

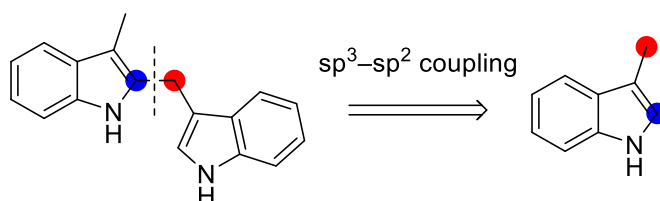
Water-Driven Formation of 2,3'-Bis(indolyl)alkanes via Unusual C(sp³)-H/C(sp²)-H Dehydrogenative Dimerization of 3-Methylindole

(School of Science, The Univ. of Tokyo) ○ Taku, KITANOSONO,* Yasuhiro YAMASHITA, Shū KOBAYASHI*

Keywords: Palladium; C-H Activation; Reaction in Water; Dehydrogenative; Indole

Bis(indolyl)alkanes (BIAs) are alkaloids bearing two indole units bonded to the same carbon, and they exhibit a broad spectrum of biological and pharmacological activities.¹ Above all, 2,3'-bis(indolyl)alkane skeletons have been recognized as an enticing pharmacophore in recent years.² The synthesis of symmetrical BIAs has been studied extensively during a long-standing quest for facile synthesis of BIAs, whereas unsymmetrical BIAs are still a challenge in the synthetic community. Although the simplest synthetic route includes dehydrogenative dimerization of 3-methylindole, selective functionalization of C(sp³)-H bonds of 3-alkylindoles remains elusive. Most of examples reported to date are limited to reactions of 2-indolyl(aryl)methanols as a substrate.

We have previously reported surfactant-aided palladium catalysis for C(sp²)-H alkylation of indoles in water³ and its application to asymmetric variants,⁴ based on stabilizing electrophilic indolylpalladium(II) intermediates. We speculated that the underlying mechanism can be applied to 3-methylindole; both C(sp³)-H bond and C(sp²)-H bond are potentially reactive under palladium catalysis. We herein report palladium-catalyzed unusual C(sp³)-H/C(sp²)-H dehydrogenative dimerization of 3-methylindole where water plays a prominent role.



- 1) Shiri, M.; Zolfigol, M. A.; Kruger, H. G.; Tanbakouchian, Z. *Chem. Rev.* **2010**, *110*, 2250–2293.
- 2) Singh, A.; Kaur, G.; Banerjee, B. *Curr. Org. Chem.* **2020**, *24*, 583–621.
- 3) Kitanosono, T.; Miyo, M.; Kobayashi, S. *Tetrahedron* **2015**, *71*, 7739–7744.
- 4) (a) Kitanosono, T.; Miyo, M.; Kobayashi, S. *ACS Sustainable Chem. Eng.* **2016**, *4*, 6101–6106; (b) Kitanosono, T.; Hisada, T.; Yamashita, Y.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2021**, *60*, 3407–3411.