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OXIDATION OF DL-METHIONINE (2-AMINO-4-METHYLTHIOBUTANOIC ACID) BY CHROMATE. MECHANISTIC INTERPRETATION ON THE BASE OF AN ONE-PLUS RATE EQUATION

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ABSTRACT. The “one-plus” rate equation is an useful tool for interpreting reaction mechanisms. The kinetic study of the oxidation of 2-amino-4-methylthiobutanoic acid (methionine) by chromate has been undertaken. The reaction obeys a “one-plus” rate law. In order to suggest a reaction mechanism, the interference of kinetic along with extra-kinetic proofs was taken into consideration. The reaction starts with a pre-equilibrium to form an intermediate from the substrate and the reactant. This step is followed by the rate determining electron-transfer process. The influence of the organic substrate and hydrogen ion concentrations was deduced from the kinetic data.

Keywords: one-plus rate law, chromate, methionine, reaction mechanism

Introduction

Each kinetic study implies the measurement of reaction rates as well as the compilation of an *empirical power-law rate equation* from extensive experimental results over a wide range of conditions. Most reactions of practical interest are multistep processes and therefore do not proceed by simple pathways. They do not obey always power-law rate equations and thus have no exact and constant reaction orders[1-5]. Hence, a traditional power-law with empirical fractional exponents cannot be expected to result from combinations of elementary steps. In contrast, “one-plus” rate equations may result from step combinations; they contain integer exponents and are therefore more likely to reflect the true mechanism[1]. Therefore, the phenomenological rate coefficients are combinations of those of the elementary steps involved in the network[1-5].

An example (see equations 1 to 7), based on literature survey as well as on experimental studies of our group, concerns the oxidation of inorganic and organic thio-derivatives by chromate[6-12]. A general mechanism for the reaction of chromium(VI) with thiols involves the formation of a chromium(VI)-thioester (reaction step 1) followed either by the redox decomposition of this intermediate (an uni-equivalent step – see process 3) or its redox reaction with a second molecule of thiocompound (a bi-equivalent step – see process 2):

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$$RSH + HCrO_4^- \rightleftharpoons RSCrO_3^- + H_2O \qquad k_1,k_{-1} \quad (1)$$

$$RSCrO_3^- + RSH \longrightarrow Cr(IV) + RSSR \qquad k_2 \quad (2)$$

$$RSCrO_3^- \longrightarrow Cr(V) + RS\bullet \qquad k_3 \quad (3)$$

These are followed by several potentially fast steps:

$$2\ RS\bullet \longrightarrow RSSR \qquad (4)$$

$$2\ RSH + Cr(V) \longrightarrow RSSR + Cr(III) \qquad (5)$$

$$Cr(IV) + Cr(VI) \longrightarrow 2\ Cr(V) \qquad (6)$$

$$Cr(IV) + RSH \longrightarrow RS\bullet + Cr(III) + H^+ \qquad (7)$$

These processes were assumed on the base of extra-kinetic proofs (free-radical and Cr(V) identification)[6-8] as well as to justify the reaction stoichiometry. Cr(V) seems to be a tetra-coordinated (or even a penta- or hexa-coordinated) species, that is a hypochromic acid reacting likewise to Cr(VI). On the other hand, Cr(IV) is a labile hexa-coordinated compound[13,14]. When the thioester is formed rapidly and in significant concentration in the pre-equilibrium (1) than: $[RSCrO_3^-]/[Cr^{VI}]_t = K[RSH]/(1+K\ [RSH])$, where $K = k_1/k_{-1}$. Hence, the overall rate law will be of the “one-plus” form below:

$$-\frac{d[Cr^{VI}]}{dt} = \frac{k_2K[RSH]^2 + k_3K[RSCrO_3^-]}{1+K[RSH]}[Cr^{VI}] \qquad (8)$$

It has two limiting forms corresponding to the cases when either the second-order (k_2) or the first-order (k_3) process prevails. In such cases substantial spectral evidence has been found to support the assumption of the thioester formation[5-12]. The latter situation has been found in the case of benzene-thiol and α-toluenethiol oxidation in acetic acid[11]. Here the uniequivalent step prevails, yet the rate law is still of the “one-plus” form:

$$-\frac{d[Cr^{VI}]}{dt} = \frac{k_3K[RSH]}{1+K[RSH]}[Cr^{VI}] \qquad (9)$$

In the case of S-methylcysteine or other disulphides, the bi-equivalent oxidation yields sulfoxide and the rate law is also of the form (8)[15-16].

EXPERIMENTAL

Employed chemicals were of guaranteed reagent grade purity, purchased from commercial sources (*Merck*, *Aldrich*, *Fluka* and *Reanal*) and used without further purification. All solutions were prepared in demineralised and tetra-distilled water.

The advance of the reaction was followed by spectrophotometrical means at 350 nm, a wavelength at which the oxidizing agent exhibits a characteristic absorption band in acidic solutions. A Jasco V-530 spectrophotometer (Japan) with a controlled-temperature cell holder as well as computerised kinetic data acquisition has been used. The reaction was initiated directly in the measurement cell by injecting the chromate solution over a mixture of the other reactants. Absorbance was recorded as a function of reaction time. The acidity and ionic strength were maintained constant by means of $HClO_4$ excess and $NaClO_4$, respectively. The temperature was controlled by means of a Lauda M-20 circulation bath. Other experimental details are also presented elsewhere[17]. At least three replicate runs were performed for each set of experimental conditions.

RESULTS AND DISCUSSION

The stoichiometry of the reaction was established by colorimetric measurements. Various reaction mixtures in acidic media, having increasing molar ratios, were allowed to react to completion (for at least 10 half times) and the remaining absorbance due to unreacted chromate was recorded at 350 nm. At excess concentration of methionine, larger than 1.5 times that of Cr(VI), the entire amount of the oxidising agent Cr(VI) is completely consumed and residual absorbencies remain small and constant. This fact suggests that the oxidised product is the corresponding sulfoxide. Even with strong oxidizing agents as peroxyanions (peroxydisulfate and peroxydiohosphate), the oxidation product was sulfoxide in the case of alkyl aryl sulphide[18] or diphenylsulfide[19].

Hence, we concluded that Cr(VI) and methionine react by a ratio of 1/1.5, so that we assumed the following overall reaction:

$$\begin{aligned} &2\,HCrO_4^- + 3\,HOOCCH(NH_2)CH_2CH_2SCH_3 + 8\,H^+ \rightarrow \\ &2\,Cr^{3+} + 3\,HOOCCH(NH_2)CH_2CH_2SOCH_3 + 5\,H_2O \end{aligned} \tag{10}$$

Kinetic experiments were carried out at various concentrations of methionine (always in large excess), at constant acidity as well as at various $HClO_4$ concentrations and constant excess of methionine. These conditions ensure pseudo-first order rate laws with respect to the coloured species. Therefore, plots of $ln(A - A_\infty)$ *vs* reaction time were linear over a large degree of reaction extent with very good correlation coefficients (0.9935 - 0.9999). A_∞ stands for the remaining absorbance at completion. Both the linearity of the plots and the identical first-order rate constants we have obtained with three different initial chromate concentrations (as limiting reagent) confirm the first-order dependence with respect to the oxidizing coloured species.

The apparent first-order rate coefficient (k_{obs}) depends upon the substrate and mineral acid concentration. By increasing the concentration of the substrate, increased first-order rate constants were measured as the slopes of semi-logarithmic plots (see results in Table 1). By plotting *lg* k_{obs} *vs lg* [Meth] to determine the reaction order with respect to methionine, a line (R = 0.9914) with a slope of 0.85 was found. This fractional order can be rationalised by the following rate equation (similar to 9):

$$-\frac{d[Cr^{VI}]}{dt}=\frac{k'[Meth]}{1+k''[Meth]}[HCrO_4^-] \tag{11}$$

Table 1.

First-order rate constants as a function of methionine concentration at 298±0.1K, $\mu = 0.34$, $[HCrO_4^-] = 1.00\times10^{-4}$ and $[HClO_4] = 8.50\times10^{-2}$ and as a function of the acid concentration at $[Meth]=7.50\times10^{-2}$, respectively. Each listed value is the mean of three replicate runs.

10^2[Meth]	10^3 k_{obs} (s^{-1})	[H^+]	10^3 k_{obs} (s^{-1})
0.38	0.76	0.042	0.59
0.56	1.12	0.085	1.23
0.75	1.23	0.128	1.69
0.94	1.83	0.170	3.11
1.13	2.02	0.191	3.45
1.50	2.31	0.213	3.73
1.88	2.97	0.255	4.73
2.25	3.57	0.298	6.62
2.50	3.75		

Rate equation (11) is similar to equation (9) that is of the “one-plus” form. If a linearization of the type (4) is used with all the data, such as follows,

$$\frac{1}{k_{obs}}=\frac{k''}{k'}+\frac{1}{k'}\frac{1}{[Meth]}\ ;\quad \frac{1}{k_{obs}}=(90\pm16)+(4.7\pm0.2)\frac{1}{[Meth]} \tag{12}$$

a good fit has been obtained (R = 0.9917). On the other hand, the reaction order with respect to hydrogen ions is of 1.22 (R = 0.9908). It may be interpreted in two ways: either by a parabolic dependence corresponding to two parallel reaction paths in which one is of first-order and the other of second-order with respect of [H^+] (see equation 13*a*), or by a dependence of the “one-plus” form (13*b*):

$$\text{(a)}\ k_{obs}=a[H^+]+b[H^+]^2\ ;\qquad \text{(b)}\ k_{obs}=\frac{c[H^+]^2}{1+d[H^+]} \tag{13}$$

Where *a,b,c* and *d* stand for some constants. If the first alternative were true, than, according to the linear form of equation (13*a*) $k_{obs}/[H^+]=a+b[H^+]$, the plot $k_{obs}/[H^+]\ vs\ [H^+]$ should result in line with good correlation coefficients. The results were: *a* = 12.1 L $mole^{-1}s^{-1}$, *b* = 29.2 L^2 $mole^{-2}s^{-1}$ and R = 0.8360. This correlation coefficient is quite poor. On the other hand, the second alternative can be proved by its linear form that gave a better fit (R = 0.9536):

$$\frac{[H^+]^2}{k_{obs}} = \frac{1}{c} + \frac{d}{c}[H^+] \qquad \frac{[H^+]^2}{k_{obs}} = (2.6 \pm 0.5) + (42 \pm 3)[H^+] \qquad (14)$$

The intercept *1/c* (see equation 14) is expressed in $L^2mole^{-2}s$ and the slope *d/c* in $L^3mole^{-3}s$, respectively. Therefore, we assume that the second alternative describes adequately the involvement of the hydrogen ion concentration. By taking into consideration both the influences of methionine and hydrogen ion concentrations, two rate laws may be written: one that contains separate terms for [Meth] and [H^+] (see equation 15) and another that dependens on the product [Meth][H^+] (see equation16):

$$-\frac{d[Cr^{VI}]}{dt} = \frac{k_a[Meth][H^+]^2[HCrO_4^-]}{1 + k_b[Meth] + k_c[H^+]} \qquad (15)$$

$$-\frac{d[Cr^{VI}]}{dt} = \frac{k_a^{'}[Meth][H^+]^2[HCrO_4^-]}{1 + k_b^{'}[Meth][H^+]} \qquad (16)$$

Rate law (15) would correspond to two independent pre-equilibria, while rate law (16) to two coupled equilibria or an overall equilibrium involving chromate, methionine as well as the hydrogen ion. The apparent first-order rate coefficient in equations (15) and (16) can be transposed into linear forms by taking the reciprocals and should therefore hold with both series of measurements. If the linear form of the apparent first-order rate coefficient of law (15) is considered while either [*Meth*] or [*H^+*] are held at constant values, the plots do not fit a line although the reproducibility of the experiments is quite good. This is true especially when [H^+]/k_{obs} is plotted as a function of 1/[H^+]. On the other hand, if we assumed that a coupled equilibria takes place, the linear form of k_{obs} as expressed from rate law (16) – see equations (17) – has a good correlation coefficient of 0.9917. Figure 1 presents the plot of equation (17) and proves the statement above.

$$\frac{[H^+]}{k_{obs}} = \frac{k_b^{'}}{k_a^{'}} + \frac{1}{k_a^{'}}\frac{1}{[Meth][H^+]}; \qquad \frac{[H^+]}{k_{obs}} = (7.6 \pm 1.3) + \frac{(3.4 \pm 0.1)10^{-2}}{[Meth][H^+]} \qquad (17)$$

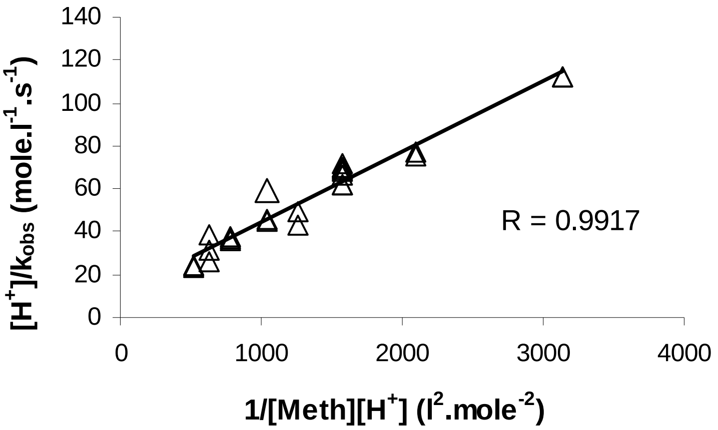

Figure 1. The plot of equation (17) with data presented in table 1.

An attempt to use this reaction system to initiate polymerization of ethylacrylate failed. This fact suggests that the reaction mechanism does not involve free radicals.

In view of the above discussion, the reaction scheme for the Cr(VI) oxidation of methionine involves the formation of an adduct by hydrogen ion. The adduct further suffers the electron and atom redistribution to yield sulfoxide and Cr(IV) during the rate determining step. This step also occurs with the assistance of hydrogen ions. Either the chromate acid or a conjugated acid of methionine will further react with the partner to form the intermediate adduct. No discrimination by kinetic experiments is possible between the two alternative pre-equilibria (18) and (19):

$$HCrO_4^- + H^+ \rightleftharpoons H_2CrO_4 \qquad K_1^{'} \qquad (18)$$

$$H_2CrO_4 + R-SCH_3 \rightleftharpoons \text{Adduct} \qquad K_2^{'} \qquad (18')$$

$$R-SCH_3 + H^+ \rightleftharpoons [RSHCH_3]^+ \qquad K_1^{''} \qquad (19)$$

$$[RSHCH_3]^+ + HCrO_4^- \rightleftharpoons \text{Adduct} \qquad K_2^{''} \qquad (19')$$

The two coupled equilibria can be written as an overall one with K = $K_1^{'} K_2^{'}$(or $K_1^{''} K_2^{''}$):

$$R-SCH_3 + H^+ + HCrO_4^- \rightleftharpoons \text{Adduct} \qquad K \qquad (20)$$

This will be followed by the electron transfer and the S=O double bond formation in the rate determining step:

$$\text{Adduct} + \text{H}^{+} \longrightarrow \text{R}-\text{SOCH}_3 + \text{Cr(IV)} \qquad k \qquad (21)$$

The process continues by potentially rapid steps of the type (6) and (7). With other words, Cr(V) may be obtained. It can also oxidize methionine to the corresponding sulfoxide.

The rate law deduced form this reaction scheme - by using the pre-equilbrium assumption - is of the form (16) in which $k_a^{'}$ = kK = (29.4 ± 0.8) $L^3mol^{-3}s^{-1}$ and $k_b^{'}$ = K = $(2.24 \pm 0.45) \cdot 10^2$ L^2mole^{-2}. A second-order rate constant k = $(1.31 \pm 0.23) \cdot 10^{-1}$ L $mole^{-1}s^{-1}$ for the rate determining step was computed under the employed experimental conditions.

CONCLUSIONS

The experimental kinetic data obey a typical “one-plus” rate law, with integer exponents. A pre-equilibrium involving the oxidant and the organic substrate is present. The bi-equivalent electron-transfer is the rate-determining step. In acidic media, the involvement of hydrogen ion favours the redox reaction. Phenomenological rate coefficients and some intermediate formation constants could be calculated. The data fit well with the rate law expressed from the proposed reaction scheme, thus supporting the suggested mechanism.

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