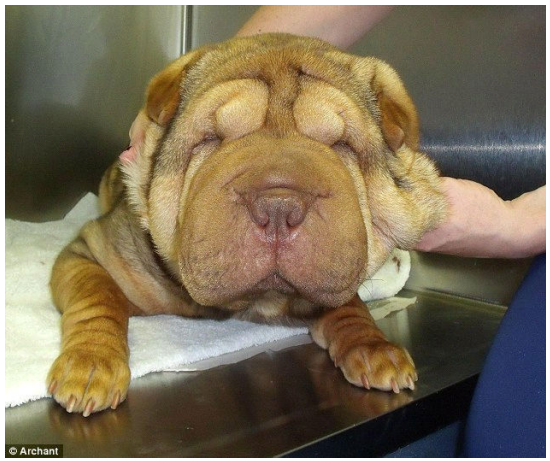
Nathan Wilde

Overbred Intermediates

This group meeting is based on a section in Hoffman's book *Elements of Synthesis Planning* called "'Overbred' Intermediates." This section defines "overbred intermediates" as intermediates en route to cyclic structures that have one or more excess C-C bonds, and these surplus bonds will need to be cleaved in subsequent steps. This goes against logical retrosynthetic planning (instead of finding good retrosynthetic *disconnections* you look for good "add bond" *connections*) and even the parameters for measuring against the ideal synthesis, but the goal of this presentation is to learn when such intermediates might be strategic.

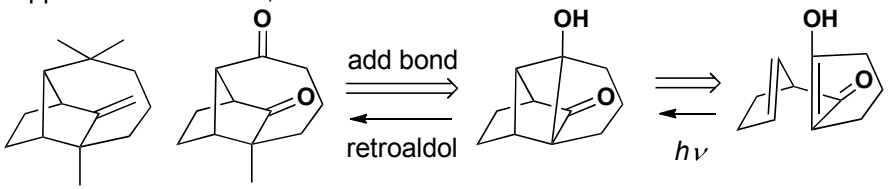
Notes:
-I only care about making and cleaving C-C bonds.
-Using DA/retro-DA to protect olefins doesn't count because I say so and because it is not interesting.
-No degradation of commercially available SM. Make the complexity and then destroy it (there may be one exception in this presentation).
-This is not meant to be a bashing party. There are lots of both good and bad examples here. We can learn from both types.
-By nature we must somehow fragment extraneous bonds in overbred intermediates, so I consider this topic a subset of Shenvi's 2005 "Fragmentation Reactions in Synthesis" group meeting.



This dog can barely squint through its overbred facial folds to see anything.

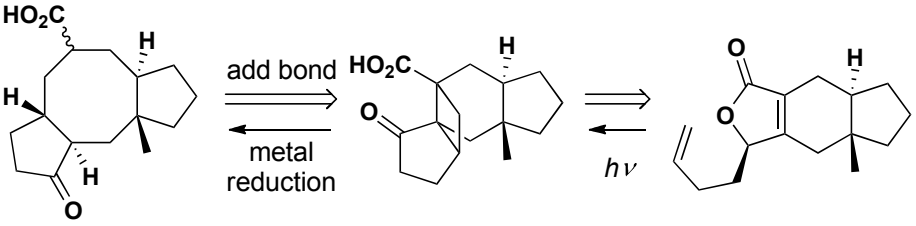
A. Medium Rings

Oppolzer. *JACS* 1978, 2583

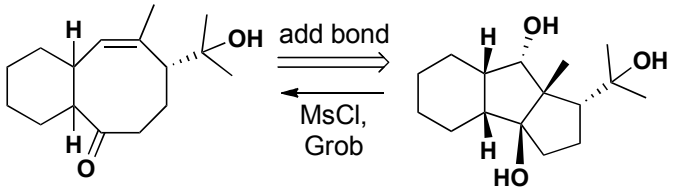


longifolene

Coates. *JACS* 1985, 3541

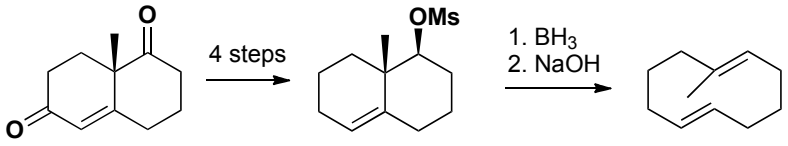


West. *JOC* 1998, 2806

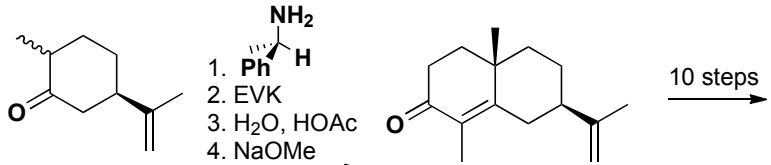


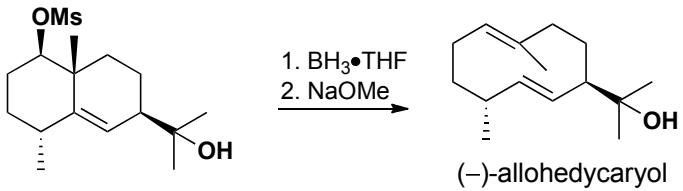
Overbred Intermediates

Marshall. *Synthesis* 1971, 229



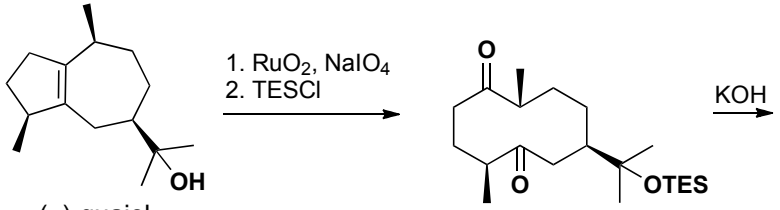
Zhabinskii. *JOC* 1996, 4022



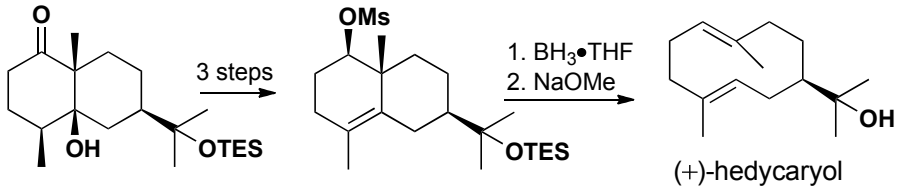


(–)-allohedycaryol

Minnaard. *Tetrahedron* 1994, 4755

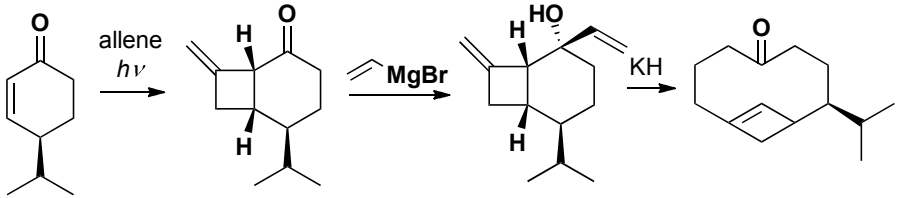


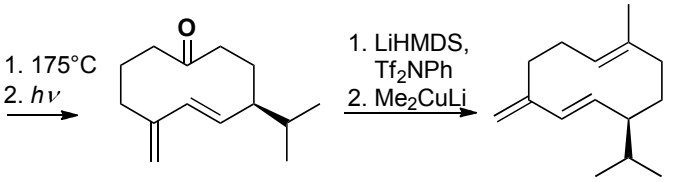
(–)-guaiol



(+)-hedycaryol

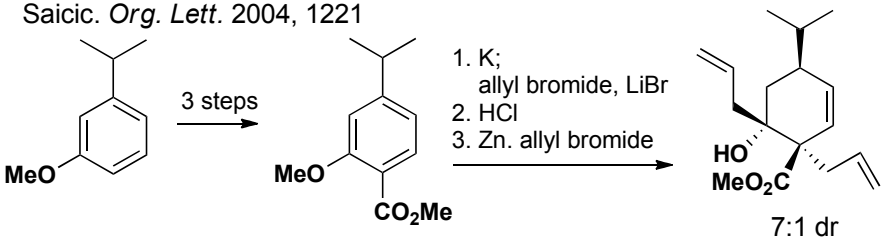
Schreiber. *Tet. Lett.* 1981, 4651
Tet. Lett. 1985, 5971



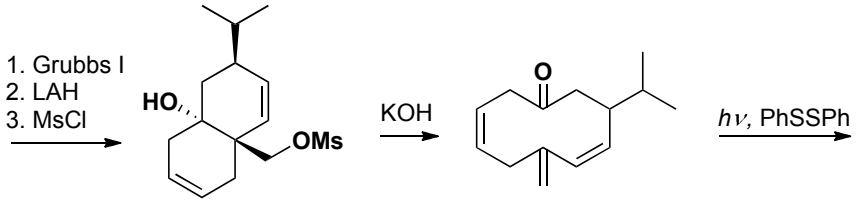


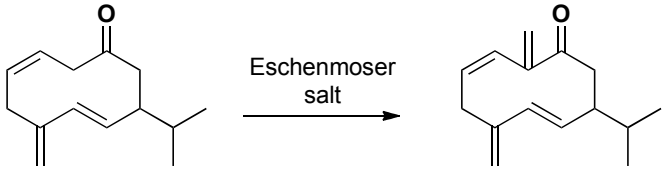
germacrene-D

Saicic. *Org. Lett.* 2004, 1221



7:1 dr



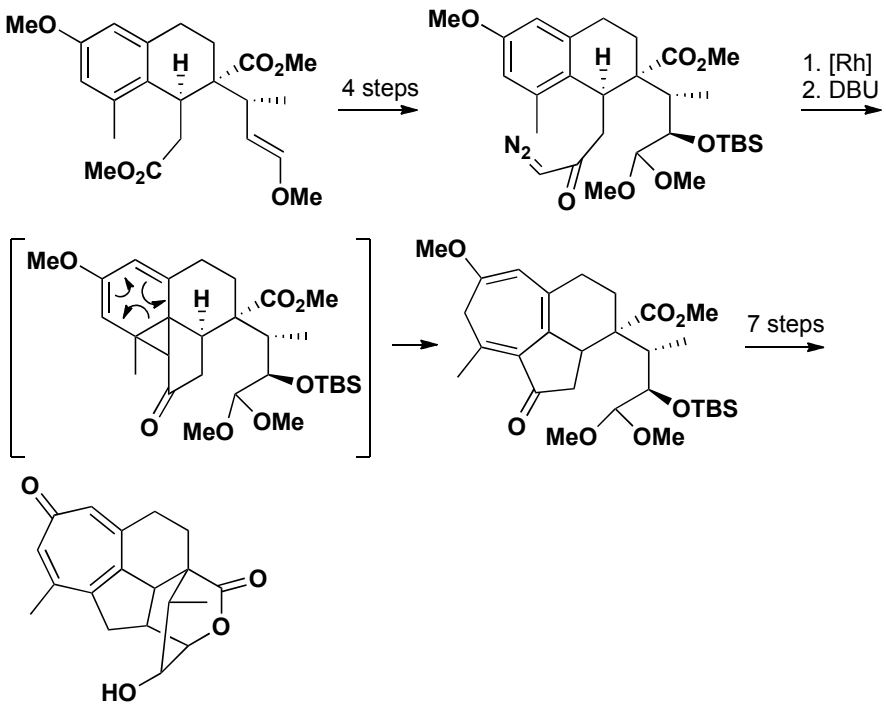


38% + 58% SM

periplanone C

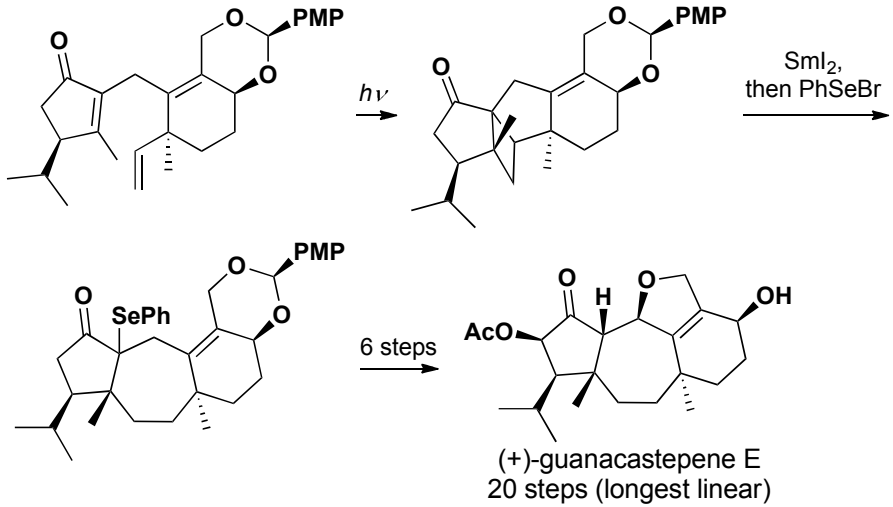
Mander. *JACS* 1998, 1914

Review: *Synlett* 2011, 2437



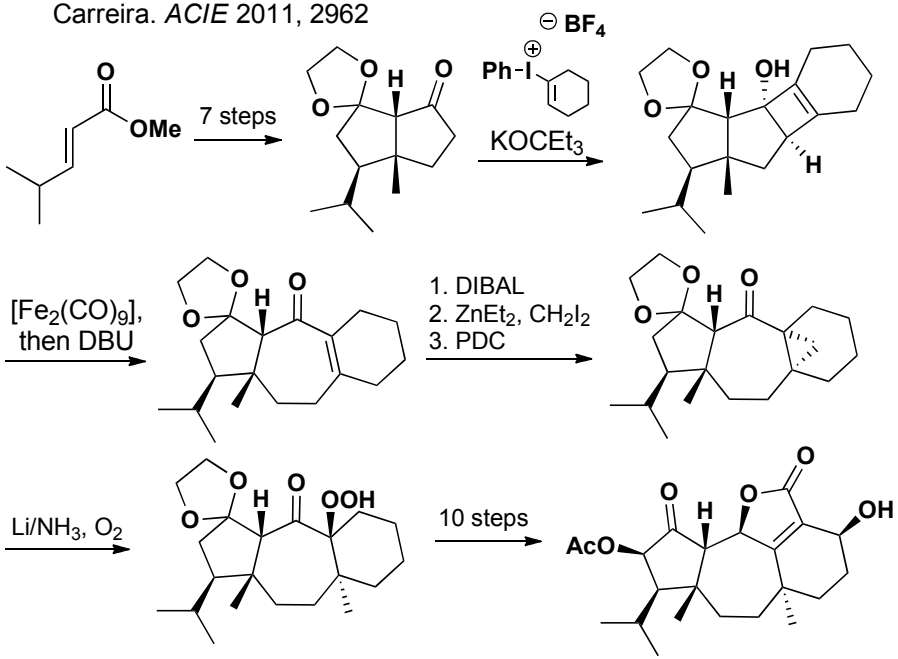
hainanolidol

Sorensen. *JACS* 2006, 7025



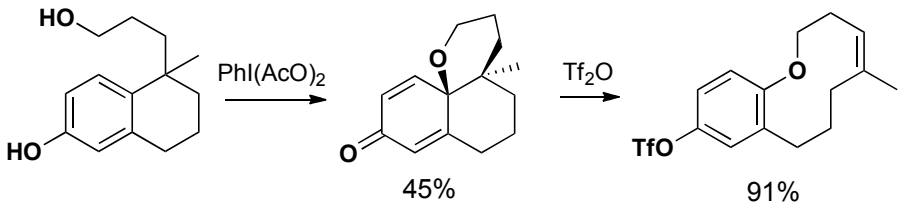
(+)-guanacastepene E
20 steps (longest linear)

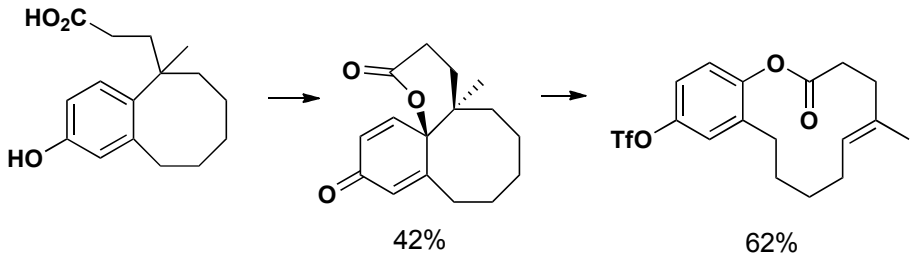
Carreira. *ACIE* 2011, 2962

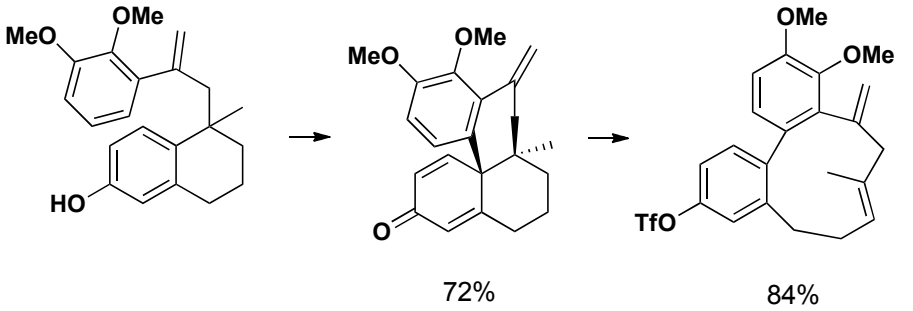


(±)-guanacastepene O

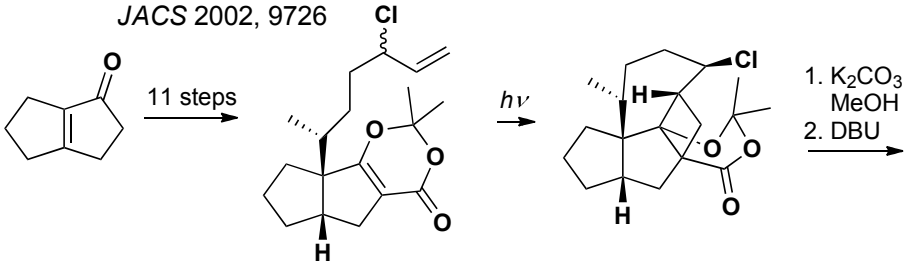
Tan. *Nat. Chem. Bio.* 2013, 21

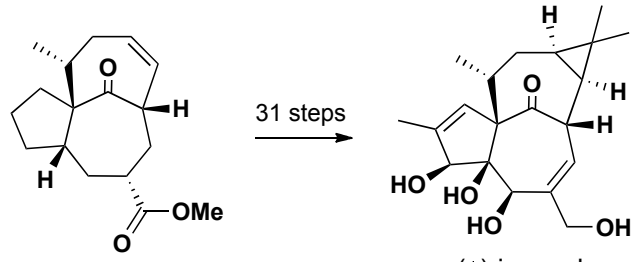






Winkler. *JACS* 1987, 2850
JACS 2002, 9726

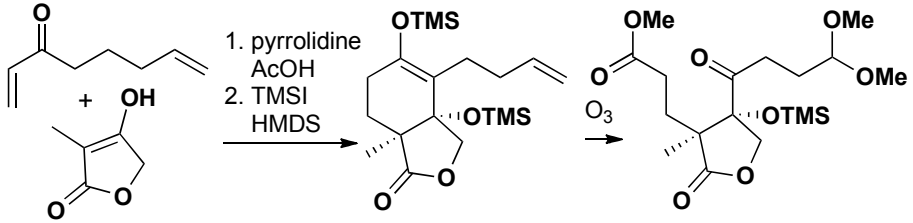


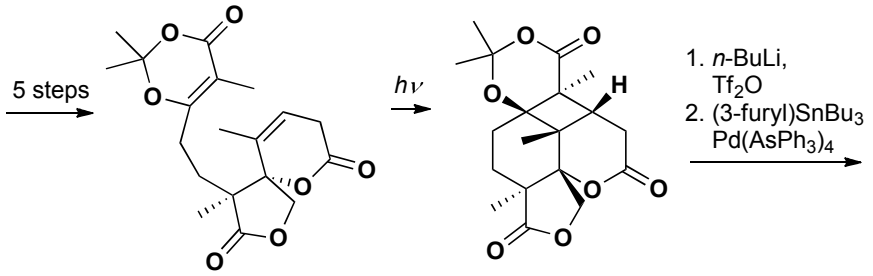


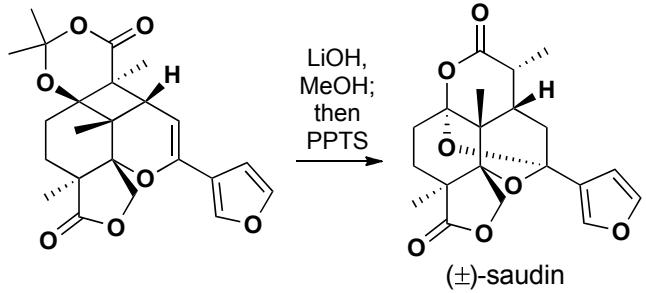
(±)-ingenol

B. Setting Cyclic Substitution

Winkler. *JACS* 1999, 7425





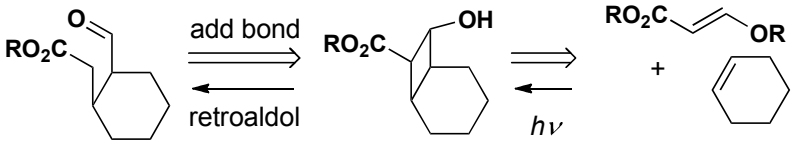


(±)-saudin

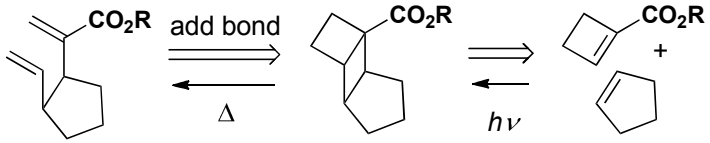
Winkler's review of 2+2 then fragmentation in synthesis:
Chem. Rev. 1995, 2003

Overbred Intermediates

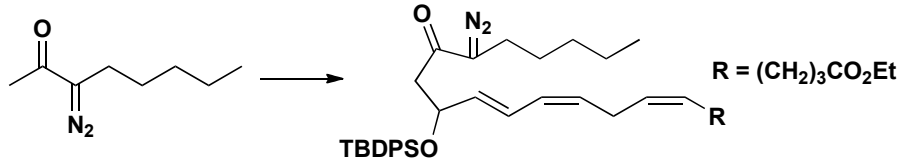
Pearlman. *JACS* 1979, 6398

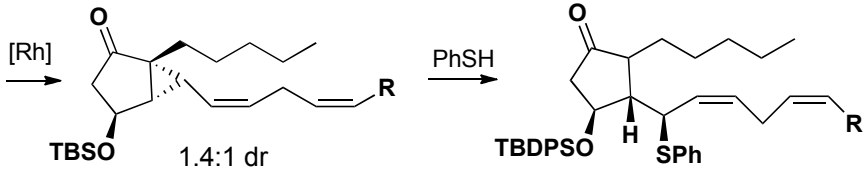


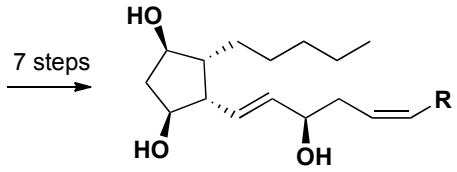
Wender. *JACS* 1977, 267



Taber. *JOC* 2001, 1876

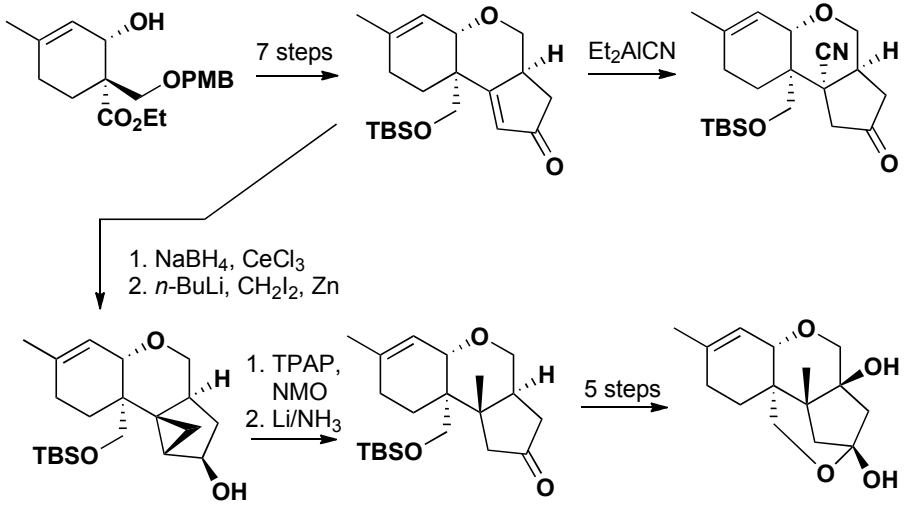






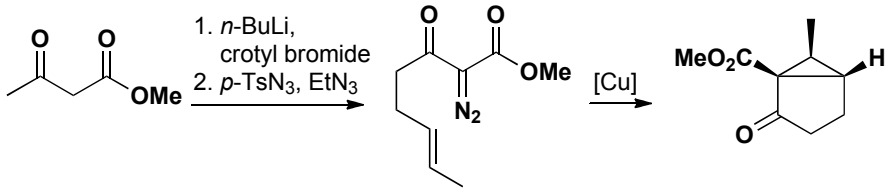
8-F_{2t}-isoprostane

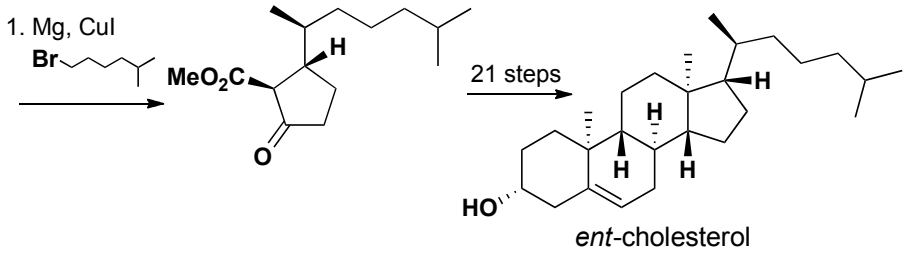
Danishefsky. *ACIE* 2007, 2199



paecilomycine A

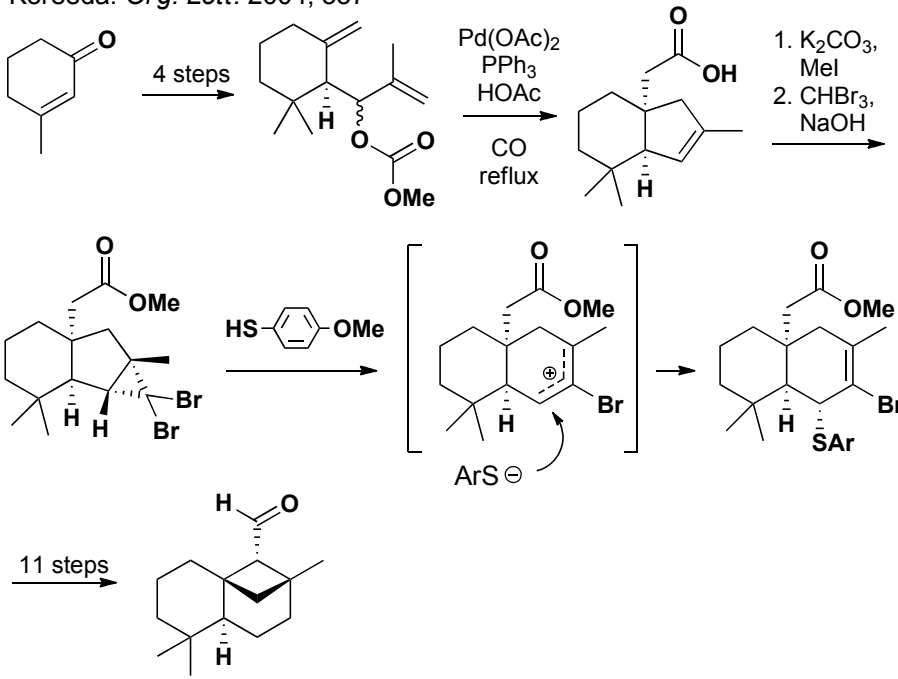
Covey. *JOC* 2002, 4893





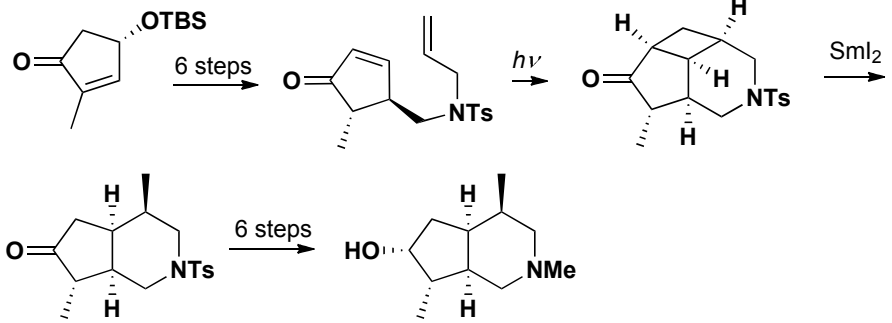
ent-cholesterol

Koreeda. *Org. Lett.* 2004, 537



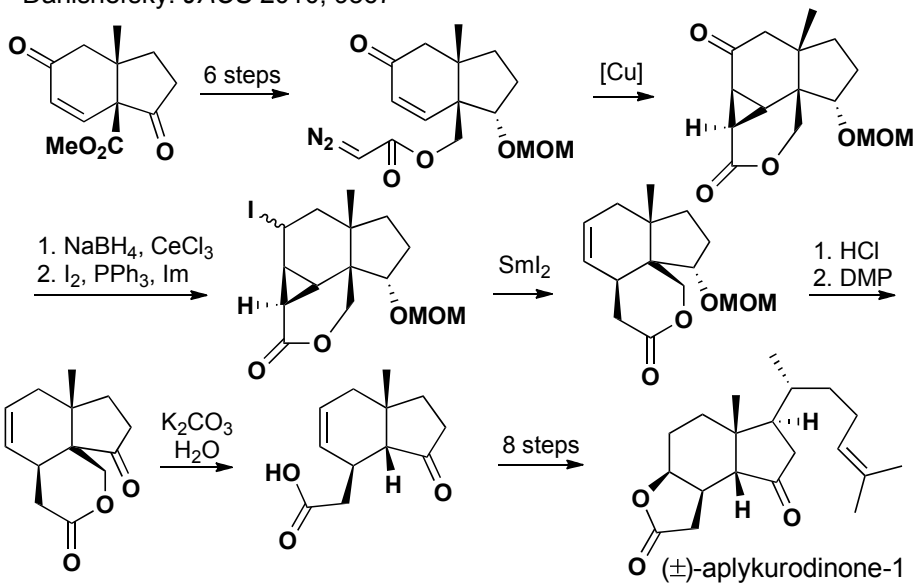
acanthodoral

Kibayashi. *Tet. Lett.* 2005, 2327



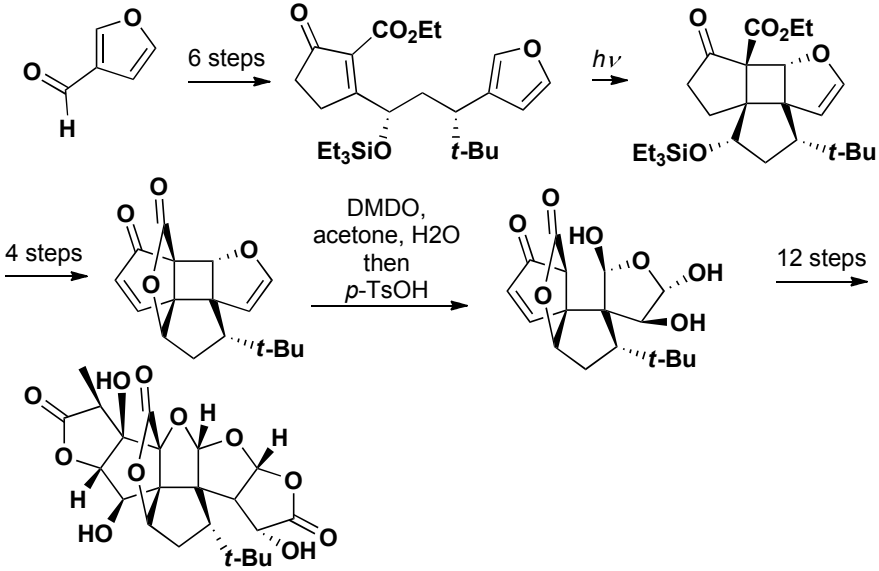
(–)-incarvilline

Danishefsky. *JACS* 2010, 9567



(±)-aplykurodinone-1

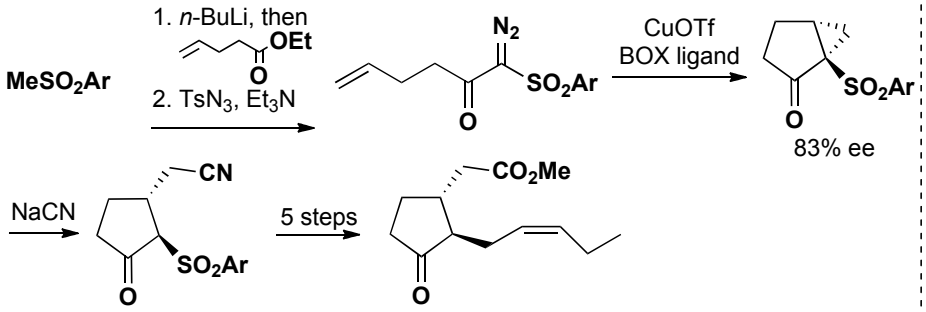
Crimmins. *JACS* 1999, 10249; *JACS* 2000, 8453



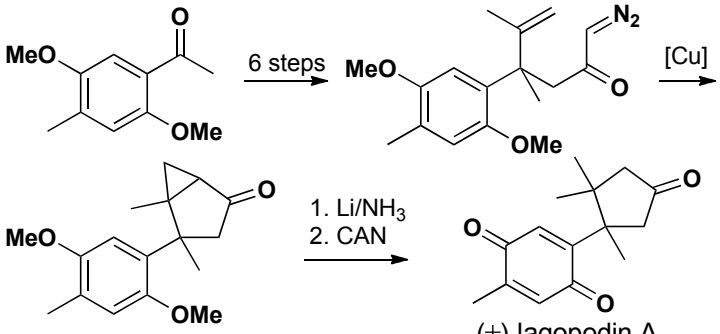
ginkgolide B

Overbred Intermediates

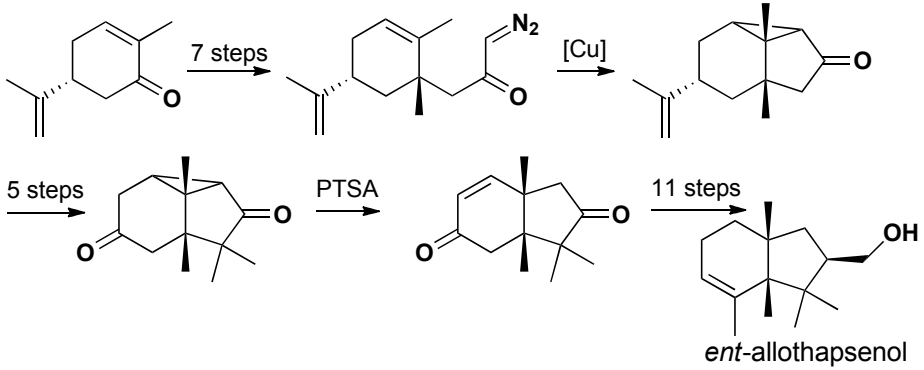
Nakada. *Tetrahedron* 2006, 8054



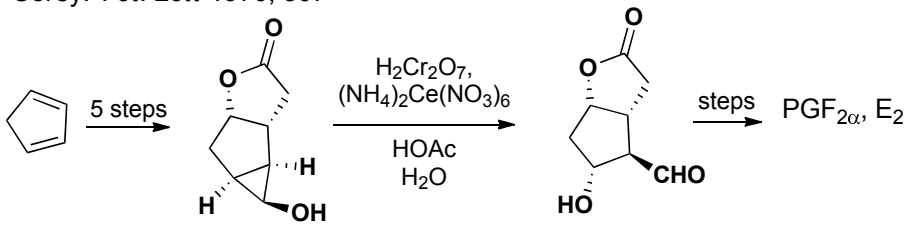
Srikrishna. *Synlett* 2007, 655



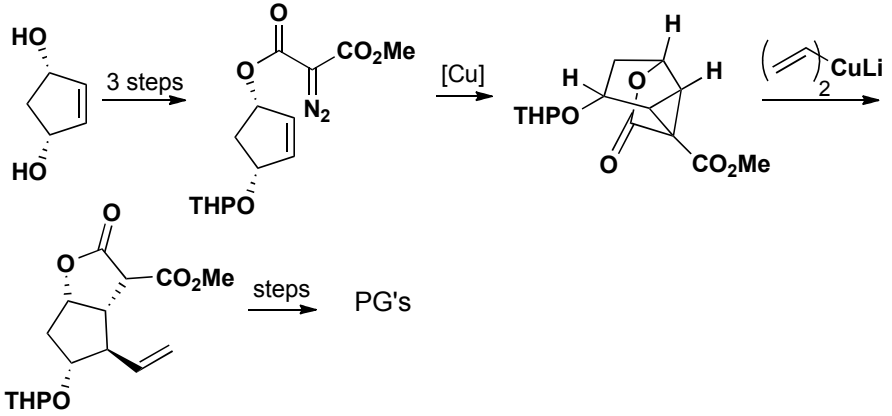
Srikrishna. *Synlett* 2012, 1021



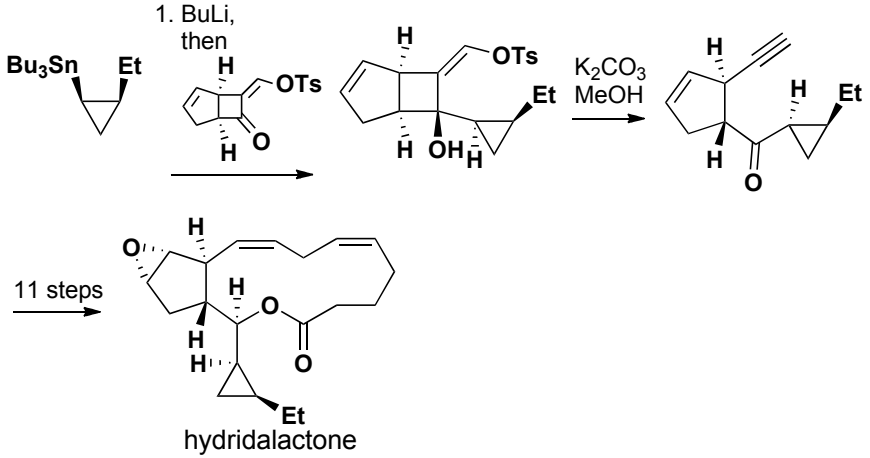
Corey. *Tet. Lett* 1970, 307



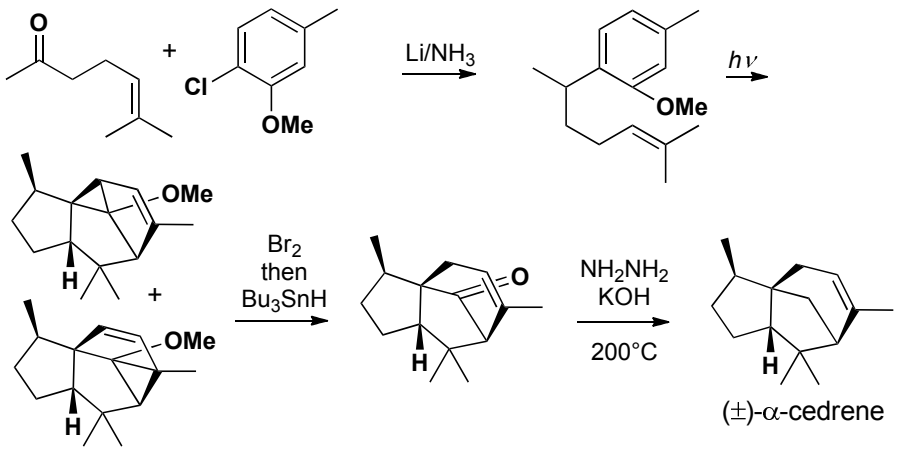
Corey. *JACS* 1972, 4014



Corey. *JACS* 1984, 2735

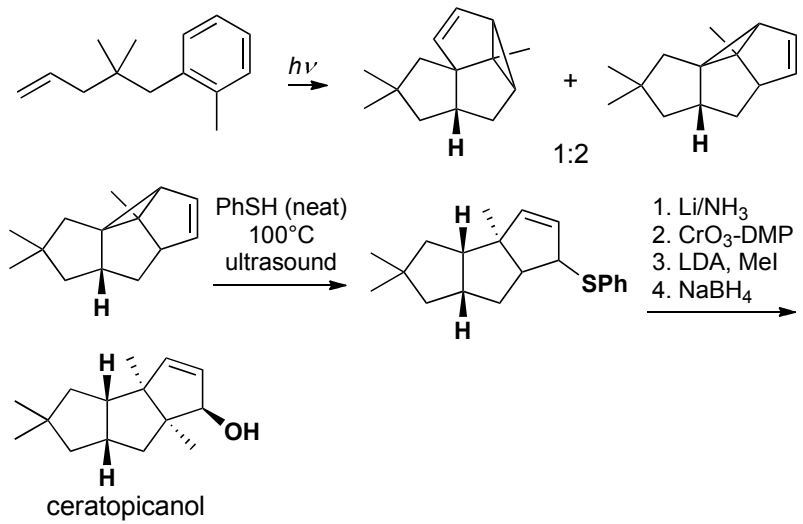


Wender. *JACS* 1981, 688



(±)-α-cedrene

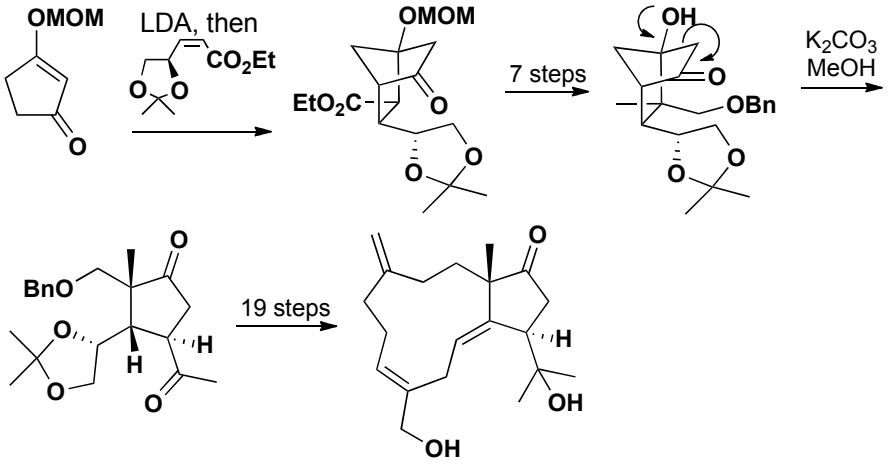
Chanon. *JOC* 1996, 3576



ceratopicanol

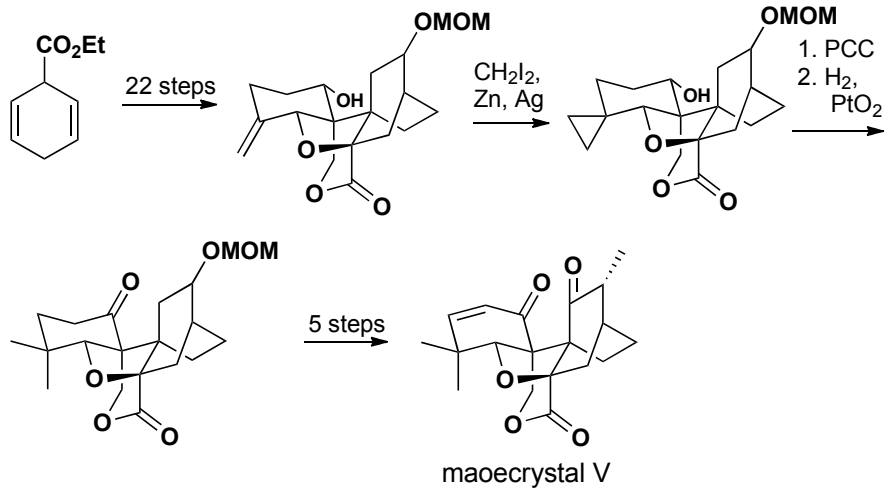
Review of meta- olefin-arene photocycloadditions:
Chem. Rev. 1993, 615

Yamada. *Tet. Lett.* 2001, 9233



stolonitriene

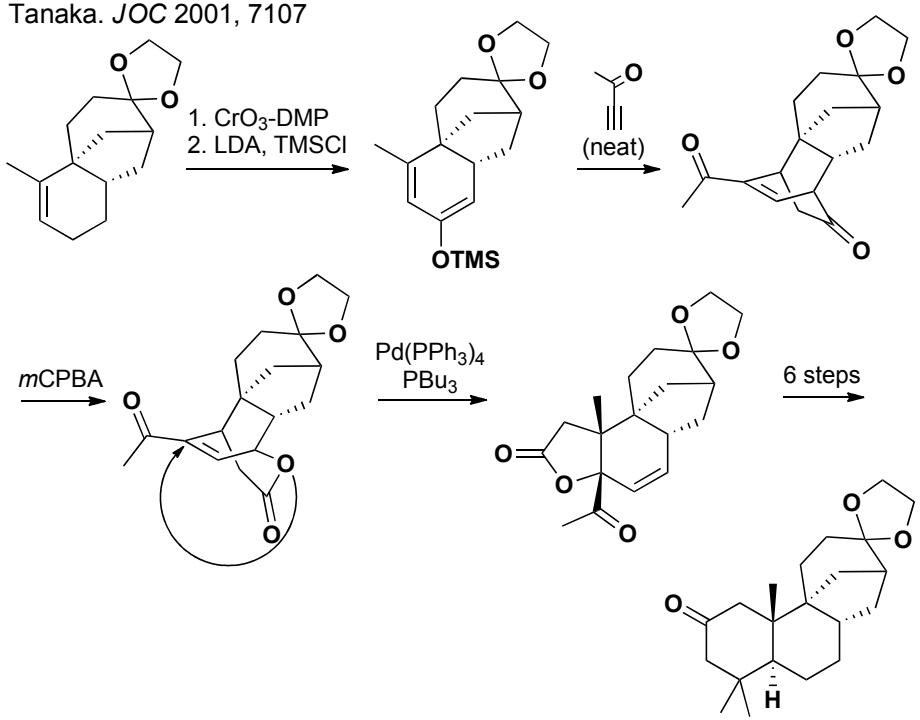
Danishefsky. *JACS* 2012, 18860



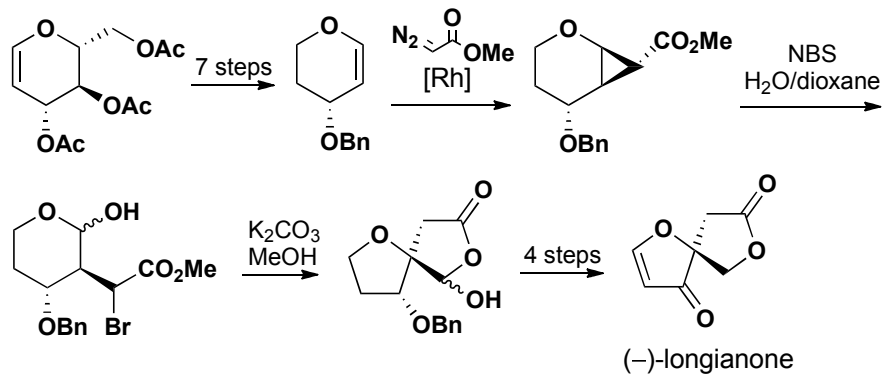
maoecrystal V

Overbred Intermediates

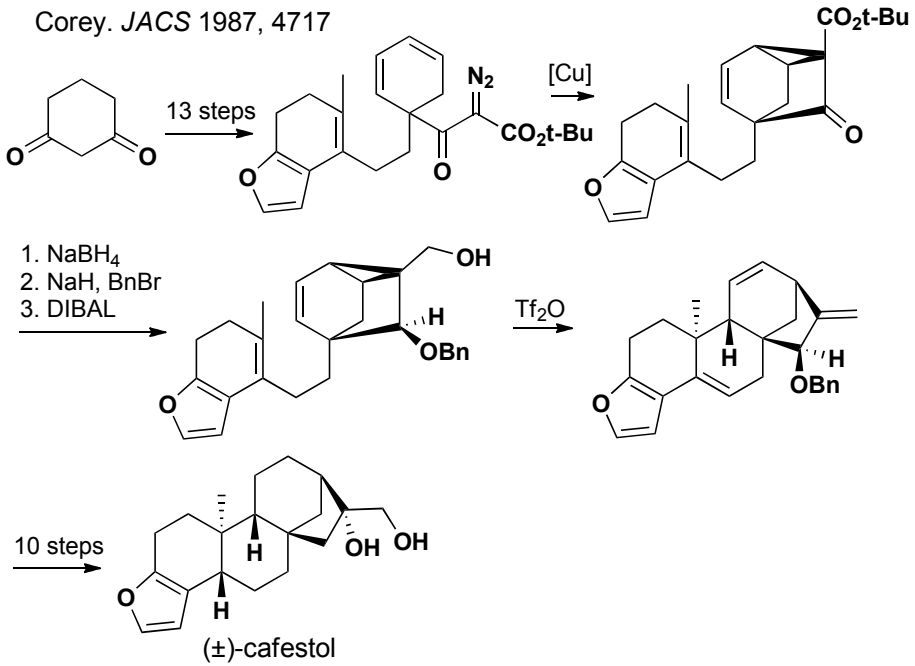
Tanaka. *JOC* 2001, 7107



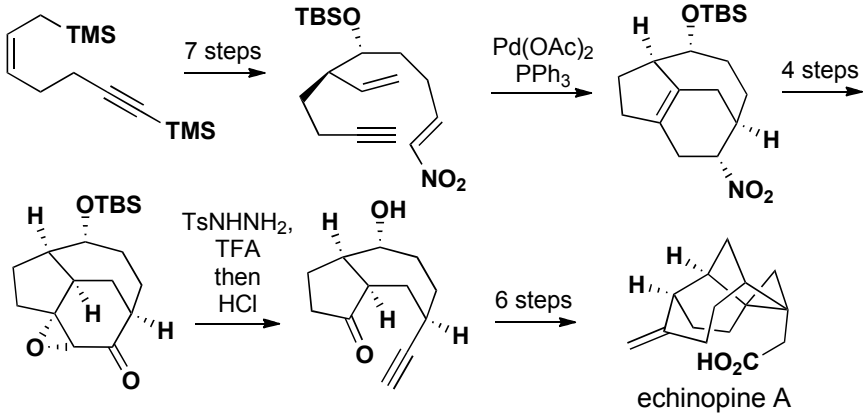
Perali. *Tetrahedron* 2012, 3725



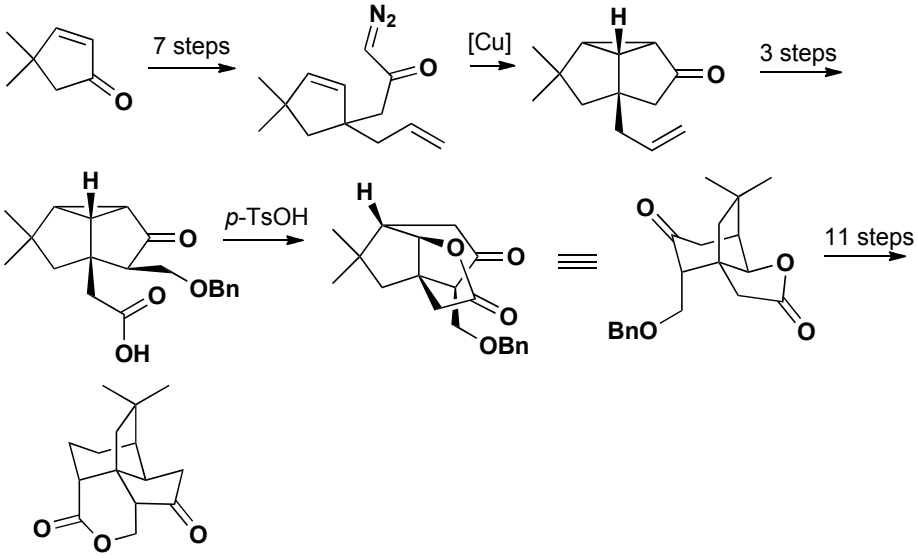
Corey. *JACS* 1987, 4717



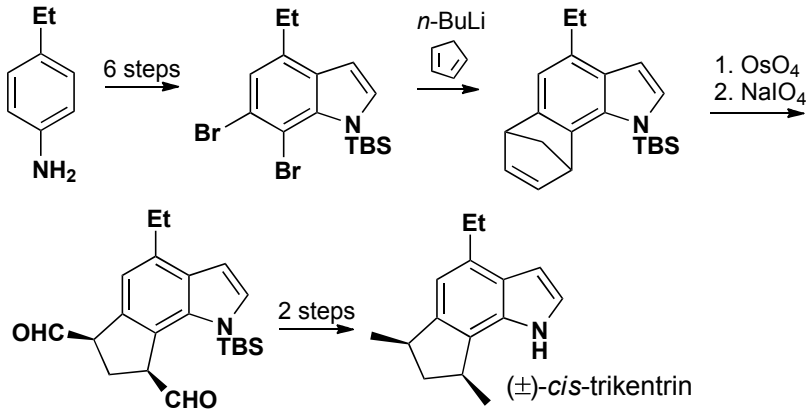
Chen. *Org. Lett*. 2011, 5724



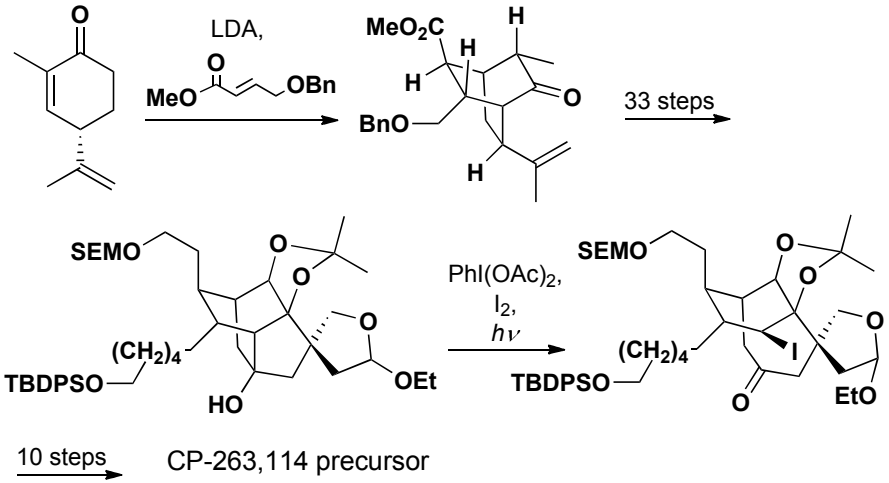
Iwata. *Tet. Lett.* 1986, 3161



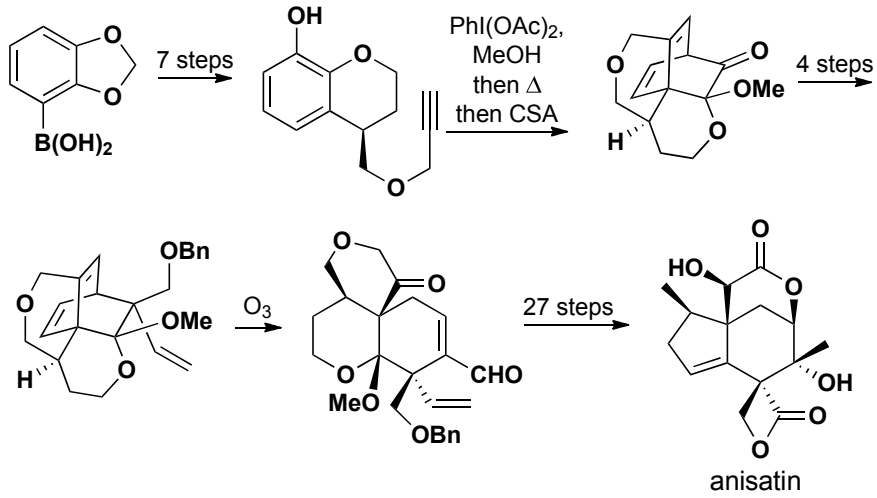
Buszek. *Org. Lett*. 2009, 201



Toshimitsu. *JOC* 2004, 9262
Org. Lett. 2000, 3751

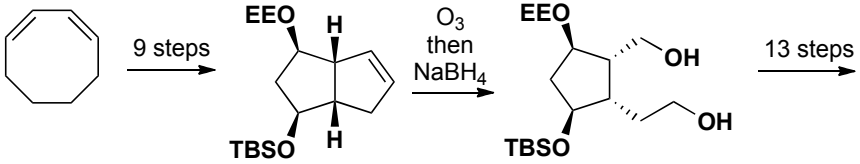


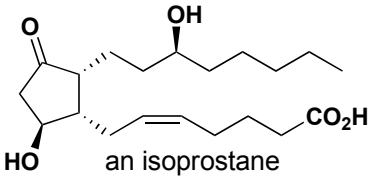
Fukuyama. *Org. Lett*. 2012, 1632



Overbred Intermediates

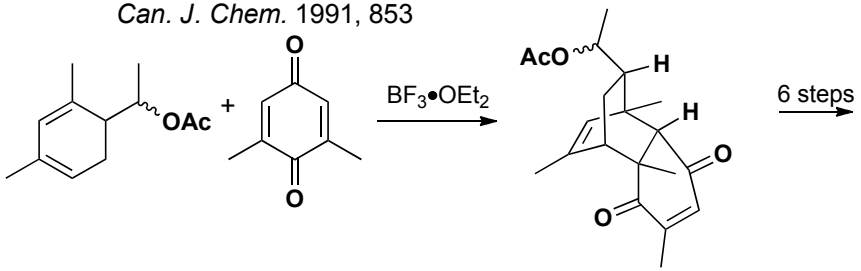
Galano. *JOC* 2010, 2411

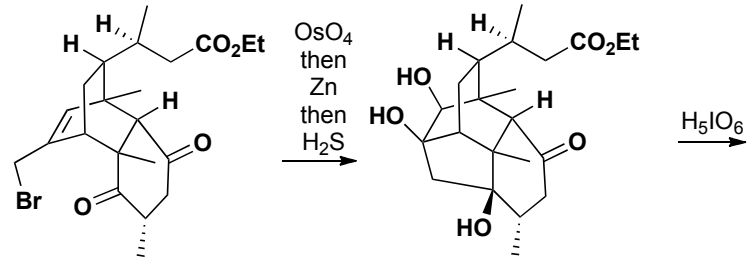


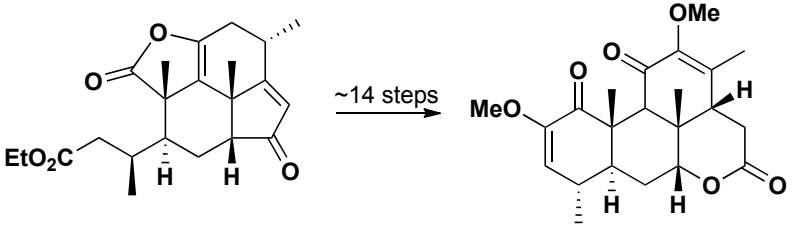


an isoprostane

Valenta. *Can. J. Chem.* 1979, 3346
Can. J. Chem. 1991, 853

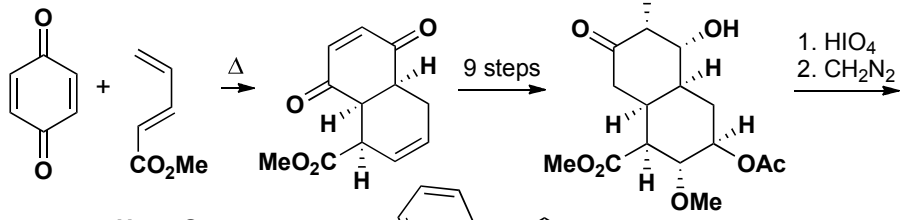


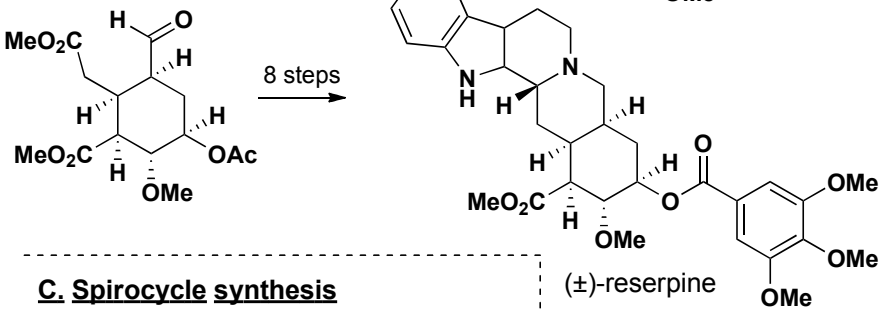




d,l-quassin

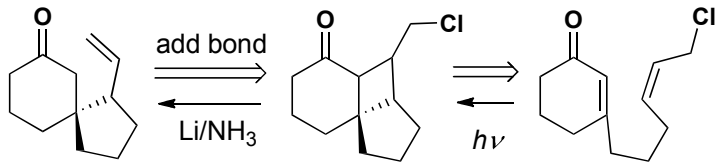
Woodward. *Tetrahedron* 1958, 1



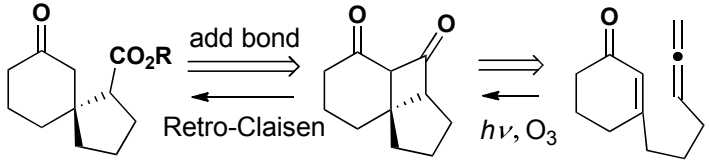


C. Spirocycle synthesis

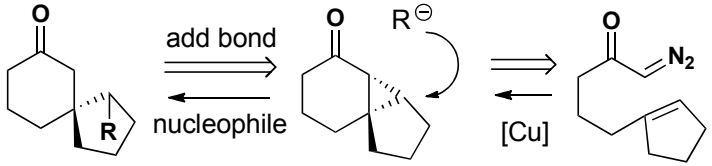
Oppolzer. *Acc. Chem. Res.* 1982, 135



Becker. *JOC* 1982, 3297

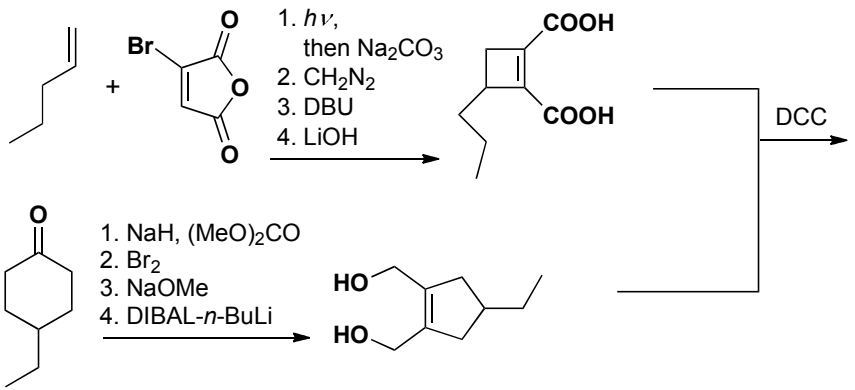


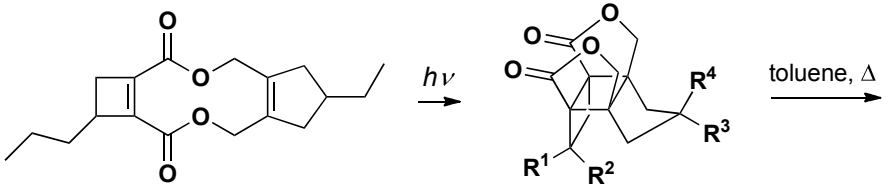
Heathcock. *Tet. Lett.* 1975, 529

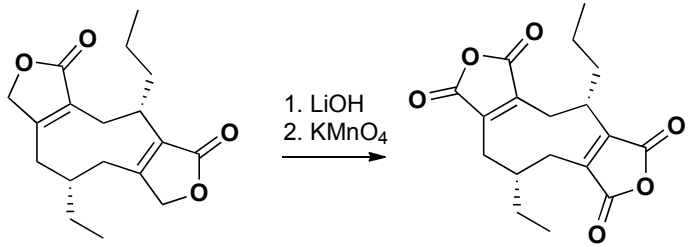


A. Olefin metathesis: [2+2]/retro [2+2]

White. *JACS* 1992, 9673



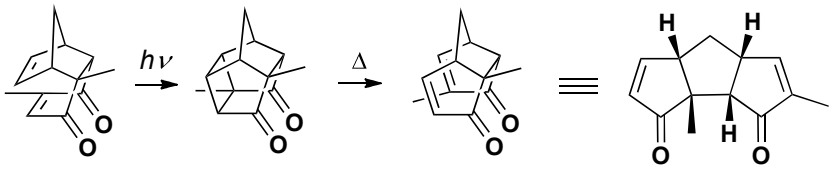


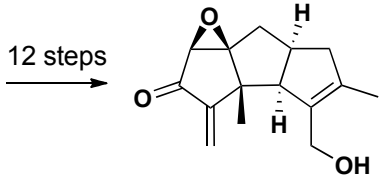


2:1 *cis*:*trans*

(±)-byssochlamic acid

Mehta. *Tet. Lett.* 2003, 5243
Tetrahedron 1981, 4543





pleurotellol