



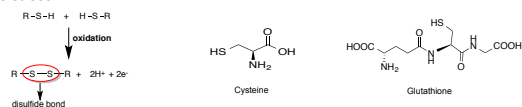
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Mechanistic Studies of Thiol Oxidation by ¹⁹F NMR

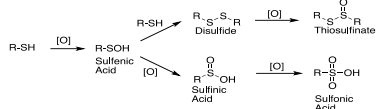
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Introduction

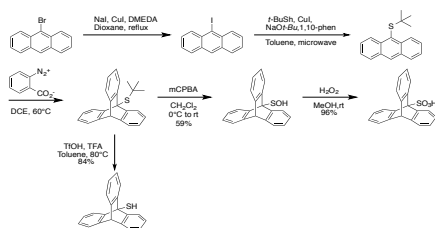
- The intermediate products of thiol oxidations have been found to play a role in a increasing number of chemical and biological processes such as signal transduction, protein folding and enzymatic processes.
- For example, glutathione, a tripeptide containing a nucleophilic thiol, is present in high concentration (up to ~5mM) in cells and offers a line of defense against oxidative stress.



- The process of thiol oxidation is much more complex than a 'textbook reaction'. This is presumably due to the high reactivity of sulfenic and sulfinic acids towards oxidation, rendering it nearly impossible to isolate.
- The isolation and characterization of these intermediates has yet to be determined.

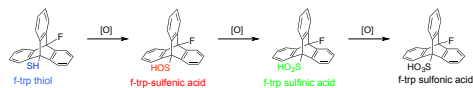


- Previous research in our laboratory enabled the synthesis of a persistent sulfenic acid; 9-triptycene sulfenic acid.



- The high steric hindrance of the triptycene backbone plays an important role as a protecting group in the stabilization of the sulfenic acid. This structure will enable the complete characterization and kinetic analysis of thiol oxidation reactions.
- Monitoring the reaction kinetics by ¹⁹F NMR is a more efficient way to collect kinetic data while minimizing product handling and cost.

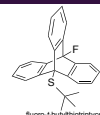
d_3 -MeOH = \$150/5g



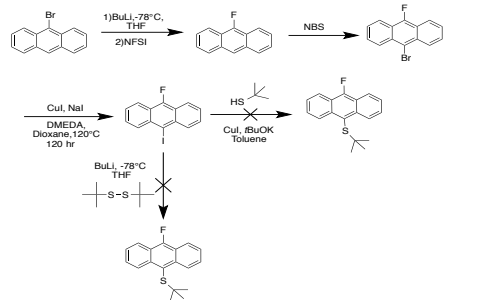
- Above are the authentic standards to be synthesized and analyzed through ¹⁹F NMR.

Synthesis of Triptycene Thiol Oxidation Products

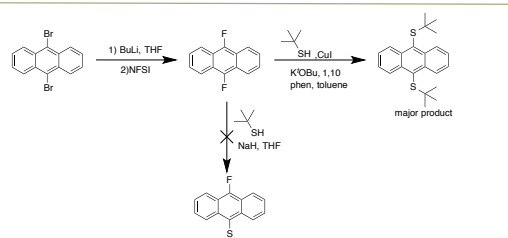
•Synthesis of the targeted fluorinated *t*-butylthiotriptycene will enable the production of the thiol, sulfenic acid and sulfonic acid standards.



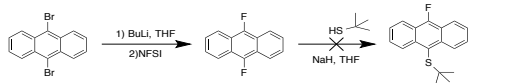
Route 1



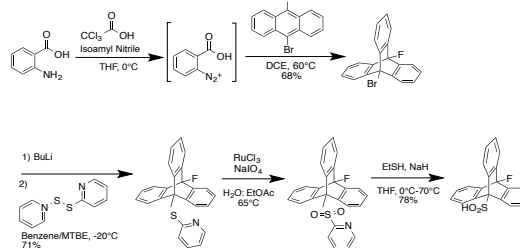
Route 2



Route 3



Synthesis of Fluoro-Triptycene Sulfinic Acid



Reaction Kinetics by ¹H NMR

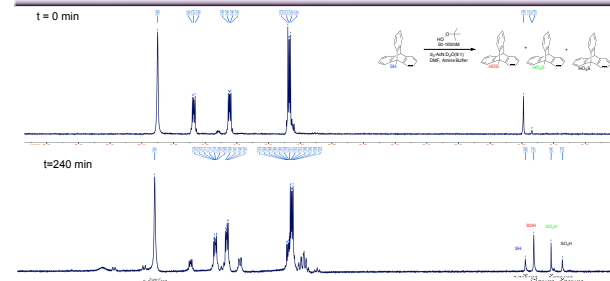


Figure 1. At $t=0$ largely only thiol is observed, but as the oxidation continues to $t=240$ min, four well separated peaks are observed. Each peak is labeled according to the observed thiol oxidation product second NMR. This obvious separation challenges the 'textbook reaction' stigma and prompts further understanding of the oxidation. A similar, yet more informative analysis is expected to be achieved through ¹⁹F NMR.

Kinetic Data

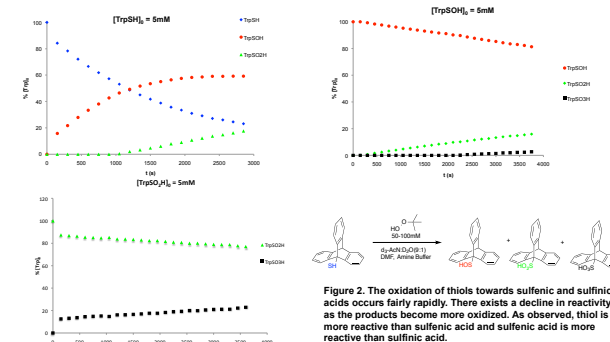
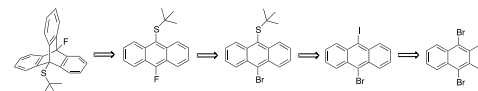


Figure 2. The oxidation of thiols towards sulfenic and sulfinic acids occurs fairly rapidly. There exists a decline in reactivity as the products become more oxidized. As observed, thiol is more reactive than sulfenic acid and sulfenic acid is more reactive than sulfonic acid.

Future Work



Method optimization to get reproducible data

- o Determine kinetics
- o Kinetics vs pH
- o Synthesis of fluorinated analogues
- o Kinetics in a variety of solvents

Reactivity with different oxidants:

- o H₂O₂
- o Alkyl-OOH
- o HOCl

References

- McGrath, A. J.; Garrett, G. E.; Valgimigli, L.; Pratt, D. A. *J. Am. Chem. Soc.* **2010**, *132*, 16759.
- Amorati, R.; Lynett, P.T.; Valgimigli, L.; Pratt, D.A. *Chem. Eur. J.* **2012**, *18*, 6370-6379.
- McGrath, A.J. *Synthesis, Redox Chemistry and Antioxidant Activity of Sulfenic Acids*. Unpublished master thesis, Queens University, Kingston, Ontario.

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Acknowledgements

