Kinetics of Chromic Acid Oxidation of Thioglycollic, Thiolactic & Thiomalic Acids

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Chromic acid oxidation of thioglycollic, thiolactic and thiomalic acids has been studied spectrophotometrically in sodium acetate-acetic acid buffer. Thiolactic and thiomalic acids are oxidized in an identical manner whereas thioglycollic acid undergoes oxidation by a different mechanism. The thermodynamic parameters for the reactions are: thioglycollic acid $\Delta E^{\ddagger} = 11 \cdot 4$ (kcal mol^{-1}), $\Delta S^{\ddagger} = -15 \cdot 6$ (cal mol^{-1} deg^{-1}); thiolactic acid $\Delta E^{\ddagger} = 4 \cdot 8$ (kcal mol^{-1}), $\Delta S^{\ddagger} = -47 \cdot 7$ (cal mol^{-1} deg^{-1}); thiomalic acid $\Delta E^{\ddagger} = 4 \cdot 8$ (kcal mol^{-1}), $\Delta S^{\ddagger} = -51 \cdot 6$ (cal mol^{-1} deg^{-1}). The formation of free radical intermediate has been demonstrated in the oxidation of thioglycollic acid whereas experimental evidence does not indicate the presence of free radicals in the oxidation of thiolactic and thiomalic acids.

I T is known that thiol group is very sensitive toward reaction with oxygen[1] and the oxidation of a thiol to its disulphide is a process of fundamental importance in biochemistry. Considerable amount of work has been done[2] on the oxidation of cysteine, thioglycollic acid and glutathione by oxygen. Eager and Winkler[3] studied the kinetics of the oxidation of RSH (R = n=C$_4$H$_9$, n=C$_8$H$_{17}$ and n=C$_{12}$H$_{25}$) by potassium perdisulphate in acetic acid-water medium. The kinetics of the oxidation of thioglycollic acid by ferricyanide have also been reported[4,5]. The oxidation of some reducing sulphur compounds by Ce(IV)[6], Co(III)[7] and V(V)[8] have also been studied. All these metal ions which are one equivalent oxidants produce free radicals in solution and finally radical dimerization occurs leading to the formation of stable products. The mechanism of the oxidation of α-mercapto acids by chromic acid has not received any attention. The present publication is concerned with an attempt to explain the kinetics of the oxidation of thioglycollic (TGA), thiolactic (TLA) and thiomalic (TMA) acids by chromic acid.

Materials and Methods

Inorganic reagents were of BDH (AR) or E. Merck (GR) grades. Freshly prepared solutions of thioglycollic (Riedel), thiolactic (Fluka, AG) and thiomalic (Koch-Light) acids were used for kinetic runs. Sodium perchlorate was prepared by the neutralization of perchloric acid with caustic soda. Deuterium oxide was supplied by Bhabha Atomic Research Centre (Trombay) and was claimed to have 99% deuterium content. All solutions were made in doubly distilled water. Sodium acetate-acetic acid buffer was employed throughout the experiment.

Kinetic measurements — All kinetic studies were done by following the decrease in absorbance at 350 nm using stoppered cells of 1 cm path length in a Beckman DU model spectrophotometer. The cell compartment was thermostated at desired temperatures. The maximum uncertainty in temperature was $\pm 0 \cdot 5°$. The air-free reactants previously equilibrated to bath temperature were mixed, flushed with nitrogen and optical densities noted at definite time intervals. α-Mercapto acids and disulphides do not show any detectable absorbance at this wavelength. The reactions were carried out under the condition in which [substrate]$\gg$[Cr(VI)]. Generally 6-8 experimental points were taken in each run. The plots (log OD versus time) gave good linearity over 90% of reaction and the pseudo-first order rate constants (k_1) were reproducible to within $\pm 5\%$ accuracy.

Stoichiometry and products — The stoichiometry was determined in excess substrates and the substrates were oxidized according to Eq. (1)

$$6RSH + 2Cr(VI) \longrightarrow 3RSSR + 2Cr(III) + 6H^+ \quad ...(1)$$

The products of the oxidation were identified as follows. Substance (1 g) was treated with calculated amount of Cr(VI) such that [substrate]$\gg$[Cr(VI)]. The reaction mixture was extracted with ether and the latter was removed. The residue was treated with toluene, refluxed for 1 hr and concentrated. The infrared spectra of the reaction products were found to be identical with the samples prepared by the oxidation of the respective α-mercapto acids by Ce(IV)[6].

Results

Effect of varying reactant concentrations — The results are presented in Tables 1 and 2. It has been observed that the reaction is independent of ionic strength over the range 0·2-1·0M (NaClO$_4$). Despite this independence, the ionic strength was adjusted to 1·0M. The pseudo-first order rate constant decreases with the increase in gross [Cr(VI)], suggesting that HCrO$_4^-$ is the main oxidizing species. The [HCrO$_4^-$] has been calculated using the relation

TABLE 1 — EFFECT OF VARYING [OXIDANT] ON THE
PSEUDO-FIRST ORDER RATE CONSTANT AT $\mu = 1.0M$

[TGA] $= 2.0 \times 10^{-3}M$; $pH = 5.48$; TEMP.$= 20°$

[Cr(VI)] $\times 10^4 M$	0.833	1.666	2.50	3.33	4.165
[HCrO$_4^-$] $\times 10^4 M$	1.550	3.04	4.45	5.78	7.07
$k_1 \times 10^3$ (sec^{-1})	1.36	1.28	1.15	0.997	0.974
$k_{corr} \times 10^3$ (sec^{-1})	0.729	0.701	0.647	0.575	0.575

[TLA] $= 2.0 \times 10^{-3}M$; $pH = 5.18$; TEMP.$= 30°$

[Cr(VI)] $\times 10^4 M$	0.833	1.70	2.50	3.30	4.10
[HCrO$_4^-$] $\times 10^4 M$	1.57	3.11	4.46	5.75	6.98
$k_1 \times 10^3$ (sec^{-1})	1.82	1.79	1.67	1.56	1.52
$k_{corr} \times 10^3$ (sec^{-1})	0.966	1.03	0.936	0.895	0.891

[TMA] $= 3.93 \times 10^{-3}M$; $pH = 5.16$; TEMP.$= 36°$

[Cr(VI)] $\times 10^4 M$	0.883	1.56	2.33	3.13	3.92
[HCrO$_4^-$] $\times 10^4 M$	1.57	2.85	4.16	5.46	6.736
$k_1 \times 10^3$ (sec^{-1})	2.71	2.63	2.48	2.35	2.15
$k_{corr} \times 10^3$ (sec^{-1})	1.43	1.44	1.39	1.26	1.25

described earlier[9]. The dissociation constants K_d and K'_d of the reactions

$$2HCrO_4^- \underset{}{\overset{K_d}{\rightleftharpoons}} Cr_2O_7^{2-} + H_2O \quad \text{and} \quad HCrO_4^- \underset{}{\overset{K'_d}{\rightleftharpoons}} H^+ + CrO_4^-$$

have been taken from results of Espenson and Kinney[10] and Tong and King[11] respectively. The values of k_{corr} $\left(\text{where } k_{corr} = \dfrac{k_1[Cr(VI)]}{[HCrO_4^-]}\right)$ are given in Table 1. The quotients, $k_1/$[substrate] have been calculated which indicate that the order with respect to both [TLA] and [TMA] is unity whereas the order with respect to [TGA] is different. However, the quotients, $k_1/$[TGA]^2 are found to be constant indicating that the order with respect to TGA is two. The average values of $k_1/$[TGA]^2, $k_1/$[TLA] and $k_1/$[TMA] in six experiments have been calculated to be 145 ± 4 (litre^2 mol^{-2} sec^{-1}), 0.87 ± 0.03 (litre mol^{-1} sec^{-1}) and 0.45 ± 0.03 (litre mol^{-1} sec^{-1}) at 20°, 40° and 35° respectively.

Effect of varying pH on the rate — The pH of each solution ($\mu = 0.2M$) was adjusted by the addition of buffer. Over the pH range 4.7-6.1, the plot of log k_1 versus pH is linear with a slope

significantly less than one. The slopes of log k_1 vs pH plots are identical (0.4) in the cases of TLA and TMA whereas the slope is different (0.2) for TGA. This is in agreement with the observation made earlier[2] in thiol oxidation that the rate is not a simple function of [H$^+$].

Solvent isotope effect — The rates of oxidation have been measured in both water and deuterium oxide. The ratios, k_{D_2O}/k_{H_2O} have been calculated to be 0.90, 1.2 and 1.2 for the oxidation of TGA, TLA and TMA respectively. It has earlier been shown[12] that for any proton-catalysed reaction, k_{D_2O}/k_{H_2O} lies between 2.0 and 2.5. This solvent isotope effect would favour all reactions involving molecular chromic acid for the equilibrium (2) is shifted by deuterium oxide in the forward direction yielding higher concentration of H_2CrO_4 than what could be present in water.

$$HCrO_4^- + H_3O^+ \rightleftharpoons H_2CrO_4 + H_2O \qquad \ldots(2)$$
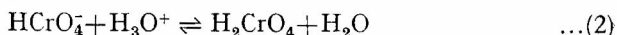
The solvent isotope effects which have been observed in the oxidations of α-mercapto acids further suggest that HCrO$_4^-$ is the reacting oxidizing species.

Effect of varying temperature on the rate — The pseudo-first order rate constants have been determined at different temperatures and the specific reaction rates have been calculated from the relations

$$k_3 = \frac{k_1}{[TGA]^2}, \quad k_2 = \frac{k_1}{[TGA]} \text{ or } \frac{k_1}{[TMA]}$$

The plots of logarithm of specific reaction rates against reciprocal of absolute temperature are linear (Fig. 1). A least square fit of each plot was used to evaluate energy of activations. Values of pZ where p is the probability or steric factor and Z the collision number at different temperatures were calculated by equating experimentally obtained rate constants with $pZe^{-E/RT}$. Entropies of activation were then computed from the relation, $pZ = e^n(RT)/Nh \exp \Delta S_{\ddagger}/R$ (where $n = 2$ for thiolactic and thiomalic acids and $n = 3$ for thioglycollic acid). The results are recorded in Table 3.

Discussion

The results obtained indicate that while TLA and TMA are oxidized by a similar mechanism, altogether

TABLE 2 — EFFECT OF VARYING [SUBSTRATES] ON THE PSEUDO-FIRST ORDER RATE CONSTANT

[Cr(VI)] $= 3.33 \times 10^{-4}M$; $pH = 5.68$; TEMP.$= 20°$

[TGA] $\times 10^3 M$	1.0	1.5	2.0	2.5	3.0	4.0
$k_1 \times 10^3$ (sec^{-1})	0.149	0.322	0.568	0.911	1.33	2.36
$k_1/$[TGA] (litre mol^{-1} sec^{-1})	0.149	0.215	0.284	0.364	0.443	0.590
$k_1/$[TGA]^2 (litre^{-2} mol^{-2} sec^{-1})	149.00	143.00	142.00	145.00	148.00	147.00

[Cr(VI)] $= 1.66 \times 10^{-4}M$; $pH = 5.60$; TEMP.$= 40°$

[TLA] $\times 10^2 M$	0.25	0.5	1.0	1.5	2.0	2.5
$k_1 \times 10^3$ (sec^{-1})	0.22	0.441	0.993	1.29	1.68	2.20
$k_1/$[TLA] $\times 10$ (litre mol^{-1} sec^{-1})	8.80	8.82	8.83	8.60	8.40	8.80

[Cr(VI)] $= 1.66 \times 10^{-4}M$; $pH = 5.60$; TEMP.$= 35°$

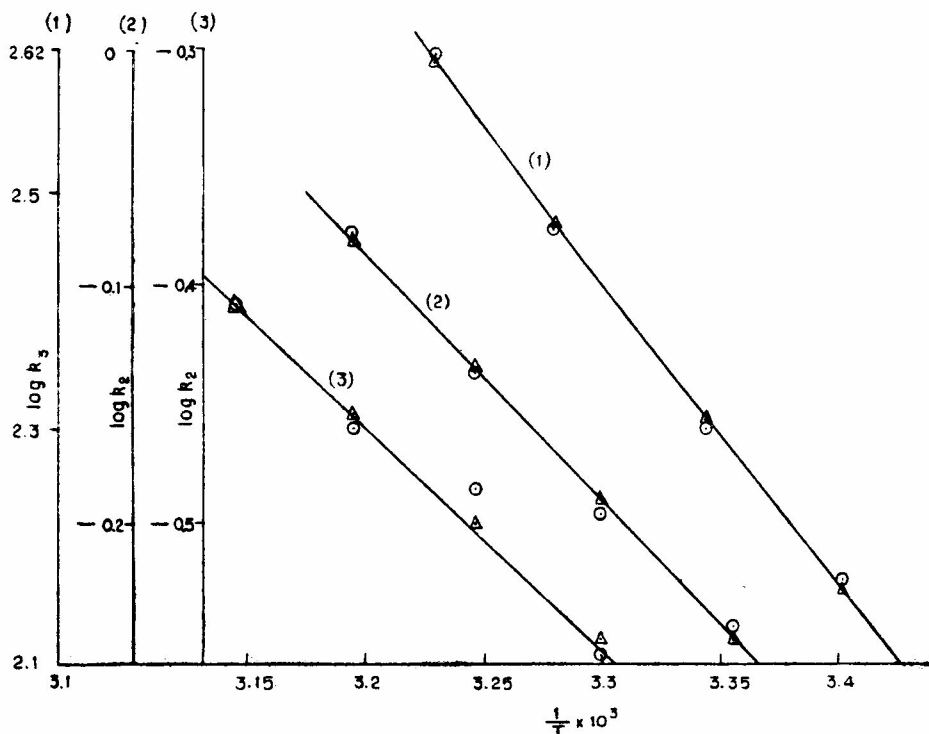| [TMA] $\times 10^3 M$	2.0	4.0	4.70	5.50	6.0	7.0
$k_1 \times 10^3$ (sec^{-1})	0.86	1.75	1.98	2.49	2.82	3.24
$k_1/$[TMA] $\times 10$ (litre mol^{-1} sec^{-1})	4.3	4.37	4.21	4.54	4.70	4.63

Fig. 1 — Plots of logarithm of specific rate constants against reciprocal of absolute temperatures [(1) Thioglycollic acid; (2) thiolactic acid; and (3) thiomalic acid. ⊙, experimental points, and △, least square points]

TABLE 3 — KINETIC EXPRESSIONS AT CONSTANT [H⁺], ORDER WITH RESPECT TO [H⁺] AND ACTIVATION PARAMETERS OBTAINED IN THE OXIDATIONS OF SOME α-MERCAPTO ACIDS AND THEIR CORRESPONDING OXYGEN ANALOGUES

Acid	$-d$ [Cr(VI)]/dt	n	E (kcal mol⁻¹)	$-\Delta S^{\ddagger}$ (cal deg⁻¹ mol⁻¹)	Reference
Thioglycollic	k_3 [Cr(VI)] [TGA]²	0·2	11·4	15·6	This work
Thiolactic	k_2 [Cr(VI)] [TLA]	0·4	4·8	47·7	do
Thiomalic	k_2 [Cr(VI)] [TMA]	0·4	4·8	51·6	do
Glycollic	$\dfrac{kK \text{ [Cr(VI)] [GA]}}{1+K \text{ [GA]}}$	0·4	13·7	25·7	15
Lactic	k_2 [Cr(VI)] [LA]	1·0	8·4	37·3	16
Malic	k_2 [Cr(VI)] [MA]	1·0	8·3	37·3	16

n = order with respect to [H⁺]. GA, LA and MA denote glycollic, lactic and malic acids respectively. k and K denote disproportionation constant and equilibrium constant of 1:1 complex formed by the interaction of GA and Cr(VI) as follows: $GA + Cr(VI) \underset{K}{\overset{k}{\rightleftharpoons}} complex \rightarrow products.$

different mechanism seems to operate in the TGA oxidation. This is in agreement with the observations made earlier[15,16] in the oxidation of corresponding oxygen analogues such as lactic, malic and glycollic acids by chromic acid (Table 3). The activation parameters (Table 3) obtained in the oxidations of thiolactic and thiomalic acids are almost identical but the values are widely different for thioglycollic acid. This suggests that thioglycollic is oxidized by a different mechanism. However, a comparison of the magnitude of the last dissociation (RSH ⇌ RS⁻+H⁺) shows that pK values[13,14] are very high (10·64-10·67) and since disulphide is produced in excess substrate it is obvious that —SH group provides the reaction site. In solutions where an excess of Cr(VI) is present,

the stoichiometry is found to increase considerably with time. This indicates that further oxidation of the disulphides to give sulphoxides and sulphones² takes place. When Cr(VI) is added to excess substrate a readily distinguishable reddish brown colour appears rapidly and then disappears. Chromium(VI) has also been shown to form complexes with some sulphur compounds and evidence for Cr(VI)-sulphur bonding[17] has been demonstrated. The oxidation of TGA by chromic acid can be explained considering that 1:1 complex is formed by the interaction of TGA and HCrO₄⁻ followed by the reaction of 1:1 complex with another substrate molecule to give 1:2 complex in which two sulphur atoms are attached symmetrically on two sides of hexacoordinated Cr(VI). The 1:2 complex decom-

poses slowly to give two RS· radicals and Cr(IV) (Eq. 3) followed by the dimerization of free radicals to give disulphide. The existence of free radicals in the TGA oxidation has been proved by the polymerization of acrylamide. Chromium(IV) may disproportionate to give chromium(V) or react rapidly with Cr(VI) to give chromium(V). The latter reacts with another substrate to give RS⁺ which then reacts with RSH to give disulphide. Although in earlier reports[4,6,7] it has been pointed out that disulphide is formed by the radical dimerization, the formation of disulphide also by the reaction between RS⁺ and RSH cannot be totally ignored[2].

$$R-S-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{C}r}-S-R \rightarrow 2RS\cdot + Cr(IV) \qquad ...(3)$$
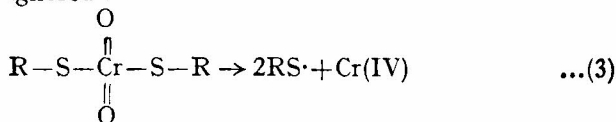
The intermediate 1:1 complexes which are formed with thiolactic and thiomalic acids readily decompose to give RS⁺ and Cr(IV) (Eq. 4) followed by the reaction of RS⁺ and RSH to give disulphide as mentioned earlier. It may be mentioned that the oxidation of TLA and TMA does not involve free radicals.

$$R-S-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{C}r}-OH \rightarrow RS^+ + Cr(IV) \qquad ...(4)$$
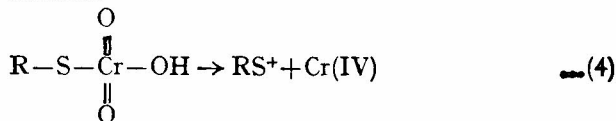
The entropies of activation obtained in the cases of thiolactic and thiomalic acids are well within the values for many bimolecular reaction[18]. On the other hand, much lower negative entropy of activation for the oxidation of TGA suggests that the reaction takes place by a different mechanism.

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