Thermal Decomposition of Ethyl Diazoacetate in Microtube Reactor: A Kinetics Study

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ABSTRACT: Ethyl diazooacetate (EDA) commonly experiences intensive decomposition as well as complex conversion concerning safety and efficiency. In this work, a careful kinetics study on the thermal decomposition of EDA was isothermally conducted in a microtube reactor to establish a mechanism-based kinetic model. The model parameters were well calibrated with experimental data including the yield of dimers and the conversion of EDA, confirming the rationality of the proposed three-step reaction route. It allows the model to concisely describe the complex species transformations during EDA decomposition, which is unavailable for an apparent kinetic model. Considering an isothermal reaction system and the tolerance of EDA consumption by thermal decomposition, this work could help reveal the requirement on the kinetic characteristics of the desired catalytic reaction in which EDA is involved, as a reference on reaction process modeling and regulation.

INTRODUCTION

Ethyl diazooacetate (EDA) is a highly welcomed chemical reagent with significance as the precursor of the carbene to synthesize some key intermediates of pesticides.1–9 For instance, EDA can conduct aldol-type condensation with aldehyde or react with ketone to obtain α-diazo-β-hydroxy ester10–17 and can provide α-carbonyl carbones to undergo O–H or C–H insertion to π-bonds to form ylides;18–20 similar to the report on the polymerization of allyl diazooacetate by Liu et al.,21 the carbene polymerization with α-carbonyl diazo compounds as carbene precursor has attracted much attention recently.22,23 It is noticed that all of these reactions involve the decomposition of EDA to generate carbones (eq 1) and the carbones could combine various transition metals to form metal carbones as active catalytic intermediates.24 Therefore, the kinetics of EDA decomposition has been the main concern. It is usually described and discussed with the apparent kinetics expression as shown in eq 2. Both first-order reaction kinetics and zero-order reaction kinetics have ever been reported for the order of EDA (y),25,26 and a consensus has not been reached until now. It indicates that EDA experiences reaction steps more complicated than what eq 1 shows. Recognizing and quantitatively modeling these reaction steps are desired to regulate the conversions that EDA participates in. To this end, experimental data corresponding to strictly controlled reaction conditions and residence time are required, which are difficult to obtain in a conventional stirred reactor because the decomposition of EDA seems to be fast and highly exothermic.27

\[
N_2CHCOEt \rightarrow :CHCOEt + N_2 \tag{1}
\]

\[
-\frac{dC_{EDA}}{dt} = k_{cat}^E C_{EDA} \tag{2}
\]

The microtube reactor with the characteristic dimension less than 1 mm is a device that could transfer the reaction time into reaction pipeline volume precisely, so it has precise control ability for reaction time.28–30 This property makes the microtube reactors especially appropriate for handling the reactions involving active reactants, products, or intermediates with a short lifetime under reaction conditions.31–34 Besides, the microtube reactors have enhanced heat transfer performance to inhibit the formation of hot spot effectively.35–37 By now, microtube reactors have been successfully used to measure the kinetics of different reactions in gas phase,38 liquid phase,39 and heterogeneous catalytic system.40

In this work, we carried out kinetic measurements on the thermal decomposition of EDA using microtube reactor by monitoring the concentrations of EDA and main products at various residence times and established a quantitative model considering simplified multistep reaction mechanism based on a comprehensive experiment data regression. And then, this kinetic model was used to predict the details of EDA consumption during thermal decomposition process and discuss the prerequisite in terms of kinetics for an effective catalytic organic synthesis involving EDA.

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Figure 1. Time profiles of EDA conversion and dimmers yield: (a) \( C_{\text{EDA},0} = 0.023 \text{ mol/L}, T = 393 \text{ K} \); (b) \( C_{\text{EDA},0} = 0.023 \text{ mol/L}, T = 403 \text{ K} \); (c) \( C_{\text{EDA},0} = 0.023 \text{ mol/L}, T = 413 \text{ K} \); (d) \( C_{\text{EDA},0} = 0.046 \text{ mol/L}, T = 413 \text{ K} \); (e) \( C_{\text{EDA},0} = 0.023 \text{ mol/L}, T = 423 \text{ K} \); and (f) \( C_{\text{EDA},0} = 0.046 \text{ mol/L}, T = 423 \text{ K} \).
RESULTS AND DISCUSSION

Data Acquisition and Process Analysis. Residence Time.
Because the decomposition of EDA could release nitrogen, the residence time is not only determined by the volume of tube and the feed flow rate, but it is also dependent on the volume ratio of nitrogen gas to liquid (ratio\_g/l) throughout the tube. Using difference method, the local value of ratio\_g/l at the end point of the \(i\)th section of the tube can be calculated as follows.

\[
\text{ratio\_g/l}_i = \frac{1000 \Delta C_{\text{EDA}}RT}{P} \quad (3)
\]

where \(\Delta C_{\text{EDA}}\) is the difference in the EDA concentration until this specific position, \(R\) is the thermodynamic constant (8.314 J/\(\text{mol K}\)), and \(P\) is the pressure. As the tube is divided into \(j\) sections, the average value of ratio\_g/l in the tube is

\[
\text{ratio\_g/l} = \frac{\sum \text{ratio\_g/l}_i + \text{ratio\_g/l}_1}{2} \quad (4)
\]

and, the residence time \((t)\) is

\[
t = \frac{V}{F(1 + \text{ratio\_g/l})} \quad (5)
\]

where \(F\) is the feed flow rate and \(V\) is the volume of the tube.

Conversion of EDA. The time profiles of the EDA conversion under specific initial EDA concentration \(C_{\text{EDA,0}}\) and temperature were determined in a thermostat microflow system and then plotted in Figure 1 (black dots and black lines). In Figure 1a−c,e, different curves correspond to different temperatures, from 393 to 423 K, but \(C_{\text{EDA,0}}\) was always kept at 0.023 mol/L. The conversion of EDA accelerates distinctly with increasing temperature. To reach 50% EDA conversion, it takes 35 min at 393 K and 3 min at 423 K. Figure 1d,f corresponding to \(C_{\text{EDA,0}} = 0.046\) mol/L show the same phenomenon. Comparing the curves in the figures obtained at the same temperature, for example, Figures 1c,d and 2e,f, we could find changing \(C_{\text{EDA,0}}\) only has little influence on the curve of EDA conversion vs residence time. This characteristic is similar with the first-order reaction kinetics to some extent.

Yield of Dimmers. Researchers have found that the decomposition of EDA could generate various products, of which two cis−trans isomers, diethyl fumarate (DEF) and diethyl maleate (DEM), are confirmed species. Both of them are so-called dimmers because they could be regarded as the dimer of carbenes. It is generally agreed that carbone species are key intermediates in alkene formation via dimerization of diazo reagents. A polymer of ethoxycarbonylcarbene could form presumably by repeated reaction of the carbene with itself or with ethyl diazoacetate, and the bulk of the carbene−carbene or carbene−diazoacetate reactions occurs in the \(\alpha\)-position. In this work, we determined the concentration of DEF and DEM separately and took the sum as the concentration of dimmers. The yield of dimmers is denoted as the ratio of dimmers concentration to 0.5\(C_{\text{EDA,0}}\). We monitored the time profiles of dimmers yield with residence time, and the results were summarized in Figure 1 (red dots and red lines). As seen, for all of the cases, the yield of dimmers reaches a peak value soon and decreases smoothly. It implies that the dimmers could transform to other products sequentially. Either DEF or DEM includes a reactive double bond. They could react with carbenes to yield trimmers with a double bond or a three-member ring.

Figure 2. Optimization process for solving reaction rate constants.

![Optimization process for solving reaction rate constants](image-url)
and also could react with EDA to yield pyrazoline.\textsuperscript{46–48} Besides, we noticed that at the same \( C_{\text{EDA},0} \), the peak value of dimmers yield increased with increasing temperature. It indicates that the reaction-generating dimmers have higher temperature sensitivity compared with the reaction-consuming dimmers, i.e., the former have a higher activation energy. Comparing Figure 1c,d and 1e,f, at the same temperature shows that \( C_{\text{EDA},0} \) has little influence on the curve of dimer yield vs residence time.

**Reaction Mechanism.** As mentioned above, the thermal decomposition of EDA involves various reactive species including EDA, carbene, and dimmers, so the actual reaction network may be quite complex. However, considering that the order of reactivity is well known as carbene \( \gg \) EDA \( > \) dimmers and EDA surpasses carbenes and dimmers overwhelmed in amount usually, it is plausible to propose a simplified reaction network as shown in Scheme 1. Three-step reactions are included. Step 1: one EDA molecular decomposes to generate one carbene and release nitrogen, of which the reaction rate parameter is \( k_1 \). Step 2: one carbene reacts with one EDA molecular to generate one dimer molecular and release nitrogen, of which the reaction rate parameter is \( k_2 \). The reaction between two carbenes is neglected because EDA is much more than carbene in the system. Step 3: one dimer reacts with one carbene to generate one trimer molecular, of which the reaction rate parameter is \( k_3 \). Herein, we neglected (1) the EDA-involved dimer consumption reaction in the absence of highly reactive intermediate like carbene, (2) the difference of DEM and DEF in reaction performance, and (3) any reaction step that trimer or larger oligomer participates in.

**Modeling Reaction Kinetics and Species Evolution.** Based on the reaction network, we can establish mathematical equations to describe the reaction kinetics, as shown in eqs 6 to 8.

\[
\frac{dC_{\text{EDA}}}{dt} = -k_1C_{\text{EDA}} - k_2C_{\text{cb}}C_{\text{EDA}} \\
\frac{dC_{\text{cb}}}{dt} = k_1C_{\text{EDA}} - k_2C_{\text{cb}}C_{\text{EDA}} - k_3C_{\text{cb}}C_{\text{dm}} \\
\frac{dC_{\text{dm}}}{dt} = k_3C_{\text{cb}}C_{\text{EDA}} - k_3C_{\text{dm}}C_{\text{cb}}
\]

where \( C_{\text{EDA}} \) is the concentration of EDA, \( C_{\text{cb}} \) is the concentration of carbene, \( C_{\text{dm}} \) is the concentration of dimmers, and \( C_{\text{tm}} \) is the concentration of trimmers. Due to the high reactivity of carbene, most of the carbenes will be consumed immediately after the generation, and the concentration of carbene is low and varies little. Supposing that the concentration of carbene complies with quasi-steady-state assumption, we could get eq 9

\[
C_{\text{cb}} = \frac{k_1C_{\text{EDA}}}{k_1C_{\text{EDA}} + k_3C_{\text{dm}}}
\]

Substituting eq 9 into eqs 6 and 8, we could get eqs 10 and 11.

\[
\frac{dC_{\text{dm}}}{dt} = k_1C_{\text{EDA}} \left( \frac{C_{\text{EDA}}}{C_{\text{EDA}} + k_3/k_2C_{\text{dm}}} - \frac{k_3/k_2C_{\text{dm}}}{C_{\text{EDA}} + k_3/k_2C_{\text{dm}}} \right)
\]

Thus, as the kinetic parameters \((k_1\text{ and } k_3/k_2)\) and the initial conditions \((C_{\text{EDA},0}\text{ and } T)\) were given, \( C_{\text{EDA}}, C_{\text{cb}}, C_{\text{dm}} \) and \( C_{\text{tm}} \) could be calculated out from eqs 10 and 11. At the same time, using microtube reactor platform, the concentration of EDA and dimmers corresponding to specific residence time could be determined experimentally. We established an objective function described as eq 12 to evaluate the deviation between the calculated values and the experimental values, where a weight factor of 100 was set for the yield of dimmers to consider the calculated values and the experimental values, where a weight factor of 100 was set for the yield of dimmers to consider the EDA conversion and the yield of dimmers comparably. Furthermore, the MATLAB programming code was written, and the Nelder–Mead simplex optimization method was used to search the optimized kinetic parameters \(k_1\) and \( k_3/k_2 \). The optimization algorithm is depicted in Figure 2.

\[
d = \sum ((C_{\text{EDA},exp} - C_{\text{EDA},cal})^2 + 100(C_{\text{dm},exp} - C_{\text{dm},cal})^2)
\]
The calibration equations were listed as follows. The activation energy for the EDA decomposition reaction to generate carbene is 114.55 kJ/mol. The difference in activation energy between dimmers-generating and -consuming reactions is 9.96 kJ/mol.

\[
k_1 = 3.999 \times 10^{11} e^{-114.55 \text{kJ/mol}/RT} \text{ s}^{-1}
\]

\[
k_3/k_2 = 2.255 e^{-9.96 \text{kJ/mol}/RT}
\]

Due to the high reactivity of carbene, the contact of two carbenes may conduct self-polymerization to form dimmers instantaneously. However, the quite a low concentration of carbene determines that the self-polymerization is a mass-transfer controlled process. As is well known, compared with the reaction rate, the mass transfer rate is usually far less sensitive to temperature. A 10 °C temperature increase may cause the reaction rate to double, whereas the mass transfer rate increases 5% or less. Equation 14 shows that the two steps, dimmers generation and consumption, have small difference in terms of activation energy. It implies that none of them is of mass transfer controlled process. In other words, it is rational to ignore the contribution of the self-polymerization of carbene to dimmers generation.

Substituting eqs 13 and 14 into eqs 10 and 11, and setting \( C_{\text{EDA,0}} \) and \( T \), the time profiles of \( C_{\text{EDA}}, C_{\text{cb}}, \) and \( C_{\text{dimmers}} \) could be calculated by numerical integration. Figure 4a shows the results when \( C_{\text{EDA,0}} = 0.023 \text{ mol/L} \) and \( T = 393 \text{ K} \). As seen, the concentration of dimmers experiences a fast rise initially and a slow fall afterward. The peak value of \( C_{\text{dimmers}} \) is about 0.00042 mol/L at 7.4 min. Most of EDA is eventually converted to trimmers. Using the above equations and calibrations, we could also discuss the conversion rate of EDA and the contribution of specific reaction step on it, as shown Figure 4b. Both decomposition of EDA to generate carbene and the reaction of EDA with carbene to generate dimmers, denoted as step 1 and step 2, respectively, consistently decelerate with time. The reaction of EDA with dimmers to generate trimmers, denoted as step 3, accelerates first and then decelerates, influenced by the dimmers’ concentration. A maximal rate of step 3 is achieved at around 3.7 min. The existence of carbene in the reaction system could promote the conversion of EDA. The total conversion rate of EDA is the sum of the rates of step 1 and step 2. One half to 1/3 of EDA is converted in the thermal decomposition of EDA in step 2. So, it is not appropriate to describe the conversion of EDA by a simple first-order reaction kinetic model. Because the carbenes participate in the conversion of EDA, we should properly consider various reactions that consume carbene and change the concentration of carbene to regulate the conversion of EDA.

Once the reaction between EDA and another reactant is the desired reaction, such as the cyclopropanation reaction between EDA and olefins, to achieve high selectivity requires that the desired reaction is much faster than the thermal decomposition of EDA. Considering an isothermal reaction system and the tolerance of EDA consumption by thermal decomposition, we can figure out a reaction window in terms of the initiation concentration of EDA, temperature, and reaction time. As the initial concentration of EDA is fixed, there will exist correspondence between the range of EDA thermal decomposition ratio and the scope that temperature and reaction time
Figure 5 shows an example, in which \( C_{\text{EDA,0}} = 0.02 \text{ mol/L} \). As seen, to reach 10% EDA thermal decomposition ratio, we need 1.6 min at 130 °C, and 25 min at 100 °C, and all of the combinations of temperature and reaction time are located on the boundary between two regions of different colors. If the desired reaction could deplete EDA under the reaction conditions in the region encircled by the boundary and two coordinate axes, we may expect a selectivity of over 90%. In other words, the simplified mechanism-based model for the thermal decomposition of EDA in organic solvent can provide a reference to model and regulate the EDA-involved catalytic organic synthesis.

### CONCLUSIONS

In summary, we established a measuring platform based on microtube reactor in thermostat to acquire the kinetic data for the thermal decomposition of ethyl diazoacetate (EDA) in organic solvent (1,2-dichloroethane) systematically. By analyzing the time profiles of the concentrations of EDA and dimmers (diethyl fumarate and diethyl maleate, as confirmed products) according to the reaction mechanism, we proposed a simplified three-step reaction kinetic model, including the decomposition of EDA to generate carbene, the reaction between carbene and EDA to generate dimmers, and the reaction between carbene and dimer to generate trimer. The parameters in kinetic equations to describe these reaction steps were obtained by calibration. Using these parameters and equations group, we could calculate the conversion of EDA and the yield of dimmers accurately and predict the contribution of carbene to the conversion of EDA. Furthermore, the reaction time/temperature dependence of EDA thermal decomposition ratio was discussed to understand the requirement on the kinetic characteristics of the desired reaction involving EDA. The simplified and quantitative mechanism-based model for the thermal decomposition of EDA in organic solvent has foundation in modeling and regulating various EDA-involving catalytic organic syntheses that are currently conducted by our group.

### EXPERIMENTAL SECTION

**Chemicals.** Ethyl diazoacetate (EDA, >91.0%; Aladdin, China), 1,2-dichloroethane (C\(_2\)H\(_4\)Cl\(_2\); DCE; Xilong, China), diethyl fumarate (DEF, 99%; Klamar, China), diethyl maleate (DEM, 96%; Sinopharm, China), and dimethyl phthalate (DMP, 99.5%; Guangfu, China) were of analytical grade and used directly without further purification.

**Experimental Setup.** The experimental setup for measuring the kinetics of EDA decomposition is shown in Figure 6. The...
solution of EDA in DCE was made up and stored at room temperature and then delivered by a constant-flux pump (Beijing Satellite). Through a preheating tube (length, 1.0 m; OD, 1.6 mm; ID, 1.0 mm), the solution came into a serial of reaction tubes (OD, 3.0 mm; ID, 2.0 mm). Both preheating tube and reaction tubes were immersed in a thermostat with polysiloxane as the heating medium. The accuracy of the temperature in the thermostat could be controlled within ±0.1 K. Two online thermocouples were placed just before and after the reaction tubes to monitor the effect of temperature control.

The maximal temperature deviation from the preset value was found to be less than 1 K. The reaction tubes were divided into six sections by a seven-way switching valve and several tees. By changing the direction of the switching valve, the volume of the EDA passing through the reaction tube(s) could be 6.8, 13.6, 20.4, 27.2, 34.0, or 40.8 mL. After the reaction tube(s), the EDA solution flowed into a cooling tube with a jacket (length, 2.0 mL; OD, 3.0 mm; ID, 2.0 mm; ice water as coolant) to quench the decomposition reaction. A back-pressure valve was placed at the end of the cooling tube to keep the back-pressure at 0.80–0.90 MPa (G). The relatively high pressure could inhibit the evaporation of DCE during the reaction, as well as reduce the influence of the generated nitrogen on the residence time. All of the valves and tubes were made of stainless steel.

**Analysis Method.** The effluent from the cooling tube was collected in a chromatographic bottle filled with the solution of DMP in DCE in advance and then weighed and analyzed by using GC 7890A (Agilent) to determine the contents of EDA, DEF, and DEM. The GC method was established by the referring literatures.41,42 In detail, the column was an INNOWAX column (length, 30 m; ID, 0.25 mm; film thickness, 0.25 μm); the oven temperature was kept at 318 K for 2 min, increased to 338 K by 5 K/min, kept at 338 K for 5 min, increased to 623 K by 50 K/min, and then held for 15 min; the flow rate of nitrogen as the carrier gas was 40 mL/min with a split ratio of 1:200; and the injector temperature was 373 K.

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**Notes**
The authors declare no competing financial interest.

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