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여러 온도 및 용매 하에서 수행된 chromen-2-one 지시약 염료들의 염기성 가수분해 반응에 대한 속도론적 연구

Ezz A. Abu-Gharib, Rafat M. EL-Khatib, Lobna A. E. Nassr, and Ahmed M. Abu-Dief*
Chemistry Deptartment, Faculty of Science, 82524, Sohag University, Sohag, Egypt
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Kinetics of Base Hydrolysis of Some Chromen-2-one Indicator Dyes in Different Solvents at Different Temperatures

Ezz A. Abu-Gharib, Rafat M. EL-Khatib, Lobna A. E. Nassr, and Ahmed M. Abu-Dief*
*Chemistry Deptartment, Faculty of Science, 82524, Sohag University, Sohag, Egypt. *E-mail: ahmed_benzoic@yahoo.com*
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요 약. 7-hydroxy-2H-chromen-2-one(HC)와 7-hydroxy-2H-chromen-2-one-4-acetic acid(HCA)의 염기성 가수분해반응을 aqueous-methanol과 aqueous-acetone 혼합물에서 283 K에서 313 K의 온도 범위에서 속도론적으로 연구하였다. 반응의 활성화 파라미터를 구하고 토의하였다. 게다가, 물, 물-에탄올, 물-아세톤 혼합물 내에서 화합물들에 대한 활성화 에너지 장벽의 변화를 속도론적 데이터로부터 추정하였다. 활성화 장벽의 변화는 HC and HCA의 가수분해 반응과 거의 같았다. HC와 HCA의 염기성 가수분해는 $k_{obs} = k_2[OH^-]$와 같은 속도법칙을 따른다. 메탄올 또는 아세톤의 비가 증가함에 따라 HC 와 HCA의 속도 상수들이 감소하는 것은 OH^- 이온이 불안정해지기 때문이다. 활성화 엔트로피가 큰 음의 값을 갖는 다는 것은 반응이 중간 착물의 형성을 경유하며 진행된다는 것을 의미하며, 또한 중간 착물이 경직성과 안정도를 갖는다는 것을 의미한다. 그러므로, 중간 착물의 고리 열림이 속도 조절 단계가 될 것이다.

주제어: Chromen-2-ones, 염기성 가수분해, 반응 메카니즘, 용매 효과, 활성화 에너지 장벽, 열역학적 파라미터

ABSTRACT. Base hydrolysis of 7-hydroxy-2H-chromen-2-one (HC) and 7-hydroxy-2H-chromen-2-one-4-acetic acid (HCA) in aqueous-methanol and aqueous-acetone mixtures were studied kinetically at temperature range from 283 to 313 K. The activation parameters of the reactions were evaluated and discussed. Moreover, the change in the activation energy barrier of the investigated compounds from water to water-methanol and water-acetone mixtures was estimated from the kinetic data. It is observed that the change in activation barriers is more or less the same for the hydrolysis of HC and HCA. Base hydrolysis of HC and HCA follows a rate law with $k_{obs} = k_2[OH^-]$. The decrease in the rate constants of HC and HCA as the proportion of methanol or acetone increases is due to the destabilization of OH^- ion. The high negative values of entropy of activation support the proposal mechanism, i.e. the investigated reaction takes place via the formation of an intermediate complex. Moreover, these values refer to the rigidity and stability of the intermediate complex. Thus, the ring opening of the intermediate complex would be the rate controlling step.

Keywords: Hydroxy-chromen-2-ones, base hydrolysis mechanism, solvent effect, activation energy barrier, kinetics

INTRODUCTION

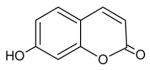
Biological importance of chromen-2-ones

Chromen-2-ones have attracted intense interest in recent years because of their diverse pharmacological properties. Among these properties, their cytotoxic effects were most extensively examined, their broad range of effects on the tumors as shown by various in vitro and *in vivo* experiments and clinical studies discussed.[1] Chromen-2-ones have important effects in plant biochemistry and physiology, acting as antioxidants,[2] enzyme inhibitors and precursors of toxic substances. In addition, these compounds are involved in the actions of plant growth hormones, growth regulators, the control of respiration and photosynthesis. Chromen-2-one derivatives have also found applications as fluorescent dyes,[3,4] anti-inflammatory agents,[5] antineoplastic agents,[6] immunomodulant agents[7] antifungals,[8] anticoagulants,[9] antibacterials,[10] antimicrobial[11,12] insecticides[13] and proliferators of HIV.[14,15] HC is widly used in estimation of enzymatic activity as fluorigenic enzyme substrates[16] and acts as a pH indicator in the range 6.5-8.9.[17,18] HCA is used as laser

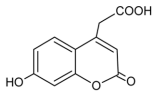
dyes for the blue-green region.[4,19]

Rate coefficient for the reaction between organic and inorganic compounds with hydroxide ions in aqueous solutions is sensitive to the nature and molar fraction of organic solvent. The dependence of the rate constants on solvent comprising binary aqueous mixtures depends on the composition of the solvent.[20,21]

Our work treats the effect of medium on the kinetics of base hydrolysis of HC and HCA in aqueous-methanol and aqueous-acetone mixtures. Also the activation parameters of the mentioned reactions were calculated by least squares of Arrhenius and Eyring plots.



7-hydroxy-2H-chromen-2-one (HC)



7-hydroxy-2H-chromen-2-one-4-acetic acid (HCA)

Materials

All materials, sodium hydroxide (99.3%), sodium chloride (99.7%), sodium nitrate (99%), oxalic acid (99.7%), methanol (99.5%) and acetone (99.5%) were obtained from BDH. 7-hydroxy-2H-chromen-2-one (99.5%) and 7-hydroxy-2H-chromen-2-one-4-acetic acid (99.5%) were obtained from Sigma. The stock solutions of NaOH (1 mol dm^{-3}), NaCl (1 mol dm^{-3}) and $NaNO_3$ (1 mol dm^{-3}) were prepared by dissolving the calculated amounts of AnalaR samples in redistilled water. The water used for preparation of the solution was deionized and distilled twice. The solution of NaOH (1 mol dm^{-3}) was standardized by volumetric (acid-base) titration with standard solution of oxalic acid (1 mol dm^{-3}) using ph.ph as indicator.

Apparatus and Experimental Method

Kinetic measurements: Kinetics of base hydrolysis of the investigated compounds were measured by following the dependence of absorbance on time using 10 mm silica cells in the thermostatted cell compartment of JASCO model V-530 spectrophotometer. The temperature was controlled at 298 ± 0.1 K using an ultrathermostate (CRIOTERM 190) water circulator connected with the spectrophotometer. Chemical reactions were monitored in solutions held at constant ionic strength (0.5 mol dm^{-3}) using appropriate amounts of sodium chloride in aqueous-methanol mixtures and sodium nitrate in aqueous-acetone mixtures over at least three half-lives. Pseudo first-order conditions were applied by mixing multifold greater concentration of NaOH (100 times) than that of the compound. The reaction of the two studied compounds with NaOH was followed spectrophotometrically by monitoring the decay of the absorbance intensity (A_t) at several time intervals at the selected wavelength (λ_{max}) corresponding to the absorption. Rate constants were calculated from the dependence on time of absorbance at 365 nm and 366 nm for HC and HCA, respectively.

RESULTS AND DISCUSSION

Kinetic results and reaction mechanism

Under the influence of alkali (0.03 M), HC and HCA, like phenols, form metal salts which can correspond to one or other of the tautomeric forms resulting in bathchromic shift i.e the λ_{max} is shifted to 373 nm and 374 nm, respectively as the pka values of HC and HCA are 8.3 and 7.8, respectively. It can be inferred from the following repeated spectral scans (cf. *Figs.* 1, 2) that the initial action

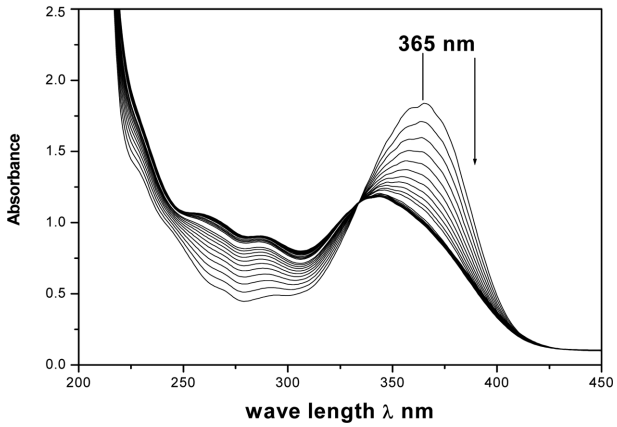


***Fig.* 1.** Repeated spectral scans of the base hydrolysis of HC at 298 K.

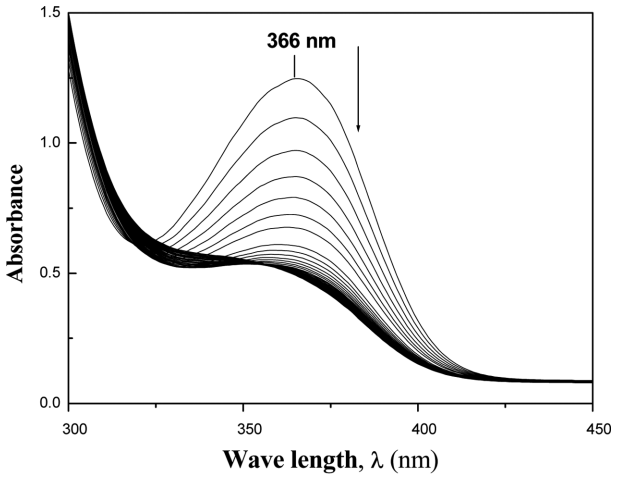


***Fig.* 2.** Repeated spectral scans of the base hydrolysis of HCA at 298 K.

on HC and HCA by NaOH takes place in one stage and leads to the rate determining opening of the pyrone ring and the formation of a salt of (2Z)-3-(2, 4-dihydroxyphenyl) acrylic acid and (2Z)-3-(2,4-dihydroxyphenyl)-2-pentenedioic acid, respectively[22,23] as shown in the suggested reaction mechanism. For HC and with prelonging the NaOH, the cis form of the salt of 3-(2,4-dihydroxyphenyl) acrylic acid converts to stable trans form at 375 nm.[24] But for HCA, the acetic acid group (bulk group) sterically hinders the rotation of the (2Z)-3-(2,4-dihydroxyphenyl)-2-pentenedioic acid to give the trans form.

The observed first-order rate constants (k_{obs}) as a function on [OH^-] and in the presence of different water-methanol and water-acetone ratios were calculated from the dependence of absorbance on time at λ_{max} for the investigated compounds using Microcal Origin program version 7.5 (cf. *Tables* 1-4) with maximum error 2%.

The observed increase in the rate constant values as the percentage of water (v/v) increases in binary solvent mixtures can be ascribed mainly to the increase in the free chromene-2-one derivative concentration due to the decrease in dispersion forces in water molecules.[23,25] The high delocalization of charge in HC and HCA compounds promotes interaction with localized dispersion centers in nearby solvent molecules. This interaction is expected to increase in following order water < methanol < acetone and stabilizes the studied compounds in the same direction. Further more, the transition state is more polar than the initial state that matches with the decrease in k_{obs} values with increasing the ratios of co-organic solvent.

The observed enhancement of the rate constant values in acetone co-solvent compared with the corresponding values in methanol co-solvent would be ascribed to the destabilization of the hydrophilic OH^- ions in acetone more than in methanol.[23,26] Also this may be due to the steric effect which results from the size of solvent molecule allowing the OH^- ions to penetrate the large acetone molecules more than the small methanol molecules.

The kinetic results conform to the pattern of equation (1)

$$-\frac{d[compound]}{dt} = k_{obs}[compound] \quad (1)$$

***Table* 1.** Observed first-order rate constant (10^4 k_{obs}, s^{-1}), second order rate constant (10^3 k_2, dm^3 mol^{-1} s^{-1}) and the change in the activation barrier ($\delta_m\Delta G^{\#}$ kJ mol^{-1}) values for the base hydrolysis of HC in various ratios (v/v) of MeOH in the presence of different [OH^-] at 298 K and I = 0.5 mol dm^{-3} (NaCl)

[OH^-], mol dm^{-3}	MeOH%(v/v)					
	0	10	20	40	50	60
	10^4 k_{obs}, s^{-1}					
0.20	19.50	15.00	12.20	9.30	7.00	4.70
0.25	25.00	18.30	15.50	11.40	8.90	5.80
0.30	28.80	22.51	18.60	13.10	10.00	6.90
0.35	34.20	26.90	22.10	16.00	12.00	8.30
0.40	39.00	30.50	24.90	18.40	13.20	9.30
0.45	44.10	33.80	28.50	20.20	15.10	10.80
10^3 k_2 dm^3 $mol^{-1}s^{-1}$	9.74	7.72	6.42	4.51	3.15	2.43
$\delta_m\Delta G^{\#}$ kJ mol^{-1}		0.58	1.03	1.90	2.79	3.44

***Table* 2.** Observed first-order rate constant (10^4 k_{obs}, s^{-1}), second order rate constant (10^3 k_2, dm^3 mol^{-1} s^{-1}) and the change in the activation barrier ($\delta_m\Delta G^{\#}$ kJ mol^{-1}) values for the base hydrolysis of HCA in various ratios (v/v) of MeOH in the presence of different [OH^-] at 298 K and I = 0.5 mol dm^{-3} (NaCl)

[OH^-], mol dm^{-3}	MeOH%(v/v)					
	0	10	20	40	50	60
	10^4 k_{obs}, s^{-1}					
0.20	25.00	20.10	17.50	13.15	10.10	7.90
0.25	32.00	24.14	22.10	17.00	13.20	9.80
0.30	37.90	29.50	27.00	19.20	16.10	12.00
0.35	44.00	34.00	30.00	23.00	18.10	13.70
0.40	50.10	39.00	35.00	25.70	20.40	15.50
0.45	57.90	44.70	39.30	29.30	23.30	18.20
10^3 k_2 dm^3 mol^{-1} s^{-1}	12.94	9.81	8.50	6.34	5.12	4.00
$\delta_m\Delta G^{\#}$ kJ mol^{-1}		0.69	1.04	1.77	2.30	2.91

***Table* 3.** Observed first-order rate constant (10^4 k_{obs}, s^{-1}), second order rate constant (10^3 k_2, dm^3 mol^{-1} s^{-1}) and the change in the activation barrier ($\delta_m\Delta G^{\#}$ kJ mol^{-1}) values for the base hydrolysis of HC in various ratios (v/v) of acetone in the presence of different [OH^-] at 298 K and I = 0.5 mol dm^{-3} ($NaNO_3$)

[OH^-], mol dm^{-3}	acetone % (v/v)					
	0	10	20	40	50	60
	10^4 k_{obs}, s^{-1}					
0.20	20.00	18.00	14.70	11.20	8.72	6.80
0.25	25.20	22.10	18.80	14.00	11.20	8.50
0.30	30.0	27.00	23.20	16.70	13.50	9.94
0.35	34.10	31.20	27.10	19.50	15.40	12.20
0.40	39.30	35.00	31.00	23.20	18.40	14.10
0.45	44.50	40.00	34.80	25.70	20.60	15.80
10^3 k_2 dm^3 mol^{-1} s^{-1}	9.70	8.63	7.94	5.91	4.79	3.67
$\delta_m\Delta G^{\#}$ kJ mol^{-1}		0.29	0.50	1.23	1.75	2.41

Maximum error is 2%

***Table* 4.** Observed first-order rate constant (10^4 k_{obs}, s^{-1}), second order rate constant (10^3 k_2, dm^3 $mol^{-1}s^{-1}$) and the change in the activation barrier ($\delta_m\Delta G^{\#}$ kJ mol^{-1}) values for the base hydrolysis of HCA in various ratios (v/v) of acetone in the presence of different [OH^-] at 298 K and I = 0.5 mol dm^{-3} ($NaNO_3$).

[OH^-], mol dm^{-3}	acetone % (v/v)					
	0	10	20	40	50	60
	10^4 k_{obs}, s^{-1}					
0.20	25.10	22.50	19.70	16.30	13.20	10.00
0.25	31.30	27.60	25.20	19.40	16.20	13.20
0.30	37.40	33.20	29.50	23.20	19.30	15.50
0.35	43.20	40.00	35.20	27.10	22.00	18.30
0.40	50.50	44.10	40.10	31.60	25.00	20.50
0.45	55.20	50.30	44.50	34.80	29.30	23.70
10^3 k_2 dm^3 mol^{-1} s^{-1}	12.23	11.20	10.07	7.66	6.22	5.30
$\delta_m\Delta G^{\#}$ kJ mol^{-1}		0.22	0.48	1.16	1.68	2.10

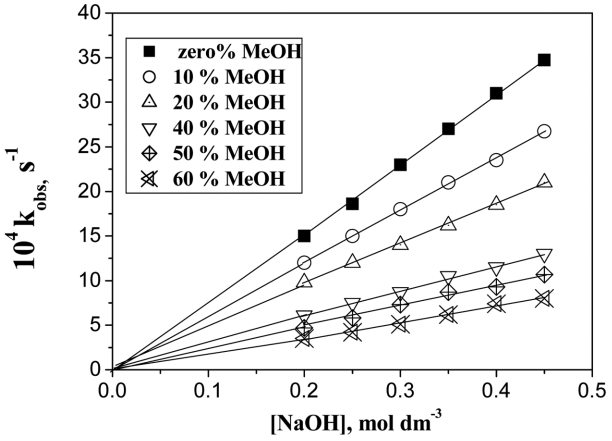


***Fig*. 3.** Plots of the observed first order rate constant of the reaction between NaOH and HC as a function of [NaOH] in aqueous-methanol mixtures at [HC] = 1×10^{-3} M, I = 0.5 M at 298 K.

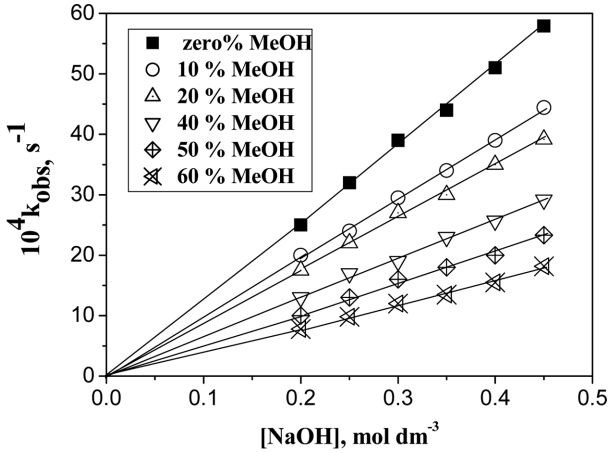


***Fig*. 4.** Plots of the observed first order rate constant of the reaction between NaOH and HCA as a function of [NaOH] in aqueous-methanol mixtures at [HCA] = 1×10^{-3} M, I = 0.5 M at 298 K.

The dependence of k_{obs} on base concentration is linear for both two compounds without significant intercept (cf. *Figs.* 3-6) hence the hydrolysis follows the rate law with:

$$k_{obs} = k_2[OH^-] \quad (2)$$

in which k_2 is the second order rate constant where [OH^-]

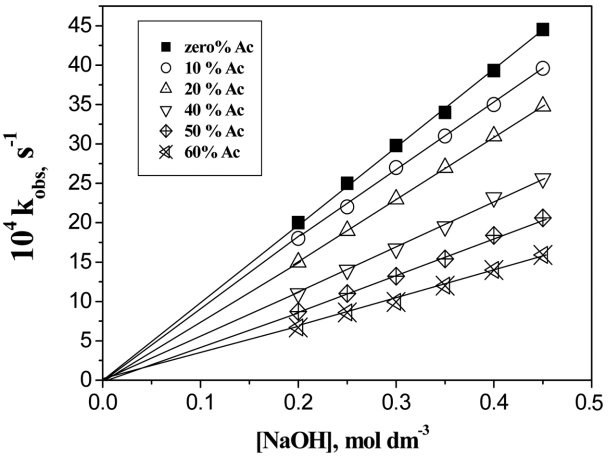


***Fig*. 5.** Plots of the observed first order rate constant of the reaction between NaOH and HC as a function of [NaOH] in aqueous-acetone mixtures at [HC] = 1×10^{-3} M, I = 0.5 M at 298 K.

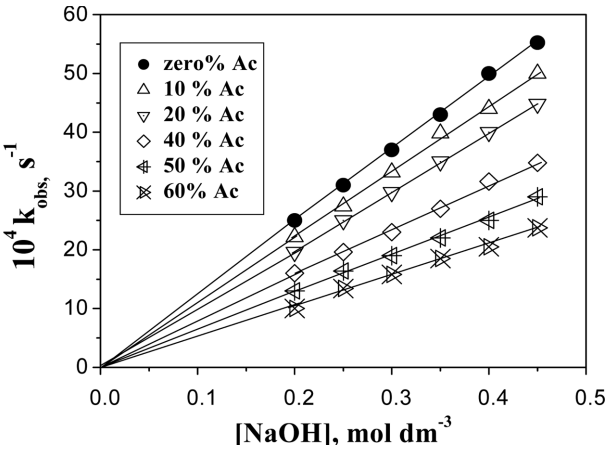


***Fig*. 6.** Plots of the observed first order rate constant of the reaction between NaOH and HCA as a function of [NaOH] in aqueous-acetone mixtures at [HCA] = 1×10^{-3} M, I = 0.5 M at 298 K.

>> [compound]. This equation indicates that the second order process is dominant in the present solvent mixtures.

On applying the steady-state approximation for the concentration of the intermediates B, C and D on the suggested reaction mechanism of HC and HCA, where the total concentration of the compound: $[A]_T=[B]+[C]+[D]$, where [A] is very small and neglectable because it reacts very fast with the base to form the intermediate B. Thus, the rate equation can be formulated as:

$$Rate = \frac{-d[compound]}{dt} = \frac{k_b k_d [OH^-][A]_T}{k_b k_c + k_c k_d + k_b k_d [OH^-]} \quad (3)$$

where

$$k_{obs} = \frac{k_b k_d [OH^-]}{k_b k_c + k_c k_d + k_b k_d [OH^-]} \quad (4)$$

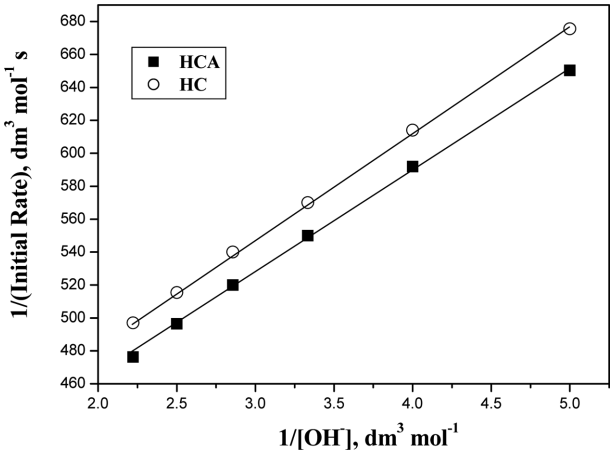
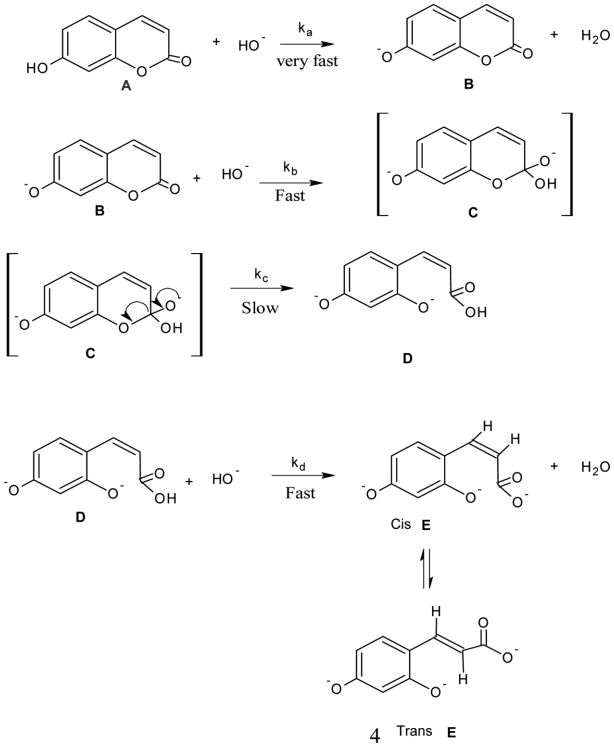
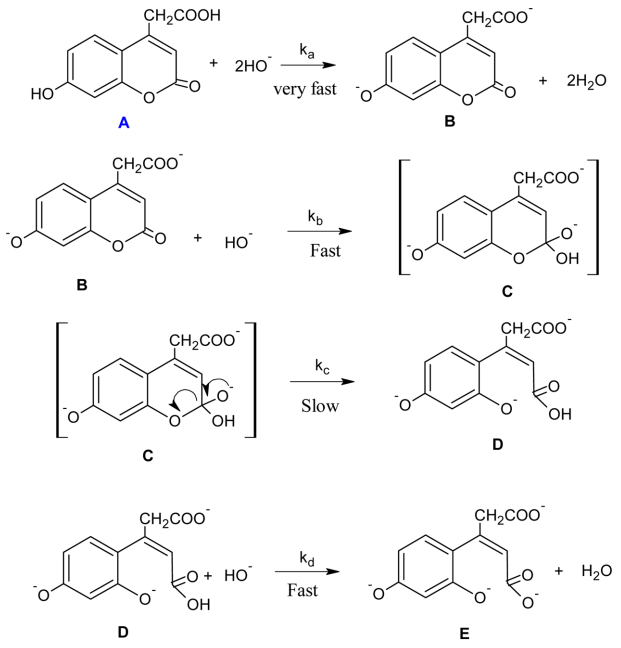


***Fig*. 7.** Lineweaver-Burk plots of the base hydrolysis of HC and HCA in aqueous solution with [compound] = 1×10^{-3} mol dm^{-3}, I = 0.5 M and 298 K.

The base hydrolysis reaction of HC and HCA exhibits Michaelis-Menten kinetics (cf. *Fig.* 7). This suggests that the reaction occurs via the formation of intermediates as shown in the suggested mechanism (cf. *Schemes* 1, 2)). From Lineweaver-Burk plots, Michaelis-Menten constants (K_M) were calculated and found to be 0.183 and 0.19 mol dm^{-3} s^{-1} for HC and HCA, respectively. The large values of K_M indicate the formation of intermediates during the reaction progress.[27-29]



***Scheme* 1.** Suggested mechanism of the base hydrolysis of HC.



***Scheme* 2.** Suggested mechanism of the base hydrolysis of HCA.

The change in the activation barrier $\delta_m\Delta G^{\#}$ is evaluated and reported in *Tables* 1-4 for both HC and HCA from the ratio of rate constants of the base hydrolysis in the aqueous-solvent (k_{2S}) to the corresponding values in the aqueous solution (k_{2W}) according to the following relation:[20]

$$\delta_m\Delta G^{*} = -RT\ln\left(\frac{k_{2s}}{k_{2w}}\right) \quad (5)$$

It is observed that the values of $\delta_m\Delta G^{\#}$ increase with increase methanol or acetone content and these matches with the decreasing of k_{obs} and k_2 values as methanol or acetone content increases.

Tables 1-4 show that the observed first-order rate constant of base hydrolysis of HCA is much faster than the corresponding value for HC. This behavior could be attributed to the easier attack of OH^- on the carbonium center in HCA. The presence of acetic acid group, electron withdrawn group, increases the activity of pyrone ring towards the attack of OH^-.

Determinations of the activation parameters

The activation parameters were calculated (cf. *Tables* 5, 6) by the least squares of Arrhenius plots (*Fig*. 8) and Eyring plots (*Fig*. 9).

It is worth mentioning that the activation parameters are important for determination of the rate of reaction and reaction mechanism. The high negative values of entropy of activation (cf. *Tables* 5, 6) support the proposal mechanism, that the investigated reaction takes place via the formation of an intermediate complex,[22,28,30] cf. the mechanism. Moreover, these values refer to the rigidity of the complex (B) and its high stability. Thus, the ring opening of the intermediate complex would be the rate controlling step (RCS) and proceeds with inner-sphere electron transfer step.

It is interesting that, the different thermodynamic functions are consistent in their trends. As entropy of activation ($\Delta S^{\#}$) increases, i.e., changes to less negative value, thus the rate constant decreases and activation energy

***Table* 5.** Second-order rate constant values (10^3 k_2, mol^{-1} dm^3 s^{-1}) and the activation parameters for the base hydrolysis of HC and HCA in various ratios (v/v) of MeOH at different at temperatures I= (0.5M)

T(K) / MeOH %	283	288	293	298	303	308	313	E_a kJ mol^{-1}	$\Delta H^{\#}$ kJ mol^{-1}	$\Delta G^{\#}$ kJ mol^{-1}	$\Delta S^{\#}$ J mol^{-1} K^{-1}	A mol^{-1} dm^3 s^{-1}
HC	10^3 k_2, mol^{-1} dm^3 s^{-1}											
0	3.68	4.90	7.31	9.74	14.60	....	....	44.35	41.8	70.00	-94.8	6.29×10^6
10	2.80	3.84	5.70	7.72	11.43	15.45	....	45.40	43.0	70.47	-92.4	4.27×10^6
20	2.41	3.24	4.81	6.42	9.71	12.90	19.52	47.13	44.6	71.40	-90.0	2.00×10^6
40	1.62	2.28	3.29	4.51	6.81	8.97	13.66	49.81	47.4	72.91	-85.7	8.89×10^5
50	1.25	1.61	2.56	3.15	5.10	6.35	10.26	51.11	48.7	73.53	-83.5	7.28×10^5
60	0.85	1.21	1.68	2.43	3.37	2.43	6.81	52.50	50.0	74.14	-81.0	3.48×10^5
HCA	10^3 k_2, mol^{-1} dm^3 s^{-1}											
0	4.75	6.37	9.45	12.94	18.97	.....	.....	42.25	39.9	68.58	-96.2	5.59×10^7
10	3.67	4.93	7.38	9.81	14.74	19.27	.....	43.42	40.9	68.84	-93.7	3.47×10^7
20	3.25	4.31	6.49	8.50	13.10	17.35	26.1	45.18	42.6	69.87	-91.5	2.25×10^7
40	2.49	3.17	4.99	6.34	9.97	12.63	19.55	47.73	45.4	71.38	-87.1	9.90×10^6
50	1.98	2.56	3.94	5.12	7.85	10.60	15.71	49.19	46.7	71.97	-84.8	7.55×10^6
60	1.54	1.92	3.07	4.00	6.30	8.39	12.87	50.45	48.1	72.80	-82.5	3.68×10^6

Maximum error is 2%

***Table* 6.** Second-order rate constant values (10^3 k_2, mol^{-1} dm^3 s^{-1}) and the activation parameters for the base hydrolysis of HC and HCA in various ratios (v/v) of acetone at different temperatures at I = (0.5 M)

MeOH % \ T(K)	283	288	293	298	303	308	313	E_a kJ mol^{-1}	$\Delta H^{\#}$ kJ mol^{-1}	$\Delta G^{\#}$ kJ mol^{-1}	$\Delta S^{\#}$ J mol^{-1} K^{-1}	A mol^{-1} dm^3 s^{-1}
HC	10^3 k_2, mol^{-1} dm^3 s^{-1}											
0	3.66	4.90	7.30	9.70	....	.....	....	40.87	39.2	68.15	-97.3	8.12×10^7
10	3.30	4.39	6.65	8.63	13.29	....	....	42.00	40.3	68.62	-94.9	6.45×10^7
20	2.77	3.85	5.57	7.94	11.13	15.70	....	43.63	41.9	69.48	-92.5	4.78×10^7
40	2.06	2.82	4.10	5.91	8.16	11.55	17.07	46.31	44.8	71.10	-88.3	4.60×10^7
50	1.67	2.30	3.29	4.79	6.50	9.38	13.3	47.61	46.0	71.60	-85.9	8.20×10^6
60	1.31	1.76	2.59	3.67	5.08	7.20	10.44	49.00	47.4	72.20	-83.4	5.60×10^6
HCA	10^3 k_2, mol^{-1} dm^3 s^{-1}											
0	4.64	6.10	9.27	12.23	....	.....	.....	38.90	37.2	66.61	-98.7	6.15×10^8
10	4.15	5.55	8.31	11.20	16.60	.....	.....	40.10	38.4	67.00	-96.1	5.30×10^8
20	3.66	5.00	7.30	10.07	14.65	20.00	....	41.65	40.0	67.96	-94.0	3.90×10^8
40	2.88	3.80	5.81	7.66	11.45	15.20	22.84	44.35	42.8	69.50	-89.6	8.90×10^7
50	2.45	3.13	4.94	6.22	9.40	12.75	18.72	45.63	44.1	70.12	-87.3	5.80×10^7
60	2.06	2.62	4.10	5.30	8.10	10.20	16.10	47.10	45.5	72.46	-85.1	3.70×10^7

Maximum error is 2%

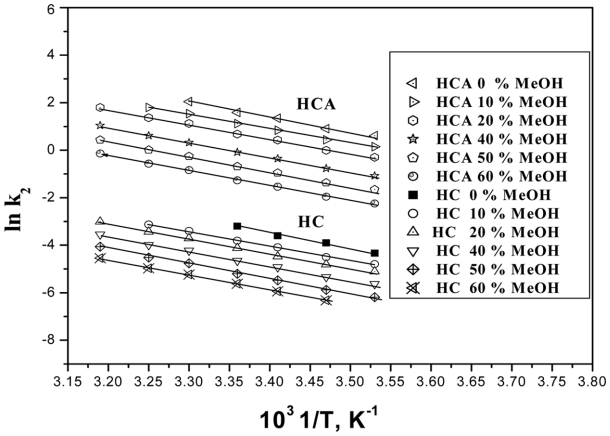


***Fig*. 8.** Plots of $\ln k_2$ against 1/T for the base hydrolysis of HC and HCA in different ratios of MeOH. For HCA, the plots are between (5+ln k_2) and 1/T.

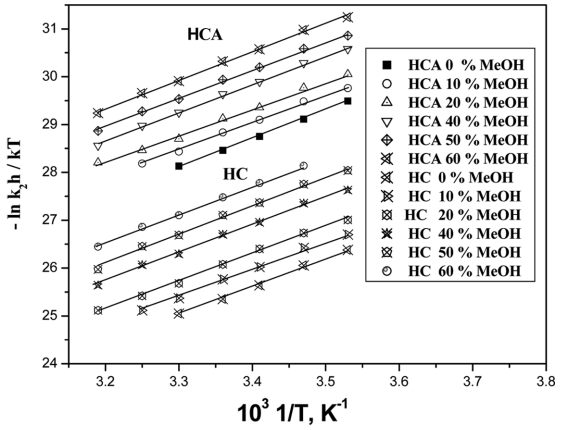


***Fig*. 9.** Plots of -$\ln k_2 h/kT$ against 1/T for the base hydrolysis of HC and HCA in different ratios of MeOH. For HCA, the plots are between (2+-ln $k_2 h/kT$) and 1/T.

increases. This behaviour can be ascribed to enhancing stability of activated complex intermediate. Again the relatively high free energy change would assume that the slow step (RCS) is the ring opening of the established intermediate (B) and many vibrational degrees of freedom have been transformed into translations.[30] The large frequency factor would suggest synergistic evidence for the proposal pathway. Furthermore, the positive free energy of transfer from water to methanol or acetone reported in *Tables* 5, 6, assumes that the transient species in hand are polar entities.[22]

CONCLUSION

Base hydrolysis of HC and HCA follow a rate law with k_{obs}=k_2[OH^-]. The decrease in the rate constants of HC and HCA as the proportion of methanol or acetone increases is due to the destabilization of OH^- ion. The values of rate constants (k_{obs} and k_2) decrease in the following order water > acetone > methanol with increasing the methanol or acetone content. The high negative values of entropy of activation supports the proposal mechanism, i.e. the investigated reaction takes place via the formation of an intermediate complex. Moreover, these values refer to the rigidity and stability of the intermediate complex. Thus, the ring opening of the intermediate complex would be the rate controlling step.

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