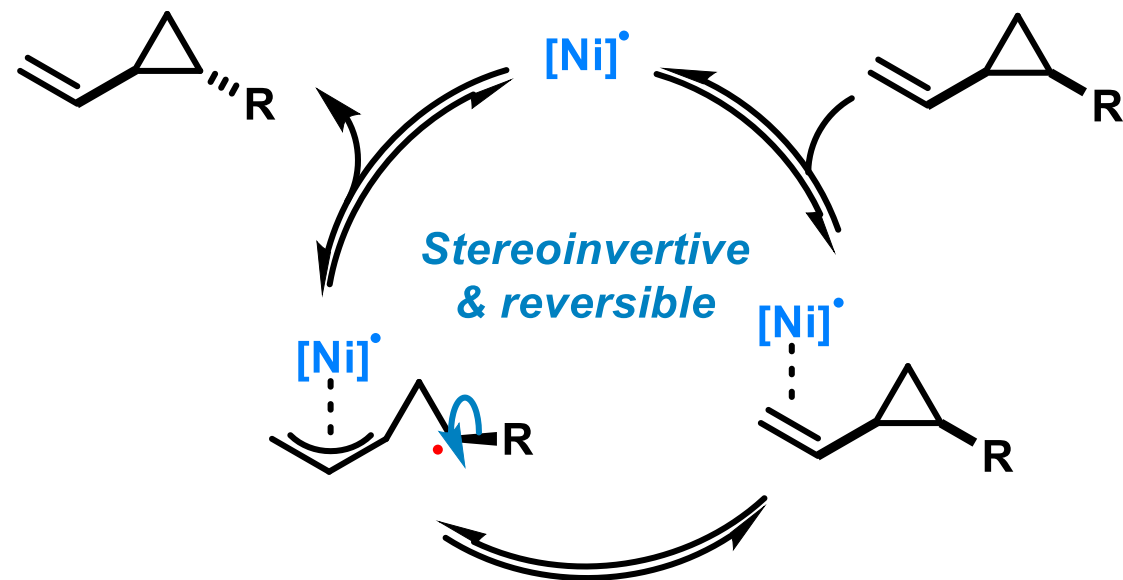


Dynamic stereomutation of vinylcyclopropanes with metalloradicals



Nature 631, 80–86 (2024).

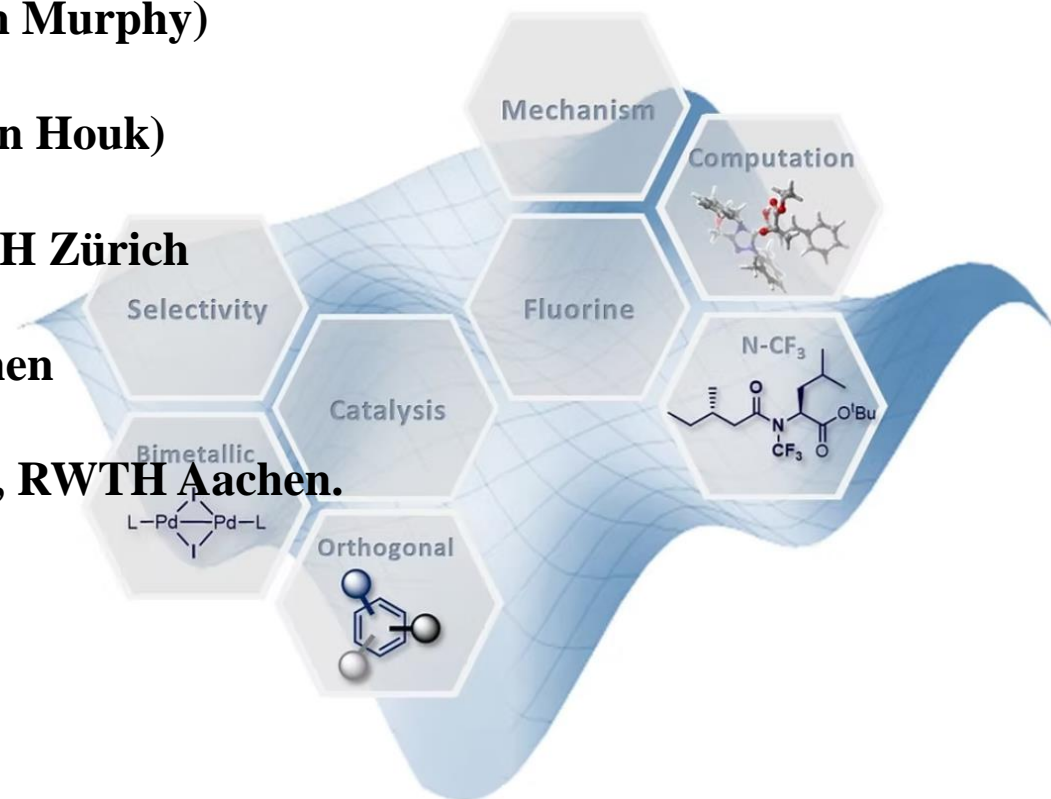
Ke Yuee
2025/01/19

Prof. Dr. Franziska Schoenebeck

RWTH Aachen University, Germany

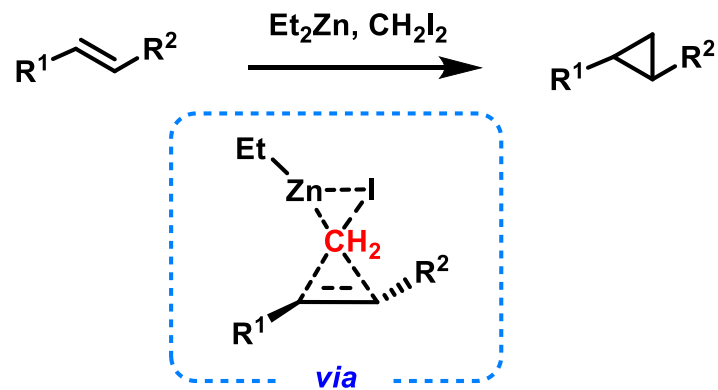


- TU Berlin (Germany) & Glasgow (UK)
- Glasgow, UK (Ph.D. with John Murphy)
- UCLA, USA (Postdoc with Ken Houk)
- 2010 – Assistant Professor, ETH Zürich
- 2013 – Professor, RWTH Aachen
- 2016 – Full Professor & Chair, RWTH Aachen.

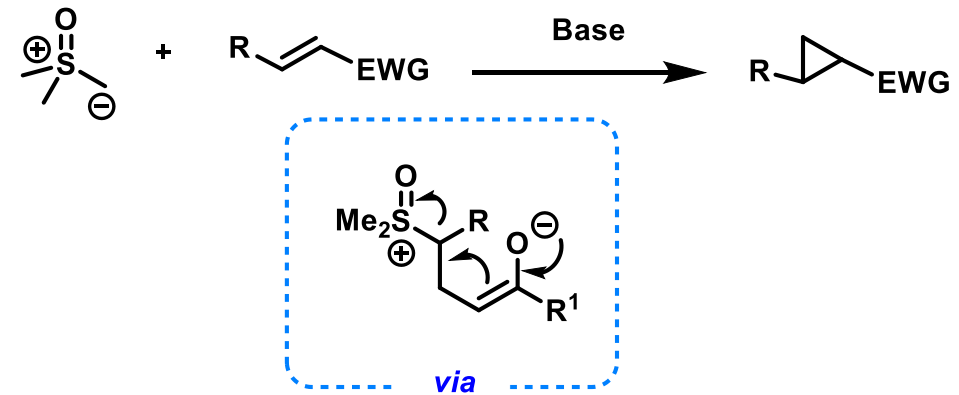


Traditional cyclopropanation reactions

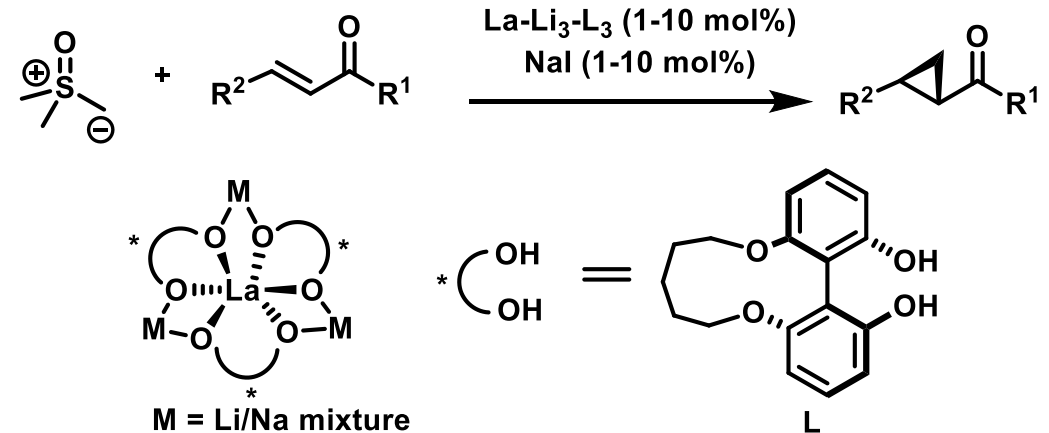
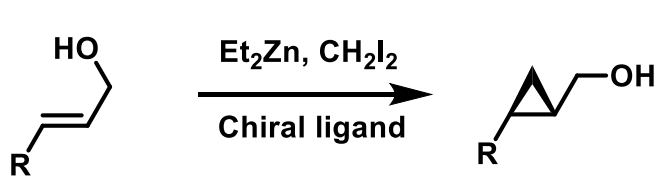
Simmons–Smith cyclopropanation



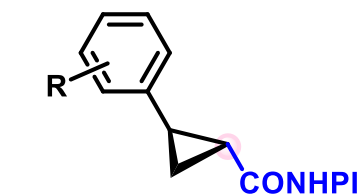
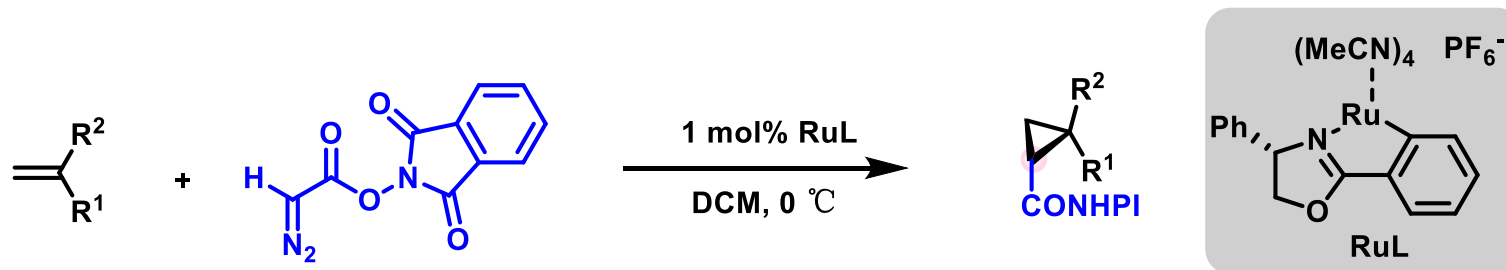
Corey–Chaykovsky cyclopropanation



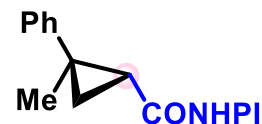
Asymmetric version



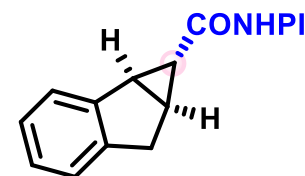
Asymmetric cyclopropanation reactions



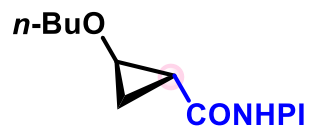
R = EWG or EDG
81-99%, >20:1 d.r., 96:4-97:3 e.r.



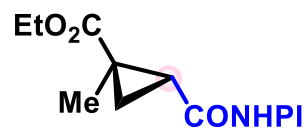
97%, 11:1 d.r., 99:1 e.r.



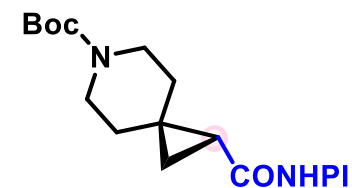
91%, 12:1 d.r., 92:8 e.r.



98%, 9:1 d.r., 97:3 e.r.

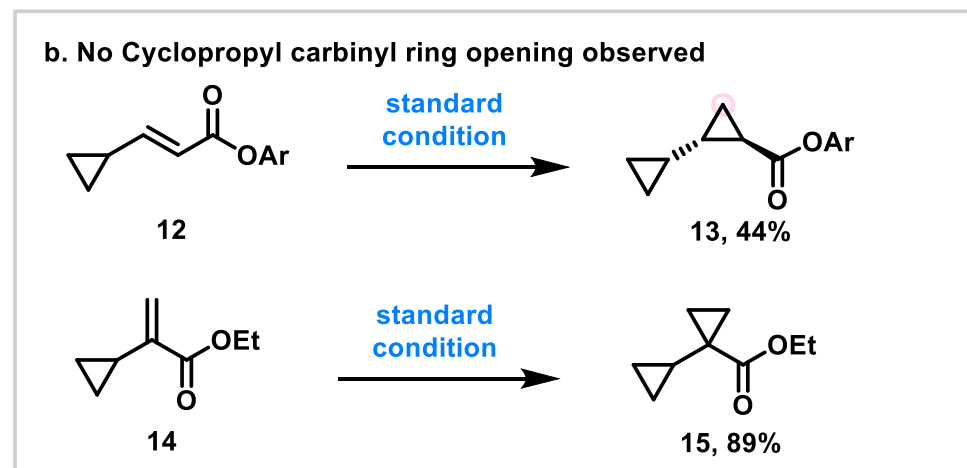
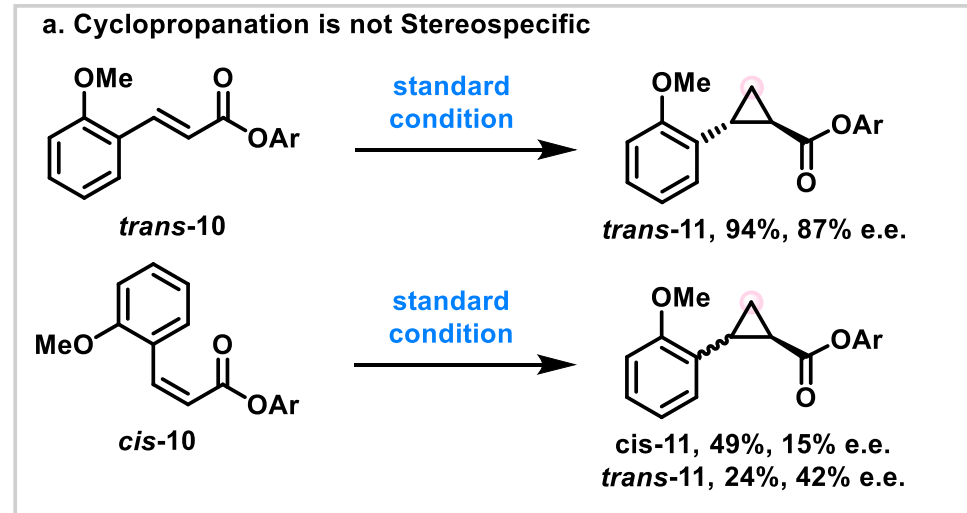
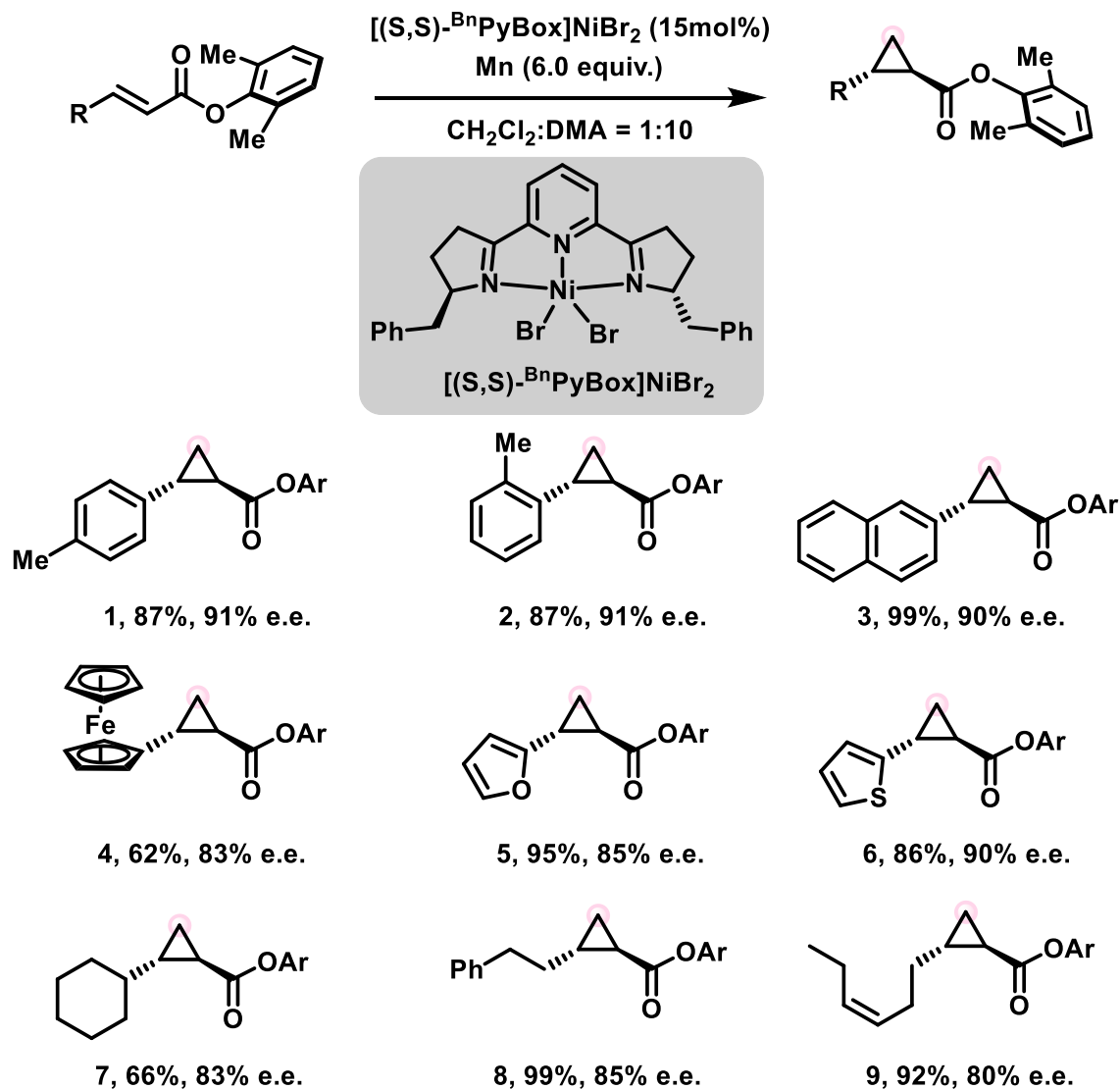


72%, 12:1 d.r., 94:6 e.r.

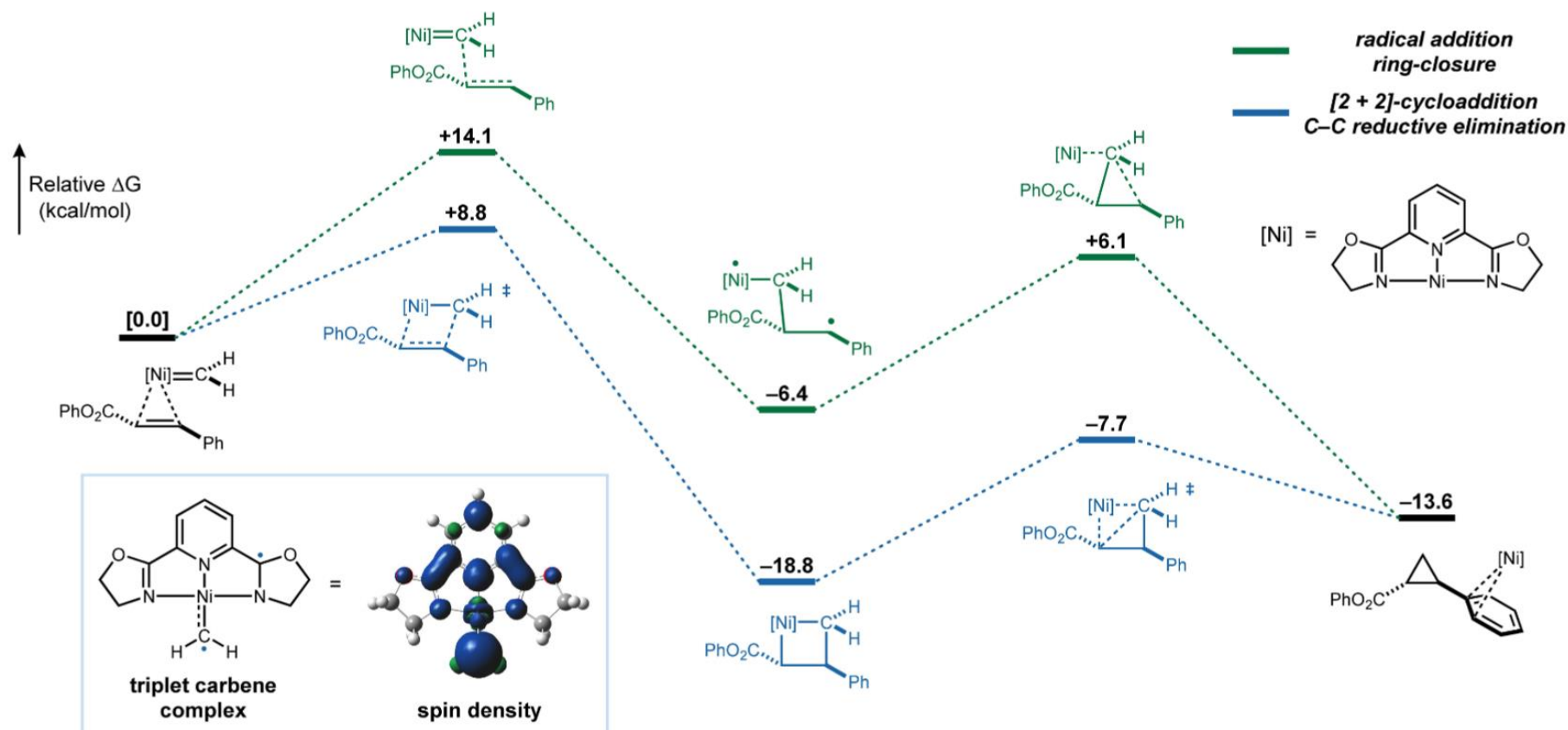
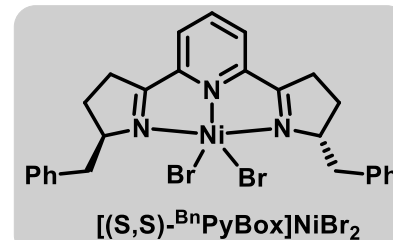
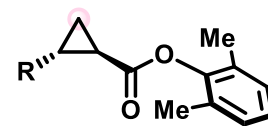
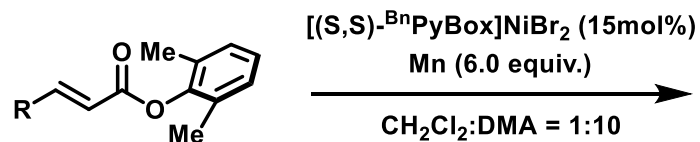


97%, 11:1 d.r., 99:1 e.r.

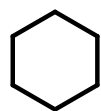
Asymmetric cyclopropanation reactions



Asymmetric cyclopropanation reactions



1) Strain Energies of ring systems (in kcal/mol)



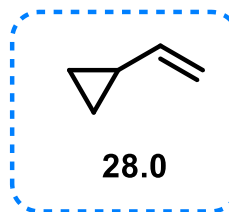
1.3



7.4



26.3

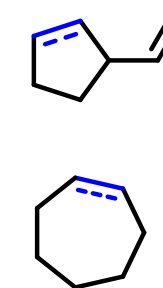
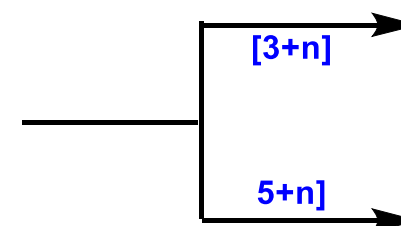
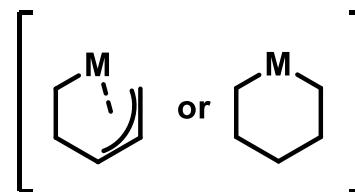
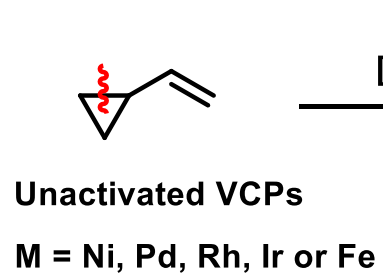
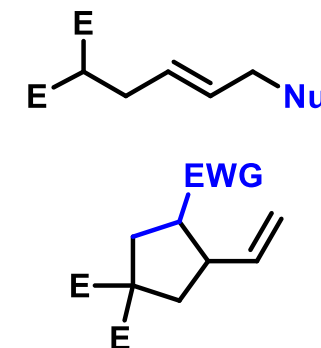
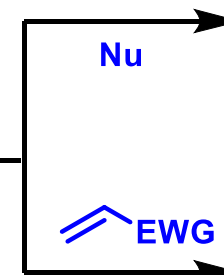
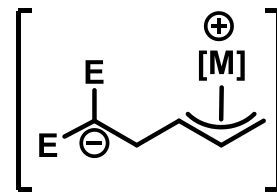
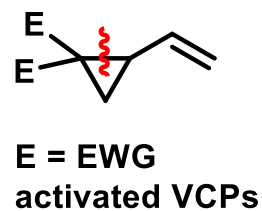


28.0

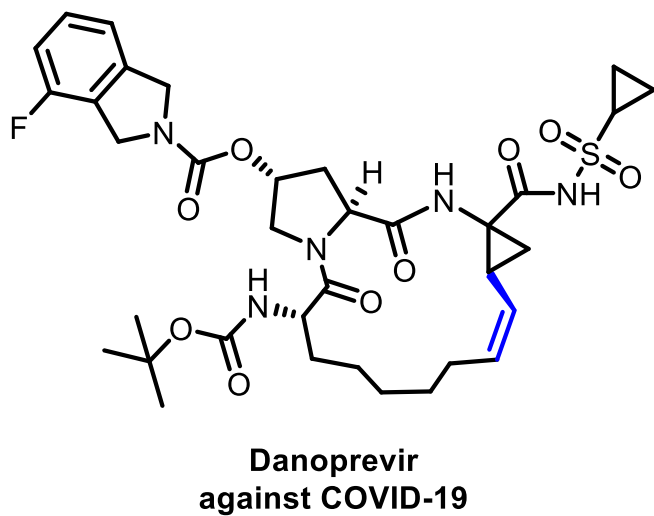
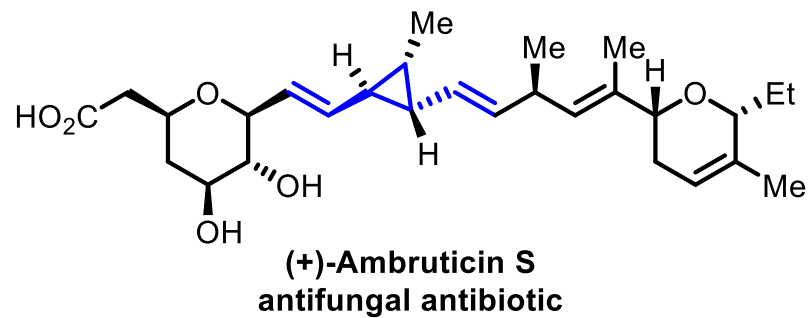


29.0

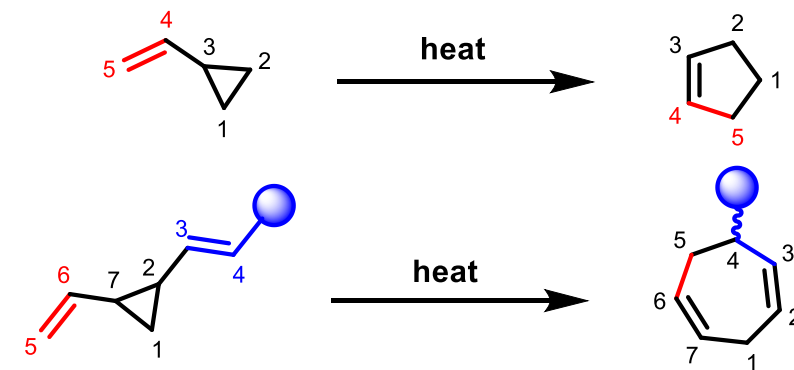
2) C-C cleavage of VCPs



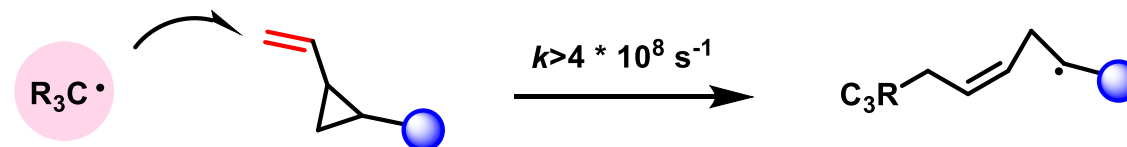
Structural units in bioactive compounds



Vinylcyclopropane rearrangement



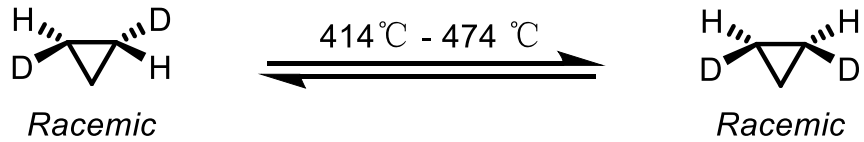
Radical clock



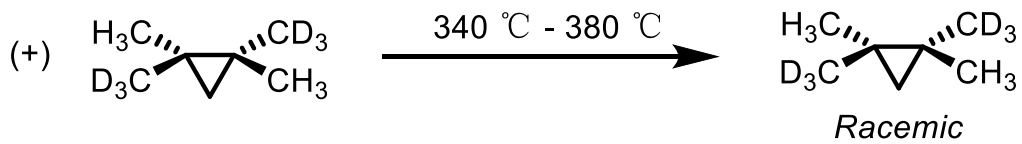
Ring-opening of cyclopropanes *via* radical pathway

Ring-opening of cyclopropanes *via di-radical*

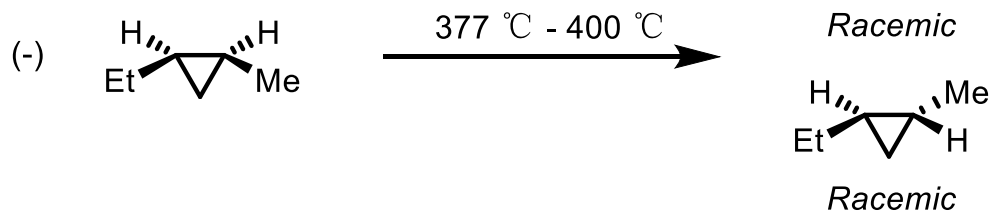
Rabinovitch, Schlag (1958)



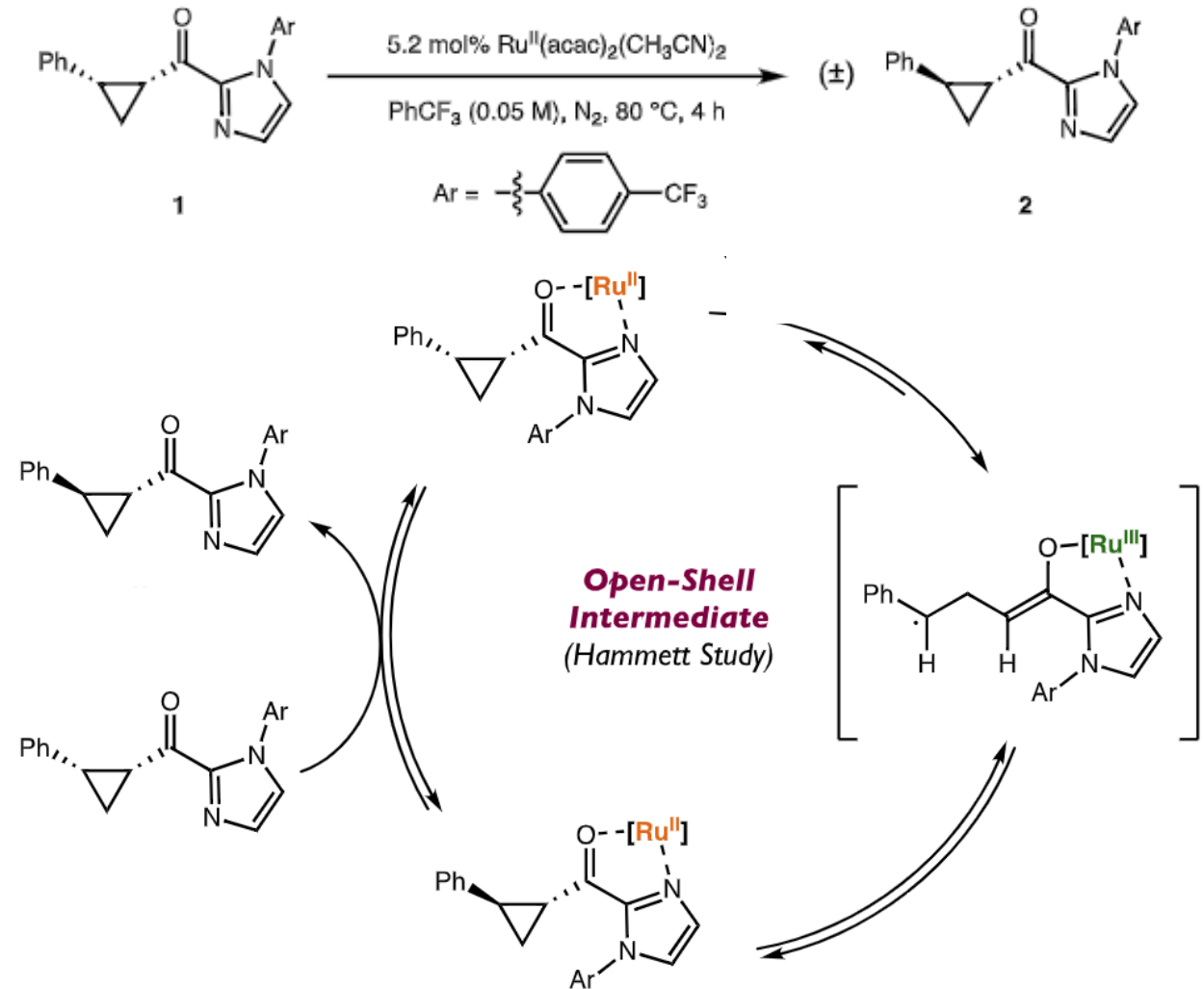
Berson, Balquist (1968)



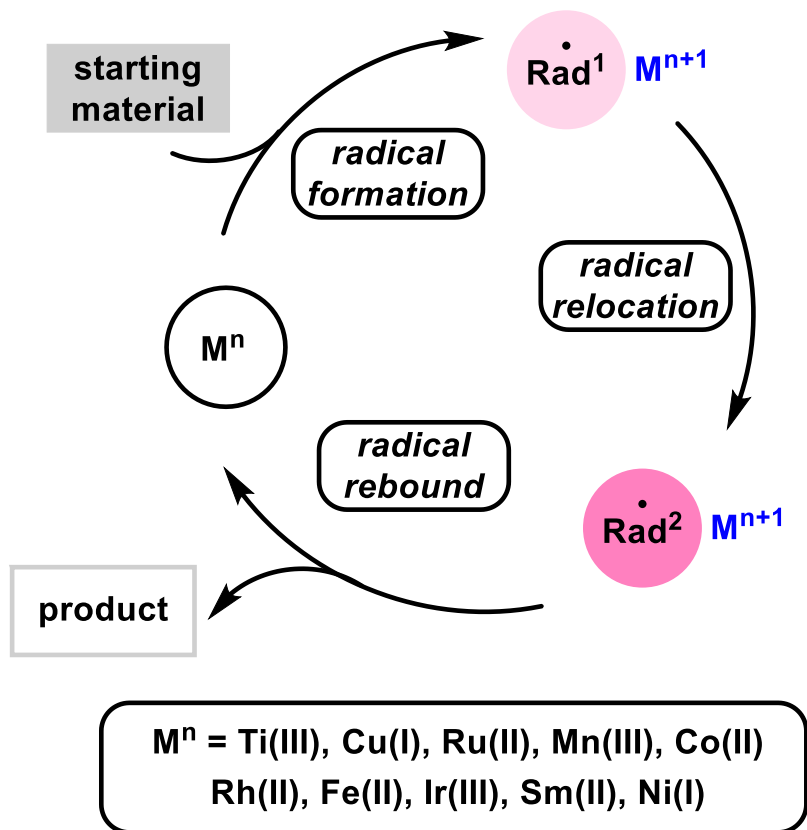
Carter, Bergman (1968)



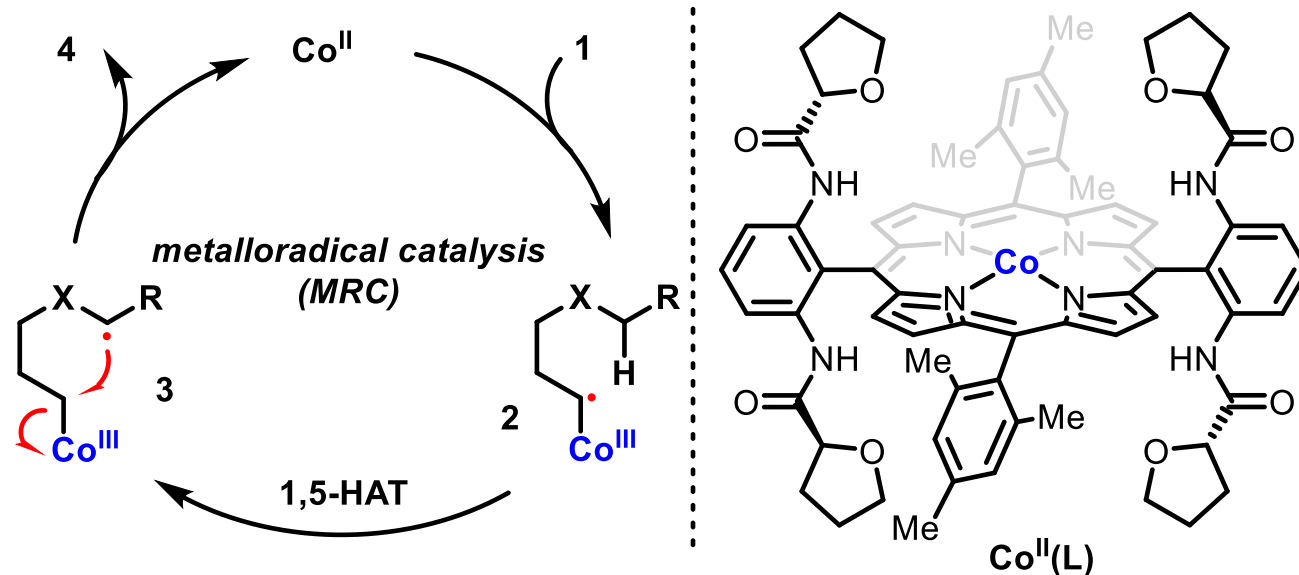
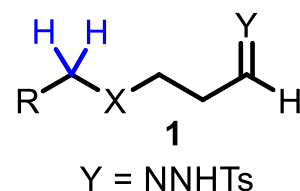
Enabled by Complexation-Induced Bond-Weakening



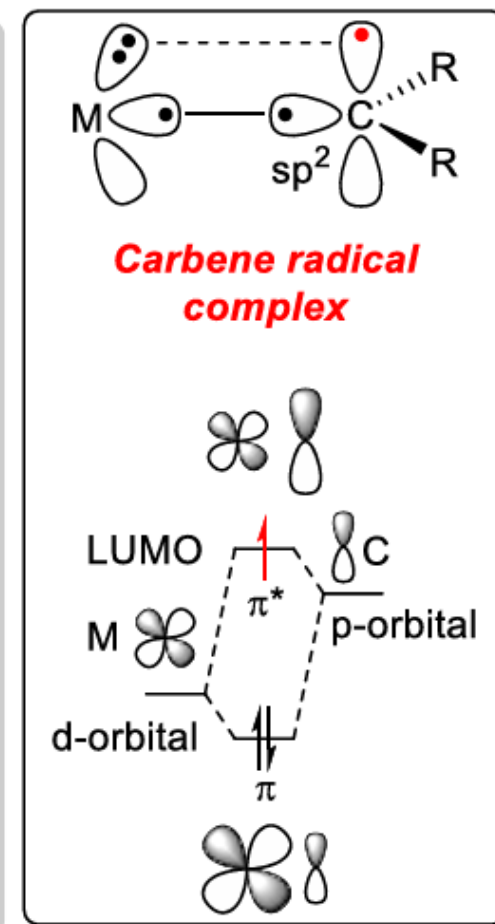
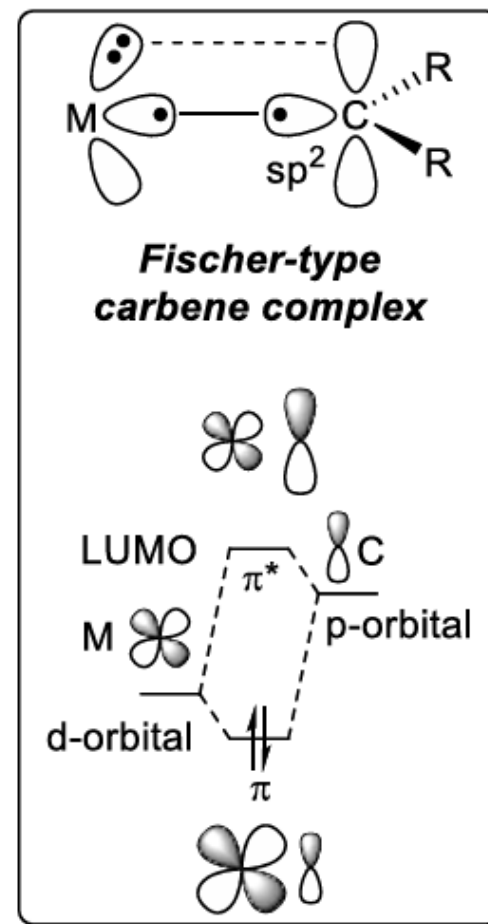
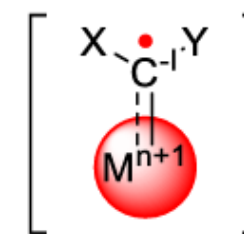
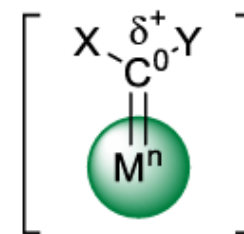
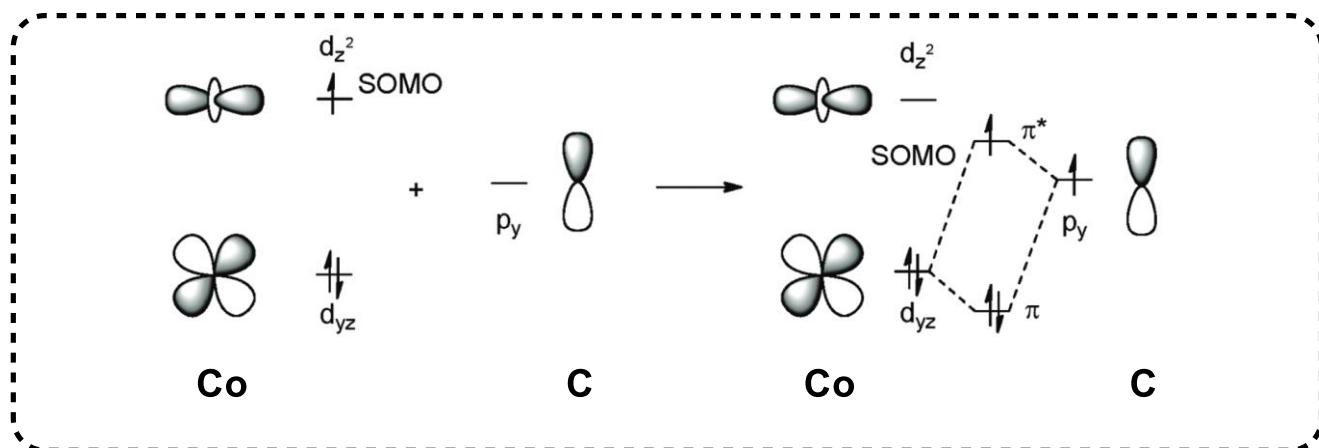
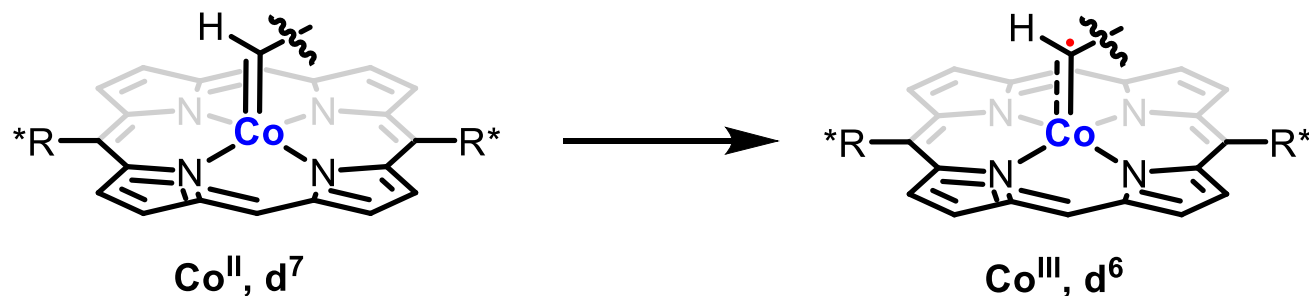
Radical relay catalysis of Mental complexes



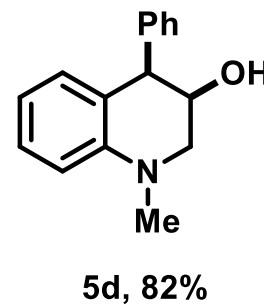
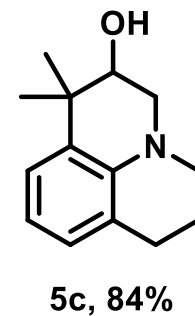
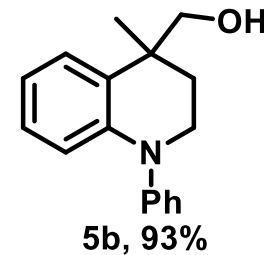
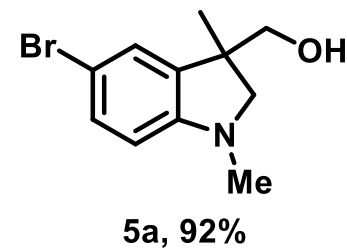
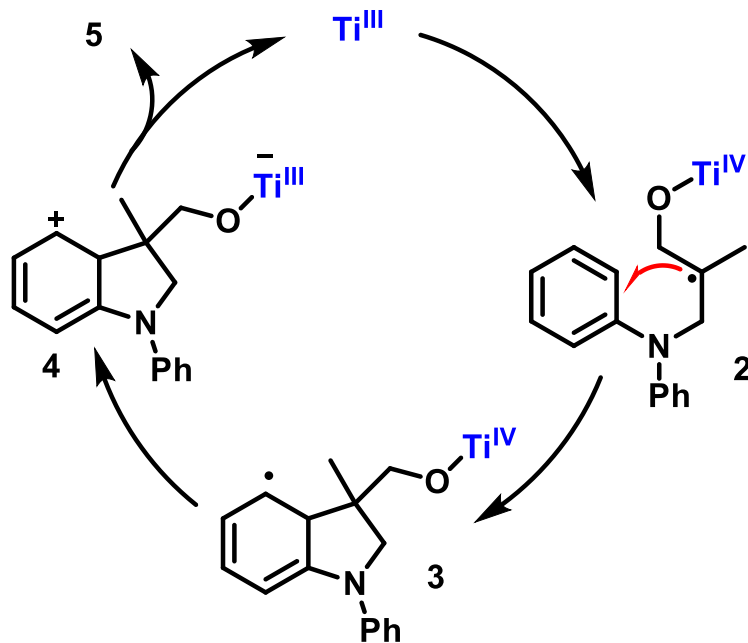
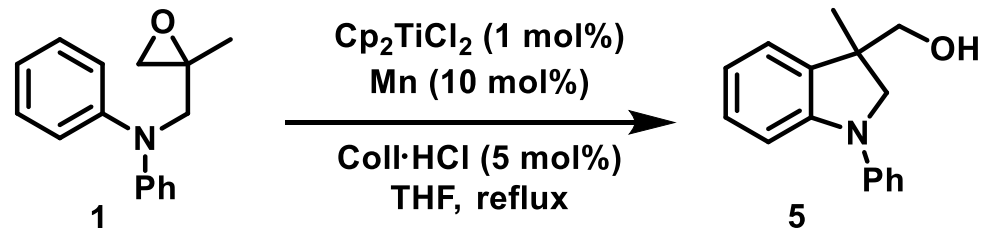
e.g. Co(II)-Catalysed cascades



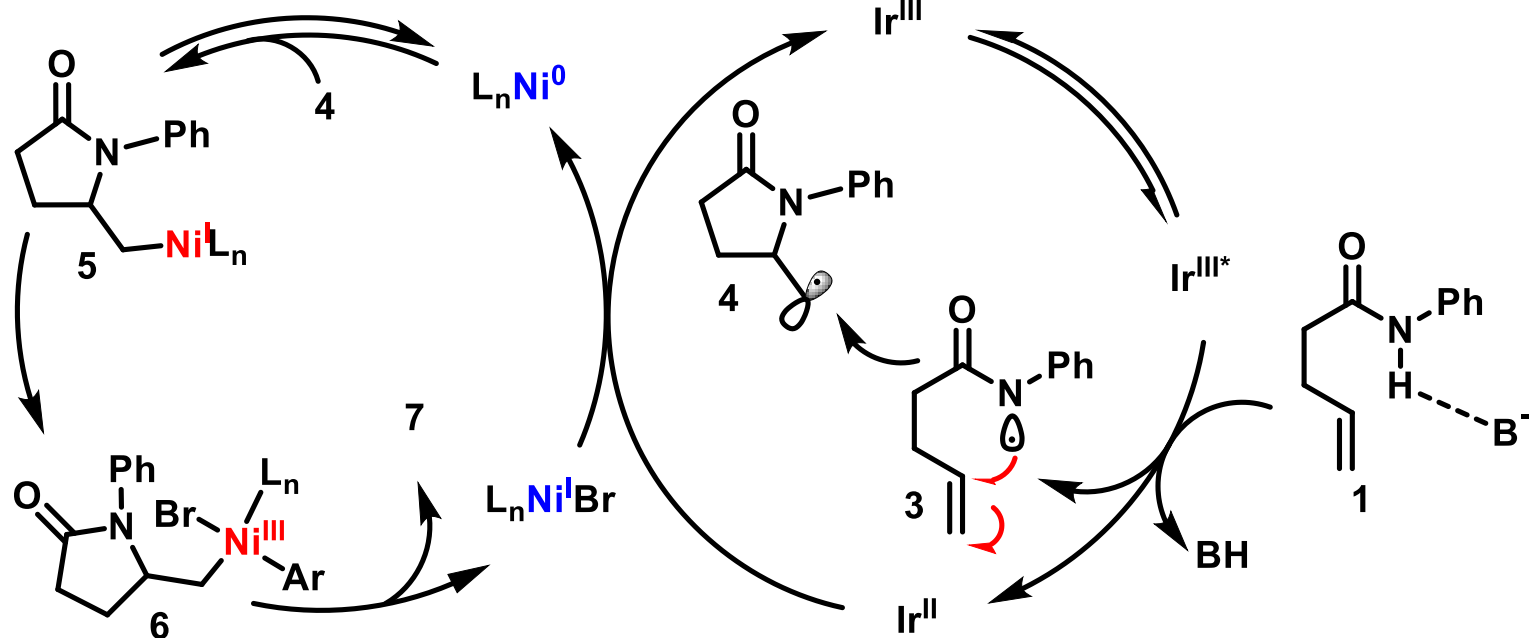
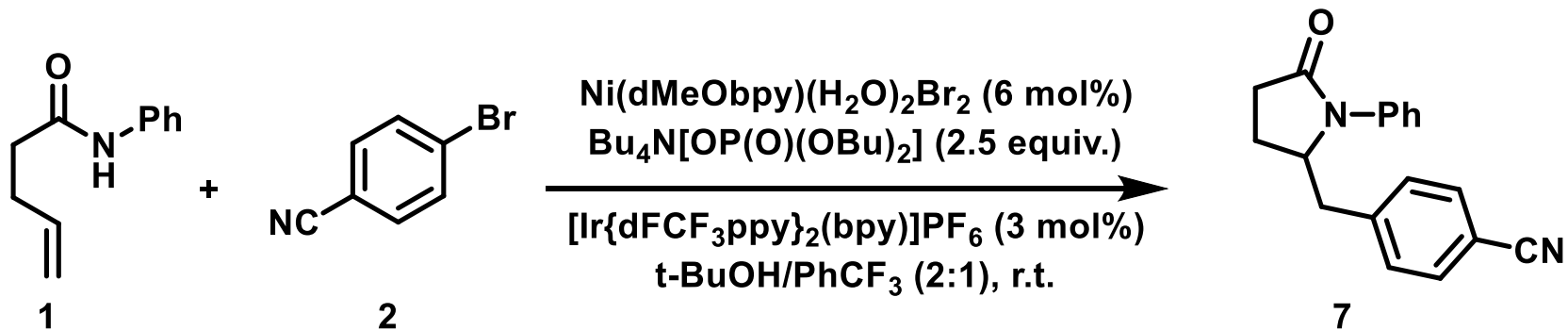
Radical relay catalysis of Mental complexes



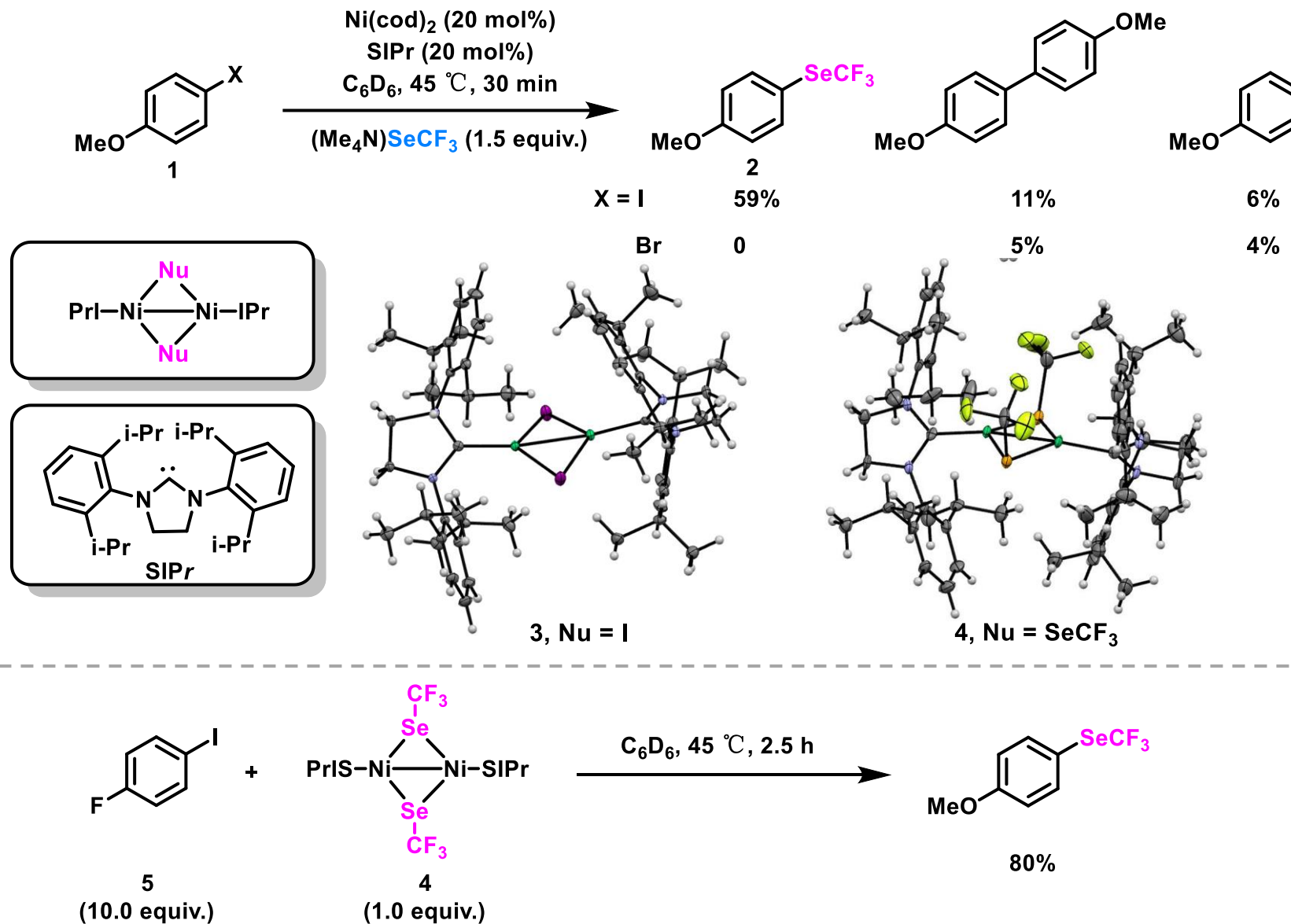
Radical relay catalysis of Mental complexes



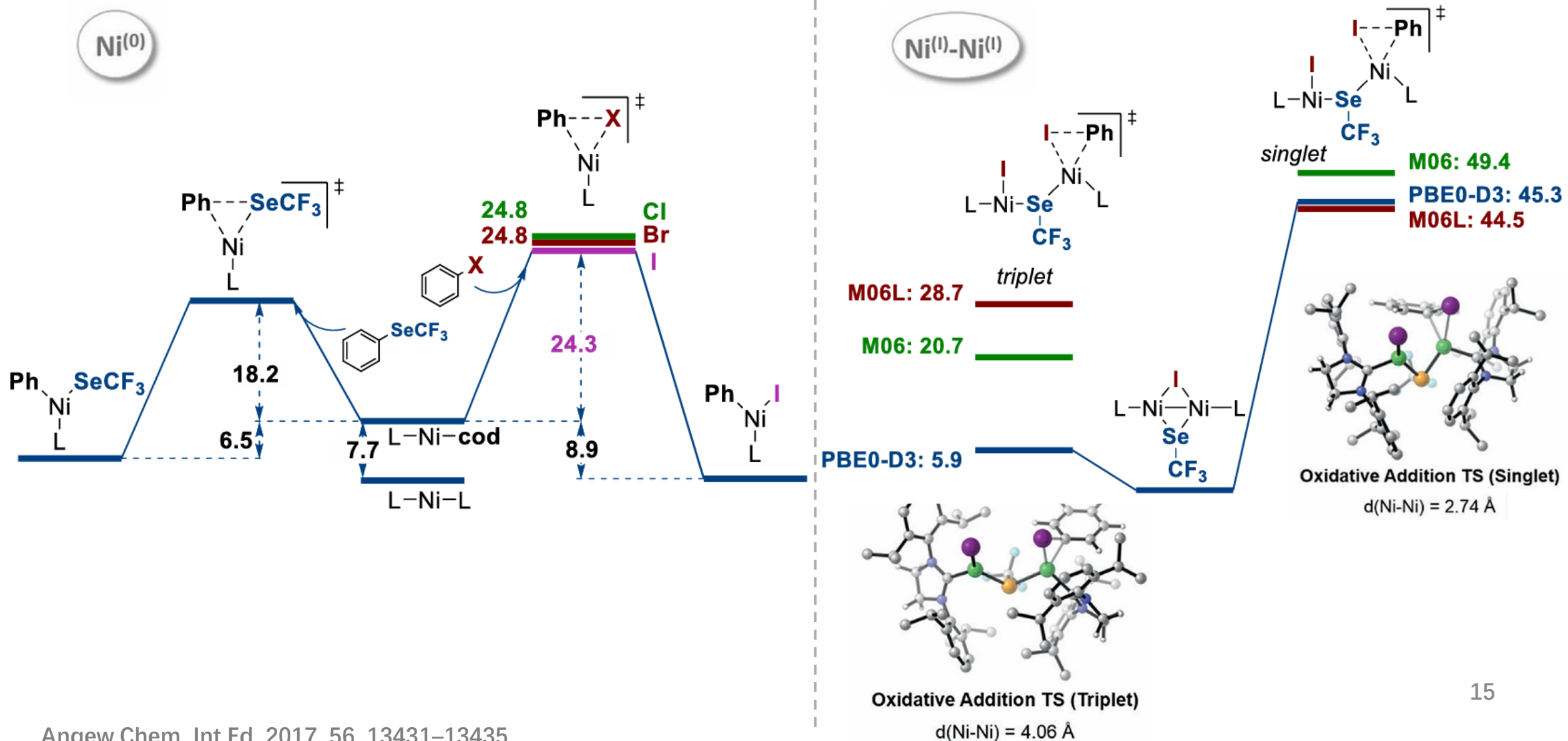
Radical relay catalysis of Mental complexes



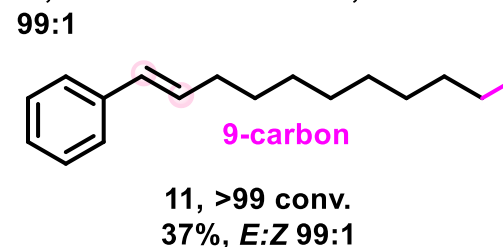
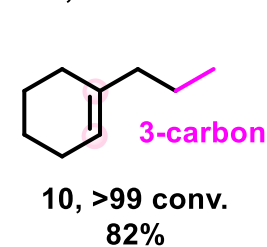
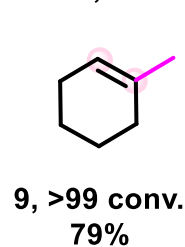
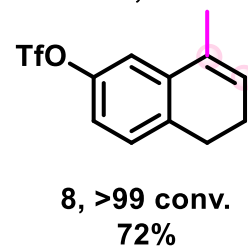
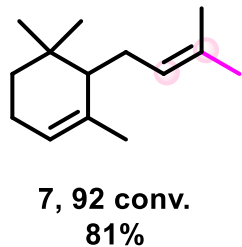
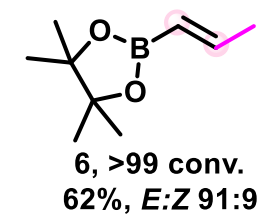
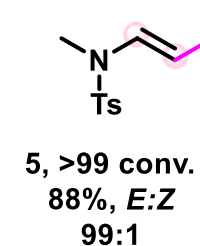
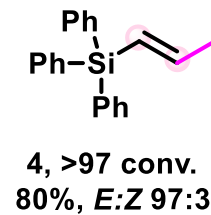
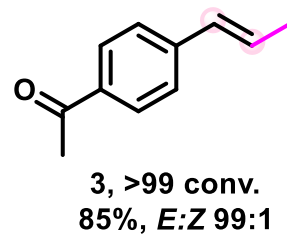
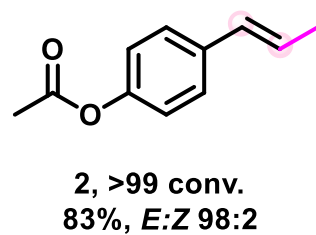
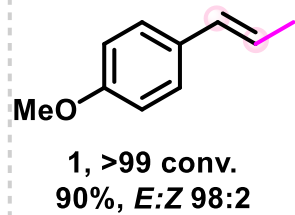
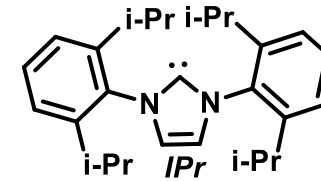
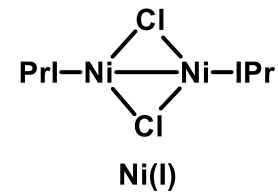
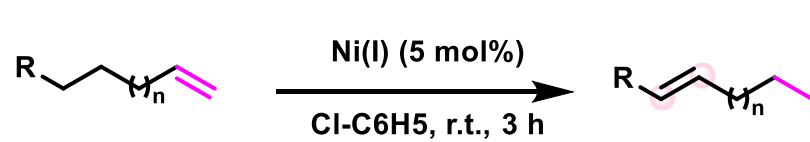
Ni(I) catalyzed Cross-coupling reaction



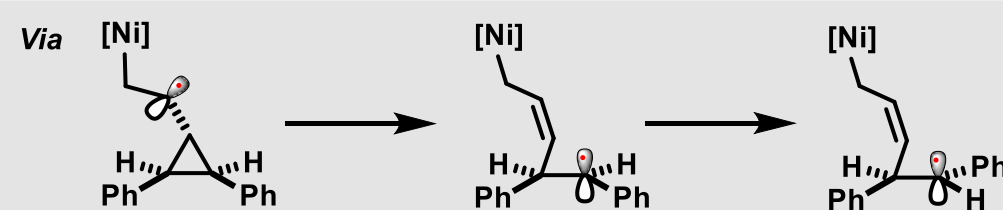
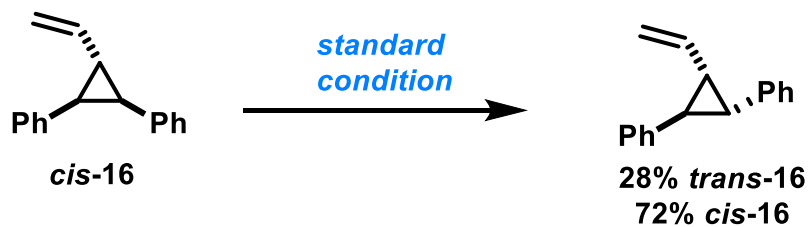
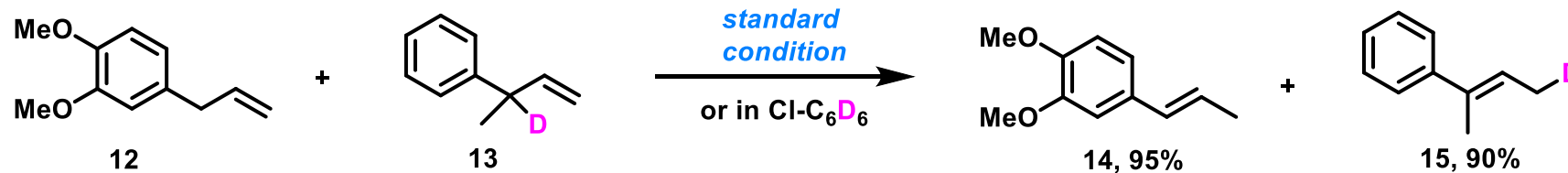
Ni(I) catalyzed Cross-coupling reaction



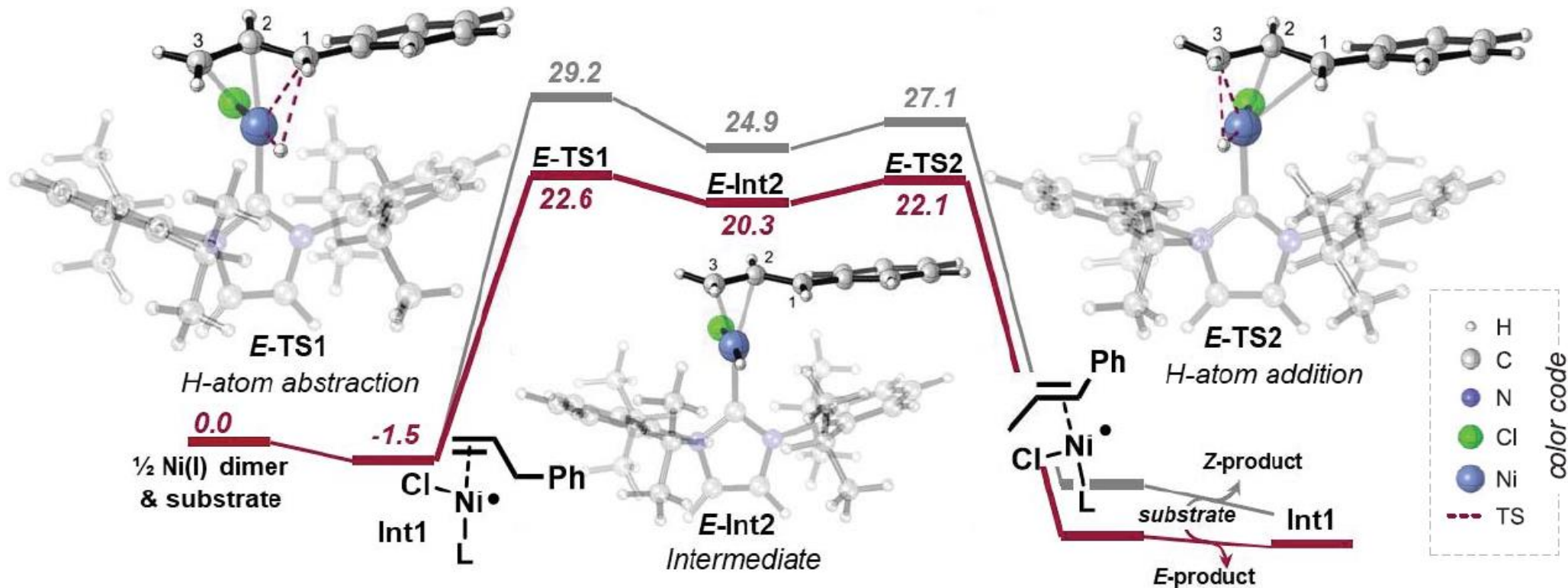
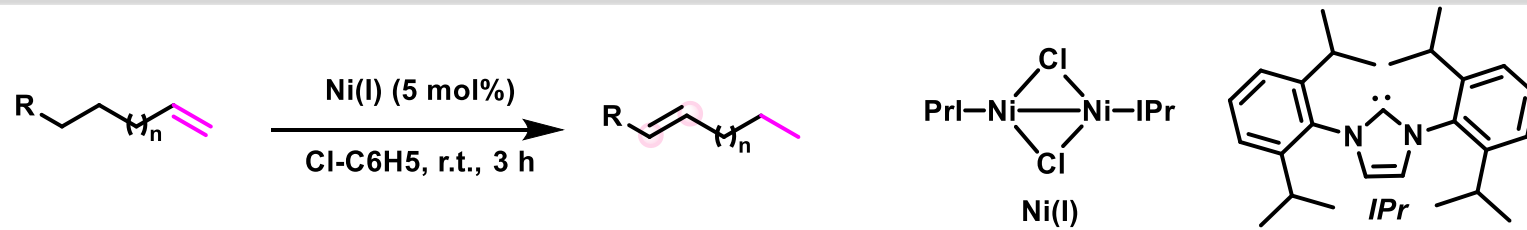
Ni(I) catalyzed double-bond migrations



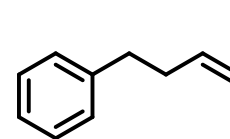
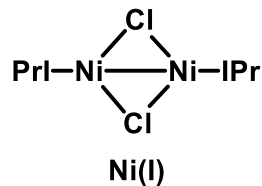
Mechanistic Tests:



Ni(I) catalyzed double-bond migrations

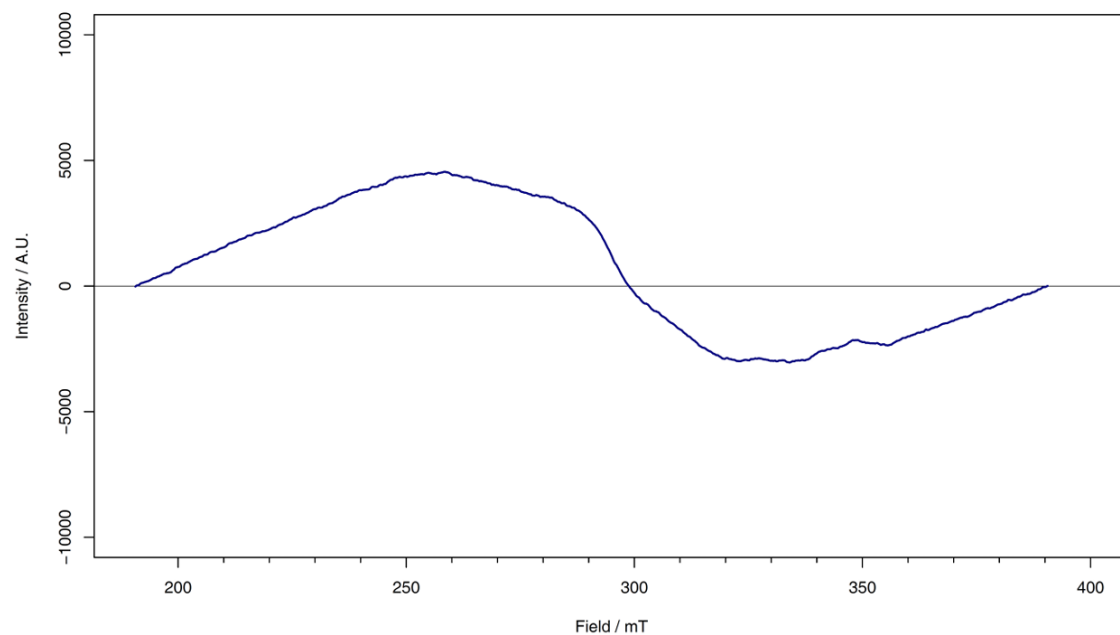


Ni(I) catalyzed double-bond migrations

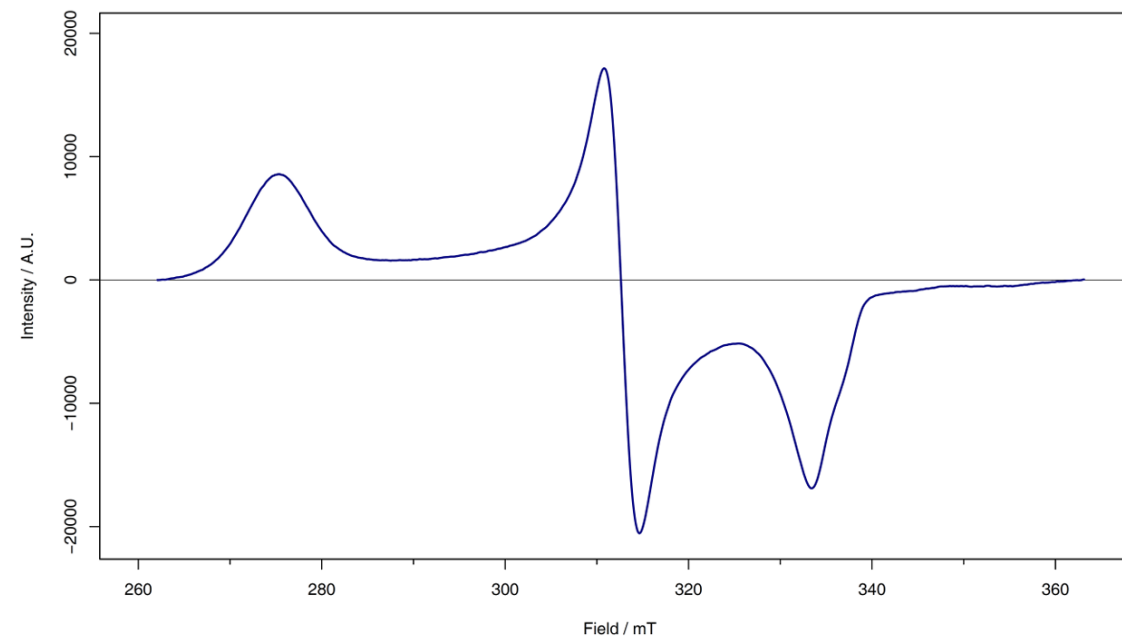


*standard
condition*

EPR spectrum

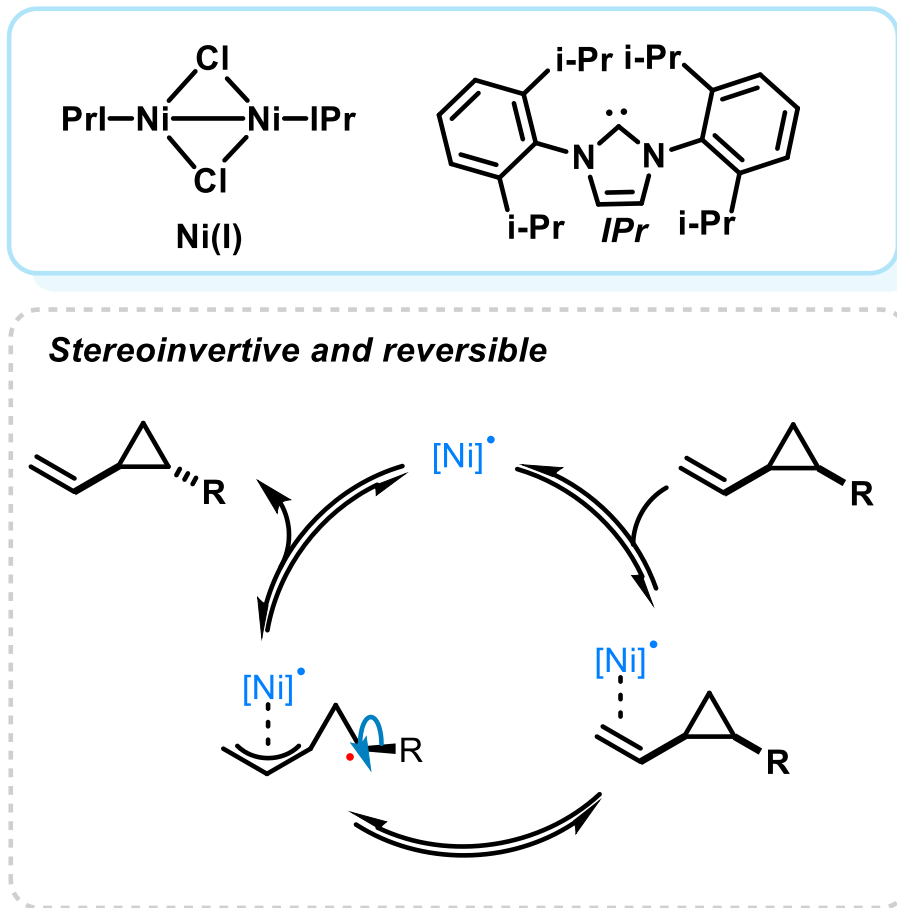
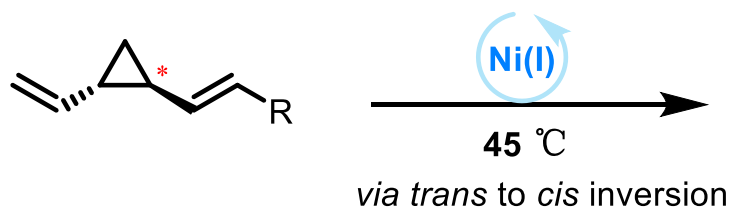
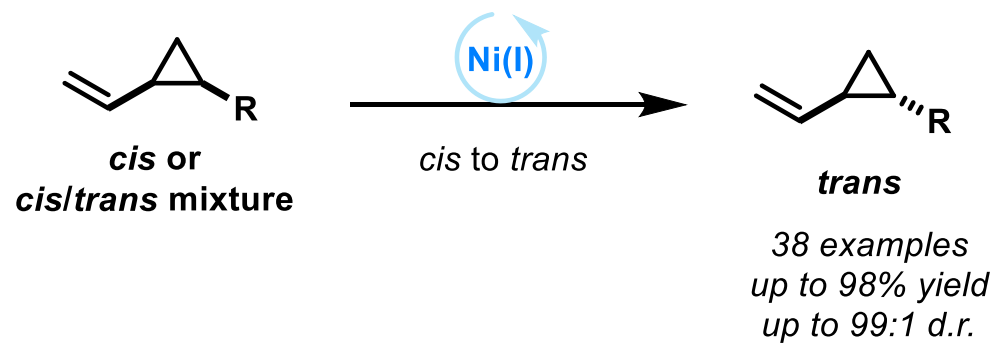


EPR spectrum of Ni(I) in chlorobenzene



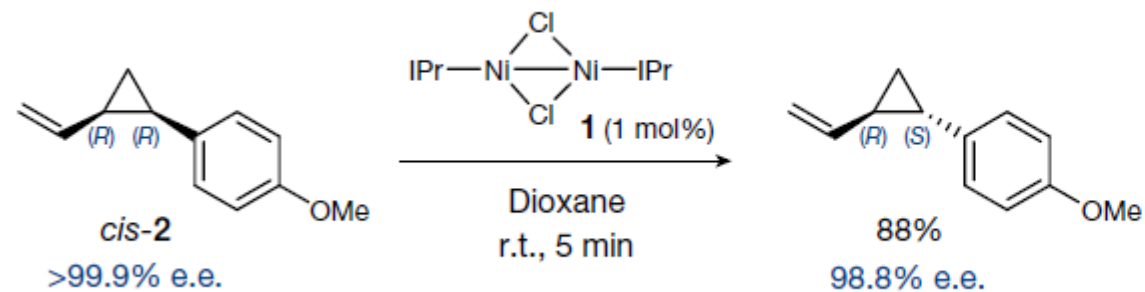
EPR spectrum of isomerization reaction

Ni(I) catalyzed Dynamic stereomutation of vinylcyclopropanes

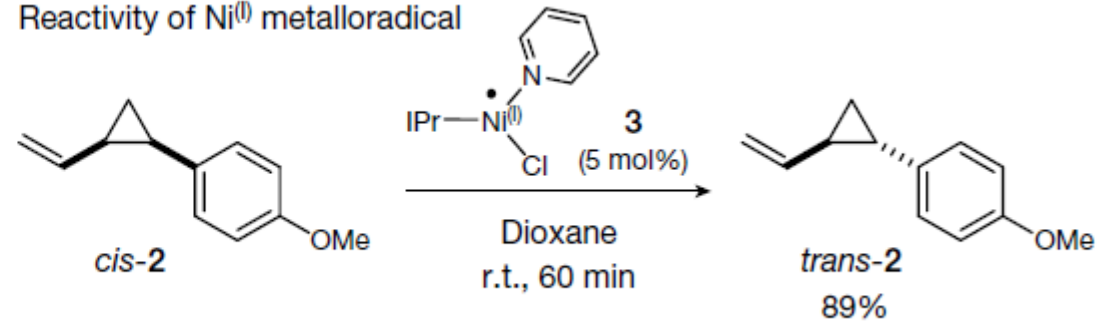


Mechanistic insight

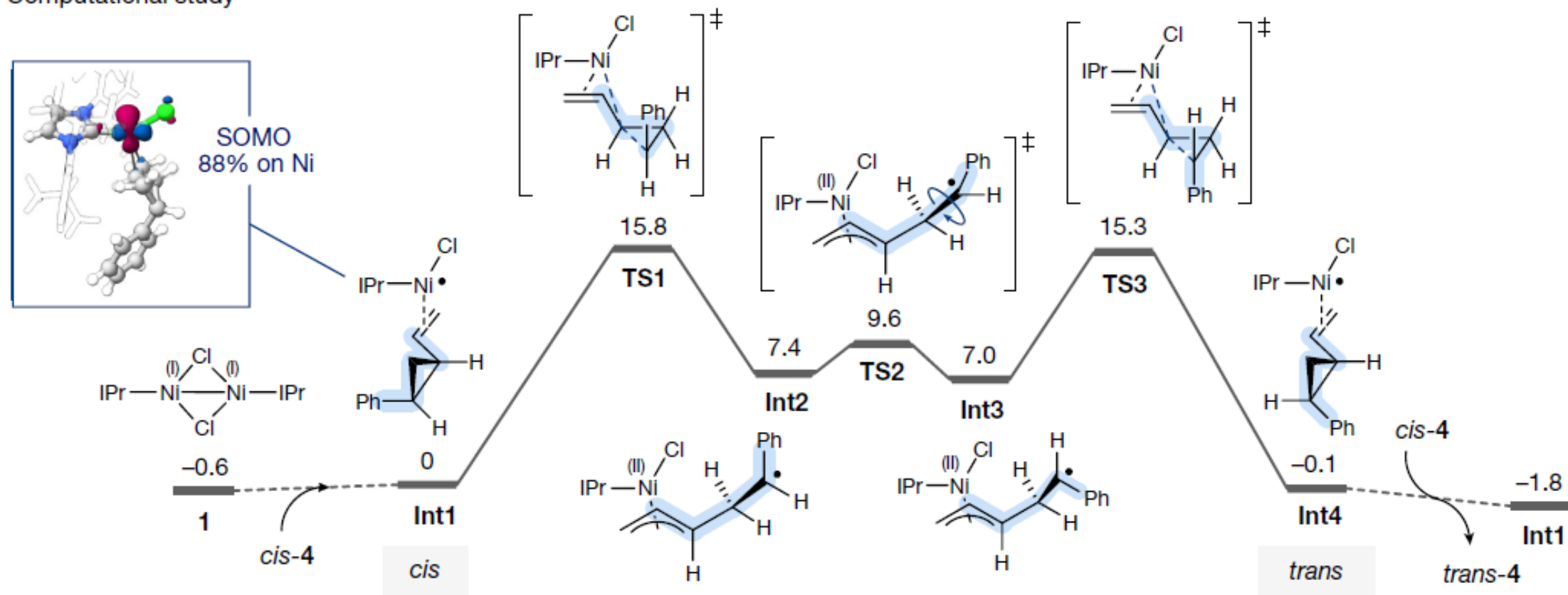
a Stereoinversion



b Reactivity of Ni⁽⁰⁾ metalloradical

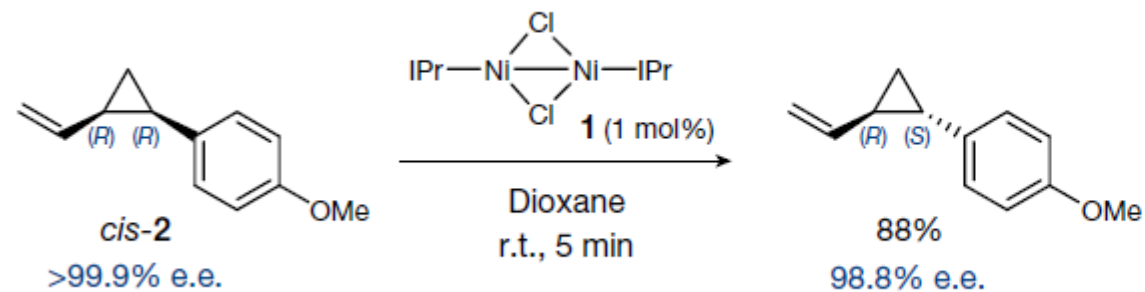


Computational study

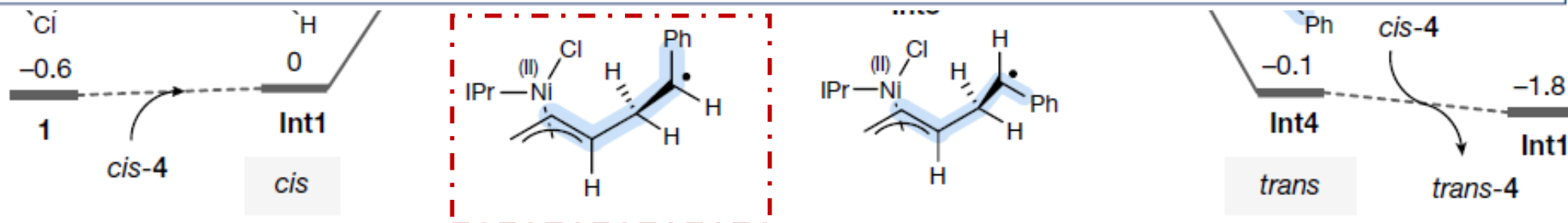
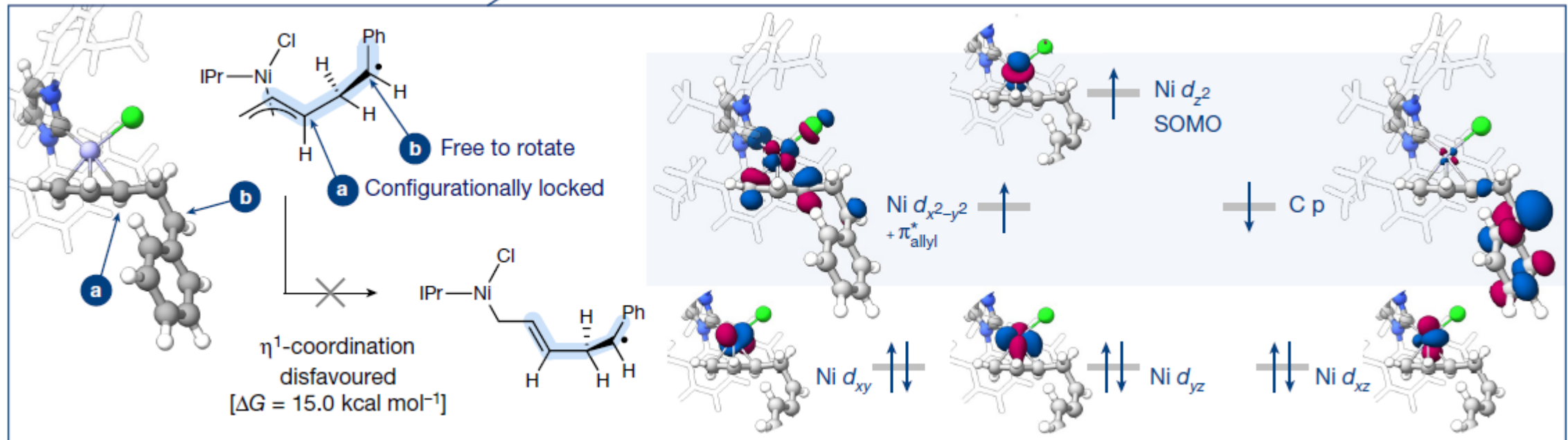
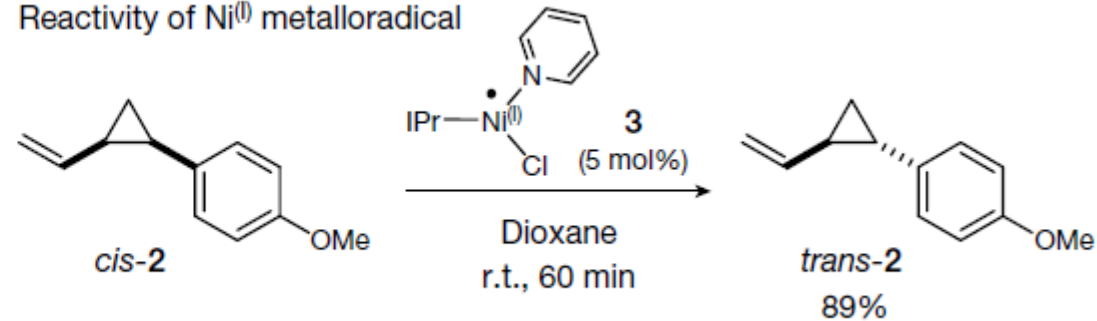


Mechanistic insight

a Stereoinversion



b Reactivity of Ni⁰ metalloradical

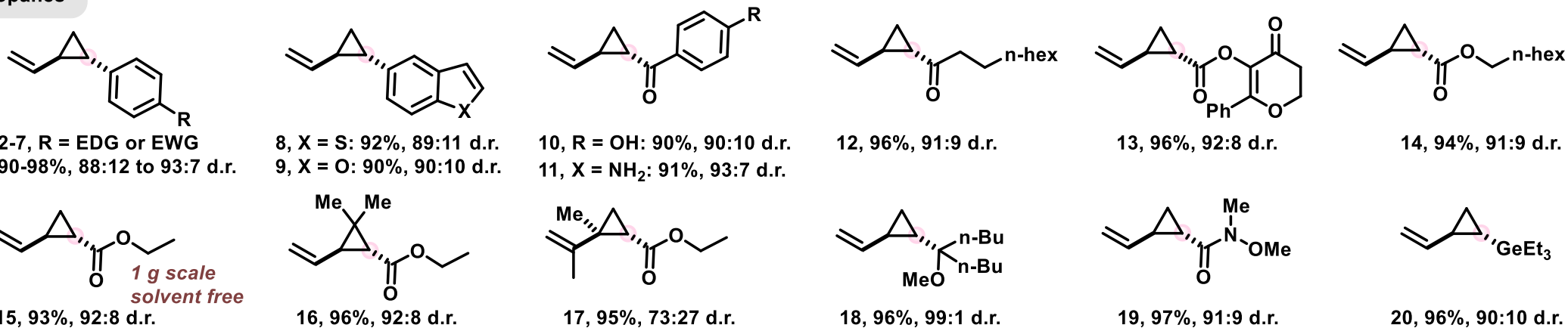


Reactivity and selectivity investigations

Scope of vinyl cyclopropanes



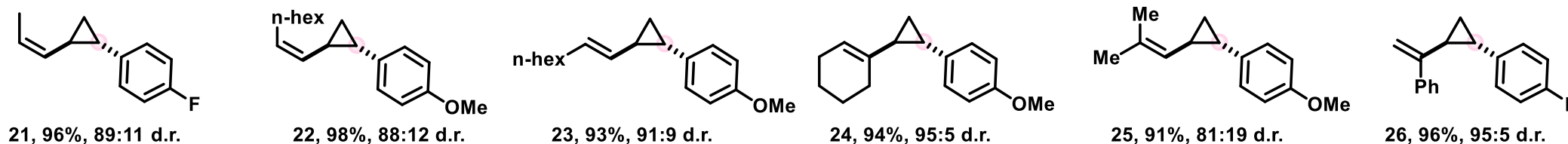
Ni(I) (1–5 mol%),
dioxane,
r.t., 5 min–1 h



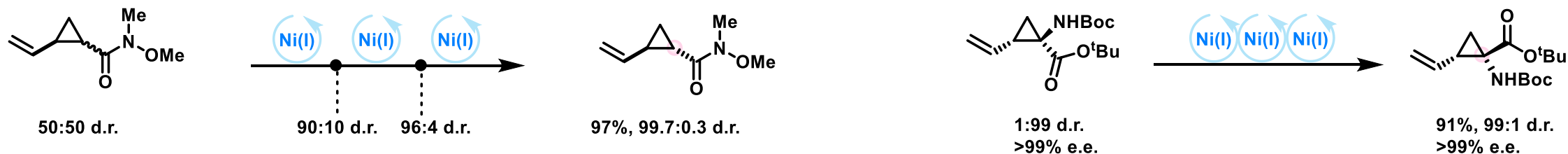
Scope of alkenyl cyclopropanes



Ni(I) (5–10 mol%),
dioxane,
r.t.–60 °C, 2–48 h

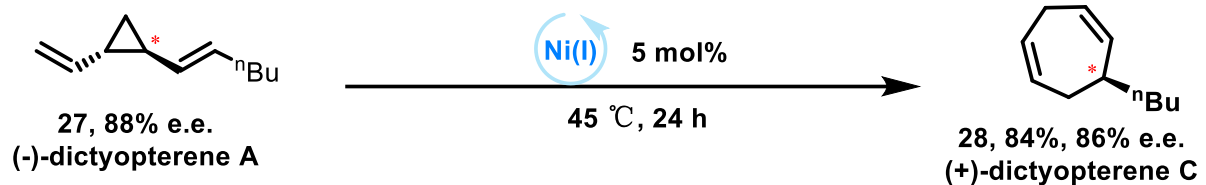


Iterative thermodynamic resolution

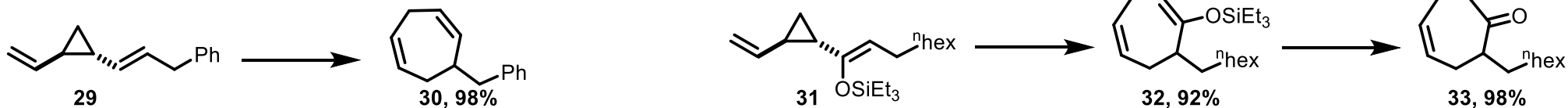
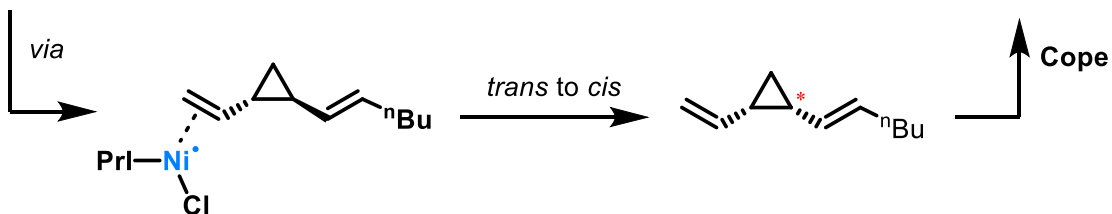
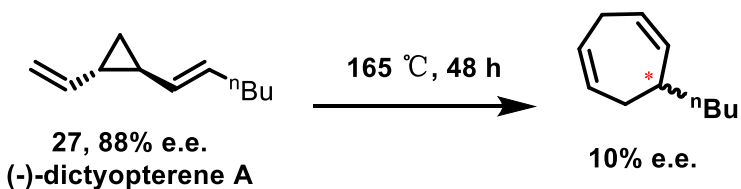


trans-to-cis isomerization/Cope rearrangement

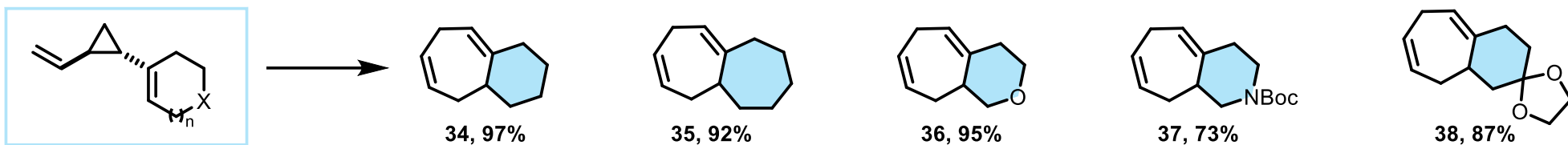
Trans-to-cis isomerization/Cope



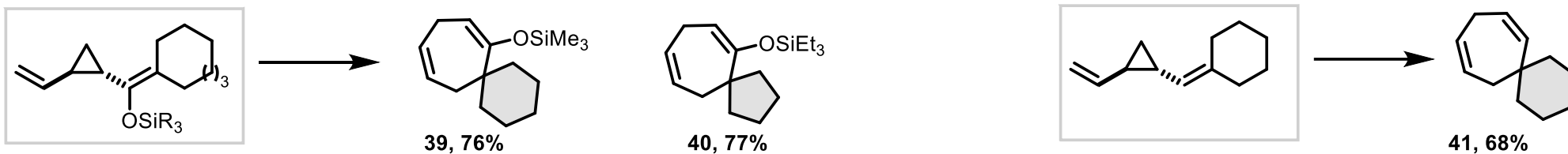
Thermal isomerization/Cope sequence



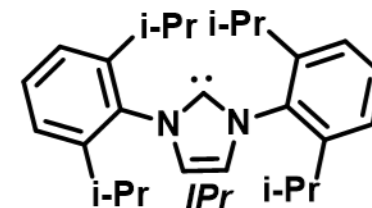
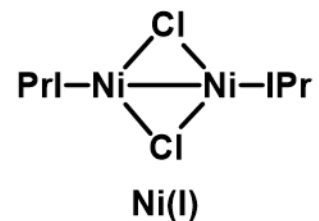
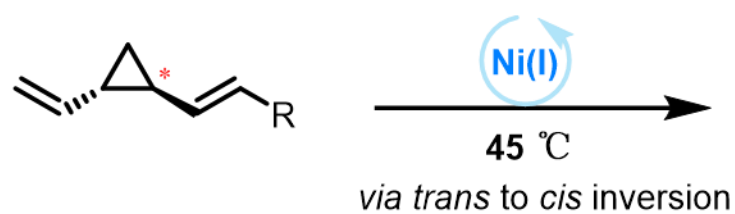
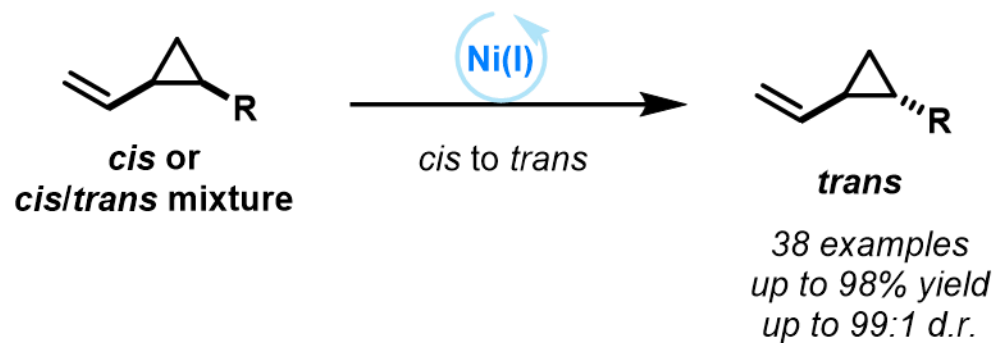
Bicycles



Spirocycles



Conclusions



Stereoinvertive and reversible

