From Process Development of a Potent Cathepsin S-Inhibitor to Efficient Syntheses of Pyrazoles

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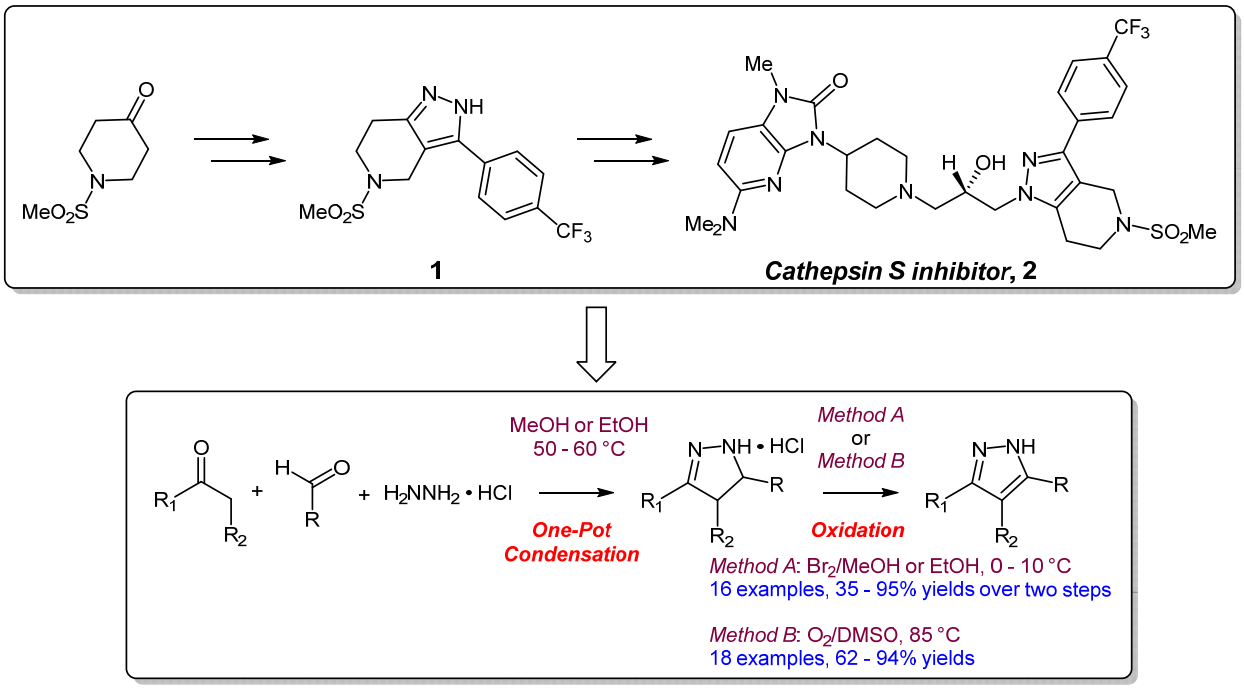

Pyrazole **1** was identified as a key intermediate towards the synthesis of Cathepsin S inhibitor **2**. A novel one-pot, metal-free synthetic protocol for pyrazole **1** was discovered and subsequently optimized for scale-up. The combination of three simple components afforded a pyrazoline intermediate under mild conditions. This was subsequently converted in situ to the target pyrazole **1** using bromine.

The scope of this operationally simple and chromatography free procedure was demonstrated to synthesize a variety of 3,4,5-substituted pyrazoles. Two approaches to the oxidation of the pyrazoline intermediate were developed using bromine or a more benign DMSO/oxygen protocol.

[1] V. Lellek, Ch. Chen, W. Yang, J. Liu, X. Ji, R. Faessler, *Synlett* **2018**, 29, A–E.