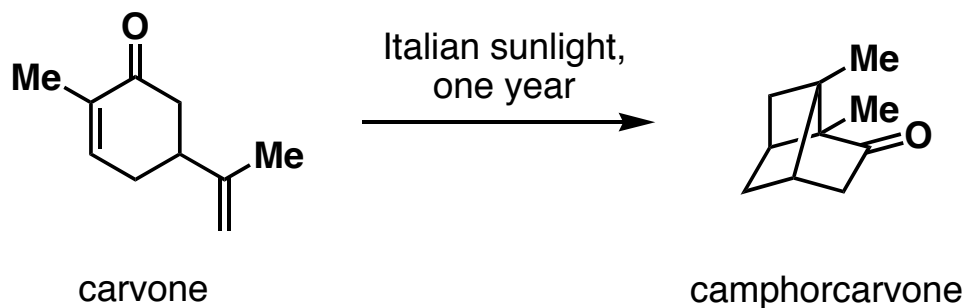

Enone Photochemistry: Fundamentals and Applications

Initial Discovery

Ciamician and Silber were the first to report a 2 + 2 light-induced cycloaddition in 1908:



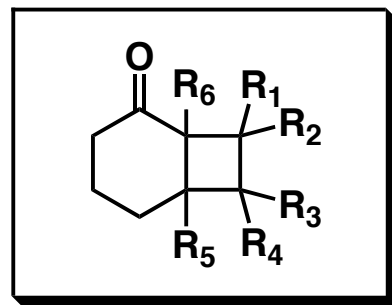
Buchi and Goldman confirmed the structure originally proposed for camphorcarvone in 1957.

Ciamician, G.; Silber, P. *Ber.*, **1908**, 41, 1928.
Buchi, G.; Goldman, I. M. *J. Am. Chem. Soc.*, **1957**, 79, 4741.

Significance

Why should we be interested in enone photochemistry?

1. It is theoretically interesting.
2. For its synthetic utility:
 - i) Efficient cyclobutane synthesis;
 - ii) Regiochemical control;
 - iii) Predictable stereochemistry at the ring fusion(s);
 - iv) Great method for accessing medium sized rings *via* fragmentation.



Mechanism, Part 1

What happens when an enone is irradiated with UV radiation?

If the radiation is of appropriate wavelength (i.e. frequency, energy), excitation will occur.

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



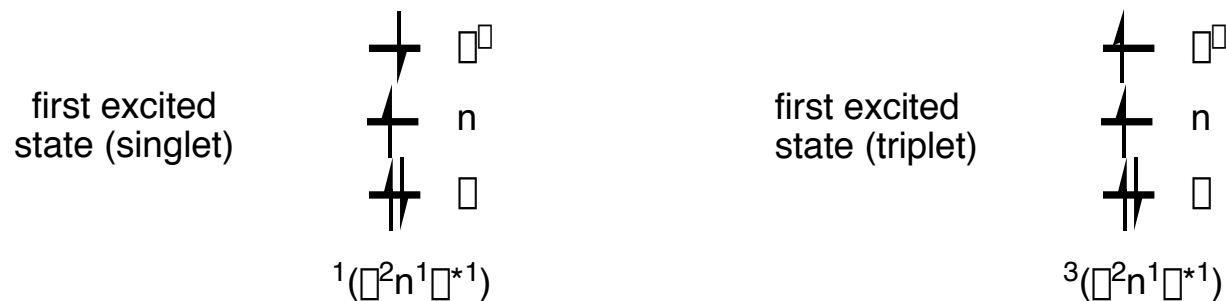
What next?

Schuster, D. I. "The Photochemistry of Enones," (p. 629-635) in:
Patai, S., Rappoport, Z. *The Chemistry of Enones*, John Wiley & Sons Ltd., 1989.

Mechanism, Part 2

An enone in the first excited state (singlet) can:

1. Return to the singlet ground state (fluorescence);
2. Undergo internal conversion to the ground state *via* "trickle down" energy loss;
3. Undergo intersystem crossing (ISC; a.k.a. spin flip) to give the lower energy triplet and proceed to the next step of product formation;
4. Skip ISC altogether and proceed to the next step.



Schuster, D. I. "The Photochemistry of Enones," (p. 629-635) in:
Patai, S., Rappoport, Z. *The Chemistry of Enones*, John Wiley & Sons Ltd., 1989.

Mechanism, Part 3

The excited enone (triplet state) can proceed to the next set of events:

1. Exciplex formation with the alkene.

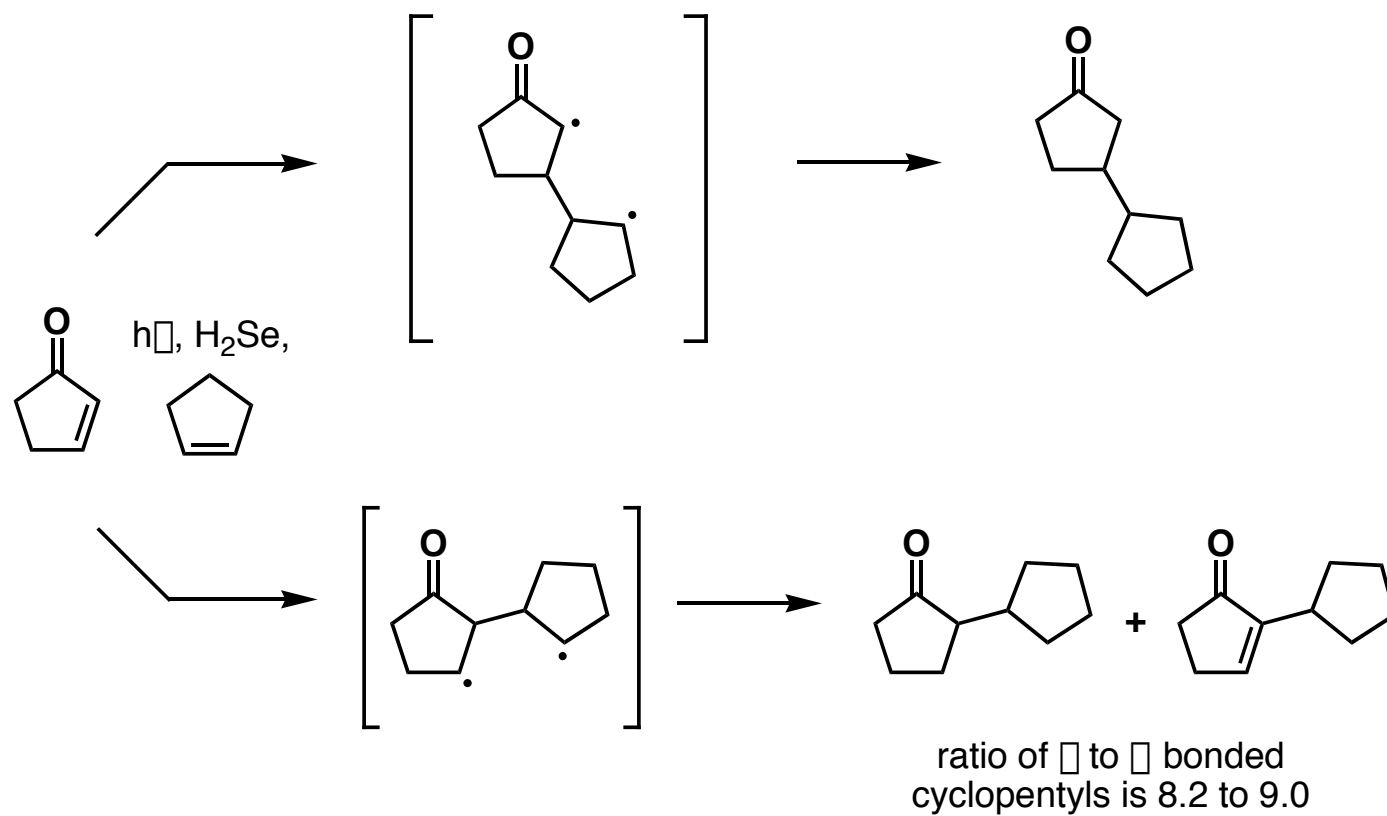
The exciplex has a lifetime of 10 to 100's of ns. In this time it can:

1. Initiate carbon-carbon bond formation at *either* the α or β carbon of the enone;
2. *Revert to starting materials. All intermediates up to the 1, 4 diradical are susceptible to this process.*

If the diradical survives long enough, it may revert to a singlet state *via* ISC to give an excited singlet state which can then form the second bond and give the product.

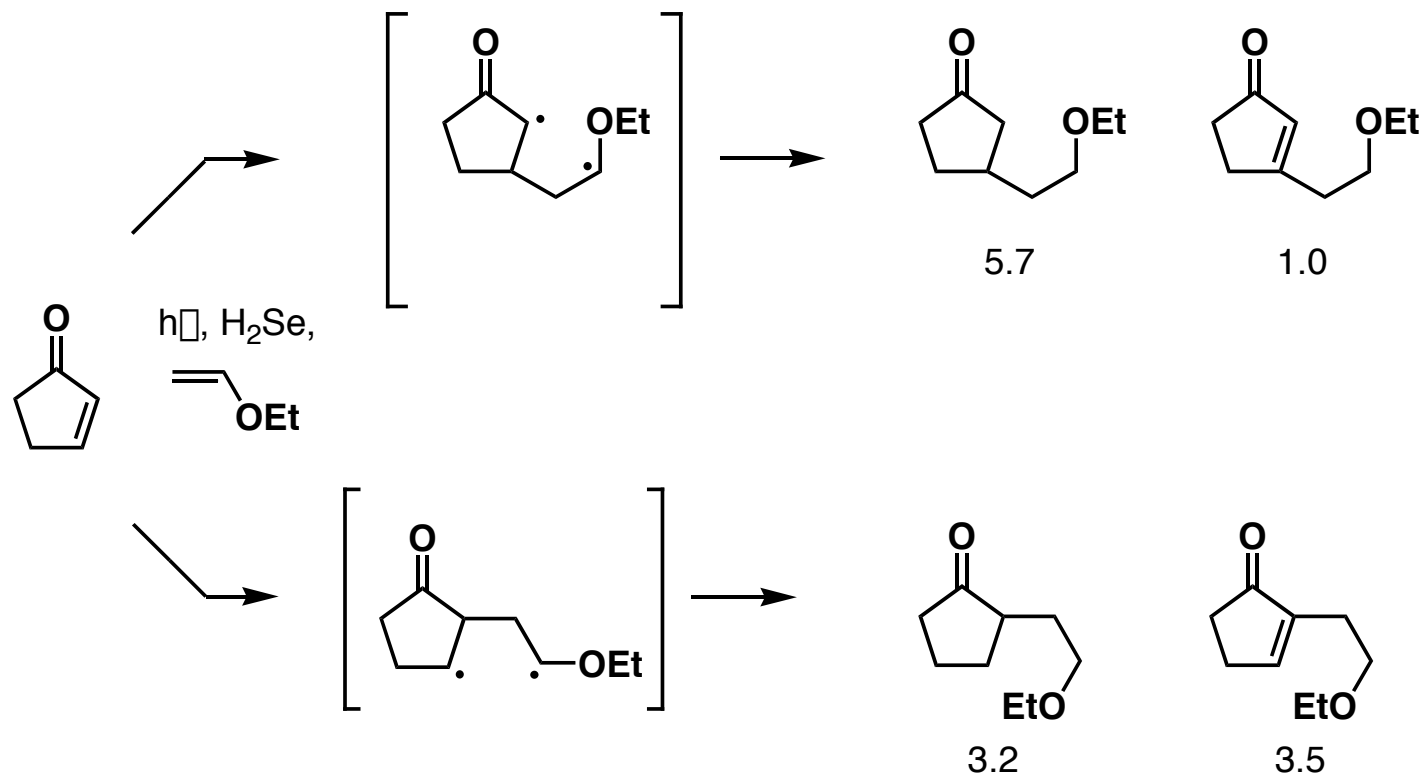
Schuster, D. I. "The Photochemistry of Enones," (p. 629-635) in:
Patai, S., Rappoport, Z. *The Chemistry of Enones*, John Wiley & Sons Ltd., 1989.

Evidence for Similar Rates of Initial Bond Formation, Part 1



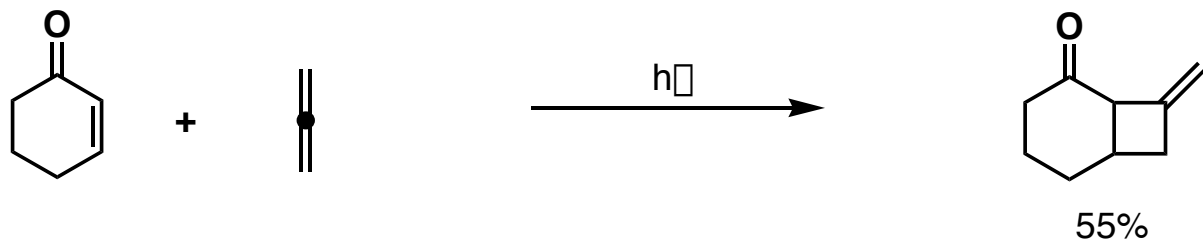
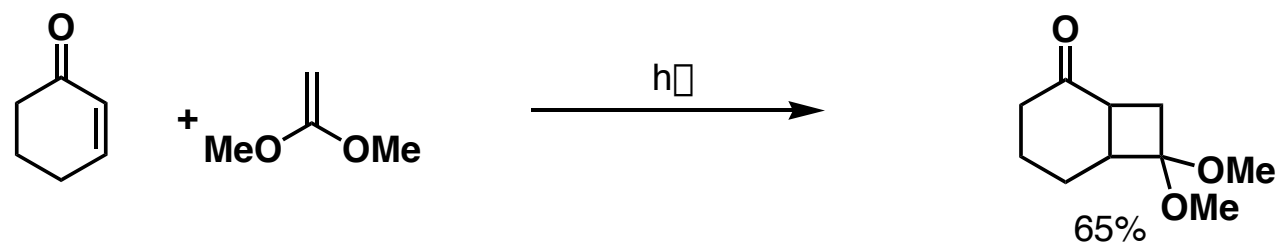
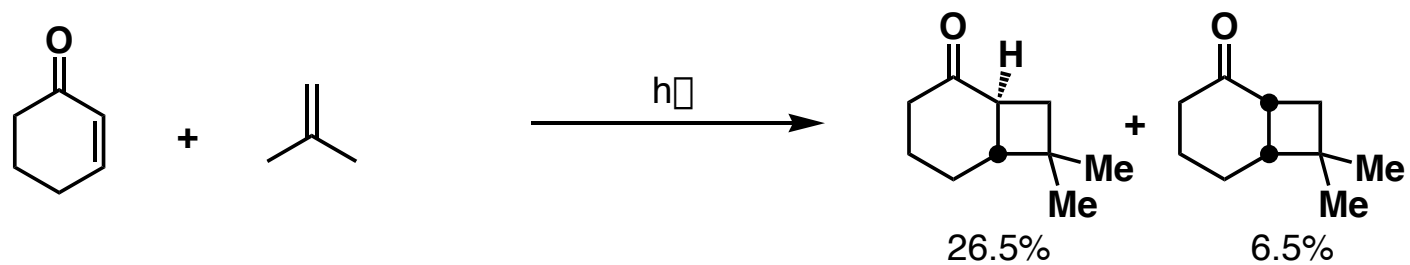
Hastings, D. J.; Weedon A. C. *J. Am. Chem. Soc.*, **1991**, *113*, 8525.

Evidence for Similar Rates of Initial Bond Formation, Part 2



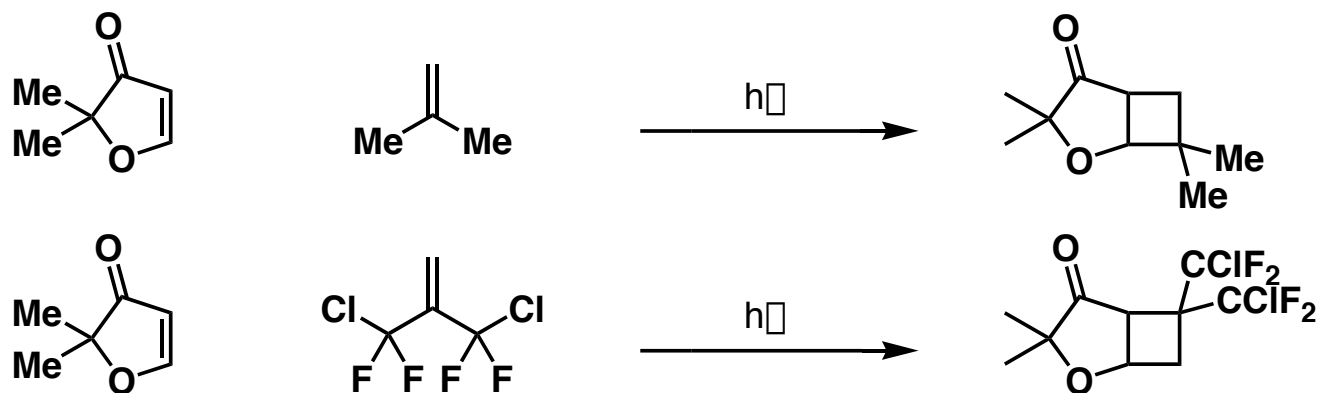
Hastings, D. J.; Weedon, A. C. *J. Am. Chem. Soc.*, **1991**, *113*, 8525.

Regioselectivity, Part 1

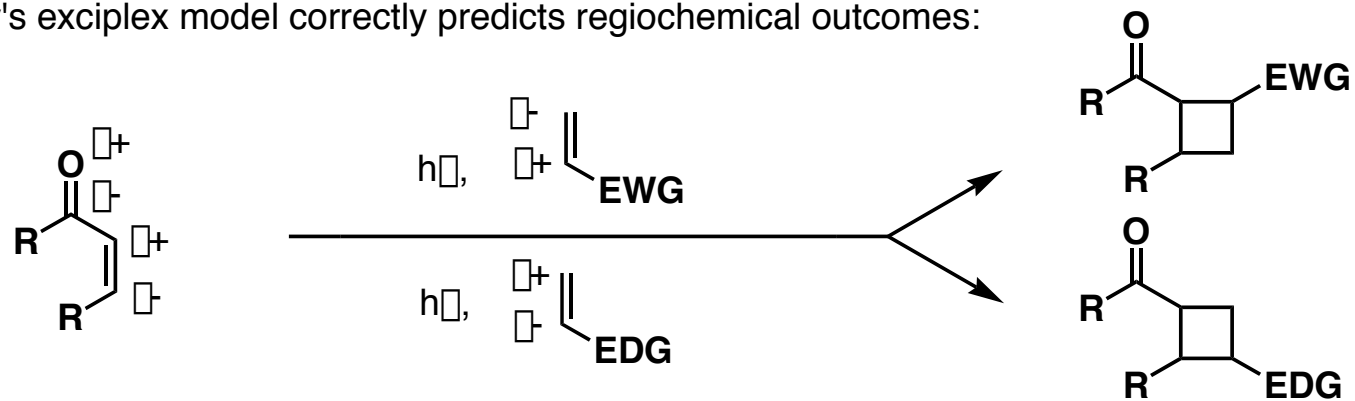


Corey, E. J.; Bass, J. D.; LeMahieu, R.; Mitra, R. B. *J. Am. Chem. Soc.* **1964**, *86*, 5570.

Regioselectivity, Part 2



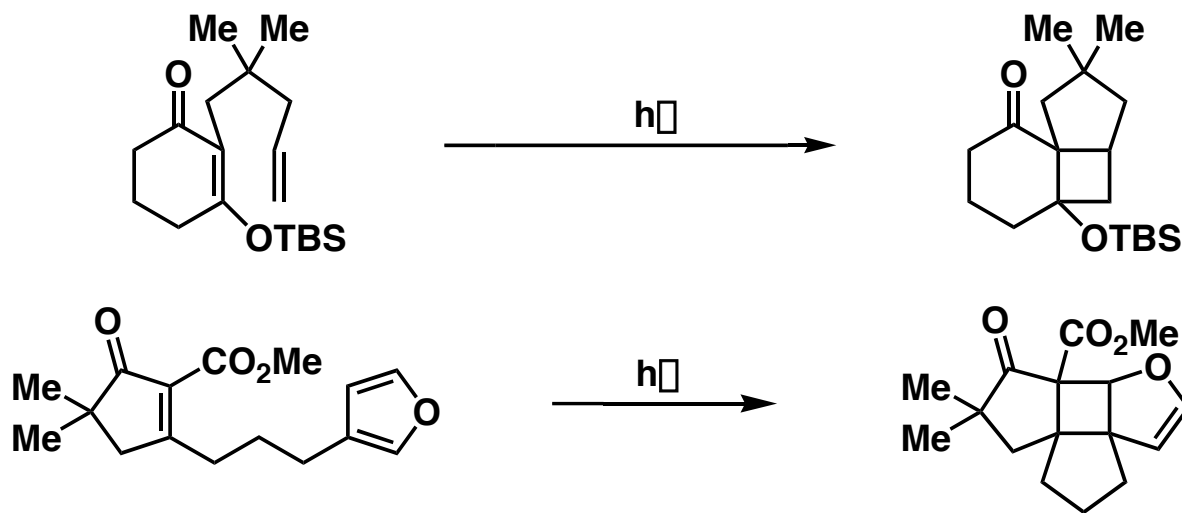
Corey's exciplex model correctly predicts regiochemical outcomes:



Regioselectivity, Part 3

Other factors that affect regiochemistry:

1. Less polar solvents favor products predicted by the Corey exciplex model;
2. Lower temperatures have the same effect;
3. In general, two to four membered tethers set regiochemistry. Examples:

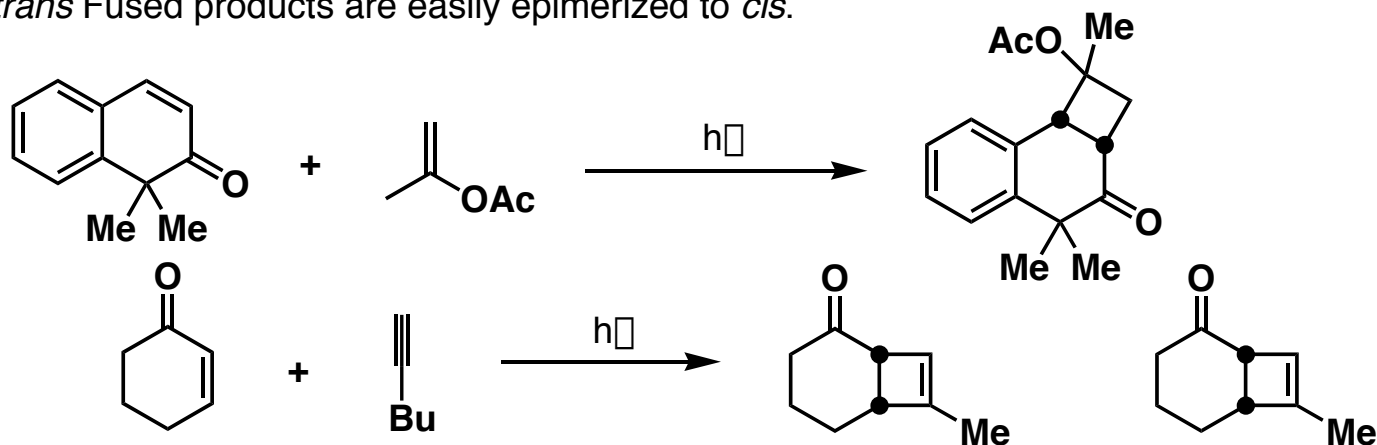


Crimmins, M. T.; Reinhold, T. L. *Org. Reactions*, **1993**, 44, 297.

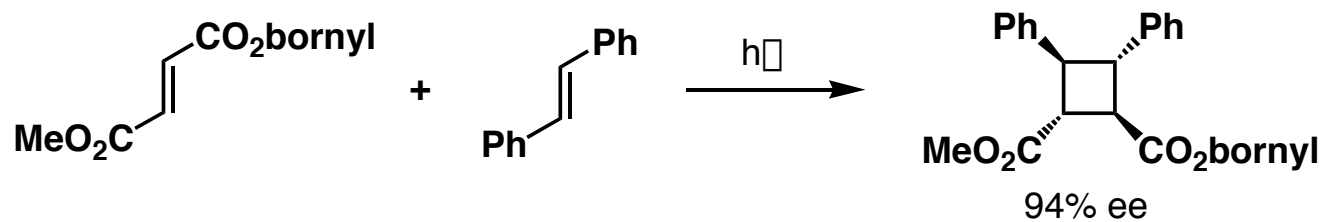
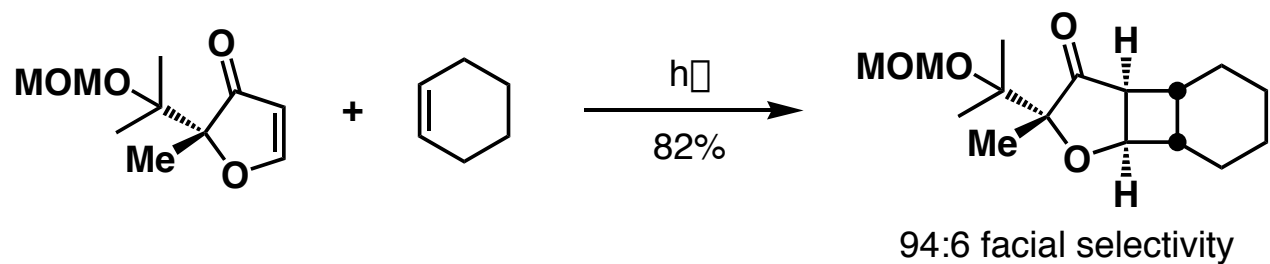
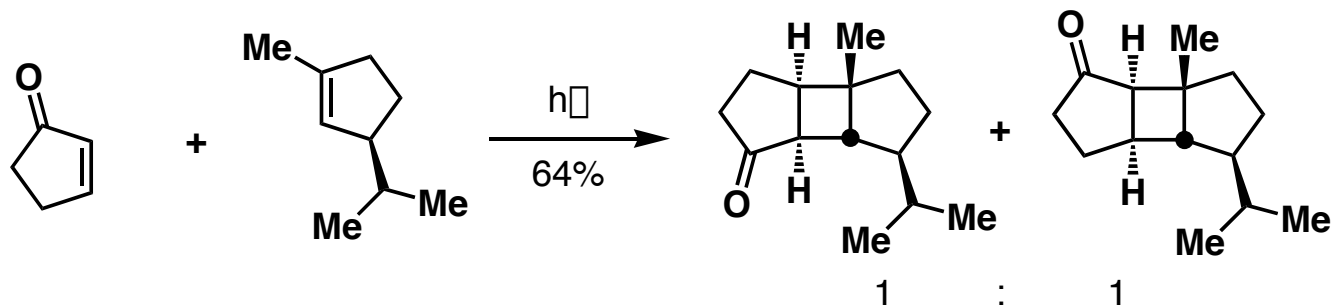
Stereochemistry, Part 1

General considerations:

1. Cyclopentenones and smaller enones give *cis* fused products;
2. Cyclohexenones give significant amounts of *trans* product;
3. Strained enones or strained cyclobutane products preclude *trans* products
4. *trans* Fused products are easily epimerized to *cis*.

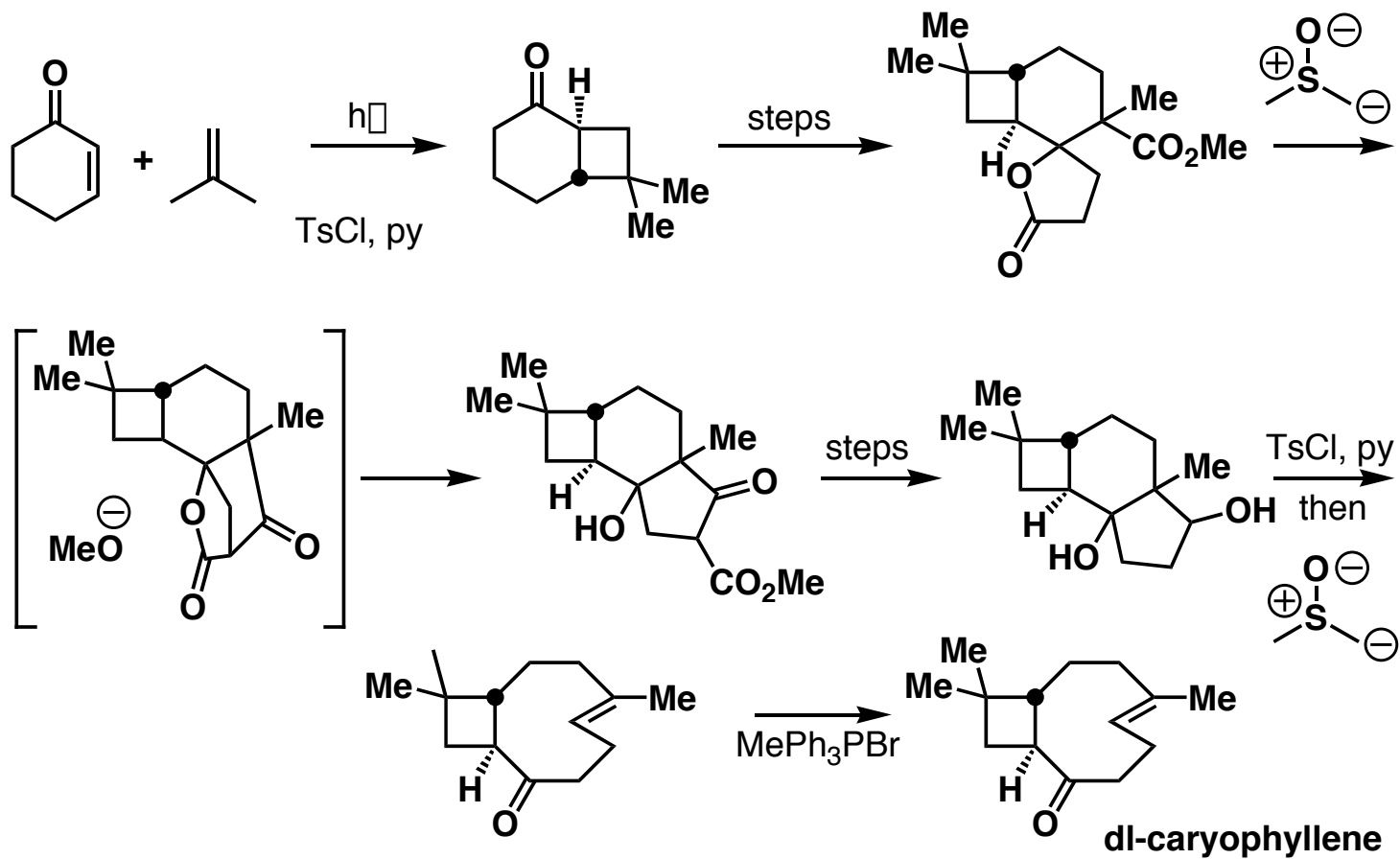


Stereochemistry, Part 2



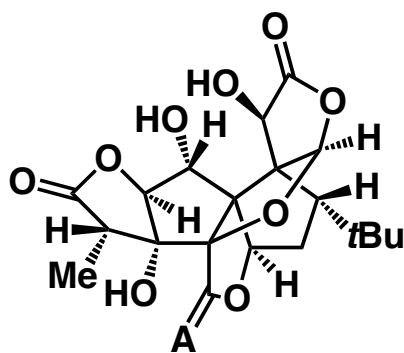
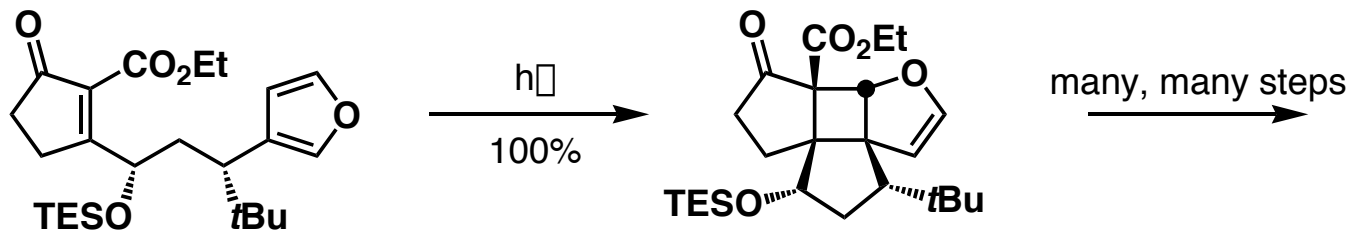
Crimmins, M. T.; Reinhold, T. L. *Org. Reactions*, **1993**, *44*, 297.

Total Synthesis, Part 1



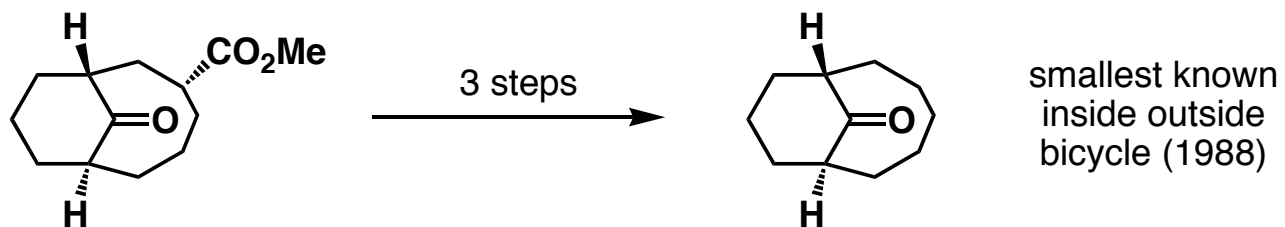
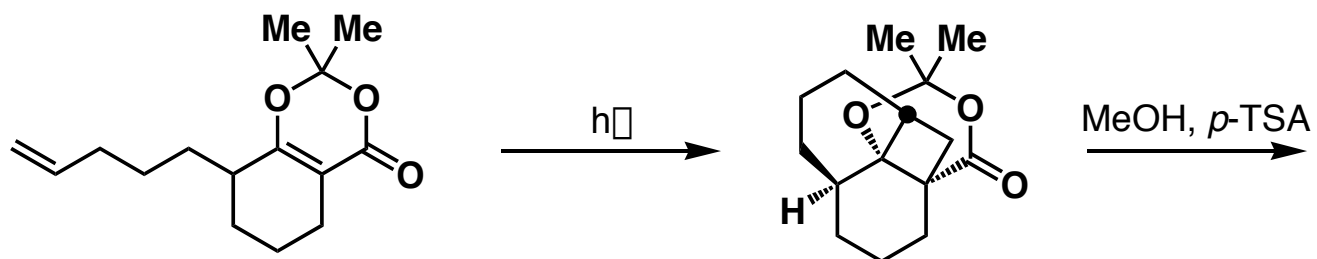
Corey, E. J.; Mitra, R. B.; Uda, H. *J. Am. Chem. Soc.* **1964**, *86*, 485.

Total Synthesis, Part 3



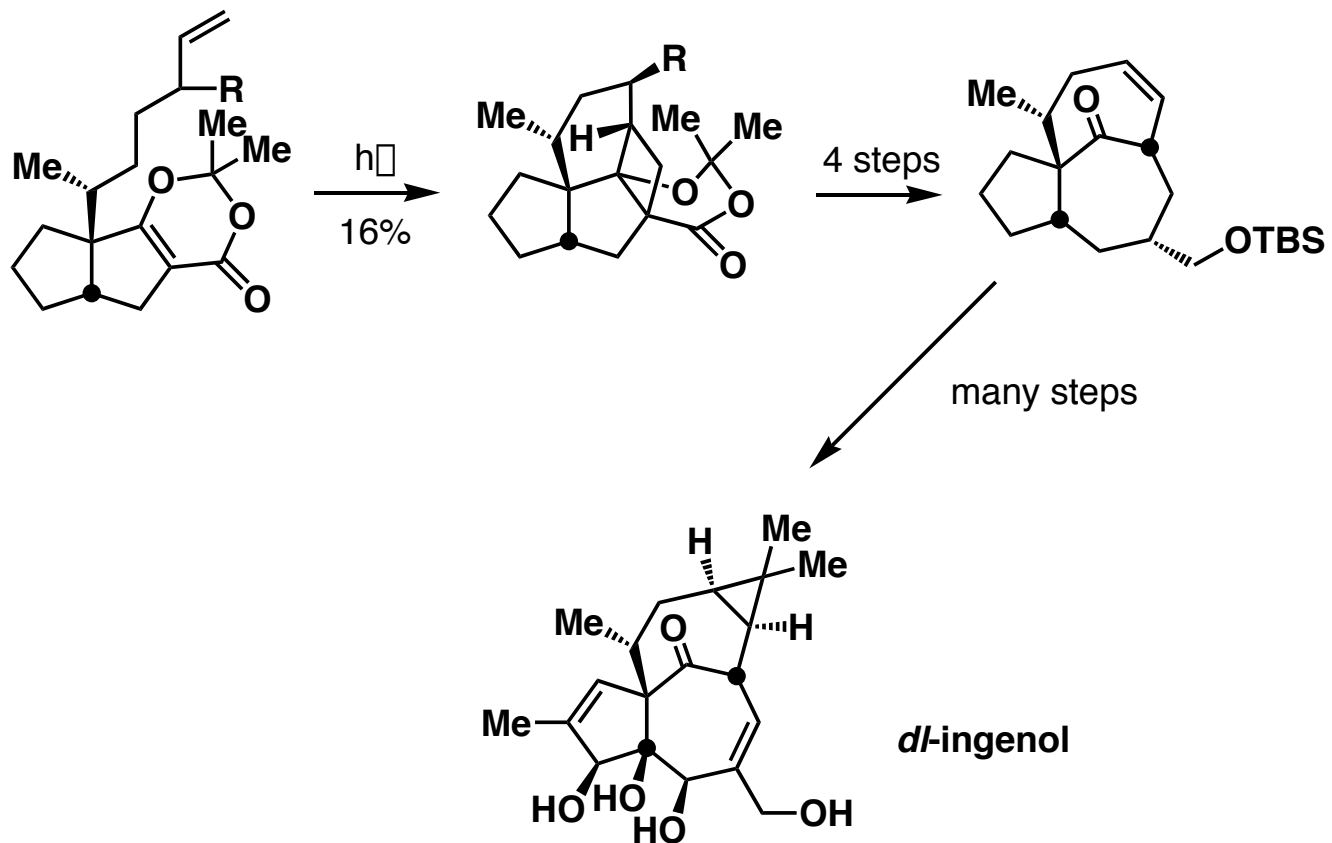
dl-ginkgolide B

Total Synthesis, Part 4



Winkler, J. D.; Hey, J. P. *J. Am. Chem. Soc.*, **1986**, *108*, 6425.

Total Synthesis, Part 5



Winkler, J. D. *et al.* *J. Am. Chem. Soc.*, **2002**, *124*, 9726.

Main Contributors to Enone Photochemistry's Development

- P. E. Eaton:** discovered that cyclopentenone and cyclopentadiene reaction under photochemical conditions; synthesized cubane to exemplify utility.
- E. J. Corey:** established the usual stereochemistry of 2 + 2 photochemical cycloadditions; advanced the notion of an exciplex to explain regioselectivity.
- P. de Mayo:** established that intermolecular 2 + 2 was feasible; invented a method for the preparation of 1, 5 diones by photochemical means, postulated that the first triplet state is the reactive one in enones; found that intermediates could revert to starting materials.
- D. I. Schuster:** determined lifetimes of reactive intermediates thereby disproving Corey's exciplex mechanism; in particular, he determined that rate constants for enones triplet quenching were previously overestimated; proved that enone triplets were reactive intermediates.
- A. C. Weedon:** determined that regioselectivity is governed by diradical lifetimes.
- H. E. Zimmerman:** explained triplet electronics and reactivity using HMO theory.
- G. S. Hammond and N. J. Turro:** carried out experiments that suggested enone triplets were reactive intermediates.