Synthesis of Bulky Copper Carbenes in a Copper Click Reaction to Determine the Impact on the Yield of Triazoles

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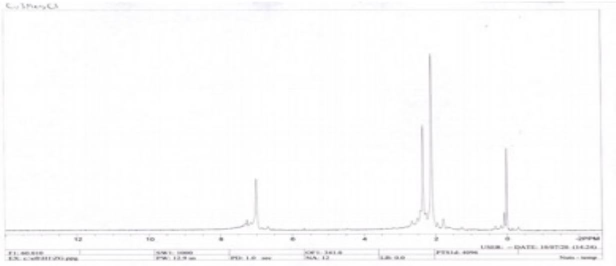
Abstract

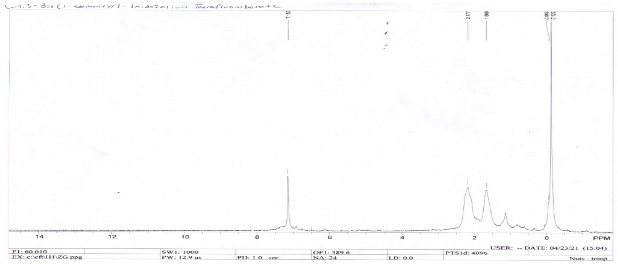
Triazole have many applications in medicinal chemistry as antifungal medications and fungicides in crop protection. Utilizing a known copper click reaction, we plan to attach copper to a series of increasingly bulky carbenes and react them the click reaction to determine their impacts on the yield of triazoles. This can determine the potential applications of different carbenes in the copper click reaction, broadening the amount of available carbenes that are able to be used as copper catalysts to create triazoles. We have confirmed that two separate methods must be used to attach copper to specific carbenes depending on the nature of the carbene. The same method of attaching copper to the carbenes cannot be used for all carbenes and not every carbene was able to accept the copper ion. Not every copper catalyst was able to react in the click reaction to synthesize triazoles.

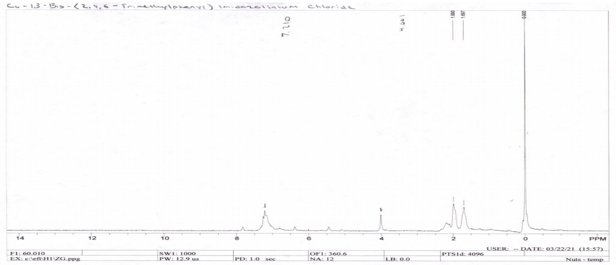
Methodology

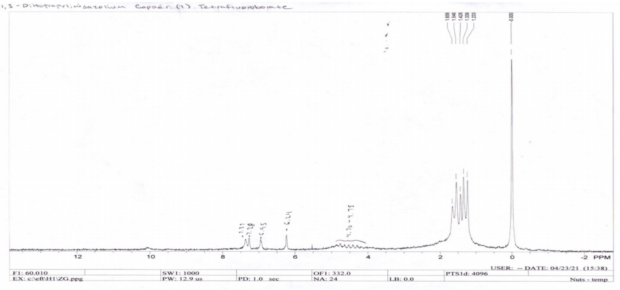
- A set of known reactions were performed to be used as a control baseline for the other experimental reactions.
- Utilizing the procedure from the control reactions, two methods were developed for the attachment of copper to the experimental carbenes.
- Once copper was attached to the carbenes, several click reactions were performed to determine the yield of 1,2,3-Triazoles from each copper catalyst.

H-NMR Copper Catalyst

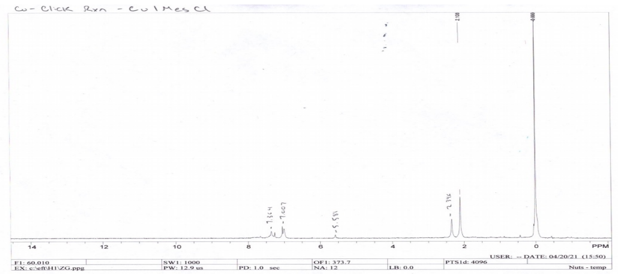


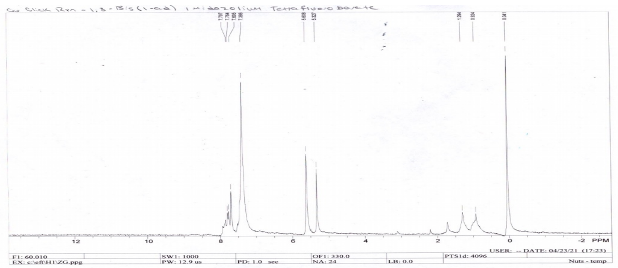


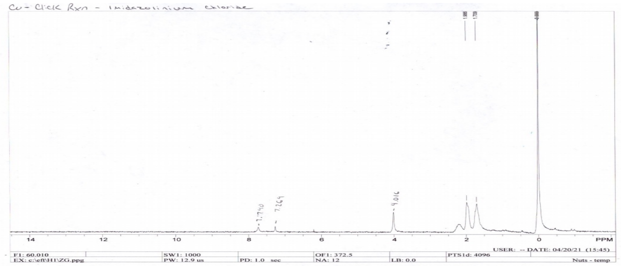


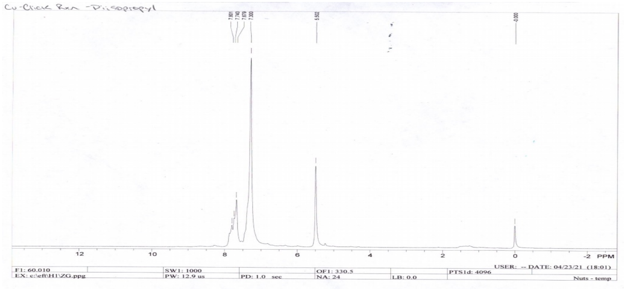


H-NMR Copper Click Reaction









Results and Discussion

- The defining peaks for successfully synthesizing the 1,2,3-Triazole are shown as a series of peaks between 6.95-7.81 ppm indicating the presence of the two Mes groups attached to the 5-membered ring as well as the peak at 5.59 ppm representing the two hydrogens bound to the carbon that links one of the Mes groups to the nitrogen on the 5-membered ring.
- The control reaction was successful in both the attachment of copper to the carbene to form the copper catalyst, shown by the disappearance of the H peak at 10.43 ppm, as well as being successful in the synthesis of the 1,2,3-Triazole shown in the series of peaks between 7.00-7.36 ppm as well as the peak at 5.58 ppm.
- The attachment of copper to the first experimental carbene containing the adamantly groups was successful utilizing the second method of copper attachment shown by the disappearance of the H peak at 8.77 ppm. The click reaction utilizing this copper catalyst also proved successful in the synthesis of 1,2,3-Triazole represented in the peaks between 7.38-7.80 ppm and the peak at 5.61 ppm.
- The attachment of copper to the second experimental carbene containing the mes groups was successful utilizing the first method of copper attachment shown by the disappearance of the H peak at 9.45 ppm. The click reaction utilizing this copper catalyst also proved successful in the synthesis of 1,2,3-Triazole represented in the peaks between 7.26-7.74 ppm and the peak at 4.02 ppm.
- The attachment of copper to the third experimental carbene containing the IPr groups was successful utilizing the second method of copper attachment shown by the disappearance of the H peak at 8.92 ppm. The click reaction utilizing this copper catalyst also proved successful in the synthesis of 1,2,3-Triazole represented in the peaks between 7.30-7.81 ppm and the peak at 5.50 ppm.

Conclusion

Utilizing the copper click reaction, copper was successfully attached to a series of increasingly bulky carbenes to create copper catalysts that held similar properties to the control copper catalyst. Due to these similar properties, the bulkier copper catalysts were able to be used in the click reaction to successfully synthesize 1,2,3-Triazole. This research showed proof of concept, expanding the available carbenes that can be used in the copper click reaction. Further research needs to be performed to improve on the efficiency of the procedure as well as the purity and the yield of the product.