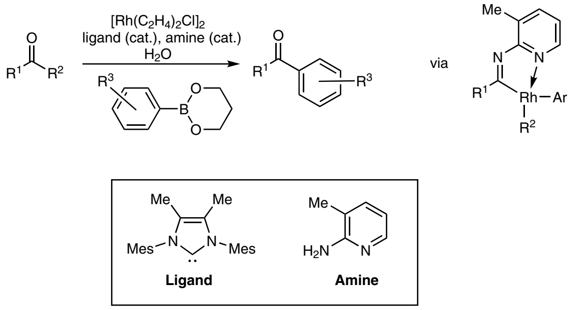
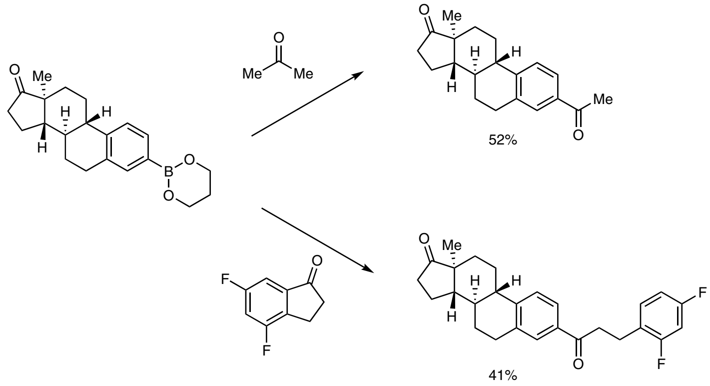
SUZUKI REACTIONS

Cross-coupling ketones

J. Am. Chem. Soc. **140**, 5347-5341 (2018)





The Suzuki–Miyaura coupling has long been a go-to reaction for the formation of carbon–carbon bonds. From its early history as a method to form Csp^2–Csp^2 bonds, continual developments have allowed it to remain at the forefront of synthetic chemistry, including the ability to work with sp^3-hybridized carbons and — largely thanks to nickel catalysis — the ability to employ a broad range of electrophiles beyond aryl and alkyl halides. Now Guangbin Dong and co-workers at the University of Chicago have expanded the electrophile scope even further by allowing cross-coupling on a wide range of simple, unstrained ketones via a C–C bond cleavage.

Prior work had shown that this was possible, though generally very specific starting ketones were needed: those containing suitable activating/directing groups or those with significant ring strain. In the current work a wide range of ketones — both cyclic and acyclic — proved capable of cross-coupling with arylboronates (pictured, top). The proposed mechanism involves the in situ formation of an intermediate imine with the amine additive, leading to coordination and subsequent insertion of the Rh(I) catalyst into the C–C bond.

Substituted cyclopentanones were ring-opened to give alkyl aryl ketones in reasonable yields, and with unsymmetrical substrates there was a slight preference for cleavage of the more sterically hindered C–C bond. In cases where aryl alkyl ketones were used as starting materials there was exclusive cleavage of the C(aryl)–C(carbonyl) bond. Dialkyl ketones such as acetone also worked with moderate yields. With respect to the boronate component *ortho*-substituted arylbornates were not efficient nucleophiles — presumably due to steric hindrance. However the system was tolerant of *meta*- and *para*-substituents, including di- and tri-substituted variants. Late-stage functionalization of more complex molecules was also demonstrated. Using boronate-functionalized steroid derivatives the group showed that ketones could be used as effective acylating reagents (pictured, bottom).

Enda Bergin

https://doi.org/10.1038/s41929-018-0087-4