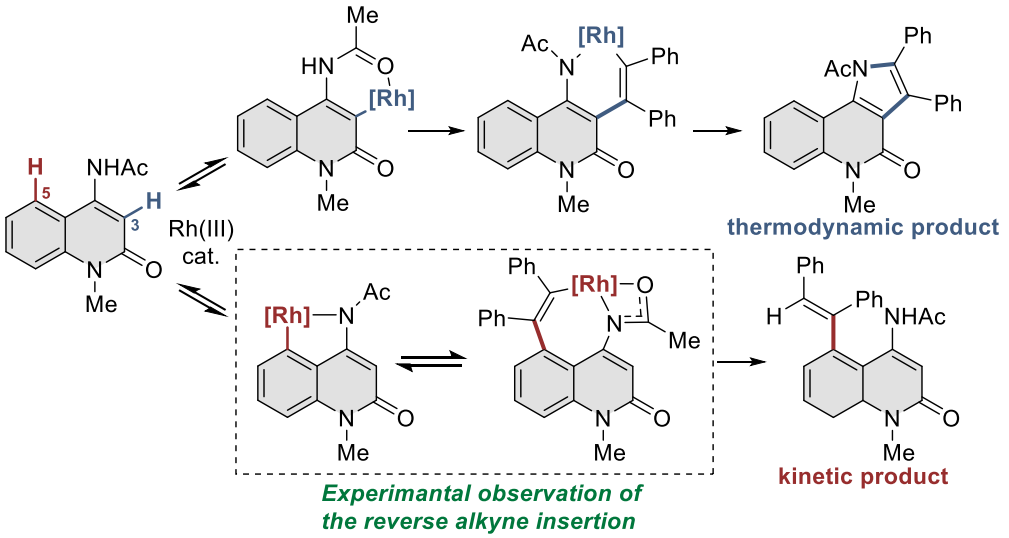
Synthesis of 3,4-Fused-2-Quinolone Derivatives via Site-Selective C–H Functionalization by Cp* Rh(III) Catalysis

([1]*Graduate School of Pharmaceutical Sciences, Nagoya University*) ○Naohiro Hirako,[1] Takeshi Yasui,[1] Yoshihiko Yamamoto[1]

Keywords: *2-Quinolone; C–H functionalization; Rhodium; Oxidative annulation*

2-Quinolone derivatives fused at the C3- and C4-positions are important motifs found in natural products, biologically active substances, and approved drugs. Therefore, the development of efficient methods for the synthesis of 3,4-fused-2-quinolones from readily available substrates is an important mission for drug discovery. Oxidative annulation of 2-quinolones with alkynes involving the C–H activation is one of the most efficient methods for the preparation of 3,4-fused 2-quinolones. However, there are no reports involving the C3-selective intermolecular C–H functionalization of 2-quinolones although the C5-selective C–H functionalization to obtain 4,5-fused 2-quinolones have been reported.[1)]

Herein, we report the oxidative annulation of 2-quinolones with alkynes to provide 3,4-fused 2-quinolones via Cp*Rh(III) catalyzed C3-selective C–H functionalization. The mechanistic study elucidated that the alkyne insertion is reversible, and the site-selectivity is thermodynamically controlled, although the alkyne insertion is generally recognized as an irreversible process because of the high activation barrier of its reverse process, β-carbon elimination, in most cases.



1) a) S. Mochida, M. Shimizu, K. Hirano, T. Satoh, M. Miura, *Chem. Asian J.* **2010**, *5*, 847. V. S. Thirunavukkarasu, M. Donati, L. Ackermann, *Org. Lett.* **2012**, *14*, 3416. c) P. K. Dutta, M. K. Ravva, S. Sen, *J. Org. Chem.* **2019**, *84*, 1176.