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Experimental and Theoretical Studies on the Oxidation of Ibuprofen by Potassium Permanganate Ion In Alkaline Medium

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Abstract: *The oxidation of ibuprofen was monitored spectrophotometrically by potassium permanganate in basic medium at λmax 525 nm at 26°C.The stoichiometry was found at 1:2 in terms of one mole of ibuprofen and two mole of permanganate ion.The products were identified by using LCMS.The effect of oxidant,substrate,sodium hydroxide,ionic strength and temperature were studied.Thermodynamics activation parameters* $\Delta H^{\#}(kJmol^{-1})$ *and* $\Delta S^{\#}(JK^{-1}mol^{-1})$ *were determined.From kinetic studies,spectral evidences and stoichiometry of the reactions suitable mechanism is proposed.*

Keywords**:** *Kinetics,Oxidation,Ibuprofen,*$KMnO_4$

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I. Introduction

Ibuprofen (IBU)was derived from propionic acid. Ibuprofen is a medication in nonsteroidal anti inflammatory drug that is used for treating pain, fever, and inflammation, painful menstruation, osteoarthritis, dental pain, headaches, and pain from kidney stones.Ibuprofen is practically insoluble in water, with solubility less than 200Mm. But very soluble in most organic solvents like ethanol (66.18 g/100mL at 40 °C for 90%EtOH),methanol,acetone and dichloromethane. Ibuprofen work by inhibiting the cyclooxygenase enzymes, which convert arachidonic acid to prostaglandin H_2 (PGH_2).PGH_2, in turn, is converted by other enzymes to several other prostaglandins (which are mediators of pain, inflammation, and fever) and to thromboxane A_2 (which stimulates platelet aggregation, leading to the formation of blood clots).Ibuprofen is a non-selective inhibitor of cyclo-oxygenase, leading to decrease synthesis of prostaglandins.In vivo and in vitro studies indicate that the S (+) isomer is responsible for the clinical activity.Ibuprofen is (+/-)-2-(pisobutylphenyl) propionic acid ($C_{13}H_{18}O_2$) with a molecular weight of 206.3; and has the structure shown below.

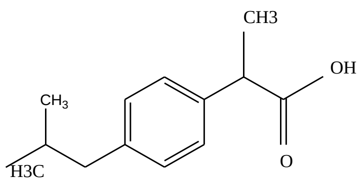


Fig 1: Structure of ibuprofen

The appearance of solid material is almost white crystalline powder.It has a density of $1.03g/cm^3$.Melting point=75°-78°C and boiling point=157°C(4mmHg).The p^{ka} is 4.8,and log octanol/water partition coefficient(kow) is 2.48 at pH 7.It is reported that approximately 70% on a mass basis of ibuprofen ingested by human is metabolized in the human body.

Many techniques and procedures have been published for the quantitative determination of Ibuprofen. These procedures include non aqueous titration[1],polarography[2], and colorimetric titration[3], and differential scanning calorimetry[4],UVspectrophotometry[5,6],colorimetry[7,8],IR spectrophotometry[9],and H^1NMR spectrophotometry[10]. In addition chromatographic procedures are also employed using TLC[11], GC[12], and HPLC[13,14,15]. According to the BP 1988 ibuprofen and its tablets are determined by an acid base titration.

Potassium permanganate discovered by Margueritte in 1846 has now been widely used for redox reactions involving a variety of chemical reactions[16]. Potassium permanganate is a chemical compound with formula $KMnO_4$.Reactions with permanganate are administrate by pH of the medium.The manganese chemistry involved in the multistep redox reactions is an important source of information as the manganese intermediates are relatively easy to identify when they have sufficiently long life times and oxidation states of the intermediates permit useful conclusions as to the possible reaction mechanism including the nature of intermediates. Among six oxidation states of manganese from +2 to+7,permanganate,Mn(VII) is the most potent oxidation state in acid as well as in alkaline medium[17].When it dissolves in water to form pink colour solution. Potassium permanganate is used for medical purposes including as an antiseptic,fungicide and also used for the treatment of skin infections.Potassium permanganate is selected as an oxidizing agent for our present study because; it is an economically low-cost material. It has high oxidation potential [E^0 =1.51 V], it can oxidize wide variety of substances and it is effective over wide range of p^H [18]. Due to high oxidizing property, permanganate is perfect source to be used for the water treatment process, so it removes magnesium and iron from water[19].

II. Experimental

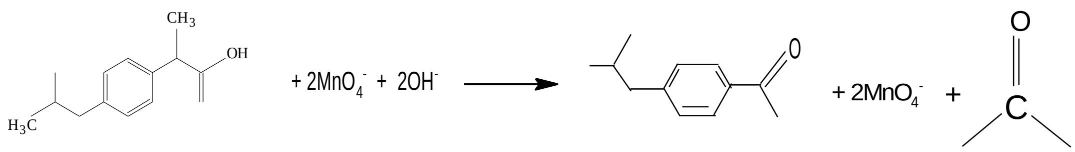
All chemicals used were of analytical grade and double distilled water used in this experiment.Stock solution of ibuprofen was prepared by dissolving the requisite amount of sample in sodium hydroxide.The solutions of potassium permanganate was prepared and standardized against oxalic acid[20].Sodium hydroxide and sodium perchlorate were used to provide alkalinity and to maintain ionic strength.

III. Kinetic Measurements

All kinetic measurements were performed under pseudo first order conditions where [Ibuprofen] >>[MnO_4^-] at constant ionic strength 1.0 mol dm^{-3}.The reaction was initiated by mixing previously thermostated solution of MnO_4^- and ibuprofen which also contains sodium hydroxide and sodium perchlorate to maintain alkalinity and ionic strength respectively.Temperature was maintained at 26°C and the reaction course was followed by decrease in the absorbance of MnO_4^- by using UV spectrophotometer at 525nm.

IV. Stoichiometry

Different reaction mixture contain excess potassium permanaganate over ibuprofen with sodium hydroxide 0.5 mol dm^{-3} ,ionic strength1.0 mol dm^{-3} were preapared in closed container.The reaction is allowed take place for 24hrs.After 24hrs remaining potassium permanganate is measured by using UV-Vis spectrophotometer.The reaction mixture is extracted with ether and studied under LCMS spectra which give M^+H+ peak at 162 mHz.The peak observe correspondence to the product isobutylacetophenone(1-[4-(2-methylpropyl)phenyl]ethanone) as shown in the figure2.



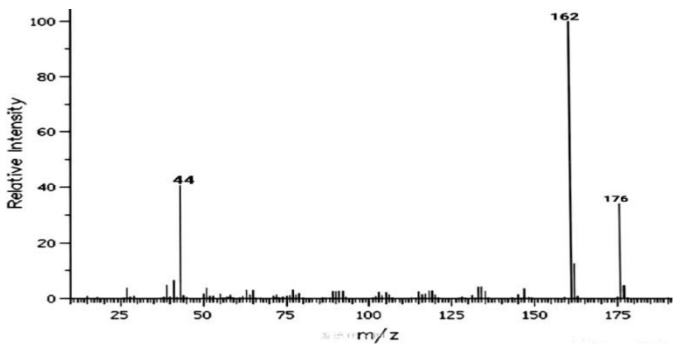


Fig 2:LCMS of Spectra of oxidation of product of ibuprofen.

V. Reaction Order

Effect of potassium permanganate

To study the effect of permanganate, concentration of permanganate was varied from 0.9X10^{-4} to 9.0X10^{-4} and ibuprofen=3X10^{-3}, OH^- =0.5 mol dm^{-3} ,sodium perchlorate=1.0 mol dm^{-3} kept constant.It has been found that the plots log aborbance v/s time were linear upto 80% of the reaction which indicate the first order with respect to oxidant shown in fig 3.

By varying [MnO_4^-] which donot show any change in pseudo first order constants(kobs) values as shown in table I.

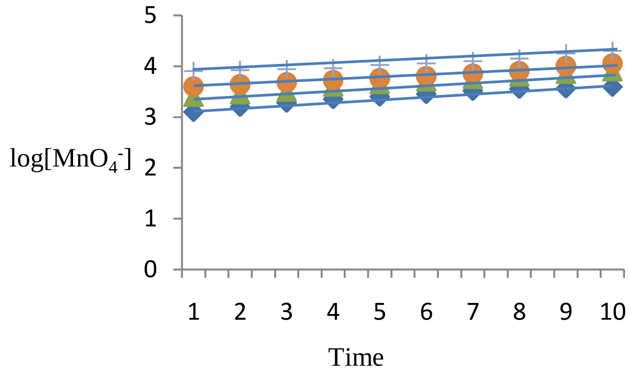


Fig 3: Pseudo first order plots of alkaline permanganate oxidation of ibuprofen at 26°C.

Effect of ibuprofen

Ibuprofen concentration was varied from $9X10^{-4}$ to $9X10^{-3}$ mol dm^{-3} at 26°C as shown in table I, keeping [permanganate]=$3X10^{-4}$, [sodium hydroxide]=0.50 mol dm^{-3} ,[sodium perchlorate]=1.0 mol dm^{-3} constant.From plot log k versus log[Ibuprofen] was found to be less than unity shown in fig.4.

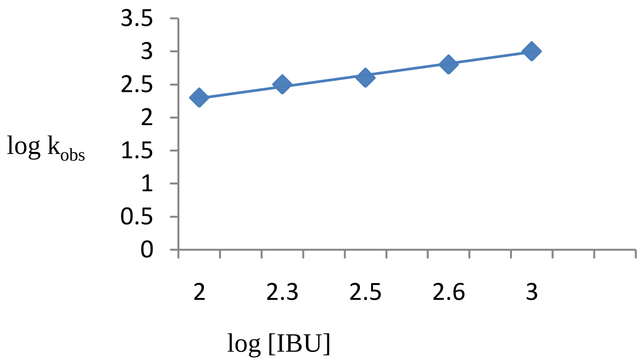


Fig 4: Order of reaction with respect to [IBU] in the oxidation of ibuprofen by alkaline permanganate.

Effect of sodium hydroxide

The OH^- was varied from 0.1 to 1.0 mol dm^{-3} and keeping ibuprofen= [$3X10^{-3}$] ,MnO_4 =[$3X10^{-4}$] ,ionic strength of 1.0 mol dm^{-3} constant.An increase in concentration of sodium hydroxide increases the rate. From plot of log k versus log[OH^-] were found to be linear indicates fractional order with respect to OH^- as shown in figure 5.

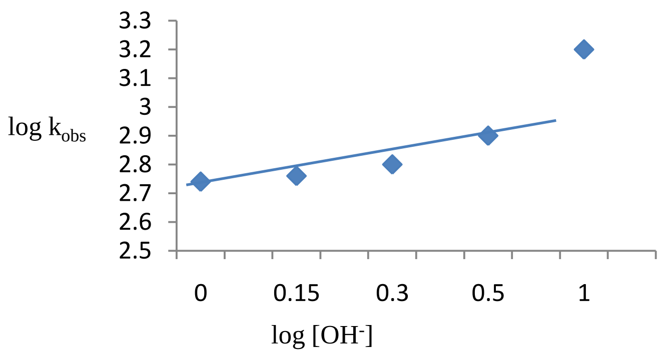


Fig 5: Order of reaction with respect to [OH^-] in the oxidation of ibuprofen by alkaline permanganate**.**

Effect of ionic strength
Sodium perchlorate was varying concentration range from 0.5 to 2.0 mol dm^{-3} at constant concentration of permanganate = [3X10^{-4}],ibuprofen=[3X10^{-3}],NaOH=[0.5] mol dm^{-3}.No major effect on rate of reaction.

Effect of halide ions
The addition of Halide ions that is NaCl had no effect on the rate of oxidation of ibuprofen.

Effect of added product
Aldehyde, Ammonia was added to the reaction mixture which did not show any effect on the rate of the reaction.

Test for free radical
The reaction mixture of ibuprofen, permanganate, sodium hydroxide kept for 2 hours with acrylonitrile and diluting with methanol. Result indicates no significant effect of free radical.

Table I.Effect of variation of [MnO_4^-],[IBU] and [OH^-] on the oxidation of Ibuprofen by alkaline permanganate at 26°C.

[MnO_4]X10^4 mol dm^{-3}	**[Ibu]X10^3 mol dm^{-3}**	**[OH^-] mol dm^{-3}**	**kobsX10^3**	**kcalX10^3**
0.9	3.0	0.5	1.56	1.65
2.0	3.0	0.5	1.58	1.65
3.0	**3.0**	**0.5**	**1.55**	**1.65**
7.0	3.0	0.5	1.56	1.65
9.0	3.0	0.5	1.56	1.65
3	0.9	0.5	0.80	0.61
3	2.0	0.5	1.41	1.19
3	**3.0**	**0.5**	**1.55**	**1.65**
3	5.0	0.5	2.0	2.37
3	9.0	0.5	2.8	3.36
3	3.0	0.1	0.6	0.59
3	3.0	0.3	1.2	1.29
3	**3.0**	**0.5**	**1.55**	**1.65**
3	3.0	0.7	1.72	1.88
3	3.0	1.0	1.8	2.13

Effect of temperature
The rate constant k were obtained from intercepts of plot of 1/kobs versus 1/[IBU] at different temperature(Fig 6).The values of k were 0.80X10^{-2} ,1.5X10^{-2} and 2X10^{-2} at 298 K,304 K, 309 K respectively. These data were calculated and tabulated in table II. From the plot of log k versus 1/T, the activation parameters were calculated and tabulated in table III.

[MnO_4^-]=3X10^{-4} [OH^-]=0.50 mol dm^{-3}

Table II

Temperature(K)	k(s^{-1})
298	0.008
304	0.015
309	0.019

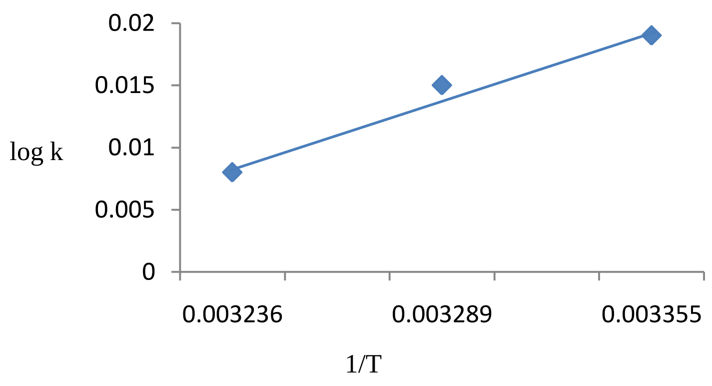


Fig 6:log k versus 1/T

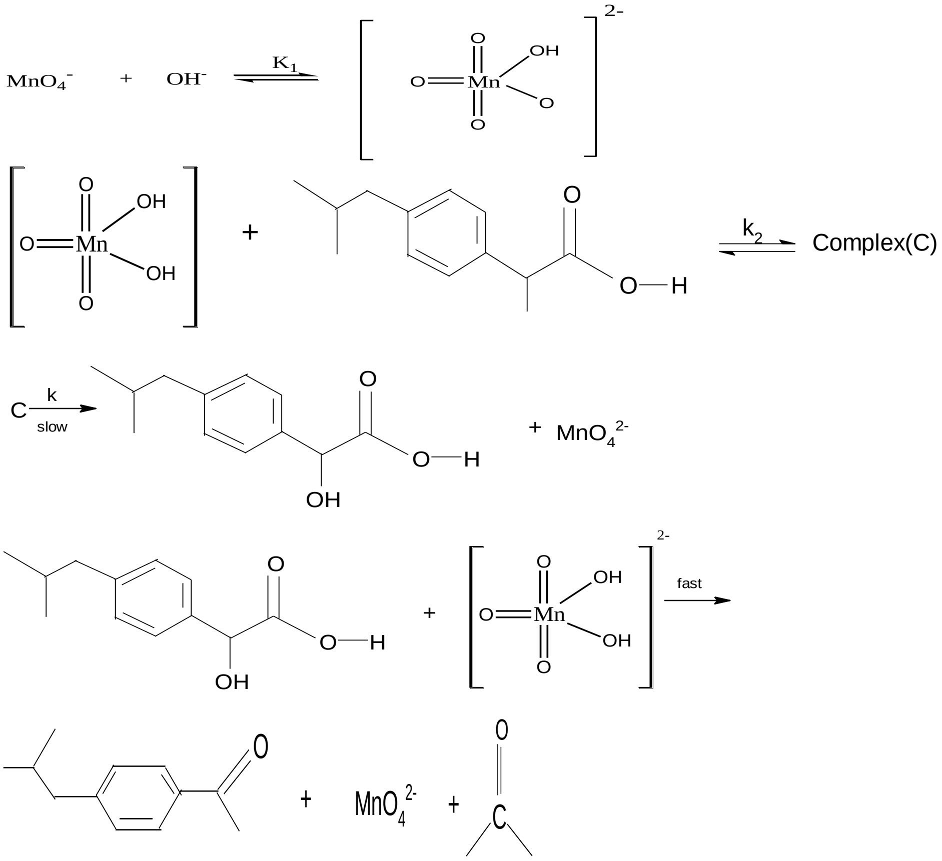
Table III: Thermodynamic activation parameters for the oxidation of ibuprofen by alkaline permanganate

Activation parameters	
Ea($kJmol^{-1}$)	60
$\Delta S^{\#}$	-65
$\Delta H^{\#}$	57
$\Delta G^{\#}$	76

VI. Discussion

Permanganate is an exclusive oxidizing agent in alkaline medium which exhibits large oxidation number.In this present paper, variation of the concentrations each of the oxidant Mn(VII), substrate (Ibuprofen) and alkali, while keeping the others constant showed that the reaction is first-order in oxidant, alkali and less than unit order in ibuprofen concentrations.The reaction between Ibuprofen and Mn(VII) in NaOH has a stoichiometry of 1:2. The result indicate that hydroxide combines with permanganate to give the intermediate $[MnO_4\ OH^-]^{2-}$ which is supported by fractional order in $[OH^-]$. $[MnO_4\ OH]^{2-}$ further reacts with ibuprofen to give complex(C).This complex decomposes in slow step to give intermediate which further reacts with another molecule of permanganate in fast step to form the product which shown in scheme I.

SCHEME I



From scheme I,the rate of the reaction can be given as

Rate = $-d[MnO_4^-]/dt = k$ [complex-C]

Rate = kK_2 [IBU] $[MnO_4.OH]^{2-}$ …………………………………(1)

$=kK_1K_2[IBU]_f\ [MnO_4^-]_f[OH^-]_f$

$[IBU]_T = [IBU]_f$ …………………………………(2)

$[MnO_4^-]_T = [MnO_4^-]_f + [MnO_4.OH]^{2-} + [C]$

$[MnO_4^-]_T = [MnO_4^-]_f + K_1[MnO_4^-]_f\,[OH^-]_f + K_1K_2[IBU]\,[MnO_4^-][OH^-]$

$[MnO_4^-]_f=[MnO_4^-]_T/\ 1+K_1[OH^-]+K_1K_2[IBU]\ [OH^-]$ …………………………………(3)

$[IBU]_T = [IBU]_f$

$[OH^-]_T = [OH^-]_f$

$Rate=kK_1K_2[IBU][MnO_4^-][OH^-]/1+K_1[OH^-]+K_1K_2[IBU][OH^-]$ ………………(4)

$Kobs= Rate/[MnO_4^-] = kK_1K_2[IBU][OH^-]\ /\ 1+K_1[OH^-]+K_1K_2[IBU][OH^-]$ ………(5)

On rearranging equation (5), we will get

$1/Kobs = 1/kK_1K_2[IBU][OH^-] + 1/kK_2[IBU] + 1/k$..(6)
According to equation (6) the plots of 1/kobs versus 1/[IBU] and 1/kobs versus 1/[OH^-] should be linear and are verified in fig (7) & (8).The slopes and intercepts of plots leads to values of k K_1 K_2 at 26°C as 0.007,1.4 dm^3 mol^{-1} and 250 respectively. Using these values rate constants at different experimental conditions were calculated and evaluated. Kobs values are in good agreement with experimental data.

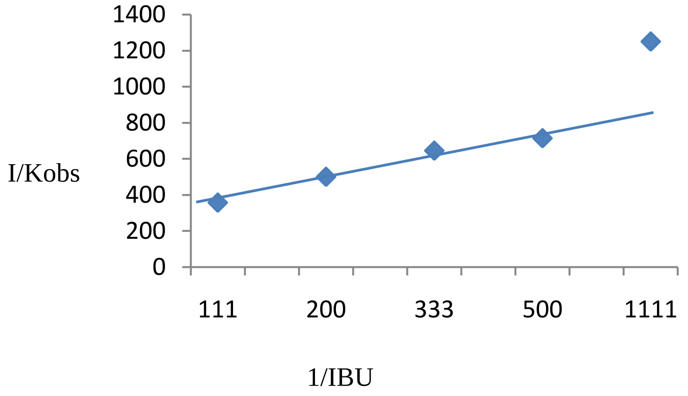


Fig 7:1/[IBU] versus 1/[Kobs]

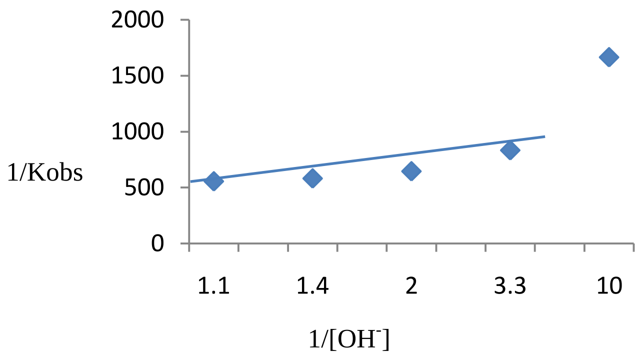


Fig 8:1/[OH^-] versus 1/Kobs

VII. Conclusion

Kinetics and oxidation of ibuprofen by potassium permanganate in alkaline medium has been investigated.Based on the experimental observations, a mechanism was proposed via the formation of an intermediate complex between ibuprofen and potassium permanganate.The rate constant of the slow step and other equilibrium constants involved in the mechanism were evaluated and activation parameters with respect to the slow step of the reaction were computed[21].The overall sequence described here is consistent with all experimental findings,including the product, and spectral,mechanistic and kinetic studies.The stiochiometry of oxidation ibuprofen and permanganate is found to be 1:2. The oxidation product was found to be isobutylacetophenone(1-[4-(2-methylpropyl)phenyl]ethanone).The reaction shows first order dependence of rate on concentration and fractional order dependence each in ibuprofen and alkali concentrations. Rate of reaction increases with increase in the temperature.The arrehnius plot shows how activation energy and temperature affect the sensitivity of the reaction rate. The large negative value of entropy($\Delta S^{\#}$) suggest that the complex is more ordered than the reactants[22].Suitable mechanism were assessed.

Reference

[1]. Kanoute G, Boucly P, Guerent Nivand E, and Guernet M. Ann. Pharm. Fr. Oct.1985:43:265-272.
[2]. Kanoute G, Nivand E, Paulet B, and Boucly P. Talanta. 1994:31:144-146
[3]. Lu J, Wang M, Wu A. and Qiu X, Shanga Yika Daxue Xuebao. 1992:17:275-277.
[4]. Mahrous M S, Abdel Khalek M M, and Abdel Hamid M E, J. Assoc. Off. Anal. Chem. 1985:68:535-539.
[5]. El-Din M K S, Abuirjeie M A, and Abdel-Hay M H, Anal. Lett. 1991:24:2187-2706.
[6]. .Matsuda R, Takeda Y, Ishibashi M, Uchiyama M, Suzuki M, and Takitani S, Bunseki Kaguku. 1986:35:151-156.

[7]. Abdel-Hay M H, Korany M A, Bedair M M, and Gazy A A, Anal. Lett. 1990:23:281-294.
[8]. Husain S, Srk A. Murthy, and Rao A R, Indian Drugs. 1989:26:185-189.
[9]. El Ragehy N A, Bulletin of fac. of pharmacy. 1991:29:1-4.
[10]. .Ge J, and He Y Zhonggue Yaoke Daxue Xuebao. 1987:18:88-95.
[11]. Rao G R, Avadhanulu A B, and Pantulu A R R, East Pharm. 1991:34:119-121
[12]. Pant S K, and G L Jain, Indian Drugs. 1991:28:216-265.
[13]. Rustom A M, J.Chromato. Ghr. Sci. 1991:29:16-20.
[14]. Goodall D M, Riley M J, Wu Z, and Wilson I D, Anal. Proc. 1992:29:253-255.
[15]. Haikla V E, Heimonen L K, and Vuorela H J, J. Pharm. Sci. 1991:80:456-458.
[16]. Dayo Felix Latona* Kinetics and Mechanism of Propane-1,3-diol Oxidation by Mn(VII) in Aqueous Medium, Advanced Journal of Chemistry-Section A.2019:3:225-233.
[17]. 17.Raviraj Kulkarni,Dinesh Bilehal,Sharanappa T Nandibewoor, Kinetics and Mechanistic Study of oxidation of Sulfamethoxazole by Alkaline Permanganate,Inorganic Reaction Mechanisms.2002:4:239-247.
[18]. Raviraj Kulkarni,Dinesh Bilehal,Sharanappa T Nandibewoor, Kinetics and Mechanistic Study of oxidation of Sulfamethoxazole by Alkaline Permanganate,Inorganic Reaction Mechanisms.2002:4:239-247.
[19]. Sayyed Hossein Rasa and Mohammad Taha Badri, Experimental Determination of the Kinetic Rate Law for the Oxidation of Acetone in Aqueous Environment by Potassium Permanganate and Sulfuric Acid at 25OC and Proposed Mechanism for the Reaction, Oriental Journal of Chemistry.2019:35:343-350.
[20]. A.I.Vogel "A Text Book of Qualitative Chemical Analysis",ELBS,Longman,Essex,UK,1996 5th edn,p 371.
[21]. Manjunath METI, Sharanappa NANDIBEWOOR, Shivamurti CHIMATADAR*, Spectroscopic investigation and oxidation of the anticholinergic drug atropine sulfate monohydrate by hexacyanoferrate(III) in aqueous alkaline media: a mechanistic approach,Turk J Chem.2014,(38): 477 – 487.
[22]. M.Sanjana,[1] A.K.Patnaik,[2] S.K.Badamali,[1] andP.Mohanty[1] , Kinetics and Mechanism of ElectronTransfer to Heptavalent Manganese by DL-Aspartic Acid in Alkaline Aqueous and Micellar Media, Journal of Chemistry.2013:1-7.

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