PhCH_2$ and X = S and $7\cdot5 \times 10^8$ and 10^6 l mol^{-1} s^{-1} for R = Me or Et, and X = O. This is due to low energy barriers for proton transfer between two like atoms as computed by quantum mechanical methods: O · · · H · · · O (in water[24]), or N · · · H · · · N (in ammonia[25,26]). The change of solvents, from protic (methanol) to dipolar aprotic (DMSO), might be expected to lead to higher rates in DMSO where anions are supposed to be free and therefore much more reactive.[27] However, this statement is not valid when applied to alcohols, since the transfer (2) occurs between alkoxide ion RO^- and an alcohol molecule bonded to it in its solvation shell. Solvent effects on these reactions are also being studied, using less polar media (nitriles, nitromethane).

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