Kinetics and mechanism of oxidation of α-hydroxy acids by Fremy’s radical in aqueous acetate-buffer solution

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Oxidation of α-hydroxy acids, viz. glycolic, lactic and mandelic acids by potassium nitrosodisulphonate (PNDS) in aqueous acetate medium of pH 6.5 shows first order dependence on [PNDS] and fractional order dependence on (α-hydroxy acid). Under the experimental conditions PNDS has been found to be quite stable. However, the little self-decomposition of PNDS found on standing for longer periods has been prevented by the addition of sulphamate ion. Increase in ionic strength of the medium has no effect on the rate of oxidation. Decrease in dielectric constant of the medium increases the reaction rate. The absorption spectrum of PNDS in the presence of α-hydroxy acid shows a shift of λ_max by 10 nm indicating the formation of adduct between PNDS and hydroxy acid. The mechanism proposed involves, a fast pre-equilibrium step leading to the formation of an adduct. The adduct disproportionate in a slow rate-determining step generating an intermediate radical. This radical reacts with another molecule of PNDS yielding the product. The equilibrium constant (K) and disproportionation constant (k) are calculated from the derived rate law. The activation parameters for the disproportionation of the adduct and thermodynamic parameters for the formation of the adduct are calculated. Mandelic acid reacts faster than glycolic or lactic acids as a result of the stabilisation of the intermediate radical R – C(OH) – COOH.

Attempts to mimic the flavin catalysed oxidation of hydroxy acids to the corresponding α-keto acids by nonenzymatic means invariably produced oxidative decarboxylation in the chemical oxidation. Oxidation of α-hydroxy acids by a variety of oxidants like lead tetraacetate, vanadium(V), manganese(III) and permanganate in acid medium are reported to cleave the C–C bond resulting in their decarboxylation. In spite of this, oxidative methods for the preparation of α-keto acids from α-hydroxy acids have been developed, which avoid or at least reduce the magnitude of the undesirable decarboxylation. For example, ceric sulphate in sulphuric acid, permanganate in alkaline medium and pyridinium hydrobromide perbromide oxidizes α-hydroxy acids to the corresponding α-keto acids.

We have recently reported that Fremy’s radical selectively oxidises some phenols to 1,4-quinones by electron transfer reactions. In our attempt to fully evaluate the stability and oxidising power of PNDS, a one-electron oxidant, we report here in our findings on the kinetics of oxidation of α-hydroxy acids viz., glycolic, lactic and mandelic acids to the corresponding α-keto acids by PNDS in aqueous acetate buffer solution.

Experimental

All the chemicals used were of highest purity. Potassium nitrosodisulphonate (Fremy’s salt) (Sigma) was used as received. The solid sample was dessicated under ammonia atmosphere. The solutions of potassium nitrosodisulphonate (PNDS) were prepared in acetate buffer solutions of pH 8.0 just before use in the presence of sufficient concentration of the sulphamate (0.20 mol dm⁻³) to prevent chain reaction initiated by nitrous acid produced by self decomposition of Fremy’s radical. The solutions of PNDS were standardised by measuring the absorbance at 545 nm and using molar absorption coefficient value of 20.8 dm³ mol⁻¹ em⁻¹ (ref. 4).

Required volumes of the reactants, PNDS and α-hydroxy acid solutions were thermally equilibrated and mixed. The absorbance of reaction-mixture at regular intervals of time was recorded on Hitachi U 1000 spectrophotometer at 545 nm which was solely due to Fremy’s radical and there is no interference at this wavelength either by the reactants or the products. The initial rates were calculated from the plots of absorbance vs time (Fig. 1A) using a computer programme.

Stoichiometry and product analysis

The stoichiometric studies under the conditions [PNDS] > [α-hydroxy acid] revealed that one mole of α-hydroxy acid consumed two moles of PNDS. The products of oxidation, were identified as the corresponding keto acids by preparing the corresponding, 2,4-dinitrophenyl hydrazone derivatives, recrystallising them from ethanol and finding their melting points (202°, 215° and 192°C for glycolic, lactic and mandelic acid respectively)
Table 1—The disproportionation constant \(k\), formation constant \(K\), activation and thermodynamic parameters for PNDS-\(\alpha\)-hydroxy acid reactions in aqueous acetate buffer solution

\[
\begin{array}{cccccc}
\text{Glycolic acid} & k \times 10^4 & \Delta H^\circ & \Delta S^\circ & K & \Delta H^\circ \\
\text{Lactic acid} & 1.93 & 24.8 & -234 & 1.08 & 34.2 \\
\text{Mandelic acid} & 5.55 & 23.0 & -232 & 4.16 & 21.3 \\
\end{array}
\]

Fig. 1—(A) Decrease in optical density of PNDS at 545 nm with time in the oxidation of lactic acid by PNDS in aqueous acetate medium. ([PNDS] = 6.2 \times 10^{-3} \text{ mol dm}^{-3}; [lactic acid] = 1.40 \text{ mol dm}^{-3}; [sodium acetate] = 1.20 \text{ mol dm}^{-3}; [sulphamate] = 0.10 \text{ mol dm}^{-3}; pH = 6.50; temp. = 303 K).

(B) Plot of \(7 + \log \text{ (initial rate)}\) versus log [PNDS] ([lactic acid] = 0.54 \text{ mol dm}^{-3}).

(C) Plot of \(7 + \log \text{ (initial rate)}\) versus log [lactic acid]. ([PNDS] = 6.25 \times 10^{-3} \text{ mol dm}^{-3}).

which agreed with those for the hydrazine derivatives of the respective keto acids.

The stoichiometric equation is

\[
\text{RCHOH - COOH} + 2\text{ON(SO}_3\text{)}_2 \rightarrow \text{R} - \text{CO} - \text{COOH} + 2\text{HON(SO}_3\text{)}_2
\]

**Results and discussion**

In all kinetic measurements unless otherwise stated [acetate] = 0.03 \text{ mol dm}^{-3}, [sulphamate] = 0.05 \text{ mol dm}^{-3} and \(pH = 6.5\). Increase in [PNDS] at fixed [\(\alpha\)-hydroxy acid] increased the initial rate and the plot of log (initial rate) versus log [PNDS] was linear with unit slope (Fig. 1B) indicating first order dependence on [PNDS]. The initial rates were calculated using the computer programme Curve fit. The best fit values were averaged and presented. Increase in [\(\alpha\)-hydroxy acid] at fixed [PNDS] increased the rate and the plot of log (initial rate) versus log [\(\alpha\)-hydroxy acid] was linear with a slope of less than one (Fig. 1C) showing fractional order dependence on [\(\alpha\)-hydroxy acid]. Increase in [sulphamate] from 0.025 \text{ mol dm}^{-3} to 0.100 \text{ mol dm}^{-3} produced only marginal effect. Ionic strength was varied from 0.05 \text{ mol dm}^{-3} to 0.44 \text{ mol dm}^{-3} using sodium perchlorate and the rate is found to be unaffected. The solvent dielectric constant was varied by the addition of different amounts of methanol. Decreasing dielectric constant of the medium increased the reaction rate. For example, under the conditions [lactic acid] = 0.60 \text{ mol dm}^{-3} [PNDS] = 4.62 \times 10^{-3} \text{ mol dm}^{-3}, [sulphamate] = 0.10 \text{ mol dm}^{-3}, [sodium acetate] = 0.2 \text{ mol dm}^{-3}, \text{ temp.} = 308K and \(pH = 6.5\), \(10^7\) [initial rate] increased from 1.79 to 6.10 \text{ mol dm}^{-3} \text{s}^{-1} when dielectric constant was decreased from 67.5 to 44.8. The plot of log (initial rate) versus 1/D was linear with a positive slope.

Potassium nitrosodisulphonate is reported to exist in the radical form in solution. This reagent is reported to be unstable in acidic as well as alkaline solutions. However, we found and confirmed that PNDS solutions were quite stable at room temperature in acetate buffer solutions. The oxidation reactions were always carried out in the presence of sulphamate to inhibit any possible self decomposition of PNDS via chain initiation by nitrous acid.

The unit order dependence of the reaction rate on [PNDS] and fractional order dependence on [\(\alpha\)-hydroxy acid] suggest that the reaction might be proceeding via fast pre-equilibrium step leading to the formation of an adduct. This adduct disproportionate in a slow rate-determining step generating an intermediate radical which is stabilised by multiple bond formation favouring substituents. This radical reacts with another molecule of PNDS yielding the product. Insensitivity of the reaction rate to added salt and the nature of sol-
vent effect observed indicates the reaction to be of ion-dipole type.

Taking lactic acid as the example, the reaction scheme can therefore be written as in Scheme 1.

\[ \text{R CHOH} - \text{COOH} + \text{O} - \text{N(SO}_3\text{)}_2 \rightarrow \text{Adduct} \]

\[ \text{Adduct} \xrightarrow{\text{slow}} \text{R} - \text{C(OH)} - \text{COOH} + \text{HON(SO}_3\text{)}_2 \]

\[ \text{Scheme 1} \]

The absorption spectra of PNDS in the presence of \( \alpha \)-hydroxy acid shows a shift of \( \lambda_{\text{max}} \) by 10 nm supporting the formation of adduct between hydroxy acid and PNDS. From Scheme 1 the rate law derived is

\[ \frac{d[\text{PNDS}]}{dt} = \frac{kK[\text{PNDS}][\alpha - \text{hydroxy acid}]}{1 + K[\alpha - \text{hydroxy acid}]} \quad \ldots (1) \]

\[ - \frac{d\ln[\text{PNDS}]}{dt} = k_{\text{obs}} = \frac{kK[\alpha-\text{hydroxy acid}]}{1 + K[\alpha - \text{hydroxy acid}]} \quad \ldots (2) \]

This rate law explains all the experimental results observed. The reciprocal of Eq. 1 is given in Eq. (3)

\[ \frac{1}{\text{rate}} = \frac{1}{k[\text{PNDS}]} \left[ \frac{1}{K[\alpha - \text{hydroxy acid}]} + 1 \right] \quad \ldots (3) \]

The plot of 1/rate versus 1/[\alpha-hydroxy acid] must therefore be linear at constant [PNDS] with an intercept on the y-axis. This is realised with all the \( \alpha \)-hydroxy acids studied in the present work supporting the proposed mechanism. From the intercept and slope, the formation constant \( (K) \) and disproportionation constant \( (k) \) have been calculated for all the hydroxy acids studied and are presented in Table 1. The activation parameters for the disproportionation step and the thermodynamic parameters for the adduct formation are also presented in Table 1. It can be observed that fastest reaction has the lowest activation energy. The data in Table 1 indicate that the reactions are accompanied by a large entropy decrease on formation of the activated complex. This further supports the contention that the activated complex is an addition complex of the substrate and \( \text{O} - \text{N(SO}_3\text{)}_2 \). Electron donating methyl group is found to facilitate the reactions as observed with lactic acid. Mandelic acid reacts much faster than glycolic or lactic acid as a result of the stabilisation of the intermediate \( \text{R} - \text{C(OH)} - \text{COOH} \) radical due to the phenyl ring.

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**References**