



Heterogeneous toluene nitration with mixed acid in microreactors: Reaction regime, characteristics and kinetic models

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ABSTRACT

It is critical for reactor design and process safety to determine the reaction kinetics for toluene nitration. Herein, a continuous-flow platform based on capillary microreactors was established. First, reaction regimes for toluene nitration and its consecutive side reaction (MNT (mononitrotoluene) nitration) were identified. On this basis, the influence of process parameters on conversion of toluene, selectivity of MNT and DNT (dinitrotoluene) and their isomer distribution were meticulously examined, including molar ratio of reactants, sulfuric acid strength, reaction temperature, and residence time. Subsequently, reaction kinetic models coupled with mass transfer were developed, allowing the simultaneous kinetic determination for toluene nitration and MNT nitration. It was found that the logarithm of the observed kinetic constant is proportional to the sulfuric acid strength. The kinetic parameters under 72.7 to 80.1 wt% sulfuric acid strengths were obtained. The outcomes provide a basis for process intensification and optimization of toluene nitration as well as other similar aromatics.

1. Introduction

Nitroaromatic compounds are vital organic intermediates extensively utilized in various industries, including dyes, perfumes, pharmaceuticals, explosives, and pesticides (Kulkarni, 2014; Patel et al., 2021). Mononitrotoluene (MNT) is one of the most representative nitroaromatic compounds. In industry, MNT is produced by the mononitration of toluene with mixed acid as the nitrating agent. As shown in Scheme 1, the product MNT includes three isomers, which can be further nitrated to dinitrotoluene (DNT, mainly 2,4-DNT and 2,6-DNT). Furthermore, the reaction is strongly exothermic with a reaction enthalpy of up to 150 kJ/mol (Chen et al., 2008; Wang et al., 2023). To control the product selectivity and process safety, it is usually carried out in multistage continuous stirred tank reactors with an effective heat transfer area typically in the range of 100 to 1000 m²/m³, where the mixed acid is slowly dripped into toluene (D'Angelo et al., 2003). There is an inherent high risk of safety issues due to long reaction time and large reactor volume. In addition, the uneven temperature/concentration distribution resulting from poor heat/mass transfer can lead to the formation of considerable amount of DNT and phenols, which increases the cost and waste disposal during product refinery (Afonso et al., 2018).

Therefore, there is urgent need to develop novel equipment and technology.

The microreaction technology has been widely applied in nitration, as well as other fast and highly exothermic reactions (Kulkarni, 2014; Li et al., 2018; Liu et al., 2023; Zhan et al., 2023). As the core equipment of the technology, microreactors exhibit significantly improved mass and heat transfer performance over conventional reactors, thanks to their small characteristic size (typically hundreds of micrometers) and large specific surface area (typically between 1,000 and 10 000 m²/m³, which is 1 to 2 orders of magnitude larger than that of conventional reactors). The excellent performance guarantees rapid fluid mixing and instant removal of reaction heat (Jensen, 2017; Wang et al., 2017; Yao et al., 2018). In this way, the product selectivity can be significantly elevated (Li et al., 2017). In addition, the smaller liquid hold-up volume in microreactors facilitates intrinsic safety. Recent applications of microreactors for toluene nitration are summarized in Table 1 (Fu et al., 2022; Song et al., 2022d; Yang et al., 2022). By analysis, it was found that the process conditions for obtaining simultaneously high toluene conversion and MNT selectivity with reference to DNT were generally either low temperature with high sulfuric acid strength or high temperature with low sulfuric acid strength. Under these operating conditions, the order of isomer distribution of MNT is generally 2-NT>4-NT>3-NT. And, we

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Nomenclature*Roman symbols*

φ	sulfuric acid strength, wt%
τ	residence time, s
δ	film thickness, m
ε	phase fraction of the reaction phase
μ	viscosity, mPa·s
ρ	density, kg/m ³
Φ	Association factors

Letters

2-NT	2-nitrotoluene
3-NT	3-nitrotoluene
4-NT	4-nitrotoluene
2,6-DNT	2,6-dinitrotoluene
2,4-DNT	2,4-dinitrotoluene
a	interfacial area, m ² /m ³
A	pre-exponential factor, L/mol/s
c	molar concentration, mol/L
d	droplet size, mm
d_i	the inner diameters of the microchanne, mm
D	diffusivity, m ² /s
DNT	dinitrotoluene
E_a	activation energy, kJ/mol
f	the relative mass correction factor
Ha	Hatta number
I_i	the distributions of the isomers of MNT and DNT
k	second-order reaction rate constants, L/mol/s
k_L	mass transfer coefficient, m/s

M	molecular weight, g/mol
MNT	mononitrotoluene
n	mole
N	HNO ₃
Q	the volumetric flow, mL/min
R	gas constant, J/mol/K
Re_M	Mean Reynolds number of two phase
S	selectivity, %
Sc	Schmidt number of sulfuric acid phase
Sh	Sherwood number
T	reaction temperature, °C
v	flow velocity, cm/s
v_m	the molecular volume at normal boiling point, m ³ /mol
V_R	the volume of the coiled capillary microreactors, mL
w	mass fraction
x	mole fraction
X	conversion of toluene, %
Y	yield, %

Subscripts

aq	aqueous phase (mixed acid phase)
MA	mixed acid
or	organic phase
S	sulfuric acid
T	toluene
W	water

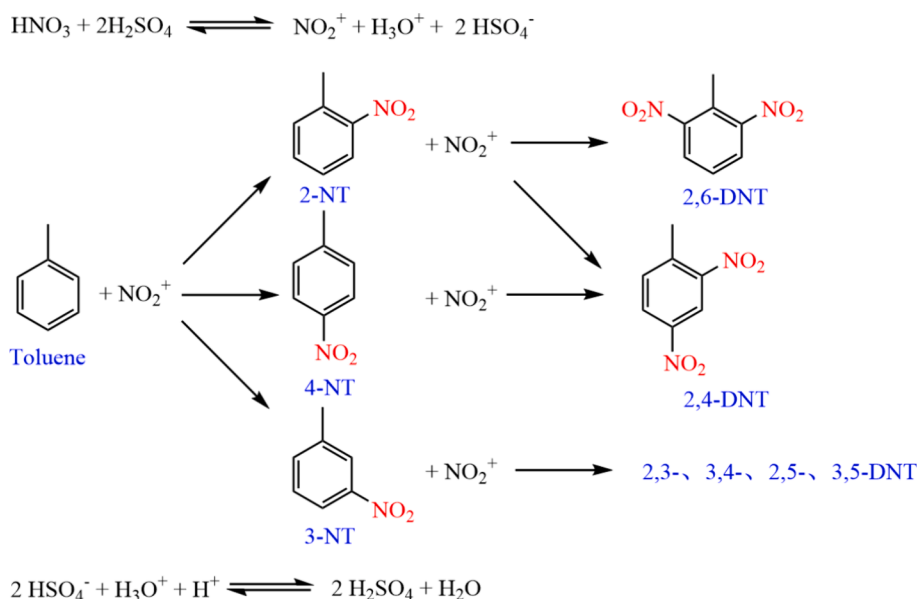
Superscripts

*	saturation solubility, mmol/ L
0	initial concentration, mol/ L

note that the latter case has a higher selectivity for MNT than the former. In addition, Song et al. (Song et al., 2022d) found that with low sulfuric acid strengths, at a conversion of about 75 %, continuing to prolong the residence time resulted in little or no increase in the conversion, albeit at a high temperature of 100 °C. This was due to the fact that the water produced by the reaction diluted the sulfuric acid, causing a significant decrease in the nitration capacity of the mixed acid. To solve this problem, they used a second feed of mixed acid to increase the sulfuric

acid strength and molar ratio of HNO₃ to toluene, allowing the reaction to be continued, but this significantly increased the burden of waste acid disposal. All in all, the existing process development for toluene nitration in microreactors is mainly focused on process parameter optimization and lacks fundamental studies on the heterogeneous reaction regime of toluene nitration in microreactors and the kinetics with coupled mass transfer.

The advantages of the microreactor also make it an efficient platform



Scheme 1. Nitration of toluene with mixed acid.

Table 1

Recent studies on nitration of toluene in microreactors.

References	φ / wt%	N/T	T / °C	τ / s	X_T / %	S_{MNT} / %
(Yang et al., 2022)	77.8	1.3	48.8	164.8	85.0	91.3
(Fu et al., 2022)	75.9	1.2	45.0	132.0	86.0	95.0
(Song et al., 2022d)	70.0	2.4 ^a	100.0	90.0	98.7	97.3

a: two stage feed with N/T=1.2 each stage.

for the determination of kinetics of the nitration reaction (Yan et al., 2022). Overall, the determination of the kinetics of the nitration reaction in microreactors is mainly divided into two methods: homogeneous and heterogeneous. For homogeneous nitration reaction kinetics, aromatic compounds, e.g., chlorobenzene (Cui et al., 2022), 2-nitrotoluene (Song et al., 2022a), 4-nitrotoluene (Song et al., 2022b), were dissolved in concentrated sulfuric acid and mixed with the mixed acid in a micromixer. By precise adjustment of the residence time of the reactants and rapid quenching of the reaction, the kinetics of the nitration reaction were precisely determined. Most of these aromatic compounds have relatively weak reactivity (generally with electron-withdrawing groups) and have a certain solubility in concentrated sulfuric acid. For heterogeneous reaction kinetics, where the reactants are in two different phases, the mass transfer rate can have an effect on the overall reaction rate. It utilizes the uniform, stable flow pattern and the fast mass transfer rate to control the reaction regime to a very slow reaction in order to eliminate the effect of mass transfer on the kinetic measurements, e.g., trifluoromethoxybenzene (Wen et al., 2018), 3-[2-chloro-4-(trifluoromethyl) phenoxy] benzoic acid (Li et al., 2022), nitrobenzene (Jin et al., 2023). However, for activated aromatic compounds such as toluene with electron-donating groups, the reactivity is very high and the intrinsic reaction rate of the nitration reaction is very fast, especially at relatively high sulfuric acid strengths, which makes it challenging to accurately determine the kinetics. Recently, Song et al. (Song et al., 2023) investigated the heterogeneous phase kinetics of toluene at sulfuric acid strengths in the range of 65 to 67.5 wt% by controlling the reaction to a very slow reaction regime. However, there is still a lack of studies on the reaction regime in the range of sulfuric acid strengths of 70 ~ 80 wt%, as well as the relation between kinetics parameters and sulfuric acid strength. This is crucial for the process design, intensification and safety evaluation (Zhang et al., 2023a; Zhang et al., 2023b).

In this work, we developed a capillary microreactor-based continuous-flow platform to determine of the kinetics of heterogeneous nitration of toluene with mixed acid. First, we determined the heterogeneous reaction regimes of toluene nitration and its consecutive side reaction MNT nitration. Then, the effects of various process parameters on the conversion of toluene and selectivity of MNT and DNT and their isomer distribution were thoroughly explored, such as molar ratio of nitric acid to toluene, sulfuric acid strength, reaction temperature, and residence time. A heterogeneous reaction kinetic model coupled with mass transfer was established based on different heterogeneous reaction regimes and the kinetic parameters under 72.7 to 80.1 wt% sulfuric acid strengths were obtained for both toluene nitration and MNT nitration. Ha numbers were calculated to validate the reaction regime of nitration of toluene and MNT. It was found that the logarithm of the observed kinetic constant is proportional to the sulfuric acid strength and a comparison with the literature also showed the reliability of our results.

2. Material and methods

2.1. Chemicals

Toluene (99.5 %) was purchased from Sinopharm Chemical Reagent Co., Ltd. 2-nitrotoluene (99.5 %), 3-nitrotoluene (99.5 %), 4-nitrotoluene (99.5 %), and nitrobenzene (99 %) were supplied by Shanghai Macklin Biochemical Co., Ltd. 2,4-DNT (99 %) and 2,6-DNT (98 %) were provided by Shanghai Aladdin Bio-Chem Technology Co., Ltd. Sulfuric

acid (98 %), fuming nitric acid (95 %), and dichloromethane (99.5 %) were obtained from Xilong Scientific Co., Ltd, Guangzhou Chemical Reagent Co., Ltd, and Damao Chemical Reagent Co., Ltd, respectively. All chemicals were used without any further purification.

2.2. Experimental setup and procedure

As depicted in Fig. 1, the microreactor system utilized two high-pressure syringe pumps (Fusion 6000, CHEMYX) to deliver toluene and mixed acid ($n_{HNO_3} : n_{H_2SO_4} = 1 : 5$) to pretreatment coiled capillaries (316 stainless steel, $\Phi 1.6 \times 0.4$ mm) and two check valves were employed to prevent backflow of reactants. Then, the two reactants were merged in a micromixer (316 stainless steel, 0.5 mm bore, VICI) and introduced into the coiled capillary microreactors (316 stainless steel, $\Phi 1.6 \times 0.4$ mm) with an effective heat transfer area of $2500 \text{ m}^2/\text{m}^3$ to initiate the reaction. Three three-way ball valves (316 stainless steel, 1.32 mm bore, flow path length 2 cm, CIR-LOK) were incorporated into the capillary microreactors to regulate the flow direction of the reactants, thus allowing adjustment of the reaction residence times. The length of the capillary microreactor between every two ball valves is 100 cm. The pretreatment coiled capillaries, micromixer, coiled capillary microreactors and three-way ball valves were all immersed in a thermostatic water bath (F25, Julabo) to obtain a uniform temperature. At the outlets, 10 ml sampling tubes filled with iced water were used to quench the reaction by diluting the mixed acid and collect the reaction products. Following the separation of the organic phase and diluted mixed acid, dichloromethane was used to extract a small quantity of dissolved organic matter from the diluted mixed acid under low temperature conditions. After vigorous shaking and layering, the diluted mixed acid was removed, and the organic phase was washed with deionized water to remove residual acid. Finally, the composition of the samples was determined using gas chromatography (GC-7890B, Agilent, Column: HP5, 30 m \times 0.32 mm \times 0.25 μm) with a flame ionization detector.

2.3. Analysis method

The samples were analyzed using gas chromatography with the following conditions: nitrogen was used as the carrier gas, the injection temperature was set to 260 °C, the column temperature was ramped from 40 to 180 °C at a rate of 10 °C/min, and the detector temperature was set to 300 °C. The sampling volume for all analyses was 0.5 μL . The typical retention times of the reactant and products under these conditions are shown in Table S1. The composition of the samples was quantified using corrected area normalization method, and the standard working curve and relative mass correction factors are shown in Fig. S1 and Table S1. All the samples were analyzed at least twice, and the average relative errors of replicates were both less than 5 %.

The conversion of toluene is calculated by Eq. (1):

$$X_T = 1 - \frac{w_T/M_T}{\sum_i^n (w_i/M_i)} \quad (1)$$

where subscripts i and T denote the components, including the reactants and products, and toluene, respectively. w and M represent mass fraction and molecular weight of substance in the sample, respectively. X_T is the conversion of toluene.

The selectivity of each product is calculated by Eq. (2):

$$S_i = \frac{w_i/M_i}{\sum_i^n (w_i/M_i) - w_T/M_T} \quad (2)$$

where S_i is the selectivity of products. And the overall selectivity and yield of MNT and DNT are defined as Eq. (3), (4), (5) and (6), respectively.

$$S_{MNT} = S_{2-NT} + S_{3-NT} + S_{4-NT} \quad (3)$$

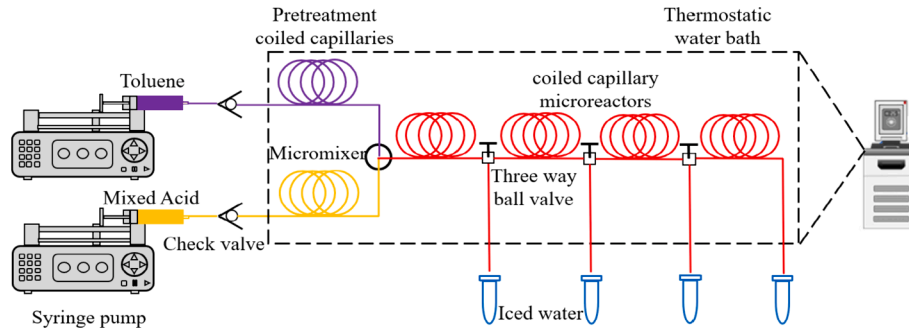


Fig. 1. Schematic diagram of the experimental setup.

$$S_{\text{DNT}} = S_{2,4\text{-DNT}} + S_{2,6\text{-DNT}} \quad (4)$$

$$Y_{\text{MNT}} = X_{\text{T}} S_{\text{MNT}} \quad (5)$$

$$Y_{\text{DNT}} = X_{\text{T}} S_{\text{DNT}} \quad (6)$$

In addition, isomer distributions of the products are essential for calculating the kinetics of each isomer. The distributions of the MNT isomers and DNT isomers are defined by Eq. (7) and (8), respectively.

$$I_i = \frac{S_i}{S_{\text{MNT}}} (i = 2 - \text{NT}, 3 - \text{NT}, 4 - \text{NT}) \quad (7)$$

$$I_i = \frac{S_i}{S_{\text{DNT}}} (i = 2, 4 - \text{DNT}, 2, 6 - \text{DNT}) \quad (8)$$

The sulfuric acid strength is defined by the Eq. (9):

$$\varphi = \frac{w_s}{w_s + w_w} \quad (9)$$

where w_s and w_w are the respective mass fractions of sulfuric acid and water in the mixed acid.

The reaction residence time and phase ratio can be calculated by the Eqs. (10) and (11), respectively:

$$\tau = \frac{V_R}{Q_{\text{MA}} + Q_{\text{T}}} \quad (10)$$

$$q = \frac{Q_{\text{MA}}}{Q_{\text{T}}} \quad (11)$$

where V_R is the volume of the coiled capillary microreactors, τ is the reaction residence time, and q is phase ratio. Q_{MA} and Q_{T} are the volumetric flow rates of the mixed acid and toluene, respectively.

In this work, the ranges of operating conditions used for the experiments were as follows: molar ratio of nitric acid to toluene (N/T) from 0.8 to 1.6, sulfuric acid strength (φ) from 72.7 to 80.1 wt%, temperature (T) from 20 to 45 °C, and residence time from 15.2 to 52.5 s.

3. Theory of reaction kinetics coupled to mass transfer

Following the review of Bourne (Bourne, 2003), for a two-phase reaction of $A+B \rightarrow P$ with a second-order kinetics, the Hatta number (Ha) that indicates the ratio of the reaction rate to the mass transfer rate is defined by:

$$Ha = \frac{\sqrt{k D_B c_{A0}}}{k_L} \quad (12)$$

The range of the Ha number defines the regime and governing equations of reaction. The concentration profile in the vicinity of the fluid interface under different reaction regimes is sketched in Fig. 2 and the according kinetic expressions coupled to mass transfer are presented in detail in Table 2.

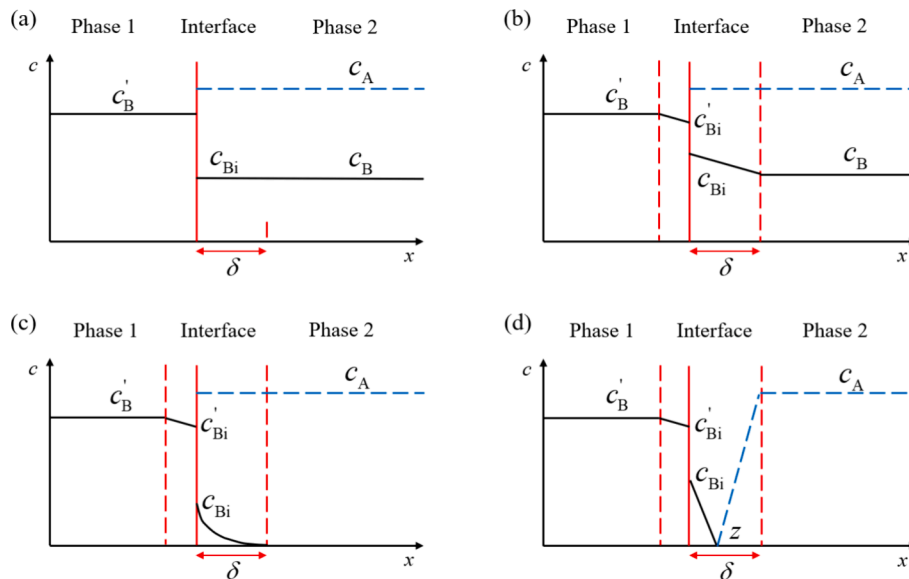


Fig. 2. The concentration profile in the vicinity of the fluid interface of different reaction regime: (a) very slow reaction; (b) slow reaction; (c) fast reaction; (d) instantaneous reaction.

Table 2

The kinetic expressions coupled to mass transfer and the recognition criteria for each reaction regime in the two-phase reaction system (Bourne, 2003).

Reaction regime	Basics equation	Recognition criteria
very slow reaction	$r = kc_A c_{Bi}$	$Ha < 0.3$
slow reaction	$r = \frac{c_B}{\frac{1}{k_L a} + \frac{1}{k c_A}}$	$0.3 < Ha < 3$
fast reaction	$r = ac_{Bi} \sqrt{k D_B c_A}$	$3 < Ha < \frac{1}{3} \left(\sqrt{\frac{D_B}{D_A}} + \frac{c_A}{2c_{Bi}} \sqrt{\frac{D_A}{D_B}} \right)$
instantaneous reaction	$r = k_L a c_{Bi} \left(1 + \frac{D_A c_A}{D_B c_{Bi}} \right)$	$Ha >> \frac{c_A}{c_{Bi}}$

4. Results and discussion

4.1. Reaction regime

Toluene nitration with mixed acid is a typical liquid–liquid heterogeneous reaction. As outlined in previous studies (Guo et al., 2023; Jin et al., 2023; Rahaman et al., 2009; Russo et al., 2019), the reaction process involves the transfer of toluene to the interface and the bulk of the acid phase, followed by its reaction with nitronium ion (NO_2^+) to

form σ -complexes, and finally deprotonation to produce MNT. Additionally, MNT can also participate in this reaction pathway to form DNT. However, due to the different nitration reactivities of toluene and MNT, they may exhibit distinct heterogeneous reaction regimes depending on the specific reactor conditions and operating parameters (Song et al., 2023; Zaldivar et al., 1995; Zaldivar et al., 1996).

In the experiment, we observed that the dispersed phase toluene was in the form of droplets at the outlet of capillary microreactor. It can be inferred that the flow state of the liquid–liquid two-phase system in the capillary microreactors is slug flow or droplet flow (Song et al., 2022c; Wen et al., 2018; Zhang et al., 2019). Increasing the flow velocity could increase the mass transfer coefficient (k_L) by enhancing the internal circulation of the droplets, thus facilitating the mass transfer rate between the two phases (Yao et al., 2020; Yao et al., 2021). Hence, in order to identify the reaction regime of nitration of toluene and MNT in the microreactors, experiments with different flow velocities at low (72.7 wt%) and high (80.1 wt%) sulfuric acid strengths were conducted. From Fig. 3(a) and (b), it can be seen that the conversion-time profile of toluene is almost unaffected by the flow rate both at low and high sulfuric acid strengths. At a sulfuric acid strength of 72.7 wt%, MNT was hardly further nitrated, whereas DNT, the product of nitration of MNT, was markedly detected at a sulfuric acid strength of 80.1 wt%. This is due to the electron-withdrawing effect of the nitro group, the nitration activity of MNT is weaker than that of toluene. As Fig. 3(c) shown, the

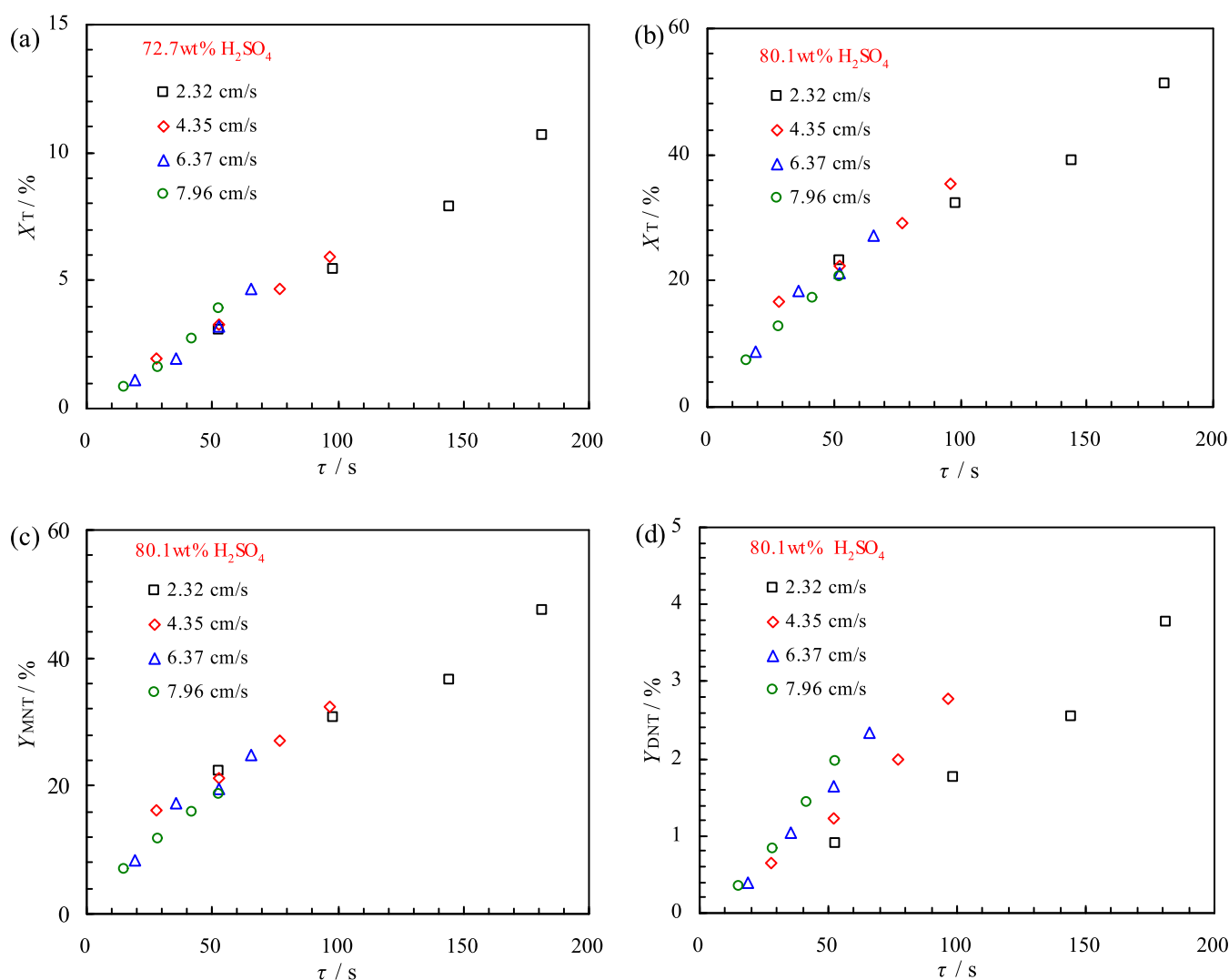


Fig. 3. Time profiles of conversion of toluene at (a) $\phi = 72.7$ wt%, (b) $\phi = 80.1$ wt%, and yield of (c) MNT and (d) DNT at $\phi = 80.1$ wt% at different flow velocities in capillary microreactors. ($N/T=1.05$, $T=30$ °C, $q = 3.9$ at $\phi = 72.7$ wt% and $q = 4.5$ at $\phi = 80.1$ wt%).

yield-time profile of MNT at 80.1 wt% sulfuric acid strength is not affected by flow rate. This is because the nitration of toluene to MNT is a fast reaction that occurs mainly at the two-phase interface. According to Table 2, the reaction rate of nitration of toluene to MNT is not affected by the k_L . However, Fig. 3(d) showed that the yield-time profile of DNT was affected by the flow velocity and when the flow velocity was increased to 6.37 cm/s, the effect was eliminated. This is because when the k_L increases with increasing flow velocity, the reaction regime for the nitration of MNT to DNT changes from a slow reaction that is affected by both the k_L and the reaction rate, to a very slow reaction regime that is affected only by the reaction rate and not by the k_L .

Based on the above analysis, the apparent nitration reaction rates of both nitration of toluene and MNT are not affected by k_L when flow velocity greater than 6.37 cm/s. The reaction regimes of nitration of toluene and MNT were proposed as shown in Scheme 2. Specifically, the nitration of toluene to MNT is a fast reaction which mainly occurs at the phase interface, whereas the nitration of MNT to DNT is a very slow reaction that primarily occurs in the bulk of the acid phase at a flow velocity greater than 6.37 cm/s and at the sulfuric acid strengths used in the present study. In all of the later studies, the flow rate was set to 7.96 cm/s to ensure that toluene nitration was in a fast reaction regime and MNT nitration was in a very slow reaction regime.

4.2. Effect of molar ratio, temperature, sulfuric acid strength and residence time

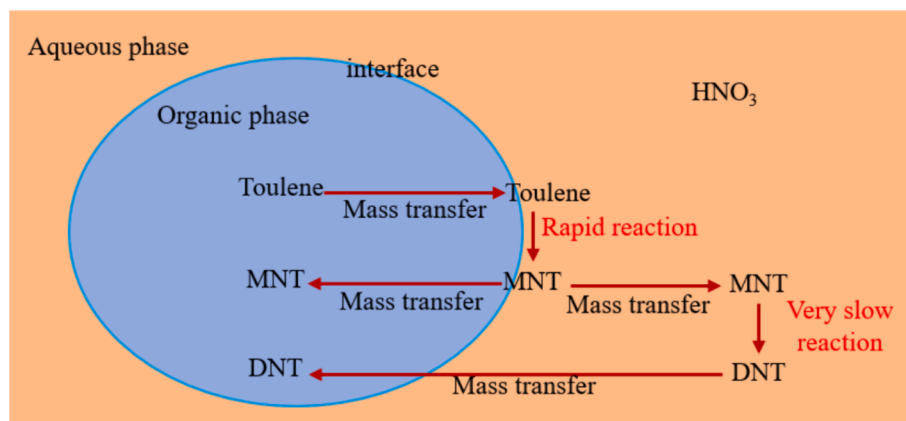
In the toluene nitration, which consists of parallel reactions and consecutive side reactions, the conversion of toluene, the total selectivity of MNT and DNT and the distribution of their isomers are important parameters to characterize the reaction performance. Therefore, it is necessary to investigate the effect of reaction conditions on the above parameters, including the molar ratio of HNO_3 to toluene (N/T), temperature, sulfuric acid strength, and residence time.

From Fig. 4(a), it can be seen that the conversion of toluene increases with increasing N/T, while the selectivity of MNT decreases with increasing N/T, on the contrary the selectivity of DNT rises. In this work, the N/T is adjusted by varying the flow ratios of mixed acid and toluene, specifically a large N/T means a large flow ratio. A larger N/T provides a greater amount of NO_2^+ at the two-phase interface and in the bulk of the acid phase, as well as slowing down the reduction of the nitration capacity of the mixed acid by the water produced by the reaction, which is beneficial for the nitration of both toluene and MNT (Jin et al., 2023; Song et al., 2022b). According to the reaction regime discussed above, a larger N/T favors the formation of smaller toluene droplets at a fixed total flow rate (Song et al., 2022c), which increases the two-phase interface area and promotes the conversion of toluene at the interface. On the other hand, a larger N/T favors the dissolution of more MNT (Su et al., 2011), promoting the mass transfer of MNT, and resulting in more

nitration of MNT to DNT in the bulk of the acid phase. N/T has almost no effect on the isomer distribution of MNT. This is reasonable because the generation of MNT isomers is a parallel reaction and the increase in N/T simultaneously increases the rate of generation of each isomer. In addition, it can be observed that the percentage of 2,6-DNT slightly increases while 2,4-DNT slightly decreases as the N/T increases. It can be seen that a suitable molar ratio is essential to control the selectivity of the nitration reaction.

Temperature is another important process parameter that affects the performance of the toluene nitration reaction. From Fig. 5(a), it can be seen that the toluene conversion increases with increasing temperature. The increase in temperature, on the one hand, increases the chemical reaction rate constants; on the other hand, it increases the solubility of toluene in the mixed acid and promotes the mass transfer (Ravikumar Bandaru and Ghosh, 2011; Su et al., 2011; Wen et al., 2018). Both of these promote the conversion of toluene. The selectivity of MNT decreases with increasing temperature, while that of DNT increases. This indicates that increasing the temperature is more favorable to promote the production of DNT. This is due to the electron-withdrawing effect of the nitro group, and the nitration reactivity of MNT is weaker than that of toluene, showing higher activation energy and thus more sensitive to temperature (Cui et al., 2022). Meanwhile, from Fig. 5(b) and (c), the variation of the isomer distributions of MNT and DNT with temperature was also observed. For MNT, the order of relative variation of isomer distribution with temperature was: 3-NT > 2-NT > 4-NT. Particularly, an increase in temperature from 20 °C to 45 °C resulted in an increase in the distribution of 3-NT from 3.6 % to 4.2 % (a relative increase of 16.7 %), an increase in the distribution of 2-NT from 57.2 % to 57.8 % (a relative increase of 1.0 %), and a decrease in the distribution of 4-NT from 39.2 % to 38.0 % (a relative decrease of 3.1 %). The relative variation of isomer distribution with temperature was calculated as $(I(T_2) - I(T_1)) / I(T_1)$. For DNT, the distributions of 2,4-DNT increased, while 2,6-DNT decreased. This is due to differences in the activation energies for the generation of the different isomers, which will be discussed and confirmed in section 4.3. It can be seen that for the toluene nitration reaction, precise control of temperature is crucial to regulating product selectivity and isomer distribution.

The effect of sulfuric acid strength was investigated in the range of 72.7 and 80.1 wt%. As shown in Fig. 6(a), toluene conversion was significantly increased by increasing the sulfuric acid strength. This is attributed to the promoted generation of NO_2^+ under high sulfuric acid strength, which accelerates the rate of the nitration reaction (Marziano et al., 1998; Russo et al., 2018). In addition, as Fig. 7 shown, increasing the sulfuric acid strength favors the dissolution of aromatics in the acid solution (the solubility of toluene was obtained from the study of Cerfontain et al. (Cerfontain and Telder, 1965) and the solubility of 2-NT was determined experimentally by UV-visible spectroscopy, detailed information is in the Section S3 of Supporting information). The



Scheme 2. The scheme of reaction regimes of heterogeneous toluene nitration with the mixed acid.

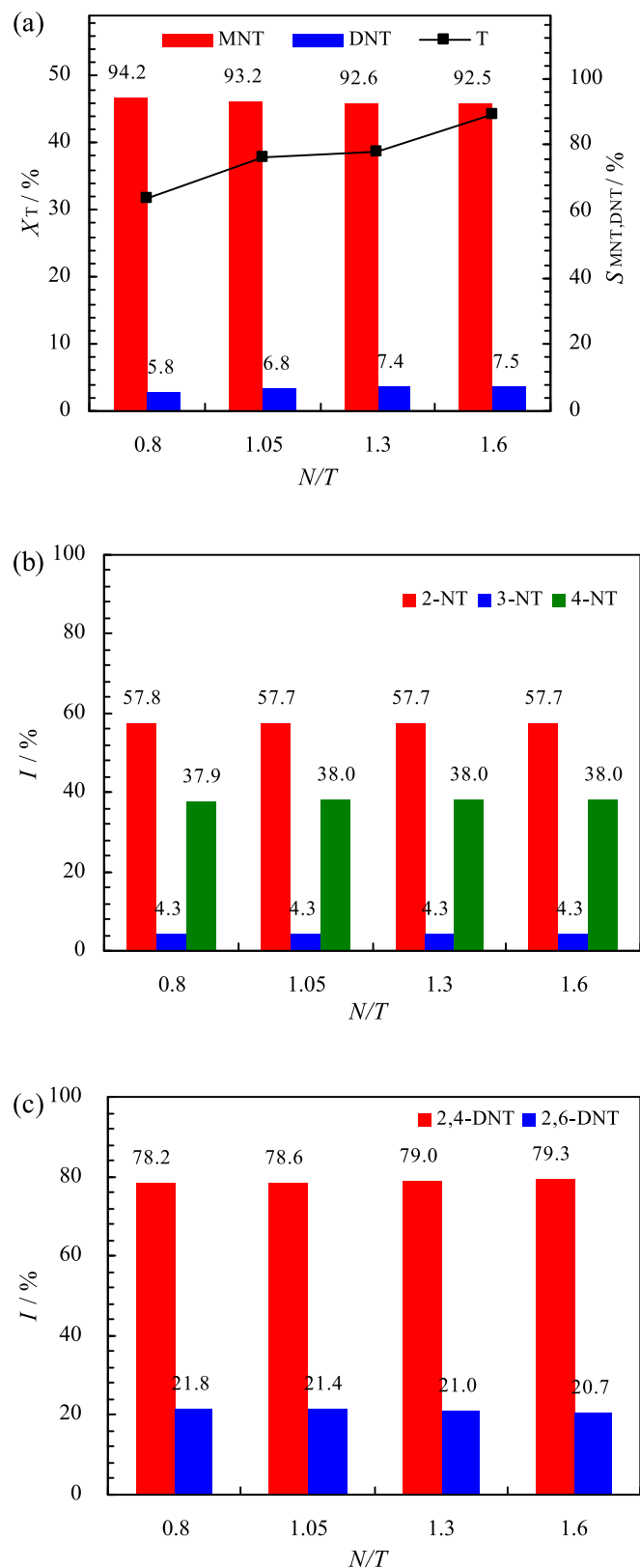


Fig. 4. Effect of the N/T on the (a) conversion of toluene and the selectivity of MNT and DNT, the isomer distribution of (b) MNT and (c) DNT. ($\varphi = 78$ wt%, $T = 50$ °C, $\tau = 52.5$ s, $v = 7.96$ cm/s, $q = 3.1 \sim 6.1$).

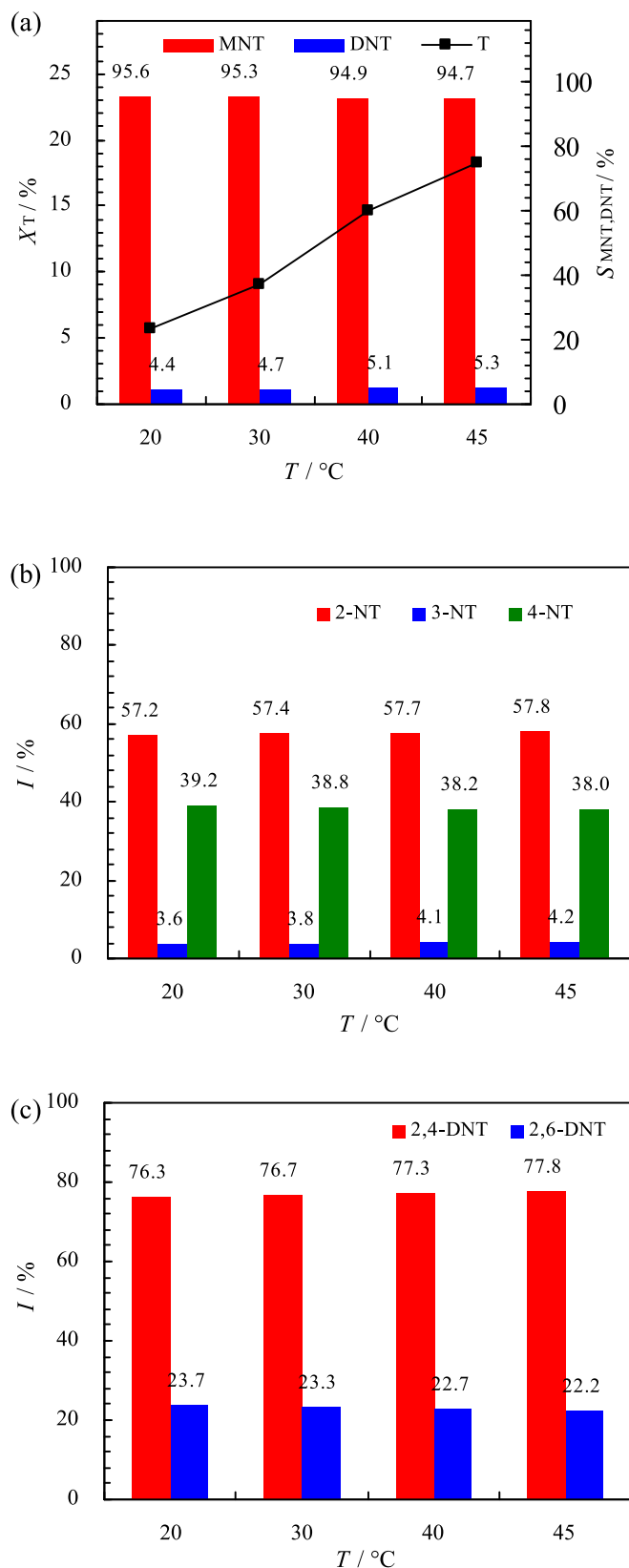


Fig. 5. Effect of reaction temperature on the (a) conversion of toluene and the selectivity of MNT and DNT, the isomer distribution of (b) MNT and (c) DNT. ($\varphi = 78.0$ wt%, $N/T = 1.05$, $\tau = 41.9$ s, $v = 7.96$ cm/s, $q = 4.1$).

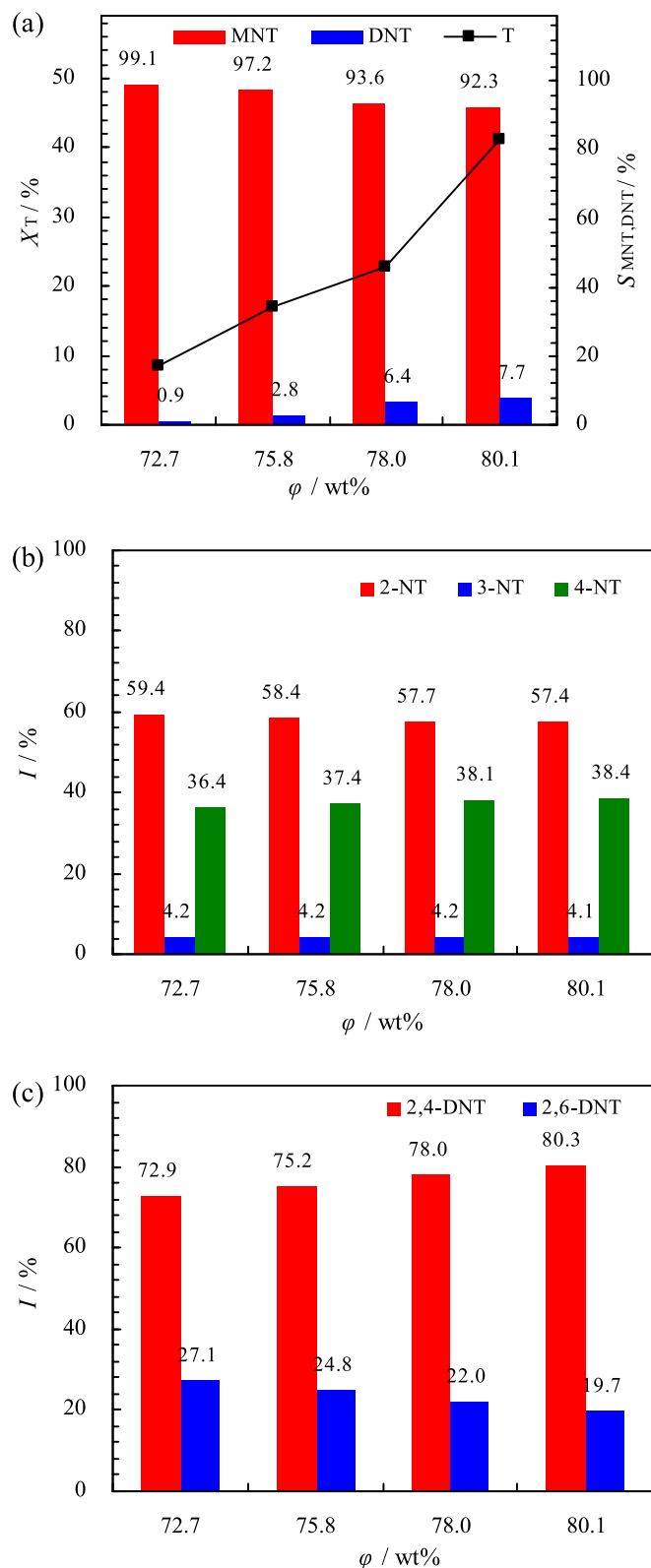


Fig. 6. Effect of sulfuric acid strength on the (a) conversion of toluene and the selectivity of MNT and DNT, the isomer distribution of (b) MNT and (c) DNT. ($T=45^\circ\text{C}$, $N/T=1.05$, $\tau=52.5$ s, $v=7.96$ cm/s, $q=3.9\sim4.5$).

solubility difference between toluene and MNT also leads to the evolution of the selectivity of MNT and DNT. The increase in solubility of MNT with increasing sulfuric acid strength was more significant than that of toluene, which resulted in more MNT being further nitrified, leading to

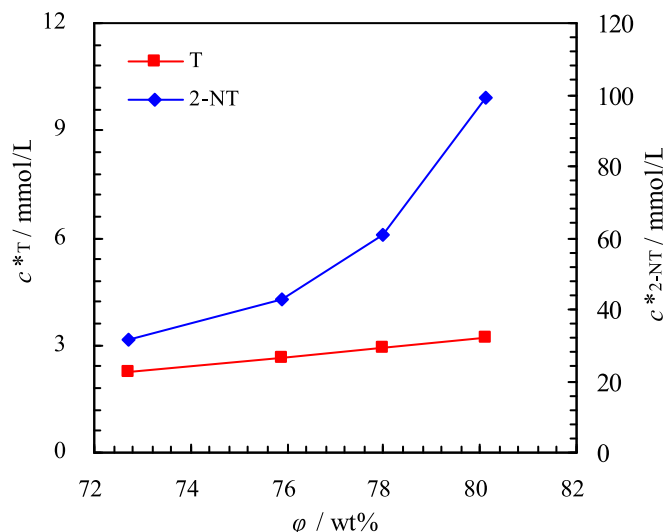


Fig. 7. Solubility of toluene and 2-NT in sulfuric acid solutions of varying sulfuric acid strength at 25°C .

increased DNT selectivity. For the distribution of isomers of MNT, the distribution of 2-NT increases almost linearly with increasing sulfuric acid strength, while the distribution of 4-NT decreases almost linearly, and the distribution of 3-NT hardly varies. This is similar to the change in isomer distribution with sulfuric acid strength for chlorobenzene nitration (Zaldivar et al., 1995). For DNT, the distribution of 2,4-DNT increases with increasing sulfuric acid strength, while 2,6-DNT decreases. This indicates that increasing the sulfuric acid strength is more favorable for the formation of 2,4-DNT, consistent with the results reported by Song et al. (Song et al., 2022a). Therefore, sulfuric acid strength is an important parameter not only for controlling toluene conversion and product selectivity, but also for regulating isomer distribution.

The residence time is also an important parameter affecting the toluene conversion and product selectivity. From Fig. 8(a), it can be seen that a linear relationship between the toluene conversion and residence time is observed. This is because at the beginning of the reaction, the reaction rate is nearly constant since the consumption in nitric acid and the decrease in sulfuric acid strength are not obvious. Therefore, the variation in the reaction kinetic parameters in the investigated experimental range of residence time/toluene conversion could be reasonably neglected. Accordingly, kinetic modeling of the toluene nitration reaction based on the heterogeneous reaction kinetics coupled with mass transfer will be discussed.

4.3. The observed reaction kinetics

As discussed in section 4.1, different regimes of liquid-liquid heterogeneous reactions for toluene and MNT were proposed, regarding the difference of nitration reactivity. Hence, based on the liquid-liquid heterogeneous reaction regime (Bourne, 2003), the net rate of formation of MNT and DNT can be expressed by Eqs. (13) and (14), respectively.

$$\frac{dc_{\text{MNT}} V_{\text{or}}}{d\tau} = ac_1^* \sqrt{k_{\text{MNT}} c_{\text{HNO}_3} D_{\text{T}} V_{\text{aq}}} - k_{\text{DNT}} c_{\text{MNT}}^* c_{\text{HNO}_3} V_{\text{aq}} \quad (13)$$

$$\frac{dc_{\text{DNT}} V_{\text{or}}}{d\tau} = k_{\text{DNT}} c_{\text{MNT}}^* c_{\text{HNO}_3} V_{\text{aq}} \quad (14)$$

where k_{MNT} and k_{DNT} are the observed rate constant of the nitration of toluene to MNT and MNT to DNT, respectively. c_{MNT} , c_{DNT} are the concentrations of MNT and DNT accumulated in the organic phase, respectively. c_{HNO_3} is the concentration of HNO_3 in the mixed acid phase. c_{T}^* and c_{MNT}^* are the solubility of toluene and MNT in the mixed

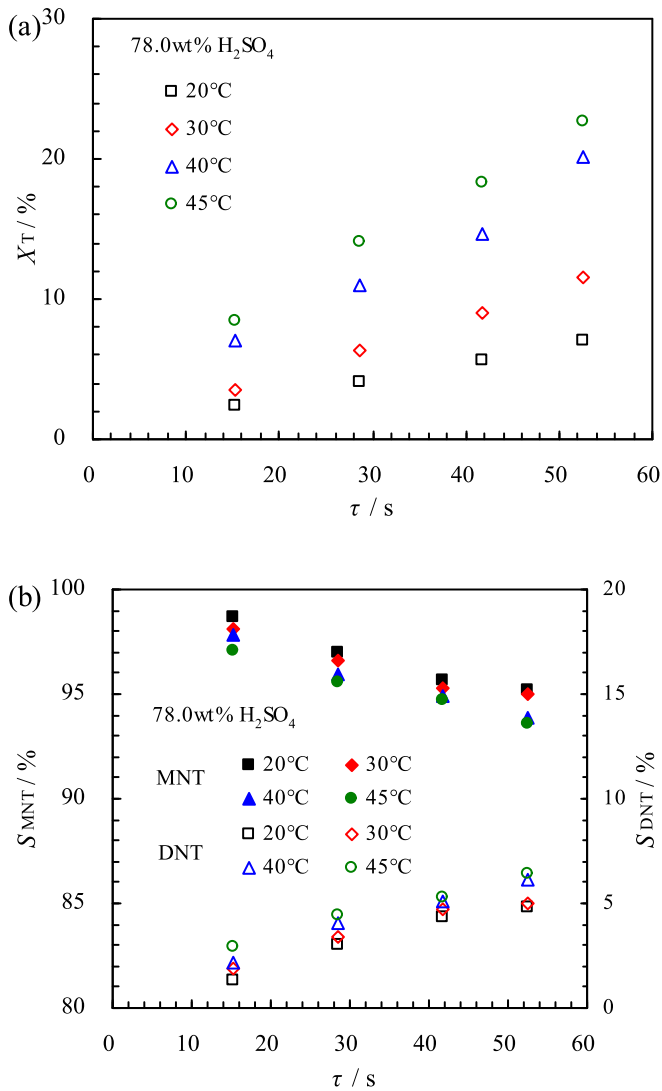


Fig. 8. Effects of the residence time on the (a) conversion of toluene and (b) selectivity of MNT and DNT. ($\varphi = 78.0$ wt%, $N/T=1.05$, $v = 7.96$ cm/s, $q = 4.1$).

acid phase. V_{or} and V_{aq} are the volumes of the organic phase and the mixed acid phase and can be expressed in terms of volumetric flow rate in the continuous flow process. In addition, a is the specific surface area based on the mixed acid phase and D_T is the diffusion coefficient of toluene in the mixed acid.

4.3.1. The observed reaction kinetics of the nitration of toluene to MNT

For the mass balance of toluene, Eq. (15) can be derived and described as follows:

$$c_T = c_T^0 - c_{\text{MNT}} - c_{\text{DNT}} \quad (15)$$

where c_T^0 is the initial concentration of toluene and c_T is the concentration of toluene at the reactor outlet.

By differentiating the time of Eq. (15), Eq. (16) can be derived and described as follows:

$$\frac{dc_T}{d\tau} = -\frac{dc_{\text{MNT}}}{d\tau} - \frac{dc_{\text{DNT}}}{d\tau} \quad (16)$$

By coupling Eqs. (13), (14) and (16), we can obtain:

$$\frac{dc_T V_{\text{or}}}{d\tau} = -ac_T^* \sqrt{k_{\text{MNT}} c_{\text{HNO}_3} D_T} V_{\text{aq}} \quad (17)$$

And Eq. (17) is easy to understand as toluene is only reacted at the phase interface. Through multiplying both sides of Eq. (17) by dc_{HNO_3}/dc_T , we can get:

$$\frac{dc_{\text{HNO}_3}}{d\tau} = -ac_T^* \sqrt{k_{\text{MNT}} c_{\text{HNO}_3} D_T} \frac{V_{\text{aq}}}{V_{\text{or}}} \frac{dc_{\text{HNO}_3}}{dc_T} \quad (18)$$

By integrating Eq. (18), Eq. (19) can be obtained and described as below:

$$\sqrt{c_{\text{HNO}_3}^0} - \sqrt{c_{\text{HNO}_3}} = \frac{1}{2} ac_T^* \sqrt{k_{\text{MNT}} D_T} \frac{V_{\text{aq}}}{V_{\text{or}}} \frac{dc_{\text{HNO}_3}}{dc_T} \tau \quad (19)$$

Eq. (19) indicates that a plot of $G = \sqrt{c_{\text{HNO}_3}^0} - \sqrt{c_{\text{HNO}_3}}$ versus residence time (τ) should be a straight line passing through the origin with a slope (l) equal to $\frac{1}{2} ac_T^* \sqrt{k_{\text{MNT}} D_T} \frac{V_{\text{aq}}}{V_{\text{or}}} \frac{dc_{\text{HNO}_3}}{dc_T}$. In this work, reaction rate constants k_{MNT} at four temperatures (20, 30, 40 and 45 °C) and four sulfuric acid strengths (72.7, 75.9, 78.0 and 80.1 wt%) were determined. As shown in Fig. 9, the fitted curves exhibited a good linear relationship, which is consistent with the hypothesis that the nitration of toluene to MNT is a fast reaction occurring mainly at the two-phase interface. And the value of reaction rate constants k_{MNT} can be calculated by Eq. (20).

$$k_{\text{MNT}} = \left(\frac{2l}{ac_T^* \frac{V_{\text{aq}}}{V_{\text{or}}} \frac{dc_{\text{HNO}_3}}{dc_T}} \right)^2 \frac{1}{D_T} \quad (20)$$

In the Eq. (20), the two phases specific surface area based on the mixed acid phase can be predicted by Eq. (21) (Zhang et al., 2019).

$$a = a_{\text{mc}} \left(1 + 0.5 \ln \left(\frac{V_{\text{or}}}{V_{\text{aq}} + V_{\text{or}}} \right) \right) \frac{V_{\text{aq}} + V_{\text{or}}}{V_{\text{aq}}} \quad (21)$$

And a_{mc} is the specific surface area of capillary microreactors and can be calculated by Eq. (22).

$$a_{\text{mc}} = \frac{4}{d_i} \quad (22)$$

where d_i is the inner diameter of capillary microreactors. The calculation results of two phases specific surface area based on the mixed acid phase are in Table S2.

The solubility of toluene in concentrated sulfuric acid was calculated based on the study of Cerfontain et al. (Cerfontain and Telder, 1965) and the results are in Table S4. The value of $V_{\text{aq}}/V_{\text{or}}$ can be calculated by the volumetric flow ratio of mixed acid and toluene in the continuous flow operation. In addition, as shown in Fig. S3, by fitting the nitric acid concentration and toluene concentration at different times, it was found that their relationship was linear and the value of dc_{HNO_3}/dc_T can be obtained and is shown in Table S6. The diffusivity of toluene (D_T) in sulfuric acid aqueous solution was obtained using the modified Wilke-Chang Equation proposed by Perkins and Geankoplis (Perkins and Geankoplis, 1969).

$$D_T = \frac{7.4 \times 10^{-8} T (\Phi \bar{M})^{1/2}}{\mu v_m^{0.6}} \quad (23)$$

where μ and v_m are the viscosity of sulfuric acid aqueous solution and the molecular volume of toluene at normal boiling point, respectively. $\Phi \bar{M}$ is defined as (Cox and Strachan, 1972a; Song et al., 2023; Wen et al., 2018):

$$\Phi \bar{M} = x_w \Phi_w M_w + x_s \Phi_s M_s \quad (24)$$

where the subscripts w and s represent water and sulfuric acid, respectively. And x , Φ , and M are the mole fraction, the association factor, and the molecular weight, respectively. The calculation results of D_T are in Table S7.

The calculated k_{MNT} at different temperatures and sulfuric acid

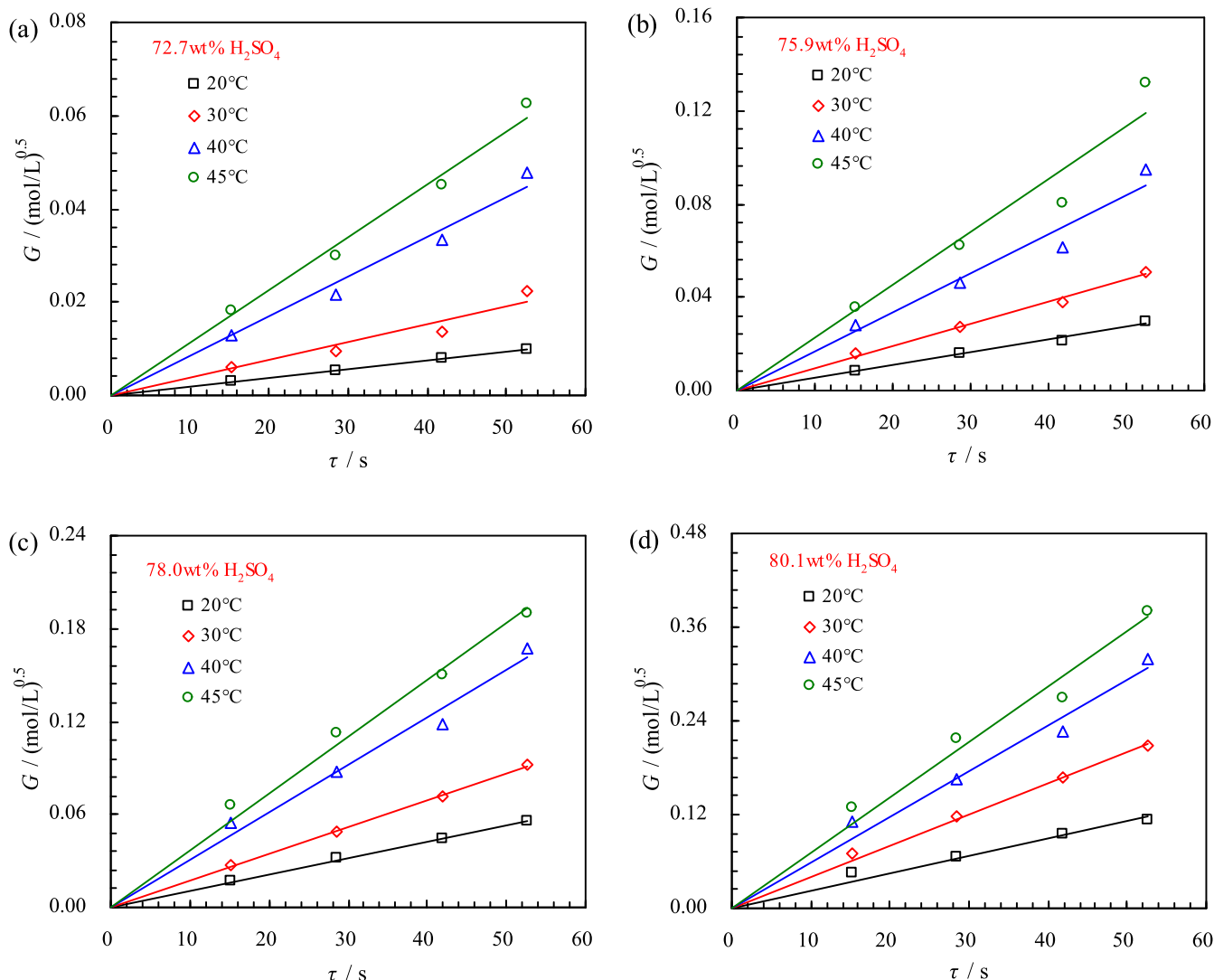


Fig. 9. Determination of k_{MNT} at sulfuric acid strengths of (a): 72.7 wt%, (b): 75.9 wt%, (c) 78.0 wt% and (d) 80.1 wt%. ($N/T=1.05$, $v = 7.96$ cm/s, $q = 3.9 \sim 4.5$).

strengths are in Table S8. Since the nitration of toluene to MNT generates three isomers at the same time, according to the distribution of the isomers, the observed reaction rate constant of each isomer can be calculated by Eq. (S4)~(S6) and the results are also in Table S8. It can be observed that k_{MNT} increases as the temperature and sulfuric acid strength increase, and the trends are more significant with increasing sulfuric acid strength compared to temperature.

The activation energy and pre-exponential factor of the nitration of toluene to MNT and production of each isomer could be obtained based on the Arrhenius Eq. (25):

$$k = Ae^{-\frac{E_a}{RT}} \quad (25)$$

where A is the pre-exponential factor, E_a is the activation energy, R is the universal gas constant, and T is the reaction temperature. Taking the logarithm of Eq. (25), we obtain:

$$\ln k = \ln A - \frac{E_a}{RT} \quad (26)$$

A plot of $\ln k$ versus $1/T$ under different sulfuric acid strength is shown in Fig. 10. From the slope of the fitted line, the activation energies for the nitration of toluene to MNT are 64.76, 32.19, 18.12 and 9.70 kJ/mol under 72.7, 75.9, 78.0 and 80.1 wt% sulfuric acid strength, respectively. The activation energy of production of each isomer under

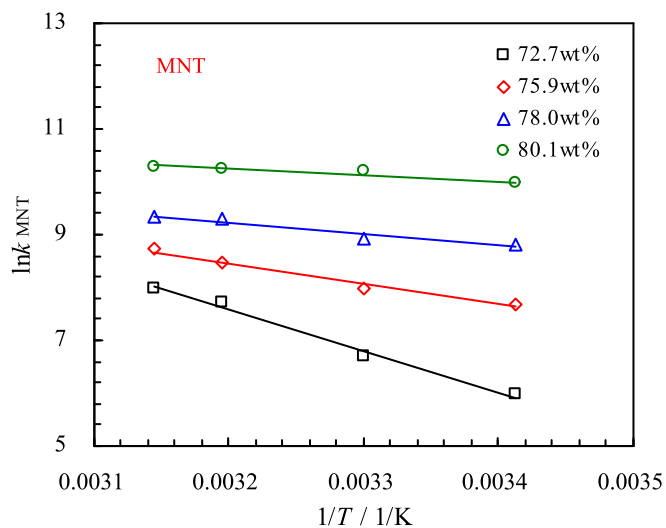


Fig. 10. Arrhenius plot of $\ln k_{\text{MNT}}$ vs. $1/T$.

different sulfuric acid strengths was also calculated based on the Arrhenius Equation, and the results are shown in Table S9. It can be seen that the activation energy for the nitration of toluene to MNT decreases with the increase of sulfuric acid strength. In addition, the activation energy of the production of each isomer is in the order of 3-NT>2-NT>4-NT (for example, the reaction activation energy is 37.41, 32.11 and 31.77 kJ/mol for 3-NT, 2-NT and 4-NT under 75.9 wt% sulfuric acid strengths, respectively), which is consistent with the relative change of isomer distribution with reaction temperature.

4.3.2. The observed reaction kinetics of the nitration of MNT to DNT

In order to obtain k_{DNT} , through multiplying both sides of Eq. (13) by dc_{HNO_3}/dc_{DNT} , we can get:

$$\frac{dc_{HNO_3}}{d\tau} = k_{DNT} c_{MNT}^* c_{HNO_3} \frac{V_{aq}}{V_{or}} \frac{dc_{HNO_3}}{dc_{DNT}} \quad (27)$$

By integrating Eq. (27), Eq. (28) can be obtained and described as follows:

$$\ln \left(\frac{c_{HNO_3}}{c_{HNO_3}^0} \right) = k_{DNT} c_{MNT}^* \frac{V_{aq}}{V_{or}} \frac{dc_{HNO_3}}{dc_{DNT}} \tau \quad (28)$$

Eq. (28) shows that a plot of $\ln(c_{HNO_3}/c_{HNO_3}^0)$ versus residence time (τ) should be a line through the origin with a slope (l) equal to $k_{DNT} c_{MNT}^* \frac{V_{aq}}{V_{or}} \frac{dc_{HNO_3}}{dc_{DNT}}$ under a constant temperature. The selectivity of MNT is always greater than 99 % when the sulfuric acid strength is 72.7 wt%. Hence, k_{DNT} at four temperatures (20, 30, 40 and 45 °C) and three sulfuric acid strengths (75.9, 78.0 and 80.1 wt%) were investigated. As shown in Fig. 11, the fitted curves show a good linear relationship, which is consistent with the assumption that the nitration of MNT to DNT is a very slow reaction that occurs mainly in the main bulk of the acid phase. And the value of k_{DNT} can be calculated by Eq. (29).

$$k_{DNT} = \frac{l}{c_{MNT}^* \frac{V_{aq}}{V_{or}} \frac{dc_{HNO_3}}{dc_{DNT}}} \quad (29)$$

The solubility of MNT in concentrated aqueous sulfuric acid, taking 2-NT as an example, is shown in the Table S5. It can be seen that the solubility of 2-NT is in the range of 30 ~ 180 mmol/l, being tens of times the solubility of toluene under identical sulfuric acid strengths.

Similar to dc_{HNO_3}/dc_T , as shown in Fig. S5, by fitting the nitric acid concentration and DNT concentration at different times, it was also found that their relationship was linear, and the value of dc_{HNO_3}/dc_{DNT} can be obtained and is shown in Table S10.

The calculated k_{DNT} at different temperatures and sulfuric acid strengths are shown in Table S11. It can be seen that the trend of k_{DNT} with temperature and sulfuric acid strength is the same as for k_{MNT} . The Arrhenius plot of k_{DNT} is shown in Fig. 12, and activation energies for the nitration of MNT to DNT are 55.46, 44.45 and 24.64 kJ/mol at 75.9, 78.0 and 80.1 wt% sulfuric acid strength, respectively. The trends in activation energy and pre-exponential factor with sulfuric acid strength were also similar to those for the nitration of toluene to MNT. It should be noted that the activation energy for the nitration of MNT to DNT is greater than that for the nitration of toluene to MNT under the same sulfuric acid strengths. This is caused by the passivation of the benzene ring by the nitro-group, which reduces the activity of the molecule in the nitration reaction.

4.3.3. Validation of the reaction regime

To further validate the hypothesis regarding the reaction regime of the nitration of toluene and MNT, the Ha numbers are calculated using Eqs. (30) and (31).

$$Ha_1 = \frac{\sqrt{k_{MNT} D_T c_{HNO_3}}}{k_{L1}} \quad (30)$$

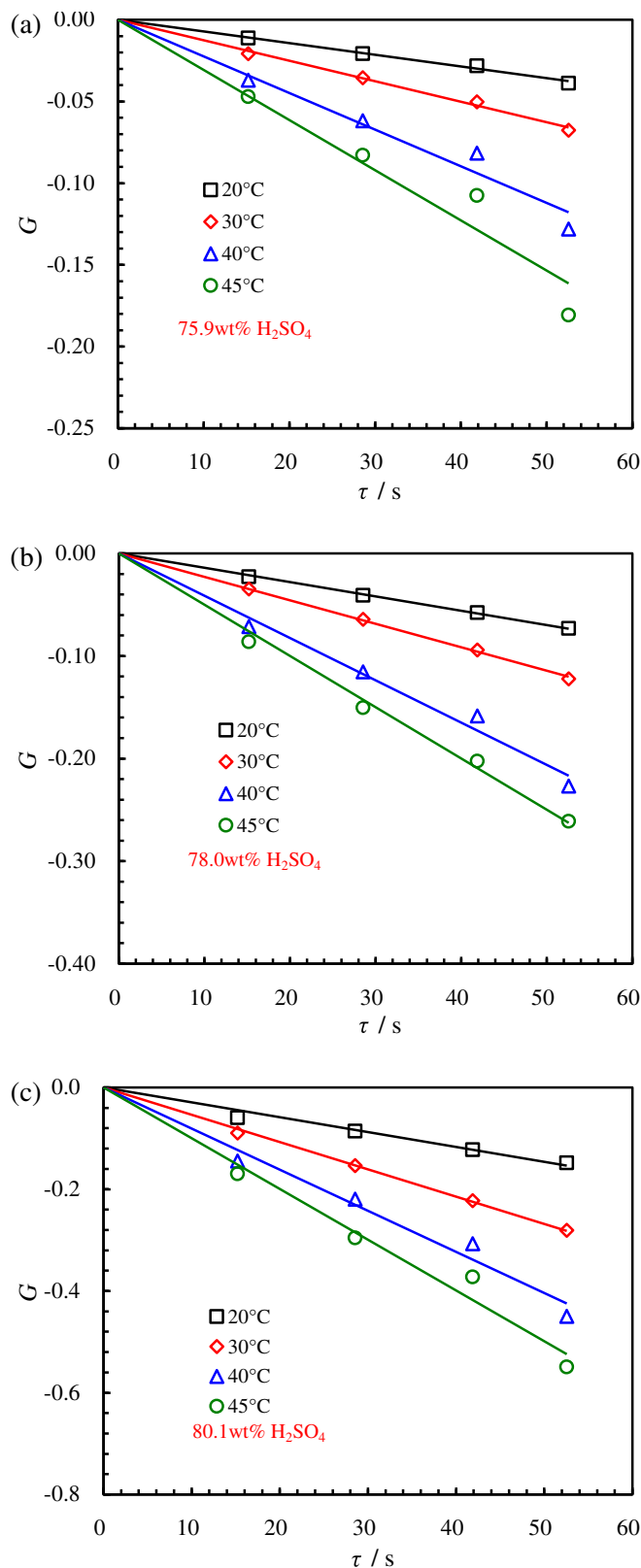


Fig. 11. Determination of the k_{DNT} at sulfuric acid strengths of (a): 75.9 wt%, (b) 78.0 wt% and (c) 80.1 wt%. ($N/T=1.05$, $v = 7.96$ cm/s, $q = 4.1 \sim 4.5$).

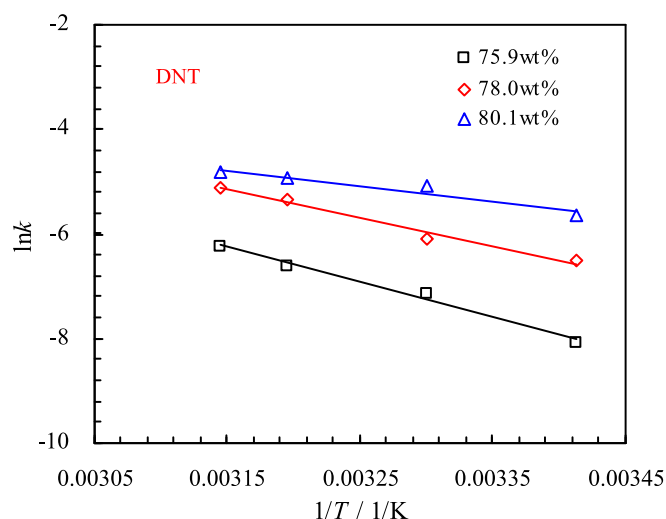


Fig. 12. Arrhenius plot of $\ln k_{\text{DNT}}$ vs. $1/T$.

$$Ha_2 = \frac{\sqrt{k_{\text{DNT}} D_{\text{MNT}} C_{\text{HNO}_3}}}{k_{\text{L2}}} \quad (31)$$

D_{T} and D_{MNT} can be calculated by Eqs. (23) and (24) as mentioned in section 4.3.1. k_{L1} and k_{L2} are the mass transfer coefficient of toluene and MNT from the organic phase to the aqueous phase.

The calculated values of k_{L} and Ha at different sulfuric acid strengths and temperatures for the nitration of toluene and MNT (detailed information is in the Section S6 of Supporting information) are presented in Table 3.

It can be seen that the Ha increases with the increase of sulfuric acid strength and temperature for the nitration both toluene and MNT. The values of Ha_1 obey the following criterion in Eq. (32):

$$3 < Ha_1 < \frac{1}{3} \left(\sqrt{\frac{D_{\text{T}}}{D_{\text{HNO}_3}}} + \frac{C_{\text{HNO}_3}}{2c_{\text{T}}} \sqrt{\frac{D_{\text{HNO}_3}}{D_{\text{T}}}} \right) \quad (32)$$

It indicates that the nitration of toluene is a fast reaction, while the low value of Ha_2 (< 0.3) for the nitration of MNT indicates that the nitration of MNT is a very slow reaction, which verifies our previous hypothesis. In other words, the utilized kinetic expression (Eqs. (13) and (14)) of the nitration of toluene and MNT are reasonable.

4.3.4. Comparison with literature

Fig. 13 summarizes the observed kinetic constants of aromatic

compounds in the literature at 25 °C for mixed acid with different sulfuric acid strengths, in order to demonstrate a comparison with the experimental results obtained in this work. It can be found that the logarithm of the observed kinetic constants for the nitration of toluene to mononitrotoluene obtained in this work is nearly proportional to the sulfuric acid strength, as shown in Eq. (33), which is consistent with previous results reported in the homogeneous nitration (Barnett et al., 1975; Coombes et al., 1968; Moodie et al., 1979) and heterogeneous nitration (Cox and Strachan, 1972b).

$$\lg k_{\text{MNT}} = 0.35\varphi - 23.59 \quad (33)$$

It should be noted that the kinetic constant for the 72.7 % case was discarded for comparison because it presented relatively large deviation (see Fig. S6). The deviation may be caused by that the Ha number for this condition was only 4.09 (Table 3) and the fast reaction regime may not be perfectly conformed. The much smaller values reported by Song et al. (Song et al., 2023) is caused by that their model did not take into account the solubility of toluene in the acid phase, but used the concentration of pure toluene instead. The excellent agreement with previous studies with different measuring methods and reaction conditions confirms the measuring accuracy of our proposed method. It also suggests that the kinetic constants obtained are close to their intrinsic values. But our method based on the microreaction technology enables a much faster and accurate measurement for fast reactions (higher sulfuric acid strength up to 80 % in the present work).

For the nitration of MNT, the logarithm of k_{obs} obtained in our heterogeneous nitration experiments can also be linearly scaled to literature studies conducted in the homogeneous nitration experiments (Song et al., 2022a; Song et al., 2022b) and the fitting equation is shown in Eq. (34).

$$\lg k_{\text{DNT}} = 0.24\varphi - 21.34 \quad (34)$$

We also compared k_{obs} at 25 °C of other aromatic substrates such as benzene (Marziano et al., 1977), chlorobenzene (Cui et al., 2022), nitrobenzene (Jin et al., 2023). Apparently, aromatics with electron-withdrawing groups are generally less reactive and need to react at higher sulfuric acid strengths. In addition, the slope of the straight line becomes larger as the activity of the substrate increases, suggesting that the more reactive substrates are more sensitive to sulfuric acid strength. These findings will provide some meaningful insights into the process intensification of aromatic nitration, as discussed below.

As discussed in section 3, for heterogeneous phase nitration, the reaction regime is determined by the Ha number. For typical operations in microreactors, the mass transfer coefficient is in the order of $O(10^{-5})$ m/s. The diffusion coefficient of aromatics in mixed acid is in the order of $O(10^{-10})$ m²/s and the concentration of nitric acid in mixed acid is in the

Table 3

The Ha of nitration of toluene and MNT.

φ / wt%	T / °C	$k_{\text{L1}} / \times 10^5$ m/s	Ha_1	$\frac{1}{3} \left(\sqrt{\frac{D_{\text{T}}}{D_{\text{HNO}_3}}} + \frac{C_{\text{HNO}_3}}{2c_{\text{T}}} \sqrt{\frac{D_{\text{HNO}_3}}{D_{\text{T}}}} \right)$	$k_{\text{L2}} / \times 10^5$ m/s	Ha_2
72.7	20	7.16	4.09	240.24	—	—
	30	8.05	6.14	202.32	—	—
	40	8.97	10.58	174.74	—	—
	45	9.51	12.45	163.60	—	—
	75.9	7.74	8.11	217.99	7.23	0.003
75.9	30	8.80	10.00	177.51	8.23	0.005
	40	9.86	13.28	149.73	9.23	0.007
	45	10.5	15.70	138.86	9.81	0.009
	78	7.97	12.97	206.58	7.43	0.006
	30	9.12	14.72	165.39	8.53	0.008
78	40	10.3	18.97	137.92	9.60	0.012
	45	10.9	19.83	127.34	10.2	0.014
	80.1	8.50	20.39	198.50	7.93	0.008
	30	9.78	24.99	156.70	9.13	0.012
	40	11.1	27.27	129.46	10.4	0.014
80.1	45	11.7	28.93	119.11	11.0	0.015

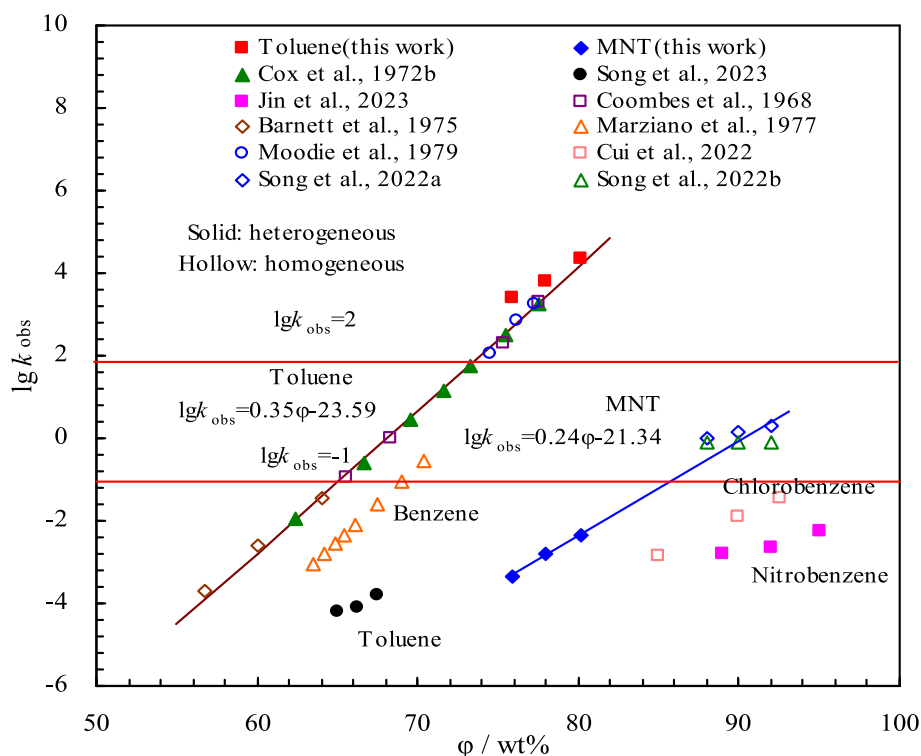


Fig. 13. The comparison of k_{obs} at 25 °C of nitration reactions of different aromatic compounds at different sulfuric acid strengths.

order of $O(1)$ mol/L. Then roughly it can be estimated that the fast reaction regime has to be controlled under $\lg k_{\text{obs}} > 2$ to 3 (>3 is suggested). When $\lg k_{\text{obs}} < -1$, the reaction can be controlled under a very slow reaction regime ($Ha < 0.3$). Theoretically, the reaction kinetics of aromatics (*i.e.*, nitrobenzene and chlorobenzene) can be conveniently determined using the microreaction platform, which then can avoid the complex measurement induced by dissolving trace substances into the sulfuric acid (Cui et al., 2022; Ravikumar Bandaru and Ghosh, 2011). This needs to be confirmed and investigated in the future.

5. Conclusions

For heterogeneous toluene nitration, accurate reaction kinetics measurements are essential for process intensification and process optimization. However, there is still a lack of kinetic studies, especially regarding the kinetics of coupled consecutive side reactions as well as mass transfer. In this work, a continuous-flow platform based on capillary microreactors was constructed. First, the reaction regimes of toluene nitration and its consecutive side reaction (MNT nitration) were verified. Then, process parameters including the molar ratio of reactants, sulfuric acid strength, reaction temperature, and residence time on the conversion of toluene, the selectivity and the isomer distribution of MNT and DNT were carefully studied and analyzed. A kinetic model was established based on different reaction regimes of the liquid–liquid heterogeneous reaction. The pre-exponential factors and activation energies of toluene nitration and MNT nitration under 72.7 to 80.1 wt% sulfuric acid strengths were obtained. It was found that the logarithm of the observed kinetic constant is proportional to the sulfuric acid strength. The calculation of the Ha number further verified our kinetic model. The results could provide a reference for the reaction kinetics of nitration of similar aromatics with mixed acid, such as *o*-xylene, mesitylene, etc., and provide insights into process intensification with a focus on improved product control and process safety.

CRediT authorship contribution statement

Rao Chen: Writing – review & editing, Writing – original draft, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Chaoqun Yao:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Methodology, Conceptualization. **Shuainan Zhao:** Writing – review & editing, Visualization, Software, Formal analysis. **Xuan Liu:** Visualization, Software, Formal analysis. **Yingjiang Lian:** Visualization, Software, Formal analysis. **Guangwen Chen:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ces.2024.120709>.

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