Thermal Hazards of Synthesizing a Grignard Reagent under Different Dosing Rates

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1. Introduction

Grignard reagents, which were discovered by the French chemist Francois Auguste Victor Grignard, are among the most useful agents for synthesizing organic intermediates [1, 2]. Grignard reagents are widely used to produce chemicals and pharmaceuticals because they can react with the carbonyl groups of aldehydes and ketones [3, 4].

Despite their significant utility, scaling-up the synthesis of Grignard reagents, which is a highly exothermic reaction, is challenging. First, the induction period in the synthesis of Grignard reagents, which is followed by a notable release of heat, can result in a runaway reaction if the cooling system is uncontrolled [5]. Additionally, the ethereal solvent, which is required for the synthesis, is flammable and explosive and is capable of forming peroxides, which are hazardous and detrimental to the reaction [6]. Furthermore, during the synthesis of the Grignard reagent, hydrogen is produced in the presence of residual water and acid in the reactor.

Grignard reagents can also undergo rapid hydrolysis, which can produce large amounts of gaseous alkanes if the condenser leaks, resulting in buildup of pressure and explosive accidents such as the one (2014) in Jiangsu province with one fatality and two injuries [7]. Thus, to ensure that Grignard reagents are safely synthesized, it is necessary to assess the hazards associated with the process.

To identify the hazards that are associated with exothermic reactions, reaction calorimetry [8, 9] and adiabatic accelerated calorimetry (ARC) [10–12], which measure the relevant thermodynamic parameters, have been used to better control the exothermic reaction. For example, Kryk et al. [13] used a reaction calorimeter to monitor the synthesis of a Grignard reagent and further used an adiabatic calorimeter to demonstrate that water had a significant impact on the exothermic process. Ferguson and Puga [14] used a reaction calorimeter to study the effects of temperature, particle size, and solvent composition on the reaction rate in synthesizing Grignard reagents and provided...
suggestions for optimizing the reaction process. A quantitative online near-infrared (NIR) spectrometer was used to monitor the formation of a Grignard reagent (as an indication of the reaction) in real-time to improve the safety of the highly exothermic process [15, 16]. In addition, a heat/mass balance-based approach, which involved real-time monitoring, was established to enhance the inherent safety of synthesizing Grignard reagents [17]. Real-time estimation of the safety-relevant parameters, such as the adiabatic temperature and corresponding pressures, has been achieved, enabling the application of advanced safety-oriented control strategies. In situ infrared technology (FTIR) was also used to definitively identify if the induction period occurred [18]. To guarantee a safe reaction, infrared absorption was used to monitor the accumulation of halides and organic halides throughout the synthesis. Moreover, Tanaka et al. [19, 20] investigated the influence of impurities and oxide layers throughout the formation of a Grignard reagent, namely, during the induction period. Additionally, for hazard evaluation in the synthesis of Grignard reagents, Cheng et al. [21] and Kadam et al. [22] studied the effect of the solvent on the process from both safety and environmental perspectives. It was found that 2-methyltetrahydrofuran, which is generally the solvent of choice, was safer than others for the industrial production of Grignard reagents. Therefore, it is necessary to vary the dosing rate to quantitatively evaluate the thermal safety of synthesizing Grignard reagents. In this study, the effect of different dosing rates on the thermal hazards associated with synthesizing Grignard reagents has been rarely reported. Notably, the dosing rate was also the main factor responsible for thermal accumulation of the reactants except for temperature, particle size, solvent, and impurity, where high dosing rates increased the reaction temperature and the risk of thermal runaway. However, the influence of the dosing rate on the thermal hazards associated with synthesizing Grignard reagents has been rarely reported. Therefore, it is necessary to vary the dosing rate to quantitatively evaluate the thermal safety of synthesizing Grignard reagents. In this study, the effect of different dosing rates on the thermal hazards associated with synthesizing a Grignard reagent is investigated. SIMULAR (reaction calorimeter, made in H.E.L) is used to analyze the thermal profile during synthesis of the Grignard reagent at different dosing rates. In addition, ARC is used to evaluate the decomposition characteristics of the Grignard reagent under adiabatic conditions. Finally, a risk matrix and a Stoessel criticality diagram are used to determine the risk level associated with synthesizing the Grignard reagent at different dosing rates. The effect of the dosing rate on the thermal hazard associated with synthesizing the Grignard reagent is also discussed. The findings presented herein are beneficial for safety design and risk management related to the industrial synthesis of Grignard reagents.

2. Experimental Section

2.1. Reaction Calorimeter Experiment. The synthesis of Grignard reagents is shown in Figure 1 and the experimental diagram is shown in Figure 2. The chemical reagents used in experiments are given in Table 1.

Before the experiments, Mg turnings were washed sequentially several times with hydrochloric acid and ethanol to remove the oxide layer on the surface of Mg, after which they were vacuum-dried [21]. p-Bromotoluene was heated at 323 K for 30 min in an oven. First, THF and the magnesium turnings were added to the reactor, and the reactor temperature ($T_i$) was set to 331.15 K; the stirring rate was 400 rpm. The reaction was initiated by adding a mixture of toluene, THF, and p-bromotoluene dropwise to the reactor at 5.0 g·min$^{-1}$. Once the reaction was initiated, the dosing rate was successively decreased from 2.0 g·min$^{-1}$ to 1.0 g·min$^{-1}$ and then to 0.5 g·min$^{-1}$. After adding the reagents, the semibatch reaction was maintained at 331.15 K for approximately 2 h until p-bromotoluene was almost consumed. Before the reaction started and after the reaction ended, the heat capacity and heat transfer coefficient of the reaction were calibrated. No sample was taken during the reaction to avoid interfering with the temperature signal. Experiments in the isothermal mode were performed twice to ensure repeatability.

After the experiment, the products were analyzed by gas chromatography (GC). GC analysis of p-bromotoluene was performed using a Shimadzu GC-2010 Plus gas chromatograph (Shimadzu, Inc., Japan). The gas analyzer consisted of a DB-17 column (30 m × 0.25 mm × 0.25 μm) with the FID detector. The GC oven was held at 323.15 K for 4 min, increased to 463.15 K with heating rate of 20 K·min$^{-1}$, and subsequently heated at 10 K·min$^{-1}$ to 563.15 K maintained for 15 min. Each sample was analyzed three times. The detector temperature was held at 573.15 K, respectively. Nitrogen was used as the carrier gas with 30 mL·min$^{-1}$ flow rate.

The maximum temperature of the synthesis reaction (MTSR) [23] is the maximum temperature as the reaction was out of control. The MTSR can be calculated by the following equations:

\[
H_a = \frac{Qm_t}{Ym}
\]

\[
H_r = \int_{t_0}^{t} q_r dt,
\]

\[
MTSR = \max(T_{cf}) = \max \left( T_r + \frac{H_r - H_a}{m_tC_p} \right).
\]

where $q_r$ is the heat flow (W); $Q$ is the total heat of the reaction ($J$); $Y$ is the yield of the Grignard reagent; $m$ is the total mass of dosing (g); $m_t$ is the mass of the dosing at time $t$; $C_p$ is the specific heat capacity of the system at time $t$ (J·g$^{-1}$·K$^{-1}$); and $T_r$ is the temperature of the reaction system before the cooling failure (K).

2.2. ARC Experiment. In the ARC experiment, 2 g Grignard reagent was put into a 1/4 Hastelloy test cell with 0.38 J·g$^{-1}$·K$^{-1}$ specific heat capacity. Then, the samples were heated from 423.15 K to 565.52 K under heat-wait-search
standard (H-W-S) mode [24]. After the decomposition was complete, the equipment was cooled down to room temperature. All the experiments were performed twice to ensure repeatability. The following test conditions were used:

- (i) Test temperature range: room temperature–773.15 K
- (ii) Test pressure range: 0–300 bar
- (iii) Detection sensitivity: 0.02 K
- (iv) Test mode: H-W-S (heat-wait-search)
- (v) Heating step: 5 K
- (vi) Waiting time: 10 min

In the adiabatic experiment, the thermal inertia \( \Phi \) was used to correct the thermodynamic parameters such as TMR\(_{ad} \) and \( \Delta T_{ad} \) [25], as the decomposed heat was transferred to samples and the test cell. Therefore, \( \Phi \) is usually defined by the following equation:

\[
\Phi = 1 + \frac{M_b C_{p,b}}{M_s C_{p,s}},
\]

where \( C_{p,b} \) is the specific heat capacity of the spherical sample bomb (J g\(^{-1}\)K\(^{-1}\)); \( M_b \) is the mass of the spherical sample bomb (g); \( M_s \) is the mass of the sample (g); and \( C_{p,s} \) is the specific heat capacity of the sample (J g\(^{-1}\)K\(^{-1}\)).

The kinetics parameters, such as preexponential factor (\( A \)) and apparent activation energy (\( E_a \)), can be obtained from the adiabatic experiments. The relationship between the heating rate and temperature under adiabatic conditions can be described by the following equations [10, 26]:

\[
\frac{dT}{dt} = A \exp\left(\frac{E_a}{RT}\right) \left(\frac{T_f - T}{\Delta T_{ad}}\right)^n \Delta T_{ad}^{n-1},
\]

\[
k^* = A \exp\left(\frac{E_a}{RT}\right) c_0^{n-1} = \frac{dT}{dt} \left(\frac{\Delta T_{ad}}{T_f - T}\right)^n \frac{1}{\Delta T_{ad}},
\]

where \( \Delta T_{ad} \) is the rise of adiabatic temperature (K); \( A \) is the preexponential factor (s\(^{-1}\)); \( E_a \) is the apparent activation energy (kJ mol\(^{-1}\)); \( R \) is general gas constant, 8.314 (J mol\(^{-1}\)K\(^{-1}\)); \( T \) is the temperature of system at time \( t \) (K); \( T_f \) is the maximum temperature of adiabatic decomposition (K); \( c_0 \) is the initial concentration of the sample; \( n \) is the reaction order; and \( k^* \) is the reaction rate constant.

The Arrhenius formula was used to obtain \( \ln(k^*) \) vs. 1/\( T \) curve, as described by the following equation:

\[
\ln k^* = \ln(Ac_0^{n-1}) - \frac{E_a}{RT}.
\]

The time to the maximum heating rate under adiabatic conditions (TMR\(_{ad}\)) is widely applied to assess the thermal risk of chemical reactions, and the temperature when TMR\(_{ad}\) is at 24 h is called \( T_{D24} \) [27, 28]. TMR\(_{ad}\) was obtained using the following equations:

\[
TMR_{ad} = t_m - t = \int_t^{t_m} \frac{dT}{A \exp\left(\frac{E_a}{RT}\right) \left(\frac{T_f - T}{\Delta T_{ad}}\right)^n \Delta T_{ad}^{n-1}}
\]

\[
TMR_{ad,s} = \frac{TMR_{ad}}{\Phi}.
\]
3. Results and Discussion

3.1. Results of Reaction Calorimeter Experiment. The yield of the Grignard reagent was determined from the area difference of p-bromotoluene detected by GC before and after the reaction, where the molar ratio of n (p-bromotoluene): n (Mg) was equal to 1:1.1. The Grignard reagent and solvents were directly transferred to another reactor and were subsequently analyzed using an accelerating rate calorimeter under dry atmosphere with no oxygen. From GC data, the yield of the Grignard reagent was 95.71 wt%, 92.15 wt%, and 87.39 wt%, respectively, indicating that the Grignard reagent was synthesized successfully.

The induction process in the synthesis of the Grignard reagent is shown in Figure 3, demonstrating that during this period, synthesis of the Grignard reagent had already been initiated [21].

The circulator temperature ($T_c$), reactor temperature ($T_r$), heat release rate ($q_r$), and amount of p-bromotoluene added during the synthesis of the Grignard reagent are shown in Figure 4. $T_c$ declined significantly when the amount of p-bromotoluene added to the reactor equaled 10 wt% of the mass of the total mixture of p-bromotoluene, toluene, and THF. This finding indicates that the reaction was successfully initiated, accompanied by rapid heat release. During the induction period, $T_r$ reached a minimum value of 310.15 K at different dosing rates, as shown in Figure 3. $T_r$ then gradually increased as Mg reacted with p-bromotoluene and was nearly equal to $T_c$ as the mixtures were added. During the reaction between Mg and p-bromotoluene, $q_r$ was maintained at 20–40 W at a dosing rate of 2.0 g·min$^{-1}$, as shown in Figure 3. However, $q_r$ was in the range of 10–20 W at 1.0 g·min$^{-1}$ dosing rate and 5–10 W at 0.5 g·min$^{-1}$ dosing rate. This finding shows that during the dosing period, the dosing rate had a significant effect on the rate of heat release from the reaction, which is consistent with a previous finding [29].

Figure 5 shows the theoretical heat (calculated using equation (1), (green)), the heat released (calculated using equation (2), (blue)), the percentage thermal accumulation (red), and the maximum temperature $T_{cf}$ (black) curves for the entire synthesis. The percentage thermal accumulation at a dosing rate of 2.0 g·min$^{-1}$ was close to 10.33% at the end of dosing, which was obviously higher than that at dosing rates of 1.0 g·min$^{-1}$ and 0.5 g·min$^{-1}$. In other words, the percentage of thermal accumulation decreased from 10.33% to 1.01% as the dosing rate decreased from 2.0 g·min$^{-1}$ to 0.5 g·min$^{-1}$ (the heat accumulation in the induction period was not considered). Thus, the dosing rate had a permanent influence on the thermal accumulation, which is the key parameter in assessing thermal hazards. However, at the end of the induction period, the percentage thermal accumulation (13.67%) at a dosing rate of 2.0 g·min$^{-1}$ was similar to that at dosing rates of 1.0 g·min$^{-1}$ and 0.5 g·min$^{-1}$, considering that the reaction was initiated at one time with the same amount of additive.

Notably, the accumulated heat during the induction period was higher than that at the end of dosing because adding the mixture at one time did not affect the dosing rate, as shown in Figure 5. Thus, the $T_{cf}$ curve had two obvious peaks in the induction and dosing periods. $T_{cf}$ at a dosing rate of 2.0 g·min$^{-1}$ increased rapidly to 359.64 K, as the generated heat could not be released rapidly in the induction period, which resulted in heat accumulation. $T_{cf}$ at a dosing rate of 2.0 g·min$^{-1}$ reached the second maximum value of 352.67 K at the end of the dosing period. $T_{cf}$ at the end of the induction period, which was calculated using equation (3), was 28 K higher than the set reactor temperature and 10 K higher than that in the dosing period. Thus, in the case of cooling failure, the most hazardous moment is the induction period, followed by the end of the dosing period. These results do not agree with a previous study [21], where the dosing period was found to be the most dangerous.

As shown in Figure 5, the heat released in the reaction at 2.0 g·min$^{-1}$ was obviously lower than the theoretical heat because the rate of heat generation was lower than the dosing rate. The difference between the theoretical heat and the heat released in the dosing period at the dosing rate of 0.5 g·min$^{-1}$ was very small compared to the difference at rates of 2.0 g·min$^{-1}$ and 1.0 g·min$^{-1}$. This finding shows that there was no heat accumulation at a dosing rate of 0.5 g·min$^{-1}$ because the rate of heat generation was equal to the dosing rate. Both $T_{cf}$ and $T_r$ were almost identical at the end of the dosing, where the dosing rate was 0.5 g·min$^{-1}$. Therefore, the dosing rate is important for decreasing heat accumulation.

The thermal parameters for synthesis of the Grignard reagent at different dosing rates are given in Table 2. As expected, the reaction is highly exothermic, given that the overall heat was between 362.69 and 397.11 kJ·mol$^{-1}$ (based on the molar amount of Grignard reagent). The enthalpy of the reaction was almost the same at different dosing rates with 373 kJ·mol$^{-1}$ [18], but higher than previously reported with 245.46 kJ·mol$^{-1}$ [21]. It was also observed that the larger the dosing rate, the higher the overall heat because of the difference in thermal accumulation. The theoretical adiabatic temperature rise, $\Delta T_{ad}$, at 2.0 g·min$^{-1}$ was 204.87 K, which indicates that during cooling failure, the reaction temperature can increase by 204.87 K. Moreover, $Q_{dosing}$ increased from 123.74 kJ to 134.09 kJ as the dosing rate increased from 0.5 g·min$^{-1}$ to 2.0 g·min$^{-1}$. Therefore, at a higher dosing rate, more heat is accumulated at the end of dosing.

3.2. Results of ARC Experiment. The key parameters for the adiabatic experiments, such as the onset temperature, self-heating rate, and pressure, are typically used to quantify runaway exothermic decomposition. The temperature vs. time curves and the pressure vs. time curves are shown in Figure 6. Decomposition of the Grignard reagent occurred in the temperature range of 500.37–551.85 K and was accompanied by a rapid rise in pressure (6 bar), which indicates that under adiabatic conditions, there is a thermal risk. The initial decomposition temperature was higher than MTSR (calculated using equation (3), 352.67 K) of synthesizing the Grignard reagent, as shown in Figure 4. This finding shows that in the case of cooling failure, the Grignard reagent is stable. Notably, the
adiabatic temperature rise for this process was 51.48 K. The adiabatic temperature increased once decomposition occurred, which likely caused the sample temperature to reach 551 K. As shown in Figure 7, the self-heating rate of the Grignard reagent increased slowly in the initial stage of decomposition and then increased rapidly to a maximum value of 1.05 K·min⁻¹.

The $k^*$ vs. 1000/T curve for the Grignard reagent is shown in Figure 8. According to equation (7), the values of $E_a$ and $A$ for the decomposition of the Grignard reagent, which were calculated from the slope and intercept of the line, were 409.07 kJ·mol⁻¹ and $4.181 \times 10^{37}$ ($R^2 = 0.9581$), respectively. Substituting $E_a$ and $A$ into equations (8) and (9), respectively, gave the TMRadm curve, as shown in Figure 8.
Figure 9. It can be seen that $T_{D24}$ of Grignard reagent was 488.20 K.

The thermal parameters, which were computed from the ARC data for the sample, are given in Table 3. In this adiabatic experiment, a $\Phi$ value of 2.3 was not considered high enough to obtain reliable data (for example, time, temperature, pressure, and heating rate). As given in Table 4, the enthalpy of the decomposition reaction was approximately $928.59$ J·g$^{-1}$. The corrected maximum heating rate reached $2.42$ K·min$^{-1}$, and the corrected adiabatic temperature rise was $118.4$ K.

3.3. Thermal Hazard Evaluation. The severity and possibility of an uncontrolled reaction were evaluated using the Zurich hazard analysis [30–32], the results of which are given in Table 4. The results show that synthesizing the Grignard reagent at different dosing rates corresponds to a level 3 hazard, which can result in serious factory losses, although the products were almost impossible to decompose. Furthermore, uncontrolled reactions during the synthesis would be infrequent because TMR$_{ad}$ was above 24 h. Thus, the risk of synthesizing the Grignard reagent is acceptable. This result indicates that the target reaction systems are safe, except for the generated heat that accumulates in the case of cooling failure. However, this accumulated heat can be eliminated by decreasing the dosing rate.

The results of the Stoessel criticality diagram [33] for assessing the risk of synthesizing the Grignard reagent are given in Table 5. The corresponding boiling point temperature of THF, considering that the reaction was performed in a closed reactor, was used to derive the maximum temperature for technical reasons (MTT), which was 339.15 K. Based on Table 5, the reactor temperature, $T_r$, was 331.15 K, and $T_{D24}$ was 488.20 K. Additionally, a previous evaluation [21] showed that MTSR was the same as $T_{cf2}$ at different rates.

Figure 5: Thermal release, thermal accumulation, dosing of p-bromotoluene, and $T_{cf}$ curves for synthesis of Grignard reagent. (a) Dosing rate of $2.0$ g·min$^{-1}$. (b) Dosing rate of $1.0$ g·min$^{-1}$. (c) Dosing rate of $0.5$ g·min$^{-1}$. $T_{cf1}$ is the maximum temperature in the induction period, and $T_{cf2}$ is the maximum temperature during the dosing period.
Therefore, the critical level was class 3 (\(T_r < MTT < MTSR < T_{D24}\)) at dosing rates of 2.0 g·min\(^{-1}\) and 1.0 g·min\(^{-1}\) and class 1 (\(T_r < MTSR < MTT < T_{D24}\)) at a dosing rate 0.5 g·min\(^{-1}\). However, when \(T_{Gr}\) was used as MTSR, the reaction risk at different dosing rates was class 3. Thus, the Grignard reagent should be synthesized at a dosing rate of 0.5 g·min\(^{-1}\) for safety. Decreasing the dosing rate can reduce the thermal accumulation in the dosing period and the risk level but has a little effect on thermal accumulation during the induction period. The main risk during the induction period is thermal accumulation, which can be controlled safely by optimizing the amount of additive introduced at one time.

<table>
<thead>
<tr>
<th>Dosing rate (g·min(^{-1}))</th>
<th>(Q_{\text{induction}}) (kJ)</th>
<th>(Q_{\text{dosing}}) (kJ)</th>
<th>(Q_{\text{total}}) (kJ)</th>
<th>(\Delta_H_m) (kJ·mol(^{-1}))(^*)</th>
<th>(\Delta T_{\text{ad,r}}) (K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>15.46</td>
<td>134.09</td>
<td>136.85</td>
<td>397.11</td>
<td>204.87</td>
</tr>
<tr>
<td>1.0</td>
<td>16.29</td>
<td>128.08</td>
<td>131.77</td>
<td>382.36</td>
<td>191.53</td>
</tr>
<tr>
<td>0.5</td>
<td>15.81</td>
<td>123.74</td>
<td>124.99</td>
<td>362.69</td>
<td>177.34</td>
</tr>
</tbody>
</table>

\(^*\Delta H_m\) is calculated from the reacted moles of \(p\)-bromotoluene and yield.

Figure 6: ARC-derived thermal decomposition curve for Grignard reagent.

Figure 7: Self-heating rate vs. temperature curve for Grignard reagent under adiabatic conditions.
Table 3: Thermal parameters for decomposition of Grignard reagent.

<table>
<thead>
<tr>
<th>$T_c$ (K)</th>
<th>$T_f$ (K)</th>
<th>$\Phi$</th>
<th>$\Delta T_{ad}$ (K)</th>
<th>$\Delta T_{ad,s}$ (K)</th>
<th>$\beta_m$ (K min$^{-1}$)</th>
<th>TMR$_{ad}$ (h)</th>
<th>$\Delta H$ (J g$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>500.37</td>
<td>551.85</td>
<td>2.3</td>
<td>51.48</td>
<td>118.40</td>
<td>3.40</td>
<td>&gt;24</td>
<td>928.57</td>
</tr>
</tbody>
</table>

$T_c$ is the initial decomposition temperature, $\beta_m$ is the maximum heating rate, and TMR$_{ad}$ is the time required to reach the maximum heating rate.

Table 4: Risk matrix for synthesis of Grignard reagent at different dosing rates.

<table>
<thead>
<tr>
<th>Dosing rate (K·min$^{-1}$)</th>
<th>$\Delta T_{ad,f}$ /K</th>
<th>Severity</th>
<th>TMR$_{ad}$/h</th>
<th>Possibility</th>
<th>Risk level</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>204.87</td>
<td>Serious factory losses</td>
<td>&gt;24</td>
<td>Infrequent</td>
<td>I: acceptable</td>
</tr>
<tr>
<td>1</td>
<td>191.53</td>
<td>Short-term damage of factories</td>
<td>&gt;24</td>
<td>Infrequent</td>
<td>I: acceptable</td>
</tr>
<tr>
<td>0.5</td>
<td>177.34</td>
<td>Short-term damage of factories</td>
<td>&gt;24</td>
<td>Infrequent</td>
<td>I: acceptable</td>
</tr>
</tbody>
</table>

Table 5: Stoessel criticality diagram for synthesis of Grignard reagent at different dosing rates.

<table>
<thead>
<tr>
<th>Dosing rate (K·min$^{-1}$)</th>
<th>$T_c$ (K)</th>
<th>MTT (K)</th>
<th>MTSR (K)</th>
<th>$T_{D24}$ (K)</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>331.15</td>
<td>339.15</td>
<td>352.56</td>
<td>488.20</td>
<td>3</td>
</tr>
<tr>
<td>1</td>
<td>331.15</td>
<td>339.15</td>
<td>344.35</td>
<td>488.20</td>
<td>3</td>
</tr>
<tr>
<td>0.5</td>
<td>331.15</td>
<td>339.15</td>
<td>332.94</td>
<td>488.20</td>
<td>1</td>
</tr>
</tbody>
</table>
4. Conclusions

SIMULAR and ARC were used to investigate the effect of the dosing rate on the thermal hazard of synthesizing a Grignard reagent.

Based on the SIMULAR results, the Grignard reagent could be successfully synthesized with a yield above 87%. The overall heat for synthesis of the Grignard reagent at dosing rates of 0.5–2.0 g·min⁻¹ was in the range of 362.69–397.11 kJ·mol⁻¹ (based on the mole of Grignard reagent). The adiabatic temperature rise, ΔTad,r, reached the maximum value of 204.87 K at dosing rate of 2.0 g·min⁻¹. Reducing the dosing rate effectively reduced the percentage thermal accumulation in the entire synthesis (except for the induction period) from 10.33% to 1.01%. Thus, the dosing rate had a permanent influence on thermal accumulation. The MTSR for the induction period at different dosing rates was higher than that at the end of the dosing period. In the case of cooling failure, the most hazardous point is the induction period, followed by the end of the dosing period.

ARC was used to investigate the thermal behavior of the Grignard reagent under adiabatic conditions. The initial decomposition temperature of the sample (500.37 K) was higher than that of MTSR, which indicates that the Grignard reagent shows stable thermal behavior. The preexponential factor and activation energy were estimated to be 4.181 × 10³⁷ and 409.074 kJ·mol⁻¹, respectively. While, TTD₂₄ was 488.20 K. The increase in the adiabatic temperature (51.48 K) cannot be ignored because the final decomposition temperature was above 500 K.

The results of the risk assessment show that the severity of the thermal runaway in synthesizing the Grignard reagent is level 3 at different dosing rates, which could result in serious factory losses, although the products were almost impossible to decompose. Thus, the risk level for synthesizing the Grignard reagent at different dosing rates is acceptable. Without considering the induction period, the Stoessel criticality diagram shows that at dosing rates of 1.0–2.0 g·min⁻¹ (Tc < MTT < MTSR < TTD₂₄), the risk level of synthesizing the Grignard reagent is class 3. However, when the induction period is considered, the risk level is class 3 at different dosing rates. Comparatively, when the dosing rate is reduced to 0.5 g·min⁻¹ (Tc < MTSR < MTT < TTD₂₄), the risk level is class 1. Thus, decreasing the dosing rate lowers risk level and thermal accumulation during the dosing period. To prevent process hazards, a dosing rate of 0.5 g·min⁻¹ is the most suitable for synthesizing the Grignard reagent. By minimizing the dosing amount while ensuring that the reaction is initiated, the heat accumulation and the risk during the induction period can be reduced.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

Wei Wang and Chenguang Shi contributed equally to this work.

Acknowledgments

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References


