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Kinetics and Mechanism of the Ring Opening of 3-carboethoxycoumarin by Sodium Hydroxide and Hydrazine

Hassan A. Ewais[1,2]*, Abdulla M. Asiri[1], Iqbal M.I. Ismail[1] Salem A. Hameed[1] and Ahmed A. Abdel-Khalek[2]
[1]Chemistry Department, Faculty of Science, King Abdulaziz University, P.O Box.80203, Jeddah 21413, SAUDI ARABIA
[2]Chemistry Department, Faculty of Science, Beni-Suef University, Beni-Suef City, EGYPTE

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Abstract

The kinetics of the ring opening of 3-carboethoxycoumarin (I) by sodium hydroxide and hydrazine have been studied spectrophotometrically over the 20 – 40 °C range. The reaction rate of 3-carboethoxy coumarin (I) with sodium hydroxide is more than it is reaction with hydrazine. The reaction is first order with respect to both [I] and [OH⁻] or [Hyd]. A possible mechanism and derived rate law for these reactions are proposed. The effects of cetyltrimethylammonium bromide (CTAB, a cationic surfactant) and sodium dodecylsulfate (SDS, an anionic surfactant), on the reaction rate have been studied. CTAB accelerates the rate of reaction while SDS inhibits. Enthalpies and entropies of activation for these reactions have been calculated.

Keywords: 3-carboethoxycoumarin; Ring opening; Hydrazine; Micelles; Thermodynamic activation parameters.

Introduction

The general chemical structure of coumarins consists of a benzene moiety fused to α-pyrone rings and most of them have a very efficient fluorescing ability. Coumarin derivatives possess a wide range of applications as anticoagulants[1], cytotoxicity[2], photosensitizers[3], anticancer[4], antimicrobial[5], chemosensor[6] and anti-inflammatory agents[7].

The base hydrolysis of both coumarin and thiocoumarin have been studied in different binary aqueous-methanol mixtures at temperature range from 288 to 313 K[8]. The activation parameters of the reactions were evaluated. Moreover, the change in the activation barrier of the investigated compounds from water to water-methanol mixtures were estimated from the kinetic data. Also, coumarin is hydrolyzed by specific hydroxyl-ion-catalyzed solvolysis and has been characterized as a function of pH[9]. The hydrolyses of 3-chlorocoumarin, 3-bromocoumarin, and 3- and 4-methylcoumarin were studied in 30% dioxane for the acid-lactone equilibrium. The halogen substituents showed pronounced accelerating effects consistent with the electronegative group acceleration of hydroxyl-ion attack on the carbonyl carbon, whereas the methyl substituents did not significantly modify the reactivity of coumarin[9].

Ionic micelles in water speed bimolecular reaction rates of counterions with micellar-bound substrates but in general second-order rate constants at the micellar pseudo-phase are not very different from those in water[10,11]**.** This observation suggests that micellar enhancement of rates of bimolecular reactions is due largely to concentration of both reactants in the small volume of the micelles.

It has been reported[12,13] that the reaction of coumarines with amines and hydrazines take place at the carbonyl group. 3-(ω-bromoacetyl) coumarin react with phenyl hydrazine, gave the corresponding hydrazone[14]. The hydrolysis of coumarin has been investigated previously by spectrophotometric method[15]. The lactone ring of a coumarin is opened by alkali to give a salt of a coumarinic acid[16]. The initial action of alkali on 3-carboethoxycoumarin (I) is always the opening of the pyrone ring[17]. The action of hydrazine hydrate on coumarines, results in ring fission and formation of salicylaldazine[18]. Also, the action of hydrazine on 3-carboethoxycoumarin (I) results in ring fission and the formation of salicylaldazine(III) and dihydrazide of malonic acid[19].

In the present work, we studied the kinetics and mechanism of the ring opening of 3-carboethoxycoumarin (I) by NaOH and hydrazine. The kinetic data gave an information about the stability of coumarin derivatives which are used in pharmaceutical field towards hydrolysis (scheme – 1).

Material and Methods

Experimental Section: Materials and Solutions: 3-carboethoxycoumarin (I) was prepared by ethylation of the corresponding 3-hydroxycoumarin made by peckmann reaction[20]. Sodium hydroxide, hydrochloric acid, absolute ethanol and hydrazine hydrate were of BHD reagent grade, cetyltrimethylammonium bromide (Fluka) and sodium dodecylsulfate (Fluka). Doubly distilled water was used in the preparation of solutions.

Apparatus and procedure: The rate of reaction of 3-carboethoxycoumarin (I) with NaOH and N_2H_4 was followed spectrophotometrically by monitoring the absorbance of the products at 385 nm, using a Milton Roy sp 601 spectrophotometer. All reactants were equilibrated at the

required temperatures before mixing in a thermostated water bath for ca. 15 min. in automatic circulation thermostat, thoroughly mixed and quickly transferred to an absorption cell. The temperature of the reacting solution was controlled, using automatic circulation thermostat. The thermostat was provided with a special pumping system for circulating water at regulated temperature in the cell holder. The average stabilizing accuracy as measured in the thermostat liquid was ±0.1 ^{o}C. Pseudo-first order conditions were maintained in all runs by the presence of a large excess (>10-fold) of sodium hydroxide and hydrazine.

Pseudo-first order rate constants, k_{obs}, obtained from the slopes of ln($A_\infty - A_t$) *versus* time plots, where A_t and A_∞ are absorbance at time *t*, and infinity, respectively. Enthalpy of activation, ΔH*, and entropy of activation ΔS*, were calculated using transition state theory equation (Eyring Equation) by plotting ln (*k*/T) against 1/T.

$$\ln k/T = \ln K/h + \Delta S^*/R - \Delta H^*/RT$$

where: K is the Boltzmann constant, h is the Plank's constant, R is the universal gas constant and T is the absolute temperature.

Results and Discussion

Kinetics of reaction of 3-carboethoxycoumarin (I) with NaOH: The kinetics of reaction of 3-carboethoxycoumarin (I) with NaOH were studied at temperatures 20 – 40 ^{o}C range for a range of NaOH and (I) concentrations. The plot of Ln(A_∞- A_t) versus time were linear up to 87 % of the reaction, where A_∞ and A_t absorbance at inifinity and at tim t respectively. The values of pseudo first-order rate constant, k_{obs}, obtained from the slopes of these plots are given in table-1. The results in table-1, show that k_{obs} was unaffected when the concentration of the (I) was varied at a constant NaOH concentration, indicating first order dependence on the (I) concentration.

Table-1
Dependence of the rate, k_{obs}, on [I][a], [NaOH] and temperatures

10^3 [OH^-] mol dm^{-3}	10^3 k_{obs} (s^{-1})				
	20 ^{o}C	25 ^{o}C	30 ^{o}C	35 ^{o}C	40 ^{o}C
0.40	0.77	0.96	1.10	1.48	1.98
0.48	0.91	1.11	1.38	1.83	2.55
0.56	1.12	1.32	1.53	2.26	2.97
0.80	1.65	2.05	2.46	3.25	4.74
1.60	2.98	3.83	4.67	5.81	8.06
2.40	4.18	5.02	6.21	7.75	9.61
3.20	5.29	6.21	7.30	9.43	11.76
4.00	6.06	7.56	8.85	12.50	18.20

[a][I] = 4.30 x 10^{-5} mol dm^{-3}; 10^3 k_{obs} = 4.48, 4.76, 4.61 and 4.69 s^{-1} at 10^5 [I] of 2.15, 6.45, 8.60 and 10.75 mol dm^{-3}, respectively at 30 ^{o}C and [OH^-]= 1.60 x 10^{-3} mol dm^{-3}.

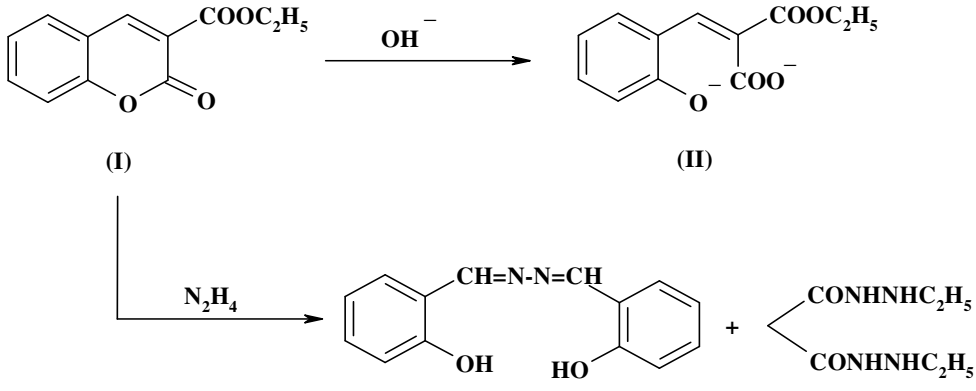
At constant concentration of (I), $1/k_{obs}$ varies linearly with $1/[OH^-]$ at different temperatures (figure-1), and the kinetic of reaction are described by equation (1).

$$\text{Rate} = \{a\,[OH^-]_T / 1 + b[OH^-]_T\}\,[I]_T \quad (1)$$

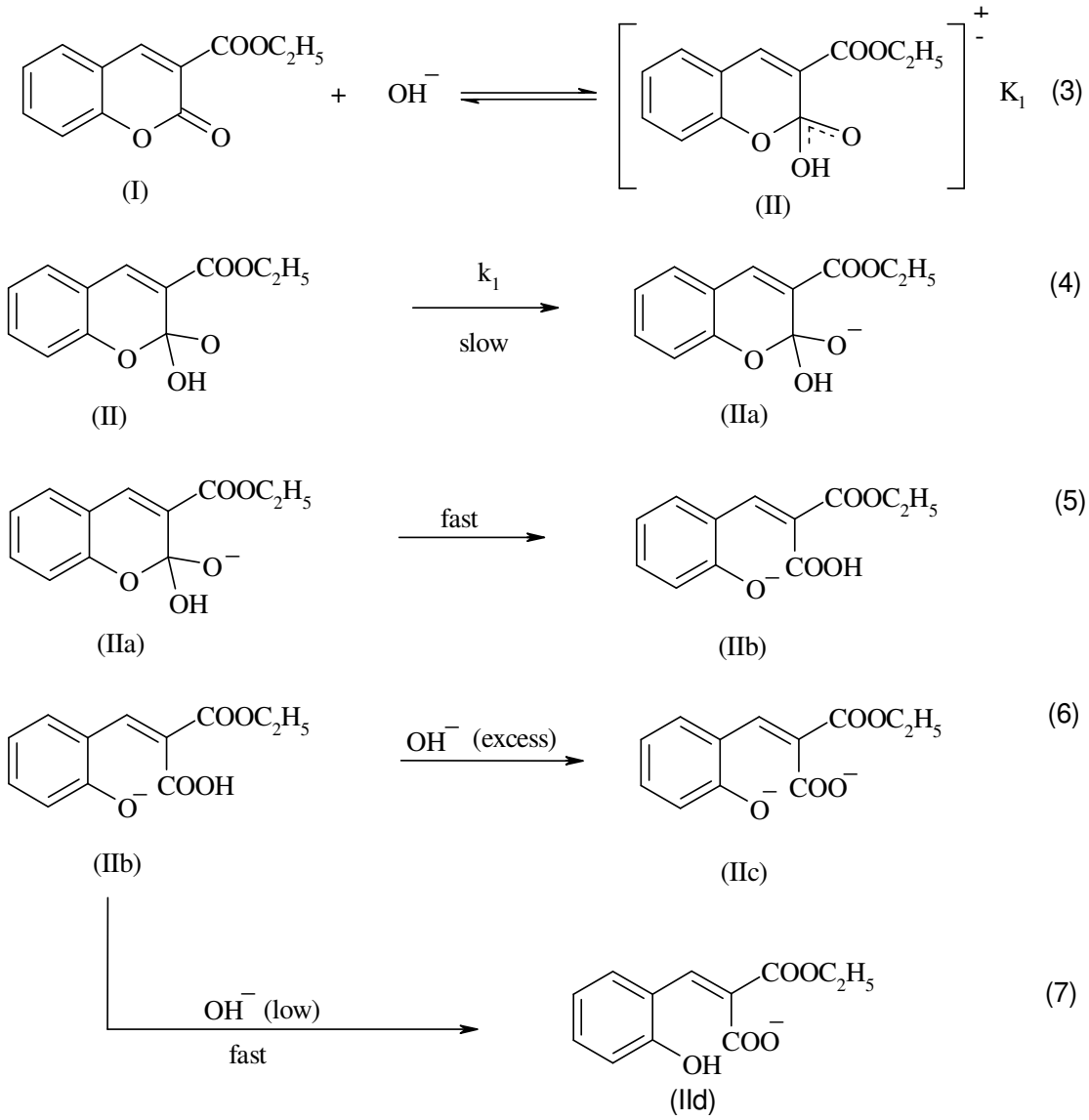
$$1/k_{obs} = 1/a\,[OH^-] + b/a \quad (2)$$

The values of a and b were obtained from the slopes and the intercepts of figure-1.

In accordance with our findings and with those previous studies[15-17] the mechanism of alkaline ring fission of 3-carboethoxycoumarin (I) consists of a rate-determining attack on the (I) carbonyl group by hydroxide ion, followed by a fast fission of the cyclic oxygen-carbonyl bond. In the presence of an excess of base, the product of the reaction is the di-anion (IIc), whereas under conditions of limited basicity, the mono-anion is formed. The proposed mechanism is described in scheme – 2.



Scheme-1



Scheme-2

From the above mechanism, the rate of reaction is given by:

$$\text{Rate} = k_1 [II] = k_1K_1[I][OH^-] \quad (8)$$

If $[I]_T$ represents the total concentration of organic substance species, then

$$[I]_T = [II] + [II_a] \quad (9)$$

By rearrangment, one gets

$$[I]_T = [I] + K_1[I][OH^-] = [I] (1 + K_1[OH^-]) \quad (10)$$

Substitution for [I] from Equation (10) into Equation (8), gives

$$\text{Rate} = k_1K_1[OH^-][I]_T / (1 + K_1[OH^-]) \quad (11)$$

$$k_{obs} = k_1K_1[OH^-] / (1 + K_1[OH^-]) = k_1K_1[OH^-] + k_1 \quad (12)$$

$$1/k_{obs} = 1/ k_1K_1[OH^-] + 1/k_1 \quad (13)$$

The values of k_1 at different temperatures are list in table-2. The values of the equilibrium constant, K_1 was calculated from equation (13) as 44.8 x 10^{-2} mol^{-1} dm^3 at 30°C. The thermodynamic activation parameters including enthalpy and entropy associated with k_1 were calculated by plotting -ln k_1/T against 1/T, (c.f. figure-2). Enthalpy of activation, ΔH^* and entropy of activation, ΔS^*, are equal to 20.5 kJ mol^{-1} and -194.7 JK^{-1} mol^{-1} respectively.

Kinetics of 3-carboethoxycoumarin (I)/ N_2H_4 reaction: The kinetics of reaction of 3-carboethoxy- coumarin (I) with hydrazine were studied at temperatures 20 – 40 °C range for a range of hydrazine and 3-carboethoxycoumarin (I) concentrations. The plot of $Ln(A_\infty - A_t)$ versus time were linear up to 85 % of the reaction, where A_∞ and A_t absorbance at inifinity and at tim t respectively. The values of pseudo first-

order rate constant, k_{obs}, obtained from the slopes of these plots are given in table-3. The results in table-3, show that k_{obs} was unaffected when the concentration of the 3-carboethoxycoumarin (I) was varied at constant hydrazine concentration, indicating that first order dependence on the 3-carboethoxycoumarin (I) concentration. The rate law at fixed $[N_2H_4]$ is given by.

$$\text{Rate} = k_{obs}[I] \quad (14)$$

Table-2
Values of k_1 at different temperatures

Temperature (^oC)	10^2 k_1(s)
20	4.09
25	5.33
30	6.50
35	7.10
40	8.76

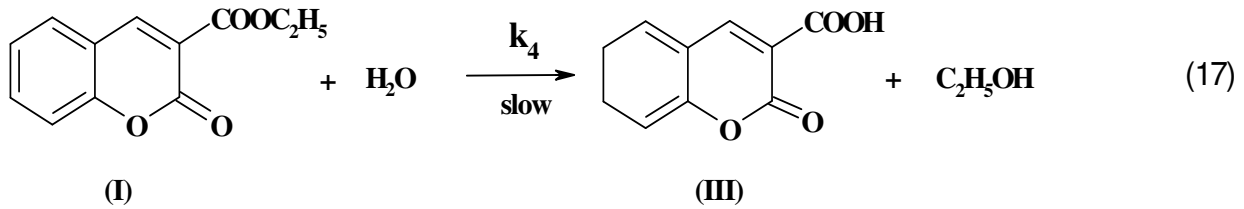
The dependence of k_{obs} on hydrazine was examined over the (1.0 – 6.0) x 10^{-2} M concentration range at different temperatures (figure-3). The results (table-3), show that k_{obs} varies linearly with $[N_2H_4]$, according to equation (15).

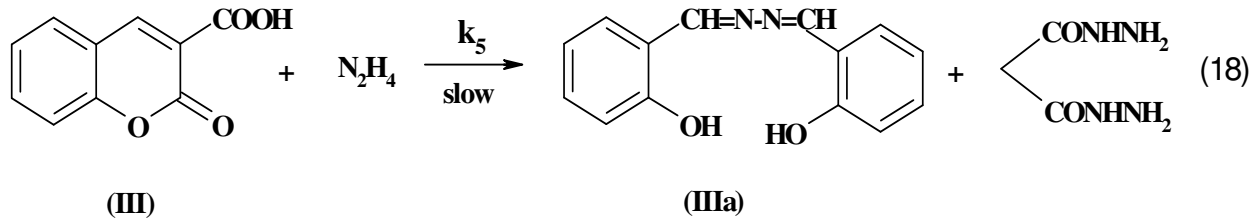
$$k_{obs} = k_2 + k_3[N_2H_4] \quad (15)$$

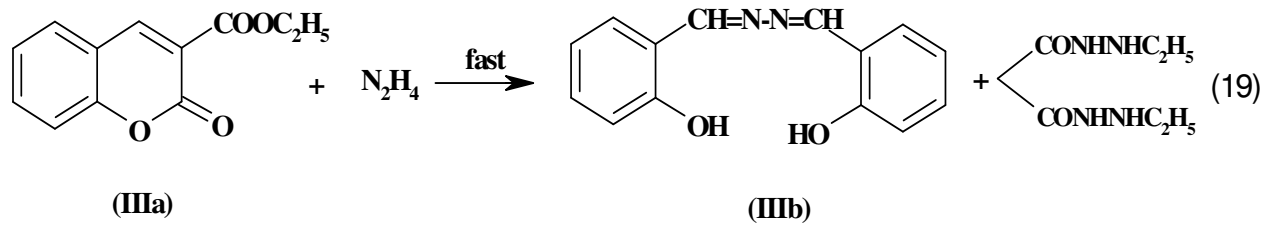
$$\text{Rate} = [I]\{k_2 + k_3[N_2H_4]\} \quad (16)$$

The k_2 and k_3 values, (table-4) over the temperature range used, were obtanied from the intercepts and the slopes respectivily of figure-3 . Thermodynamic activation parameters associated with k_2 and k_3 obtained from from linear least-square fit to the transition state theory equation and figure-4 at different temperatures were calculated by plotting $\ln k_2/T$ and $\ln k_3/T$ against 1/T (figures-4). The enthalpy of activation ΔH_2^* and ΔH_3^* associated with k_2 and k_3 are 36.1 and 23.4 $kJmol^{-1}$, respectively, The corresponding entropies of activation ΔS_2^* and ΔS_3^* were calculated as -185.5 and -190.3 JK^{-1} mol^{-1} respectively.

From equation (15), it was found that one path of the reaction is independent of hydrazine. This observation has drawn our attention to the possibility of hydrolysis of 3-carboethoxycoumarin (I) by H_2O. The action of hydrazine on 3-carboethoxycoumarin (I), which results in ring fission and formation salicylaldazine (III_a) and dihydrazide of malonic acid[19]. The mechanistic pathway for the reaction of 3-carboethoxy- coumarin (I) with hydrazine may be represented in scheme – 3.







Scheme-3

Table-3
Dependence of the rate, k_{obs}, on [I][a], [Hydrazine] and temperatures.

10^2 [Hyd]	10^3 k_{obs} (s^{-1})				
mol dm^{-3}	20 °C	25 °C	30 °C	35 °C	40 °C
1.0	0.80	1.22	1.45	1.73	1.89
2.0	1.23	1.82	2.08	2.33	2.91
3.0	1.65	2.10	2.70	3.15	3.75
4.0	2.18	2.66	3.38	4.12	4.81
5.0	2.50	3.22	3.95	4.87	5.52
6.0	2.81	4.03	4.76	5.42	5.94

[a][I] = 4.30 x 10^{-5} mol dm^{-3}; 10^3 k_{obs} = 2.54, 2.76, 2.82 and 2.68 s^{-1} at 10^5[I] of 2.15, 6.45, 8.60 and 10.75 mol dm^{-3}, respectively at 30 °C and [Hyd] = 3.0 x 10^{-2} mol dm^{-3}.

Table-4
Values of k_2 and k_3 at different temperatures.

Temperature (°C)	10^4 k_2 (s^{-1})	10^2 k_3 (mol^{-1} dm^3 s^{-1})
20	4.23	4.11
25	6.27	5.37
30	7.69	6.53
35	8.99	7.73
40	12.00	8.35

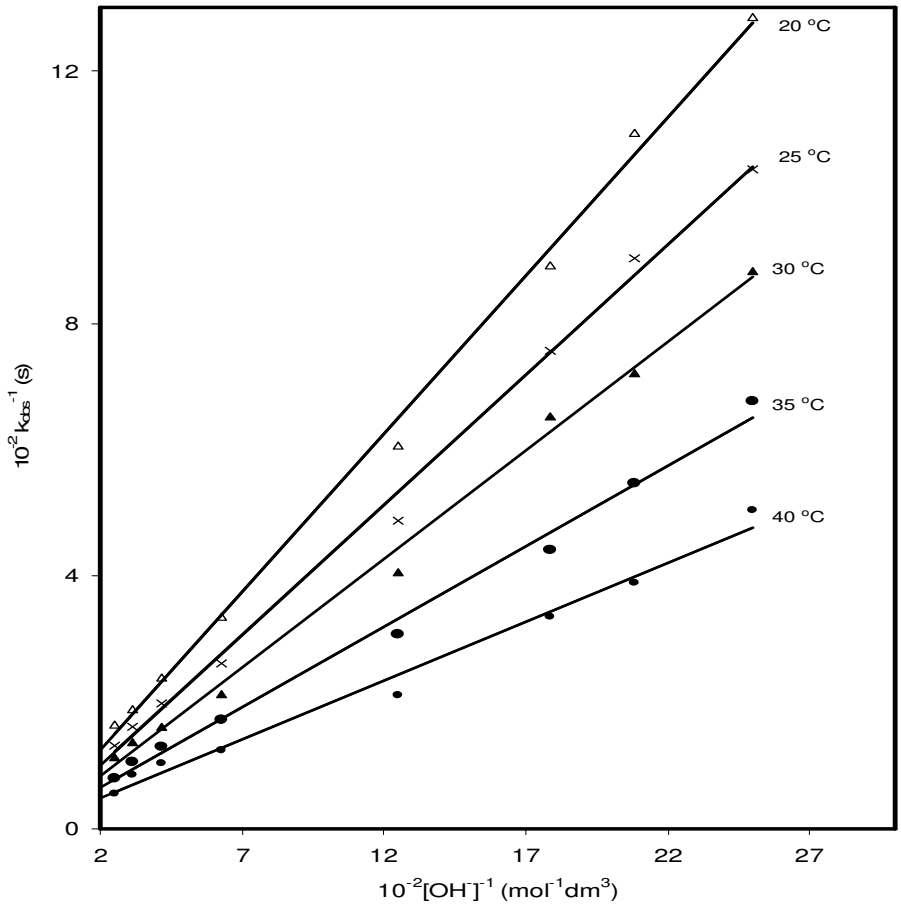


Figure-1
Plot of $1/k_{obs}$ versus 1/[OH] at different temperatures

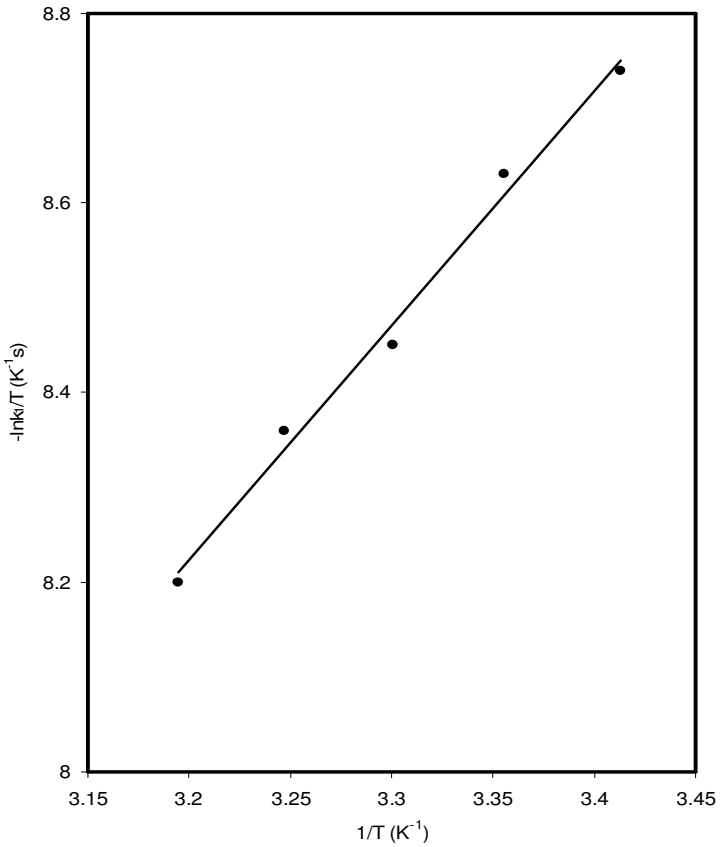


Figure-2
Plot of Ink$_1$/T versus 1/T

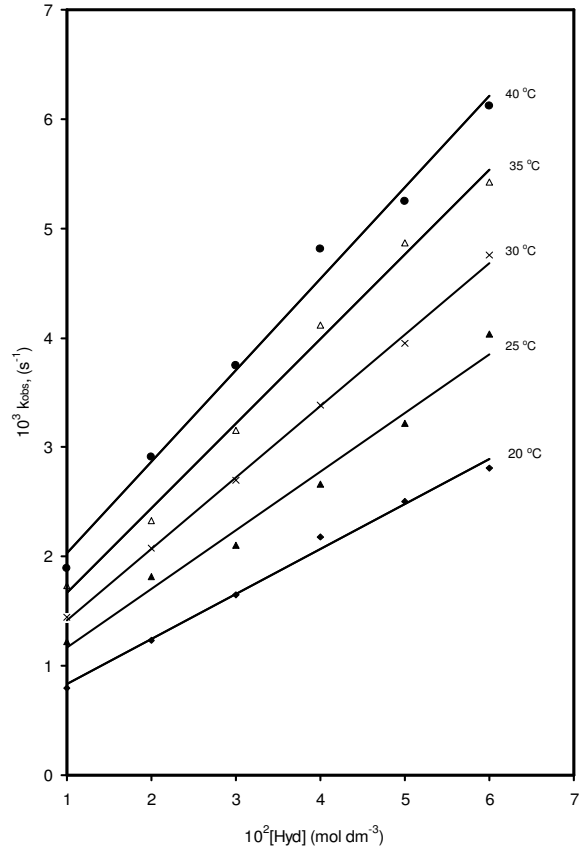


Figure-3
Plot of k obs versus [Hyd] at different temperatures

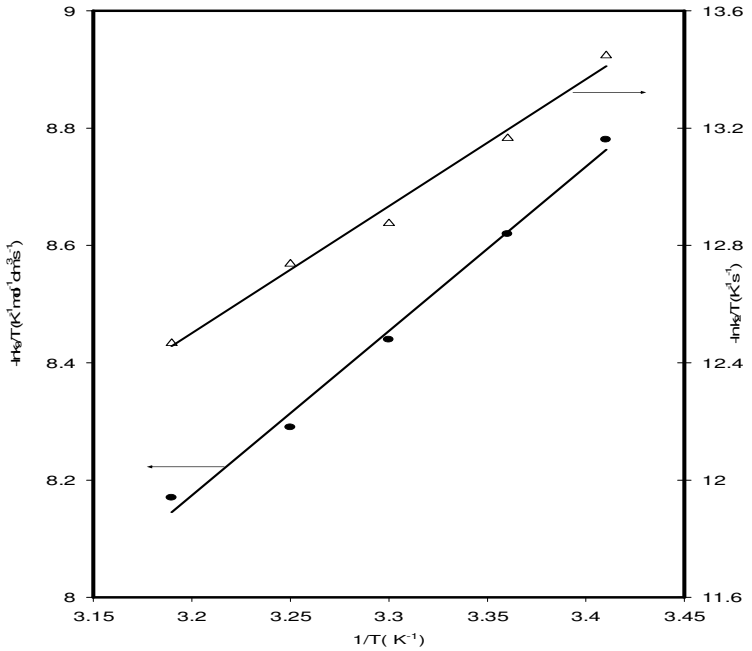


Figure-4
Plot of In K2/T and Ink2/T versus 1/T

From the above mechanism, the rate of the reaction is given by

$$\text{Rate} = k_4[I][H_2O] + k_5[I][N_2H_4] = [I]\{k_4[H_2O] + k_5[N_2H_4]\} \quad (20)$$

If $k_4[H_2O]$ is large, $k_4[H_2O]$ is equal constant (k_6)

$$\text{Rate} = [I]\{k_5[N_2H_4] + k_6\} \quad (21)$$

The rate law is given by equation (21) which is consistent with the experimental rate law equation (16). A comparsion of equations (16) and (21), shows: $k_2 = k_6$ and $k_3 = k_5[N_2H_4]$

Alkaline hydrolysis of 3-carboethoxycoumarin (I) with sodium hydroxide and hydrazine which results in the ring opening of the coumarin ring. At the same condition, the rate of reaction of 3-carboethoxycoumarin (I) with sodium hydroxide is more than it is reaction with hydrazine. This may be due to sodium hydroxide is more basic than hydrazine.

The ring opening step is endothermic as indicated by the positive ΔH^* value. Thus the relatively small enthalpy of activation, ΔH^*, can be explained in terms of the formation of a more solvated intermediate[21]. The negative ΔS^* value was claimed to be largely the result of substantial mutual ordering of the solvated water molecules on the intermediate[21].

Effect of micelles on the rate of reaction of 3-carboethoxycoumarin (I) with NaOH: Micellar catalysis has received considerable attention in view of the analogies drawn between micellar and enzyme catalyses[11,22]. Micelles increase rates of bimolecular reactions by concentrating both the reactants at their surfaces. Electrostatic-, approximation-, and medium-effects are responsible for the incorporation of reactants into or onto a micelle. In order to verify the role of micelles on the hydrolysis of 3-carboethoxycoumarin (I) by NaOH, cationic and anionic micelles were chosen. The effect of micelles (CTAB & SDS) on the reaction of 3-carboethoxycoumarin (I) with NaOH was carried at [I] = 4.30 x 10^{-5} mol dm^{-3}, [OH^-] = 1.60 x 10^{-3} mol dm^{-3} and T = 30.0^{o}C over the micelles concentration range (2.0–20.0) x 10^{-3} mol dm^{-3}. Figure-5, shows the effect of CTAB cationic micelles on the sensitivity for the range 2.0×10^{-3} mol dm^{-3} to 20.0×10^{-3} mol dm^{-3}. The reaction rate increases with increasing [CTAB] up to $\geq 16.0 \times 10^{-3}$ mol dm^{-3} and remains constant at higher [CTAB]. This may be due to the dilution effect. The role of CTAB micelles in catalysis can be explained by incorporation/ solubilisation of [I]/[OH^-] in the Stern layer of CTAB micelles through electrostatic and hydrophobic interactions. These results are in good agreement with our previous observations.[23] The effect of SDS anionic micelles on the reaction rate for the range 2.0×10^{-3} mol dm^{-3} to 20.0×10^{-3} mol dm^{-3} was studied. Figure-5, show a continuous decrease of the reaction rate, k_{obs}, with increasing of [SDS]. This behavior could be rationalized in terms of anionic micelles repel the hydroxide ions.

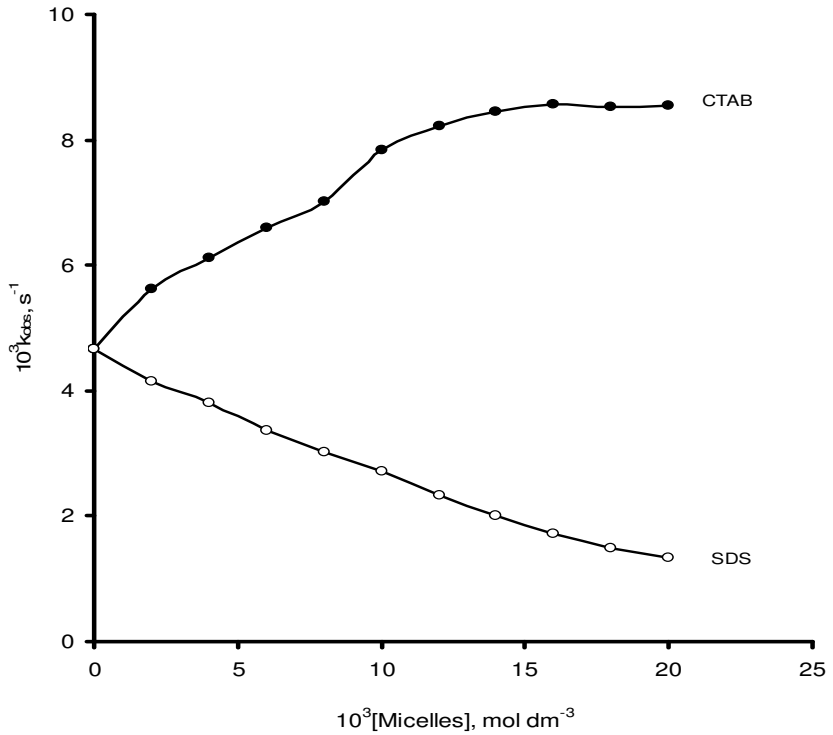


Figure-5
Variation of k_{obs} with [micelles] (CTAB or SDS) at 30^{0}C

Conclusion

The action of sodium hydroxide on the ring opening of 3-carboethoxycoumarin (I) is more than its action with hydrazine. In two cases, the reaction is pseudo-first order and the rate of reaction increases with increasing of temperature. CTAB increases the reaction rate while SDS decreases. The step of ring opening of 3-carboethoxycoumarin is endothermic as indicated by the positive ΔH^* value.

Acknowledgments

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