

Asymmetric Photochemistry

MacMillan Group Meeting
October 18, 2000

Tehshik Yoon

- 1. Circularly polarized light**
- 2. Solid-phase**
- 3. Solution-phase**
 - **Covalently-bound chiral auxiliaries**
 - **Chiral complexing agents**
 - **Chiral sensitizer**

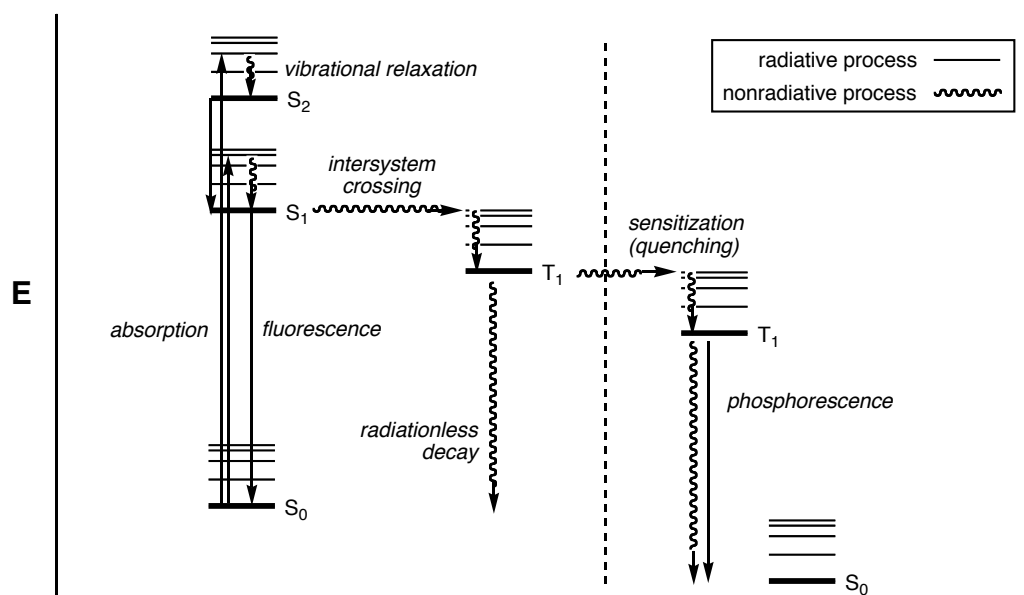
Reviews: Inoue, Y., in *Organic Molecular Photochemistry*, Ramamurthy, V., Schanze, K. S., Eds.; Dekker: New York, 1999, pp 71-130.
Inoue, Y. *Chem. Rev.* **1992**, *92*, 741-770.
Rau, H. *Chem. Rev.* **1983**, *83*, 535-547.

Why Study Asymmetric Photochemistry?

- **Prebiotic photochemistry — enantiomeric excess of biomolecules may have been generated by circularly polarized light (CPL)**
- **Environmentally benign processes — light requires no workup, generates no waste**
- **Different mode of reactivity — access to novel, strained compounds which are thermally inaccessible or difficult to synthesize**

Photophysical processes

Generalized Jablonski diagram



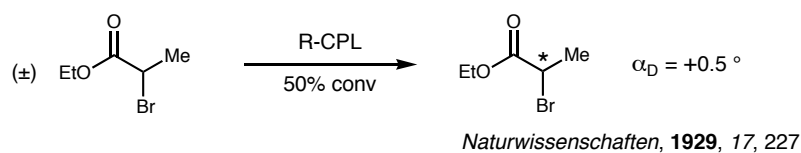
- Photochemistry can happen from either S₁ or T₁ state, but normally T₁
- Spin-allowed processes (S to S, T to T) tend to be faster, so T₁ is usually longer-lived ($k_d \sim 0.4 \text{ s}^{-1}$)
- $E(T_1/S_1) \sim 10^2 \text{ kcal/mol}$ for most useful organic photochemistry

see, e.g., Carroll, *Structure and Mechanism in Organic Chemistry*, Pacific Grove, CA: Brooks/Cole Ch. 12.

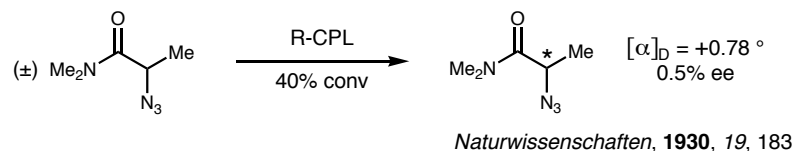
Asymmetric photodestruction with CPL

- van't Hoff first suggested the possibility of asymmetric photochemistry with CPL in 1897

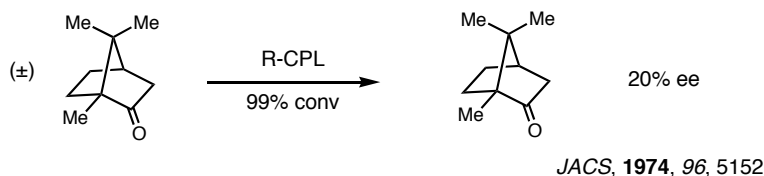
- Kuhn and Braun (1929)



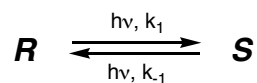
- Kuhn and Knopf (1930)



- Kagan (1974)



Photoresolution using CPL



- enantiomers absorb nonpolarized or linearly polarized light with equal intensity
- enantiomers can absorb circularly polarized light with different intensities; the rate of reaction is proportional to the absorption coefficients (ϵ_R and ϵ_S)
- a photostationary state (pss) is achieved when $k_1[R] = k_{-1}[S]$

$$\epsilon_R[R] = \epsilon_S[S]$$

$$\text{optical purity} = ([R]-[S])/([R]+[S]) = g/2$$

$$\text{where } g = (\epsilon_R - \epsilon_S)/\epsilon; \quad \epsilon = (\epsilon_R + \epsilon_S)/2$$

- g depends on wavelength of irradiation

Stevenson *JACS* **1978**, *90*, 2974

Photoresolution using CPL

- Stevenson and Verdick, *JACS* **1968**, *90*, 2974

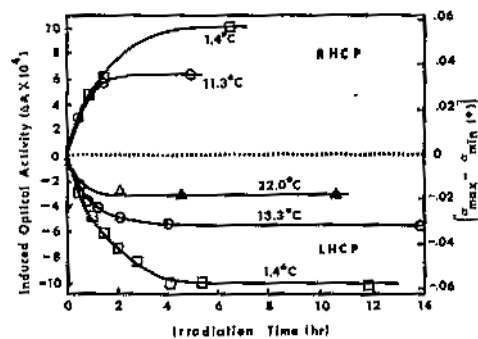
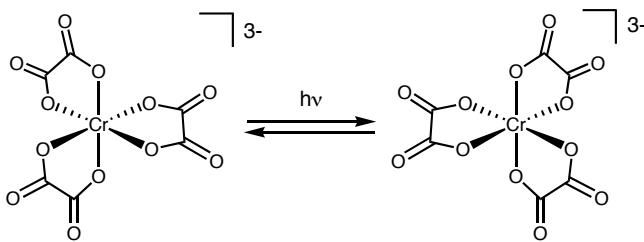
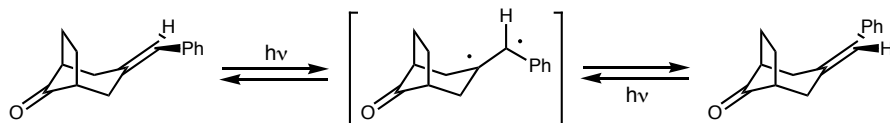


Figure 1. Photoresolution of trioxalatochromate(III), 2.6×10^{-3} M, in RHCP and LHCP light at 546 nm.

- Schuster (1995): $g_{313} = 0.0502$

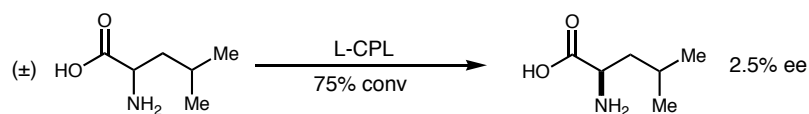


CPL induces observed 1.6% ee
JOC, **1995**, *60*, 7192

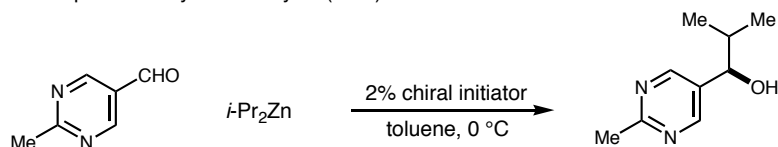
Photochemistry with CPL—prebiotic origin of optical activity?

■ Bonner (1977)

JACS, 1977, 99, 3622



■ Chiral amplification by autocatalysis (Soai)

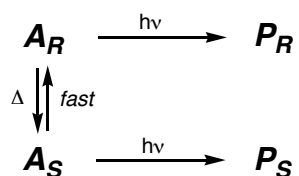


initiator	yield	ee
L-valine (2% ee)	82%	21%
(0.5% ee)	89%	54%
(0.1% ee)	not given	79%

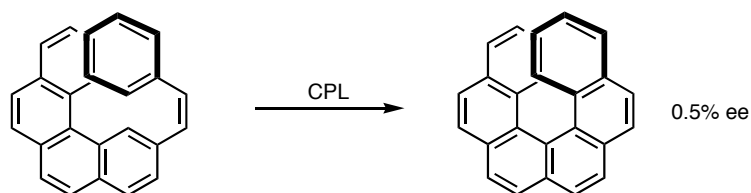
JACS 1998, 120, 12157

Enantioselective photofixation using CPL

Asymmetric photofixation possible by preferential photoexcitation of one of a pair of rapidly equilibrating enantiomeric conformers



■ Helicenes (Kagan)

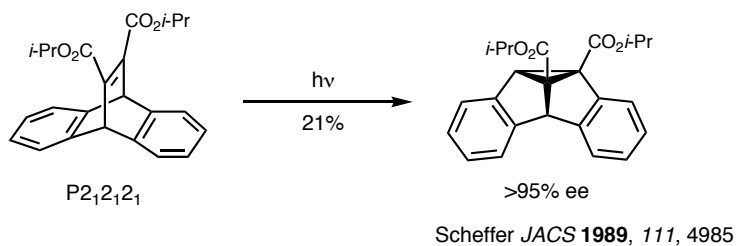


Tetrahedron, 1975, 31, 2139)

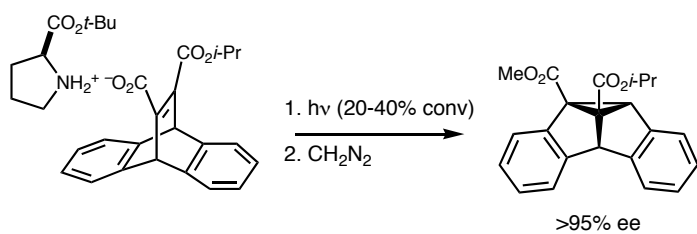
Large *g* values are required for appreciable ee's; however, conformational flexibility allows averaging of CD spectra with opposite signs.

Enantioselective solid-phase photochemistry

- Achiral compounds can crystallize into chiral point groups



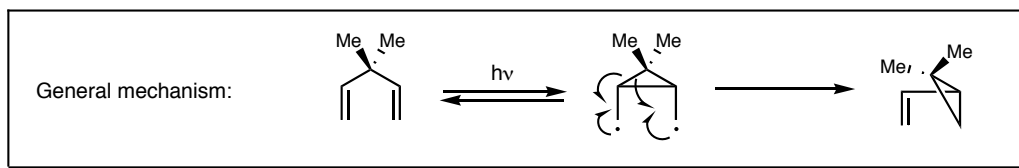
- Introduction of chiral "handles" induces chiral crystals



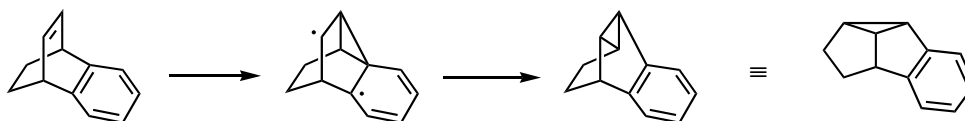
the solution-phase reaction gives racemic product and 1:1 regioselectivity

Scheffer, *Acc. Chem. Res.* **1996**, 29, 203

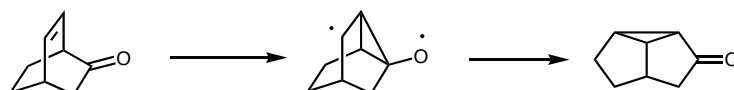
The di- π -methane rearrangement



- olefin-arene rearrangement



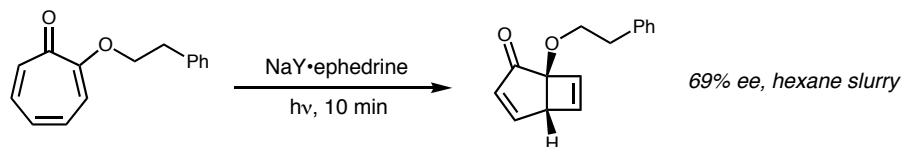
- olefin-carbonyl rearrangement



Enantioselective solid-phase photochemistry

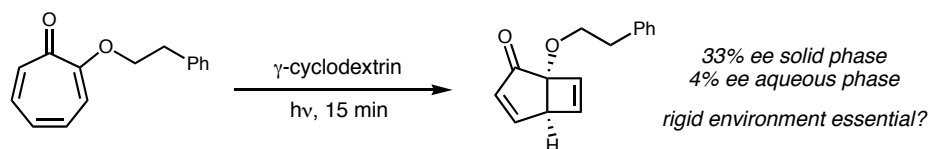
■ Modified zeolites as hosts

Ramamurthy, *Org. Lett.* **2000**, *2*, 119

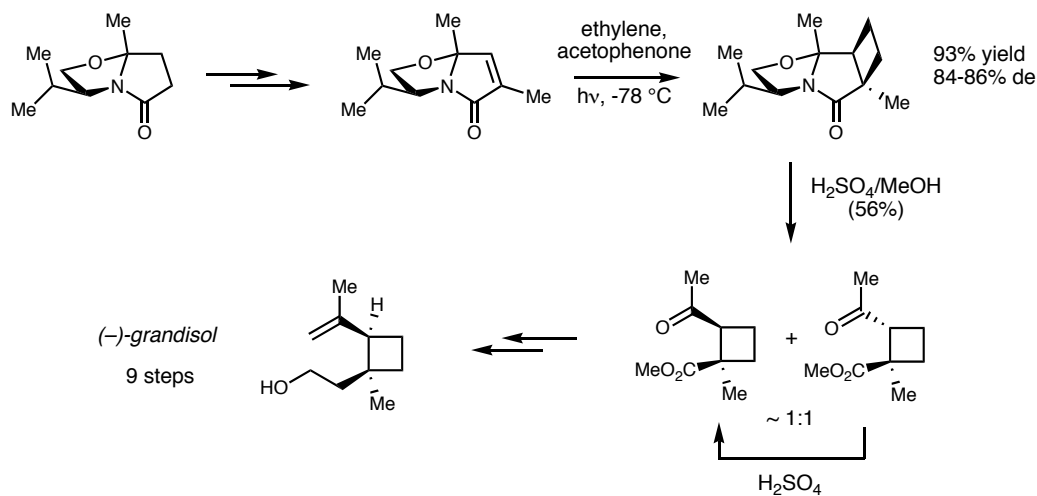


■ Cyclodextrin hosts:

Ramamurthy, *Tetrahedron* **2000**, *56*, 7005



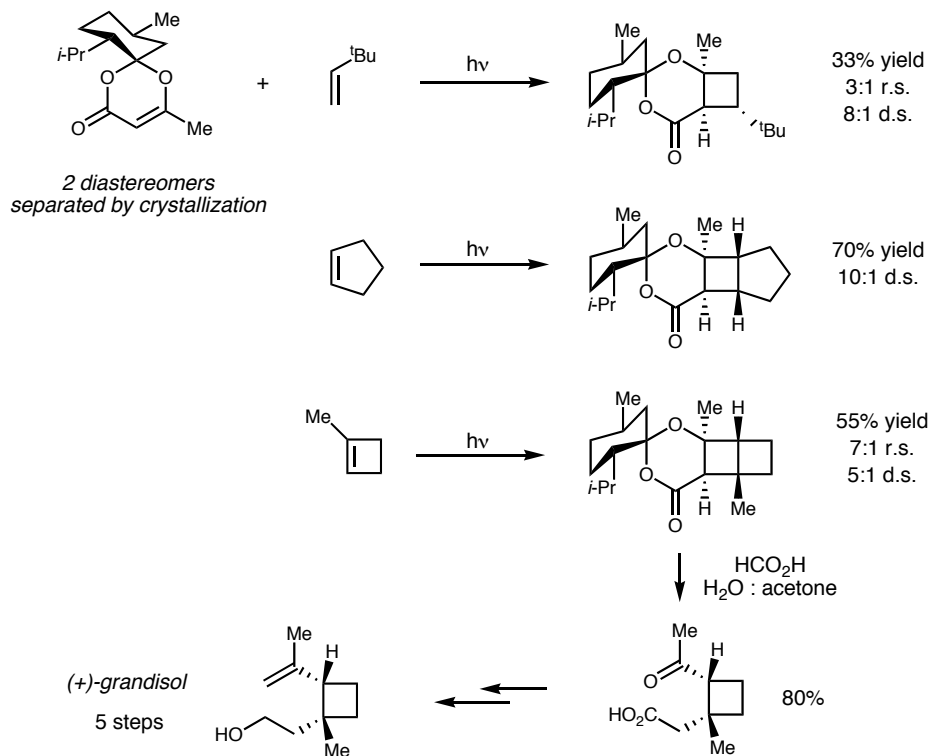
Meyers' chiral lactam auxiliary



No other examples reported

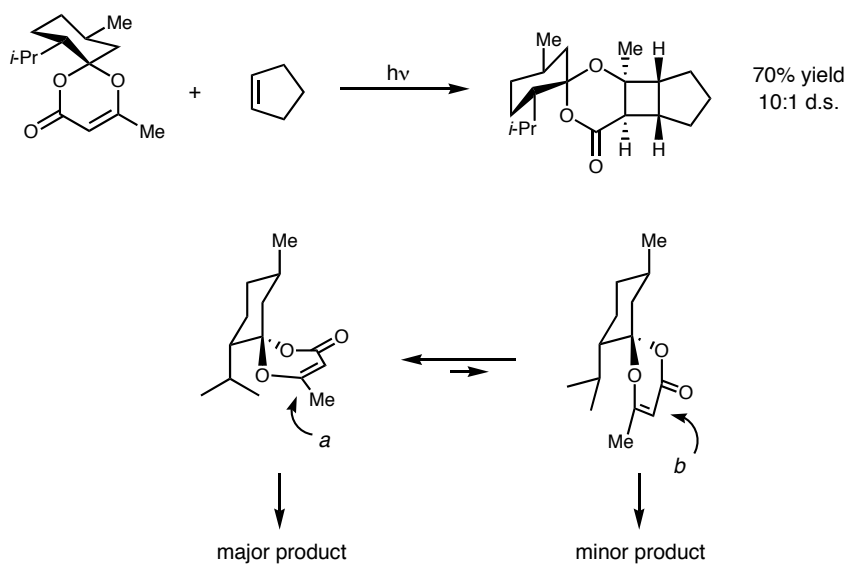
Meyers, A. I. *JACS*, **1986**, *108*, 306

Menthone-derived spirodioxinone



Demuth *ACIEE* **1986**, 25, 1117

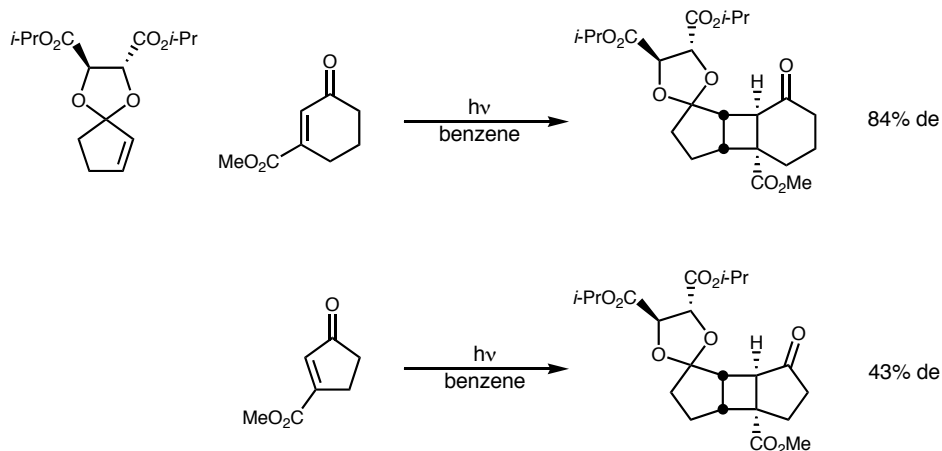
Menthone-derived spirodioxinone



"Though the b-side attack of the alkene on **A** is not completely denied, it is more reasonable to assume that the minor adduct... may be formed via the less stable conformer (**B**) by the attack of the alkene from the b-side."

[2+2] cycloadditions with tartarate auxiliary

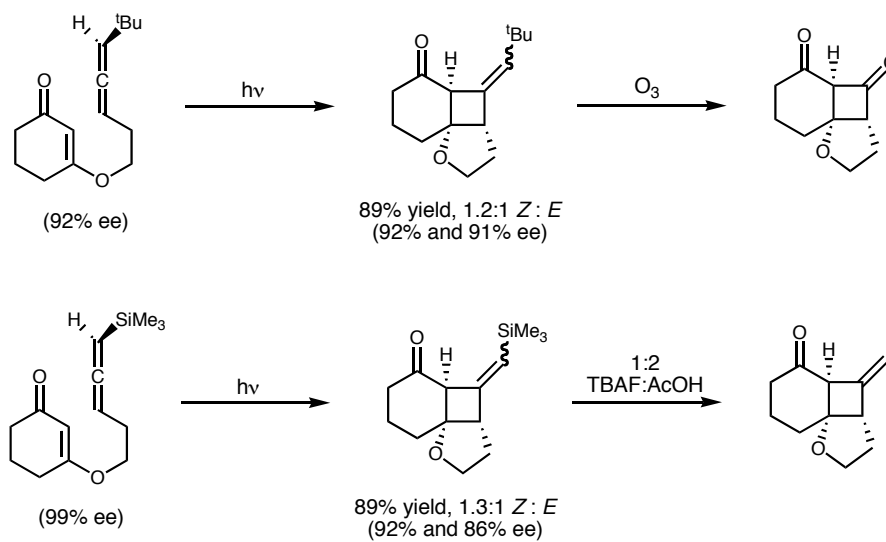
- Chiral auxiliaries on the alkene component of alkene-enone photocycloadditions as much rarer



2-fold excess of ketal — isolated yields only 30-45%

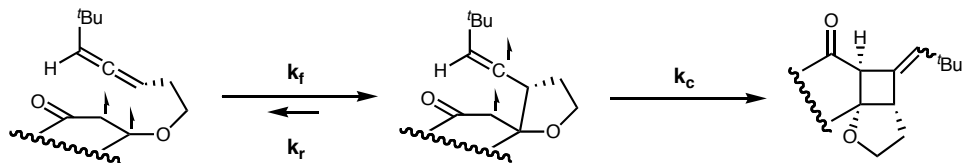
Lange, *TL*, **1988**, *29*, 2613

Chiral allene-enone [2+2] photocycloadditions



Carreira *JACS*, **1994**, *116*, 6622
JACS, **1997**, *119*, 2597

Chiral allene-enone [2+2] photocycloadditions

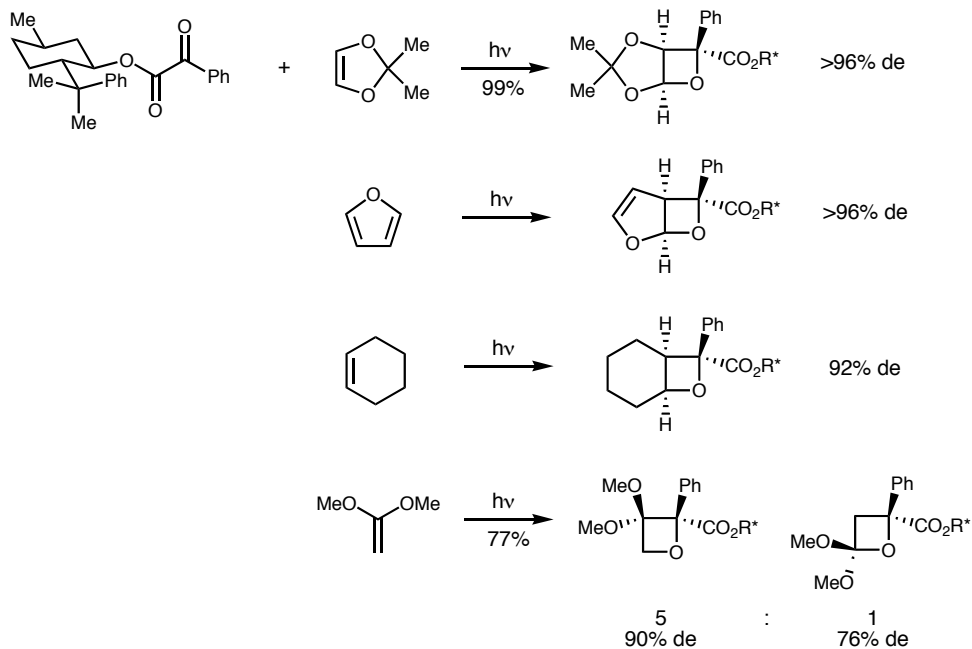


- *exo* approach of allene: ring ↔ H vs ring ↔ tether
- enone approaches opposite *t*-Bu group
- free bond rotation at 1,4-diradical; cycloreversion is not competitive with ring closure ($k_r \ll k_c$)

Carreira *JACS*, **1994**, *116*, 6622
JACS, **1997**, *119*, 2597

The Paterno-Buchi Reaction

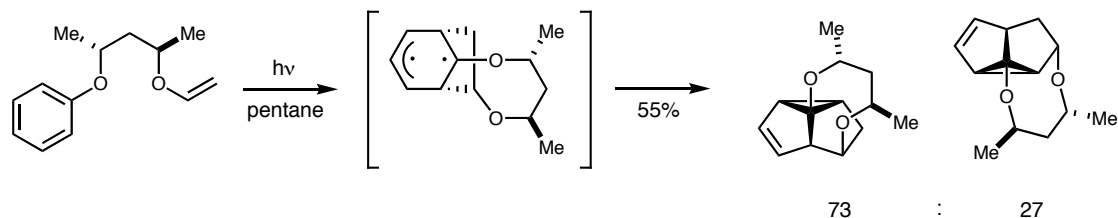
8-phenylmenthol auxilliary control



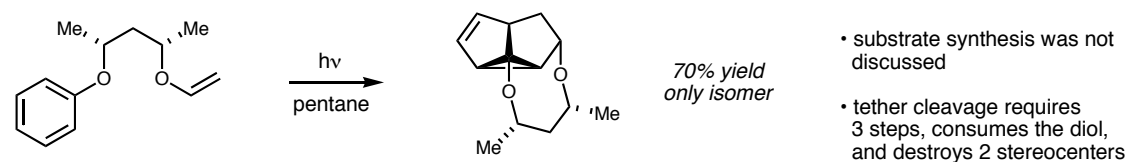
Scharf, *ACIEE* **1991**, *30*, 477

Asymmetric meta-arene-alkene photocycloaddition

- C₂-symmetric diol tether gives excellent facial selectivity



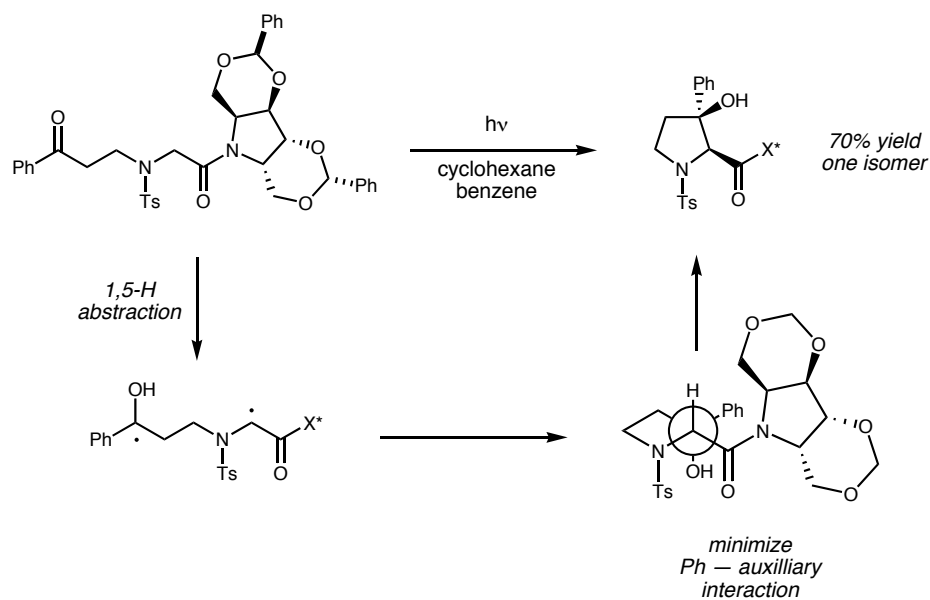
- Selectivity of the cyclopropane closure can be achieved by adjusting the tether



Sugimura, Tai *Tet. Asymm.* **1994**, 5, 1163

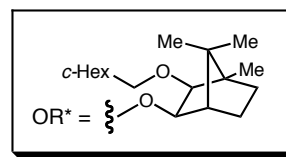
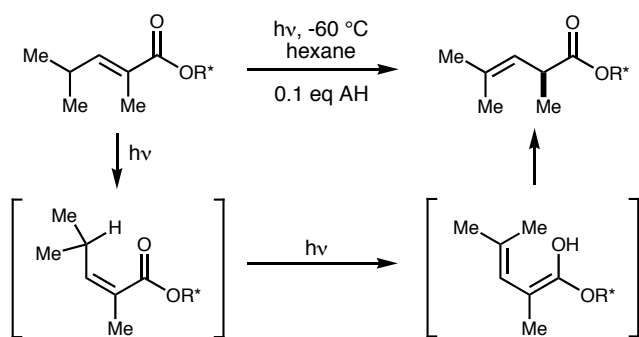
Asymmetric photoinduced radical cyclization

- Synthesis of 3-hydroxyproline derivatives



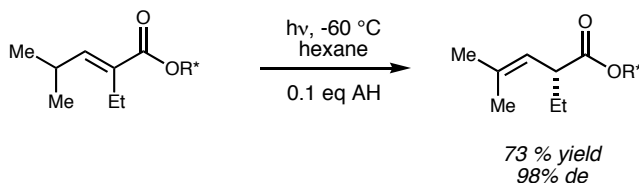
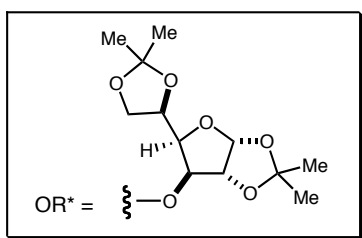
Wessig, *Helv. Chim. Acta* **1994**, 77, 829

Photodeconjugation of esters with chiral auxiliaries



AH	yield	dr
<i>i</i> -Pr ₂ NH	71%	94%
(+)-ephedrine	65%	52%
(-)-ephedrine	69%	48%

Pete, *Tet. Asym.* **1991**, 2, 1101

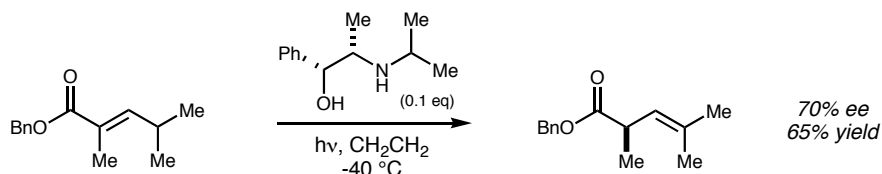


Piva, *Tet. Asym.* **1992**, 3, 759

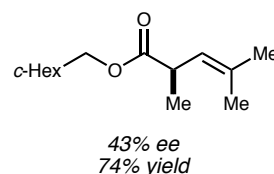
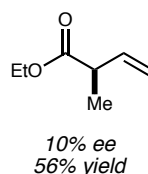
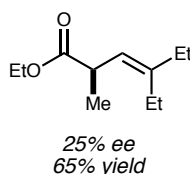
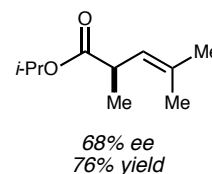
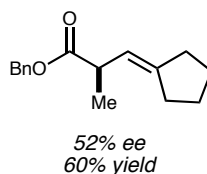
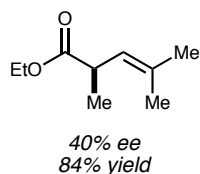
enantiodifferentiating step is protonation of the enol—
not a photoprocess

Asymmetric photodeconjugation of achiral esters

- High levels of enantioselectivity can be achieved with catalytic amounts of additive



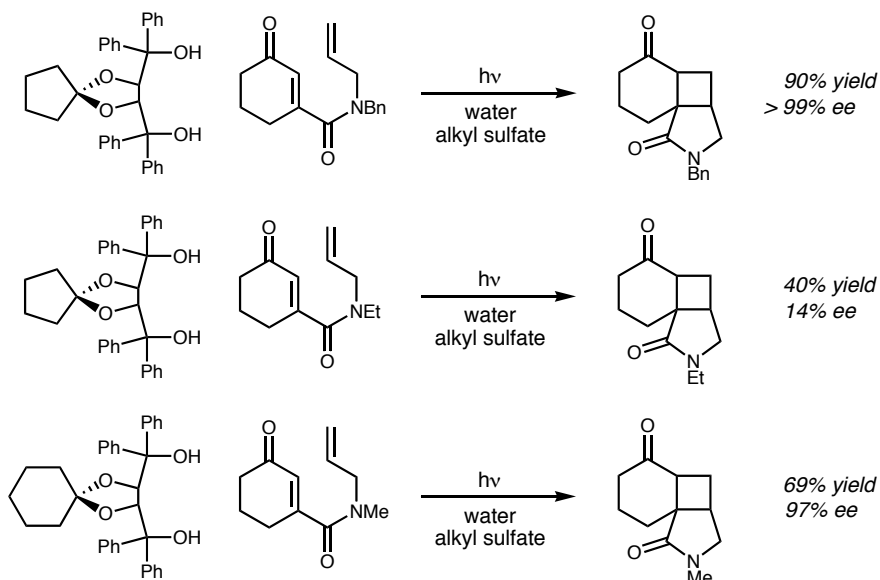
- Selectivity is highly substrate-dependent



Piva, *JACS*, **1990**, 112, 9263

Cycloadditions using chiral complexing agents

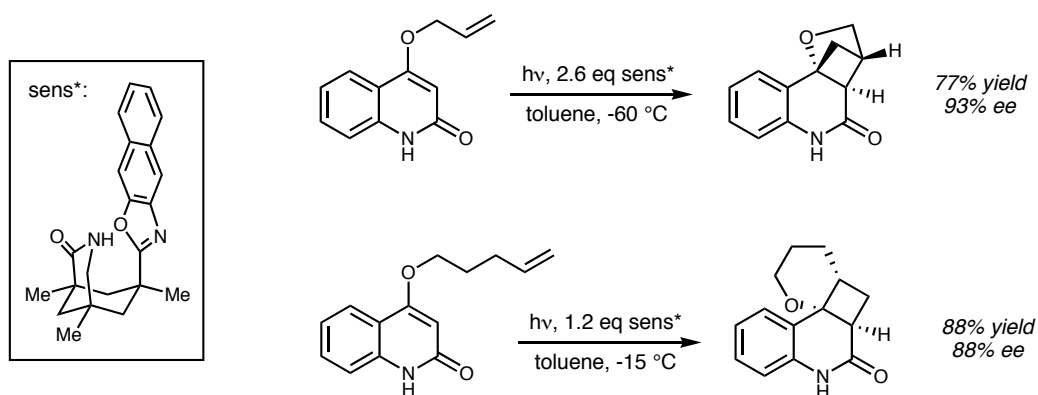
■ 2:1 host:guest complexes



- *N*-benzyl groups work well; *N*-alkyl, *N*-aryl, and *N*-allyl give poorer results
- Aqueous suspensions made from powdered 2:1 host:guest co-crystals.
Is this really a solution-phase reaction?

Toda, *JCS, Chem. Comm.* **1995**, 621

Cycloadditions using chiral complexing agents

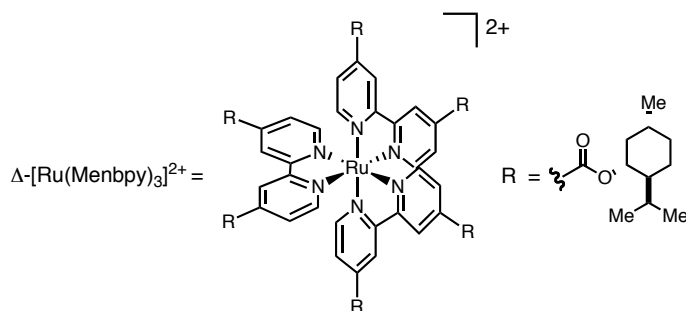
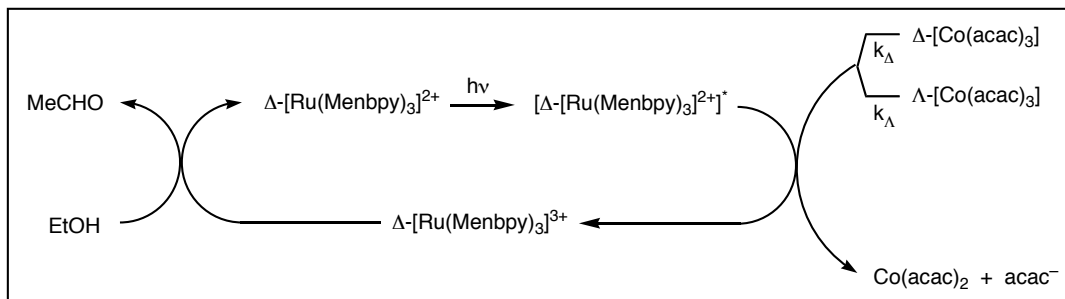


- Stereoselectivity based host-guest recognition: amide–amide interaction
- Best enantioselectivity in a solution-phase photochemical reaction to date

Bach, *ACIEE*, **2000**, 39, 2302

Enantioselective sensitized photodestruction

- Inorganic systems can work well



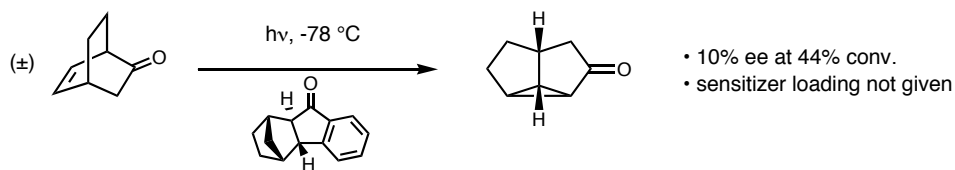
- 1.3 mol% sensitizer used
- $k_{\Delta}/k_{\Lambda} = 14.7$ (94% ee) in 9:1 EtOH:water at 30% conversion
- Enantioselectivity is critically solvent-dependant: $k_{\Delta}/k_{\Lambda} = 8.7$ in 8:1 EtOH:water

Inoue *JCS, Chem. Comm.* **1993**, 1423

Enantioselective organic photosensitized reactions

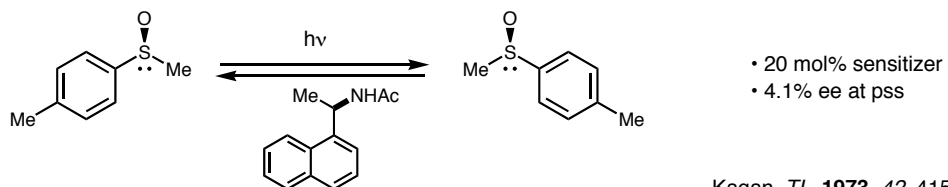
- Organic systems work less well

- Di- π -methane rearrangement



Demuth *Helv. Chim. Acta* **1980**, 63, 2434

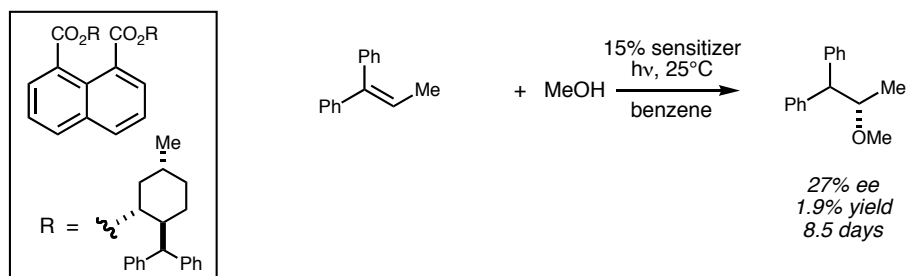
- Sulfoxide isomerization



Kagan *TL* **1973**, 42, 4159

Enantioselective photosensitized polar addition

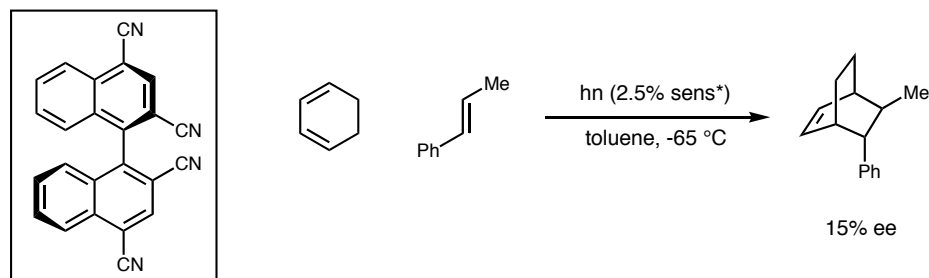
- Photosensitized ant-Markovnikov methanol addition to 1,1-diphenylpropene



- The intermediacy of an electron-transfer exciplex is invoked
- Addition occurs to the radical cation intermediate
- Increasing concentration of MeOH lowers ee, indicating that polar effects are important in the symmetry-breaking step

Inoue *JCS, Chem Comm* **1993**, 718

Enantioselective photosensitized [4+2] cycloaddition



- No yields given
- Reaction of electron-rich diene with electron-rich dienophile
- Enantioselectivity presumably arises from selective capture of diastereomeric exciplexes

Schuster *JACS* **1990**, 112, 9635

Conclusions

- Photochemistry with circularly-polarized light gives poor enantiomeric excesses, but CPL can't be ruled out as the prebiotic origin of biological homochirality
 - Solid-phase asymmetric photochemistry can work very well, but has limited range
 - Solution-phase photochemistry can have good enantioselectivity, particularly with [2+2] photocycloadditions using chiral auxiliaries
 - Asymmetric photochemistry using chiral sensitizers is usually poorly selective
-