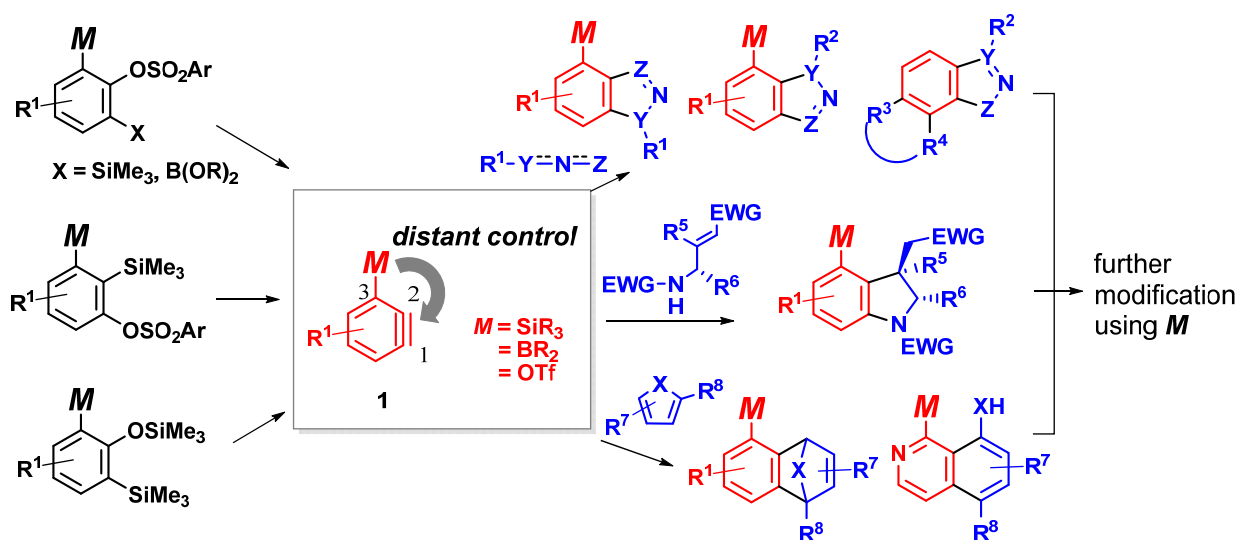


## Arynes as Powerful Platforms for Regioselective Construction of Fused Heteroaromatic Compounds

Takashi Ikawa and Shuji Akai\*

Graduate School of Pharmaceutical Sciences, Osaka University  
Suita, Osaka 565-0871, Japan

Benzo-fused nitrogen-containing heterocycles are abundant in biologically active compounds. One of the most effective methods for preparing such heterocycles is the cycloaddition reactions of benzyne with nitrogen-containing compounds. However, the reactions of unsymmetrically substituted benzyne generally show low regioselectivity to produce mixtures of two regioisomers. In this symposium, we present the synthesis of both regioisomers of multisubstituted benzo-fused azoles through the regiocomplementary (3 + 2) cycloaddition reactions of 3-boryl-, 3-silyl, and 3-triflyloxy-benzyne **1** with 1,3-dipoles, in which the substituent *M* at the C3-position effectively control the reaction site of **1**.<sup>[1-3]</sup> Similar preparations of multisubstituted indolines and other fused nitrogen-containing heterocyclic compounds are also available by using **1**.<sup>[4]</sup> The substituent *M* of the cycloaddition products is applicable to installation of a range of carbon-, nitrogen-, and oxygen-substituents at its ipso position. The improved generation of the functionalized benzyne **1** as well as benzdienes from new precursors and the analysis of mechanisms for these regioselective cycloaddition reactions by density functional theory calculations will also be discussed.<sup>[5]</sup>



[1] Akai, S.; Ikawa, T.; Takayanagi, S.; Morikawa, Y.; Mohri, S.; Tsubakiyama, M.; Egi, M.; Wada, Y.; Kita, Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 7673.

[2] Ikawa, T.; Takagi, A.; Kurita, Y.; Saito, K.; Azechi, K.; Egi, M.; Kakiguchi, K.; Kita, Y.; Akai, S. *Angew. Chem., Int. Ed.* **2010**, *49*, 5563.

[3] Kaneko, H.; Ikawa, T.; Yamamoto, Y.; Arulmozhiraja, S.; Tokiwa, H.; Akai, S. *Synlett* **2018**, *29*, 943.

[4] Ikawa, T.; Sumii, Y.; Masuda, S.; Wang, D.; Emi, Y.; Takagi, A.; Akai, S. *Synlett* **2018**, *29*, 530.

[5] Ikawa, T.; Masuda, S.; Takagi, A.; Akai, S. *Chem. Sci.* **2016**, *7*, 5206.