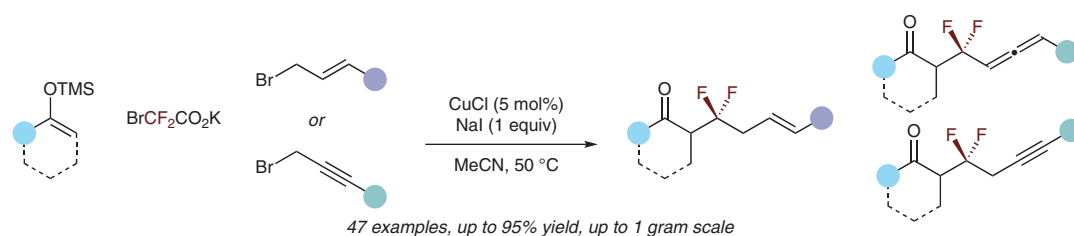


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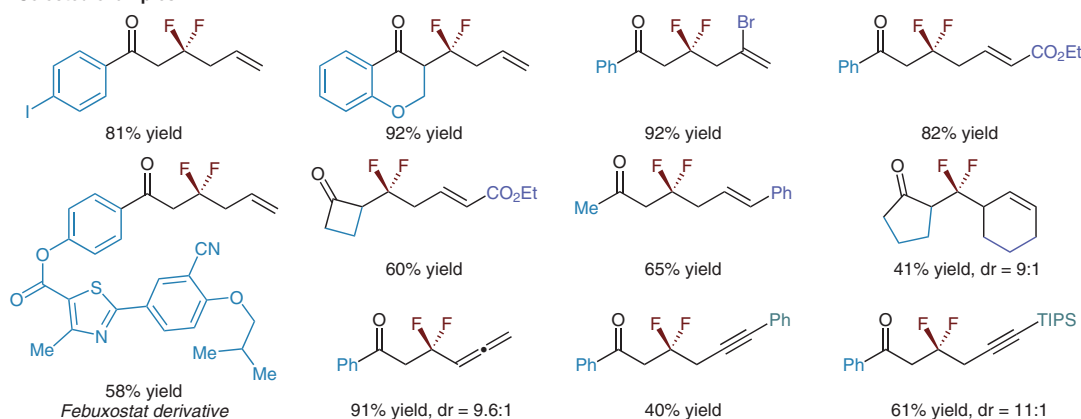
Copper-Catalyzed Difluorocarbene Transfer Enables Modular Synthesis

Nat. Chem. 2023, 15, 1064–1073, DOI: 10.1038/s41557-023-01236-8.

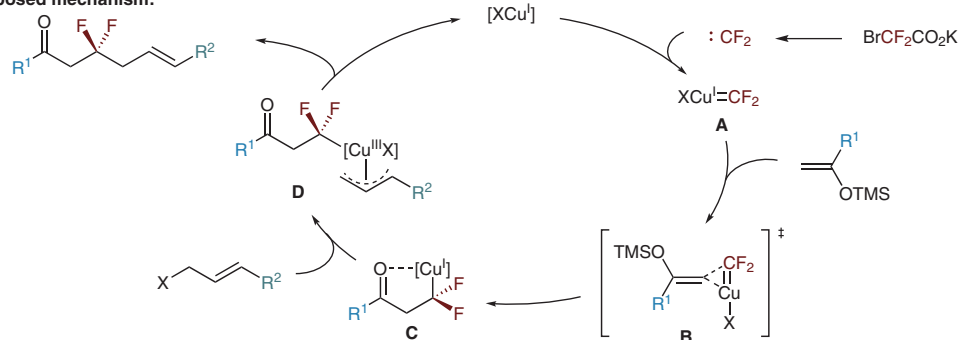
Copper-Catalyzed Difluoroalkylation of Silyl-Enol Ethers



Selected examples:



Proposed mechanism:



Significance: A copper-catalyzed difluorocarbene transfer reaction is reported. This strategy couples a difluorocarbene, generated from a bromodifluoroacetate precursor, with two inexpensive feedstocks. A silyl enol ether and allyl/propargyl bromides engage to access difluoroalkylated compounds in up to 95% yield. A broad substrate scope features a range of cyclic and acyclic silyl enol ethers and differently substituted allyl bromides. The methodology is also efficient when applied in a gram-scale reaction.

Comment: Mechanistic and computational studies were used to elucidate the mechanism. The reaction of the copper(I) salt and the in situ generated difluorocarbene generates the isolable electrophilic carbene A. Subsequent nucleophilic addition (B), and desilylation generates difluoroalkylcopper species C. Oxidative addition of C with the allyl halide and then reductive elimination delivers the product.

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