Photochemistry and Applications in Synthesis

Jason M. Rohde

September 1, 2004

Photochemistry

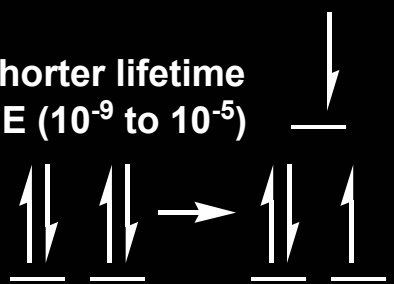
-chemical reactions initiated by light
-energy is absorbed or emitted by matter in discrete quanta called photons

$$E = h\nu = hc/\lambda$$

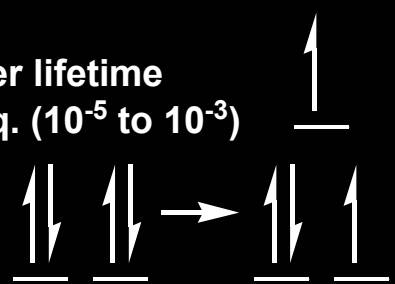
short λ light corresponds to high energy

-absorption of light leads to an electronic excitation (ground state$\rightarrow$excited state)
-promote an e^- like $n\rightarrow\pi^*$ or $\pi\rightarrow\pi^*$
-most chemistry takes place from S_1 and T_1 excited states

S_1 have a shorter lifetime and higher E (10^{-9} to 10^{-5})



T_1 have a longer lifetime b/c spin flip req. (10^{-5} to 10^{-3})



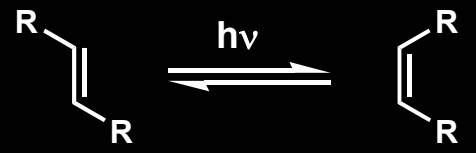
Photochemistry

-If a molecule absorbs energy, it can undergo a reaction or undergo loss of energy by two methods:

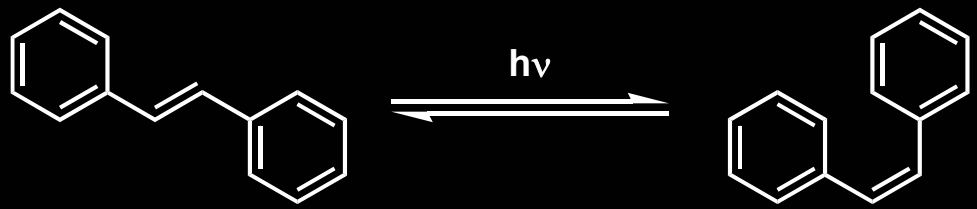
- •radiative processes-involve emission of a photon
  - -phosphorescence-relaxation to a lower state with different multiplicity, such as $T_1 \rightarrow S_0$ (spin forbidden)
  - -fluorescence-relaxation to lower state of same multiplicity, such as $S_1 \rightarrow S_0$ (spin allowed)
- •non-radiative processes-no emission
  - -internal conversion-involves no spin change, such as $S_1 \rightarrow S_0$
  - -intersystem crossing-involves change in spin multiplicity
    - •one way competes with phophorescent decay of the lowest triplet state to the ground state
    - •another way converts the lowest excited singlet state to the lowest triplet state (competes with fluorescence and IC)[gives access to triplet state]

-Excitation by E transfer is Sensitization (deactivation is Quenching)

Geometrical Isomerism

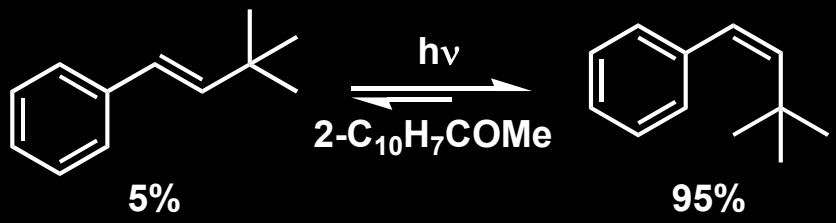


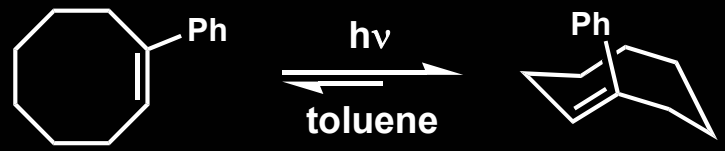
-*cis*/*trans* (*E* / *Z*) isomerism under photochemical conditions commonly leads to thermodynamically less stable*cis*-isomer
-*cis*-isomer typically absorbs at a lower λ due to decreased conjugation b/c of non-bonded interactions
-reactions come to photostationary state unless optical pumping is performed (irradiation of just 1 isomer to drive the equilibrium)

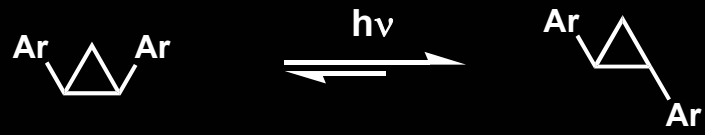


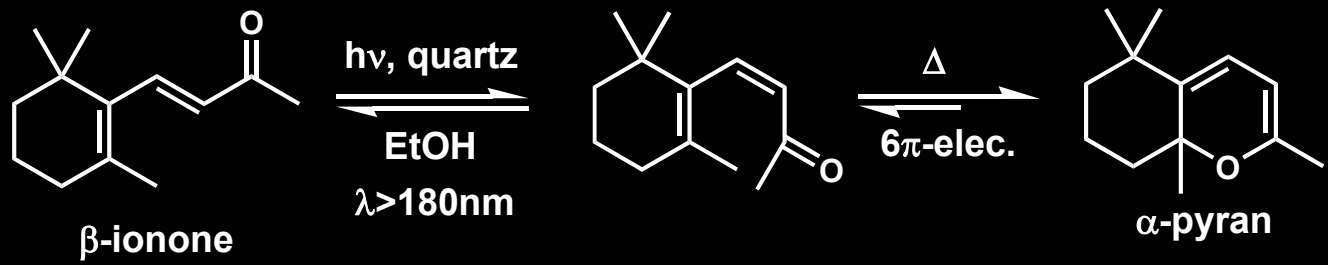
w/o sensitizer photostationary state: *E* / *Z* : 8/92
w sensitizer photostationary state: *E* / *Z* :50/50

Geometrical Isomerism



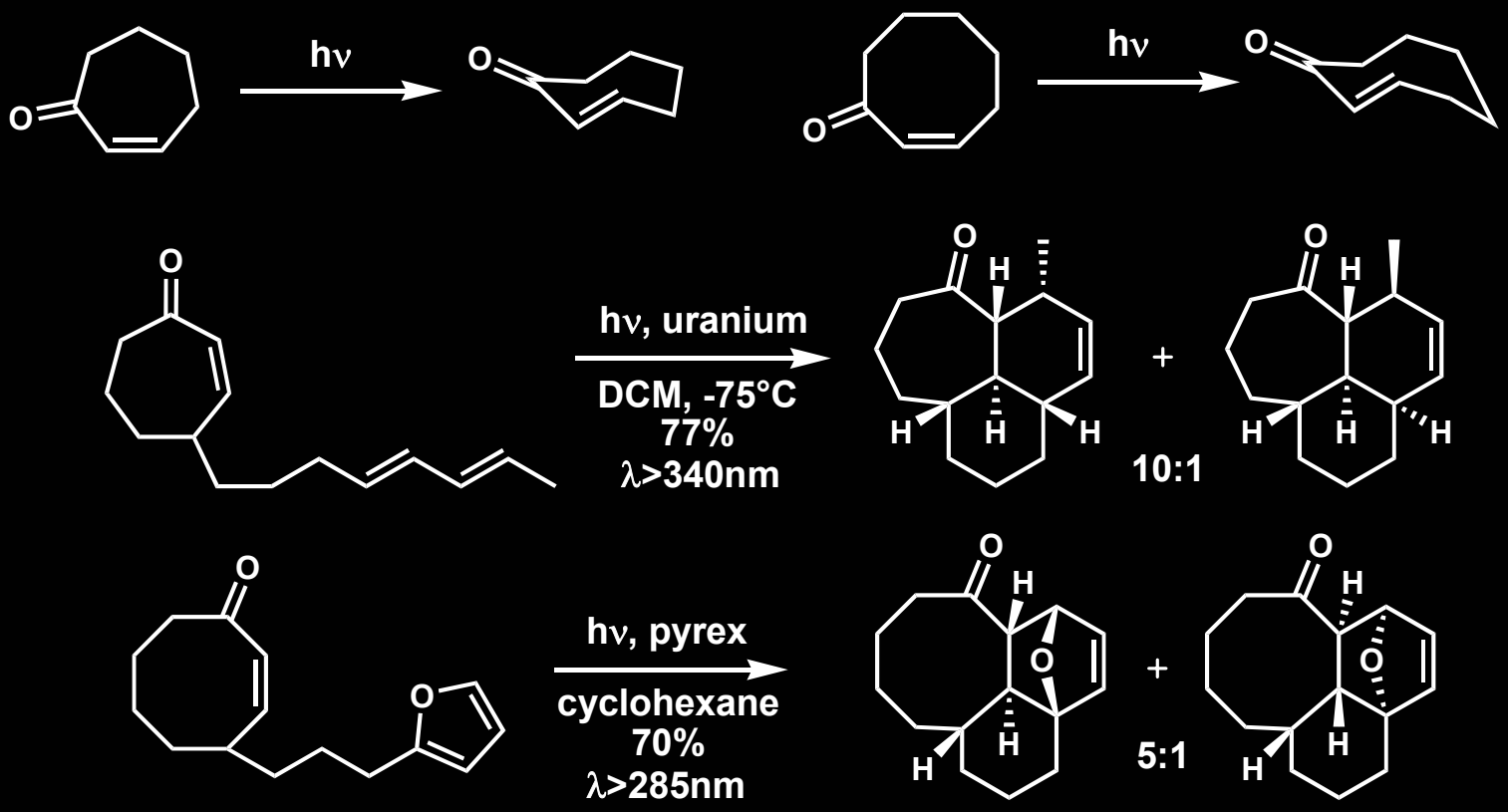






α-pyran: G. Büchi and N.C. Yang *J. Am. Chem. Soc.* **1957**, *79*, 2318.

Geometrical Isomerism



H. Dorr, V. Rawal *J. Am. Chem. Soc.* **1999**, *121*, 10229

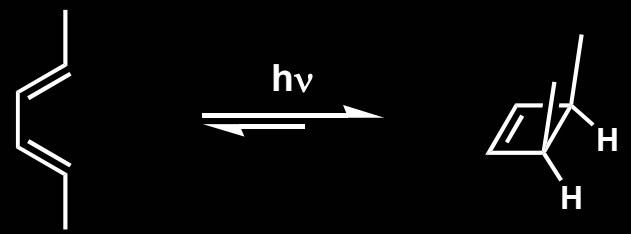
Electrocyclizations

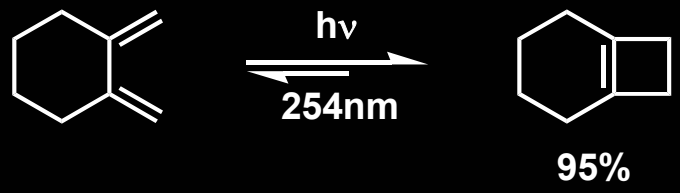
-reactions generate a new σ-bond between the termini of the conjugated π-system
-concerted process-bond breaking occurs at the same time as bond formation
-reactions also come to photostationary state based on absorption coefficient at the λ of irradiation

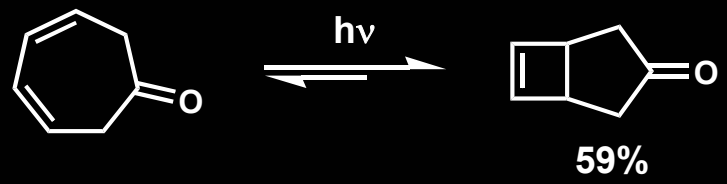
Thermal Reactions	Photochemical Reactions
-occur via HOMO	-occur via LUMO
4n - conrotatory	4n - disrotatory
4n + 2 - disrotatory	4n + 2 - conrotatory

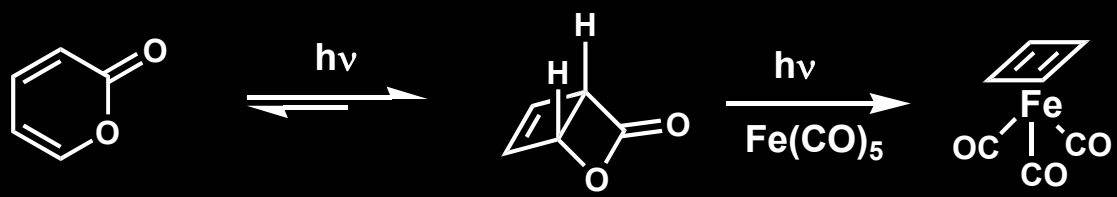
4π-Electrocyclizations

4π-electrocyclizations occur with disrotatory ring closure under photochemical conditions



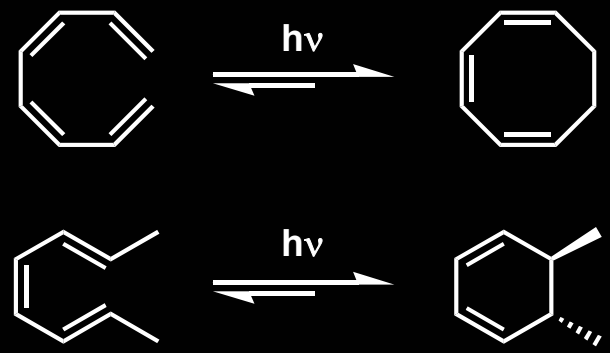


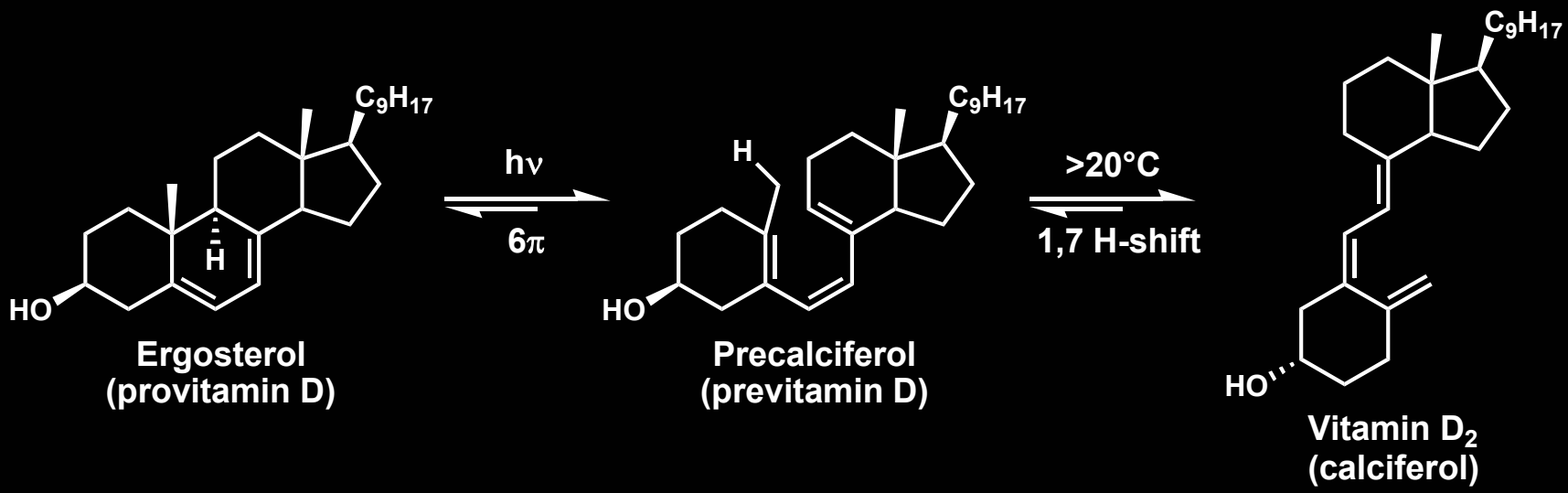




8 and 6π-Electrocyclizations

8π-electrocyclizations occur with disrotatory ring closure under photochemical conditions and 6π-systems undergo conrotatory ring closure



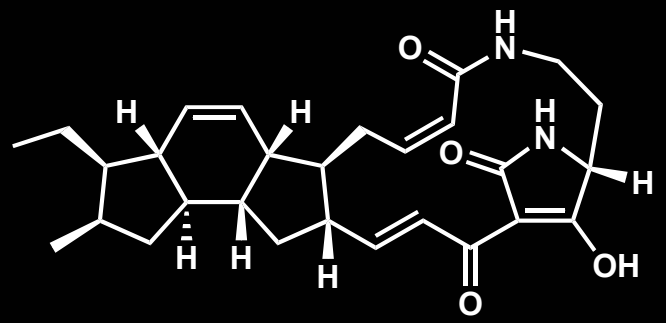


Ergosterol (provitamin D)

Precalciferol (previtamin D)

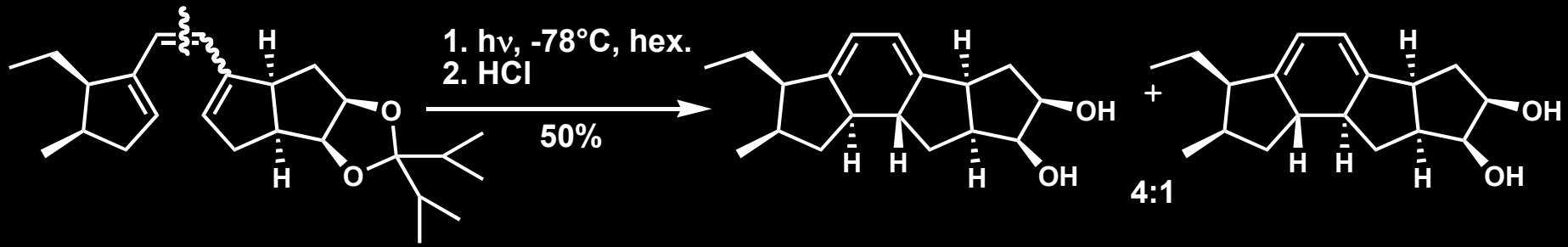
Vitamin D_2 (calciferol)

6π-Electrocyclization in Synthesis



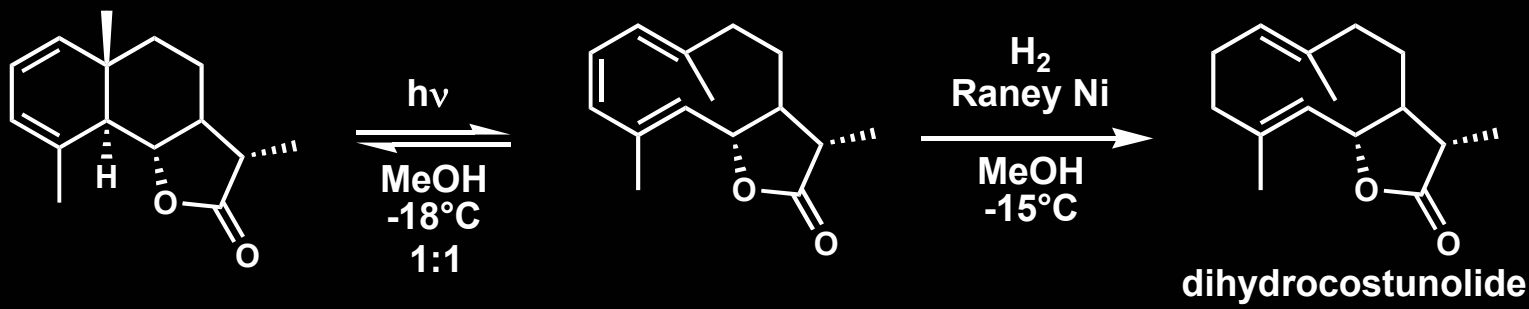
Ikarugamycin

Wittig Reaction



J. Whitesell and M. Minton *J. Am. Chem. Soc.* **1987**, *109*, 6403

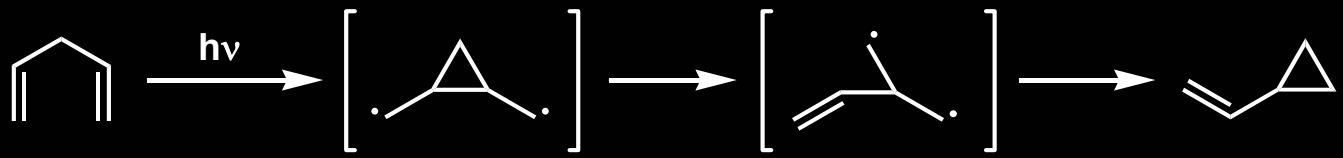
retro-6π-Electrocyclization

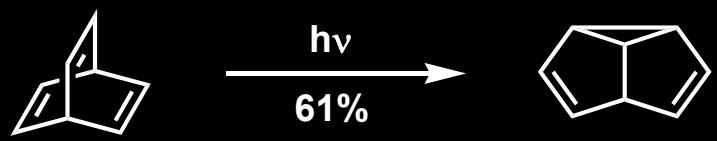


E. Corey and A. Hortmann *J. Am. Chem. Soc.* **1963**, *85*, 4033

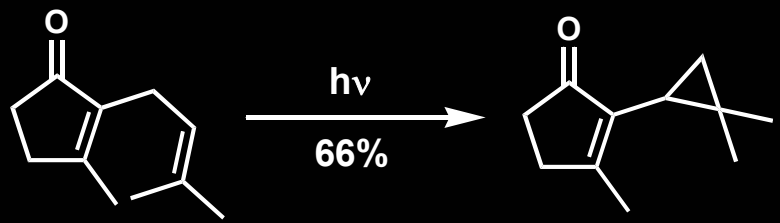
Di-π-methane rearrangement

-Howard E. Zimmerman has studied this reaction extensively
-Reaction takes 1,4-dienes or 3-phenylalkenes to vinyl or phenyl cyclopropanes

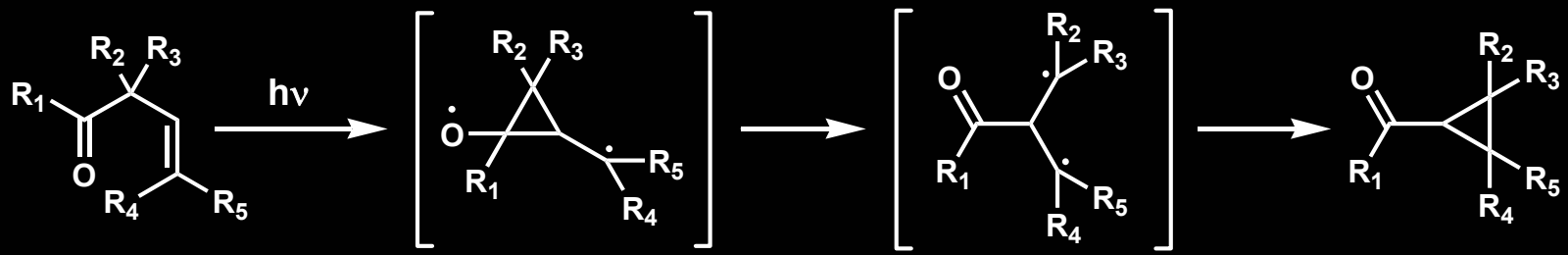


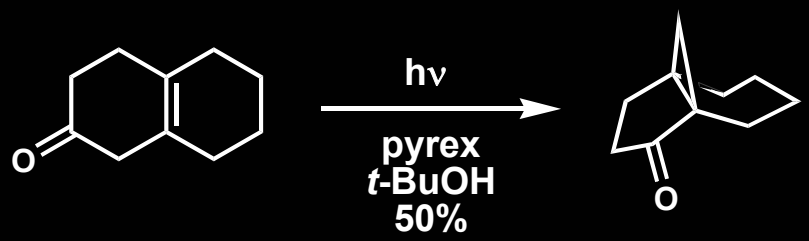


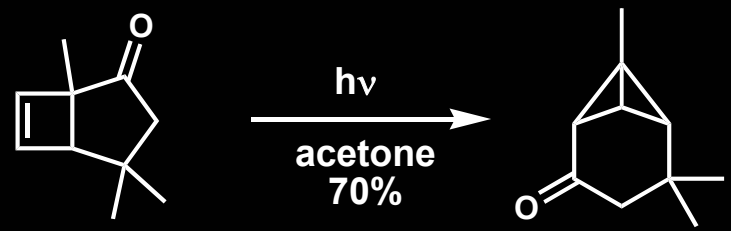
barrelene semibullvalene



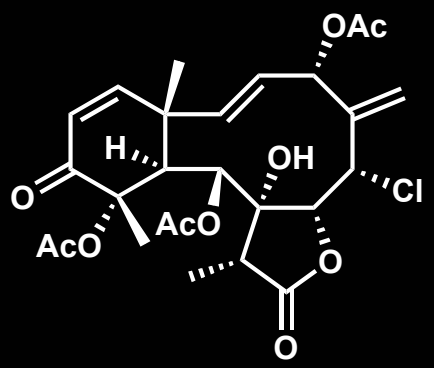
Oxa-di-π-methane rearrangement







Di-π-methane rearrangement in Natural Products

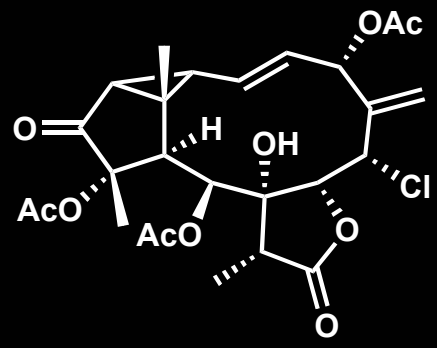


erythrolide B

hν

quartz
PhH
87% conv
in 3 hr

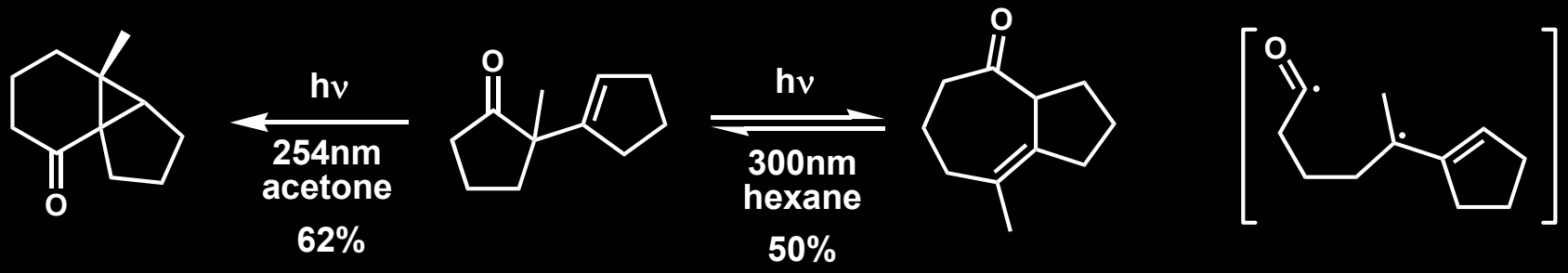
or
5% methanolic
seawater
(glass)
with
sunlight
37% conv
in 8 days

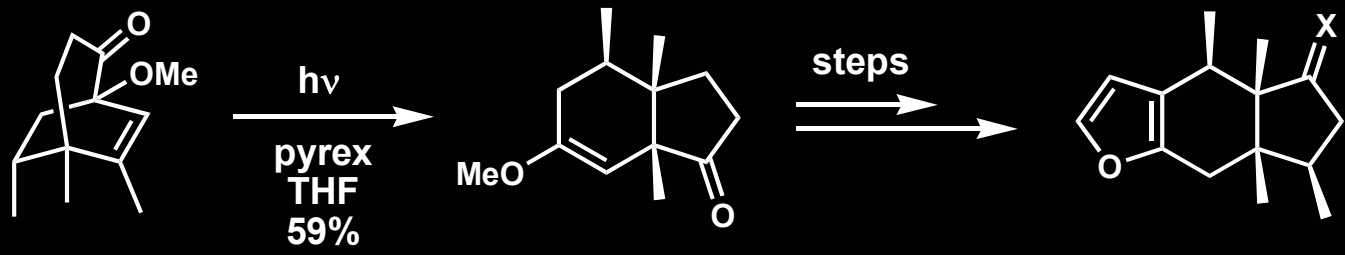


erythrolide A

S. Look, W. Fenical, D. Van Engen, J. Clardy *J. Am. Chem. Soc.* **1984**, *106*, 5026.

Oxa-di-π-methane vs. 1,3-Acyl Migration

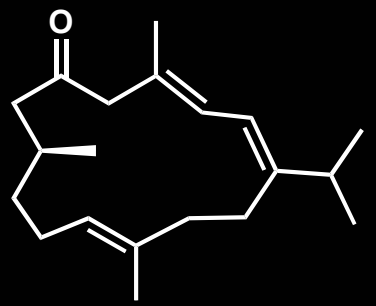




X = O pinguisone
X = H_2 deoxypinguisone

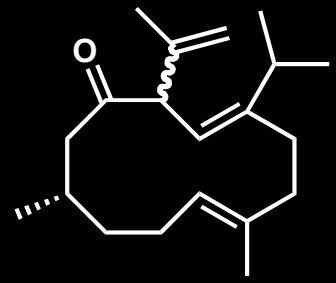
T. Uyehara, Y. Kabasawa, T. Kato *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2521

1,3-Acyl Migration in Natural Products

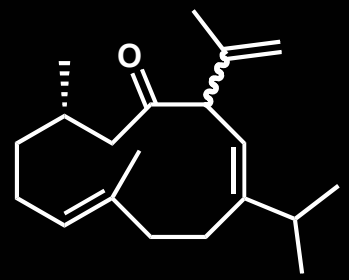


hν

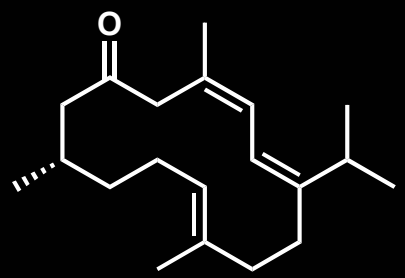
quartz
PhH
3h



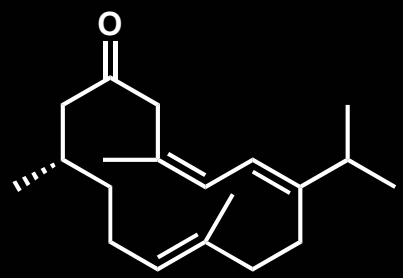
calyculone D back 8.8%
calyculone E 6.2%



calyculone F up 10.6%
calyculone G 15.9%



cembratriene 10.6%

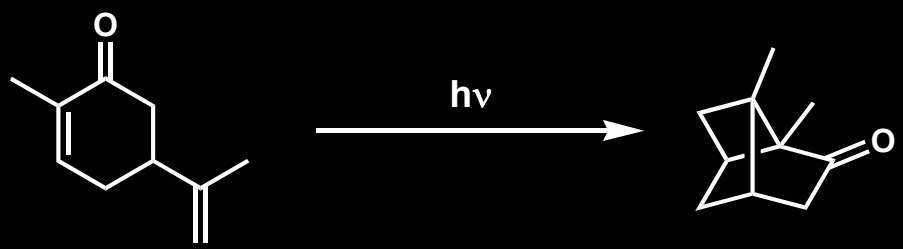


cembratriene 11.5%

J. Shin, W. Fenical *J. Org. Chem.* **1991**, *56*, 1227

[2 + 2] Cycloaddition

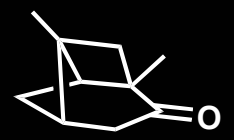
-[2+ 2] photocycloadditon is the cyclization of two olefinic units to provide a cyclobutane (generate 2 new C-C bonds and up to four new stereocenters)
-1908 Ciamician observed the first [2 + 2] reaction when exposure to Italian sunlight for 1 year generated carvone camphor from carvone



carvone

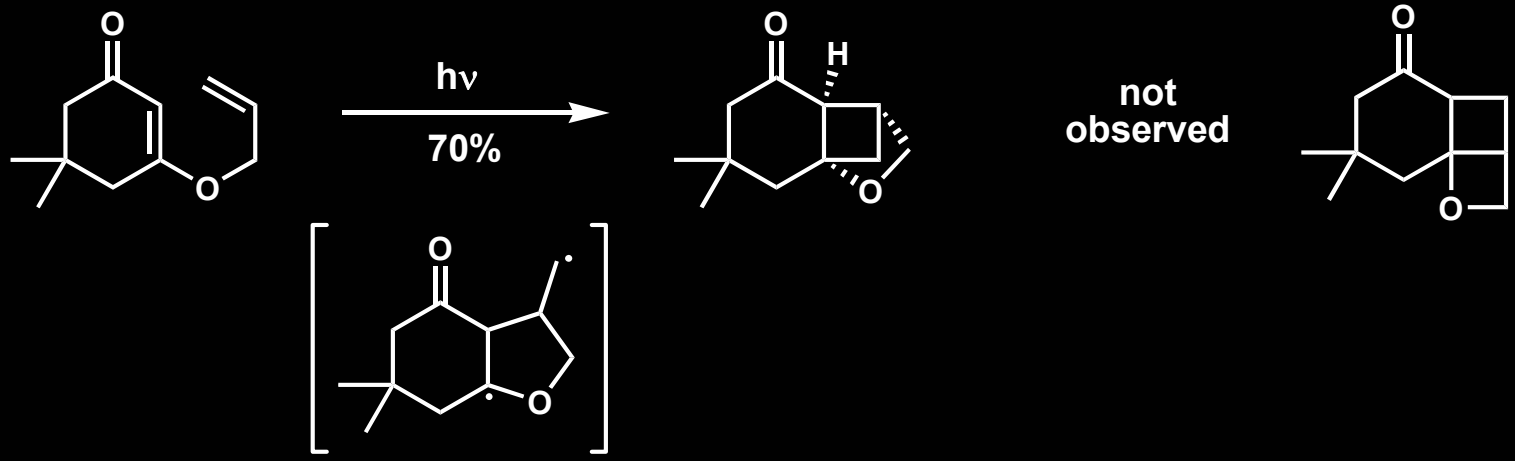
carvone camphor

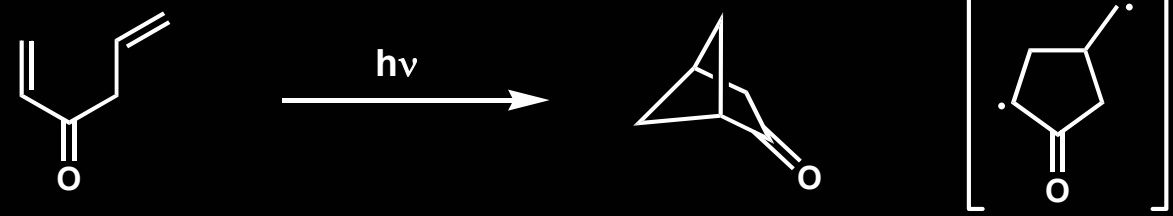
-photochemical conditions create charge like umpolung of enone (β-carbon is electron rich)
-intermolecular variants also well known, but regioselec. can be highly dependent on both olefinic partners
-this [2 + 2] follows the "rule of 5" and none of the other regioisomer is observed



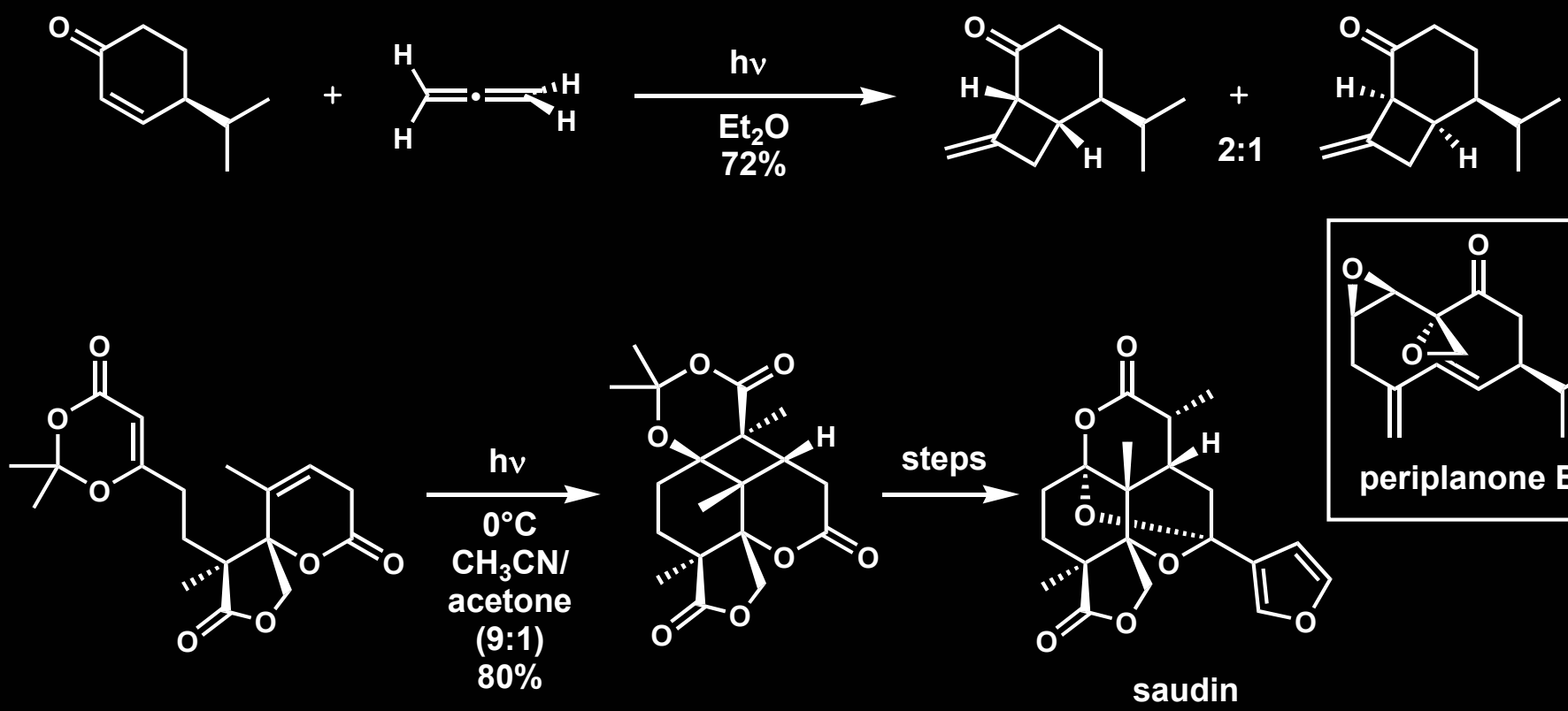
not observed

"Rule of 5"



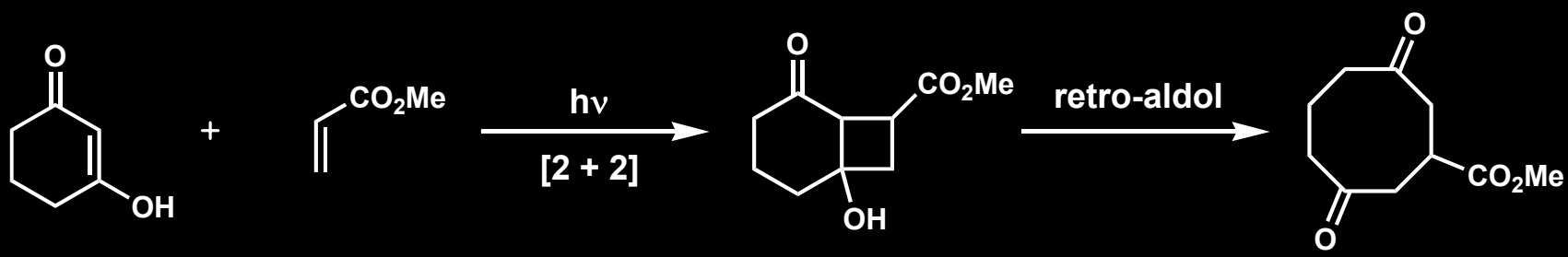


[2 + 2] Cycloaddition in Synthesis



periplanone: S. Schreiber, C. Santini *Tetrahedron Lett.* **1981**, *22*, 4651
saudin: J. Winkler, E. Doherty *J. Am Chem. Soc.* **1999**, *121*, 7425

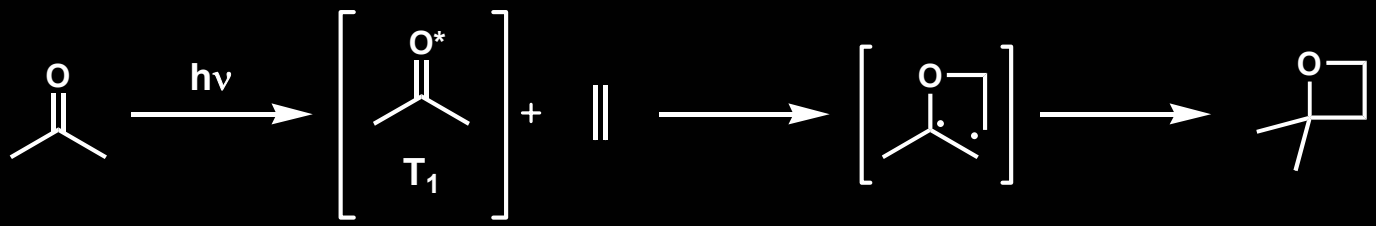
de Mayo Reaction



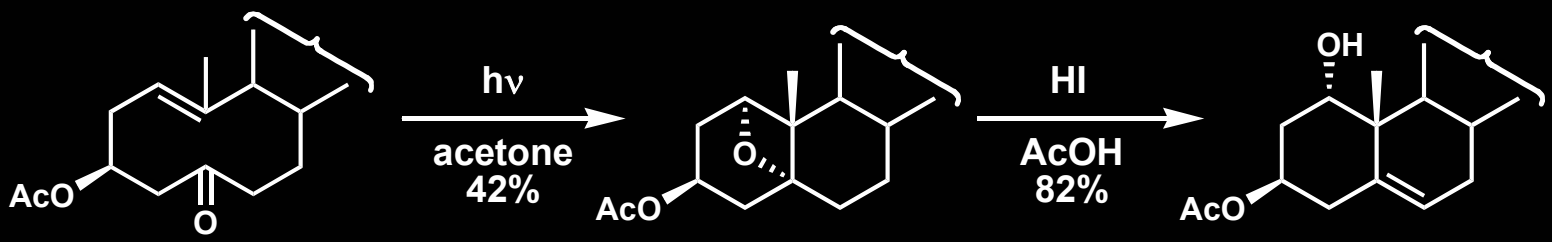
-[2 + 2] cycloaddition involving double bond of an enol and another olefin and the retro-aldol reaction

Paterno-Büchi Reaction

-Paterno and Chieffi observed the first example of a [2 + 2] cycloaddition between a carbonyl and an olefin to make an oxetane

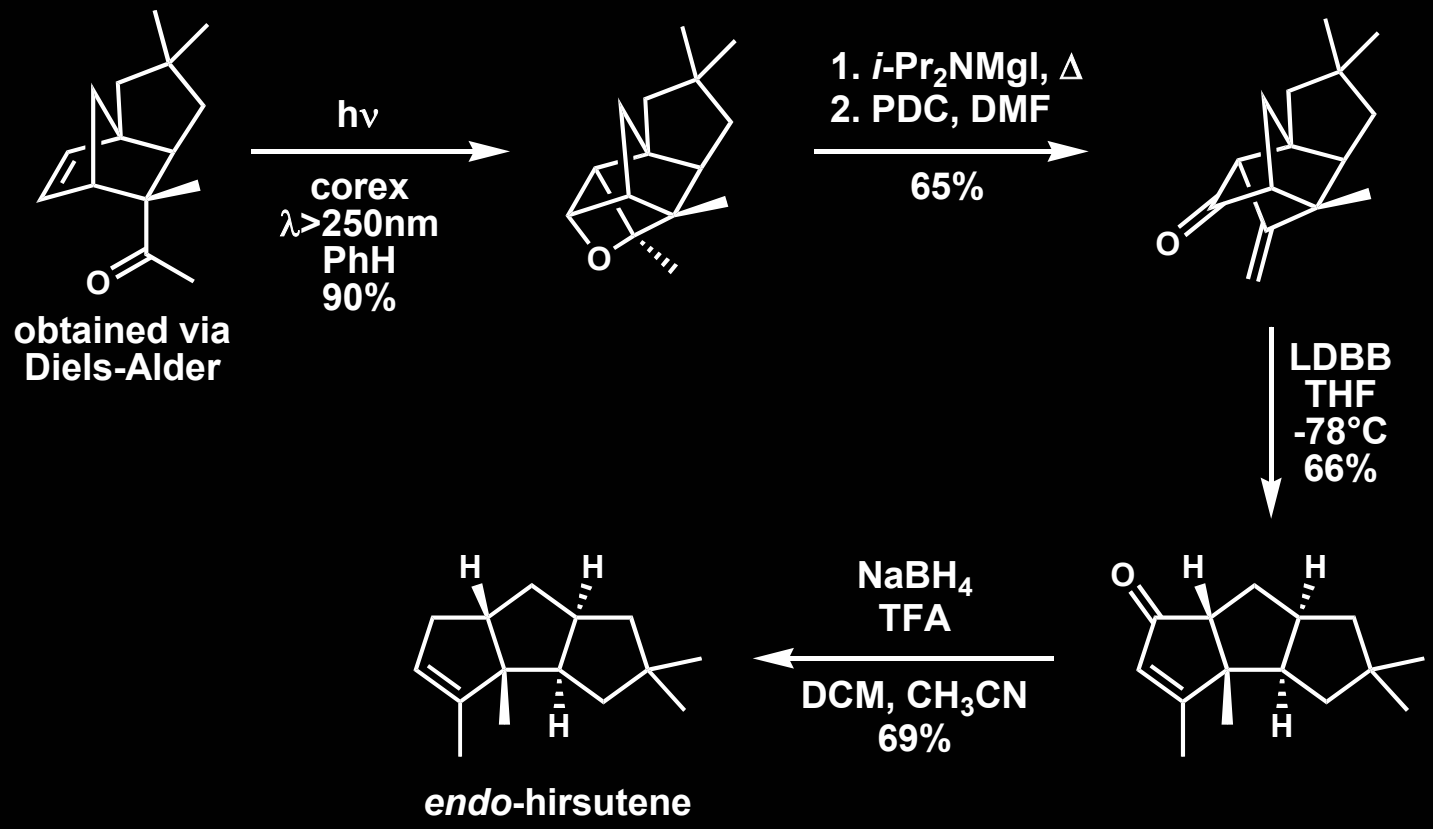


-many examples of intermolecular reaction, but regioselectivity and product distributions are highly case dependent
-many synthetic examples of intramolecular variant



vitamin D_3 analogs: M. Mihailovic, L. Lorenc, V. Pauolvic, J. Kalvoda *Tetrahedron* **1977**, *33*, 441

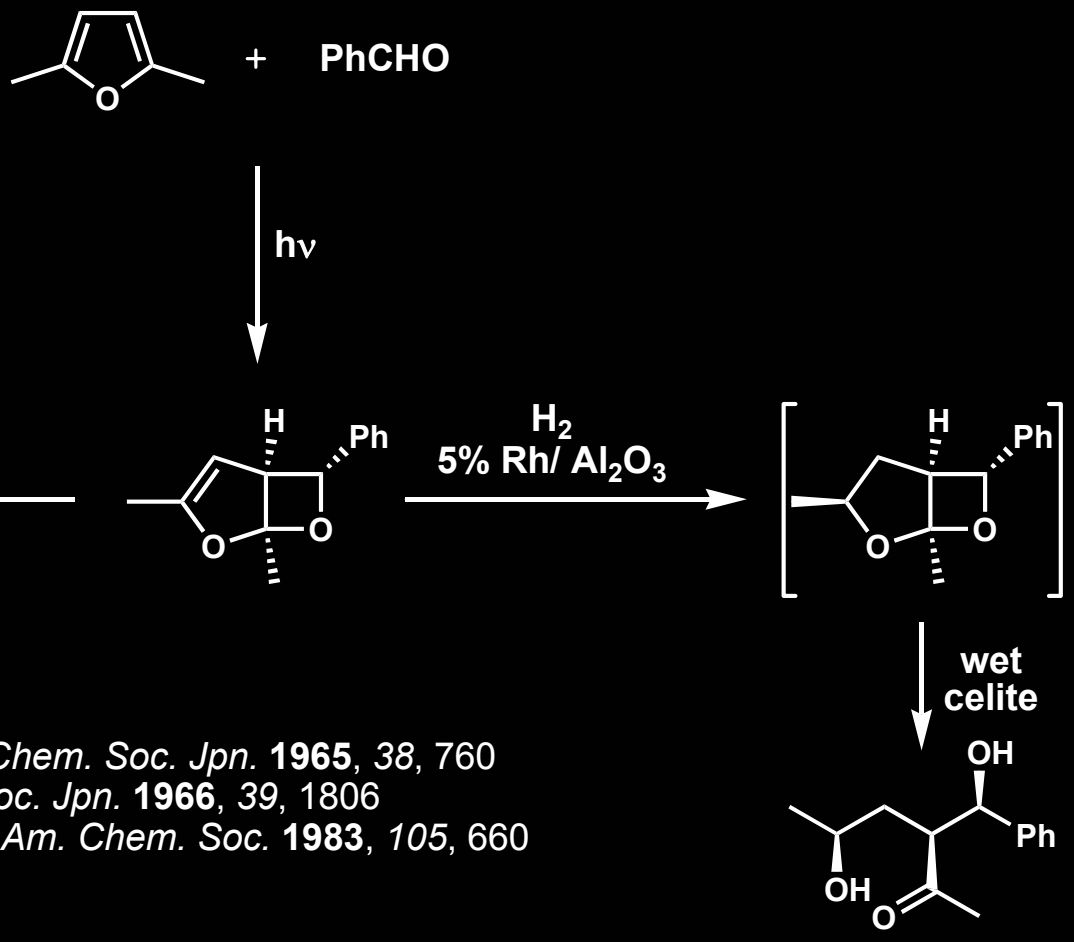
Paterno-Büchi Reaction in Synthesis



V. Rawal, A. Fabré, S. Iwasa *Tetrahedron Letters* **1995**, *36*, 6851

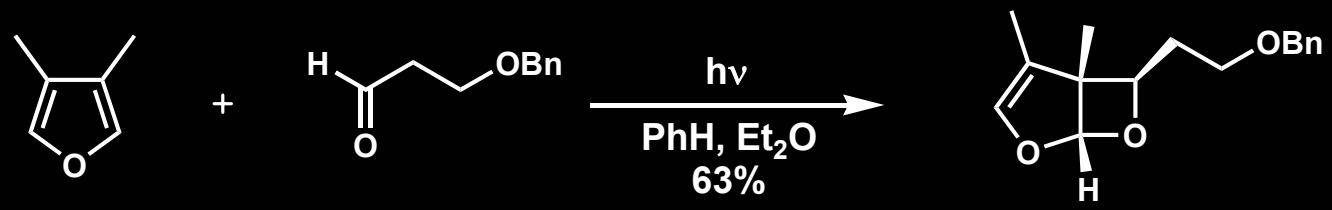
Furan-Carbonyl Variant of the Paterno-Büchi Reaction

-this variant of the [2 + 2] offers a photochemical variant of the aldol reaction through transformations of the photoadduct

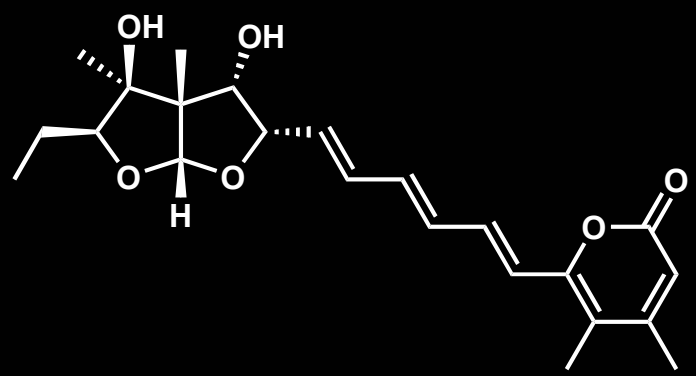


S. Toki, K. Shima, H. Sakurai *Bull. Chem. Soc. Jpn.* **1965**, *38*, 760
K. Shima, H. Sakurai *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1806
S. Schreiber, A. Hoyveda, H. Wu *J. Am. Chem. Soc.* **1983**, *105*, 660

Furan-Carbonyl Variant of the Paterno-Büchi Reaction



establishes 2 sterocenters present in asteltoxin (architecture used to install remaining stereocenters in next few steps)



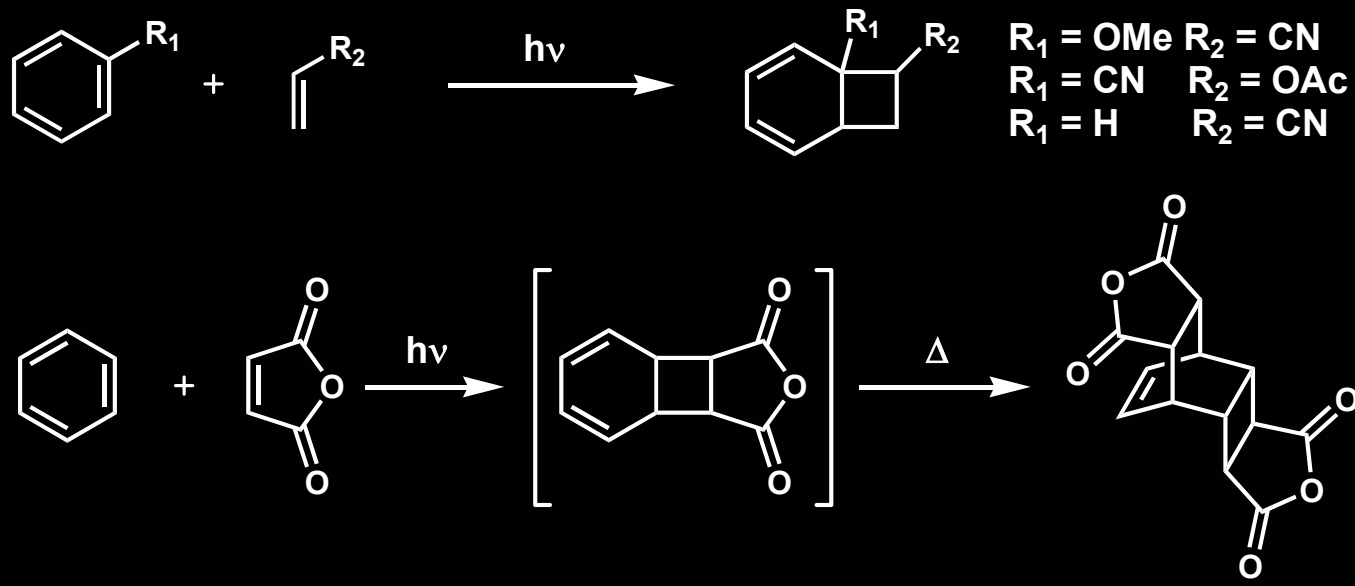
asteltoxin

S. Schreiber, K. Satake *J. Am. Chem. Soc.* **1983**, *105*, 6723
S. Schreiber, K. Satake *J. Am. Chem. Soc.* **1984**, *106*, 4186

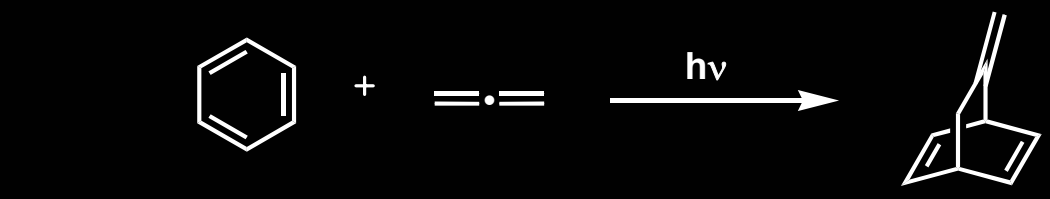
Arene-Olefin Cycloadditions

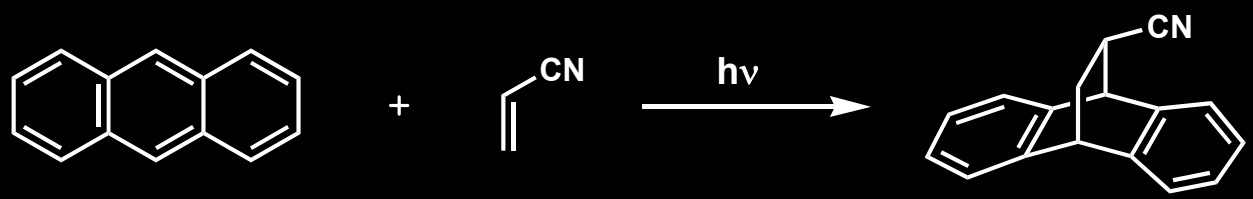
-cycloadditions between arenes and an olefin
- •ortho cycloadditions-[2 + 2]
- •para cycloadditions-[4 + 2]
- •meta cycloadditions-[3 + 2]

ORTHO CYCLOADDITIONS



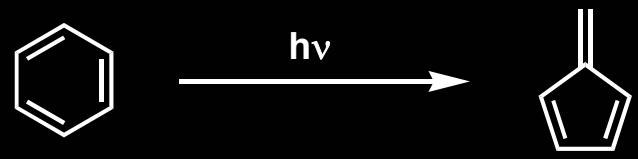
Para Cycloadditions



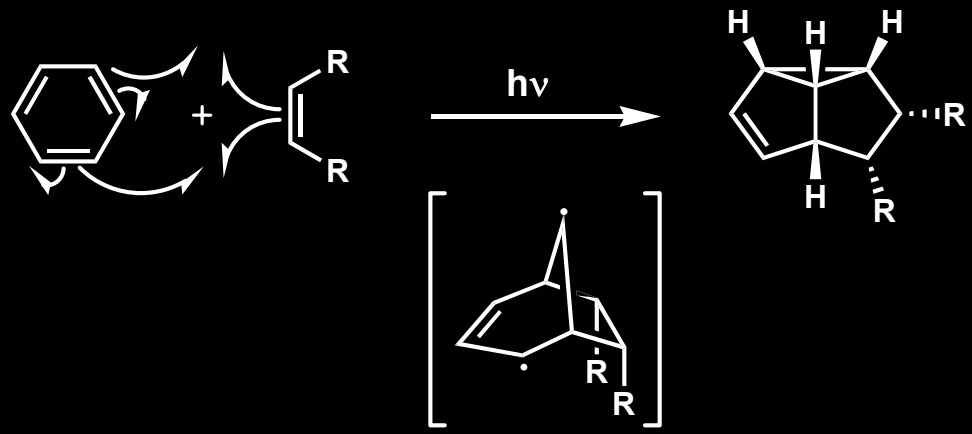


Meta Cycloadditions

Bryce-Smith and Blair dispelled the long standing myth that arenes are photochemically inert

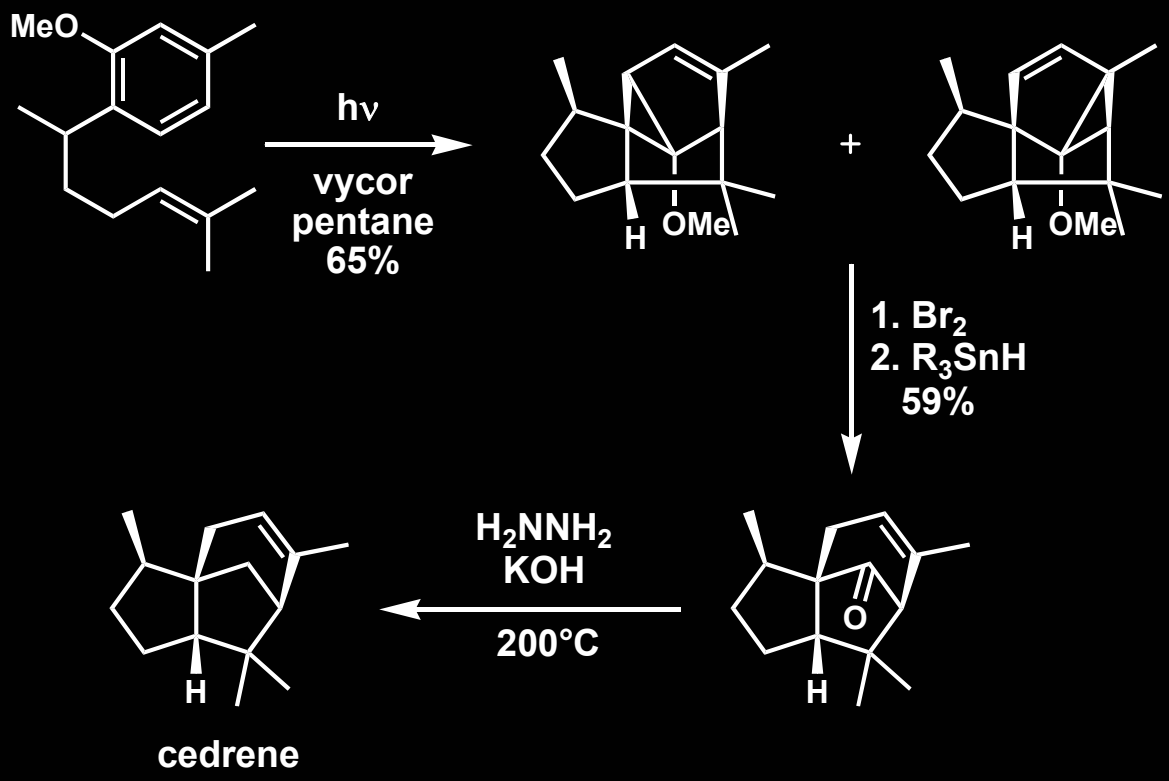


In 1966, Wilzbach and Kaplan and Bryce-Smith, Gilber and Orger codiscovered the meta arene olefin cycloaddition



Meta Cycloadditions in Synthesis

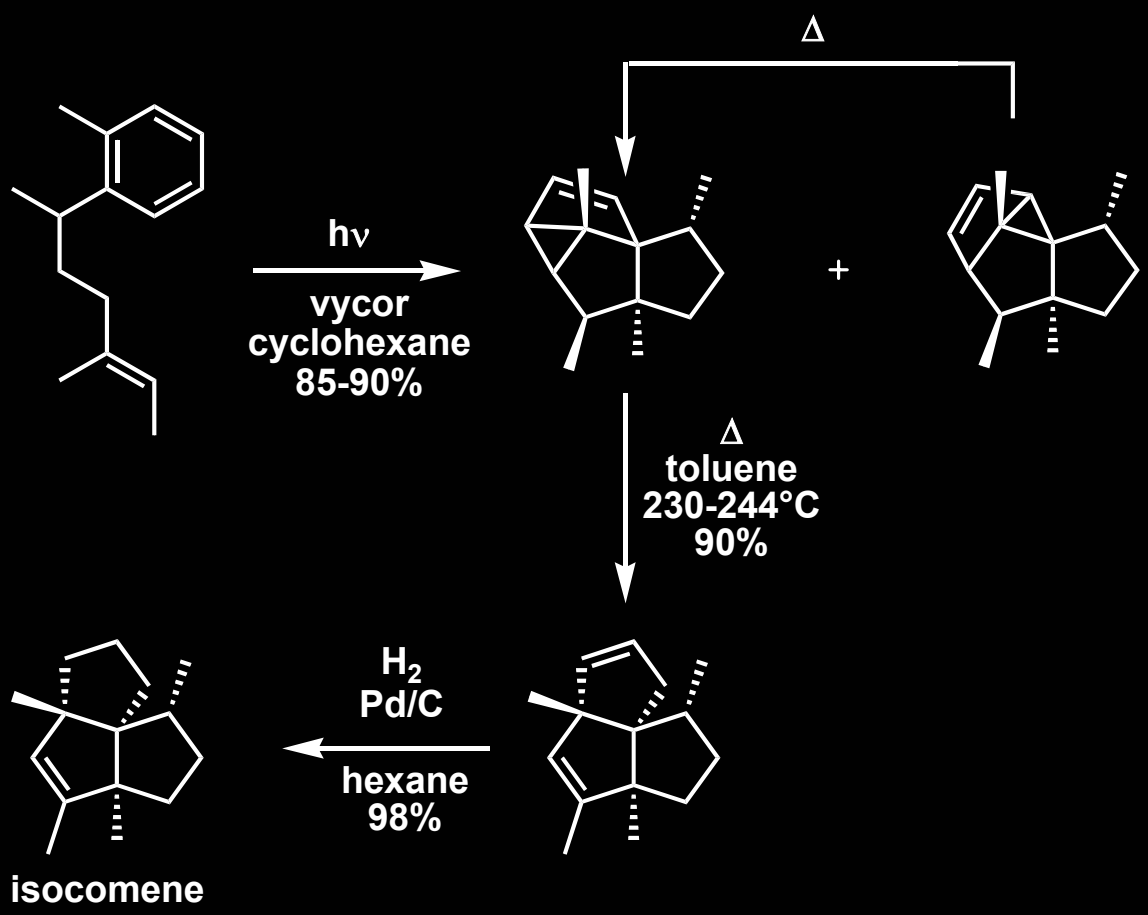
Wender pioneered the use of [3 + 2] arene/olefin cyc loadditions in synthesis



cedrene

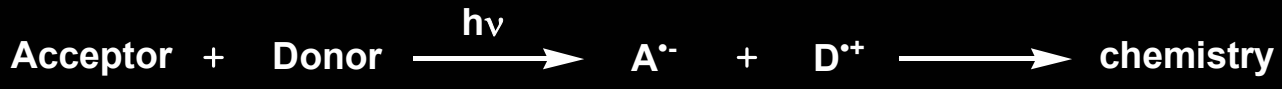
P. Wender, J. Howbert *J. Am. Chem. Soc.* **1981**, *103*, 688

Meta Cycloadditions in Synthesis



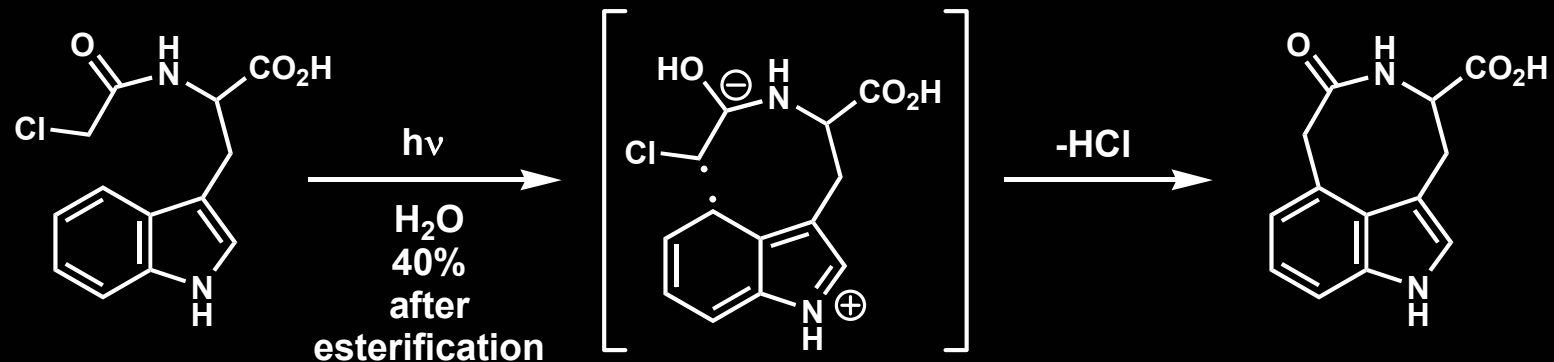
P. Wender, G. Dreyer *Tetrahedron* **1981**, *37*, 4445

Photoinduced Electron Transfer



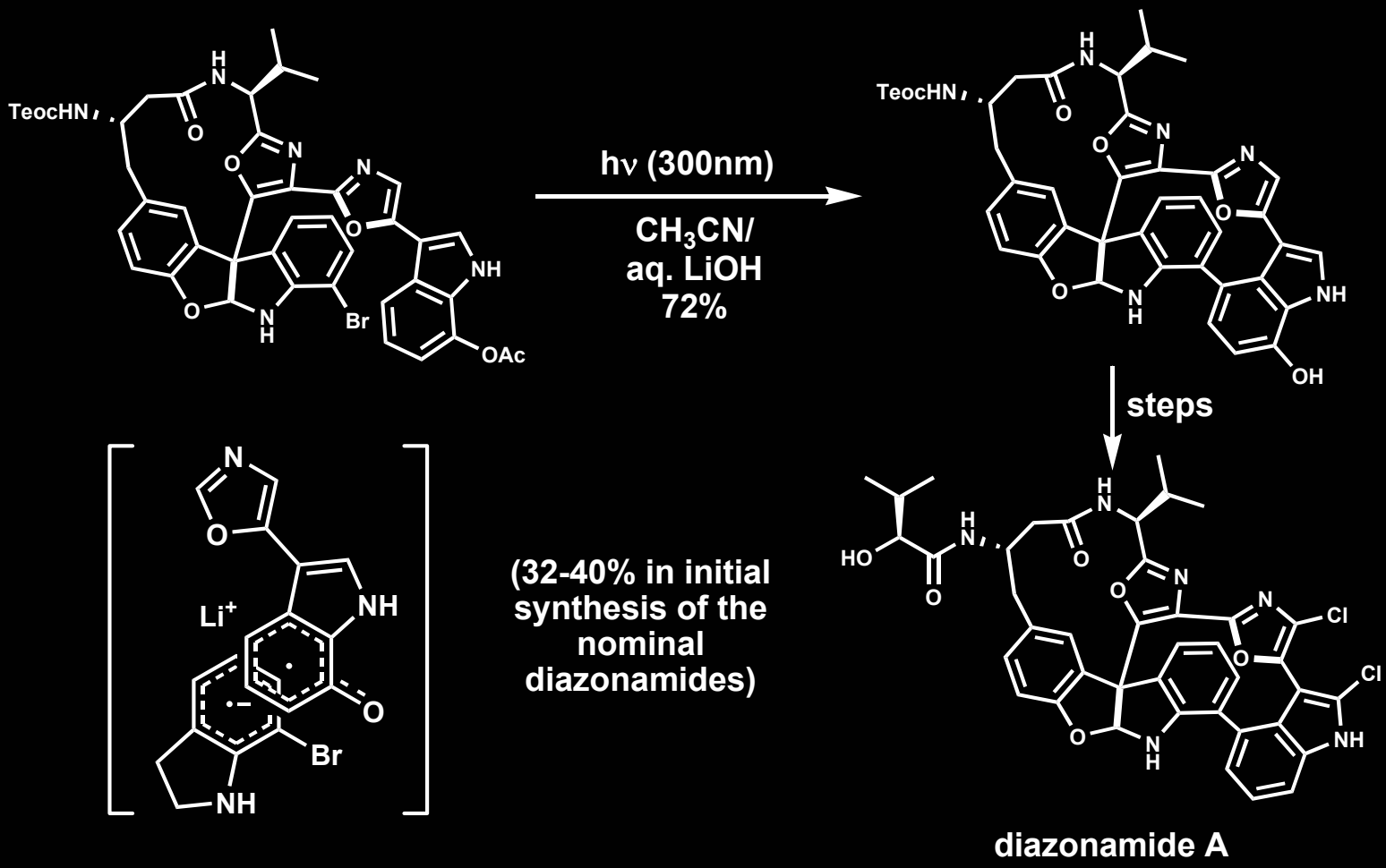
polar solvents facilitate the generation of radical ions and subsequent chemical reactions

Witkop Cyclization



O. Yonemitsu, P. Cerutti, B. Witkop *J. Am. Chem. Soc.* **1966**, *88*, 3941

Witkop Cyclization in Synthesis

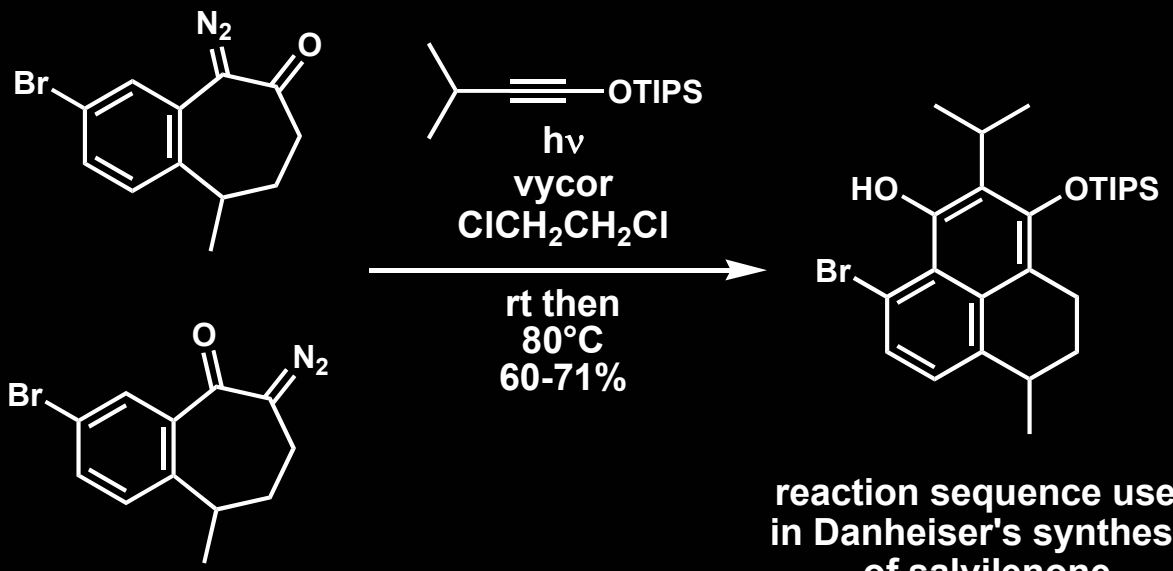


A. Burgett, Q. Li, Q. Wei, P. Harran *Angew. Chem. Int. Ed.* **2003**, *42*, 4961

Additional Photochemical Reactions

-Norrish Type I and II (α-cleavage of carbonyl and H-abstraction and fragmentation)
-nitrogen extrusion (generate carbenes such as the Wolff rearrangment or to give diradical)
-sigmatropic rearrangements such as (1,3), (1,5), and (1,7)
-^{1}O reactions
-deprotections (such as cleavage of nitroarenes)
-many other PET reactions
- •isomerizations
- •rearrangements
- •fragmentations
- •arene substitutions and reductions
- •photooxygenations
- •and many more reactions

Problem 1 (Were you paying attention to the last slide?)

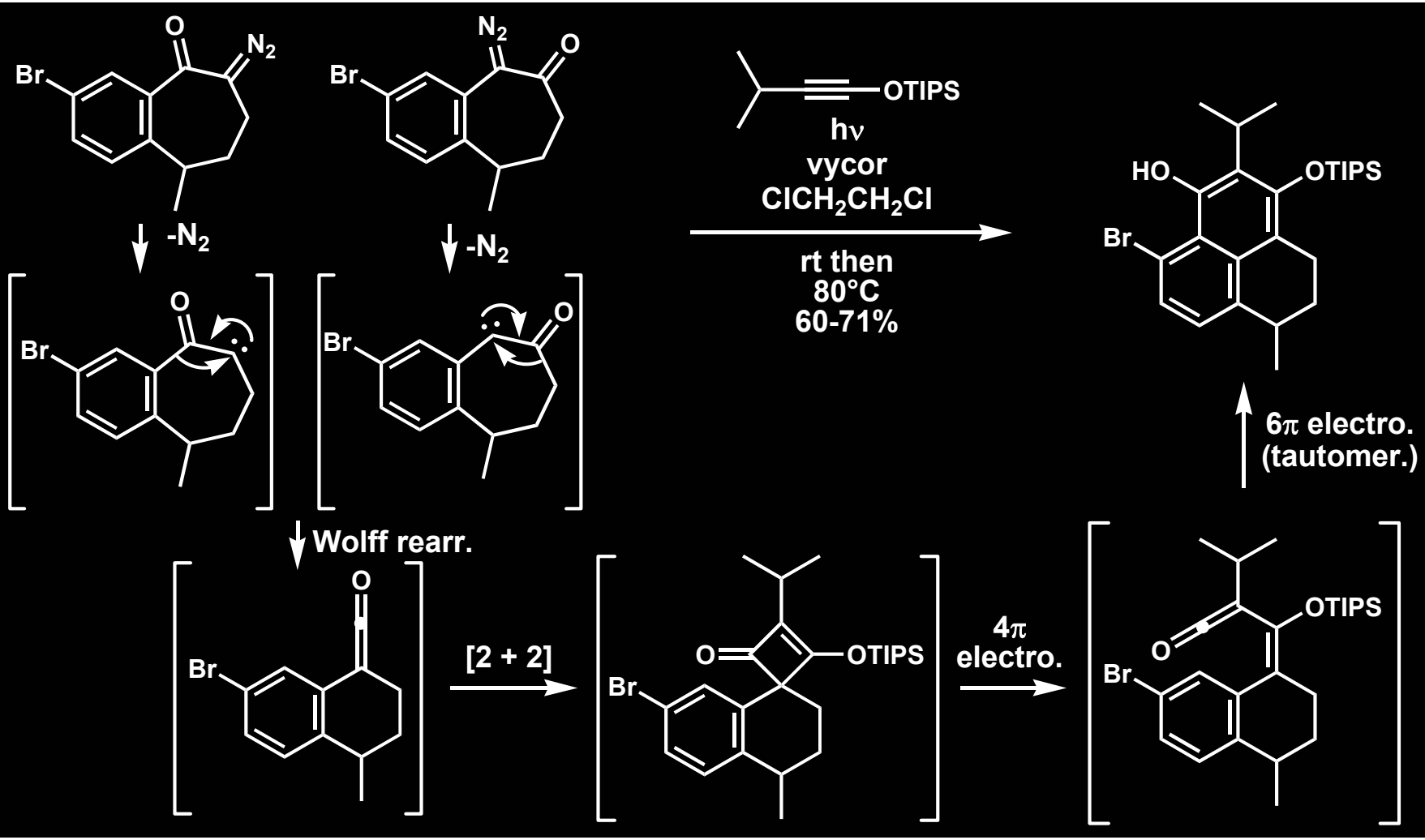


either substrate can be used to generate the product and both give essentially the same yield of tricycle

reaction sequence used in Danheiser's synthesis of salvilenone

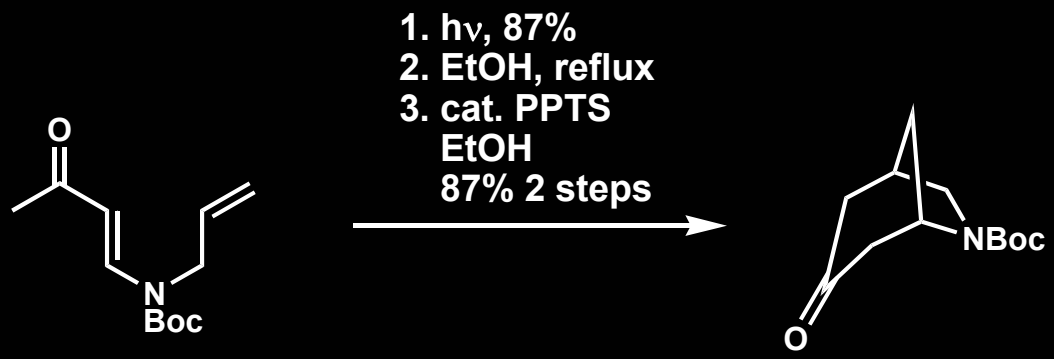
R. Danheiser, A. Helgason *J. Am. Chem. Soc.* **1994**, *116*, 9471

Problem 1 Solution



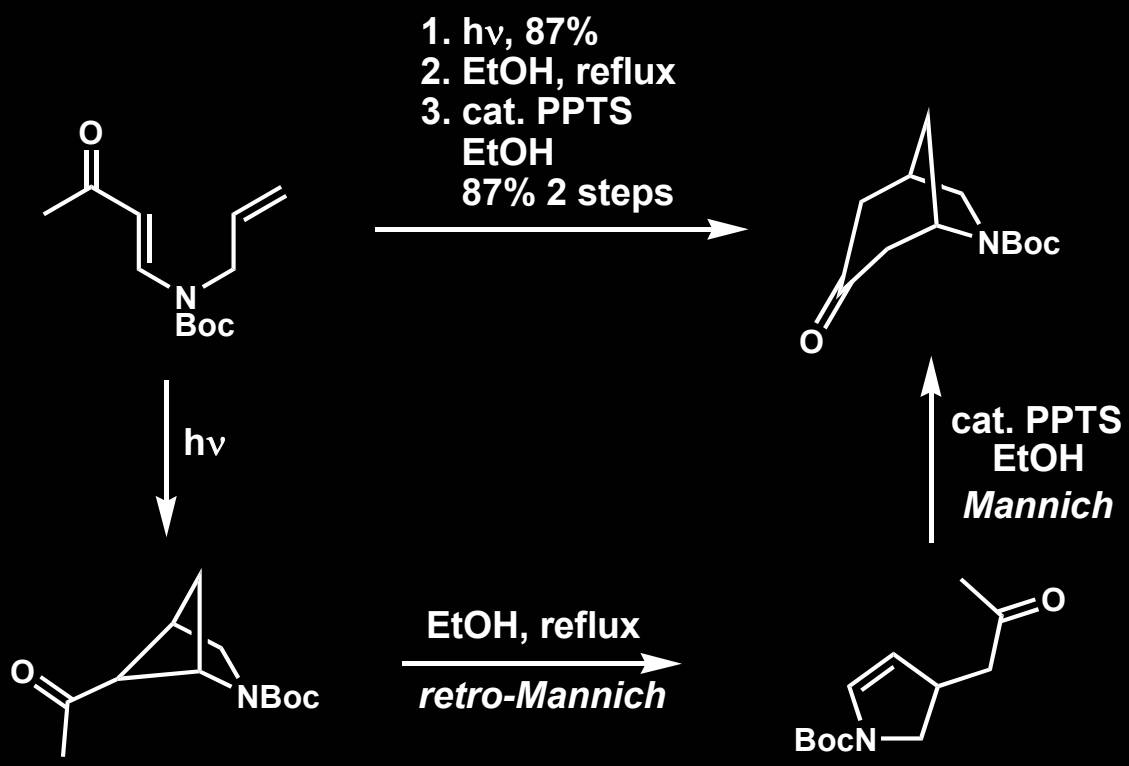
R. Danheiser, A. Helgason *J. Am. Chem. Soc.* **1994**, *116*, 9471

Problem 2



Y. Kwak, J. Winkler *J. Am. Chem. Soc.* **2001**, *123*, 7429

Problem 2 Solution



Y. Kwak, J. Winkler *J. Am. Chem. Soc.* **2001**, *123*, 7429