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Research Article

Polyethylene Glycols as Efficient Catalysts for the Oxidation of Xanthine Alkaloids by Ceric Ammonium Nitrate in Acetonitrile: A Kinetic and Mechanistic Approach

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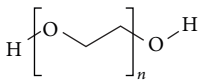
Kinetics of oxidation of xanthine alkaloids, such as Xanthine (XAN), hypoxanthine (HXAN), caffeine (CAF), theophylline (TPL), and theobromine (TBR), have been studied with ceric ammonium nitrate (CAN) using poly ethylene glycols (PEG) as catalysts. Reaction obeyed first order kinetics in both [CAN] and [Xanthine alkaloid]. Highly sluggish CAN-xanthine alkaloid reactions (in acetonitrile media even at elevated temperatures) are enhanced in presence PEGs (PEG-200, -300, -400, -600). An increase in [PEG] increased the rate of oxidation linearly. This observation coupled with a change in absorption of CAN in presence of PEG, $[H–(OCH_2–CH_2)_n–O–NH_4Ce(NO_3)_4(CH_3CN)]$ (PEG bound CAN species), is considered to be more reactive than CAN. The mechanism of oxidation in PEG media has been explained by Menger-Portnoy's enzymatic model.

1. Introduction

There has been an increasing interest in the kinetics of electron transfer reactions since more than half a century because of their ever green importance in understanding the mechanisms of industrially, pharmaceutically, and biologically important redox reactions [1–11]. A special focus has been paid to single electron transfer (SET) oxidations [1–18]. In this context, ceric ammonium nitrate (CAN) has emerged as one of the most valuable and notable SET oxidants for a variety of reactions [19–30], due to its relative abundance, ease of preparation, low cost, and low toxicity. During the oxidation of organic substrates, the initial formation of a radical or radical cation is usually followed by rearrangement or follow-up reactions that led to other free radical intermediates. Typically, the free radical reacts with another substrate (olefin, etc.) to form a new C–C bond and a product radical. Oxidation of the free radical intermediate to a cation leads to capture of solvent or nitrate expelled from CAN upon its reduction to Ce(III) and these alternative mechanistic pathways result in many of the side products prevalent in oxidations. Therefore, preparative Ce(IV) initiated oxidations cannot be achieved in many instances. Chemical intuition suggests that these pathways can be depressed by understanding the interrelationship between the mechanism of oxidation by Ce(IV), the effect of solvent on the stability of the initially formed radical cation intermediate, and the rates (mechanisms) of various available pathways.

Polyethylene glycol (PEG) is a polyether compound with many applications from industrial manufacturing to medicine. It has also been known as polyethylene oxide (PEO) or polyoxyethylene (POE), depending on its molecular weight. PEG is a neutral, hydrophilic polyether and less expensive. It avoids the use of acid or base catalysts and reagent can be recovered and reused. Thus, it offers a convenient, inexpensive, nonionic, nontoxic, and recyclable reaction medium for the replacement of volatile organic solvents (see Scheme 1).

Polyethylene glycol (PEG) is a condensation polymer of ethylene oxide and water with the general formula $[H(OCH_2CH_2)_nOH]$, where n is the average number of repeating oxyethylene groups typically from 4 to about 180. The low molecular weight members from $n = 2$ to 4 are diethylene glycol, triethylene glycol, and tetra ethylene glycol,



Scheme 1: Structure of polyethylene glycol (PEG).

respectively, which are produced as pure compounds. The wide range of chain lengths provides identical physical and chemical properties for the proper application selections directly or indirectly in the field of chemical and biological sciences. In recent past polyethylene glycols (PEGs) have been used as catalysts and catalyst supports and also have been found to be an inexpensive, non-toxic, environmentally friendly reaction medium, which avoid the use of acid or base catalysts. Moreover PEG can be recovered after completion of the reactions and recycled/reused [31–37] in another batch. Inspired by the striking features of PEG the author wants to use it as a catalyst by avoiding the use of acid in the present study, namely, ceric ammonium nitrate (CAN) triggered oxidation of certain xanthine alkaloid compounds. Acetonitrile is used as solvent in order to facilitate kinetic studies.

2. Experimental Details

Poly ethylene glycols were procured from E-Merck and other materials used were similar to those given in previous chapters. Thermostat was adjusted to desired reaction temperature. Flask containing known amount of ceric ammonium nitrate (CAN) in acetonitrile solvent and another flask containing the substrate (Xanthine alkaloid) and suitable amount of PEG solutions were clamped in a thermostatic bath. Reaction was initiated by mixing requisite amount of CAN to the other contents of the reaction vessel. The entire reaction mixture was mixed thoroughly. 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 CAN content could be estimated from the previously constructed calibration curve showing absorbance versus [CAN]. Absorbance values were in agreement to each other with an accuracy of ±3% error.

2.1. Determination of the Order of Reaction and Salient Kinetic Features

(1) Reactions were conducted under two different conditions. Under pseudo first order conditions [CAF] ≫ [CAN], plots of $\ln(A_0/A_t)$, that is, $\ln[a/(a-x)]$ versus time, were straight lines with positive slopes, passing through origin indicating first order (x) with respect to [oxidizing agent] (Figure 1).

(2) This reaction is also conducted under second order conditions with equal concentrations of $[CAF]_0 = [CAN]_0$. Under these conditions, kinetic plots of $[1/(A_t)]$ versus time have been found to be linear with a positive gradient and definite intercept on ordinate (vertical axis), indicating overall second order kinetics (Figure 2). Since the order with respect to [CAN] is already verified as one under pseudo conditions this observation suggests that order in [CAF] is also one.

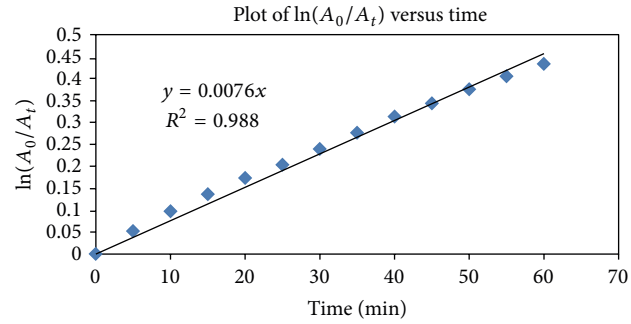


Figure 1: Pseudo first order kinetic plots of caffeine with MeCN at 310 K. [CAF] = 0.016 mol dm^{-3}; [CAN] = 0.0041 mol dm^{-3}; [PEG-300] = 0.062 mol dm^{-3}.

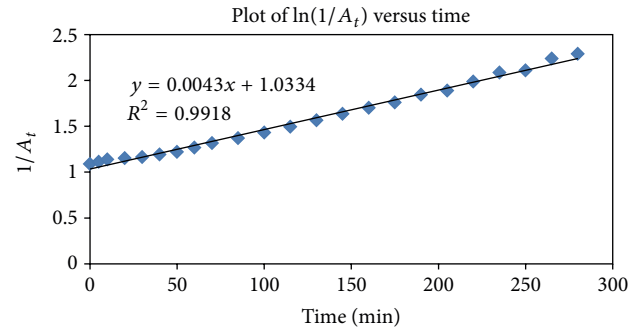


Figure 2: Second order kinetic plots of caffeine with MeCN at 310 K. [CAF] = 0.002 mol dm^{-3}; [CAN] = 0.002 mol dm^{-3}; [PEG-300] = 0.375 mol dm^{-3}.

(3) In PEG mediated reactions an increase in the [PEG] increased the reaction rates depending on the nature of PEG. By and large reaction rates were found high in PEG-200 media over other PEGs (Tables 2, 3, 4, 5, and 6).

(4) In the present study, kinetic data have been collected at three to four different temperatures within the range of 300 to 320 K. Activation parameters such as $\Delta H^{\#}$ and $\Delta S^{\#}$ have been evaluated by Eyring's equation. Free energy of activation ($\Delta G^{\#}$) is obtained from Gibbs-Helmholtz equation. The data related to activation parameters are compiled in Tables 2 to 6.

(5) Addition of olefin monomer (acryl amide and acrylonitrile) to the reaction mixture decreased the reaction rate. When heated, the contents of the reaction mixture turned viscous and indicated dense polymer formation. This observation can be explained due to the induced vinyl polymerization of added monomer, showing the presence of free radicals in the system.

Table 1: Binding constants of [CAN-PEG] at 303°K using Benesi-Hildebrand method.

S. N.	PEG	Benesi-Hildebrand Equation	K	ε	$-\Delta G$ (kJ/mol)
1	PEG-200	$y = 7E-05x + 0.052$	743	19.23	16.7
2	PEG-300	$y = 9E-05x + 0.055$	611	18.18	16.2
3	PEG-400	$y = 5E-05x + 0.071$	1420	14.08	18.3

Table 2: Activation parameters of caffeine in different PEG media.

Type of PEG	PEG % (V/V)	k'' at 300 K	Equation obtained for plot of $\ln(k''/T)$ versus $(10^3/T)$	R^2	$\Delta H^{\#}$ kJ/mol	$\Delta G^{\#}$	$-\Delta S^{\#}$ J/Kmol
PEG-200	0.5	0.4	$y = -4.1044x + 7.088$	0.985	34.1	75.2	138
	1.0	0.5	$y = -3.9118x + 6.686$	0.963	32.4	74.7	141
	2.0	0.6	$y = -3.4191x + 5.218$	0.968	28.3	74.5	154
	3.0	0.6	$y = -5.24x + 11.28$	0.989	43.5	74.7	103
	4.0	0.7	$y = -4.4927x + 8.922$	0.999	37.2	74.2	123
	5.0	0.9	$y = -3.9922x + 7.503$	0.999	33.1	73.6	135
PEG-300	0.5	0.2	$y = -5.7209x + 11.77$	0.997	47.5	76.6	99.7
	1.0	0.3	$y = -4.4045x + 7.775$	1.00	36.5	76.1	132
	2.0	0.4	$y = -4.1044x + 7.088$	0.986	34.1	75.5	138
	3.0	0.5	$y = -3.0174x + 3.654$	0.998	25.0	75.1	167
	4.0	0.6	$y = -2.1466x + 0.948$	0.995	17.8	74.5	189
	5.0	0.7	$y = -1.8624x + 0.153$	0.996	15.4	73.5	196
PEG-400	0.5	0.2	$y = -4.0901x + 6.298$	0.992	33.9	75.6	139
	1.0	0.4	$y = -1.6439x - 1.125$	0.974	13.6	70.0	188
	2.0	0.5	$y = -1.3085x - 2.031$	0.998	10.8	64.8	180
	3.0	0.6	$y = -1.0727x - 2.636$	0.999	8.90	61.4	175
	4.0	0.7	$y = -3.0329x + 4.079$	0.971	25.1	74.0	163
	5.0	0.8	$y = -3.0238x + 4.168$	0.992	25.0	73.6	162
PEG-600	0.5	0.2	$y = -4.9831x + 9.337$	0.980	41.3	77.0	119
	1.0	0.3	$y = -3.7714x + 5.687$	0.988	31.3	76.3	150
	2.0	0.4	$y = -3.0286x + 3.490$	0.992	25.1	75.5	168
	3.0	0.6	$y = -1.6344x - 0.784$	0.966	13.5	70.8	191
	4.0	0.7	$y = -1.3993x - 1.412$	0.963	11.6	67.1	185
	5.0	0.9	$y = -0.6541x - 3.627$	0.999	5.42	55.5	167

2.2. CAN-PEG Binding Studies. UV-Visible Spectrophotometric studies were performed in order to throw light on CAN binding with PEG (Poly ethylene glycol). Absorption spectra of CAN in acetonitrile indicated a band at 459 nm; this band underwent a hypsochromic shift from 459 nm to 441 nm in presence of 0.1 mol PEG, suggesting the interaction of PEG with CAN (Figure 3):

$$\underset{\text{(PEG)}}{\text{H}-(\text{OCH}_2-\text{CH}_2)_n-\text{OH}} + \underset{\text{(CAN)}}{(\text{NH}_4)\left[\text{Ce}(\text{NO}_3)_5\,(\text{ACN})\right]} \overset{K}{\rightleftharpoons} \underset{\text{Complex (C) or [PEG-CAN]}}{\left[\text{PEG}-\text{NH}_4\text{Ce}(\text{NO}_3)_5\right]\,(\text{ACN}).} \quad (1)$$

The [CAN-PEG] binding constants were evaluated by Benesi-Hildebrand equation according to the method reported in the literature [38], as elaborated in our earlier paper.

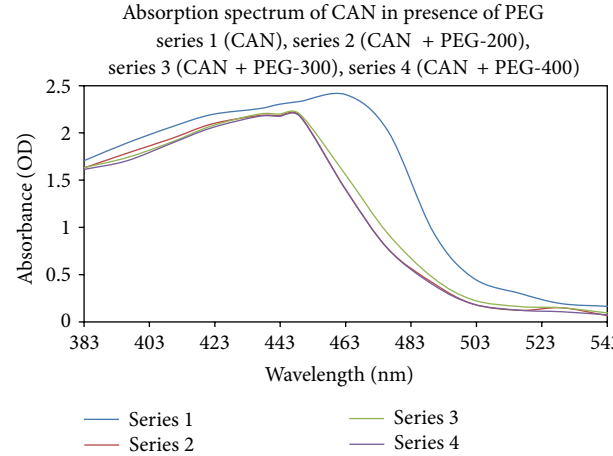


Figure 3: Absorption of spectra of CAN in presence of PEG.

Table 3: Activation parameters of Xanthine in different PEG media.

Type of PEG	PEG % (V/V)	k'' at 300 K	Equation	R^2	$\Delta H^{\#}$ kJ/mol	$\Delta G^{\#}$	$-\Delta S^{\#}$ J/Kmol
PEG-200	0.5	0.09	$y = -6.7533x + 14.44$	0.987	56.0	79.2	77.5
	1.0	0.11	$y = -7.6965x + 17.79$	0.989	63.9	78.7	49.6
	2.0	0.14	$y = -7.2183x + 16.39$	0.999	60.0	78.3	61.3
	3.0	0.16	$y = -7.2597x + 16.71$	0.986	60.2	77.7	58.6
	4.0	0.18	$y = -7.225x + 16.72$	0.977	59.9	77.4	58.5
	5.0	0.21	$y = -6.8661x + 15.69$	0.971	57.0	77.1	67.1
PEG-300	0.5	0.07	$y = -6.3772x + 12.96$	0.961	52.9	79.8	89.8
	1.0	0.09	$y = -6.2301x + 12.70$	0.983	51.7	79.0	91.9
	2.0	0.11	$y = -7.0542x + 15.55$	0.987	58.8	79.2	68.2
	3.0	0.14	$y = -6.7082x + 14.77$	0.951	55.7	78.1	74.7
	4.0	0.14	$y = -6.7034x + 14.74$	0.966	55.6	78.1	75.0
	5.0	0.16	$y = -6.4505x + 14.04$	0.958	53.5	77.7	80.8
PEG-400	0.5	0.11	$y = -2.0567x - 1.059$	0.999	17.0	73.4	188
	1.0	0.14	$y = -1.6434x - 2.177$	0.980	13.6	67.3	179
	2.0	0.14	$y = -4.9725x + 8.909$	0.999	41.2	78.1	123
	3.0	0.21	$y = -4.4045x + 7.418$	0.999	36.5	77.0	135
	4.0	0.28	$y = -3.7414x + 5.514$	0.991	31.0	76.3	151
	5.0	0.30	$y = -3.5601x + 4.983$	0.985	29.5	76.3	156
PEG-600	0.5	0.16	$y = -3.4399x + 3.886$	0.957	28.5	78.0	165
	1.0	0.18	$y = -3.4127x + 3.971$	0.995	28.3	77.5	164
	2.0	0.18	$y = -4.5044x + 7.594$	1.00	37.3	77.5	134
	3.0	0.21	$y = -4.1343x + 6.498$	0.994	34.3	77.2	143
	4.0	0.30	$y = -2.6889x + 2.060$	0.999	22.3	76.3	180
	5.0	0.39	$y = -2.2924x + 0.992$	0.999	19.0	75.7	189

The equilibrium constant $K = [C]/[CAN][PEG]$, where [CAN], [PEG], and [C] are equilibrium concentrations of acceptor (CAN), donor (PEG), and complex, respectively. For the above equilibrium, concentration of [PEG-CAN] complex ([C]) can be correlated to the formation constant (K) by the following relationship. If $[CAN]_0$ and $[PEG]_0$ represent initial concentrations of CAN and PEG, respectively, then

$$[C] = \frac{K[CAN]_0[PEG]_0}{1 + K[PEG]_0}. \quad (2)$$

But according to Lambert-Beer's law absorbance, $(A) = \epsilon cl$.

In the above equations, l is path length, d is absorbance, ϵ is the molar extinction coefficient, and K is formation constant of the complex, respectively. For one cm path length, above equation can be written as, $(A) = \epsilon c$,

$$[C] = \frac{A}{\epsilon l} = \frac{K[CAN]_0[PEG]_0}{1 + K[PEG]_0}. \quad (3)$$

Further, taking the reciprocals to the above equation, it rearranges to

$$\frac{[CAN]_0}{A} = \frac{1}{K[PEG]_0\epsilon} + \frac{1}{\epsilon}. \quad (4)$$

However, the absorbance of CAN and [CAN-PEG] absorb in the same region significantly; therefore the observed absorbance (A) could be written as

$$A = A_{(CAN)} + A_{(Complex)},$$
$$A_{(Complex)} = \Delta A = A \sim A_{(CAN)}. \quad (5)$$

Therefore, a plot of $([CAN]_0/\Delta A)$ versus $1/[PEG]_0$ should give a straight line according to the above equation. These plots have been realized in the present study (Figure 4). Formation constant (K) has been calculated from the ratio of intercept to slope, while inverse of the intercept gave molar extinction coefficient (ϵ) and is represented in Table 1.

3. Results and Discussion

3.1. Mechanism of CAN Oxidation of Xanthine Alkaloids in MeCN Medium. Earlier reports on CAN oxidation studies from our laboratory and elsewhere show that a variety of CAN species such as $Ce(NO_3)_6^{2-}$, $Ce(NO_3)_5^{-}$, $Ce(OH)(NO_3)_4^{-}$, $Ce(NO_3)_4$, and $Ce(OH)^{3+}$ may exist in nitric acid medium [39–43]. However, CAN species in MeCN medium could be entirely different. Since MeCN is large

Table 4: Activation parameters of hypoxanthine in different PEG media.

Type of PEG	PEG % (V/V)	k'' at 300 K	Equation	R^2	$\Delta H^{\#}$ kJ/mol	$\Delta G^{\#}$	$-\Delta S^{\#}$ J/Kmol
PEG-200	0.5	0.04	$y = -9.0666x + 12.37$	0.976	75.2	103	94.7
	1.0	0.09	$y = -5.8149x + 11.36$	0.978	48.3	79.2	103
	2.0	0.11	$y = -5.7982x + 11.48$	0.962	48.1	78.7	102
	3.0	0.18	$y = -4.2045x + 6.604$	0.998	34.8	77.4	142
	4.0	0.21	$y = -4.1526x + 6.623$	0.965	34.4	77.3	143
	5.0	0.02	$y = -4.3082x + 7.221$	0.981	35.7	76.8	137
PEG-300	0.5	0.14	$y = -4.3602x + 6.862$	1.00	36.1	78.1	140
	1.0	0.16	$y = -4.344x + 6.985$	0.972	36.0	77.1	139
	2.0	0.18	$y = -4.2045x + 6.604$	0.998	34.9	77.5	142
	3.0	0.21	$y = -4.2723x + 6.939$	0.988	35.4	77.1	139
	4.0	0.23	$y = -3.9753x + 6.107$	0.982	33.0	76.8	146
	5.0	0.25	$y = -4.145x + 6.761$	0.978	34.4	76.7	141
PEG-400	0.5	0.16	$y = -4.3194x + 6.817$	0.971	35.8	77.8	140
	1.0	0.18	$y = -4.1982x + 6.561$	0.997	34.8	77.7	143
	2.0	0.21	$y = -3.9535x + 5.901$	0.997	32.8	77.2	148
	3.0	0.23	$y = -3.9681x + 6.058$	0.999	32.9	77.0	147
	4.0	0.25	$y = -4.2862x + 7.204$	0.998	35.5	76.6	137
	5.0	0.28	$y = -4.0984x + 6.692$	0.998	32.7	75.0	141
PEG-600	0.5	0.14	$y = -3.0095x + 2.327$	0.963	24.9	78.3	178
	1.0	0.21	$y = -3.0241x + 2.815$	1.00	25.0	77.2	174
	2.0	0.25	$y = -2.6271x + 1.673$	0.997	21.8	76.7	183
	3.0	0.30	$y = -2.4203x + 1.15$	0.995	20.0	76.4	188
	4.0	0.35	$y = -2.5077x + 1.581$	0.974	20.8	76.0	184
	5.0	0.42	$y = -2.283x + 1.035$	0.999	18.9	75.3	188

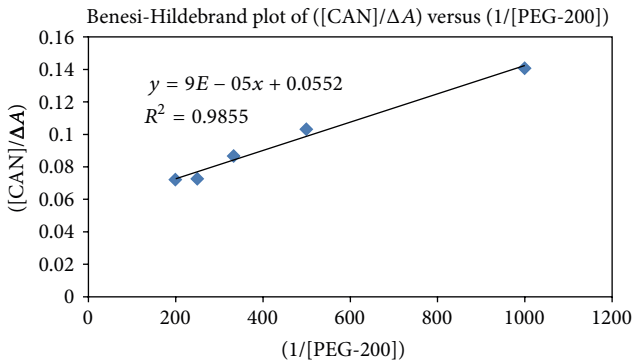


Figure 4: Benesi-Hildebrand plot of CAN-PEG-200.

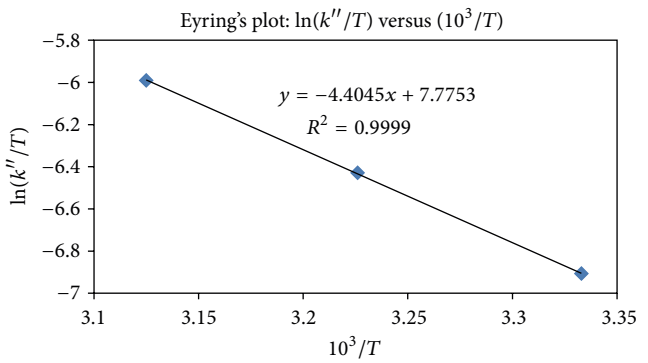


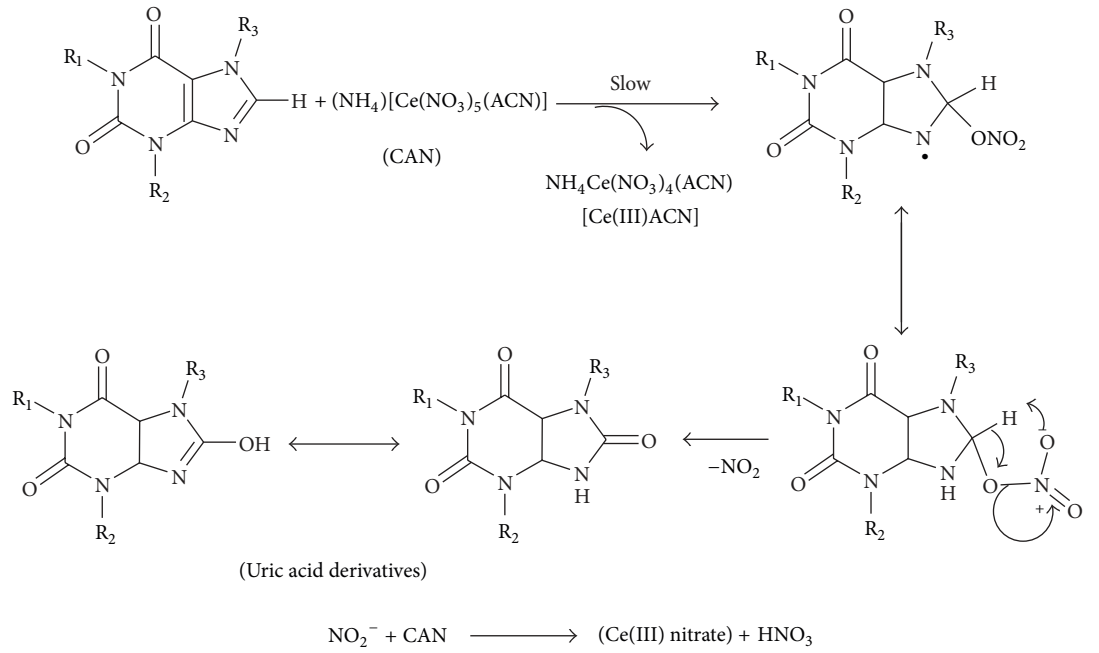
Figure 5: Eyring's plot: PEG-300 catalysed oxidation of caffeine by CAN.

excess over [CAN], MeCN may penetrate into the coordination spheres of Ce(IV) and form *solvated CAN species* according to the following equilibrium:

$$\underset{\text{(CAN)}}{(NH_4)_2Ce(NO_3)_6} + CH_3CN \rightleftharpoons \underset{\text{(Solvated CAN)}}{[(NH_4)\,Ce(NO_3)_5\,(CH_3CN)]} + NH_4NO_3. \quad (6)$$

Solvated CAN may be able to oxidize the substrate to afford uric acid as product, when Xanthine alkaloid is added to the reaction mixture (see Scheme 2).

3.2. Mechanism of Oxidation in PEG Media. Progress of the reaction has been studied in the presence of a set of poly oxy ethylene compounds (PEGs) with varied molecular weights ranging from 200 to 6000 units, and it was



Scheme 2: CAN oxidation of xanthine alkaloids in ACN medium.

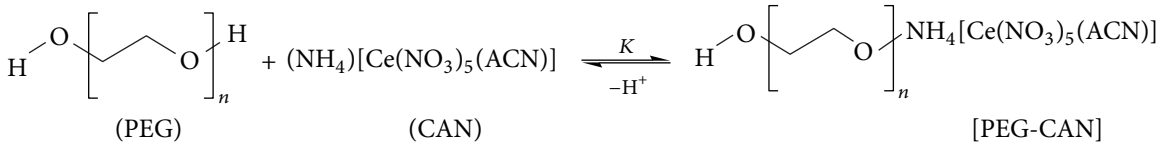
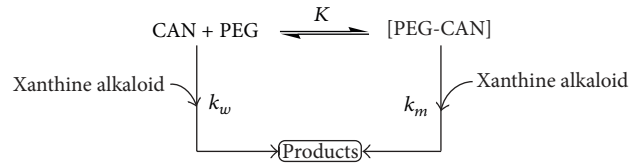


Figure 6

found that the reaction is enhanced remarkably in all PEGs. Reaction times were reduced from 24 hrs to few hours. The catalytic activity was found to be in the decreasing order: PEG-200 > PEG-300 > PEG-400 > PEG-600. UV-Visible Spectroscopic results presented in Figure 5 clearly indicated a bathochromic/hypsochromic shift from 459 nm to around 442 nm, followed by hypochromic shift clearly indicate CAN and PEG interactions to afford "PEG bound CAN" [PEG-CAN] according to the following equilibrium (see Figure 6).

The plots of k_m (rate constant of PEG reaction) versus C_{PEG} (concentration of PEG) indicated a rate maxima nearly in the vicinity of 1.50 mol dm^{-3} PEG-200, 0.99 mol dm^{-3} PEG-300, 0.75 mol dm^{-3}, PEG-400, 0.500 mol dm^{-3}, and PEG-600. Mechanism of PEG mediated CAN-xanthine alkaloids reactions was explained in the lines of micellar catalysis because PEG resembles the structure of non-ionic micelles such as Triton-X. Menger and Portnoy model is used to explain PEG effects, which closely resemble that of an enzymatic catalysis [44–48]. According to this model, formation of PEG bound reagent (PEG-Ce(IV)) could occur in the preequilibrium step due to the interaction of Ce(IV) with PEG. The complex thus formed may possess higher or lower reactivity to give products. A general



Scheme 3: CAN oxidation mechanism in presence of PEG.

mechanism is proposed by considering the bulk phase and micellar phase reactions as shown in Scheme 3, where k_m and k_0 or (k_w) represent rate constants for PEG and bulk phases, respectively, and K is the [PEG-Ce(IV)] binding constant. For the above mechanism, rate law could be derived according to the following sequence of steps in the lines of micellar catalyzed reactions. From Scheme 3 rate (V) of the reaction comes out as

$$V = \{k_0\,[\mathrm{CAN}] + k_m\,[\mathrm{PEG\_CAN}]\}\,C_S,$$
$$\frac{V}{C_S} = k' = k_0\,[\mathrm{CAN}] + k_m\,[\mathrm{PEG\_CAN}]\,. \tag{7}$$

Table 5: Activation parameters of theophylline in different PEG media.

Type of PEG	PEG % (V/V)	k'' at 300 K	Equation	R^2	$\Delta H^{\#}$ kJ/mol	$\Delta G^{\#}$	$-\Delta S^{\#}$ J/Kmol
PEG-200	0.5	0.39	$y = -1.426x - 1.899$	0.993	11.8	66.1	181
	1.0	0.49	$y = -2.6456x + 2.392$	0.993	21.9	75.0	177
	2.0	0.51	$y = -2.8259x + 3.021$	0.984	23.4	75.0	172
	3.0	0.53	$y = -3.3595x + 4.821$	0.964	27.8	74.9	157
	4.0	0.56	$y = -3.5908x + 5.700$	0.995	29.8	74.8	150
	5.0	0.65	$y = -3.8286x + 6.599$	0.984	31.7	74.3	142
PEG-300	0.5	0.23	$y = -5.1973x + 10.21$	0.952	43.1	76.7	112
	1.0	0.30	$y = -4.348x + 7.607$	0.992	36.0	76.2	134
	2.0	0.37	$y = -3.7544x + 5.847$	0.979	31.1	75.5	148
	3.0	0.39	$y = -3.6694x + 5.622$	0.970	30.4	75.4	150
	4.0	0.44	$y = -3.2984x + 4.504$	0.969	27.3	75.3	160
	5.0	0.51	$y = -3.0744x + 3.877$	0.998	25.5	75.0	165
PEG-400	0.5	0.16	$y = -5.2588x + 9.971$	0.995	43.6	77.8	114
	1.0	0.25	$y = -3.8986x + 5.902$	0.999	32.3	76.7	148
	2.0	0.28	$y = -4.1044x + 6.732$	0.986	34.0	76.3	141
	3.0	0.30	$y = -4.2289x + 7.215$	0.988	35.1	76.2	137
	4.0	0.32	$y = -4.4535x + 8.039$	0.978	36.9	75.9	130
	5.0	0.44	$y = -3.187x + 4.113$	0.993	26.4	75.3	163
PEG-600	0.5	0.11	$y = -4.8443x + 8.296$	0.956	40.2	78.6	128
	1.0	0.21	$y = -3.2573x + 3.634$	0.953	27.0	77.1	167
	2.0	0.25	$y = -3.1274x + 3.359$	0.981	25.9	76.6	169
	3.0	0.35	$y = -2.1206x + 0.333$	0.979	17.6	75.8	194
	4.0	0.44	$y = -1.5663x - 1.290$	0.980	13.0	68.8	186
	5.0	0.60	$y = -0.7623x - 3.664$	0.958	6.33	56.4	167

Considering the total concentration of (C_S) as the algebraic sum of free species and PEG bound CAN complex (PEG-CAN) species,

$$C_{\text{CAN}} = [\text{CAN}] + [\text{PEG-CAN}]. \tag{8}$$

From PEG-CAN binding equilibrium,

$$K = \frac{[\text{PEG-CAN}]}{[\text{PEG}]\,[\text{CAN}]} \quad \text{or} \quad [\text{CAN}] = \frac{[\text{PEG-CAN}]}{K\,[\text{PEG}]}. \tag{9}$$

Substitution of [CAN] in (7) gives

$$\begin{aligned} C_{\text{CAN}} &= \frac{[\text{PEG-CAN}]}{K\,[\text{PEG}]} + [\text{PEG-CAN}] \\ &= \frac{[\text{PEG-CAN}] + K\,[\text{PEG}]\,[\text{PEG-CAN}]}{K\,[\text{PEG}]} \\ \text{or } [\text{PEG-CAN}] &= \frac{K\,[\text{PEG}]\,C_{\text{CAN}}}{1 + K\,[\text{PEG}]}. \end{aligned} \tag{10}$$

Similarly free substrate [CAN] is written as, $[\text{CAN}] = C_{\text{CAN}} - [\text{PEG-CAN}]$,

$$[\text{CAN}] = C_{\text{CAN}} - \frac{K\,[\text{PEG}]\,C_{\text{CAN}}}{1 + K\,[\text{PEG}]}. \tag{11}$$

After simplification, the above equation reduces to

$$[\text{CAN}] = \frac{C_{\text{CAN}}}{1 + K\,[\text{PEG}]}. \tag{12}$$

Substitution of [PEG-CAN] and [CAN] in rate equation (7) gives

$$k' = \frac{k_0 C_{\text{CAN}}}{1 + K\,[\text{PEG}]} + \frac{k_m K\,[\text{PEG}]\,C_{\text{CAN}}}{1 + K\,[\text{PEG}]}, \tag{13}$$

$$\text{or } k_\varphi = \frac{k_0 + k_m K\,[\text{PEG}]}{1 + K\,[\text{PEG}]}, \tag{14}$$

$$k_\varphi = \frac{k_0 + k_m K\,[\text{PEG}]}{1 + K\,[\text{PEG}]}, \tag{15}$$

where $k_\varphi = (k'/[\text{CAN}])$, the second order rate constant in PEG media. Subtracting k_0 from both the sides of equation and rearranging,

$$k_\varphi - k_0 = \frac{(k_m - k_w)\,K\,[\text{PEG}]}{1 + K\,[\text{PEG}]}. \tag{16}$$

However, since the reactions are too sluggish in the absence of [PEG], the rate constant (k_0) would be much smaller than

Table 6: Activation parameters of theobromine in different PEG media.

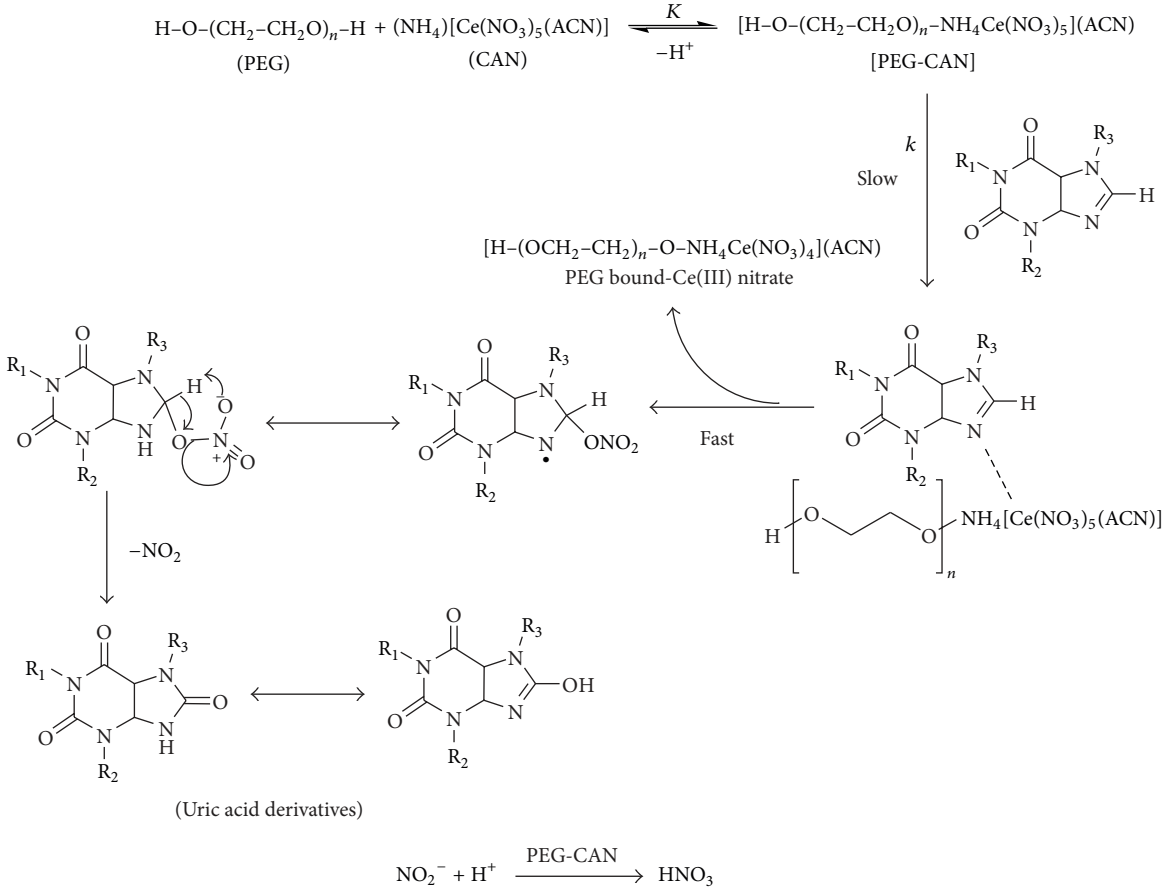
Type of PEG	PEG % (V/V)	k'' at 300 K	Equation	R^2	$\Delta H^{\#}$ kJ/mol	$\Delta G^{\#}$	$-\Delta S^{\#}$ J/Kmol
PEG-200	0.5	0.21	$y = -5.2713x + 10.31$	0.999	43.7	80.0	111
	1.0	0.23	$y = -5.9167x + 12.54$	0.999	49.1	77.0	93.3
	2.0	0.30	$y = -4.7454x + 8.893$	0.996	39.3	76.2	123
	3.0	0.32	$y = -4.6086x + 8.510$	0.999	38.2	76.0	126
	4.0	0.35	$y = -4.4002x + 7.950$	0.979	36.5	75.8	131
	5.0	0.44	$y = -3.5467x + 5.326$	0.981	29.4	75.3	153
PEG-300	0.5	0.16	$y = -5.8962x + 12.17$	0.973	48.9	77.7	96.3
	1.0	0.21	$y = -4.983x + 9.385$	0.980	41.3	77.0	119
	2.0	0.23	$y = -5.2059x + 10.27$	0.987	43.0	76.6	112
	3.0	0.30	$y = -5.236x + 10.41$	0.972	43.4	76.7	111
	4.0	0.35	$y = -4.632x + 8.798$	0.956	38.4	75.6	124
	5.0	0.42	$y = -4.6308x + 8.917$	0.962	38.4	75.3	123
PEG-400	0.5	0.14	$y = -6.9315x + 15.48$	0.987	57.5	78.1	68.8
	1.0	0.21	$y = -6.0803x + 13.08$	0.953	50.4	77.0	88.8
	2.0	0.30	$y = -4.5372x + 8.261$	0.971	37.6	76.0	128
	3.0	0.35	$y = -5.2988x + 10.96$	0.972	43.9	75.7	106
	4.0	0.35	$y = -6.2994x + 14.29$	0.978	52.3	108	186
	5.0	0.42	$y = -5.7161x + 12.49$	0.997	47.4	76.1	93.7
PEG-600	0.5	0.18	$y = -3.4127x + 3.971$	0.995	28.3	77.5	164
	1.0	0.21	$y = -3.0241x + 2.815$	1.00	25.0	77.2	174
	2.0	0.28	$y = -2.0791x - 0.0386$	0.996	17.2	76.3	197
	3.0	0.32	$y = -2.3784x + 1.079$	0.998	19.7	79.4	188
	4.0	0.42	$y = -1.7943x - 0.569$	0.963	14.8	72.4	192
	5.0	0.51	$y = -2.9311x + 3.403$	0.995	24.3	75.0	169

($k_m K$[PEG]), that is, ($k_0 \lll k_m K$[PEG]). Therefore the (k_0) term could be neglected in the above equation. On the basis of the foregoing discussion, the most plausible mechanism for PEG catalysed reaction could be given as in Scheme 4. The rate law for Scheme 4, could then be considered as

$$k_\varphi = \frac{k_m K\,[\text{PEG}]}{1 + K\,[\text{PEG}]}. \tag{17}$$

This rate law resembles Michaelis-Menten type rate law that is used for enzyme kinetics. Interestingly the plots of rate constant (k_φ), that is, second order rate constant of PEG mediated reaction versus [PEG], indicated Hill type curves (i.e., a gradual increase with an increase in [PEG] passing through a maximum point in the profile). This observation points out that beyond certain concentration, PEG bound [CAN] inhibits the reaction rates. This could be attributed to the fact that [CAN] is tightly bound to PEG and surrounded by PEG environment, giving less scope for rate accelerations. In view of this reaction kinetics are studied in detail at various PEG concentrations in order to have an insight into the variation in the enthalpies and entropies of activation with [PEG].

3.3. Effect of Structure on Enthalpy and Entropy Changes. The enthalpy and entropy of activation ($\Delta H^{\#}$ and $\Delta S^{\#}$) are the two parameters typically obtained from the slope and intercepts of Eyring's plot of $\ln(k''/T)$ versus $(1/T)$ as shown in Figure 5. The positive values for $\Delta S^{\#}$ suggest a dissociative mechanism, while negative $\Delta S^{\#}$ values indicate an associative mechanism. Values near zero are difficult to interpret [26, 49, 50]. Almost similar magnitude of $\Delta G^{\#}$ in a series of closely related reactions generally indicates a similar type of mechanism operative for closely related reactions under study. Overall free energy of reaction (ΔG) may be considered to be the driving force of a chemical reaction. When $\Delta G < 0$ the reaction is spontaneous; when $\Delta G = 0$ the system is at equilibrium and no net change occurs; and when $\Delta G > 0$ the reaction is not spontaneous. Entropies of activation data compiled in Tables 1 to 6 of the present study are highly negative, which are in accordance with an associative mechanism leading to a well-organized transition state. These results probably support the association of PEG with CAN, which brings about changes in the transition state and cause simultaneous association and dissociation of species causing disorderness in the transition state leading to a chemical



Scheme 4

reaction. Similar type of trends is recorded in all the PEGs used in this study.

4. Conclusions

We have studied oxidation of Xanthine alkaloids such as Xanthine (XAN), hypoxanthine (HXAN), caffeine (CAF), theophylline (TPL), and theobromine (TBR), by a common laboratory desktop reagent CAN in catalytic amounts. Oxidation of xanthine derivatives afforded uric acid derivatives. Even though the reaction is too sluggish in acetonitrile media even at reflux temperatures, it underwent smoothly in presence of Poly ethylene glycols (PEG). Reaction kinetics indicated first order in both [CAN] and [Xanthine alkaloid]. Rate of oxidation is accelerated with an increase in [PEG] linearly. Mechanism of oxidation in PEG media has been explained by Menger-Portnoy enzymatic model with the oxidation of PEG bound oxidant (PEG-CAN) as more reactive species than (CAN) itself.

References

[1] L. Eberson, *Electron Transfer Reactions inOrganic Chemistry*, Springer, Berlin, Germany, 1987.

[2] K. B. Wiberg, *Oxidations in Organic Chemistry (Part A)*, Academic Press, 1965.

[3] W. S. Trahanosky, *Oxidations in Organic Chemistry (Part B)*, Academic Press, 1968.

[4] P. Renaud and M. P. Sibi, *Radicals in Organic Synthesis*, vol. 1, Wiley-VCH, Weinheim, Germany, 2001.

[5] N. L. Bauld, "Hole and electron transfer catalyzed pericyclic reactions," in *Advances in Electron Transfer Chemistry*, vol. 2, pp. 1–66, 1992.

[6] M. Chanon, M. Rajzmann, and F. Chanon, "One electron more, one electron less. What does it change? Activations induced by electron transfer. The electron, an activating messenger," *Tetrahedron*, vol. 46, no. 18, pp. 6193–6299, 1990.

[7] M. Schmittel, "Ketene-diene [4 + 2] cycloaddition products via cation radical initiated Diels-Alder reaction or vinylcyclobutanone rearrangement," *Journal of the American Chemical Society*, vol. 115, no. 6, pp. 2165–2177, 1993.

[8] M. Schmittel and C. Wöhrle, "Electron transfer initiated Diels-Alder reaction with allenes as dienophiles," *Tetrahedron Letters*, vol. 34, no. 52, pp. 8431–8434, 1993.

[9] A. Gieseler, E. Steckhan, O. Wiest, and F. Knoch, "Photochemically induced radical cation Diels-Alder reaction of indole and electron-rich dienes," *Journal of Organic Chemistry*, vol. 56, no. 4, pp. 1405–1411, 1991.

[10] M. Schmittel, "Ammoniumyl salt-induced Diels-Alder reaction of ketenes-control of [2 + 2] versus [4 + 2] selectivity," *Angewandte Chemie*, vol. 30, no. 8, pp. 999–1001, 1991.

[11] N. L. Bauld, "Cation radical cycloadditions and related sigmatropic reactions," *Tetrahedron*, vol. 45, no. 17, pp. 5307–5363, 1989.

[12] P. E. Floreancig, "Development and applications of electron-transfer-initiated cyclization reactions," *Synlett*, no. 2, pp. 191–203, 2007.

[13] M. Schmittel, "Umpolung of ketones via enol radical cations," in *Topics in Current Chemistry*, vol. 169, pp. 183–230, 1994.

[14] M. Schmittel and A. Burghart, "Understanding reactivity patterns of radical cations," *Angewandte Chemie*, vol. 36, no. 23, pp. 2550–2589, 1997.

[15] M. Schmittel and A. Langels, "A short-lived radical dication as a key intermediate in the rearrangement of a persistent cation: the oxidative cyclization of 2,2-dimesityl-1-(4-N,N-dimethylaminophenyl)ethenol," *Angewandte Chemie*, vol. 36, no. 4, pp. 392–395, 1997.

[16] M. Rock and M. Schmittel, "Controlled oxidation of enolates to a-carbonyl radicals and a-carbonyl cations," *Journal of the Chemical Society, Chemical Communicationspp*, no. 23, pp. 1739–1741, 1993.

[17] V. Nair, L. Balagopal, R. Rajan, and J. Mathew, "Recent advances in synthetic transformations mediated by Cerium(IV) ammonium nitrate," *Accounts of Chemical Research*, vol. 37, no. 1, pp. 21–30, 2004.

[18] V. Nair, J. Mathew, and J. Prabhakaran, "Carbon-carbon bond forming reactions mediated by cerium(IV) reagents," *Chemical Society Reviews*, vol. 26, no. 2, pp. 127–132, 1997.

[19] E. Baciocchi and R. Ruzziconi, "1,2- and 1,4-addition in the reactions of carbonyl compounds with 1,3-butadiene induced by cerium(IV) ammonium nitrate," *Journal of Organic Chemistry*, vol. 51, no. 10, pp. 1645–1649, 1986.

[20] A. B. Paolobelli, P. Ceccherelli, F. Pizzo, and R. J. Ruzziconi, "Regio- and stereoselective synthesis of unsaturated carbonyl compounds based on ceric ammonium nitrate-promoted oxidative addition of trimethylsilyl enol ethers to conjugated dienes," *The Journal of Organic Chemistry*, vol. 60, no. 15, pp. 4954–4958, 1995.

[21] J. R. Hwu, C. N. Chen, and S. S. Shiao, "Silicon-controlled allylation of 1,3-dioxo compounds by use of allyltrimethylsilane and ceric ammonium nitrate," *The Journal of Organic Chemistry*, vol. 60, no. 4, pp. 856–862, 1995.

[22] V. Nair and J. Mathew, "Facile synthesis of dihydrofurans by the cerium(IV) ammonium nitrate mediated oxidative addition of 1,3-dicarbonyl compounds to cyclic and acyclic alkenes. Relative superiority over the manganese(III) acetate," *Journal of the Chemical Society, Perkin Transactions 1*, no. 3, pp. 187–188, 1995.

[23] V. Nair, J. Mathew, and S. Alexander, "Synthesis of spiroannulated dihydrofurans by cerium(IV) ammonium nitrate mediated addition Of 1,3-dicarbonyl compounds to exocyclic alkenes," *Synthetic Communications*, vol. 25, no. 24, pp. 3981–3991, 1995.

[24] B. B. Snider and T. Kwon, "Oxidative cyclization of .delta., .epsilon.- and .epsilon.,.zeta.-unsaturated enol silyl ethers and unsaturated siloxycyclopropanes," *The Journal of Organic Chemistry*, vol. 57, no. 8, pp. 2399–2410, 1992.

[25] A. J. Clark, C. P. Dell, J. M. McDonagh, J. Geden, and P. Mawdsley, "Oxidative 5-endo cyclization of enamides mediated by ceric ammonium nitrate," *Organic Letters*, vol. 5, no. 12, pp. 2063–2066, 2003.

[26] M. Schmittel, G. Gescheidt, and M. Rock, "The first spectroscopic identification of an enol radical cation in solution: the anisyl-dimesitylethenol radical cation," *Angewandte Chemie*, vol. 33, no. 19, pp. 1961–1963, 1994.

[27] M. Schmittel and A. Langels, "Enol radical cations in solution. Part 12: synthesis and electrochemical investigations of a stable enol linked to a ferrocene redox centre," *Journal of the Chemical Society, Perkin Transactions 2*, no. 3, pp. 565–572, 1998.

[28] M. Schmittel and A. Langels, "Enol radical cations in solution. 13. First example of a radical dication rearrangement. One-electron oxidation of dihydrobenzofuranyl cations leads to drastic rate enhancement in the oxidative benzofuran formation from enols," *The Journal of Organic Chemistry*, vol. 63, no. 21, pp. 7328–7337, 1998.

[29] V. N. Vasudevan and S. V. Rajendra, "Microwave-accelerated Suzuki cross-coupling reaction in polyethylene glycol (PEG)," *Green Chemistry*, no. 3, pp. 146–148, 2001.

[30] A. Haimov and R. Neumann, "Polyethylene glycol as a non-ionic liquid solvent for polyoxometalate catalyzed aerobic oxidation," *Chemical Communications*, no. 8, pp. 876–877, 2002.

[31] L. Heiss and H. J. Gais, "Polyethylene glycol monomethyl ether-modified pig liver esterase: preparation, characterization and catalysis of enantioselective hydrolysis in water and acylation in organic solvents," *Tetrahedron Letters*, vol. 36, no. 22, pp. 3833–3836, 1995.

[32] S. Chandrasekar, C. Narsihmulu, S. S. Shameem, and N. R. Reddy, "Osmium tetroxide in poly(ethylene glycol)(PEG): a recyclable reaction medium for rapid asymmetric dihydroxylation under Sharpless conditions," *Chemical Communications*, no. 14, pp. 1716–1717, 2003.

[33] K. Tanemura, T. Suzuki, Y. Nishida, and T. Horaguchi, "Aldol condensation in water using polyethylene glycol 400," *Chemistry Letters*, vol. 34, no. 4, pp. 576–577, 2005.

[34] R. Kumar, P. Chaudhary, S. Nimesh, and R. Chandra, "Polyethylene glycol as a non-ionic liquid solvent for Michael addition reaction of amines to conjugated alkenes," *Green Chemistry*, vol. 8, no. 4, pp. 356–358, 2006.

[35] K. V. Rao and S. S. Muhammed, "Studies in the two phases system sodium formate-yridine. Extraction of nickel and separation from chromium," *Bulletin of the Chemical Society of Japan*, vol. 36, no. 8, pp. 941–943, 1963.

[36] S. S. Muhammed and B. Sethuram, "Upper carboniferous flora from the Mecsek Mts (Southern Hungary)—summarized results," *Acta Geologica Hungarica*, vol. 46, no. 1, pp. 115–125, 1965.

[37] M. Santappa and B. Sethuram, "Oxidation studies. IV. Kinetics of oxidation of HCHO and some alcohols by ceric salts in HNO_3 medium," *Proceedings of the Indian Academy of Sciences A*, vol. 67, pp. 78–89, 1968.

[38] N. Dutt, R. R. Nagori, and R. N. Mehrotra, "Kinetics and mechanisms of oxidations by metal ions. Part VI. Oxidation of a-hydroxy acids by cerium(IV) in aqueous nitric acid," *Canadian Journal of Chemistry*, vol. 64, no. 1, pp. 19–23, 1986.

[39] K. C. Rajanna, Y. R. Rao, and P. K. Saiprakash, "Kinetic and mechanistic study of isopropanol and acetone by Ceric sulphate in aqueous sulphuric acid medium," *Indian Journal of Chemistry A*, vol. 17, p. 270, 1977.

[40] J. H. Fendler and R. J. Fendler, *Catalysis in Micellar and Micro-Molecular Systems*, Academic Press, New York, NY, USA, 1975.

[41] J. Van Stam, S. Depaemelaere, and F. C. De Schryver, "Micellar aggregation numbers—a fluorescence study," *Journal of Chemical Education*, vol. 75, no. 1, pp. 93–98, 1998.

[42] J. H. Fendler and W. L. Hinze, "Reactivity control in micelles and surfactant vesicles. Kinetics and mechanism of base-catalyzed hydrolysis of 5,5'-dithiobis(2-nitrobenzoic acid) in water, hexadecyltrimethylammonium bromide micelles, and dioctadecyldimethylammonium chloride surfactant vesicles," *Journal of the American Chemical Society*, vol. 103, no. 18, pp. 5439–5447, 1981.

[43] L. S. Romsted, "A general kinetic theory of rate enhancements for reactions between organic substrates and hydrophilic ions in micellar systems," in *Micellization, Solubilization, and Microemulsions*, K. L. Mittal, Ed., vol. 2, pp. 509–530, Plenum Press, New York, NY, USA, 1977.

[44] F. M. Menger and C. E. Portnoy, "On the chemistry of reactions proceeding inside molecular aggregates," *Journal of the American Chemical Society*, vol. 89, no. 18, pp. 4698–4703, 1967.

[45] F. M. Menger, "Groups of organic molecules that operate collectively," *Angewandte Chemie*, vol. 30, no. 9, pp. 1086–1099, 1991.

[46] K. A. Connors, *Chemical Kinetics: The Study of Reaction Rates in Solution*, VCH, New York, NY, USA, 1990.

[47] J. Espenson, *Chemical Kinetics and Reaction Mechanism*, McGraw-Hill, 1981.

[48] J. E. Leffler and E. Grunwald, *Rates and Equilibria of Organic Reactions*, Wiley, New York, NY, USA, 1963.

[49] H. Maskill, *The Physical Basis of Organic Chemistry*, Oxford University Press, Oxford, UK, 1986.

[50] V. Jagannadham, "The change in entropy of activation due to solvation/hydration—a one hour graduate classroom lecture," *Chemistry*, vol. 18, no. 4, p. 89, 2009.