

Metal-Free Functionalization of Heteroatom Nucleophiles with Iodine(III) Reagents

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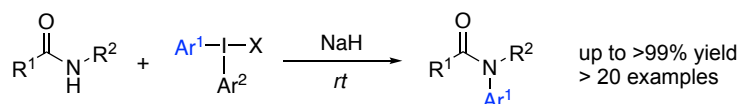
Aniline and amide derivatives are ubiquitous in Nature, in medicinal applications and material science. Consequently, the research focus on development of efficient synthetic methodology for *N*-arylation of nitrogen nucleophiles remains intense. While transition metal-catalyzed cross couplings have been successful with a wide variety of nitrogen nucleophiles, the drawbacks associated with transition metal catalysis, including toxicity, cost, need for substrate-dependent designer ligands, and risk of product contamination has led to an increased focus on development of metal-free methodology for C-N bond formation.¹

Diaryliodonium salts are sustainable, reactive and selective electrophilic arylation reagents.² We have developed several one-pot syntheses of diaryliodonium salts and other iodine(III) reagents, making these reagents easily available. We have also demonstrated their efficiency in arylation of various heteroatom and carbon nucleophiles under mild and metal-free conditions.

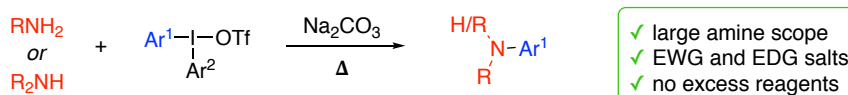
In the lecture, our recent results on the *N*-arylation of amides,³ aliphatic amines⁴ and nitrite⁵ will be presented. The first one-pot reaction, where diaryliodonium reagents are formed from iodine(I), and subsequently trapped by *in situ* addition of *N*-centered nucleophiles, will also be described.⁵

In contrast to amides, the arylation of thioamides proceeds with high *S*-selectivity to provide aryl thioimides.⁶ Mechanistic studies of nucleophiles with several nucleophilic sites (enolates, amides, thioamides, nitrite) will be discussed, and our recent findings of tetracoordinated intermediates in *O*-arylations will be presented.⁷

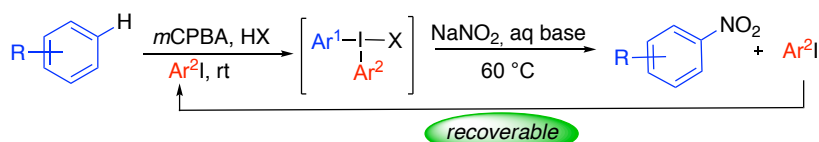
Amides:



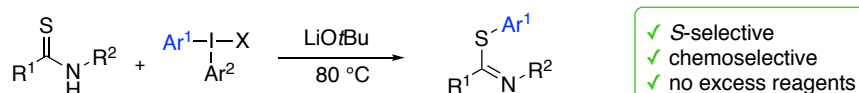
Aliphatic amines:



One-pot reaction with nitrite:



Thioamides:



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(2) Merritt, E. A.; Olofsson, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 9052-9070.

(3) Tinnis, F.; Stridfeldt, E.; Lundberg, H.; Adolfsson, H.; Olofsson, B. *Org. Lett.* **2015**, *17*, 2688-2691.

(4) Purkait, N.; Kervfors, G.; Linde, E.; Olofsson, B. *Angew. Chem. Int. Ed.* **2018**, *57*, 11427-11431.

(5) Reitti, M.; Villo, P.; Olofsson, B. *Angew. Chem. Int. Ed.* **2016**, *55*, 8928-8932.

(6) Villo, P.; Kervfors, G.; Olofsson, B. *Chem. Commun.* **2018**, *54*, 8810-8813.

(7) Stridfeldt, E.; Lindstedt, E.; Reitti, M.; Blid, J.; Norrby, P.-O.; Olofsson, B. *Chem. Eur. J.* **2017**, *13249-13258*.