

# One-electron Redox Potentials of $\text{RSSR}^{+\cdot}$ - $\text{RSSR}$ Couples from Dimethyl Disulphide and Lipoic Acid

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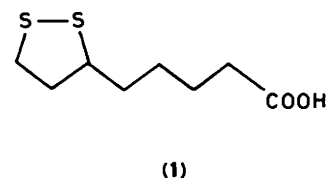
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One-electron redox potentials have been measured for three  $(\text{RSSR})^{+\cdot}/\text{RSSR}$  couples by reference to  $(\text{SCN})_2^{2-}/2 \text{SCN}^-$  and/or  $\text{I}_2^{2-}/2 \text{I}^-$  in pulse radiolysis experiments:  $E^\circ(\text{CH}_3\text{SSCH}_3^{+\cdot}/\text{CH}_3\text{SSCH}_3) + (1.391 \pm 0.003) \text{ V}$ ;  $E^\circ[\text{lip}(\text{SS})_{\text{COOH}}^{+\cdot}/\text{lip}(\text{SS})_{\text{COOH}}] + (1.13 \pm 0.01) \text{ V}$ ; and  $E^\circ[\text{lip}(\text{SS})_{\text{COO}^-}^{+\cdot}/\text{lip}(\text{SS})_{\text{COO}^-}] + (1.10 \pm 0.01) \text{ V}$  [ $\text{lip}(\text{SS}) = \text{lipoic acid}$ ]. The paper also includes equilibrium constants for the underlying  $\text{RSSR} + \text{X}_2^{2-} \rightleftharpoons \text{RSSR}^{+\cdot} + 2 \text{X}^-$  equilibria ( $\text{X} = \text{SCN}$  or  $\text{I}$ ), and rate constants for the respective back and/or forward reactions. The results are discussed in the light of structural considerations and in relation to other redox couples involving sulphur-centred radical species.

One-electron oxidation of organic disulphides leads to radical cations  $(\text{RSSR})^{+\cdot}$ . Such species have been well characterized in a number of publications, e.g. from pulse radiolysis investigations in aqueous solutions,<sup>1-4</sup> or e.s.r. measurements in  $\text{CH}_2\text{Cl}_2$  as a solvent.<sup>5</sup> A characteristic physical property of  $(\text{RSSR})^{+\cdot}$  is optical absorption which typically peaks in the 400–450 nm range.<sup>2</sup> Electronically the sulphur-sulphur bond assumes a partial  $\pi$ -character in the radical cation owing to an interaction of the unpaired  $p$ -electron of the primarily oxidized sulphur with the  $p$ -electron pair of the second sulphur atom. As a result, the already existing  $\sigma$ -bond is strengthened by the combined effect of two bonding  $\pi$ - and one antibonding  $\pi^*$ -electrons. This shows up, for example, in the optical absorption spectra of  $\text{RSSR}^{+\cdot}$  which depend on the nature of  $\text{R}$ ,<sup>2</sup> and also in an increased rigidity of the radical cation compared with the unoxidized disulphide.<sup>5</sup>

Chemically,  $(\text{RSSR})^{+\cdot}$  species have been found to exhibit oxidizing properties, e.g. towards  $\text{Fe}^{2+}$ ,  $\text{Fe}(\text{CN})_6^{4-}$ , and thiolates  $\text{RS}^-$ .<sup>2,6</sup> Their formation, on the other hand, can be induced by e.g.  $\cdot\text{OH}$ ,  $\text{Br}_2^{2-}$ , and radical cations generated from organic monosulphides,  $\text{R}_2\text{S}^{+\cdot}$ .<sup>3</sup> So far it has not been possible to evaluate the oxidation potential for any  $\text{RSSR}^{+\cdot}$  or other sulphur-centred radical; only a crude estimate of ca. +1 V has been given for  $\text{RS}^{\cdot}/\text{RS}^-$  couples from theoretical considerations.<sup>7</sup> The  $\text{RSSR}^{+\cdot}/\text{RSSR}$  redox potential in general can thus be expected to be somewhat more positive and to lie in between this value and that of the  $\text{Br}_2^{2-}/2 \text{Br}^-$  couple of ca. +1.7 V.<sup>8</sup>

Particularly interesting among the disulphides are cyclic five-membered-ring compounds since they show some significantly different features compared to their open-chain analogues. A prominent representative of the former is lipoic acid (1) further denoted as  $\text{lip}(\text{SS})$ . Its well established biological action as a coenzyme is based on redox reactions of the disulphide bridge.<sup>9-11</sup> In five-membered-ring structures the S-S bond has been found to suffer a much faster reductive and/or nucleophilic attack than in the open-chain derivatives.<sup>12</sup>  $\text{CO}_2^{2-}$ , for example, readily reduces lipoic acid to the  $\text{lip}(\text{S}\cdot\text{S})^-$  three-electron-bonded radical anion<sup>13</sup> while such a reaction has not been observed for cystamine, cystine, or glutathione disulphide.<sup>6,14</sup> A main reason for this general difference in behaviour is considered to be a smaller CS-SC torsional angle in the cyclic structures which results in a comparatively higher electron density of the disulphide bridge. Experimentally this has been corroborated by photoionization and chemical experiments which show that  $\text{lip}(\text{SS})$  and similar five-membered-ring systems are much easier to oxidize than the non-cyclic disulphides.<sup>5</sup> This in turn suggests that the disulphide radical cations also exhibit different redox properties, with the



open-chain  $\text{RSSR}^{+\cdot}$  being a comparatively more powerful oxidant than the corresponding cyclic  $\text{lip}(\text{SS})^{+\cdot}$  radical cation.

In this paper we present radiation chemical pulse radiolysis measurements on various redox reactions involving lipoic acid and  $\text{CH}_3\text{SSCH}_3$  which corroborate these considerations, and for the first time allow an evaluation of the standard redox potentials of the associated  $\text{RSSR}^{+\cdot}/\text{RSSR}$  couples.

## Experimental

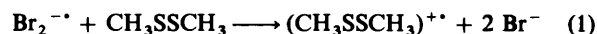
All chemicals were of purest grade commercially available (Merck, Fluka) and used as received. Solutions were prepared from deionized, Millipore system-purified water the quality of which corresponded to triply quartz-distilled water. The pH of the solutions was generally adjusted with  $\text{NaOH}$  and  $\text{HClO}_4$ . Deoxygenation was obtained by bubbling with  $\text{N}_2$ . The solutions were subsequently saturated with  $\text{N}_2\text{O}$  to convert  $e_{\text{aq}}^-$  into  $\cdot\text{OH}$  radicals ( $\text{N}_2 + e_{\text{aq}}^- \longrightarrow \text{N}_2 + \cdot\text{OH} + \text{OH}^-$ ).

Pulse radiolysis experiments were performed with high-energy electrons from a 1.6 MeV Van-de-Graaff accelerator and pulse durations of ca. 0.5–5  $\mu\text{s}$ . Dosimetry was based on the  $\cdot\text{OH}$ -radical-induced oxidation of thiocyanate [ $\cdot\text{OH} + 2 \text{SCN}^- \longrightarrow (\text{SCN})_2^{2-} + \text{OH}^-$ ]. Absorbed doses per pulse were generally in the range of 1–10 Gy which correspond to an  $\cdot\text{OH}$  radical concentration of ca.  $(0.6\text{--}6) \times 10^{-6} \text{ mol l}^{-1}$  per pulse in  $\text{N}_2\text{O}$ -saturated solutions. Details of the pulse radiolysis equipment and the evaluation of data from time-resolved optical measurements have already been described.<sup>15,16</sup>

All experiments have been carried out at room temperature.

## Results

(1) *Reaction of  $(\text{SCN})_2^{2-}$  with  $\text{CH}_3\text{SSCH}_3$ .*—In an earlier study<sup>3</sup> we have shown that dimethyl disulphide is readily and irreversibly oxidized by  $\text{Br}_2^{2-}$  according to equation (1). The



rate constant for this reaction was measured as  $2.2 \times 10^9 \text{ l mol}^{-1} \text{ s}^{-1}$



Figure 1. Trace of optical absorption at 500 nm versus time from pulse-irradiated, N<sub>2</sub>O-saturated, pH ca. 4 solution containing 5 × 10<sup>-3</sup>M-KSCN and 2 × 10<sup>-3</sup>M-CH<sub>3</sub>SSCH<sub>3</sub>.

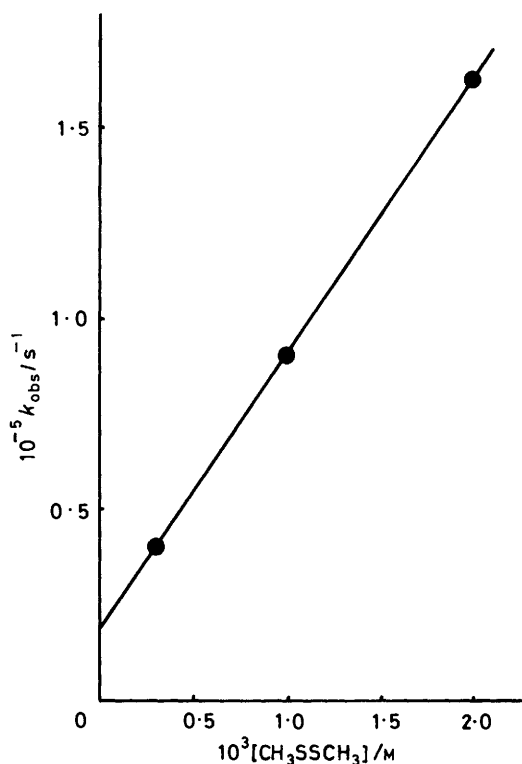


Figure 2. Plot of  $k_{\text{obs}} = \ln 2/t_{1/2}$  referring to the exponential part of the  $(\text{SCN})_2^{2-}$  decay versus  $[\text{CH}_3\text{SSCH}_3]$  in pulse-irradiated, N<sub>2</sub>O-saturated, pH ca. 4 solutions of 10<sup>-1</sup>M-KSCN and various CH<sub>3</sub>SSCH<sub>3</sub> concentrations

mol<sup>-1</sup> s<sup>-1</sup> by monitoring the decay of the Br<sub>2</sub><sup>-</sup> absorption ( $\lambda_{\text{max}}$ , 365 nm) or the formation of the (CH<sub>3</sub>SSCH<sub>3</sub>)<sup>++</sup> radical cation ( $\lambda_{\text{max}}$ , 440 nm<sup>2</sup>). Similar experiments have now been conducted with  $(\text{SCN})_2^{2-}$  and I<sub>2</sub><sup>-</sup> as oxidants.

Pulse radiolysis of an N<sub>2</sub>O-saturated, pH ca. 4 solution of high concentrations of KSCN ( $\geq 10^{-3}$ M) leads to an immediate and quantitative conversion of <sup>•</sup>OH radicals into  $(\text{SCN})_2^{2-}$  radical anions by the overall process (2). The  $(\text{SCN})_2^{2-}$  species



exhibit a strong optical absorption at 480 nm. Addition of CH<sub>3</sub>SSCH<sub>3</sub> to the solution resulted in an exponential decay of this absorption, with  $t_{1/2}$  being inversely proportional to the disulphide concentration. An experimental example is given in Figure 1 which shows an absorption-time trace recorded at 500 nm from a pulsed N<sub>2</sub>O-saturated, pH ca. 4 solution of 5 × 10<sup>-3</sup>M-KSCN and 2 × 10<sup>-3</sup>M-CH<sub>3</sub>SSCH<sub>3</sub>. It is noted that the absorption does not decay to its baseline and that the spectrum of the remaining long-lived absorption still resembles that of  $(\text{SCN})_2^{2-}$  in the  $\approx 480$  nm range [at lower wavelengths (CH<sub>3</sub>SSCH<sub>3</sub>)<sup>++</sup> also contributes to the overall absorption].

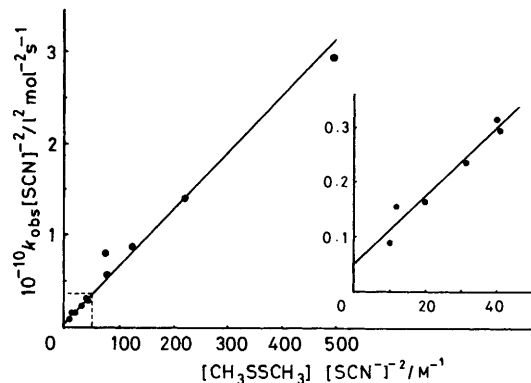
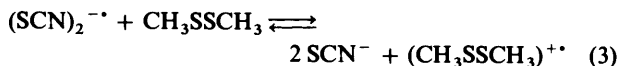


Figure 3. Plot of  $k_{\text{obs}}/[\text{SCN}^-]^2$  versus  $[\text{CH}_3\text{SSCH}_3]/[\text{SCN}^-]^2$  according to equations (II) with  $k_{\text{obs}}$  referring to the exponential part of the  $(\text{SCN})_2^{2-}$  decay in pulse-irradiated, N<sub>2</sub>O-saturated, pH ca. 4 solutions of various CH<sub>3</sub>SSCH<sub>3</sub> and KSCN concentrations. Insert: enlarged low concentration-ratio range

Looking at the results obtained at different solute concentrations it is further noticed that the yield of the long-time absorption at 500 nm increases with increasing  $[\text{KSCN}]/[\text{CH}_3\text{SSCH}_3]$  ratio. All these observations suggest that the oxidation of dimethyl disulphide by  $(\text{SCN})_2^{2-}$  in contrast to the Br<sub>2</sub><sup>-</sup> reaction [equation (1)] is a reversible process (3).



Experimental verification of this equilibrium has been achieved by kinetic and yield measurements. Figure 2 shows, for example, a plot of the pseudo-first-order rate constants  $k_{\text{obs}} = \ln 2/t_{1/2}$  calculated from the exponential part of the  $(\text{SCN})_2^{2-}$  decay as a function of the dimethyl disulphide concentration [solutions: N<sub>2</sub>O-saturated, pH ca. 4, 10<sup>-2</sup>M-KSCN, (0.3–2.0) × 10<sup>-3</sup>M-CH<sub>3</sub>SSCH<sub>3</sub>]. A straight line is obtained, but it does not go through the origin. This is typical of equilibrium conditions and allows, in fact, an evaluation of the equilibrium constant via  $K = k_3/k_{-3}$ . The above mentioned observed rate

$$k_{\text{obs}} = k_3 [\text{CH}_3\text{SSCH}_3] + k_{-3} [\text{SCN}^-]^2 \quad (I)$$

constant includes the rate constants for the forward reaction,  $k_3$ , and the back reaction,  $k_{-3}$ , of the equilibrium as well as the solute concentrations. Rearrangement of (I) leads to (II). A

$$\frac{k_{\text{obs}}}{[\text{SCN}^-]^2} = k_3 \frac{[\text{CH}_3\text{SSCH}_3]}{[\text{SCN}^-]^2} + k_{-3} \quad (II)$$

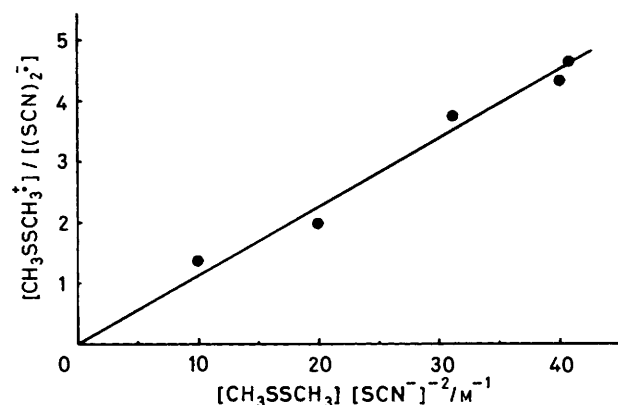
corresponding plot of  $k_{\text{obs}}/[\text{SCN}^-]^2$  versus  $[\text{CH}_3\text{SSCH}_3]/[\text{SCN}^-]^2$  yields the expected straight line as shown in Figure 3 (the insert exhibits the initial part at expanded scales). The rate constants  $k_3$  and  $k_{-3}$  can be derived from the slope and intercept, respectively. Their numerical values are listed in the Table. Since the back-reaction of equilibrium (3) takes place between charged species the Table also lists a rate constant  $k_{-3,\text{corr}}$ , which corrects for the kinetic salt effect (the ionic strength of the solution was generally kept to  $\mu$  0.01 by addition of NaClO<sub>4</sub>). It is noted that the oxidation of CH<sub>3</sub>SSCH<sub>3</sub> by  $(\text{SCN})_2^{2-}$  ( $k_3$ ) is slower by almost two orders of magnitude than that by Br<sub>2</sub><sup>-</sup>.

The  $k_3/k_{-3}$  ratio yields an equilibrium constant of  $K_3 = 12.4 \times 10^{-2}$  mol l<sup>-1</sup> for the  $\mu$  0.01 solutions while  $k_3/k_{-3,\text{corr}} = K_{3,\text{corr}} = 9.8 \times 10^{-2}$  mol l<sup>-1</sup> for the equilibrium constant extrapolated to zero ionic strength. The error limits of all these kinetic and thermodynamic values are estimated to be  $\pm 10\%$ .

**Table.** Rate and equilibrium constants for various  $\text{RSSR} + \text{X}_2^{2-} \rightleftharpoons \text{RSSR}^{+} + 2 \text{X}^-$  equilibria and standard redox potentials for  $\text{RSSR}^{+}/\text{RSSR}$  couples

Equilibria	$\bar{k}/\text{l mol}^{-1} \text{s}^{-1}$	$\bar{k}/\text{l}^2 \text{mol}^{-2} \text{s}^{-1}$	$K/\text{mol l}^{-1}$ (from $\bar{k}/\bar{k}$ )*	Redox couple	$E^\circ/\text{V}$ versus NHE
$\text{CH}_3\text{SSCH}_3 + (\text{SCN})_2^{2-} \rightleftharpoons \text{CH}_3\text{SSCH}_3^{+} + 2 \text{SCN}^-$	$6.2 \times 10^7$	$5.0 \times 10^8$	$9.84 \times 10^{-2}$	$\text{CH}_3\text{SSCH}_3^{+}/\text{CH}_3\text{SSCH}_3$	$+(1.391 \pm 0.003)$
$\text{lip}(\text{SS})_{\text{COOH}} + \text{I}_2^{2-} \rightleftharpoons \text{lip}(\text{SS})_{\text{COOH}}^{+} + 2 \text{I}^-$	$6.8 \times 10^8$	$1.44 \times 10^{10}$	$2.27 \times 10^{-2}$	$\text{lip}(\text{SS})_{\text{COOH}}^{+}/\text{lip}(\text{SS})_{\text{COOH}}$	$+(1.13 \pm 0.01)$
$\text{lip}(\text{SS})_{\text{COOH}} + (\text{SCN})_2^{2-} \rightleftharpoons \text{lip}(\text{SS})_{\text{COOH}}^{+} + 2 \text{SCN}^-$	$1.9 \times 10^9$	$5.0 \times 10^5$	$1.72 \times 10^3$	$\text{lip}(\text{SS})_{\text{COOH}}^{+}/\text{lip}(\text{SS})_{\text{COOH}}$	$+(1.14 \pm 0.05)$
$\text{lip}(\text{SS})_{\text{COO}^-} + \text{I}_2^{2-} \rightleftharpoons \text{lip}(\text{SS})_{\text{COO}^-}^{+} + 2 \text{I}^-$	$5.2 \times 10^8$	$3.5 \times 10^9$	$6.29 \times 10^{-2}$	$\text{lip}(\text{SS})_{\text{COO}^-}^{+}/\text{lip}(\text{SS})_{\text{COO}^-}$	$+(1.10 \pm 0.01)$
	$\bar{k}_{\text{corr.}} = 2.2 \times 10^8$				

\* Corrected for salt effects.

**Figure 4.** Plot of  $[(\text{CH}_3\text{SSCH}_3)^+]/[(\text{SCN})_2^{2-}]$  (equilibrium radical concentrations) versus  $[\text{CH}_3\text{SSCH}_3]/[\text{SCN}^-]^2$  according to equation (IV). Solutions as for Figure 3

The second possibility of evaluating  $K_3$  is based on equation

$$K_3 = \frac{[\text{SCN}^-]^2 [(\text{CH}_3\text{SSCH}_3)^+]}{[(\text{SCN})_2^{2-}] [\text{CH}_3\text{SSCH}_3]} \quad (\text{III})$$

$$\frac{[(\text{CH}_3\text{SSCH}_3)^+]}{[(\text{SCN})_2^{2-}]} = K_3 \frac{[\text{CH}_3\text{SSCH}_3]}{[\text{SCN}^-]^2} \quad (\text{IV})$$

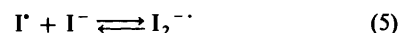
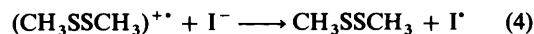
(III) which in its rearranged form (IV) implies a linear relationship between the ratios of the equilibrium radical concentrations and  $[\text{CH}_3\text{SSCH}_3]/[\text{SCN}^-]^2$ . The  $(\text{SCN})_2^{2-}$  yields were evaluated from absorption measurements at 500 nm where the  $(\text{CH}_3\text{SSCH}_3)^+$  hardly absorbs. The  $(\text{CH}_3\text{SSCH}_3)^+$  yields were then calculated as the difference between the initial  $\cdot\text{OH}$  ( $G$  5.5) and the  $(\text{SCN})_2^{2-}$  yield. A direct measurement was not possible because the absorption of  $(\text{CH}_3\text{SSCH}_3)^+$  is small compared with that of  $(\text{SCN})_2^{2-}$  at all wavelengths. For solutions with a concentration ratio  $[\text{SCN}^-]/[\text{CH}_3\text{SSCH}_3] < 10$  the results were corrected for the fact that the direct reaction of  $\cdot\text{OH}$  with  $\text{CH}_3\text{SSCH}_3$  yields  $(\text{CH}_3\text{SSCH}_3)^+$  radical cations only with 50% efficiency.<sup>1</sup> Figure 4 shows that a thus evaluated radical yield ratio, if plotted according to equation (IV), does indeed give a straight line going through the origin. Considering that all the underlying experiments have been carried out with solutions of an ionic strength  $\mu$  0.01 the equilibrium constant  $K_3 = 11.3 \times 10^{-2} \text{ mol l}^{-1}$  derived from the slope has to be compared with  $K_3 = 12.4 \times 10^{-2} \text{ mol l}^{-1}$  from the uncorrected kinetic measurements. The two values are in excellent agreement.

Assuming ideal thermodynamic conditions and taking the zero ionic strength  $K_{3,\text{corr.}}$  value the Gibbs free energy at 289 K may be calculated:  $\Delta G^\circ = -RT \ln K_{3,\text{corr.}} = 5.75 \times 10^3 \text{ J mol}^{-1}$ . From this it is then possible to calculate the difference

in standard redox potentials  $\Delta E^\circ = \Delta G^\circ/F = E^\circ [(\text{CH}_3\text{SSCH}_3)^+/\text{CH}_3\text{SSCH}_3] - E^\circ [(\text{SCN})_2^{2-}/2 \text{SCN}^-] = 0.060 \text{ V}$  with an estimated error limit of  $\pm 0.003 \text{ V}$ . Taking the known  $E^\circ [(\text{SCN})_2^{2-}/2 \text{SCN}^-] = +1.331 \text{ V}$ <sup>17</sup> the standard one-electron redox potential of the  $(\text{CH}_3\text{SSCH}_3)^+/\text{CH}_3\text{SSCH}_3$  couple amounts to  $E^\circ = +(1.391 \pm 0.003) \text{ V}$ .

(2) *Reaction of  $(\text{CH}_3\text{SSCH}_3)^+$  with  $\text{I}^-$  Ions.*—Considering that the one-electron redox potential of the  $\text{I}_2^{2-}/2 \text{I}^-$  couple ( $E^\circ$  1.03 V)<sup>8,17-21</sup> is much lower than that of the dimethyl disulphide couple derived above it can be expected that  $\text{I}_2^{2-}$  radical anions will not be able to oxidize  $\text{CH}_3\text{SSCH}_3$ . This is indeed found to be the case, i.e. the decay kinetics of the  $\text{I}_2^{2-}$  absorption ( $\lambda_{\text{max}}$  385 nm, observable in pulsed,  $\text{N}_2\text{O}$ -saturated solutions of  $\text{I}^-$ ) could not be accelerated even at the highest possible  $\text{CH}_3\text{SSCH}_3$  concentrations.

On the other hand, the  $(\text{CH}_3\text{SSCH}_3)^+$  radical cation can easily oxidize  $\text{I}^-$  ions to yield  $\text{I}_2^{2-}$  via reactions (4) and (5).



Appropriate experiments were carried out with  $\text{N}_2\text{O}$ -saturated, pH ca. 4 solutions with a high ( $2 \times 10^{-3} \text{ M}$ )  $\text{CH}_3\text{SSCH}_3$  concentration while the  $\text{I}^-$  concentration was kept comparatively low ( $(0.2-1.0) \times 10^{-4} \text{ M}$ ). Under these conditions the initially formed  $\cdot\text{OH}$  radicals practically all react with the disulphide. The reaction sequence (4) and (5) can be monitored by the formation of the  $\text{I}_2^{2-}$  absorption. The latter is found to grow exponentially, with  $t_{1/2}$  being inversely proportional to the  $\text{I}^-$  concentration, yielding a straight line if plotted as  $k = \ln 2/t_{1/2}$  versus  $[\text{I}^-]$ . This plot incidentally goes through the origin, i.e. the results do not indicate any equilibrium conditions, as expected. The bimolecular rate constant derived from these kinetic data amounts to  $k$   $5.5 \times 10^9 \text{ l mol}^{-1} \text{ s}^{-1}$ . This value is close to  $k_5$   $7.6 \times 10^9 \text{ l mol}^{-1} \text{ s}^{-1}$  published for the forward reaction of equilibrium (5).<sup>22</sup> It is therefore not possible unambiguously to assign our rate constant to either of the two reactions involving  $\text{I}^-$  ions. But it is quite clear that the oxidation of  $\text{I}^-$  by  $(\text{CH}_3\text{SSCH}_3)^+$  is in any case a fast and practically diffusion-controlled process.

(3) *Reactions of  $\text{I}_2^{2-}$  and  $(\text{SCN})_2^{2-}$  with Lipoic Acid.*—In contrast to dimethyl disulphide the cyclic disulphide lipoic acid could readily be oxidized by  $\text{I}_2^{2-}$ , suggesting that the redox potential of the  $\text{lip}(\text{SS})^+/\text{lip}(\text{SS})$  couple is considerably lower than that of the  $(\text{CH}_3\text{SSCH}_3)^+/\text{CH}_3\text{SSCH}_3$  couple. Pulse radiolysis experiments carried out on the decay of the  $\text{I}_2^{2-}$  absorption at 385 nm in  $\text{N}_2\text{O}$ -saturated, pH 3.6 and pH 9 solutions of various  $\text{I}^-$ -lipoic acid concentration ratios gave the results shown in Figure 5. They are principally the same as

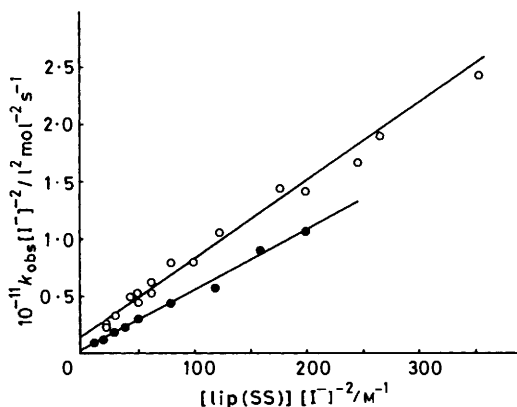


Figure 5. Plots of  $k_{\text{obs}}/[I^-]^2$  versus  $[\text{lip}(\text{SS})]/[I^-]^2$  with  $k_{\text{obs}}$  referring to the exponential part of the  $I_2^{--}$  decay at 380 nm in pulse-irradiated,  $N_2O$ -saturated solutions of various KI and lipoic acid concentrations at pH 3.6 (O) and pH 9 (●)

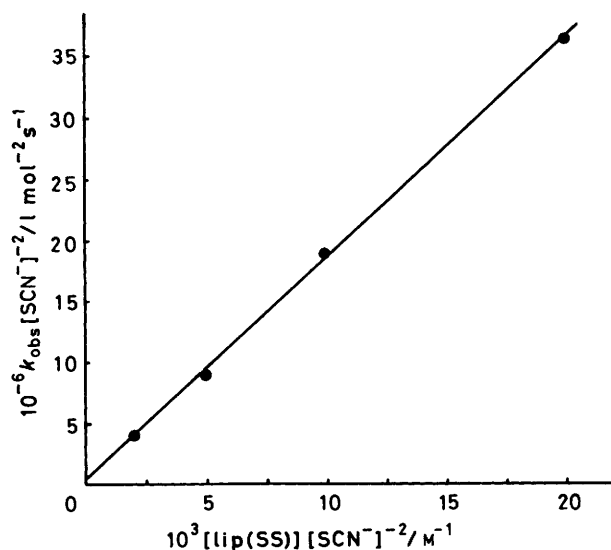


Figure 6. Plot of  $k_{\text{obs}}/[\text{SCN}^-]^2$  versus  $[\text{lip}(\text{SS})]/[\text{SCN}^-]^2$  with  $k_{\text{obs}}$  referring to the exponential part of the  $(\text{SCN})_2^{--}$  decay in pulse-irradiated,  $N_2O$ -saturated, pH 3.6 solutions of various KSCN and lipoic acid concentrations

discussed in connection with Figure 2. The most important aspect is a positive intercept in the  $k_{\text{obs}}/[I^-]^2$  versus  $[\text{lip}(\text{SS})]/[I^-]^2$  plot [analogous to equation (II)] which clearly suggests the establishment of equilibria. Furthermore, this applies to both the neutral  $\text{lip}(\text{SS})_{\text{COOH}}$  as well as the anionic  $\text{lip}(\text{SS})_{\text{COO}^-}$  form the lipoic acid ( $pK$  5.4), *i.e.* equilibria (6) and



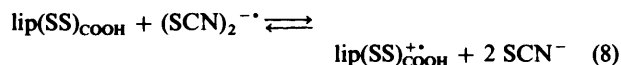
(7). The rate constants for the respective forward and back reactions and the equilibrium constants derived therefrom are listed in the Table. For the evaluation of  $K_6$  and  $K_7$  the rate constants  $k_{-6}$  and  $k_7$  were corrected for the ionic strength of  $\mu$  0.1 generally applied in these experiments.

Calculation of equilibrium constants from radical yields was not feasible in these systems since the  $I_2^{--}$  absorption ( $\lambda_{\text{max}}$  385 nm) overlaps too much with that of  $\text{lip}(\text{SS})_{\text{COOH}}^{+\cdot}$  ( $\lambda_{\text{max}}$  390 nm) or  $\text{lip}(\text{SS})_{\text{COO}^-}^{+\cdot}$  ( $\lambda_{\text{max}}$  425 nm).<sup>23</sup>

From the equilibrium constants the differences in standard

redox potentials are calculated as  $\Delta E^\circ = E^\circ [\text{lip}(\text{SS})_{\text{COOH}}^{+\cdot}/\text{lip}(\text{SS})_{\text{COOH}}] - E^\circ (I_2^{--}/2 I^-) = -(RT \ln K_6)/F = 0.097 \text{ V}$  and  $\Delta E^\circ = E^\circ [\text{lip}(\text{SS})_{\text{COO}^-}^{+\cdot}/\text{lip}(\text{SS})_{\text{COO}^-}] - E^\circ (I_2^{--}/2 I^-) = -(RT \ln K_7)/F = 0.071 \text{ V}$  at 298 K. Taking  $E^\circ (I_2^{--}/2 I^-) = +1.03 \text{ V}$  as an average literature value<sup>8,17-21</sup> the one-electron redox potentials are derived as  $E^\circ [\text{lip}(\text{SS})_{\text{COOH}}^{+\cdot}/\text{lip}(\text{SS})_{\text{COOH}}] = +1.13 \text{ V}$  and  $E^\circ [\text{lip}(\text{SS})_{\text{COO}^-}^{+\cdot}/\text{lip}(\text{SS})_{\text{COO}^-}] = +1.10 \text{ V}$ , both with an estimated error limit of  $\pm 0.01$ .

Although these redox potentials are considerably lower than that of the  $(\text{SCN})_2^{--}/2 \text{SCN}^-$  couple it was still possible to establish equilibrium (8) with the neutral form of lipoic acid but



not with the anionic form. The rate constant  $k_{-8}$  for the back-reaction became already very small. Also, the  $k_{\text{obs}}/[\text{SCN}^-]^2$  versus  $[\text{lip}(\text{SS})_{\text{COOH}}]/[\text{SCN}^-]^2$  plot in Figure 6 exhibits almost no intercept.

Evaluation of the kinetic data yielded  $\Delta E^\circ -0.191 \text{ V}$  from which  $E^\circ [\text{lip}(\text{SS})_{\text{COOH}}^{+\cdot}/\text{lip}(\text{SS})_{\text{COOH}}] = +1.140 \text{ V}$  is calculated. Despite the relatively large error limits which should be allowed for these values  $E^\circ$  is nevertheless in excellent agreement with that obtained from the iodide-containing system.

## Discussion

The present investigation for the first time provided standard redox potentials for one-electron redox couples involving sulphur-centred radical species. A remarkable observation is the significant difference between  $E^\circ$  of the dimethyl disulphide and the lipoic acid-derived  $(-\text{SS}-)^{+\cdot}/(-\text{SS}-)$  couples of almost 0.3 V. Accordingly the  $(\text{CH}_3\text{SSCH}_3)^{+\cdot}$  radical cation is a much stronger oxidant than the sulphur-centred radical cations derived from lipoic acid and lipoate. On the other hand, the latter substrates are comparatively easier to oxidize. These observations correlate very well with other findings made for the gas phase.<sup>5</sup> Photoelectron spectroscopy has thus revealed a relatively low first ionization energy for lipoic acid (8.06 eV) compared with  $\text{CH}_3\text{SSCH}_3$  (8.97 V). Even more striking are the differences between the first and second ionizations which have been measured as 1.79 and 0.24 eV for the two respective disulphides. The rationale for these findings is based on structural considerations. The CS-SC torsional angle is *ca.* 90° in  $\text{CH}_3\text{SSCH}_3$  but only *ca.* 35° in lipoic acid. This leads to a comparatively much higher electron density in the disulphide bridge in the latter facilitating ionization. Energetically this process is further favoured since the formation of a partial  $\pi$ -bond between the two sulphur atoms in the radical cation<sup>4,5</sup> results in a release of ring strain associated with a structural flattening and a shortening of the sulphur-sulphur distance in the oxidized lipoic acid.<sup>5</sup> [The sulphur-sulphur bond in  $(\text{RSSR})^{+\cdot}$ -type radical cations contains 2  $\sigma$ , 2  $\pi$  and 1 antibonding  $\pi^*$  electrons.<sup>4</sup>] These arguments are considered to apply to five-membered-ring disulphides in general.

A small difference in redox potential has been found between the neutral carboxy and the anionic carboxylate form of lipoic acid with the radical cation of the former seemingly being the slightly better oxidant. The difference is, however, only marginal and thus within expectation according to which the far distant carboxy group should have only little influence on the electronic situation in the disulphide bridge.

The evaluation of redox potentials for our  $(\text{RSSR})^{+\cdot}/\text{RSSR}$  couples also allows a semiquantitative extrapolation to the redox potentials of other sulphur-containing systems. Thus  $\text{CH}_3\text{SSCH}_3$  is readily oxidized, for example, by the radical cation from dimethyl sulphide,  $(\text{CH}_3)_2\text{S}^{+\cdot}$ , with a practically

diffusion-controlled rate constant ( $4 \times 10^9 \text{ l mol}^{-1} \text{ s}^{-1}$ )<sup>24</sup> suggesting that the redox potential of the  $(\text{CH}_3)_2\text{S}^{++}/(\text{CH}_3)_2\text{S}$  couple should clearly exceed +1.4 V.  $(\text{CH}_3\text{SSCH}_3)^{+}$  and also  $\text{lip}(\text{SS})_{\text{COO}^-}^{\bullet}$  radical cations, on the other hand, have been found to oxidize thiolate,  $\text{RS}^-$ , to the corresponding thiyl radicals,  $\text{RS}^\bullet$  ( $\text{R} = \text{e.g. alkyl, aminoalkyl, and several amino-acid residues}$ ).<sup>6</sup> The  $\text{RS}^\bullet/\text{RS}^-$  redox potential has thus to be located below +1.1 V. Since  $\text{RS}^\bullet$  can, however, themselves still act as oxidants, *e.g.* towards  $\alpha$ -tocopherol (Vit E) and ascorbate (Vit C),<sup>25</sup> their oxidation potentials may indeed be close to the value of *ca.* +1.0 V estimated by Armstrong in his theoretical consideration.<sup>7</sup> The proximity of the  $\text{lip}(\text{SS})^{\bullet}/\text{lip}(\text{SS})$  and  $\text{RS}^\bullet/\text{RS}^-$  redox potentials may have some bearing on the biological function of the lipoic acid.

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