

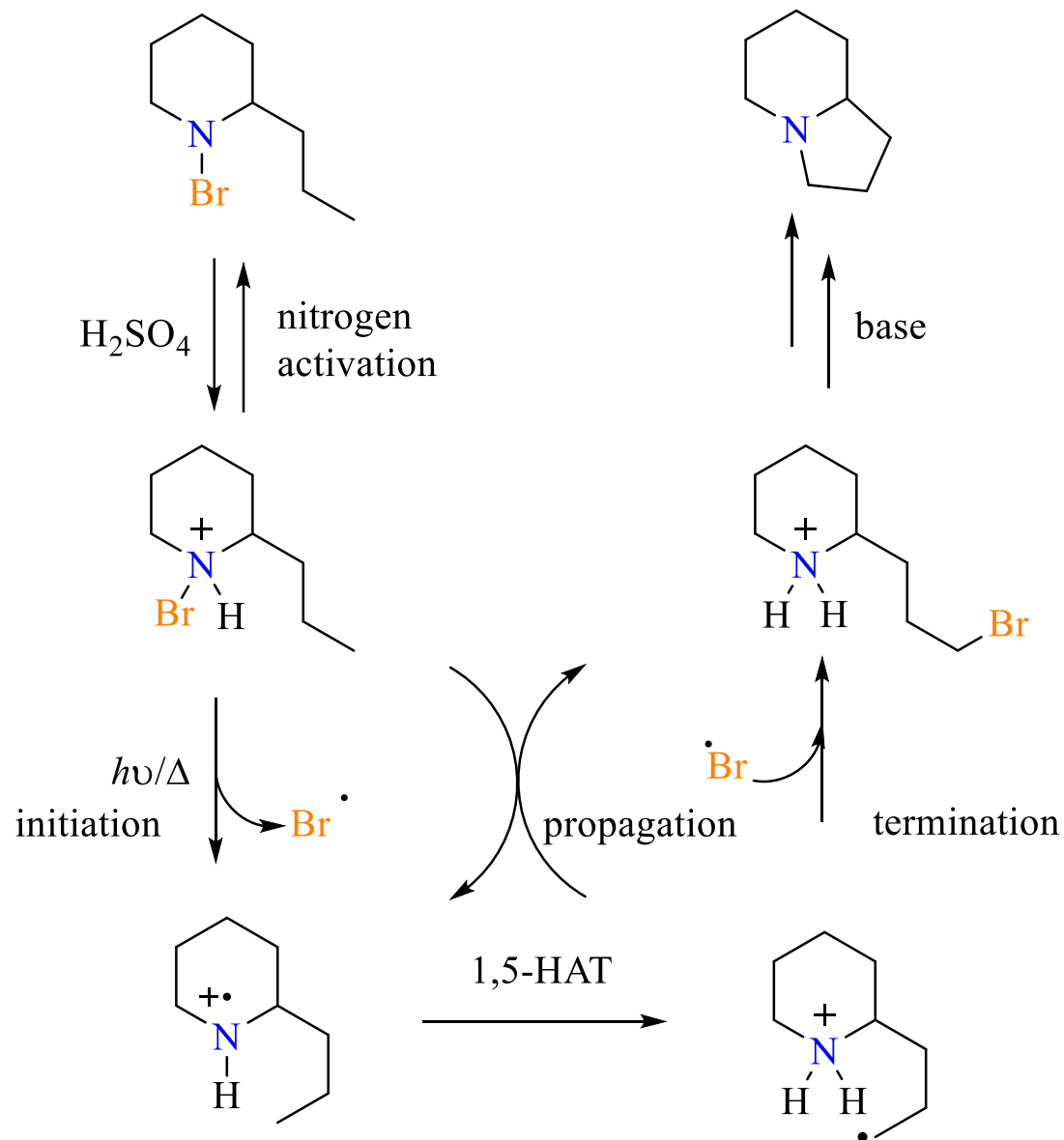
EPR and NMR Investigation of Hofmann–Löffler–Freitag Reaction: Detection of N-centered Radical



Gabrijel Zubčić

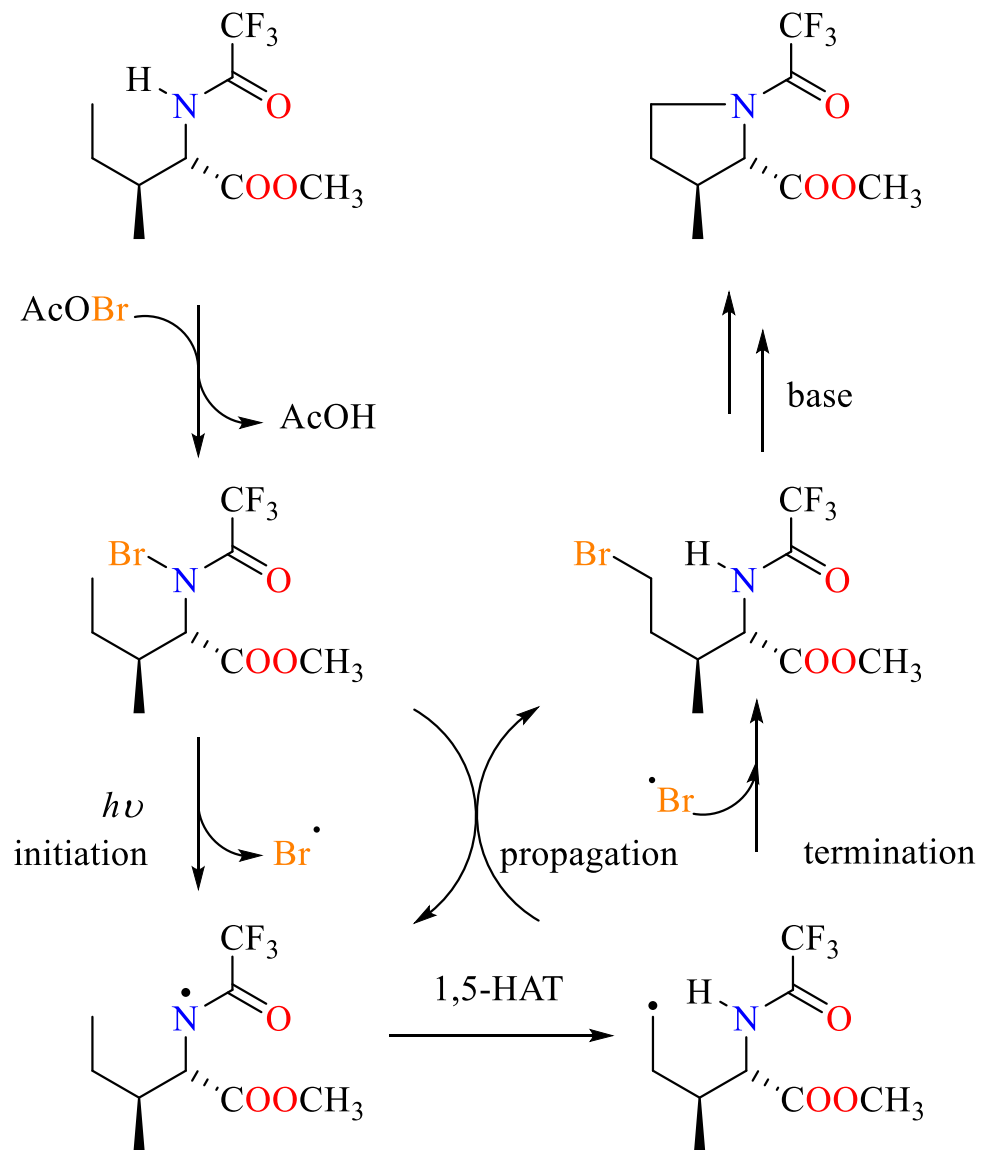


Original Hofmann-Löffler-Freytag (HLF) reaction

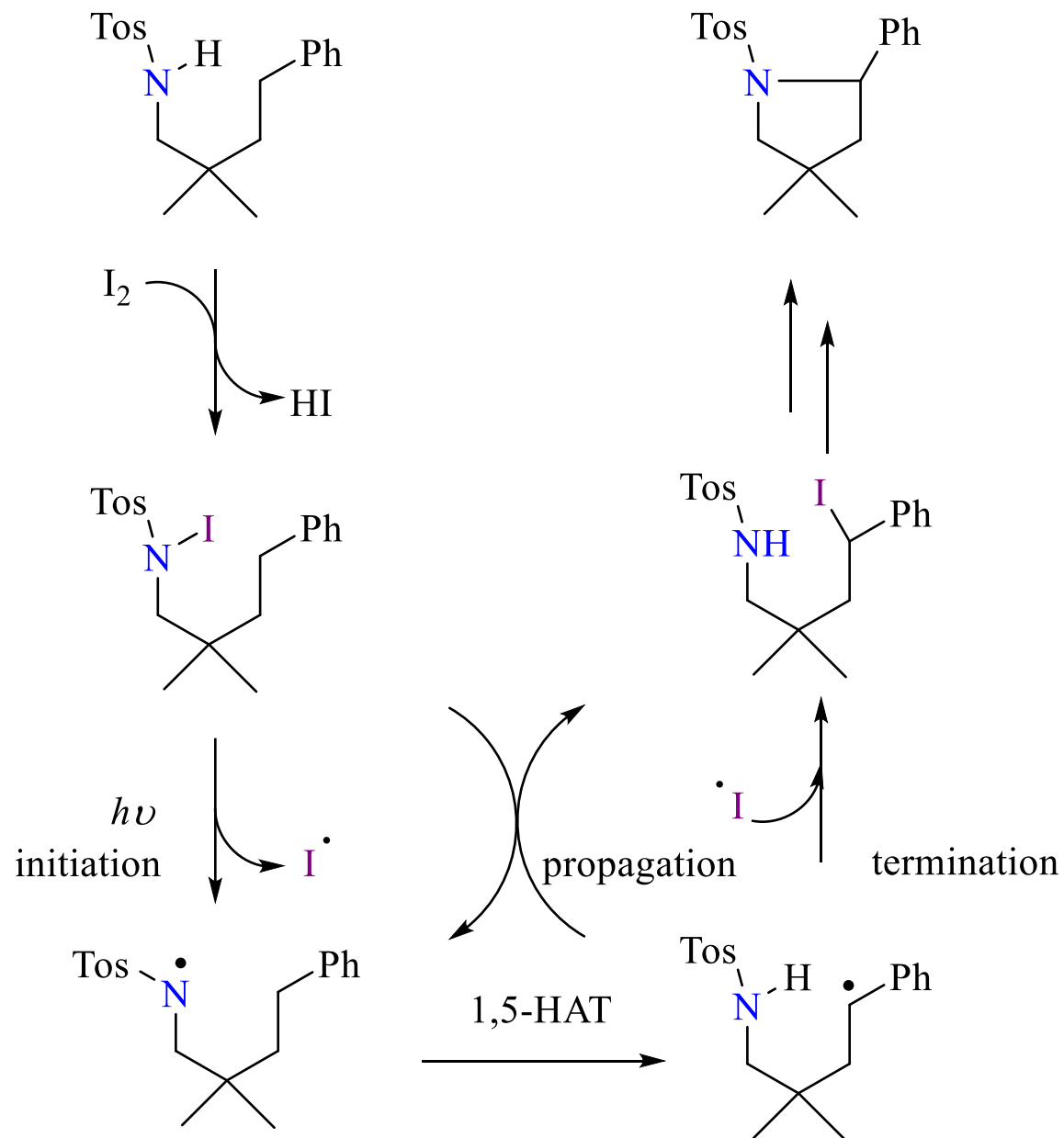


a) Hofmann, A. W. *Ber. Dtsch. Chem. Ges.* **1881**, 14, 2725; b) Hofmann, A. W. *Ber. Dtsch. Chem. Ges.* **1883**, 16, 558; c) Hofmann, A. W. *Ber. Dtsch. Chem. Ges.* **1885**, 18 (5), 109 d) Löffler, K., Freytag, C. *Ber. Dtsch. Chem. Ges.* **1909**, 42, 3427

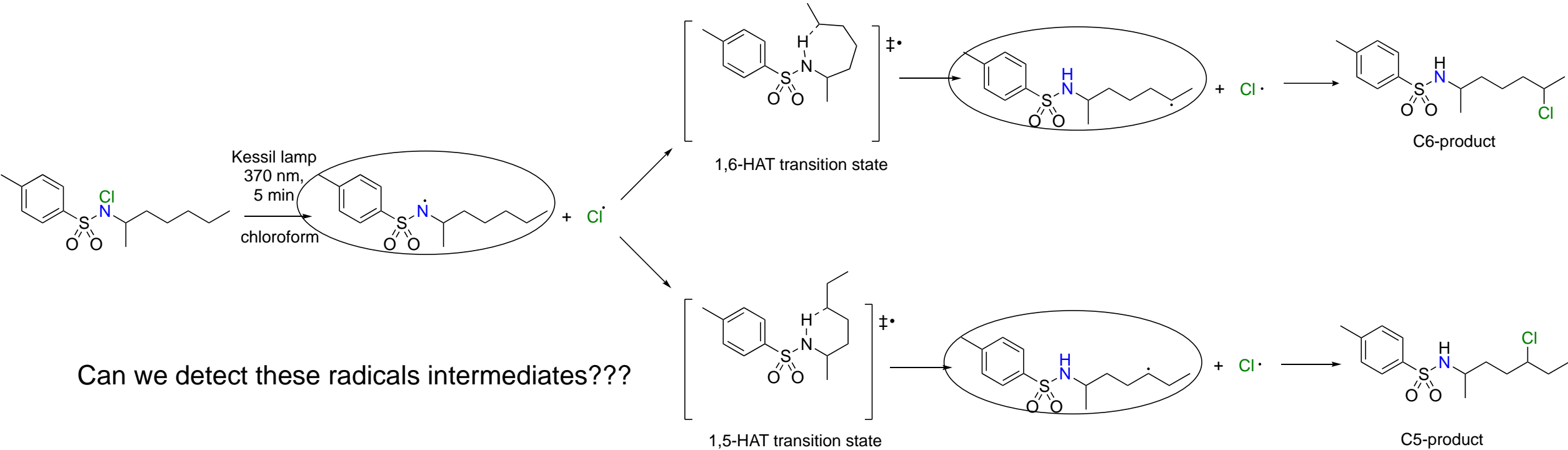
"Corey modification" of the HLF procedure



"Suarez modification" of the HLF reaction

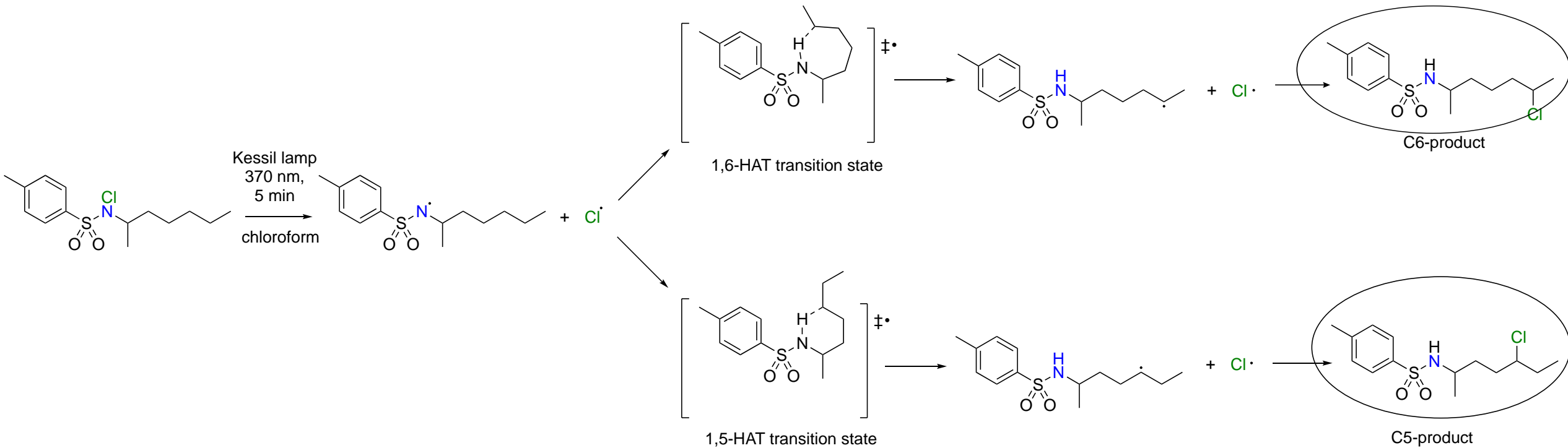


Goals of our work



Can we detect these radicals intermediates???

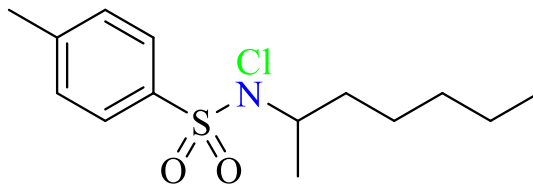
Goals of our work



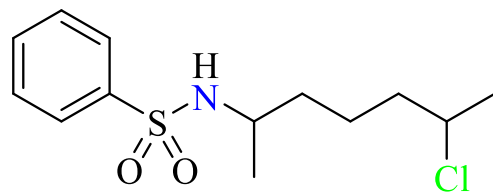
Regioselectivity explained???
C5 vs C6 products???

NMR experiments

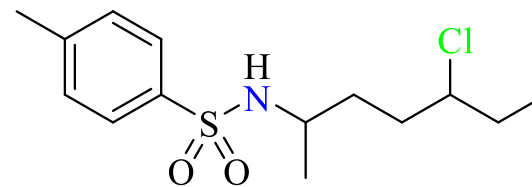
Reactant



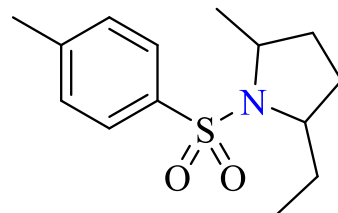
Expected products according to the literature



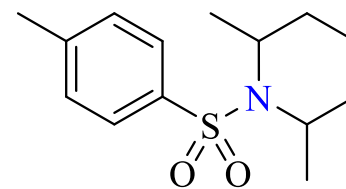
1



2

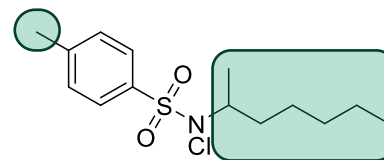
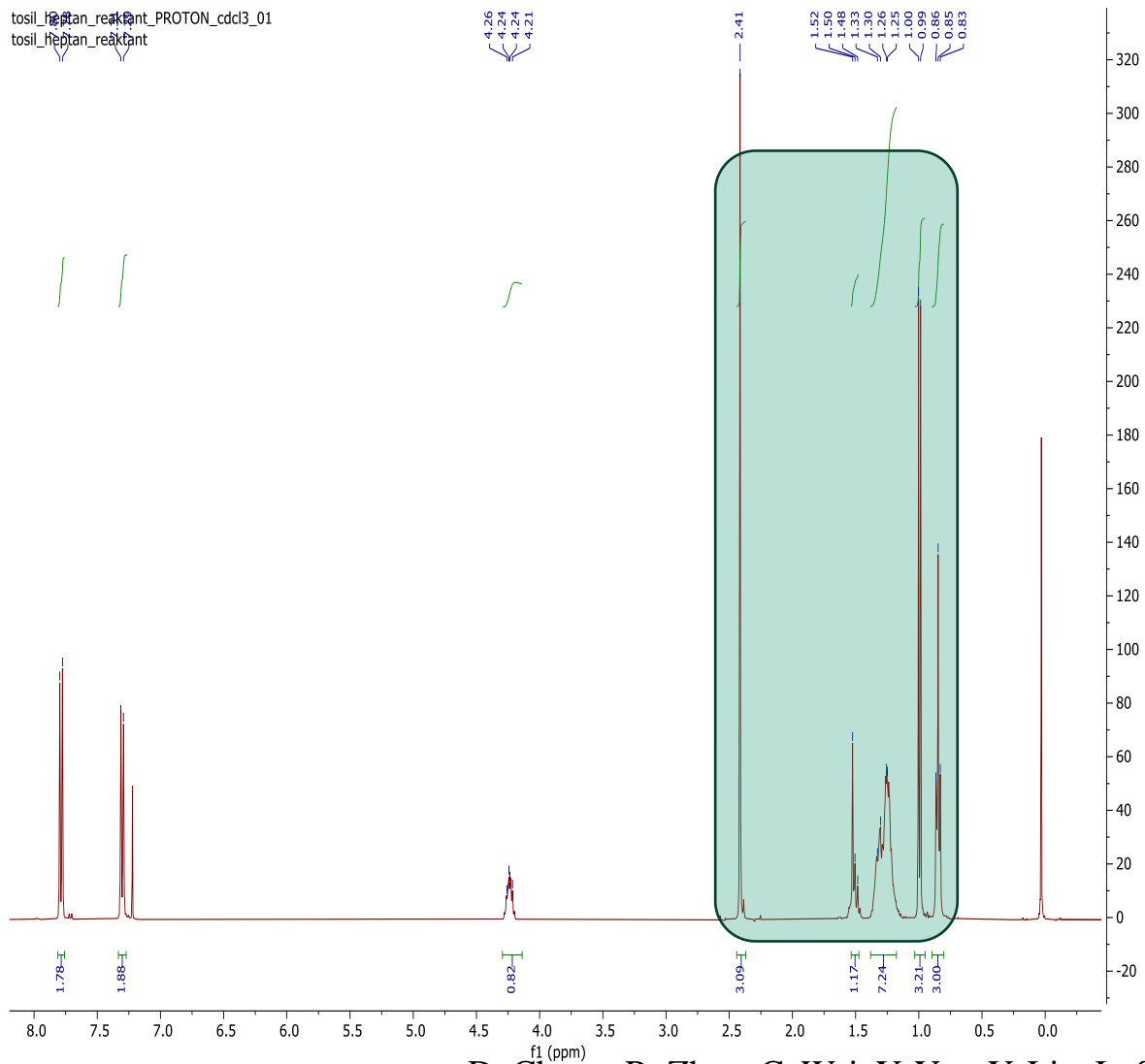


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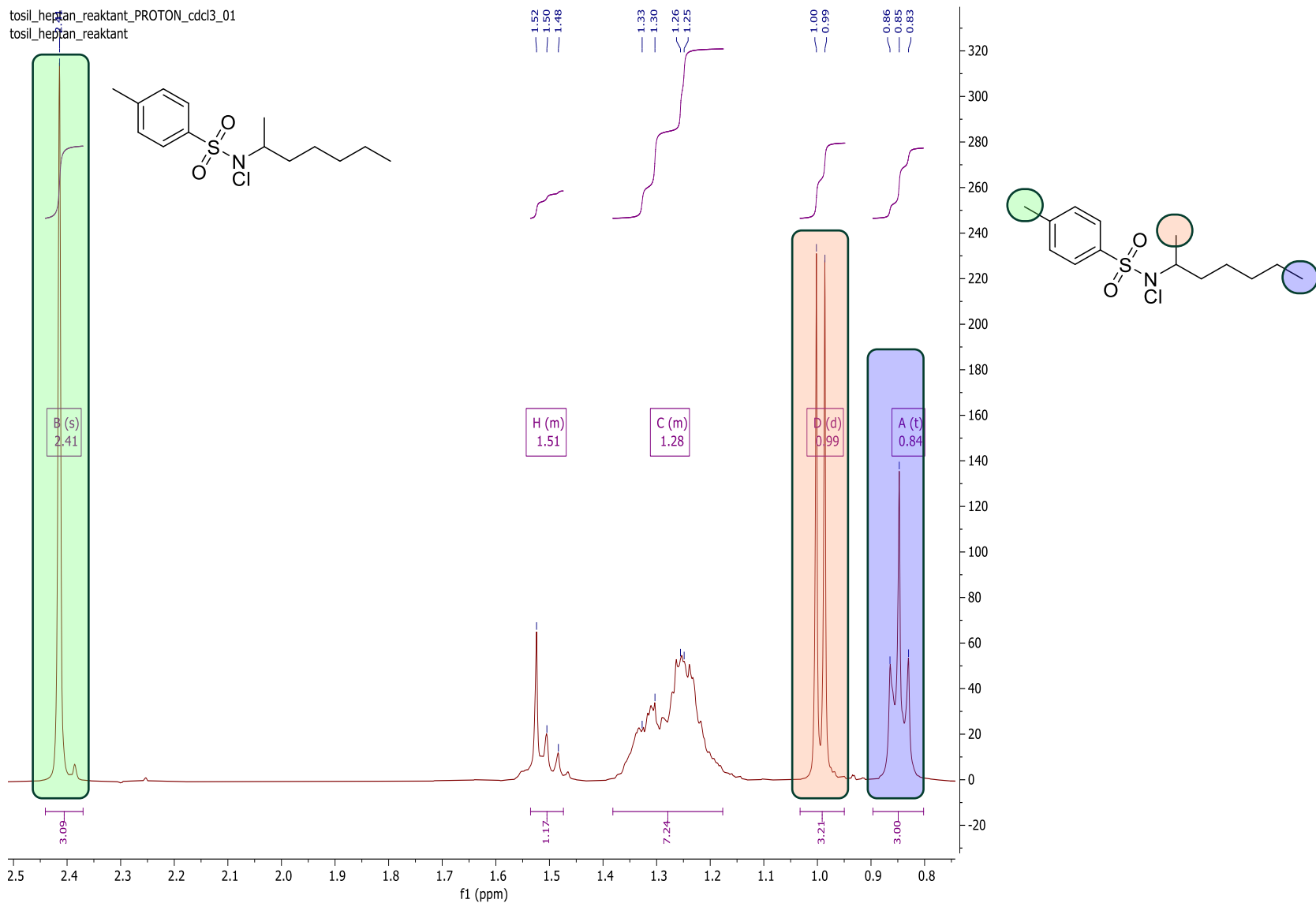


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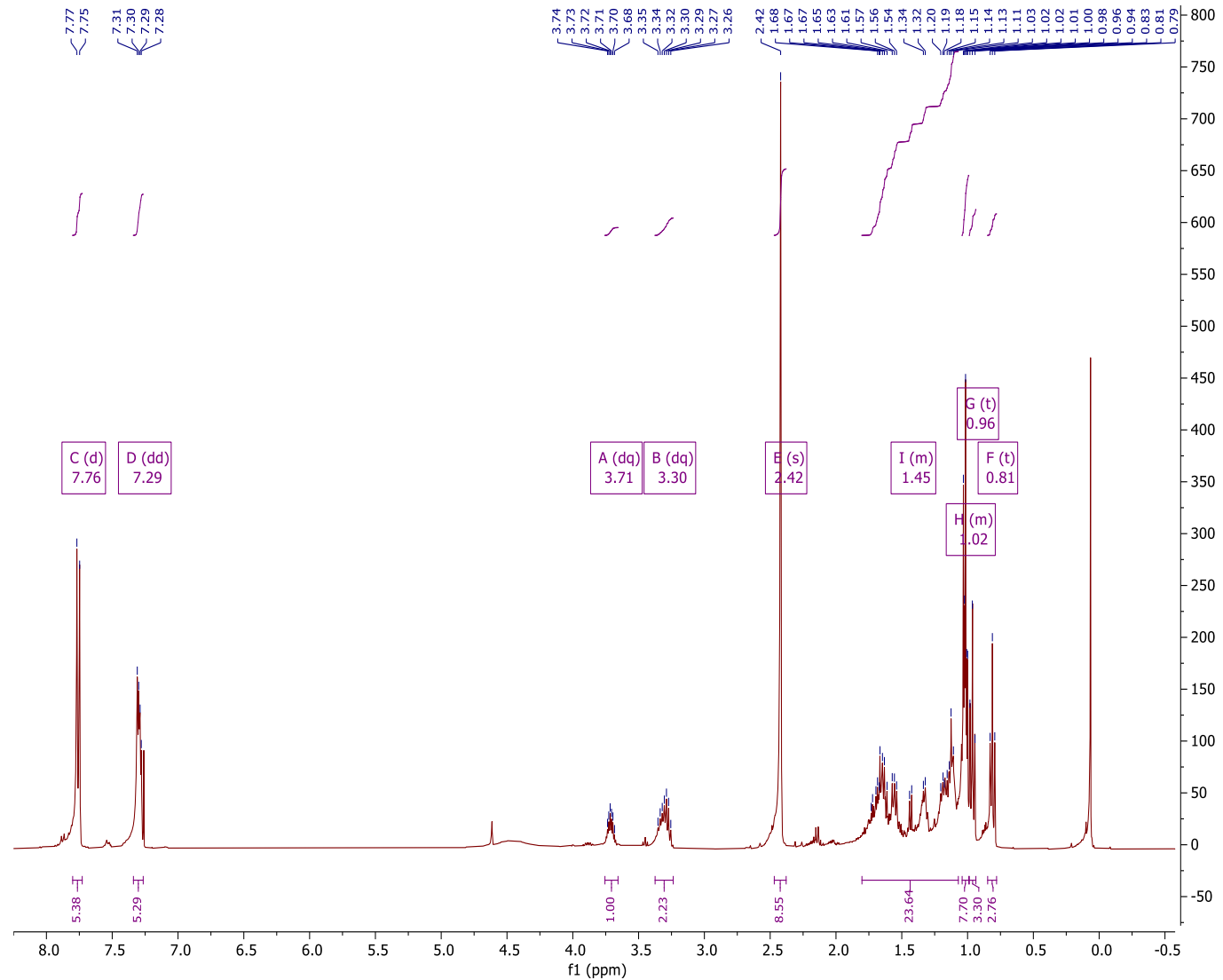
^1H NMR spectrum of the *N*-chlorinated tosyl 2-heptyl amine



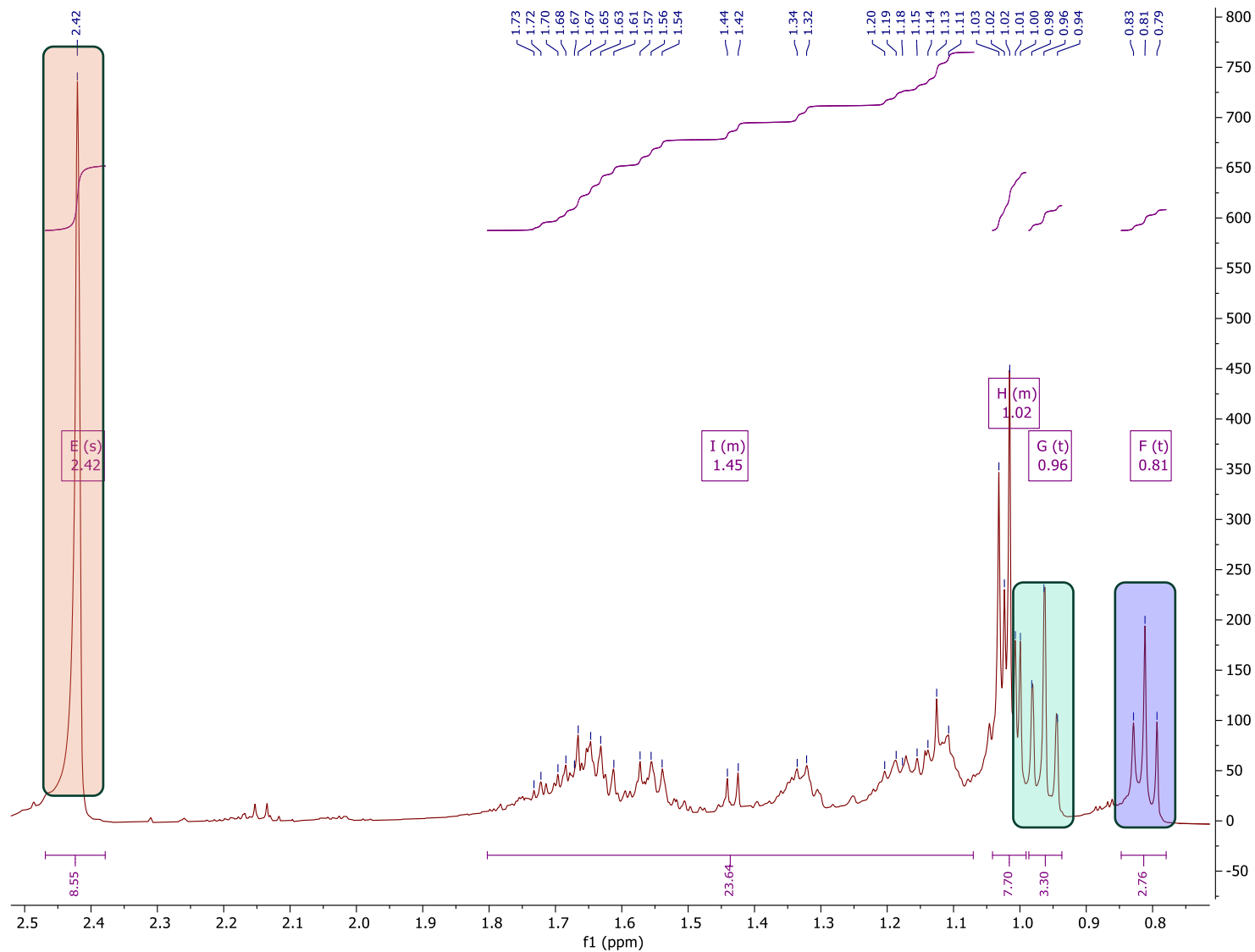
¹H NMR spectrum of the *N*-chlorinated tosyl 2-heptyl amine



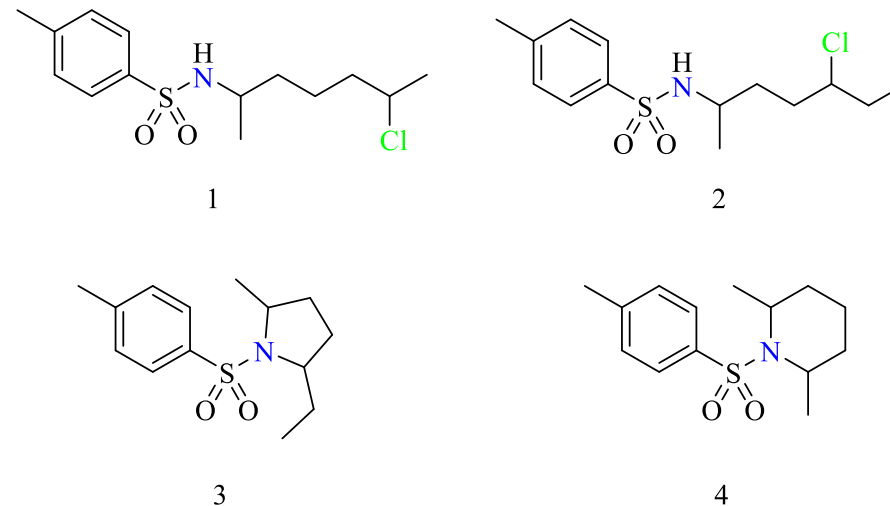
^1H NMR spectrum of the product mixture



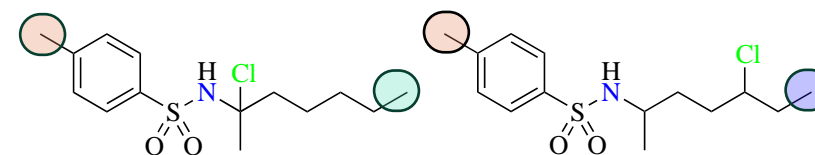
Product mixture



Expected products according to the literature

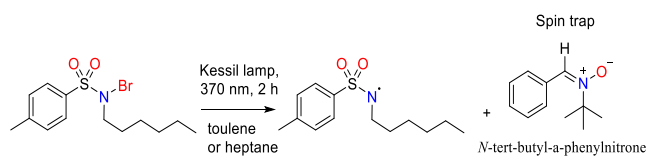


Actual products determined by NMR experiments

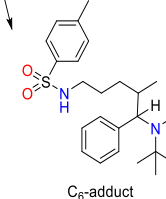
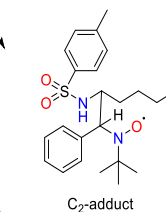
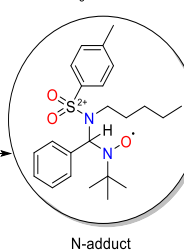
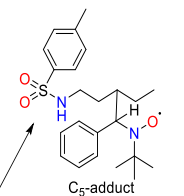
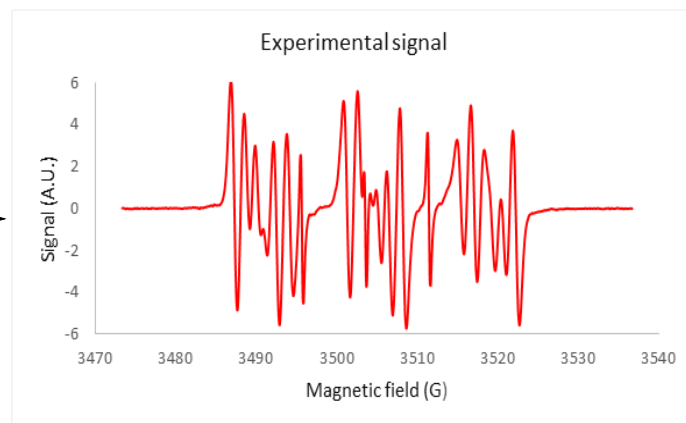


N. Herron, C.-P. Hsu, J.-Q. Yu, *Org. Lett.* **2022**, 24, 3652–3656.
 A. N. Herron, C.-P. Hsu, J.-Q. Yu, *Org. Lett.* **2022**, 24, 3652–3656.
 K. O. Marichev, J. M. Takacs, *ACS Catal.* **2016**, 6, 2205–2210.

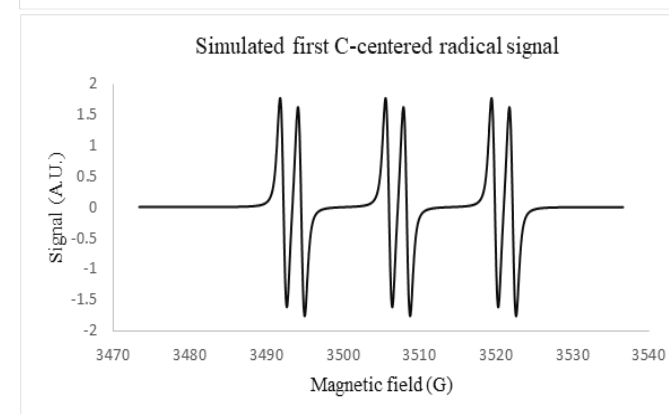
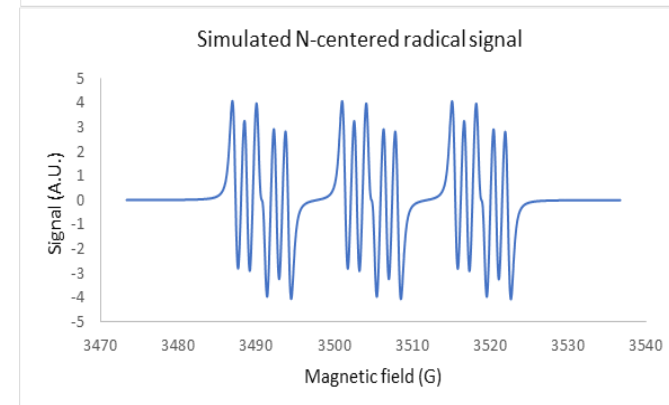
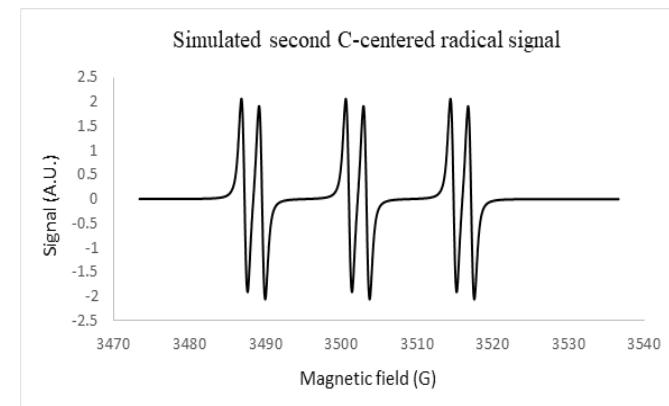
EPR experiments



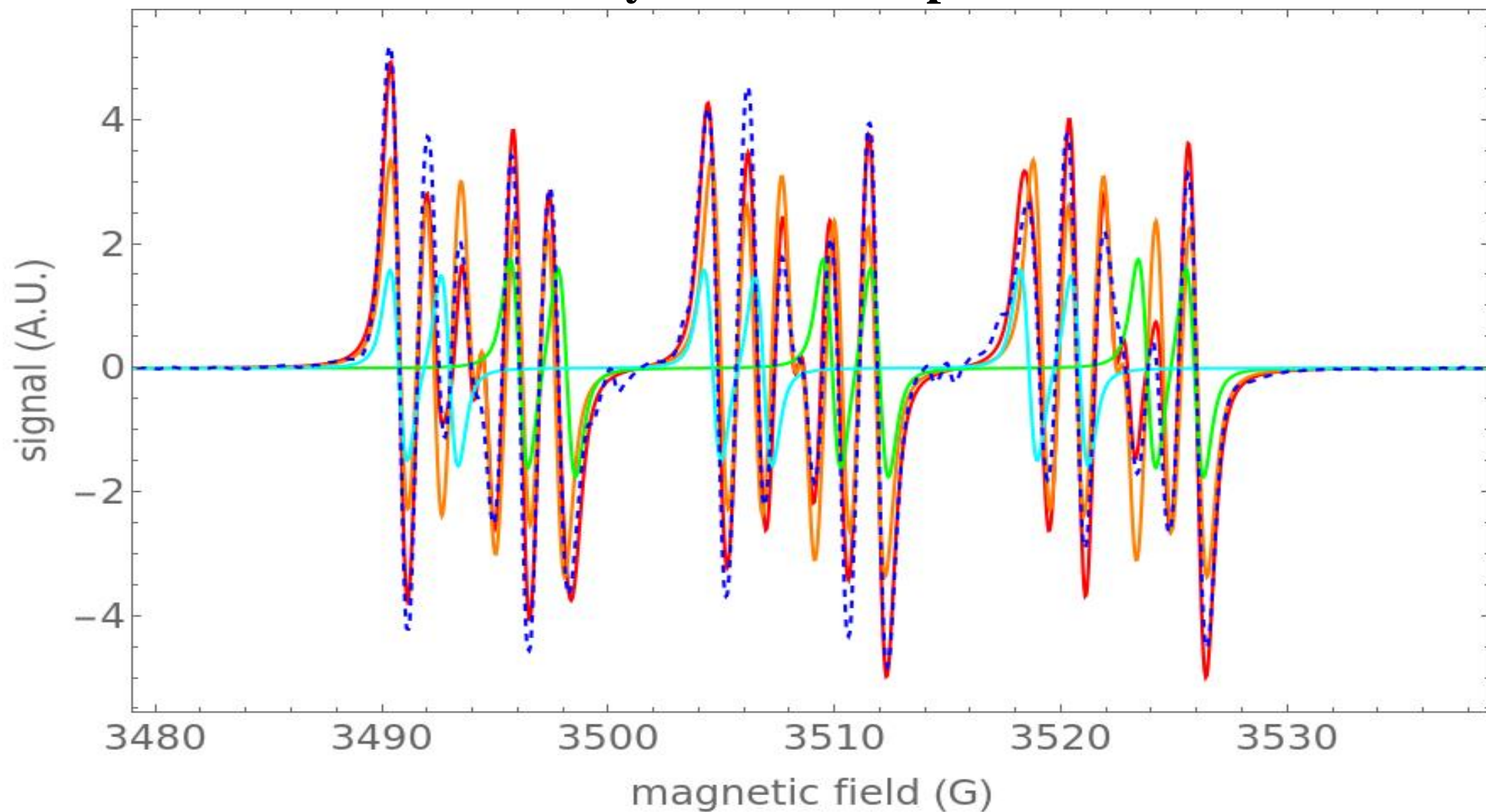
EPR



Desomposition and simulation in Mathematica



Decomposition of the experimental spectrum of *N*-brominated tosyl hexyl amine in heptane.



Summary

- 1,5- and 1,6-HAT processes are crucial elementary steps of the HLF reaction mechanism.
- Regioselectivity of the reaction is affected by a reverse 1,5-HAT process.
- Final confirmation of the N-centered radical will imply EPR experiments with ^{15}N labeled compounds.
- HLF reaction involves radical intermediates.
- We have indirectly observed Cl- N- and C-centered radical adducts at the same time point in the experiment.

Thank you for your attention!

Gabrijel
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Maria
Kolypadi
Marković



Hendrik
Zipse



Valerije
Vrček



Fabian
Zott



Salavat
Ashirbaev



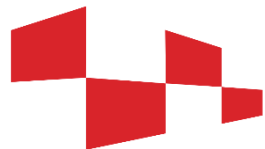
Jiangyang
You



Erim
Bešić



Davor
Šakić



HRZZ
Croatian Science
Foundation

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HRZZ project UIP-2020-02-4857

