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Kinetic and Mechanistic Study of the Oxidative Deamination and Decarboxylation of *L*-Valine by Alkaline Permanganate

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Summary. The kinetics of the oxidation of *L*-valine, (*L*-Val) by permanganate in aqueous alkaline medium at a constant ionic strength of $0.50\,\mathrm{mol \cdot dm^{-3}}$ was studied spectrophotometrically. The reaction is of first order in [permanganate ion] and of fractional order in both [*L*-Val] and [alkali]. Addition of products has no significant effect on the reaction rate. However, increasing ionic strength and decreasing dielectric constant of the medium increase the rate. The oxidation process in alkaline medium has been shown to proceed *via* two paths, one involving the interaction of *L*-valine with permanganate ion in a slow step to yield the products, and the other path the interaction of alkali with permanganate ion to give manganate. Some reaction constants involved in the mechanism were determined; calculated and observed rate constants agree excellently. The activation parameters were computed with respect to the slow step of the mechanism.

Keywords. Kinetics; Oxidation; *L*-Valine; Activation parameters.

Introduction

Oxidation with permanganate has found extensive application in organic syntheses [1–7], especially after the advent of phase transfer catalysis [3, 4, 6] which permits the use of solvents like dichloromethane and benzene. The manganese chemistry involved in these multistep redox reactions is an important source of information as the manganese intermediates are relatively easy to identify when they have sufficiently long life times. In strongly alkaline medium, the stable reduction product of permanganate is the manganate ion, MnO_4^{2-} [8]. No mechanistic information is available allowing to distinguish between a direct one electron reduction to manganese (VI) (Scheme 1) or the prior formation of hypomanganate in a two electron step followed by a fast reaction (Scheme 2).

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$$\mathrm{Mn(VII)} + S \xrightarrow{k'_1} \mathrm{Mn(VI)} + S^{\cdot}$$
$$\mathrm{Mn(VII)} + S^{\cdot} \xrightarrow{k'_2} \mathrm{Mn(VI)} + \mathrm{Products}$$
$$(S = \text{substrate}, k'_2 \gg k'_1)$$

Scheme 1

$$\mathrm{Mn(VII)} + S \xrightarrow{k'_3} \mathrm{Mn(V)} + \mathrm{Products}$$
$$\mathrm{Mn(VII)} + \mathrm{Mn(V)} \xrightarrow{k'_4} 2\mathrm{Mn(VI)}$$
$$(S = \text{substrate}, k'_4 \gg k'_3)$$

Scheme 2

Amino acids have been oxidised by a variety of oxidants [9] leading to different products [10]; the dependence of the behaviour of amino acids towards the oxidant is of importance because of their biological significance.

A variety of organic [11] and inorganic [8] substrates are oxidized by permanganate in aqueous alkaline medium. However, there are only a few reports on the oxidation of amino acids by aqueous alkaline permanganate [12]. Although the oxidation of *rac*-serine by alkaline permanganate has been studied recently [12], the behaviour of *L*-valine towards the same reagent is of interest to verify nature of the active species, the actual site of oxidation, changes in mechanism, *etc*.

Results and Discussion

Reaction order

The reaction orders were determined from the slopes of $\log k_{\mathrm{obs}}$ *vs*. log *c* plots by varying the concentration of oxidant, reductant, and alkali in turn while keeping the others constant. The potassium permanganate concentration was varied in the range of 5.0×10^{-5} to $5.0 \times 10^{-4}\,\mathrm{mol\cdot dm^{-3}}$, and the linearity of plots of $\log[\mathrm{MnO_4^-}]$ *vs*. time indicates an order of 1 in $[\mathrm{MnO_4^-}]$. This was confirmed by the fact that variation of $[\mathrm{MnO_4^-}]$ did not influence the *pseudo*-first-order rate constants (Table 1). [*L*-Val] was varied in the range of 5.0×10^{-4} to $5.0 \times 10^{-3}\,\mathrm{mol\cdot dm^{-3}}$ at 27°C; the order with respect to [*L*-Val] was found to be less than unity (Table 1).

Effect of initially added products

Initially added reaction products, such as manganate, aldehyde, and ammonia, did not show any significant effect on the rate of the reaction.

Effect of alkali

The effect of alkali on the reaction was studied at constant concentrations of *L*-valine and potassium permanganate, $I = 0.50\,\mathrm{mol\cdot dm^{-3}}$, and 27°C. The rate constants increased with increasing $[\mathrm{OH^-}]$ (Table 1).

Table 1. Effects of [*L*-valine], [MnO_4^-], and [OH^-] on the oxidation of *L*-valine by permanganate in aqueous alkaline medium at 27°C ($I = 0.5\,mol \cdot dm^{-3}$)

$\frac{[L\text{-Val}] \times 10^3}{mol \cdot dm^{-3}}$	$\frac{[MnO_4^-] \times 10^4}{mol \cdot dm^{-3}}$	$\frac{[OH^-]}{mol \cdot dm^{-3}}$	$\frac{k_{obs} \times 10^3}{s^{-1}}$	
			Expt.	Calcd.[a]
0.5	2.0	0.3	0.49	0.50
1.0	2.0	0.3	0.76	0.70
2.0	2.0	0.3	1.15	1.10
3.0	2.0	0.3	1.70	1.51
5.0	2.0	0.3	2.60	2.32
2.0	0.5	0.3	1.15	1.10
2.0	1.0	0.3	1.15	1.10
2.0	2.0	0.3	1.15	1.10
2.0	3.0	0.3	1.15	1.10
2.0	5.0	0.3	1.15	1.10
2.0	2.0	0.05	0.32	0.32
2.0	2.0	0.10	0.56	0.55
2.0	2.0	0.20	0.82	0.85
2.0	2.0	0.30	1.15	1.10
2.0	2.0	0.50	1.54	1.45

[a] Calculations of rate constants are performed on the basis of Eq. (2) using $5.14\,dm^3 \cdot mol^{-1}$, $0.66\,dm^3 \cdot mol^{-1} \cdot s^{-1}$, and $1.0 \times 10^{-3}\,dm^3 \cdot mol^{-1} \cdot s^{-1}$ for K, k_1, and k_2, respectively

Effect in ionic strength and solvent polarity

The effect of ionic strength was studied by varying the sodium perchlorate concentration from 0.3 to $2.0\,mol \cdot dm^{-3}$ at constant concentrations of permanganate, *L*-valine, and alkali. It was found that the rate of reaction increased with increasing concentration of $NaClO_4$; the plot of $\log k_{obs}$ *vs.* $I^{1/2}$ is linear with a positive slope (Fig. 1).

The relative permittivity effect was evaluated by variation of the *t*-butanol content while keeping all other conditions constant. Attempts to measure the relative permittivities failed; however, they were computed from the values of pure liquids as in Ref. [13]. There was no reaction of the solvent with the oxidant. The rate constants k_{obs} increase with decreasing dielectric constant of the medium, and the plot of $\log k_{obs}$ *vs.* $1/D$ is linear (Fig. 1).

Test for free radicals

The intervention of free radicals was examined as follows. The reaction mixture, to which a known quantity of acrylonitrile scavenger had been added initially, was kept in an inert atmosphere for one hour. Upon diluting the reaction mixture with methanol, a precipitate resulted, suggesting the participation of free radicals in the reaction.

The permanganate ion is a powerful oxidant in aqueous alkaline medium. As it exhibits a multitude of oxidation states, the stoichiometric results and the *pH* of

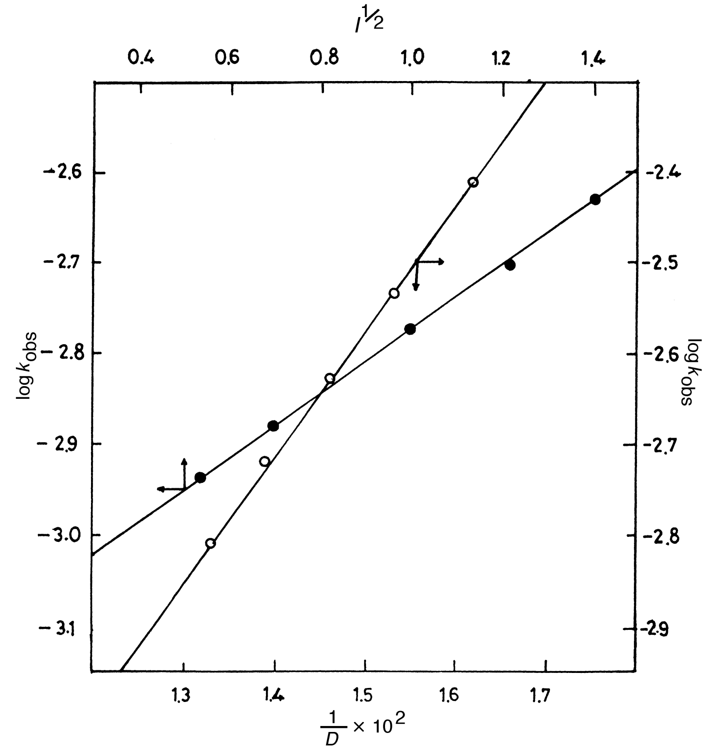
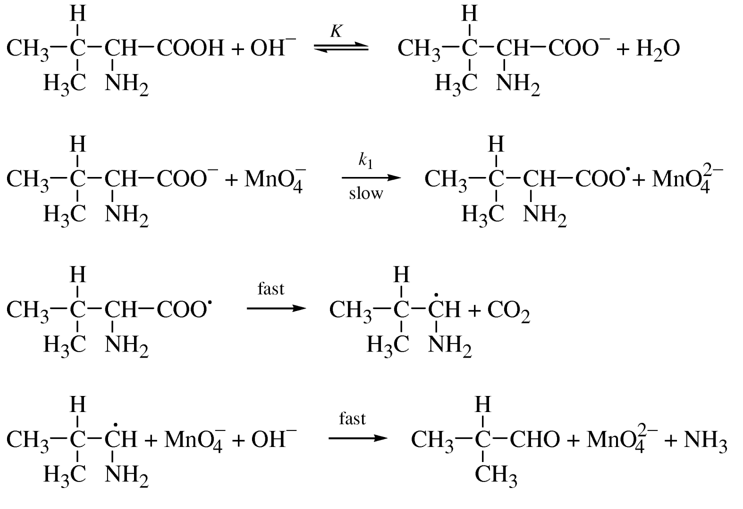


Fig. 1. Plot of $\log k_{obs}$ *vs.* $I^{1/2}$ and $\log k_{obs}$ *vs.* $1/D$

reaction media play a significant role. Diode array rapid scan spectrophotometer (DARSS) studies have shown that at $pH > 12$ the product of the reaction of Mn(VII) is Mn(VI), and no further reduction was observed [8]. However, upon prolonged standing Mn(VI) is slowly reduced to Mn(IV).

Path I

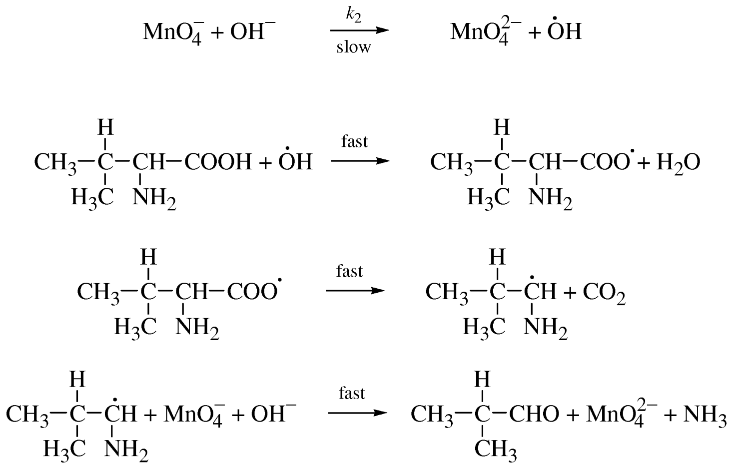


$$CH_3-\overset{H}{\underset{H_3C}{C}}-\underset{NH_2}{CH}-COOH + OH^- \overset{K}{\rightleftharpoons} CH_3-\overset{H}{\underset{H_3C}{C}}-\underset{NH_2}{CH}-COO^- + H_2O$$

$$CH_3-\overset{H}{\underset{H_3C}{C}}-\underset{NH_2}{CH}-COO^- + MnO_4^- \xrightarrow[\text{slow}]{k_1} CH_3-\overset{H}{\underset{H_3C}{C}}-\underset{NH_2}{CH}-COO^{\bullet} + MnO_4^{2-}$$

$$CH_3-\overset{H}{\underset{H_3C}{C}}-\underset{NH_2}{CH}-COO^{\bullet} \xrightarrow{\text{fast}} CH_3-\overset{H}{\underset{H_3C}{C}}-\underset{NH_2}{\dot{C}H} + CO_2$$

$$CH_3-\overset{H}{\underset{H_3C}{C}}-\underset{NH_2}{\dot{C}H} + MnO_4^- + OH^- \xrightarrow{\text{fast}} CH_3-\overset{H}{\underset{CH_3}{C}}-CHO + MnO_4^{2-} + NH_3$$



Path II

Scheme 3

The reaction between permanganate and *L*-valine in alkaline medium has a stoichiometry of 2:1 with fractional order on alkali and *L*-valine concentrations and first order on permanganate concentration. The observed kinetic and other results may be explained by a mechanism proceeding *via* two pathways, one of which depends on substrate concentration, whereas the other does not (Scheme 3).

The observed fractional order in alkali concentration may be due to the existence of *L*-valine in its anionic form in alkaline medium [14]. This anionic form will react with MnO_4^- under decarboxylation in a slow step, giving a radical of *L*-valine which reacts further with another molecule of permanganate in a fast step to afford the products. Since permangante is a one-electron oxidant in alkaline medium, the reaction between substrate and oxidant would give rise to a radical intermediate as indicated by a free radical scavenging experiment. This type of radical intervention in the oxidation of amino acids has also been observed earlier [12].

The combined rate law is given by Eqs. (1) and (2):

$$-\frac{\mathrm{d}[\mathrm{MnO_4^-}]}{\mathrm{dt}} = \frac{K \cdot k_1 \cdot [\mathrm{MnO_4^-}] \cdot [\mathrm{L-Val}] \cdot [\mathrm{OH^-}]}{1 + K \cdot [\mathrm{OH^-}]} + k_2 \cdot [\mathrm{MnO_4^-}] \cdot [\mathrm{OH^-}] \qquad (1)$$

$$k_{\mathrm{obs}} = \frac{K \cdot k_1 \cdot [\mathrm{L-Val}] \cdot [\mathrm{OH^-}]}{1 + K \cdot [\mathrm{OH^-}]} + k_2 \cdot [\mathrm{OH^-}] \qquad (2)$$

According to Eq. (2), a plot of k_{obs} *vs.* [*L*-valine] gave a better correlation than a reciprocal plot (Fig. 2). From intercept of the linear plot, the value of k_2 was obtained as $1.0 \times 10^{-3}\,\mathrm{dm^3 \cdot mol^{-1} \cdot s^{-1}}$.

Rearrangement of Eq. (2) leads to

$$\frac{1}{k_{\mathrm{obs}} - k_2 \cdot [\mathrm{OH^-}]} = \frac{1}{K \cdot k_1 \cdot [L - \mathrm{Val}] \cdot [\mathrm{OH^-}]} + \frac{1}{k_1 \cdot [L - \mathrm{Val}]} \qquad (3)$$

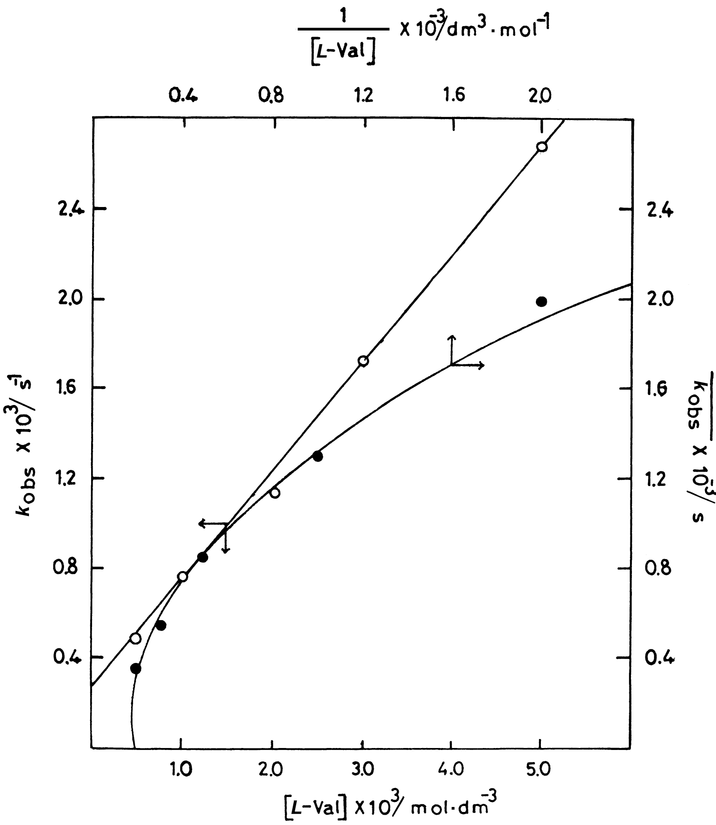


Fig. 2. Plot of k_{obs} *vs.* [*L*-valine] and $1/k_{obs}$ *vs.* 1/[*L*-valine] (conditions as in Table 1)

According to Eq. (3), a plot of $1/k_{obs} - k_2[OH^-]$ *vs.* $1/[OH^-]$ is expected to be linear (Fig. 3). Intercept and slope of this plot lead to $k_1 = 0.66 \pm 0.03\,dm^3 \cdot mol^{-1} \cdot s^{-1}$ and $K = 5.14 \pm 0.25\,dm^3 \cdot mol^{-1}$ at 27°C. These values were used to calculate the rate constants under different experimental conditions. There is a reasonable agreement between the calculated and observed rate constants (Table 1); the value of k_2 thus obtained agrees with earlier investigations [15].

Effect of temperature

The rate constants (k_1 and k_2) of the slow steps of Scheme 3 were obtained from the intercepts of plots of k_{obs} *vs.* [*L*-valine] and $1/k_{obs} - k_2[OH^-]$ *vs.* $1/[OH^-]$ at different temperatures and used to calculate the activation parameters. The values of k_1 are 0.66, 1.0, 1.34, and 1.99 $dm^3 \cdot mol^{-1} \cdot s^{-1}$, those of k_2 1.0×10^{-3}, 1.66×10^{-3}, 2.33×10^{-3}, and $3.20 \times 10^{-3}\,dm^3 \cdot mol^{-1} \cdot s^{-1}$ at 27, 32, 37, and 42°C, respectively. Two sets of activation parameters (for Path I and Path II of Scheme 3) corresponding to these constants were evaluated from the plots of log(k_1 or k_2) *vs.* $1/T$ (Table 2).

The effect of increasing ionic strength on the rate of reaction explains qualitatively the reaction between two negatively charged ions (Scheme 3). However, increasing the content of *t*-butanol in the reaction medium leads to an increase of the

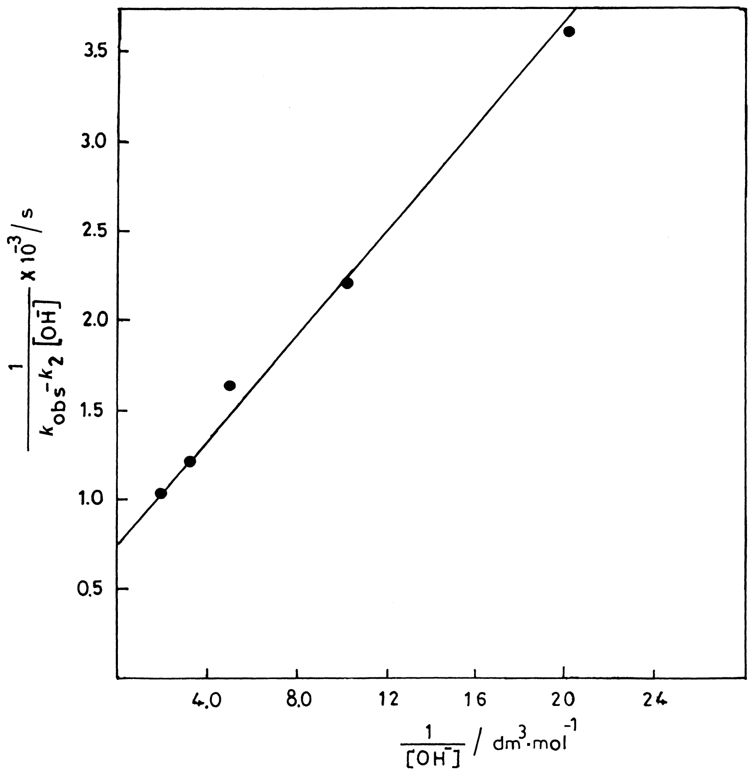


Fig. 3. Plot of $\frac{1}{k_{obs} - k_2[OH^-]}$ *vs.* $\frac{1}{[OH]^-}$ (conditions as in Table 1)

Table 2. Activation parameters for the oxidation of *L*-valine by alkaline permanganate with respect to the slow step of the reaction (Scheme 3)

Activation parameters	Path I	Path II
E_a/kJ · mol^{-1}	42 ± 4	51 ± 5
log*A*	9.6 ± 3.0	7.6 ± 2.0
$\Delta H^{\#}$/kJ · mol^{-1}	40 ± 3	48.6 ± 4.0
$\Delta S^{\#}$/J · K^{-1} · mol^{-1}	-116 ± 6	-140 ± 7
$\Delta G^{\#}$/kJ · mol^{-1}	75 ± 4	90 ± 4

reaction rate, which is contrary to the expected slower reaction between ions of the same polarity in media of lower relative permittivity. Perhaps the effect is opposed substantially by an increased formation of active reaction species in low-permittivity media, thus leading to the observed net increase in the rate [16]. The values of $\Delta S^{\#}$, within the range for radical reactions, have been ascribed to the nature of electron pairing and unpairing processes and to the loss of degrees of freedom formerly available to the reactands upon the formation of a rigid transition state [17].

It is interesting to note that the oxidant species [MnO_4^-] requires $pH > 12$; at lower values, the system gets disturbed, and the reaction proceeds further to give a reduced product of the oxidant, Mn(IV), which slowly, develops yellow turbidity. Thus, the role of *pH* is crucial in this reaction. It is also noteworthy that under the conditions studied the reaction occurs in two successive one-electron reductions (Scheme 3) rather than as a two-electron reduction in a single step (Scheme 2).

Experimental

Materials

Series of stock solutions of *L*-valine (Sisco-Chem. Ltd.) and $KMnO_4$ (BDH) were prepared by dissolving the appropriate amounts of samples in doubly distilled water. The stock solution of $KMnO_4$ was standardized against oxalic acid [18]. K_2MnO_4 solution was prepared as described in Ref. [19] as follows: A solution of $KMnO_4$ was heated to boiling (above 120°C) in an aqueous 8.0 M KOH solution until a green colour developed. The solid K_2MnO_4 formed upon cooling was recrystallized from the same solvent. The stock solution of K_2MnO_4 was prepared in aqueous potassium hydroxide. The solution was standardized by measuring its absorbance using a Hitachi 150–20 spectrophotometer with a 1 cm cell at 608 nm ($\varepsilon = 1530 \pm 20\,\mathrm{dm^3 \cdot mol^{-1} \cdot cm^{-1}}$). All other reagents were of analytical grade purity, and their solutions were prepared by dissolving the required amounts of sample in doubly distilled conductivity water. NaOH and $NaClO_4$ were used to provide the required alkalinity and to maintain the correct ionic strength, respectively.

Kinetic measurements

All kinetic measurements were performed under *pseudo*-first-order conditions with [*L*-valine]:$[MnO_4^-] \geq 10{:}1$ at a constant ionic strength of $0.5\,\mathrm{mol \cdot dm^{-3}}$. The reaction was initiated by mixing previously thermostatted solutions of MnO_4^- and *L*-valine which also contained the required quantities of NaOH and $NaClO_4$ to maintain the required alkalinity and ionic strength. The temperature was kept at 27 ± 0.1°C. The progress of the reaction was followed by monitoring the decrease in the absorbance of MnO_4^- in a 1 cm quartz cell of a Hitachi 150–20 spectrophotometer at 526 nm as a function of time. Preliminarily it was checked that there is negligible interference from other reagents at this wavelength. The application of *Beer*'s law for MnO_4^- at 526 nm had earlier been verified, giving $\varepsilon = 2083 \pm 50\,\mathrm{dm^3 \cdot mol^{-1} \cdot cm^{-1}}$ (Ref. [8]: $\varepsilon = 2200$). The first-order plots were linear up to 85% completion of the reaction in almost all cases, and k_{obs} were reproducible within ± 5%. In the course of the measurements the colour of the solution changed from violet to blue and further to green. The spectrum of the green solution was identical to that of MnO_4^{2-}. It was empirically found that the blue colour originated from a mixture of violet (MnO_4^-) and green (MnO_4^{2-}) rather than from the formation of hypomanganate. The formation of Mn(VI) was also evidenced by the decrease of the absorbance of Mn(VII) at 526 nm and the increase of that of Mn(VI) at 608 nm during the course of reaction (Fig. 4).

The effect of dissolved oxygen on the rate of reaction was checked by preparing the reaction mixture and following the reaction in an atmosphere of nitrogen. No significant difference between the results was observed. Added carbonate had no effect on the reaction rate.

Stoichiometry

The reaction mixtures containing an excess of permanganate over *L*-valine (see above) were mixed in the presence of 0.30 *M* NaOH adjusted to a constant ionic strength of $0.50\,\mathrm{mol \cdot dm^{-3}}$. After completion of the reaction, solid KI was added, followed by acidification by 10% H_2SO_4. The remaining MnO_4^- was then titrated against standard sodium thiosulfate [20]. The results indicated that two moles of MnO_4^- consumed one mole of *L*-valine (Eq. (4)). The main oxidation products

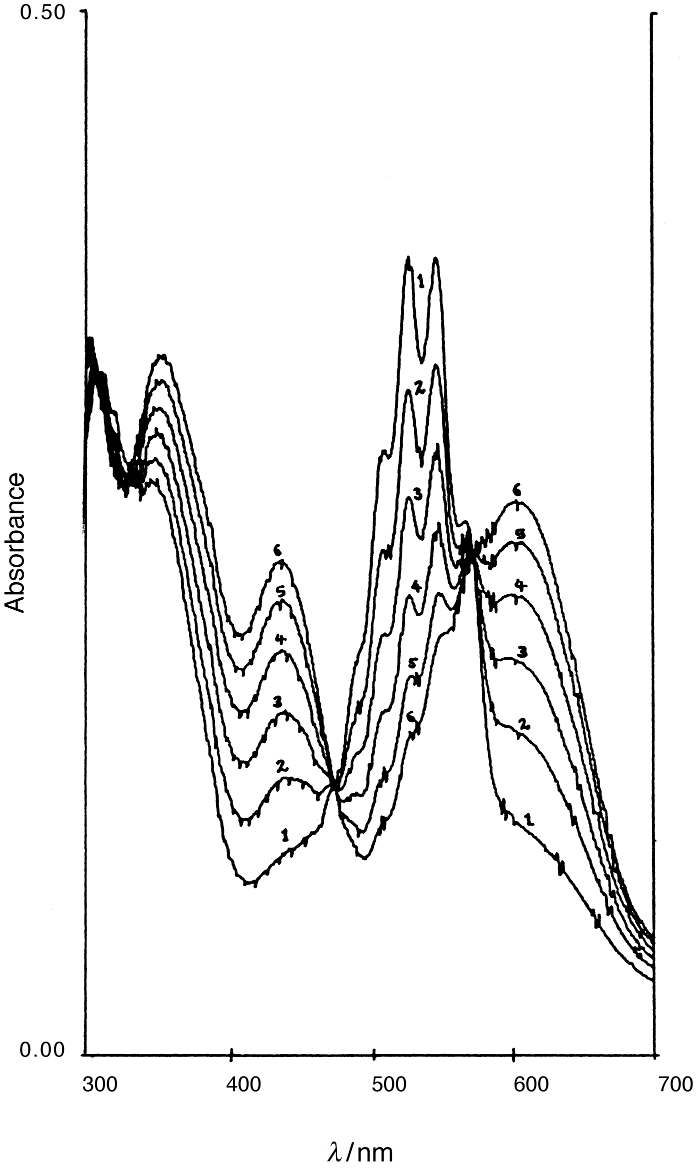


Fig. 4. Spectral changes during the oxidation of *L*-valine by alkaline permanganate; $[MnO_4^-] = 2 \times 10^{-4}$, [*L*-valine] $= 2 \times 10^{-3}$, $[OH^-] = 0.30, I = 0.5\,mol \cdot dm^{-3}$, scanning time interval 2.0 min, 27°C

were identified as isobutylaldehyde (spot test [21]), ammonia (*Nessler*'s reagent [22]), and MnO_4^{2-} (UV/Vis spectrum). CO_2 was qualitatively detected by bubbling N_2 gas through the acidified reaction mixture and passing the liberated gas through a tube containing lime water. The nature of the aldehyde was confirmed by recording its IR spectrum and by preparing its 2,4-*DNP* derivative. The IR spectrum showed a carbonyl stretching vibration at $1729\,cm^{-1}$ and a band at $2928\,cm^{-1}$ for aldehydic C-H stretching, thus confirming the presence of isobutylaldehyde. The aldehyde did not undergo further oxidation under the applied experimental conditions.

$$(CH_3)_2-CH-\underset{\displaystyle NH_2}{\underset{|}{CH}}-COOH + 2MnO_4^- + 2OH^- \longrightarrow (CH_3)_2-CH-CHO+CO_2+NH_3 \\ +2MnO_2^{2-}+H_2O \tag{4}$$

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