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Reactivity Trends in the Base Hydrolysis of 6-Nitro-2H-chromen-2-one and 6-Nitro-2H-chromen-2-one-3-carboxylic Acid in Binary Mixtures of Water with Methanol and Acetone at Different Temperatures[1]

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Abstract—Kinetics of the base hydrolysis of 6-nitro-2H-chromen-2-one (NC) and 6-nitro-2H-chromen-2-one-3-carboxylic acid (NCC) in water–methanol and water–acetone mixtures was studied at temperature range from 283 to 313 K. The activation parameters of the reactions were evaluated and discussed. The change in the activation barrier of the investigated compounds from water to water–methanol and water–acetone mixtures were estimated from the kinetic data. The base hydrolysis of NC and NCC in the water–methanol and water–acetone mixtures follows a rate law with $k_{obs} = k_2[OH^-]$ and $k_{obs} = k_1 + k_2[OH^-]$, respectively. The decrease in the rate constants of NC and NCC hydrolysis, as the proportion of methanol and acetone increases, is accounted for by the destabilization of the OH^- ion. The activation and thermodynamic parameters were determined.

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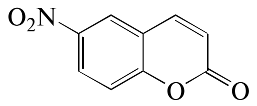
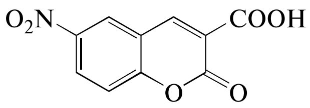
Chromen-2-one is the parent organic compound of a class of naturally occurring photochemicals found in many plant species such as meliot, tonca beans, lavender, sweet clover grass and licorice. It occurs in food plants such as strawberries, apricots, cherries, and cinnamon. It is thought to work as a pesticide for the plants that produce it. This oxygen heterocycle is best known for its fragrance described as a vanilla-like odor or the aroma of freshly mowed hay. It is the odoriferous principle of wood ruff, which led to its wide-spread use as a perfumery chemical in industry [1]. Chromen-2-one derivatives have also found applications as fluorescent dyes [2, 3], antitumor agents [4], antioxidants [5], antiinflammatory agents [6], antineoplastic agents [7], immunomodulant agents [8] antifungals [9], anticoagulants [10], antibacterials [11], antimicrobial [12] and insecticides agents [13], proliferators of HIV [14, 15], and particular human malignant cell lines *in vitro* [16, 17], as well as affecting tumor activity of several tumor types *in vivo* [18–20]. The synthesis of nitro-substituted chromen-2-ones has been undertaken as part of a general scheme of search for physiologically active compounds, in view of the fact that nitro-substituted compounds have a unique place in the attack against pathogenic microorganisms [21].

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 cosolvent. The rate constants in binary aqueous mixtures depend on the composition of the solvent [22, 23].

In our work, we report here the effects of methanol and acetone, as organic cosolvents, on the kinetics of the base hydrolysis of 6-nitro-2H-chromen-2-one (**NC**) and 6-nitro-2H-chromen-2-one-3-carboxylic acid (**NCC**) at different temperatures to gain more information about the activation parameters of base hydrolysis of these two compounds.



6-Nitro-2H-chromen-2-one (NC)



6-Nitro-2H-chromen-2-one-3-carboxylic acid (NCC)

EXPERIMENTAL

Materials

All materials, sodium hydroxide, sodium chloride, sodium nitrate, methanol, and acetone were obtained from “BDH”. The stock solutions of NaOH, NaCl

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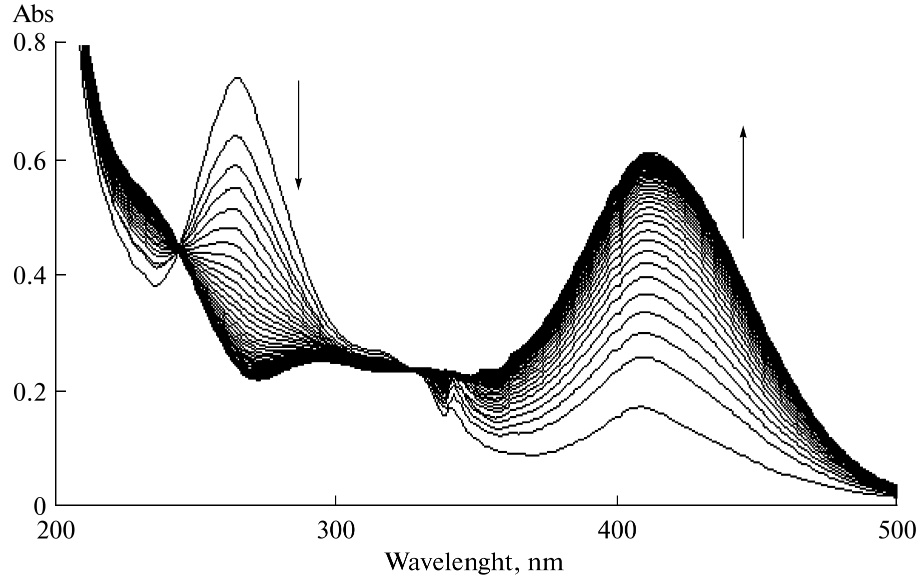


Fig. 1. Repeated spectral scans of NC in aqueous solution at $[OH^-] = 1.7 \times 10^{-4}$ mol/L, $[NC] = 3.5 \times 10^{-6}$ mol/L, $I = 1.8 \times 10^{-4}$ mol/L and 298 K with time interval of 2 min.

and $NaNO_3$ were prepared by dissolving the calculated amounts of AnalaR samples in redistilled water. 6-Nitro-2H-chromen-2-one and 6-nitro-2H-chromen-2-one-3-carboxylic acid were obtained from “Sigma”.

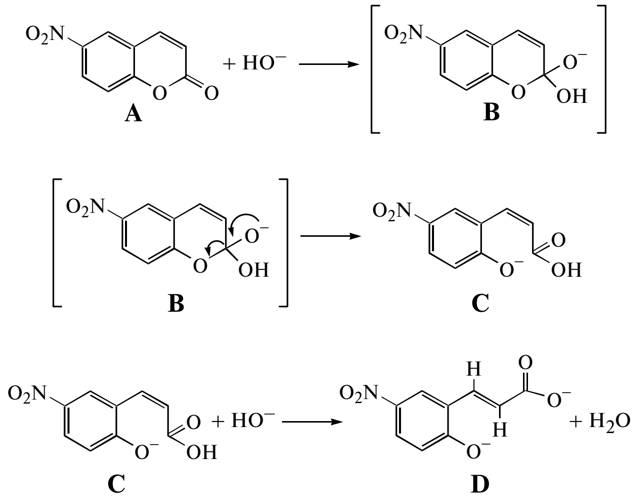
Kinetic Measurements

Kinetics of base hydrolysis were measured by following the time-dependence of absorbance using 10 mm silica cells in a thermostated cell compartment of a JASCO’s model V-530 spectrophotometer. The temperature (25°C ± 0.1°C and other temperatures) were adjusted by a CRIOTERM 190 ultrathermostate. The required volumes of the isothermal reacting stock solutions were syringed out and mixed in 10 mm cells in the thermostated cell jacket compartment. Chemical reactions were monitored in solutions held at constant ionic strength using appropriate amounts of sodium chloride for methanol and sodium nitrate for acetone over at least three half-live times. The reaction was carried out under pseudo first-order conditions in respect to a substrate by mixing multifold greater concentration of NaOH than that of the compound. Rate constants were calculated from the time-dependence of absorbance at 412 nm for NC and 407 nm for NCC. The substances were added to the cell according to the following order: (1) substrate, (2) methanol or acetone fraction, (3) salt, (4) water, and finally NaOH. The total volume of the cell is 3 mL. Before NaOH was added into the cell, the cell was allowed to take the required temperature of the jacket compartment of the spectrophotometer. The run started simultaneously after addition of NaOH. It was confirmed that there is no interference from other reagents at the selected wavelength absorption maxima for the investigated compounds.

RESULTS AND DISCUSSION

Kinetic Results and Reaction Mechanism

It can be inferred from repeated spectral scan (Fig. 1) that the initial action on NC and NCC 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 (2*E*)-3-(2-hydroxy-5-nitrophenyl) acrylic acid and (2-hydroxy-5-nitrobenzylidene) malonic acid [24, 25] as shown in Schemes 1 and 2.



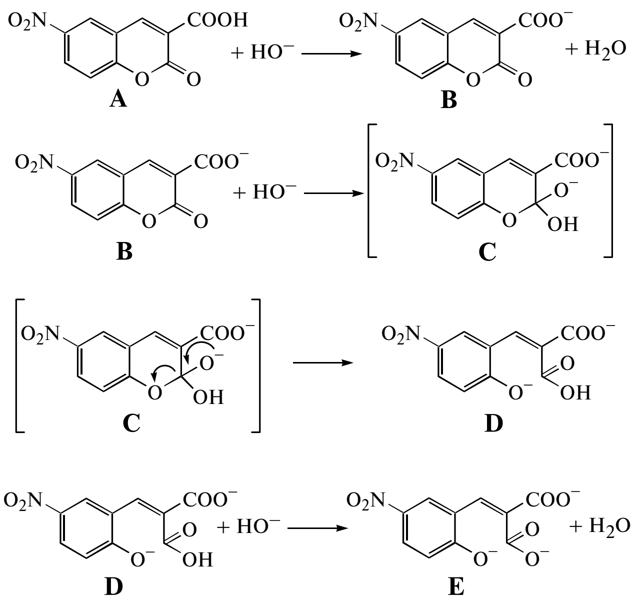
Scheme 1.

Table 1. The observed first-order rate constant k_{obs}, second-order rate constant k_2 and the activation energy barrier values $\delta_m G^{\#}$ for the base hydrolysis of NC at various ratios (v/v) of MeOH and acetone in the presence of different [OH$^-$] at 298 K and $I = 1.8 \times 10^{-4}$ mol/L

[OH]×10^5, mol/L	MeOH, vol %						Acetone, vol %				
	0	10	20	40	50	60	10	20	40	50	60
	k_{obs}, s^{-1}										
7	3.5	2.8	2.5	1.9	1.5	1.2	3.3	2.8	2.3	2.2	1.7
9	4.7	3.7	3.2	2.4	2.1	1.6	4.2	3.6	2.9	2.5	2.1
11	5.6	4.6	3.9	3.0	2.6	1.9	5.2	4.5	3.5	3.2	2.7
13	6.5	5.3	4.7	3.5	2.9	2.3	6.1	5.4	4.2	3.7	3.2
15	7.5	6.1	5.3	4.1	3.3	2.7	7.0	6.4	4.9	4.2	3.4
17	8.6	7.1	6.2	4.8	3.8	3.0	7.9	7.1	5.5	4.7	3.9
k_2, L mol^{-1}s^{-1}	5.0	4.2	3.6	2.8	2.3	1.8	4.5	4.2	3.2	2.6	2.2
$\delta_m\Delta G^{\#}$, kJ/mol	–	0.43	0.76	1.45	1.93	2.54	0.24	0.43	1.1	1.6	2.1

Table 2. The observed first-order rate constant k_{obs}, second-order rate constant k_2 and the activation energy barrier values $\delta_m G^{\#}$ for the base hydrolysis of NCC in various ratios (v/v) of MeOH and acetone in the presence of different [OH$^-$] at 298 K and $I = 1.8 \times 10^{-4}$ mol/L

[OH] × 10^5, mol/L	MeOH, vol %						Acetone, vol %				
	0	10	20	40	50	60	10	20	40	50	60
	k_{obs}, s^{-1}										
7	6.4	5.6	4.9	4.5	4.0	3.7	6.1	5.6	5.2	4.6	4.3
9	7.7	6.5	5.9	5.1	4.7	4.3	7.3	6.5	5.7	5.4	4.8
11	9.1	7.4	6.9	5.8	5.3	4.7	8.4	7.6	6.4	6.1	5.4
13	10.3	8.6	7.7	6.5	5.8	5.2	9.5	8.6	7.2	6.7	5.9
15	11.5	9.7	8.7	7.2	6.3	5.7	10.6	9.7	8.2	7.5	6.6
17	12.7	10.6	9.4	7.8	7.0	6.1	11.8	10.6	8.8	8.0	7.2
k_2, L mol^{-1}s^{-1}	6.4	5.1	4.5	3.4	2.9	2.4	5.7	5.0	3.9	3.5	3.0
$\delta_m\Delta G^{\#}$, kJ/mol	–	0.58	0.85	1.58	2.04	2.42	0.24	0.43	1.1	1.6	2.1



Scheme 2.

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

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

The slight enhancement of k_{obs} in acetone cosolvent compared with the corresponding values in meth-

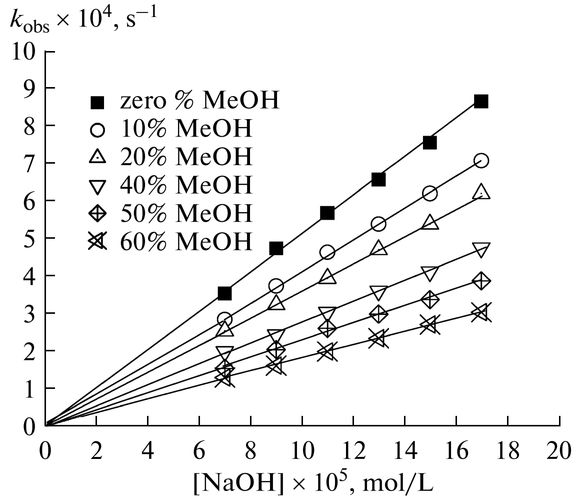


Fig. 2. Plots of the observed first-order rate constant of the reaction between NaOH and NC as a function of [NaOH] in H_2O—MeOH mixtures at [NC] = 3.5 × 10^{-6} mol/L, $I = 1.8 \times 10^{-4}$ mol/L at 298 K.

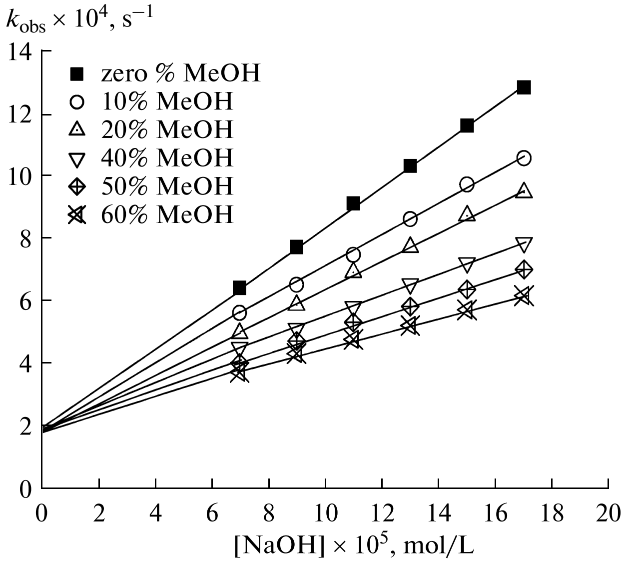


Fig. 3. Plots of the observed first-order rate constant of the reaction between NaOH and NCC as a function of [NaOH] in H_2O–MeOH mixtures at [NCC] = 3.5 × 10^{-6} mol/L, $I = 1.8 \times 10^{-4}$ mol/L at 298 K.

anol cosolvent would be ascribed to the destabilization of the hydrophilic OH^- ions in acetone more than in methanol.

The dependence of k_{obs} on the base concentration is linear for NC in methanol and acetone without significant intercept (Fig. 2). Hence, the hydrolysis follows the rate law (1)

$$k_{obs} = k_2[OH^-], \quad (1)$$

where k_2 is the second-order rate constant at $[OH^-] \gg$ [NC]. This equation indicates that the second-order process is dominant in the solvent mixtures.

For NCC, the dependence of k_{obs} on the base concentration is linear with an intercept (Fig. 3), hence the hydrolysis follow the rate law (2)

$$k_{obs} = k_1 + k_2[OH^-], \quad (2)$$

where k_1 is the rate constant for the NCC hydrolysis in the absence of alkali. The value of $k_1 = 2 \times 10^{-4}$ s^{-1} is independent of the presence of a cosolvent.

The change in the activation barrier $\delta_m\Delta G^{\#}$ is evaluated and reported in Tables 1 and 2 for both NC and NCC from the ratio of rate constants of the base hydrolysis in the binary solvent (k_{2s}) to the corresponding values in the aqueous solution (k_{2w}) according to the following relation [22]:

$$\delta_m\Delta G^* = -RT\ln\left(\frac{k_{2s}}{k_{2w}}\right). \quad (3)$$

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

Tables 1 and 2 show that the observed first-order rate constant values of base hydrolysis of NCC are slightly higher than the corresponding values for NC. This behavior could be attributed to the easier attack of OH^- on the carbonium center in NCC. The presence of the electron withdrawing carboxylic group increases the activity of pyrone ring towards the attack of OH^-.

Determination of Activation Parameters

The activation parameters were calculated by the least squares of Arrhenius and Eyring plots (Tables 3, 4). It is worth mentioning that the activation parameters are important for determination of the reaction rate and mechanism. The high negative values of entropy of activation (Table 3, 4) indicate the role of solvation in the mechanism [25, 26].

It is interesting that the different thermodynamic functions are consistent in their trends. As entropy of activation ($\Delta S^{\neq}$) increases, changing to less negative values, the rate constant decreases, and activation energy increases. This behavior can be ascribed to enhancing stability of activated complex intermediate. Also the relatively high free energy of transfer ($\Delta G^{\#}$) would indicate that the slow step is the ring opening, and many vibrational degrees of freedom have been transformed into translations. The positive free energy of transfer from water to methanol or acetone reported in Table 3 assumes that the transient species in hand are polar entities [24, 25, 27, 28].

The values of activation enthalpies ($\Delta H^{\neq}$) and activation entropies ($\Delta S^{\neq}$) are important in controlling the reaction rate. The values of $\Delta H^{\neq}$ are plotted versus the values of $\Delta S^{\neq}$ (Fig. 4) and straight line is obtained. The

Table 3. Second-order rate constant (k_2, L mol^{-1} s^{-1}) and the hydrolysis of NC and NCC at various ratios MeOH (vol %) activation parameters for the base at different temperatures at $I = 1.8 \times 10^{-4}$ mol/L

MeOH vol %	T, K							E_a	$\Delta H^{\neq}$	$\Delta G^{\neq}$	$\Delta S^{\neq}$	$A \times 10^9$
	283	288	293	298	303	308	313	kJ/mol	kJ/mol	kJ/mol	J mol^{-1}K^{-1}	mol^{-1} L s^{-1}
			NC k_2, L mol^{-1} s^{-1}									
0	1.9	2.5	3.8	5.0	7.8	10.1	15.8	34.1	31.6	63.3	−106.2	4.65
10	1.5	2.1	3.1	4.2	6.2	8.4	12.6	35.2	32.7	63.6	−103.7	4.17
20	1.3	1.8	2.7	3.6	5.5	7.5	11.2	36.2	33.9	64.1	−101.5	3.27
40	1.1	1.4	2.1	2. 8	4.3	5.5	8.5	37.9	36.2	65.1	−97.1	2.14
50	0.8	1.1	1.7	2.3	3.5	4.4	6.9	38.7	37.1	65.3	−94.8	1.97
60	0.6	0.9	1.3	1.8	2.7	3.5	5.6	39.8	38.2	65.7	−92.5	1.64
			NCC k_2, L mol^{-1} s^{-1}									
0	2.3	3.2	4.8	6.4	9.4	12.8	18.6	32.6	30.1	62.9	−110.2	5.00
10	1.9	2.5	3.7	5.1	7.3	10.1	14.4	33.8	31.2	63.3	−107.6	4.65
20	1.7	2.2	3.3	4.5	6.6	9.0	13.1	34.5	32.5	64.0	−106.5	4.25
40	1.3	1.7	2.5	3.2	5.0	6.8	9.9	36.5	34.9	65.2	−101.7	3.96
50	1.1	1.5	2.2	2.9	4.5	5.7	9.0	37.3	35.9	65.2	−98.7	3.00
60	1.0	1.2	2.0	2.4	3.9	4.8	7.7	38.2	36.7	65.5	−96.5	2.82

Table 4. Second-order rate constant values (k_2, L mol^{-1} s^{-1}) and the activation parameters for the base hydrolysis of NC and NCC in various ratios (v/v) of acetone at different temperatures at $I = 1.8 \times 10^{-4}$ mol/L

Aceton, %	T, K							E_a	$\Delta H^{\neq}$	$\Delta G^{\neq}$	$\Delta S^{\neq}$	$A \times 10^9$
	283	288	293	298	303	308	313	kJ/mol	kJ/mol	kJ/mol	J mol^{-1}K^{-1}	mol^{-1} L s^{-1}
			NC k_2, L mol^{-1} s^{-1}									
0	1.9	2.5	3.8	5.0	7.6	…	…	31.7	29.1	61.5	−108.6	4.65
10	1.7	2.3	3.5	4.5	7.1	9.1	…	32.5	30.1	61.7	−106.1	0.417
20	1.5	2.1	3.0	4.2	6.1	8.4	12.1	33.8	31.4	62.4	−103.9	0.291
40	1.2	1.8	2.5	3.2	4.9	6.3	9.6	35.7	33.4	63.2	−99.6	0.197
50	1.0	1.3	1.9	2.6	4.0	5.2	8.0	36.4	34.5	63.5	−97.4	0.164
60	0.8	1.1	1.6	2.2	3.3	4.3	6.5	37.9	35.7	64.0	−95.1	0.094
			NCC k_2, L mol^{-1} s^{-1}									
0	2.4	3.1	4.7	6.3	9.4	…	…	30.1	27.6	61.2	−112.6	13.0
10	2.1	2.8	4.2	5.7	8.5	11.5	…	31.2	28.7	61.5	−110.1	6.50
20	1.9	2.5	3.8	5.0	7.6	9.8	15.3	32.4	30.0	62.4	−108.9	4.50
40	1.5	2.0	3.0	3.9	6.0	7.9	12.1	34.5	32.1	62.8	−103.1	2.50
50	1.3	1.7	2.6	3.5	5.2	7.0	10.4	35.3	33.1	63.0	−100.2	2.16
60	1.1	1.5	2.3	3.0	4.5	6.0	9.0	36.2	34.2	63.7	−98.9	1.68

isokinetic temperature (β) was determined by least square of the slope and found to be 305 K, which is greater than the average experimental temperature (T_{exp} = 298 K) indicating that the reaction rate is enthalpy controlled [28, 29]. The straight line obtained, provides that the base hydrolysis of NC and

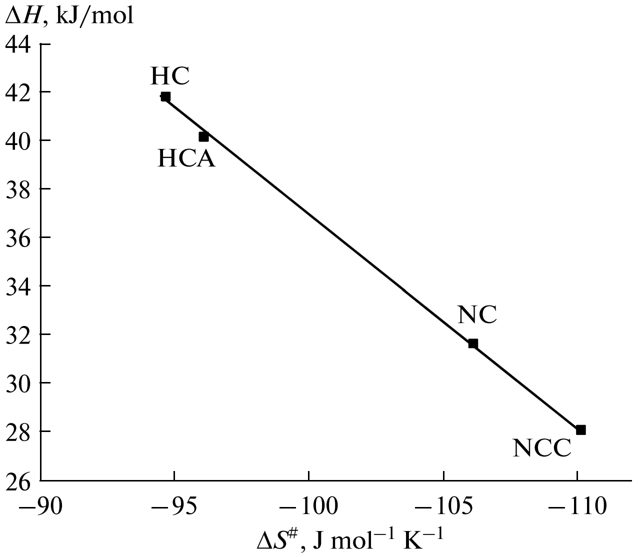


Fig. 4. Isokinetic plot of the reaction of OH^- ion with chromen-2-one derivatives in aqueous solution. 7-Hydroxy-2H-chromen-2-one (HC) and 7-hydroxy-2H-chromen-2-one-4-acetic acid (HCA) are taken from reference [25].

NCC follows the same mechanism via the same rate determining step either in aqueous solution or water—organic solvent mixtures.

Base hydrolysis of NC and NCC at the excess of alkali follows Eqs. (1) and (2), respectively. The decrease in the rate constants of NC and NCC, as the methanol or acetone content increases, is due to the destabilization of OH^- ion. The values of the rate constants (k_{obs} and k_2) decrease in the following order water > acetone > methanol with increasing methanol or acetone content.

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