Hessisches Kompetenzzentrum
für Hochleistungsrechnen

Selective Organic Reactions Enabled by Isotope-Controlled Tunneling Reactivity



Project Manager
Prof. Dr. Peter R. Schreiner

Researchers
Dr. Fumito Saito

Principal Investigator
Prof. Dr. Peter R. Schreiner

Project Term
2018 - 2019

Clusters
Goethe-HLR Frankfurt

Software
GAUSSIAN

Additional Software
CFOUR

Institute
Institute of Organic Chemistry

University
Justus Liebig University Giessen

Introduction

A large kinetic isotope effect (KIE) is one of the criteria that indicates quantum mechanical tunneling in a chemical reaction. A larger mass lowers zero-point vibrational energy, resulting in broader energy barrier a particle has to penetrate. Besides tunneling probes, this phenomenon could be a useful tool to enable the desired selectivity in organic reactions. In 2017, an example of isotope-controlled selectivity in a chemical reaction was reported where two products can form by two distinct tunneling pathways (Figure 1). The computational studies predicted that carbene **1** would undergo [1,2]H-tunneling to give vinylcyclopropane **2**. On the other hand, the ring expansion would proceed to yield **3** when d_3-**1** is used. Our goal is to realize these reactions that would be the first example of the selective organic synthesis enabled by isotope-controlled selectivity.

Methods

The project consists of experimental and computational parts. In the experimental part, we synthesize suitable carbene precursors, one of which is *N*-aziridinyl imine **4** (Figure 1). Using **4** as an initial test substrate, we conduct matrix isolation experiments to capture and characterize reactive carbene species generated by flash vacuum pyrolysis or UV irradiation. The identification of reactive intermediates captured in a matrix at 3 K is performed by IR spectroscopy. In the computational part, we compute IR spectra of possible (reactive) intermediates at B3LYP/6-31G(d,p). We also perform computations of IR

JUSTUS-LIEBIG-UNIVERSITÄT GIESSEN
TECHNISCHE UNIVERSITÄT DARMSTADT
UNIKASSEL VERSITÄT
Philipps Universität Marburg

spectra at CCSD(T)/cc-pVTZ for the optimized structures. The computed IR spectra are used for comparison with experimental spectra.

Results

The synthesis of *N*-aziridinyl imine **4** was performed starting with commercially available (–)-ethyl L-lactate (Scheme 1). Protection of the hydroxyl group with the 2-tetrahydropyranyl (THP) group was followed by the cyclopropanol formation to give **5**. The free hydroxyl group was methylated, and the THP group was removed to reveal secondary alcohol, which was oxidized to give ketone **6**. The condensation with hydrazine **7** afforded hydrazone **4**. Its deuterated variant d_3-**4** was also prepared following a-deuteration of **6**.

Next, we carried out matrix isolation experiments using **4** as a substrate. After deposition of **4** in an argon matrix at 12 K, photochemical decomposition of **4** to carbene **1** via diazoalkane **8** was attempted at 3 K. Irradiation at 313 nm resulted in the formation of **8**, which was assigned based on the strong, characteristic C=N=N absorption at 2060 cm^{-1}. However, diazoalkane **8** was unexpectedly stable against UV irradiation and decomposition of **8** to **1** has not been achieved under photochemical conditions.

Discussion

N-aziridinyl imines (also known as Eschenmoser hydrazones) is known to generate diazoalkanes – common carbene precursors – without the need for an external base. This would be advantageous when one considers the generation of carbenes thermally by flash vacuum pyrolysis or photochemically in a matrix. In fact, *N*-aziridinyl imines have been utilized by other research groups to study reactivities of carbenes under matrix isolation conditions. Although photochemical conditions failed in our hands, we envision generation of carbene **1** (via **8**) by flash vacuum pyrolysis.

Outlook

We will establish conditions for thermal generation of carbene **1** by examining reaction parameters such as temperature, length and diameter of quartz tube. Once the method is established, we investigate reactivity of **1** (expectedly [1,2]H-tunneling to form vinylcyclopropane **2**). At the same time, we also explore reactivity of d_3-**1** and see if it undergoes ring expansion to give **3** by carbon tunneling.

Publications

Nandi, A.; Gerbig, D.; Schreiner, P. R.; Borden, W. T.; Kozuch, S.: "Isotope-controlled selectivity by quantum tunneling: hydrogen migration versus ring expansion in cyclopropylmethylcarbenes", J. Am. Chem. Soc. 2017, 139, 9097–9099, 2017 https://doi.org/10.1021/jacs.7b04593

Last Update: 2022-06-14 20:36