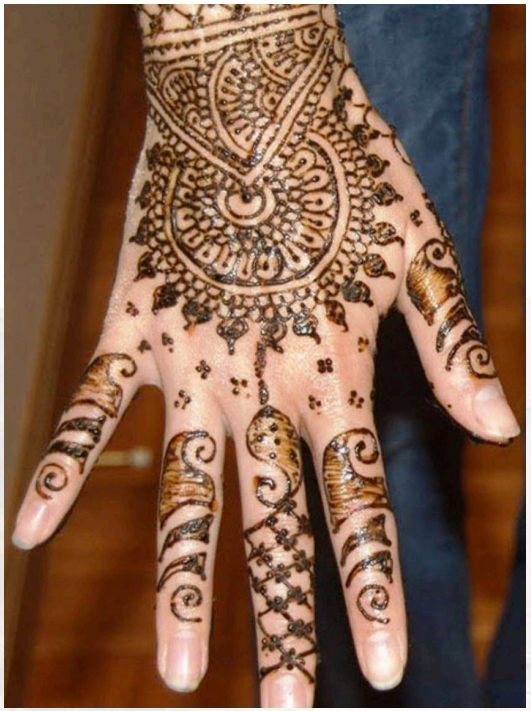
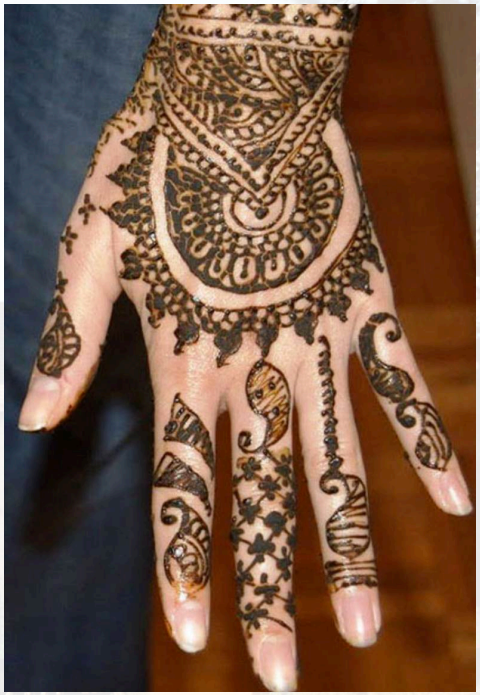
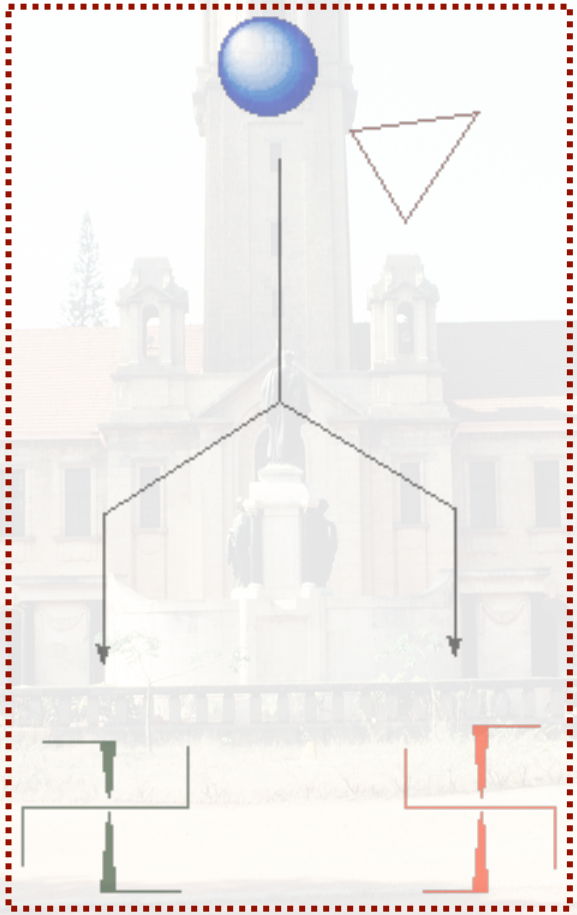
Chiral Photochemistry



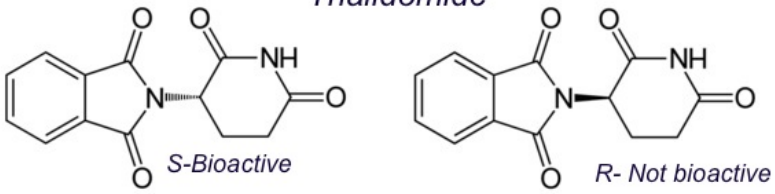


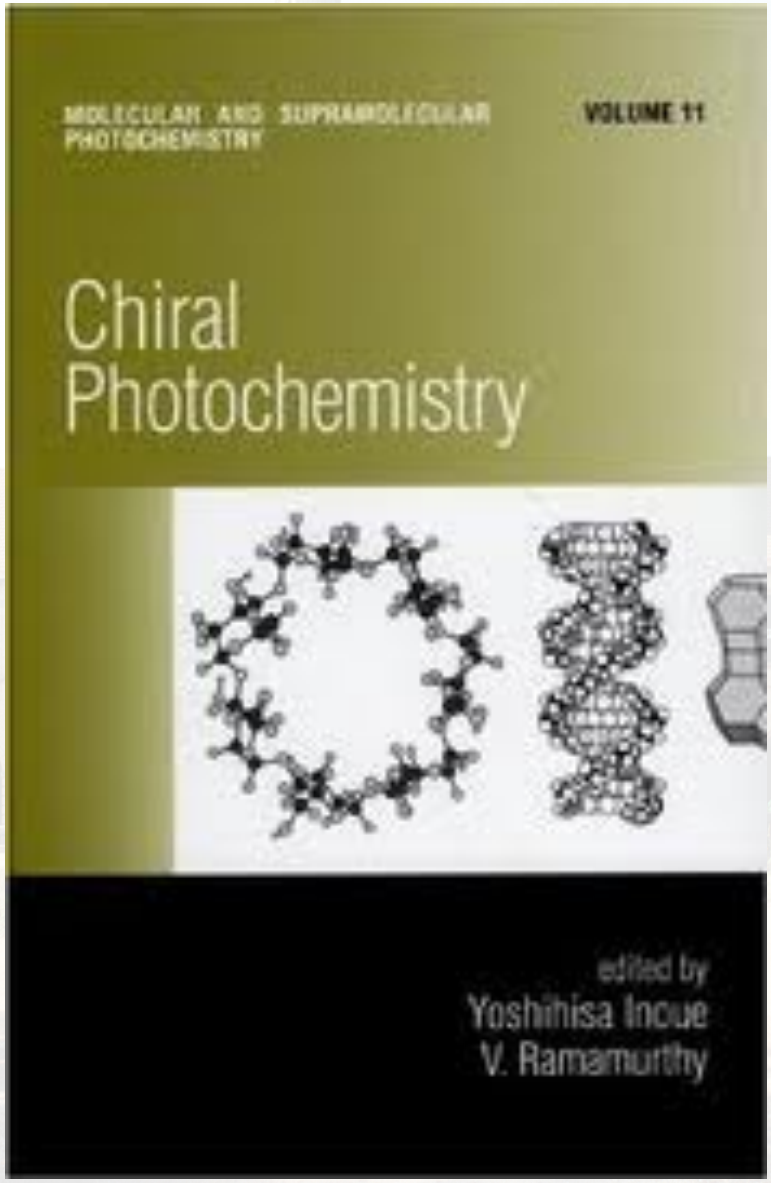
- Crystals
- Zeolites
- Solution

Why Chiral Chemistry



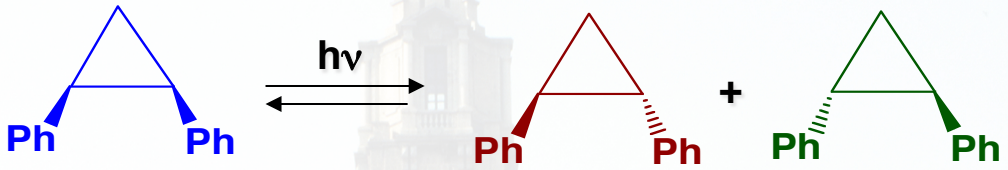
Thalidomide



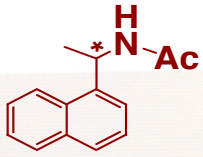

MOLECULAR AND SUPRAMOLECULAR PHOTOCHEMISTRY
VOLUME 11
Chiral Photochemistry
edited by
Yoshihisa Inoue
V. Ramamurthy

Photochemistry in Water

The beginnings of chiral organic photochemistry

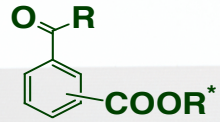


Hammond, G. S. and Cole, R. S.
J. Am. Chem. Soc. **1965,** p-3256



ee = 6.7%

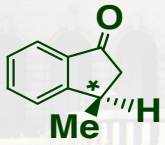
Horner, L. and Klaus, J.
Liebigs Ann. Chem., **1979**, p-1232



R* - Menthyl

ee = 4.0 %

Ouannes, C. Beugelmans, R. and Roussi, G.
J. Am. Chem. Soc., **1973**, p-8472

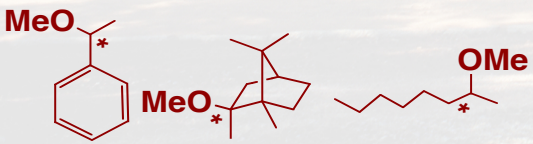


ee = 3.0%

Vondenhof, M. and Mattay, J.
Chem. Ber., **1990,** p-2457

ee = 3.5%

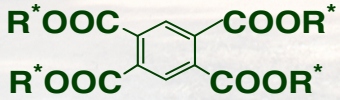
Faljoni, A. Zinner, K. and Weiss, R. G.
Tetrahedron lett., **1974**, p-1127



As chiral solvents

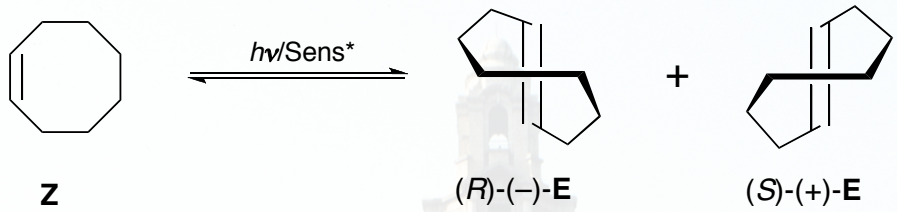
ee = 2.3%

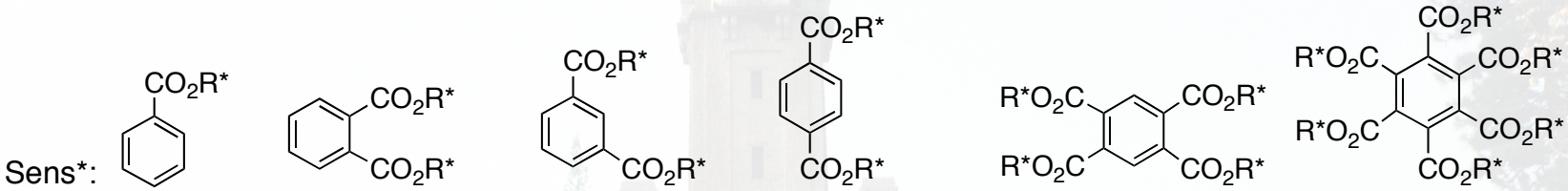
Inoue, Y. Shimoyama, H. Yamasaki, N. and Tai, A.
Chem, lett., **1991,** p-593

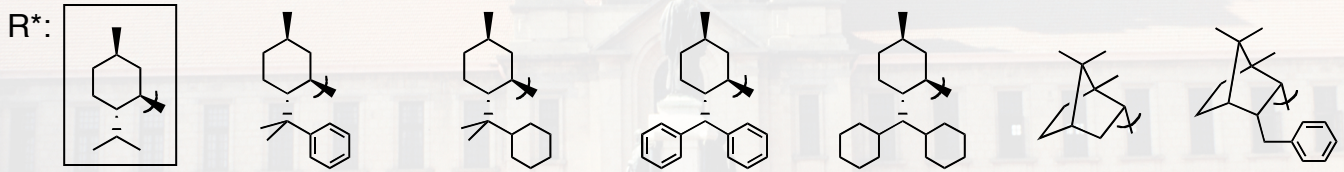


R* - Menthyl, Bornyl

ee = 10.4 %



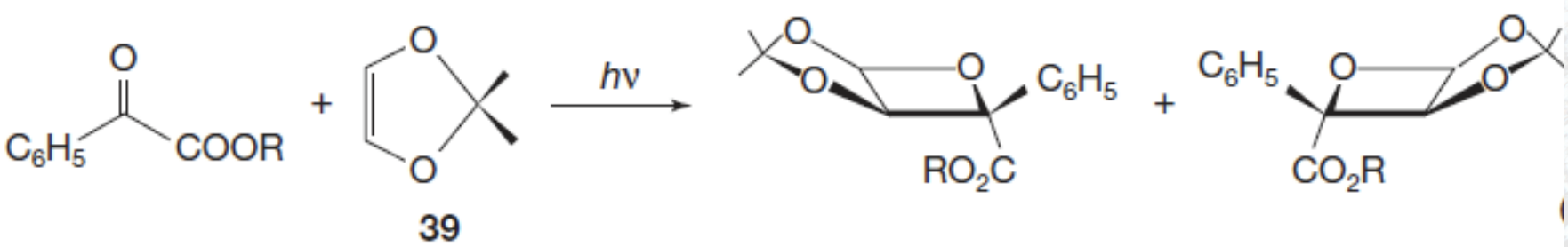




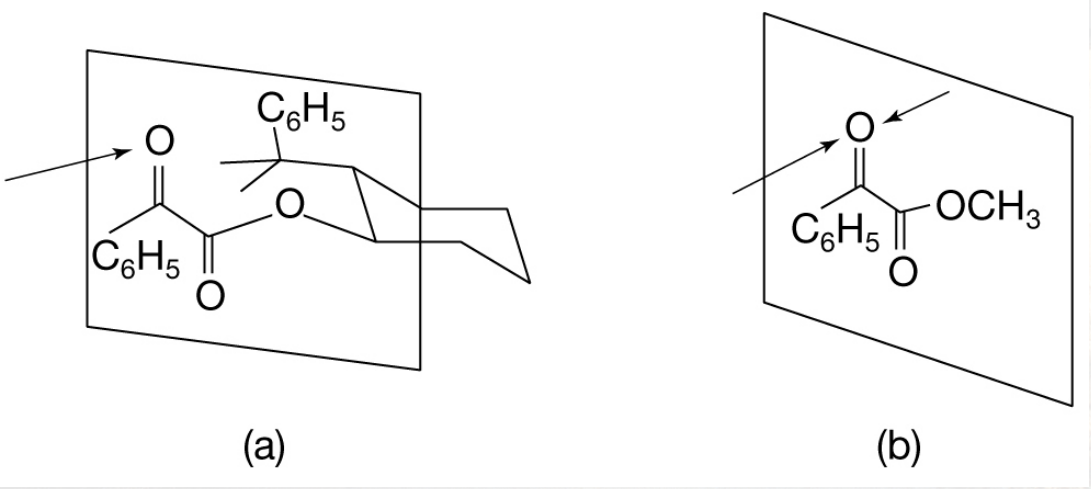
Temperature
Pressure
Solvent

73% ee at -110°C in pentane

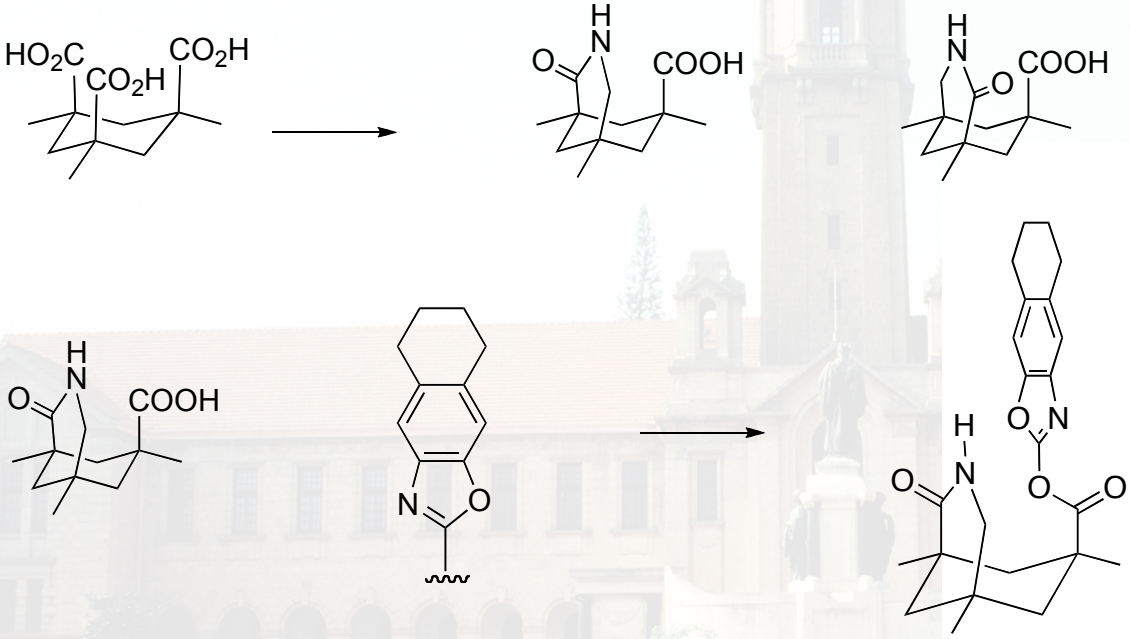
Chiral photochemistry in solution through covalent chiral auxiliary

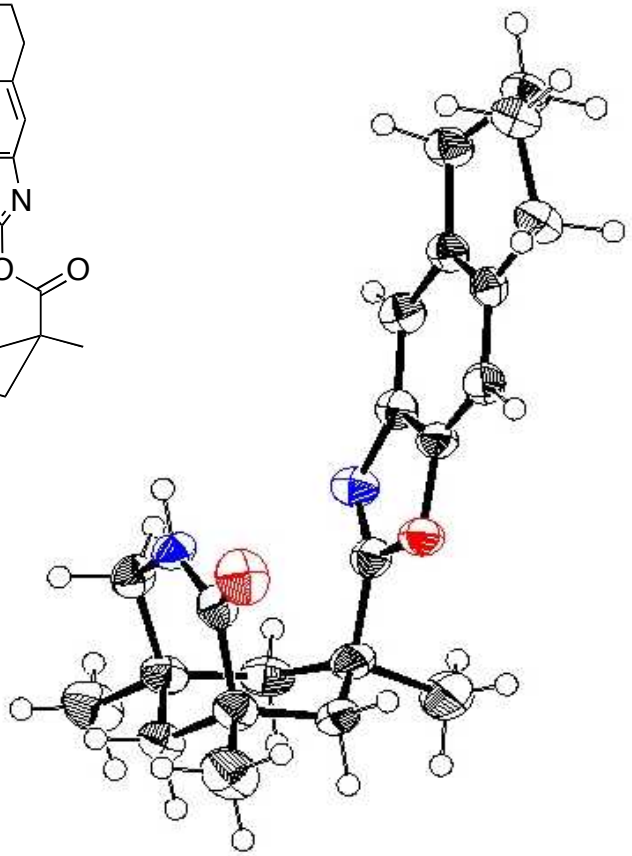


R	*de*
(–)-8-C_6H_5-Menthyl	≥96%
(–)-Menthyl	57%

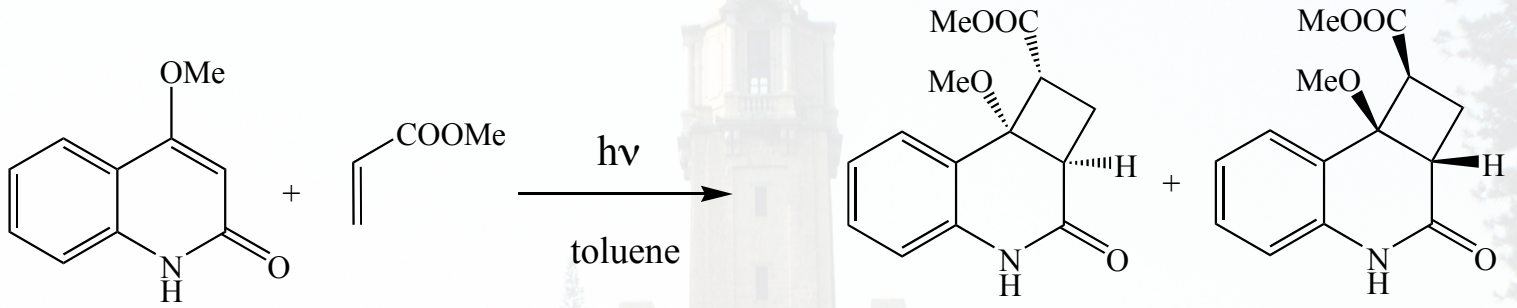


Chiral photochemistry in solution through templation



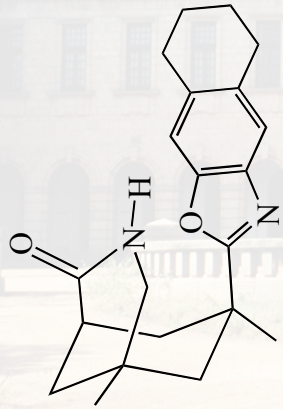


Chiral photochemistry in solution through templation

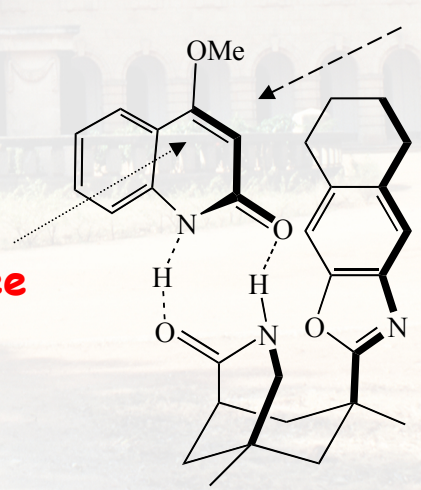


In the absence of template; e.e.: 0

In the presenceof template; e.e.: 82%



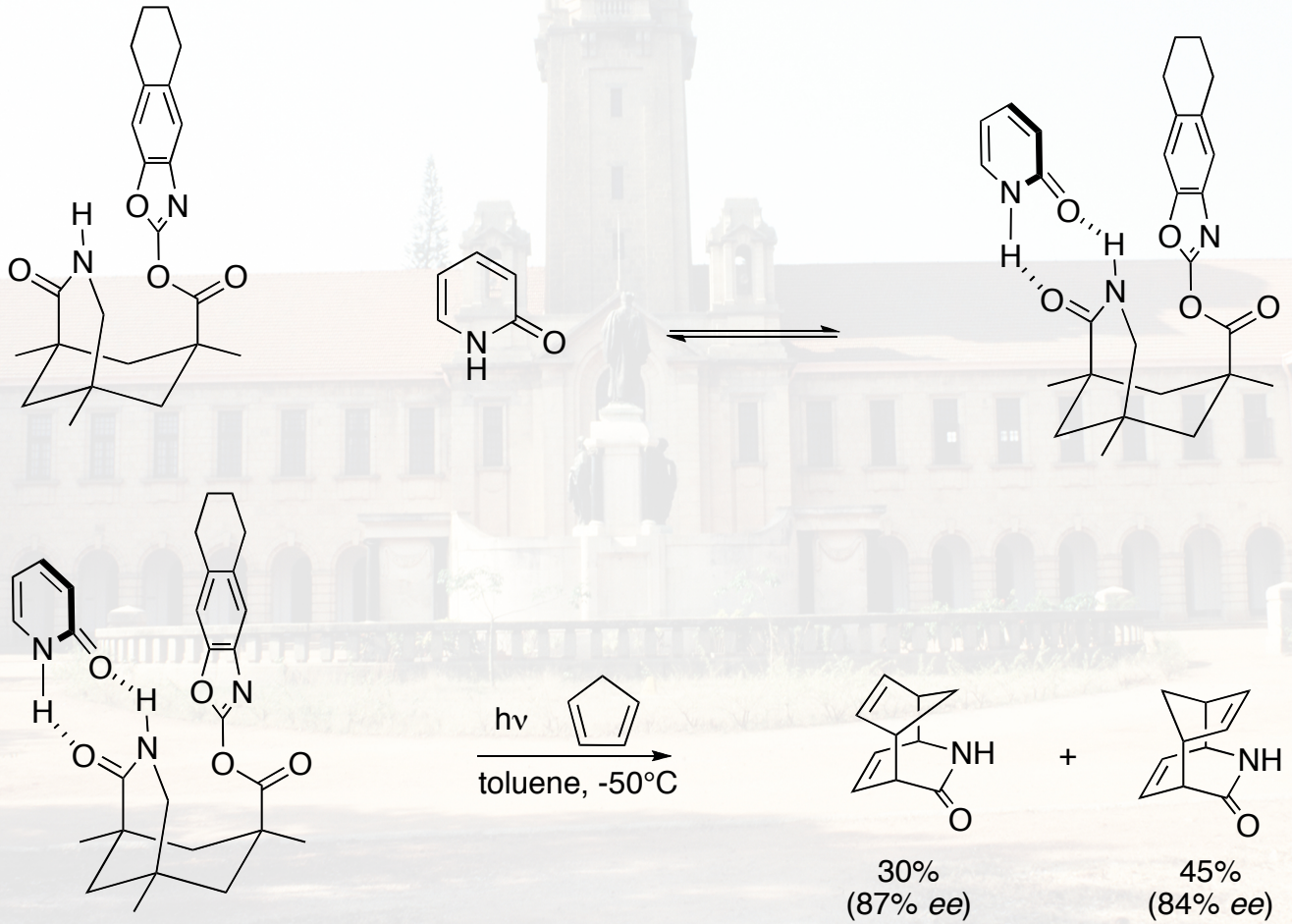
Template

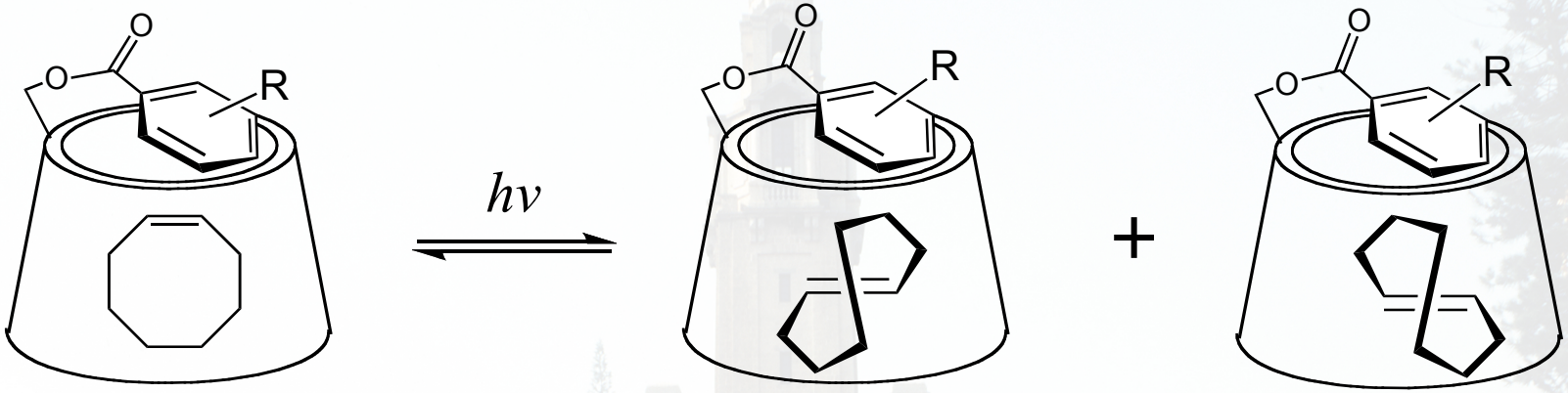


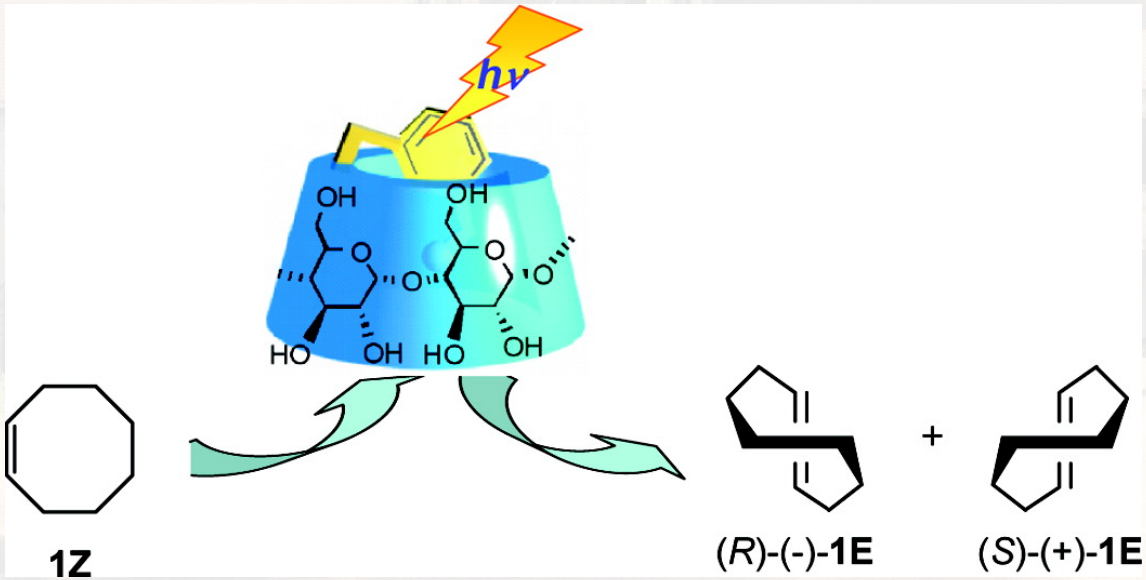
Free

One mode of approach blocked

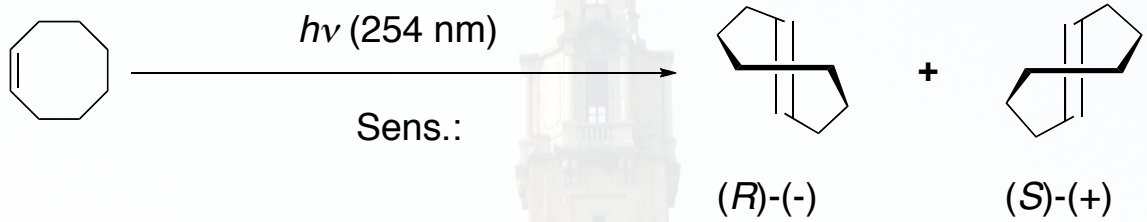
Chiral photochemistry in solution through templation



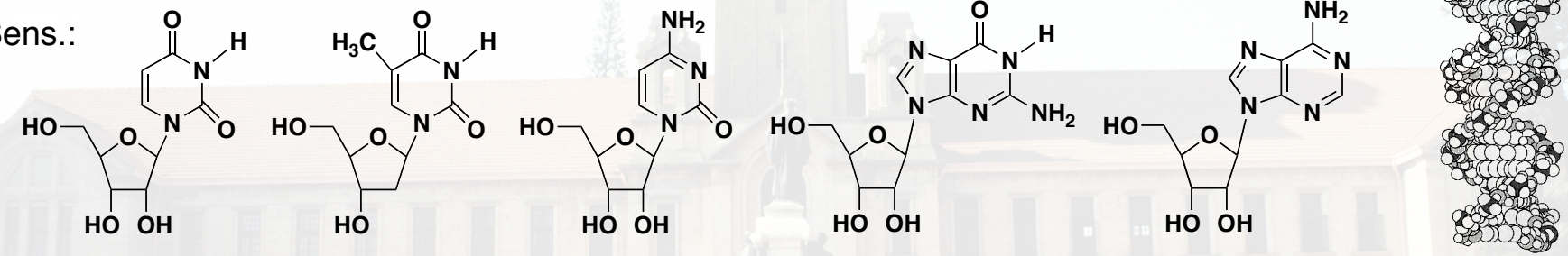




46% ee

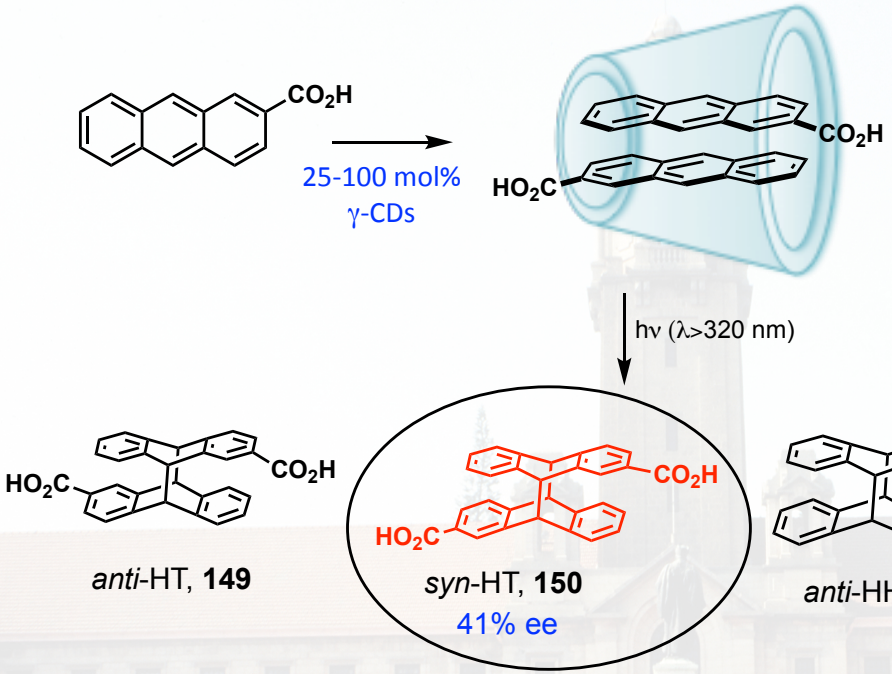


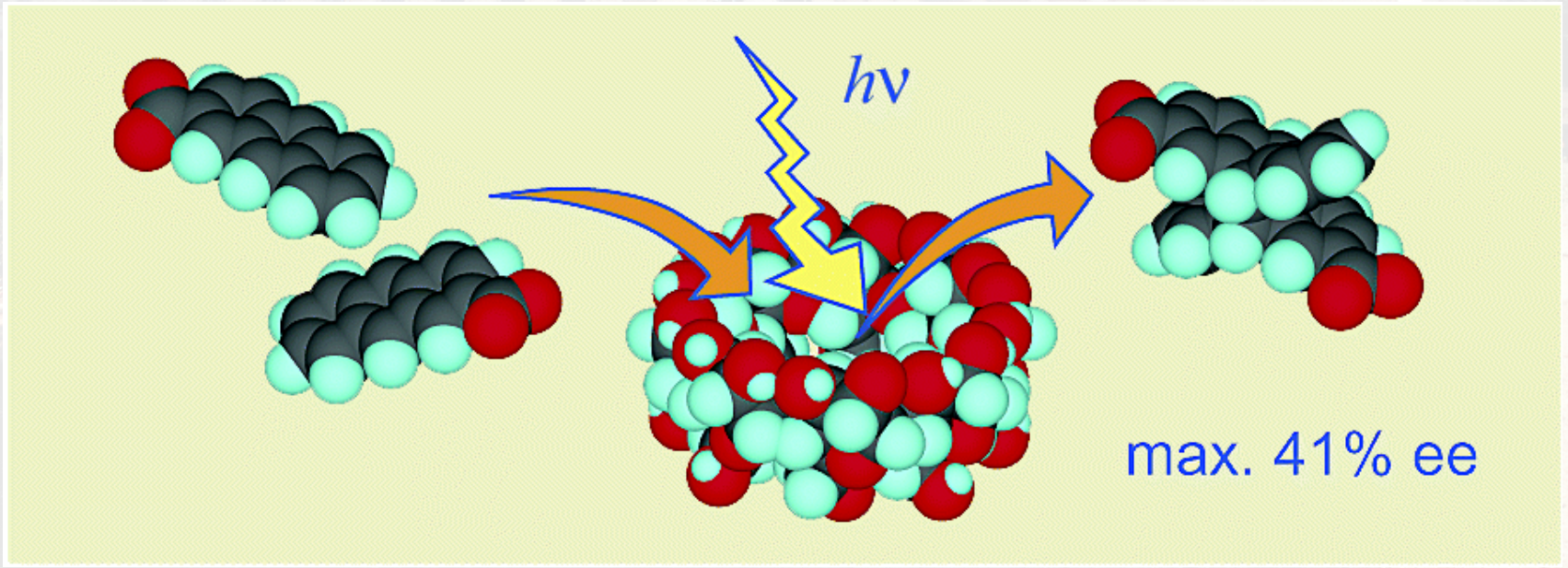
Sens.:

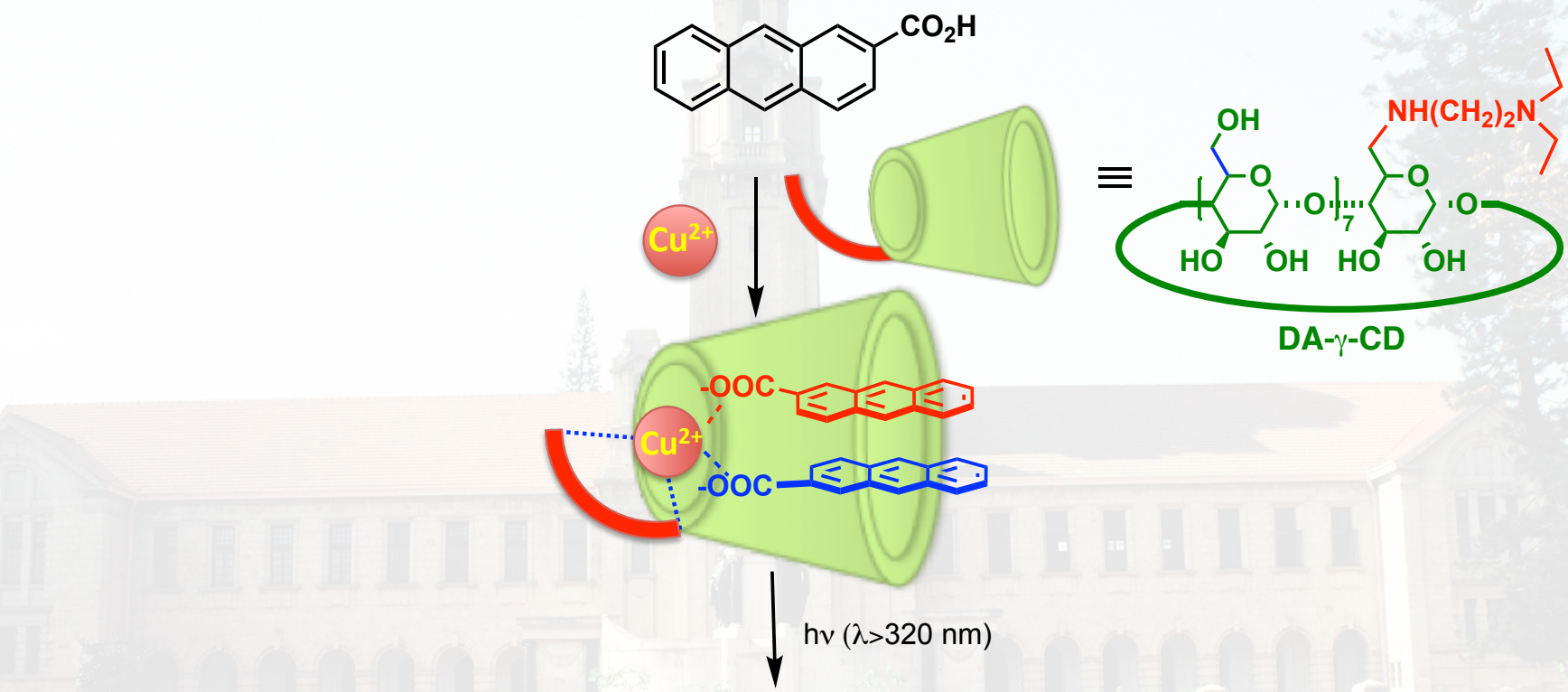


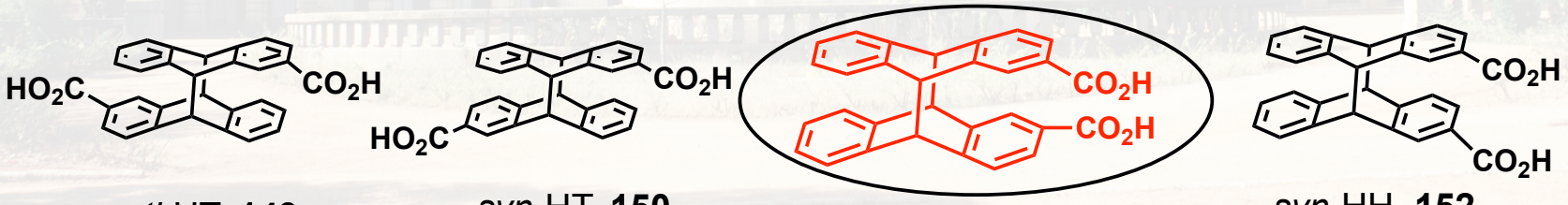
Calf Thymus DNA

18.8% ee


CO2H
25-100 mol%
γ-CDs
HO2C
CO2H
hν (λ>320 nm)
HO2C
CO2H
anti-HT, 149
HO2C
CO2H
syn-HT, 150
41% ee
CO2H
CO2H
anti-HH, 151
CO2H
CO2H
syn-HH, 152


hν
max. 41% ee





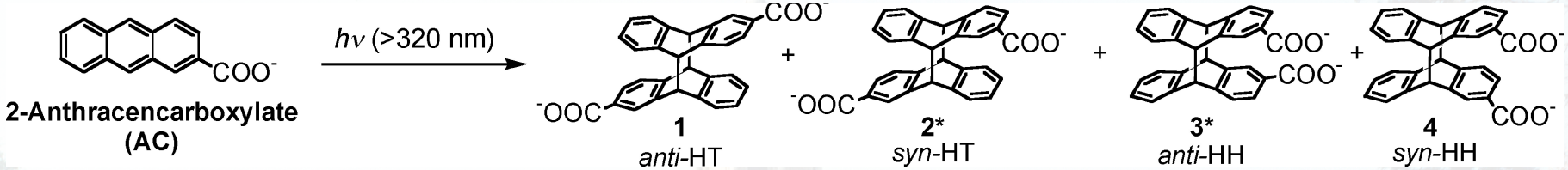
anti-HT, **149**

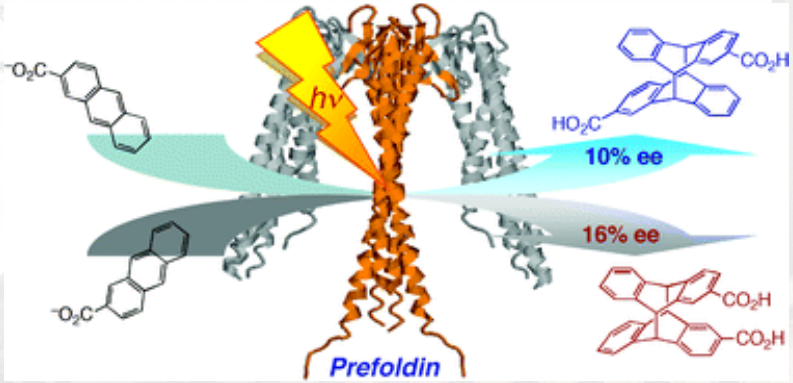
syn-HT, **150**

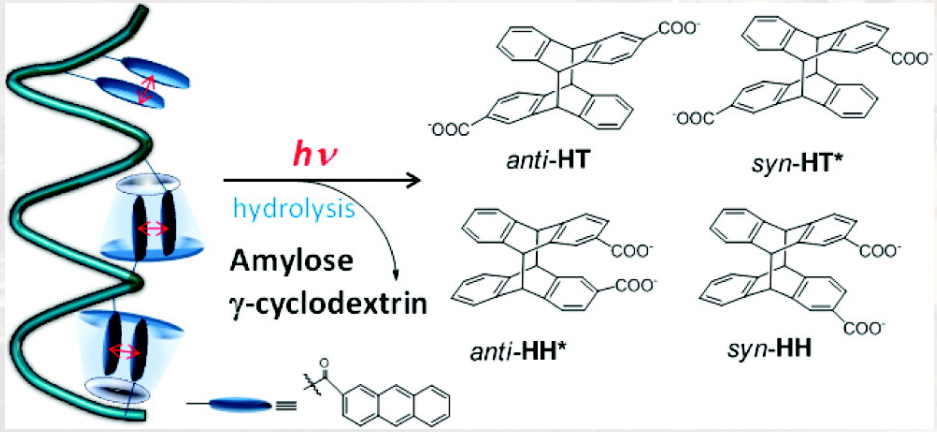
anti-HH, **151**

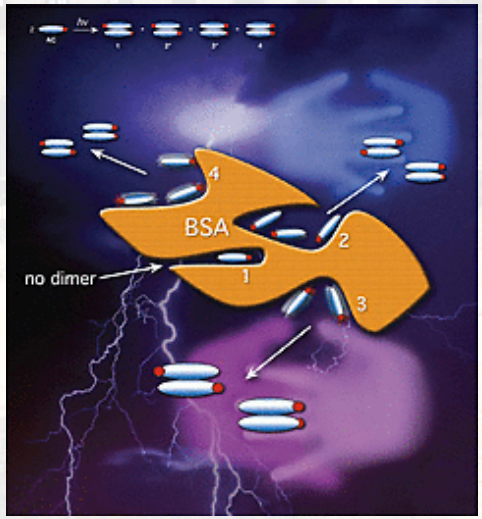
70% ee

syn-HH, **152**









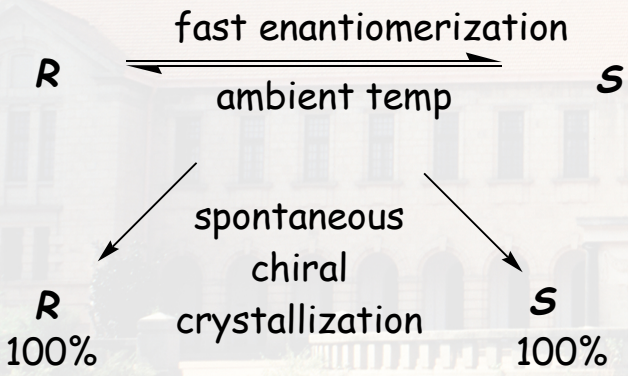
15% ee for syn HT amylose
37% ee for syn HT amylose + γ-cyclodextrin

38% ee for syn HT
58% ee for anti HH

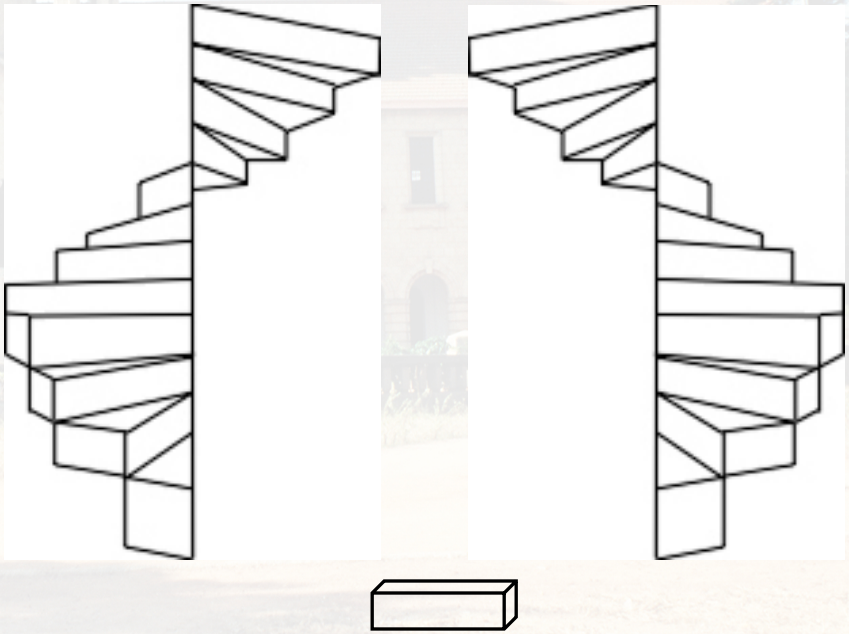
Photochemistry in Solid State

Chiral crystallization

Achiral molecule may crystallize in achiral space group.
e.g., quartz, urea, maleic anhydride,



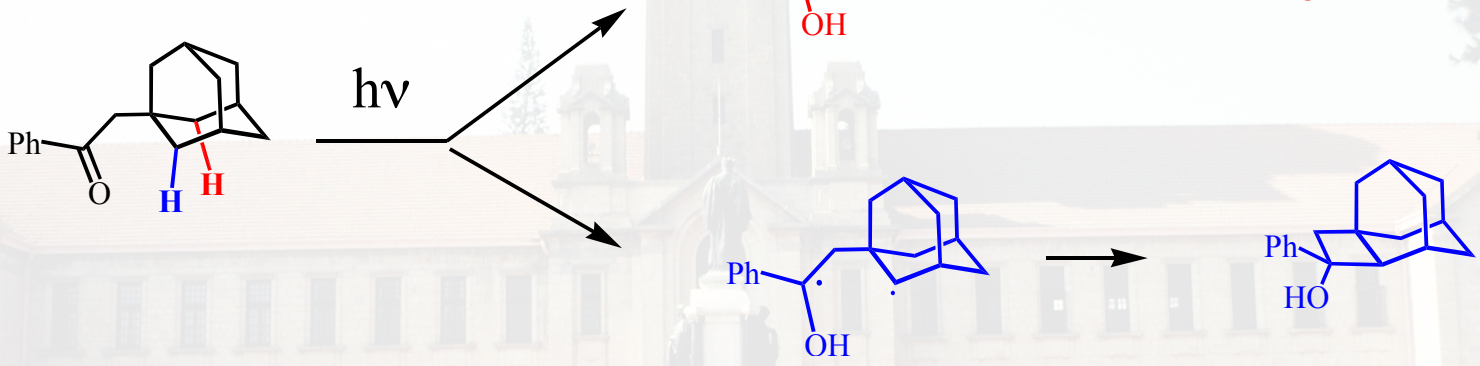
Chiral crystallization of achiral materials

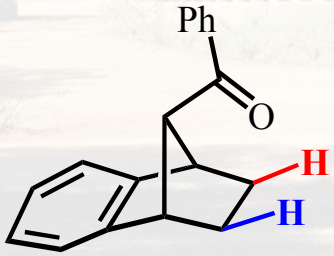


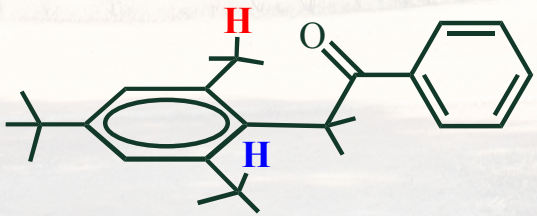
The most common space groups of organic crystalline compounds based upon a survey of 29059 crystal structure determinations

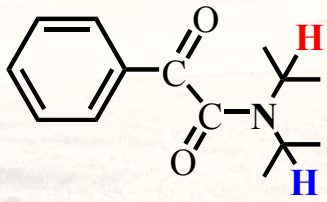
space group	number	percentage
$P2_1/c$	10450	36.0
$P\text{-}1$	3986	13.7
$P2_12_12_1$*	3359	11.6
$P2_1$*	1957	6.7
$C2/c$	1930	6.6
$Pbca$	1261	4.3
$Pnma$	548	1.9
$Pna2_1$	513	1.8
$Pbcn$	341	1.2
$P1$*	305	1.1

*Chiral space group.

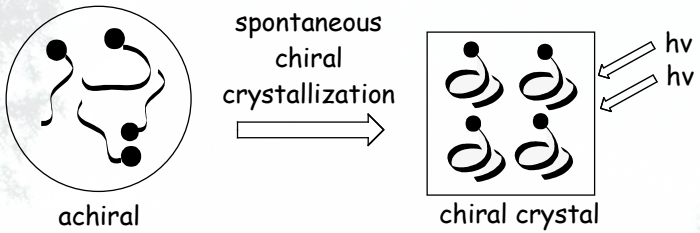

Ph
O
H
H
hν
Ph
OH
Ph
HO
Ph
OH
Ph
HO


Ph
O
H
H


H
O
H


O
C
C
N
O
H
H

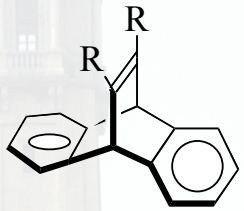
Chiral crystallization



optically active materials with permanent chirality

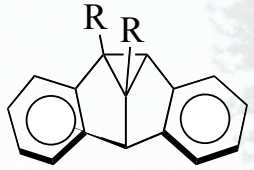
Absolute asymmetric synthesis in the chiral crystalline environment

Achiral → Chiral



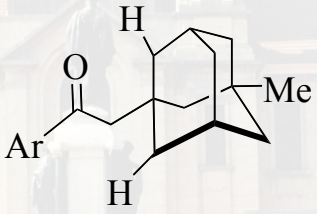
R = COO*i*-Pr

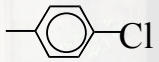
hν



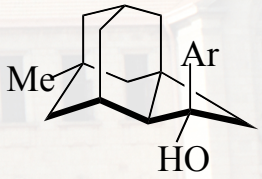
Solution e.e : 0%

Crystals e.e : 100%



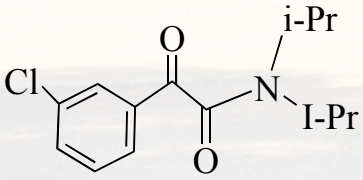
Ar = 

hν

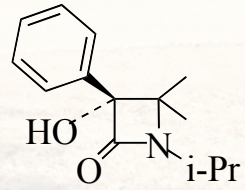


Solution e.e : 0%

Crystals e.e : 82%

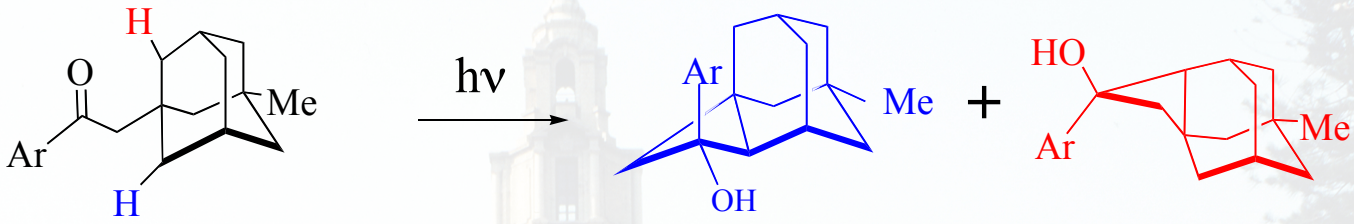


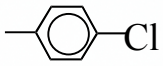
hν



Solution e.e : 0%

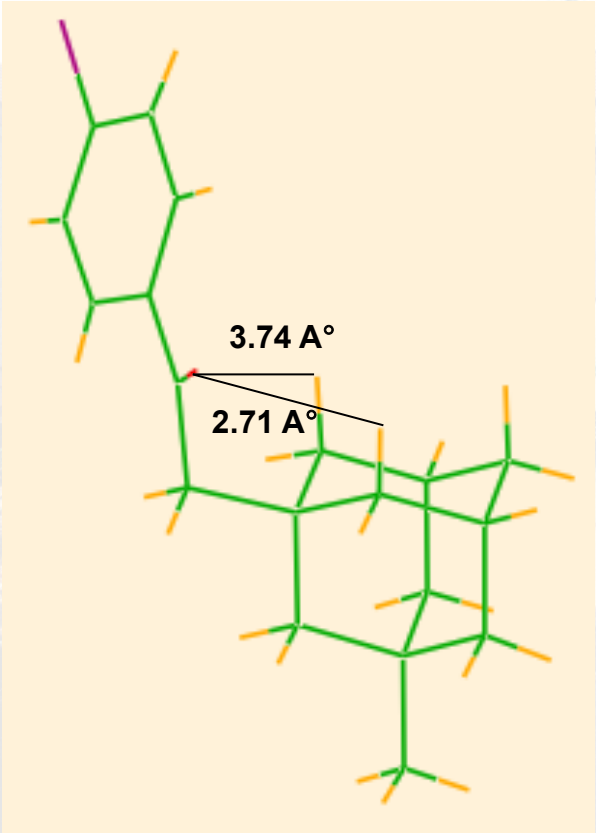
Crystals e.e : 100%



Ar = 

Solution e.e : 0%

Crystals e.e : 82%



Note that the two prochiral hydrogens are not equidistant from the carbonyl chromophore.

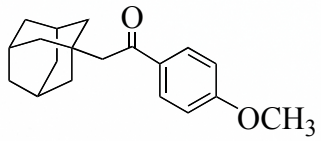
The molecule being present in a chiral space group does not have another molecule that is mirror symmetric.

Since only one prochiral hydrogen would be abstracted only one cyclobutanol enantiomer would be formed.

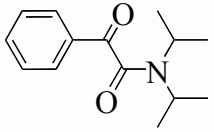
Essential Criteria for Asymmetric Photochemistry in the Crystalline State

Molecules must crystallize in a chiral space group (non-centro symmetric form)

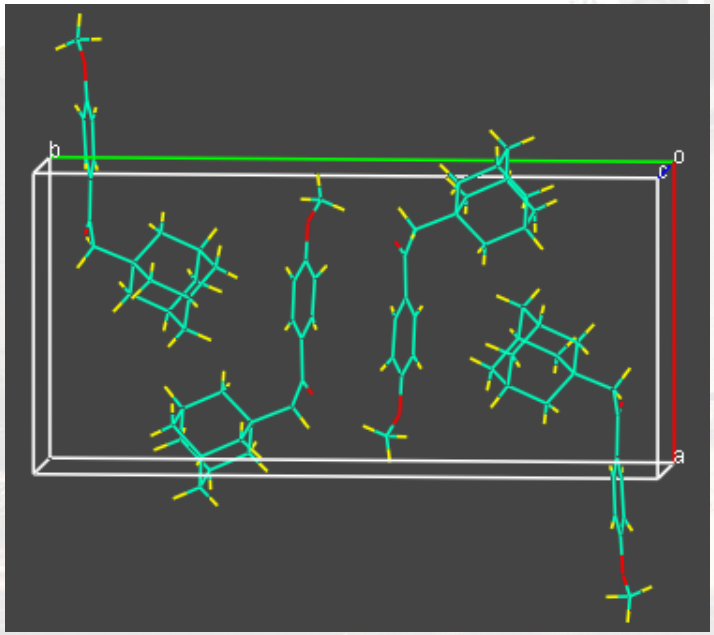
Majority of achiral molecules crystallize in a non chiral space group (symmetric packing)

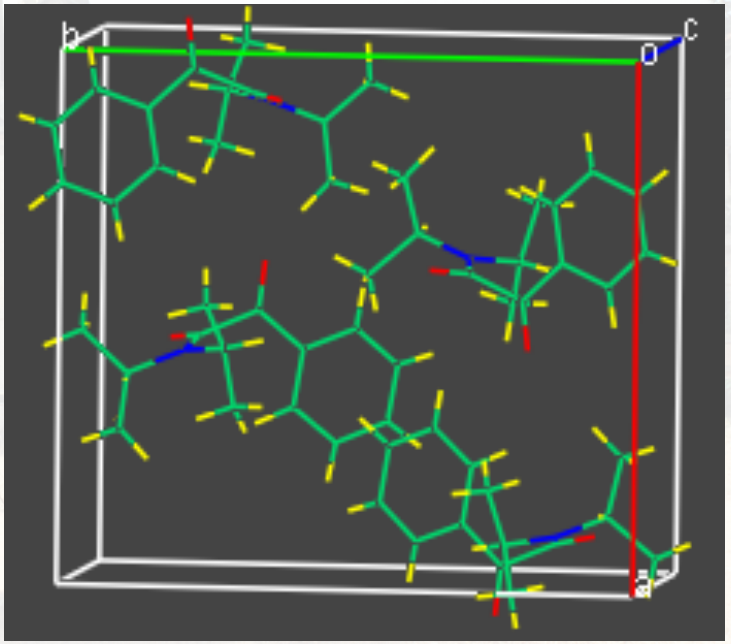


% ee: 0



% ee: 100





$P2_1/n$

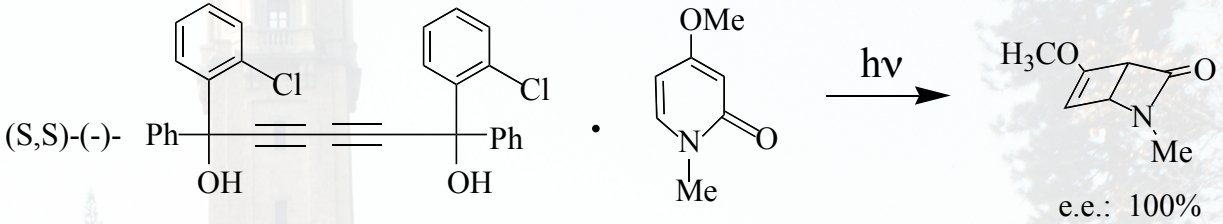
centrosymmetric

$P2_12_12_1$

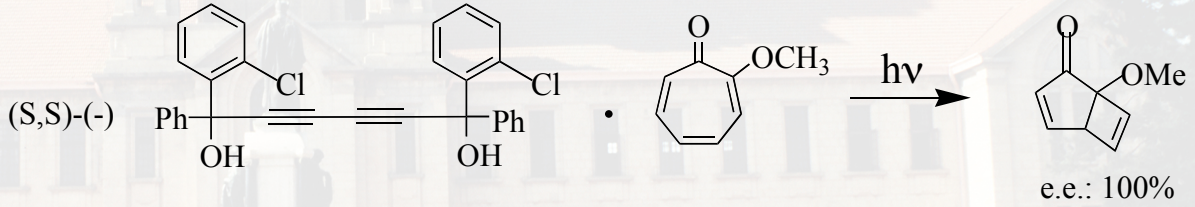
non-centrosymmetric

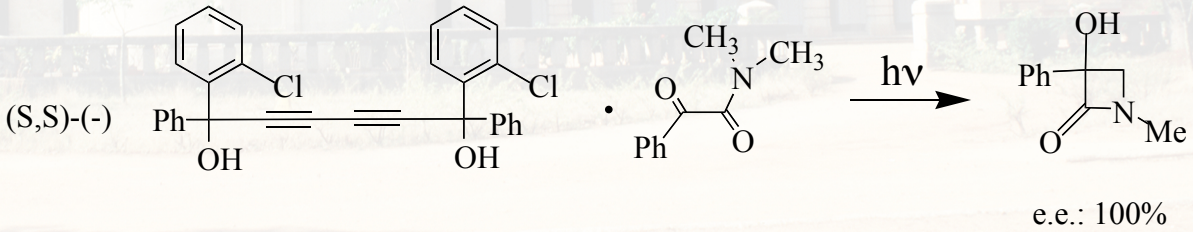
Use of chiral hosts: Solid state photochemistry

Chiral hosts upon inclusion of an achiral molecule may induce chirality on the achiral molecule.



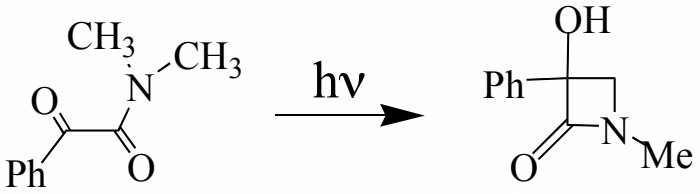
The above host-guest complexation would lead to diastereomeric (instead of enantiomeric) transition states .



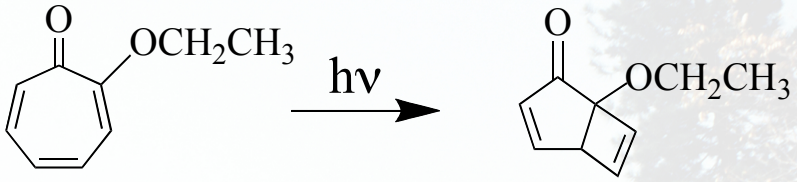


In solution no chiral induction is obtained.

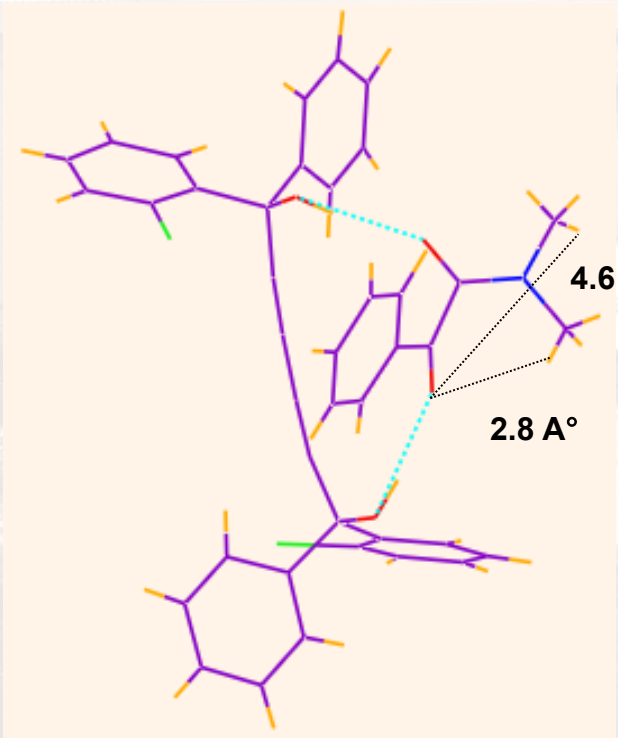
Use of chiral hosts: Unimolecular reactions

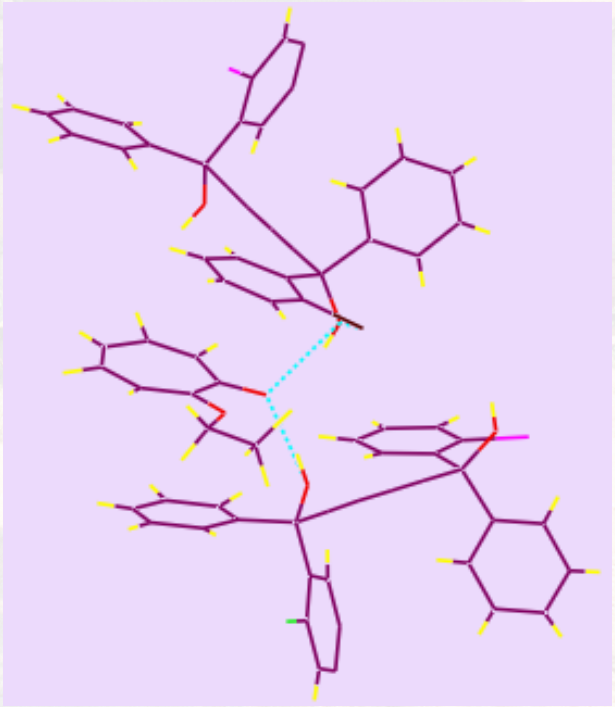


e.e.: 100%

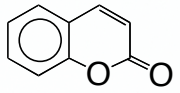


e.e.: 100%





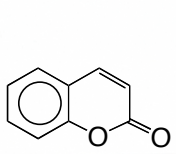
Use of chiral hosts: Bimolecular reactions



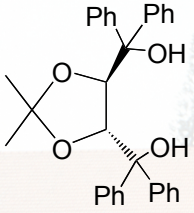
hν

Crystal

No dimer

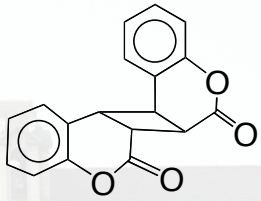


+

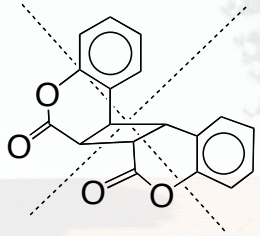


hν

Crystal

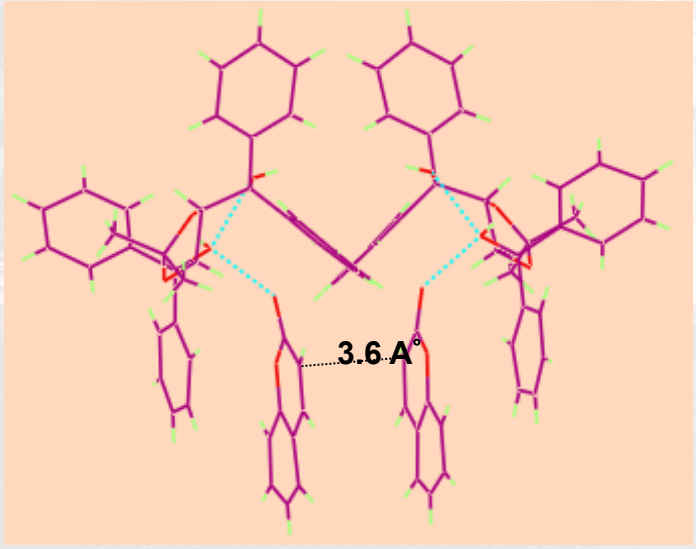


+

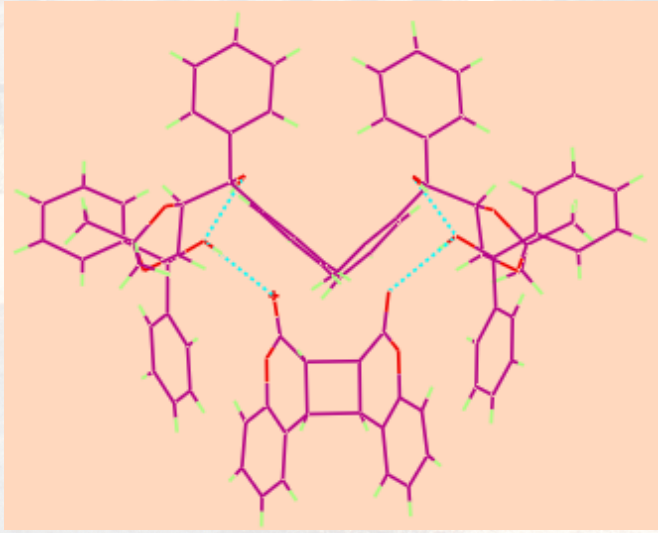


96% ee

1:1 complex



hυ



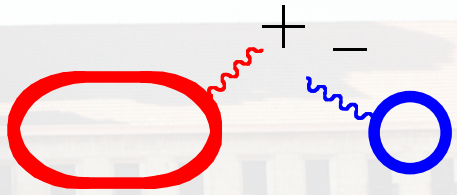
Most commonly occurring space groups

230 unique space groups of which only 65 are chiral space groups
Chiral space groups (symmetry elements are rotational, translational and combinations of these)
achiral space groups (symmetry elements are mirror, glide plane or center of inversion)

Space group	Total no. of crystals	%
$P2_1/c$	10450	36.0
$P_{?1}$	3986	13.7
$P2_12_12_1$	3359	11.6
$P2_1$	1957	6.7
C_2/c	1930	6.6
P_{bca}	1261	4.3
Pnma	548	1.9
$Pna2_1$	513	1.8
P_{bcn}	341	1.2
P1	305	1.1

Chiral space group

Ionic Chiral Auxillary Approach



Reactive part Chiral auxliary

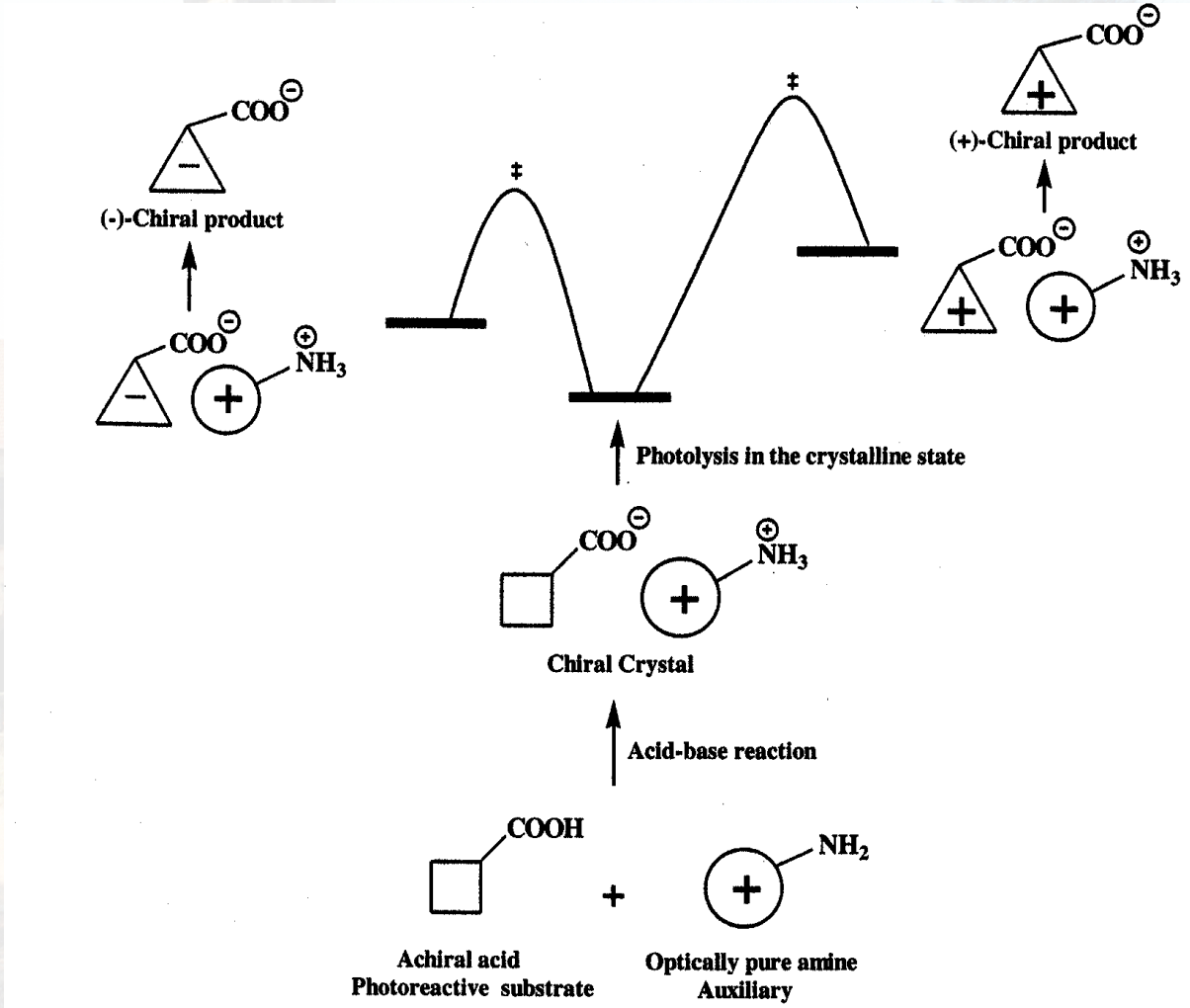
Covalent Chiral Auxillary Approach

Reactive part Chiral auxliary

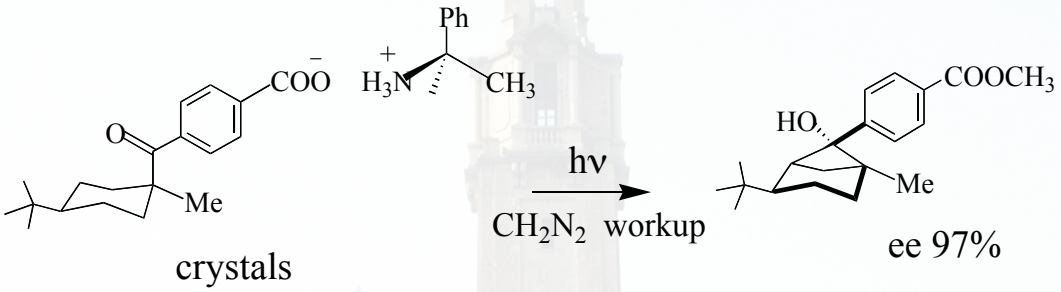
Ionic chiral auxiliary approach: Solid state photochemistry

The chiral auxiliary ensures that the reactant molecule crystallizes in a chiral space group.

This would make the two diastereomeric reaction pathways to have different activation energies.

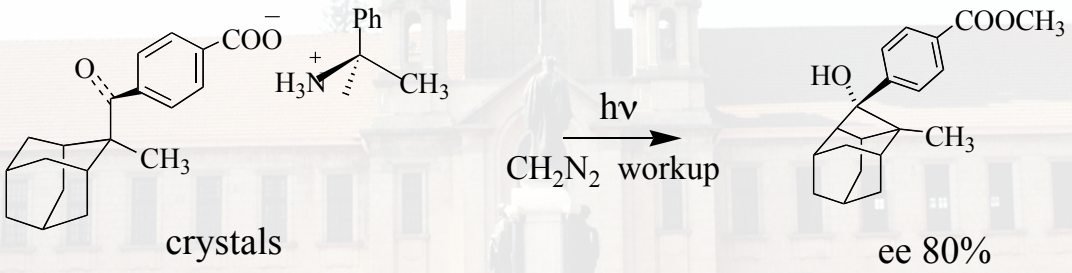


Ionic chiral auxiliary approach



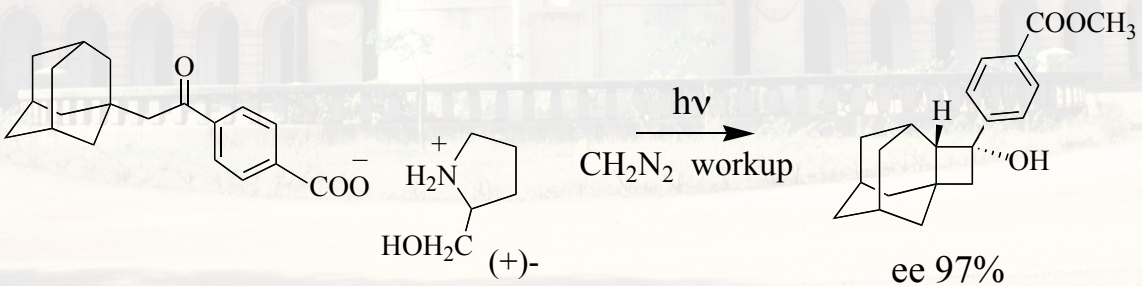
crystals

ee 97%



crystals

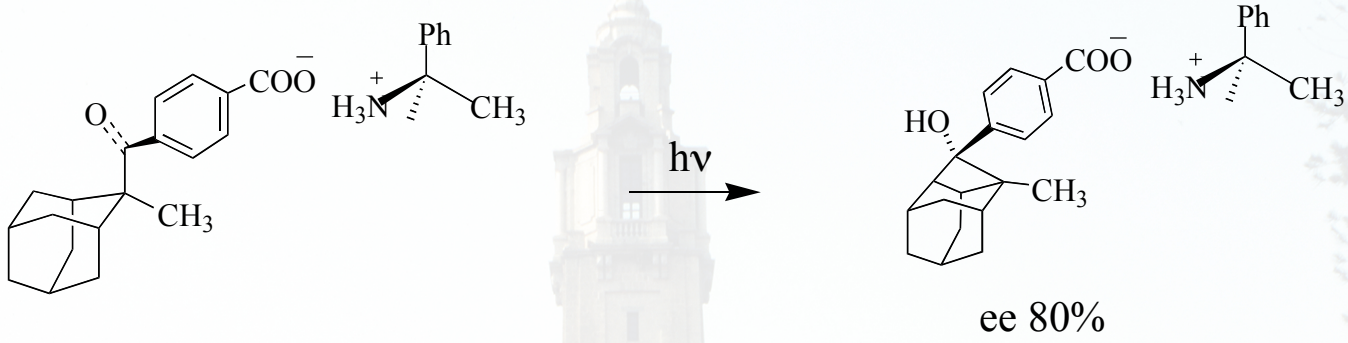
ee 80%



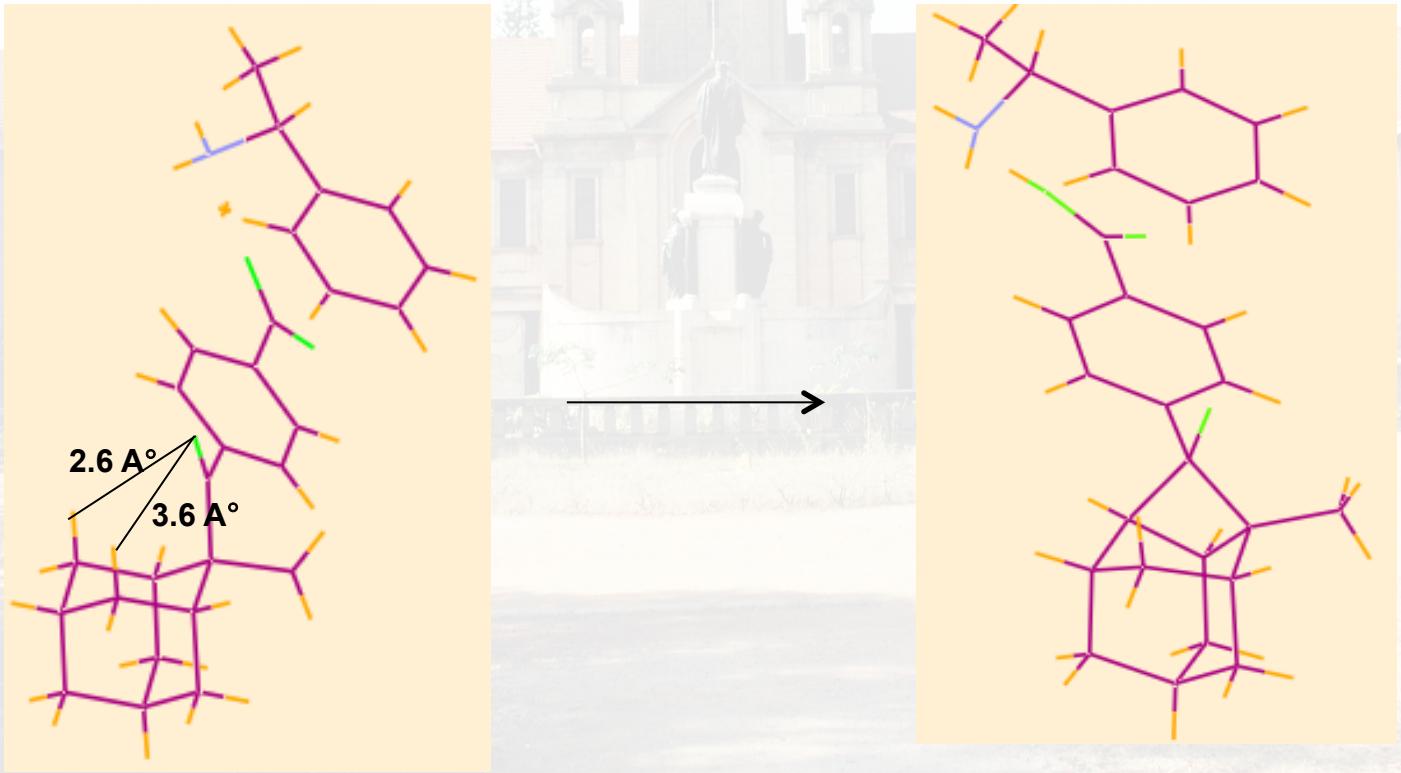
crystals

ee 97%

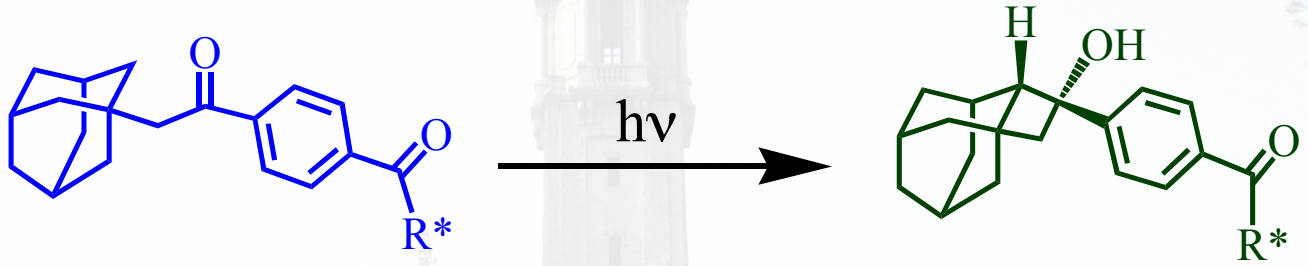
The two prochiral hydrogens are distinguishable in the crystalline state.
In solution no chiral induction is obtained.

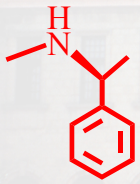
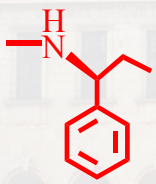
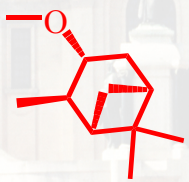
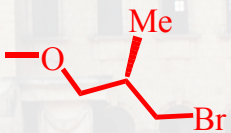
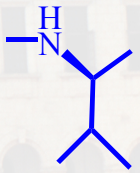
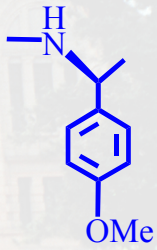


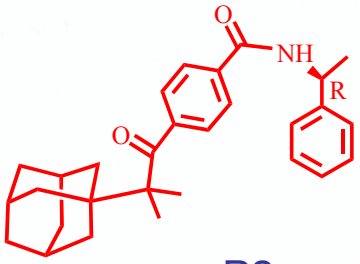
ee 80%



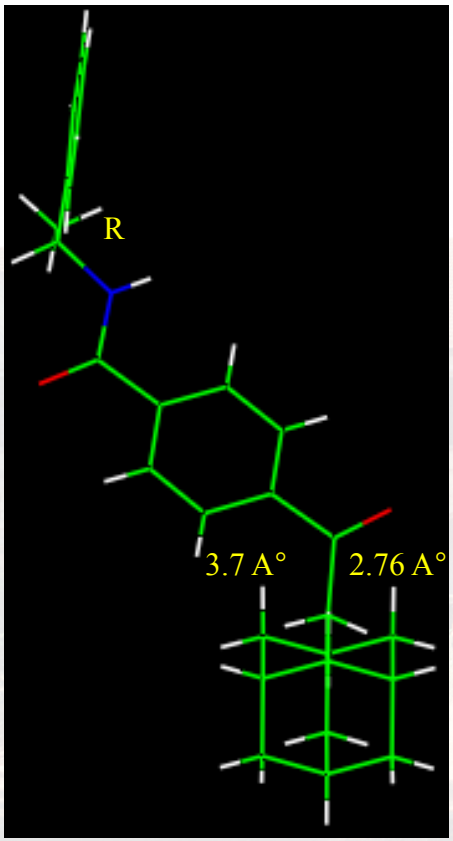
Covalent chiral auxiliary approach



R*						
% de	97	90	92	80	22	5

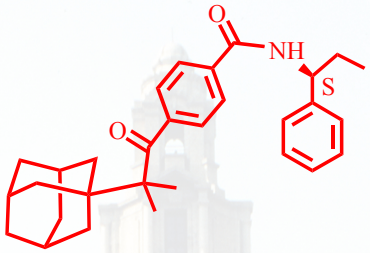


$P2_1$

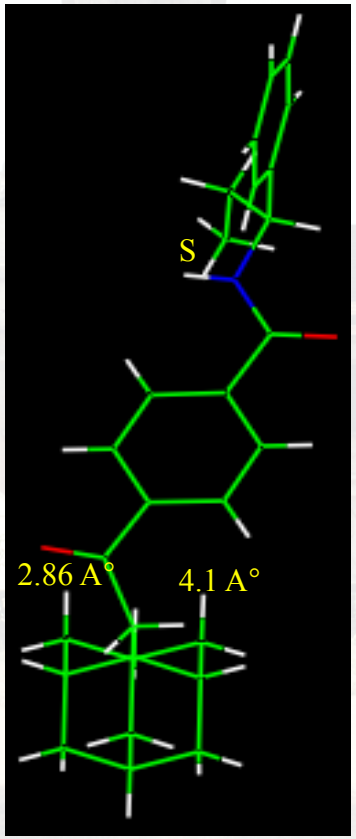


Trans CB

% de 97

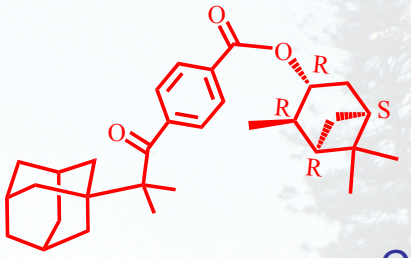


$P2_1$

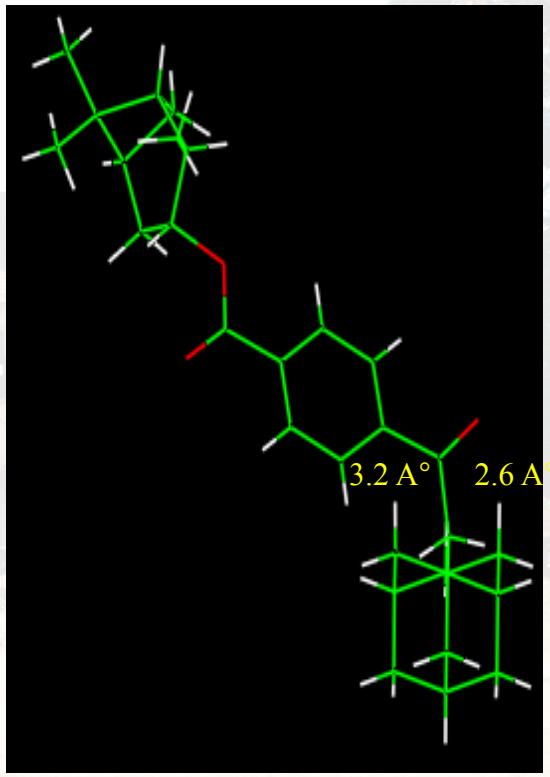


Trans CB

90



C2

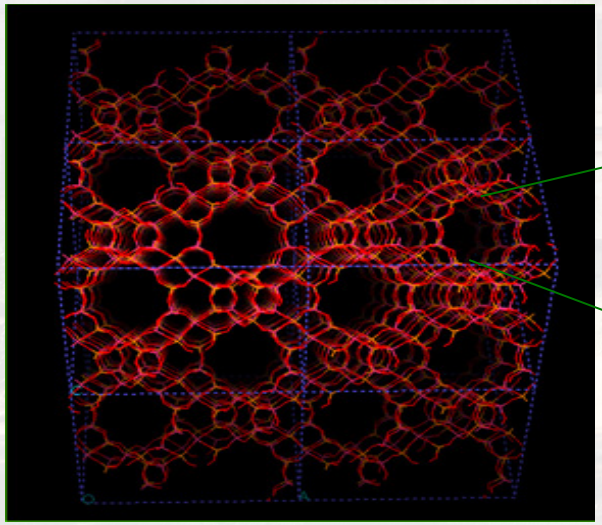


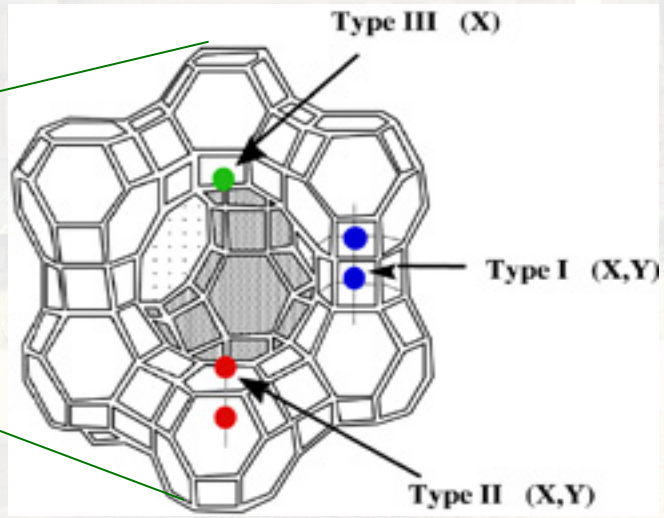
Trans CB

92

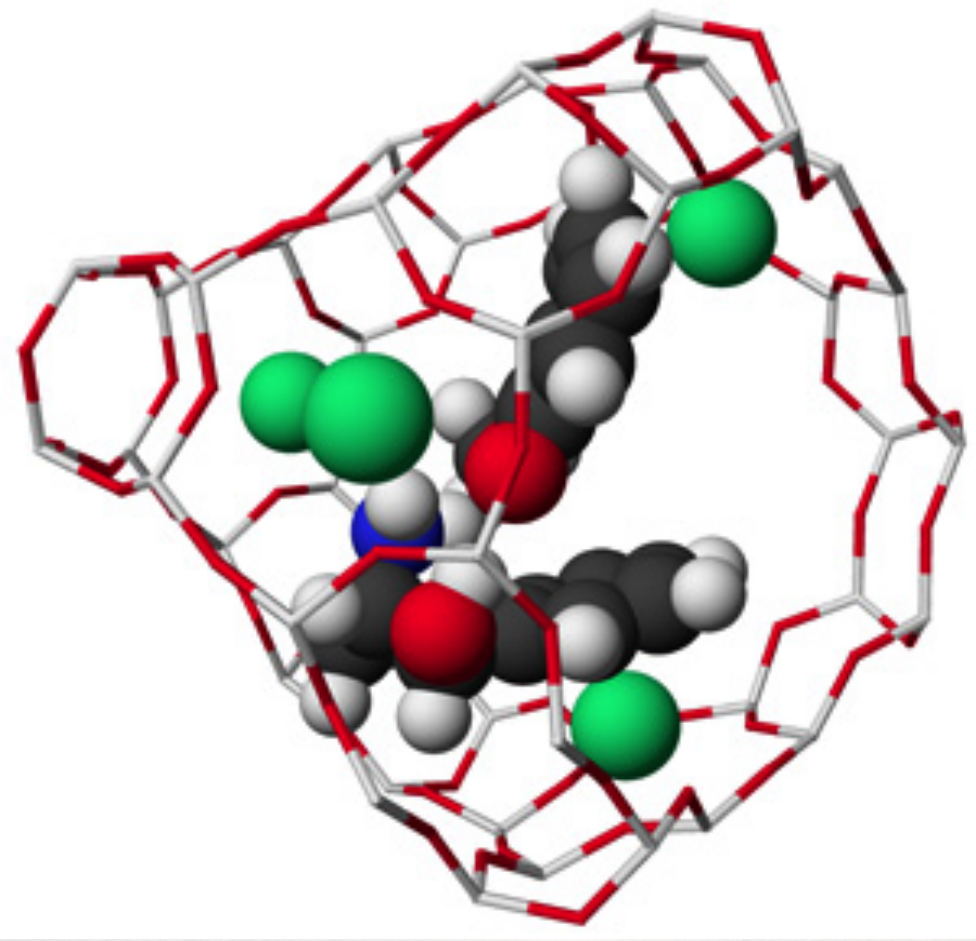
Asymmetric photoreactions within zeolites

- Key is the cation binding to the included organic molecule. Confined space also imposes restrictions.
- Details yet to be understood.



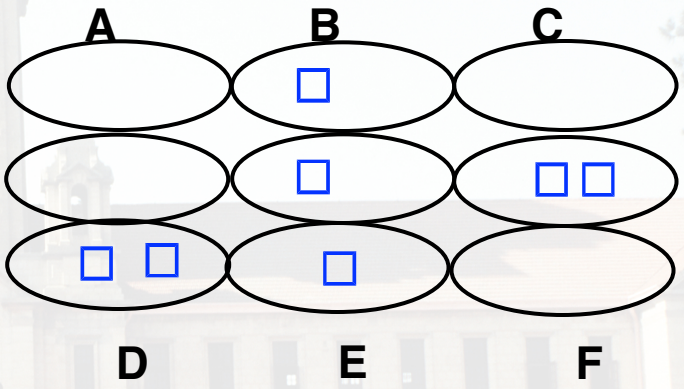


Asymmetric Photoreactions Within Zeolites



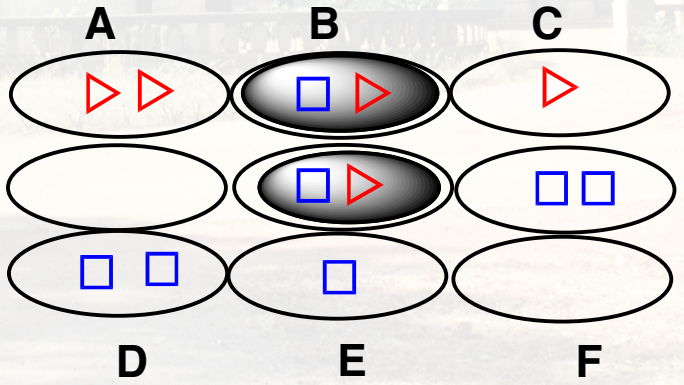
Chiral inductor approach

Chiral Inductor

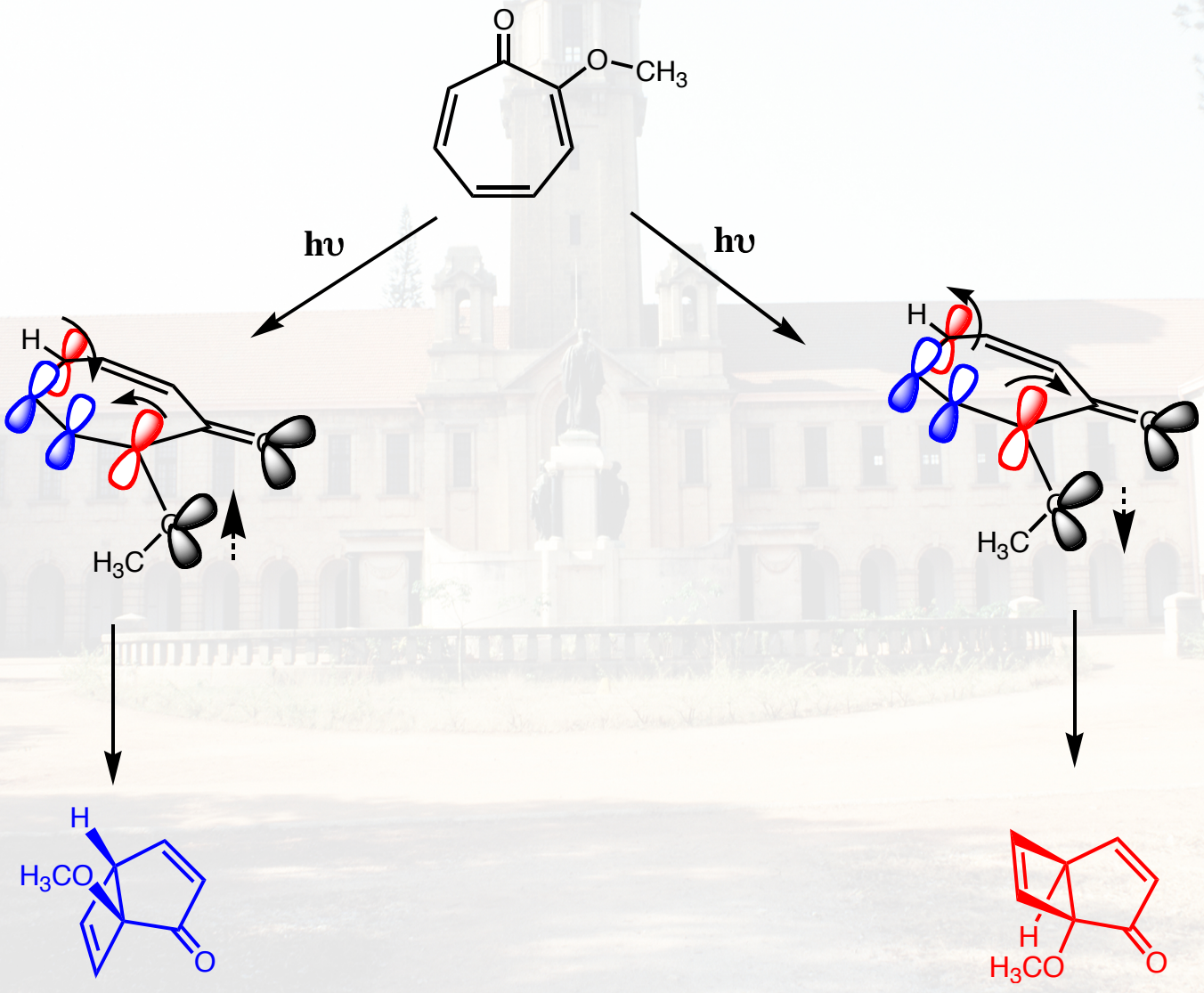


Achiral Reactant

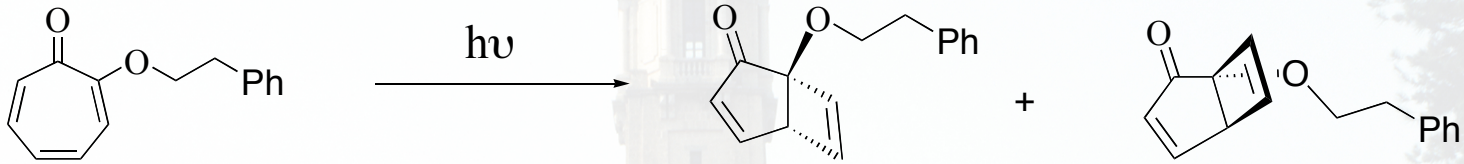
Chiral Inductor

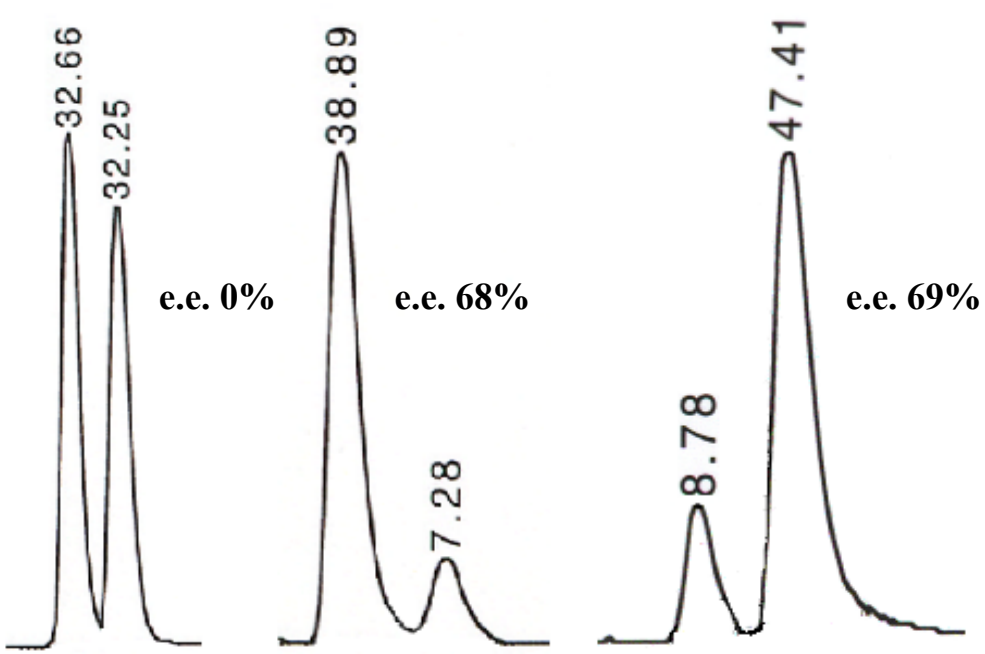


Enantioselective Electrocylization of Achiral Tropolones



Chiral Induction: Solution *vs.* Zeolite

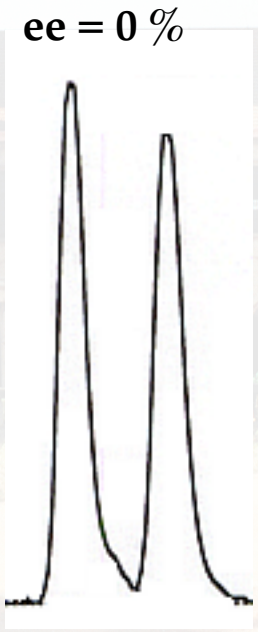




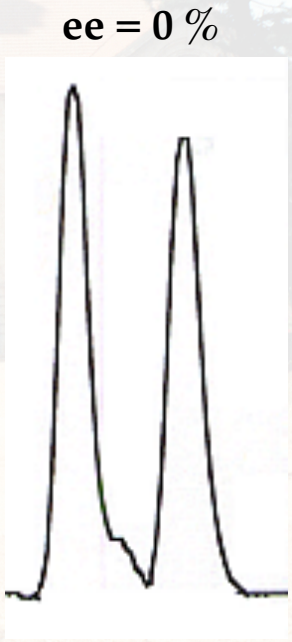
NaY

NaY / (-)-Ephedrine

NaY / (+)-Ephedrine



Hexane-methylene chloride/(-)-Ephedrine

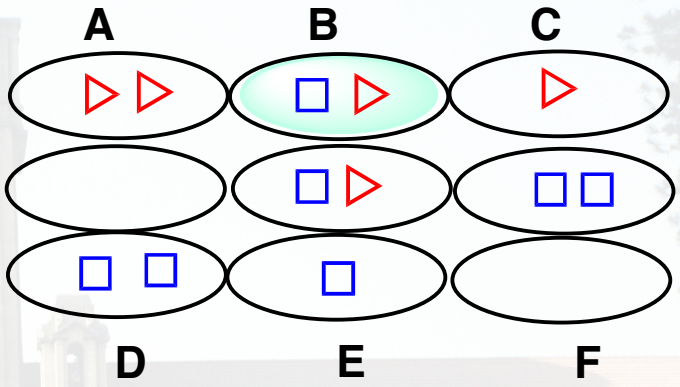


Silica gel/(-)-Ephedrine

Chiral inductor approach

Achiral Reactant

Chiral Inductor

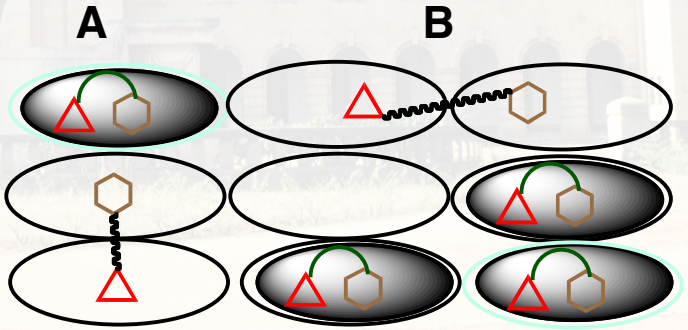


Chiral auxiliary approach

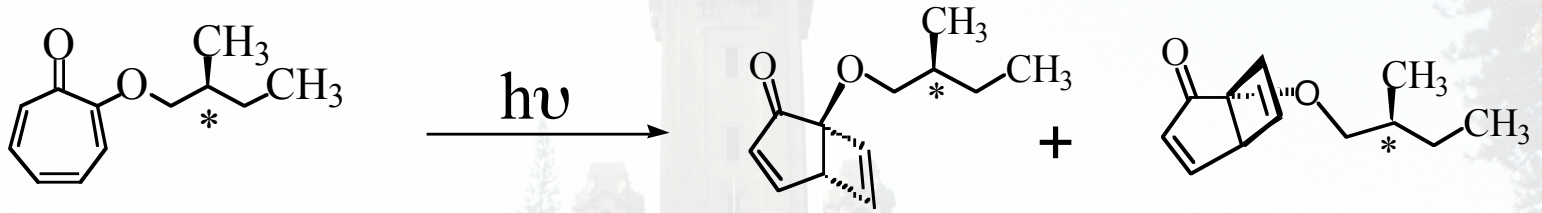
Achiral Reactant

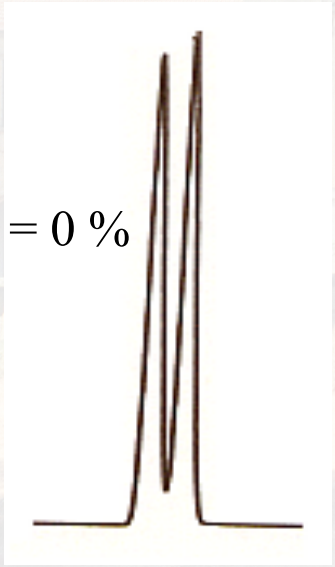
Covalent bond

Chiral Auxiliary



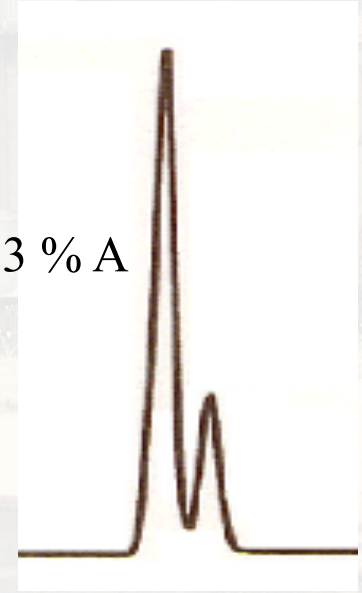
Chiral Induction (Diastereoselectivity)
Solution *vs.* Zeolite





d.e. = 0 %

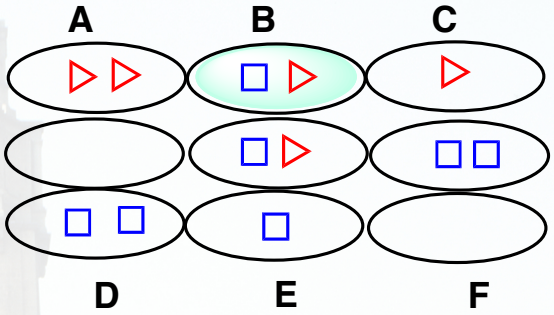
Hexane



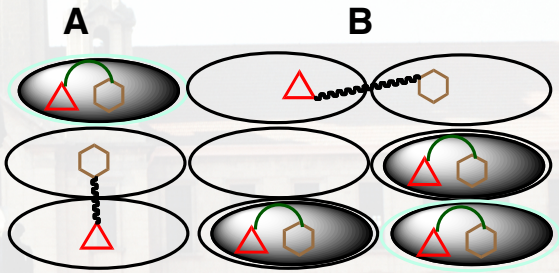
53 % A

NaY

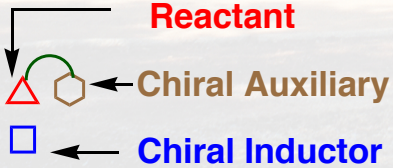
Chiral inductor approach

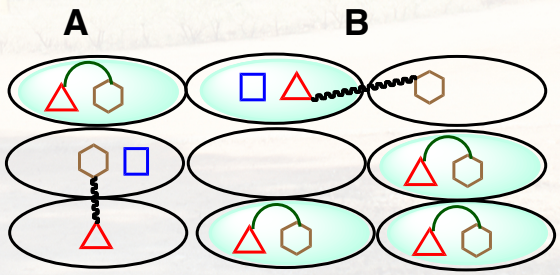


Chiral auxiliary approach

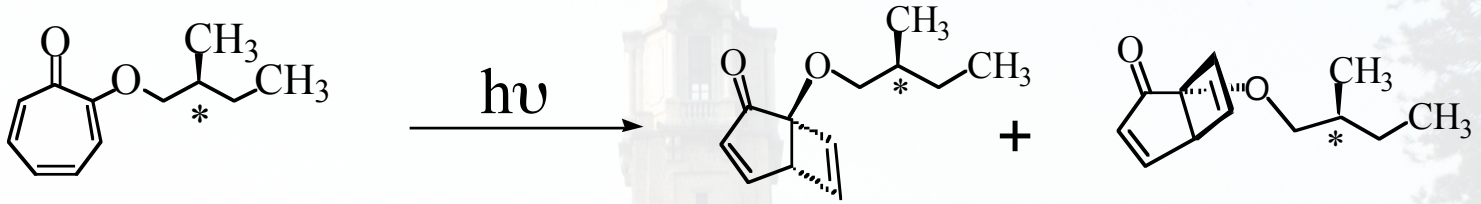


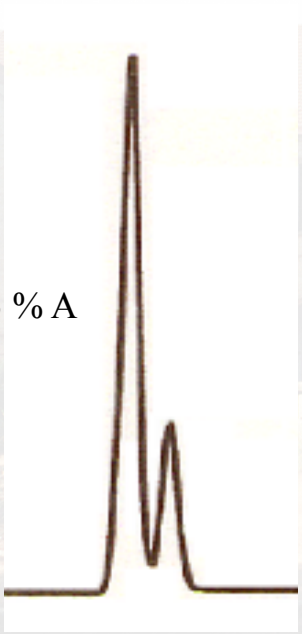
Gumbo approach



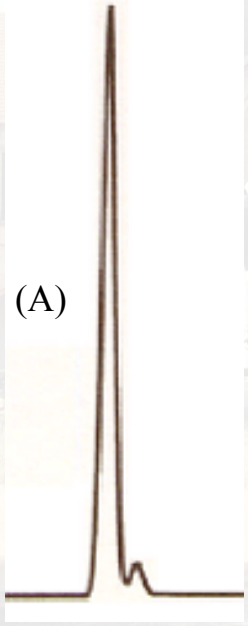


Chiral induction within a chirally modified zeolite



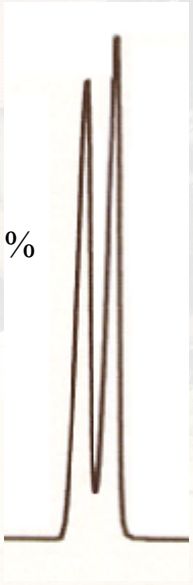


NaY



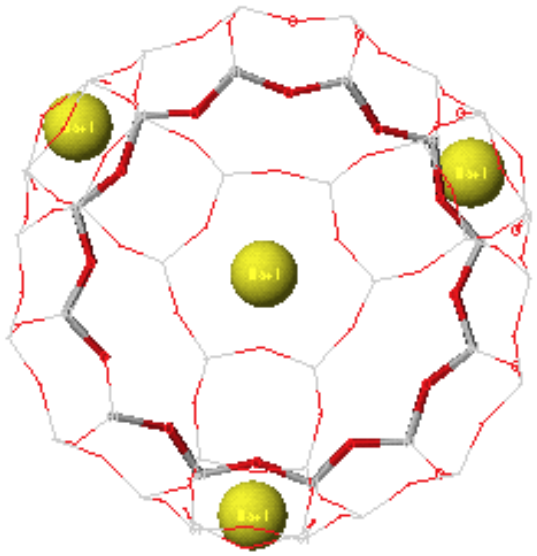
(-)-ephedrine / NaY

Silica gel /
(-)-ephedrine



(CH_2Cl_2 / hexane)
(-)-ephedrine

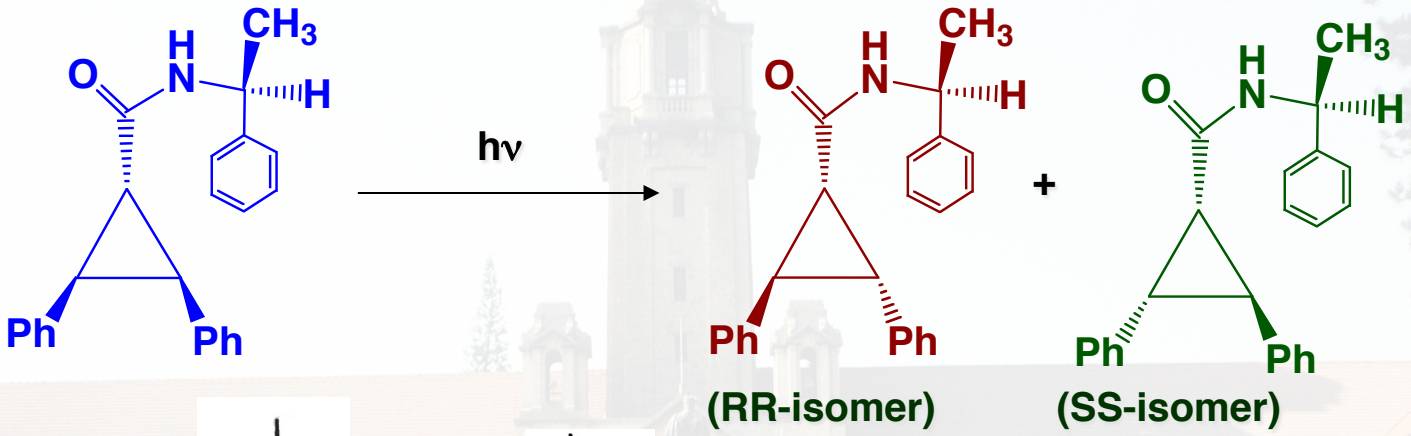
Asymmetric Photoreactions Within Zeolites



- Chiral Induction Depends on
  - Nature of the Cation
  - Number of Cations (Si/Al ratio)
  - Water Content

Cation is the Key

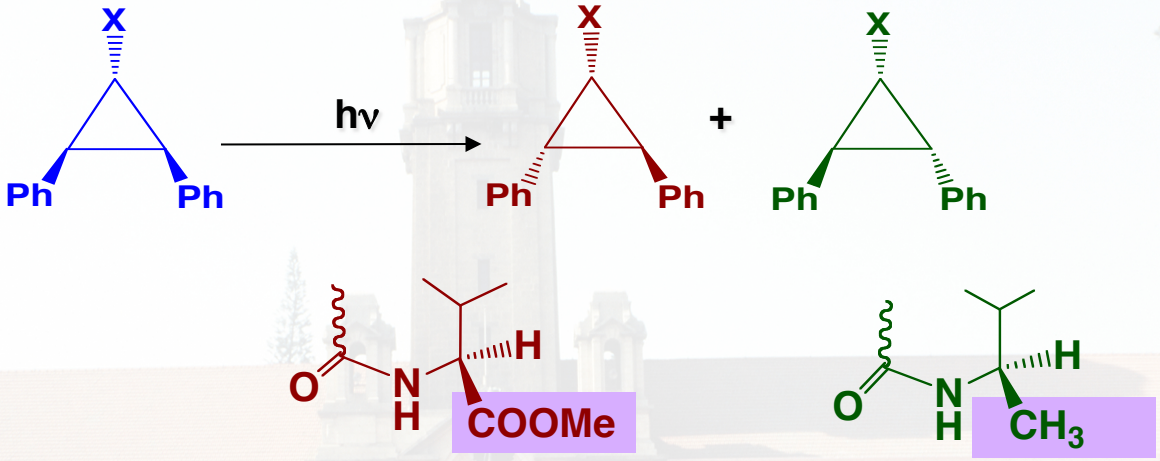
Chiral Induction Depends on the Nature Alkali Metal Ion



Solution	LiY	NaY	KY	RbY	CsY
2 (SS)	80 (SS)	28 (RR)	14 (RR)	5 (RR)	5 (RR)

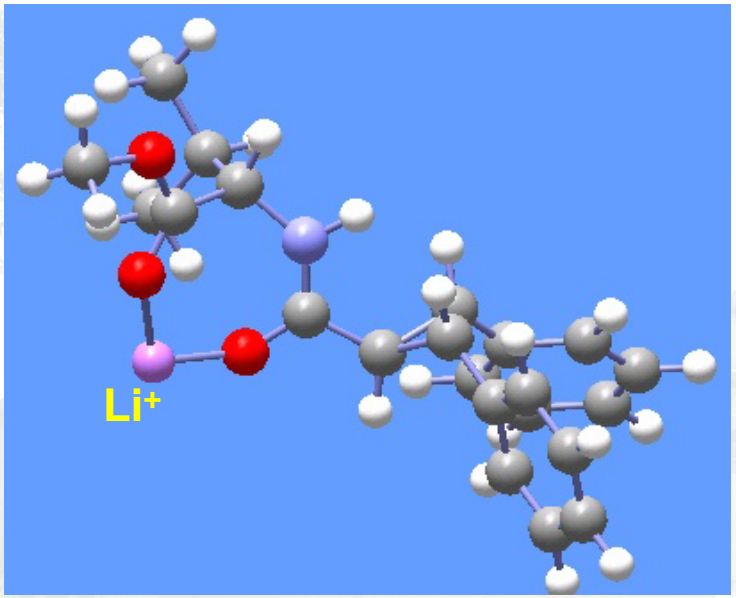
Role of Cation-Carbonyl Dipolar Interaction

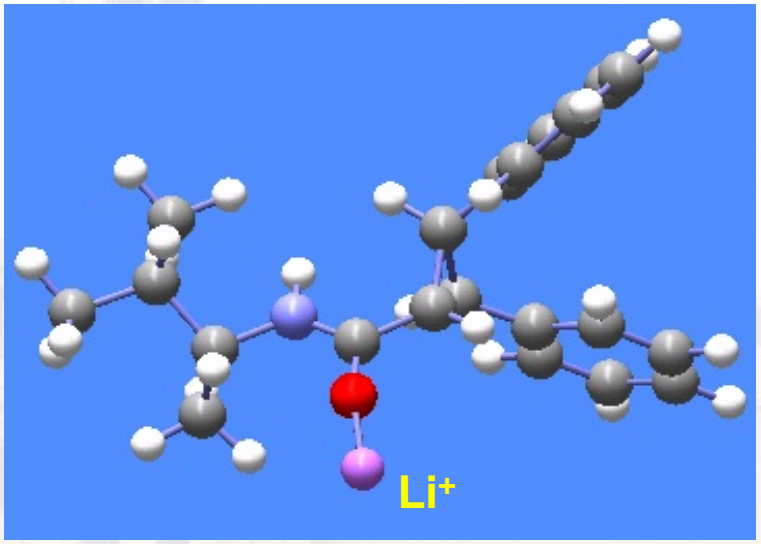
Carboalkoxy *vs* Alkyl



Zeolite	% d.e.	% d.e.
LiY	83-B	7-A
NaY	28-A	7-A
KY	80-A	7-B
RbY	47-A	12-B
Solution	2-B	2-B

Role of Cation-Carbonyl Dipolar Interaction





HF / 3-21G

BA = 104.10 kcal/mol

BA = 79.63 kcal/mol