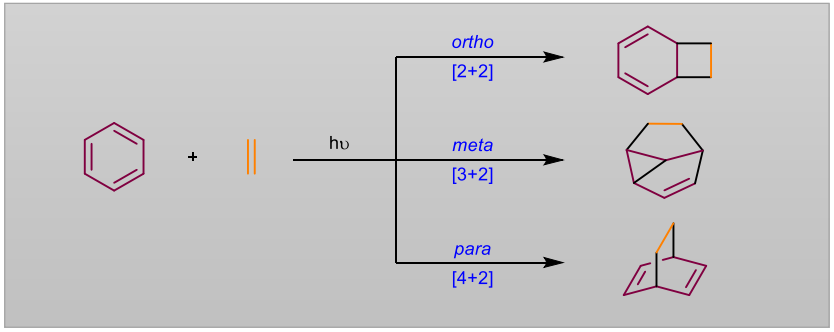
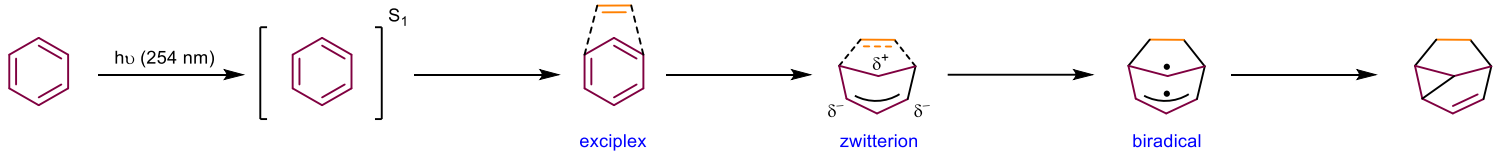
meta-Photocycloaddition



- The *meta*-photocycloaddition was first reported in 1966 by Wilzbach and Kaplan.
- 3 Sigma bonds and up to 6 stereocenters are formed in the reaction.
- The intramolecular version has been extensively used in total synthesis (mostly by Wender).

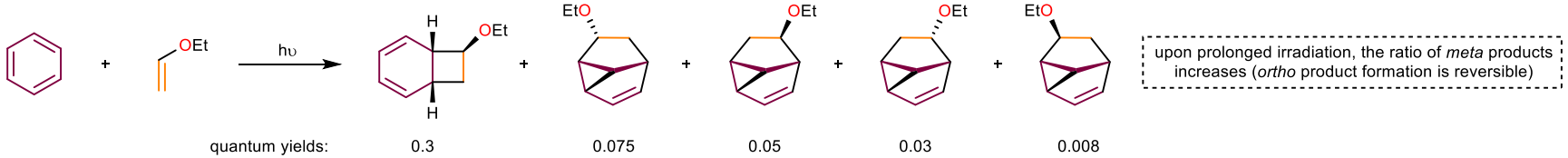
Cornelisse, J. *Chem. Rev.* **1993**, *93*, 615 https://doi.org/10.1021/cr00018a002
Bochet, C. G. *Beilstein, J. Org. Chem.* **2011**, *7*, 525 https://doi.org/10.3762/bjoc.7.61
Bochet, C. G. *Chem. Rev.* **2016**, *116*, 9816 https://doi.org/10.1021/acs.chemrev.6b00005
Stephenson, C. *Chem. Rev.* **2016**, *116*, 9683 https://doi.org/10.1021/acs.chemrev.5b00760

Mechanism:



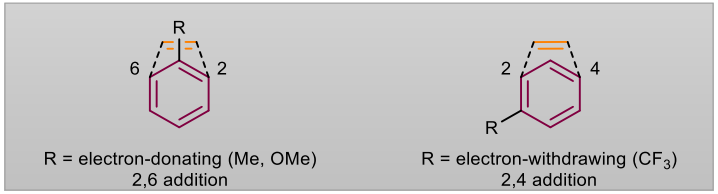
Selectivity:

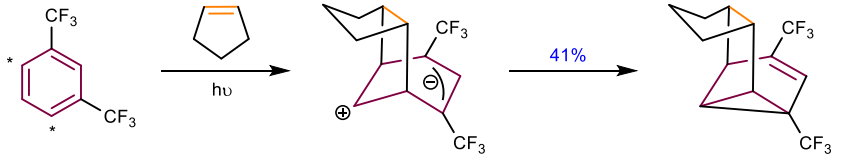
- Intermolecular photocycloaddition shows lack of selectivity:



Taylor, G. N. J. *Chem. Soc. Perkin. Trans. 1*, ***1980***, 869 https://doi.org/10.1039/P19800000869

- Regioselectivity is influenced by electronic properties of the substituents on the aromatic ring, based on stabilization of the zwitterionic intermediate:

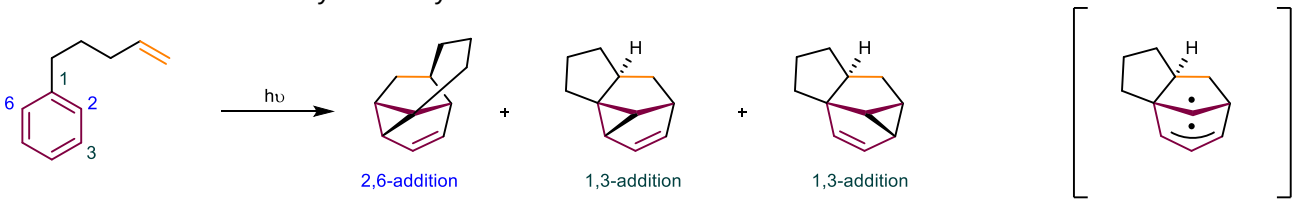




Mattay, G. *J. Chem. Soc. Perkin. Trans. 1* **1987**, 2333 https://doi.org/10.1039/P19870002333

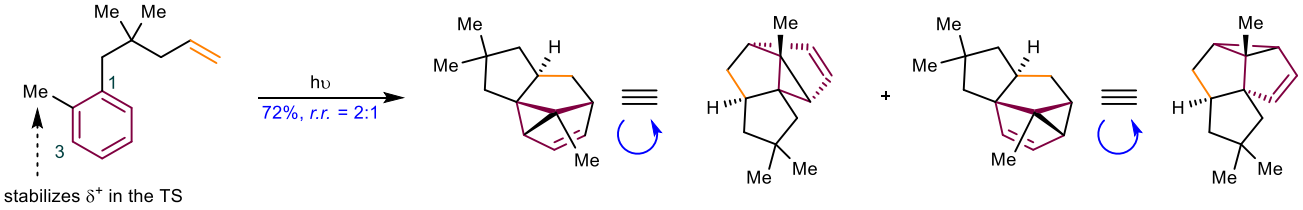
meta-Photocycloaddition

- The intramolecular variation is much more synthetically useful. It is most efficient when the tether contains three atoms.



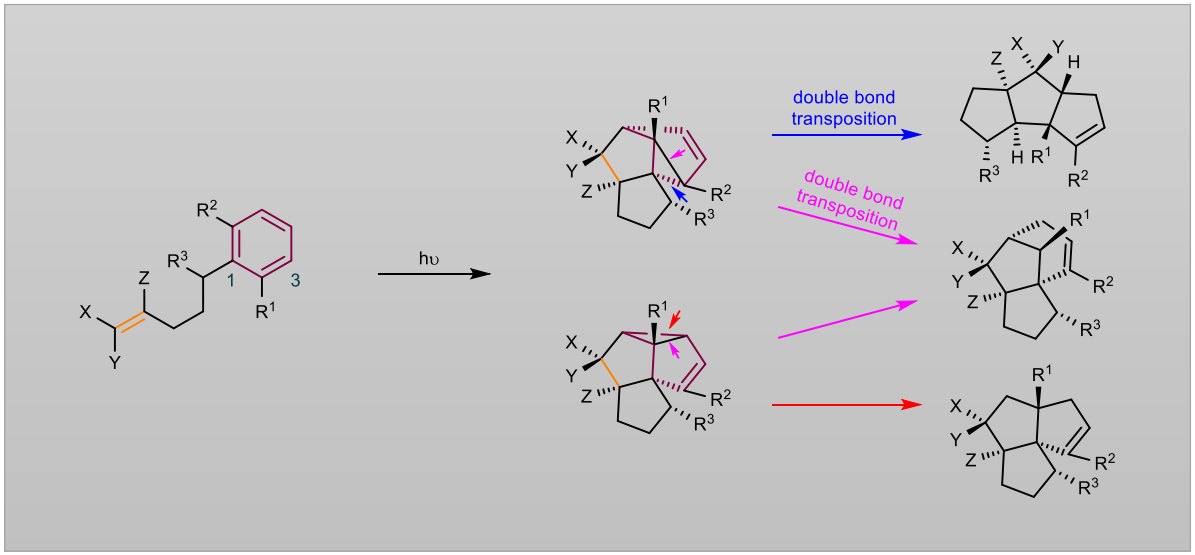
Taylor, G. N. *J. Chem. Soc. Chem. Commun.* **1979**, 229 https://doi.org/10.1039/C39790000229

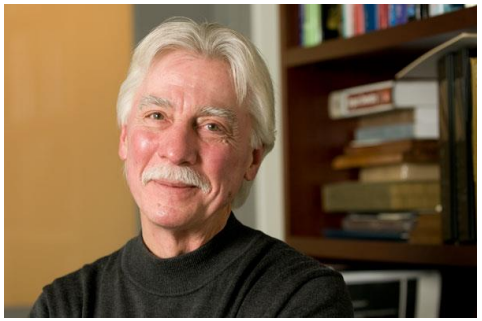
- 1,3 Addition is favored over 2,6 addition when the aromatic ring contains two substituents in the *ortho* position, due to sterics:



Julliard. M. *J. Org. Chem.* **1996**, *61*, 3576 https://doi.org/10.1021/jo960382k

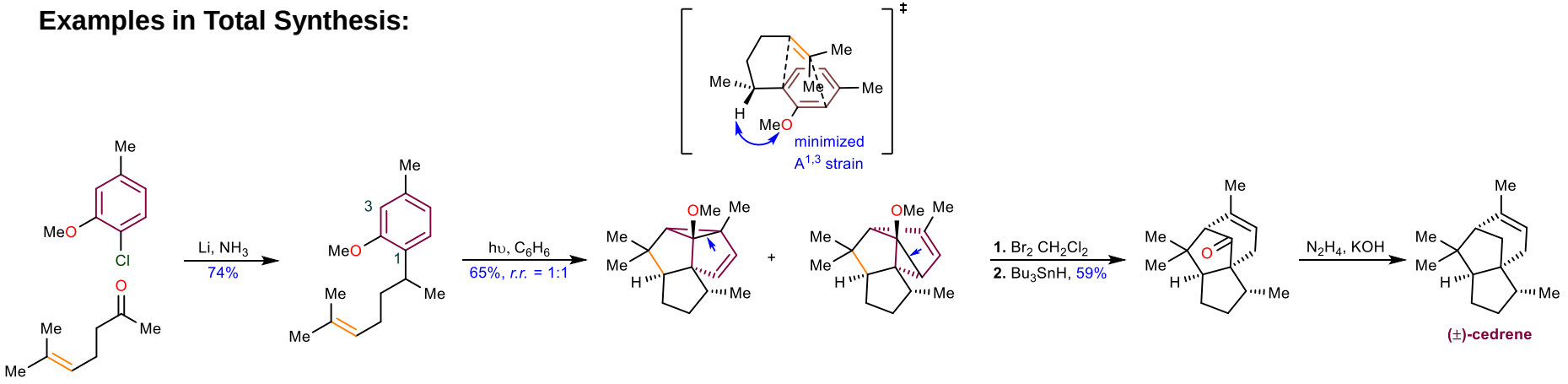
- Different polycyclic ring systems can be accessed through fragmentation of the cyclopropane obtained from a 1,3 addition:



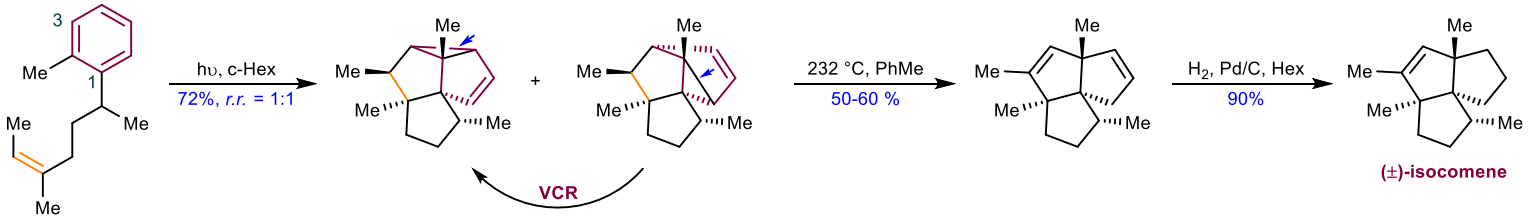


meta-Photocycloaddition

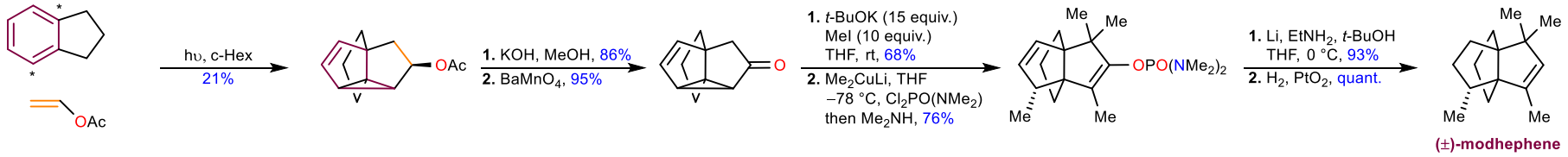
Examples in Total Synthesis:



Wender, P. A. *J. Am. Chem. Soc.* **1981**, *103*, 688 https://doi.org/10.1021/ja00393a041

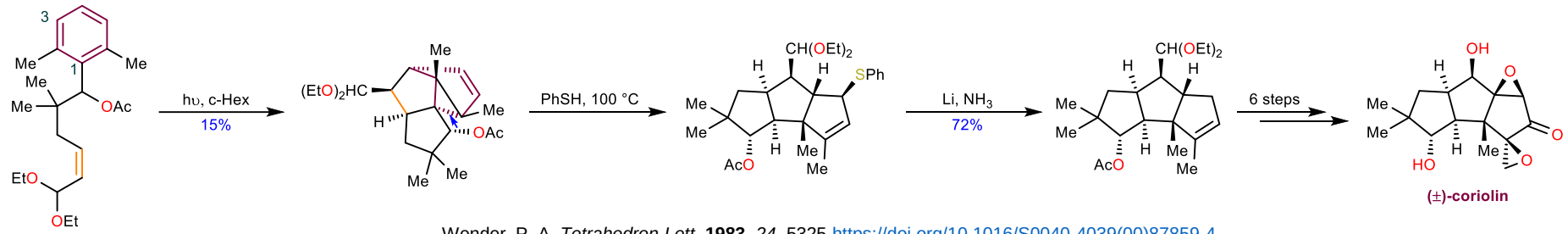


Wender, P. A. *Tetrahedron* **1981**, *37*, 4445 https://doi.org/10.1016/0040-4020(81)80011-7

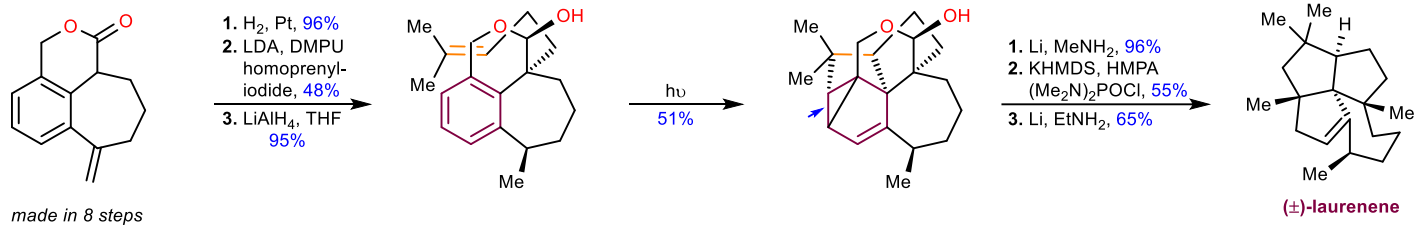


Wender, P. A. *J. Am. Chem. Soc.* **1982**, *104*, 5805 https://doi.org/10.1021/ja00385a051

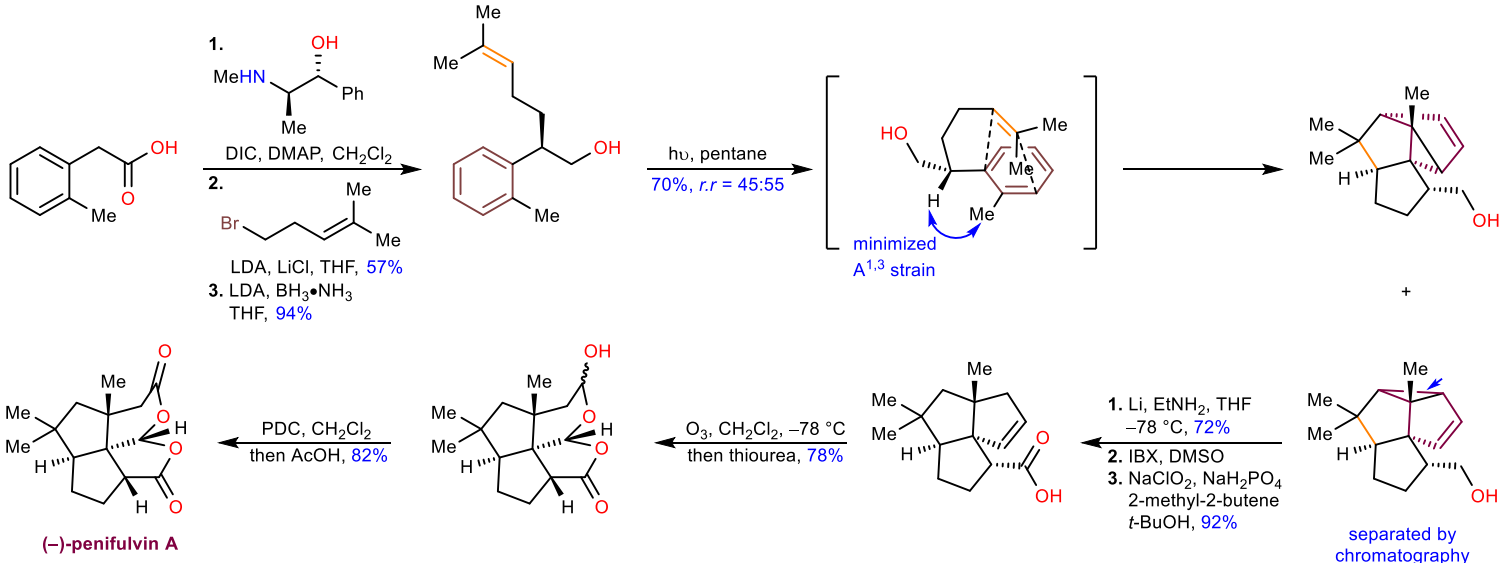
meta-Photocycloaddition



Wender, P. A. *Tetrahedron Lett.* **1983**, *24*, 5325 https://doi.org/10.1016/S0040-4039(00)87859-4



Wender, P. A. *J. Am. Chem. Soc.* **1988**, *110*, 4858 https://doi.org/10.1021/ja00222a072



Mulzer, J. *J. Am. Chem. Soc.* **2009**, *131*, 452 https://doi.org/10.1021/ja8083048