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Oxidation of some catecholamines by sodium N-chloro-p-toluenesulfonamide in acid medium: A kinetic and mechanistic approach

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Abstract: The kinetics of the oxidation of five catecholamines viz., dopamine (A), L-dopa (B), methyldopa (C), epinephrine (D) and norepinephrine (E) by sodium N-chloro-p-toluenesulfonamide or chloramine-T (CAT) in presence of $HClO_4$ was studied at 30 ± 0.1 °C. The five reactions followed identical kinetics with a first-order dependence on $[CAT]_o$, fractional-order in $[substrate]_o$, and inverse fractional-order in $[H^+]$. Under comparable experimental conditions, the rate of oxidation of catecholamines increases in the order D > E > A > B > C. The variation of ionic strength of the medium and the addition of p-toluenesulfonamide or halide ions had no significant effect on the reaction rate. The rate increased with decreasing dielectric constant of the medium. The solvent isotope effect was studied using D_2O. A Michaelis–Menten type mechanism has been suggested to explain the results. Equilibrium and decomposition constants for CAT–catecholamine complexes have been evaluated. $CH_3C_6H_4SO_2NHCl$ of the oxidant has been postulated as the reactive oxidizing species and oxidation products were identified. An isokinetic relationship is observed with $\beta = 361$ K, indicating that enthalpy factors control the reaction rate. The mechanism proposed and the derived rate law are consistent with the observed kinetics.
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Keywords: Catecholamines, oxidation kinetics, chloramine-T, acid medium

1 Introduction

Catecholamines are compounds with amines attached to a benzene ring bearing two hydroxy groups. Several catecholamines act as neurotransmitters [1-6]. The most important

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endogenously produced compounds of this group are epinephrine (adrenalin), norepinephrine (noradrenalin) and dopamine (3,4-dihydroxyphenethylamine). The main sites of production of the catecholamines are the brain, chromaffin cells of the adrenal medulla and the sympathetic neurons. Epinephrine is quantitatively the most important substance produced by the adrenal medulla, whereas norepinephrine is the major substance liberated by the postganglionic sympathetic nerves. Epinephrine is used to stimulate the heart, tones up the blood pressure and above all affords relaxation of the musculature of the intestine and bronchi. Norepinephrine is the transmitter at smooth muscle junctions that are invervated by sympathetic nerve fibers, in contrast to parasympathetic junctions in which acetylcholine is the transmitter. Dopamine is an important neurotransmitter and imbalance of it is attributed to two major disorders in the central nervous system, Parkinson's disease and schizophrenia. The hydrochloride salt of dopamine is widely used in the treatment of shock and in acute congestive failure.

L-dopa (3-(3, 4-dihydroxyphenyl)-L-alanine) is a neutral amino acid precursor of dopamine. L-dopa is particularly effective in the treatment of tremors and hyperkinesia. It can be widely used as a universal antiparkinsonian drug, as it improves all the manifestations of Parkinsonism. Methyldopa (3-(3,4-dihydroxyphenyl)-2-methyl-L-alanine) is a potent antihypertensive and hypotensive drug that acts centrally by stimulating α-adrenergic receptors. It is widely employed to treat patients having moderate to severe hypertension by reducing the blood pressure. Hence, these catecholamines find a number of applications in pharmaceutical, metabolic, and biochemical research. It is noted that despite the importance of the above drugs, relatively little is known about their mode of action at the molecular level.

The chemistry of aromatic sulfonylhaloamines (N-haloamines) has evoked considerable interest, as they are sources of halonium cations, hypohalite species and N-anions, which act both as electrophiles and as nucleophiles. The prominent member of this class is sodium N-chloro-p-toluenesulfonamide or chloramine-T (CAT), which is a by-product in the manufacture of saccharin. Generally, CAT undergoes a two-electron change in its reactions, forming p-toluenesulfonamide (PTS) and sodium chloride. The oxidation potential of CAT-PTS couple varies with the pH of the medium (1.139 V at pH 0.65, 0.778 V at pH 7.0 and 0.614 V at pH 9.7). The mechanistic aspects of CAT reactions have been well documented [7-12].

Although the kinetics of oxidation of dopamine by chloramine-B, bromamine-B and bromamine-T under various experimental conditions has been reported from our laboratory [13-15], there seems to be no report in the literature on the oxidation of L-dopa, methyldopa, epinephrine, and norepinephrine by N-haloamines from the viewpoint of their kinetic and mechanistic aspects.

In light of the information available and in continuation with our extensive studies on the oxidation kinetics of catecholamines with N-haloamines [13-15], we have taken up a systematic investigation of the oxidation of dopamine, L-dopa, methyldopa, epinephrine and norepinephrine by CAT in acid medium to explore the mechanistic aspects of these oxidations and also to assess their relative rates. The studies were also extended to

deduce the appropriate rate law and to establish the isokinetic relationship through the computed thermodynamic parameters.

2 Experimental

2.1 Materials

Chloramine-T (S.D. Fine Chem. Ltd.) was purified by the method of Morris et al [16]. An aqueous solution of CAT was prepared, standardized by the iodometric method and preserved in brown bottles to prevent its photochemical deterioration. The catecholamines, dopamine HCl (Spectrochem), L-dopa and methyldopa (Acros), epinephrine (S.D. Fine Chem. Ltd.) and norepinephrine (Fluka) were used as received. Aqueous solutions of catecholamines were prepared and employed. All other chemicals were of analytical grade. Heavy water (D_2O 99.4 %) was supplied by BARC, India. The permittivity of the reaction mixture was altered by the addition of methanol in varying proportions (v/v), and the values of the permittivity (dielectric constant) of methanol-water mixtures reported in the literature [17] were employed. Triply distilled water was used throughout the course of reaction. A regression analysis of the experimental data was carried out on an fx-100w scientific calculator to obtain the regression coefficient (r).

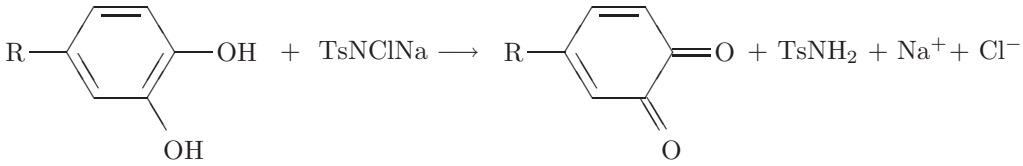
2.2 Kinetic procedure

Kinetic runs were performed under pseudo-first-order conditions by keeping an excess of the catecholamine over oxidant. The reaction was carried out in glass stoppered Pyrex boiling tubes whose outer surface was coated black to eliminate photochemical effects. For each kinetic run, requisite amounts of solutions of the substrate, acid and water (to maintain a constant total 50 ml volume) were introduced into the tube and thermostatted at 30 ± 0.1 ^{o}C until thermal equilibrium was attained. A measured amount of CAT solution, also thermostated at the same temperature, was added rapidly to the above mentioned mixture to initiate the reaction. The mixture was periodically shaken to ensure uniform concentration, and the progress of the reaction was monitored by an iodometric determination of unreacted CAT in a measured aliquot (5 ml each) of the reaction mixture at different time intervals. The reaction was followed for more than two half-lives. The pseudo-first-order rate constants (k'), calculated from linear plots of log [CAT] versus time, were reproducible within ± 5 %.

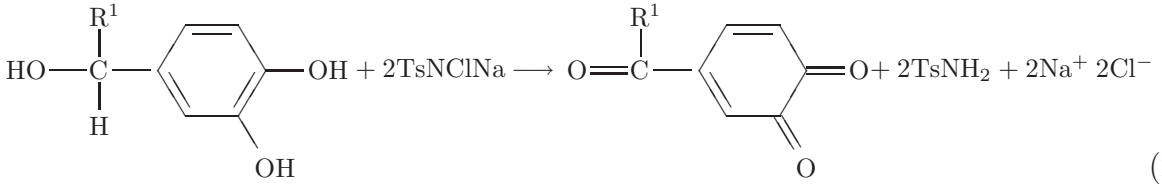
2.3 Stoichiometry and product analysis

Reaction mixtures containing varying proportions of CAT and catecholamines were equilibrated at 30 °C in presence of 0.01 mol dm^{-3} $HClO_4$. An iodometric determination of the unconsumed CAT in the reaction mixture showed that dopamine, L-dopa, and methyldopa consumes one mole of CAT per mole of catecholamine while epinephrine and

norepinephrine take up two moles of CAT per mole of catecholamine, confirming the following stoichiometries:



(1)



(2)

where Ts = $CH_3C_6H_4SO_2-$, R = $-CH_2CH_2NH_2$ for dopamine, -$CH_2CH(COOH)NH_2$ for L-dopa, -$CH_2C(COOH)(CH_3)NH_2$ for methyldopa, R^1 =$-CH_2NH(CH_3)$ for epinephrine and $-CH_2NH_2$ for norepinephrine.

The reduction product of CAT, p-toluenesulfonamide ($TsNH_2$), among the reaction products was identified by paper chromatography [11] using benzyl alcohol saturated with water as the solvent system ascending irrigation and using 0.5 % vanillin in 1 % HCl in EtOH as the spray reagent (R_f = 0.905). The oxidation products of catecholamines are corresponding o-benzoquinones under the kinetic conditions employed in the present work. The oxidation products of dopamine, L-dopa, methyldopa, epinephrine, and norepinephrine are 4-(2-aminoethyl) benzo-1,2-quinone, 2-amino-3-(3,4-dioxo-1,5-cyclohexadienyl) propionic acid, 2-amino-3-(3,4-dioxo-1,5-cyclohexadienyl)-2-methyl propionic acid, 4-(2-methyl aminoacetyl) benzo-1,2-quinone and 4-(2-aminoacetyl) benzo-1,2-quinone respectively. These are identified by conventional spot test analysis [18] and further characterized by 2, 4-DNP derivative [19]. Further these products polymerizes to a brown gel after some time. The same oxidation products have been reported for the oxidation of several catecholamines with different oxidizing agents by several researchers [4, 5, 13-15, 20].

3 Results and discussion

The kinetics of oxidation of five catecholamines (henceforth abbreviated as substrate or S) by CAT was investigated at several initial concentrations of the reactants in $HClO_4$ medium. Identical kinetic oxidation behaviour was observed for all the five catecholamines studied in the present investigation.

Under pseudo–first–order conditions of $[substrate]_o \gg [oxidant]_o$ at constant $[substrate]_o$, $[HClO_4]$ and temperature, plots of log [CAT] versus time were linear ($r > 0.9946$) indicating a first-order dependence of the reaction rate on $[CAT]_o$. The values of pseudo-first-order constants (k') were unaltered with variation in $[CAT]_o$, confirming

the first-order dependence on $[CAT]_o$ (Table 1). The rate increases with an increase in $[substrate]_o$. Plots of log k' versus log [substrate] were linear ($r > 0.9974$) with fractional slopes (0.42-0.75), indicating a fractional-order dependence on $[substrate]_o$ (Table 1). Furthermore, plots of k' versus [S] are linear ($r > 0.9910$) with a y-intercept, confirming fractional-order dependence on $[substrate]_o$. The rate of reaction decreased with an increase in $[HClO_4]$ (Table 2). Plots of log k' versus log $[HClO_4]$ were linear ($r > 0.9963$) with negative fractional slopes (0.26-0.30), indicating a inverse fractional-order dependence on $[H^+]$.

The ionic strength of the reaction system was varied from 0.1 to 0.5 mol dm^{-3} with $NaClO_4$ solution at constant other experimental conditions. It was found that ionic strength has negligible effect on the reaction rate, indicating that non-ionic species are involved in the rate-limiting step. Hence, no attempt was made to keep ionic strength constant for kinetic runs. Addition of the reaction product, p-toluenesulfonamide (PTS; $4.0 \times 10^{-4} - 10.0 \times 10^{-4}$ mol dm^{-3}) and Cl^- or Br^- ions in the form of NaCl or NaBr (0.1 – 0.5 mol dm^{-3}) had no pronounced effect on the rate. The dielectric constant (D) of the medium was varied by adding methanol (0 - 30 % v/v) to the reaction mixture. The rate increases with an increase in methanol content (Table 3). The plots of log k' versus 1/D were linear ($r > 0.9957$) with positive slopes. Blank experiments with methanol indicated that the oxidation of methanol was negligible. Studies of the rate in D_2O medium for L-dopa and norepinephrine revealed that while $k'(H_2O)$ is 10.0×10^{-4} s^{-1} and 13.1×10^{-4} s^{-1}, $k'(D_2O)$ is 8.38×10^{-4} s^{-1} and 10.8×10^{-4} s^{-1} respectively. The solvent isotope effect k' $(H_2O)/k$ (D_2O) is 1.19 for L-dopa and 1.21 for norepinephrine.

The reaction was studied at five different temperatures (293, 298, 303, 308 and 313 K), and from the Arrhenius plots of log k' versus 1/T ($r > 0.9962$), values of activation parameters ($\Delta H^{\neq}$, $\Delta S^{\neq}$ and $\Delta G^{\neq}$) for the overall reaction for each temperature were calculated and the average values for each parameters are reported along with errors. These results are summarized in Table 4. The reaction mixture could not initiate polymerization in acrylamide solution, demonstrating the absence of free radical species in the reaction.

Chloramine-T behaves as a strong electrolyte in aqueous solutions [21]. Depending on pH of the medium, CAT furnishes [16, 21-23] following types of reactive species in solutions:

$$TsNClNa \rightleftharpoons TsNCl^- + Na^+ \quad (3)$$

$$TsNCl^- + H^+ \rightleftharpoons TsNHCl \quad (4)$$

$$2TsNHCl \rightleftharpoons TsNH_2 + TsNCl_2 \quad (5)$$

$$TsNHCl + H_2O \rightleftharpoons TsNH_2 + HOCl \quad (6)$$

$$TsNCl_2 + H_2O \rightleftharpoons TsNHCl + HOCl \quad (7)$$

$$HOCl \rightleftharpoons H^+ + OCl^- \quad (8)$$

$$HOCl + H^+ \rightleftharpoons H_2OCl^+ \quad (9)$$

Therefore, the possible oxidizing species in acidified CAT solutions are TsNHCl, $TsNCl_2$, HOCl, and possibly H_2OCl^+. If $TsNCl_2$ were to be the reactive species, then the rate law predicts a second-order dependence of rate on $[CAT]_o$, which is contrary to the experimental observations. If HOCl is primarily involved, a first-order retardation of rate by added p-toluenesulfonamide is expected. Since no such effect is noticed, HOCl can be ruled out as the oxidizing species. Hardy and Johnston [22], who have studied the pH-dependent relative concentrations of the species present in acidified CAT solutions of comparable molarities, have shown that TsNHCl is the likely oxidizing species in acid medium. Hence, TsNHCl is the most probable oxidizing reactive species for the oxidation of catecholamines in the present system. Further, formation of species of the type $TsNH_2Cl^+$ has been reported [24, 25] with CAT and the protonation constant for the reaction,

$$TsNHCl + H^+ \rightleftharpoons TsNH_2Cl^+ \tag{10}$$

is found to be 1.02×10^2 at 25 °C.

In the present investigations, the retardation of rate by H^+ ion indicates that the unprotonated oxidant (TsNHCl) is the active oxidizing species. In view of preceding discussion and experimental facts, Scheme 1 is proposed to explain the reaction mechanism for the oxidation of catecholamines by CAT in $HClO_4$ medium:

$$\begin{aligned}
TsNH_2Cl^+ &\overset{K_1}{\rightleftharpoons} TsNHCl + H^+ && \text{(i) fast}\\
TsNHCl + S &\overset{K_2}{\rightleftharpoons} X && \text{(ii) fast}\\
X &\xrightarrow{k_3} X' && \text{(iii) slow and rate limiting step}\\
X' + nTsNHCl &\xrightarrow{k_4} Products && \text{(iv) fast}
\end{aligned}$$

Scheme 1 A general mechanistic scheme for the oxidation of catecholamines by CAT in acid medium.

where n=1 for epinephrine and norepinephrine. A possible mechanistic pathway of catecholamine - CAT reaction in acid medium is presented in Schemes 2 and 3, in which the complex intermediate species X and X′ structures are shown.

If $[CAT]_t$ is total effective concentration of CAT, then

$$[CAT]_t = [TsNH_2Cl^+] + [TsNHCl] + [X] \tag{11}$$

From step (i) of Scheme 1,

$$K_1 = \frac{[TsNHCl][H^+]}{[TsNH_2Cl^+]}$$

$$\text{or} \qquad [TsNH_2Cl^+] = \frac{[TsNHCl][H^+]}{K_1} \tag{12}$$

From step (ii) of Scheme 1,

$$K_2 = \frac{[X]}{[TsNHCl][S]}$$

$$\text{or} \qquad [\text{TsNHCl}] = \frac{[\text{X}]}{K_2[\text{S}]} \tag{13}$$

By substituting for [TsNHCl] from equation 13 into equation 12 one obtains,

$$[\text{TsNH}_2\text{Cl}^+] = \frac{[\text{X}][\text{H}^+]}{K_1K_2[\text{S}]} \tag{14}$$

By substituting for [TsNHCl] and $[\text{TsNH}_2\text{Cl}^+]$ from equation 13 and 14 respectively into equation 11 and solving for [X], we get:

$$[\text{CAT}]_t = \frac{[\text{X}][\text{H}^+]}{K_1K_2[\text{S}]} + \frac{[\text{X}]}{K_2[\text{S}]} + [\text{X}]$$

$$[\text{CAT}]_t = [\text{X}]\left\{\frac{[\text{H}^+]}{K_1K_2[\text{S}]} + \frac{1}{K_2[\text{S}]} + 1\right\}$$

$$\text{or} \qquad [\text{X}] = \frac{K_1K_2[\text{CAT}]_t[\text{S}]}{[\text{H}^+] + K_1 + K_1K_2[\text{S}]} \tag{15}$$

From slow step of Scheme 1,

$$\text{rate} = \frac{-[\text{CAT}]_t}{\text{dt}} = k_3[\text{X}] \tag{16}$$

By substituting for [X] from equation 15 into equation 16, the following rate law is obtained:

$$\text{rate} = \frac{K_1K_2k_3[\text{CAT}]_t[\text{S}]}{[\text{H}^+] + K_1 + K_1K_2[\text{S}]} \tag{17}$$

Rate law 17 is in good agreement with the experimental results, wherein a first-order dependence of rate on $[\text{CAT}]_o$, fractional-order on $[\text{S}]_o$ and inverse fractional-order on $[\text{H}^+]$ was observed.

Since rate = k' $[\text{CAT}]_t$, equation 17 can be transformed into equations 18–20,

$$k' = \frac{K_1K_2k_3[\text{S}]}{[\text{H}^+] + K_1 + K_1K_2[\text{S}]} \tag{18}$$

$$\frac{1}{k'} = \frac{1}{K_2k_3[\text{S}]}\left\{\frac{[\text{H}^+]}{K_1} + 1\right\} + \frac{1}{k_3} \tag{19}$$

$$\frac{1}{k'} = \frac{[\text{H}^+]}{K_1K_2k_3[\text{S}]} + \frac{1}{K_2k_3[\text{S}]} + \frac{1}{k_3} \tag{20}$$

Double reciprocal plots of $1/k'$ versus $1/[\text{S}]$ ($r > 0.9862$) and $1/k'$ versus $[\text{H}^+]$ were linear ($r > 0.9832$) and from the intercept and slope of these plots, values of equilibrium constants K_1 and K_2 and decomposition constant k_3 were calculated using equations 19 and 20 for each catecholamine at 30 °C. These values are recorded in Table 5. Since the rate was fractional-order in [S], Michaelis-Menten kinetics [26] were adopted and the values of k_3 were calculated for each substrate at different temperatures (293 – 313 K). The activation parameters for the rate-limiting step of catecholamine-CAT complex were

evaluated using Arrhenius plots of log k_3 versus 1/T (r > 0.9921). These results are compiled in Table 6.

The proposed mechanism and the derived rate law are supported by the following experimental findings:

A change in the solvent composition by varying the methanol content in methanol-water affects the reaction rate. The effect of solvent on the reaction kinetics has been described in detail in the well-known monographs of Moelwyn-Hughes [27], Benson [28], Frost and Pearson [29], Laidler [30], Amis [31], and Entelis and Tiger [32]. For the limiting case of zero angle of approach between two dipoles or an ion dipole system, Amis [31] has shown that a plot of log k' versus 1/D gives a straight line, with a negative slope for a reaction between a negative ion and a dipole or between the dipoles, while a positive slope results for a positive ion-dipole interaction. The latter concept agrees with the present observations, where a positive ion and a dipole are involved in the rate-limiting step of the proposed scheme.

The observed solvent isotope effect supports the proposed mechanism and the derived rate expression. Since D_3O^+ is ∼2 to 3 times [33, 34] stronger than H_3O^+, for acid catalyzed reactions the solvent isotope effect $k'(H_2O)/k'(D_2O) < 1$. But for reactions retarded by H^+ ion, this ratio should be greater than unity, as was observed in the present investigations. The magnitude however is small, which can be attributed to the inverse fractional - order dependence of rate on $[H^+]$.

From an inspection of the rate data, the rate of oxidation of catecholamines follows the order: epinephrine > norepinephrine > dopamine > L-dopa > methyldopa. In case of epinephrine and norepinephrine oxidation, benzylic ketone is generated, which increases the reactivity of the phenolic function and therefore the reactivity of epinephrine and norepinephrine is faster compared to dopamine, L-dopa and methyldopa. Here two moles of oxidant are required. Epinephrine is faster than norepinephrine because of the presence of N-methyl group in epinephrine. On the other hand, we observed that the reactivity of dopamine is faster compared to L-dopa which in turn is faster than methyldopa. Since there are additional bulky groups COOH in L-dopa and COOH and CH_3 in methyldopa, it is reasonable to expect that steric effects may play a role in deciding the rates of oxidation. However, electronic effects do not appear to be important in the oxidation of dopamine, L-dopa and methyldopa, as the reacting OH group is in the phenyl ring. Here, one mole of oxidant is consumed in the oxidation reaction. Hence the order of reaction is in concurrence with the experimental observation ie., dopamine > L-dopa > methyldopa. Therefore, the overall reactivity of these catecholamines has been found to be epinephrine > norepinephrine > dopamine > L-dopa > methyldopa.

It can be seen from Table 4 that the activation energy is highest for the slowest reaction, and *vice versa*, indicating that the reaction is enthalpy-controlled. Further, it is verified by calculating the isokinetic temperature (β) from the slope of the linear plot of $\Delta H^{\neq}$ versus $\Delta S^{\neq}$ (Fig. 1; r = 0.9998) β is found to be 361 K, which is much higher than the experimental temperature (T = 303 K). The relation was proved to be genuine through the Exner criterion [35]by plotting log $k'_{(303K)}$ versus log $k'_{(293K)}$. The value of β

was calculated from this linear plot (Fig. 1; r = 0.9874) using the relation $\beta = T_1(1\text{-}q) / (T_1/T_2\text{-}q)$, where q is the slope of the Exner plot and is found to be 351 K. There is evidence in the literature for a large number of reactions [36-40] for which β is higher than experimental temperature. The proposed mechanism is also supported by the moderate values of energy of activation and thermodynamic parameters (Table 4). The fairly high positive values of free energy of activation and enthalpy of activation indicate that the transition state is highly solvated while the high negative entropy of activation suggests the formation of a rigid associative transition state with a reduction in the degrees of freedom of molecules in each case.

The reduction product of CAT ($TsNH_2$) does not influence the rate, showing that it is not involved in pre-equilibrium. Further, addition of halide ions has no effect on the rate indicating that no interhalogen or chlorine is formed. These observations provide additional evidence for the mechanism proposed.

4 Conclusions

The stoichiometry and oxidation products are found to be different for dopamine, L-dopa, methyldopa, epinephrine and norepinephrine but it is interesting to note that the oxidation of these catecholamines by CAT in presence of $HClO_4$ exhibits identical kinetics and follows the rate law, $-d[CAT]/dt = k[CAT][S]^x[H^+]^{-y}$, where x and y < 1. Reaction mechanism proposed is consistent with all the observed experimental results, in which TsNHCl has been postulated as the reactive species of CAT. The rate of oxidation of catecholamines increased in the order epinephrine > norepinephrine > dopamine > L-dopa > methyldopa. Activation parameters and reaction constants involved in the reaction scheme support the proposed mechanism.

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10^4 [CAT]$_o$ (mol dm^{-3})	10^3 [substrate]$_o$ (mol dm^{-3})	$10^4\,k'$ (s^{-1})				
		A	B	C	D	E
2.0	6.0	11.7	10.0	9.30	15.0	13.2
4.0	6.0	11.6	10.1	9.29	15.2	13.2
6.0	6.0	11.7	10.0	9.25	14.9	13.1
8.0	6.0	11.5	10.2	9.30	14.8	13.2
12.0	6.0	11.7	10.1	9.20	14.9	13.2
6.0	2.0	6.15	4.85	4.50	9.54	8.65
6.0	4.0	9.10	8.10	7.05	12.6	11.6
6.0	6.0	11.7	10.0	9.25	14.9	13.2
6.0	8.0	14.4	13.0	11.7	17.8	15.7
6.0	12.0	17.0	16.3	14.1	20.7	18.2

Table 1 Effect of varying reactant concentrations on the reaction rate at $[HClO_4] = 1.0 \times 10^{-2}$ mol dm^{-3}; temp = 303 K.

10^2 [$HClO_4$] (mol dm^{-3})	$10^4\ k'$ (s^{-1})				
	A	B	C	D	E
0.2	18.0	14.6	13.9	23.6	22.0
0.6	12.9	11.3	10.6	17.8	16.4
1.0	11.7	10.0	9.25	14.9	13.1
2.0	9.10	8.05	7.45	12.6	11.5
4.0	7.85	6.71	5.90	10.3	9.09

Table 2 Effect of varying acid concentration on the reaction rate at $[CAT]_o = 6.0 \times 10^{-4}$ mol dm^{-3}; $[substrate]_o = 6.0 \times 10^{-3}$ mol dm^{-3}; temp = 303 K.

MeOH (v/v)	D	$10^4\ k'$ (s^{-1})				
		A	B	C	D	E
0	76.73	11.7	10.0	9.25	14.9	13.1
5	74.50	13.0	11.4	10.2	16.1	14.4
10	72.37	14.6	12.6	11.5	18.1	15.7
20	67.48	18.0	16.5	14.0	21.1	19.2
30	62.71	23.0	21.1	18.0	26.0	24.5

Table 3 Effect of varying dielectric constant (D) of medium on the reaction rate at $[CAT]_o = 6.0 \times 10^{-4}$ mol dm^{-3}; $[substrate]_o = 6.0 \times 10^{-3}$ mol dm^{-3}; $[HClO_4] = 1.0 \times 10^{-2}$ mol dm^{-3}; temp = 303 K.

Temperature (K)	$10^4\ k'$ (s^{-1})				
	A	B	C	D	E
293	5.00	4.51	4.00	7.46	6.25
298	8.05	6.45	6.35	11.2	8.65
303	11.7	10.0	9.25	14.9	13.1
308	17.0	16.2	14.3	19.1	17.9
313	22.0	21.1	19.2	26.9	25.5
E_a/kJ mol^{-1}	55.2	59.6	64.9	42.1	50.1
$\Delta H^{\neq}$/kJ mol^{-1}	52.6±0.09	57.1±0.07	62.4±0.15	39.5±0.15	47.6±0.10
$\Delta G^{\neq}$/kJ mol^{-1}	90.8±0.91	91.6±0.73	91.2±1.01	90.7±1.20	91.9±1.10
$\Delta S^{\neq}$/J K^{-1} mol^{-1}	-127±0.41	-114±0.42	-97.4±0.50	-168±0.40	-143±0.16

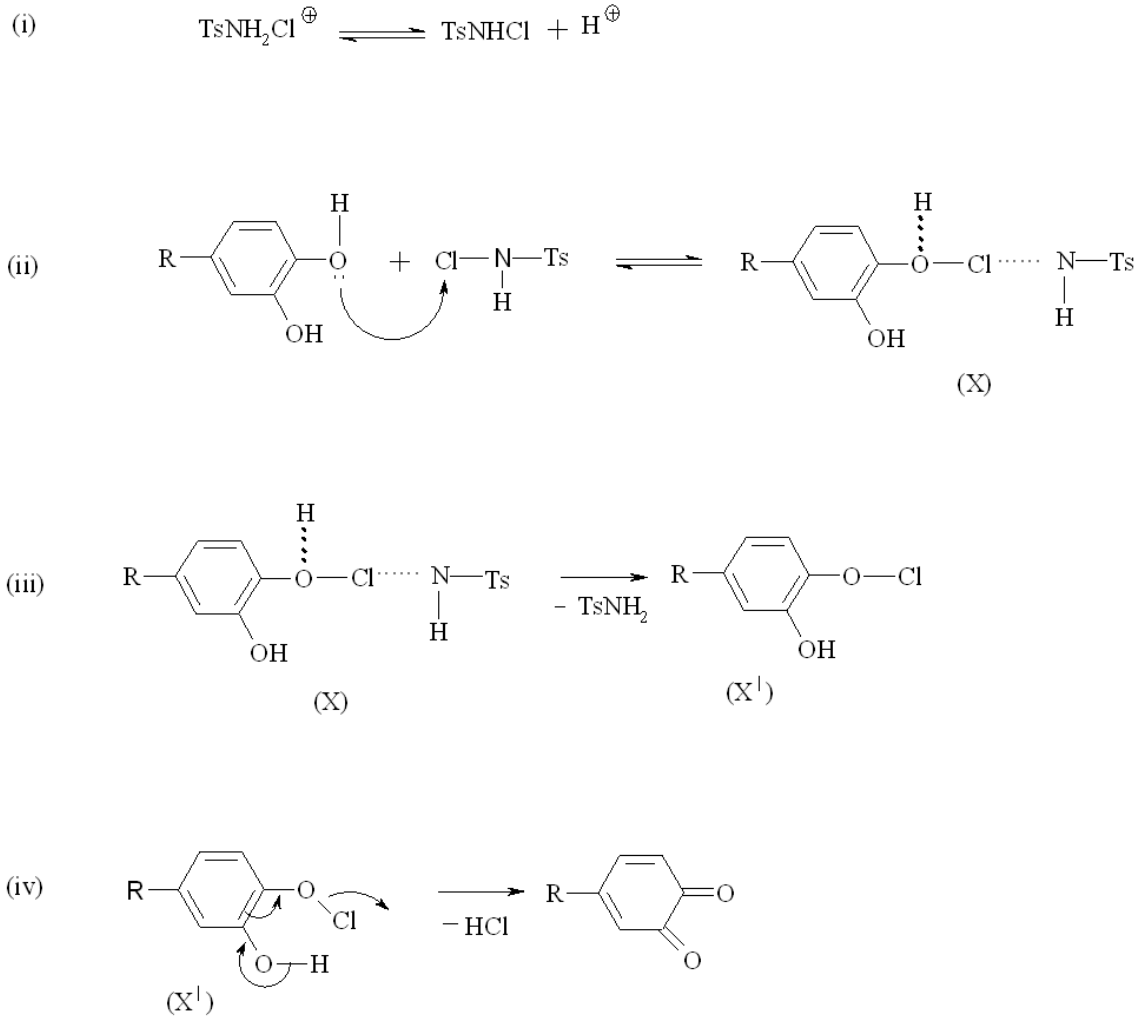
Table 4 Effect of temperature on the reaction rate and activation parameters for the oxidation of catecholamines by CAT in acid medium at $[CAT]_o = 6.0 \times 10^{-4}$ mol dm^{-3}; $[substrate]_o = 6.0 \times 10^{-3}$ mol dm^{-3}; $[HClO_4] = 1.0 \times 10^{-2}$ mol dm^{-3}.

	$10^3 K_1$ ($dm^3\ mol^{-1}$)	$10^{-2} K_2$ ($mol\ dm^{-3}$)	$10^3 k_3$ (s^{-1})
A	11.9	1.45	3.35
B	10.0	1.95	2.76
C	6.07	4.16	2.00
D	13.5	1.20	5.12
E	12.4	1.30	4.51

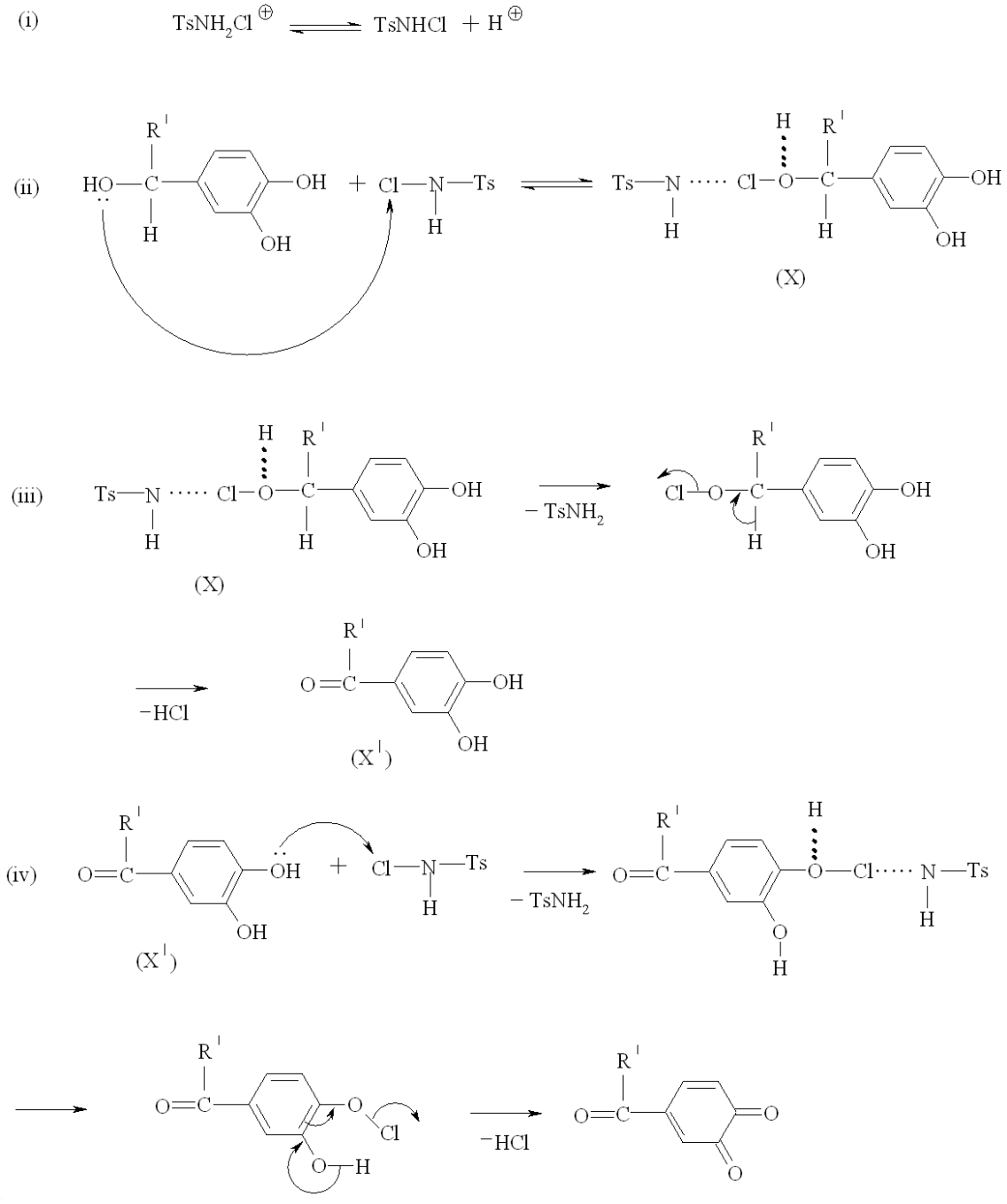
Table 5 Values of equilibrium and decomposition constants at $[CAT]_o = 6.0 \times 10^{-4}$ mol dm^{-3}; $[substrate]_o = 6.0 \times 10^{-3}$ mol dm^{-3}; $[HClO_4] = 1.0 \times 10^{-2}$ mol dm^{-3}; temp = 303 K.

Temperature (K)	$10^3\ k'$ (s^{-1})				
	A	B	C	D	E
293	2.00	1.53	1.00	2.80	2.50
298	2.50	2.24	1.43	4.05	3.20
303	3.55	2.76	2.00	5.12	4.51
308	5.10	4.00	3.32	7.15	6.42
313	7.14	6.25	5.26	10.0	8.32
E_a/kJ mol^{-1}	44.3	50.2	57.0	35.9	39.7
$\Delta H^{\neq}$/kJ mol^{-1}	41.8±0.07	47.7±0.26	54.4±0.13	33.4±0.09	37.2±0.12
$\Delta G^{\neq}$/kJ mol^{-1}	88.7±1.10	89.2±1.10	89.5±0.78	88.4±0.81	88.5±0.92
$\Delta S^{\neq}$/J K^{-1} mol^{-1}	-154±0.48	-137±0.56	-117±0.71	-179±0.62	-167±0.52

Table 6 Decomposition constants of substrate-oxidant complex at different temperatures and activation parameters for rate-limiting step.



Scheme 2 Oxidation of dopamine, L-dopa and methyldopa.



Scheme 3 Oxidation of epinephrine and norepinephrine.

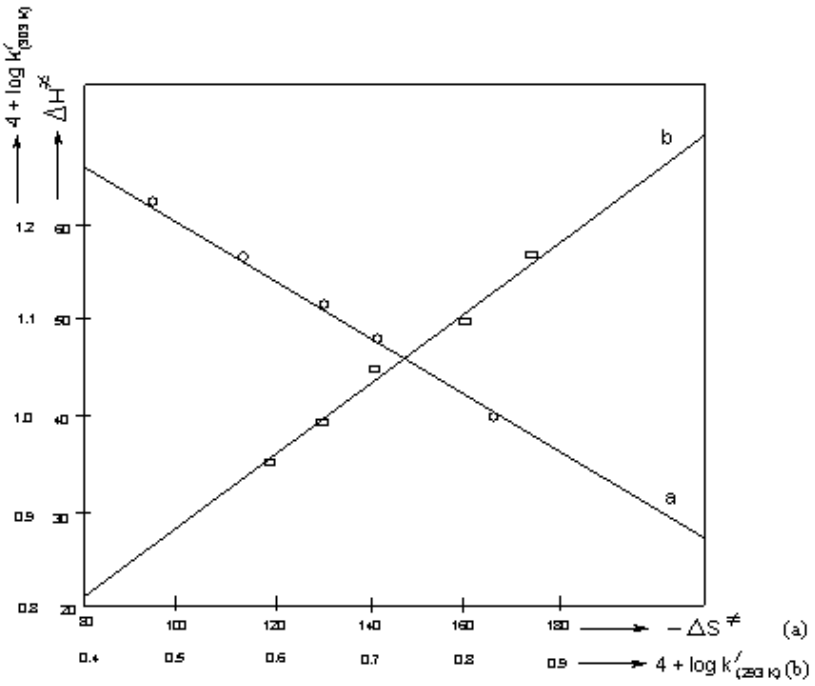


Fig. 1 Isokinetic plots of (a) $\Delta H^{\neq}$ versus $\Delta S^{\neq}$ and (b) $\log k'_{(303K)}$ versus $\log k'_{(293K)}$.