

Research Article

Kinetic and Mechanistic Investigation of Pyrano[2,3-d]pyrimidine Formation in the Presence of Catalyst under Novel One-Pot Three-Component Reaction

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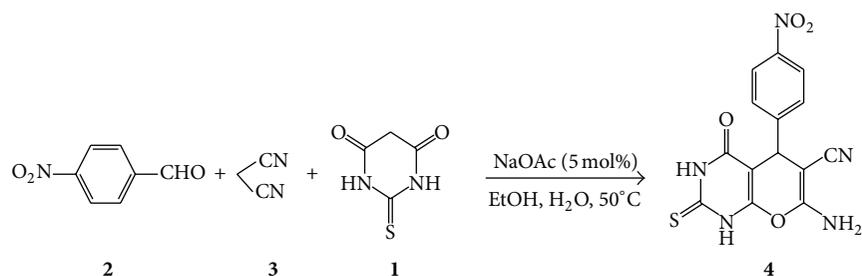
Sodium acetate was applied as an efficient catalyst for the one-pot, three-component condensation reactions consisting of 4-nitrobenzaldehyde **2**, malononitrile **3**, and thiobarbituric acid **1**. Use of nontoxic reaction components, short reaction times, environmental, easy work-up, and high yields are some remarkable advantages of this method. Kinetics and mechanism of the reaction were spectrally studied and the second order rate constant ($k_{\text{ovr}} = k_1$) was automatically calculated by the standard equations contained within the program. The second order rate constant [$\ln(k_{\text{ovr}} = k_1)$, $\ln(k_{\text{ovr}} = k_1)/T$] that depended on reciprocal temperature was in good agreement with the Arrhenius and Eyring equations, respectively. This data provided the suitable plots for calculating the activation energy and parameters (E_a , ΔG^\ddagger , ΔS^\ddagger , and ΔH^\ddagger) of the reaction. Furthermore, from studying the effects of solvent, concentration, and catalyst on the reaction rate, useful information was obtained regarding the mechanism. The results showed that the first step of the reaction mechanism is a rate determining step (RDS). The proposed mechanism was confirmed in accordance with the experimental data and also the steady state approximation.

1. Introduction

Multicomponent reactions (MCRs) involving pot, atom, and step-economy have received substantial consideration from the organic community due to their advantages over conventional multistep synthesis [1–6]. This kind of reactions have some advantages over conventional linear syntheses, including shorter reaction times, lower costs, high atom-economy, energy saving, the possibility for combinatorial surveying of structural variations, and environmental friendliness.

The benzopyrans and their derivatives, in particular, have shown several biological and pharmacological properties, such as spasmolytic, diuretic, antianaphylactin, antisterility, and anticancer agents [7–10]. The polyfunctionalized benzopyrans were used as cosmetics, pigments, and biodegradable agrochemicals [11, 12]. Due to their applications, the syntheses of heterocyclic derivatives of these ring systems have great importance in medicinal chemistry and organic

synthesis. Strategies for the synthesis of these compounds have varied from one-pot to multistep approaches [13]. In recent years, the syntheses of pyrano[2,3-d]pyrimidine were reported using a plethora of reagents in the presence of catalyst, such as *L*-proline [14], microwave irradiation [15], $\text{H}_6\text{P}_2\text{W}_{18}\text{O}_{62}\cdot 18\text{H}_2\text{O}$ [16], 4-(dimethylamino) pyridine (DMAP) [17], and diammonium hydrogen phosphate [18]. However, some of these methods have drawbacks, such as long reaction times, unsatisfactory yields. Furthermore, some of the used catalysts are either expensive or difficult to prepare. Owing to the importance of pyrano[2,3-d]pyrimidine from a pharmaceutical and biological point of view, there is still a need to develop an efficient, mild reaction benign protocol for the synthesis of pyrano[2,3-d]pyrimidine. As a part of our current studies on development of efficient multicomponent reactions for the preparation of interesting bioactive molecules [19–22], especially the synthesis of pyrano[2,3-d]pyrimidine [23], we report here, a simple



SCHEME 1

and efficient procedure for the synthesis of pyrano[2,3-d]pyrimidine via a one-pot, three-component condensation reaction between 4-nitrobenzaldehyde **2**, malononitrile **3**, and thiobarbituric acid **1** in the presence of catalytic amounts of NaOAc 5 mol% in a mixture of aqueous ethanol at 50°C (Scheme 1).

The kinetics and mechanism of the mentioned reaction were monitored using the UV-vis spectrophotometry apparatus. Kinetics and mechanism of numerous reactions have been previously studied using the UV-vis technique [24–28]. In recent years, we have endeavored to expand the synthesis of phosphorous ylides along with developing experimental and theoretical studies on the kinetics and mechanisms of these reactions [29–36]. In these studies, reactions occurred by at least three steps. The first step of the proposed mechanism was recognized as a rate-determining step and this was confirmed based upon the steady-state approximation. Moreover, the overall reaction order followed second-order kinetics. The rate of all reactions was increased in solvents with upper dielectric constant value that could be related to the differences in stabilization of the reactants and the zwitterionic intermediate by the solvents [29–36]. In present work, we describe kinetic results together with detailed mechanistic studies for the one-pot, three-component condensation reactions consisting of 4-nitrobenzaldehyde **2**, malononitrile **3**, and thiobarbituric acid **1** in the presence of sodium acetate as a catalyst in methanol and environmental friendly solvents (mixture of ethanol and H₂O 50/50) based on a global kinetic analysis methodology using the UV-vis spectrophotometry apparatus.

2. Experimental

In order to optimize the reaction conditions, the synthesis of reaction between 4-nitrobenzaldehyde **2** (1 m mol), malononitrile **3** (1 m mol), and thiobarbituric acid **1** (1 m mol) was carried out using different quantities of sodium acetate under different conditions. It was found that the best results were obtained under condition with 5 mol% sodium acetate under H₂O : EtOH (4 : 1, 5 mL) at 50°C (Table 1).

2.1. Chemicals and Apparatus. The 4-nitrobenzaldehyde **2**, malononitrile **3**, thiobarbituric acid **1**, and sodium acetate were obtained from Merck (Darmstadt, Germany), Acros (Geel, Belgium), and Fluka (Buchs, Switzerland) and used

without further purification. All extra pure solvents including the methanol and ethanol were also obtained from Merck (Darmstadt, Germany). A Cary UV/Vis spectrophotometer model Bio-300 with a 10 mm light-path quartz spectrophotometer cell was employed throughout the current work.

2.2. General Procedure for the Synthesis of a Pyrano[2,3-d]pyrimidine. A mixture of 4-nitrobenzaldehyde **2** (1 m mol), malononitrile **3** (1 m mol), thiobarbituric acid **1** (1 m mol), and sodium acetate (5 mol%) in water and ethanol (4 : 1, 5 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 filtered and the precipitated solid re-crystallized from ethanol 98% to give compound **4** in high yield. Spectroscopic data of product **4** is given below: 7-Amino-6-cyano-5-(4-nitrophenyl)-4-oxo-2-thioxo-5H-pyrano [2, 3-d]pyrimidinone. Yellow solid, Yield: 98% = 0.337 g; IR (KBr) ν : 3369 (NH₂), 3191 (N–H), 2201 (C≡N), 1684 (C=O), 1572 (C=S), 1278 (C–O) cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ : 4.48 (1H, s, CH), 7.30 (2H, s, NH₂), 7.55–8.15 (4H, m, H–Ar), 12.46 (1H, brs, NH), 13.50 (1H, brs, NH) ppm.

3. Kinetics Studies

3.1. Method. Kinetics measurements of the reaction between 4-nitrobenzaldehyde **2**, malononitrile **3**, and thiobarbituric acid **1** in the presence of sodium acetate as a catalyst were 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*, 10⁻² M solution of each compound **1**, **2**, **3** and 10⁻² M solution of sodium acetate were prepared in methanol as solvent. The relevant spectrum of each compound was recorded over the wavelength range 200–600 nm. In the *second experiment*, the reaction mixture was started into a 10 mm black quartz spectrophotometer cell along with a 10⁻² M solution of each compound (**1**, **2** and **3**) and 10⁻² M sodium acetate according to stoichiometry of each compound in the overall reaction. The reaction was monitored by conducting scans of the entire spectrum with 10-second intervals during the whole reaction time at ambient temperature. The typical UV spectra are shown in Figure 1. Herein, the upward direction of the arrow indicates the progress of product versus time. From this, the appropriate

TABLE 1

Entry	Substrate	1,3-Dicarbonyl	Product	Time (min)	Yield (%) ^a	M.P observed (°C)	M.P reported (°C)
1	4-NO ₂ C ₆ H ₄	3	4	14	98	234-236	235-236 [5]

^aYields refer to the pure isolated products.

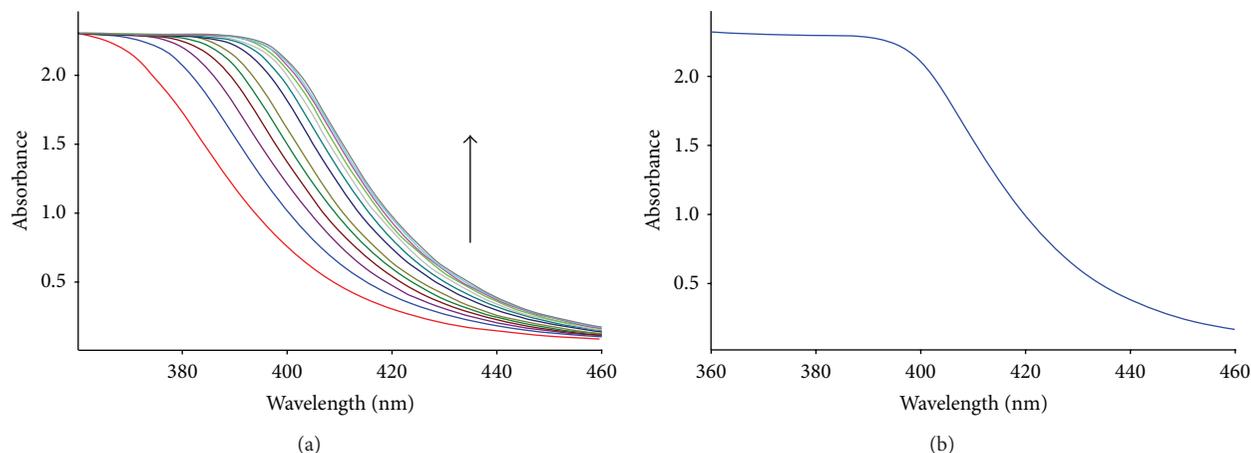


FIGURE 1: (a) The UV-vis spectra of the reaction between 4-nitrobenzaldehyde **2** (10^{-2} M), malononitrile **3** (10^{-2} M), and thiobarbituric acid **1** (10^{-2} M) in the presence of sodium acetate as a catalyst in methanol as reaction proceeds into a 10 mm light-path cell. Herein, the upward direction of the arrow indicates the progress of product versus times. (b) The UV spectrum of the final product.

wavelength was discovered to be 390, 415, 420, 430, and 435 nm. Since at these wavelengths, compounds **1**, **2**, **3**, and sodium acetate have relatively no absorbance value, it gave us the chance to find the practical conditions that allow kinetics and a mechanistic investigation of the reaction. Herein, in all the experiments, the UV-vis spectrum of the compound product was measured over the concentration range (10^{-3} M \leq M product $\leq 10^{-2}$ M) to confirm a linear relationship between the absorbance and concentrations values.

In the *third experiment* under the same concentration of each compound (10^{-2} M), experimental absorbance curve was recorded versus time at 25°C temperature and wavelength 430 nm. Figure 2 shows that the experimental curve (dotted line) is fitted to second order curve (solid line). It is obvious that the reaction is second order. Then, the rate constant ($12.64 \text{ min}^{-1} \cdot \text{M}^{-1}$) of the reaction was automatically calculated by the software associated [38] within the UV-vis spectrophotometer.

In this case, overall order of rate law can be written as $\alpha + \beta + \gamma = 2$. Consider the following:

$$\text{Rate} = k_{\text{ovr}}[\mathbf{3}]^{\alpha}[\mathbf{2}]^{\beta}[\mathbf{1}]^{\gamma}[\text{Cat}]. \quad (1)$$

4. Result and Discussion

4.1. Effects of Concentration. Partial order of the reactants is obtained under pseudoorder. In the *fourth experiment*, we followed the reaction kinetics by plotting the UV-vis absorbance versus time at wavelength 420 nm for the 10^{-2} M, 10^{-2} M, and 10^{-3} M solution of each compound (**1**, **2**, and **3**),

respectively, at 25.0°C along with 10^{-2} M solution of sodium acetate. For this case, the rate law can be expressed as follows:

$$\begin{aligned} \text{Rate} &= k_{\text{ovr}}[\mathbf{3}]^{\alpha}[\mathbf{2}]^{\beta}[\mathbf{1}]^{\gamma}[\text{Cat}] \\ \text{Rate} &= k_{\text{obs}}[\mathbf{3}]^{\alpha} \end{aligned} \quad (2)$$

$$k_{\text{obs}} = k_{\text{ove}}[\mathbf{2}]^{\beta}[\mathbf{1}]^{\gamma}[\text{Cat}].$$

The infinity absorbance (A_{∞}) is the absorbance at reaction completion and is obtainable from Figure 3 at $t = 85$ min. With respect to this value, the zero, first, or second curve fittings can be drawn automatically for the reaction using the software [38] associated with the UV/Vis instrument. The original experimental absorbance against time data made a pseudo-first-order available fit curve at 420 nm, which exactly fits the experimental curve (dotted line) and is displayed in Figure 3. Herein, observation rate constant (k_{obs}) was automatically calculated for (2) by the software associated within the UV/Vis instrument. It is obvious that the reaction is of the first order type with respect to malononitrile **3**, $\alpha = 1$.

Also to gain a partial order of the reaction with respect to 4-nitrobenzaldehyde **2**, (10^{-3} M), under pseudoorder condition, compounds **3** and **1** were used in excess (10^{-2} M). *Fifth experiment* was employed as the previous experiment (fourth). The rate law can be written as follows:

$$\begin{aligned} \text{Rate} &= k_{\text{ovr}}[\mathbf{3}]^{\alpha}[\mathbf{2}]^{\beta}[\mathbf{1}]^{\gamma}[\text{Cat}] \\ \text{Rate} &= k_{\text{obs}}[\mathbf{2}]^{\beta} \end{aligned} \quad (3)$$

$$k_{\text{obs}} = k_{\text{ovr}}[\mathbf{3}]^{\alpha}[\mathbf{1}]^{\gamma}[\text{Cat}].$$

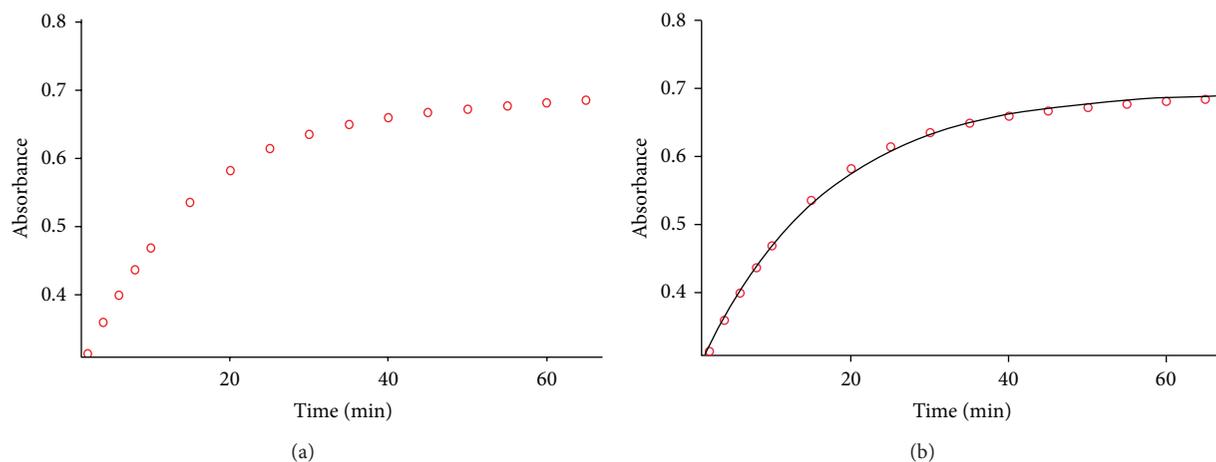


FIGURE 2: (a) The experimental absorbance values for reaction compounds **1**, **2**, **3**, and catalyst in a mixture of ethanol and water. (b) The experimental absorbance change (dotted line) along with the second order fit curve (solid line) against time for the reaction between 4-thiobarbituric acid **1** (10^{-2} M), malononitrile **3** (10^{-2} M), 4-nitrobenzaldehyde **2** (10^{-2} M), and (10^{-2} M) catalyst, at 430 nm, 25.0°C, and in methanol.

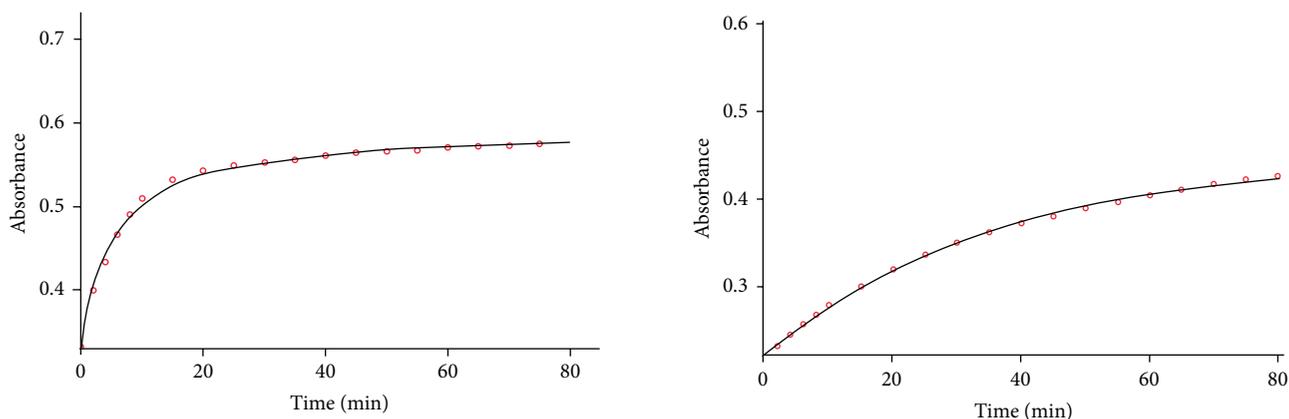


FIGURE 3: First pseudoorder fit curve (solid line) along with the original experimental curve (dotted line) in relation to malononitrile **3**, for the reaction between **1** (10^{-2} M), **2** (10^{-2} M), and **3** (10^{-3} M) which was processed in methanol at 25°C and 420 nm.

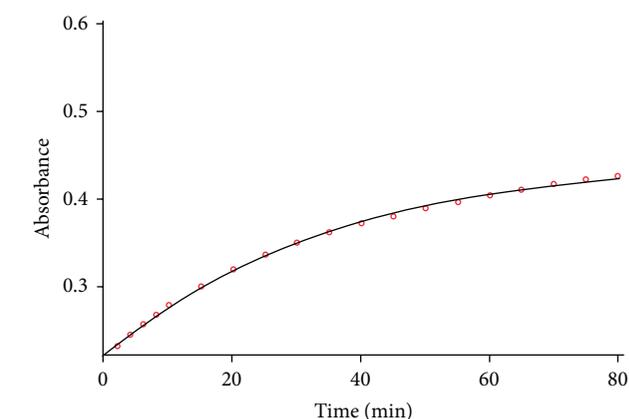


FIGURE 4: First pseudoorder fit curve (solid line) accompanied by the original experimental curve (dotted line) with respect to 4-nitrobenzaldehyde **2**, for the reaction between **1** (10^{-2} M), **3** (10^{-2} M), and **2** (10^{-3} M) which proceeded in methanol at 25°C and 415 nm.

The original experimental absorbance against time data (Figure 4) creates a first order fit curve (full line) at 415 nm, which fits the experimental curve precisely. Therefore, the reaction is of the first order type with respect to (**3**) in relation to the 4-nitrobenzaldehyde **2**, $\beta = 1$.

In the *sixth experiment*, the reaction was followed in the presence of an excess of compounds **3** and **2** (10^{-2} M of each) along with 10^{-3} M of compound **1**, so the rate law can be expressed as follows:

$$\begin{aligned} \text{Rate} &= k_{\text{ovr}}[\mathbf{3}]^{\alpha}[\mathbf{2}]^{\beta}[\mathbf{1}]^{\gamma}[\text{Cat}] \\ \text{Rate} &= k_{\text{obs}}[\mathbf{1}]^{\gamma} \quad (4) \\ k_{\text{obs}} &= k_{\text{ovr}}[\mathbf{3}]^{\alpha}[\mathbf{2}]^{\beta}[\text{Cat}]. \end{aligned}$$

The experimental absorbance curve versus time along with a second-order fit was recorded at 25°C and wavelength 435 nm

(Figure 5). Then, the rate constant ($k_{\text{obs}} = 12.40 \text{ min}^{-1} \cdot \text{M}^{-1}$) of the reaction was automatically obtained by the software programme. In fact, the obtained rate constant (12.40) for (4) from the sixth experiment is equal to second order rate constant (12.64) of third experiment ((1) for 10^{-2} M of each compound). Although in both (sixth and third) experiments, whole conditions are the same, with the exception of concentration of compound **1**, that is, 10^{-3} M and 10^{-2} M, respectively; nevertheless, in the two cases, the reaction is second order and independent of concentration **1**; this is possible when γ is zero in both (1) and (4). It means that the reaction is zero and of the second order type in relation to compound **1** and sum of **2** and **3** ($\alpha + \beta = 2$), respectively. As a result, the overall order of reaction is two which is the same as the previous experiment (third experiment).

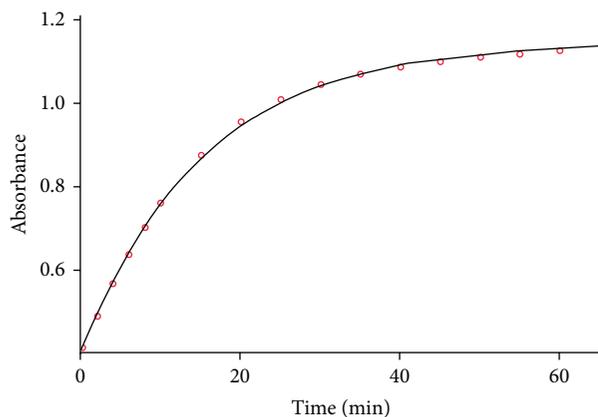


FIGURE 5: Second order fit curve (solid line) along with the original experimental curve (dotted) for the reaction between 4-hydroxycoumarin **1** (10^{-3} M), malononitrile **3** (10^{-2} M), and 4-nitrobenzaldehyde **2** (10^{-2} M) which was proceed in methanol at 25.0°C and 435 nm.

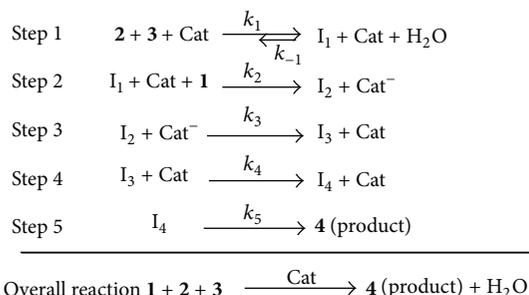


FIGURE 6: The simplified Scheme for the proposed reaction mechanism [14, 18, 37].

Utilizing the above results, the simplified scheme of the proposed reaction mechanism (Scheme 2, [29–31]) as a possible explanation is shown in Figure 6 [14, 18, 37].

To investigate which steps of the proposed mechanism is the rate-determining step, the rate law was written using the final step of reaction as follows:

$$\text{Rate} = k_5 [\mathbf{I}_4]. \quad (5)$$

The steady state approximation can be applied for obtaining the concentration of $[\mathbf{I}_4]$, which is generated from the following equations:

$$\frac{d[\mathbf{I}_4]}{dt} = k_4 [\mathbf{I}_3] [\text{Cat}] - k_5 [\mathbf{I}_4] = 0 \quad (6)$$

$$k_4 [\mathbf{I}_3] [\text{Cat}] = k_5 [\mathbf{I}_4]. \quad (7)$$

The value of (7) can be replaced in (5) so the rate equation becomes

$$\text{Rate} = k_4 [\mathbf{I}_3] [\text{Cat}]. \quad (8)$$

For obtaining the concentration of intermediate $[\mathbf{I}_3]$, the following equation is yielded by applying the steady state assumption:

$$\frac{d[\mathbf{I}_3]}{dt} = k_3 [\mathbf{I}_2] [\text{Cat}^-] - k_4 [\mathbf{I}_3] [\text{Cat}] = 0, \quad (9)$$

$$k_3 [\mathbf{I}_2] [\text{Cat}^-] = k_4 [\text{Cat}] [\mathbf{I}_3],$$

and with the replacement of (9) in (8), the following equation is obtained:

$$\text{Rate} = k_3 [\mathbf{I}_2] [\text{Cat}^-]. \quad (10)$$

And we can obtain the value of $[\mathbf{I}_2]$ as follows which can be replaced in (10) for generation of (13):

$$\frac{d[\mathbf{I}_2]}{dt} = k_2 [\mathbf{I}_1] [\text{Cat}^-] [\mathbf{1}] - k_3 [\mathbf{I}_2] [\text{Cat}^-] = 0 \quad (11)$$

$$k_2 [\mathbf{I}_1] [\text{Cat}] [\mathbf{1}] = k_3 [\mathbf{I}_2] [\text{Cat}^-] \quad (12)$$

$$\text{Rate} = k_2 [\mathbf{I}_1] [\mathbf{1}] [\text{Cat}]. \quad (13)$$

The concentration of intermediate $[\mathbf{I}_1]$ is obtained using steady state approximation, and by substituting (15) into (13), (16) is yielded as follows:

$$\frac{d[\mathbf{I}_1]}{dt} = k_1 [\mathbf{2}] [\mathbf{3}] [\text{Cat}] - k_{-1} [\mathbf{I}_1] [\text{Cat}] [\text{H}_2\text{O}] \quad (14)$$

$$- k_2 [\mathbf{I}_1] [\mathbf{1}] [\text{Cat}]$$

$$[\mathbf{I}_1] = \frac{k_1 [\mathbf{2}] [\mathbf{3}]}{k_{-1} [\text{H}_2\text{O}] + k_2 [\mathbf{1}]} \quad (15)$$

$$\text{Rate} = \frac{k_1 k_2 [\mathbf{1}] [\mathbf{2}] [\mathbf{3}] [\text{Cat}]}{k_{-1} [\text{H}_2\text{O}] + k_2 [\mathbf{1}]} \quad (16)$$

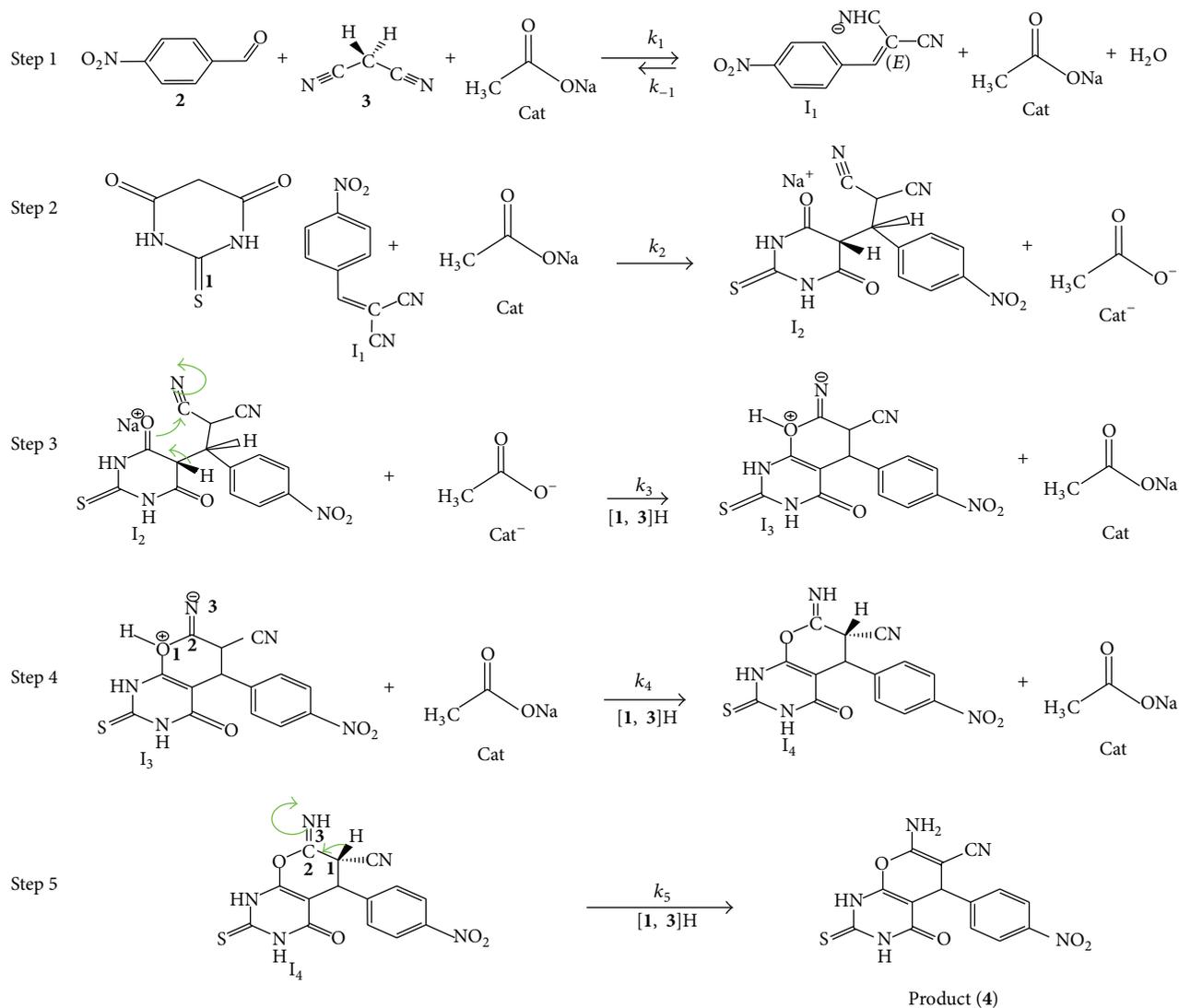
Equation (16) is not compatible with the experimental data

$$\text{Rate} = k_{\text{ovr}} [\mathbf{2}] [\mathbf{3}] [\text{Cat}]. \quad (17)$$

Therefore, the rate constants k_{-1} and k_2 have no chance to be a rate determining step; nevertheless, if $k_2 \gg k_{-1}[\text{H}_2\text{O}]$, the following equations can be obtained:

$$\text{Rate} = (k_1 = k_{\text{ovr}}) [\mathbf{2}] [\mathbf{3}] [\text{Cat}]. \quad (18)$$

The final equation (18) (remerge from steady state assumption) indicates that the overall order of the reaction is two; additionally, in accordance with this equation, the order of reaction with respect to each compound (**3**, **2** and **1**) is 1, 1, and zero, respectively, which was previously confirmed by the experimental data (17). It is obvious that overall constant (k_{ove}) in (17) is equal to rate constant (k_1) in (18). Because of the presence of k_1 in the rate law (18), it is 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 (see Scheme 2, step 1) in reaction carries a dispersed charge effect of solvent (next section, mixture of water and ethanol, 50/50) which has higher dielectric constant ($\epsilon = 52.12$) more than methanol



SCHEME 2

(with lower dielectric constant $\epsilon = 32.6$) on this dispersed charge which would be much stronger compared to that on reactants (2 and 3) that do not have any charge. The solvent thus stabilizes the species at the transition state more than it does the reactants, and therefore E_a would be lower and speeding up the reaction rate (see Table 2, effect of both solvents). As is evident, the concentration of sodium acetate as a catalyst appears in the rate law (18), since, at the end of mechanism, (Scheme 2) sodium acetate is generated once again, and keep a constant value in its concentration. With respect to (18), k_1 is a rate determining step; therefore, the activation parameters which involve ΔG^\ddagger , ΔS^\ddagger , and ΔH^\ddagger can be now calculated for the first step (rate determining step, k_1), as an elementary reaction, on the basis of Eyring equation (a) of Figure 7(a), $\text{Ln}(k_1 = k_{\text{ove}})/T$ versus $1/T$ and also a different linearized form of Eyring equation (b) of Figure 7(b), $T \times \text{Ln}(k_1 = k_{\text{ove}})/T$ against (T) [39]. The results are accumulated in Figures 7(a) and 7(b). Statistical analysis of the Eyring equation clearly confirms that the standard errors of ΔS^\ddagger and

ΔH^\ddagger correlate (T_{av} is the center of the temperature range used) as follows:

$$\sigma(\Delta S^\ddagger) = \frac{1}{T_{\text{av}}}\sigma(\Delta H^\ddagger). \quad (19)$$

It follows that in most solution phase studies $\sigma(\Delta S^\ddagger) \approx \sigma(\Delta H^\ddagger) \times 0.003 \text{ K}^{-1}$. This correlation has been mentioned elsewhere [39, 40]. The standard errors for activation parameters have been calculated according to the above instructions [39–41] and they have been reported along with these parameters in Figures 7(a) and 7(b). With respect to the values of ΔS^\ddagger and ΔH^\ddagger (see Figures 7(a) and 7(b)), ($\Delta G^\ddagger = 54.32 \text{ kJ mol}^{-1}$) is reported for the reactions between 1, 2, and 3 in a mixture of ethanol and water at 430 nm and 298.2 K.

4.2. Effect of Solvents and Temperature. In order to determine the effect of change in temperature and solvent environment on the reaction rate, various experiments were arranged

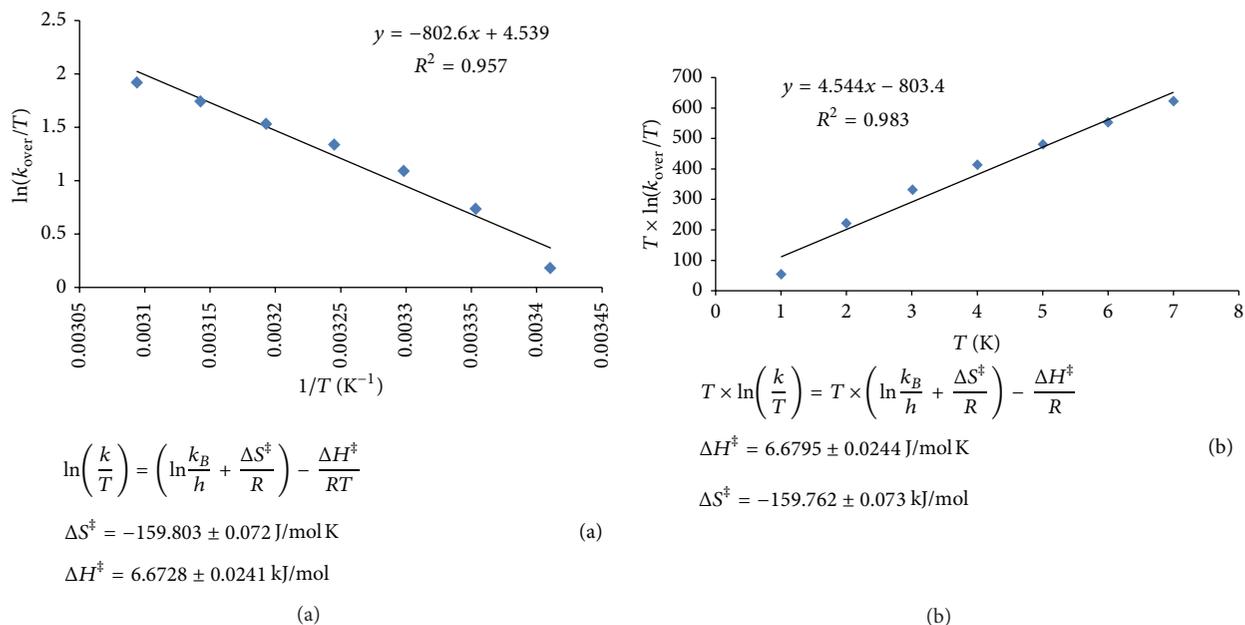


FIGURE 7: (a, b) Eyring plots according to (1) and (2), for the reaction between **1**, **2**, **3**, and sodium acetate catalyst in methanol.

TABLE 2: Rate constants k_{obs} ($\text{min}^{-1} \text{M}^{-1}$), $k_1 = k_{\text{ove}}$ ($\text{min}^{-1} \text{M}^{-2}$) for the reaction between **2** (10^{-2}M), **3** (10^{-2}M), and **1** (10^{-2}M) in the presence of sodium acetate (as a catalyst) and both solvents methanol (32.6)^a and a mixture of ethanol and water (ethanol : water, 1 : 1), (52.12)^d.

Solvent: methanol (32.6) ^a							
T (°C)	$T = 20^\circ\text{C}$	$T = 25^\circ\text{C}$	$T = 30^\circ\text{C}$	$T = 35^\circ\text{C}$	$T = 40^\circ\text{C}$	$T = 45^\circ\text{C}$	$T = 50^\circ\text{C}$
k_{obs}	3.5092 (0.0011) ^b	6.2492 (0.0094)	9.0095 (0.0102)	11.7607 (0.0065)	14.50 (0.0189)	18.15 (0.0099)	22.10 (0.0199)
k_{ove}^c	350.92	624.92	900.95	1176.07	1450	1815	2210
Solvent: mix ethanol/water (52.12) ^d							
T (°C)	$T = 20^\circ\text{C}$	$T = 25^\circ\text{C}$	$T = 30^\circ\text{C}$	$T = 35^\circ\text{C}$	$T = 40^\circ\text{C}$	$T = 45^\circ\text{C}$	$T = 50^\circ\text{C}$
k_{obs}	9.4693 (0.007) ^b	12.6398 (0.0093)	14.9811 (0.0116)	17.7596 (0.0139)	20.507 (0.0164)	24.609 (0.0186)	29.705 (0.0193)
k_{ove}	946.93	1263.98	1498.11	1775.96	2050.7	2460.9	2970.5

^{a,d}Dielectric constant.

^bSD (standard deviation).

^cIs overall rate constant.

with different temperatures and solvent polarity under the same conditions with the previous experiment. For this purpose, dry methanol and a mixture of ethanol and water (ethanol : water, 1 : 1) have been used in the experiment. The results showed that the rate of reaction speeds up in solvent with high dielectric constant (ethanol and water) compared to lower dielectric constant (methanol) at all investigated temperatures (see Table 2).

Also, as can be seen in Table 2, rate of the reaction increases by raising the temperature. In the studied temperature range, the second-order rate constant ($\ln k_1$) of the reaction was inversely proportional to the temperature, which is in agreement with the Arrhenius equation. This behavior is shown in Figure 7. The activation energy, for the reaction between **1**, **2**, and **3** was obtained in lone a mixture of ethanol

and water (1 : 1) ($45.98 \pm 0.25 \text{ kJ} \cdot \text{mol}^{-1}$) form the slope of Figure 8.

4.3. Effect of Catalyst. The rate of reaction was reduced in the presence of $\text{Zn}(\text{CH}_3\text{CO}_2)_2$ as a second catalyst in a mixture of ethanol and water (1 : 1) in comparison with the first catalyst (NaCH_3CO_2). It seems that Zn^{+2} ions have more interactions with polar solvent in relation to Na^+ ions. This reduces the rate of reaction in the second catalyst media (see Table 3).

5. Conclusion

In this work, we report a novel three-component one-pot synthesis of functionalized pyrano[2,3-d]pyrimidine in the presence of NaOAc and $\text{Zn}(\text{OAc})_2$ as the highly effective

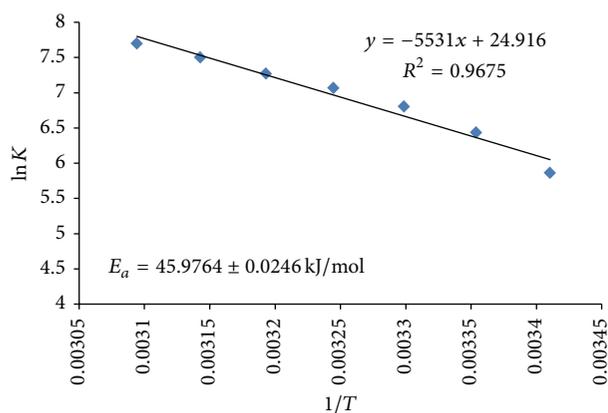


FIGURE 8: The dependence 12 of the second order rate constant ($\ln k_1$) on reciprocal temperature for the reaction between compounds **1**, **2**, and **3** measured in methanol at wavelength of 430 nm according to the Arrhenius equation.

TABLE 3: Effect of various catalysts on a reaction between **1**, **2**, and **3** compounds in the presence of methanol solvent.

Catalyst	$k_1 \times 10^2$ ($\text{min}^{-1} \cdot \text{M}^{-2}$)	SD
$T = 25^\circ\text{C}$		
NaCH_3CO_2	6.25	0.0118
$\text{Zn}(\text{CH}_3\text{CO}_2)_2$	2.08	0.0160

base catalyst under thermal conditions. The catalyst shows an environmentally friendly character, which is inexpensive, clean, safe, nontoxic, and easily obtained. Moreover, the procedure offers several advantages including high yields, operational simplicity, clean reaction conditions, and minimum pollution of the environment, which makes it a useful and attractive process for the synthesis of these compounds.

Also, the following results are obtained from kinetics and mechanism studies.

- (1) The overall order of the reaction followed second-order kinetics and the reaction order of each reactant 4-nitrobenzaldehyde **2**, malononitrile **3**, and thiobarbituric acid **1** is one, one, and zero, respectively.
- (2) The overall rate constants of all reactions were calculated successfully at all investigated solvents and temperatures.
- (3) In solvents with higher dielectric constants, the rate of all reactions increased and this can be related to the stabilization differences of the reactants and the activated complex by the solvent in the transition state.
- (4) Based on the experimental data, the first step of suggested mechanism was identified as a rate-determining step (k_1) and this was confirmed by the steady-state assumption.
- (5) The activation energy ($45.9764 \pm 0.246 \text{ kJ} \cdot \text{mol}^{-1}$) and parameters of the reaction involving ΔG^\ddagger , ΔS^\ddagger , and ΔH^\ddagger have been calculated, on the basis of both Eyring equation and a different linearized form.
- (6) The rate of reaction speeds up in the presence of catalyst with more charge potential (counter ion Zn^{+2} versus Na^+).

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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References

- [1] C. C. A. Cariou, G. J. Clarkson, and M. Shipman, "Rapid synthesis of 1,3,4,4-tetrasubstituted β -lactams from methyleneaziridines using a four-component reaction," *Journal of Organic Chemistry*, vol. 73, no. 24, pp. 9762–9764, 2008.
- [2] S. M. Kupchan, Y. Komoda, W. A. Court et al., "Maytansine, a novel antileukemic ansa macrolide from *Maytenus ovatus*," *Journal of the American Chemical Society*, vol. 94, no. 4, pp. 1354–1356, 1972.
- [3] R. W. Armstrong, A. P. Combs, P. A. Tempest, S. D. Brown, and T. A. Keating, "Multiple-component condensation strategies for combinatorial library synthesis," *Accounts of Chemical Research*, vol. 29, no. 3, pp. 123–131, 1996.
- [4] G. Ren, J. Zhang, Z. Duan, M. Cui, and Y. Wu, "A simple and economic synthesis of propargylamines by CuI-catalyzed three-component coupling reaction with succinic acid as additive," *Australian Journal of Chemistry*, vol. 62, no. 1, pp. 75–81, 2009.
- [5] C. Mukhopadhyay, A. Datta, and R. J. Butcher, "Highly efficient one-pot, three-component Mannich reaction catalysed by boric acid and glycerol in water with major 'syn' diastereoselectivity," *Tetrahedron Letters*, vol. 50, no. 29, pp. 4246–4250, 2009.
- [6] C. Mukhopadhyay, P. K. Tapaswi, and M. G. B. Drew, "Room temperature synthesis of tri-, tetrasubstituted imidazoles and bis-analogues by mercaptopropylsilica (MPS) in aqueous methanol: application to the synthesis of the drug trifenagrel," *Tetrahedron Letters*, vol. 51, no. 30, pp. 3944–3950, 2010.
- [7] Y. Morianka and K. J. Takahashi, *Japanese Kokai*, vol. 17, p. 498, 1977.
- [8] J.-B. Montandon, F. J. Zijlstra, J. H. P. Wilson, E. M. Grandjean, and L. Cicurel, "In-vitro versus in-vivo activities of new 5-lipoxygenase inhibitors with antiinflammatory activity," *International Journal of Tissue Reactions*, vol. 11, no. 3, pp. 107–112, 1989.
- [9] G. T. Brooks, "The effect of some furochromene and benzochromene analogues of 2,2-dimethyl-7-methoxychromene (precocene I) and benzofuran precursors on *Oncopeltus fasciatus* (dallas) and *Locusta migratoria migratorioides* (R&F)," *Journal of Pesticide Science*, vol. 22, pp. 41–50, 1998.
- [10] T. Hyana and H. Saimoto, "Preparation of (furan) pentenylchromene derivatives as anticancer agents," *Jpn Patent JP 621812768*, 1987.

- [11] E. A. A. Hafez, M. H. Elnagdi, A. G. Ali Elagamey, and F. M. A. A. El-Taweel, "Nitriles in heterocyclic synthesis: novel synthesis of benzo[c]-coumarin and of benzo[c]pyrano[3,2-c]quinoline derivatives," *Heterocycles*, vol. 26, no. 4, pp. 903–907, 1987.
- [12] F. M. Abdel-Galil, B. Y. Riad, S. M. Sherif, and M. H. Elnagdi, "Activated nitriles in heterocyclic synthesis: a novel synthesis of 4-azoloyl-2-aminoquinolines," *Chemistry Letters*, vol. 11, no. 8, pp. 1123–1126, 1982.
- [13] M. El-Agrody, *Journal of Chemical Research*, p. 280, 1994.
- [14] M. Bararjanian, S. Balalaie, B. Movassagh, and A. M. Amani, "One-pot synthesis of pyrano[2,3-d]pyrimidinone derivatives catalyzed by L-proline in aqueous media," *Journal of the Iranian Chemical Society*, vol. 6, no. 2, pp. 436–442, 2009.
- [15] M. Kidwai and S. Saxena, "Convenient preparation of pyrano benzopyranes in aqueous media," *Synthetic Communications*, vol. 36, no. 18, pp. 2737–2742, 2006.
- [16] M. M. Heravi, B. A. Jani, F. Derikvand, F. F. Bamoharram, and H. A. Oskooie, "Three component, one-pot synthesis of dihydropyrano[3,2-c]chromene derivatives in the presence of $H_6P_2W_{18}O_{62} \cdot 18H_2O$ as a green and recyclable catalyst," *Catalysis Communications*, vol. 10, no. 3, pp. 272–275, 2008.
- [17] A. T. Khan, M. Lal, S. Ali, and M. M. Khan, "One-pot three-component reaction for the synthesis of pyran annulated heterocyclic compounds using DMAP as a catalyst," *Tetrahedron Letters*, vol. 52, no. 41, pp. 5327–5332, 2011.
- [18] S. Balalaie, S. Abdolmohammadi, H. R. Bijanzadeh, and A. M. Amani, "Diammonium hydrogen phosphate as a versatile and efficient catalyst for the one-pot synthesis of pyrano[2,3-d]pyrimidinone derivatives in aqueous media," *Molecular Diversity*, vol. 12, no. 2, pp. 85–91, 2008.
- [19] N. Hazeri, M. T. Maghsoodlou, S. M. Habibi-Khorassani, J. Aboonajmi, M. Lashkari, and S. S. Sajadikhah, "A green protocol for one-pot three-component synthesis of α -amino phosphonates catalyzed by succinic acid," *Research on Chemical Intermediates*.
- [20] N. Hazeri, M. T. Maghsoodlou, S. M. Habibi-Khorassani, J. Aboonajmi, and S. S. Sajadikhah, " $Fe(NO_3)_3 \cdot 9H_2O$ as efficient catalyst for one-pot synthesis of highly functionalized piperidines," *Journal of the Chinese Chemical Society*, vol. 60, no. 4, pp. 355–358, 2013.
- [21] M. Lashkari, N. Hazeri, M. T. Maghsoodlou et al., "Synthesis and crystal structure study of diethyl aryl(benzo[d]thiazol-2-ylamino)methyl phosphonates," *Heteroatom Chemistry*, vol. 24, no. 1, pp. 58–65, 2013.
- [22] M. R. Mousavi, J. Aboonajmi, M. T. Maghsoodlou, N. Hazeri, S. M. Habibi-Khorassani, and M. Safarzaei, " $La(NO_3)_3 \cdot 6H_2O$ catalyzed one-pot highly diastereoselective synthesis of functionalized piperidines," *Letters in Organic Chemistry*, vol. 10, no. 3, pp. 1570–1786, 2013.
- [23] N. Hazeri, M. T. Maghsoodlou, M. R. Mousavi, J. Aboonajmi, and M. Safarzaei, "Potassium sodium tartrate as a versatile and efficient catalyst for the one-pot synthesis of pyran annulated heterocyclic compounds in aqueous media," *Research on Chemical Intermediates*.
- [24] O. J. Nielsen, J. Sehested, S. Langer, E. Ljungström, and I. Wängberg, "UV absorption spectra and kinetics for alkyl and alkyl peroxy radicals originating from di-tert-butyl ether," *Chemical Physics Letters*, vol. 238, no. 4-6, pp. 359–364, 1995.
- [25] S. Langer, E. Ljungström, T. Ellermann, O. J. Nielsen, and J. Sehested, "Pulse radiolysis study of reactions of alkyl and alkylperoxy radicals originating from methyl tert-butyl ether in the gas phase," *Chemical Physics Letters*, vol. 240, no. 5-6, pp. 499–505, 1995.
- [26] V. V. Ivanov and C. Decker, "Kinetic study of photoinitiated frontal polymerization," *Polymer International*, vol. 50, no. 1, pp. 113–118, 2001.
- [27] P. C. Fung, K. M. Sin, and S. M. Tsui, "Decolorisation and degradation kinetics of reactive dye wastewater by a UV/ultrasonic/peroxide system," *Journal of the Society of Dyers and Colourists*, vol. 116, no. 5-6, pp. 170–173, 2000.
- [28] F. Misiti, M. Castagnola, C. Zuppi, B. Giardina, and I. Messana, "Role of ergothioneine on S-nitrosoglutathione catabolism," *Biochemical Journal*, vol. 356, no. 3, pp. 799–804, 2001.
- [29] M. Shaharaki, S. M. Habibi-Khorassani, A. Ebrahimi, M. T. Maghsoodlou, and A. Pakanahad, "Theoretical, kinetic and mechanistic studies of the reaction between dialkyl acetylenedicarboxylates, triphenylphosphine and pyrrole in organic solvents," *Progress in Reaction Kinetics and Mechanism*, vol. 37, no. 4, pp. 321–343, 2012.
- [30] S. M. Habibi-Khorassani, M. T. Maghsoodlou, M. Zakari-anezhad, M. Nassiri, M. A. Kazemian, and P. Karimi, "A facile synthesis of stable phosphorus ylides derived from 3,6-dibromocarbazole and kinetic investigation of the reactions by UV spectrophotometry technique," *Heteroatom Chemistry*, vol. 19, no. 7, pp. 723–732, 2008.
- [31] S. M. Habibi-Khorassani, A. Ebrahimi, M. T. Maghsoodlou et al., "Theoretical study, an efficient synthesis route to, and kinetic investigation of, stable phosphorus ylides derived from benzamide," *Progress in Reaction Kinetics and Mechanism*, vol. 34, no. 3, pp. 261–288, 2009.
- [32] S. M. Habibi Khorassani, M. T. Maghsoodlou, A. Ebrahimi, M. Zakari-anezhad, and M. Fattahi, "Kinetics and mechanism of the reactions between triphenylphosphine, dialkyl acetylenedicarboxylates and a NH-acid, pyrazole, by UV spectrophotometry," *Journal of Solution Chemistry*, vol. 36, no. 9, pp. 1117–1127, 2007.
- [33] S. M. Habibi-Khorassani, M. T. Maghsoodlou, E. Aghdaei, and M. Shahraki, " 1H NMR technique for kinetic investigation of equilibrium between the Z- and E-isomers in a stable phosphorus ylide involving a 2-indolinone," *Progress in Reaction Kinetics and Mechanism*, vol. 37, no. 3, pp. 301–310, 2012.
- [34] M. A. Kazemian, P. Karimi, S. M. Habibi-Khorassani, A. Ebrahimi, M. T. Maghsoodlou, and F. J. Milani, "Synthesis of stable phosphorus ylides from 6-chloro-2-benzoxazolinone and kinetic investigation of the reactions by uv spectrophotometry," *Progress in Reaction Kinetics and Mechanism*, vol. 34, no. 1, pp. 77–96, 2009.
- [35] S. M. Habibi Khorassani, M. T. Maghsoodlou, A. Ebrahimi, M. Zakari-anezhad, P. Mojhammadzadeh, and M. Shahraki, "Kinetic study and mechanism investigation of the reactions between triphenylphosphine, dialkyl acetylene dicarboxylates and NH-acid such as Harman," *Oriental Journal of Chemistry*, vol. 24, no. 1, pp. 73–82, 2008.
- [36] S. M. Habibi-Khorassani, A. Ebrahimi, M. T. Maghsoodlou, M. Zakari-anezhad, H. Ghasempour, and Z. Ghahghayhi, "Theoretical, nmr study, kinetics and a mechanistic investigation of the reaction between triphenylphosphine, dialkyl acetylenedicarboxylates and 2-aminothiophenol," *Current Organic Chemistry*, vol. 15, no. 6, pp. 942–952, 2011.
- [37] S. Mashkouri and M. R. Naimi-Jamal, "Mechanochemical solvent-free and catalyst-free one-pot synthesis of pyrano[2,3-d]pyrimidine-2,4(1H,3H)-diones with quantitative yields," *Molecules*, vol. 14, no. 1, pp. 474–479, 2009.

- [38] L. M. Schwartz and R. I. Gelb, "Alternative method of analyzing first-order kinetic data," *Analytical Chemistry*, vol. 50, no. 11, pp. 1592–1594, 1978.
- [39] G. Lente, I. Fábián, and A. J. Poë, "A common misconception about the Eyring equation," *New Journal of Chemistry*, vol. 29, no. 6, pp. 759–760, 2005.
- [40] J. H. Espenson, *Chemical Kinetics and Reaction Mechanisms*, McGraw-Hill, New York, NY, USA, 2nd edition, 1995.
- [41] A. J. Poe, "Mechanisms of inorganic and organometallic reaction," in *Mechanisms of Inorganic and Organometallic Reaction*, M. V. Twigg, Ed., vol. 8, chapter 10, p. 220, Plenum Press, New York, NY, USA, 1994.



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