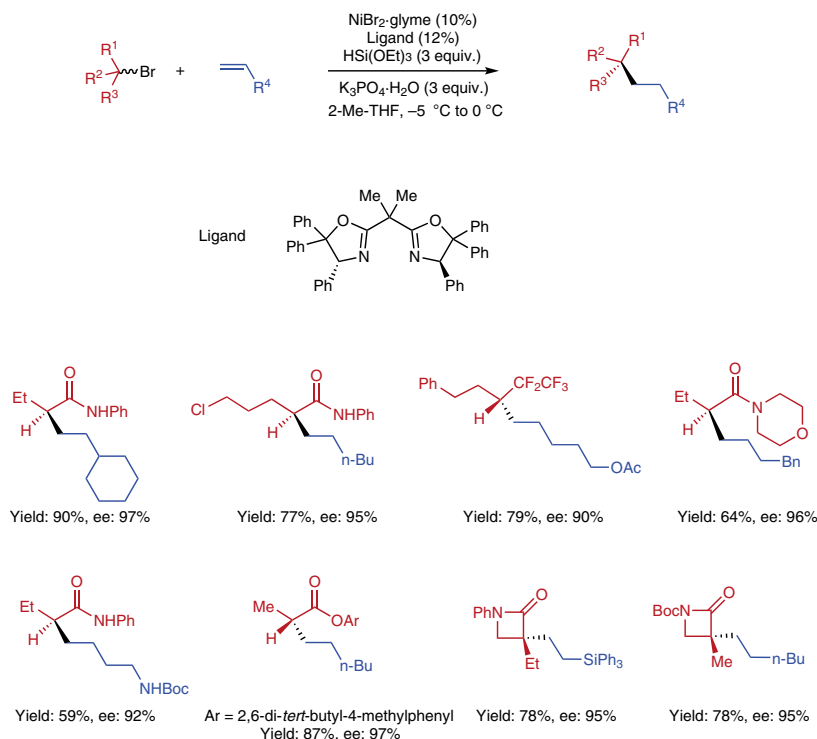


## ENANTIOCONVERGENT CROSS-COUPLING

## Alkyl-alkyl bond formation

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Asymmetric cross-coupling reactions allow the formation of new carbon–carbon bonds in addition to the selective formation of new stereocentres. One successful example of this is the enantioconvergent cross-coupling between an alkyl halide and an alkyl metal nucleophile (including organo-magnesium, silicon, zirconium and boron compounds) to form a new alkyl–alkyl bond.

However, the use of organometallic species can cause difficulties due to their limited structural variability and, in some cases, poor stability. Now, Gregory Fu and co-workers at the California Institute of Technology have reported enantioconvergent coupling between racemic alkyl halides and simple olefins. Using a chiral nickel complex, the researchers showed broad substrate scope in both reaction partners. For the alkyl bromide electrophile, all substituents — R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> in the figure — could be varied (and it is worth noting that a single catalyst worked in all cases). Although most examples included amide groups, esters or perfluoroalkyl substituents were also tolerated. Furthermore, tertiary alkyl bromides (in the form of  $\alpha$ -halo- $\beta$ -lactams) could be used, resulting in the formation of quaternary stereocentres — something

that is challenging even in achiral processes. Flexibility with respect to the olefin nucleophile was also observed, and in cases where the starting material contained chiral centres, the enantioselectivity of the product was determined largely by the catalyst. Although most examples were mono-substituted alkenes, some intriguing early results showed that internal alkynes also produce cross-coupled products in high yields and enantioselectivities.

As for a mechanism, hydrosilylation of the olefin followed by cross-coupling with the resulting organosilicon compound (Hiyama-type coupling) was ruled out by pre-forming this species and showing that it was not an effective reaction partner. Rather, the team propose insertion of the olefin into a nickel hydride complex, followed by coupling with an alkyl bromide-derived radical.

Given the availability and stability of olefins, the mild conditions and the reasonably broad substrate scope of this reaction, this work is a big step forward in enantioconvergent couplings.

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