Nickel Catalyzed Enantioselective C-H Benzylic Carbamoylation

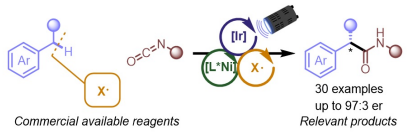
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Lignin is a useful and sustainable source of relevant building blocks in organic chemistry. Valuable aromatic compounds can be obtained by reductive depolymerization, including alkylarenes, and thus, new tools to derivatize these products are in high demand. One straightforward approach relies on the functionalization of the benzylic C-H bond because of the relatively low BDE. Recently, halogen-mediated radical abstraction of hydrogen has merged with nickel metallaphotoredox catalysis to forge enantioenriched benzylic derivatives.[1] These protocols represent an attractive alternative to classical functionalization methods and are devoid of highly unstable intermediates.

In the last years, the use of isocyanates as electrophilic coupling partners in nickel catalysis has been well studied, providing elegant alternatives to the classical synthesis of amides.[2] However, asymmetric variants for this reaction are yet to be developed.

Here, we present the combination of the benzylic hydrogen abstraction with isocyanates as coupling partner via nickel metallaphotoredox (See Scheme below).[3] This strategy allows to straightforward generate valuable enantioenriched 2-arylamides, a scaffold found in a plethora of product of interest with bioactive properties or intermediates in total synthesis. In this work we present a scope of 30 examples with enantiomeric ratios up to 97:3. Additionally, several control experiments and DFT calculations allow to propose a plausible mechanism.



[1] a) Z. Lu *et. al*. *Nat. Commun.* **2019**, 10, 3549; b) H. Haohua *et. al*. *Nat. Commun.* **2021**, 10, 3536; c) G. Liu *et. al*. *J. Am. Chem. Soc.* **2022**, 144, 13468–13474; d) Z. Lu *et. al*. *ACS Catal.* **2021**, 11, 11059–11065.
[2] a) R. Martin *et. al. Angew. Chem. Int. Ed*. **2016**, 55, 11207–11211; b) G. Molander *et. al. ACS Catal*. **2017**, 7, 7957–7961.
[3] C. Nevado *et al. Submitted manuscript.*