

Site-selective α -C(sp^3)-H Alkylation of Alcohols and Primary Amines Promoted by Photoredox, HAT, and Bond-Weakening Hybrid Catalysis

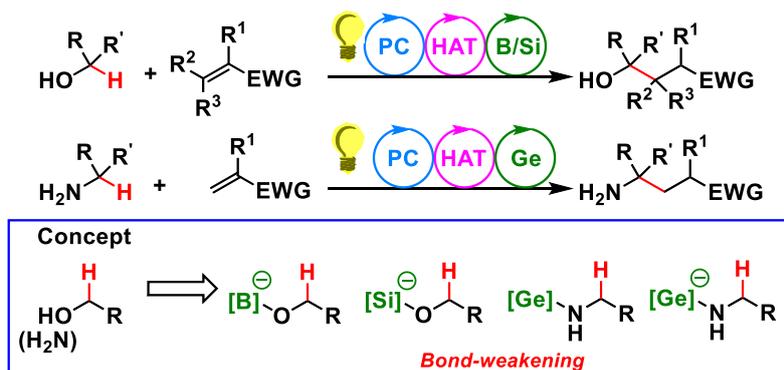
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The development of catalytic C(sp^3)-H functionalization reactions can explore various applications, such as the discovery of functional materials and drugs. To realize functionalization of unreactive C(sp^3)-H bonds, hydrogen atom transfer (HAT) catalysts have been attracting much attention because of their mild reaction conditions.¹ However, most of reported HAT catalysis have limited substrate scopes, which can only target the weakest or highly hydridic C(sp^3)-H bonds in the substrate. Targeting other C(sp^3)-H bonds in high regioselectivity under catalyst-control remains challenging.

We would like to report ternary hybrid catalyst systems consisting of photoredox (PC), HAT, and bond-weakening catalysts.² The bond-weakening catalyst design is based on DFT calculations uncovering that α -C(sp^3)-H bonds of alcohol^{3a,3b} and primary amine^{3c} substrates were effectively weakened by complexation as silicates, borates, and germane/germate species. These bond-weakening phenomena accelerates the HAT process of specific C(sp^3)-H bonds, leading to catalyst-controlled site-selectivity of C(sp^3)-H functionalization.

In this talk, we would like to focus mainly on the α -C(sp^3)-H alkylation of primary amines promoted by the PC-HAT-Ge hybrid system.



1) Capaldo, L.; Quadri, L. L.; Ravelli, D., *Green Chem.*, **2020**, 22, 3376. 2) Precedents of the hybrid system: a) MacMillan, D. W. C. and co-workers, *Science* **2015**, 349, 1532. b) Taylor, M. S. and co-workers, *J. Am. Chem. Soc.*, **2019**, 141, 5149. 3) a) **Sakai, K.**; Oisaki, K.; Kanai, M., *Adv. Synth. Catal.*, **2020**, 362, 337. b) **Sakai, K.**; Oisaki, K.; Kanai, M., *Synthesis*, **2020**, 52, 2171. c) **Sakai, K.**; Oisaki, K.; Kanai, M., *manuscript in preparation*