In Situ Raman Monitoring of Silver(I)-Aided Laser-Driven Cleavage Reaction of Cyclobutane

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The cyclobutane cleavage reaction is an important process and has received continuous interest. Herein, we demonstrate the visible laser-driven cleavage reaction of cyclobutane in crystal form by using in situ Raman spectroscopy. Silver(I) coordination-induced strain and thermal effects from the laser irradiation are the two main driving forces for the cleavage of cyclobutane crystals. This work may open up a new avenue for studying cyclobutane cleavage reactions, as compared to the conventional routes using ex situ techniques.

The cyclobutane cleavage reaction, as a key step in DNA repair (e.g. in the case of thymine cyclobutane dimer), is a very important reaction process and has received wide-spread interest.[1,2] Thermally induced ion or molecule movement at the molecular level can lead to unit-cell dilation, crystal structure altering, and cyclobutane isomerization/cleavage.[3–7] It has been reported that pyridyl-substituted cyclobutane coordinated with metallic ions can undergo isomerization/cleavage reactions upon thermal treatments[8–11] and recently, metal–organic organopolymeric hybrid frameworks have been produced by using [2+2] cycloaddition reactions.[12,13] Besides conventional heat resources, laser irradiation can also be applied to induce cleavage reaction.[14,15] Typically, ex situ techniques such as nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry are used to study the yield of the cyclobutane cleavage reactions, which fail to monitor the whole reaction process.[16,17] In situ time-resolved Raman spectroscopy is an advanced technique that can monitor the reaction processes and structure changes of molecules.[12,15–18] Moreover, Raman spectroscopy is ultrasensitive to bond vibration,[11,16–18] as opposed to in situ X-ray diffraction, which is only sensitive to crystalline structure, so Raman spectroscopy can even be applied to amorphous materials during the reaction process.[22–24] In our previous work,[25] we managed to monitor the dimerization reaction process of pyridyl-substituted olefins into cyclobutenes through the in situ Raman spectra, where the laser is the heat source and silver(I) ions act as a template to control the pyridyl-substituted paralleled olefins’ distance to within 4.2 Å. However, the newly formed cyclobutane would not undergo cleavage in ambient conditions, owing to its chemically stable conformation.

Herein, we demonstrate the monitoring of silver(I)-aided laser-driven cyclobutane cleavage in the melted state by using an in situ Raman technique, and this cyclobutane cleavage reaction is sensitive to the applied laser power (local temperature induced by laser irradiation). We synthesized a crystalline material by mixing diethyl 3,4-di(pyridin-4-yl)cyclobutane-1,2-dicarboxylate (DCCB) with silver trifluoroacetate (AgTFA) in tetrahydrofuran (THF), and then layered it with n-hexane (see the Experimental Details in the Supporting Information). An [Ag(DCCB)][TFA] crystal (CCDC No. 1054463) was obtained for single-crystal diffraction, and the structure is illustrated in Figure 1; the crystal data can be found in Table S1. There are two types of coordination bonds: the nitrogen atom on a pyridyl ring coordinated with silver(I) (Py–Ag), and the carbonyl C=O group coordinated with silver(I) (C=O–Ag–O=C), and the silver ions were bridged with TFA groups, leading to a two-dimensional (2D) network. For a comparison study, a DCCB crystal was also obtained by using a similar technique.

It was found that the [Ag(DCCB)][TFA] crystal could undergo the cleavage reaction at the cyclobutane position under laser irradiation, whereas the DCCB crystal could not (Figure 2a). As shown in Figure 2b, the Raman spectrum of DCCB is dominated by the pyridine ring stretching at approximately 1610 cm⁻¹, pyridine ring breathing at 1020 cm⁻¹, the cyclobutane skeletal C–C stretching mode and C(cyclobutane)–C(pyridine) at 1145 and 845 cm⁻¹, respectively, as well as CH₂ deformation at 1430 and 1370 cm⁻¹.[25] For the [Ag(DCCB)][TFA] crystal, besides the Raman fingerprints of DCCB, one new band at approximately 943 cm⁻¹ can be found, corresponding to the bisaceta C–C symmetric vibration of C=O–Ag–O=C.[26,27] Importantly, upon 633 nm laser (100 % power, 3 mW) irradiation,
another new band at 1637 cm$^{-1}$ was formed, which can be ascribed to C=C double bond stretching. This result clearly indicates that under laser irradiation, cyclobutane in the [Ag$_3$(DCCB)][TFA]$_3$ crystal can undergo a cleavage reaction into vinyl structures. However, ring opening is catalyzed by crystal formation through complexation between the carbonyl and Ag ion (AgTFA), and the DCCB crystal alone remains inert under laser irradiation.

It is widely accepted that laser irradiation can be a unique thermal source for inducing chemical reactions, whereas here we found that under identical laser irradiation, the cyclobutane cleavage reaction only occurs on the [Ag$_3$(DCCB)][TFA]$_3$ crystal, which is an indication that the thermal effect from laser irradiation is not the sole driving force for this cleavage reaction. This phenomenon prompts curiosity about the crystal structure of the obtained [Ag$_3$(DCCB)][TFA]$_3$, a coordinated complex comprised of DCCB molecules and silver trifluoroacetate (AgTFA). The most distinguished difference in the [Ag$_3$(DCCB)][TFA]$_3$ structure from the dimerization precursor [Ag$_2$(PEA)$_4$][TFA]$_2$ (PEA = ethyl-(pyridine-4-yl)prop-2-enolate) is that two carbonyl groups in DCCB were coordinated with one silver(I) ion, and each pyridyl ring was coordinated with one silver(I) ion, giving a compact 2D polymeric structure (see Figures S1–S4). Here, we propose that, under laser irradiation, the silver(I) ions coordinated to the pyridyl ring (Py–Ag) and to the carbonyl C=O (C=O–Ag–O=C) may trigger the strenuous movement of the pyridyl rings and carbonyl groups, adding additional stress to cyclobutane in DCCB. Coupled with the laser energy, the cyclobutane ring is then cleaved into two vinyl groups.

Monitoring this cleavage reaction by using in situ Raman spectroscopy is only possible in the melted state, as can be seen from the line-mapping Raman spectra in Figure 2c. We pre-melted the part under a laser beam for 5 s, and then line mapping was carried out through the pre-melted center. It can be seen that only the melted part shows distinguishable Raman features, whereas almost no Raman signals can be collected from the non-melted part. For the Ag$_3$(DCCB)][TFA]$_3$ crystal, the new band at approximately 1637 cm$^{-1}$ ascribed to the C=C double bond can be clearly seen, indicating the occurrence of the cyclobutane cleavage reaction. For the DCCB crystal (Figure 2d), a similar phenomenon with a stronger Raman signal appears in the melted part, but no cleavage reaction can be detected.

Interestingly, the cyclobutane cleavage reaction of the [Ag$_3$(DCCB)][TFA]$_3$ crystal is found to be laser-power dependent (Figure 3). With 100% power (3 mW) of the 633 nm laser, the [Ag$_3$(DCCB)][TFA]$_3$ crystal can be melted within 5 s, and strong Raman signals can be obtained. The intensity of the Raman peak corresponding to the C=C double bond gradually gets stronger with increasing irradiation time, showing the increasing yield of pyridine-substituted olefins. However, it is found that the intensities of the peak at approximately 845 and 1145 cm$^{-1}$ (owing to cyclobutane) remain unchanged. We think this can be rationalized by the fact that during the reaction process, the surrounding [Ag$_3$(DCCB)][TFA]$_3$ crystal will be continuously melted and moved toward the laser irradiation spot, and therefore, the DCCB content might be kept stable. When 50% power (1.57 mW) was applied, the melting process takes about 5 min, after which the Raman signal of [Ag$_3$(DCCB)][TFA]$_3$ can be observed. However, even in the melted state, no cyclobutane cleavage reaction can be discovered at this power level, as no Raman peaks for the C=C double bond can be found. With 10% power (0.3 mW) of the 633 nm laser, it cannot melt the [Ag$_3$(DCCB)][TFA]$_3$ crystal even after 30 min (see Figure S5). One may notice slight frequency shifts of the characteristic Raman peaks, which have frequently changed.
been seen and attributed to strain generated by ion movement in the melted state.\cite{34} We also tried this reaction with a 532 nm laser, but found that the crystal easily suffers from carbonization, even with a relatively low power (Figure S6).

The above results clearly show that, for this laser-driven cyclobutane cleavage reaction, silver(I) coordination and laser power are two key factors that make this reaction feasible. On one hand, laser-driven silver(I) ion thermal movement in melted [Ag₃(DCCB)][TFA]₃ may increase the ring strain of the cyclobutane, and thus increase the possibility of the ring-opening reaction. On the other hand, laser irradiation, as a unique heat source, provides the necessary thermal energy to melt the [Ag₃(DCCB)][TFA]₃ crystal and induce the cyclobutane cleavage reaction, rendering an in situ monitoring of the reaction process by Raman spectroscopy possible. Notably, the laser power should be high enough to melt the [Ag₃(DCCB)][TFA]₃ crystal, otherwise no cleavage reaction can be seen from the Raman spectra, or even no Raman signal can be collected from the solid-state crystal.

As the cleavage of [Ag₃(DCCB)][TFA]₃ is thermally driven and laser-power dependent, we are eager to understand the thermal behavior of the as-prepared crystal. Figure 4a shows the differential scanning calorimetry and thermogravimetric analysis (DSC–TGA) curves of the [Ag₃(DCCB)][TFA]₃ crystal under a N₂ atmosphere. One can see two weight-loss regions in the TGA curve, corresponding to the evaporation of the solvent remaining in the crystal (an endothermic process), as well as carbonization and release of gaseous small molecules (an exothermic process), respectively. It is interesting to find another endothermic peak in the DSC curve in the range of 160–200°C, which we believe is ascribed to the crystal melting and cyclobutane cleavage. To confirm this, we thermally treated the [Ag₃(DCCB)][TFA]₃ crystal under two different temperatures, 200 and 300°C, and then Raman spectra were collected (Figures 4b and 4c). It can be seen that the sample treated at 300°C displays no distinct peaks, without Raman signals from either the cyclobutane or vinyl groups, presumably owing to the carbonization and formation of amorphous carbon under this condition. For the sample treated at 200°C, one can still see distinguishable Raman signals from the [Ag₃(DCCB)][TFA]₃ crystal, as well as a strong peak corresponding to the C=C double bond at approximately 1637 cm⁻¹. From the above results, we can conclude that cleavage reaction of [Ag₃(DCCB)][TFA]₃ is quite temperature sensitive and happens within a narrow temperature range (160–200°C), above which carbonization of the sample can occur and the production of pyridyl-substituted olefins is prohibited. A control experiment by heating the DCCB crystal at 200°C indicates that DCCB will not undergo the cleavage reaction, as no Raman signals from the vinyl group can be detected. Whereas, heat treatment at 300°C directly leads to full carbonization, as typical D and G bands of carbon materials can clearly be seen from the Raman spectrum (see Figure S7). Therefore, we can positively conclude that, during the laser-driven cleavage reaction of cyclobutane, a thermal effect from laser irradiation is an important driving force.

Figure 3. Laser-power dependent cyclobutane cleavage reaction of a [Ag₃(DCCB)][TFA]₃ crystal under 633 nm laser irradiation: a) Raman spectra collected with 100% power (3 mW), with a 5 s interval, and b) Raman spectra collected with 50% power (1.57 mW), with a 60 s interval. The arrows show the sequence of collecting the Raman spectra.

Figure 4. a) DSC–TGA curves of the [Ag₃(DCCB)][TFA]₃ crystal and Raman spectra of [Ag₃(DCCB)][TFA]₃ after heat treatment at b) 300°C and c) 200°C.
force, but stress added to the cyclobutane ring by silver(I) ion movement is also very critical. Moreover, the laser-induced melting of \([Ag_3(DCCB)][TFA]_3\) crystals renders the in situ Raman monitoring of the cleavage reaction possible.

In conclusion, in situ Raman monitoring of the cleavage reaction of diethyl 3,4-dipyrindin-4-yl)cyclobutane-1,2-dicarboxylate (DCCB) has been made possible from \([Ag_3(DCCB)][TFA]_3\) crystals in a melted state. This cleavage reaction shows laser-power dependent reaction kinetics, and a control experiment indicates that this reaction occurs within a narrow temperature range \((160–200 \, ^\circ \text{C})\) and that a higher temperature induces the carbonization of this organic material. Besides the thermal effect from the laser, silver(I) coordination to the pyridyl rings can add stress to the cyclobutane ring upon laser irradiation, which is thought to be a crucial factor that leads to the cleavage reaction. We believe this work may open up a new avenue for studying the cyclobutane cleavage reactions, as compared to the conventional routes using ex situ techniques.

### Experimental Section

#### Materials and Reagents

Ethyl-(pyridine-4-yl)prop-2-enolate (PEA) was prepared according to the literature method.\(^{[25]}\) Silver (I) trifluoroacetate (AgTFA) was purchased from Sigma–Aldrich. Methanol, tetrahydrofuran (THF), and n-hexane were purchased from Sinopharm Chemical Reagent Co., Ltd.

#### Synthesis of DCCB

Diethyl 3,4-dipyrindin-4-yl)cyclobutane-1,2-dicarboxylate (DCCB) was obtained under UV light irradiation through photodimerization reaction, according to the literature method.\(^{[25,26,27]}\) In detail, PEA was dissolved in THF solution. A crystal was obtained within 3 days of THF evaporation. The crystalline material was photodimerized with UV irradiation for at least 48 h. The dimer was purified with column chromatography. \(^1\)H NMR: \((400 \, \text{MHz, CDCl}_3, \text{ppm})\); \(\delta 8.300 \) (d, 4 H, J = 4.4 Hz, pyridine \(\alpha\)H), 6.932 (d, 4 H, J = 5 Hz, pyridine \(\beta\)H), 4.398 (d, 2 H, J = 6 Hz, Py-cyclobutane H), 4.195 (dd, 4 H, 7 Hz, 7 Hz, cyclobutane H), and 3.836 (d, 6 H, 6 H, \(-\text{CH}_2\)–). 1.236 (t, 6 Hz, 6 H, \(-\text{CH}_3\)).

#### Preparation of \([Ag_3(DCCB)][TFA]_3\) Crystals

The crystalline material \([Ag_3(DCCB)][TFA]_3\) was prepared through the layer-to-layer diffusion method. DCCB was mixed with AgTFA in THF solution, and layered with n-hexane. After 3 days, a crystal suitable for single-crystal X-ray diffraction was obtained.

#### Characterization

X-ray single-crystal diffraction was carried out on Bruker APEX II. TGA–DSC curves were recorded on a TA SDT Q600. Raman spectra were collected on a Renishaw in Via Raman system, with a 633 nm laser.

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### Keywords:

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Checking out the cleavage: A visible laser-driven cyclobutane cleavage reaction is monitored by using in situ Raman spectroscopy. The silver(I) coordination-induced strain and the thermal effect after laser irradiation are the two main driving forces for this cleavage reaction.