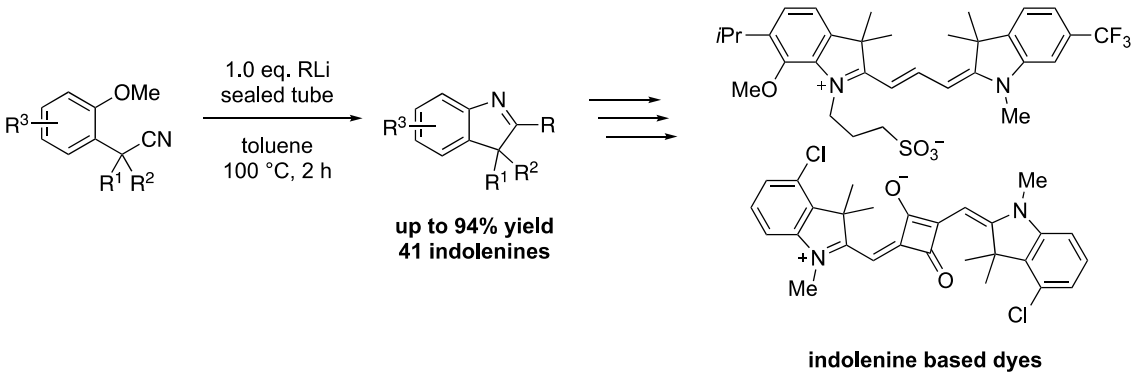
PREPARATION OF INDOLENINES VIA NUCLEOPHILIC AROMATIC SUBSTITUTION

Joel Roesslein, Florian Huber and Karl Gademann

Department of Chemistry, University of Zurich, Winterthurerstrasse 190,
8057 Zürich, Switzerland

The indolenine core structure is a popular motive among many natural products.[1] Besides its use in natural product synthesis, indolenines are also used as precursors in the synthesis of indolenine based dyes that are employed in many differed fields such as *in vivo* and *ex vivo* imaging.[2] Nowadays most indolenines are synthesized via the interrupted Fischer indolization, which application is mainly limited to substitutions at the 5-position.[3] In this context, we have developed a new method for the synthesis of indolenines via a nucleophilic aromatic substitution using easy accessible benzyl nitriles as starting materials.[4] Our cyclization method is high yielding (up to 94%) and tolerates a wide range of functional groups, which is exemplified by the substrate scope of 41 indolenines. Substitutions at all possible positions of the aromatic ring as well as electron rich and poor benzyl nitriles are well tolerated. Furthermore, we investigated the mechanism of this reaction. Finally, we applied our new method for the synthesis new indolenine-based dyes, which are difficult to access with current literature known procedures.



[1] Ishikura, M.; Abe, T.; Choshi, T.; Hibino, S. *Nat. Prod. Rep.* **2015**, *32*, 1389−1471.

]2] Collot, M.; Fam, T. K.; Ashokkumar, P.; Faklaris, O.; Galli, T.; Danglot, L.; Klymchenko, A. S. *J. Am. Chem. Soc.* **2018**, *140*, 5401−5411.

[3] Witkop B.; Patrick J. B. *J. Am. Chem. Soc.* **1951**, *73*, 1558–1564.

[4] Huber F.; Roesslein J.; Gademann K. *Org. Lett.* **2019**, *21*, 2560–2564.