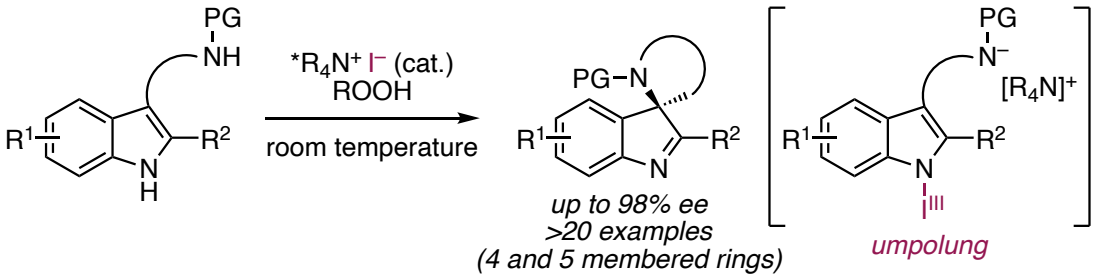
Ammonium Hypoiodite-catalyzed Oxidative Umpolung of Indoles for Dearomatization

(*Graduate School of Engineering, Nagoya University*) ○Hiroki Tanaka, Muhammet Uyanik, Kazuaki Ishihara

Keywords: *Hypoiodite Catalysis; Oxidation; Cyclization; Indole; Umpolung*

Indole derivatives are key structural units of several biologically active compounds. To date, numerous synthetic methods for those compounds have been developed. Among them, the dearomatization of indoles is one of the most powerful tools for the synthesis of substituted or polycyclic indole derivatives.[1] In most dearomatization strategies, indoles have been utilized as nucleophiles due to the high nucleophilicity of the indole nucleus at C-3. Only a few methods using C-3 electrophilic indoles have been reported.[2] On the other hand, in our laboratory, quaternary ammonium hypoiodite salt catalysis has been developed for environmentally benign oxidative coupling reactions.[3] In this catalytic oxidation system, hypoiodite salts are generated *in situ* from the corresponding quaternary ammonium iodides in the presence of hydrogen peroxide or alkyl hydroperoxides as an environmentally benign oxidant.

Here, we describe the hypoiodite-catalyzed oxidative dearomatization of indole derivatives.[4,5] Mechanistic studies suggest umpolung reactivity of the C-3 position of indoles by iodination of the indole nitrogen atom. In addition, enantioselective dearomative spirocyclization of indoles using chiral quaternary ammonium iodide as a catalyst gave the corresponding spiroindolenines with high enantioselectivity. Moreover, site-selective spirocyclization of tryptamine at C-3 position was achieved to give the difficult-to-access spiroazetidine in an enantioselective manner. We anticipated that this unusual "electrophilic indole" strategy would allow improving the synthetic portfolio for indole manipulation significantly.



1) C. Zheng, S.-L. You, *Nat. Prod. Rep.* **2019**, *36*, 1589.
2) M. Bandini, *Org. Biomol. Chem.* **2013**, *11*, 5206.
3) M. Uyanik, K. Ishihara, *ChemCatChem* **2012**, *4*, 177.
4) M. Uyanik, H. Tanaka, K. Ishihara, *Org. Lett.* **2020**, *22*, 8049.
5) M. Uyanik, H. Tanaka, K. Ishihara, *Asian J. Org. Chem.* **2021**, *10*, 164.