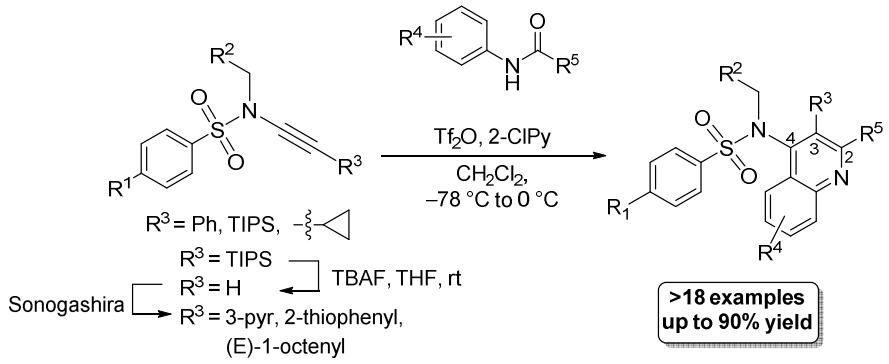
Synthesis of Highly Functionalized 4-Aminoquinolines

Tim Wezeman, Sabilla Zhong, Stefan Bräse

Institute of Organic Chemistry, Karlsruhe Institute of Technology, Karlsruhe, Germany

A method for the synthesis of highly functionalized 4-aminoquinolines from sulphynamides and amides is presented. The amides are activated by triflic anhydride (Tf_2O) and 2-chloropyridine (2-ClPy) and, as Movassaghi *et al.* have shown, can be used to prepare a wide range of heterocyclic structures.[1] Sulphynamides can be prepared using copper catalysis and alkyl bromides[2] and further derivatized by using Sonogashira chemistry.[3] The main challenge in existing quinoline syntheses is the functionalization at the C-2 and C-3 positions. By combining the Sonogashira approach with the ynamide/amide methodology a wide range of substitutions at C-3 is possible and the C-2 and C-5 to C-8 positions are also accessible. In order to show the broad applicability of the methodology, it was found that the ynamides also readily react with paracyclophane-based amides, creating very interesting planar chiral compounds.



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[2] Y. Zhang, R. P. Hsung, M. R. Tracey, K. C. M. Kurtz, E. L. Vera, *Org. Lett.* **2004**, *6*, 1151-1154

[3] M. R. Tracey, Y. Zhang, M. O. Frederick, J. A. Mulder, R. P. Hsung, *Org. Lett.* **2004**, *6*, 2209-2212.