GOING SUB-STOICHIOMETRIC: THE EVOLUTION OF SAMARIUM(II) CATALYSIS

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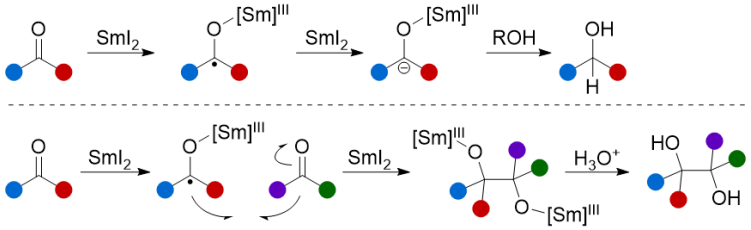
INTRODUCTION

The utility of samarium in synthetic organic chemistry was first reported by Kagan in 1977, wherein it was discovered to be a powerful reagent for reduction and coupling reactions via single-electron transfer (SET) (Scheme 1).[1] Since this discovery, SmI_2 has been used extensively in the synthesis of complex molecules.[2] However, owing to the mechanistic limitation of SET, stoichiometric amounts of SmI_2 must be used to generate radical intermediates. This limitation arises from the strong Sm-O bond (619 kJ/mol) formed after SET, which requires strongly reducing conditions to turnover oxidized Sm(III) minimizing substrate scope. The development of mild, catalytic Sm(II) methods will allow chemists to bypass the cost and scale limitations of stoichiometric use of this reagent.



Scheme 1. Classical reactions using stoichiometric amounts of SmI_2.

THE BIRTH OF SAMARIUM CATALYSIS: CHEMICAL REDUCTANTS

Reduction of Sm(III) intermediates was first reported by Sonoda in 1992. In this work, the authors were able to reduce the catalytic loading of SmI_2 to 55 or 110 mol % by employing samarium metal or magnesium, respectively.[3] Though this discovery was a proof-of-concept for samarium catalysis, it required expensive samarium metal as the reductant to lower the SmI_2 loading. Inspired by this work, Endo later disclosed a novel system employing magnesium and chlorotrimethylsilane (TMSCl) that allowed the loading of SmI_2 to be lowered more than 5-fold. In this system, Sm(III) is liberated from the pinacolate intermediate by TMSCl as $SmClI_2$ prior to reduction with magnesium (Figure 1).[4] However, the harsh reducing ability of magnesium likely limited the substrate scope presented. The next pioneering study came from the Reisman and See groups in 2023 wherein they discovered that the redox potential of Sm (III) species is strongly influenced by the coordination strength of the counter anions. For example, $SmCl_3$ is completely redox inactive but when this anion is exchanged for bromide, iodide, or triflate the redox potential is restored with varying degrees

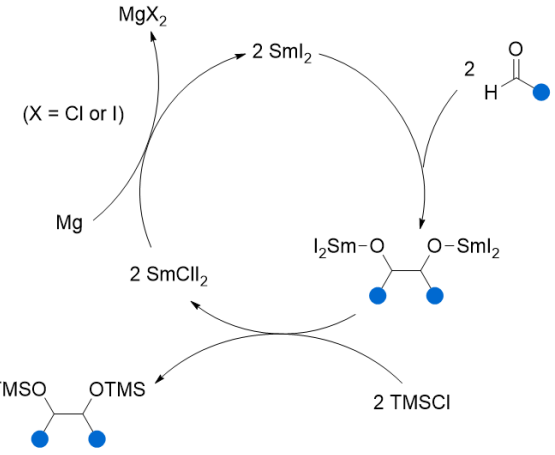


Figure 1. Catalytic cycle for Endo's system.

of reversibility (Figure 2).[7a] This discovery was soon adapted to a catalytic system disclosed by Reisman and co-workers that employs either chemical reduction with zinc or electrochemical reduction.[7b] Their system using a chemical reductant co-employed a weak acid additive as a proton source to activate the samarium-alkoxide intermediate for reduction. With this, they were able to induce reduction under mild conditions with zinc (redox potential of -0.76 V as compared to -2.37 V for magnesium).

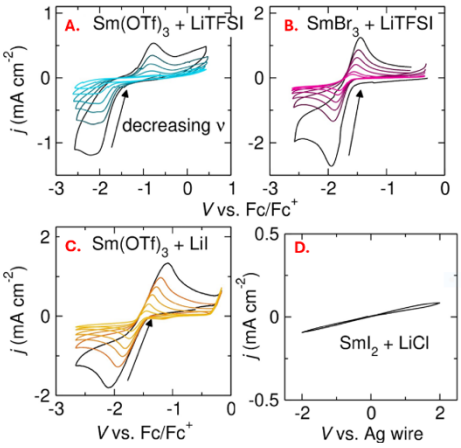


Figure 2. Effects of counter anion on redox reversibility.

ELECTROCHEMISTRY TURNS A NEW STONE

Electrochemical reduction of Sm(III) is the current preferred method being developed for catalysis. First pioneered by Périchon and coworkers in the early 1990s, it was shown that Sm(II) could be generated *in situ* from commercially available $SmCl_3$ under the presence of sacrificial amounts of Mg or Zn anodes to synthesize a wide variety of products.[5a-f] Using this method, air and moisture sensitive SmI_2 can be avoided entirely. Nearly 20 years passed before further developments took place, in which Mellah and coworkers exploited a samarium anode-platinum cathode pair to generate SmI_2 on demand (Figure 3).[6a] This reduces the volume of solvent required by 4-fold as active SmI_2 is replaced as its consumed during the reaction. In this system, tetraalkylammonium salts were used as electrolytes and butane and butene are observed as side products from reduction of the electrolyte. The electrochemically generated SmI_2 effectively performs carbonyl-carbonyl and carbonyl-alkyl halide coupling but lacked catalytic capability. This work was pursued further by the same group to render the system catalytic by employing a samarium cathode to reduce Sm(III) back to the active species.[6b] Slight modifications to the electrode pair were made to expand the scope to benzylic carboxylation and hydrocarboxylation of styrenes.[6c-d]

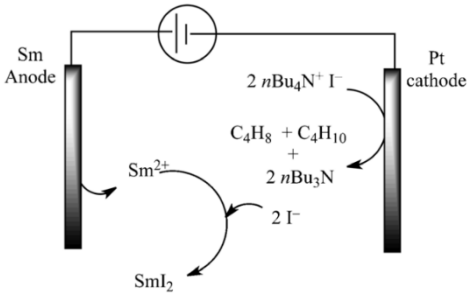


Figure 3. Electrochemical generation of SmI_2.

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