

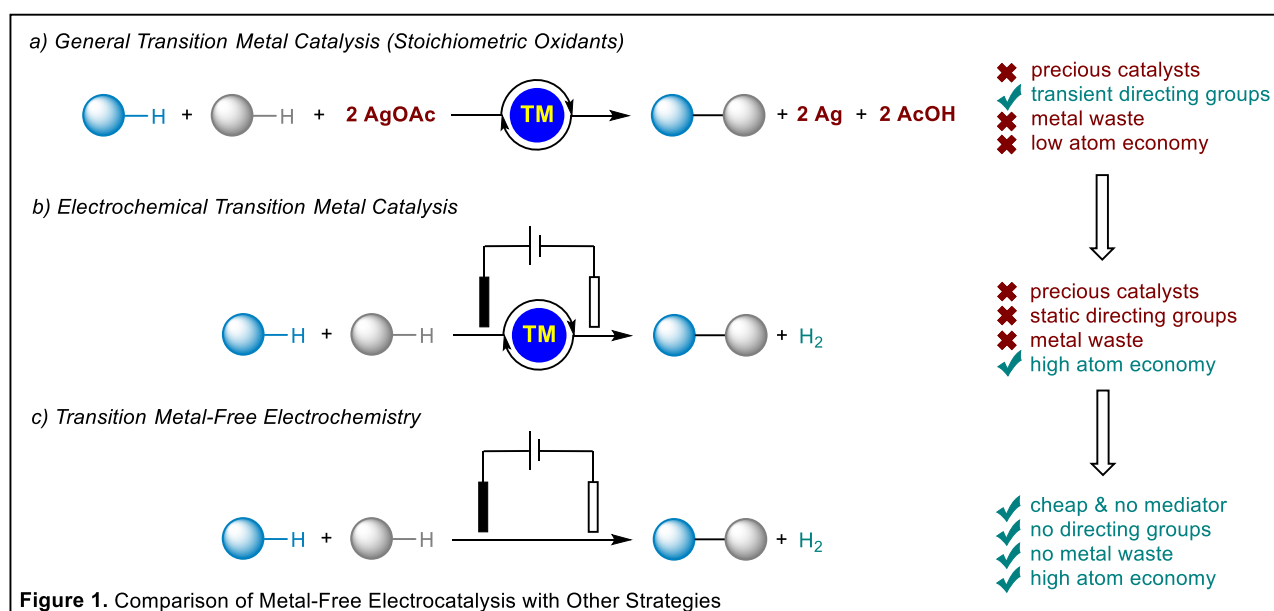
TRANSITION METAL-FREE ELECTROCHEMICAL C-H FUNCTIONALIZATION

Reported by Cheng Yang

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INTRODUCTION

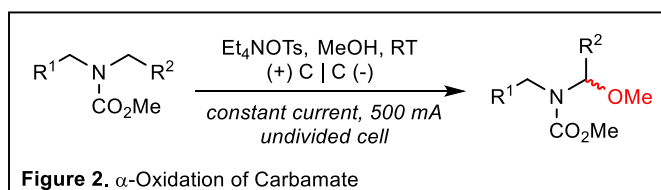
Transition metal-catalyzed C-H functionalization is a research hotspot of organic chemistry in recent years. The ability to drastically shorten the synthetic route makes this method a novel choice for retrosynthesis. However, the use of expensive metal catalysts and stoichiometric oxidants restricts its scalability and sustainability (**Figure 1a**). Therefore, using electrons as the alternative to replace both costly stoichiometric oxidant as well as the precious metal catalysts is an attractive choice to improve



current C-H activation strategy, as it not only increases the atom economy but also reduces the cost of treating the metal waste (**Figure 1b, c**). Over the past decades, transition metal-free electrochemical C-H functionalization has gained considerable impetus. Many synthetically useful and scalable transformations have been reported, focusing on carbon-oxygen, carbon-nitrogen and carbon-carbon formation.

C-O BOND FORMATION

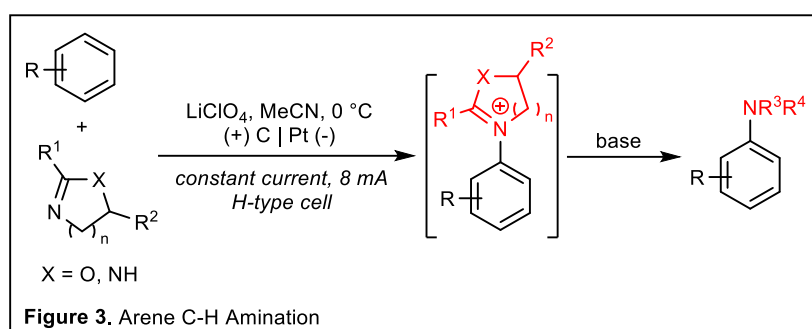
Shono group reported the electrochemical α -oxidation of carbamates (**Figure 2**)² in 1975, which is named as Shono Oxidation and represents one of the most widely utilized electrochemical reactions to this day. In 2016, Baran group reported a radical-mediated electrochemical allylic C-H bonds oxidation³. The use of inexpensive and readily available materials enables the potential



of this strategy on industrial application. By changing the mediator, Baran group also realized the direct oxidation of unactivated sp^3 C-H bond⁴. Furthermore, electrochemical oxidation of benzylic C-H bonds to form acetal is also reported, greatly expanding the benzylic oxidation methodology.

C-N BOND FORMATION

Electrochemical C-H bond amination is suggested to be challenging because of the facile overoxidation of the amine products which have similar potentials with substrates. By applying imine-type nitrogen source, Yoshida group successfully realized electrochemical arene C-H amination

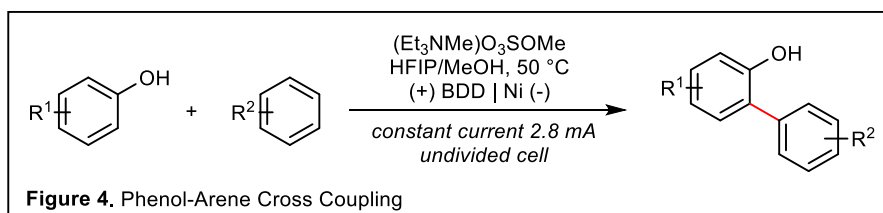


(**Figure 3**)⁵. The iminium ion intermediate is immune to overoxidation because of its high oxidative potential. Both intra and intermolecular sp^3 C-H amination are also reported, while both

benzylic and unactivated sp^3 C-H bonds are suitable substrates^{6a, 6b, 6c}.

C-C BOND FORMATION

Direct oxidative coupling of two C-H bonds to form C-C bonds represents an attractive strategy due to its high atom economy. Waldvogel group reported the first electrochemical oxidative phenol-arene cross-coupling promoted by boron-doped diamond (BDD) electrode in 2010 (**Figure 4**)⁷, which was later expanded to other heterocyclic compounds as well. Cathodic reduction initiated arene-arene cross coupling was also reported in 2019⁸, which substantially broaden the substrate scope of this



method. Besides, Lei group exploited the sulfonamide as mediator and realized electrochemical C-H arylation of unactivated sp^3 C-H bond⁹.

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