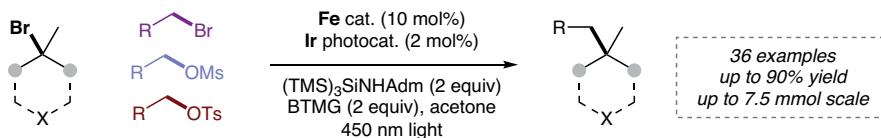


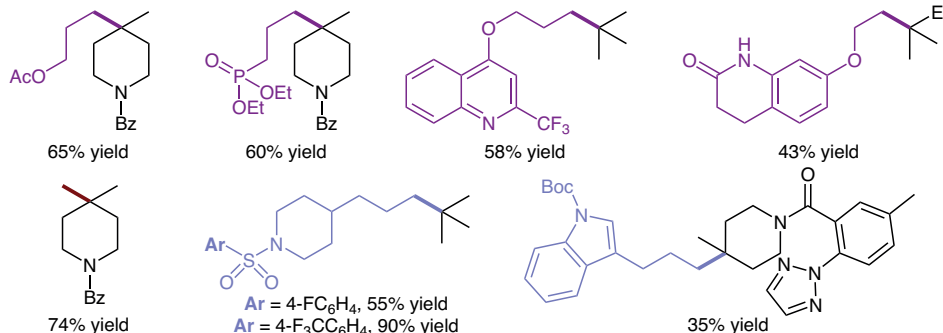
A. L. PACE, F. XU, W. LIU, M. N. LAVAGNINO, D. W. C. MACMILLAN*
(PRINCETON UNIVERSITY, USA)

Iron-Catalyzed Cross-Electrophile Coupling for the Formation of All-Carbon Quaternary Centers
J. Am. Chem. Soc. **2024**, *146*, 32925–32932, DOI: 10.1021/jacs.4c14942

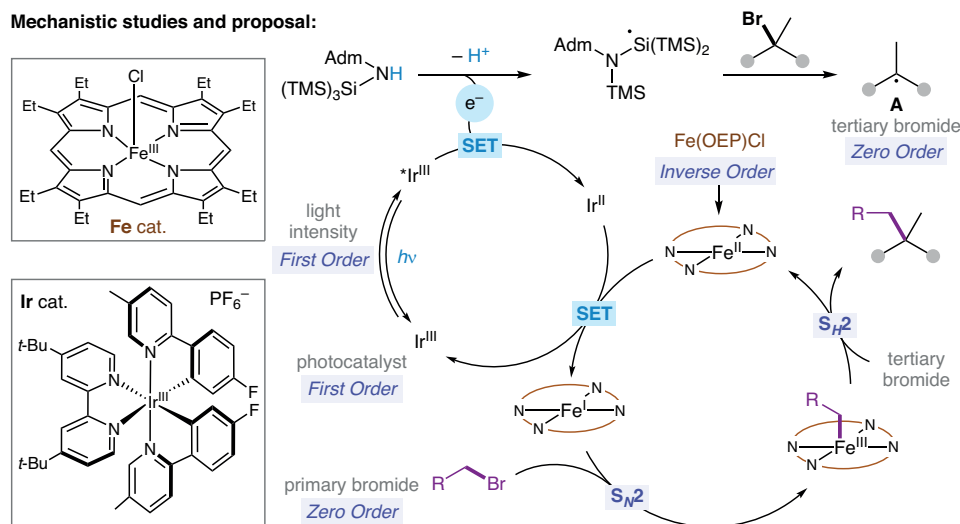
Cross-Electrophile Coupling via Iron-Mediated Tandem $S_{\text{N}}2/S_{\text{H}}2$ -Type Reaction



Selected examples:



Mechanistic studies and proposal:



Significance: MacMillan and colleagues report the cross-electrophile coupling of tertiary bromides and primary alkyl electrophiles using iron catalysis. By harnessing an iron(I)-mediated $S_{\text{N}}2$ reaction of alkyl electrophiles, followed by a bimolecular homolytic substitution ($S_{\text{H}}2$) reaction with in situ generated tertiary radical species, a variety of molecules bearing a quaternary center can be synthesized. The authors demonstrate that a range of alkyl bromides and alkyl sulfonates can effectively participate in the coupling reaction.

Comment: In-depth mechanistic studies are reported, including variable time normalization analysis, which provides insights into the kinetic orders of the reaction components. Photonuclear magnetic resonance studies confirm the intermediacy of Fe(I) and Fe(III) complexes under the reaction conditions. Notably, the detection of Fe(I) before the Fe(III) complex supports the proposal that the formation of Fe(I) is a crucial step for the subsequent formation of the Fe(III)–alkyl complex through an $S_{\text{N}}2$ -type pathway.

SYNFACTS Contributors: Mark Lautens, Alexa Torelli
Synfacts 2025; 21(02), 144 Published online: 28.01.2025
DOI: 10.1055/a-2497-0099; Reg-No.: L01925SF

© 2025, Thieme. All rights reserved.
Georg Thieme Verlag KG, Oswald-Hesse-Strasse 50, 70469 Stuttgart, Germany