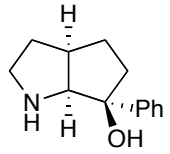
Richter

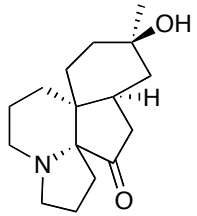
Nitrogen Centered Radicals

3/31/04
Group Meeting

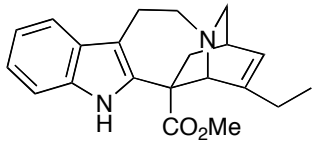
Syntheses Discussed:



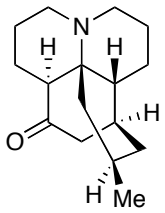
Corey, CBS Ligand
TL, 1989, 5547



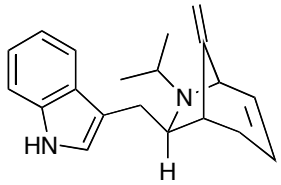
Zard, 13-Deoxyserratine
ACIEE, 2002, 1783



Fukuyama, Catharanthine
Heterocycles, 2002, 313



Grieco, Lycopodine
JACS, 1998, 5128



Weinreb, Peduncalarine
T, 2001, 8779

Partial List of Transforms Discussed:

1. Hofmann-Löffler-Freytag Reaction
2. Ireland-Claisen Rearrangement
3. Pauson-Khand Reaction
4. Beckmann Rearrangement
5. Stieglitz Rearrangement

Relevant or Related Reveiws:

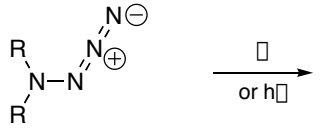
1. Gansäuer, A. *Angew. Chem. Int. Ed. Eng.* **2003**, *42*, 5556
2. Bowman, W.R. *J. Chem. Soc. Perkin Trans. 1.* **2002**, 2747
3. Friestad, G.K. *Tetrahedron.* **2001**, *57*, 5461
4. Yet, L. *Tetrahedron.* **1999**, *55*, 9349
5. Stella, L. *Angew. Chem. Int. Ed. Eng.* **1983**, *22*, 337
6. Neale, R.S. *Synthesis*, **1971**, *1*, 1
7. Wolff, M.E. *Chem. Rev.* **1963**, *63*, 55

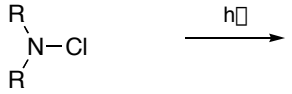
Important Note: The term nitrogen centered radical refers to a species where the initiating radical is localized on a nitrogen atom, not to transformations that terminate with a nitrogen radical. Numerous examples of the latter are known and are not discussed here.

Three types of Nitrogen Radicals:

1. Neutral Aminyl Radicals

a. Generation



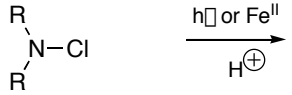


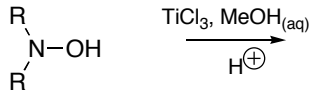
b. Reactivity
- – Dimerize to form hydrazines, which disproportionate to form imines and amines
- – Abstract allylic hydrogens preferrably
- – Can add to styrenes and arenes, if there are no allylic protons

Nitrogen Centered Radicals

2. Protonated Aminyl Radicals

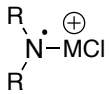
a. Generation



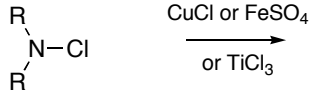


b. Reactivity
– Adds to unsaturated hydrocarbons and arenes
– Abstract protons if favorably disposed and activated

3. Aminyl Radicals Complexed to Metal Ions



a. Generation

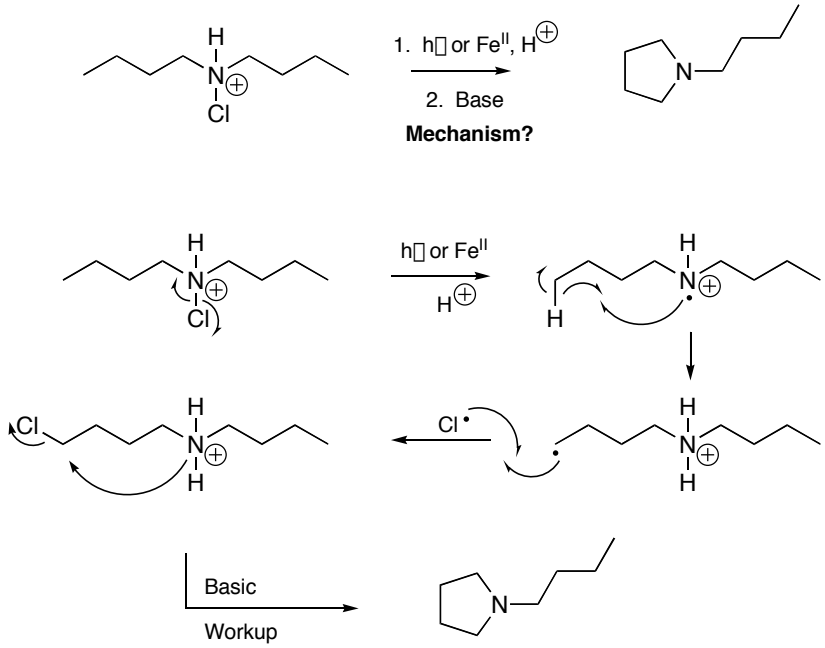


Must use neutral conditions to generate, otherwise protonated aminyl radicals are obtained

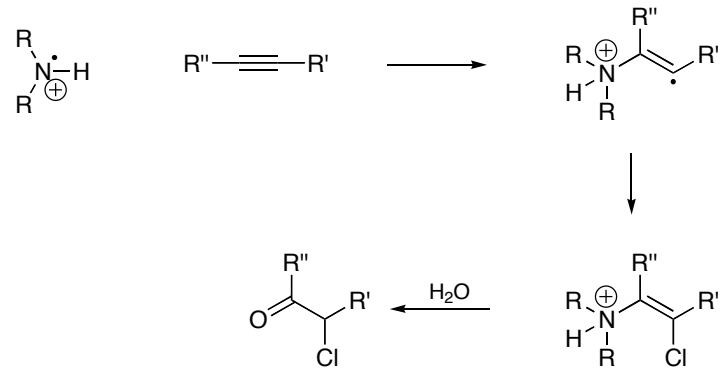
b. Reactivity
– Add to dienes, acetylenes, or alkenes
– No acid prevents electrophilic chlorination of the substrate

Selected Transformations:

1. Hofmann-Löffler-Freytag Reaction:



2. Synthesis of -Chloroketones from Alkynes:

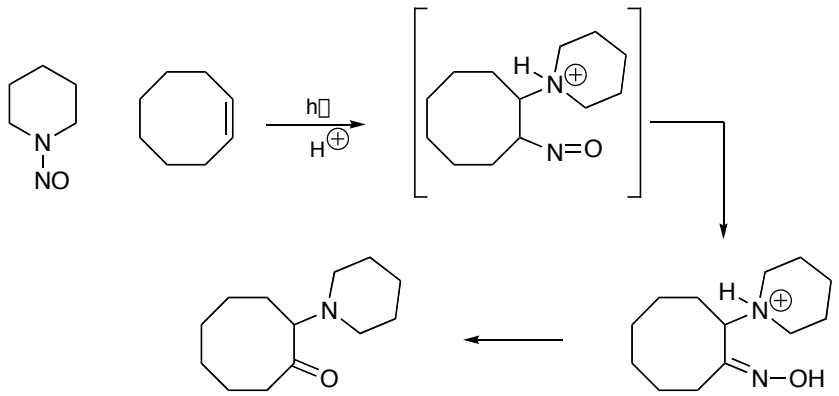


Stella, L. *Angew. Chem. Int. Ed. Eng.* **1983**, *22*, 337; Neale, R.S. *Synthesis.* **1971**, *1*, 1

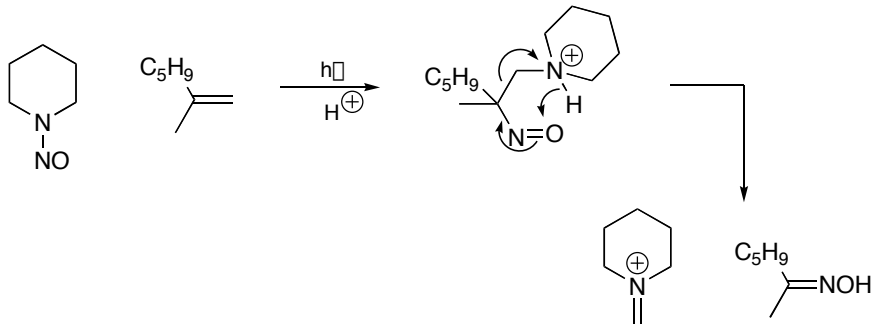
Neale, R.S. *Synthesis.* **1971**, *1*, 1; Wolff, M.E. *Chem. Rev.* **1961**, *63*, 55

Nitrogen Centered Radicals

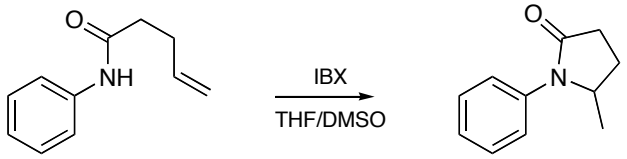
3. Synthesis of β-Amino Ketones from Alkenes:



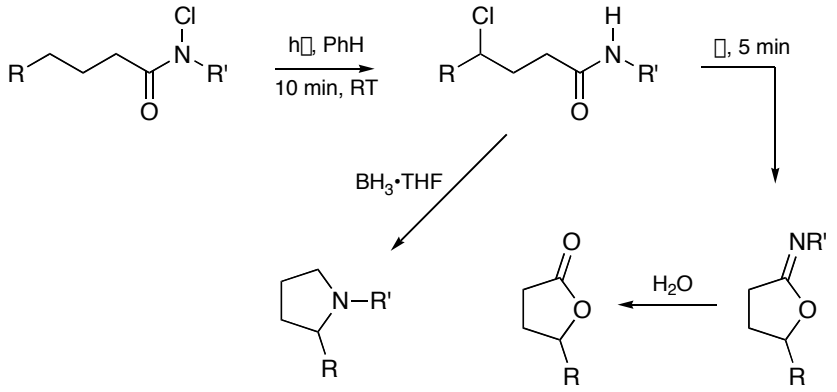
4. Synthesis of Oximes from Alkenes:



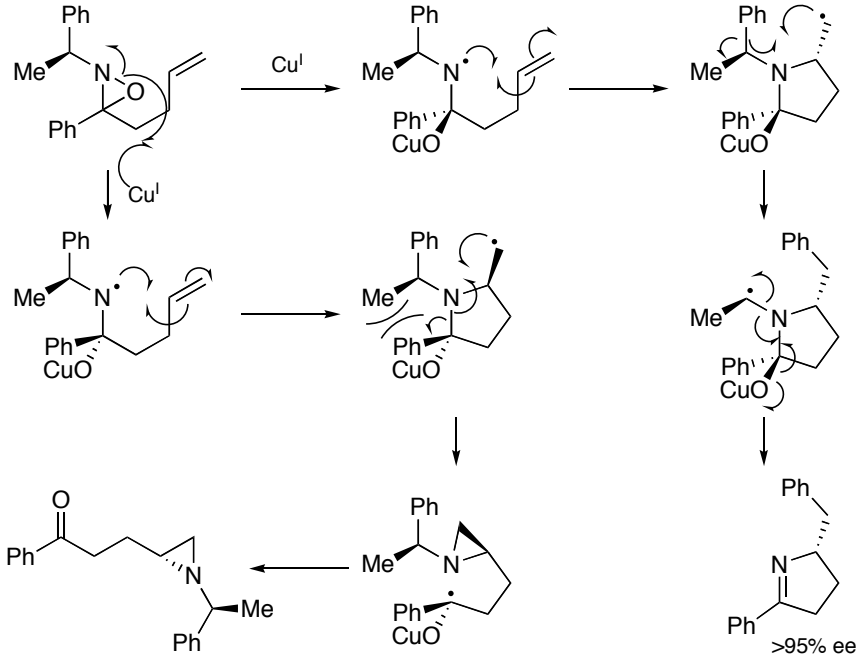
5. IBX Reactions:



6. Synthesis of γ-Lactones or Pyrrolidines:



7. Aubé, J. *J. Am. Chem. Soc.* 1992, *114*, 5466:



Neale, R.S. *Synthesis.* **1971**, *1*, 1; Nicolaou, K.C. *Angew. Chem. Int. Ed. Eng.* **2001**, *40*, 202

Neale, R.S. *Synthesis.* **1971**, *1*, 1; Aubé, J. *J. Am. Chem. Soc.* **1992**, *114*, 5466

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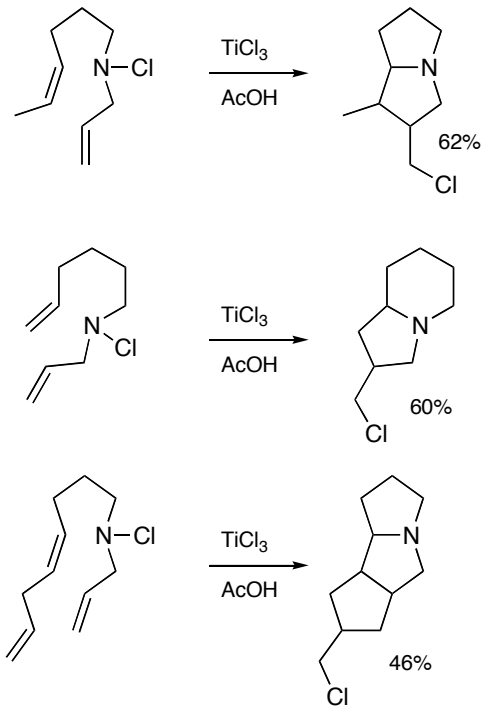
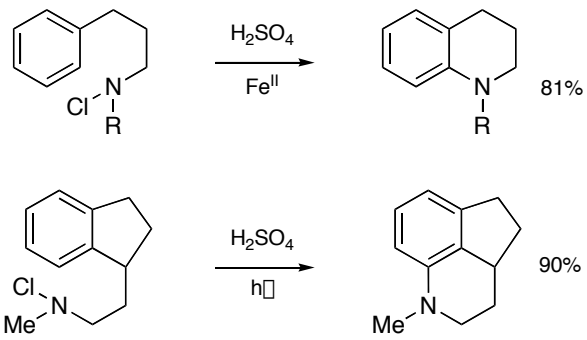
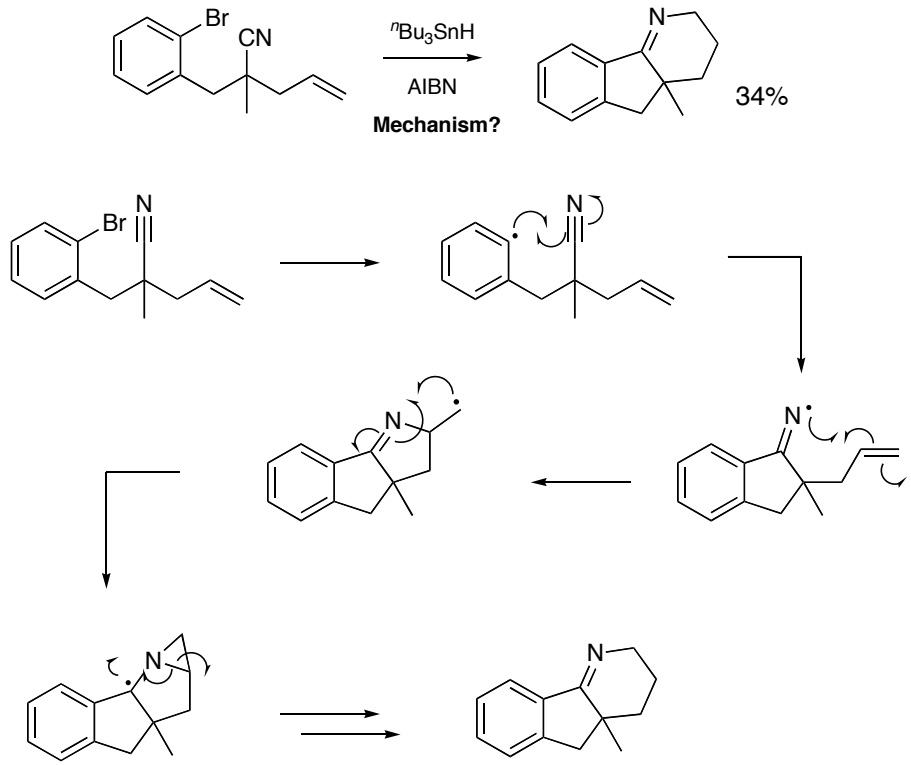
8. An Alternative to Nitrogen Stitching:



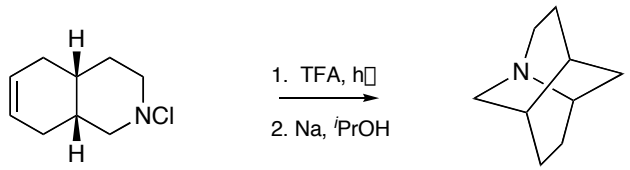
9. Aryl Amination:



10. Cyclizations involving Nitriles:



11. Synthesis of a Twistane:



Stella, L. *Angew. Chem. Int. Ed. Eng.* **1983**, *22*, 337

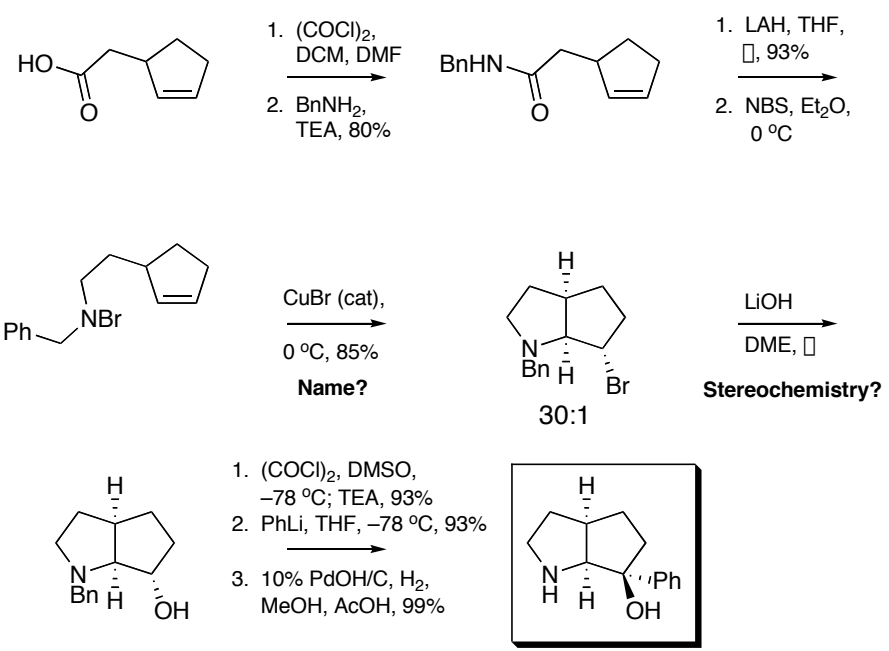
Bowman, W.R. *Tetrahedron Lett.* **2000**,*41*, 8989; Heusler, K. *Tetrahedron Lett.* **1970**, *11*, 97

Nitrogen Centered Radicals

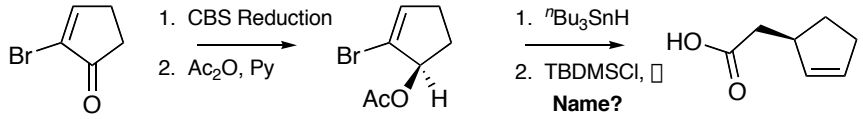
Syntheses:

1. A Chemzymatic Ligand

Corey, E.J. *Tetrahedron Lett.* 1989, *30*, 5547:

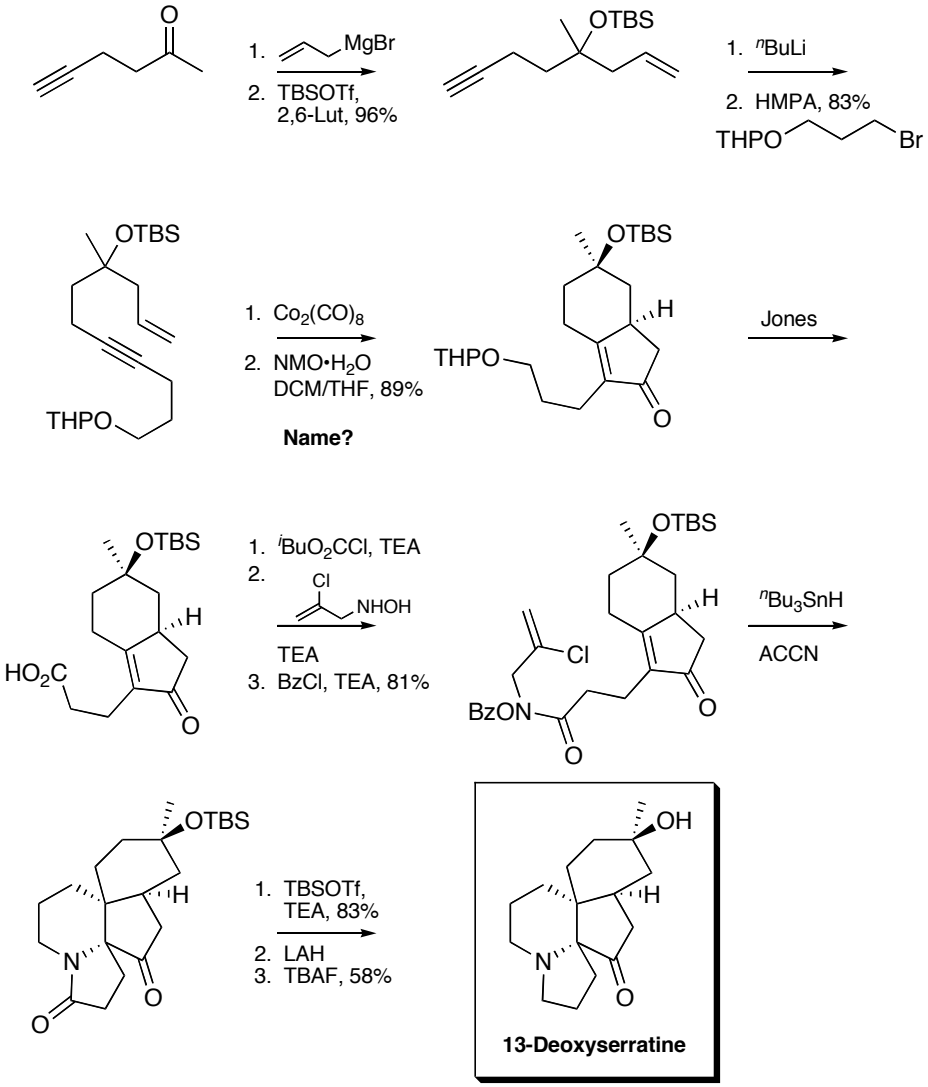


Synthesis of Chiral Starting Material Using a CBS Reduction.



2. (±)-13-Deoxyserratine

Zard, S.Z. *Angew. Chem. Int. Ed. Eng.* 2002, *41*, 1783:



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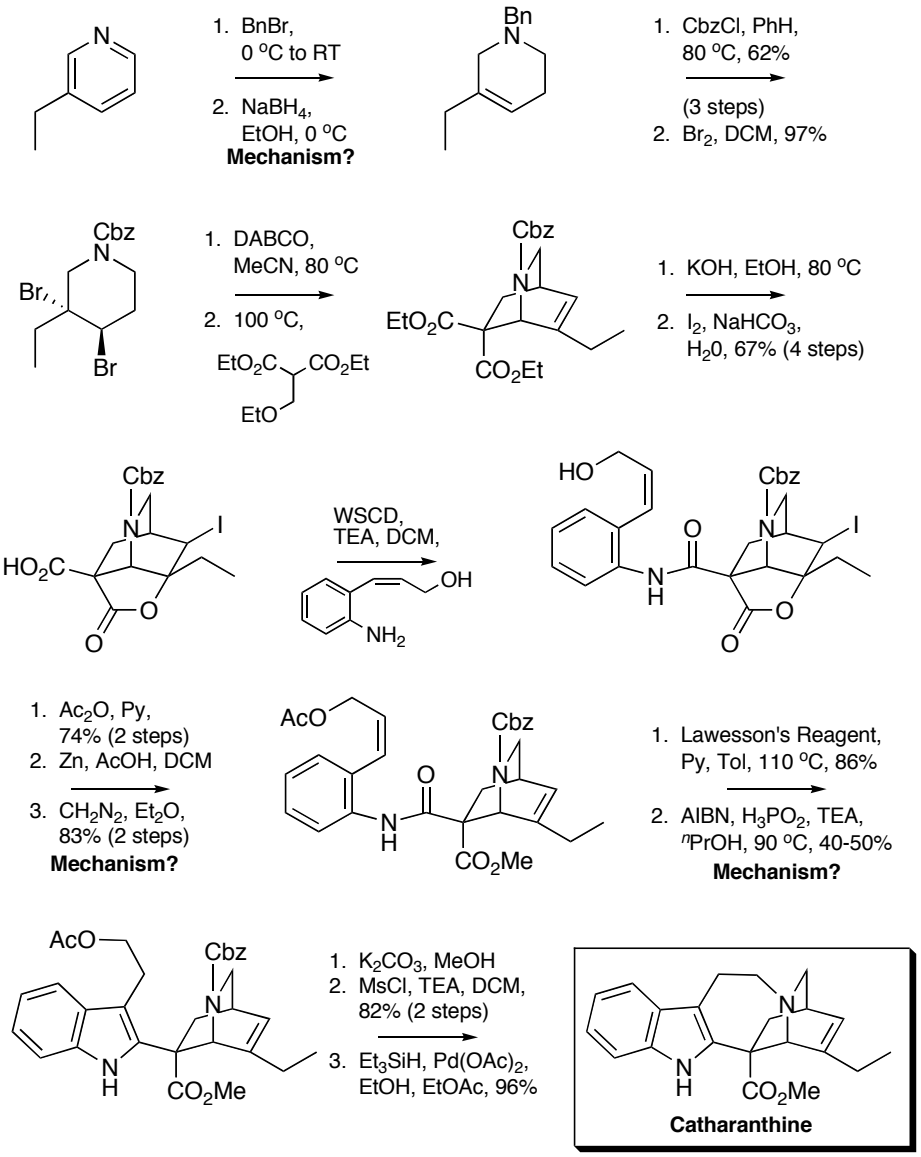
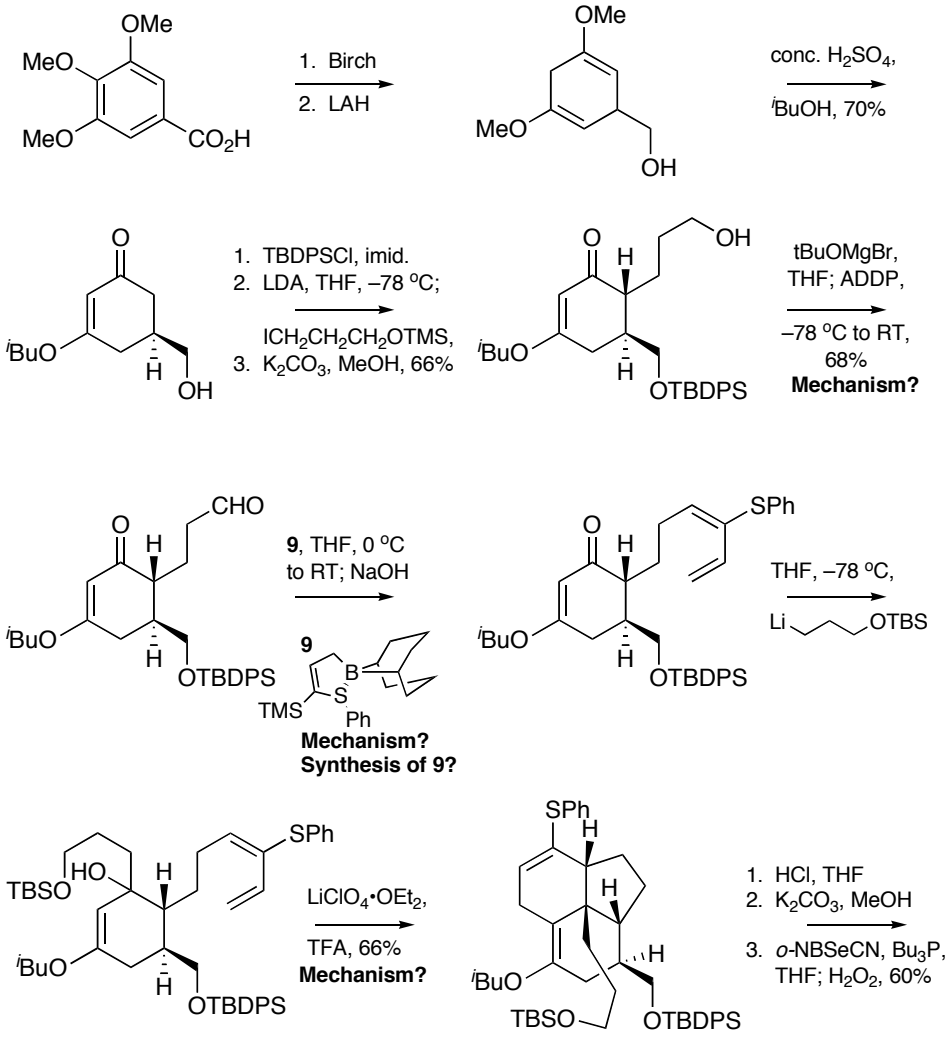
3. (±)-Catharanthine
Fukuyama, T. *Heterocycles*. 2002, *56*, 313:



4. (±)-Lycopodine
Grieco, P.A. *J. Am. Chem. Soc.* 1998, *120*, 5128:



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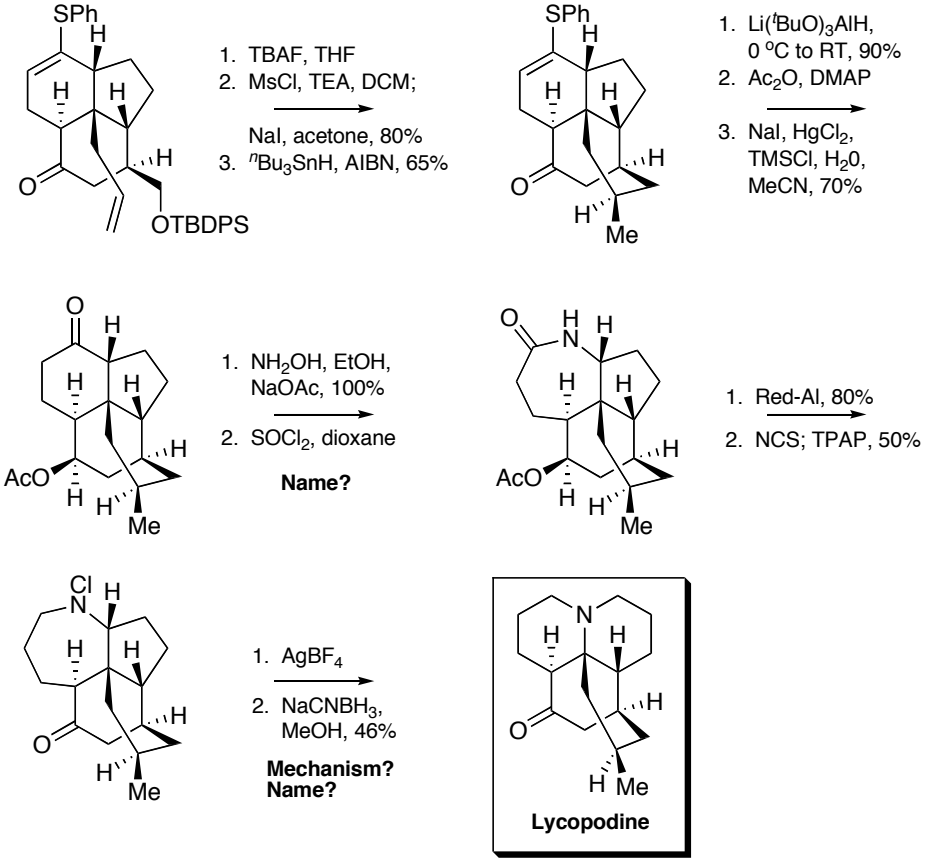
4. (±)-Lycopodine (Continued)
Grieco, P.A. *J. Am. Chem. Soc.* 1998, *120*, 5128:



5. Peduncularine (Formal)
Weinreb, S.M. *Tetrahedron* 2001, *57*, 8779
Hiemstra, H. *J. Am. Chem. Soc.* 1989, *111*, 2588