Theoretical Insights into the Mechanism of the Copper Catalysed Azomethine Imine-Alkyne Cycloaddition Reaction

H. Bhakhoa*, L. Rhyman and P. Ramasami

Computational Chemistry Group, Department of Chemistry, Faculty of Science, University of Mauritius, Réduit, Mauritius

*Author for correspondence e-mail: hbhakhoa@gmail.com

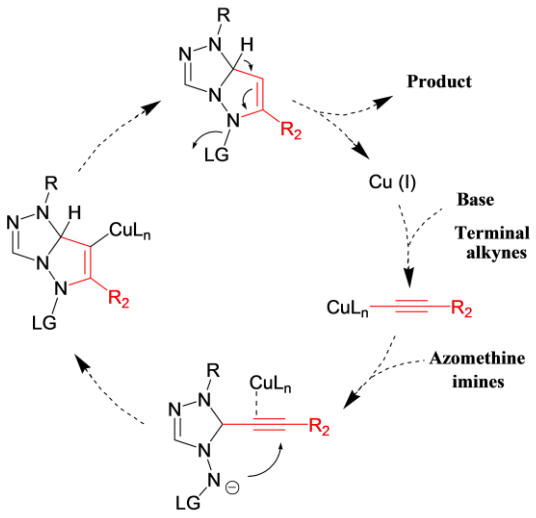
Cycloaddition reactions are among the most powerful processes with both synthetic and mechanistic interest in organic chemistry. In particular, the copper catalysed [3+2] cycloaddition reaction (32CA), which is an effective route for the synthesis of the nitrogen containing five membered heterocyclic structures, stands as a popular example of click reactions.

Recently, in an attempt to spur the development of catalytic processes in the field of click chemistry, Katritzky's group [1] conducted the copper (I) catalysed 32CA of a wide scope of C,N-cyclic azomethine imines with terminal alkynes, *via* a novel and efficient process and ultimately proposed a stepwise catalytic mechanism (Scheme 1) for this particular reaction. However, there is still neither experimental nor theoretical proof for the key steps and intermediates of this catalytic cycle.

Thus, a DFT study has been carried out to shed light on the proposed mechanism of the copper (I) mediated 32CA of the azomethine imines with terminal alkynes [2]. En route, an in-depth comparison of the uncatalysed and catalysed reaction were also made to have a better understanding on the role of the copper (I) catalyst.

Interestingly, the transformation from the uncatalysed 32CA to the catalysed stepwise process, lowers the activation barrier considerably. The detailed insight obtained herein, can be used to predict *a priori* the reactivity of a wider range of azomethine imines with terminal alkynes before embarking on a resource-consuming synthetic undertaking. We hope that this theoretical study incites experimentalists to isolate and characterise the intermediates.

Scheme 1: Proposed mechanism of Cu (I) mediated azomethine imine-alkyne cycloaddition



References

1. D. Jishkariani, C. D. Hall, A. A. Oliferenko, D. Leino, and A. R. Katritzky, Journal of Organic Chemistry, 77, 2012, 5813-5818.
2. H. Bhakhoa, L. Rhyman, P. Ramasami, L. R. Domingo, A. A. Oliferenko, and A. R. Katritzky, Journal of Organic Chemistry, 2013 (*In preparation).*