Asymmetric Nickel-Catalyzed Intramolecular Hydroalkenylation

Significance: Nickel catalysis has been explored in recent years as a cost-effective alternative to palladium. Zhu, Zhou, and co-workers report the enantioselective nickel-catalyzed isomerizations of dienes to yield chiral piperidines or tetrahydro- pyrans, which are found in a number of natural products and drug structures.

Comment: The reaction was proposed to involve a nickel-hydride intermediate, which was generated through $\beta$-hydride elimination of the alkyl nickel species. The approach was successful with a variety of substituents on the olefin, and all the reactions proceeded with high enantioselectivities.

Selected examples:

- TsN
  - 69% yield, 99% ee

- TsN
  - 88% yield, 99% ee

Example applied in the enantioselective synthesis of (+)-femoxetin:

1. NBS, Bu$_3$P (61% yield)
2. n-Bu$_3$SnH, Et$_3$B, 91% yield

1. MsCl, Et$_3$N
2. NaH, DMF
4-methoxyphenol (52% yield over two steps)

1. napthalene/Na
2. AcOH, (CH$_2$O)$_n$, NaBH$_3$CN
(42% yield over two steps)