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Brønsted Acid Catalysis in the Oxidation of Purine Based Alkaloids by Mn(VII) in Aqueous Acetonitrile and Sodium Fluoride Medium: A Kinetic Approach

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Brønsted acid ($HClO_4$, H_2SO_4) catalyzed Mn(VII) oxidation of purine alkaloids such as caffeine, theophylline and theobromine in aqueous acetonitrile and sodium fluoride medium revealed first order kinetics in both [(Mn(VII)] and [Alkaloid] at constant acidity and temperature. Sodium fluoride was added to the reaction mixture in order to avoid/suppress auto catalytic reaction due to the generation of Mn(III) and Mn(IV) species during the course of Mn(VII) oxidations in acidic solutions. An increase in the Brønsted acids ($HClO_4$, H_2SO_4) concentration accelerated the rate of oxidation. Rate enhancements observed here in are analyzed by Zucker-Hammett, Bunnett and Bunnett-Olsen criteria of acidity functions. On the basis of observed Bunnett-Olsen criteria of acidity functions, the most plausible mechanism has been proposed with the involvement of water molecule in the slow step (as proton transferring agent).

Keywords: Mn(VII) oxidation, Purine alkaloids, Brønsted acid catalysis, Zucker-Hammett, Bunnett, Bunnett-Olson acidity functions.

INTRODUCTION

Caffeine (3,7-dihydro-1,3,7-trimethyl-1*H*-purine-2,6-dione), theophylline (3,7-dihydro-1,3-dimethyl-1*H*-purine-2,6-dione) and theobromine (3,7-dihydro-3,7-dimethyl-1*H*-purine-2,6-dione) are some of the important purine alkaloids, which are widely distributed in plant products and beverages like tea, coffee, cacao and mate [1-4]. Many of these alkaloids find their use as stimulants and vasodilators [5-7]. It is one of the most widely used, consumed and socially accepted stimulants, which also exhibit relaxant properties. But theophylline is explored as much more important drug for curing bronchial asthma because of its enhanced relaxant properties [8-10].

On the other hand, permanganate species (MnO_4^-) is a versatile oxidizing agent and extensively used in organic synthesis in aqueous acidic and alkaline solutions [11-19]. It is one the foremost synthetic regents which is explored as efficient phase-transfer catalyst [20]. In continuation of our ongoing work on the oxidation of xanthine alkaloids [21,22], certain kinetic aspects pertaining to Mn(VII) oxidation of caffeine (CAF), theophylline (TPL), theobromine (TBR) in aqueous Brønsted acids ($HClO_4$, H_2SO_4) media are presented. However, the reactions with xanthine and hypoxanthine did not proceed either in $HClO_4$ or H_2SO_4 media even at elevated temperatures.

The literature reports on permanganate oxidation of theophylline and caffeine [23,24] in perchloric acid medium revealed that the plots of [log (Absorbance)] *versus* time plots deviated from linearity beyond 60 to 65% reaction. This deviation was explained due to the autocatalysis of Mn(II) generated *in situ* during the course of reaction. Mn(II) thus produced in turn reduces permanganate (MnO_4^-) to other efficient oxidizing species like Mn(III) and Mn (IV) in acidic media.

$$MnO_4^- + 3Mn^{2+} + 8H^+ \longrightarrow 3Mn^{3+} + Mn^{4+} + 4H_2O$$

The as *in situ* generated Mn(III) is also strong oxidant, which could play an important role during the oxidation of organic compounds by Mn(VII) in aqueous acid solutions. A perusal of literature revealed that Mn(III) and its hydrolysis products have very short life period of few seconds in aqueous solutions, which could be stabilized by adding suitable ligands like fluoride (F^-), pyrophosphate ($P_2O_7^{2-}$) and sulfate (SO_4^{2-}). Thus the addition of excess of NaF forms to permanganate oxidations in acid media converts Mn(III) and Mn(IV) complexes kinetically inactive [25-30], under the conditions [NaF] >> [Mn(VII)]. Thus, we could also overcome the non-linearity of [log (Absorbance)] *versus* time plots. The current preliminary kinetic studies indicated perfect linearity of [log (Absorbance)] *versus* time plots, under both the conditions.

EXPERIMENTAL

All chemicals used were of analytical grade and procured from the commercial sources. Doubly distilled water (distilled over alkaline $KMnO_4$ and acid dichromate in an all glass apparatus) was used whenever required. Acetonitrile and other solvents were HPLC grade and used as such.

Kinetic studies: Flask containing known amount of substrate (purine alkaloid), Brønsted acid ($HClO_4$/H_2SO_4), sodium fluoride (NaF) and required amount of solvent (water) were clamped in a thermostatic (constant temperature) bath. In another flask, $KMnO_4$ solution (Mn(VII)) was taken, which was also clamped in the same thermostatic bath. After attaining thermal equilibrium, reaction was initiated by mixing requisite amount of Mn(VII) to the other contents of the reaction vessel and mixed thoroughly and instantaneously. Flask was coated black from outside to prevent the photochemical effects. Aliquots of the reaction mixture were withdrawn into a cuvette and placed in the cell compartment of the laboratory visible spectrophotometer. Cell compartment was provided with an inlet and outlet for circulation of thermostatic liquid at a desired temperature. The Mn(VII) content could be estimated from the previously constructed calibration curve showing Absorbance *vs.* [Mn(VII)] at 525 nm. Absorbance values were in agreement to each other with an accuracy of ± 3% error.

Determination of order of reaction: The graphical method of approach to determine order of reaction according to literature procedures [31,32]. Plots of ln [(A_0)/ (A_t)] *versus* time (t) were found linear passing through origin indicating first order kinetics in [Mn(VII)] (Few plots are shown in Figs. 1 to 4), under pseudo conditions (without NaF) and with NaF as additive by taking [NaF] >> [Substrate] >> [Mn(VII)]:

$$\ln\left(\frac{A_o}{A_t}\right) = (k')t \qquad (1)$$

Herein, A_o and A_t represent the absorbance values at zero time (the time of initiating the reaction) and at a given instant of time (during the progress of reaction), respectively. Further, A_o is proportional to initial concentration of $KMnO_4$ $[Mn(VII)]_0$, while A_t is proportional to the concentration of Mn(VII) at a given time 't' ($[Mn(VII)]_t$). Further, under second order conditions, when equimolar solutions of Mn(VII) and xanthene alkaloid (substrate) were taken in the reaction mixture (*i.e.* when $[Mn(VII)]_0 = [substrate]_0$), the plots of [$1/(A_t)$] *vs.* time, have been found to be linear with a positive gradient and definite intercept on vertical axis indicating over all second order kinetics (Figs. 5 and 6), according to the following expression:

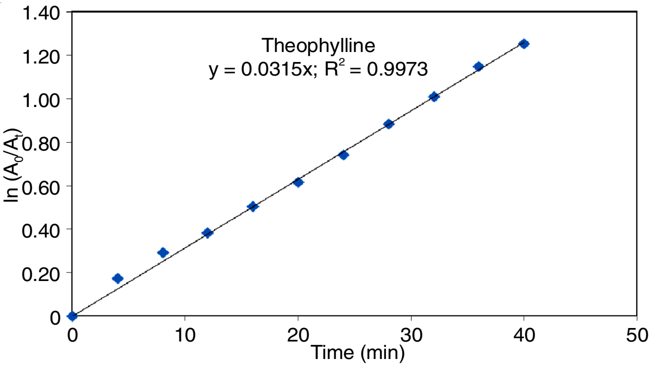


Fig. 1. Plot of ln (A_0/A_t) *vs.* time for oxidation of theophylline in aq. H_2SO_4 medium at 298 K (10^4 [$KMnO_4$] =2.50 mol/dm^3; 10^3 [Theoph] = 2.50 mol/dm^3; [NaF] = 0.01 mol/dm^3; [H_2SO_4] = 1.00 mol/dm^3)

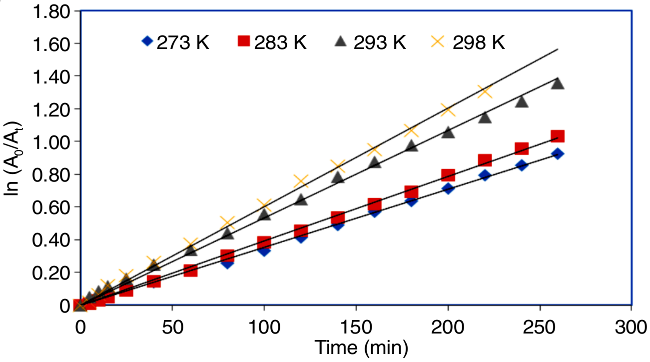


Fig. 2. First order plot of ln (A_0/A_t) *vs.* time for oxidation of caffeine in aqueous H_2SO_4 medium at different temperatures (10^4 [$KMnO_4$] = 4.0 mol/dm^3; 10^3 [Caff] = 4.0 mol/dm^3; [NaF] = 0.01 mol/dm^3; [H_2SO_4] = 0.6 mol/dm^3)

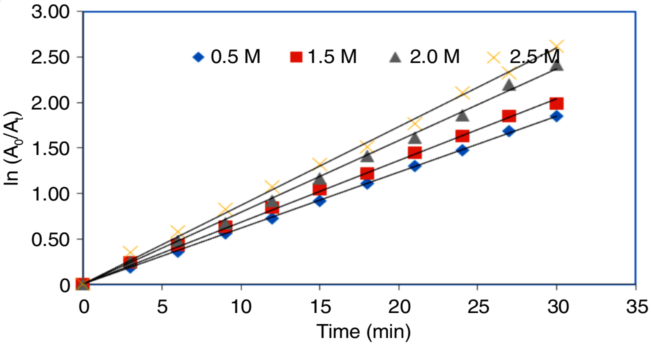


Fig. 3. Plot of A_0/A_t *vs.* time for oxidation of theophylline in aqueous $HClO_4$ medium at different concentrations (variation of perchloric acid) (10^4 [$KMnO_4$] = 2.5 mol/dm^3; 10^3 [Theophylline] = 2.5 mol/dm^3; Temp. = 298 K)

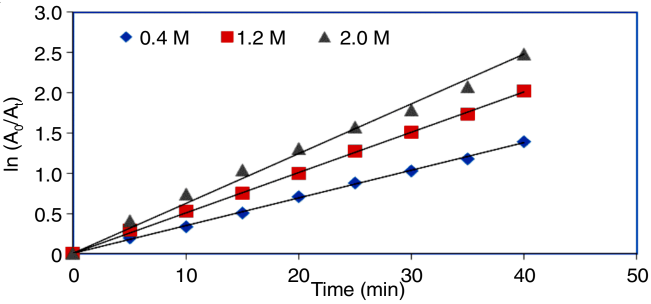


Fig. 4. Plot of A_0/A_t *vs.* time for oxidation of theobromine in aq. $HClO_4$ medium at different concentrations (10^4 [$KMnO_4$] = 4.0 mol/dm^3; 10^3 [Theobromine] = 4.0 mol/dm^3; [NaF] = 0.01 mol/dm^3; Temp. = 298 K)

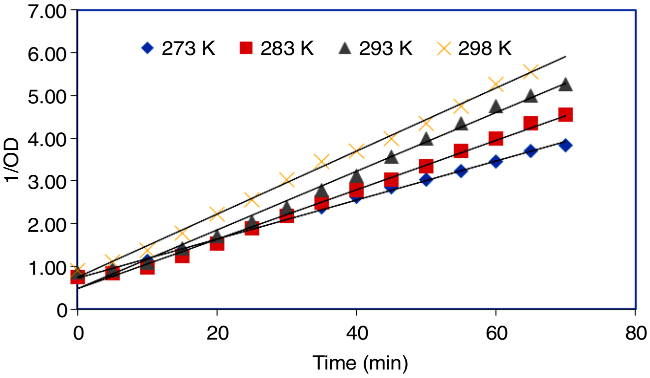


Fig. 5. Plot of 1/OD *vs*. time for oxidation of theophylline in aqueous H_2SO_4 medium at different temperatures (10^4 [$KMnO_4$] = 5 mol/dm^3; 10^4 [Theophylline] = 5.0 mol/dm^3; [NaF] = 0.01 mol/dm^3 ; [H_2SO_4] = 0.75 mol/dm^3)

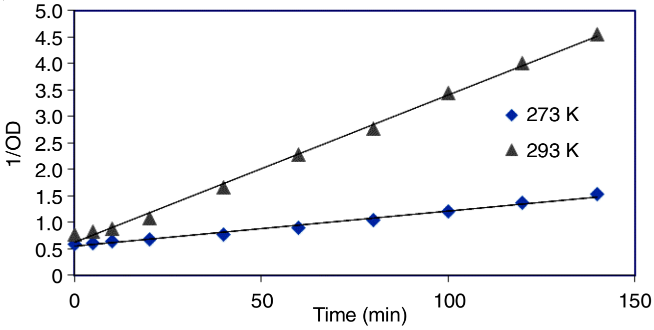


Fig. 6. Plot of 1/OD *vs*. time for oxidation of theobromine in aqueous H_2SO_4 medium at different temperatures (10^4 [$KMnO_4$] = 5.0 mol/dm^3; 10^4 [Theobromine] = 2.0 mol/dm^3; [NaF] = 0.01 mol/dm^3; [H_2SO_4] = 0.75 mol/dm^3)

$$\frac{1}{A_t} = \frac{k}{(\varepsilon)} t + \frac{1}{A_o} \quad (2)$$

where ε = $[Mn(VII)]_o/(A_o)$.

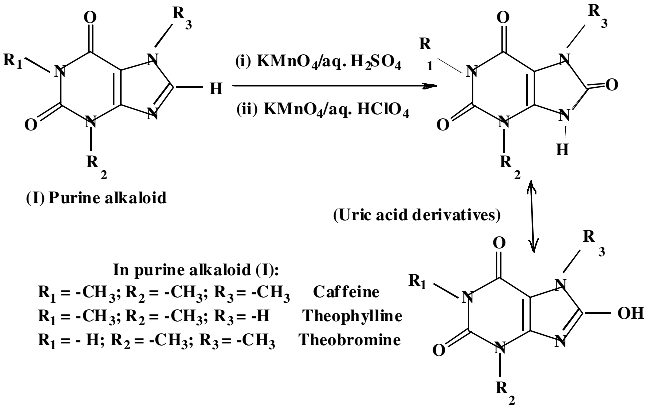
Substitution of ε into the above equation leads to

$$\frac{1}{A_t} = \frac{k[Mn(VII)]_0}{(A_0)} t + \frac{1}{A_0} \quad (3)$$

The foregoing observations revealed that reaction kinetics follow overall second order at constant acidity and linearity of [$\ln(A_0/A_t)$] *versus* time indicate first order in [Mn(VII)], it is understood that order in [substrate] is also one. Thus, second order rate constant (k) can be calculated from the ratio of the observed slope and intercept of second order plot (k = slope/(Intercept × $[Mn(VII)]_0$)). However, in the present work, second order rate constant (*k*) is obtained from the slopes of k′ *versus* [Substrate].

Generation for free radicals: Addition of olefinic monomer (acrylamide or acrylonitrile) to the reaction mixture did not induce vinyl polymerization of added monomers even at elevated temperatures and inert atmosphere. Besides, none of the oxidation reactions did not induce precipitation of mercurous chloride, when mercuric chloride was added to the reaction mixture. These observations revealed that free radical intermediates are not formed during the oxidation of caffeine, theophylline and theobromine by permanganate.

Oxidation products: In a typical experiment, xanthine alkaloid (0.01 mol substrate) and Mn(VII) (0.015 mol) were made up to 50 mL in aqueous acid media. After completion, contents of the reaction mixture were extracted into dichloromethane (2 × 25 mL) and washed with water (40 mL). Dichloromethane (DCM) layer was separated and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by flash column chromatography (SiO_2, ethyl acetate-hexane 1:2) to obtain end product (**Scheme-I**). The NMR and mass spectroscopic studies indicated that of the end products are uric acid derivatives. These results are similar to earlier observations [21,22].



Scheme-I: Oxidation of purine alkaloid to uric acid derivative

1,3,7-Trimethyl uric acid (oxidation product of caffeine): Mass (*m/z*) 210; NMR: δ 3.35(N-CH_3); δ 3.41(N-CH_3), δ 3.73 (N-CH_3); δ 13.49(O-H).

3,7-Dimethyl uric acid (oxidation product of theobromine): Mass (*m/z*) 196; NMR: δ 9.45 (N-H); δ 3.24 (N-CH_3), δ 3.73 (N-CH_3); δ 13.49 (O-H).

1,3-Dimethyl uric acid (oxidation product of theophylline): Mass (*m/z*) 196: NMR: δ 3.35 (N-CH_3); δ 3.41 (N-CH_3); δ 13.43 (O-H); δ 13.92 (N-H).

Temperature effect and the computation of activation parameters: Kinetic studies for the oxidation of purine alkaloids (caffeine, theophylline and theobromine) have been taken up at different temperatures range of 273-335 K, depending on the nature of substrate. An increase in temperature increased the reaction rate remarkably. The free energy of activation ($\Delta G^\#$) at a given temperature (T) is calculated using Eyring's equation according to the well-known theory of reaction rates [31,32],

$$\Delta G^\# = RT\ 1n\ (RT/Nhk) \quad (4)$$

Substituting the values for R (8.314 J/mol K), N (6.022 × 10^{23}/mol), h (6.626 × 10^{-34} J s) and T (Kelvin) respectively, $\Delta G^\#$ could be simplified accordingly as:

$$\Delta G^\# = 8.314 \times T\ [23.7641 + \ln(T/k)] \quad (5)$$

Enthalpy and entropies of activation ($\Delta H^\#$ and $\Delta S^\#$) were obtained from the plot of ($\Delta G^\#$) *versus* temperature (T) according to the Gibbs-Helmholtz eqn. 6.

$$\Delta G^\# = \Delta H^\# - T\Delta S^\# \quad (6)$$

RESULTS AND DISCUSSION

Mechanism of oxidation of purine alkaloids by Mn(VII) in Brønsted acid media: In aqueous acid media, $KMnO_4$ is known to exist as MnO_4^- (permanganate anion) and $HMnO_4$ (permanganic acid) due to protonation of MnO_4^-, according to the following protonation equilibrium [19].

$$H^+ + MnO_4^- \xrightleftharpoons{K} HMnO_4$$

$$(K = 2.99 \times 10^{-3}\ dm^3/mol\ at\ 25\ ^\circ C)$$

But, several earlier literature reports revealed that permanganate ion (MnO_4^-) reduces to Mn^{2+} according to the following equation:

$$MnO_4^- + 8H^+ + 5e^- \longrightarrow Mn^{2+} + 4H_2O$$

The Mn^{2+} species, as-formed, in turn reacts with permanganate ion (MnO_4^-) to afford Mn^{3+} and Mn^{4+} species as follows:

$$MnO_4^- + 3Mn^{2+} + 8H^+ \rightleftharpoons 3Mn^{3+} + Mn^{4+} + 4H_2O$$

It is well known that both Mn^{3+} and Mn^{4+} are also oxidizing species, which probably compete with acid permanganate ($HMnO_4$) to take part in the reaction. As a result, the plots of [log (Absorbance)] *versus* time may deviate from linearity showing autocatalytic behaviour of Mn(II). In such case, initial addition of Mn(II) should accelerate the rate of oxidation, while the addition of [F^-] should retard the rate of oxidation as suggested earlier [25-29]. However, in the present study a non-linearity is not observed in first order plots, but initial addition of [F^-] retarded the rate of oxidation, probably because the interaction of [F^-] with Mn(II) and/or Mn(III) to form inactive species. In view of these results (Table-1), it is observed that the pseudo first rate constant (k′) is the sum of the rate constants of Mn(VII) and Mn(III) contributions.

$$k' = k'_{Mn(VII)} + k'_{Mn(III)}$$

According to this contention, kinetic study in presence of known excess of NaF as additive ([NaF] > > [Mn(VII)]) should be equal to the observed rate constant corresponds to only due to permanganate oxidation ($k'_{Mn(VII)}$). Further, it is of interest to note that the difference between the gross rate constant (k′) (without NaF) and $k'_{Mn(VII)}$ (with NaF as additive), should give the contribution of Mn(III) oxidation path [($k'_{(Mn(III))}$) = k′ − $k'_{Mn(VII)}$]. We have separately prepared Mn(III) reagents and studied few reactions with a view to confirm and support this discussion. Table-2 clearly shows that $k'_{Mn(III)}$ values obtained using Mn(III) reagents are equal to the difference values [k′ − $k'_{Mn(VII)}$].

Acid catalysis and acidity functions: In dilute acids (when acid concentration < 0.10 mol dm^{-3}), the dependence of rate constant (k′) is generally interpreted as a function of pH. But in highly acidic solutions (when acidity ≥ 0.100 mol/dm^3), rate accelerations with an increase in acidity could be interpreted using different types of acidity functions, which were developed by Zucker- Hamett, Bunnett and Bunnett-Olson [30-40].

Accordingly, in the present study, the observed rate accelerations (Table-2) in different Brønsted acid concentrations were characterized by Zucker- Hamett (log (k) *vs.* (H_0); log k *vs.* log [Acid]), Bunnett ([log k + H_0] *vs.* log a_w; [log k − log acid] *vs.* log (a_w)) and Bunnett-Olson ((log k + H_0) *vs.* (H_0 + log [H^+]); (log k) *vs.* (H_0 + log [H^+]) plots were linear, with characteristic slopes, showing good to excellent correlation coefficients (0.995 > R^2 > 0.980) (Figures are not shown).

Observed slopes of Zucker- Hamett (m and $m^\#$), Bunnett (ω and $\omega^\#$) and Bunnett-Olsen (ϕ, or ϕ^*) plots pertaining to this study are compiled presented in Table-3, which were helpful to suggest the participation of water molecule and its significance in the rate determining step of the mechanism.

Table-3 clearly revealed that both the Zucker-Hammett's plots of log k *vs.* H_f and log k *vs.* log [Acid] are linear for all the substrates but none of them indicated ideal unit slopes suggesting water molecule participation in the rate determining step. At the same time, Bunnett's slopes gave unassumingly high slopes. However, Bunnett-Olsen's slopes are somewhat

TABLE-1
PSEUDO FIRST ORDER RATE CONSTANTS FOR THE OXIDATION OF XANTHINE ALKALOIDS USING Mn(VII) IN PRESENCE AND ABSENCE OF NaF AND ALSO Mn(III) REAGENTS (10^4 [Mn(VII)] = 4.00 mol/dm^3; 10^3 [Substrate] = 4.00 mol/dm^3; [Acid] = 0.200 mol/dm^3; 10^3 [NaF] = (a) Nil (b) 8.00 mol/dm^3; Temp. = 298 K)

[Acid] (mol/dm^3)	(k'/min) in H_2SO_4 medium			(k'/min) in $HClO_4$ medium		
	Caffeine	Theophylline	Theobromine	Caffeine	Theophylline	Theobromine
0.200	0.007	0.027	0.029	0.009	0.045	0.029
0.400	0.008	0.027	0.033	0.010	0.062	0.035
0.800	0.009	0.031	0.035	0.012	0.065	0.041
1.200	0.010	0.032	0.036	0.030	0.068	0.049
1.600	0.011	0.036	0.038	0.014	0.079	0.054
2.000	0.013	0.038	0.041	0.015	0.085	0.059

TABLE-2
EFFECT OF VARIATION OF [ACID] IN Mn(VII) OXIDATION OF ALKALOIDS

Brønsted acid	Xanthine alkaloid (substrate)	Observed rate constant values		$(k')_{Mn(III)}$	
		Without NaF (k')	With NaF $(k')_{Mn(VII)}$	Difference in (k')-$(k')_{Mn(VII)}$	Using Mn(III) reagent
H_2SO_4	Theobromine	0.084	0.053	0.031	0.025
	Theophylline	0.028	0.006	0.021	0.027
$HClO_4$	Theobromine	0.029	0.013	0.016	0.015
	Theophylline	0.045	0.037	0.008	0.008

TABLE-3
ACIDITY FUNCTION PLOTS (XANTHINE DERIVATIVES) IN DIFFERENT ACID MEDIA

Compound	Theory/Plot	Parameter	H_2SO_4		$HClO_4$	
			Slope	R^2	Slope	R^2
Theobromine	Zucker-Hammett-I	m	0.128	0.976	0.311	0.989
	Zucker-Hammett-II	m*	-0.108	0.983	-0.303	0.947
	Bunnett-III	ω	14.2	0.956	7.93	0.959
	Bunnett-IV	ω*	-12.9	0.913	-10.2	0.940
	Bunnett-Olsen-V	ϕ	-1.11	0.941	-0.701	0.833
	Bunnett-Olsen-VI	ϕ*	1.21	0.998	1.43	0.998
Theophylline	Zucker-Hammett-I	m	0.156	0.913	0.243	0.925
	Zucker-Hammett-II	m*	-0.104	0.966	-0.173	0.883
	Bunnett-III	ω	16.3	0.994	10.8	0.991
	Bunnett-IV	ω*	-10.9	0.940	-11.5	0.936
	Bunnett-Olsen-V	ϕ	-1.48	0.965	-1.22	0.925
	Bunnett-Olsen-VI	ϕ*	1.16	0.998	1.38	0.996
Caffeine	Zucker-Hammett-I	m	0.220	0.964	0.222	0.980
	Zucker-Hammett-II	m*	-0.187	0.979	-0.220	0.969
	Bunnett-III	ω	12.9	0.974	8.91	0.976
	Bunnett-IV	ω*	-15.9	0.929	-10.2	0.940
	Bunnett-Olsen-V	ϕ	-0.101	0.938	-0.798	0.870
	Bunnett-Olsen-VI	ϕ*	1.31	0.997	1.33	0.997

in the range of suggesting water molecule participation either as a nucleophile or as a proton transfer reagent in the slow step (Table-4).

Effect of structure on enthalpy and entropy changes: The entropy of activation ($\Delta S^{\#}$) provides useful information about the molecularity of the rate determining step in a reaction, *i.e.* whether the reactants are bonded to each other or not. Positive values for $\Delta S^{\#}$ suggest that entropy increases upon achieving the transition state, which often indicates a dissociative mechanism. Negative values for $\Delta S^{\#}$ indicate that entropy decreases upon achieving the transition state, which often indicates an associative mechanism [30-32]. An insight into the activation parameters data presented in Table-5 indicated that entropy of activation is negative for Mn(VII) oxidation of caffeine, theophylline and theobromine in both sulfuric acid and perchloric acid. This observation suggests associative mechanism followed by greater solvation (water molecule participation) in the transition state. On the basis foregoing negative magnitude of entropy of activation (Table-4) together with the slopes of Bunnett-Olsen's plots, it can be concluded that water participates in the slow step as a proton transfer reagent through hydration in the transition state. Accordingly, the most plausible mechanism is shown in **Scheme-II**.

Rate law for the above mechanism could be given as:

$$\frac{-d[\text{Mn(VII)}]}{dt} = kK[\text{Mn(VII)}][\text{Substrate}][\text{Acid}]$$

At constant acidity ([H_2SO_4] or [$HClO_4$], rate law comes out as:

$$\frac{-d[\text{Mn(VII)}]}{dt} = k[\text{Mn(VII)}][\text{Substrate}]$$

where k″ = kK[Acid] and Substrate = Caffeine, theophylline or theobromine.

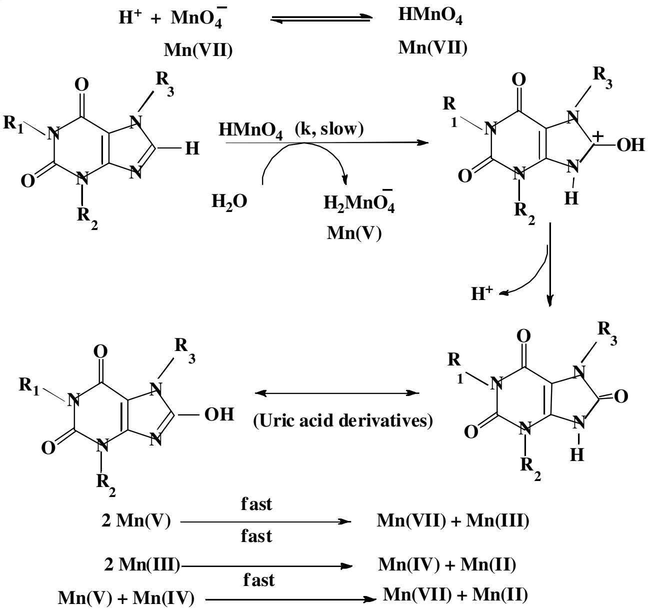
Above rate law is in accordance with the observed kinetics at any given temperature and acidity.

TABLE-4
ZUCKER-HAMMETT, BUNNETT AND BUNNETT-OLSEN's HYPOTHESIS

Type of acidity functions and kinetic plots	Slope value	Function of water molecule in the rate determining step
Zucker-Hammett (H_0) plots		
log (k) *vs.* (H_0)	(m) = 1.00	H_2O molecule is not involved
log (k) *vs.* log [Acid]	(m*) ≠ 1.00	H_2O molecule may involve
Bunnett Plots [log (k + (H_0)] *vs.* log a_{H_2O}	(ω) = –2.5 to 0.0	H_2O not involved
	(ω) = +1.2 to 3.3	H_2O as a nucleophilic agent
	(ω) = +3.3 to 7.0	H_2O as a proton abstracting agent
Bunnett Plots [log (k) - log(acid)] *vs.* log a_{H_2O}	(ω*) < (–2)	H_2O as a nucleophilic agent
	(ω*) > (–2)	H_2O as a proton abstracting agent
Bunnett-Olsen Plots (for weakly basic compounds) (log k + H_0) *vs.* (H_0 + log [H^+])	(ω) = –0.34 to 0	H_2O molecule is not involved
	(ϕ) = +0.18 to 0.47	H_2O as a nucleophilic agent
	(ϕ) > 0.47	H_2O as a proton transfer agent
Bunnett-Olsen plots (for moderately basic compounds) (log k) *vs.* (H_0 + log [H^+])	($\phi^{\#}$) = –0.34 to 0	H_2O molecule is not involved
	($\phi^{\#}$) = +0.18 to 0.47	H_2O as a nucleophilic agent
	($\phi^{\#}$) > 0.47	H_2O as a proton transfer agent

TABLE-5
TEMPERATURE DEPENDENT OF KINETIC AND ACTIVATION PARAMETERS

Substrate	Temp.	(k) ($dm^3/mol/min$)	$\Delta G^{\#}$ (kJ/mol)	GH Eq.	$\Delta H^{\#}$ (kJ/mol)	$-\Delta S^{\#}$ (J/K/mol)
Sulfuric acid medium						
Theobromine	273	8.60	62.0	y = 0.1611x + 17.492	17.5	166
	283	15.4	63.0			
	293	20.0	64.5			
	303	21.0	67.0			
Theophylline	273	18.3	60.0	y = 0.1884x + 8.537	8.54	188
	283	23.0	62.0			
	293	27.4	64.0			
	303	29.4	66.0			
Caffeine	298	0.900	73.0	y = 0.207x + 11.726	11.7	207
	313	1.00	77.0			
	323	1.50	78.0			
	333	1.50	81.0			
Perchloric acid medium						
Theobromine	273	6.55	62.4	y = 0.228x + 0.1635	16.3	228
	283	6.72	64.7			
	293	6.95	67.0			
	298	7.22	68.1			
Theophylline	273	16.2	60.3	y = 0.2205x + 0.1434	14.3	220
	283	16.6	62.6			
	293	17.0	64.8			
	298	18.0	65.8			
Caffeine	273	1.95	65.1	y = 0.2342x + 1.2306	12.3	234
	283	2.00	67.6			
	293	2.12	69.9			
	298	2.28	70.9			



Scheme-II: Acid catalyzed Mn(VII) oxidation of xanthine alkaloids

Conclusion

The oxidation of purine alkaloids *viz.* caffeine, theophylline, theobromine by hypervalent Mn reagent ($KMnO_4$) in aqueous sulfuric and perchloric acid media were studied. The reactions did not occur in in the absence of acid, but are accelerated by the addition of sulfuric acid and perchloric acid remarkably. Reactions are faster in perchloric acid media as compared to those in sulfuric acid. The observed rate accelerations were analyzed by Zucker-Hammett, Bunnett and Bunnett-Olsen criteria of acidity functions. Observed slope values (ϕ or ϕ^*) of Bunnett-Olsen plots indicate the involvement of water molecule in the slow step (as proton transferring agent).

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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