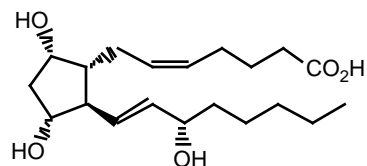
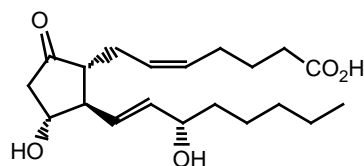
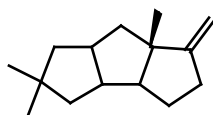
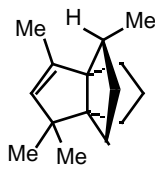


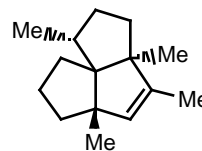
5 Membered Rings

PGF₂PGE₂

Hirsutene



Modhephane



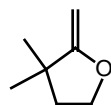
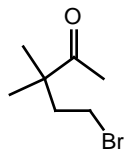
Isocumene

1. Intramolecular S_N2 Reactions
2. Intramolecular Aldol Condensation and Michael Addition
3. Intramolecular Wittig Olefination
4. Ring Expansion and Contraction Reactions
 - a. 3 5
 - b. 4 5
 - c. 6 5
5. 1,3-Dipolar additions
6. Nazarov Cyclization
7. Arene-Olefin Photocyclization
8. Radical Cyclizations
9. Others

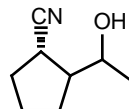
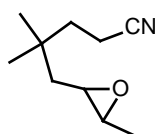
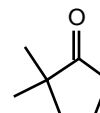
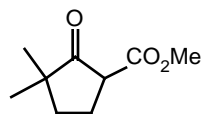
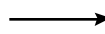
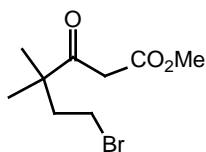
Synthesis **1973**, 397; *ACIEE* **1982**, 21, 480;

Intramolecular S_N2 Reaction

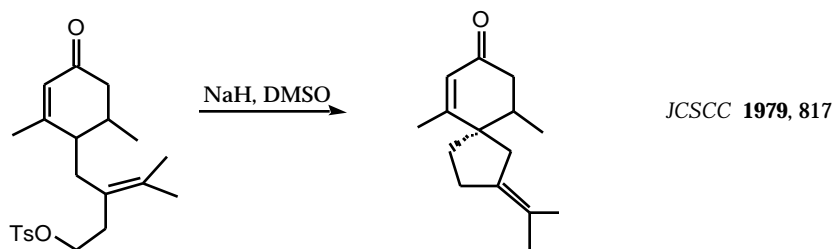
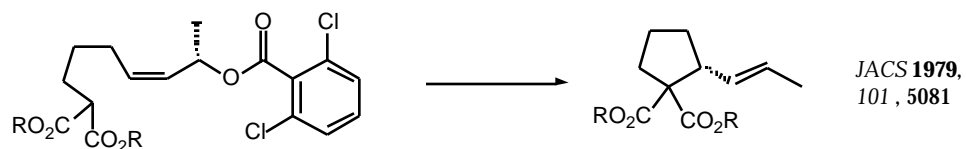
5-exo-tet: favored



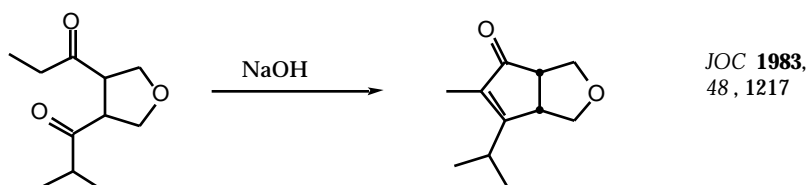
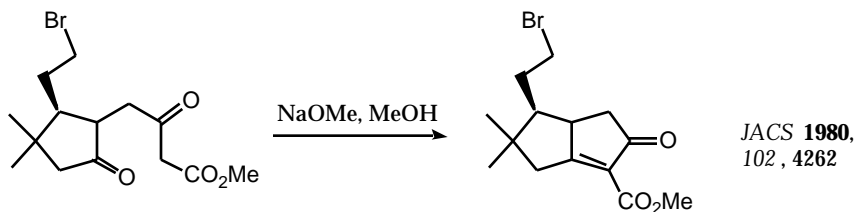
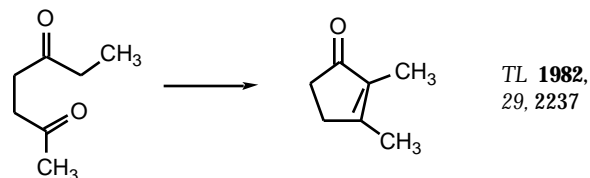
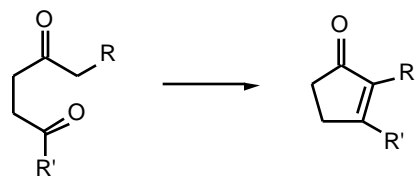
JCSCC **1973**, 233



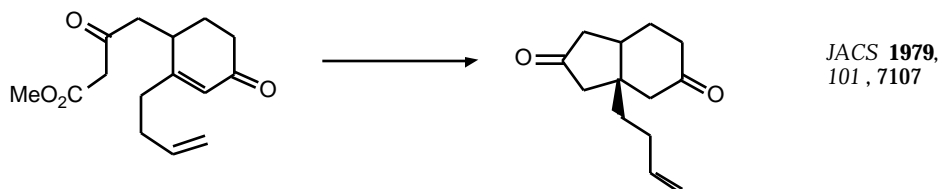
JACS **1974**, 96, 5268



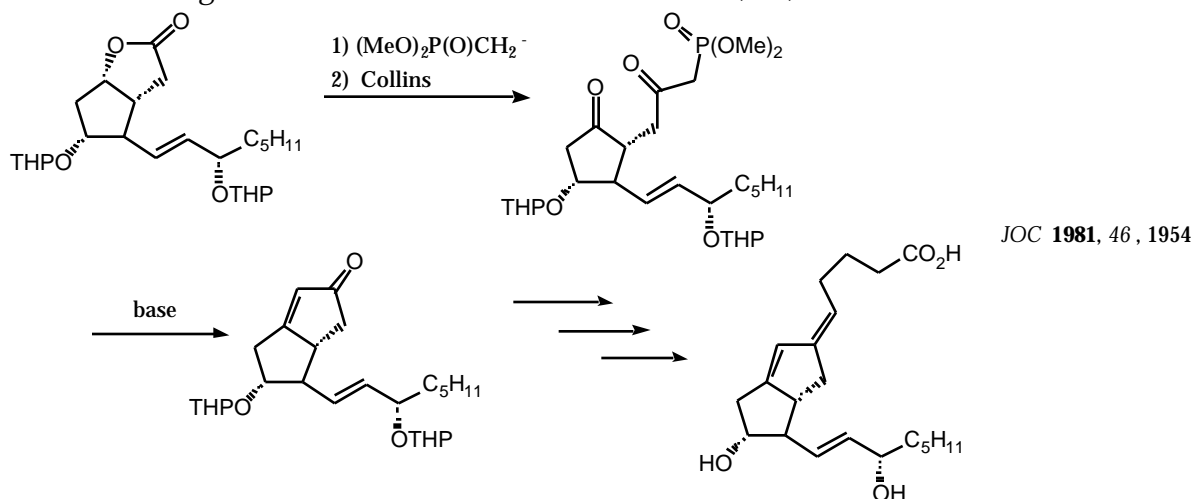
Intramolecular Aldol Condensation 5-exo-trig: favored
intramolecular aldol condensation of 1,4-diketones



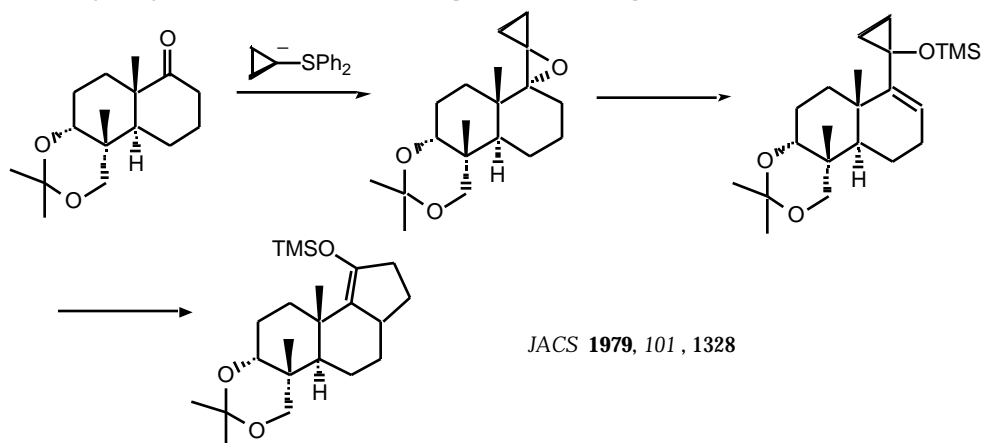
Intramolecular Michael Addition 5-exo-tet: favored
Organic Reactions **1995**, 47, 315-552



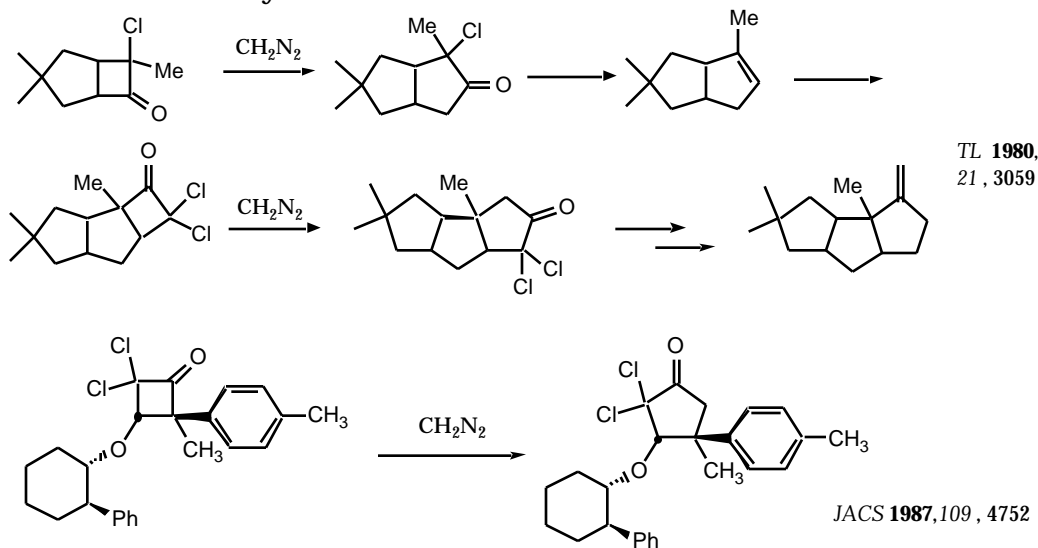
Intramolecular Wittig Olefination

Tetrahedron **1980**, 36, 1717

Ring Expansion Reactions

- 3 5: Vinyl Cyclopropane Rearrangement *Organic Reactions* **1985**, 33, 247.

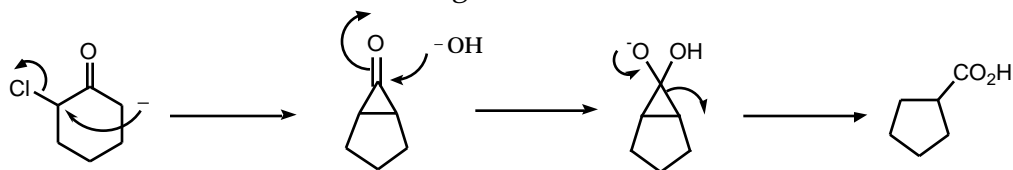
- 4 5: Reaction of cyclobutanones with Diazomethane



Ring Contraction Reactions

- 6 5: Favorskii Reaction

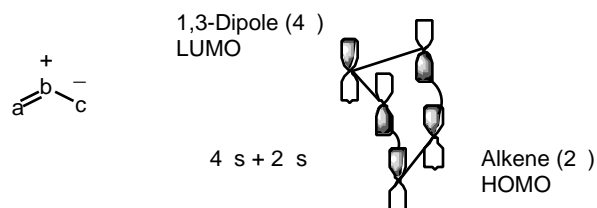
Organic Reactions **1960**, 11, 261



1,3-Dipolar Addition to Olefins

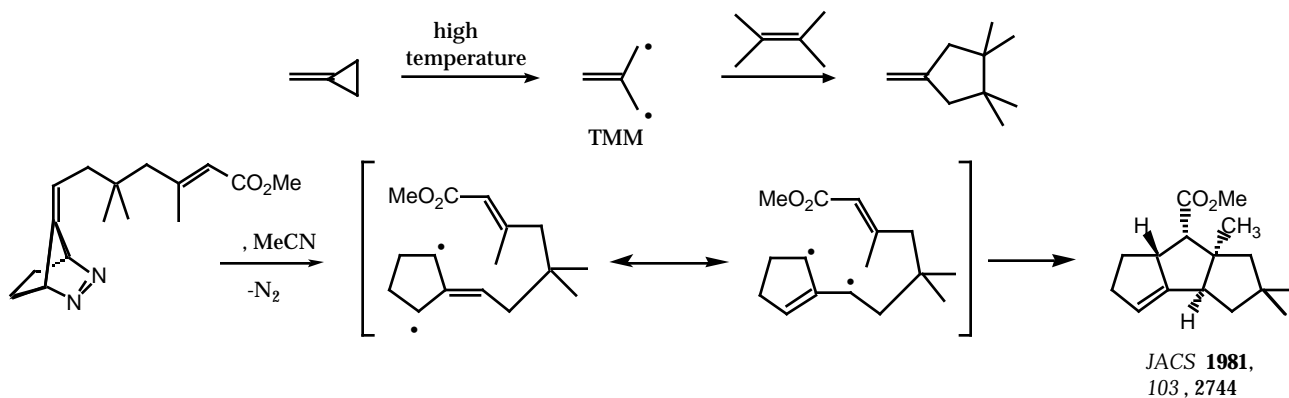
1,3-Dipolar Cycloaddition Chemistry, vol 1 & 2 (A.

Padwa ed.) (Wiley, NY 1984); ACIEE **1977**, 16, 10. Chem Rev. **1998**, 98, 863.

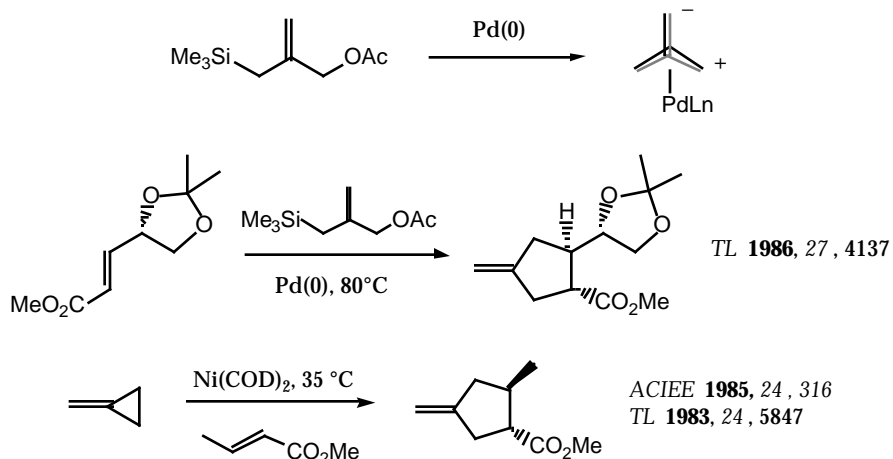


- trimethylenemethane (TMM)

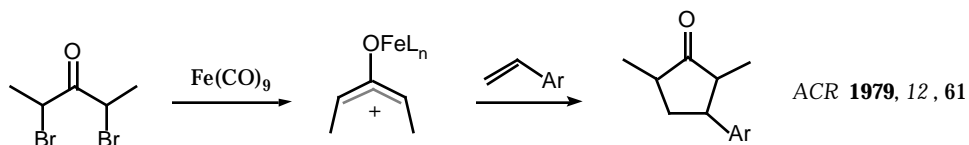
ACIEE **1986**, 25, 1. Synlett **1992**, 107.



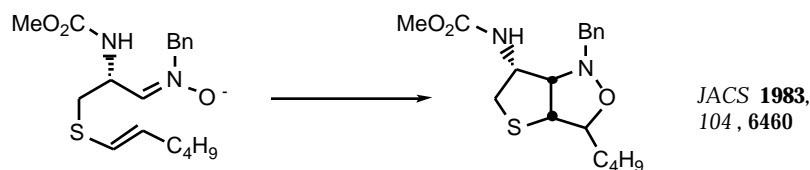
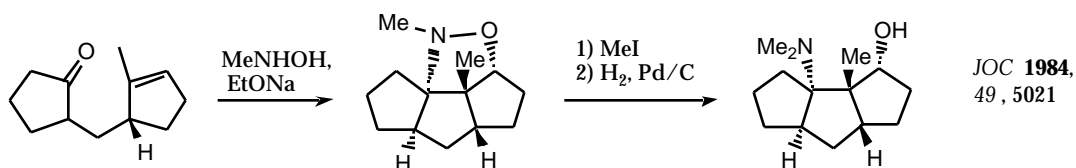
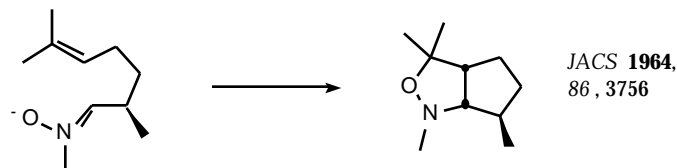
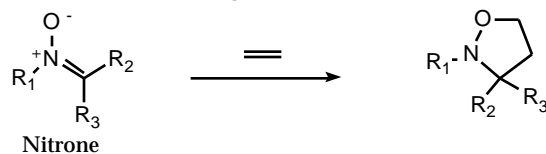
note: TMM usually reacts poorly w/ electron deficient olefins



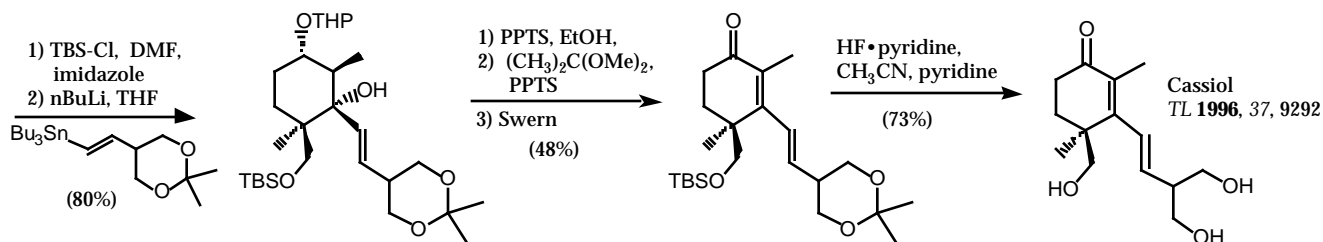
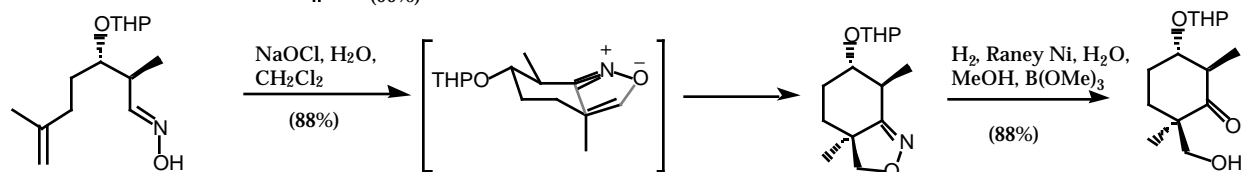
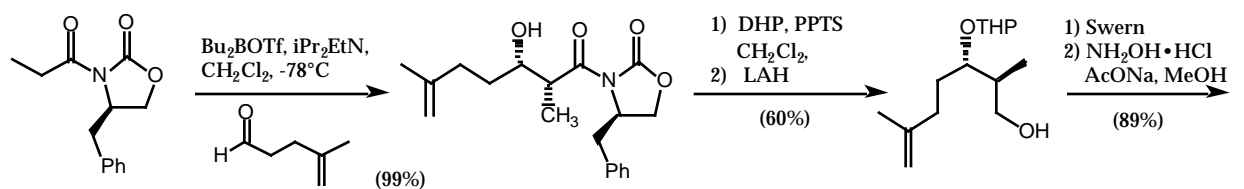
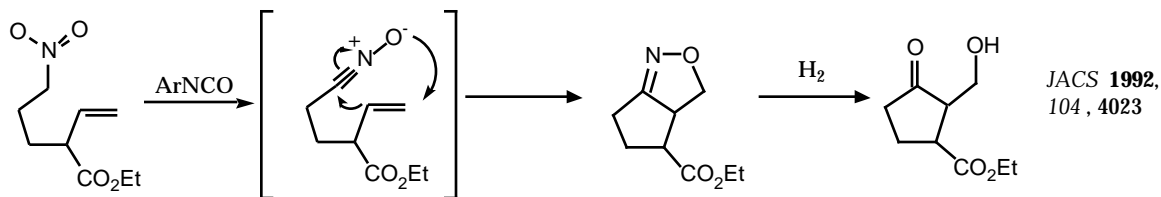
- , '-dihaloketones

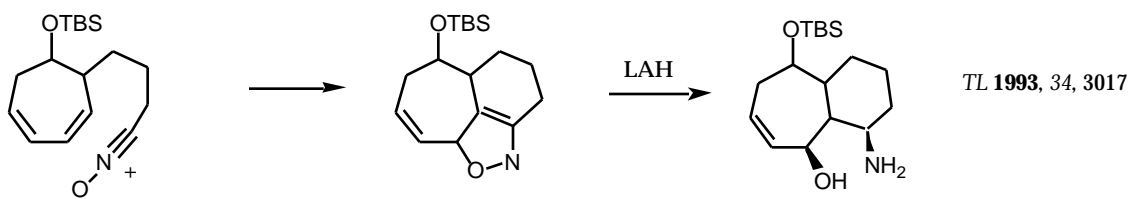


- nitrones ACR **1979**, 12, 396; *Organic Reactions*, **1988**, 36, 1

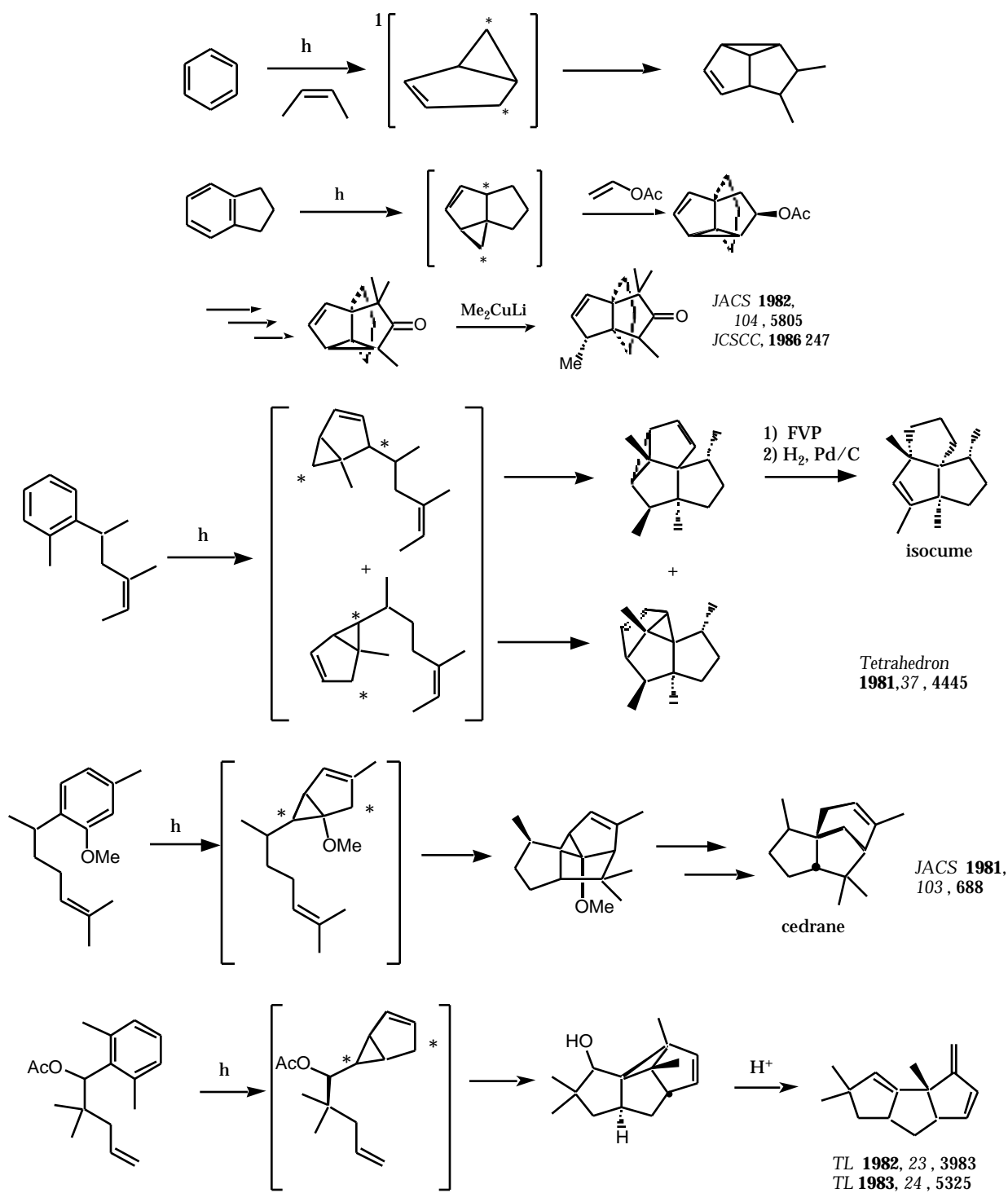


- nitrile oxides



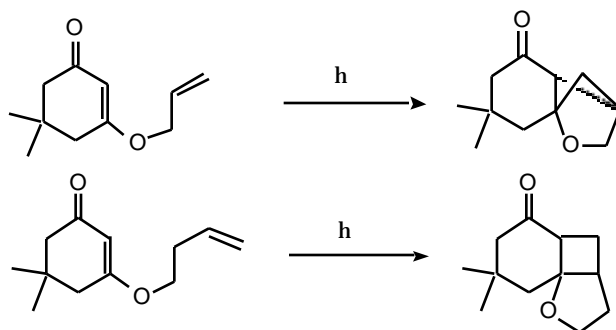


Arene-Olefin Photocyclization *Organic Photochemistry* **1989**, 10, 357
 - the photochemistry of benzene is dominated by the singlet state



Intramolecular Photochemical [2+2]

"Rule of Five"



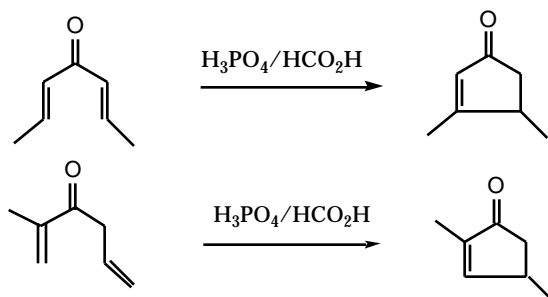
JOC **1975**, 40, 2702
 JOC **1979**, 44, 1380

Nazarov Cyclization

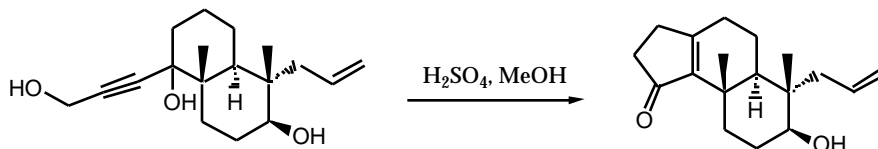
 review: *Synthesis* **1983**, 429

Organic Reaction **1994**, 45, 1

- cyclization of allyl vinyl or divinyl ketones

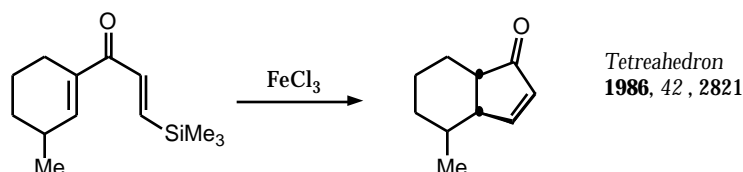


- 1,4-hydroxy-acetylenes



JOC **1989**,
 54, 3449

- Silicon-Directed Nazarov



Tetrahedron
1986, 42, 2821

 - Tin -directed Nazarov *TL* **1986**, 27, 5947

Radical Cyclization

 B. Giese *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*

 (Pergamon Press; NY) **1986**; *Bull. Soc. Chim. Fr.* **1990**, 127, 675; *Tetrahedron* **1981**, 37, 3073; *Tetrahedron* **1987**, 43, 3541; *Advances in Free Radical Chemistry* **1990**, 1, 121.

Organic Reactions **1996**, 48, 301-856.

Radical Addition to multiple bonds:

1. Free radical addition is a two stage process involving an addition step followed by an atom transfer step.
2. In general, the preferred regioselectivity of the addition is in a manner to give the most stable radical (thermodynamic control)

Advantages of free radical reactions:

1. non-polar, little or no solvent effect
2. highly reactive- good for hindered or strained systems
3. insensitive to acidic protons in the substrates (i.e. hydroxyl groups do not necessarily need to be protected)

Mechanism of radical chain reactions

1. initiation
2. propagation
3. termination (bad)

Formation of carbon centered radicals:

tin hydride reduction of

alkyl, vinyl and aryl halides,
alcohol derivatives:

xanthates, thionocarbonate, thiocarbonylimidazolides

organoselenium & boron compounds

carboxylic acid derivatives (Barton esters)

reduction of organomercurials

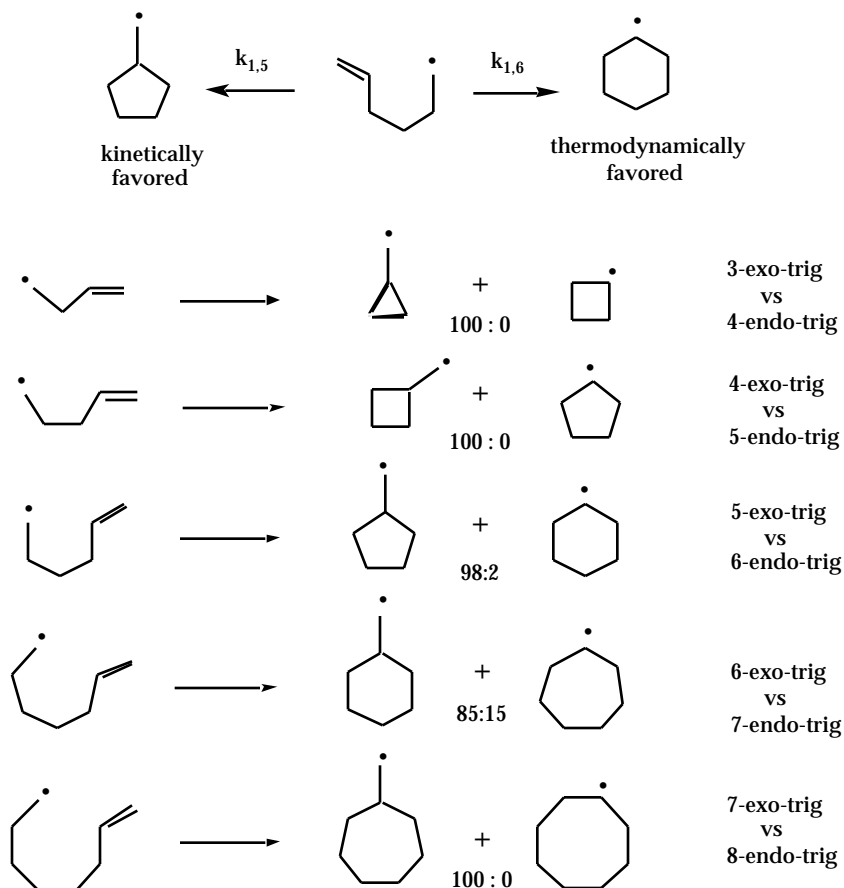
thermolysis of organolead compounds

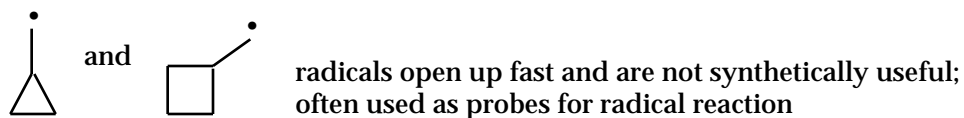
thermolysis or photolysis of azoalkanes.

Radical Ring Closure

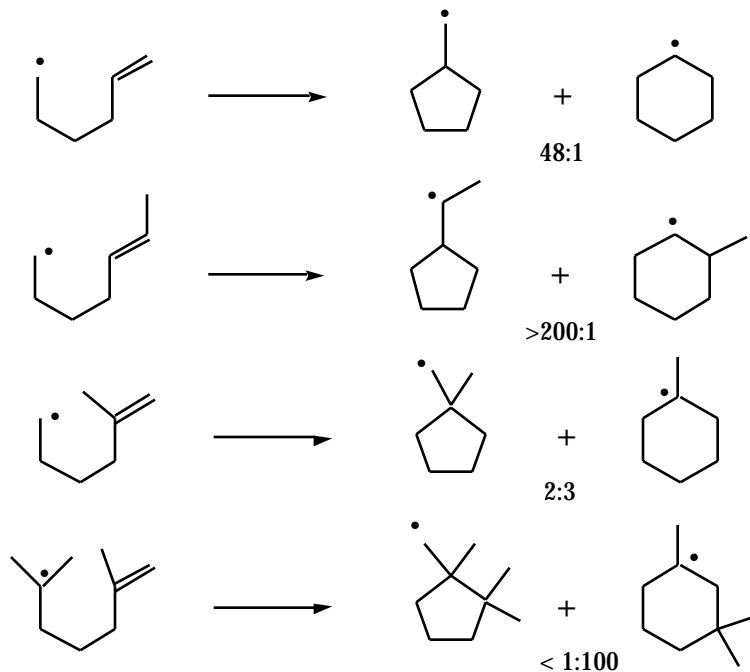
For irreversible ring closure reaction, the kinetic product will predominate.

Both the 5-exo-trig and 6-endo-trig are favored reactions, with the 6-exo-trig mode producing the most stable radical. However, the 5-exo-trig is about 50 times faster





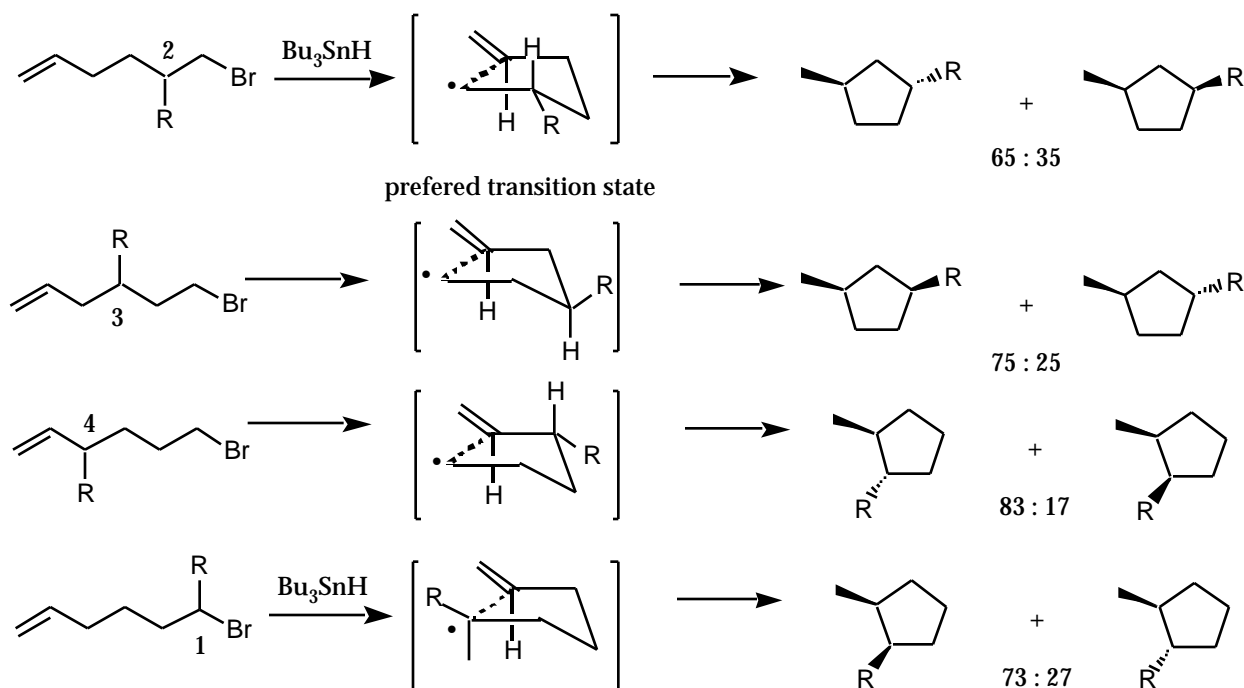
Effects of substituent on the regiochemistry of the 5-hexenyl radical cyclization

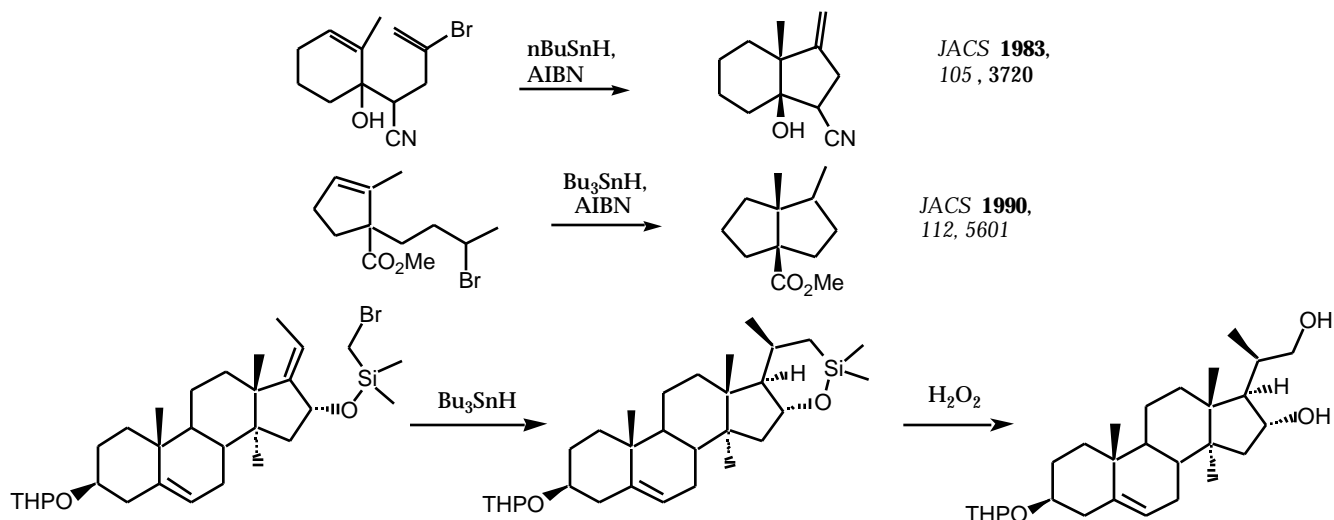


Stereochemistry of 5-hexenyl radical cyclization

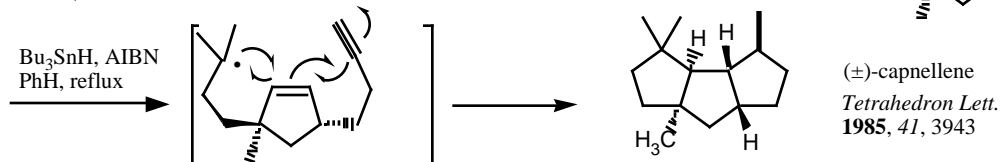
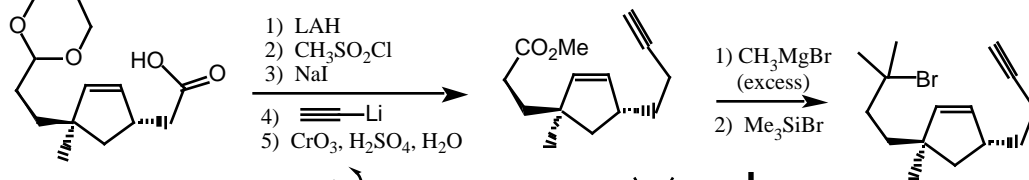
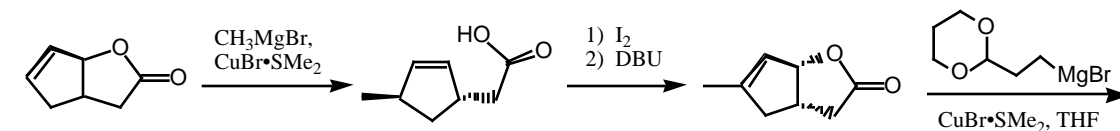
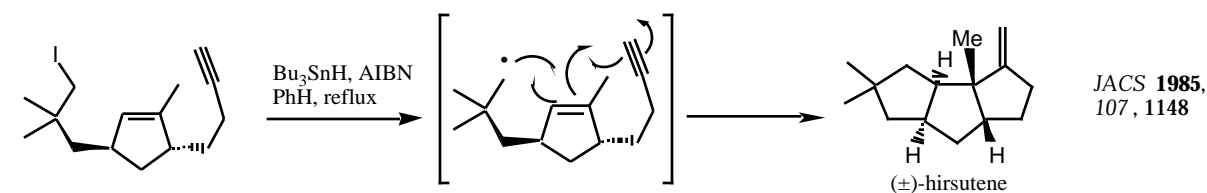
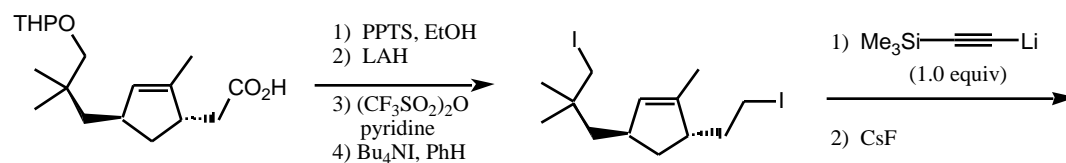
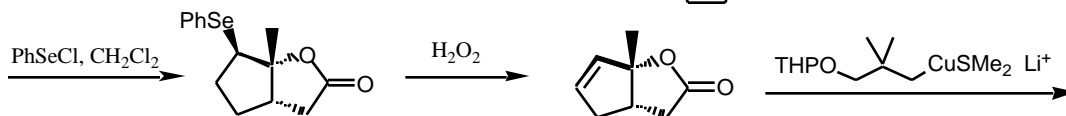
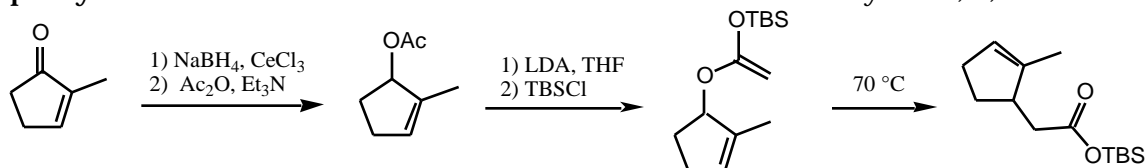
1-, or 3-substituted 5-hexenyl radicals give cis disubstituted cyclopentanes

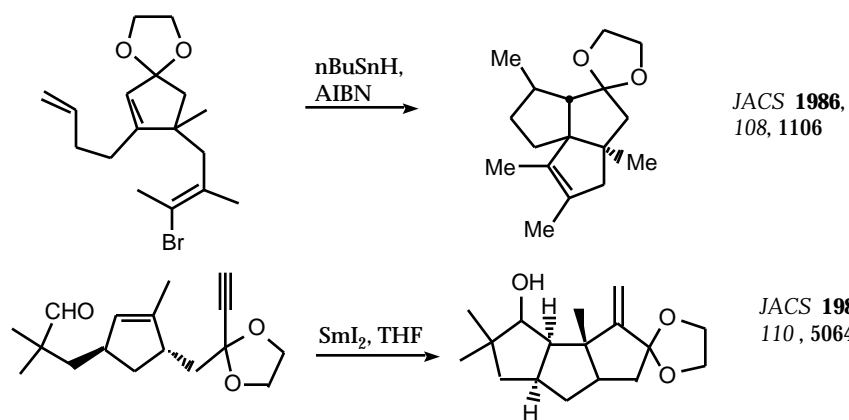
2-, or 4-substituted 5-hexenyl radicals give trans disubstituted cyclopentanes



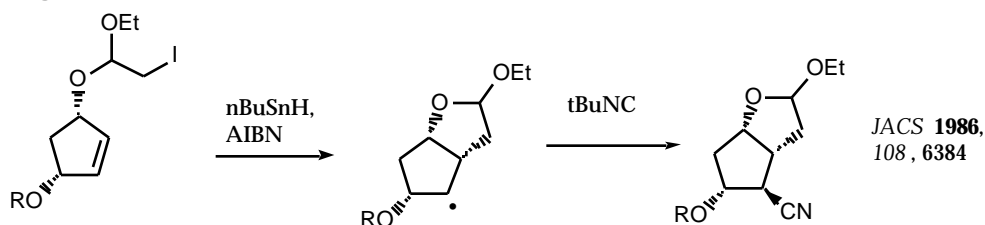


multiple cyclizations: D. Curran *Advances in Free Radical Chemistry* **1990**, 1, 121.

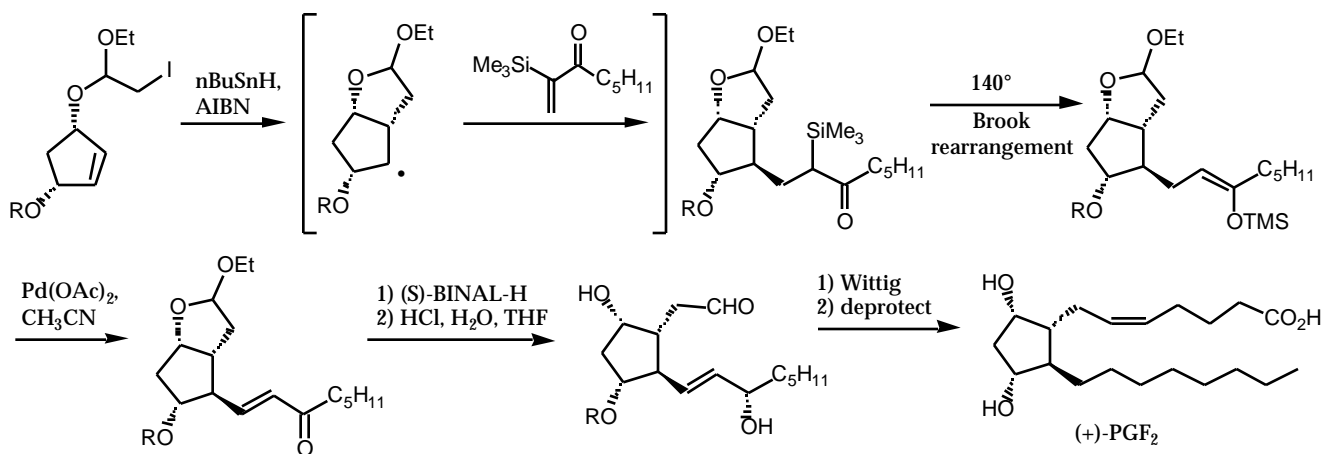




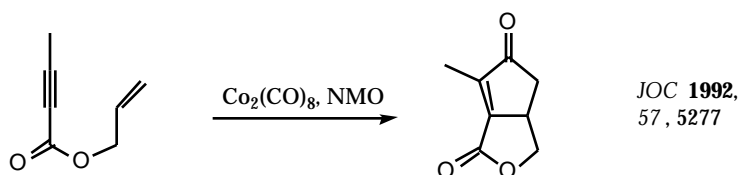
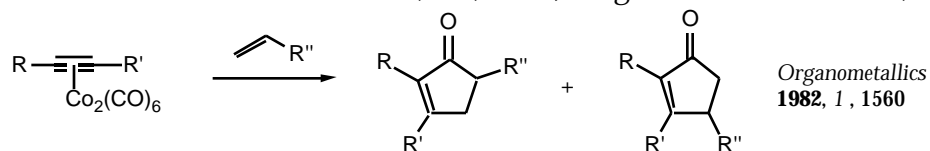
radical trapping

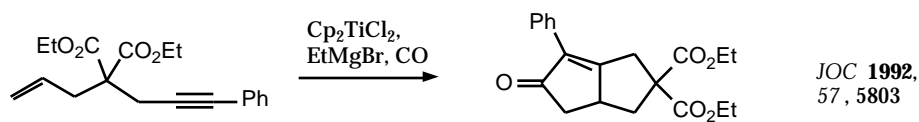


can also be trapped with acrylate esters or acrylonitrile.

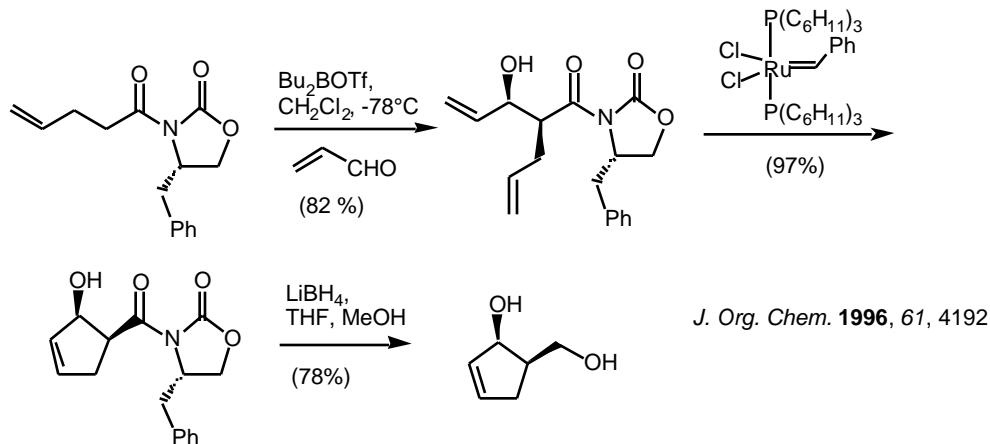


Paulson-Khand Reaction *Tetrahedron* **1985**, 41, 5855; *Organic Reactions* **1991**, 40, 1.

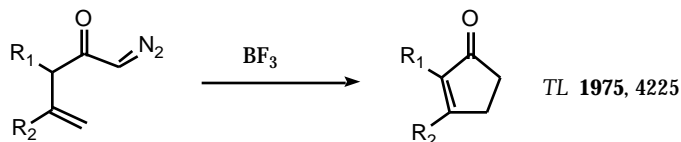




Ring-Closing Metathesis *Tetrahedron* **1998**, *54*, 4413, *Acc. Chem. Res.* **1995**, *25*, 446.



Diazoketones *Tetrahedron* **1981**, *37*, 2407; *Organic Reactions* **1979**, *26*, 361



FVP of Acetylenic Ketones

