# CHIRAL AND NON CHIRAL *N*-BOC PROTECTED 7-AZAINDOLINES IN BATCH AND FLOW

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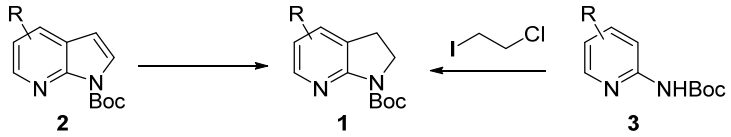
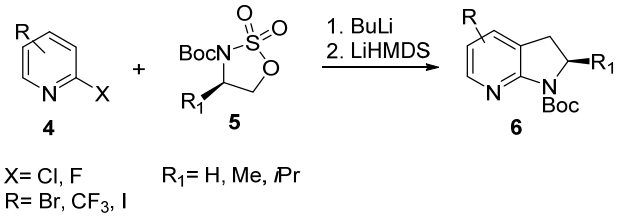
7-Azindolines are a common structural motif in modern drugs.[1] Despite this fact only a couple of general methods have been developed to synthesise these compounds. Especially *N*-Boc protected 7-azaindolines with a variety of halogenated substituents have only been reported a few times mainly through reduction of Azaindoles **2**[2] or the alkylation of *N*-Boc protected 2-aminopyridines **3** (Scheme 1).[3]




Scheme 1

In our ongoing efforts to make new chiral building blocks for the pharmaceutical and agricultural industries as well as academia we have developed a general method from commercially available pyridines **4** and (*R*) or (*S*) *N*-Boc 1,2,3-oxathiazolidine-2,2-dioxides **5** to make chiral and non chiral *N*-Boc 7-azaindolines **6** in a 2 step procedure (Scheme 2, only one enantiomer shown for clarity).[4]




Scheme 2.

We will present our findings in optimizing the two synthetic steps in multi-gram scale. Challenges, limitations and solutions for the synthesis using conventional batch reactors will be discussed and we will also show our results for the cyclisation using a flow chemistry reactor.

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[1] *e.g.* MISSION THERAPEUTICS LIMITED; Gibson, K. R.; Jones, A.; Kemp, M. I.; Madin, A.; Stockley, M. L.; Whitlock, G. A.; Woodrow, M. D. **WO2017/141036**

[2] *e.g.* Makida, Y.; Saita, M.; Kuramoto, T.; Ishizuka, K.; Kuwano, R. *Angew. Chem. Int. Ed.* **2016**, *55*, 11859-11862.

[3] *e.g.* Davies, A. J.; Brands, K. M. J.; Cowden, C. J.; Dolling, U.-H.; Lieberman, D. R. *Tetrahedron Lett.* **2004**, *45*, 1721-1724.

[4] a) Hebeisen, P.; Alker, A.; Berkler, M. *Heterocycles* **2012**, 85, 65-72. b) Nguyen, H. N.; Wang, Z. J. *Tetrahedron Lett.* **2007**, *48*, 7460-7463.