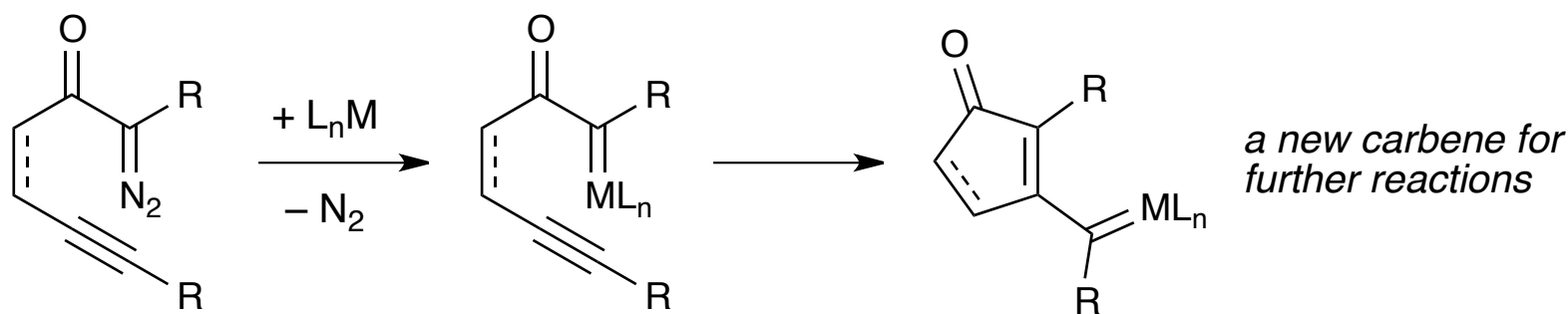
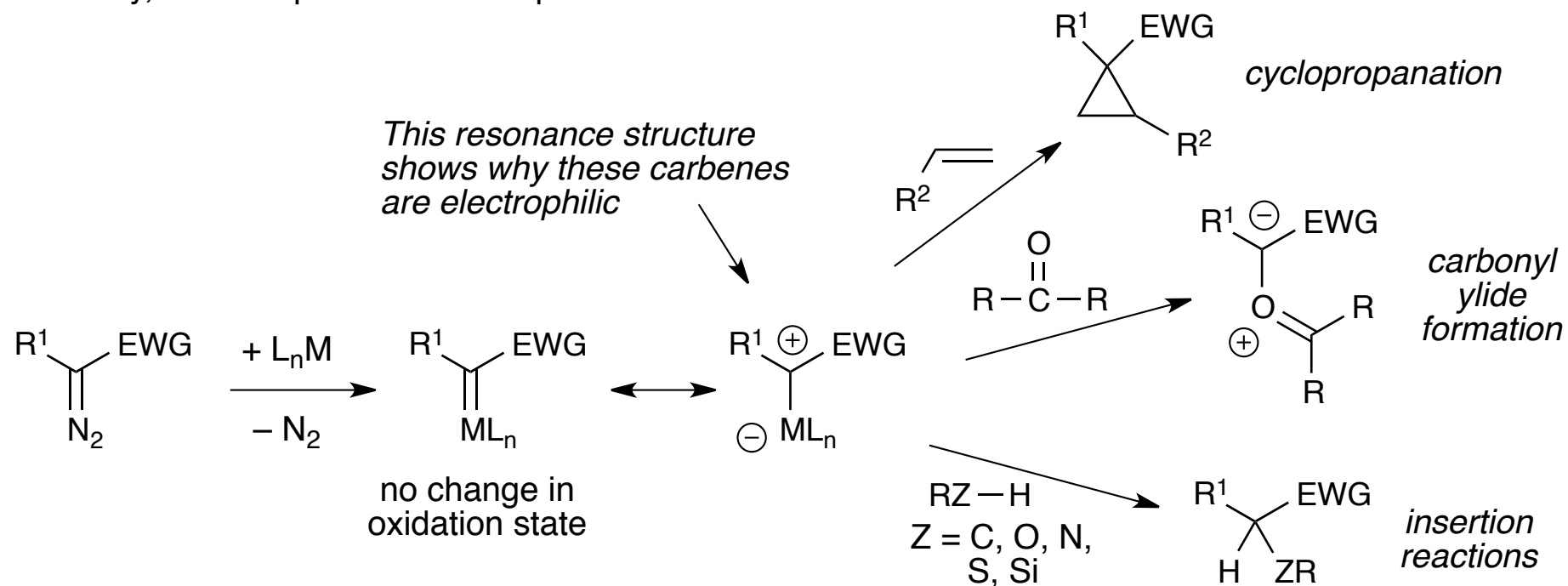


Electrophilic Carbenes

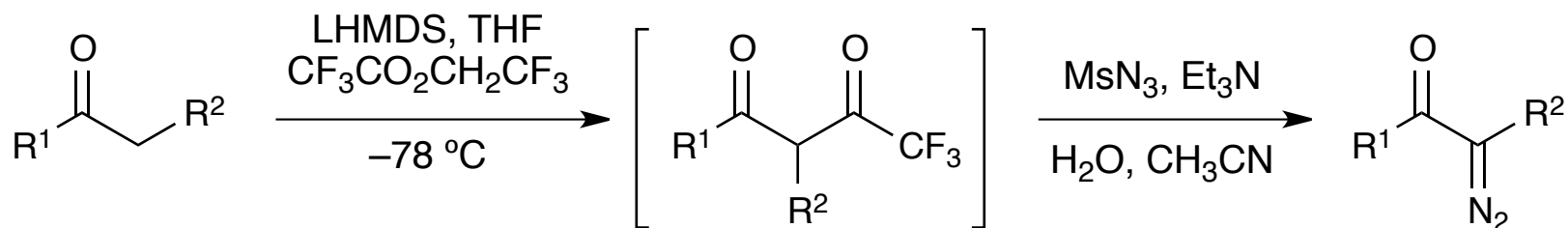
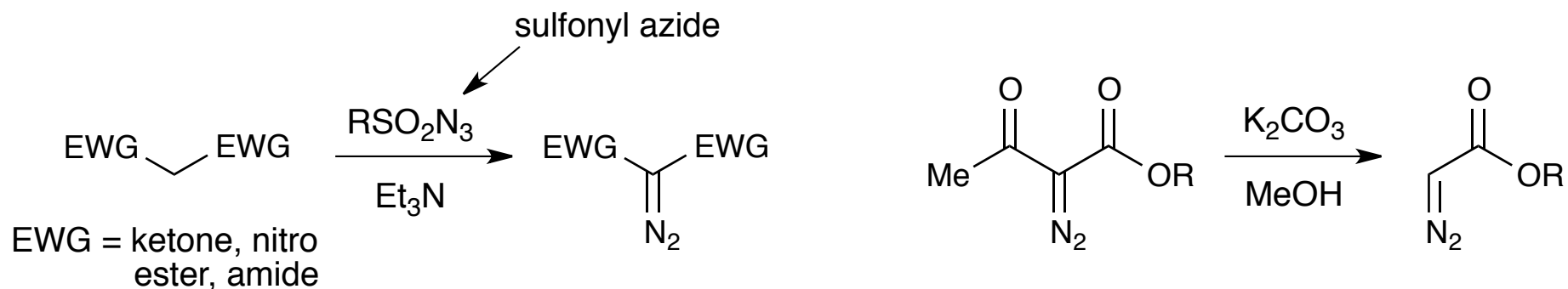
The reaction of so-called stabilized diazo compounds with late transition metals produces a metal carbene intermediate that is electrophilic. The most common catalysts are Cu(I) triflate and Rh(II) acetate and related complexes. Others include Pd(II) salts and $\text{Rh}_6(\text{CO})_{16}$. These intermediates engage in very rich chemistry, often as part of cascade processes.



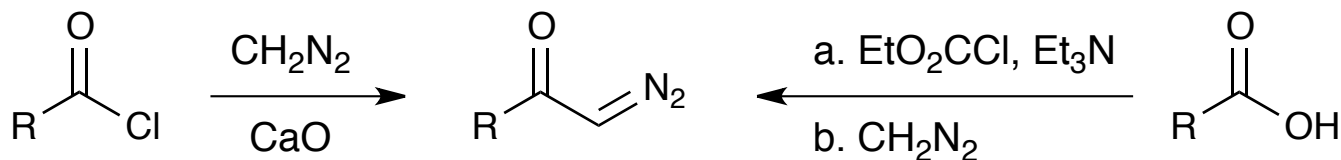
Diazo Formation

While diazo alkanes are normally reactive and unstable, those that are conjugated to electron-withdrawing groups (typically carbonyls) are often quite stable. Several methods available for their production.

Diazo transfer reactions

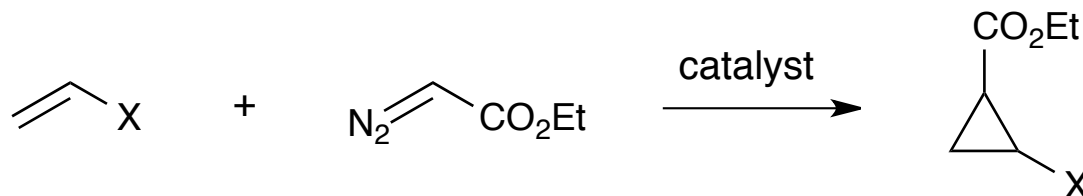


J. Org. Chem. **1990**, *55*, 1959.



Cyclopropanation

If formed in the presence of an olefin, the carbene can form cyclopropanes. Both inter- and intramolecular reactions are possible. Because the carbenes are electrophilic, they react much faster with electron-rich olefins.



X = CH₂Br, CH₂Cl, OPh, Bu, OAc, OEt, OBu, *i*-Pr, *t*-Bu, CH₂=CPh, CH₂=CMe, CH₂=C*t*-Bu, CH=CHOMe, CH=CHCl, CH=CHPh, CH=CHMe
catalyst = Rh₂(OAc)₄, CuCl-P(*Oi*-Pr)₃, Rh₆(CO)₁₆, PdCl₂(PhCN)₂

Order of reactivity: electron-rich > "neutral" >> electron poor
β-substitution on olefin slows reactivity & *cis* > *trans*

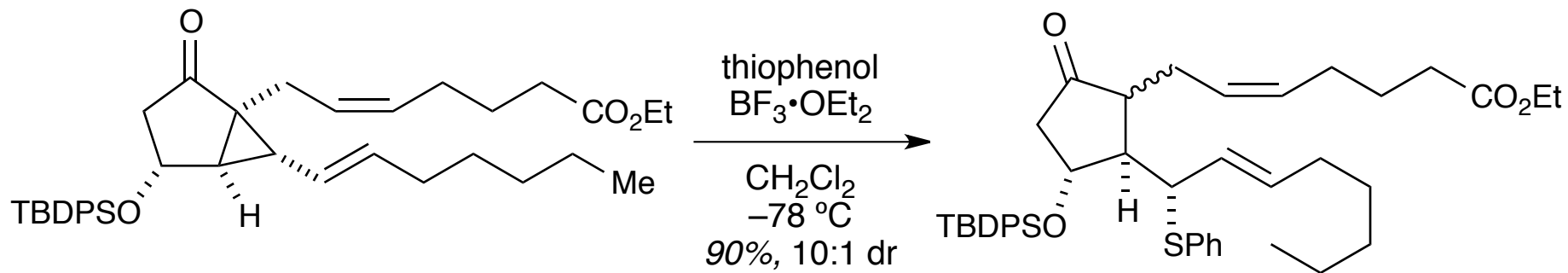
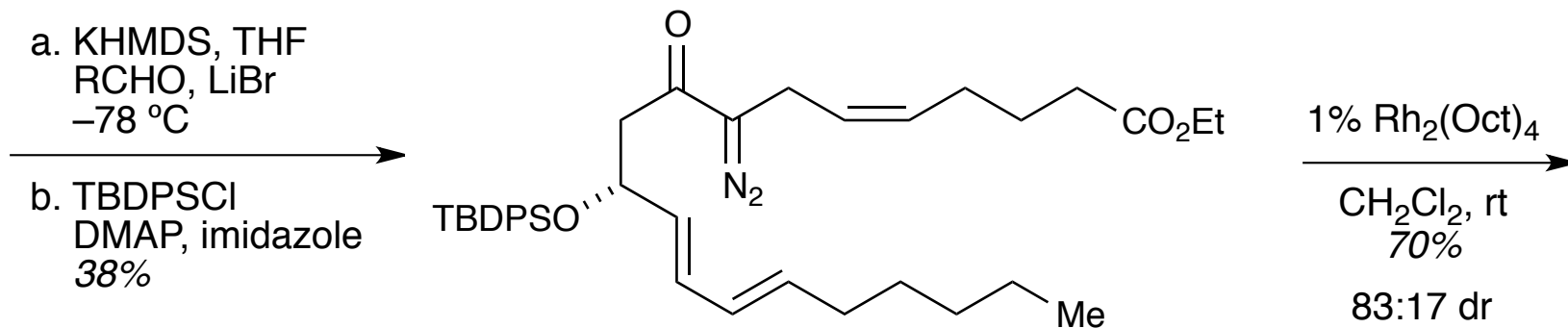
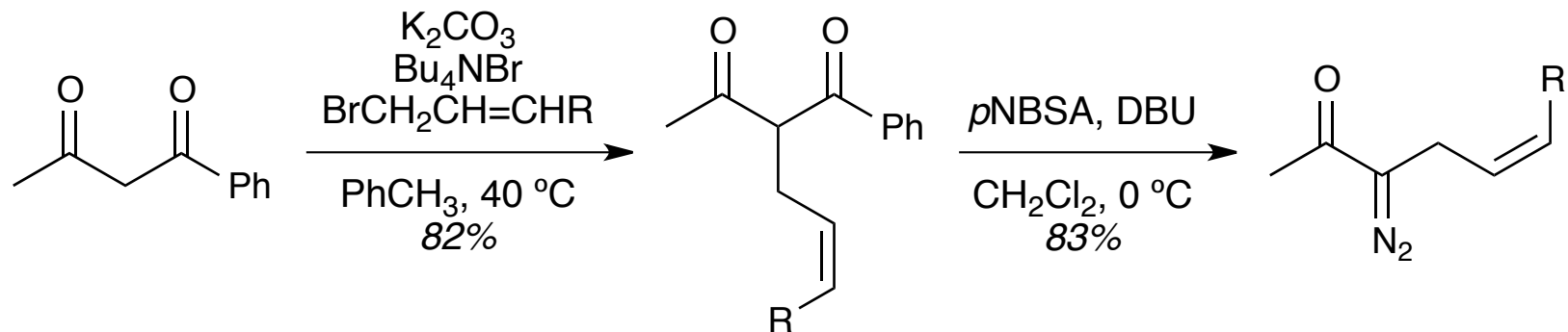
Alkene geometry is maintained, but little stereoselectivity for diazo-bearing carbon

Other reactive groups: dienes, alkynes, **aromatic rings**, and **heteroaromatic rings**

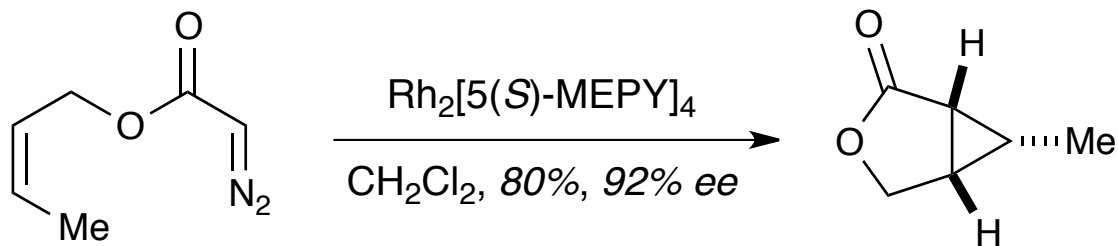
Asymmetric reactions are possible with chiral ligands on Rh and Cu catalysts.

Intramolecular reactions usually prefer to form 5-membered rings. With polyenes, the regioselectivity is usually good, but can depend on catalyst choice.

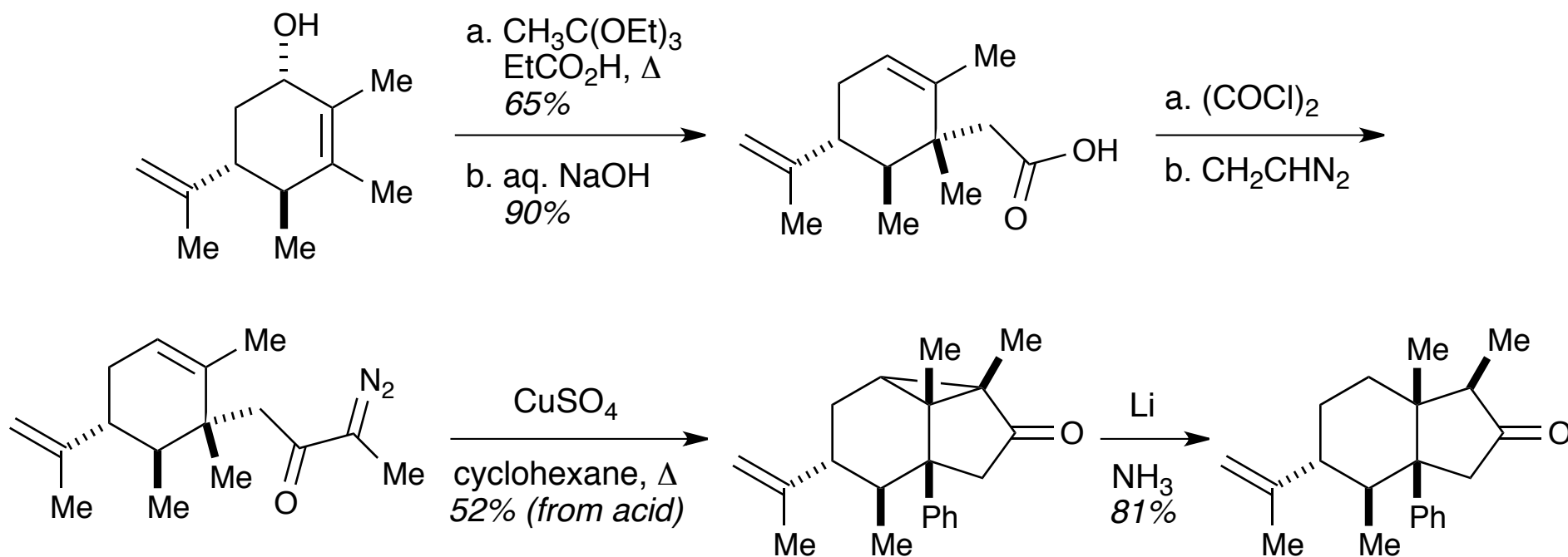
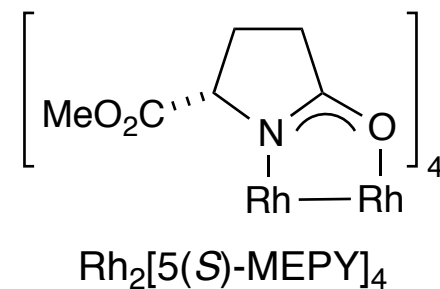
Cyclopropanation



Cyclopropanation



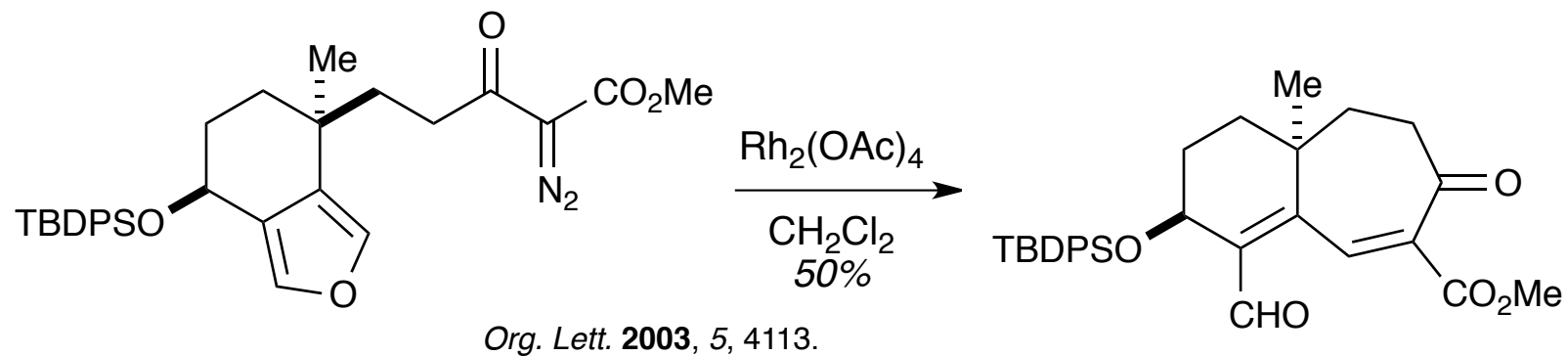
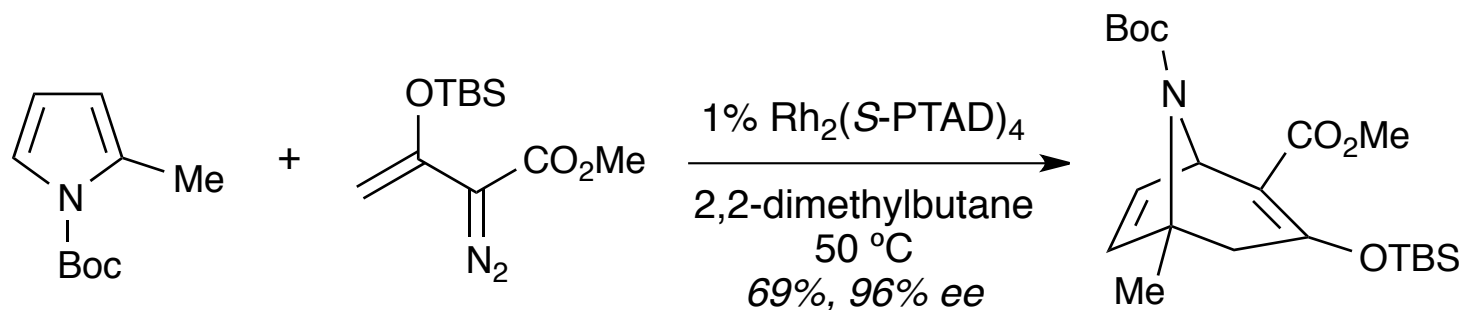
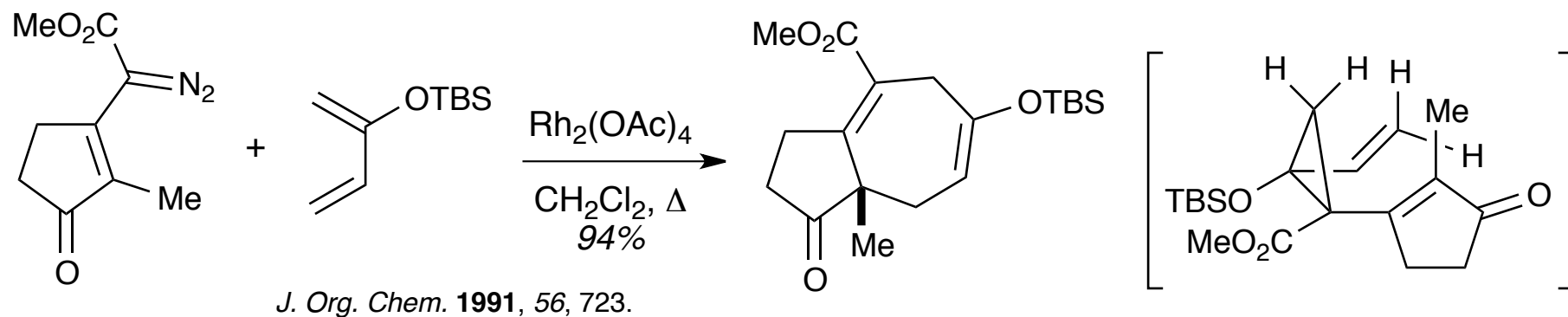
J. Am. Chem. Soc. **2001**, *123*, 12432.



J. Chem. Soc., Perkin Trans 1 **2000**, 2583

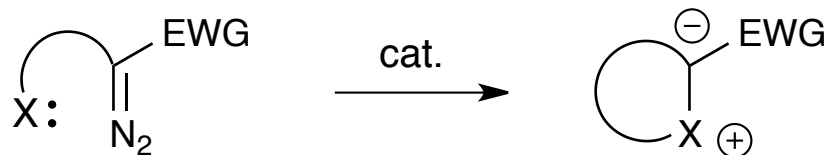
Cyclopropanation

With appropriate substitution patterns, cascade reactions are possible



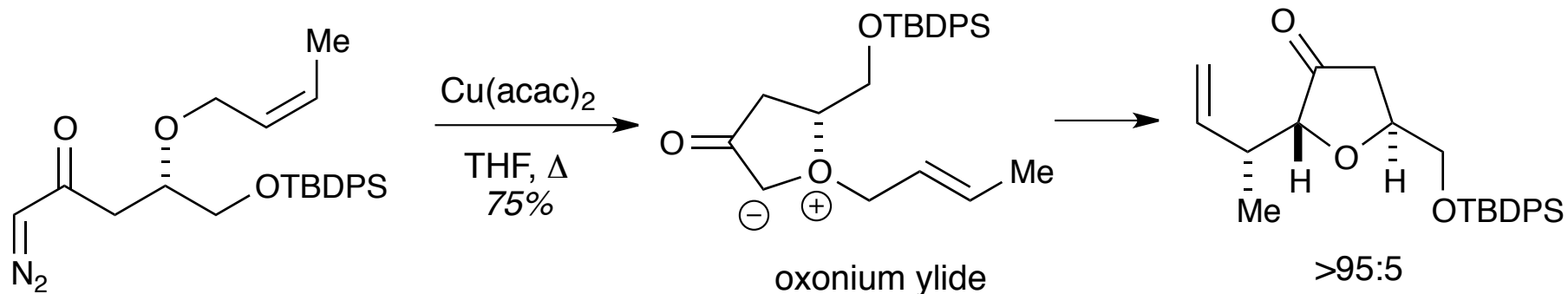
Ylide Formation

The electrophilic nature of the carbenes means they are also capable of reacting with Lewis basic groups such as carbonyls, ethers, and sulfides. This will form an ylide structure. If appropriate functionality is present, other reactions will take place (cycloadditions, rearrangements). Intramolecular formation of ylides are most common.

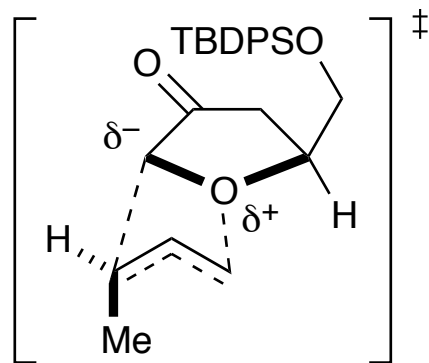


ylyde

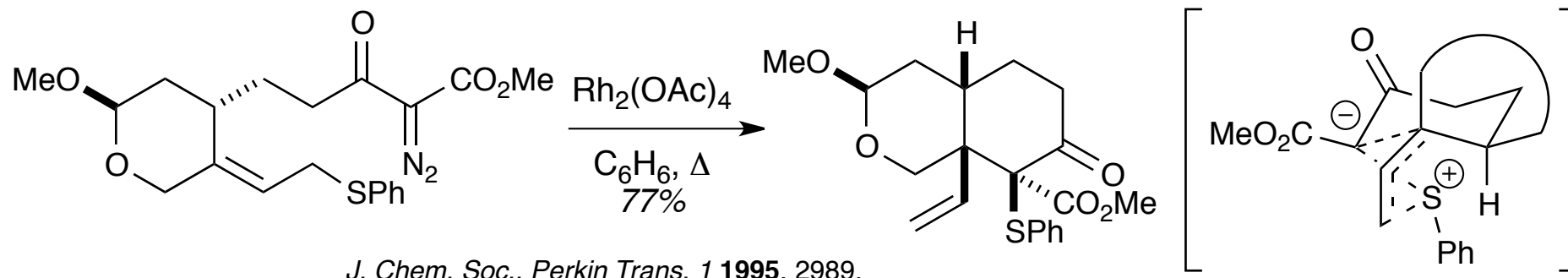
[2,3]-rearrangements



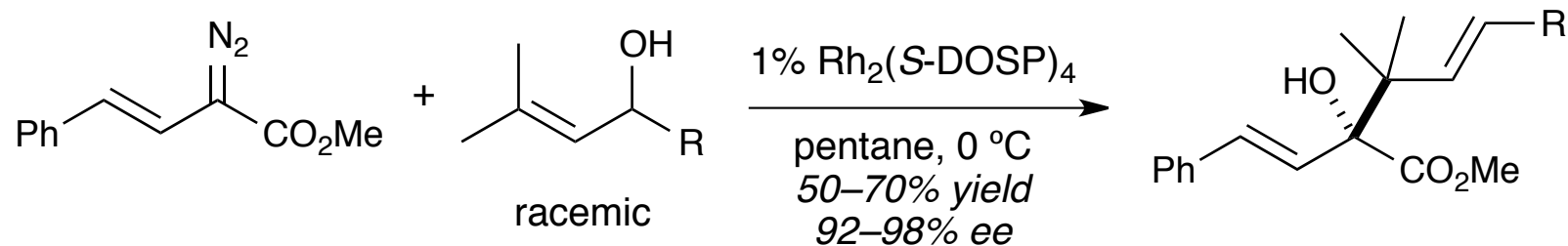
Org. Lett. **2004**, *6*, 1773.



Ylide Formation

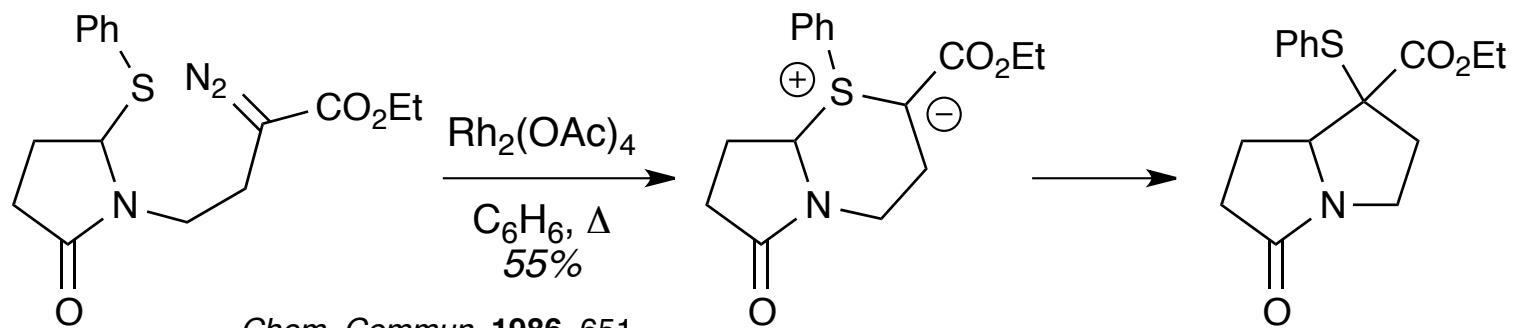


J. Chem. Soc., Perkin Trans. 1 **1995**, 2989.



J. Am. Chem. Soc. **2010**, 132, 396.

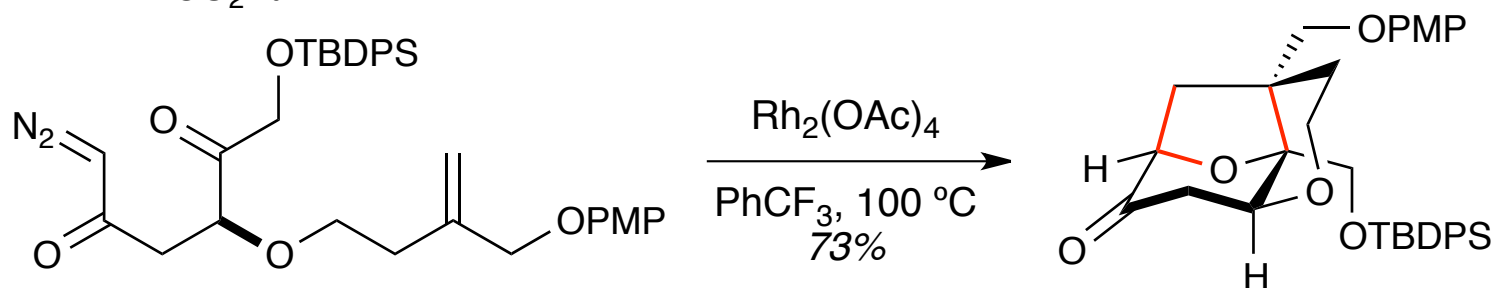
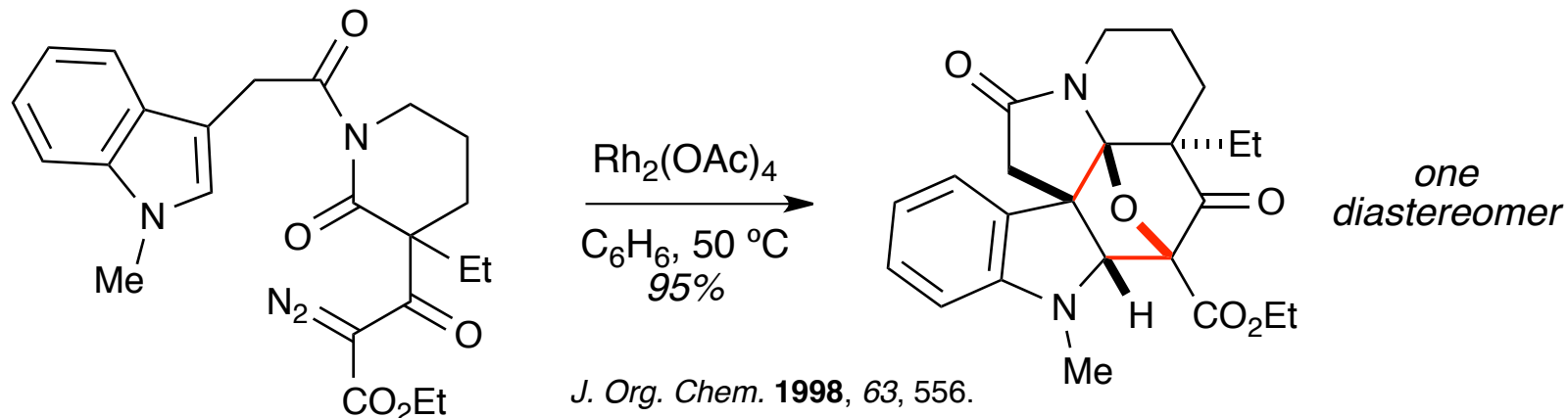
Stevens-type rearrangement



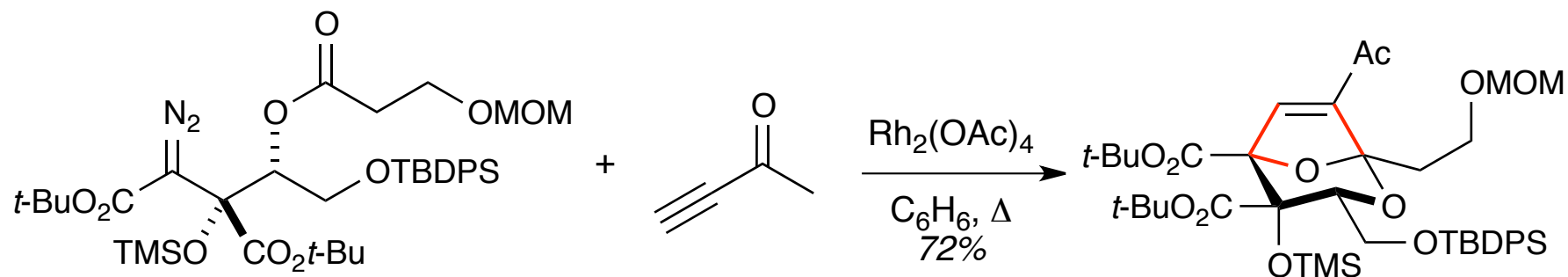
Chem. Commun. **1986**, 651.

Ylide Formation

Dipolar Cycloadditions – Addition of carbonyls will form a carbonyl ylide. These are 1,3-dipoles that can undergo cycloaddition reactions with electron deficient olefins/alkynes.



Angew. Chem. Int. Ed. **2006**, *45*, 6532.



Angew. Chem. Int. Ed. **2003**, *42*, 5351.

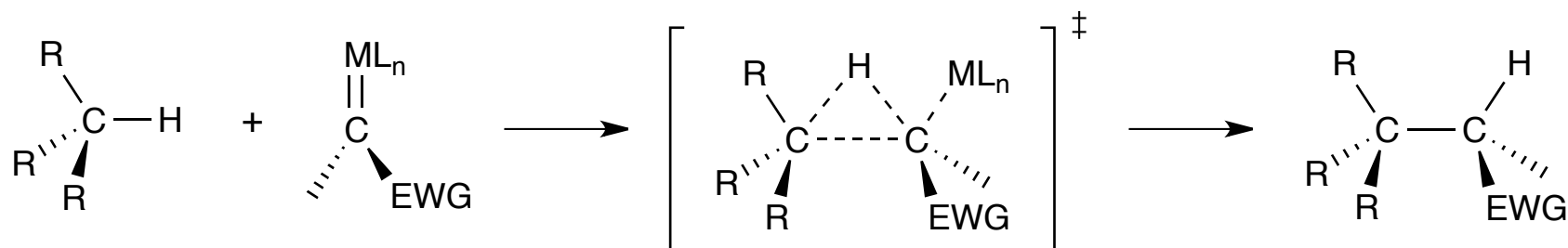
Insertion Reactions

Rh(II) catalysts promote the insertion of diazoalkanes into C–H, O–H, N–H, S–H, and Si–H bonds. Likely involves a three-center transition state. Chiral ligands can be used for enantioselective reactions. Intramolecular reactions generally favor 5-membered ring formation. Fluorinated carboxylate ligands on the metal promote insertion into aromatic C–H bonds.

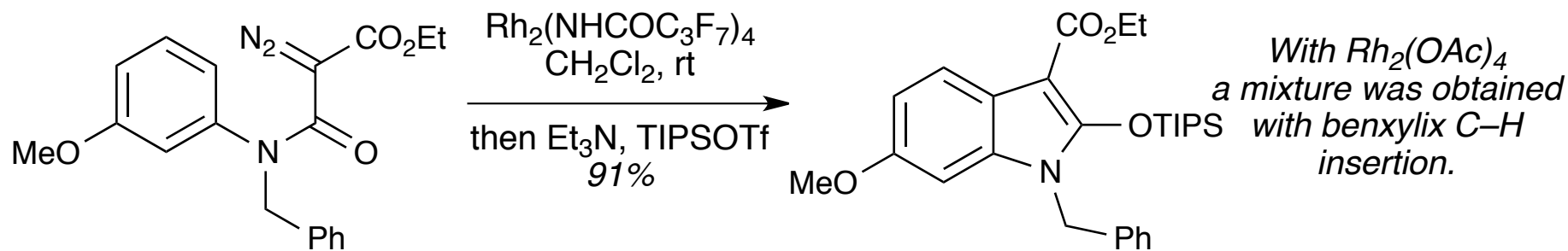
General order of reactivity for C–H bonds: $2^\circ > 1^\circ \approx 3^\circ$, but is catalyst dependent

Electron-withdrawing groups deactivate C–H bonds, electron-donating groups activate

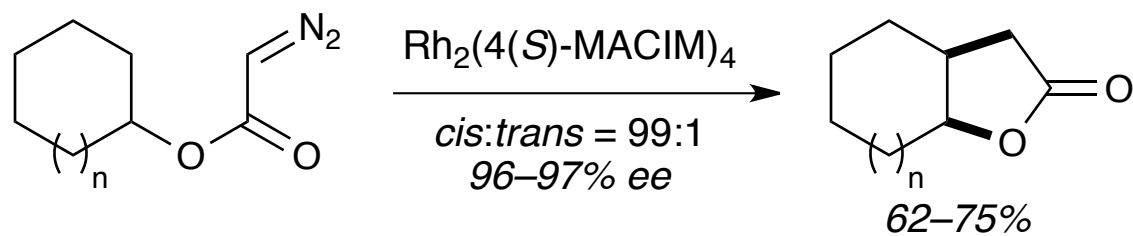
Proposed transition state: *J. Am. Chem. Soc.* **1993**, 115, 958.



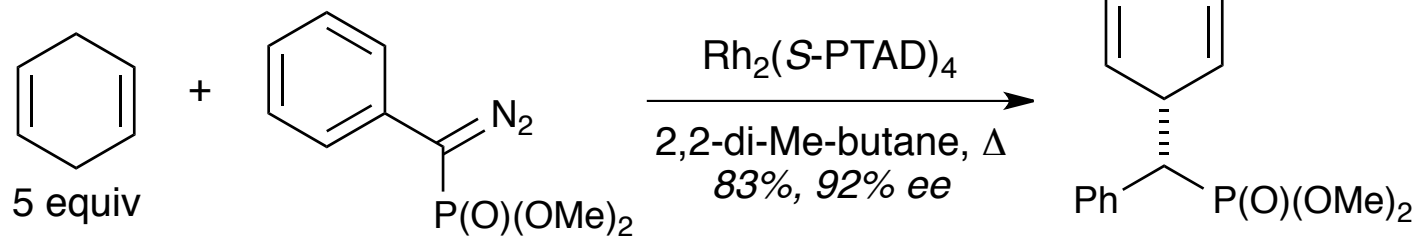
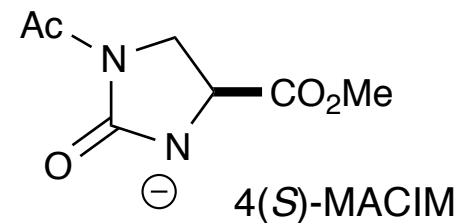
This mechanism implies that the insertion reaction is stereospecific



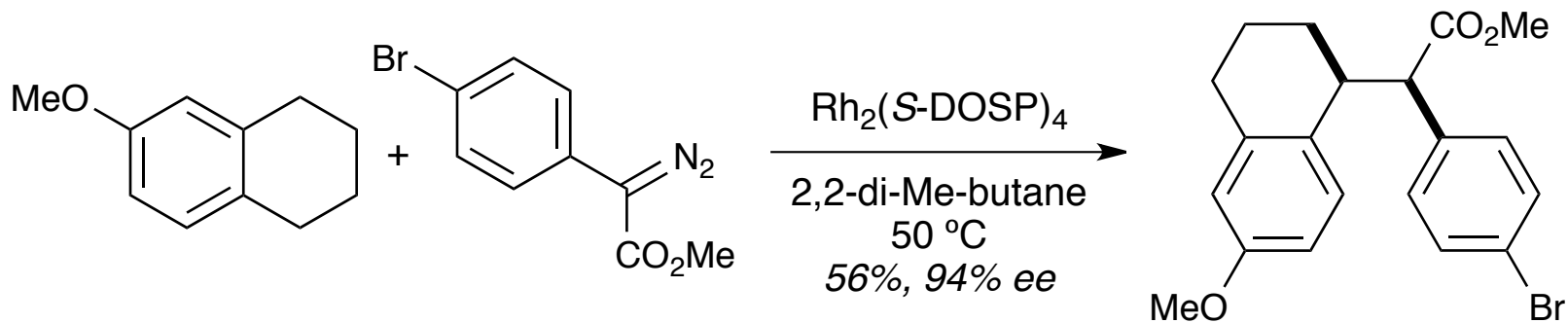
Insertion Reactions



J. Am. Chem. Soc. **1994**, *116*, 450.



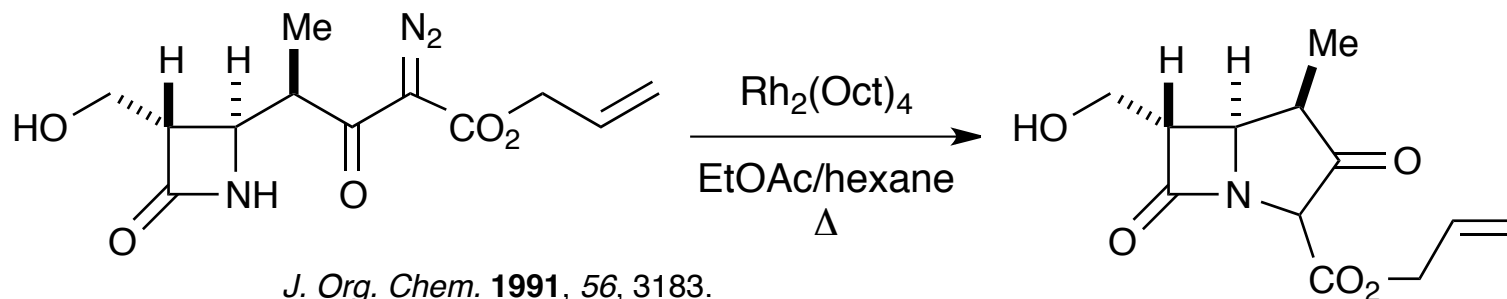
Org. Lett. **2006**, *8*, 3437.



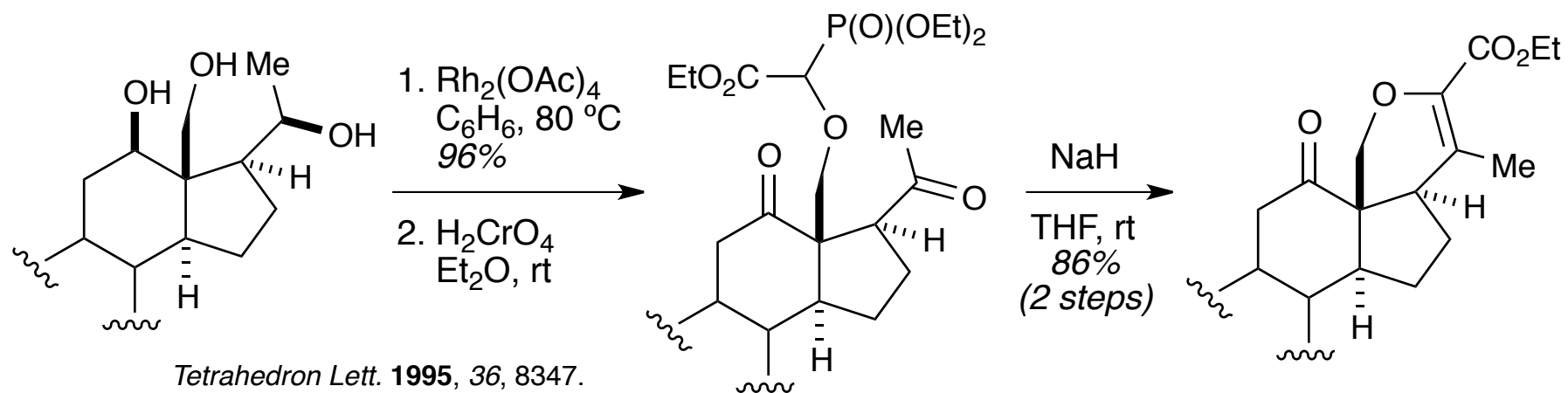
J. Org. Chem. **2002**, *67*, 4165.

Insertion Reactions

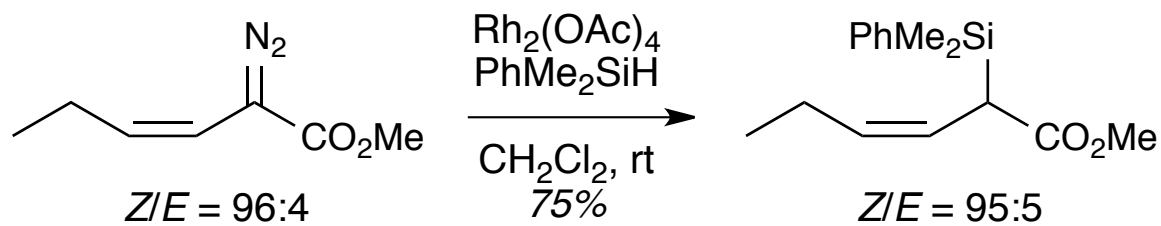
N-H insertions



O-H insertions



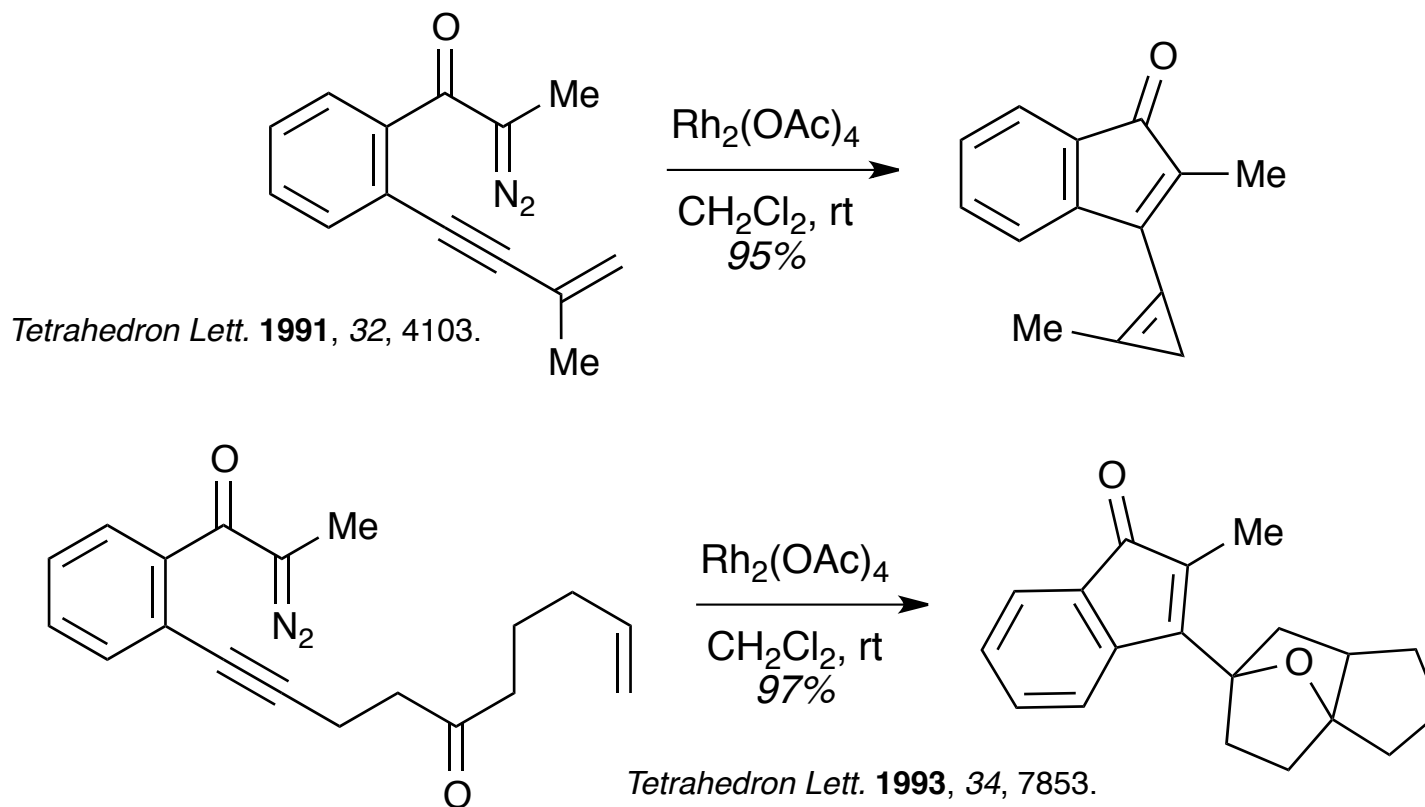
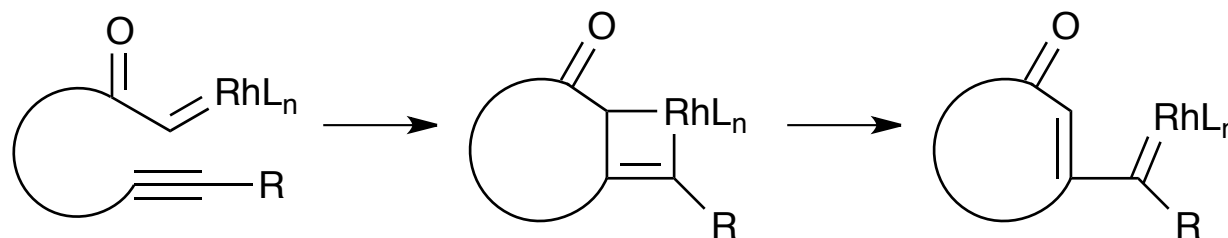
Si-H insertions



Tetrahedron Lett. **1994**, *35*, 9549.

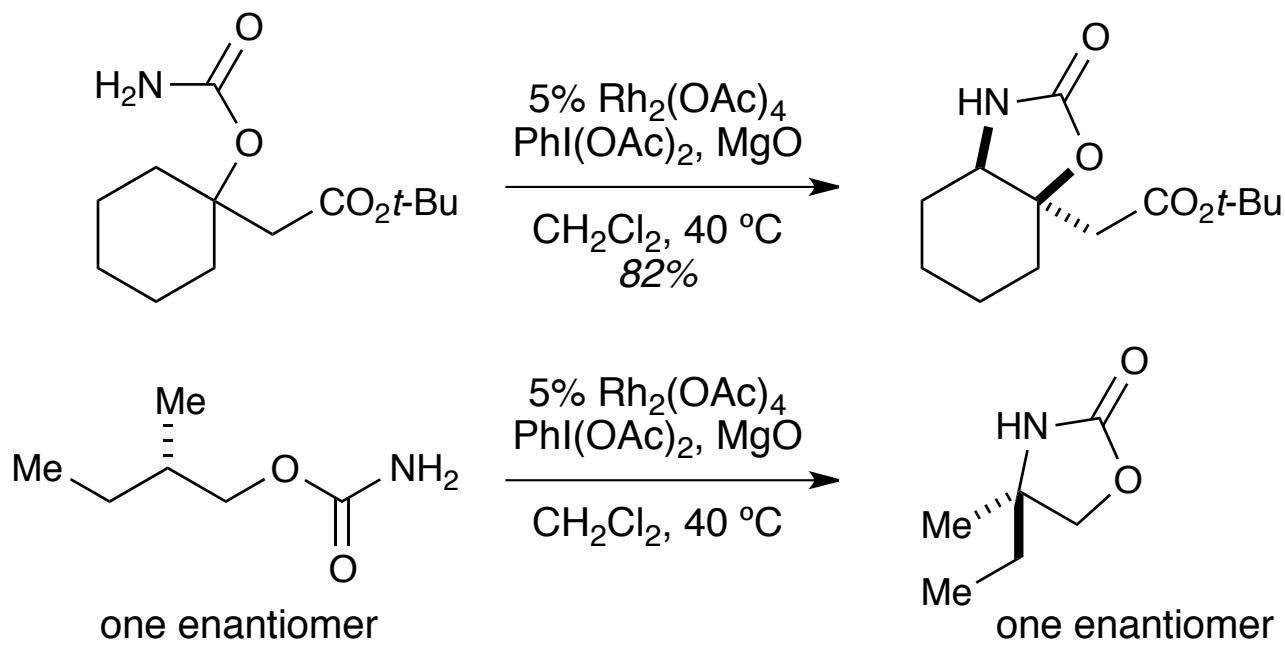
Metathesis with Alkynes

Once formed, Rh carbenoids can undergo "metathesis"-type chemistry with alkynes. This generates a new Rh carbene that can undergo other processes, such as those we have already discussed.



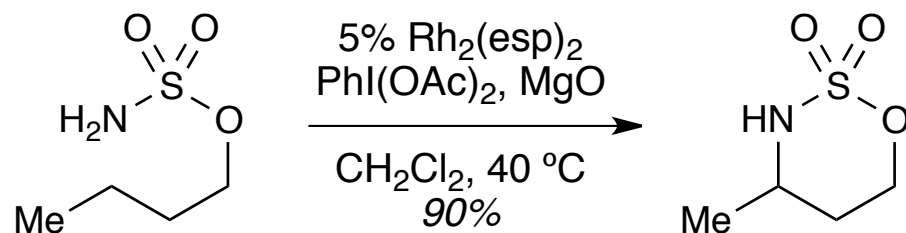
Nitrenoid Intermediates

Much like metal-catalyzed decomposition of diazo compounds produces carbenoid intermediates, it is also possible to generate nitrenoid intermediates. This typically involves the in situ oxidation of a non-basic primary nitrogen atom (sulfonamide, amide, carbamate, urea, etc.).



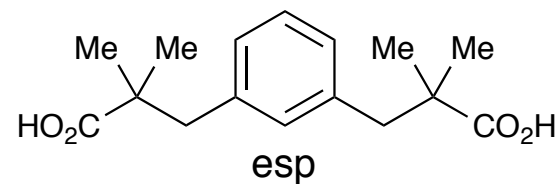
carbonyl groups prefer 5 membered rings, sulfonyls prefer 6 membered rings.

Angew. Chem. Int. Ed. **2001**, 40, 598.

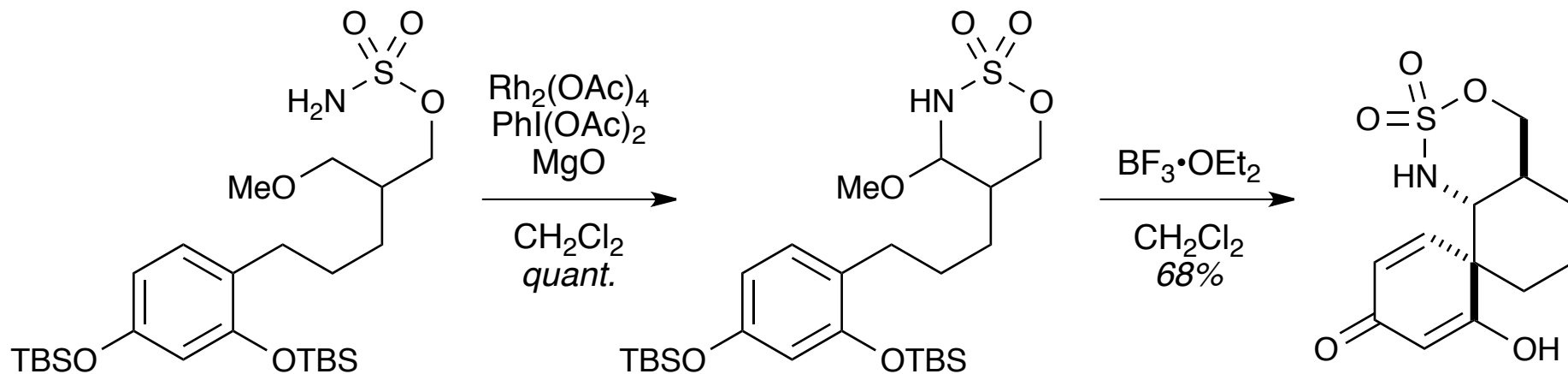


J. Am. Chem. Soc. **2004**, 126, 15378.

intermolecular are possible:
J. Am. Chem. Soc. **2007**, 129, 562.

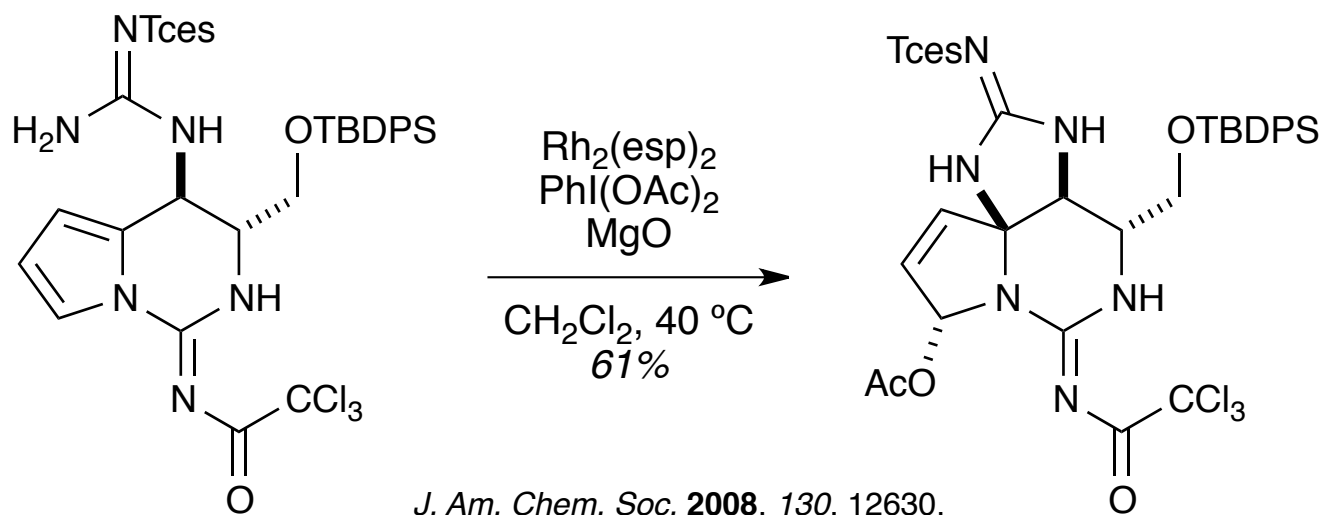


Nitrenoid Intermediates



Org. Lett. **2007**, *9*, 5465.

Other types of reactions are possible besides C–H insertions



J. Am. Chem. Soc. **2008**, *130*, 12630.