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Diversity Oriented Synthesis of Sulfur Containing Epoxide Compounds

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Introduction

The opening of the epoxide ring with amine nucleophiles has shown to create products that are potentially active in a pharmaceutical setting. Through diversity oriented synthesis, a relatively quick and simple procedure was created to generate sulfur containing compounds.

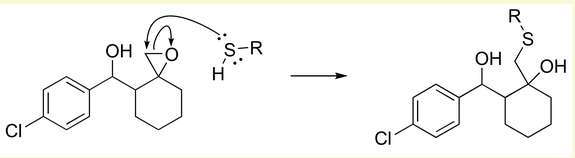


Figure 1: Sn2 mechanism for the opening of the epoxide ring and addition of a thiol group.

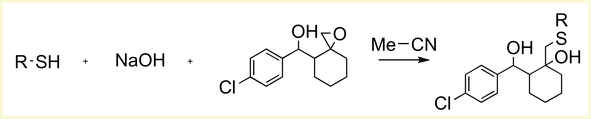


Figure 2: Procedure used for the opening of the epoxide ring and addition of a thiol group.

Results and Discussion

Table 1 shows three products that were successfully synthesized and verified by NMR.

We let our reactions occur at room temperature and verified using TLC that starting material was no longer present (~30 min). After liquid-liquid extraction, we dried and rotovapped the products to remove solvent. An NMR was done to confirm the reaction went as planned. We used flash chromatography to separate the product from impurities if needed.

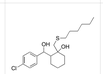
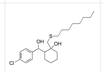
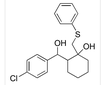
Thiol	Product	Yield
		61%
		55%
		24%

Table 1: Thiol reagents that were used in the reaction shown in figure 2, their products, and percent yield.

We attempted to react sodium hydrosulfide with epoxide to create a product as seen in figure 4a. The reaction conditions from figure 2 failed to result in the predicted product and we have yet to find a successful set of reaction conditions. We also attempted to react sodium sulfide and epoxide to create a product as seen in figure 4b. In addition, the sodium in figure 4b can potentially result in the opening of another epoxide ring as seen in figure 4c, which has heightened complexity compared to other products.

Again, the reaction conditions displayed in figure 2 did not result in our anticipated product and we have yet to create a more favorable set of reaction conditions.

We attempted four new, more complex thiol groups with the same reaction conditions as shown in figure 2, but we have not received clear results. It appears that some of the more complex thiols result in a product that has an episulfide, but the structure of the episulfide compound has yet to be confirmed.

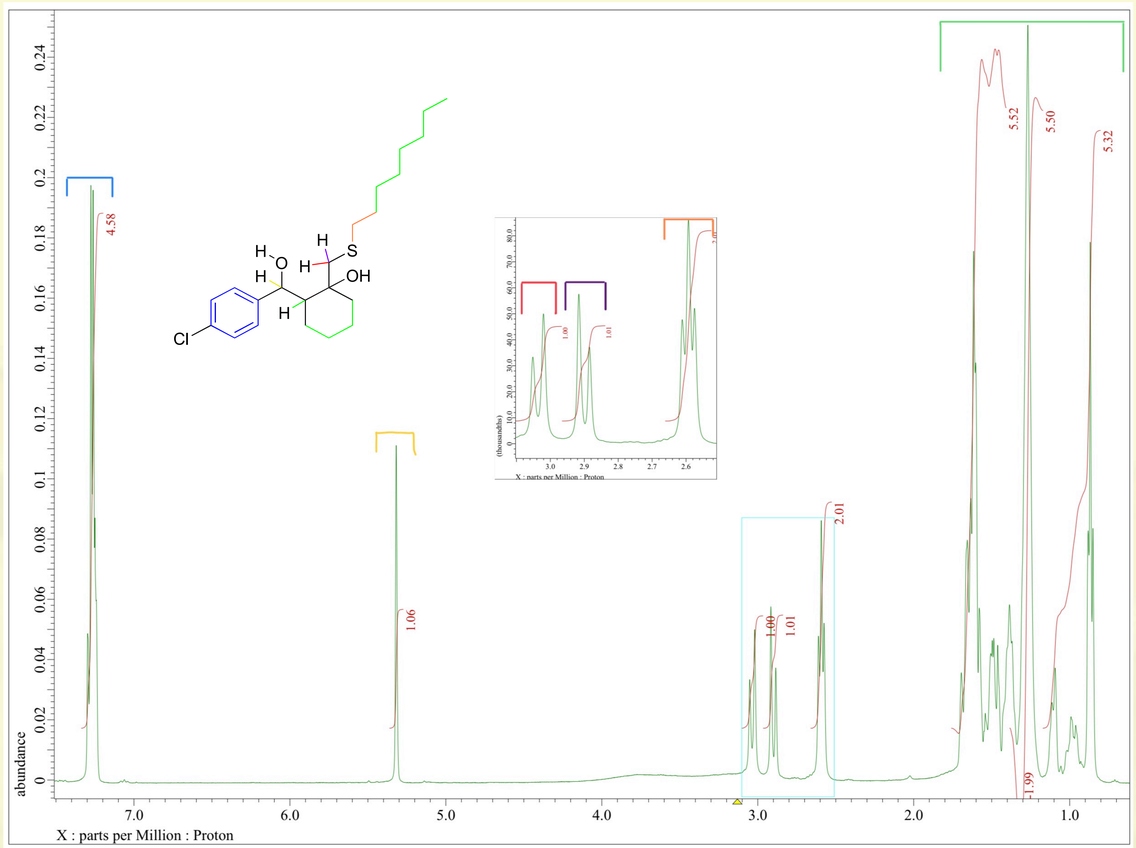


Figure 3: Proton NMR of our octanethiol product. The colored bonds on the structure indicate hydrogens that correspond with colored sections of the spectrometry.

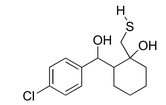
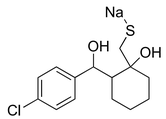
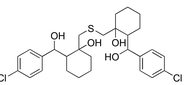
A	
B	
C	

Figure 4a: Desired product resulting from reaction of epoxide and NaSH.
Figure 4b: Desired product resulting from reaction of equal parts epoxide and Na_2S.
Figure 4c: Desired product resulting from reaction of excess epoxide and Na_2S.

Future Work

Our future work includes the synthesis of new products as seen in table 2. We suspect to have created the following products, but have yet to verify the products using NMR and mass spectrometry.

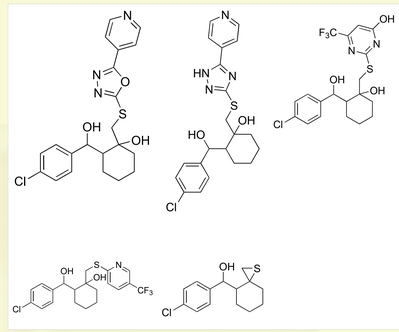


Table 2: Potential products that have yet to be synthesized and verified.

Acknowledgements

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References

1. Hansen, J. Diastereoselective sulfur ylide promoted aldol/epoxidation. *Tetrahedron Letters* **2006**, *47 (40)*, 7209-7212.