Asymmetric Copper-Catalyzed Defluoroalkylation

Significance: Defluorination of trifluoromethyl alkenes has become a popular strategy in the past few years to introduce a new stereocenter and synthesize gem-difluoroalkenes. Gem-Difluoroalkenes are useful handles for further functionalizations and they are also useful moieties in medicinal chemistry. Shi and co-workers report the enantioselective addition of alkyl Grignard reagents to trifluoromethyl alkenes with the assistance of an arylboronate.

Comment: The reaction uses alkyl magnesium bromide reagents which initially react with the organoboron species to form a tetraorganoborate. The tetraalkylboron species reacts with the copper catalyst to undergo an enantioselective addition to the trifluoromethyl alkene followed by β-fluoride elimination. The reaction was successful with a variety of substituents on the trifluoromethyl alkenes including aryl, alkenyl, alkynyl, and alkyl groups. Unfunctionalized Grignard reagents were most extensively investigated in the reaction.

Proposed mechanism:

Selected examples:

- 65% yield, 87% ee
- 72% yield, 92% ee
- 93% yield, 99% ee
- 36% yield, 88% ee
- 51% yield, 93% ee
- 67% yield, 71% ee
- 80% yield, 83% ee
- 69% yield, 88% ee
- 96% yield, 96% ee
- 73% yield, 92% ee