HEAVY ATOM TUNNELING IN ORGANIC CHEMISTRY

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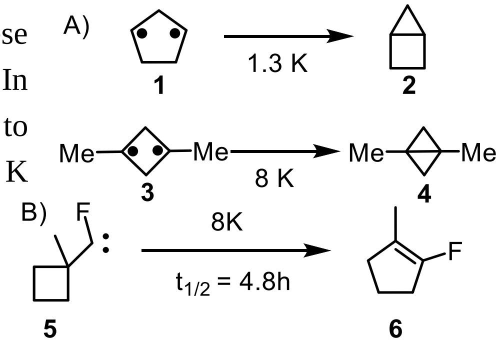
Introduction

Tunneling is the quantum property where an atom is observed to travel across a barrier for which the requisite potential energy is not met. Through the JWKB reaction (**eq. 1**), the tunneling probability can be determined with only the knowledge of the barrier width, barrier height, and mass of the tunneling particles. An important takeaway from this equation is the larger significance of barrier width over mass: barrier width has a linear dependence whereas the mass has a square root dependence. Heavy atom tunneling describes the quantum tunneling events associated with atoms larger than helium. While the probability of heavy atom tunneling is severely reduced relative to hydrogen and helium, low enough barrier widths (< 0.75 Å) can led to relatively high probabilities of quantum tunneling.[1] Unfortunately, until 1975, it was thought impossible that atoms larger than helium would be capable of tunnelling.

$$P(E) = \mathrm{e}^{-\pi^2 w\sqrt{2m(V_0 - E)}/h} \tag{1}$$

Literature Survey

The first examples of heavy atom tunneling in the literature include the decomposition of diradicals to their respective bicycles (**Scheme 1A**).[1] In both examples it was noted that there was large deviance from the Arrhenius equation and the rates of the reactions in matrix isolation were temperature independent, indicating that these reactions likely proceed through a heavy atom tunneling event. In 2003, it was observed the carbene insertion of carbene **5** to cyclopentene **6** occurred in matrix isolation in the dark at 9 K (**Scheme 1B**).[2] Classical transition state theory would have predicted a rate 10^{160} times slower than the observed rate of the reaction, providing evidence that heavy atom tunneling plays a significant role in this reaction. Further computation discovered that this reaction proceeds through the 0th vibrational state, a level where reactivity is generally perceived to be impossible.



Scheme 1. A) closure of diradicals in matrix isolation B) C-C carbene insertion in matrix isolation

Heavy atom tunneling is observed in the opening of cyclopropyl carbinyl radical (**Figure 1**). Through an elegant intermolecular natural abundance $^{12}C/^{13}C$ KIE experiment, the population of ^{13}C could be used to deduce the contribution of tunneling.[1] The results demonstrated a large deviation from the linear expectations of the Arrhenius equation and experimental evidence is also in complete agreement with computationally determined values (which incorporated heavy atom tunneling). A key extrapolation was that greater than 50% of the rate contribution at – 80 °C was a function of heavy atom tunneling, indicating the importance of a reaction that organic chemists encounter frequently both in the literature and in the lab.

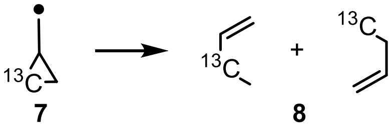
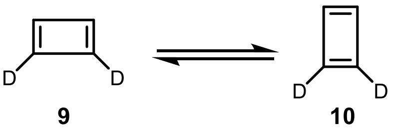


Figure 1. Intramolecule KIE experiment to determine contribution of tunneling in cyclopropyl carbinyl radical

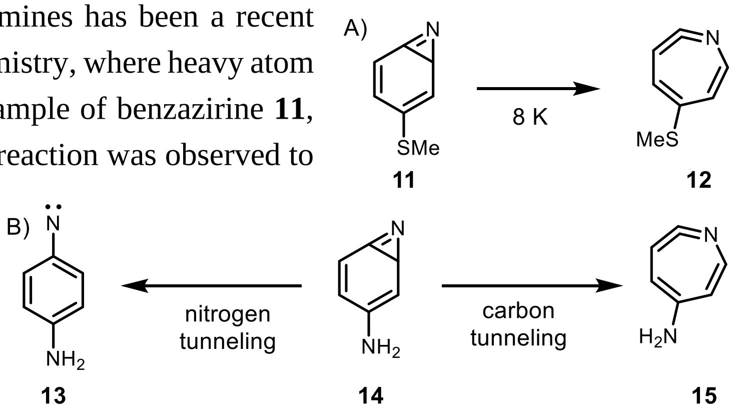


9 **10**

Figure 2. automerization of cyclobutadiene-d_2

Automerization in many cases has been demonstrated to involve heavy atom tunneling, and the example explored here is the case of cyclobutadiene (**Figure 2)**. This was first observed by Carpenter in 1982, where it was found that the isomerization of cyclobutadiene proceeds at a much faster rate than could be described classically.[1] It was found that below 0 °C, the rate of heavy atom tunneling accounts for >95% of the actual rate of the reaction. Experimentally, an elegant trapping of a regiospecifically generated cyclobutadiene-d_2 through a [4+2] cycloaddition led to the determination of the rates of automerization.

The conversion of benzaziranes to ketenimines has been a recent area of interest in the field of physical organic chemistry, where heavy atom tunneling was first observed in 2013 with the example of benzazirine **11**, converting to ketenimine **12** (**Scheme 2A**).[3] This reaction was observed to rapidly undergo the transformation in the dark in matrix isolation, suggesting a quantum-controlled reaction. With amino benzazirane **14** (**Scheme 2B**), high rates of both ring opening and nitrene formation reactions in matrix isolation suggests competitive tunneling events. This is the third example of a reaction tunneling by nitrogen, and the first case of an organic molecule undergoing a nitrogen tunneling event.[4]



11 **12** **13** **14** **15**

Scheme 2. A) Benzazirane ring expansion to form ketenimine B) competitive carbon tunneling vs. nitrogen tunneling

Utility in Organic Chemistry

A recent study was performed analyzing the tunneling contributions in 13 different organic reactions.[5] It was found that transfomations such as the Diels-Alder cycloaddition and SN_2 reactions have significant contributions of heavy atom tunneling. Reactions that agree with intuition that have high tunneling contributions include [3,3]-sigmatropic rearrangements as well as electrocylizations. In these cases, heavy atom tunneling ranges from as a little as 10% of the rate to greater than 95%. As a result, heavy atom tunneling is an important contributor to the rates of organic reactions which cannot be ignored.

Outlook

The fundamental insights obtained from heavy atom tunneling as well as the experiments and methodologies developed may be useful for the study of reactive intermediates in organic/organometallic reactions. It would be interesting to see if heavy atom tunneling could be utilized to change product selectivities relative to the expected transition state outcome. As well, the study of methodologies utilized by organic chemists such as the giese reaction or radical decarboxylaton would also be reactions of interest. Finally, in complex molecule synthesis it would be interesting to observe heavy atom tunneling in reactions with high pre-organizational requirement: for example, polyene cyclizations.

References: 1) *WIREs Comput. Mol. Sci.*, **2016**, *6*, 20-46 2) *Science* **2003**, *299*, 867 3) *J. Am. Chem. Soc.*, **2013**, *135*, 10246 4) *J. Am. Chem. Soc.*, **2019**, *36*, 14340 5) *Angew. Chem. Int. Ed.*, **2017**, *56*, 13099