

Literature Review  
Organic Synthesis

**Organic Photochemistry – Tapping on light**

January 24<sup>th</sup>, 2013

❖ Fundamentals – How do they work?

❖ Practical considerations when starting a photochemical reaction

❖ Photochemistry as key steps in organic synthesis

❖ [2+2] photochemistry

❖ Photochemistry for the future

“ There is frequently a thin line between diverse photochemical reaction pathways, and slight changes in the structure of the substrate can lead to an entirely different outcome.

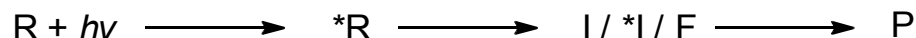
In combination with the unfamiliar photochemical equipment, this has resulted in many synthetic chemists being reluctant to use photochemical reactions. This reserve is not justified... ”

T. Bach et al, Angew Chem Int Ed **2011**, 50, 1000

■ Definition of organic photochemistry

It is a science concerned with the structures and dynamic processes that result from the interaction of light with organic molecules.

Organic photochemistry involves the overall process of:



**\*R:** An electronically excited molecule that has absorbed a photon ( $h\nu$ ) of the right frequency

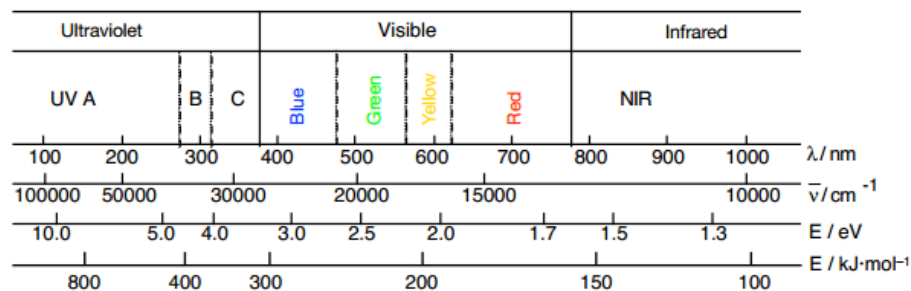
**I:** Formation of a discrete reactive intermediate that have the characteristics of a radical pair, a biradical or a zwitterion (most commonly observed for organic photochemical reactions)

**\*I:** Electronically excited intermediate

**F:** Funnel which is a non-discrete reactive intermediate.

■ Range of photon energies in the Electromagnetic Spectrum

Concerned with wavelengths of 200 nm to 1000 nm. The shorter the wavelength, the higher the energy.



## ■ Fundamental laws

- Grotthuss-Draper law (1812):** Light must be absorbed by a compound in order for a photochemical reaction to take place.
- Stark-Einstein law (1908-1913):** For each photon of light absorbed by a chemical system, only one molecule is activated for a subsequent photochemical reaction. Also known as the photo-equivalence law.

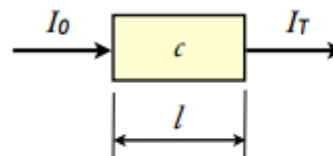
$$\Delta G_{\text{molecule}} = N_A \cdot h\nu = N_A \cdot \frac{hc}{\lambda}$$

## ■ From the fundamental laws...

- Energy/wavelength of light used is crucial, where a higher intensity of a higher wavelength of light may have the same total energy, but will not be able to effect the reaction.**
- Even though a photon of light may be absorbed by a chemical system, photophysical processes may take place where there are radiative (fluorescence and phosphorescence) and non-radiative return pathways, resulting in no chemical change of the reactant.
- The efficiency of which a given photochemical process occurs is given by its quantum yield which is the ratio of amount of product formed over amount of photons (of a certain wavelength) absorbed.
- If the quantum yield is smaller than 0.01, the conversion is very slow and exhaustive irradiation times may be required while high yields of the product may still be obtained.

## ■ Laws of absorption

### Beer-Lambert Law



$$A = -\log \frac{I_T}{I_0} = -\log T = \epsilon \cdot c \cdot l \quad [-]$$

$c$  molar concentration [mol l<sup>-1</sup>]

$l$  optical pathlength [cm]

$\epsilon$  molar decadic extinction coefficient

Example:  $c = 10^{-3}$  M,  $\epsilon = 10^4$  mol<sup>-1</sup> · l · cm<sup>-1</sup>

⇒  $T = 0.01$ ,  $A = 2$  ⇒ 99% of the light is absorbed within the first 2 mm of the solution

Depending on the photophysical properties of the absorbing species, light penetration is commonly limited to a narrow layer with the reaction mixture. Consequently, high dilutions or narrow reaction vessels are typically applied to allow for improved light penetration.

## ■ Kasha's rule

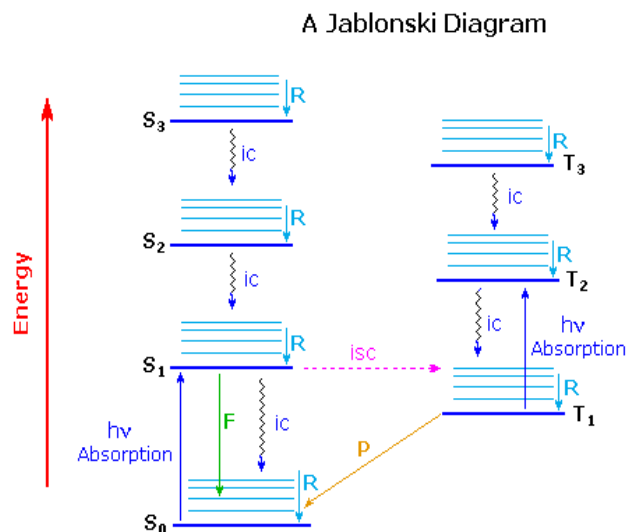
The rule states that photon emission (fluorescence or phosphorescence) occurs in appreciable yield only from the lowest excited state of a given multiplicity.

## ■ Franck-Condon Principle

When light of the specific frequency is absorbed by a molecule, the consequence of the Born-Oppenheimer approximation is that electronic transitions occur much faster than the nuclei can respond. After completion of the electronic transition, the nuclei will experience the new electronic negative force field of the new wavefunction until the nuclear geometry is adjusted to it.

Therefore, the most probable transitions between electronic states occur when the wavefunction of the initial vibrational state most closely resembles the wavefunction of the final vibrational state.

## ■ Jablonski Diagram / State Energy Diagram



Process	Transition	Timescale (sec)
Light Absorption (Excitation)	$S_0 \rightarrow S_n$	ca. $10^{-15}$ (instantaneous)
Internal Conversion	$S_n \rightarrow S_1$	$10^{-14}$ to $10^{-11}$
Vibrational Relaxation	$S_n^* \rightarrow S_n$	$10^{-12}$ to $10^{-10}$
Intersystem Crossing	$S_1 \rightarrow T_1$	$10^{-11}$ to $10^{-6}$
Fluorescence	$S_1 \rightarrow S_0$	$10^{-9}$ to $10^{-6}$
Phosphorescence	$T_1 \rightarrow S_0$	$10^{-3}$ to 100
Non-Radiative Decay	$S_1 \rightarrow S_0$	$10^{-7}$ to $10^{-5}$
	$T_1 \rightarrow S_0$	$10^{-3}$ to 100

Non-radiative decays may take place by intermolecular transfer to other molecules (quenching/ sensitisation)

Excited states may be classified as singlet or triplet based upon their electron spin angular momentum.

Typically we only consider the lowest excited singlet state (S<sub>1</sub>) or the lowest triplet state (T<sub>1</sub>) as likely candidates for the initiation of an emission (Kasha's rule)

Internal conversion of excited states to lower energy states of the same multiplicity takes place rapidly with loss of heat energy (relaxation).

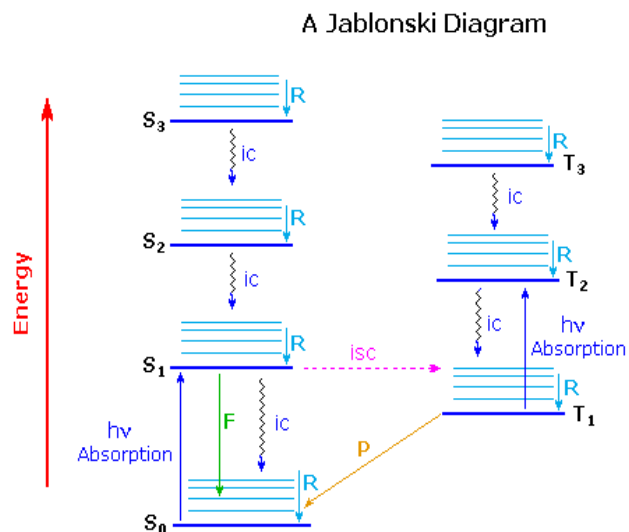
Conversion of a singlet state to a lower energy triplet state, or vice versa is termed intersystem crossing and is slower than internal conversion.

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## ■ Jablonski Diagram / State Energy Diagram



S = singlet state  
 T = triplet state  
 ic = internal conversion  
 isc = intersystem crossing  
 R = relaxation  
 F = fluorescence  
 P = phosphorescence

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## ■ Photosensitisation

For many molecules intersystem crossing (S1 to T1) is not very efficient, and such as if it is the only way to reach T1, T1 will be very limited.

**Photosensitisation is the process where a molecule (Donor) is selectively excited that produce T1 in high yield by ISC and then the energy can be transferred to a second molecule (Acceptor). Here the Donor molecule is also known as the photosensitiser. This is especially useful in providing a new group of potentially new reactive molecules. Aldehydes and ketones are widely employed as sensitisers.**

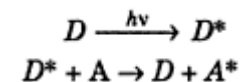
The basic requirement is that the energy of the donor should be 5kcal/mol more energy than the energy required for the excitation of the acceptor molecule.

In the event where D\* is the molecule of interest, the acceptor will be also known as a quencher.

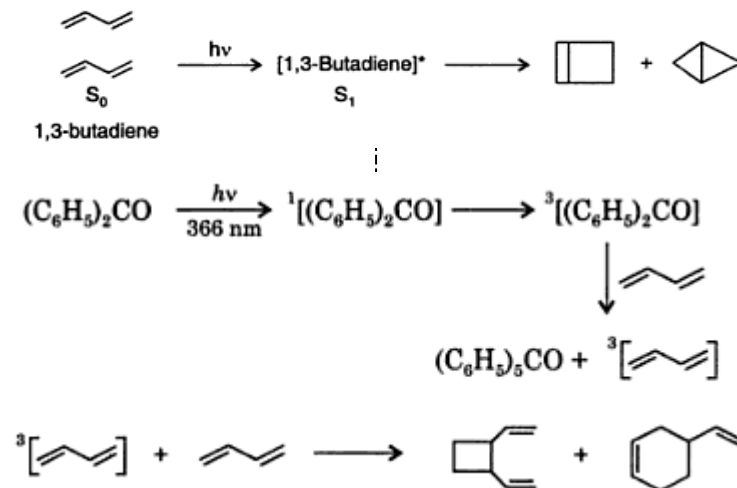
## ■ Requirements of photosensitiser

1. It must be excited by the irradiation used.
2. Present in sufficient concentration and absorb more strongly than the other reactants so that it is the major light absorber.
3. Energy of triplet state of sensitiser must be greater than that of the reactant.
4. Must be able to transmit energy to reactant.

Sensitiser	Triplet energy ( $E_T$ ) in kcal/mole
Benzophenone	69
Acetophenone	74
Fluorenone	53
Benzene	85
Nepthalene	61
Biacetyl	56
Benzil	53



Presence of photosensitiser can highly alter the fate of the reaction!!!



### 1. Purity of starting material is highly important.

Photochemistry is very sensitive to coloured or light absorbing impurities – not only merely the starting material, but unwanted compounds that are formed during the reaction. These may interfere with the photoprocesses and kill the reaction.

### 2. Taking UV spectra of substrate/all reagents may be a good idea before running your experiment.

From the UV spectra recorded with different compound concentrations, the extinction coefficients of all bands can be obtained even for the weak absorptions that may be of importance. UV spectra from the reaction mixture may help to identify the ground state interactions of compounds and guide the way to best reaction conditions. If possible, having UV spectra of the product may be useful in optimising yields as well.

#### HOMO-LUMO transitions in organic molecules

Chromophore	Transition	$\lambda_{\max}$ / nm	$\epsilon_{\max}$ / mol <sup>-1</sup> ·l·cm <sup>-1</sup>
N=O	n- $\pi^*$	~ 660	200
C=S	n- $\pi^*$	~ 520	100
N=N	n- $\pi^*$	~ 350	100
C=C=O	n- $\pi^*$	~ 350	30
C=O	n- $\pi^*$	~ 280	20
NO <sub>2</sub>	n- $\pi^*$	~ 270	20
C $\equiv$ N	n- $\pi^*$	~ 260	150
S=O	n- $\pi^*$	~ 210	1.5 · 10 <sup>3</sup>
benzene ring	$\pi$ - $\pi^*$	~ 260	200
C=C=O	$\pi$ - $\pi^*$	~ 220	2 · 10 <sup>5</sup>
C=C=C	$\pi$ - $\pi^*$	~ 220	2 · 10 <sup>5</sup>
C=C	$\pi$ - $\pi^*$	~ 180	1 · 10 <sup>5</sup>
C-C	$\sigma$ - $\sigma^*$	< 180	1 · 10 <sup>5</sup>
C-H	$\sigma$ - $\sigma^*$	< 180	1 · 10 <sup>3</sup>

### 3. Usage of solvents

1. Solvent should be able to dissolve reactant
2. Solvent should be free of impurities.
3. The extinction coefficient of the solvent at the particular wavelength should not be too high as this will result in a significant filter effect.

Table 1: Solvents used for photoreactions<sup>1</sup>

Solvent	Cut-off wavelength <sup>2</sup>	$\epsilon_T$ <sup>3</sup>	ET(30) <sup>4</sup>
water	185	78.30	63.1
acetonitrile	190	35.94	45.6
n-hexane	195	1.88	31.0
ethanol	204	24.5	51.9
methanol	205	32.66	55.4
cyclohexane	215	2.02	30.9
diethyl ether	215	4.20	34.5
1,4-dioxane	230	2.21	36.0
methylene chloride	230	8.93	40.7
chloroform	245	4.81	39.1
tetrahydrofuran	245	7.58	37.5
ethyl acetate	255	6.02	38.1
acetic acid	250	6.17	51.7
carbon tetrachloride	265	2.23	32.4
dimethylsulfoxide	277	46.45	45.1
benzene	280	2.27	34.3
toluene	285	2.38	33.9
pyridine	305	12.91	40.5
acetone	330	20.56	42.2

<sup>1</sup> taken from C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry* 1988, VCH, Weinheim.

#### 4. Usage of glassware

Type of Glass	Wavelength Cut-off
Pyrex	< 275 nm
Corex	< 260 nm
Vycor	< 220 nm
Quartz	< 170 nm

#### 5. Irradiation apparatus

##### (a) Low-pressure Mercury Arc Lamps

- $10^{-5}$  atm under operating conditions
- Most of the emission occurs at 254 nm, supplied as quartz tubes.
- Heating under such conditions is modest.
- "rotating merry go round" device can ensure equivalent irradiation in all positions.

##### (b) Medium-Pressure Mercury Arc Lamps

- 1-10atm
- Emission consists of a range of lines over a continuum (313, 366, 405, 550 nm being most prominent) with 254 nm strongly diminished
- Considerable amount of heat produced with forced circulation of cooling water.
- Can be adapted to lower temperature setups

#### 6. Effects of Impurities, Oxygen and Temperature

- With the lifetime of the excited state being short, for a chemical reaction to compete with an unproductive physical decay, it has to be fast.
- **Effects of impurities are small and extensive purification of reagents and solvents is not generally required.**
- **The exception is oxygen, which quenches excited states at a diffusion-controlled rate. In many air-equilibrated organic solvents the amount of oxygen is in the range of 0.002 to 0.003M, which is large enough to quench more than 90% of the longlived triplets. ==> Overcome by flushing with inert gas**
- Photochemical reactions are generally unaffected by temperature, but temperature may affect the reaction steps before or after the photochemical steps and lead to very different reagents being excited.

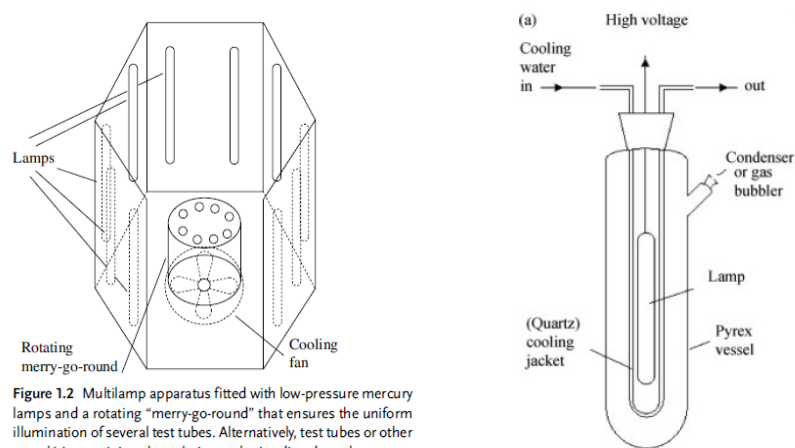


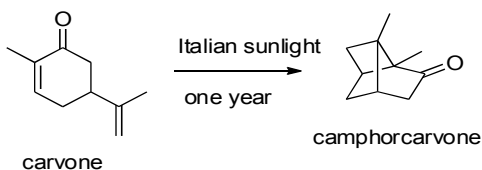
Figure 1.2. Multilamp apparatus fitted with low-pressure mercury lamps and a rotating "merry-go-round" that ensures the uniform illumination of several test tubes. Alternatively, test tubes or other vessel(s) containing the solution to be irradiated can be accommodated.

Medium Pressure Mercury Arc





## Initial Discovery

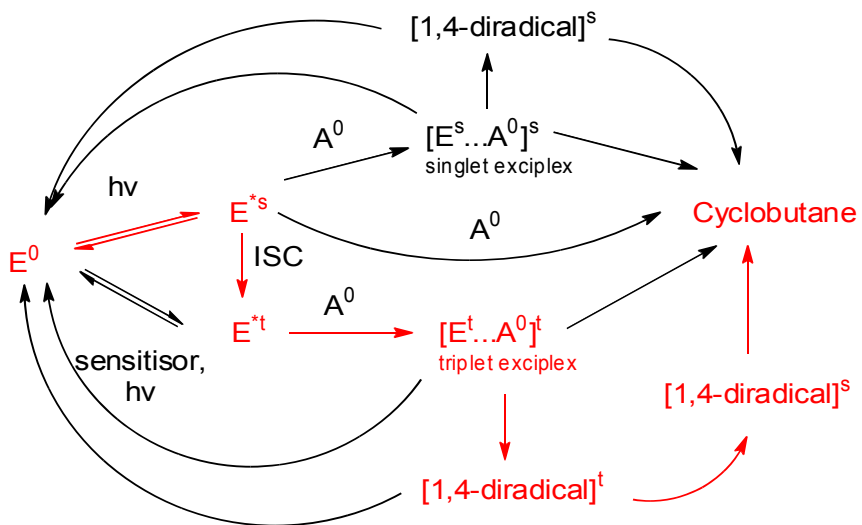


Ciamician, G; Silber, P. Ber., **1908**, 41, 1928

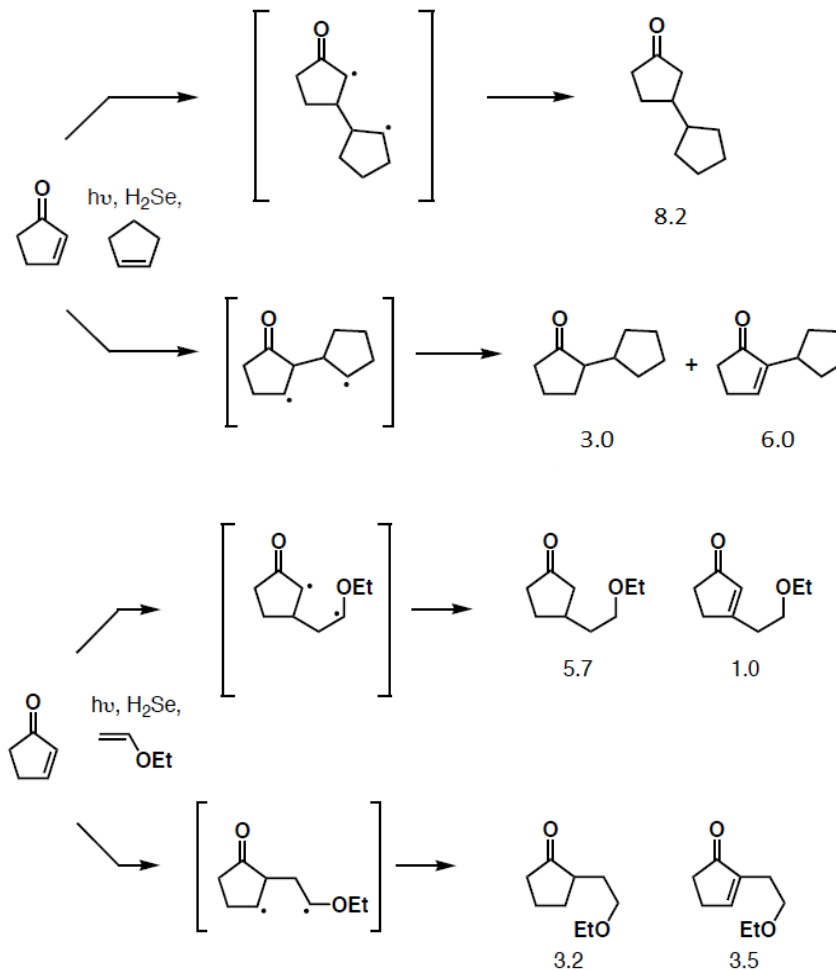
Confirmation of structure by Buchi and Goldman using a 'modified' procedure (6.5 months with Californian sunshine)

Buchi, G.; Goldman, I. M. *J. Am. Chem. Soc.*, **1957**, 79, 4741.

## Mechanistic Discussion



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

Evidence for Similar Rates of Initial Bond Formation on  $\alpha$  or  $\beta$  carbon

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

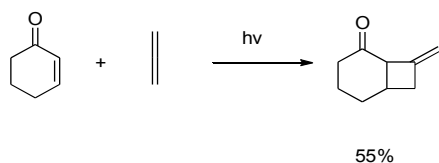
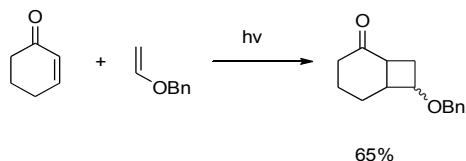
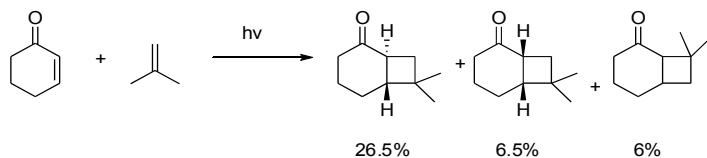
### Factors

Ratio of isomeric photoadducts (head-to-tail or head-to-head products) is generally thought to be controlled by:-

- 1) **Electronic interactions in the excited state complex**
- 2) **Steric interactions between the substituents on the two double bonds.**

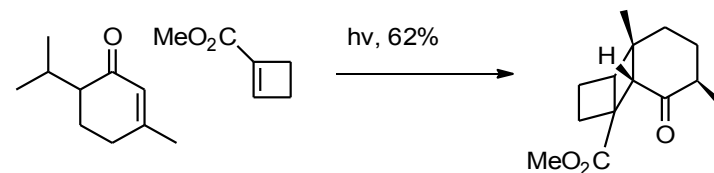
### Electronic factor: Polar Exciplex theory

The charge distribution of the excited enone is the exact opposite of its ground state configuration where the enone beta-carbon bears a partial negative charge. During exciplex formation, the ground state alkene and the excited state enone are oriented to maximise electrostatic interactions.



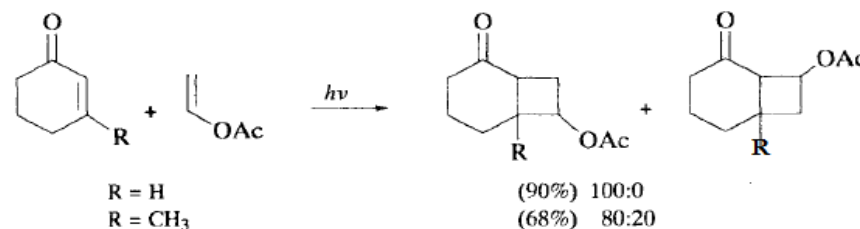
Corey, E. J. et al. *J. Am. Chem. Soc.* **1964**, *86*, 5570.

While this electrostatic interpretation can be a useful predictive tool, regioselectivity can be greatly influenced by the rate at which each initially formed exciplex or 1,4-diradical proceeds to products or reverts to ground state.



Wender, P. A. *J. Am. Chem. Soc.* **1978**, *100*, 4321

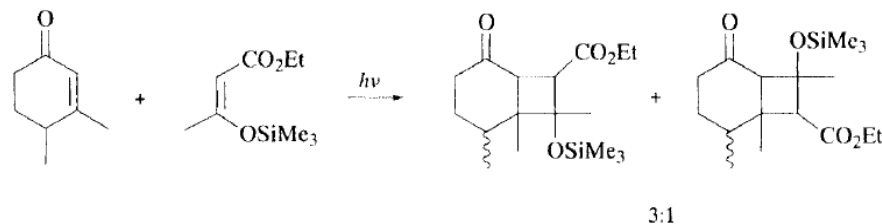
### Steric interactions



Hunter, N. R. *Can. J. Chem.* **1970**, *48*, 1436..

### Counteracting electronic and steric influences

While a strong electronic preference (with minimal steric effect) for one regioisomer can control the outcome of the reaction (and vice versa), selectivity can suffer when two effects counteract one another.



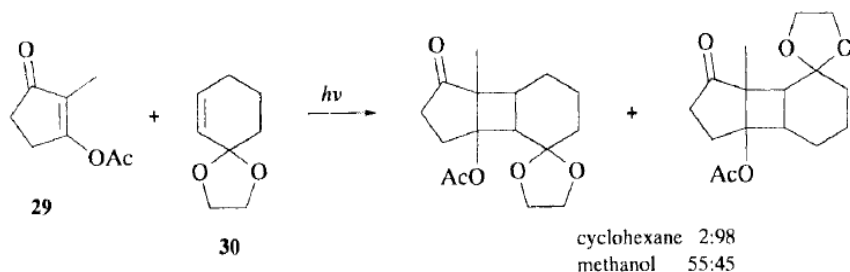
Liu, H. S. et al. *Tetrahedron Letters*, **1982**, *23*, 295.

### Other Factors that affect regioselectivity

#### 1) Choice of solvent

- The polar exciplex model predicts that solvent polarity can affect the regioselectivity of a photocycloaddition by influencing the charge transfer interaction in the exciplex.

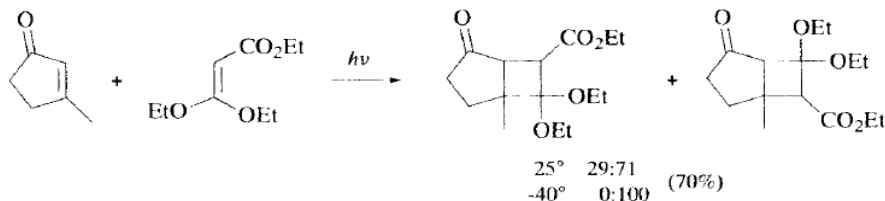
- Nonpolar solvents tend to favour the products predicted by the model, while more polar solvents tend to temper electrostatic interactions and result in a higher proportion of the minor product.



Challand, B. D. ; DeMayo, P. *Chem Soc, Chem Commun* **1968**, 16, 982.

#### 2) Temperature

- Typically lowering the temperature tends to enhance the selectivity in favour of the major regioisomer.



Van Audenhove, M. *Tetrahedron Letters* **1978**, 2057.

### Intramolecular photocycloaddition

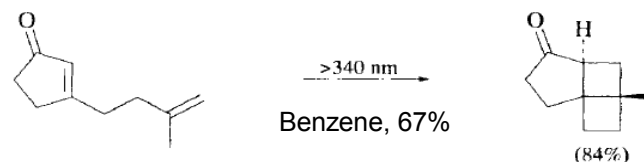
- Geometric constraints that are placed on intramolecular systems can usually override the problems that lead to multiple products in the analogous intermolecular reaction.

#### - Preference for formation of five membered rings followed by six membered rings

- In general, two to four membered tethers set regioselectivity. When the tether between the enone and alkene is more than four atoms, the straight adducts usually predominates.

#### 1) Two-membered tethers

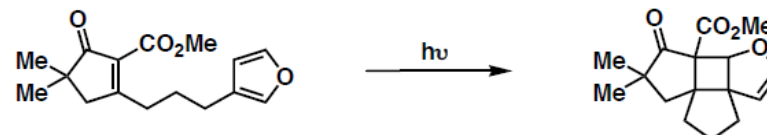
- While initiation formation of five membered rings are usually preferred, substitution on the internal carbon of the alkene retards five-membered ring formation and 1,6-cyclisation dominates.



Wolff, S.; Agosta, W.C. *J. Org Chem.*, **1981**, 46, 4821.

#### 2) Three/four-membered tethers

- Predictable regioselectivity control that generally gives the straight adduct as the exclusive product through initial five/six-membered ring formation. Overrides the normal electronic preference observed in the intermolecular reaction.



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

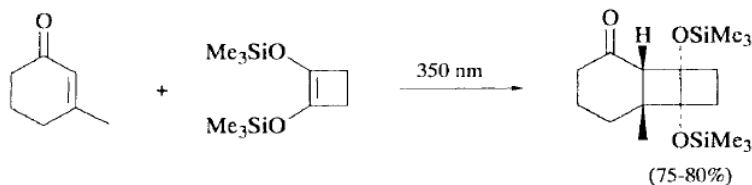
### Important Considerations

- Photocycloaddition is NOT concerted and proceeds through an intermediate 1,4-diradical  $\rightarrow$  Rotation about single bonds in the diradical can result in scrambling of alkene geometry IF:-

1) Alkene is acyclic.

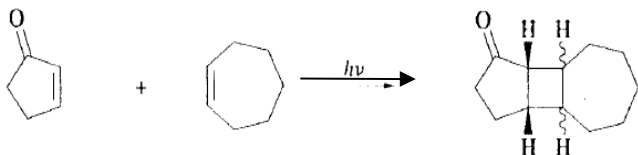
2) Double bond is contained in a ring larger than six.

- When cyclic alkenes which have ring sizes of five members or less are used as the alkene partner, the alkene geometry is preserved since cis-trans isomerisation is inhibited.

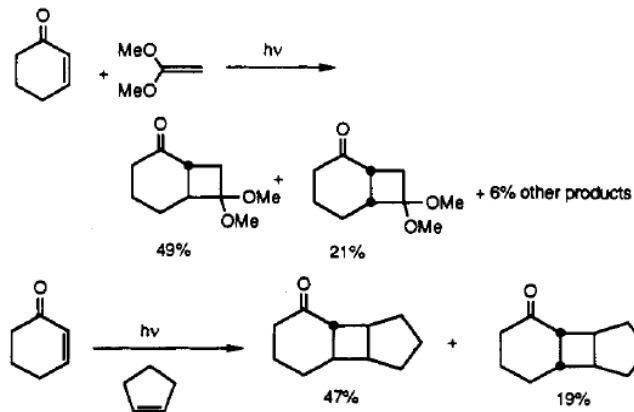


Van Audenhove, M. *Tetrahedron Letters* **1980**, 1979.

- Use of larger rings can result in loss of alkene stereochemistry.



Duc, L et al. *Tetrahedron Letters* **1968**, 6173.



Corey, E. J. et al. *J. Am. Chem. Soc.* **1964**, 86, 5570.

Spectroscopic evidence indicates that some cyclohexenone triplets are substantially twisted about the C-C double bond and permits bond formation on one side of the ring at the alpha carbon while bond formation at the opposite face on the beta carbon. However, trans-fused products are easily epimerised to cis, so this is normally of no consequence.



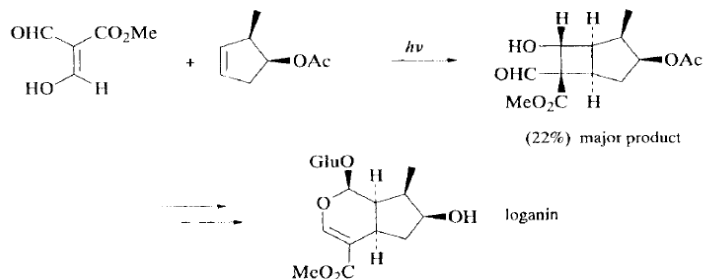
Eaton, P.E. *J. Am. Chem. Soc.* **1962**, 84, 2344

**Facial selectivity: Tends to favour exo or cis-anti-cis geometry**

- result of steric interactions between the alkene substituents and the enone ring carbons in the cis-syn-cis isomer

**Presence of preexisting stereogenic centre on either the excited state enone OR ground state alkene**

- Excited state enone will normally undergo addition to the sterically most accessible face of the ground state alkene.

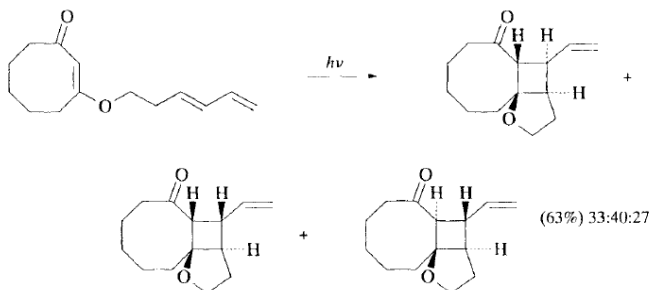


Buchi G. et al, *J. Am. Chem. Soc.*, **1973**, 95, 540.

**Intramolecular photocycloaddition**

Intramolecular photocycloadditions are generally highly stereoselective. Additionally, stereogenic centres in the starting enone-alkene can be utilized to dictate the stereogeneity of newly formed stereocentres in the photoadduct.

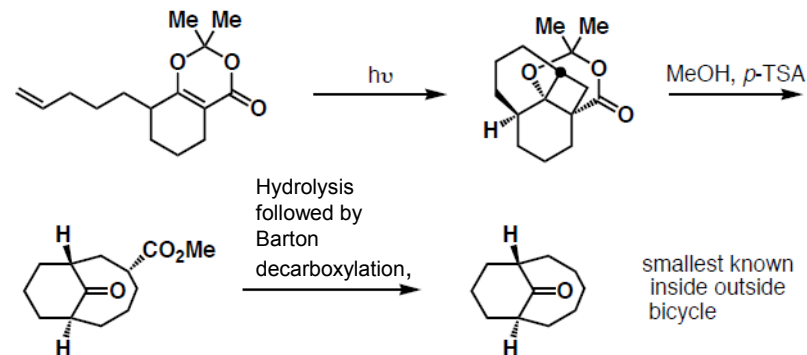
Stereochemistry of ring fusion between cyclobutane and other rings in the photoadducts is almost always cis. Exceptions result when the enone ring contains seven or more atoms or when the enone-alkene tether can easily accommodate the transcyclobutane. (example below)



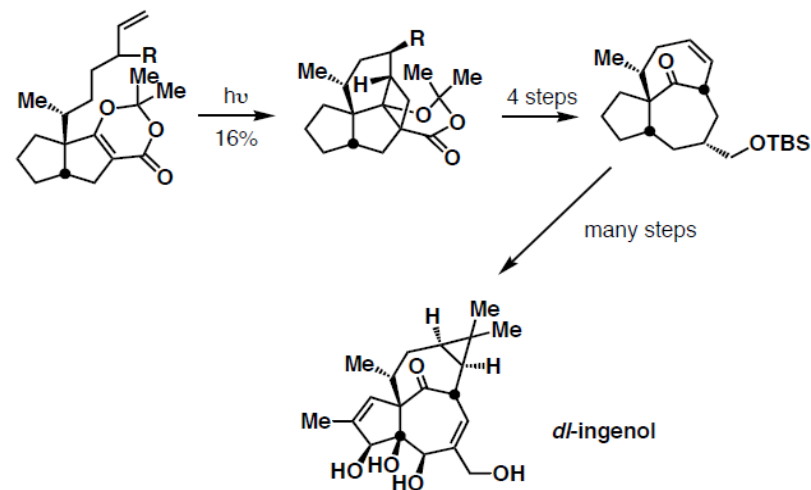
Pirrung M.C. et al, *Tetrahedron Letters*, **1986**, 27, 3983.

**Example: Synthesis of ingenol**

A noteworthy exception where the dioxolene which produces exclusively the trans 6-4 junction in cycloadduct.

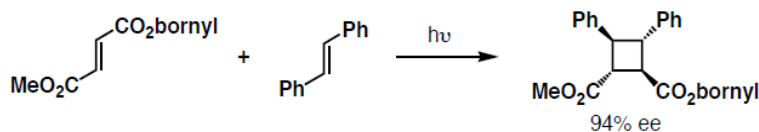


Winkler, J. D.: Hev, J. P. *J. Am. Chem. Soc.*, **1986**, 108, 6425.



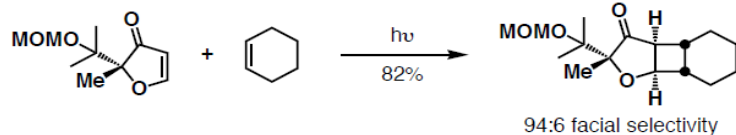
Winkler, J. D. et al. *J. Am. Chem. Soc.*, **2002**, 124, 9726.

Few reports have appeared regarding control of absolute asymmetry in photocycloadditions. The first example of the use of a “removable” chiral auxiliary is the photocycloaddition of bornyl fumarate to stilbenes to provide impressive enantioselectivity.



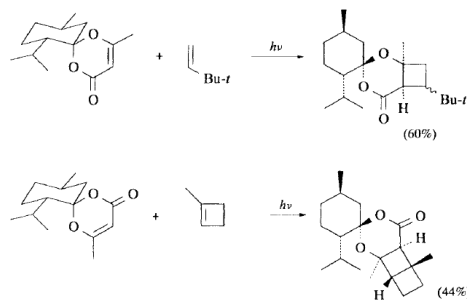
Tolbert, L. M.; Ali, M. B. *J. Am. Chem. Soc.*, **1982**, *104*, 1742.

Excellent facial selectivity is also possible in the photoaddition of compounds where the stereogenic centre that controls diastereoselectivity can be excised to afford products of high enantiomeric purity.



Baldwin, S.W et al. *Tetrahedron Letters*, **1986**, *27*, 5975.

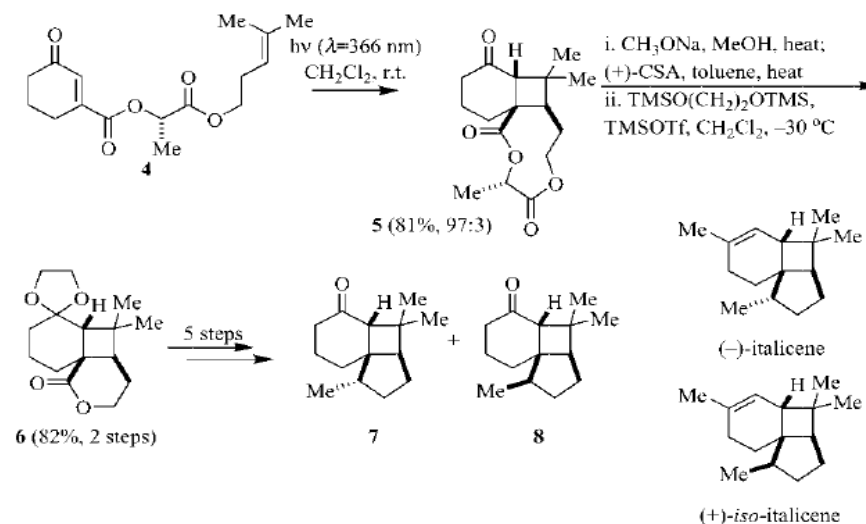
Sterically based dioxolenones also show promise for asymmetric syntheses based on [2+2] photocycloadditions.



Demuth, M. *Pure and Applied Chem*, **1986**, *58*, 1233.

**Example: Achieving enantioselectivity through the influence of a homochiral tether between two reaction moieties in making (-)-italicene and (+)-iso-italicene**

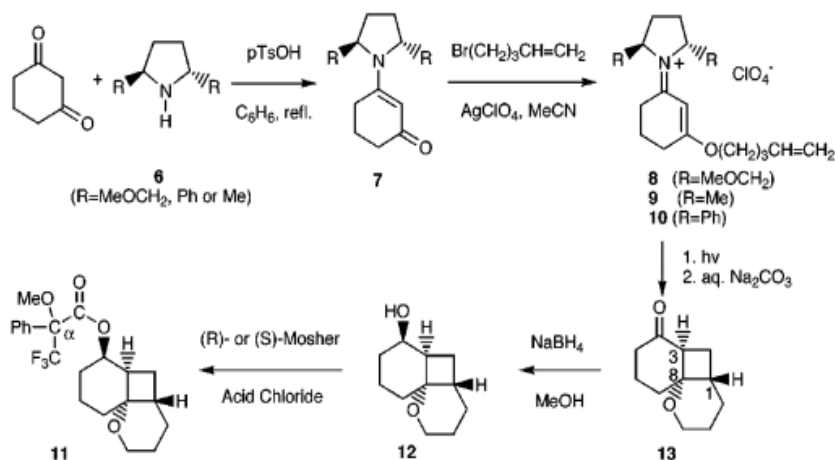
The approach made use of (S)-lactic acid as a chiral removable tether group, which determined the excellent facial selectivity achieved in the key photoaddition step.



Faurea, S. ; Piva O. *Tetrahedron Letters*, **2001**, *42*, 255.

**Example: Using eniminium salt as surrogate for enones to direct enantioselectivity**

Since the iminium salts possess only  $\pi \rightarrow \pi^*$  excited states, ISC from singlet to triplet states expected to be slow. As such, photocycloaddition reactions of the substrates could occur from singlet excited states and follow concerted mechanistic pathways.



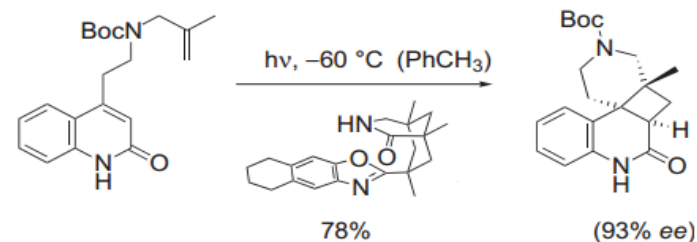
**Table 2.** Facial Selectivities (% ee) in Intramolecular [2 + 2] Photocycloadditions of the C<sub>2</sub>-Chiral Eniminium Perchlorates **8** and **9**

eniminium perchlorate	conditions <sup>a</sup>			% ee <sup>b</sup> tricyclic ketone <b>13</b>
	conversion (%) <sup>c</sup>	temperature (°C)	yield (%)	
<b>8</b>	90	20	51	63
<b>8</b>	56	20	65	75
<b>8</b>	40	20	61	82
<b>8</b>	60	4	60	78
<b>8</b>	46	4	56	80
<b>9</b>	53	20	20	37
<b>9</b>	51	20	25	31
<b>9</b>	48	20	31	37

<sup>a</sup> All photoreactions were run in MeCN by using Correx glass-filtered light. <sup>b</sup> From the % de of the ester derivative, formed by reaction of alcohol **12** with (R)-(-)-Mosher acid chloride, by using HPLC on a Chiralcel-OJ column with 9:1 hexane-*i*-PrOH as eluant. <sup>c</sup> Determined by UV-spectroscopic monitoring of the photolyzate.

**Example: Complexing with template structures where enantioselectivity is induced inside a host/guest structure**

Photochemical reactions have been carried out in host/guest structures where stereochemistry can be induced inside.

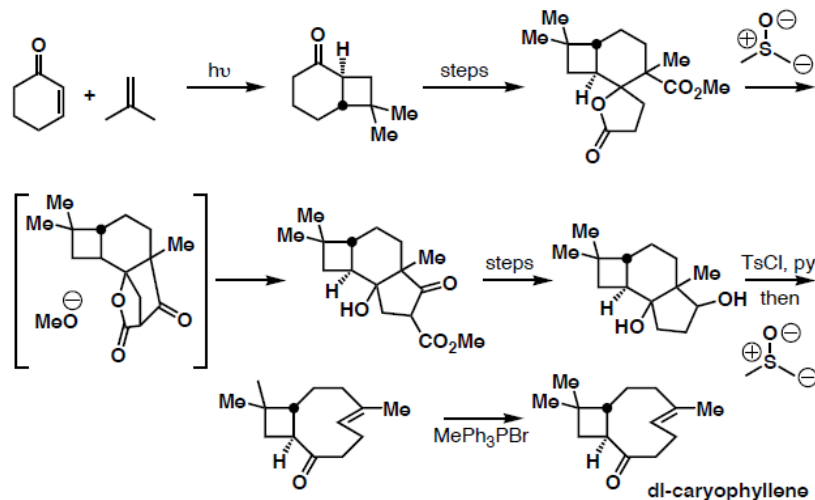


Brandes, S; Selig, P; Bach T. *Synlett.* **2004**, *14*, 2588.

### Total synthesis of caryophyllene

In 1964, the first elegant synthesis was reported by Corey and coworkers, where the nine-membered ring was generated by bond scission of two fused smaller rings.

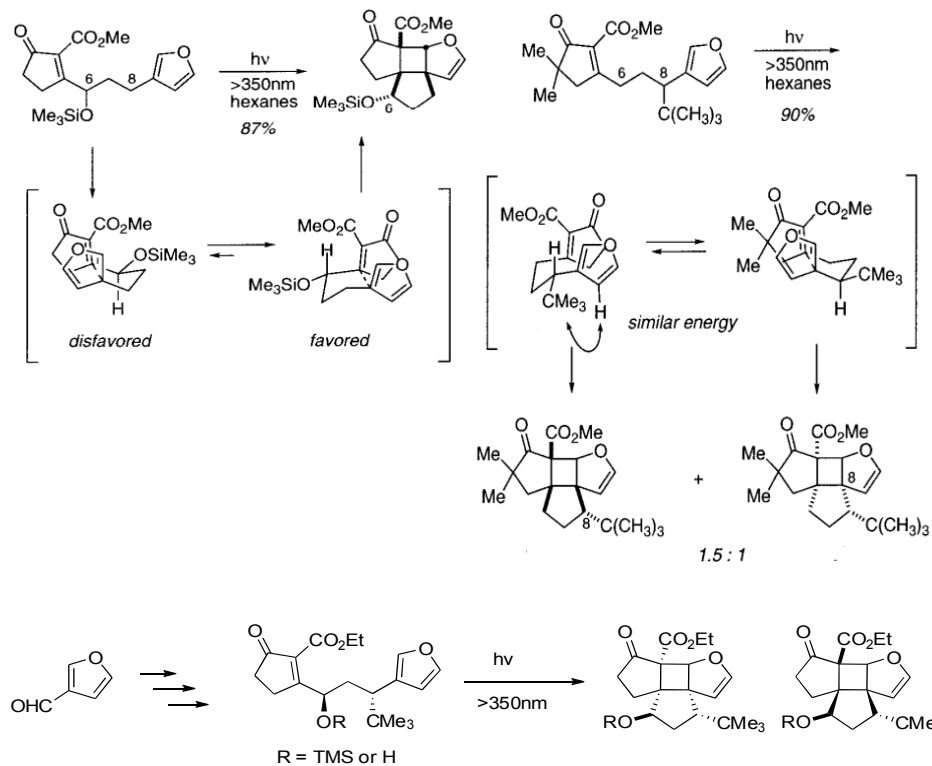
The very first step involves the photoaddition of 2-cyclohexanone to isobutylene where the unstable trans isomer is produced in larger amount than to the cis form (which has already been discussed in regioselectivity factors).



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

### Total synthesis of dl-ginkgolide B

One of the key steps in the total synthesis of dl-ginkgolide B is the double diastereoselective enone-furan [2+2] photocycloaddition. Similar photocycloadditions had been examined on stereochemically simplified systems as shown.



	Solvent	ratio	yield
R = Me <sub>3</sub> Si	hexanes/C <sub>6</sub> H <sub>6</sub>	>25 : 1	85%
R = Me <sub>3</sub> Si	MeOH	>25 : 1	80%
R = H	hexanes/C <sub>6</sub> H <sub>6</sub>	1 : 1 : 1	77%
R = H	THF	7 : 1	79%
R = H	MeOH	>25 : 1	75%

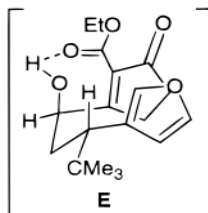
Crimmins, M. T. et al. *J. Am. Chem. Soc.*, **2000**, *122*, 8453.



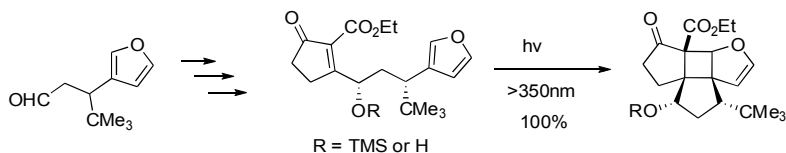
### Total synthesis of dl-ginkgolide B (continued)

Following the results regarding solvent effect, it was deduced that a hydrogen bonding interaction between the secondary hydroxyl and the ester carbonyl might be responsible for altering the diastereoselectivity of the photocycloaddition.

With amide carbonyls being more Lewis basic than ester carbonyls, the possibility was studied and the product ratio improved to 3:1 in favour of the desired product



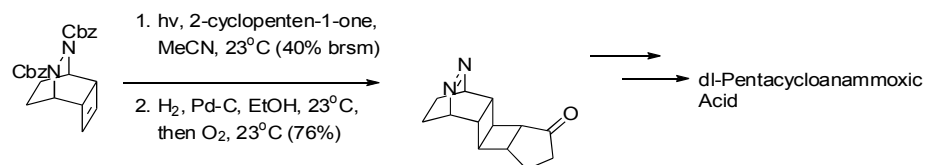
A syn diastereomer of starting material was then postulated to permit a transition state where both substituents at carbon 6 and 8 would be in pseudoequatorial orientations in chairlike conformation, and the strategy was modified.



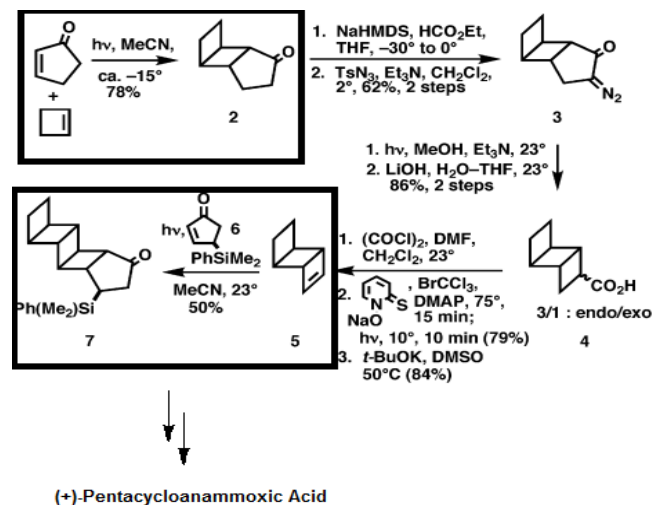
Crimmins, M.T. et al. *J. Am. Chem. Soc.*, **2000**, 122, 8453.

### Total synthesis of (+/-) and (+)-pentacycloammonic acid

In both approaches, [2+2] photochemical cycloaddition proves vital in building cyclobutane rings in the ladderanes.



V. Mascitti, E. J. Corey, *J. Am. Chem. Soc.* **2004**, 126, 15664.



V. Mascitti, E. J. Corey, *J. Am. Chem. Soc.* **2006**, 128, 3118.

### Introduction

While alkenes conjugated to a pi system such as enones have absorption maxima around 300 nm and can easily be led to triplet excited states on direct irradiation, nonconjugated alkenes have UV absorption maxima at 190-200 nm and thus require high energy for excitation that is not available from conventional photochemical equipment.

However, in the presence of transition metal salts, such alkenes exhibit UV absorption maxima around 240 nm. CuOTf has been found to be the most efficient and selective for [2+2]-cycloaddition, where it leads preferentially to a single diastereoisomer especially in the case of intramolecular reactions.

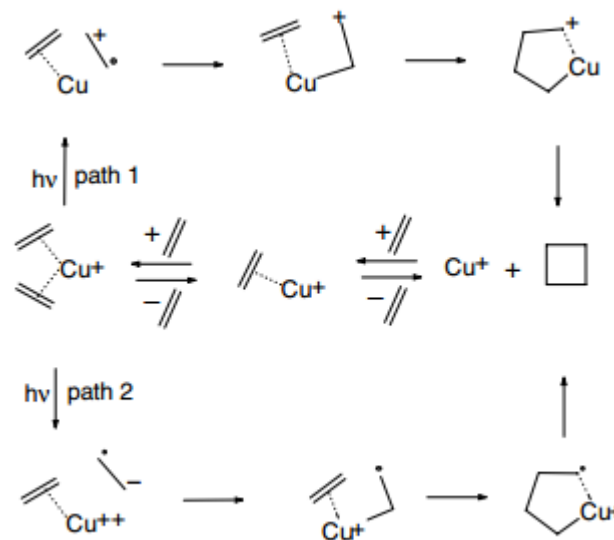
### Mechanism of Catalysis

While norbornene and CuBr separately are almost transparent in UV, an intense UV absorption band at 239 nm was observed for a solution with both. In the presence of excess norbornene and irradiation for 149 hr in vycor glassware, the dimer can be formed.

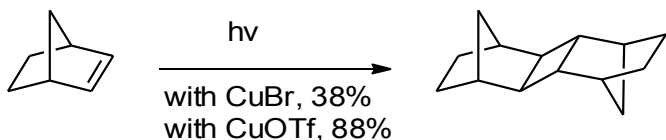
Discovery of the role of the cuprous reagent as a catalyst with over 40 molecules of dimer formed for every 1 molecule of cuprous salt present. And that the photocycloaddition requires ground-state coordination of both reacting alkene bonds with a single Cu(I)

The CuOTf-norbornene complex shows two UV-absorption maxima at 236 nm ( $\epsilon$  3400) and 272 nm ( $\epsilon$  2000). The shorter wavelength absorption possibly arises through a metal-to-alkene ligand charge transfer (MLCT) excitation while the longer wavelength absorption is assumed to be due to an alkene ligand-to-metal charge transfer (LMCT) excitation.

Assuming the bond formation to be a sequential process, LMCT (path 1) and MLCT (Path 2) excitation may proceed through cationic or radical paths. A concerted pathway has also been supported by intermolecular cycloaddition studies.

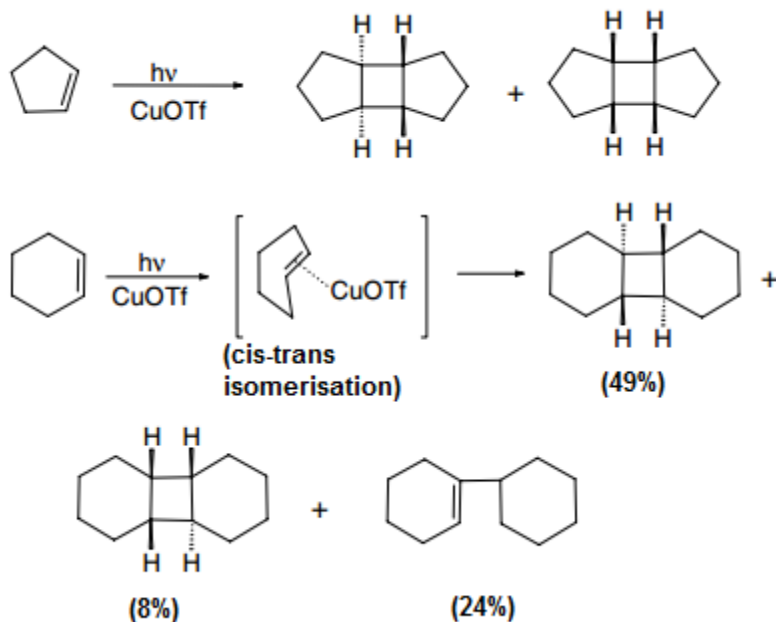


From the CRC Handbook of Organic Photochemistry and Photobiology, 2<sup>nd</sup> Edition, Chapter 18 Pg 18-3



### Intermolecular Photocycloadditions

It requires that one of the reacting alkenes to be **highly strained and reactive**.

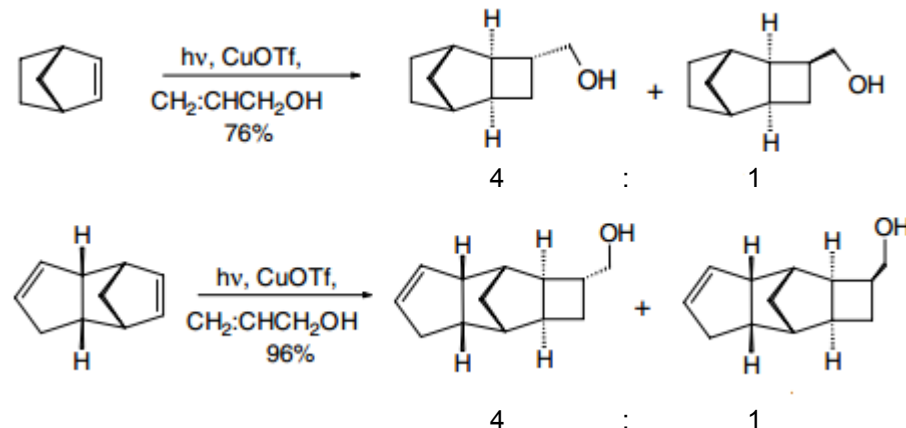


Salomon, R. G. et al. *J. Am. Chem. Soc.*, **1974**, 96, 1145.

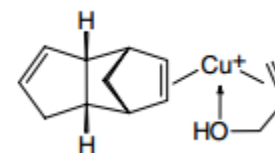
Cycloheptenes on the other hand produces all trans-fused trimer as the sole product. No dimerisation has been observed for cyclooctene and acyclic olefins. However, mixed photocycloaddition occurs with cyclooctene if the other olefin is sufficiently reactive.

Salomon, R. G. and Kochi, J. K., *J. Am. Chem. Soc.*, **1974**, 96, 1137.  
Salomon, R. G. et al. *J. Am. Chem. Soc.*, **1974**, 96, 1145.

Photocyclization of allyl alcohol to strained cycloalkenes



The additional coordinative interaction by the OH group of the allyl alcohol favour such complex formation.

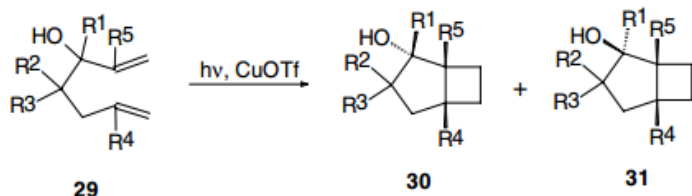


Salomon, R. G. and Sinha, A. *Tetrahedron Lett*, **1978**, 1367.

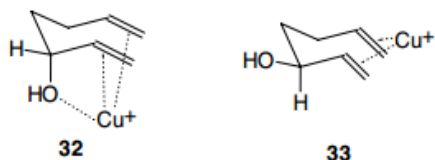
## Intramolecular Photocycloadditions

## [2+2] Cycloaddition of 1,6-heptadienes

While acyclic olefins often fail to undergo intermolecular [2+2] cycloaddition reactions, intramolecular [2+2] cycloaddition reactions are possible.



a, R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = R<sup>4</sup> = R<sup>5</sup> = H; b, R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = R<sup>4</sup> = H, R<sup>5</sup> = Me;  
 c, R<sup>1</sup> = R<sup>4</sup> = R<sup>5</sup> = H, R<sup>2</sup> = R<sup>3</sup> = Me; d, R<sup>1</sup> = R<sup>4</sup> = H, R<sup>2</sup> = R<sup>3</sup> = R<sup>5</sup> = Me;  
 e, R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = H, R<sup>4</sup> = R<sup>5</sup> = Me; f, R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = R<sup>5</sup> = H, R<sup>4</sup> = Me;  
 g, R<sup>1</sup> = Me, R<sup>2</sup> = R<sup>3</sup> = R<sup>4</sup> = R<sup>5</sup> = H



The thermodynamically less stable endo product is preferred in this case. The transition state in **32** with Cu(I) as a tridentate ligand is favoured.

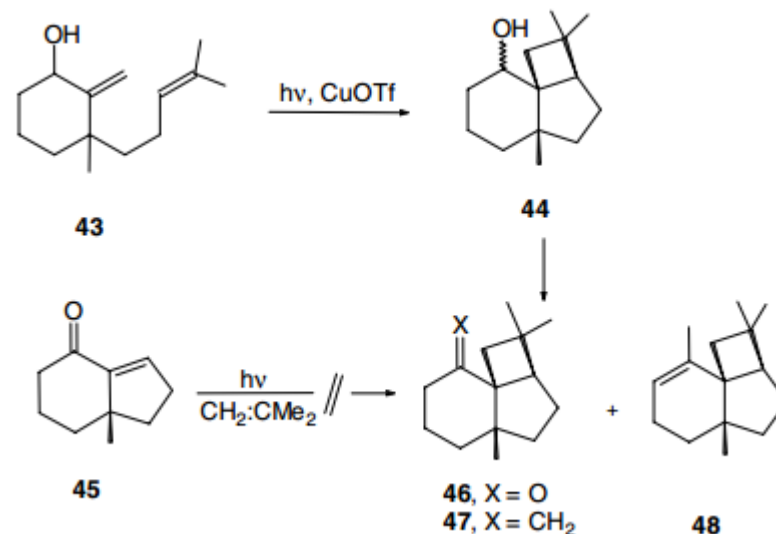
TABLE 18.1 Copper(I)-Catalyzed Photocycloaddition of 1,6-Heptadiene-3-ols

Entry	Diene	Bicyclo[3.2.0]heptanes	endo:exo	Yield (%)
1	29a	30a, 31a	9:1	86
2	29b	30b, 31b	6:1	81
3	29c	30c, 31c	9:1	91
4	29d	30d, 31d	3:2	83
5	29e	30e, 31e	>20:1	*
6	29f	30f, 31f	5:1	78
7	29g	30g, 31g	>20:1	89

\* 40% conversion after 24 h.

From the CRC Handbook of Organic Photochemistry and Photobiology, 2<sup>nd</sup> Edition, Chapter 18

Example: total synthesis of the sesquiterpenes  $\alpha$ -panasinsene and  $\beta$ -panasinsene



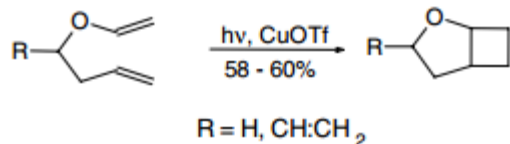
Key photochemical step was achieved under 24 h, and gave a single tricyclic product in 45% yield.

It is noteworthy that direct access to the requisite intermediate involving **45** with isobutylene failed and illustrate the importance of the copper(I)-catalysed photocycloaddition of 1,6-heptadienols.

McMurry, J. E. and Choy, W. *Tetrahedron Lett.*, **1980**, *21*, 2477.

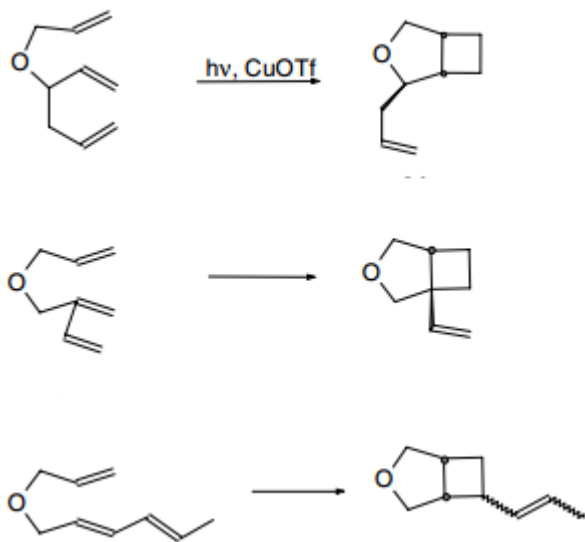
## Intramolecular Photocycloadditions

## [2+2] Photocycloaddition of Diallyl Ethers and Homoallyl Vinyl Ethers



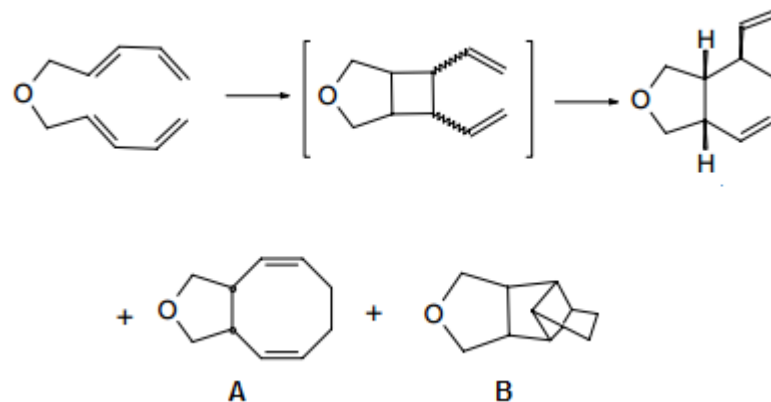
Raychaudhuri, S. R. et al. *J. Am. Chem. Soc.*, **1982**, *104*, 6841.

Copper(I)-catalysed intramolecular [2+2] photocycloaddition is selective for 1,6-dienes only. **The 1,5 and 1,7-dienes do not react.**



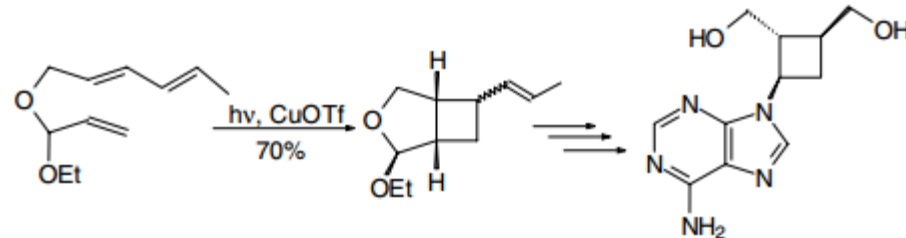
Ghosh, S. et al. *J. Org. Chem.*, **1987**, *52*, 83.

CuOTf-catalysed photocycloaddition of the tetraene produces a mixture of products of which the divinyl cyclobutane formed initially underwent further reaction on prolonged radiation to form these products. In fact, the tricyclic compound B arises from intramolecular addition of cyclooctadiene derivative.



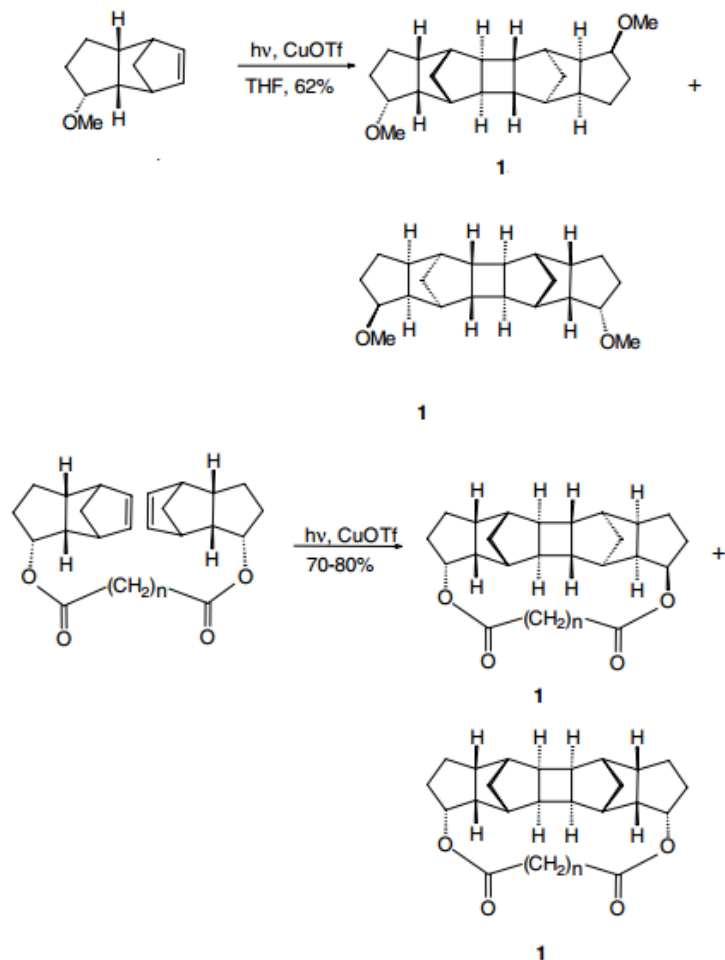
Herte, R. et al. *J. Am. Chem. Soc.*, **1991**, *113*, 657.

Synthesis of cyclobut-A, an inhibitor of HIV has been accomplished using the CuOTf catalysed photocycloaddition as the key step

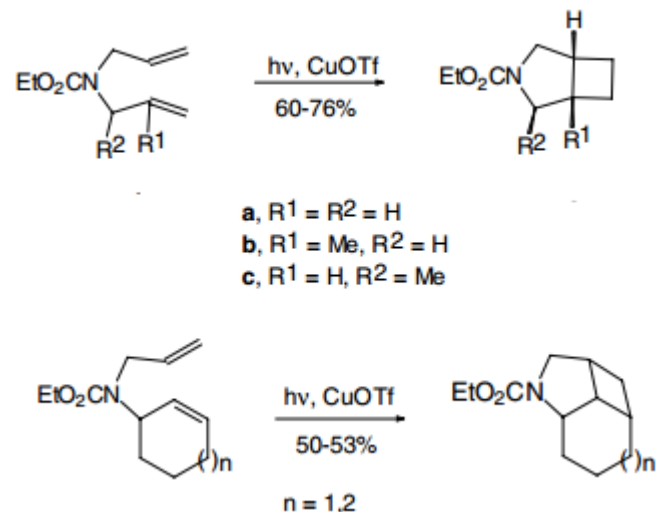


Panda, J. et al. *J. Chem. Soc., Perkin Trans*, **2001**, *1*, 3013.

## Tethered Intramolecular Photocycloadditions

Galoppini, E. et al. *J. Org. Chem.*, **2001**, 66, 162.

## [2+2] photocycloaddition of diallyl carbamates

Salomon R. G. et al. *Tetrahedron Lett.*, **1984**, 25, 3167.

It is important to note that N,N-diallyl acetamide and N,N-diallylformamide do not undergo [2+2]-photocycloaddition under these conditions. The failure of these photoreactions is possibly due to excitation of the amide functional groups rather than photoactivation of the Cu(I)-diene complex.