Oxidation of Thioglycolic Acid and Glutathione by (*trans*-Cyclohexane-1,2-diamine-*N,N,N',N'*-tetraacetato)manganate(III) in Aqueous Media†

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The kinetics of the electron-transfer reactions of the manganese(III) complex of *trans*-cyclohexane-1,2-diamine-*N,N,N',N'*-tetraacetate ($cdta^{4-}$) with two thiols thioglycolic acid and glutathione has been investigated at 30 °C in aqueous media in the range pH 2.0–10.33 with varying reductant concentrations at constant ionic strength, $I = 0.20$ mol dm^{-3} ($NaClO_4$). The reactions are first order both in complex and reductants and follow the general rate law, $-d[Mn^{III}(cdta)^-]/dt = k_{obs}[Mn^{III}(cdta)^-] = k[Mn^{III}(cdta)^-][reductant]$. Both the reactions have been assumed to proceed *via* an inner-sphere mechanism with support for this coming from the observation of a rapid initial increase in absorption followed by a slower decay. This indicates the formation of an inner-sphere associated species which decomposes unimolecularly leading to the transfer of the electron from the thiol to the oxidant. Additional support for this mechanism comes from a comparison of the water-exchange rate of $[Mn(cdta)(H_2O)]^-$ with the higher limit of the electron-transfer rates. The pH–rate profiles are bell-shaped curves and were successfully modelled by fitting the experimental data to a computer-fitted program thereby evaluating the reactivity of all the reacting species of the reductants.

Thiols are recognised to be the most active groups found in cells, and are easily oxidised to disulfides by biochemical oxidants such as flavins, cytochrome c, dehydroascorbic acid, quinones, amino acids and fumarates.[1] These studies have led to several proposals which enhance the understanding of their roles as electron-transfer enzymes. In general, the oxidation of thiols to disulfides occurs through either electron transfer preceded by the formation of an intermediate of significant thermodynamic stability[2–7] or by simple electron transfer without any prior complexation.[8,9]

In an attempt to investigate the kinetic behaviour of trivalent manganese towards biologically relevant molecules, redox studies on the interaction of (*trans*-cyclohexane-1,2-diamine-*N,N,N',N'*-tetraacetato)manganate(III), $[Mn^{III}(cdta)]^-$ with thioglycolic acid $HSCH_2CO_2H$ and glutathione $H_2NCH(CO_2H)CH_2CH_2CONHCH(CH_2SH)CONHCH_2CO_2H$ have been carried out by us. Thioglycolic acid is a simple thiol whereas glutathione contains a γ-glutamyl locus along with a sulfhydryl group of a cysteinyl residue, and is considered to be the major low-molecular weight thiol found in living plant or animal cells. The significance of the structure of glutathione for its biological function is of continued interest, and thereby the present investigation over a wide range of pH could furnish a reasonably accurate understanding of the electron-transfer characteristics of these two types of thiol.

Experimental

Materials and Reagents.—The potassium salt of (*trans*-cyclohexane-1,2-diamine-*N,N,N',N'*-tetraacetato)manganate(III), $K[Mn(cdta)]\cdot 2.5H_2O$ {hereafter designated as $[Mn^{III}(cdta)]^-$} was prepared, characterised and standardised as reported earlier.[10] Thioglycolic acid (AnalaR grade) was distilled under reduced pressure before use. Glutathione was purchased from Sigma, and the purity of both the thiols was checked by iodine titration.[11] Recrystallised sodium perchlorate was used to maintain the ionic strength of the medium, and the pH was adjusted by using perchloric acid, acetic acid–sodium acetate and sodium dihydrogenphosphate–sodium hydroxide buffers as required. Although the measured pH is usually defined in terms of the activity of the hydrogen ion, the concentration of the hydrogen ion for each solution was obtained by calibrating the pH electrode with analytically prepared solutions maintained at the desired ionic strength.

Kinetic Measurements.—The kinetics under various reaction conditions was monitored by stopped-flow spectrophotometry at 510 and 448 nm for the aqua, $[Mn^{III}(cdta)(H_2O)]^-$ and hydroxo, $[Mn^{III}(cdta)(OH)]^{2-}$ forms (to be discussed later) of the complex respectively. A Union RA-401 stopped-flow spectrophotometer (Otsuka Electronics, Japan) interfaced with a data processor RA-451 was used for this purpose. The observed rate constants were evaluated by treating the kinetic curves of the average of at least five runs by a least-squares curve-fit method. The pseudo-first-order rate constants thus evaluated varied within an error limit of ±3%. pH Measurements were done with a Systronics digital pH-meter (model 335, India). The reaction temperature (±0.1 °C) was controlled by a Haake F3 thermostat. All the solutions were prepared immediately prior to use and deaerated by bubbling dinitrogen for at least 25 min to suppress aerial oxidation of thiols.

Polymerisation Study.—The generation of free radicals in the reaction mixture was tested by the method reported earlier.[12] The precipitation of white polymers of acrylonitrile indicates that both reactions proceed *via* the generation of free radicals. No polymerisation was encountered when the complex and the reagents were treated separately with acrylonitrile.

Stoichiometry and Reaction Products.—The stoichiometries of the reactions were determined under various concentrations of the oxidant and reductants at pH 5.0 with $I = 0.2$ mol dm^{-3} ($NaClO_4$) and at 25 °C under deaerated conditions. With excess of oxidant ($[Mn^{III}(cdta)]^- = (2.0–8.0) \times 10^{-3}$ mol dm^{-3} and [reductant] $= 1.0 \times 10^{-3}$ mol dm^{-3}), the unreacted complex

† *Supplementary data available* (No. SUP 56989, 4 pp.): observed rate constants at different $[H^+]$. See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1994, Issue 1, pp. xxiii–xxviii.

was determined spectrophotometrically at 510 nm after the completion of the reactions (*ca.* 30 min after mixing the reactants). The results showed that 1 mole of $[Mn^{III}(cdta)]^-$ is reduced per mole of reductants. The stoichiometry under the kinetically investigated reaction conditions *i.e.*, with excess of reductant over the oxidant was also determined. For this purpose the contents (25 cm^3) of the four vials with excess of thiols (RSH) of concentrations 0.01, 0.03, 0.05 and 0.09 mol dm^{-3} were treated at room temperature with $[Mn^{III}(cdta)^-] = 5.0 \times 10^{-3}$ mol dm^{-3} at pH 5.0, and the unreacted thiols were estimated by iodine titration.[11] In each case a 1.02 ± 0.05:1 stoichiometric ratio with respect to oxidant was obtained. The stoichiometry under both conditions is thus represented by equation (1).

$$2[Mn^{III}(cdta)]^- + 2RSH \longrightarrow 2[Mn^{II}(cdta)]^{2-} + RSSR + 2H^+ \quad (1)$$

Product Analysis.—The expected oxidation products of thioglycolic acid and glutathione are dithiodiglycolic acid and glutathione disulfide. To characterise the products of the reactions, $[Mn^{III}(cdta)]^-$ (0.67 g, 0.14 mol) and the thiols [0.14 mol dm^{-3}, 0.13 g (thioglycolic acid), 0.43 g (glutathione)] were allowed to react.[13] After the completion of the reaction, the metal ions were removed by ion exchange. The eluent in each case was then added to ice-cold ethanol whereby white powdered precipitates of the disulfide products were obtained. The mixtures were then warmed to redissolve the precipitate, filtered and allowed to cool. The white powder formed was collected and dried *in vacuo*. Oxidation of the thiols by iodine also produces the corresponding disulfides.[11,14] A comparison of the melting points of the disulfides obtained by both methods, 100 ± 2 and 178 ± 5 °C (decomposition), for dithiodiglycolic acid and glutathione disulfide respectively showed them to be the same. Further support for their formulation comes from a study of their IR spectra which show S–S stretching bands at 455 and 435 cm^{-1} for dithiodiglycolic acid and glutathione disulfide respectively.

Preliminary Kinetic Observations.—Typical reaction traces at 510 nm for the reduction of $[Mn^{III}(cdta)]^-$ by thioglycolic acid and glutathione showed an initial rise in absorption within 20–30 ms followed by a slow fall. The initial rise in absorbance can be ascribed to the existence of a transient intermediate which is believed to be a complex between $[Mn^{III}(cdta)]^-$ and the thiols, while the slower decay may be due to the decomposition of this complex to form Mn^{II}. Further information was gathered from the spectrum generated in the oxidation of thioglycolic acid by observing the rise in absorption as a function of wavelength in the range 340–800 nm at 20 nm intervals (Fig. 1). This shows that the maximum change in absorbance pertaining to the formation of the intermediate is wavelength dependent for a given set of reactant concentrations. The spectrum exhibits a single maximum at *ca.* 510 nm which is characteristic of the parent $[Mn^{III}(cdta)]^-$ complex. The redox decomposition of the intermediate may therefore interfere in an accurate study of the complex formation, however the conditions were set appropriately to lower pH so as to ensure that the rate of formation was sufficiently high compared to the electron-transfer process.

Results and Discussion

The electron-transfer reactions of $[Mn^{III}(cdta)]^-$ with thioglycolic acid and glutathione were followed at 30 °C under various concentrations of reductants and pH at constant ionic strength (I = 0.2 mol dm^{-3}, $NaClO_4$). A first-order dependence of the rate on $[Mn^{III}(cdta)^-]$ for both the reactions was established from the linearity of plots of $-\log A_t$ *vs.* t (the symbols have their usual significance) up to 4–5 half-lives of the reactions. The plots of k_{obs} *vs.* [reductant] yielded straight lines passing through the origin, indicating a first-order dependence of rate on reductant (Table 1). A general rate expression for these reactions is given in equation (2).

$$\frac{d[Mn^{III}(cdta)^-]}{dt} = k[\text{reductant}][Mn^{III}(cdta)^-] = k_{obs}[Mn^{III}(cdta)^-] \quad (2)$$

The effect of pH on the rates of reaction was followed in the range pH 2.0–10.33 in order to ascertain the contributions of the various reacting species. As shown in Fig. 2(*a*) and 2(*b*), for plots of k_{ox} *vs.* $-\log [H^+]$ the rate of reaction increases and reaches a maximum at $-\log [H^+]$ 8.46 (pH 8.75) and 8.0 (pH 8.25) for the oxidation of thioglycolic acid and

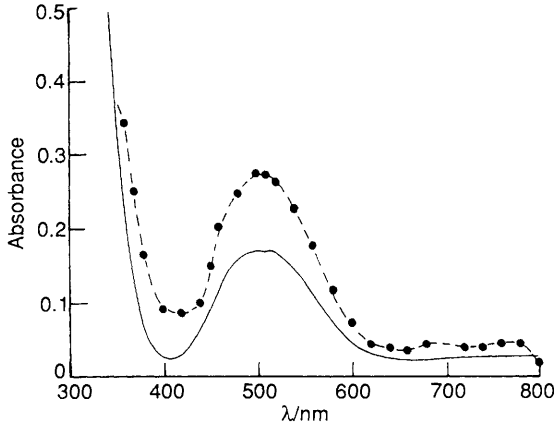


Fig. 1 Representative absorbance plot of the reaction intermediate for the oxidation of thioglycolic acid by $[Mn^{III}(cdta)]^-$ with $[Mn^{III}(cdta)^-] = 4.96 \times 10^{-4}$ mol dm^{-3}, $[H_2A] = 0.01$ mol dm^{-3}, I = 0.2 mol dm^{-3} ($NaClO_4$), pH = 4.50 and 30 °C, (– – –) spectrum of the intermediate, (——) spectrum of $[Mn^{III}(cdta)]^-$

Table 1 Pseudo-first-order rate constants at pH 4.75 (or 5.47) and 9.5[a] for the oxidation of thioglycolic acid and glutathione by $[Mn^{III}(cdta)]^-$ (5.0×10^{-4} mol dm^{-3}), I = 0.2 mol dm^{-3} ($NaClO_4$), [acetate][b] or [phosphate] = 0.02 mol dm^{-3} and at 30 °C

		k_{obs}/s^{-1}	
Reductant (R)	[R]/mol dm^{-3}	pH 4.75[c]	9.5
Thioglycolic acid	0.01	15.01	15.30
	0.02	25.96	
	0.025		45.20
	0.03	47.09	
	0.05	62.70, 63.0, 67.23	94.60
	0.07	91.10	132.60
	0.10	140.0	187.0
Glutathione	0.002		20.10
	0.004		38.90
	0.005	1.05	
	0.006		61.50
	0.007	1.65	
	0.008		78.20
	0.01	2.09, 2.59	100.0, 98.0
	0.012		121.80
	0.03	7.20	
	0.05	10.20	

[a] Complete data given in SUP 56989. [b] The pseudo-first-order rate constants (k_{obs}) increase by *ca.* 2–3% on addition of 0.02 mol dm^{-3} acetate buffer compared to unbuffered solutions and is considered within the limit of experimental error. However, on increasing [buffer] at a given pH, the rate increases further (*e.g.* 0.05 mol dm^{-3} $[O_2CMe^-]$ causes an 8–10% increase in rate). [c] For glutathione pH 5.47.

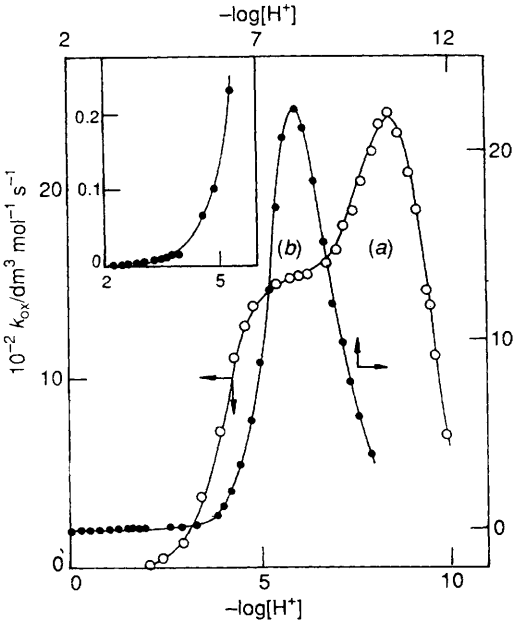


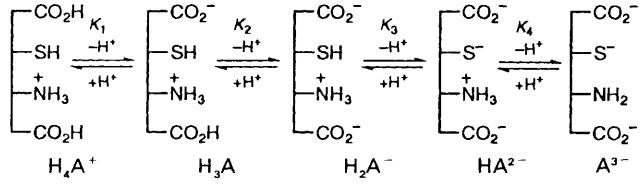
Fig. 2 Variation of $k_{ox} = k_{obs}/[\text{reductant}]$ as a function of $-\log[H^+]$ for the oxidation of (*a*) thioglycolic acid and (*b*) glutathione at 30 °C with $[Mn^{III}(cdta)^-] = 5.0 \times 10^{-4}$ mol dm^{-3}, and $I = 0.20$ mol dm^{-3} ($NaClO_4$); the inset indicates the initial portion of (*b*) on an enlarged scale. The solid line represents calculated values, and the experimental values are shown by points

glutathione respectively and then decreases steadily. Such behaviour is associated with deprotonation of the aqua species $[Mn^{III}(cdta)(H_2O)]^-$ [equation (3), $K_m = 7.76 \times 10^{-9}$ mol

$$[Mn^{III}(cdta)(H_2O)]^- \overset{K_m}{\rightleftharpoons} [Mn^{III}(cdta)(OH)]^{2-} + H^+ \quad (3)$$

dm^{-3} ^{10}] and where the hydroxo species is inactive towards the electron-transfer process.[15-19]

The inertness of the hydroxo species is due to the decrease in redox potential of the deprotonated species relative to the corresponding conjugate acid.[20] As the basicity of the medium increases, the equilibrium in equation (3) is shifted to the right. It is also imperative to consider the acid dissociation constants of thioglycolic acid (H_2A) and glutathione (H_3A). For the former $pK_1 = 3.58$ and $pK_2 = 9.78$ for the processes $HSCH_2CO_2H \rightleftharpoons H^+ + HSCH_2CO_2^-$ and $HSCH_2CO_2^- \rightleftharpoons H^+ + {}^-SCH_2CO_2^-$ respectively.[21] The equilibria involving fully protonated glutathione (H_4A^+)[22] are as shown schematically below.



The L-glutamyl carboxylic group is considered to be the most acidic with $pK_1 = 2.05$, the second ionisation constant corresponds to the glycyl carboxylic proton ($pK_2 = 3.40$), the third ionisation from the sulfhydryl group (pK_3) and the fourth from the ammonium group (pK_4) are 8.72 and 9.49 respectively.

In the oxidation of thioglycolic acid by $[Mn^{III}(cdta)^-]$, the reacting species H_2A, HA^- and A^{2-} are likely to be present in the experimental range of pH 2.10–10.33. If one considers the reactivity of the aqua species $[Mn^{III}(cdta)(H_2O)]^-$ alone, a possible electron-transfer scheme can be given by equations (4)–(7) ($R^\bullet$ = $HA^\bullet$ or $A^{\bullet-}$).

$$[Mn^{III}(cdta)(H_2O)]^- + H_2A \xrightarrow{k_0} [Mn^{II}(cdta)(H_2O)]^{2-} + HA^\bullet + H^+ \quad (4)$$

$$[Mn^{III}(cdta)(H_2O)]^- + HA^- \xrightarrow{k_1} [Mn^{II}(cdta)(H_2O)]^{2-} + A^{\bullet-} + H^+ \quad (5)$$

$$[Mn^{III}(cdta)(H_2O)]^- + A^{2-} \xrightarrow{k_2} [Mn^{II}(cdta)(H_2O)]^{2-} + A^{\bullet-} \quad (6)$$

$$R^\bullet + R^\bullet \xrightarrow{\text{fast}} R\text{-}R \text{ (disulfide)} \quad (7)$$

The general rate expression corresponding to the above scheme is given by equation (8) where $k_{ox} = k_{obs}/[H_2A]_{tot}$.

$$k_{ox} = \frac{k_0[H^+]^2 + k_1K_1[H^+] + k_2K_1K_2}{[H^+]^2 + K_1[H^+] + K_1K_2}\left\{\frac{[H^+]}{K_m + [H^+]}\right\} \quad (8)$$

The evaluation of rate parameters is best achieved by considering suitable acidity regions where particular types of reacting species exist. Thus in the range pH 2.1–5.5, the first proton dissociation of H_2A (K_1) is operative, and therefore the reactive species of thioglycolic acid are H_2A and HA^- leading to the rate expression (9). Experimental data were fitted to

$$k_{ox} = \frac{k_0[H^+] + k_1K_1}{[H^+] + K_1} \quad (9)$$

equation (9) by means of a non-linear least-squares program and the evaluated parameters are $k_0 = 1.55 \pm 0.28$ dm^3 mol^{-1} s^{-1}, $k_1 = (1.56 \pm 0.00) \times 10^3$ dm^3 mol^{-1} s^{-1} and $K_1 = (1.0 \pm 0.00) \times 10^{-4}$ mol dm^{-3} ($pK_1 = 4.0$).

Similarly on considering the reactivity of HA^- and A^{2-} ($pK_2 = 9.78$) and the proton dissociation constant of the complex ($pK_m = 8.11$), the rate expression in the range pH 7.05–10.33 is given by equation (10).

$$k_{ox} = \frac{k_1[H^+] + k_2K_2}{[H^+] + K_2}\left\{\frac{[H^+]}{K_m + [H^+]}\right\} \quad (10)$$

This has been solved by using a computer-fitted non-linear least-squares program. The evaluated parameters were: $k_1 = (1.51 \pm 0.02) \times 10^3$ dm^3 mol^{-1} s^{-1}, $k_2 = (1.08 \pm 0.01) \times 10^5$ dm^3 mol^{-1} s^{-1}; $K_2 = (3.56 \pm 0.03) \times 10^{-10}$ mol dm^{-3} ($pK_2 = 9.45$) and $K_m = (1.32 \pm 0.01) \times 10^{-8}$ mol dm^{-3} ($pK_m = 7.88$). The good agreement between the reported and observed proton dissociation constants of thioglycolic acid highlights the self-consistency between the equilibrium scheme and the rate expressions, and provides justification for adopting them.

The reactivities of all the glutathione species were ascertained by a similar approach. All the five species (H_4A^+, H_3A, H_2A^-, HA^{2-} and A^{3-}) are likely to be present in the pH range studied. A plausible mechanism consistent with our results is given by equations (11)–(16) ($R^\bullet$ = $H_2A^\bullet$, $HA^{\bullet-}$ or $A^{2\bullet-}$) and the general

$$[Mn^{III}(cdta)(H_2O)]^- + H_4A^+ \xrightarrow{k_0} [Mn^{II}(cdta)(H_2O)]^{2-} + H_3A^\bullet + H^+ \quad (11)$$

$$[Mn^{III}(cdta)(H_2O)]^- + H_3A \xrightarrow{k_1} [Mn^{II}(cdta)(H_2O)]^{2-} + H_2A^\bullet + H^+ \quad (12)$$

$$[Mn^{III}(cdta)(H_2O)]^- + H_2A^- \xrightarrow{k_2} [Mn^{II}(cdta)(H_2O)]^{2-} + HA^{\bullet-} + H^+ \quad (13)$$

$$[Mn^{III}(cdta)(H_2O)]^- + HA^{2-} \xrightarrow{k_3} [Mn^{II}(cdta)(H_2O)]^{2-} + HA^{\bullet -} \quad (14)$$

$$[Mn^{III}(cdta)(H_2O)]^- + A^{3-} \xrightarrow{k_4} [Mn^{II}(cdta)(H_2O)]^{2-} + A^{2\bullet -} \quad (15)$$

$$R^\bullet + R^\bullet \xrightarrow{fast} R\text{–}R \text{ (disulfide)} \quad (16)$$

rate expression is given by equation (17).

$$\frac{-d[ox]}{dt} = \frac{k_0[H^+]^4 + k_1K_1[H^+]^3 + k_2K_1K_2[H]^2 + k_3K_1K_2K_3[H^+] + k_4K_1K_2K_3K_4}{[H^+]^4 + K_1[H^+]^3 + K_1K_2[H^+]^2 + K_1K_2K_3[H^+] + K_1K_2K_3K_4} \left\{\frac{[H^+]}{[H^+] + K_m}\right\} \quad (17)$$

A judicious choice of pH regions enables one to evaluate various rate and equilibrium parameters. In the region pH 2.0–4.0, where the reacting species are H_4A^+, H_3A, H_2A^- and $[Mn^{III}(cdta)(H_2O)]^-$, the rate expression is given by equation (18) and the best fit of the experimental data was achieved by

$$k_{ox} = \frac{k_0[H^+]^2 + k_1K_1[H^+] + k_2K_1K_2}{[H^+]^2 + K_1[H^+] + K_1K_2} \quad (18)$$

employing a computer-fitted non-linear least-squares program of five variables. The evaluated parameters were $k_0 = 0.34 \pm 0.01$ dm^3 mol^{-1} s^{-1}, $k_1 = 1.32 \pm 0.004$ dm^3 mol^{-1} s^{-1}, $k_2 = (24.7 \pm 0.01)$ dm^3 mol^{-1} s^{-1} and $K_1 = (8.51 \pm 0.06) \times 10^{-3}$ mol dm^{-3} ($pK_1 = 2.07$), $K_2 = (1.76 \pm 0.001) \times 10^{-4}$ mol dm^{-3} ($pK_2 = 3.75$). The close agreement between the reported and experimentally obtained values of K_1 and K_2 is of note.

In the range pH 6.07–10.33 reactivities of H_2A^-, HA^{2-} and A^{3-} should be considered, and again assuming $[Mn^{III}(cdta)(OH)]^{2-}$ as an unreactive species, the appropriate rate expression is given by equation (19). A best fit of experimental data

$$k_{ox} = \frac{k_2[H^+]^2 + k_3K_3[H^+] + k_4K_3K_4}{[H^+]^2 + K_3[H^+] + K_3K_4} \times \left\{\frac{[H^+]}{K_m + [H^+]}\right\} \quad (19)$$

was achieved through a non-linear least-squares program of six variables. This yields $k_2 = (24.76 \pm 8.42)$ dm^3 mol^{-1} s^{-1}, $k_3 = (7.91 \pm 0.0) \times 10^4$ dm^3 mol^{-1} s^{-1}, $k_4 = (7.0 \pm 0.01) \times 10^5$ dm^3 mol^{-1} s^{-1} and $K_3 = (1.29 \pm 0.0) \times 10^{-8}$ mol dm^{-3} ($pK_3 = 7.89$), $K_4 = (1.69 \pm 0.0) \times 10^{-10}$ mol dm^{-3} ($pK_4 = 9.77$), $K_m = (1.27 \pm 0.0) \times 10^{-8}$ mol dm^{-3} ($pK_m = 7.90$).

The kinetically obtained parameters from the two reactions can now be entered into equations (8) (thioglycolic acid) or (17) (glutathione), and the k_{ox} values calculated at different pH values. The validity of the proposed mechanism for both reactions is established from the concurrency of calculated and experimentally obtained values of k_{ox} [Fig. 2(*a*) and 2(*b*)].

A large number of reports on the redox reactions of $[Mn^{III}(cdta)]^-$ with a variety of cross-reactants have appeared in recent years. The majority of these are believed to proceed *via* an inner-sphere mechanism[23–31] though in most cases direct evidence for inner-sphere association was not encountered. Spectral evidence is of critical importance to establish such a process. The results of the present investigation have clearly demonstrated the formation of an inner-sphere intermediate as evidenced from the rapid initial increase in optical absorption followed by the relatively slower decay of the formed species. It is also supported from the comparison of electron transfer rate constants *vis-a-vis* the water exchange rate constant (k_{ex}) of $[Mn^{III}(cdta)(H_2O)]^-$ ($k_{ex} \approx 4.4 \times 10^8$ dm^3 mol^{-1} s^{-1}).[26] The upper limit of the electron-transfer rates are $k_2(A^{2-}) = 1.08 \times 10^5$ dm^3 mol^{-1} s^{-1} and $k_4(A^{3-}) = 7.0 \times 10^5$ dm^3 mol^{-1} s^{-1} for the thioglycolic acid and glutathione systems respectively. It can be easily seen that k_{ex} is $\approx 10^3$ orders of magnitude higher than the corresponding rate constants of electron transfer in the present reactions strengthening further the proposition for an inner-sphere route. Association with the manganese(III) centre in $[Mn^{III}(cdta)]^-$ could occur either through the displacement of the co-ordinated water molecule or through the partial unwrapping of the carboxylate arms of the co-ordinated cdta ligand[32,33] and co-ordination of either the carboxylate group or sulfur atom of the thiol. The latter is more probable during the oxidation of the thiol to the disulfide[34–36] since the available d orbitals of the sulfur lead to greater stability of the intermediate complex. Also electron transfer from sulfur to the metal centre would be more facile than that from the more electronegative oxygen atom. From preliminary experiments we have also observed that the reduction of $[Mn^{III}(cdta)]^-$ by glycolic acid is extremely slow in comparison to that by thioglycolic acid and this supports the above view. Formation of radical intermediates in the redox chemistry of sulfur systems is well documented, and the greater stability of sulfur relative to oxygen radicals is evidenced through the formation of disulfide products in most cases.[34–37] On the other hand, in the case of oxygen radicals, delocalisation of electrons takes place throughout the entire radical which is able to complex with another metal ion with the subsequent very fast decomposition of this intermediate. This leads to decarboxylation and formation of either lower aldehydes or their corresponding acids.[34] Our observations for a 1:1 reaction stoichiometry and formation of disulfides as the only reaction products are diagnostic for an inner-sphere association in which transient Mn–S bonds are formed.

Such an association may be represented as shown below for the thioglycolic acid systems [equations (20) and (21)] with

$$[Mn^{III}(cdta)(H_2O)]^- + A^{2-} \overset{K}{\rightleftharpoons} [Mn^{III}(cdta)(A)]^{3-} + H_2O \quad (20)$$

$$[Mn^{III}(cdta)(A)]^{3-} \xrightarrow{k} [Mn^{II}(cdta)]^{2-} + A^{\bullet -} \quad (21)$$

$k_2 = kK$. Alternative pathways such as (22) and (23) are

$$[Mn^{III}(cdta)(OH)]^{2-} + HA^- \overset{K}{\rightleftharpoons} [Mn^{III}(cdta)(A)]^{3-} + H_2O \quad (22)$$

$$[Mn^{III}(cdta)(A)]^{3-} \xrightarrow{k} [Mn^{II}(cdta)]^{2-} + A^{\bullet -} \quad (23)$$

kinetically indistinguishable to (20) and (21). It might be expected that replacing a co-ordinated water molecule by a hydroxo group would increase the lability of the metal species but OH^- is difficult to replace owing to its high nucleophilicity. Such an inner-sphere process (22) should also be facilitated by an increase in reaction rate with pH as increasing deprotonation of the thiols has been found to lead to higher reactivity. In the present system however, while reactivity does increase with pH, it then reaches a maximum value and increasing the pH further slows the reaction down. This thus indicates the non-participation of the hydroxo species of the complex in the redox process.

The inactivity of the hydroxo species $[Mn^{III}(cdta)(OH)]^{2-}$ may be ascribed to the strong nucleophilic character of the OH^- group compared to aqua or mercapto groups making it difficult to replace OH^- by –SH of the thiols. Additionally the

negative charge on the complex increases upon deprotonation, and this electrostatically hinders the close approach of a negatively charged thiolate species at higher pH. A decrease in reduction potential on deprotonation of the oxidant might also make it a weaker electron acceptor.

The significance of the present investigation lies in the evaluation of the reactivity of all the possible reactive species. Earlier kinetic studies with thioglycolic acid and glutathione were confined either to the acidic[9,38] or neutral or alkaline pH range[8,14,39,40] while the present study enables us to comment on the reactivity of all types of species. The general feature that appears on comparing the kinetic results is increasing reactivity with increasing deprotonation of the thiols, and this is in agreement with the ease of oxidation based on thermodynamic considerations: $H_2A < HA^- < A^{2-}$ and $H_4A^+ < H_3A < H_2A^- < HA^{2-} < A^{3-}$ for the thioglycolic acid and glutathione systems respectively.

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References

1 Y. M. Torchinski, *Sulfhydryl and Disulfide Groups of Proteins*, Consultants Publishing Corporation, New York, 1974.
2 J. P. McCann and A. McAuley, *J. Chem. Soc., Dalton Trans.*, 1975, 783.
3 M. A. Olatunji and A. McAuley, *Can. J. Chem.*, 1977, **55**, 3335.
4 N. Kujundic and J. Everse, *Biochem. Biophys. Res. Commun.*, 1978, **82**, 1211.
5 G. Davies, *Inorg. Chem.*, 1972, **11**, 2488.
6 F. Cristani and A. Diaz, *Inorg. Chim. Acta*, 1977, **24**, L7.
7 Z. Amzad and A. McAuley, *Inorg. Chim. Acta*, 1977, **25**, 127.
8 J. F. Martin and J. Spence, *J. Phys. Chem.*, 1970, **74**, 2863.
9 G. A. Ayoko and M. A. Olatunji, *Polyhedron*, 1983, **2**, 577.
10 R. E. Hamm and M. A. Suwyn, *Inorg. Chem.*, 1967, **6**, 139.
11 R. Kuhn, L. Brikhofer and F. W. Quackenbush, *Ber. Dtsch. Chem. Ges.*, 1939, **72**, 407.
12 M. Ali, S. K. Saha and P. Banerjee, *J. Chem. Soc., Dalton Trans.*, 1990, 187.
13 W. R. Cullen, B. C. Mcbride and J. R. Reglinski, *J. Inorg. Biochem.*, 1984, **21(1)**, 45.
14 J. F. Martin and J. T. Spence, *J. Phys. Chem.*, 1970, **74**, 3589.
15 S. Gangopadhyay, M. Ali and P. Banerjee, *Bull. Chem. Soc. Jpn.*, 1992, **65**, 517.
16 S. Gangopadhyay, M. Ali, S. K. Saha and P. Banerjee, *J. Chem. Soc., Dalton Trans.*, 1991, 2729.
17 S. Gangopadhyay, M. Ali and P. Banerjee, *J. Chem. Soc., Perkin Trans. 2*, 1992, 781.
18 D. H. Macartney and D. W. Thompson, *Inorg. Chem.*, 1989, **28**, 2195.
19 R. G. Wilkins and R. E. Yelin, *Inorg. Chem.*, 1968, **7**, 2667.
20 A. Chakravorty, *Comments Inorg. Chem.*, 1985, **4**, 1.
21 *Stability Constants of Metal Ion Complexes*, eds. L. G. Sillen and A. E. Martell, The Chemical Society, London, Special Publ. no. 17, 1964, p. 376.
22 D. L. Rabenstein, *J. Am. Chem. Soc.*, 1973, **95**, 2797.
23 D. J. Boone, R. E. Hamm and J. P. Hunt, *Inorg. Chem.*, 1972, **11**, 1060.
24 T. E. Jones and R. E. Hamm, *Inorg. Chem.*, 1974, **13**, 1940.
25 W. H. Woodruff and D. W. Margerum, *Inorg. Chem.*, 1974, **13**, 2578.
26 T. E. Jones and R. E. Hamm, *Inorg. Chem.*, 1975, **14**, 1027.
27 J. Stein, J. P. Fackler, jun., G. J. McCline, J. A. Fee and L. T. Chan, *Inorg. Chem.*, 1979, **18**, 4511.
28 P. Arselli and E. Mentasti, *J. Chem. Soc., Dalton Trans.*, 1983, 689.
29 S. Gangopadhyay, S. K. Saha and P. Banerjee, *Transition Met. Chem.*, 1991, **16**, 355.
30 V. M. Bobba, G. Giraudi and E. Mentasti, *Transition Met. Chem.*, 1988, **13**, 256.
31 S. Gangopadhyay, S. K. Saha, M. Ali and P. Banerjee, *Int. J. Chem. Kinet.*, 1991, **23**, 105.
32 G. Giraudi and E. Mentasti, *Transition Met. Chem.*, 1981, **4**, 230.
33 E. Mentasti, *J. Chem. Soc., Dalton Trans.*, 1982, 721; D. S. Everhart and R. F. Evilia, *Inorg. Chem.*, 1977, **16**, 120.
34 J. Hill and A. McAuley, *J. Chem. Soc. A*, 1968, 156.
35 J. Hill and A. McAuley, *J. Chem. Soc. A*, 1968, 2405.
36 Z. Amjad, G. Chambers and A. McAuley, *Can. J. Chem.*, 1977, **55**, 3575.
37 J. Hill, A. McAuley and W. F. Pickering, *Chem. Commun.*, 1967, 573.
38 G. A. Ayoko and M. A. Olatunji, *Inorg. Chim. Acta*, 1983, **80**, L15.
39 P. O'Brien and Z. Ozolins, *Inorg. Chim. Acta*, 1989, **161**, 261.
40 Z. Abedinzadeh, M. Gardes-Albert and C. Ferradini, *Can. J. Chem.*, 1989, **67**, 1247.

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