Homogenizing Heterogeneous Catalysis: Synthetic Applications of Single Atom Catalysis

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Introduction

The field of organic chemistry has a rich history of utilizing both homo- and heterogeneous transition metal catalyzed reactions to achieve otherwise difficult transformations. Despite decades of academic research towards improved homogeneous catalysis methods, an extreme discrepancy between the two modes exists in industry owing to their different properties (**Fig 1**).[1] One of the leading solutions to bridge this gap has been heterogenous Single Atom Catalysis.[2,3] A single atom catalyst contains isolated active metal centers stabilized by a non-active support. In recent years, synthetic applications of single atom catalysis have been greatly expanded to demonstrate their unique reactivity, unprecedented selectivity, and precise electronic tunability.
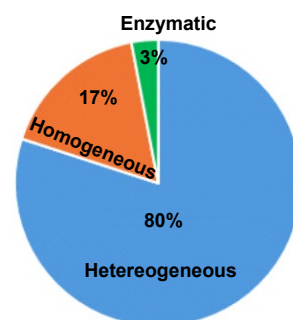

Figure 1. Market share of different catalyst types

Aziridination via Cobalt SAC

Aziridines are a well-established functional handle to install amines and amides selectively into olefins. Traditional methods of aziridine synthesis involve rare earth metals, high temperature degradation of azides, or utilize complex ligand systems.[4-6] The Tang group has developed a cobalt based single atom catalyst to aziridinate olefins in moderate yields based on Zhang's cobalt metalloradical chemistry (**Fig. 2**).[7] This catalyst is the first example of olefin functionalization via single atom catalysis, demonstrating the powerful reactivity of these systems. Notably, the reaction scope and systemic limitations are in line with current state of the art cobalt aziridination catalysts. This system demonstrates the ability of single atom catalysts to bridge the gap between current homogeneous methods and desired heterogeneous reactivity.
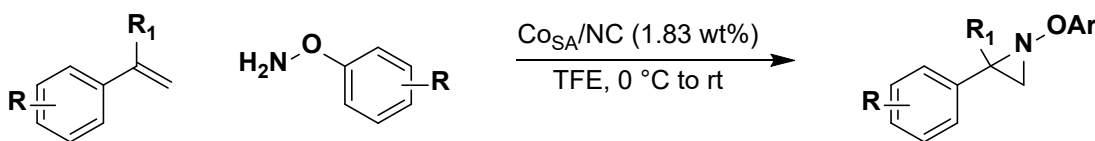

Figure 2. Reaction scheme for the single atom catalyt mediated aziridination of olefins

Regioselective C-O Bond Formation by SAC Catalyzed Carbene Insertion

Carbenoid insertion has proven to be a reliable and widely utilized method of forming C-O bonds; however, there are no literature examples of catalyst driven regioselective bond formation. Inspired by the unique reactivity of single atom catalysis, the Toste group developed an iridium based single atom catalyst to regioselectively form C-O bonds (**Fig. 3**).[8] In a direct head-to-head comparison between the SAC and state of the art homogenous catalyst for C-O insertion with an sp^2 and sp^3 alcohol, it was shown that the single atom catalyst provided consistently higher yields and better selectivities for Csp^3 insertion. This system demonstrates the incredible selectivity of single atom catalysts in the context of organic synthesis.
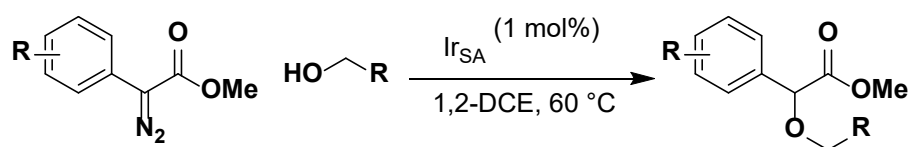

Figure 3. Single atom catalyst mediated OH insertion

Selective Reduction of Nitroarenes to Anilines via a Cobalt SAC

Anilines are a highly privileged motif in organic synthesis FDA approved drugs. One method of constructing these motifs is reduction of nitroarenes. Existing heterogeneous methods utilize harsh conditions and have extensive functional group incompatibilities.[9,10] Taking advantage of the unique electronic tunability of single atom catalysts, the Cao group developed a cobalt based single atom catalyst to reduce nitroarenes to anilines in the presence of other reduction sensitive functional groups via precise electronic tuning of the metal center (**Fig 4**).[11] This was achieved by adding a phosphorous atom into the metal coordination sphere. The reaction system was demonstrated to be highly efficient, achieving excellent yields of traditionally difficult substrates and showing significantly higher reduction rates than other similar systems. This catalyst clearly demonstrates the ability to electronically tune single atom catalysts for any desired reactivity.
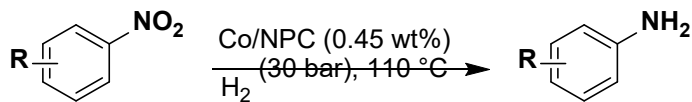

Figure 4. Single atom catalyzed reduction of nitroarenes

References

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