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COMMUNICATION

# Metal nanoparticle catalyzed cyclobutane cleavage reaction

Dengtai Chen, Xijiang Han,\* Wen Jin, and Bin Zhang\*

Received 00th January 20xx,  
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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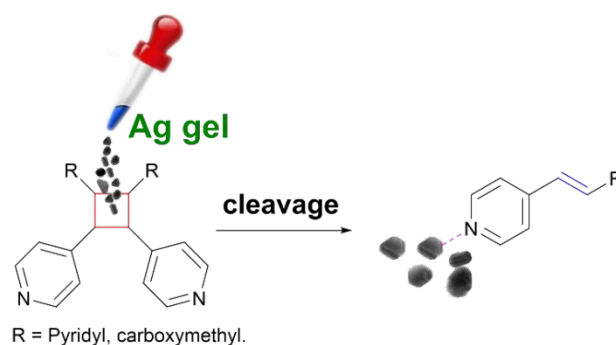
**Pyridine substituted cyclobutane cleavage reaction can be catalyzed directly by the high surface energy of metallic silver/gold nanoparticles.**

Cyclobutane cleavage reaction, as a reverse reaction of cycloaddition, is a key step in organic synthesis,<sup>1</sup> DNA damage repair,<sup>2-4</sup> and ring expansion reactions.<sup>5-8</sup> Cyclobutane strain force usually accounts for the cleavage reaction, and many environmental factors can trigger this reaction, such as laser irradiation,<sup>9, 10</sup> thermal treatment,<sup>11, 12</sup> photolysis,<sup>3, 4, 13, 14</sup> reducing reagents (e.g. vitamin C),<sup>13</sup> radicals,<sup>5, 15, 16</sup> and radiolytic method.<sup>17</sup> With high surface energy, metallic silver/gold nanoparticles (Ag/Au NPs) are normally used as surface-enhanced Raman scattering (SERS) platforms<sup>18</sup> to detect dyes and pyridyl/thiol substituted compounds.<sup>19</sup> To the best of our knowledge, there is no report concerning the surface energy catalyzed cyclobutane cleavage reaction. 1,2,3,4-tetra(pyridin-4-yl)cyclobutane (TPCB), and dimethyl 3,4-di(pyridin-4-yl)cyclobutane-1,2-dicarboxylate (DMCB) are among the most studied and ideal pyridyl substituted cyclobutane compounds.<sup>20, 21</sup> In addition to cyclobutane strain force, pyridyl functional groups' rigid linear monodentate coordination mode is also crucial for cleavage reaction.<sup>22, 23</sup>

When pyridyl is coordinated with Ag/Au NPs, the bend coordination bond tends to adjust to linear configuration,<sup>24, 25</sup> giving the cyclobutane additional strain.<sup>26</sup> Pyridyl group coordinated with Ag/Au NPs would destroy metal NPs' dielectric layer to induce agglomeration and settling. Once pyridyl group is coordinated with Ag/Au NPs, desorption is very difficult due to the coordination bond stability between Ag/Au nanoparticles and pyridyl group,<sup>27</sup> which excludes the influence of reactant and product adsorption/desorption.<sup>28</sup>

*In-situ* Raman spectroscopy is a powerful tool to study reaction mechanism for its sensitivity to the chemical bond's force constants,<sup>29, 30</sup> and this technique has been successfully

applied to monitor the laser-induced dimerization of aminothiophenol (PATP).<sup>28, 31, 32</sup> Combined with thin layer chromatography (TLC) technique,<sup>33, 34</sup> SERS is suitable for cyclobutane compound detection. In addition, as a mature method, TLC can conquer the TPCB/DMCB crystallization issue which is commonly induced by metallic Ag/Au NPs in the solution.<sup>35</sup> In this communication, pyridyl substituted cyclobutane cleavage reaction was detected on Ag/Au gel surface and monitored by Raman spectroscopy (Scheme 1). The cleavage reaction was catalyzed by the high surface energy of metallic Ag/Au NPs. This study may give a new and green way to realize cyclobutane cleavage with potential application in nanomedicine to cure DNA photo damage.



**Scheme 1.** Schematic illustration of Pyridyl substituted cyclobutane (TPCB, DMCB) cleavage on metal nanoparticle surface.

TPCB and DMCB were synthesized through solid-state photodimerization of their monomers (see experimental details in ESI†).<sup>20, 24, 36</sup> Ag nanostructures supported on polyaniline substrate,<sup>37</sup> and Ag/Au nanoparticles were prepared according to the literature method (see Fig. S1-S3 in ESI†).<sup>19</sup> Cleavage reaction was accidentally discovered by the appearance of characteristic olefin vibration peak  $\nu(\text{C}=\text{C})$  at  $\sim 1635 \text{ cm}^{-1}$  and disappearance of the cyclobutane vibration at  $\sim 1150$  and  $\sim 844 \text{ cm}^{-1}$  when SERS substrate (Ag nanostructures supported on polyaniline) was immersed in TPCB solution ( $0.5 \text{ mM}$ ). TPCB is stable in methanol solution even in open air for one month, as proved by the UV-vis spectra (Fig. S4 in ESI†),

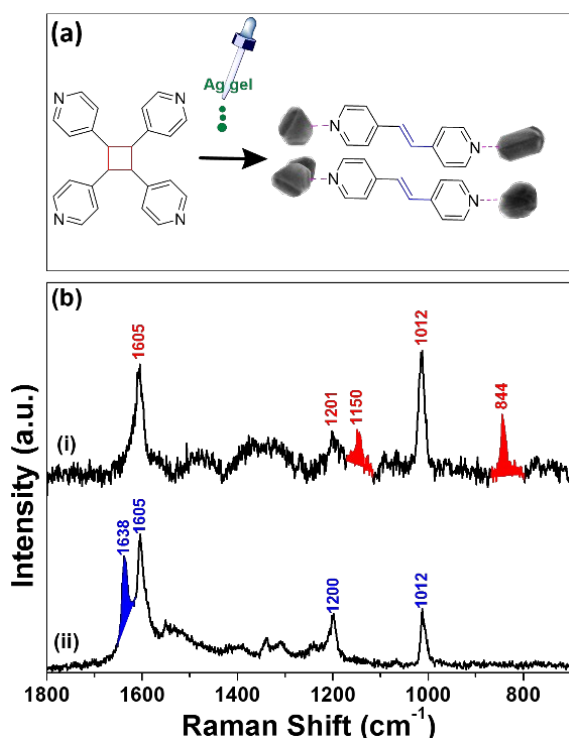
Department of Chemistry, Harbin Institute of Technology, Harbin, 150001, China.

Email: zhangbin\_hit@aliyun.com; hanxijiang@hit.edu.cn

Electronic Supplementary Information (ESI) available: Experimental section, Figure S1-S17, and Video 1. See DOI: 10.1039/x0xx00000x

which means the fresh-made Ag nanostructures may catalyze this cyclobutane cleavage reaction. This phenomenon inspires us to explore this surface reaction.

We measured the Raman and SERS spectra of TPCB and its monomer *trans*-1,2-bis(4-pyridyl)-ethylene (BPE), and DMCB and its monomer (E)-methyl-3-(pyridin-4-yl)acrylate (PMA) for reference (Fig. S5-S8 in ESI<sup>†</sup>). In order to avoid TPCB/DMCB crystalline deposition (Fig. S9-S11 in ESI<sup>†</sup>), TLC technique was applied to get reliable experimental results (Fig. S12 in ESI<sup>†</sup>). In detail, TPCB/DMCB was firstly developed onto TLC plate to give well-distributed thin layer TPCB/DMCB spot, silver gel was then sprayed onto the spot, and dried in open air for SERS measurements.

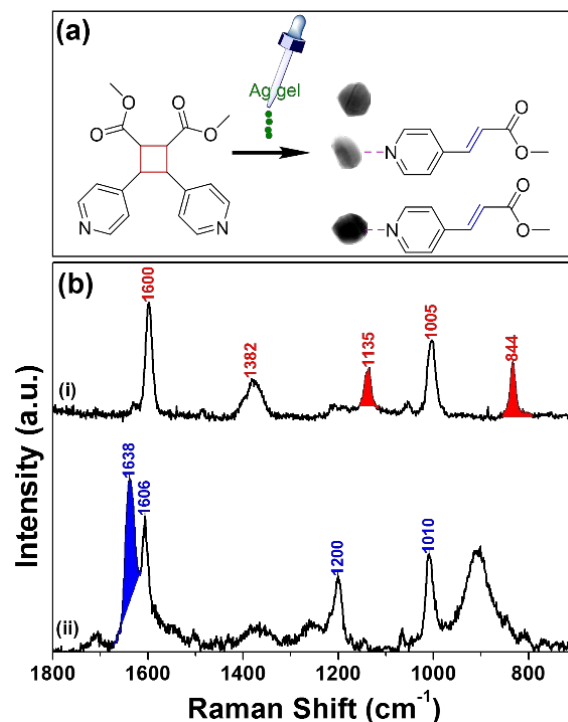


**Fig. 1** (a) Schematic illustration of TPCB cleavage reaction with the assistance of Ag NPs; (b) Raman spectra of (i) TPCB developed on TLC plate, and the peaks at 844 & 1150 cm<sup>-1</sup> (red) were assigned to cyclobutane moiety; (ii) SERS spectra of TPCB after Ag NPs were dropped on, which is identical to SERS spectra of BPE, and the peak at 1638 cm<sup>-1</sup> (blue) was assigned to C=C double bond.

TPCB cleavage reaction was detected on the Ag NPs surface, as shown Fig. 1a. SERS spectrum of BPE was discovered from the TPCB spot (Fig. 1b), as proved by the disappearance of cyclobutane moiety vibrations at 844 cm<sup>-1</sup> and 1150 cm<sup>-1</sup>, and the formation of C=C moiety vibration at 1638 cm<sup>-1</sup>. Experimental reliability lied in the facts that, firstly, TPCB and BPE were developed with different  $R_f$  values of 0.1 and 0.6, respectively; secondly, this process can be seen as a purification process, and the pencil-circled area would be pure TPCB/BPE molecules. To test the reproducibility of TPCB cleavage reaction, Raman mapping was carried out on randomly selected area and 418 Raman spectra were collected (see Fig. S13 in ESI<sup>†</sup>). We tentatively define relative intensity

(RI) of double bond (1635 cm<sup>-1</sup>) vs pyridine skeletal breathing stretching (1605 cm<sup>-1</sup>),  $RI = I_{1635} / I_{1605}$ , as the reaction process index. Mean values of  $I_{1635}$  and  $I_{1605}$  were adopted to give  $RI = 1.01$ , which indicates that the intensity of the double bond in the final products can be as high as that of the pyridine ring.

Cleavage mechanism was studied by time-dependent *in-situ* SERS spectra with 1 second time-step (Fig. S14 in ESI<sup>†</sup>, Video 1). At the beginning, the obtained Raman spectrum from TPCB spot was just straight lines. After Ag NPs was dropped on, the characteristic peak at 1635 cm<sup>-1</sup> assigned to C=C vibration can be seen immediately, indicating the instant occurrence of TPCB cleavage reaction. Strained cyclobutane was stable in solution or coordinated with metallic ions,<sup>9,22</sup> and proton acids,<sup>38</sup> therefore here we think the high surface energy of metal NPs accounts for the cleavage reaction.<sup>39</sup> The coordination interaction between Ag NPs and pyridyl group can be accomplished instantly, and the cleavage reaction occurs simultaneously. It is suggested that the cyclobutane cleavage reaction is driven by the increased strain force due to the coordination interaction, and there would be no free radical intermediates.



**Fig. 2** (a) Schematic illustration of DMCB cleavage reaction with the assistance of Ag NPs; (b) Raman spectra of solid state DMCB (i), and SERS spectra of DMCB after Ag NPs were dropped on (ii). DMCB cleavage reaction was certified with the disappeared cyclobutane peaks at 844 & 1135 cm<sup>-1</sup> and the appeared C=C double bond at 1638 cm<sup>-1</sup>.

DMCB cleavage reaction was also studied with this TLC-SERS technique, utilizing metallic NPs as catalyst (Fig. 2a). DMCB solid-state Raman spectrum showed similar cyclobutane moiety characteristic peaks at 1135 and 844 cm<sup>-1</sup>. Cleavage reaction was approved with double bonds at 1638 cm<sup>-1</sup> when

Ag NPs was dropped on (Fig. 2b). Laser wavelength-dependent and laser power-dependent SERS spectra were also studied with 532/633 nm laser with different power. It showed that the cleavage reaction could be carried out almost immediately at both lasers at different powers. However, carbonization can be observed with 100% power (6.40 mW) of 633 nm laser, and above 10% power (2.39 mW) of 532 nm laser (Fig. S15 in ESI<sup>†</sup>). We also applied Au NPs for this cleavage reaction, and found similar results (Fig. S16-S17 in ESI<sup>†</sup>). Disappearance of cyclobutane moiety vibrations, and formation of C=C moiety vibration can be well distinguished from the SERS spectra collected on Au NPs, which again verifies that the high surface energy of the metallic NPs can trigger this cyclobutane cleavage reaction.

In summary, pyridyl substituted cyclobutane being cleaved into monomers could be proved with SERS spectra on metallic Ag/Au NPs surface. Both pyridyl linear coordination mode and strained cyclobutane account for the cleavage reaction. This metallic Ag/Au NPs catalyzed cleavage reaction can shed new light on the green chemistry and nanomedicine for DNA damage repairs.

## Acknowledgements

We thank the financial support from NSFC (No. 21471039, 21203045), Fundamental Research Funds for the Central Universities (Grant No. HIT. NSRIF. 2010065 and 2011017, PIRS of HIT A201502 and HIT. BRETH. 201223), China Postdoctoral Science Foundation (2014M560253), Postdoctoral Scientific Research Fund of Heilongjiang Province (LBH-Q14062, LBH-Z14076), Natural Science Foundation of Heilongjiang Province (B2015001), Open Project Program of Key Laboratory for Photonic and Electric Bandgap Materials, Ministry of Education, Harbin Normal University, China (PEBM 201306), Open Project of State Key Laboratory of Urban Water Resource and Environment, Harbin Institute of Technology (No. ES201411), and Open Foundation of State Key Laboratory of Electronic Thin Films and Integrated Devices (KFJJ201401).

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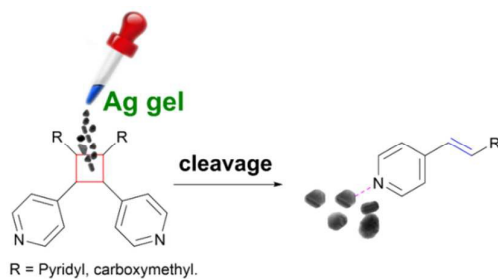
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