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# Kinetics and a mechanistic investigation of one-pot multicomponent reaction for 2-amino-4H- chromene formation using glucose as a catalyst

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**Abstract:** Glucose is applied as an efficient catalyst for the three-component reaction consisting of aromatic aldehydes, malononitrile and resorcinol in a mixture of water and ethanol media as green solvents. The advantages of this method are excellent yeilds, inexpensive catalyst and more environmentally friendly. Mechanistic insight into the synthesis of 2-amino-4H-chromene included spectral kinetics approaches is revealed.

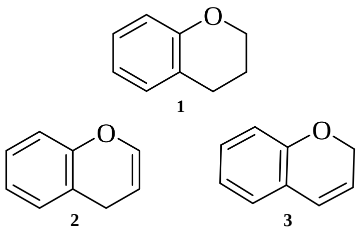
**Keywords:** Glucose, Catalyst, Kinetics, Mechanism, Chromene derivatives.

## Introduction

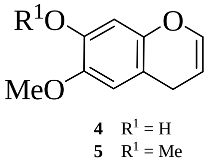
Chemistry as a central science is facing a steadily increasing demand for new chemical entities [1]. Multicomponent reactions (MCRs) are those reactions in which three or more reactants come together in a single reaction vessel to form a new product which contains portions of all the components [2,4]. MCRs tool allows compounds to be synthesized in a few steps and in a one-pot operation [5]. The usefulness of MCRs is correlated to several factors [6]: high atom economy, resource efficient (time & cost), operationally simple: in one-pot, energy saving, avoidance of expensive purification processes, more environmentally friendly [7-10].

The 1-benzopyrans include structural skeletons such as chromane **1**, 4H-chromene **2** and 2H-chromene **3** as depicted in Scheme **1**.

As a class of compounds the 4H-chromenes **2** (also known as 4H-1-benzopyrans) only a few examples of natural products containing this structure have been isolated [10]. An example of a naturally occurring 4H-chromene is 7-hydroxy-6-methoxy-4H-chromene **4** [12]. This natural product, which reportedly has interesting organoleptic properties, was isolated from the plant Wisteria sinensis along with the related compound, 6,7-dimethoxy-4H-chromene **5** (Scheme **2**) [11].



**Scheme 1:** The 1-benzopyrans include structural skeletons such as chromane **1**, 4H-chromene **2** and 2H-chromene **3**



**Scheme 2:** The structure of 6,7-dimethoxy-4H-chromene

The chromene skeletons have also elicited pharmaceutical interest as structural elements in drug-like compounds. In recent years, the ring-closing

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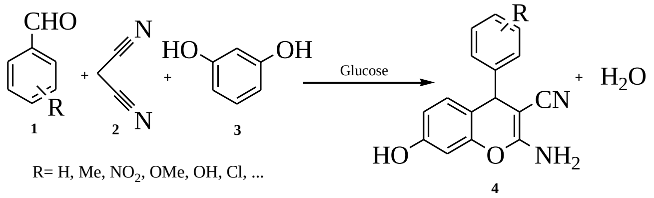
*Corresponding author. Tel: (+98) 541 2446565, Fax: (+98) 541 2446565, E-mail: smhabibi@chem.usb.ac.ir metathesis (RCM) reaction has been used to synthesize both the 2H- and 4H-chromene classes [13].

A simple and environmentally benign synthesis of 2-amino-4H-chromene is described using hydrotalcite as a solid base catalyst in aqueous medium. The catalysts were prepared by a co-precipitation method and well characterized by various techniques such as XRD, FT-IR, SEM and the basicity was found using the phenol adsorption method [14].

In this work we report an simple and efficient procedure for the synthesis of 2-amino-4H-chromene via a one-pot, three-component condensation reaction between, benzaldehyde **1**, malononitrile **2**, resorcinol **3**, in the presence of catalytic amounts of glucose 20 mol % in a mixture of aqueous ethanol and water 1:9 at room temperature (Scheme **3**). Although kinetics studies of these new compounds are important, but they have not been investigated completely yet. In recent years, we have attempted to expand experimental and theoretical studies on the kinetics and mechanisms of some organic reactions [15-27]. We now describe full kinetics and a mechanistic study of mentioned reaction in below.



**Scheme 3:** The reaction between benzaldehyde **1**, malononitrile **2** and resorcinol **3** in the presence of glucose.

## Results and discussion

*Optimize the synthesis conditions:*

For optimize the conditions, first the effect of amount of the catalyst was investigated on this reaction. Accordingly, with the mixture of benzaldehyde **1**, malononitrile **2** and resorcinol **3** in the presence of 10 mol% glucose, the product was obtained in 55% yield at 70 ˚C in water and ethanol for 12 hr. Increasing amount of catalyst from 20 mol% to 40 mol %, yields of 78%, 72% and 45% were obtained, respectively. Use of just 20 mol% glucose is sufficient to urge the reaction forward. Therefore, 20 mol% was chosen as a suitable amount of catalyst for this reaction (Table **1**).

Now we tested the effect of various solvents. It is remarkable to mention that the polar solvents such as water and ethanol or methanol, provide better yields than nonpolar ones, and a mixture of water and ethanol is the most effective solvent( Table **2**).

Then, the same reaction was carried out in a mixture of water and ethanol at different temperatures to estimate the effect of temperature to the reaction yield. It was observed that yield was the function of temperature. With increasing temperature, at 80 °C, the product was obtained in an excellent yield. At the higher temperature (90 °C) did not observe the increasing yield (Table **3**).

**Table 1:** Optimization of catalyst in synthesis of 2-amino-4H-chromene.

| Entry | Catalyst (mol%) | Time ( hr ) | Yield (%) |
|---|---|---|---|
| 1 | 10 | 12 | 55 |
| 2 | 20 | 12 | 78 |
| 3 | 30 | 9 | 72 |
| 4 | 40 | 10 | 45 |

**Table 2:** Optimization of solvent in synthesis of 2-amino-4H-chromene.

| Entry | Solvent | )°C(Temperature | Ratio | Yield (%) |
|---|---|---|---|---|
| 1 | $H_2O$ | 80 | - | 79 |
| 2 | $H_2O$/EtOH | 80 | 1:3 | 88 |
| 3 | $H_2O$/EtOH | 80 | 2:3 | 80 |
| 4 | $H_2O$/EtOH | 80 | 1:1 | 76 |
| 5 | EtOH | 80 | - | 70 |

**Table 3:** Optimization of temperature in synthesis of 2-amino-4H-chromene.

| **Entry** | **)°C(Temperature** | **Catalyst (mol%)** | **Time ( hr )** | **Yield (%)** |
|---|---|---|---|---|
| 1 | 50 | 20 | 24 | - |
| 2 | 60 | 20 | 24 | - |
| 3 | 70 | 20 | 12 | 78 |
| **4** | **80** | **20** | **8.5** | **88** |
| 5 | 90 | 20 | 9 | 67 |

*Data of some selected compounds:*

Compound a: mp: 230-231℃, yield: 88%, IR (KBr) (vmax, $cm^{-1}$): 3500 (OH),3330, 3215 ($NH_2$), 2185 (C≡N).

Compound g: mp: 202-203℃, yield: 94%, IR (KBr) (vmax, $cm^{-1}$): 300-3500 (OH,$NH_2$), 2180 (C≡N), 1000-1400(C-F).

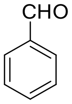
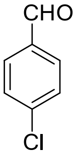
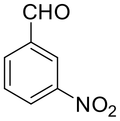
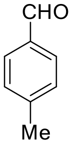
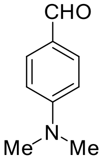
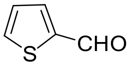
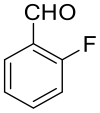
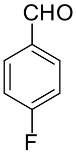
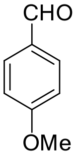
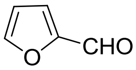
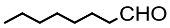
Compound c: mp: 168-170℃, yield: 90%, IR (KBr) (vmax, $cm^{-1}$): 3425, 3325($NH_2$), 3205 (OH), 2192 (C≡N), 1527, 1346($NO_2$).

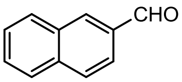
Compound b: mp: 159-161℃, yield: 96%, IR (KBr) (vmax, $cm^{-1}$): 3470 (OH), 3325, 3190 ($NH_2$), 2195 (C≡N), 600-800(CCl).

Compound e: mp: 192-193℃, yield: 68%,IR (KBr) (vmax, $cm^{-1}$):3300-3655(OH,$NH_2$), 2200 (C≡N).

Compound i: mp: 110-112℃, yield: 75%, IR (KBr) (vmax, $cm^{-1}$): 3430 (OH,$NH_2$), 2180 (C≡N), 1028,1248(C-OMe).

**Table 4:** Synthesis of 2-amino-4H-chromene derivatives using glucose.

| Entry | Derivatives | Product | Time ( hr ) | Yield(%) | MP(Obsd)(°C) | MP(Lit)(°C) |
|---|---|---|---|---|---|---|
| 1 |  | a | 8.5 | 88 | 230-231 | 232-234[28] |
| 2 |  | b | 5.5 | 96 | 159-161 | 161-162[28] |
| 3 |  | c | 6 | 90 | 168-170 | 170-171[28] |
| 4 |  | d | 8 | 76 | 181-182 | 184-186[28] |
| 5 |  | e | 9 | 68 | 192-193 | 189-191[29] |
| 6 |  | f | 9 | 86 | 188-190 | 190-191[29] |
| 7 |  | g | 6 | 94 | 202-203 | 200-202[28] |
| 8 |  | h | 4.5 | 96 | 188-190 | 187-189[28] |
| 9 |  | i | 8.5 | 75 | 110-112 | 112-114[29] |
| 10 |  | j | 9 | 87 | 191-192 | 189-191[29] |
| 11 |  | k | 6 | 89 | 124-125 | 124-126[30] |

| | | | | | | |
|---|---|---|---|---|---|---|
| 12 |  | l | 9.5 | 83 | 229-230 | 230-232[30] |

*kinetice studies:*

Full kinetics study of the reaction between benzaldehyde **1**, malononitrile **2**, and resorcinol **3**, in the presence of catalyst of glucose was performed, using the UV/Vis spectrophotometry technique. Firstly, it was necessary to find the suitable wavelength for the kinetic study of the reaction. For this reason in the first experiment, $10^{-3}$ M solution of each compound **1**, **2**, **3** and $2\times10^{-4}$ M solution of glucose were prepared in a mixture of water and ethanol 9:1 as solvent. The spectrum of each compound was recorded over the wavelength range 190 - 500 nm (Figures **1**, **2**, **3** and **4**).

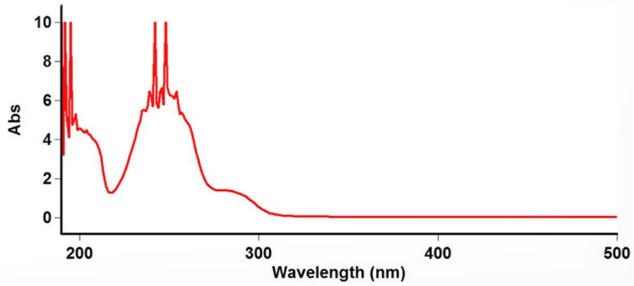


**Figure 1**: The UV/Vis spectrum of $10^{-3}$M benzaldehyde **1** in water and ethanol 9:1.

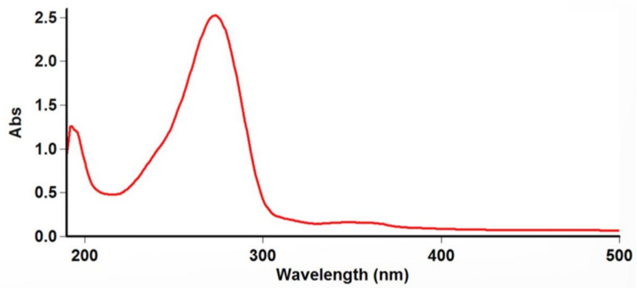


**Figure 2**: The UV/Vis spectrum of $10^{-3}$M malononitrile **2** in water and ethanol 9:1.

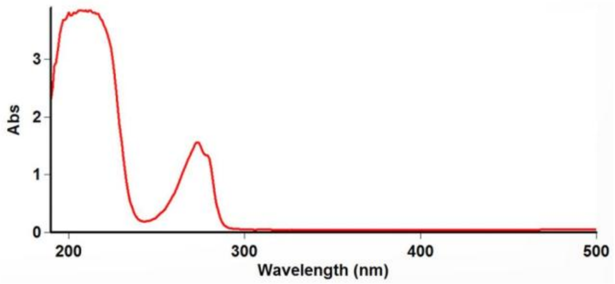


**Figure 3**: The UV/Vis spectrum of $10^{-3}$M resorcinol **3** in a mixture of water and ethanol (9:1).

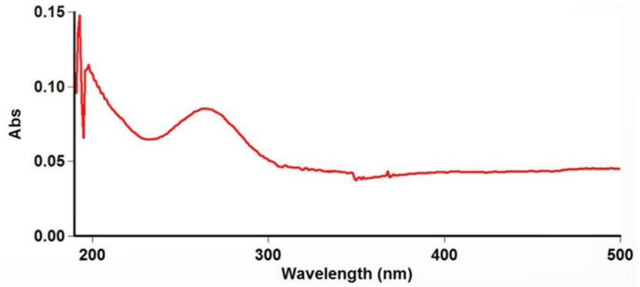


**Figure 4**: The UV/Vis spectrum of $10^{-3}$M glucose as a catalyst in a mixture of water and ethanol (9:1).

In the Second experiment, 0.8 mL aliquot of $8\times10^{-4}$ M solution catalyst and 0.8 mL aliquot of $4\times10^{-3}$ M solution of reactants **1** and **2** were pipetted into a quartz spectrophotometer cell then 0.8 mL aliquot of $4\times10^{-3}$ M solution of reactant **3** was added to the mixture according to stoichiometry of each reactant in the overall reaction. The reaction was monitored by recording scans of the entire spectra with 10 minute intervals during the whole reaction time at the ambient temperature (Figure **5**). In fact, the upward of direction of the arrow indicate that the progress of product versus time. From this, the proper wavelength was discovered to be 345, 340 and 335 nm (corresponding mainly to the product **4a**). At these wavelengths, compounds **1**, **2**, **3** and glucose have not absorbance value; it gave us the leisure to find the practical conditions for kinetics and a mechanistic investigation of the reaction. Thus, for performance this reaction was selected 340 nm (Because at this wavelength, there is enough absorbance and reactants also have no absorbance value). In all experiments, the UV/Vis spectrum of the product was measured over the concentration range ($10^{-4}$M $\leq$ M product $\leq 10^{-3}$M) to confirm a linear relationship between the absorbance and concentrations values.

In the third experiment under same concentration of each compound ($10^{-3}$M), absorbance curve was recorded versus time at 26 $^{o}$C temperature and wavelength 340 nm. This is shown in Figure **6**.

This curve, exactly fits to second order experimental curve (solid line), Figure **7**. In this case, overall order of rate low can be written as:

$$\alpha + \beta + \gamma = 2.$$

$$Rate = k_{Ove}[\mathbf{1}]^{\alpha}[\mathbf{2}]^{\gamma}[\mathbf{3}]^{\beta}[Cat] \qquad (1)$$

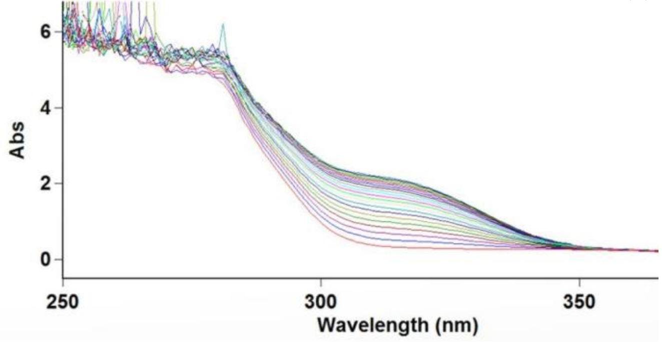


**Figure 5**: The UV/Vis spectrum of the reaction between benzaldehyde **1** **(**$10^{-3}$ M), malononitrile **2** ($10^{-3}$ M**)** and resorcinol **3** ($10^{-3}$ M**)** in the presence of glucose ($2\times10^{-4}$ M) as a catalyst in a mixture of water and ethanol 9:1 as reaction proceeds into a 10 mm light-path cell. Herein, the upward of direction of the arrow indicate that the progress of product versus times.

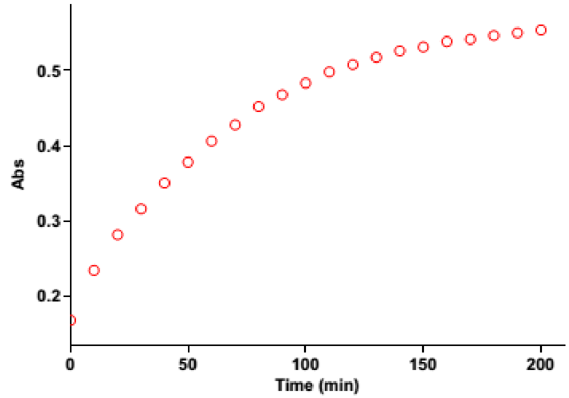


**Figure 6:** The experimental absorbance values for reaction compounds **1**, **2**, **3** and catalyst in a mixture of water and ethanol 9:1.

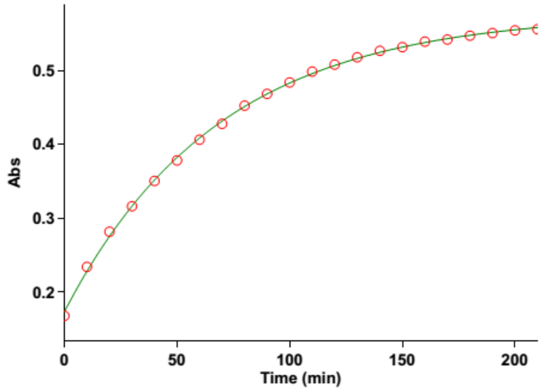


**Figure 7**: The experimental absorbance change (dotted line) along with the second order fit curve (solid line) against time for the reaction between compounds **1**, **2**, **3** and catalyst in a mixture of water and ethanol 9:1, at 340 nm, 26 °C.

### *Effect of concentration:*

For obtain a partial order of reaction respecting benzaldehyde **1** (nomination of α), pseudo-order conditions were performed for the reaction. Thus in the fourth experiment, we followed the reaction kinetics by UV/Vis absorbance versus time at wavelength 340 nm for the $10^{-3}$ M solution of each compound **2** and **3**, and $5\times10^{-4}$ M solution of compound **1**, at 26° C, together with $2\times10^{-4}$ M solution of glucose. For this case the rate law can be expressed:

$$Rate = k_{Ove}[\mathbf{1}]^{\alpha}[\mathbf{2}]^{\gamma}[\mathbf{3}]^{\beta}[Cat]$$
$$Rate = k_{Obs}[\mathbf{1}]^{\alpha} \qquad (2)$$
$$k_{Obs} = k_{Ove}[\mathbf{3}]^{\beta}[\mathbf{2}]^{\gamma}[Cat]$$

The infinity absorbance (A∞), is the absorbance at reaction completion, that can be obtained from Figure **8** at t = 200 min. With respect to this value, the zero, first or second curve fittings can be drawn automatically for the reaction using the software [31]. The original experimental absorbance curves versus times provided a pseudo-first order (Figure **8.A**). Herein, according to aquation 2, partial order with respect to compound **1** is 1(α=1). In the fifth experiment, we followed the reaction kinetics at 340 nm, for $5\times10^{-4}$ M each of compound **1** and **2** (nomination of γ), $10^{-3}$ M of the compound **3** at 26 °C. For this reaction the rate law can be written:

$$Rate = k_{Ove}[\mathbf{1}]^{\alpha}[\mathbf{2}]^{\gamma}[\mathbf{3}]^{\beta}[Cat]$$
$$Rate = k_{Obs}[\mathbf{1}]^{\alpha}[\mathbf{2}]^{\gamma} \qquad (3)$$
$$k_{Obs} = k_{Ove}[\mathbf{3}]^{\beta}[Cat]$$

The experimental absorbance curve against times along with a second-order fit was obtained (Figure **8.B)**. Hence, the total partial orders in relation to equation **3** is α+ γ =2. In previous experiment (fourth) α was equal to 1. As a result, it is reasonable to accept that the partial order with respect to reactant **2** is one (γ =1). Therefore, with respect to the third experimental result (α+β+ γ =2), fourth experiment (α=1) and the fifth experiment (γ =1) the partial order of β can be determined as zero (β=0). So the experimental rate law can be expressed:

$$Rate=K_{obs}[1][2] \qquad (3a)$$
$$Kobs= k_1[cat]$$

### *Effect of solvents and temperature:*

In order to investigate the effect of temperature and solvent on the reaction rate, Various experiments were repeated under different temperatures and solvents. So that, a mixture of water and ethanol 5:1 with lower dielectric constant has been used in the experiment. This solvent was studied at all temperatures (Table **5**).

We did not use from a mixture of water and ethanol 3:1, because the rate of reaction was very low in this solvent.

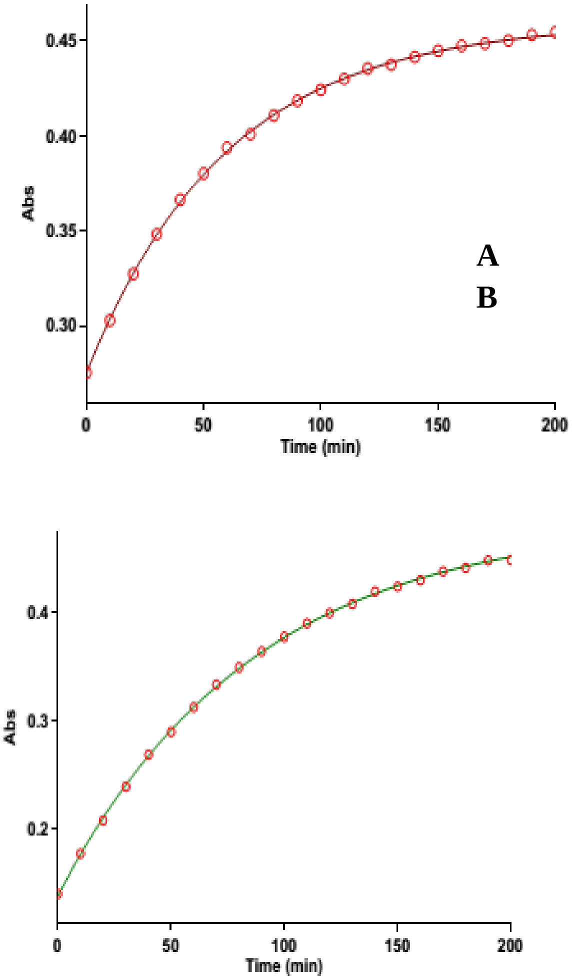


**Figure 8**: **A.** First pseudo order fit curve (solid line) along with the original experimental curve (dotted line) in relation to benzaldehyde **1**, for the reaction between **1** ($5\times10^{-4}$ M), **2** ($10^{-3}$M), **3** ($10^{-3}$ M) and sucrose ($2\times10^{-4}$ M) which was processed in a mixture of water and ethanol (3:1) at 26 $^{o}$C and 340 nm. **B).** Second pseudo order fit curve (solid line) along with the original experimental curve (dotted line), for the reaction between **1** ($5\times10^{-4}$ M), **2** ($5\times10^{-4}$ M), **3** ($10^{-3}$ M) and sucrose ($2\times10^{-4}$ M) which was processed in a mixture of water and ethanol (3:1) at 26 $^{o}$C and 340 nm.

With respect to this Table **5**, the rate of reaction increases at higher temperatures in each solvent. In addition, it seems that rate of reaction increase in solvent with higher dielectric constant, and this can be related to the stabilization differences of the reactants and the activated complex (charged species) in the transition state (TS1). Thus, the second-order rate constant (Ln $K_1$) of the reaction was inversely proportional to the temperature (Arrhenius equation), for the reaction between **1**, **2**, **3** and glucose in a mixture of water and ethanol 9:1, the activation energy was obtained from the slope of Figure **10**.

*Effect of catalyst:*

In the presence of xylose as a second catalyst in a mixture of water and ethanol 9:1, rate of reaction was increased in comparison with the glucose. It means that xylose has less interaction with polar solvent than glucose (Table **6**), and can be free more for performance of catalytic role.

Utilizing the above results, the simplified scheme of the proposed reaction mechanism [32-34] as a possible interpretation is shown in scheme **4**.

To examine which steps of the proposed mechanism is a rate-determining step (RDS), the rate law was written for the final step of reaction:

$$Rate=K_4[I_3] \qquad [4]$$

The steady state approximation was useable for obtaining the concentration of $[I_3]$:

$$\frac{d[I_3]}{dt} = k_3[I_2][cat^-] - k_4[I_3] = o$$

$$[I_3] = \frac{k_3[I_2][cat^-]}{k_4}$$

The $[I_3]$ of equation 5 can be replaced in the equation 4 so the rate equation becomes:

$$Rate=K_3[I_2][cat^-] \qquad [6]$$

Now, for obtaining the concentration of intermediate $[I_2]$ by the steady state assumption can be written:

$$\frac{d[I_2]}{dt} = k_2[\mathbf{3}][I_1][Cat] - k_3[I_2][cat^-] = o$$

$$[I_2] = \frac{k_2[3][I_1]}{k_3[cat^-]}[Cat] \qquad (7)$$

With the replacement of the equation 7 in equation 6, the equation 8 is obtained:

$$Rate = k_2[3][I_1][Cat] \qquad (8)$$

And the value of $[I_1]$ can write as below:

$$\frac{d[I_1]}{dt} = k_1[\mathbf{1}][\mathbf{2}][cat] - k_2[\mathbf{3}][I_1][Cat] - k_{-1}[I_1][H_2O][Cat] = 0$$

$$[I_1] = \frac{k_1[1][2][Cat]}{(k_2[3]+k_{-1}[H_2O])[Cat]} \qquad (9)$$

After the replacement of the equation 9 in 8, the equation 10 is extracted:

$$Rate = \frac{k_1k_2[1][2][3][Cat]}{k_2[3]+k_{-1}[H_2O]} \qquad (10)$$

Equation 10 is not compatible with the experimental data, therefore if $k_2[3] >> k_{-1}[H_2O]$, the following equation for return step (first step) can be obtained [15]:

$$Rate = \frac{k_1k_2[1][2][3][Cat]}{k_2[3]} \qquad (11)$$

This equation is not compatible with the experimental data too. Thus with considering went step, in the first step, we can express:

$$Rate= K_1[1][2][cat] \qquad [12]$$

$$Kobs=K_1[cat] \qquad [13]$$

$$Rate= k_{obs}[1][2] \qquad [14]$$

**Table 5**: The rate of constant $k_1\ (M^{-2}min^{-1})$ for the reaction between **1** ($10^{-3}$M), **2** ($10^{-3}$M) and **3** ($10^{-3}$M) in the presence of glucose ($2\times10^{-4}$ M) in different solvent media and temperatures.

| Solvent: mix of water/ethanol (5:1) (70.72)[a] | | | | |
|---|---|---|---|---|
| T | T= 16° C +x | T= 21° C +x | T= 26°C +x | T= 31° C +x |
| $k_{Obs}$ | 0.35<br>(0.009)[b] | 1.92<br>(0.008) | 7.26<br>(0.021) | 10.9<br>(0.034) |
| $k_1$ [c] | $1.75\times10^{-3}$ | $9.60\times10^{-3}$ | $3.63\times10^{-3}$ | $5.45\times10^{-3}$ |
| Ln $k_1$ | 7.47 | 9.17 | 10.50 | 10.90 |
| Ln ($k_1$/T) | 1.80 | 3.48 | 4.80 | 5.19 |
| **Solvent: mix of water/ethanol (9:1) (74.3)[a]** | | | | |
| T | T= 16° C +x | T= 21° C +x | T= 26° C +x | T= 31° C +x |
| $k_{Obs}$ | 1.49<br>(0.006)[b] | 3.18<br>(0.0033) | 8.53<br>(0.016) | 11.64<br>(0.027) |
| $k_1$ [c] | $7.45\times10^{-3}$ | $1.59\times10^{-3}$ | $42.65\times10^{-3}$ | $5.82\times10^{-3}$ |
| Ln $k_1$ | 8.91 | 9.67 | 10.66 | 10.97 |
| Ln ($k_1$/T) | 3.25 | 3.99 | 4.96 | 5.25 |

a: dielectric constant (D)
b: standard deviation (SD).
c: $k_1= k_{Obs}$ /[Cat]
x: 273.15

**Table 6**: Effect of various catalysts on rate of reaction between **1**, **2** and **3** compounds in a mixture of water and ethanol 9:1.

| Catalyst | T= 26° C | |
|---|---|---|
| | $k_{Obs}$ | $k_1$ [a] |
| Glucose ($2\times10^{-4}$ M) | 8.53<br>(0.016)[b] | $4.26\times10^{-3}$ |
| Xylose ($2\times10^{-4}$ M) | 10.22<br>(0.0045)[b] | $5.11\times10^{-3}$ |

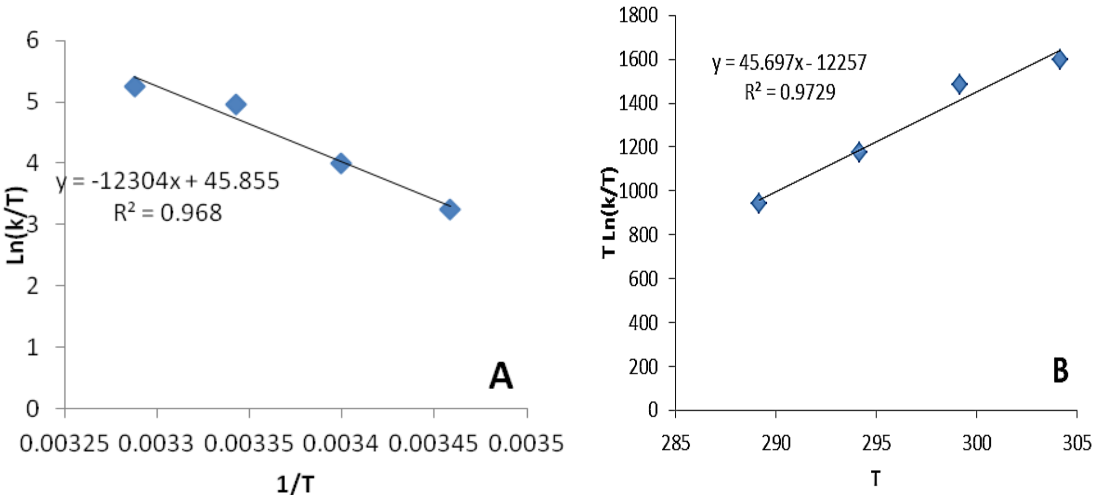
a: $k_1= k_{Obs}$ /[Cat]
b: standard deviation (SD).

The equation 14 that appeared from steady state assumption and the mechanism of the reaction (Scheme **4**) is agreement with the experimental equation (3a) which previously indicated that the overall order of the reaction is two. Also equation 14 clears that order of reaction for each compound (**1**, **2** and **3**) is 1, 1 and zero, respectively. The presence of $k_1$ in the rate low (equation 14) obvious that first step ($k_1$) is a rate determining step and $k_2$ should be a fast step. In this case, the transition state (Scheme **4**, step 1) transports a dispersed charge, hence, different solvents (Next section) with higher dielectric constant speed up reaction rate by stabilizing the species at the transition state more than reactants, and therefore $E_a$ would be lower (Table **5**). The activation parameters which involve $\Delta H^{\ne}$, $\Delta S^{\ne}$ and $\Delta G^{\ne}$, can be calculated for the first step (rate determining step, $K_1$), as an elementary reaction, on the basis of Eyring equation (15), Figure **9-A**, and also a different linearized form of Eyring equation (16), Figure **9-B**, [35]. Statistical analysis of the Eyring equation confirms the standard errors of $\Delta H^{\ne}$ and $\Delta S^{\ne}$ correlate:

$$\sigma(\Delta S^{\ne}) = 1/T_{av}\, \sigma(\Delta H^{\ne}) \qquad (17)$$

$T_{av} = the\ center\ of\ the\ temperature\ range\ used$

It follows that in solution phase studies [35, 36] $\sigma(\Delta S^{\ne}) \approx\ 0.003\ K^{-1} \times\ \sigma(\Delta H^{\ne})$. The standard errors for activation parameters have been calculated according to above instructions [35-37] in Figure **9 (A-B).**



$$ln(\frac{k_1}{T}) = (ln\frac{k_B}{h} + \frac{\Delta S^{\neq}}{R}) - \frac{\Delta H^{\neq}}{RT} \qquad (15)$$

$$T\ln(\frac{k_1}{T}) = T(\ln\frac{k_B}{h} + \frac{\Delta S^{\neq}}{R}) - \frac{\Delta H^{\neq}}{R} \qquad (16)$$

$$\Delta H^{\neq} = 102 \pm 0.67 \frac{kJ}{mol} \qquad \Delta H^{\neq} = 101 \pm 0.67 \frac{kJ}{mol}$$

$$\Delta S^{\neq} = 183 \pm 1.22 \frac{J}{mol\ K} \qquad \Delta S^{\neq} = 182 \pm 1.22 \frac{J}{mol\ K}$$

**Figure 9 (A,B):** Eyring plots according to equations (15 and 16), for the reaction between 1, 2, 3 and glucose in a mixture of water and ethanol (9:1).

With consideration to the vales of $\Delta H^{\neq}$, $\Delta S^{\neq}$ and equation of $\Delta G^{\neq} = \Delta H^{\neq} - T\Delta S^{\neq}$, ($\Delta G^{\neq} = 46.55\ \mathrm{kJ}\ mol^{-1}$) is reported for the reactions between **1**, **2** and **3** in a mixture of water and ethanol 9:1 at 340 nm and 299.15 K (26 $^{o}$C).

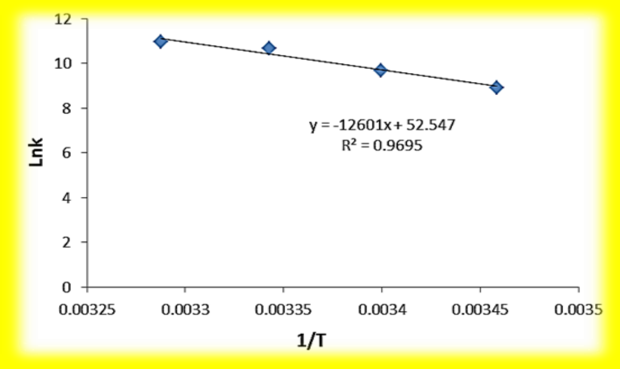


**Figure 10**: The Dependence of the second order rate constant (Ln $k_1$) on reciprocal temperature for the reaction between **1**, **2, 3** and glucose in a mixture of water and ethanol 9:1 in 340 nm.

## Conclusion

We report a novel three-component one-pot synthesis of 2- amino -4H-chromene in the presence of glucose and xylose as effective catalysts under mentioned conditions. The catalyst is environmental friendly, inexpensive, clean, safe, nontoxic and easily obtained.

The results of the kinetic investigations on these reactions can be explained as follow:

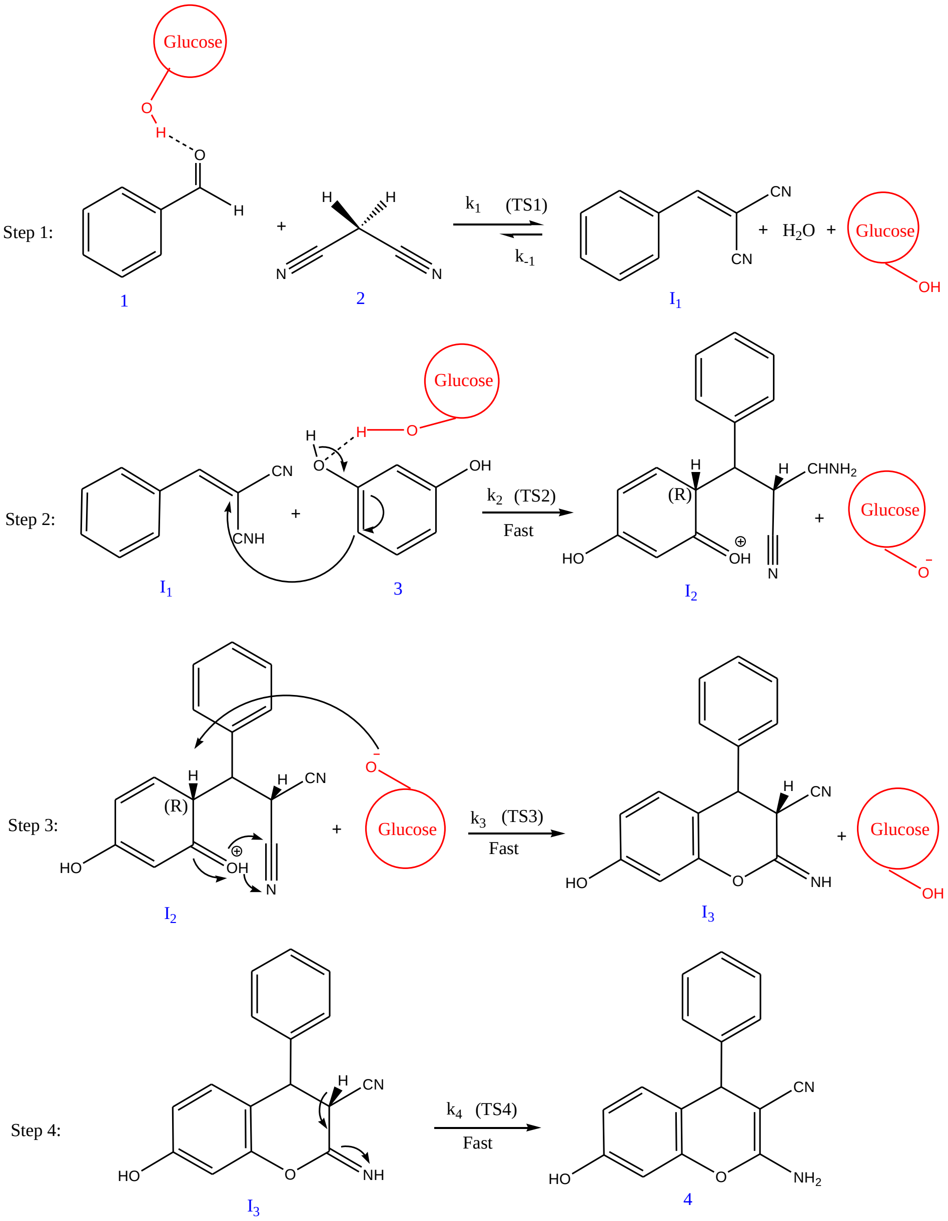
1. The overall order of the reaction obtained second-order and the reaction order of each reactant benzaldehyde **1**, malononitrile **2** and resorcinol **3** is one, one and zero, respectively.
2. Using the solvents with higher dielectric constants increased the rate of all reactions and this can be related to the stabilization differences of the reactants and the activated complex in the transition state.
3. The first step of suggested mechanism was nominated as a rate-determining step ($k_1$) with using the experimental results and this was shown to be true by the steady-state assumption.
4. The activation energy ($105 \pm 0.67\ kJ.mol^{-1}$) and activation parameters of the reaction ($\Delta H^{\neq}$, $\Delta S^{\neq}$ and $\Delta G^{\neq}$ ) have been calculated, with Arrhenius equation and both Eyring equations.
5. The rate of reaction changes in the presence of different catalyst, and this can be relevant to its interaction differences with polar solvent.

## Experimental

In order to optimize the reaction conditions, the synthesis of reaction between, benzaldehyde **1**, malononitrile **2** and resorcinol **3** was carried out using amounts of glucose 20 mol % under different conditions.

*Chemicals and Apparatus used:*

Benzaldehyde **1**, malononitrile **2**, resorcinol **3** and glucose catalyst were obtained from Merck (Darmstadt, Germany), and Fluka (Buchs, Switzerland), and used without purification. Pure solvent of ethanol was also obtained from Merck (Darmstadt, Germany). A UV/Vis spectrophotometer apparatus model Cary Bio-300 with a 10 mm light-path quartz spectrophotometer cell was employed throughout the current work.



**Scheme 4.** The proposed reaction mechanism between benzaldehyde **1**, malononitrile **2**, resorcinol **3**, in the presence of glucose as a catalyst.

*General procedure for the synthesis of 2-amino-4H-chromene:*

A mixture of an aromatic aldehyde **1** ( 1 mmol ), malononitrile **2** ( 1 mmol ), resorcinol **3** ( 1 mmol ) and glucose ( 20 mol% ) in a mixture of water and ethanol ( 1:3, 4 mL ) was heated for an appropriate length of time. During the procedure, the reaction was monitored by TLC. After completion of the reaction, the mixture was filtrate and the precipitated solid re-crystallised from ethanol 95% to give compound **4** in high yields.

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