Chemoselective α,β and γ-functionalization of substituted alkylamides

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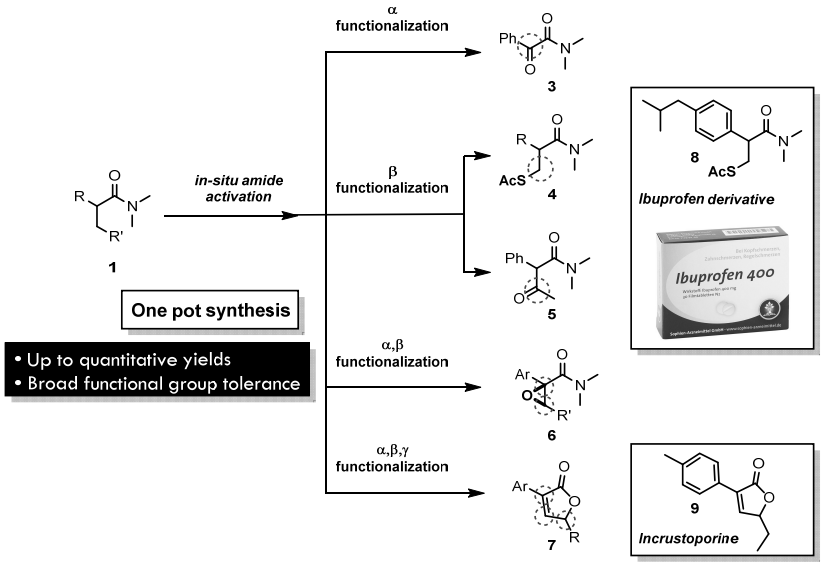
The selective functionalization of C(sp^3)-H bonds in alkanes remains a challenging topic of current research.[1] Herein, we present a flexible C-H functionalization of aliphatic amides at different chain positions in a one pot fashion.[2,3] As shown below (Scheme 1), α-carbonylation to α-ketoamides **3** is possible, while β-functionalization delivers β-thio-amides **4**. Derivatives of relevant bioactive substances such as Ibuprofen were functionalized at the β-C(sp^3)-H bond in order to demonstrate the potential utility of this approach. Further epoxidations and allylic oxidations are also possible, culminating in a short synthesis of the natural product Incrustoporine.[4]



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[1] For recent reviews on C-H functionalization see: a) P. Gandeepan, T. Müller, D. Zell, G. Cera, S. Warratz, L. Ackermann *Chem. Rev.* **2019** 10.1021/acs.chemrev.8b00507 b) C. Ma, P. Fang, T.-S. Mei *ACS Catal.* **2018**, *8*, 7179–7189.

[2] A. Bauer, N. Maulide, *Manuscript in preparation*.

[3] Review on electrophilic amide activation: D. Kaiser, A. Bauer, M. Lemmerer, N. Maulide *Chem. Soc. Rev.* **2018**, *47*, 7899.

[4] A. Lu, J. Wang, T. Liu, J. Han, Y. Li, M. Su, J. Chen, H. Zhang, L. Wang, Q. Wang., *J. Agric. Food Chem.* **2014**, *62*, 8799.