

Giuliana Judge^{1,3}, Ping Yan^{2,3}, Corey Acker^{2,3}, Leslie Loew²

¹University of Connecticut, Storrs, CT ²Center for Cell Analysis and Modeling, UConn Health, Farmington, CT

³Potentiometric Probes, Farmington, CT

Introduction

Voltage sensitive dyes (VSDs) allow for fluorescent imaging of action potentials in certain cells that rely on electrical signals such as neurons and cardiomyocytes and are essential in circumstances where it is difficult or impossible to use other methods of measuring electronic changes across the membrane, such as patch-clamp.¹ The VSDs described here rely on a fast response electrochromic mechanism which leads to changes in fluorescence that correspond to membrane potential changes, allowing for real-time imaging.² Recent research has focused on developing fluorescent dyes with emission in the near-infrared range (NIR), due to decreased noise in this range.¹ One way to achieve this is to extend the conjugation of existing dyes; however, this must be done without compromising the voltage sensitivity of the dye. We present progress that has been made toward the synthesis of chromene-based voltage sensitive dyes with a phenyl group between the donor and acceptor moieties, as well as a 2*H*-Naphtho[2,3-*b*]pyran-based dye.

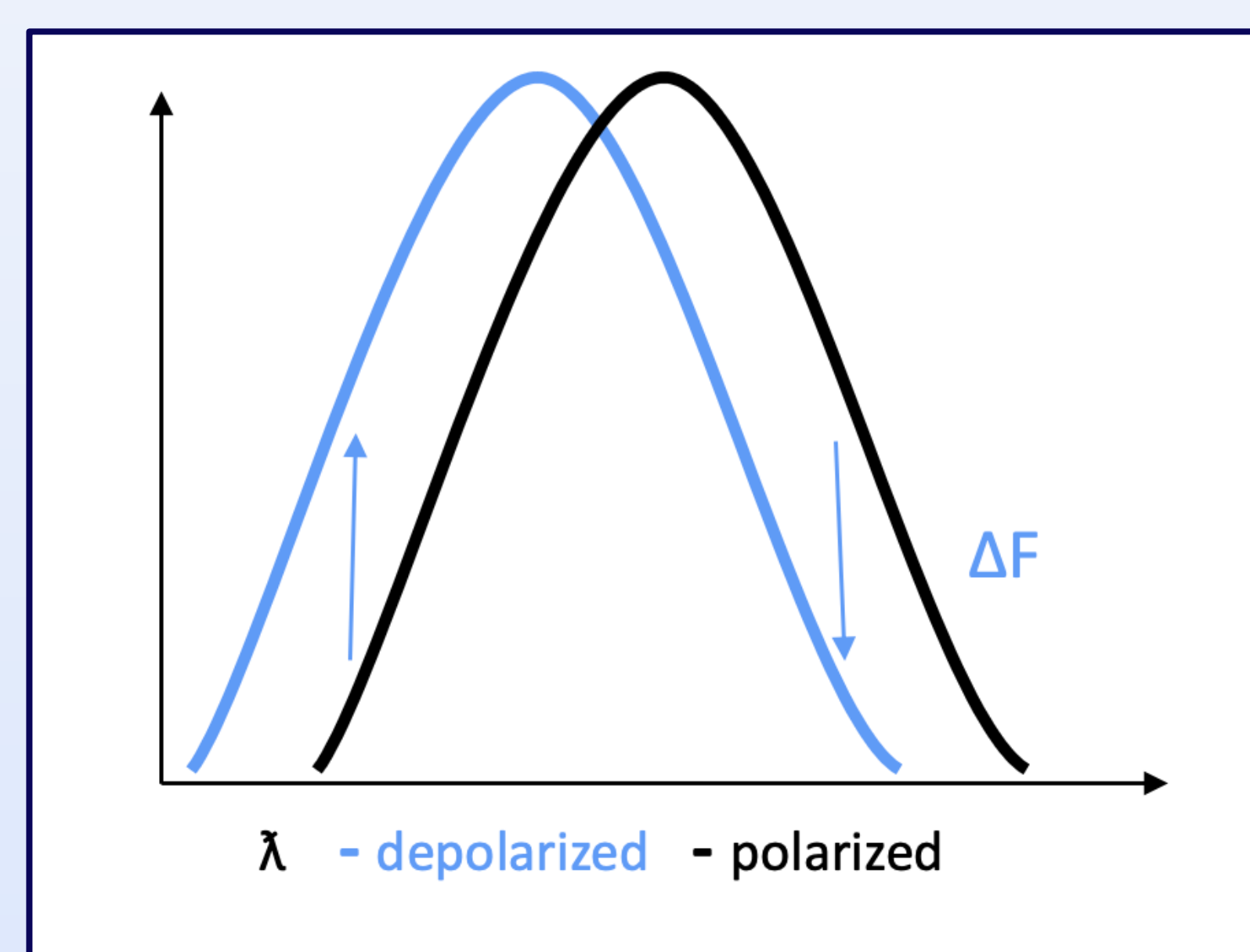
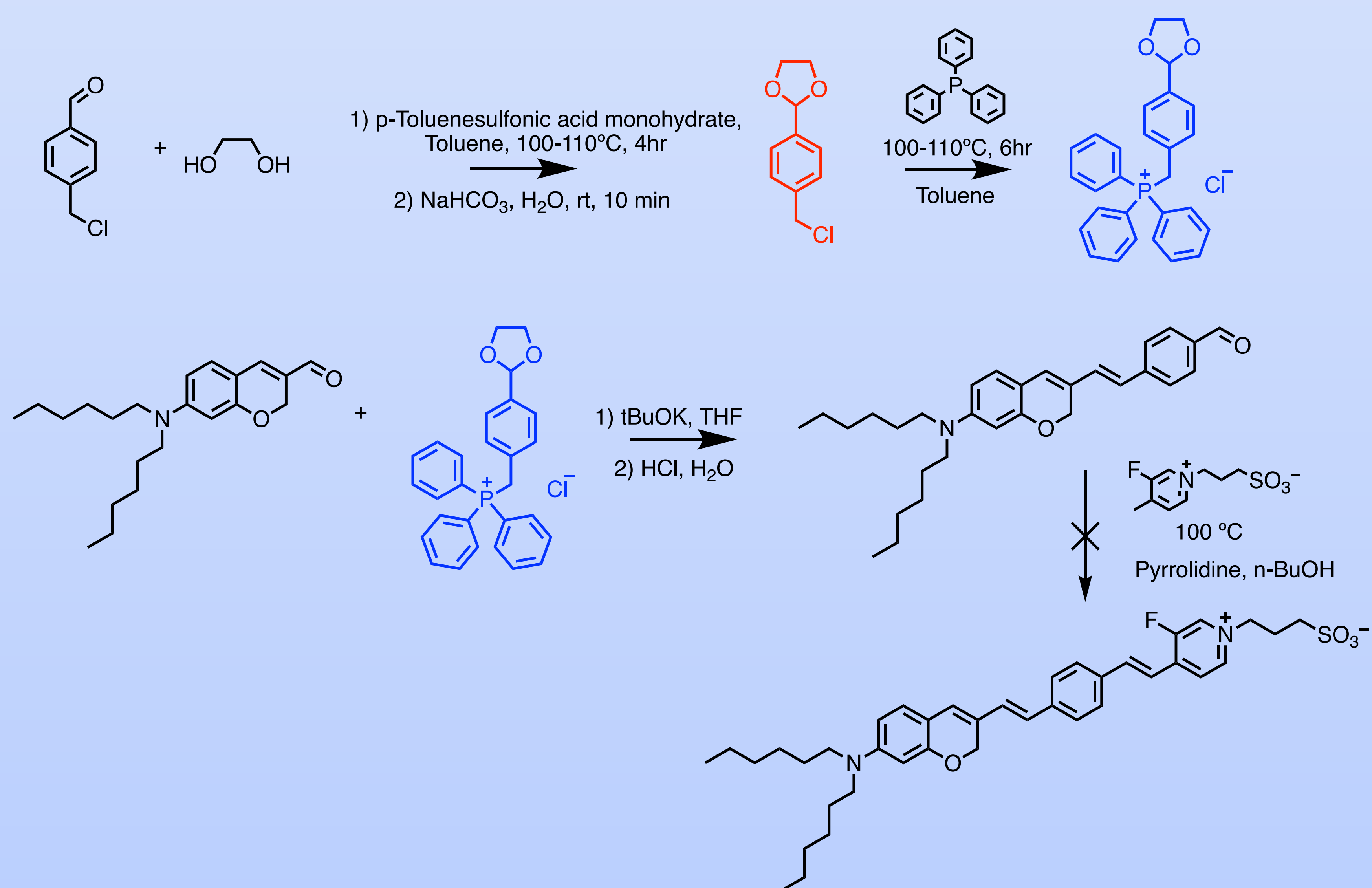


Figure 1. The Effect of Voltage Changes Across Cellular Membranes on Fluorescence of VSDs. When a cell depolarizes, more energy is required to excite the dye, so the fluorescence spectrum shifts to the left.²

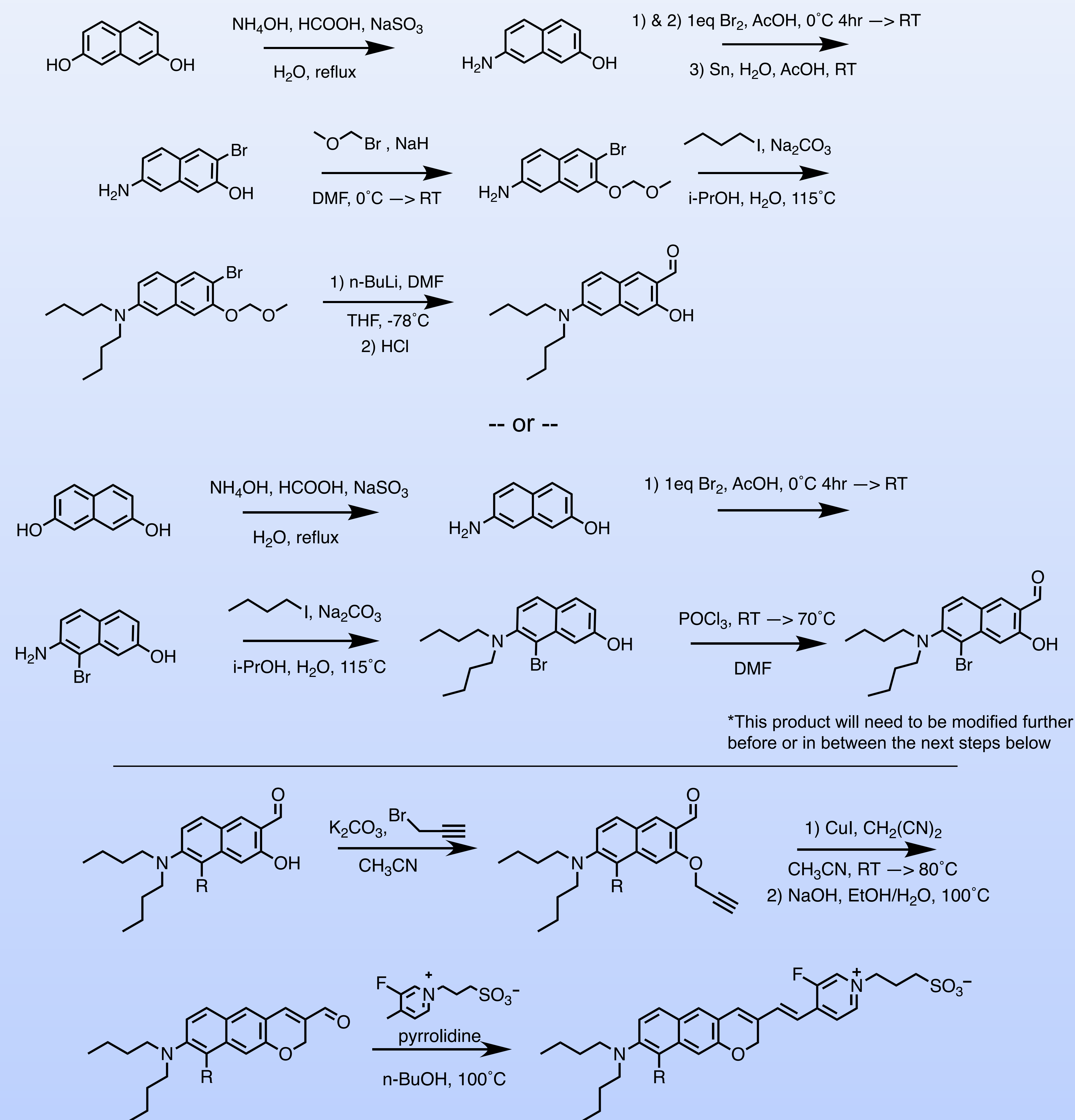
Synthesis



- The last reaction in the sequence consistently produced a low yield, and the product was unable to be confirmed by NMR to date.
- Different acceptor molecules have been reacted with similar results.

Giuliana Judge
giuliana.judge@uconn.edu

Current Project/Future Directions



References

- (1) Yan, P.; Acker, C. D.; Biasci, V.; Judge, G.; Monroe, A.; Sacconi, L.; Loew, L. M. Near-Infrared Voltage-Sensitive Dyes Based on Chromene Donor. *Proceedings of the National Academy of Sciences* **2023**, *120* (34), e2305093120. <https://doi.org/10.1073/pnas.2305093120>. (1)
- (2) Loew, L. M. Design and Characterization of Electrochromic Membrane Probes. *Journal of Biochemical and Biophysical Methods* **1982**, *6* (3), 243–260. [https://doi.org/10.1016/0165-022X\(82\)90047-1](https://doi.org/10.1016/0165-022X(82)90047-1).

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