

# Determination of the kinetics of chlorobenzene nitration using a homogeneously continuous microflow

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## Abstract

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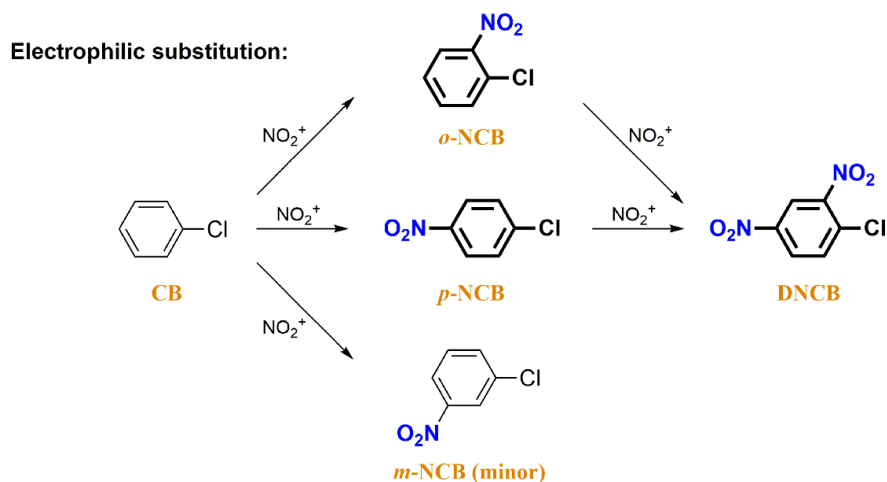
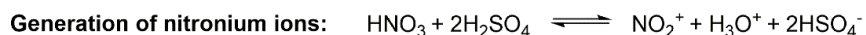
## Keywords

kinetics, nitration of chlorobenzene, microreactor, homogeneous microflow

## 1. Introduction

The nitration of aromatics is one of the oldest and most ubiquitous reactions utilized in industrial production and laboratory research. Similar to the nitration of benzene and toluene,<sup>1,2</sup>the nitration of chlorobenzene

(CB) is representative, and its products are important raw materials and intermediates, that are widely applied in dyes, pharmaceuticals, explosives, pesticides, and spices.<sup>3</sup> Generally, the nitration of aromatics is a liquid-liquid heterogeneous reaction. The reaction mainly takes place in the acid phase containing a large excess of sulfuric acid, and the amount of nitric acid is stoichiometrically proportional to that of the aromatic hydrocarbons. Taking the nitration of CB as an example, when nitric acid reacts with sulfuric acid, its hydroxyl group is protonated, and a molecule of water is removed to form nitronium ions ( $\text{NO}_2^+$ ). The general consensus that is the true nitrating agent in the nitration.<sup>4</sup> CB molecules diffuse into the acid phase and undergo an electrophilic substitution reaction with nitronium ions to generate three isomers: 1-chloro-2-nitrobenzene (*o*-NCB), 1-chloro-4-nitrobenzene (*p*-NCB), and a very small amount of 1-chloro-3-nitrobenzene (*m*-NCB). These isomers can further react with nitronium ions to form the secondary nitration product 1-chloro-2,4-dinitrobenzene (DNCB). The reactions are shown in **Scheme 1**.



**SCHEME 1** Reactions for the nitration of CB with mixed acid

Sulfuric acid provides a necessary environment for the generation of  $\text{NO}_2^+$ . In addition, sulfuric acid as a solvent can absorb reaction heat, which can prevent local overheating and reduce the occurrence of side reactions. Therefore, in industrial production processes, the nitration of CB is usually carried out at high sulfuric acid concentrations, which undoubtedly increases the viscosity of the system and the mass transfer resistance for CB traveling from the organic phase to the acid phase;<sup>5</sup> in addition, CB nitration is a fast and highly exothermic reaction. It remains a challenge for batch reactors to provide rapid feedback and sufficient mass and heat transfer rates. The uneven distribution in chemical concentrations, residence times and temperatures leads to side reactions and rapidly increasing temperature, making it difficult to control the selectivity of the reaction. Moreover, the volume of traditional nitrification reactors is large. If an accident occurs, the high chemical oxygen demand (COD) value of the waste acid and the emission of nitrogen oxides can cause serious damage to the environment. To ensure a safe production environment, the reaction is often operated at low temperatures and drip rates. Therefore, the problems associated with these conditions, such as a low space-time yield and high energy consumption, are prominent.

The smaller characteristic size and larger specific surface area of microreactors significantly improve heat and mass transfer rates,<sup>6-8</sup> easily meeting the requirements of isothermal conditions and effectively controlling the selectivity of the reaction. A lesser degree of liquid holdup is conducive to the realization of intrinsic safety, rapid mixing provides the system with a uniform chemical concentration distribution and precise residence time, and the enclosed space of the microreactor system effectively inhibits the decomposition of concentrated nitric acid.<sup>9,10</sup> In addition, microchemical systems have the advantages of easy automatic

control and integrated amplification;<sup>11</sup> as such, they act as a safe, efficient and green platform for the nitration of CB. In recent years, many examples of continuous-flow nitration have emerged in which the advantages of microreactors and the various needs of aromatic nitration are combined.<sup>12,13</sup> Burns et al.<sup>2</sup> carried out the nitration of benzene and toluene in a stainless steel and polytetrafluoroethylene (PTFE) capillary microchannel reactor, respectively. Rapid interphase mixing and mass transfer were realized, and the industrial potential of microreactors in chemical production was preliminarily explored. Kulkarni et al.<sup>14</sup> carried out the nitration of benzaldehyde safely and continuously in a microreactor system. Given the high heat transfer efficiency of the microreactor, the reaction time was shortened to 2 min by increasing the temperature. Using a microreactor system, Chen et al.<sup>15</sup> continuously synthesized dinitro herbicides in a single step. In contrast to the traditional two-step batch process, there was no need to separate the reaction intermediates, which greatly reduced the amount of solvent required. Yu et al.<sup>16</sup> used *p*-difluorobenzene as a raw material and fumed nitric acid to continuously synthesize 2,5-difluoronitrobenzene. Compared with the yield achieved with a batch reactor (80%), the yield achieved with the microreactor was increased (98%), and the reaction time was shortened from 1 h to 2.3 min. Luo et al.<sup>17</sup> carried out the nitration of acetyl guaiacol in a microreactor using nitric acid/acetic acid as the nitrating agent. The established kinetic model could accurately predict the experimental results observed at high temperature. The reaction conditions were further optimized, and the product yield reached 90.7%. Chen et al. studied the nitration of 2-ethylhexanol<sup>18</sup> and trifluoromethoxybenzene<sup>19</sup> in a microreactor. The kinetic model could accurately predict the reaction conversion. Somma et al.<sup>20</sup> studied the nitration of benzaldehyde in a microreactor embedded in a static mixer. The results showed that the microreactor exhibited better performance than batch reactors. The effect of reduced mass transfer between the two phases on the reaction rate was greatly reduced.

Accurate kinetic data are essential for understanding the characteristics of nitration in depth and guiding the design of reactors. Early studies confirmed that the nitration of CB is a second-order reaction, and the reaction rate for both CB and nitric acid is described by first-order kinetics. Cox et al.<sup>3</sup> measured the rate of CB nitration in sulfuric acid with a mass fraction of 70.2%. The rate constants at different temperatures and the activation energy were obtained. Tselinskii et al.<sup>21</sup> used nitric acid as a nitrating agent to determine the rate of homogeneous CB nitration in 70-90% nitric acid and obtained the rate constants and activation energy. The above studies were all carried out in a batch reactor. Because nitration is a fast reaction, the reaction parameters can change significantly within only a few seconds of sampling and quenching, so the residence time cannot be precisely controlled. Therefore, earlier studies were often carried out at low sulfuric acid concentrations to avoid the large residence time error caused by the rapid reaction. As such, kinetic data for CB nitration at high sulfuric acid concentrations are relatively lacking. In addition, the nitration of CB is a liquid-liquid heterogeneous reaction. It is difficult to eliminate the effect of reduced mass transfer between the two phases on the reaction in a batch reactor, which leads to deviations in the obtained kinetic parameters. Unfortunately, to date, accurate kinetic data for the CB nitration with concentrated mixed acids have not been systematically and comprehensively reported.

The purpose of this study was to accurately measure the kinetics of CB nitration at high mixed acid concentrations. A continuous-flow microreactor system and a homogeneous reaction condition were applied. The effects of temperature, residence time and sulfuric acid concentration on the conversion and selectivity of the reaction were investigated systematically. According to the conversion, the observed reaction rate constants were obtained at different temperatures and sulfuric acid concentrations. The concentration of is not easy to measure directly, and is indispensable to explain the relationship between the reaction rate and sulfuric acid concentration. In this paper, by integrating the experimental data reported in the literature, a mathematical model that can accurately estimate nitric acid equilibria in aqueous sulfuric acid as a function of sulfuric acid concentration and temperature is proposed. Using this model, the rate constants based on are obtained, and the activation energy of CB nitration is calculated.

## 2. Experimental

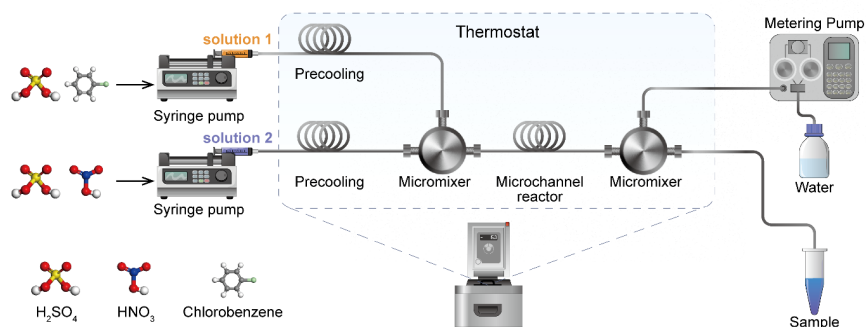
### 2.1 Materials

CB (99%) was obtained from Shanghai Aladdin Bio-Chem Technology Co., Ltd. (Shanghai, China). Sulfuric acid (18.4 kmol/m<sup>3</sup>) was procured from Beijing Lanyi Chemical Products Co., Ltd. (Beijing, China). Lower-concentration sulfuric acid solutions were prepared by diluting the concentrated acid in water. Fuming nitric acid (98 wt%) was purchased from Sinopharm Chemical Reagent Co., Ltd. (Beijing, China). High-performance liquid chromatography (HPLC)-grade methanol (99.9%) was procured from Shanghai Titan Scientific Co., Ltd. (Shanghai, China). Nitrobenzene (>99.8%) as an internal standard was obtained from Shanghai Macklin Biochemical Co., Ltd. (Shanghai, China). Standard samples of *o*-NCB (>99%), *p*-NCB (>99.5%), *m*-NCB (>99.5%) and DNCB (99%) were procured from Shanghai Aladdin Bio-Chem Technology Co., Ltd. (Shanghai, China).

## 2.2 Experimental setup

To eliminate the influence of interphase mass transfer on the reaction and reduce measurement error, the kinetics of CB nitration were studied under homogeneous conditions. A known amount of CB was added to a sealed glass vessel containing sulfuric acid. The mixture was stirred for 1 h with a magnetic stirrer (RCT basic, IKA, Germany) at room temperature to form a homogeneous solution (solution 1). According to the literature,<sup>5</sup> a sulfonation reaction between CB and sulfuric acid is not expected to occur at the temperature. Sulfuric acid and fuming nitric acid were mixed to form the acid phase (solution 2). The molar ratio of nitric acid to CB was adjusted by changing the amount of nitric acid added to solution 2. The mass fraction of sulfuric acid used in the experiment was between 85% and 95%.

As shown in **Figure 1**, solution 1 and solution 2 were loaded into two airtight syringes (50 mL, CHEMYX, USA) and delivered by two syringe pumps (Fusion 6000, CHEMYX, USA). The two solutions were allowed to pass through a sufficiently long, precooled capillary loop so that they could reach the preset reaction temperature. After being mixed in the first micromixer (316 stainless steel, 250 μm bore, VICI, USA), the solutions entered the microchannel reactor for reaction, and the residence time was controlled by adjusting the length of the reaction capillary. In the second micromixer (316 stainless steel, 250 μm bore, VICI, USA), the reaction was quenched in situ by a large amount of water, which was delivered by a metering pump (2PB-3020, Szweico, China). According to the literature,<sup>22,23</sup> when the concentration of mixed acid is substantially diluted by water, the concentration of will decrease to the extent that the reaction immediately stops. Due to the large amount of water, the contact between water and sulfuric acid during quenching does not significantly increase the temperature of the solution, and no side reactions such as sulfonation occur. The outer and inner diameters of all stainless steel capillaries were 1/16 inch and 0.5 mm, respectively. The entire microreactor system, consisting of precooling, mixing, reaction and quenching stages, was submerged in a circulating thermostat (CORIO CD-200F, Julabo, Germany) to obtain a uniform reaction temperature.



**FIGURE 1** Schematic of the microreactor system used to determine the kinetics of CB nitration

It is worth noting that due to the limited solubility of CB in sulfuric acid, the mass ratio of sulfuric acid to nitric acid in solution 2 was kept at approximately 240 to meet the molar ratio of nitric acid to CB. The large amount of sulfuric acid as a solvent can absorb the reaction heat. In addition, the reaction conversion

was controlled at a low level, and the thermostat was used to continuously remove the reaction heat. The calculated increase in the reaction temperature was less than 0.3 °C, which can be completely negligible. The calculation process is provided in the Supporting Information. It can be considered that the reaction proceeded under isothermal conditions. Each experiment was repeated three times. The error bars are marked in figures, and the final results are the average values of the three measurements.

## 2.3 Sample analysis

After the reaction was quenched, a 1 mL sample was collected in a 10 mL centrifuge tube. The internal standard method was used to quantify the composition of the products. A known quantity of nitrobenzene was added to the centrifuge tube as the internal standard, and then methanol was added to dilute the mixture. After the sample was evenly mixed, a small amount of the sample was extracted and analyzed by ultra-performance liquid chromatography (UPLC) using an ACQUITY UPLC I-Class system (Waters, USA) equipped with an ACQUITY UPLC BEH C18 column (2.1 × 100 mm, 1.7 μm). The injection volume was 1 μL. The mobile phase consisted of methanol (50%) and water (50%), and its flow rate was 0.2 mL/min. The column temperature was 30 °C. The detection wavelength of the UV detector was 200-300 nm. For the peaks observed for each substance by UPLC, please refer to the Supporting Information (**Figure S1**).

In the internal standard method, standard curves were obtained by varying the proportions of each substance and the internal standard can be found in the Supporting Information (**Figure S2**). The correction factor for each substance was calculated with Equation (1), and the mass of the various substances in the sample was calculated with Equation (2). The goodness of fit ( $R^2$ ) for each standard reached 0.999.

The subscript  $i$  represents CB,  $o$ -NCB,  $p$ -NCB,  $m$ -NCB or DNCB. The subscript  $s$  represents nitrobenzene,  $f$  is the correction factor obtained from the standard curve,  $A$  is the liquid chromatographic peak area, and  $m$  is the mass of the substance in the sample.

The CB conversion can be calculated with the following equations:

where  $c$  is the molar concentration of the substance in the sample,  $M$  is the molar mass of the substance, and  $X_{CB}$  is the CB conversion.

The selectivity of each product can be calculated with the following equations:

where  $S_{NCB}$  is the selectivity of mononitrochlorobenzene and  $S_{DNCB}$  is the selectivity of DNCB.

The residence time in the capillary is calculated with the following equation:

where  $V$  is the volume of the capillary and  $Q_{or}$  and  $Q_{ac}$  are the volumetric flow rates of the two solutions, respectively.

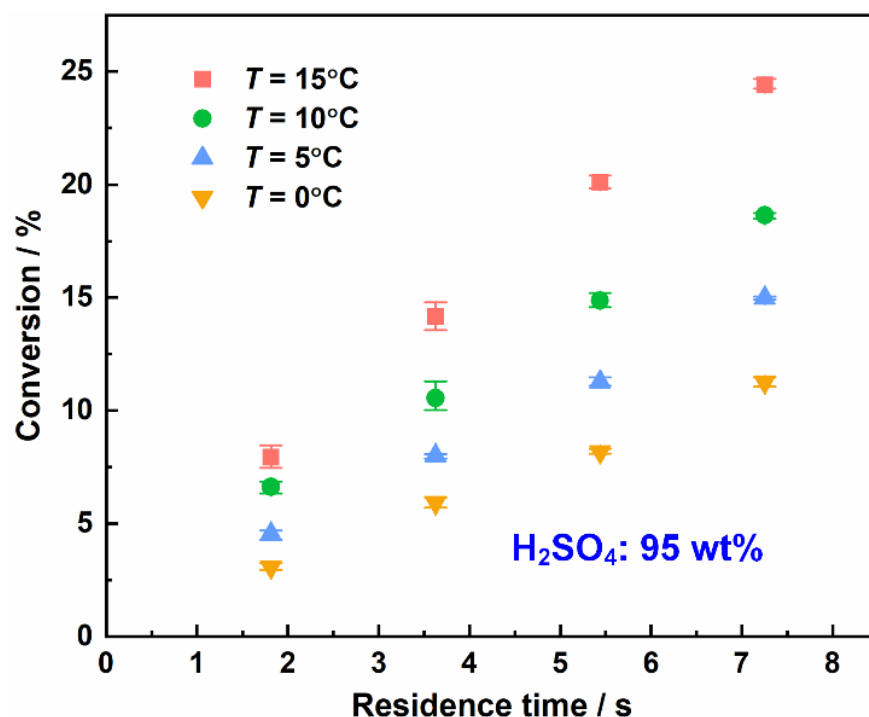
## 3. Results and discussion

### 3.1 Mixing performance in the microreactor system

In this work, since a small amount of CB was dissolved in sulfuric acid, the reaction involved a homogeneous liquid system. Because the nitration reaction is rapid, it is necessary to ensure sufficient mixing performance, which is related to the flow rates of the two streams.<sup>24,25</sup> The concentration distribution of CB in the mixed solution was simulated by computational fluid dynamics (CFD). The flow rates of the solution 1 and solution 2 were 0.4 mL/min and 0.9 mL/min, respectively, as shown in **Figure S3**. The mixing performance of the two fluid streams was significantly enhanced at the intersection of the T-micromixer. The distance at which the substance concentration was homogenized was only 3 mm. By knowing the total flow rate, the mixing time of the two streams can be calculated, and it was found to be much less than the reaction time, indicating that mixing was not the limiting factor in the nitration reaction. In addition, the properties of the two fluids were very similar due to the low solubility of CB in sulfuric acid. To eliminate any mixing limitations, all of the following experiments were operated at the same flow rate.

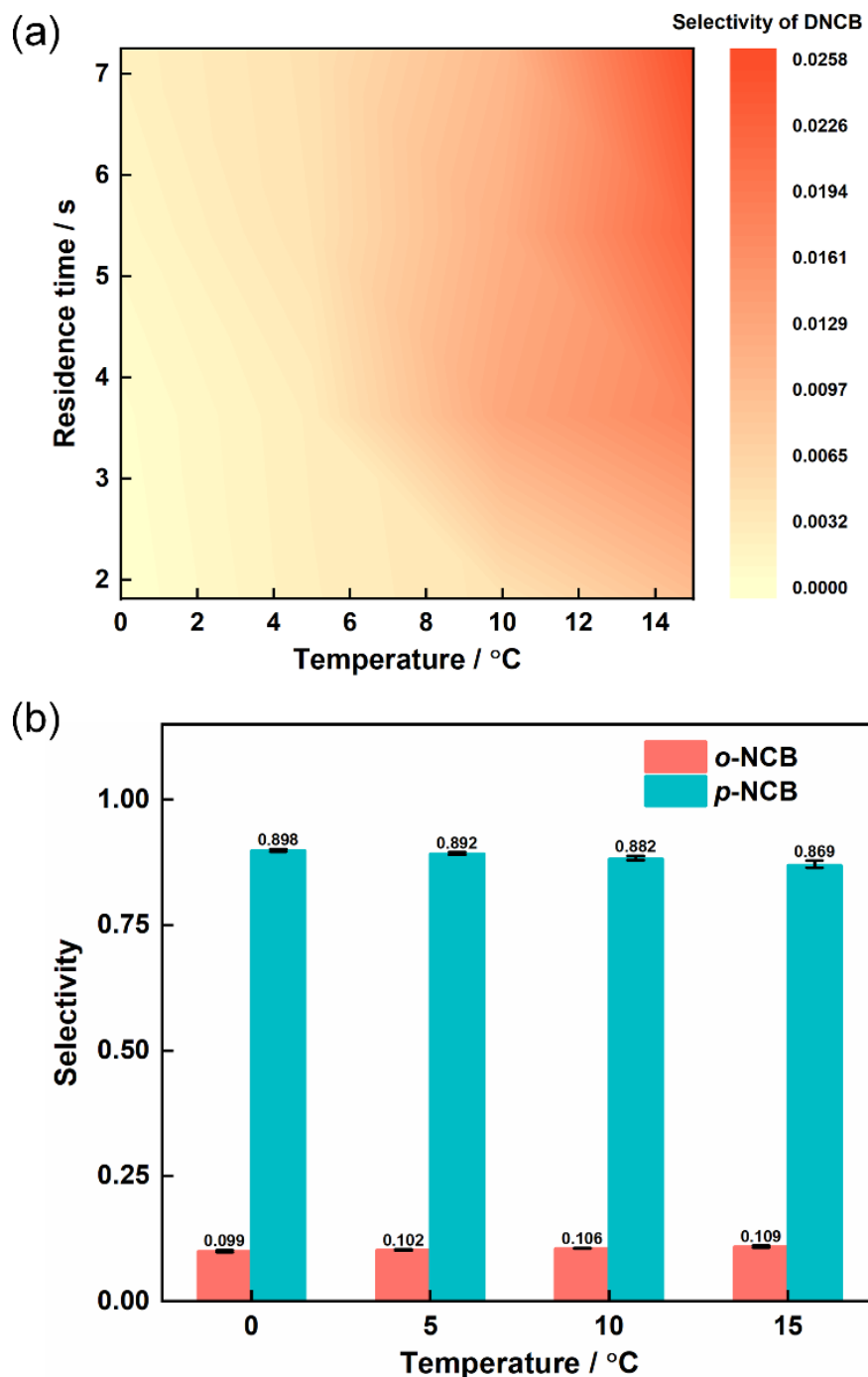
### 3.2 Effect of temperature and residence time

The CB conversion is an important parameter that can be used to characterize the reaction process and measure the reaction rate; it also affects the selectivity. The CB conversion was investigated as a function of temperature and residence time, as shown in **Figure 2**. The mass fraction of sulfuric acid was 95%. The results showed that under the condition of incomplete CB conversion, the conversion increased with increasing residence time, and at the same residence time, the conversion increased with increasing temperature, indicating that higher temperatures significantly increased the reaction rate. It is worth noting that the reaction was carried out at a low temperature and with a short residence time. When the conversion was very low, the concentration of nitric acid did not obviously decrease and was approximated to be constant. Therefore, the conversion of CB increased linearly and in accordance with pseudo-first-order reaction kinetics.



**FIGURE 2** Effect of temperature and residence time on the conversion of CB. The mass fraction of  $\text{H}_2\text{SO}_4 = 95\%$ , molar ratio of  $\text{HNO}_3$  to CB = 1.3,  $Q_{\text{or}} = 0.4$  mL/min, and  $Q_{\text{ac}} = 0.9$  mL/min

It is worth mentioning that DNCB is an undesirable byproduct, and to obtain accurate kinetic data for the nitration of CB, the selectivity of DNCB needs to be controlled to a low level. The selectivity of each CB nitration product was investigated as a function of the reaction temperature, as shown in **Figure 3**. As the temperature and residence time increased, NCB was further nitrated to form DNCB, resulting in an increase in the selectivity of DNCB. However, at the low temperature used in this work and with the short residence time, the selectivity of DNCB remained below 1%. In addition, lowering the temperature had a more obvious inhibitory effect than shortening the residence time on the formation of DNCB. Therefore, the formation of DNCB had a negligible effect on the accuracy of the primary CB nitration kinetic data. When substituents are introduced on the benzene ring, the nitration difficulty will change. For example, in the tertiary nitration of CB, because the introduced nitro functional group is an electron-withdrawing group, the electron cloud density of the benzene ring decreases, and a certain steric hindrance is generated, making nitration more difficult. Therefore, no 1-chloro-2,4,6-trinitrobenzene was detected after reaction.



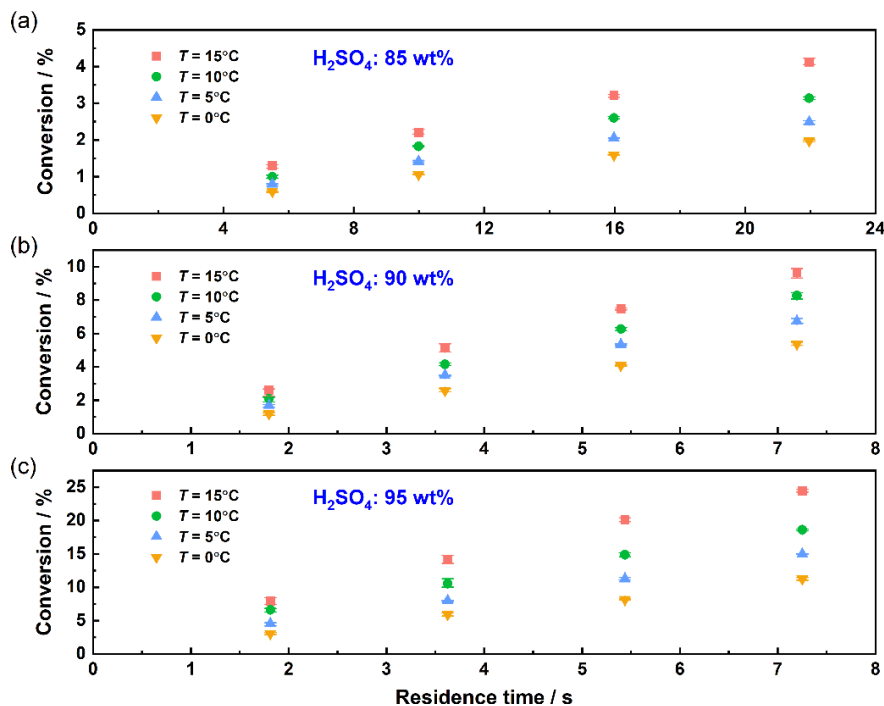
**FIGURE 3** Effect of temperature on the selectivity of (a) DNCB and (b) NCB. The mass fraction of  $\text{H}_2\text{SO}_4 = 95\%$ , molar ratio of  $\text{HNO}_3$  to CB = 1.3,  $Q_{\text{or}} = 0.4$  mL/min, and  $Q_{\text{ac}} = 0.9$  mL/min

**Figure 3b** shows the effect of temperature on the selectivity of NCB. The selectivity of *o*-NCB increased slightly with increasing temperature, while the selectivity of *p*-NCB decreased. This was due to the difference in the activation energy of the parallel reactions generating these two isomers, which resulted in the two reactions exhibiting different sensitivities to temperature. Specific results will be discussed in Section 3.5.2.

Under the experimental conditions, the selectivity of *m*-NCB ranged from 1 with that reported by Chen et al.<sup>19</sup> Generally, electron-donating groups are ortho- and para-positioning groups, and electron-withdrawing groups are meta-positioning groups; however, halogen is an exception. The electronegativity of halogen atoms is larger than that of carbon atoms. Considering the induction effect, halogen is a strong electron-withdrawing and passivating group and reduces the electron cloud density of the benzene ring. However, due to the conjugation effect of unshared electron pairs in halogen atoms, the relative stability of ortho- and para-  $\sigma$  complexes is enhanced. However, when attacks the meta position, the conjugation effect is not observed. Therefore, halogen is an ortho- and para-positioning group. It is worth noting that the continuous-flow microreactor system provides an excellent heat transfer rate and precise temperature control, and the selectivity of each primary nitration product did not vary much with the residence time.

### 3.3 Effect of sulfuric acid concentration

Numerous related studies<sup>19,26,27</sup> have shown that the rate of nitration is strongly related to the concentration of sulfuric acid. Within a certain range, the higher the concentration of sulfuric acid is, the faster the rate of aromatic nitration. The effect of the mass fraction of sulfuric acid (85~95 wt%) on CB conversion was investigated, as shown in **Figure 4**. When the temperature was 15 °C and the mass fraction of sulfuric acid was 95%, the conversion of CB reached 25% in less than 8 s. When the mass fraction of sulfuric acid was 90%, the conversion of CB was less than 10% under the same conditions. For the lower sulfuric acid concentration (85 wt%), when the residence time was 22 s, the reaction conversion was less than 5%, indicating that the reaction rate was greatly reduced. As shown in **Scheme 1**, sulfuric acid provides the necessary environment for the generation of  $\text{NO}_2^+$ . The experimental results of Deno<sup>28</sup> and Marziano<sup>29</sup> showed that as the mass fraction of sulfuric acid was reduced below 90%, the proportion of  $\text{NO}_2^+$  in nitric acid decreases exponentially, resulting in a decrease in the amount of the effective nitration agent and a significant reduction in the reaction rate. Variation in the concentration of  $\text{NO}_2^+$  in the mixed acid will be discussed in Section 3.5.2.



**FIGURE 4** Effect of the mass fraction of H<sub>2</sub>SO<sub>4</sub> on the conversion of CB. The mass fraction of H<sub>2</sub>SO<sub>4</sub> was (a) 95%; (b) 90% and (c) 85%. Molar ratio of HNO<sub>3</sub> to CB = 1.3,  $Q_{or}$  = 0.4 mL/min, and  $Q_{ac}$  = 0.9 mL/min



### 3.4 The observed reaction rate constant

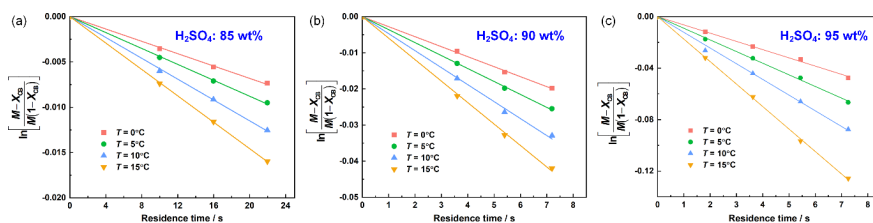
Most aromatic nitration processes in mixed acids are liquid-liquid heterogeneous processes. Because decoupling the reaction from mass transfer is very difficult, these reactions are usually regarded as pseudo-homogeneous in kinetic studies.<sup>30</sup> In this work, solution 1 is a solution formed by the addition of a small amount of CB to sulfuric acid, and the nitration of CB can be regarded as quasi-homogeneous.<sup>18,31</sup> The reaction follows second-order kinetics, which has been widely accepted with respect to aromatic nitration, with CB and nitric acid following first-order kinetics.<sup>3,21</sup> Therefore, the rate of nitration can be expressed in terms of the concentration of the reactants as follows:

where  $k_{\text{obs}}$  is the observed second-order rate constant and  $C_{\text{CB}}$  and  $C_{\text{HNO}_3}$  are the concentrations of CB and nitric acid in solution, respectively. Equation (7) can be described as follows by considering the initial concentration and conversion of CB:

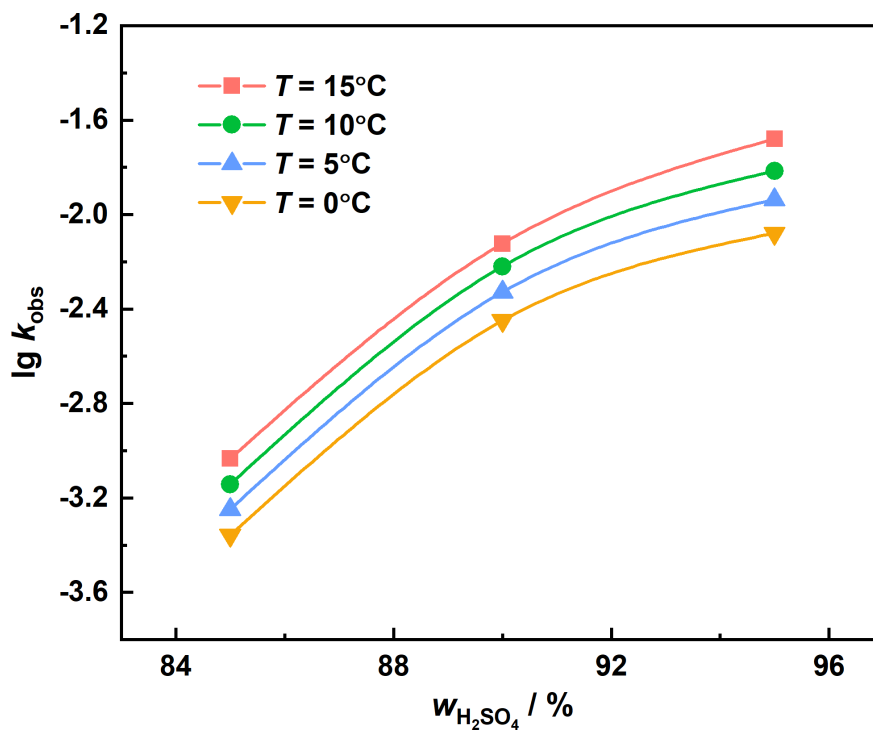
where  $C_{\text{CB},0}$  and  $C_{\text{HNO}_3,0}$  are the initial concentrations of CB and nitric acid, respectively. Under homogeneous conditions, the reaction rate of CB nitration can be described by the following equation:<sup>27</sup>

By integrating Equations (8) and (9), we obtain:

Therefore, a plot of  $\ln \left[ \frac{M - X_{\text{CB}}}{M(1 - X_{\text{CB}})} \right]$  vs. residence time ( $t$ ) should be a straight line passing through the origin with a slope equal to  $k_{\text{obs}}$ . The observed second-order rate constants can be calculated from the slope. The observed reaction rate constants at four temperatures (0, 5, 10 and 15 °C) and three sulfuric acid mass fractions (85, 90 and 95 wt%) were investigated. As shown in **Figure 5**, the fitting curve exhibited good linearity, which is in accordance with the hypothesis that the reaction is a second-order reaction. Plots of  $k_{\text{obs}}$  versus temperature and sulfuric acid concentration are shown in **Figure 6**. The observed rate constant increases with increasing temperature and sulfuric acid concentration, which is consistent with the trends observed for CB conversion discussed in Section 3.3. The values of  $k_{\text{obs}}$  at different temperature and sulfuric acid concentration are shown in **Table 1**.



**FIGURE 5** Determination of the observed reaction rate constants with H<sub>2</sub>SO<sub>4</sub> mass fractions of (a) 85 wt%; (b) 90 wt% and (c) 95 wt%. Molar ratio of HNO<sub>3</sub> to CB = 1.3,  $Q_{\text{or}} = 0.4$  mL/min, and  $Q_{\text{ac}} = 0.9$  mL/min



**FIGURE 6** Variation in  $k_{\text{obs}}$  with  $\text{H}_2\text{SO}_4$  mass fraction at different temperatures

**TABLE 1** Values of  $k_{\text{obs}}$  for different  $\text{H}_2\text{SO}_4$  mass fractions and at different temperature

Mass fraction of $\text{H}_2\text{SO}_4$ (wt%)	$T$ ( $^{\circ}\text{C}$ )	$k_{\text{obs}} \times 10^3$ ( $\text{L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$ )
85	0	$0.439 \pm 0.020$
	5	$0.564 \pm 0.023$
	10	$0.721 \pm 0.025$
	15	$0.926 \pm 0.017$
90	0	$3.558 \pm 0.141$
	5	$4.701 \pm 0.141$
	10	$6.036 \pm 0.347$
	15	$7.539 \pm 0.295$
95	0	$8.339 \pm 0.037$
	5	$11.57 \pm 0.041$
	10	$15.32 \pm 0.078$
	15	$20.95 \pm 0.038$

### 3.5 The rate constant based on

The observed reaction rate constant cannot explain the relationship between the reaction rate and sulfuric acid concentration very well. Therefore, it is necessary to study the rate constant based on . Extensive studies have shown that the rate-determining step for homogeneous aromatic nitration in mixed acids is the attack of nitrate ions on the aromatics, and the reaction rate can be expressed by the concentration of CB and nitronium ions as follows:<sup>3,32</sup>

where is the observed rate constant expressed for , and is the concentration.

Based on the Brønsted-Bjerrum rate law (transition-state theory),<sup>33,34</sup> the nitration rate can be expressed as follows:

where  $k^*$  is the rate constant based on and  $\gamma$ , and  $\gamma^*$  are the activity coefficients for CB, nitronium ions and the transition-state intermediate, respectively.

The value of the activity coefficient is not easy to obtain. To calculate the  $pK_a$  of weak bases in a study of acid-base equilibrium, Marziano et al.<sup>26,34</sup> introduced the activity coefficient function  $M_c$  to describe the change in the activity coefficient with acid strength:

where  $n$  is a thermodynamic parameter related to the type of aromatic compounds. The  $M_c$  for sulfuric acid represents a general scale describing its acidity, and its value depends only on the concentration of sulfuric acid at a given temperature. Therefore, the value corresponding to describes the variation in the activity coefficient ratio of Equation (12) as a function of the sulfuric acid concentration, and the effective concentration of the reactant is taken into consideration.

Combining Equations (7) and (13), the relationship between  $k^*$  and  $k_{obs}$  can be expressed as follows:

Taking the logarithm of Equation (14), we obtain:

Therefore, taking as the ordinate and  $M_c$  as the abscissa, the values of  $n$  and  $k^*$  can be obtained by the slope and intercept of the resulting straight line. However, before this can be done, the values of  $M_c$  and need to be determined.

### 3.5.1 $M_c$

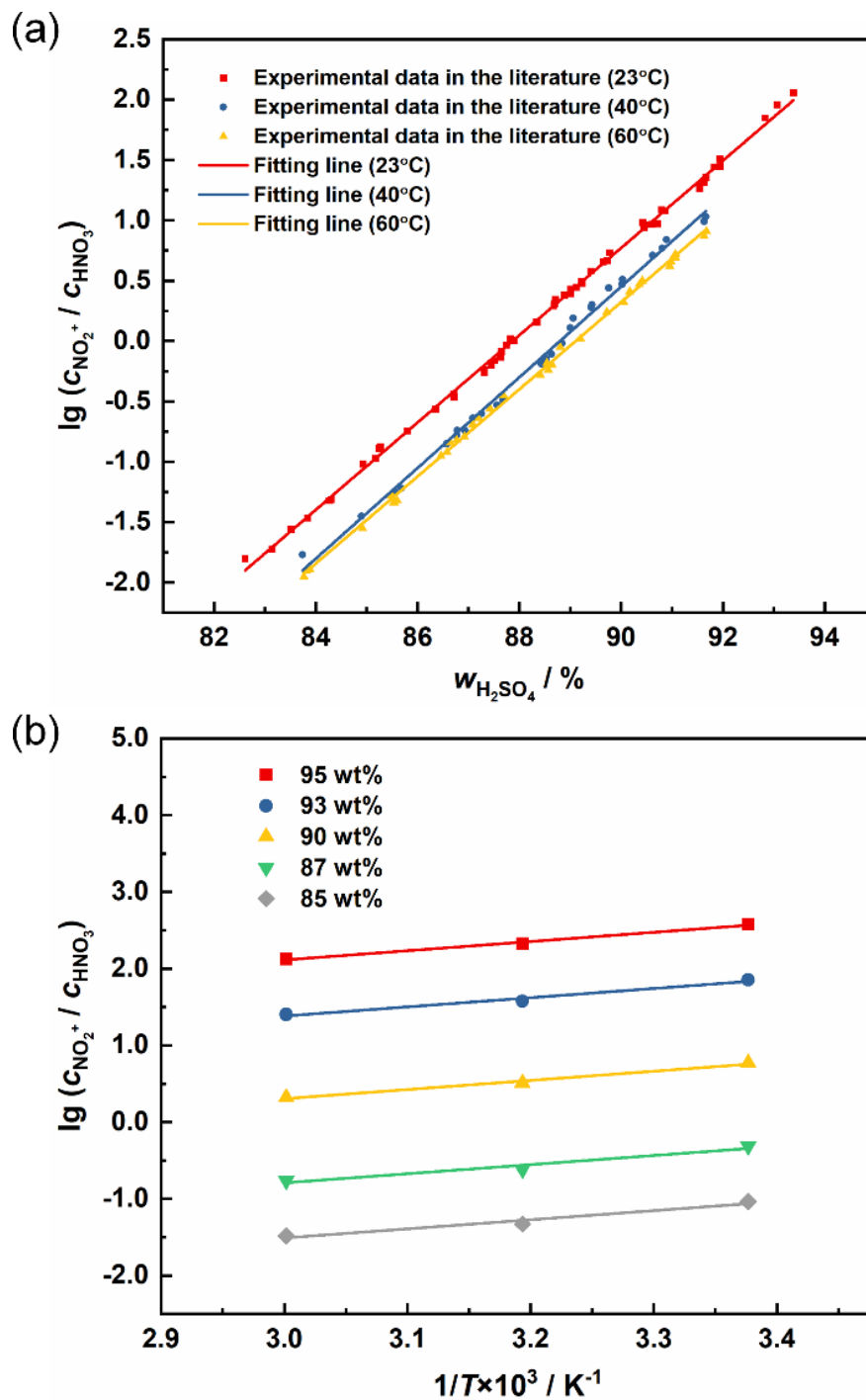
The value of  $M_c$  is related to temperature and the sulfuric acid concentration. Marziano et al.<sup>35</sup> predicted the values of  $M_c$  at different sulfuric acid concentrations using experimental acid-base equilibrium data. By fitting the predicted data, Equation (16), in which the sulfuric acid concentration is a variable, can be obtained at a given temperature, and the applicable sulfuric acid concentration range is 15.2~18.4 kmol/m<sup>3</sup>. A plot of  $M_c$  versus sulfuric acid concentration is shown in the Supporting Information (**Figure S4**).

An equation describing  $M_c$  as a function of temperature was proposed in another work by Marziano:<sup>36</sup>

### 3.5.2

In the nitration process, nitro groups are introduced into the nitrified compound. The essence of this process is realized by the mutual transfer of nitrating agents and nitrified compounds under certain conditions. A nitrating agent is a macroscopic concept, and there are numerous ions and groups in its system. For instance, there are  $HNO_3$ , and unionized, molecular nitric acid in mixed acids.<sup>37-39</sup> It can be seen from the structural formula of nitric acid that the most easily broken bonds are the H-O bond and N-O bond, by which  $H^+$  and are generated via acidic ionization and basic ionization, respectively. Sulfuric acid is referred to as a nitration activator. It has a greater acidity than nitric acid and can donate protons to nitric acid, resulting in further basic ionization of nitric acid and the formation of  $H_2NO_2^+$ . Therefore, a nitrating agent composed of nitric acid and sulfuric acid is a much stronger nitrating agent than nitric acid alone and is more applicable in industrial production.

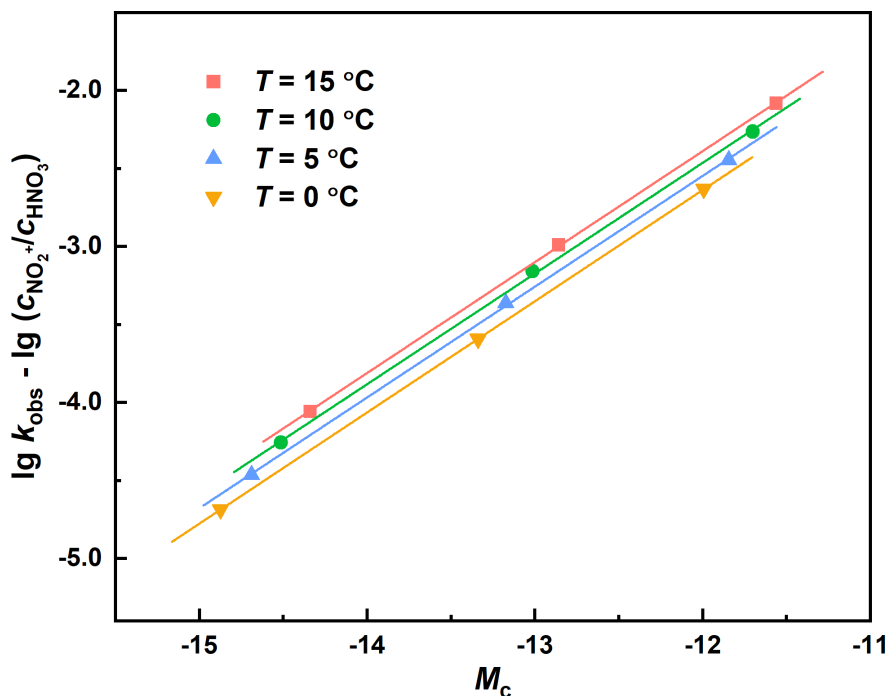
Since  $HNO_3$  is the substance that actually plays a role in nitration,<sup>4</sup> an accurate estimation of its concentration is crucial to understanding the underlying reaction mechanism and kinetics. The concentration of molecules and ions in nitric acid and aqueous sulfuric acid has been extensively studied by various spectroscopy techniques, such as Raman,<sup>28,40</sup> UV<sup>29,41</sup> and NMR<sup>42</sup> spectroscopy. Several studies<sup>28,36,42</sup> have reported values at different temperatures (mainly 23, 40, and 60 °C) and sulfuric acid concentrations. A plot of versus the mass fraction of sulfuric acid was prepared by summarizing these data. The fitting curve exhibited a good linear correlation, as shown in **Figure 7a**. According to the fitted model, the values of within the investigated sulfuric acid concentration range (85~95 wt%) can be calculated at temperatures of 23, 40 and 60 °C. By plotting versus  $1/T$ , a series of straight lines at different sulfuric acid concentrations can be obtained, as shown in **Figure 7b**. In this way, equilibrium data for nitric acid in a sulfuric acid solution can be obtained at other temperatures.



**FIGURE 7** Variations and fitting of as a function of (a) the mass fraction of sulfuric acid at 23, 40 and 60 °C; (b)  $1/T$  at different sulfuric acid concentrations

Based on the above analysis, the value of  $n$  can be calculated. A plot of  $\lg k^*$  versus  $M_c$  is shown in **Figure 8**. At all temperatures, the experimental data fit well to the resulting straight line. The values of  $n$  and  $\lg k^*$  can be obtained from the slope and intercept of the fitting line, respectively, as shown in **Table 2**. The value of

$k^*$  increases with increasing temperature, and the value of  $n$  remains essentially unchanged.  $n$  is a specific thermodynamic parameter that is characteristic of different aromatic compounds, which is consistent with the conclusions reported in other studies.<sup>18,19,27</sup>



**FIGURE 8** Determination of the reaction rate constants  $n$  and  $k^*$  at different temperatures

**TABLE 2** Values of  $n$  and  $\lg k^*$  at different temperatures

$T$ ( $^{\circ}\text{C}$ )	$n$	$\lg k^*$
0	$0.713 \pm 0.007$	$5.902 \pm 0.096$
5	$0.711 \pm 0.061$	$5.979 \pm 0.808$
10	$0.710 \pm 0.089$	$6.055 \pm 0.163$
15	$0.712 \pm 0.036$	$6.151 \pm 0.473$

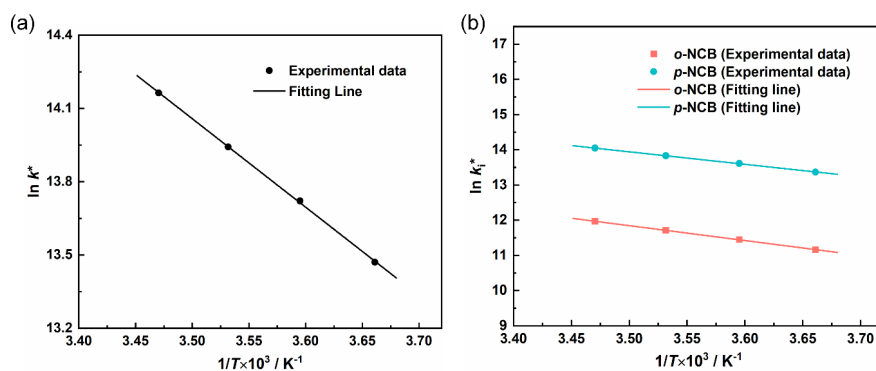
Considering the values of  $k^*$  at different temperatures, the activation energy ( $E_a$ ) corresponding to the electrophilic attack of on CB molecules can be determined according to the Arrhenius equation:

where  $A$  is the pre-exponential factor ( $\text{L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$ ),  $E_a$  is the activation energy ( $\text{J}/\text{mol}$ ),  $R$  is the universal gas constant ( $8.314 \text{ J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$ ), and  $T$  is the reaction temperature ( $\text{K}$ ). Taking the logarithm of Equation (18), we obtain:

A plot of  $-\ln k^*$  versus  $1/T$  is shown in **Figure 9a**. The data are in good agreement with the fitting line. From the slope of the straight line,  $E_a$  for CB nitration was calculated to be  $30.11 \pm 1.68 \text{ kJ}/\text{mol}$ . As mentioned in Section 3.2, under the experimental conditions investigated, the yields of  $m$ -NCB and DNCB were both less than 1 could be concluded that there were only two parallel reactions that generated  $o$ -NCB and  $p$ -NCB. The rate equation for the parallel reactions is given by Equation (20). According to the definition of reaction selectivity, the ratio of the rate constants for the two parallel reactions is equal to the ratio of their respective selectivity.

In the above equations,  $r_i$  and  $S_i$  are the reaction rate and selectivity, respectively, and subscript  $i$  represents either  $o$ -NCB or  $p$ -NCB.

The selectivity of the two products at the investigated temperature is shown in **Figure 3**. The experimental results also indicated that the selectivity of  $o$ -NCB and  $p$ -NCB did not change much with the sulfuric acid concentration. Given the rate constant of the overall reaction and the selectivity of the products, the rate constants of the two parallel reactions can be calculated. The activation energies for  $o$ -NCB and  $p$ -NCB were calculated to be  $35.12 \pm 1.79$  kJ/mol and  $29.52 \pm 1.02$  kJ/mol, respectively, according to the Arrhenius equation (**Figure 9b**). The greater activation energy for  $o$ -NCB indicates that the molecule needs to cross a higher energy barrier to transform from its normal state into the active state prone to reaction, and an increase in temperature improves the selectivity of this reaction. It can be verified by the data in **Figure 3b** that as the temperature increases, the selectivity of  $o$ -NCB increases, while the selectivity of  $p$ -NCB decreases.



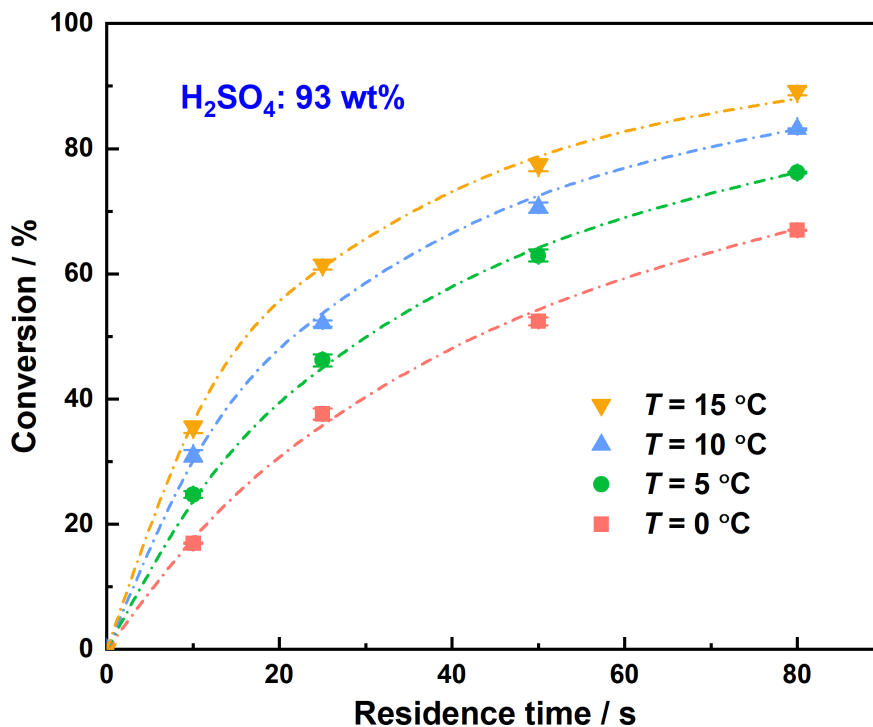
**FIGURE 9** Arrhenius plots of (a)  $\ln k^*$  and (b)  $\ln k_i^*$  versus  $1/T$

### 3.6 Verification of the reaction kinetics model

From Equations (11) and (13), the calculated values of the observed rate constant expressed for can be obtained:

From Equations (7) and (11), the experimental values of can also be obtained:

A comparison of the calculated and experimental values of at different temperatures and different sulfuric acid concentrations is provided in Table S1. These two values are very close. Furthermore, the effectiveness of the kinetic model in predicting the nitration of CB was verified by a series of experiments, as shown in **Figure 10**. The mass fraction of sulfuric acid was changed to 93%, and the conversion of CB was investigated at different temperatures. Under both the conditions of a short residence time (low conversion) and a long residence time (high conversion), the experimental results of CB conversion are in good agreement with the values predicted by the model, indicating that even if the concentration of sulfuric acid changes, the model can still predict the kinetic parameters for CB nitration.



**FIGURE 10** Comparison of the experimental (data points) and predicted (dotted lines) values for CB conversion at different temperatures. The mass fraction of  $\text{H}_2\text{SO}_4 = 93\%$ ,  $Q_{\text{or}} = 0.4 \text{ mL/min}$ , and  $Q_{\text{ac}} = 0.9 \text{ mL/min}$

#### 4. Conclusions

In this work, a continuous-flow microreactor system was proposed for the rapid and accurate measurement of CB nitration kinetics at high mixed acid concentrations. The influence of mass transfer between the two phases on the kinetic measurements was eliminated by dissolving CB in concentrated sulfuric acid, which allowed for a homogeneous reaction environment. The effects of temperature, residence time and sulfuric acid concentration on conversion and selectivity were systematically investigated, and it took only a few seconds to obtain a single data point. The results demonstrated that at the same residence time, the conversion of CB and the selectivity of *o*-NCB increased slightly with increasing reaction temperature (from 0 to 15 °C), while the selectivity of *p*-NCB slightly decreased. The selectivity of *m*-NCB ranged from 1rate and accurate temperature control realized in the microreactor system, the selectivity of each nitration product did not change much with changes in the residence time. Similar to the nitration of other aromatic compounds, the nitration of CB is a second-order reaction, with both CB and nitric acid exhibiting first-order kinetics. Based on conversion data obtained at different times, a kinetic model was established to obtain the observed reaction rate constants. The results showed that the nitration rate was highly related to temperature and the sulfuric acid concentration. As the temperature increased,  $k_{\text{obs}}$  increased; at the same temperature, as the mass fraction of sulfuric acid increased from 85% to 95%,  $k_{\text{obs}}$  increased by more than 1 order of magnitude. To explain the relationship between the reaction rate and sulfuric acid concentration, a polynomial equation describing  $M_c$  as a function of sulfuric acid concentration was fitted. The essence of the homogeneous nitration of aromatics in mixed acids involves the attack of on the aromatics. By summarizing data reported in the literature, a prediction model for concentration as a function of sulfuric acid concentration and temperature was established. Based on the above analysis, the reaction rate parameters based on were obtained. With increasing temperature, the value of  $k^*$  increased.  $n$  is a specific thermodynamic parameter that is characteristic of different aromatic compounds and was approximately 0.71 in this work.  $E_a$  for CB nitration was  $30.11 \pm 1.68 \text{ kJ/mol}$ , and  $E_a$  for *o*-NCB and *p*-NCB was  $35.12 \pm 1.79 \text{ kJ/mol}$  and  $29.52 \pm$

1.02 kJ/mol, respectively, indicating that *o*-NCB was more sensitive to the reaction temperature. Finally, at a sulfuric acid mass fraction of 93%, the kinetic model was used to predict the reaction performance. The experimental results were in good agreement with the values predicted by the model, indicating that the model is of crucial theoretical significance and practical value for optimizing the reactor design and understanding nitration processes in-depth. We envisage that the kinetics-based study of other fast and highly exothermic reactions is possible with this continuous-flow microreactor system. In our future work, more kinetics studies on nitration will be carried out.

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