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RESEARCH ARTICLE

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Kinetics and related studies of the formation of 2,3dihydroquinazolin-4(1H)-ones in the presence of different benzaldehyde derivatives

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Abstract

The kinetics and activation parameters for the reaction between 2-aminobenzamide and some benzaldehyde derivatives in the presence of formic acid have been reported and discussed. A linear plot of lnk vs l/T showed that the reactions obey the Arrhenius equation. Both the Arrhenius and the Eyring equations were used to calculate the activation energy. The effect of nitro groups was studied on different positions of benzaldehyde. For all substituents, the reactions followed second-order kinetics, and the partial orders of reactions were recognized with respect to each reactant. Comparisons between the magnitudes of ΔH^{\ddagger} and $T\Delta S^{\ddagger}$ showed that the reactions were enthalpy controlled. The validity of the isokinetic relationship and the compensation effect was tested, and the isokinetic temperature (β) was obtained. A linear enthalpyentropy plot (ΔH^{\ddagger} versus ΔS^{\ddagger}) showed that the compensation effect is established, and this process occurs via a same mechanism across a series of reactions. From the Van't Hoff and Exner's plots, the isokinetic temperature was obtained.

KEYWORDS

compensation effect, dihydroquinazolin, isokinetic temperaturekineticssubstituent effects

1 | INTRODUCTION

The goal of any kinetic study is the investigation of how different experimental conditions can influence the speed of a chemical reaction and yield information regarding the reaction's mechanism and transition state. In order to study the nature of the reaction mechanism, it is important to study the effect of different factors on the rate of the reaction and determine the various kinetic and activation parameters. The isokinetic relationship is helpful in determining whether a series of reactions are following same mechanism.^[1,2] A number of methods have been developed to obtain experimental kinetic data and analyze them to arrive at a true explanation of the reaction mechanism. Numerous kinetic researches over a large

area of different reactions have previously been reported using the UV/vis technique.^[3–9] The main purpose of this study is to achieve a general overview on the kinetic behavior of the reaction between 2-aminobenzamide with benzaldehyde in the presence of formic acid as a catalyst for the generation of 2, 3-dihydroquinazolin-4(1H)-ones (Scheme 1). Quinazolin-4(3H)-ones are an important class of fused heterocycles that are used as chemotherapeutic agents for the treatment of diseases resulting from different microorganisms, and currently there has been a major expansion in the number of quinazolinone derivatives as drugs.^[10–18] 2, 3-Dihydroquinazolinone derivatives have been reported to possess a wide range of pharmacological attributes such as anti-inflammatory, analgesic,^[19] antitumor,^[20] anticancer,^[21] antibacterial,^[22] and diuretic



SCHEME 1 Reaction of the formation of 2, 3-dihydroquinazolin-4(1H)-ones

attributes.^[23] These unique biological properties have made quinazolinone synthetic studies over the years very attractive.^[24] It is notable that the kinetics and synthesis studies have been reported for these reactions.^[2,25] Herein, we investigate the validity of the isokinetic relationship and compensation effect in addition to the kinetic studies.

2 | EXPERIMENTAL

2.1 | Chemicals and apparatus used

2-Amino-benzamide **1**, some benzaldehyde derivatives **2** (which are listed in Table 1), and formic acid (as a solvent) were obtained from Merck (Darmstadt, Germany), Acros (Geel, Belgium), and Fluka (Buchs, Switzerland) and used without further purifications. 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

The progress of the reaction between 2-aminobenzamide1 and some benzaldehyde derivatives 2 (listed in Table 1) in the presence of formic acid were studied by UV-vis spectrophotometer. The following procedures were carried out. In the first experiment, 10^{-3} M solutions of each reactant were prepared using formic acid as the solvent. The relevant spectrum of each compound was recorded at a wavelength range of 200 to 600 nm. Afterwards, the absorbance changes of the mixed solution



FIGURE 1 The expanded absorption changes versus wavelength in the safe region for the reaction between compound $1 (10^{-3} \text{ M})$ and 4-nitro benzaldehyde 2 (10^{-3} M) in the presence of formic acid as a solvent. The upward direction of the arrow indicates the progress of reaction versus time

involving 10^{-3} M solutions of each compound (1and 2) were recorded until the reaction was finished. The progress of the reaction was monitored via expanded absorbance changes as a function of wavelengths (Figure 1). From these spectra and the single spectrum of each reactant, the appropriate wavelength was discovered, providing the opportunity to investigate the kinetics and mechanism of the reaction. Determination of the rate law and overall order of the reaction is the main objective of the kinetic studies. Hence, increases in the absorbance of the product were followed versus time under same concentrations of each compound at 298.15 K and an appropriate wavelength of 390 nm (Figure 2). Results showed that the experimental curve (dotted line) fit the second-order curve (solid line) $(\beta + \alpha = 2)$. The second-order rate constants k were automatically evaluated using the standard equations within the program.^[26] All the reactions followed a second-order rate law at different temperatures. Same

TABLE 1 The listed benzaldehyde derivatives which have been used for the investigated reactions in Scheme 1

2-Nitrobenzaldehyde	3-Nitrobenzaldehyde	4-Nitrobenzaldehyde
NO2 CHO	20N CHO	20N CHO
4-Methylbenzaldehyde	Benzaldehyde	
Н ₃ С СНО	Сно	



FIGURE 2 The original experimental absorbance curve versus time for the reaction between compound $1 (10^{-3} \text{ M})$ and 4-nitro benzaldehyde $2 (10^{-3} \text{ M})$ in the presence of formic acid as a solvent at 293.15 K and 390 nm. The dotted line is the experimental values, and the solid line is the fitted curve

results were deducted for other benzaldehyde derivatives (listed in Table 1) which relevant spectra and experimental absorbance curve and fitted curve have been reported in supplemental material files (SMF). Pseudo-order conditions indicated that the partial order of the reaction was one with respect to each reactant ($\alpha = 1$) and ($\beta = 1$). For this case, the rate law can be expressed as Equation 2. The subscripts exp and ove denote experimental and overall, respectively.

$$rate_{exp} = k_{ove}[1]^{\alpha}[2]^{\beta}[cat]$$
(1)

$$rate_{exp} = k_{obs}[1][2]$$
(2)

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$$k_{obs} = k_{ove}[cat] \qquad (3)$$

3 | RESULTS AND DISCUSSION

3.1 | Kinetic and activation parameters

The kinetic investigation of the reactions was carried out at different temperatures and same concentrations of each reactant to obtain the activation and kinetic parameters. The second-order rate constants k_{obs} were calculated at different temperatures which are reported in Table 2.

The results show that the rate of the reactions was increased at higher temperatures. When the Ln k_{ove} (rate constant) is plotted against the inverse of the temperature, 1/T, a straight line is obtained which is in agreement with the Arrhenius equation 5 (Figure 3).

$$\mathbf{k} = \mathbf{A}\mathbf{e}^{-\frac{E_a}{RT}} \tag{4}$$

$$Ln k = LnA - \frac{E_a}{RT}$$
(5)

The activation energies of the reactions were obtained from the slopes of the curves in Figure 3. Other activation parameters were calculated using the values of activation energy and the following equations 1.

$$\operatorname{Ln}\left(\frac{\mathrm{k}}{\mathrm{T}}\right) = \left(\operatorname{Ln}\frac{\mathrm{k}_{\mathrm{B}}}{\mathrm{h}} + \frac{\Delta \mathrm{S}^{\ddagger}}{\mathrm{R}}\right) - \frac{\Delta \mathrm{H}^{\ddagger}}{\mathrm{R}\mathrm{T}} \tag{6a}$$

$$\Gamma \operatorname{Ln}\left(\frac{k}{T}\right) = T\left(\operatorname{Ln}\frac{k_{B}}{h} + \frac{\Delta S^{\ddagger}}{R}\right) - \frac{\Delta H^{\ddagger}}{R}$$
 (6b)

TABLE 2 Second-order rate constants at various temperatures for the reaction between compound **1** and different substituents of compound **2** in the presence of formic acid as the solvent

			k _{obs}		
Substituent of compound 2	T(K)	293.15	298.15	303.15	308.15
4-Nitrobenzaldehyde (reaction 1)		72.3 (0.014) ^a	$(0.018)^{a}$	253.2 (0.010) ^a	344.0 (0.015) ^a
3-Nitrobenzaldehyde (reaction 2)		57.3 (0.009) ^a	115.4 (0.011) ^a	155.7 (0.007) ^a	215.4 (0.012) ^a
2-Nitrobenzaldehyde (reaction 3)		29.9 (0.008) ^a	44.7 (0.009) ^a	59.9 (0.011) ^a	74.7 (0.012) ^a
Benzaldehyde (reaction 4)		40 (0.009)a	46 (0.007)a	68.64 (0.004)a	107.47 (0.005)a
4-Methylbenzaldehyde (reaction 5)		21.47 (0.012)a	28.2 (0.014)a	44 (0.016)a	52 (0.015)a

^aStandard deviation.



FIGURE 3 The dependence of the second-order rate constant ($Ln k_{ove}$) on the reciprocal temperature for the reaction between compound **1** and different substituents of compound **2** in the presence of formic acid as a solvent

FIGURE 4 A, Eyring plot according to Equation 7a for the reaction between compound 1 and different substituent of compound 2 in the presence of formic acid as a solvent. B, Eyring plot according to Equation 7b for the reaction between compound 1 and different substituents of compound 2 in the presence of formic acid as a solvent

$\Delta G^{\ddagger} = \Delta \mathbf{H}^{\ddagger} - T \Delta \mathbf{S}^{\ddagger} \tag{7}$

The Arrhenius equation is often applied to gas-phase kinetics, whereas the Eyring equation is used to describe the relationship between the reaction rate and temperature for reactions in solution media, Equation 6a or 6b.

The values of the activation parameters were determined from a Ln $(\frac{k}{T})$ vs $\frac{1}{T}$ plot Equation 6a and Figure 4 A. In addition, the activation parameters (ΔS^{\ddagger} and ΔH^{\ddagger}) also could be calculated from the linearized form of Eyring equation 6b shown in Figure 4B. Morever, ΔG^{\ddagger} is subsequently calculated from Equation 7.

Thus, the kinetic and activation parameters are accumulated in Table 3. Herein, Eyring equations suggest that the standard errors of ΔS^{\ddagger} and ΔH^{\ddagger} are related to each other through Equation 8.

$$\sigma(\Delta S^{\ddagger}) = \frac{1}{Tav} \sigma(\Delta H^{\ddagger})$$
(8)

In this equation, $T_{\rm av}$ is known to be the centre of the temperature range that is used in this investigation. It

follows that in the 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.^[27]

The activation Gibbs free energy is essentially the energy required for molecule (or a mole of them) to undergo the reaction. Activation energies below 42 kJ mol⁻¹ generally indicate diffusion-controlled processes, and higher values represent chemically controlled reaction processes, so the reactions of this study are chemically controlled.^[28,29] Activation Gibbs's free energies are considered to be the difference in free energy between the activated complex and the reactants from which it was formed. The large and positive ΔG^{\neq} and ΔH^{\ddagger} values suggested that these reactions require energy to convert reactants into products. As can be seen from the data in Table 3, ΔH^{\ddagger} is larger than $T\Delta S^{\ddagger}$ for each of the substituents. Therefore, ΔG^{\neq} and the rates of these reactions are controlled by ΔH^{\ddagger} .^[30] Furthermore, the large negative values of ΔS^{\ddagger} for reactions **3**, **4**, and **5** compared with reactions 2 and 1 indicated that the activated complex for reaction 3 (involving 2-nitrobenzaldehyde) has a more ordered or more rigid structure than the other reactions (1and 2). Nevertheless, the positive values of ΔH^{\ddagger} for

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TABLE 3 Activation parameters (ΔH^{\ddagger} , ΔG^{\ddagger} , ΔS^{\ddagger} , and E_a) for the reaction between compound **1** (10⁻³ M) and different substituent of compound **2** (10⁻³ M) in the presence of formic acid as a solvent in accordance with 2 Equations 6a and 6b

4- Nitrobenzaldehyde (reaction 1)								
$\Delta H^{\ddagger} (kJ.mol^{-1})$	$\Delta G^{\ddagger} (kJ.mol^{-1})$	$\Delta S^{\ddagger}(J.mol^{-1}.K^{-1})$	$T\Delta S^{\ddagger}(kJ.mol^{-1})$	$E_a (kJ.mol^{-1})$	А			
$(74.5 \pm 3.8)^{\rm a}$	$(60.7 \pm 9.2)^{a}$	$(46.3 \pm 12.7)^{a}$	13.5	$(77.0 \pm 3.5)^{\rm c}$	4.31×10^{15}			
$(74.1 \pm 4.6)^{\rm b}$	$(60.7 \pm 9.2)^{\rm b}$	$(44.7 \pm 15.5)^{\rm b}$	13.1					
3-Nitrobenzaldehyde (reaction 2)								
$(61.5 \pm 3.1)^{a}$	$(61.6 \pm 6.1)^{a}$	$(0.7 \pm 0.1)^{\rm a}$	0.2	$(64.3 \pm 2.9)^{\rm c}$	1.06×10^{13}			
$(61.5 \pm 3.1)^{\rm b}$	$(61.6 \pm 6.0)^{\rm b}$	$(-0.4 \pm 0.1)^{\rm b}$	0.1					
2-Nitrobenzaldehyde (reaction 3)								
$(43.2 \pm 1.3)^{\rm a}$	$(63.7 \pm 2.5)^{\rm a}$	$(-68.8 \pm 4.3)^{\rm a}$	20.1	$(45.7 \pm 1.2)^{\rm c}$	3.58×10^9			
$(43.0 \pm 1.3)^{\rm b}$	$(63.7 \pm 2.4)^{\rm b}$	$(-69.3 \pm 4.3)^{\rm b}$	20.3					
		Benzaldehyde (reaction 4)						
$(47.2 \pm 2.7)^{a}$	$(63.2 \pm 5.3)^{\rm a}$	$(-51.5 \pm 8.9)^{\rm a}$	15.3	$(50.38 \pm 2.5)^{\rm c}$	3.4×10^{10}			
48.21 \pm 2.7 $^{\rm b}$	$(63.2 \pm 5.4)^{\rm b}$	$(-50.46 \pm 9)^{\rm b}$	15.0					
		4-Methylbenzaldehyde (reaction 5)						
$(44.0 \pm 1.7)^{a}$	$(64.63 \pm 3.4)^{\rm a}$	$(-68.92 \pm 5.8)^{\rm a}$	20.54	$(46.5 \pm 1.6)^{\rm c}$	4.2×10^{9}			
$(43.9 \pm 1.7)^{\rm b}$	$(64.62 \pm 3.4)^{\rm b}$	$(-69.17 \pm 5.7)^{\rm b}$	20.62					

^a. Obtained from Equation 6a.

^b. Obtained from Equation 6b.

^c. Obtained from Figure 3.

reaction 3 are less than both reactions 2 and 3. Therefore, a competition between both unfavorable ΔS^{\ddagger} (negative and unfavorable) and favorable ΔH^{\ddagger} (low value) makes a difficult reaction of nitro-substituent in the orto position of the benzaldehyde ring (reaction 3) relative to the other positions (meta and para in reactions **2** and **1**, respectively). Where comparing ΔG^{\neq} values for the reactions (Table 3), the activation energy for the nitro-substituent in the orto position (reaction 3) is less than (meta and para in reactions 2 and 1, respectively), so it is expected that the rate of reaction 3 will be more than the reactions 2 and 1, but as shown in Equation 4 rate constant is a combination of different factors such as frequency factor and activation energy. The frequency factor A is related to the frequency of collisions and the probability that the collisions are favorably oriented for the reaction. Ln A and ΔS^{\ddagger} give informations about the degree of order in the transition state.

$$A = \frac{ek_BT}{h}e^{\frac{\Delta S^{\neq}}{R}+2}$$
(9)

Low values of Ln A correspond to negative values of ΔS^{\ddagger} , suggesting that entropy reduces upon achieving the transition state for reaction 3, 4, and 5 (compared with reactions 2 and 1).

3.2 | Substituent effects

(Structural effect).

In the present work, several experiments were carried out to achieve further understanding about the effect of the functional group on the rate of the reaction. Results showed that the effectiveness of the investigated substituent in increasing the rate of reaction follows the following order:

4-nitrobenzaldehyde > 3-nitrobenzaldehyde > benzaldehyde > 2-nitrobenzaldehyde > 4-methylbenzaldehyde.

Nitro group is the electron-withdrawing group (EWG) and increases the reactivity of benzaldehyde with nucleophiles so increases the rate of reaction, but because of steric effect the rate of reaction in the presence of 2-nitrobenzaldehyde(reaction 3) is lower than reaction 4.

The rate of reaction in the presence of 4methylbenzaldehyde is less than that of benzaldehyde; because carbon is slightly more electronegative than hydrogen, there will be a little dipole moment pulling electron density away from hydrogen toward carbon. This slight build-up of electron density on the carbon results in the methyl group having an electron donating effect by induction, thus decreasing the rate of reaction.



FIGURE 5 The proposed mechanism for the reaction between compound **1** and compound **2** in the presence of formic acid for the generation of **3** (product)

3.3 | Mechanism investigation

A simplified scheme of the proposed reaction mechanism shown in Figure 5 is presented in Figure **6**.

On the basis of experimental observations, 3 possibilities can be considered.

First, if step₃ (k_3) are considered as the rate-determining step (RDS), step₂ (k_2) should appear as the equilibrium state with forward (k_2) and return (k_{-2}) rate constants, respectively. So, the simplified scheme of the proposed reaction mechanism can be stated (Figure 7) as:

By applying the steady-state approximation, the general rate law can be written:

$$rate = \frac{k_1 k_3 \ [1][2][cat]}{k_{-2}[cat][H_2O] + k_3} \tag{10}$$

When $step_3$ is practically the RDS, the following assumption is logical:

$$k_{-2}[cat][H_2O] >> k3 \text{ rate} = \frac{k_1 k_3 [1][2]}{k_{-2}[H_2O]} \text{ kobs}$$
$$= \frac{k_1 k_3}{k_{-2}[H_2O]}$$
(10a)

$$rate_{mech} = k_{obs}[1][2]$$
(10b)

As a result, 5 significant points can be stated:

 When step₃ (k₃) is the RDS, under this condition, the rate law that was deduced from the mechanism is rate_{mech} = k_{obs} [1, 2] (10b).



3(product)

FIGURE 6 Simplified scheme for the proposed reaction mechanism

Step₁ 1 + 2 + Cat
$$\xrightarrow{k_1}$$
 I₁

Step₂
$$I_1$$
 $\xrightarrow{k_2}$ $I_2 + Cat + H_2O$

Step₃
$$I_2 \xrightarrow{\text{RDS(slow)}}_{k_3}$$

- 2. This equation follows a second-order kinetics and agrees with the experimental rate law, $rate_{mech} = k_{obs}$ [1, 2] (Equation 2).
- 3. When step₃ (k₃) is practically the RDS, intermediate I₂ is converted to main product 3 (**see** Figure 5) along with a 6-membered ring forming within compound. As expected, formation of such a ring in step₃ reduces the number of degrees of freedom which subsequently slows the entropy down ($\Delta S^{\ddagger} >> 0$).
- 4. Practically, only reaction 3 had a large negative value of $\Delta S^{\ddagger} \Delta S^{\ddagger} = -68.8 \text{ j.mol}^{-1}.\text{k}^{-1}$), Table 3) with participation of 2-nitrobenzaldehyde in a reaction environment; hence, it has an associative mechanism.
- 5. Therefore, for reaction 3, RDS is step₃ (k₃), and the second-order rate Law is Equation 10b with the observed rate constant, $k_{obs} = \frac{k_3 k_1}{K_{-1} H2O}$

Second, if step₂ (k_2) is considered as the RDS, step₁ (k_1) should appear as the equilibrium state with forward (k_1) and return (k_{-1}) rate constants, respectively. So, the simplified scheme of the proposed reaction mechanism can be expressed (see Figure **8**) as:

So, the general rate law can be obtained as:

rate =
$$\frac{k_1 k_2 [1][2][cat]}{k_{-1} + k_2}$$
 (11)

When step₂ is practically the RDS, the following assumption is acceptable:

$$k_{-1} >> k2 \text{ rate} = \frac{k_1 k_2 [1][2][cat]}{k_{-1}} \text{ kobs}$$
$$= \frac{k_1 k_2 [cat]}{k_{-1}}$$
(11a)

$$rate_{mech} = k_{obs}[1][2]$$
(11b)

Herein, 5 significant points can be exposed:

1. when $step_2 (k_2)$ is the RDS, under this circumstance, the rate law that was obtained from the mechanism is

$$rate_{mech} = k_{obs}[1, 2].$$
(11c)

- 1. This equation follows a second-order kinetics and is an agreement with the experimental rate law, rate_{exp} = k_{obs} [1, 2] (Equation 2).
- 2. When step₂ is practically the RDS, intermediate I₁ with a rate constant (k₂) is converted to intermediate I₂ through a dehydration process. In this case, I₁ species are divided into 2 species such as I₂ and H₂O; as expected, the number of degrees of freedom increases and subsequently speeds the enthalpy up ($\Delta S^{\ddagger} >> 0$).
- 3. Practically, only reaction 1 had a large positive value of $\Delta S^{\ddagger}(\Delta S^{\ddagger} = 46.3 \text{ j.mol}^{-1}.\text{k}^{-1})$ with the participation of 4-nitrobenzaldehyde in the reaction environment; hence, it has a dissociative mechanism. When ΔS^{\ddagger} is bigger than $-10 \text{ j.mol}^{-1}.\text{k}^{-1}$, it generally predicates a dissociative mechanism.^[30] For this reason, reaction 2 with the participation of 3-nitrobenzaldehyde follows a dissociative mechanism.
- 4. Therefore, for both reactions 1 and 2, RDS is step₂ (k₂), and the second-order rate law is Equation 11b with the observed rate constant, $k_{obs} = \frac{k_2 k_1 [ca]}{K_1}$

Third, when k_{-1} k_2 , the simplified scheme becomes Figure **9**:

Herein, the general rate law can be stated as:

$$rate = k_1[1][2][cat]$$
 (12)

$$kobs = k_1[cat] \tag{12a}$$

$$rate_{mech} = k_{obs}[1][2]$$
(12b)

3(product)

Equation 12b follows second-order kinetics and agrees with the experimental rate law (Equation 2). When step₁ (k_1) is the RDS, both reactants (**1**,**2**) with rate constant (k_1) along with a nucleophilic attack of compound 1 on the carbonyl group of compound **2** are converted to I₁.

Step₁ 1 + 2 + Cat
$$\xrightarrow{k_1}$$
 I_1

 I_2

$$I_1 \xrightarrow{k_2} I_2 + Cat + H_2O$$

fast

k3

FIGURE 8 Simplified scheme for the reaction mechanism when step₂ is the RDS

Step₂

Step₃



same rate (or equilibrium) constant. As shown in Figure 10, plotting the enthalpy changes vs the entropy changes gives a straight line. Obviously, there is a significant linear correlation between the enthalpy an entropy changes (correlation coefficient = 0.999) and, therefore, an excellent compensation effect. The value of the

in Figure 10 (270/2 K). As previously mentioned, the isokinetic effect can be distinct from the compensation effect. Therefore, the correlation between ΔH^{\ddagger} and ΔS^{\ddagger} does not serve as good evidence for the existence of the isokinetic relationship.

isokinetic temperature β is given by the slope of the curve

Validity of the isokinetic relationship can be investigated in different ways, 1 way of finding a real isokinetic (or isoequilibrium) relationship is to plot the free energy changes vs the temperature (Figure 11) and look for a point of common intersection among the lines. If no point of common intersection exists, then an isokinetic (or isoequilibrium) relationship cannot be said to exist. Figure 11 shows that there is a temperature at which all the free energy of the set of reactions are fairly close to each other (273.15 K), so there is an isoequilibrium effect. In a series of compounds with little a difference in structures, which are undergoing a reaction by essentially the same mechanism, the ΔG^{\ddagger} values may be more or less constant with relative changes in ΔH^{\ddagger} and ΔS^{\ddagger} .^[31]



is independent of temperature. It seems that at the temperature β , all the reactions in the series should have the

(13)

FIGURE 10 Enthalpy-entropy compensation plot

This conversion is accompanied with a reduction in ΔS^{\ddagger} , which is in agreement with the recorded data for reactions 1, 2, and 3 where $\Delta S^{\ddagger} << 0$ in Table 3. Nevertheless, when the nitro group is placed on the orto-position of the benzaldehyde ring, its steric effect prevents the nucleophilic attack of the amine group of compound 1 on the carbonyl group of compound 2 (see step₁, Figure 5). For this reason, the reaction is difficult and required high values of ΔH^{\ddagger} , while it is not practically so high for the 2-nitro substituent(reaction3) in Table 3. It seems that in reaction 3, step₃ (k₃) with low value of ΔH^{\ddagger} is a suitable RDS, while step₁ (k₁) that needs high value of ΔH^{\ddagger} which couldn't be compatible with the low experimental value of $\Delta H^{\ddagger}(\Delta H^{\ddagger}=43.2 \text{ kj.mol}^{-1})$ is not a good candidate for the RDS of this reaction.

4 | VALIDITY OF THE ISOKINETIC **RELATIONSHIP AND COMPENSATION EFFECT**

Where the isokinetic relationship or the compensation effect for a series of reactions is sufficiently similar, one may expect the same mechanism to be operating across reactions. Historically, the isokinetic relationship and compensation effect were considered to be synonymous, but Lei Liu et al demonstrated that the compensation effect and isokinetic (or isoequilibrium) effect are not necessarily synonymous, and the occurrence of one does not necessarily imply the occurrence of the other. The basic aim of the present article is to clarify if the isokinetic relationship or compensation effect or both are appeared in the mentioned reactions. Sometimes, it is found that there is a linear relationship between the activation enthalpy and entropy changes of the series of reactions. This behavior is known as the compensation effect or, more precisely, enthalpy-entropy compensation.

 $\Delta H^{\ddagger} = \beta \Delta S^{\ddagger} + \alpha$

 β is therefore named the isokinetic temperature, and it



FIGURE 11 Van't Hoff plot

Exner has recommended an alternative method for calculating the isokinetic relationship and the value of β . It consists of plotting the logarithms of the rate constants at 2 temperatures ($T_2 > T_1$) against each other according to Equation 14.

$$\log k_2 = a + b\log k_1 \tag{14}$$

The value of the isokinetic temperature β can be calculated from the following expression

$$\beta = \frac{T_2 T_1 (b-1)}{T_2 b - T_1} \tag{15}$$

In this study, a plot of log k_2 (at 298/15 K) vs log k_1 (at 293.15 K) (Figure 12) was found to be linear. The value of β calculated by this method is 282.6 K, which is in relative agreement with that evaluated from Figures 11 (273.15) and 10 (270.2 K).



FIGURE 12 Exner's plot (relationship between log k_1 (at $T_1 = 293.15$ K) and log k_2 (at $T_2 = 298.15$ K)

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5 | CONCLUSION

The detailed kinetic investigation of the reactions between 2-amino-benzamide and some benzaldehyde derivatives in the presence of formic acid as an acid-catalyst and solvent was calculated using UV/vis spectrophotometry technique. The results can be summarized as follows:

It was experimentally found that the reactions followed second-order rate law, so the overall order of the reactions is 2, and the partial order of the reaction, with respect to each reactant, is one. Rate of reactions speeds up at higher temperatures, which agrees well with the Arrhenius equation. Activation parameters ($\Delta H^{\ddagger}, \Delta S^{\ddagger}$, and ΔG^{\ddagger}) were obtained from the Eyring equation. Based on these parameters, it was found that the reactions were enthalpy controlled for the investigated systems. Based on the experimental data, the second step of the suggested mechanism was identified as a rate determining step (k₂) with a second-order rate law, when para or meta-substituents were used as reactants during the reaction. According to the experimental data (activation parameter), the third step of the proposed mechanism was determined as a rate determining step (k_2) with the second-order rate law, when the meta substituent was employed as reactant within the reaction environment. A linear relationship in the enthalpyentropy plot (ΔH^{\ddagger} versus ΔS^{\ddagger}) showed that the compensation effect is established and this process occurs via a same mechanism along the series of reactions. Existence of a common intersection point of Van't Hoff lines serves as evidence for the isokinetic relationship. The value of the isokinetic temperatures, β , which are obtained from Exner's plot, are in good agreement with the values that are calculated from Van't Hoff plots.

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