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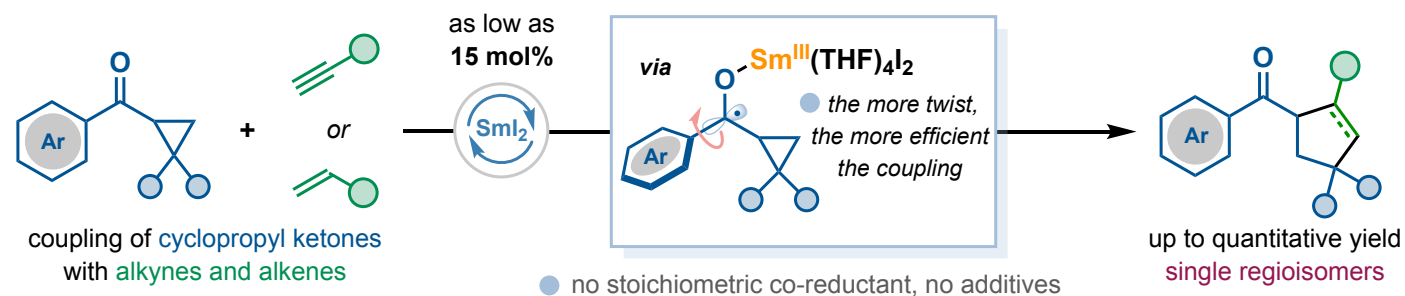
Title

Sml₂-Catalyzed Intermolecular Couplings by Radical Relay

Soumitra Agasti, Giacomo E. M. Crisenza, and David J. Procter*

Department of Chemistry, The University of Manchester, Oxford Road, Manchester, M13 9PL (UK)

E-mail: david.j.procter@manchester.ac.uk

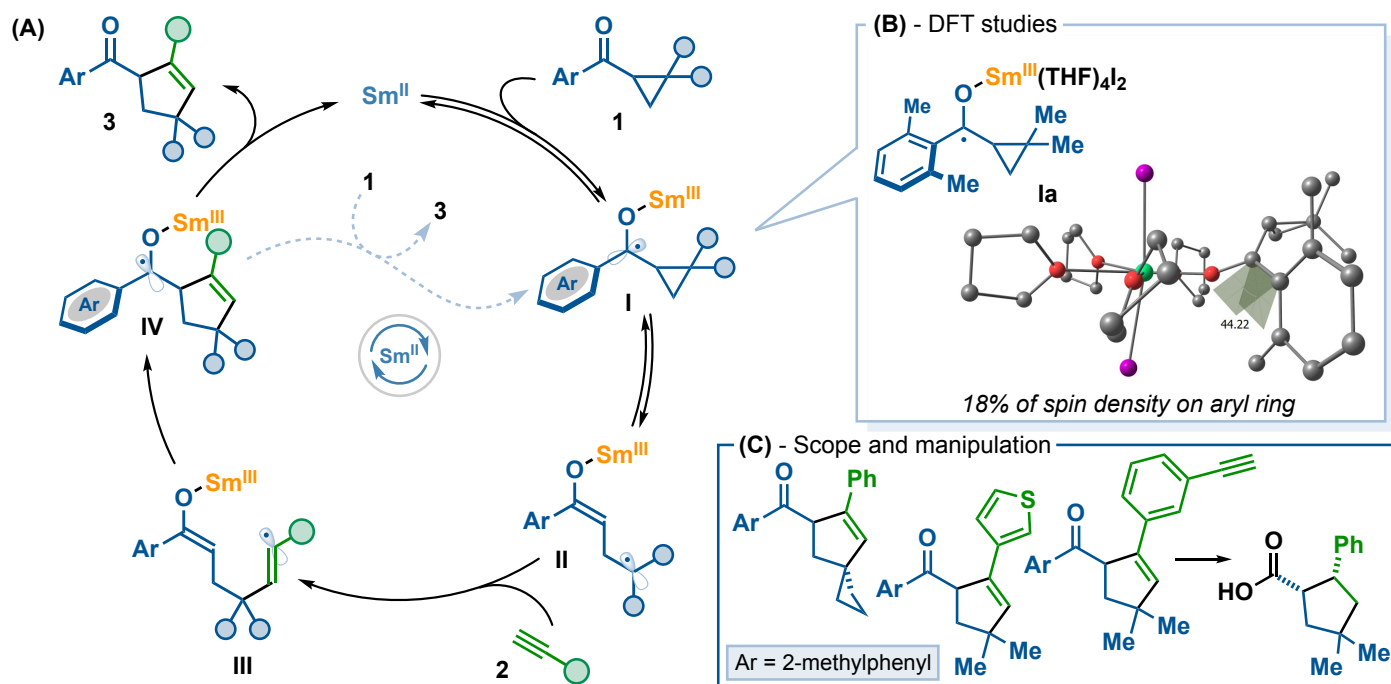


Origin

Sml₂ (Kagan's reagent) remains one of the most versatile and selective single electron transfer (SET) reagents. The chemistry of Sml₂ has provided unique solutions to synthetic problems in many fields, however, its use in super-stoichiometric amounts raises concerns over sustainability. The few methods catalytic in Sml₂ have to rely on the presence of super-stoichiometric metal co-reductants to regenerate Sm(II). We reported a radical-relay approach to catalysis with Sml₂ that negates the need for co-reductants and additives.

Reaction Mechanism

Building on our prior *intra*-molecular process, a more challenging and unprecedented Sml₂-catalyzed *inter*-molecular radical coupling between cyclopropyl ketones and unsaturated hydrocarbons has been developed. Here, reversible SET from Sml₂ to ketone **1** generates ketyl radical **I**, which undergoes fragmentation to reveal samarium(III) β-enoyl-radical **II** (A). Intermolecular coupling with alkyne **2**, and ensuing radical rebound addition to the Sm(III)-enolate moiety within intermediate **III**, produces new ketyl radical **IV**. Back electron transfer (BET) from **IV** to the Sm(III)-center regenerates the active Sm(II) species, while yielding densely-functionalized cyclopentenyl product **3**. It is also possible that ketyl radical **IV** directly reduces starting ketone **1**, feeding an electron transfer chain mechanism. The key aspects driving the observed reactivity are: i) the use of Sml₂ in catalytic amounts (as low as 15 mol%) – lower concentrations of the reagent prevent competing reduction of radical intermediate **II** to the corresponding carbanion, and; ii) the instability of the starting ketyl radical **I**, which promotes fragmentation and pushes the reaction equilibrium towards the formation of a more stable product ketyl radical **IV**. Computational studies were used to predict the conformation of samarium ketyl radical **Ia**, and show that the ketyl aryl substituent is twisted out of plane, thus vouching for the instability of the corresponding ketyl radical **I** (B). Remarkably, our study unveils an intriguing link between ketone conformation and efficient cross-coupling in Sml₂-catalysis.



Importance

The SmI_2 -catalyzed process provides synthetic access to highly-decorated cyclopentene scaffolds, suitable for further derivatization (C). Of mechanistic importance, our radical relay strategy not only enables SmI_2 -catalysis in the absence of super-stoichiometric co-reductant and additives, but also facilitates intermolecular radical processes under Sm(II) conditions, which are inherently challenging due to competing reduction of radicals to carbanions. This study provides further insight into the mechanism of radical relays involving SmI_2 , and paves the way for the future use of this classical reagent in modern radical catalysis.

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