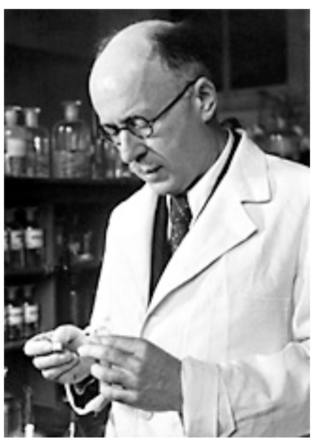
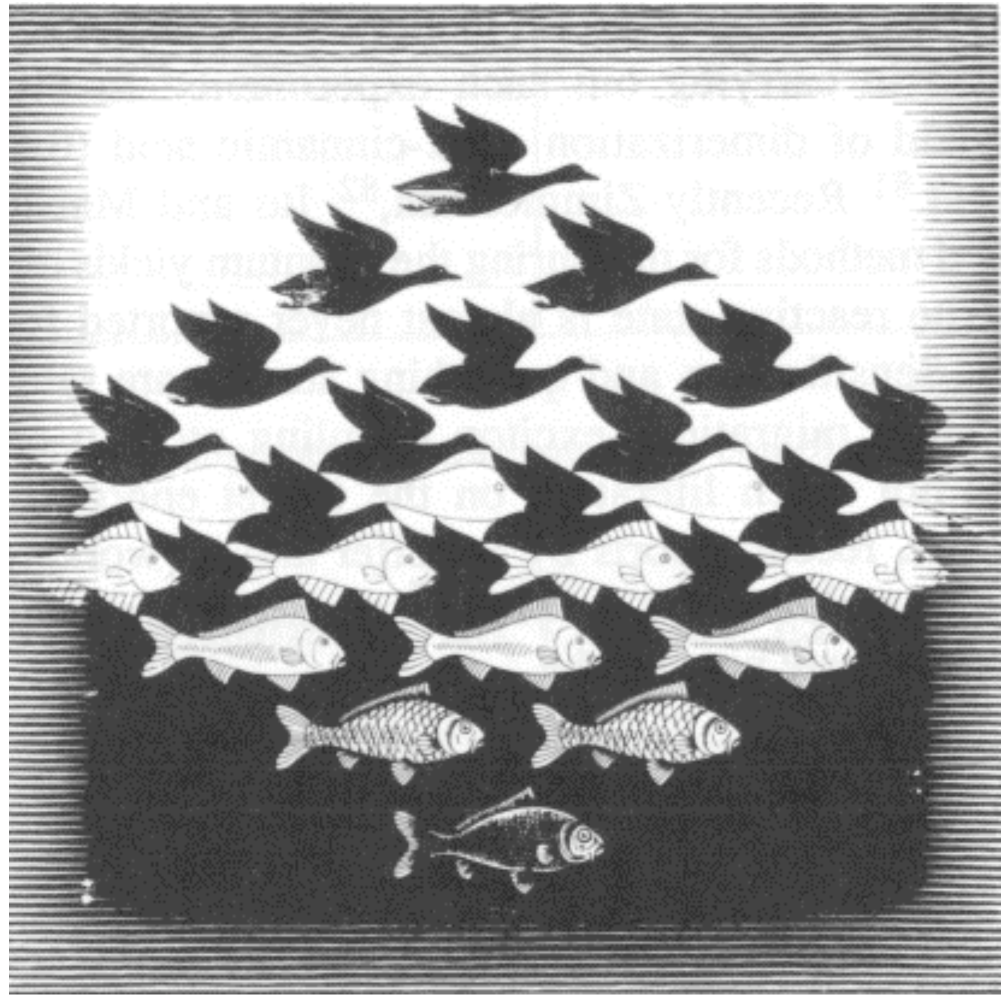
Crystalline State Photochemistry

The Nobel Prize in Chemistry 1964
"for her determinations by X-ray techniques of the structures of important biochemical substances"

Photoreactions in Crystals



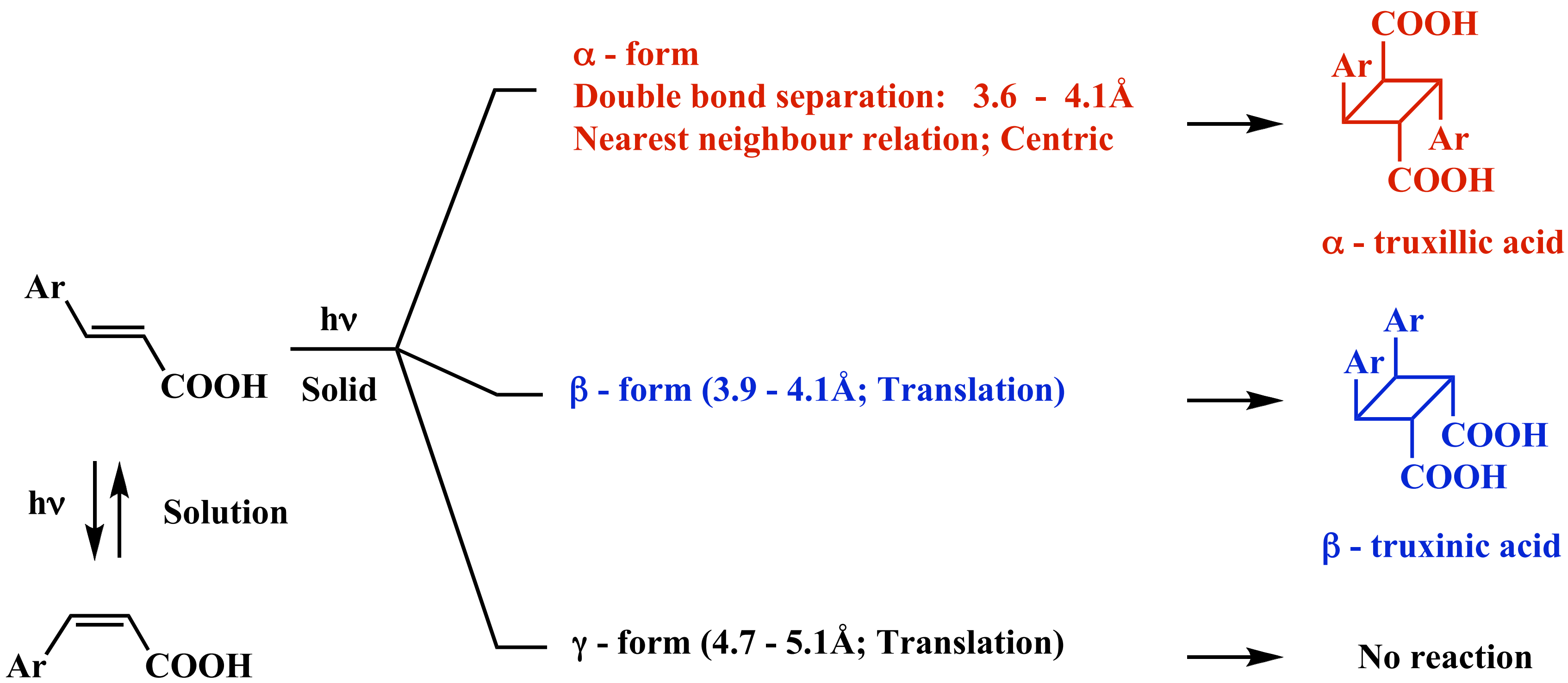


Esher's drawings

"A crystal is a chemical cemetery"

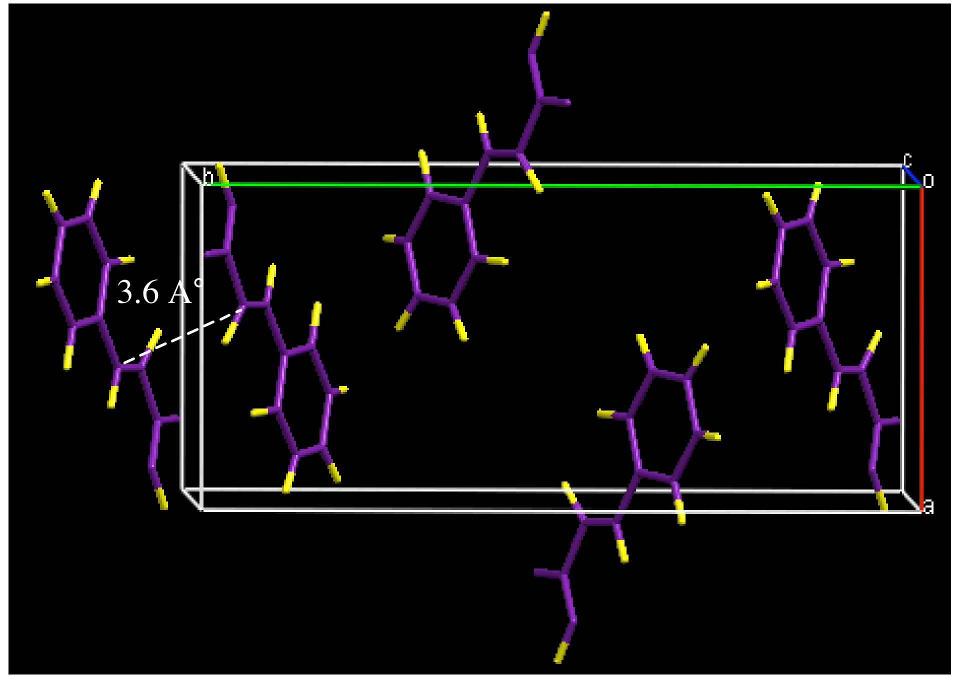
Nobel Laureate L. Ruzika (1930s)

Photodimerization of *trans*-Cinnamic acids



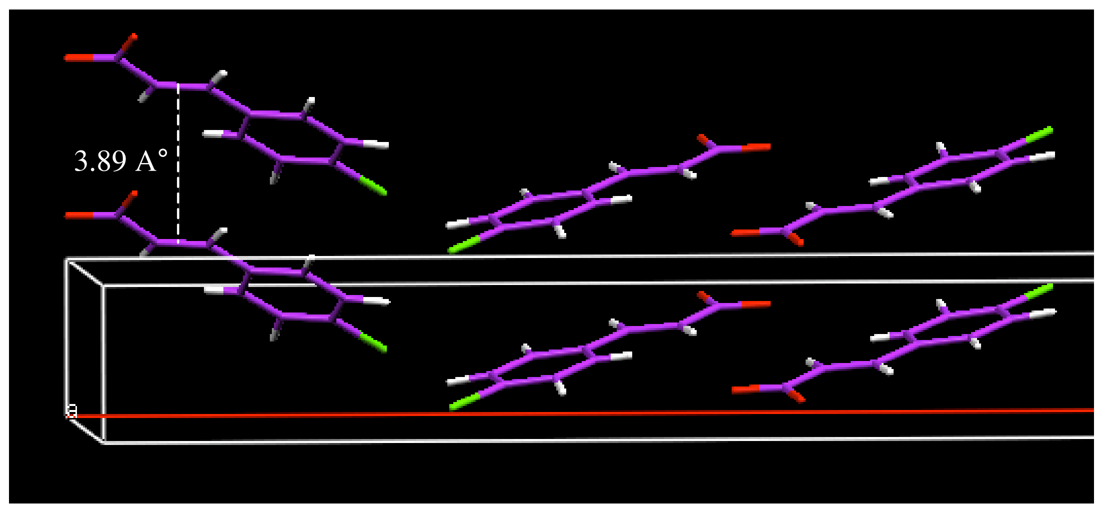
α-*trans*-Cinnamic acid

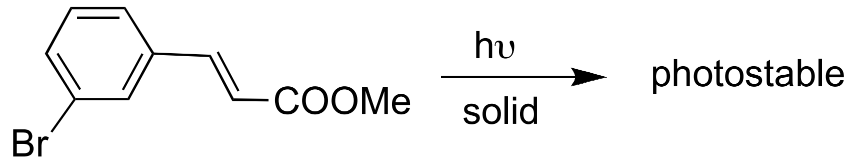
Leads to centrosymmetric dimer

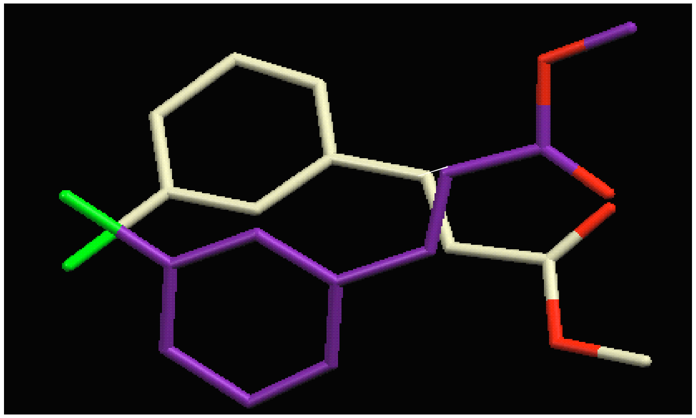


β-*trans*-Cinnamic acid

Leads to mirror symmetric dimer

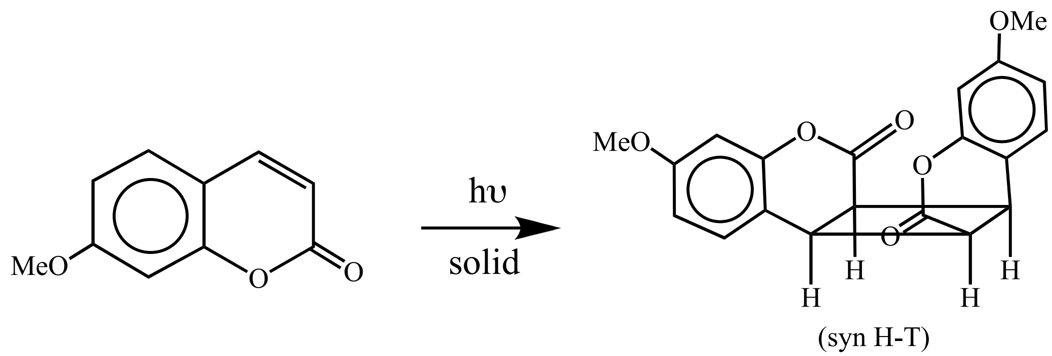


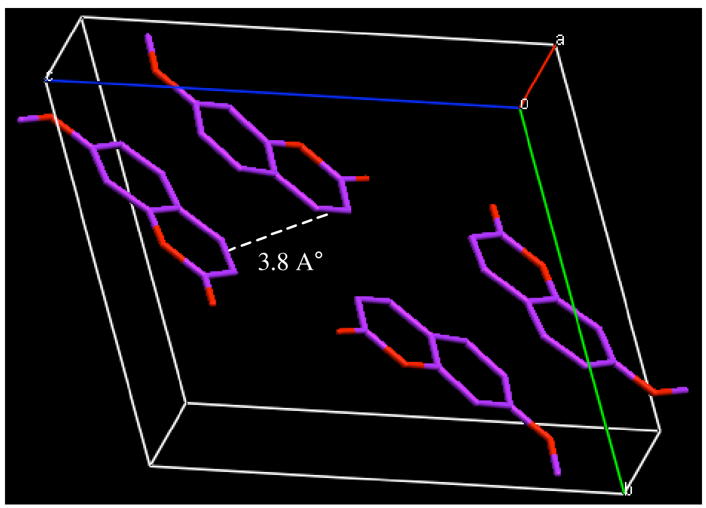


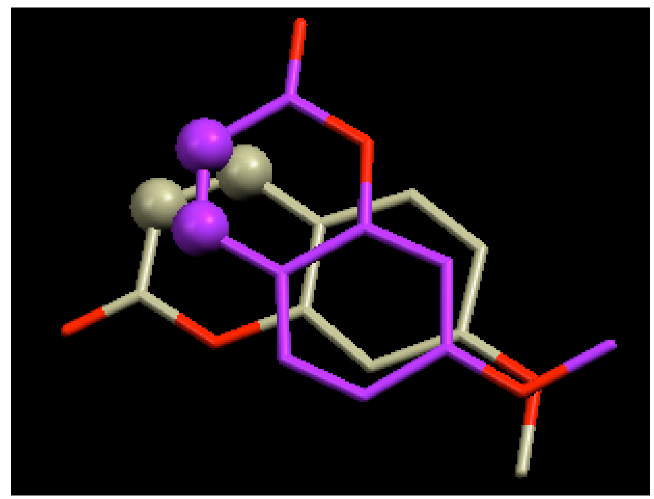


Topochemical principle: Reactions in the solid state take place with minimum atomic movements.

G. M. J. Schmidt et al. '*Solid State Photochemitsry, A Collection of Papers*', Verlag Chemie, 1976.







K. Venkatesan, V. Ramamurthy et. al., (1984)

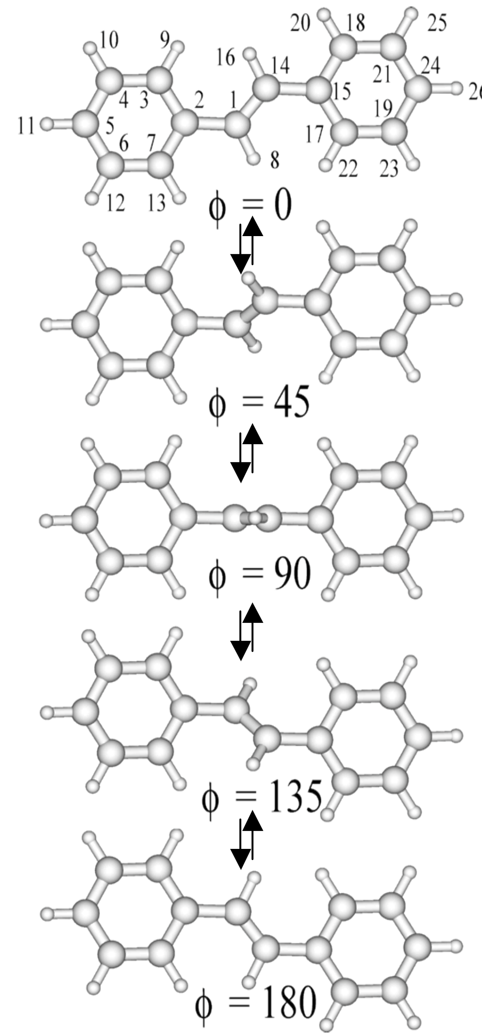
"The next decade will surely see ----- large-amplitude molecular motions in the solid state."

J. D. Dunitz, V. Schomaker and K. N. Trueblood (1988)

~~"A crystal is a chemical cemetery"~~

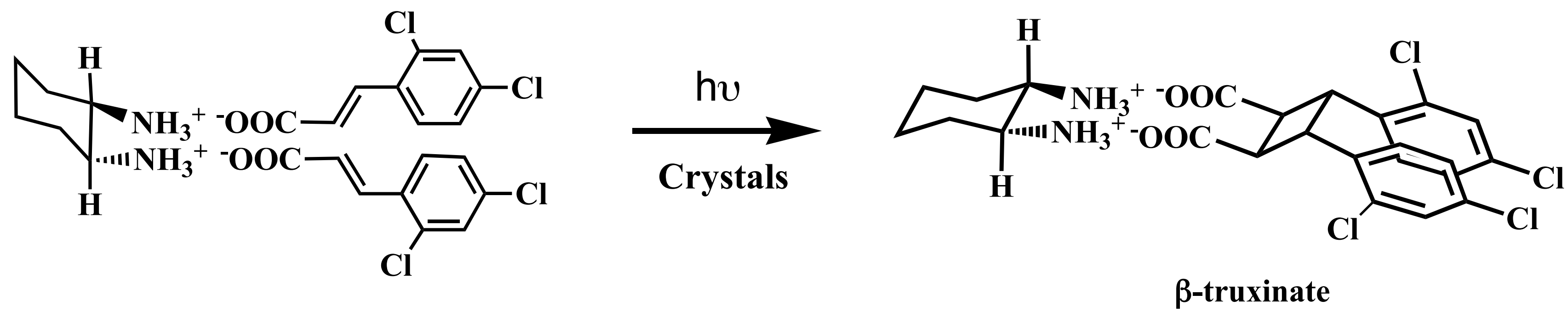
L. Ruzika (1930s)

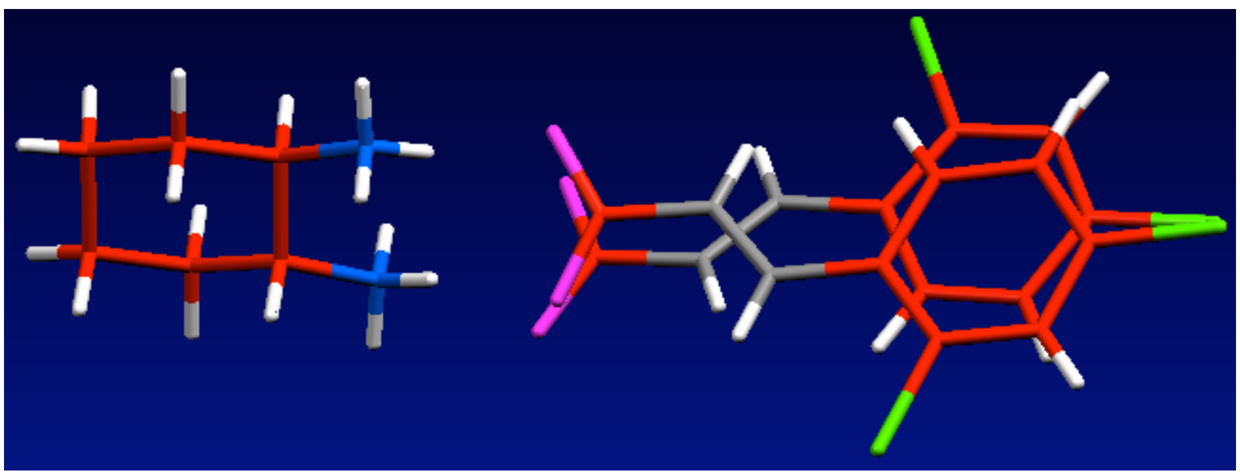
Pedal motion of stilbenes



Harada and Ogawa, JACS (2004).

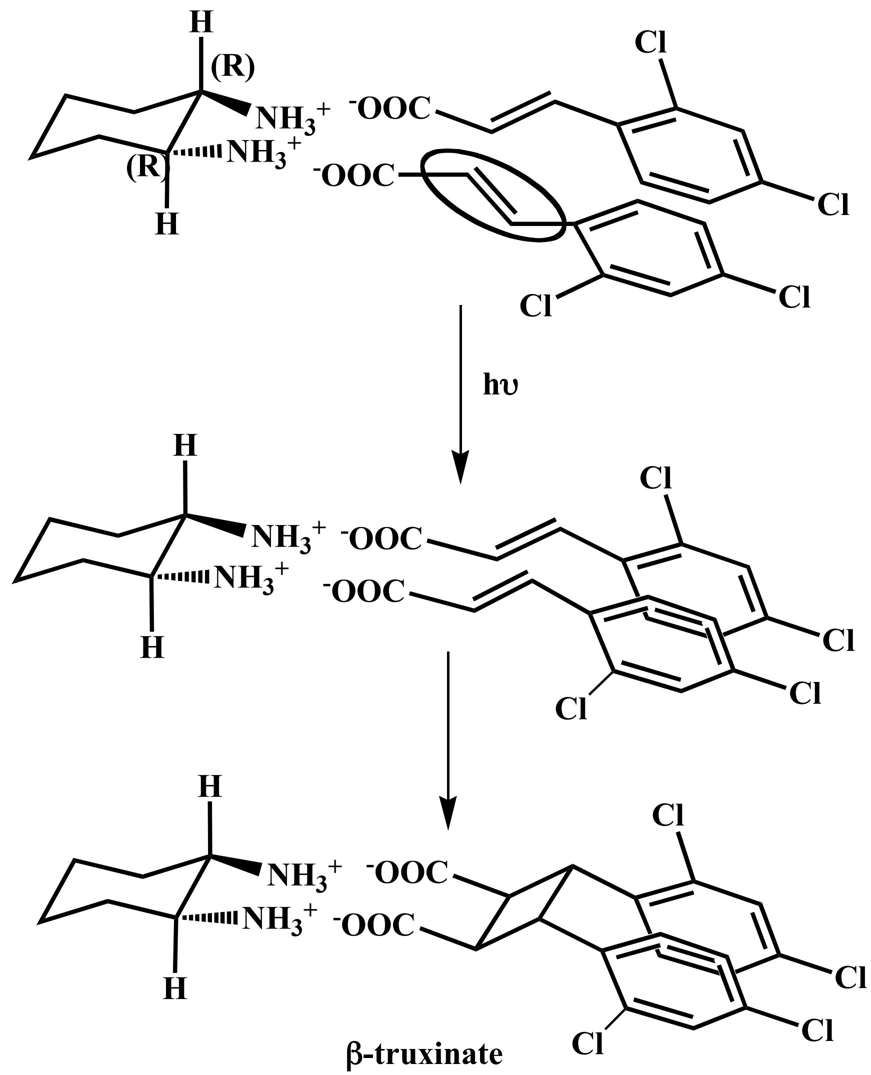
Photodimerization of criss-cross alkenes



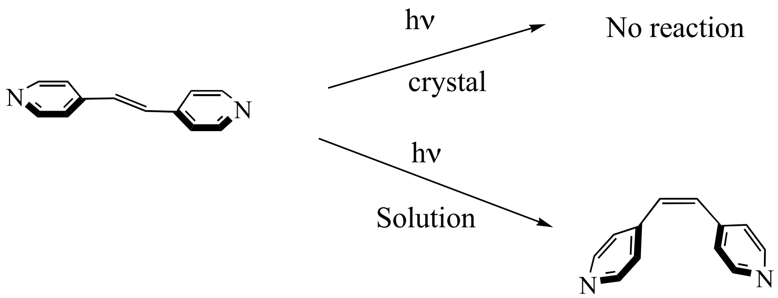


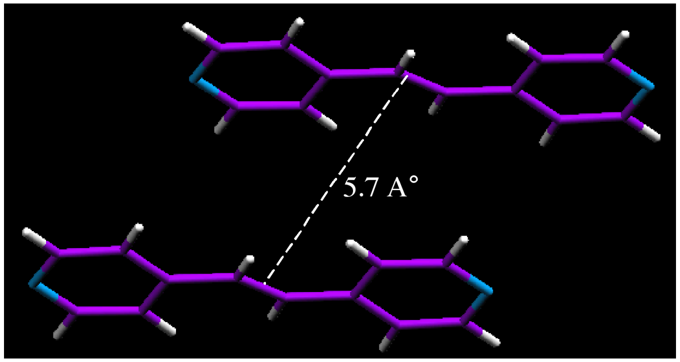
Large motions are tolerated in the crystal

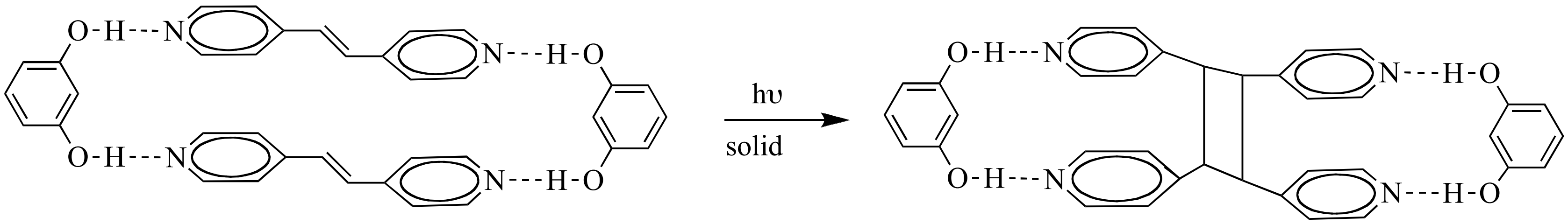
- Pedal-like conformational change by one of the cinnamic acid molecules is required for β-dimer formation.

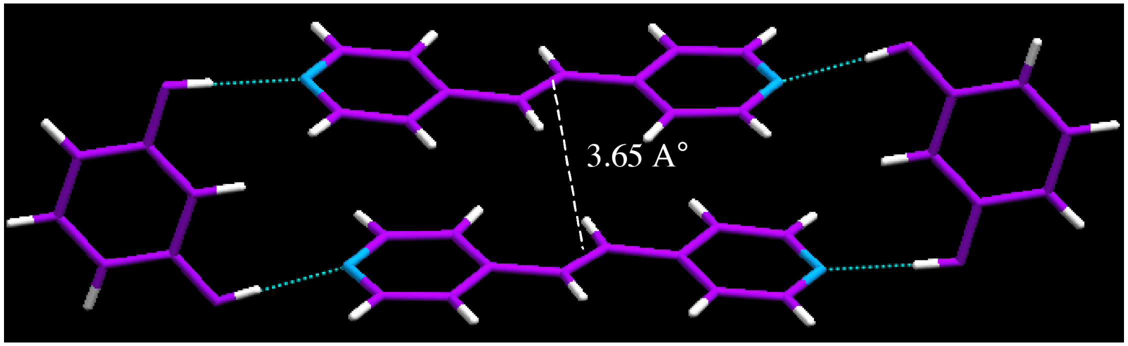


Pre-organization with a guest: Non reactive molecule made to react



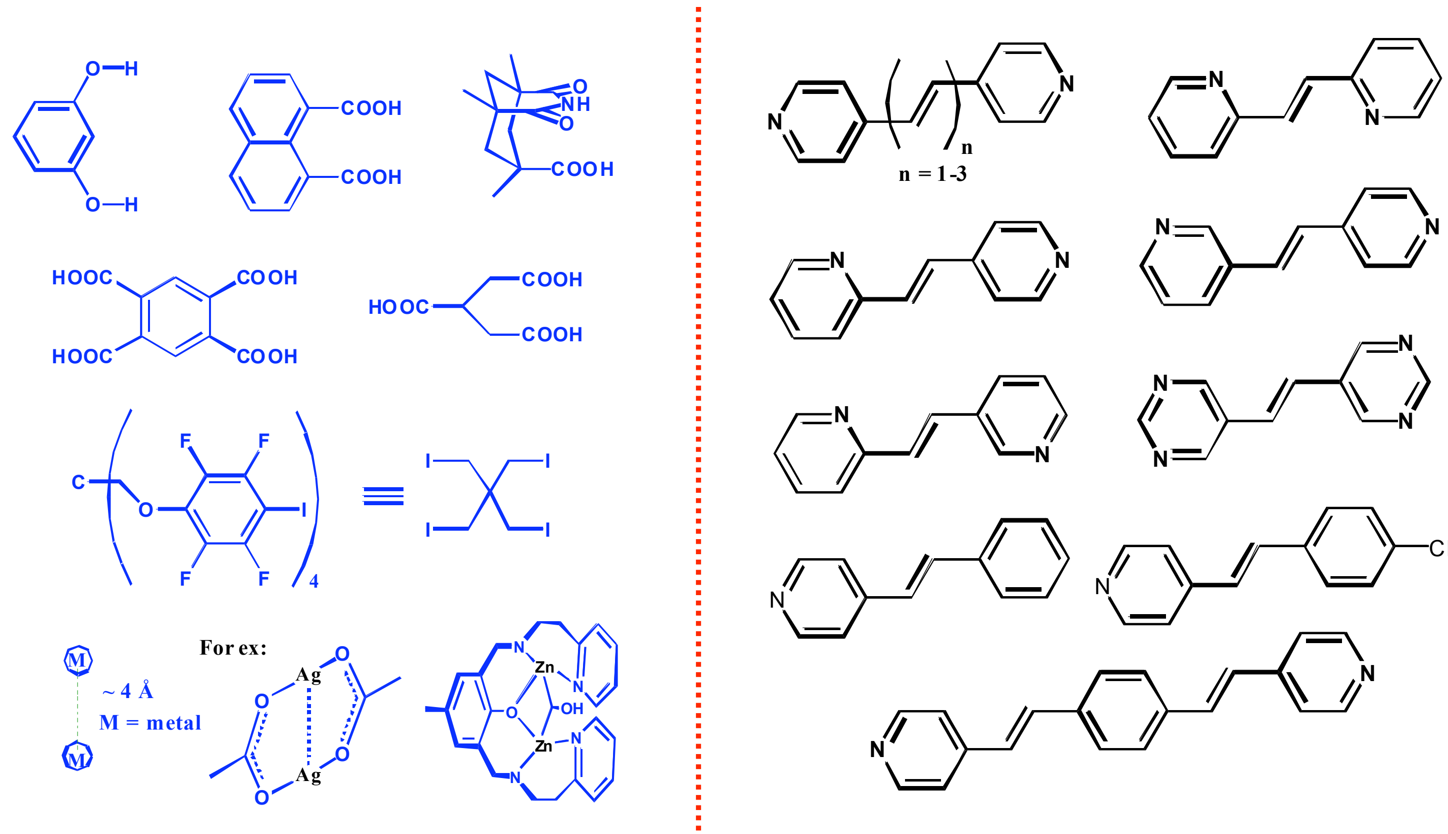




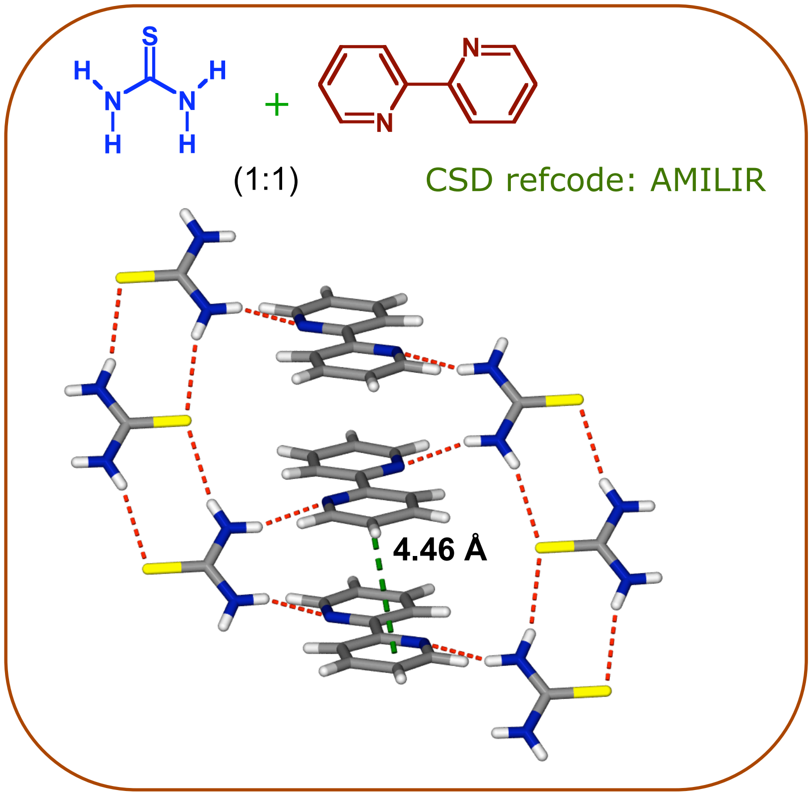


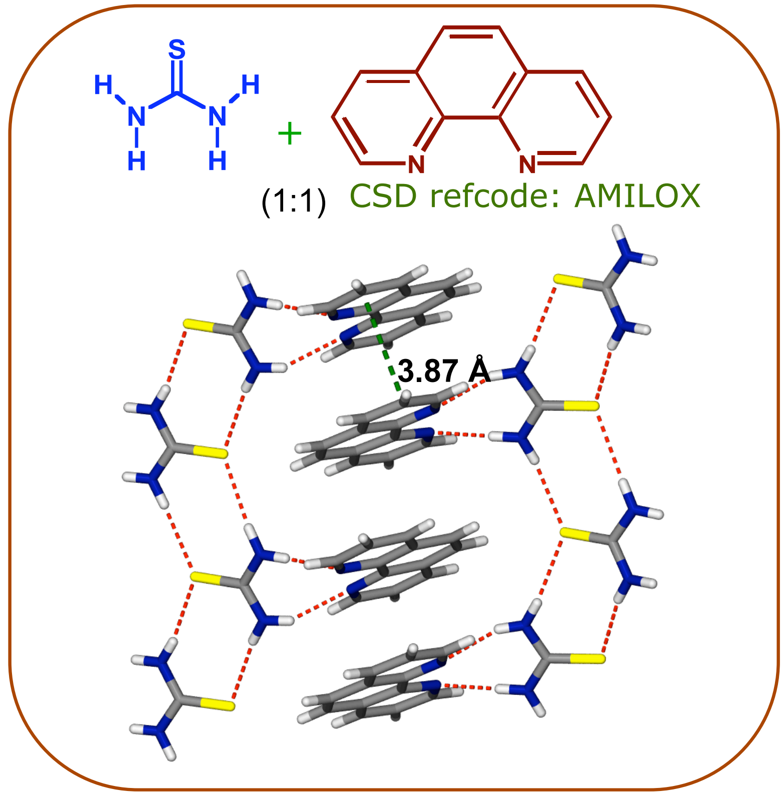
MacGillivray et. al., *JACS*, 2000, *122*, 7817.

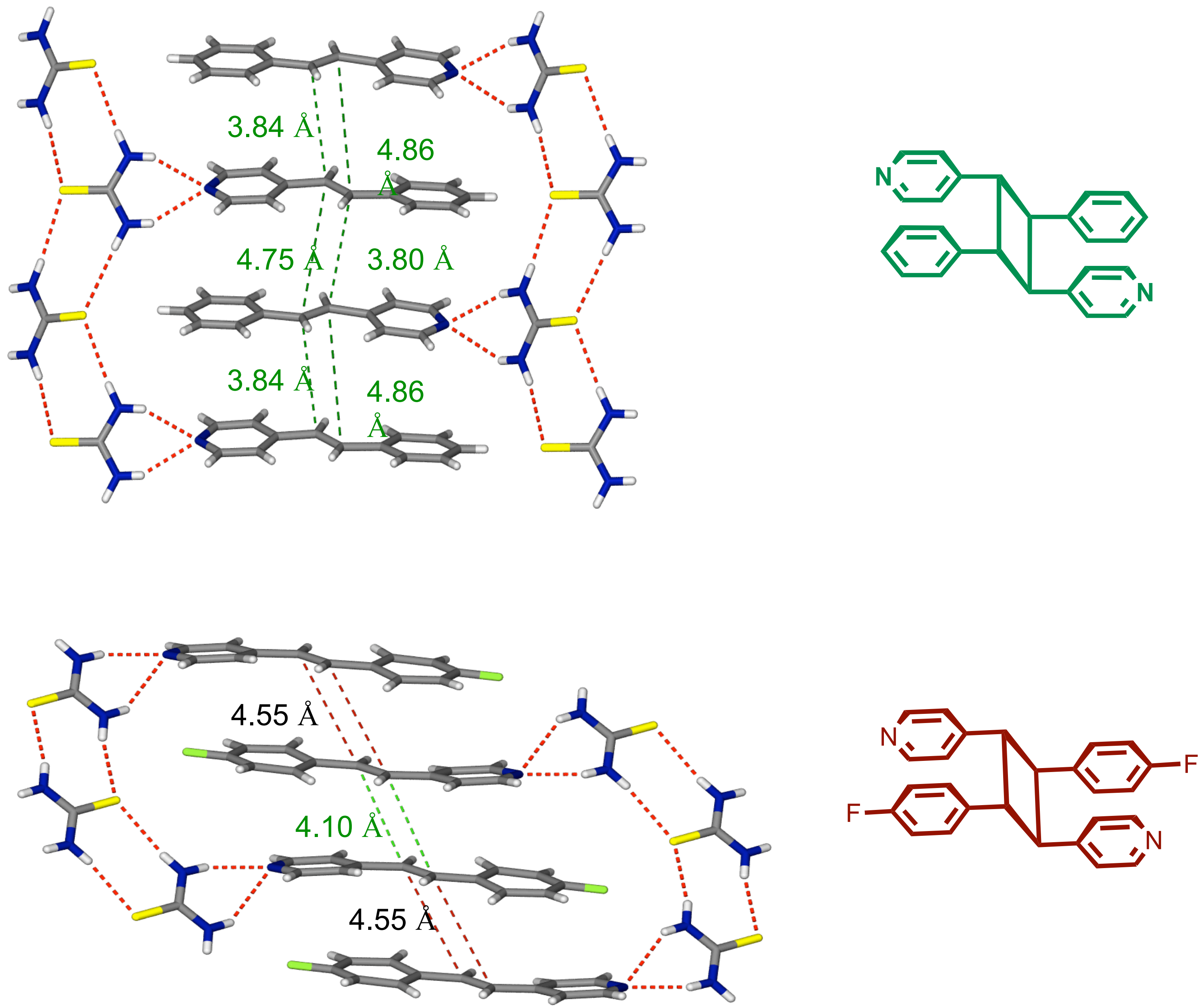
Overview of templated dimerization of olefins in solid-state



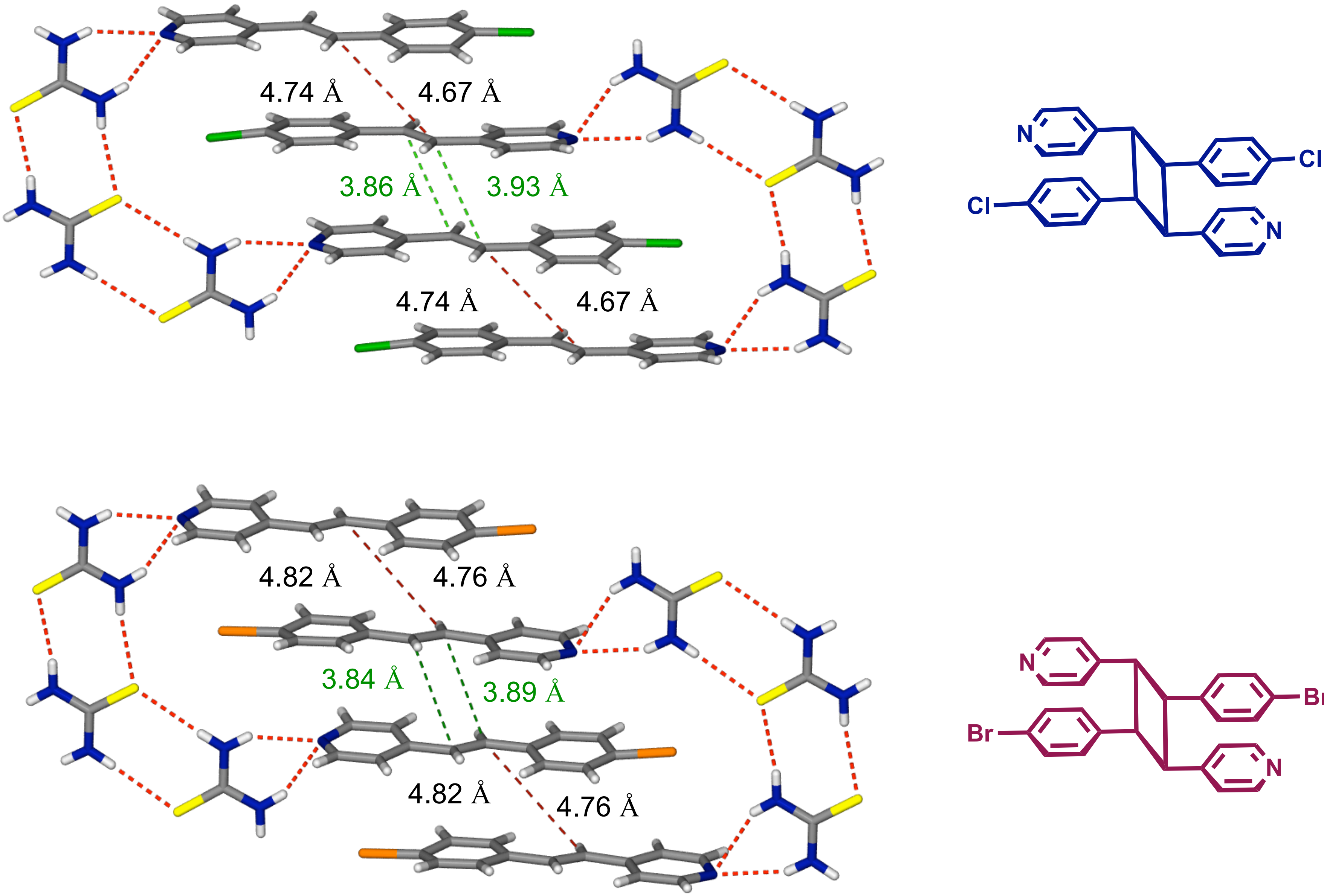
Thiourea as a possible template (Cambridge Structural Database)

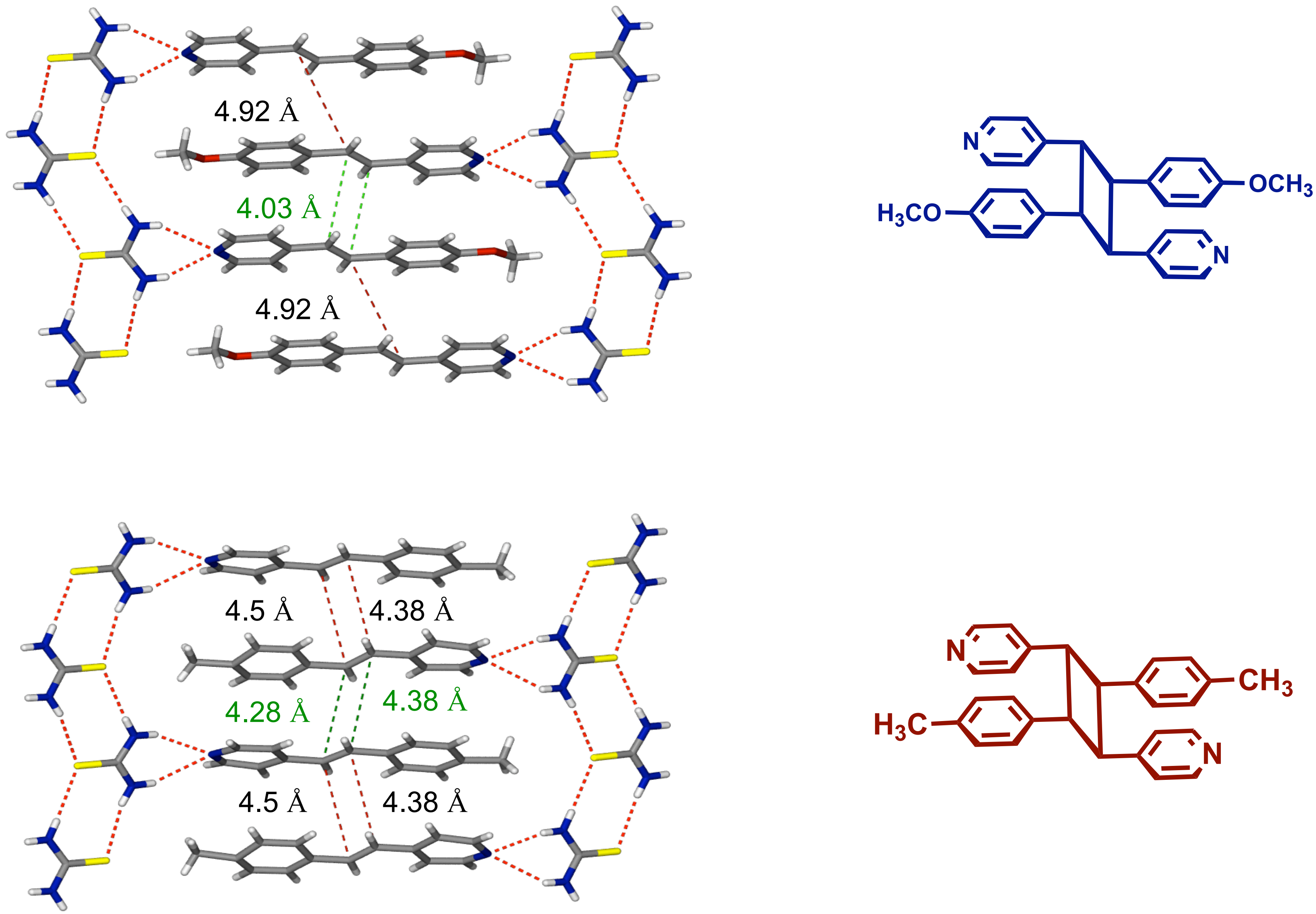


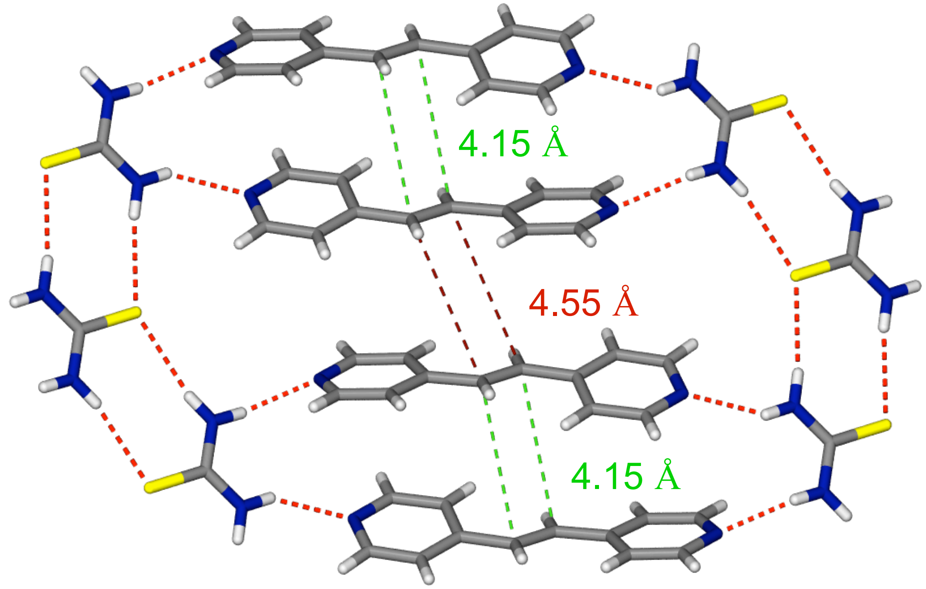


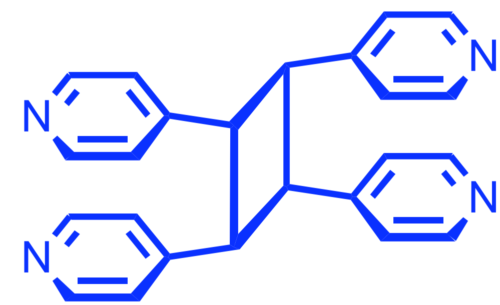


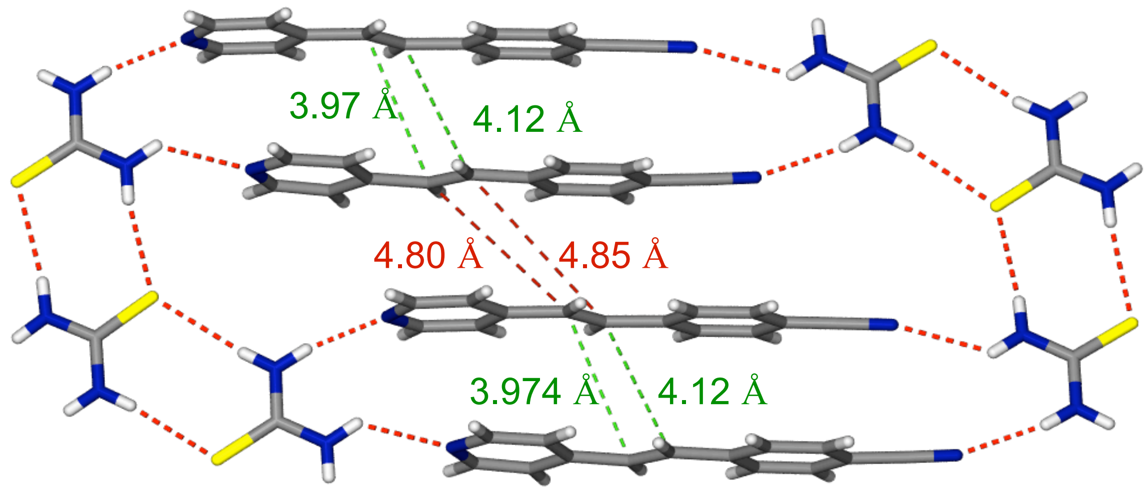
3.84 Å
4.86 Å
4.75 Å
3.80 Å
3.84 Å
4.86 Å
N
N
4.55 Å
4.10 Å
4.55 Å
N
F
F
N

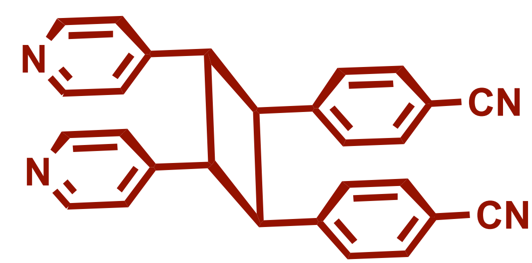

4.74 Å
4.67 Å
3.86 Å
3.93 Å
4.74 Å
4.67 Å
N
Cl
Cl
N
4.82 Å
4.76 Å
3.84 Å
3.89 Å
4.82 Å
4.76 Å
N
Br
Br
N


4.92 Å
4.03 Å
4.92 Å
N
OCH3
H3CO
N
4.5 Å
4.38 Å
4.28 Å
4.38 Å
4.5 Å
4.38 Å
N
CH3
H3C
N

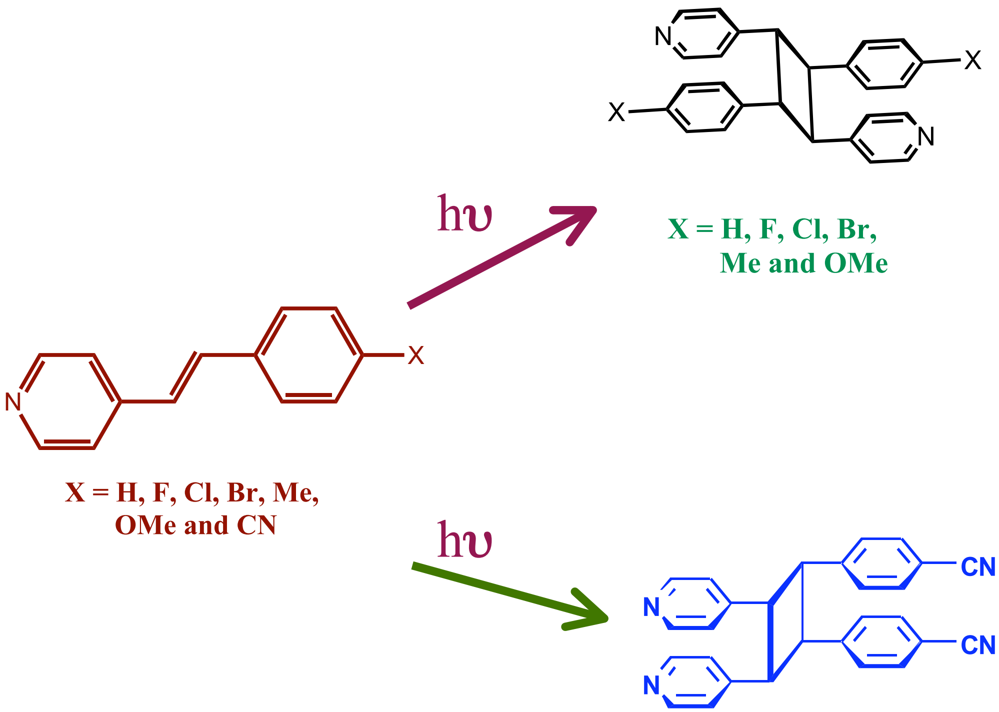

4.15 Å
4.55 Å
4.15 Å

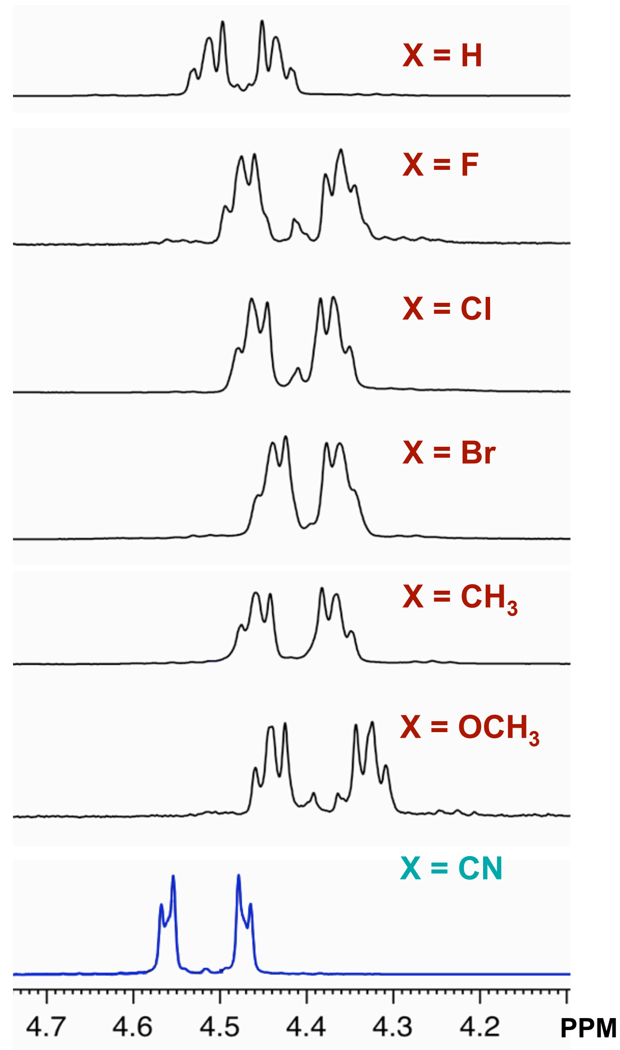

N
N
N
N


3.97 Å
4.12 Å
4.80 Å
4.85 Å
3.974 Å
4.12 Å


N
N
CN
CN

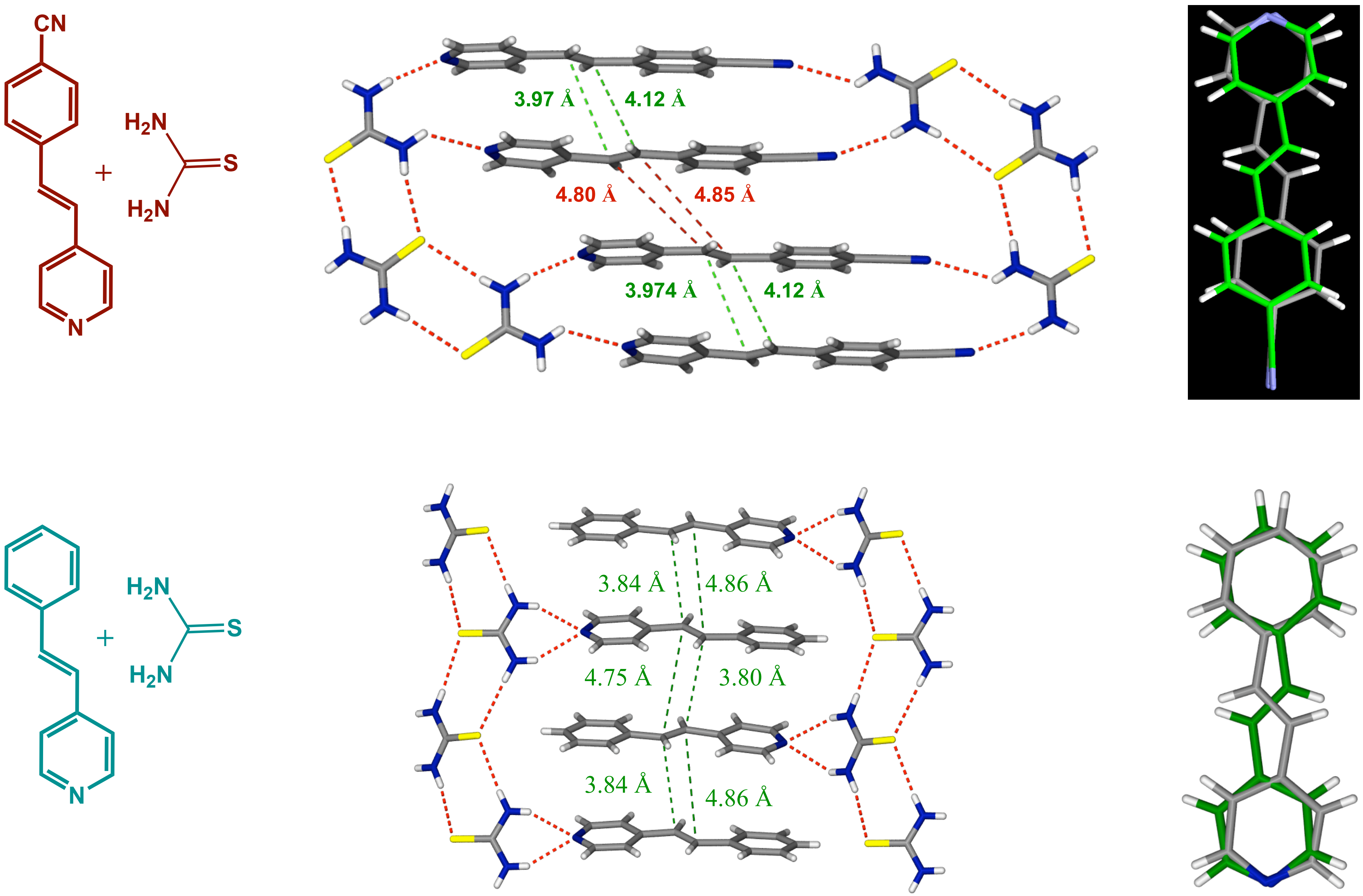
An overview of photochemistry of stilbazoles in thiourea co-crystals

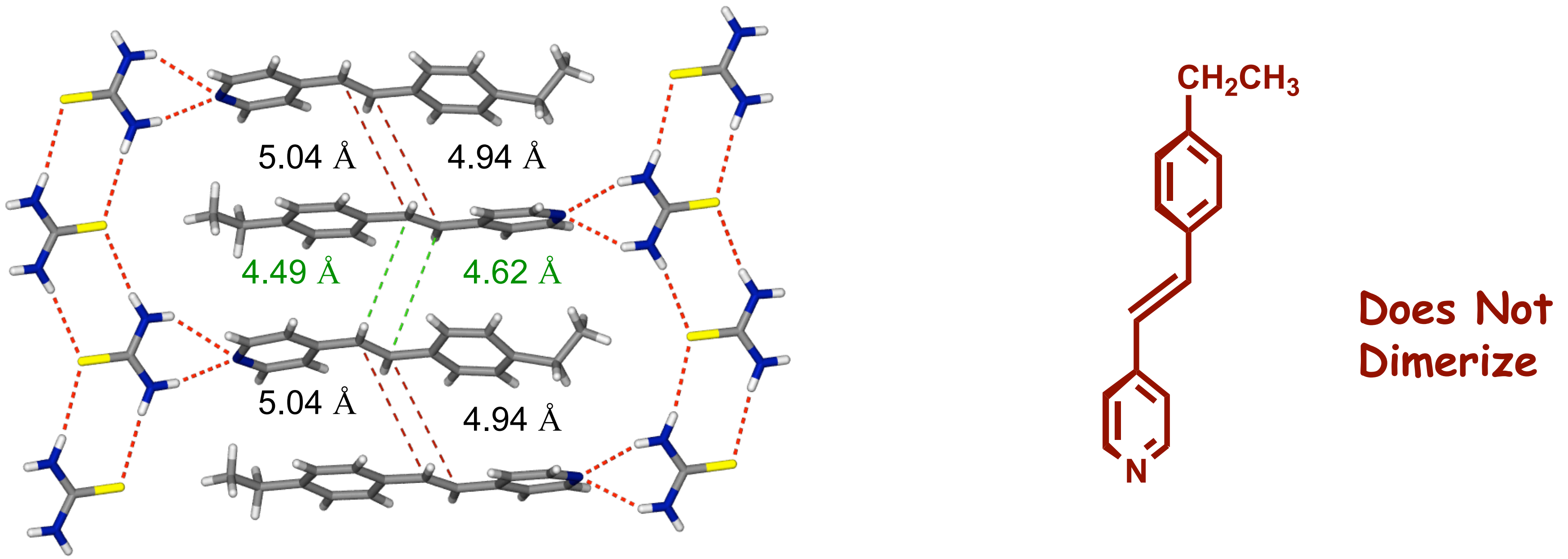


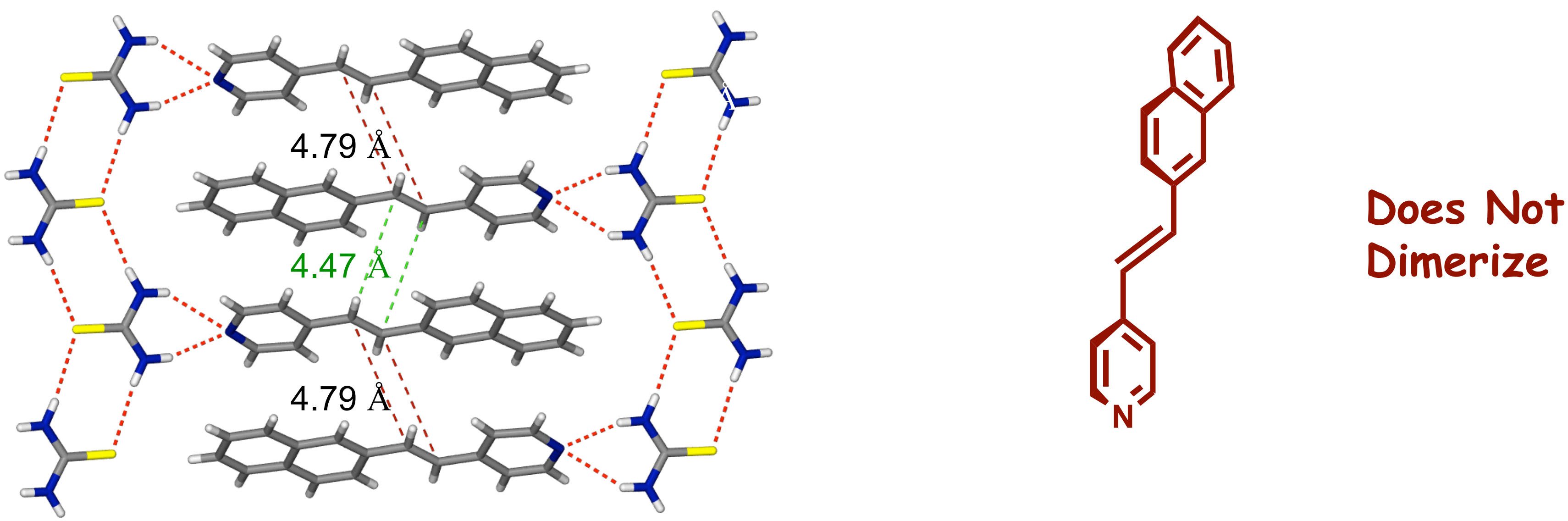


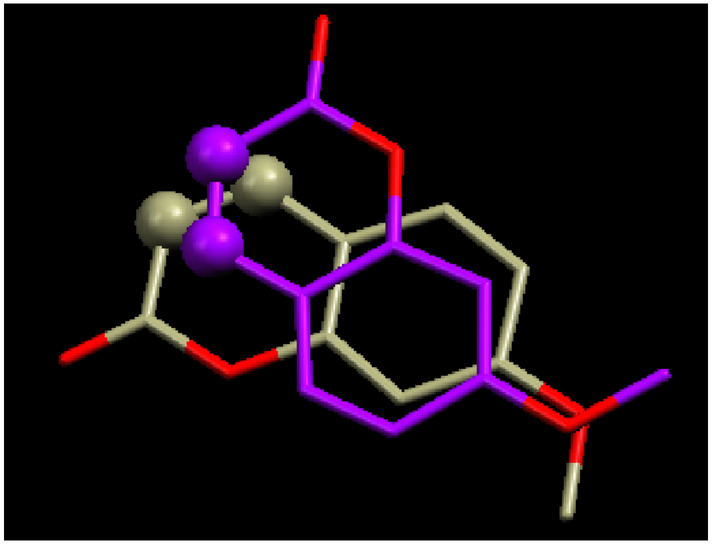
[1]H NMR ($CDCl_3$) of cyclobutane protons in dimer products

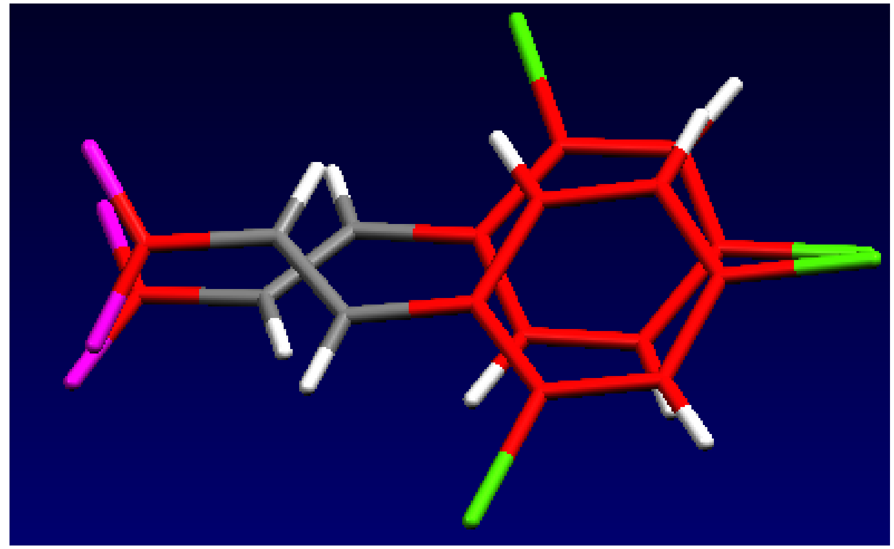
Anomalous orientation of 4-cyanostilbazole in thiourea co-crystals

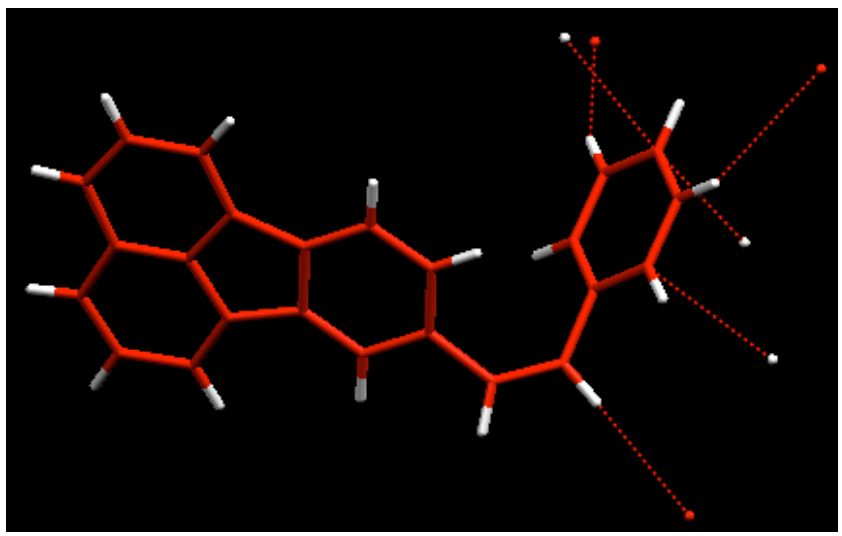



5.04 Å
4.94 Å
4.49 Å
4.62 Å
5.04 Å
4.94 Å
CH2CH3
N
Does Not
Dimerize


4.79 Å
4.47 Å
4.79 Å
N
Does Not
Dimerize

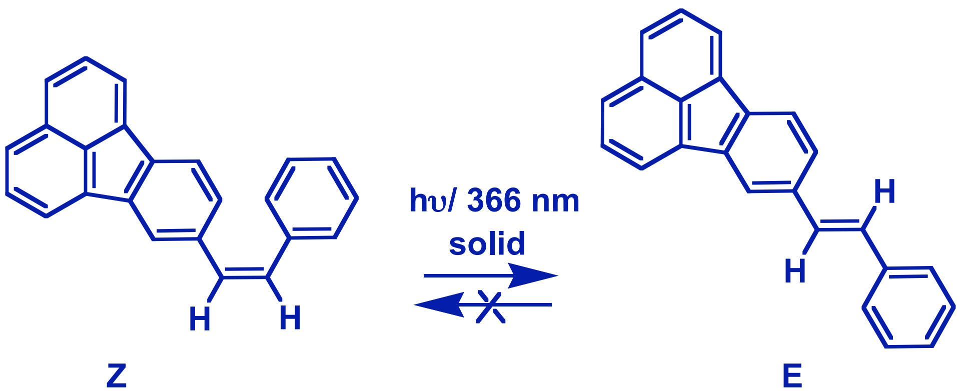


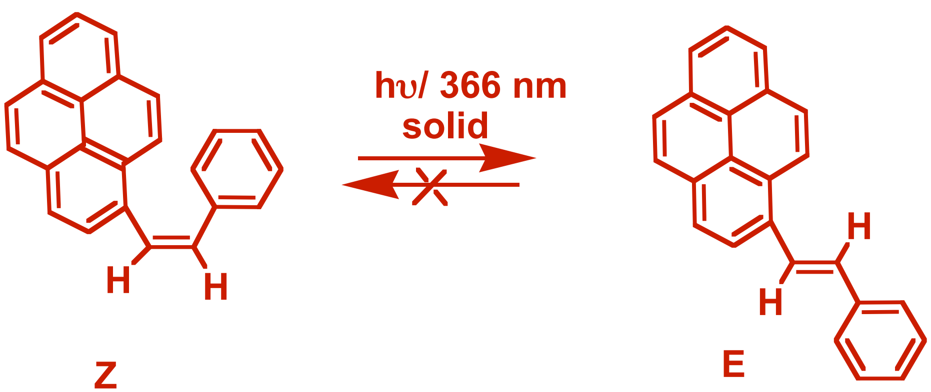




??

Cis-Trans Photoisomerization in Crystals

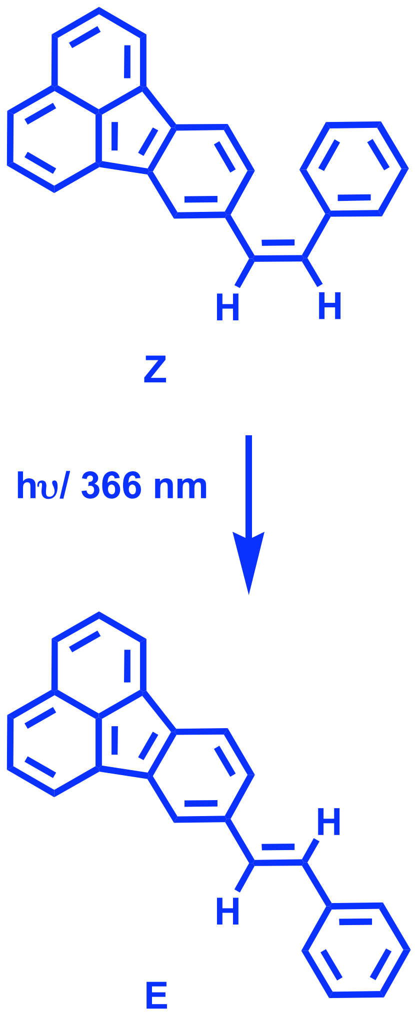


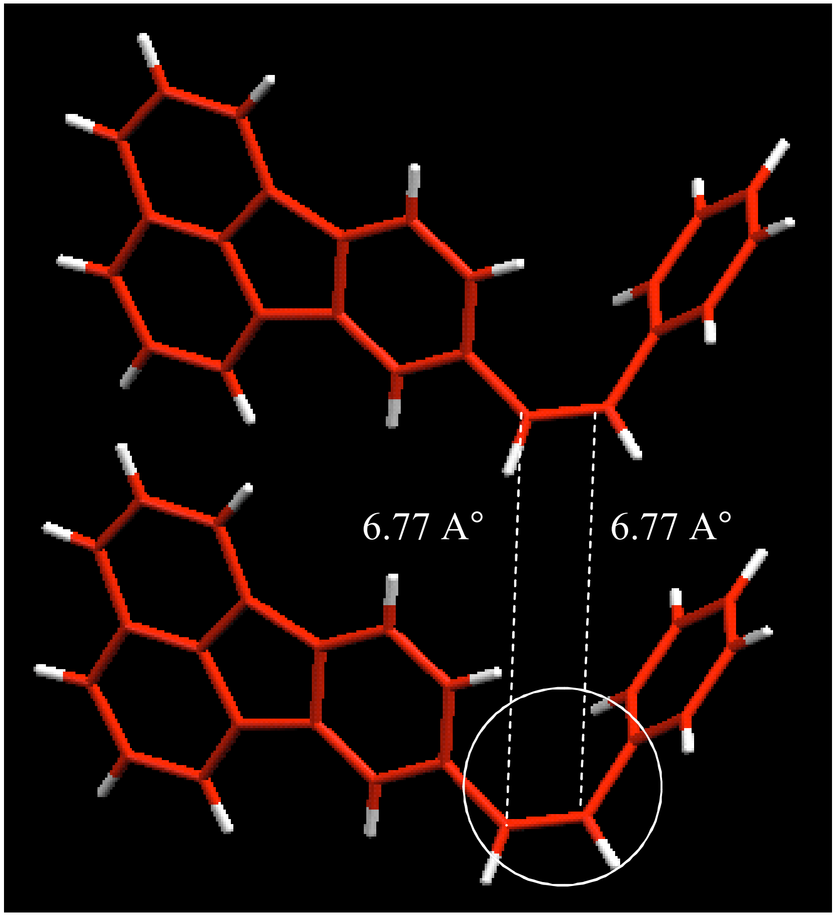


Temp °C	Duration	%Conversion
RT	12	100
50°C	6	100
RT	12	15
50°C	18	60
RT	45	80
50°C	21	100

T. Arai

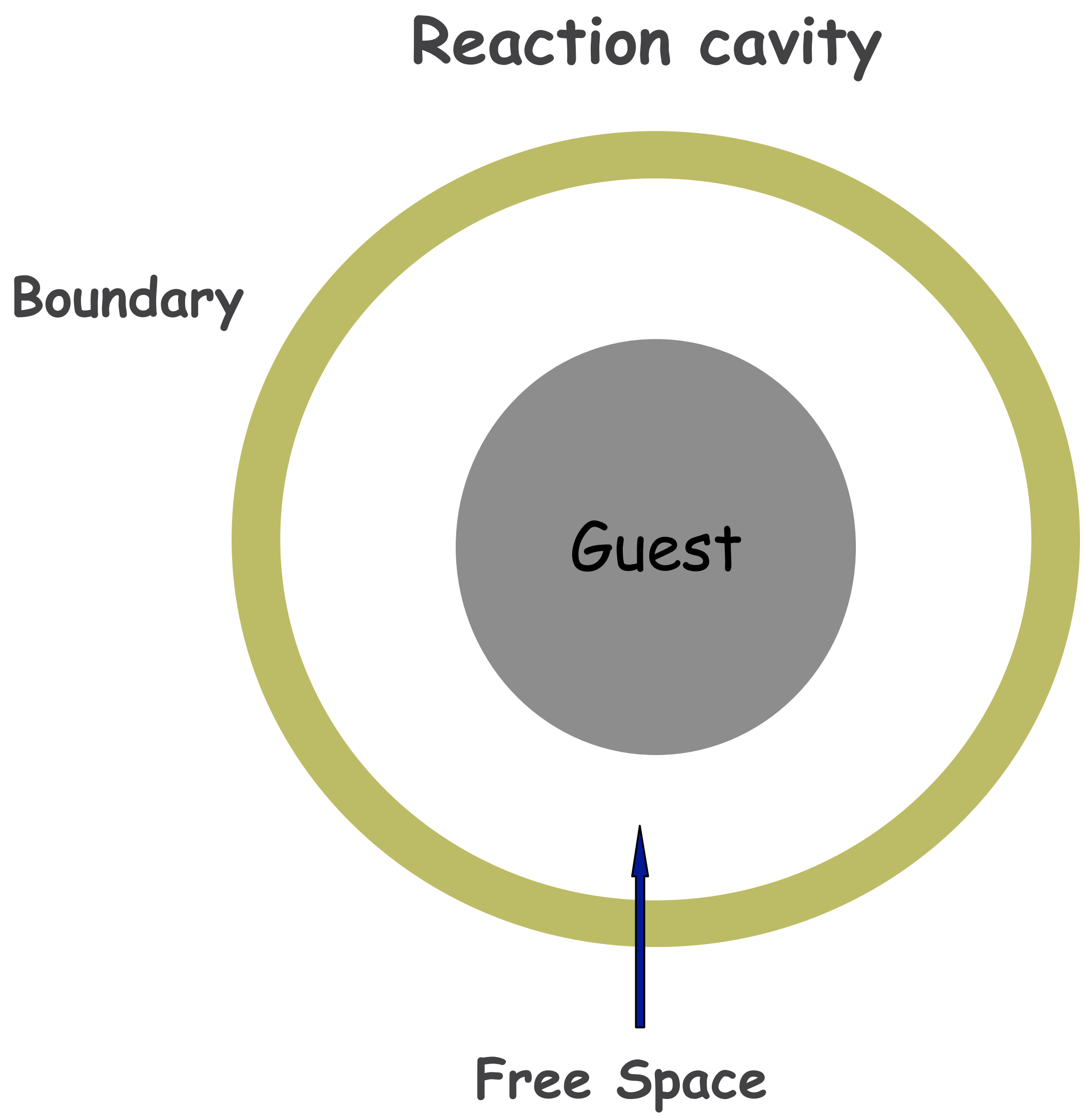
Photoisomerization of *cis*-8-fluoranthenyl styrene





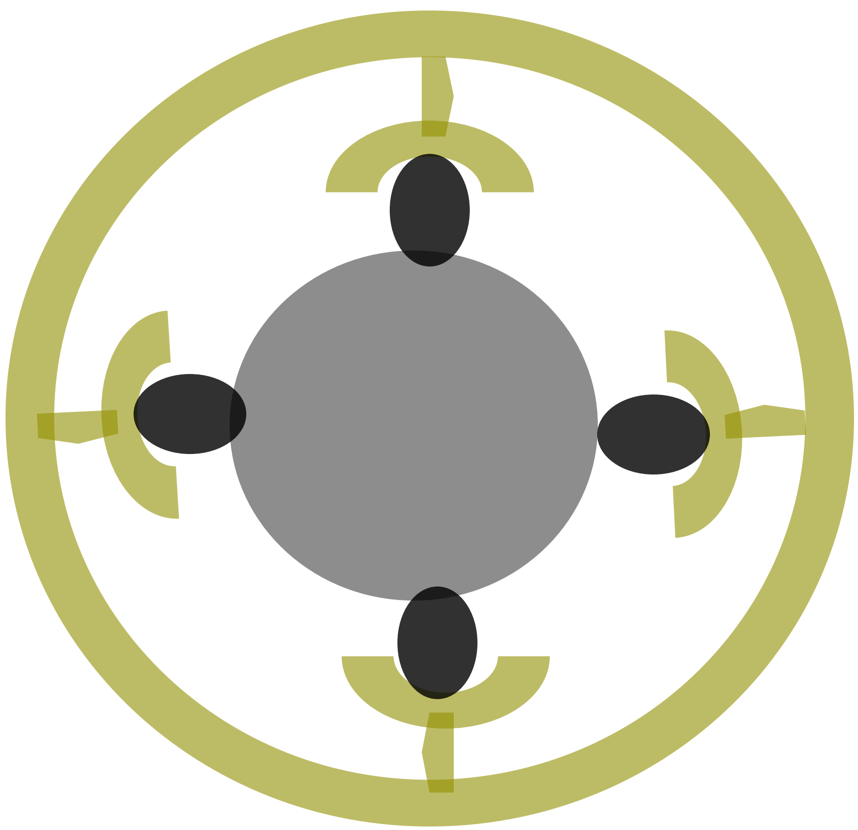
Large distance between the reactive double bonds 6.77 A° precludes cyclobutane intermediate.

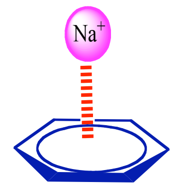
Supramolecular Containers



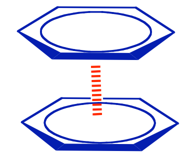
Cohen and Schmidt

Role of Weak Interactions

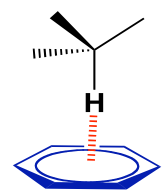




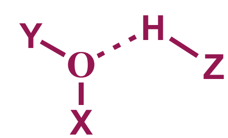
Cation---π



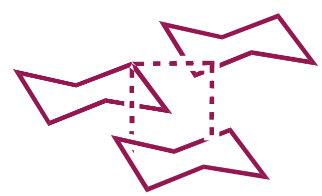
π---π



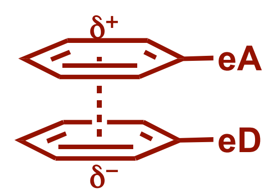
C–H---π



Hydrogen bond

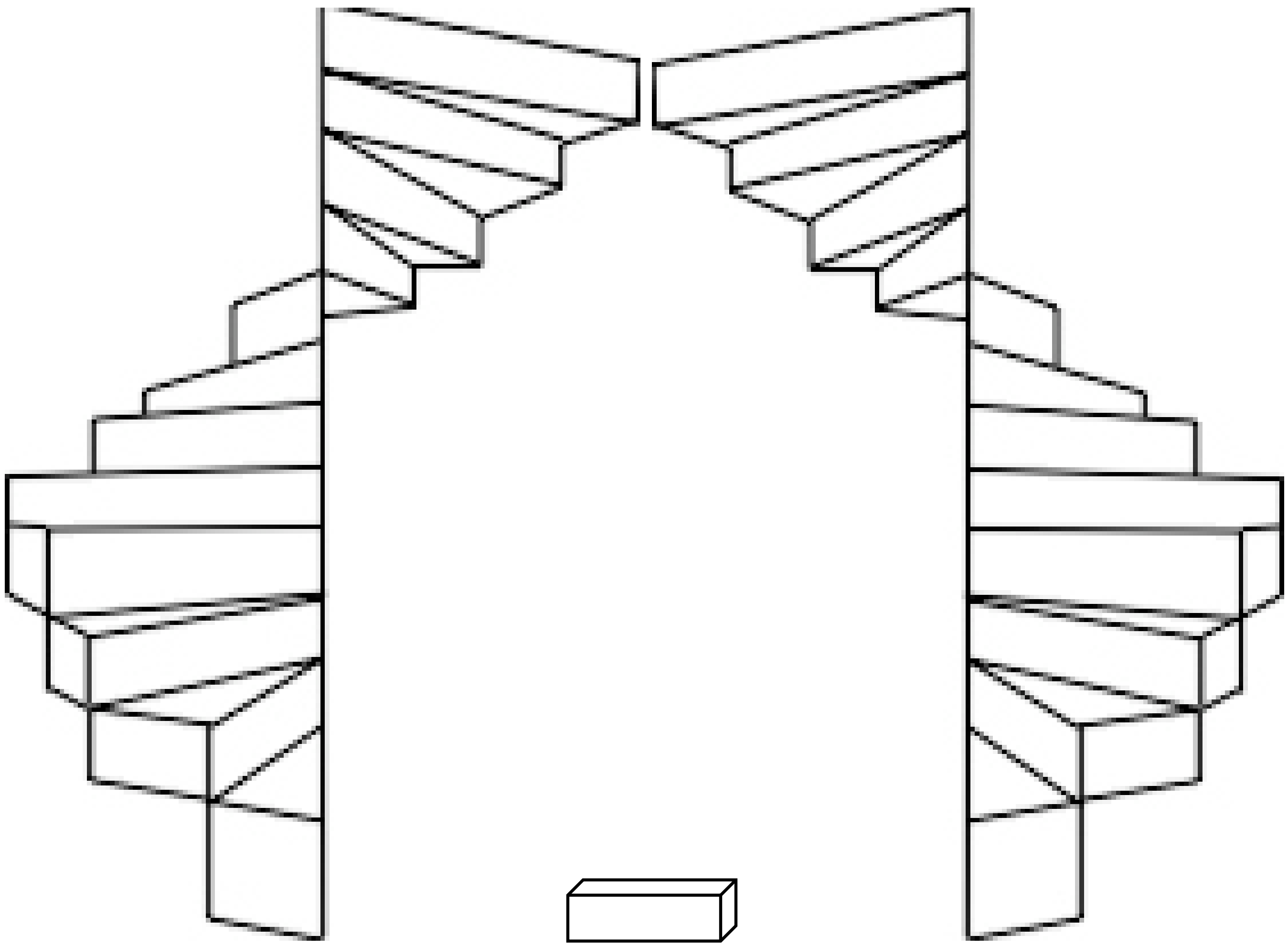


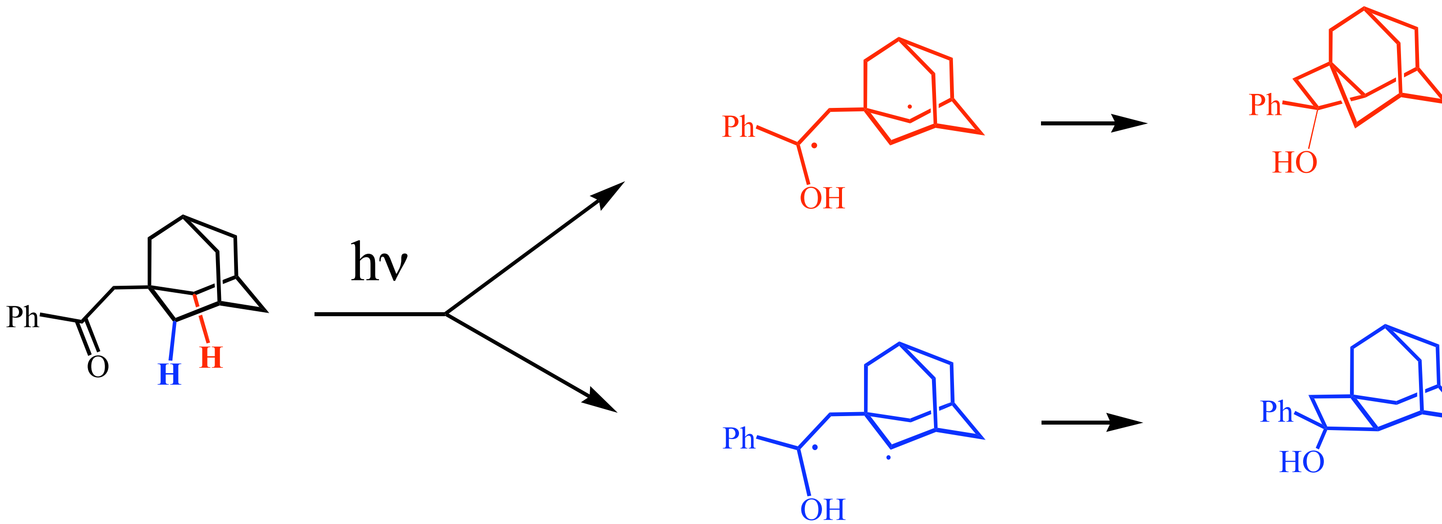
van der Waals

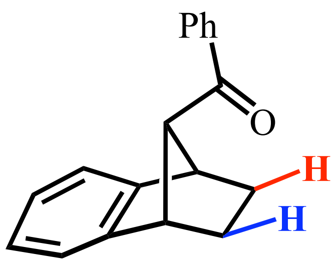


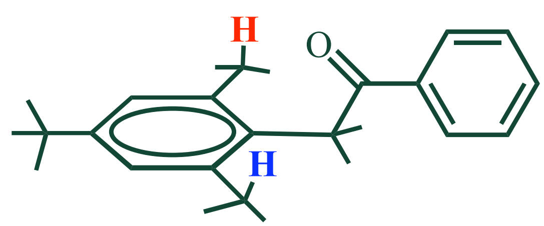
Charge transfer

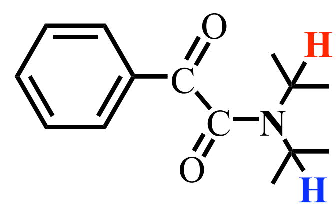
Asymmetric Photochemistry in Crystals



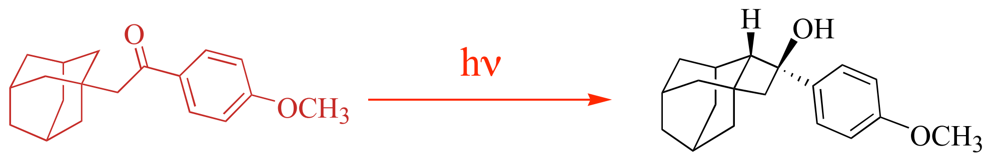

Ph
O
H
H
hν
Ph
OH
Ph
HO
Ph
OH
Ph
HO

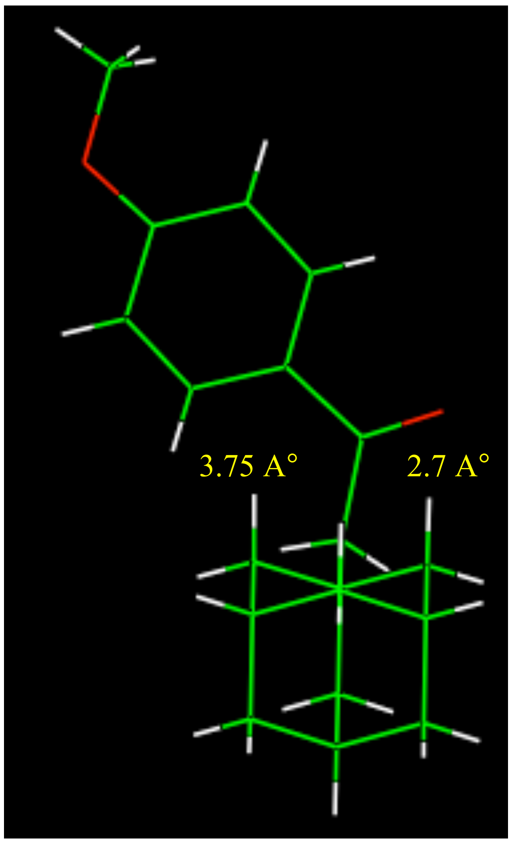

Ph
O
H
H


H
O
H

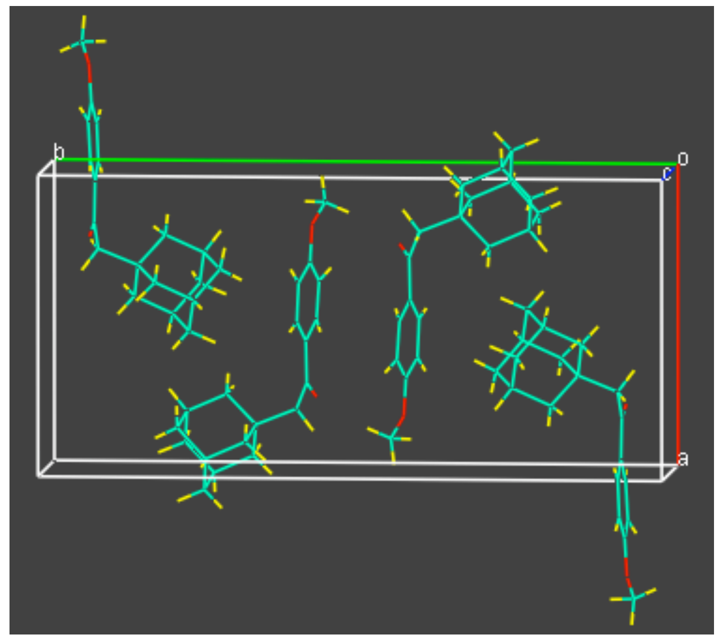

O
C
C
N
O
H
H

Adamantyl acetophenone derivatives





% ee = 0



P2$_1$/n

centrosymmetric

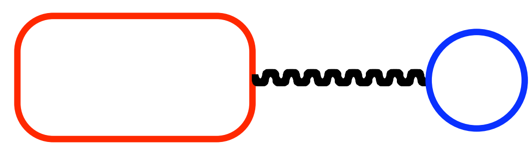
Most commonly occurring space groups

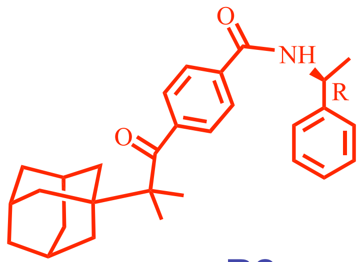
230 unique space groups of which only 65 are chiral space groups
Chiral space groups (symmetry elements are rotational, translational and combinations of these)
achiral space groups (symmetry elements are mirror, glide plane or center of inversion)

Space group	Total no. of crystals	%
$P2_1/c$	10450	36.0
$P\bar{1}$	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

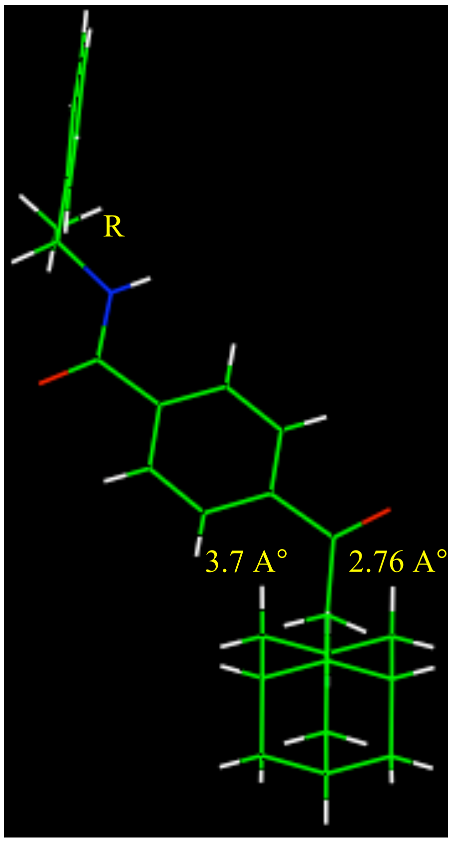
Chiral space group

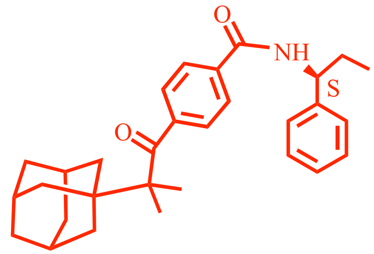
Covalent Chiral Auxillary Approach



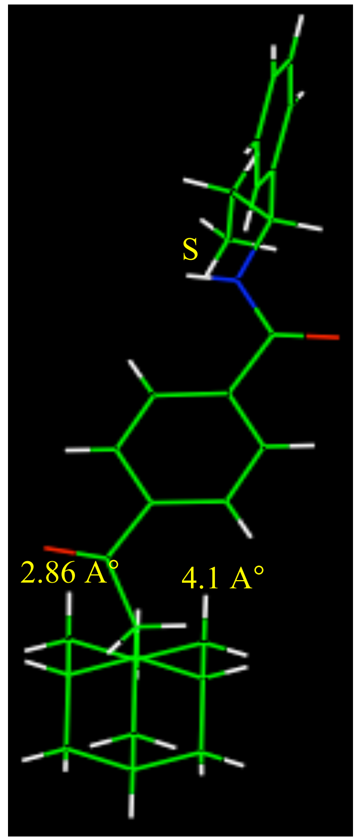


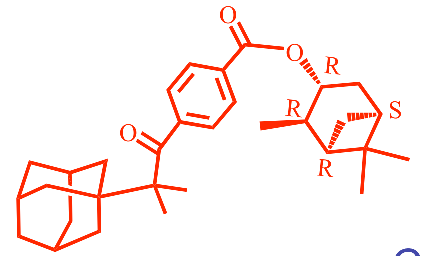
$P2_1$



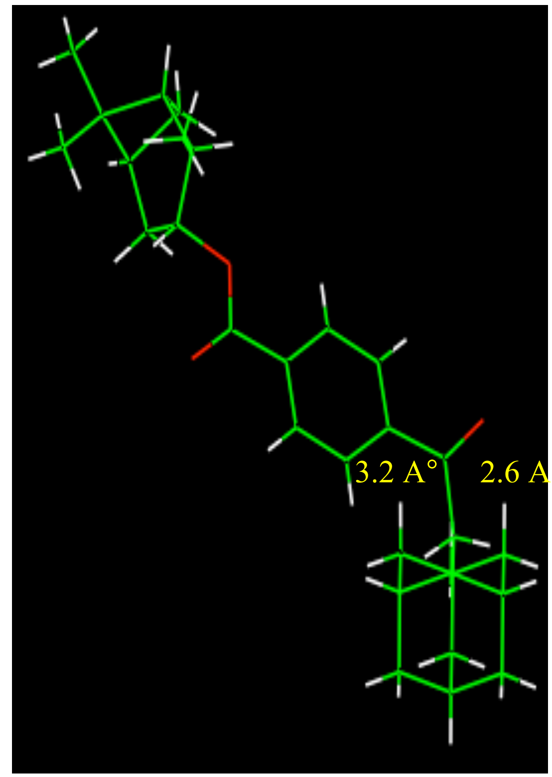


$P2_1$



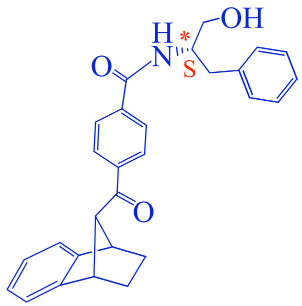


C2



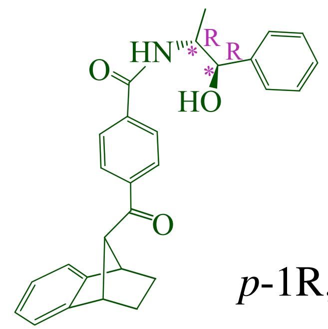
	Trans CB	Trans CB	Trans CB
% de	97	90	92

Conformational isomerism



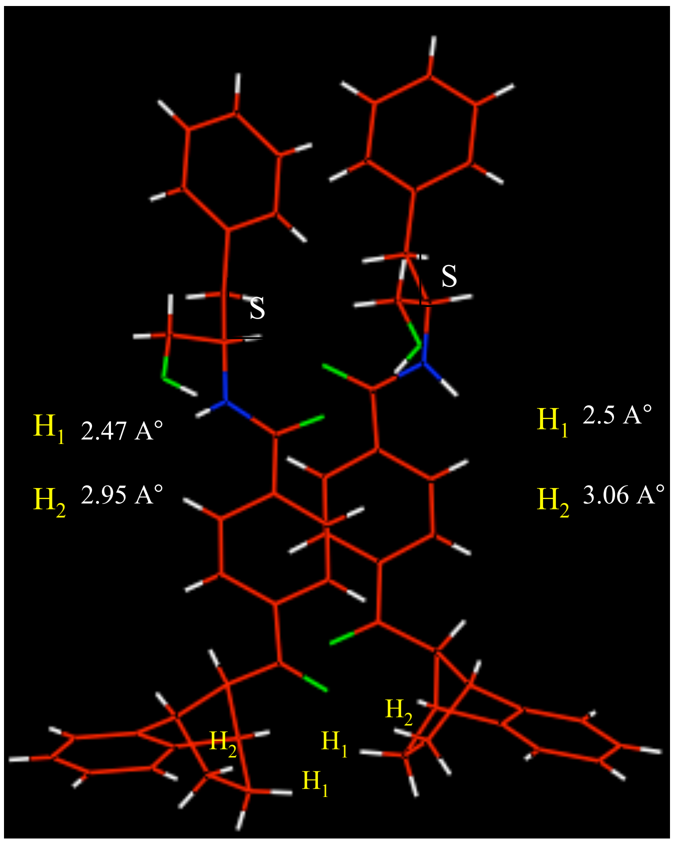
C2

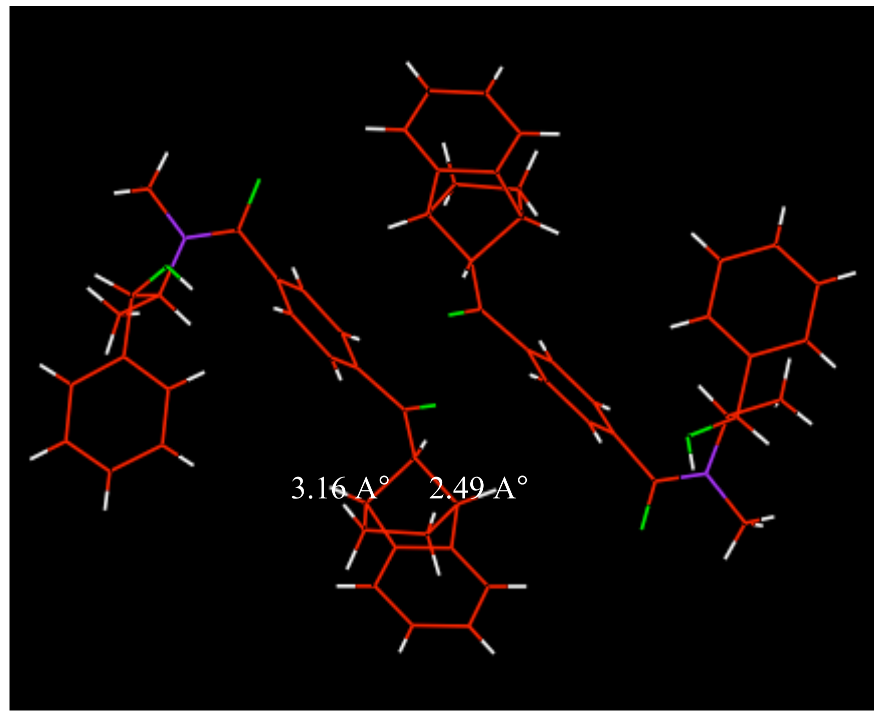
p-L-pheylalaninol



$P2_1$

p-1R,2R-pseudoephedrine





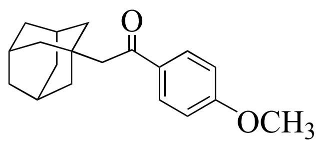
%de **1** **3**

"Crystallization with equal amounts of two independent and mirror image related conformers"

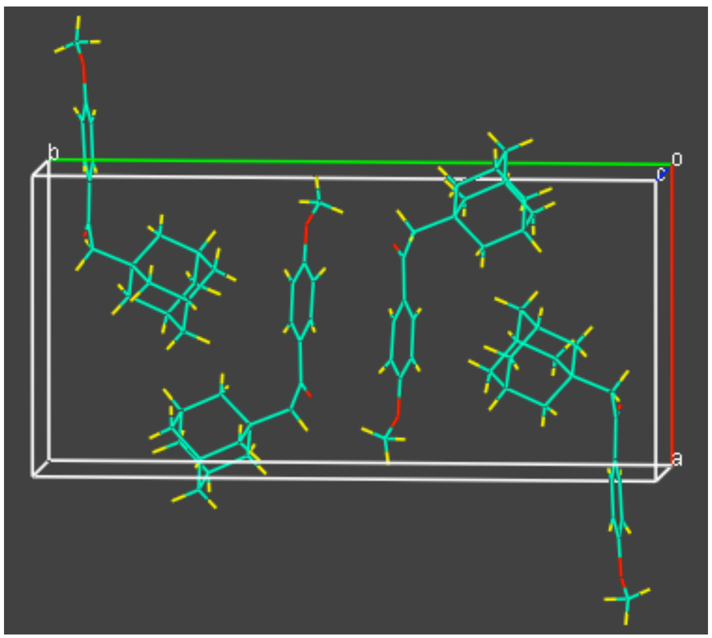
Essential Criteria for Asymmetric Photochemistry in the Crystalline State

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)

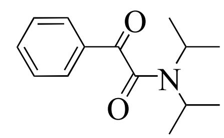


% ee: 0

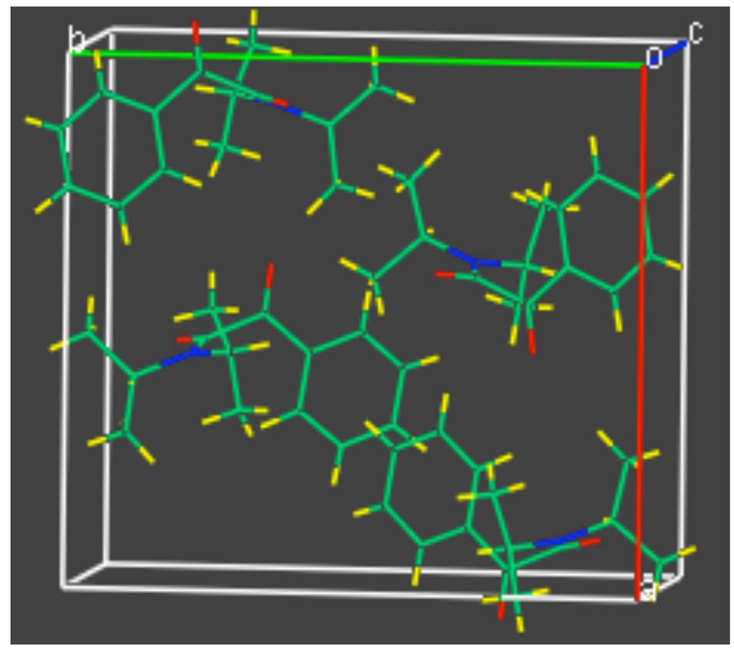


$P2_1/n$

centrosymmetric



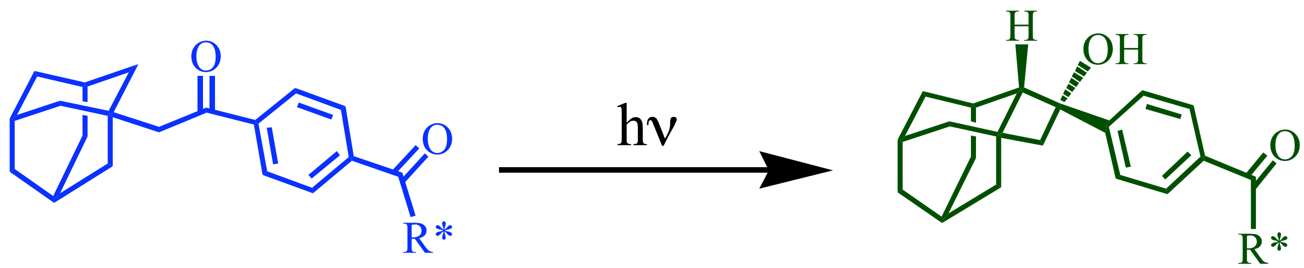
% ee: 100



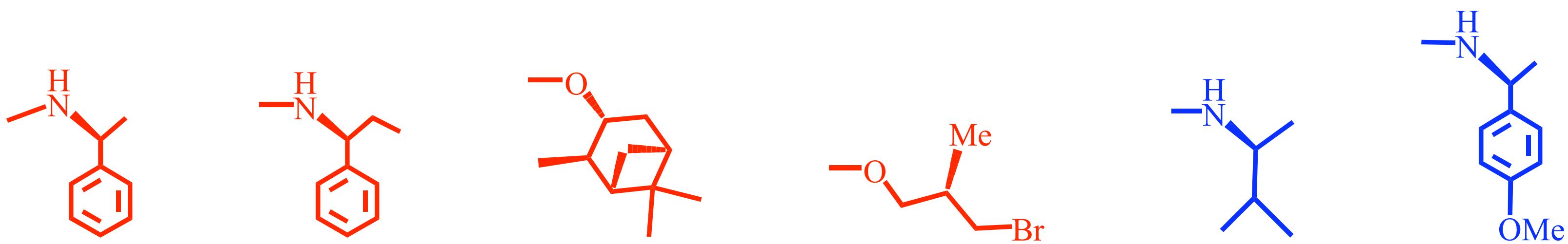
$P2_12_12_1$

non-centrosymmetric

Diastereoselective Photoreactions in the Crystalline State

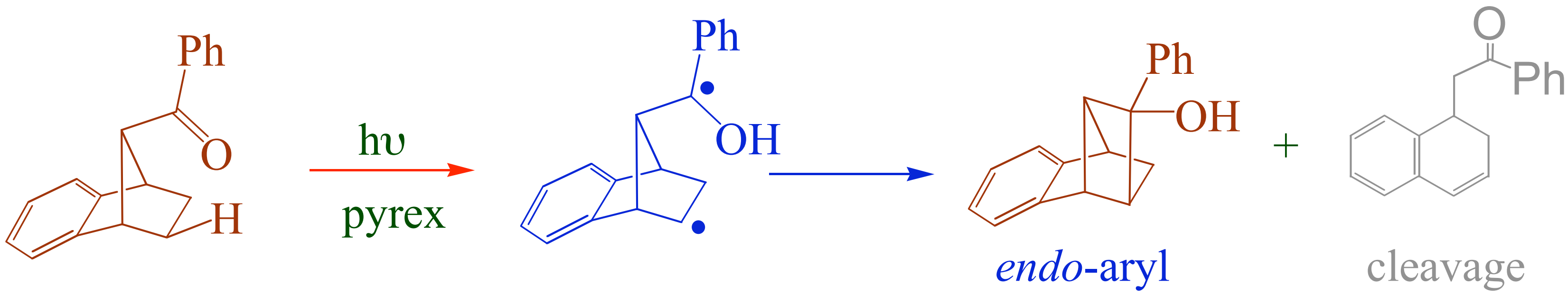


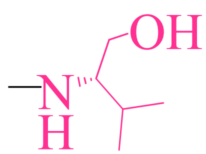
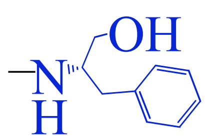
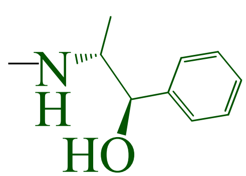
R*



% de	97	90	92	80	22	5

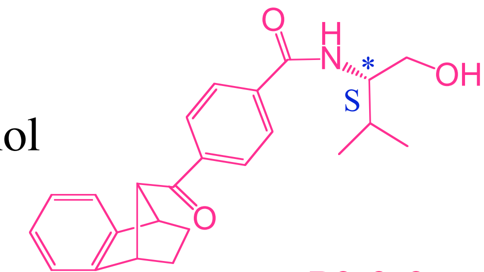
Generality and limitation of covalent chiral auxiliary strategy



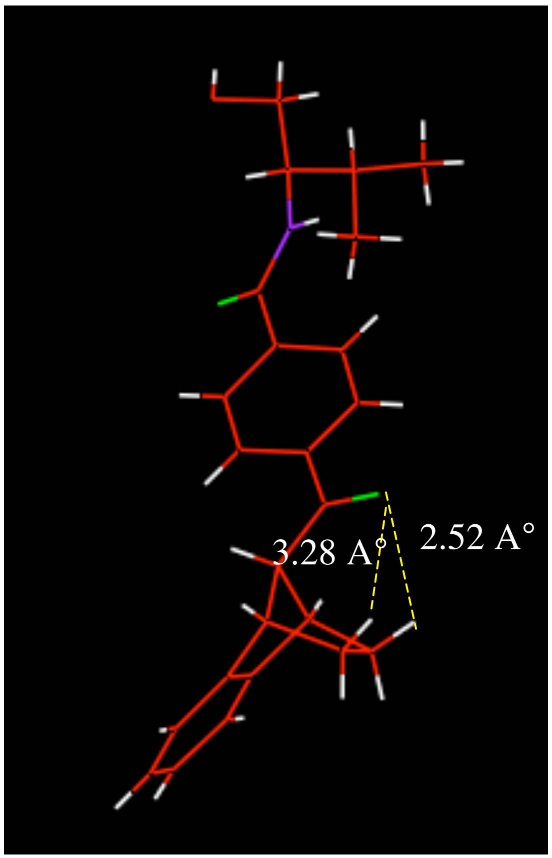
R*	% Conversion	%de (*endo*)
	25 100	100 65
	27 95	91 73
	5	1
	20	3

Crystal irradiation of Benzonorbornadiene derivatives

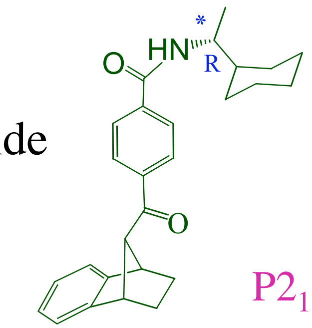
p-L-valinol



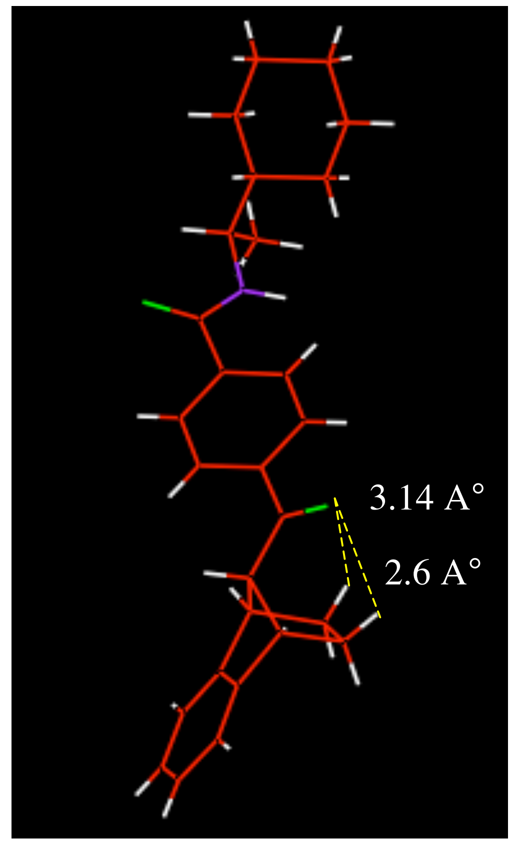
$P2_12_12_1$



p-R-cyclohexylethylamide

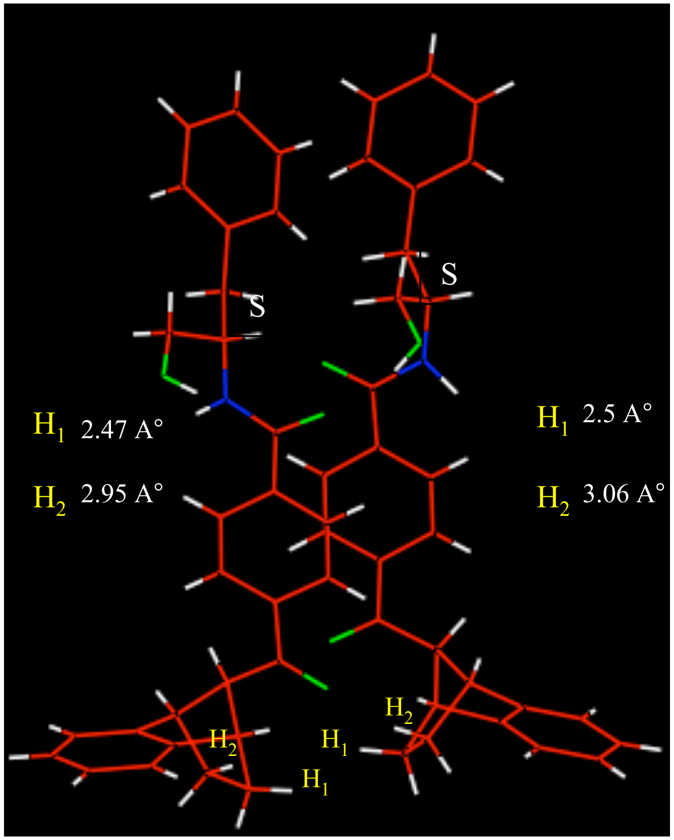


$P2_12_12_1$

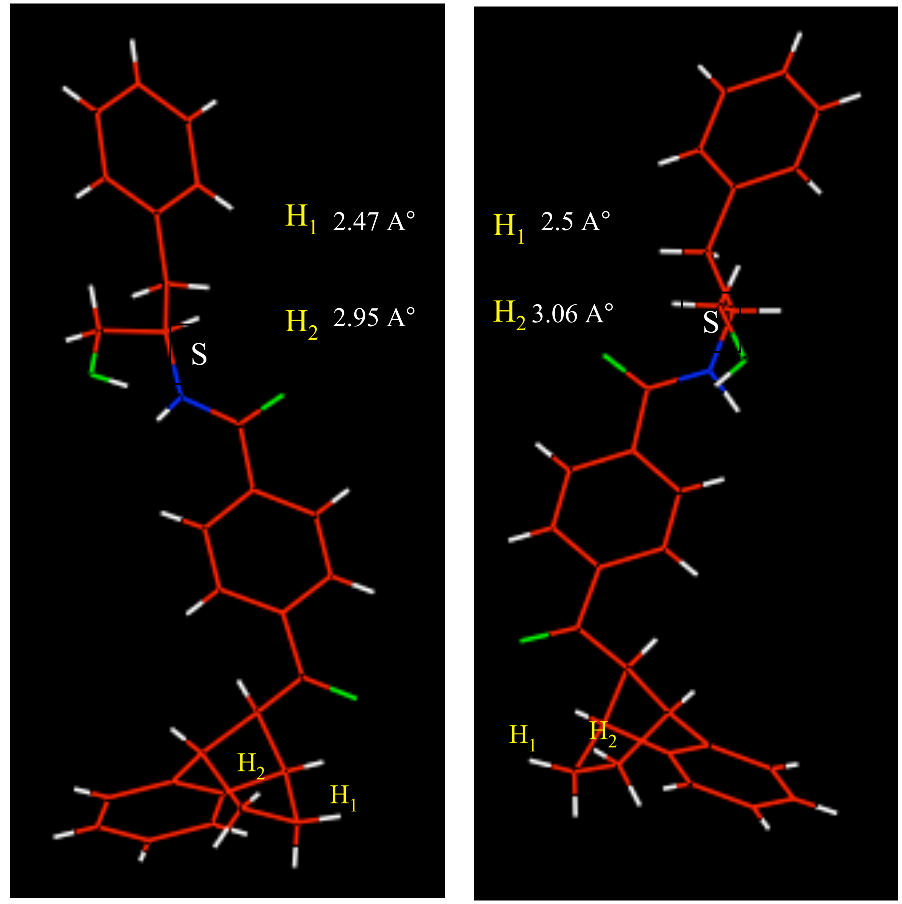


%de	100	91

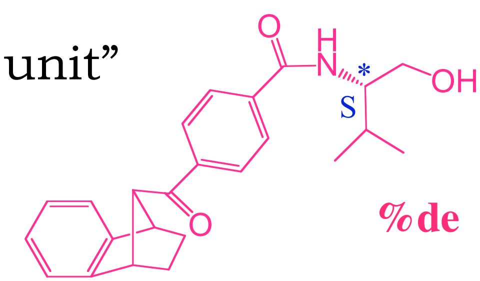
Mirror image related conformers



“In the asymmetric unit”

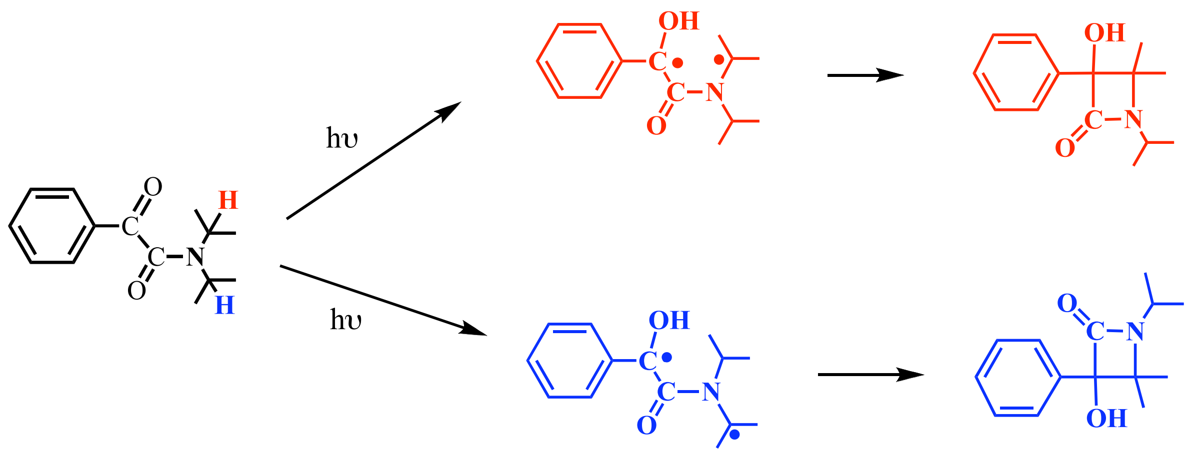


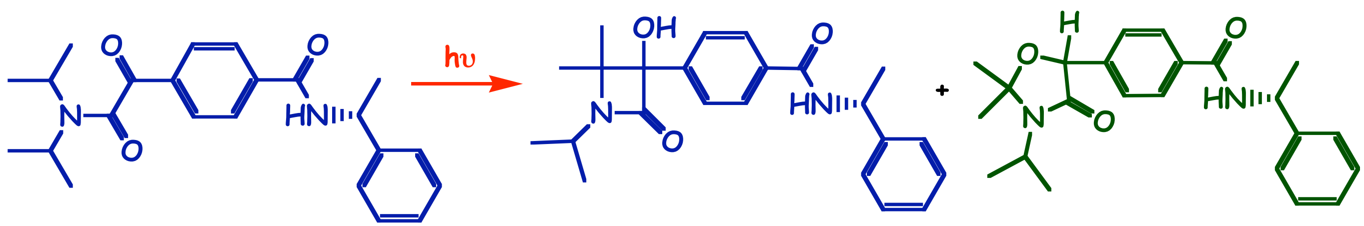
“Independent view”



%de 1

Photochemistry of α-Oxoamides

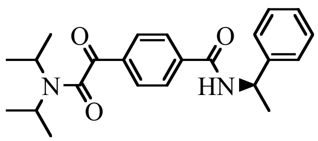
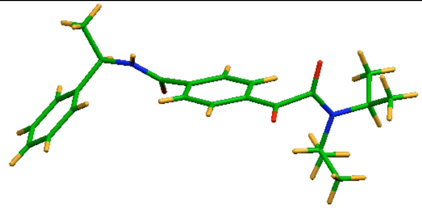
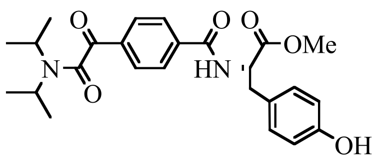
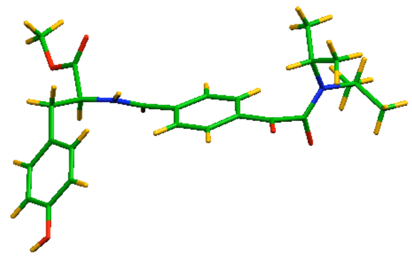
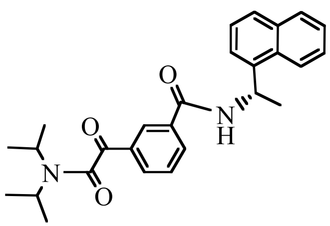
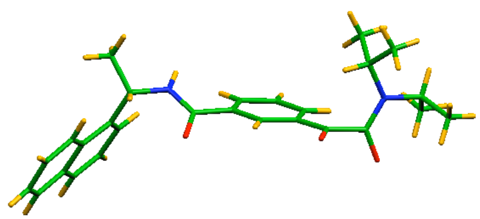
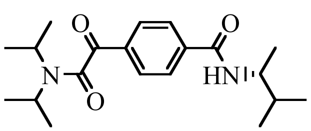
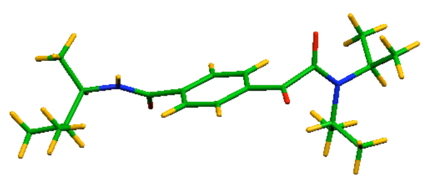
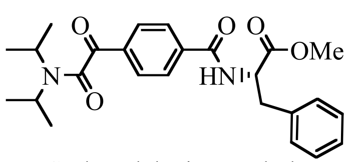
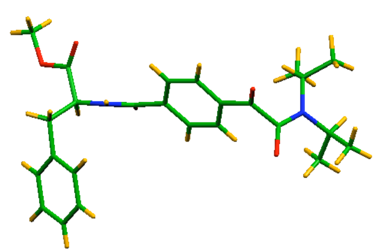


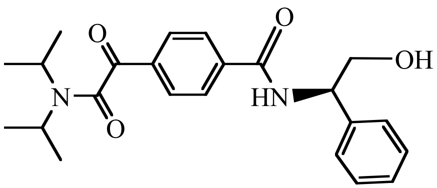
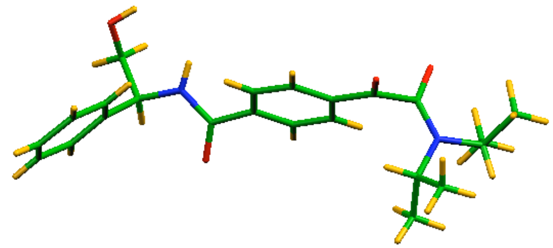
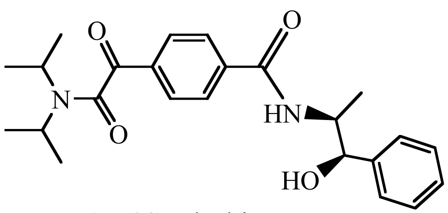
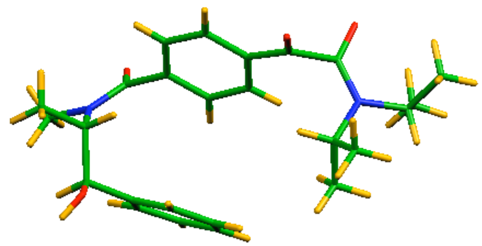
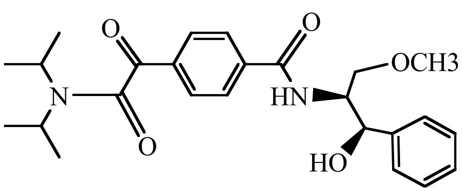
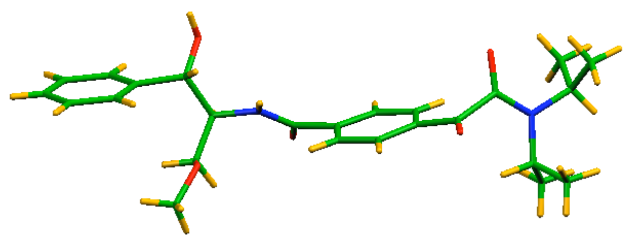
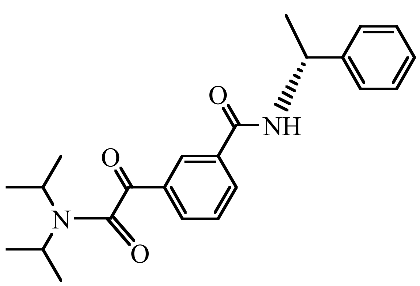
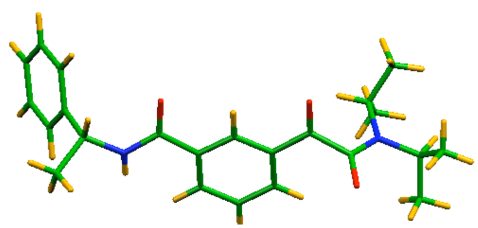


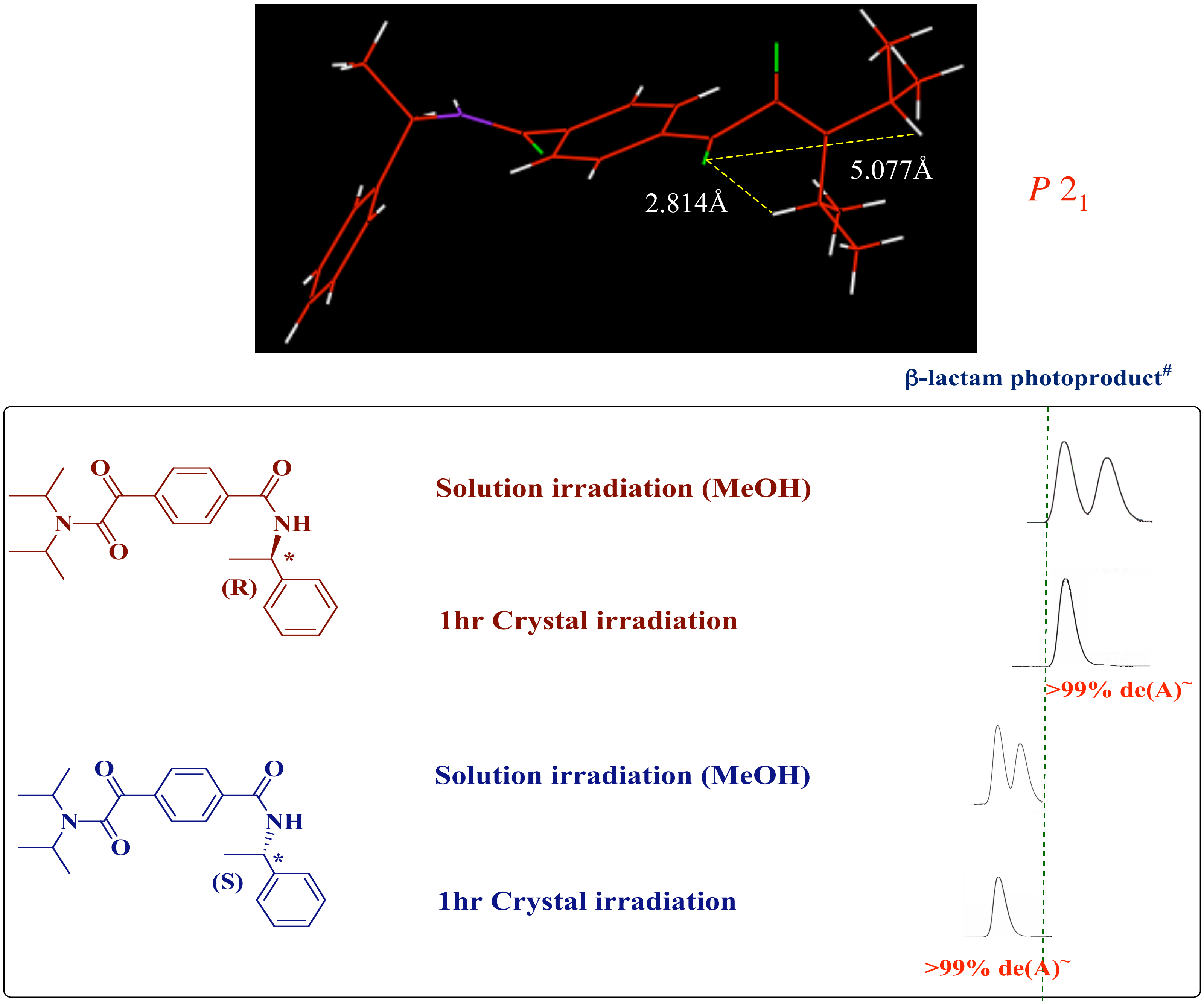
1 2 3

Medium	1	2	3
Solution (CH_3CN)	19	35	46
Crystal	0	100	0

Diastereoselectivity obtained with various chiral auxiliaries in solid state

		Crystal structures	C=O....γ-H_1	C=O....γ-H_2	%de of β-lactam
a)	 *p*-R-phenylethylamide		2.814 A^o	5.077 A^o	>99(A)
b)	 p-S-tyrosine methylesteramide		2.562 A^o	5.091 A^o	>99(B)
c)	 m-S-napthylethylamide		2.737 A^o	5.214 A^o	>99(B)
d)	 *p*-R-secondarybutylmide		2.781 A^o	5.052 A^o	96(B)
e)	 *p*-S-phenylalanine methyl esteramide		2.618A^o	5.130 A^o	82(A)

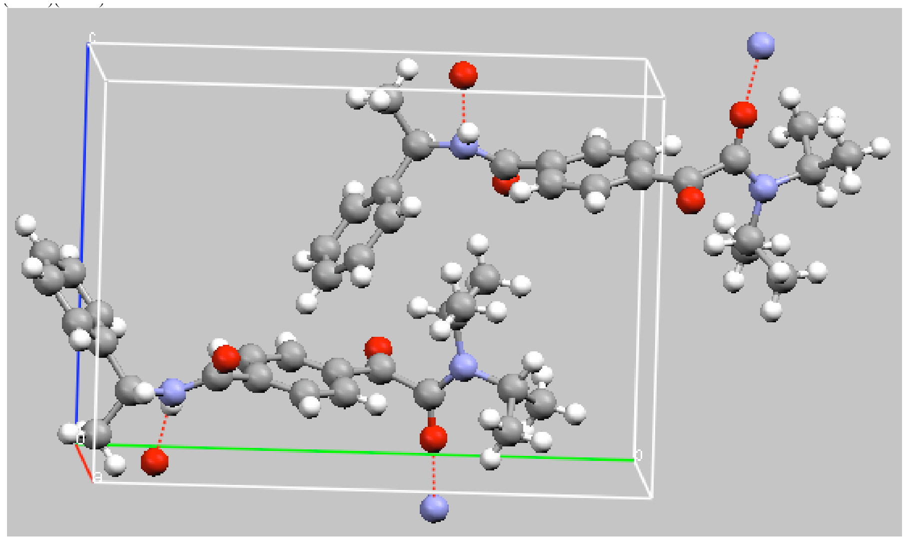
		Crystal structures	C=O....γ-H_1	C=O....γ-H_2	%de of β-lactam
f)	 p-R-phenylglycinol		2.776 A^{o}	5.025 A^{o}	93(B)
g)	 p-1R, 2S-ephedrine		2.804 A^{o}	5.030 A^{o}	87(B)
h)	 p-S-amidomethylphenylpropanol		2.662 A^{o}	5.034 A^{o}	85(B)
i)	 m-R-phenylethylamide		2.713 A^{o}	4.850 A^{o}	80(A)

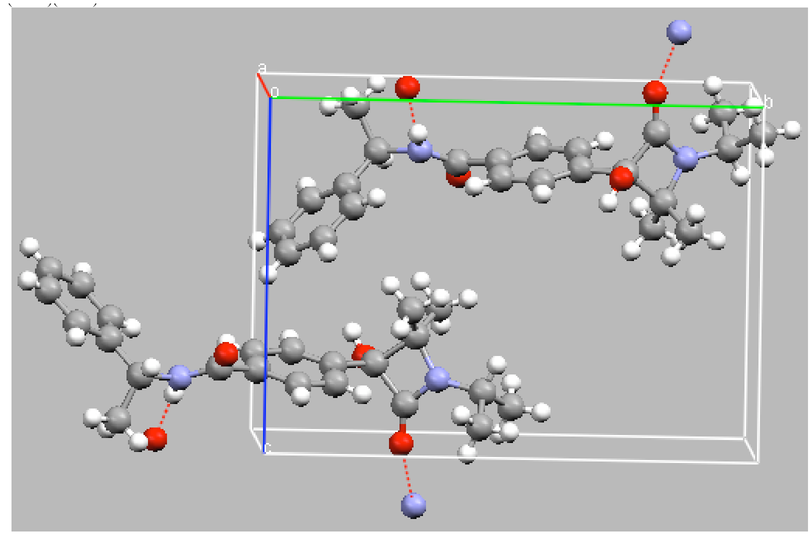


Photoproducts analyzed on HPLC chiralcel-OD

~ A: First peak on HPLC

Single crystal-to-Single Crystal Phototransformation





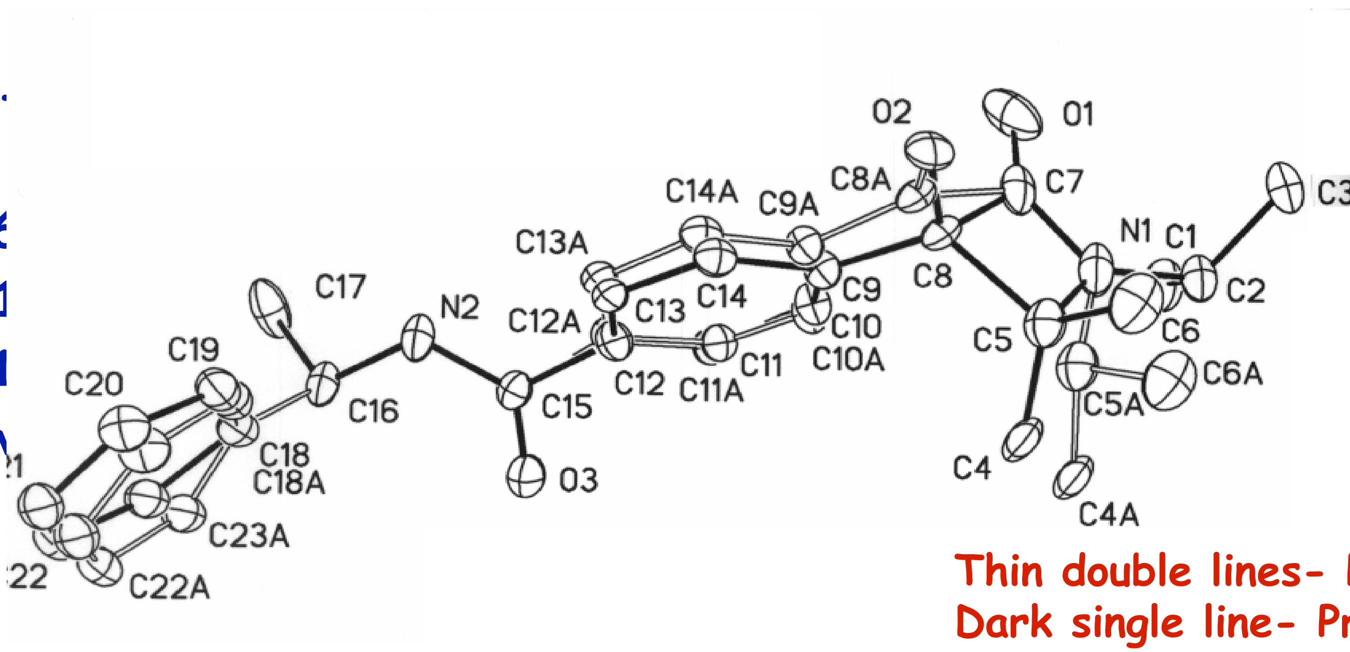
Reac … crystal; $P2_1$)

a = 6 …

b = 1 …

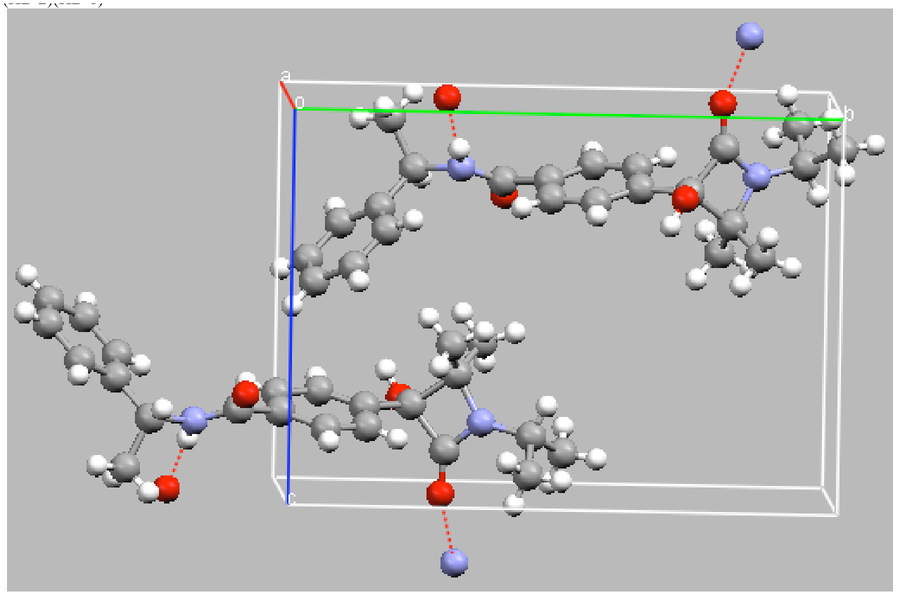
c = 1 …

Cell v … Å^3



Thin double lines- Precursor

Dark single line- Product



Photoproduct as Formed ($P2_1$)

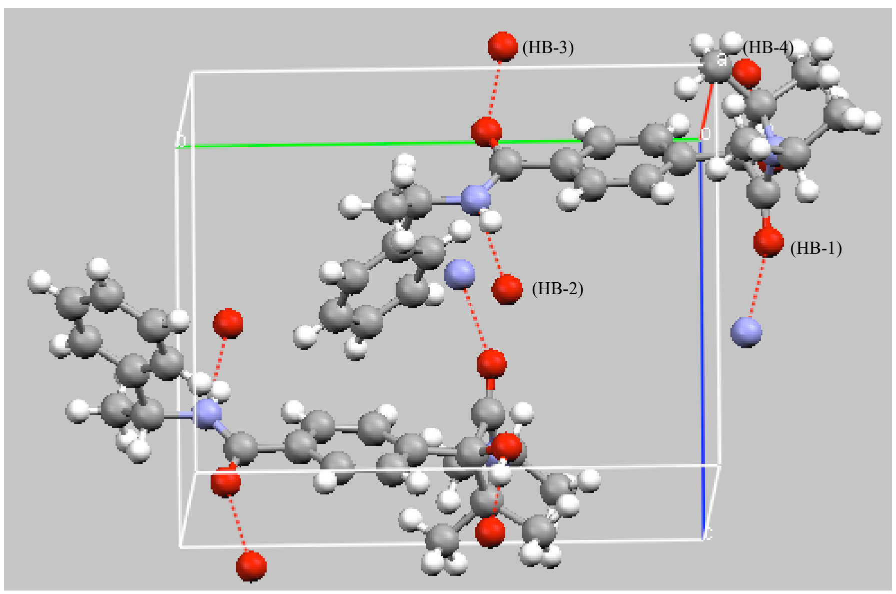
a = 6.4821 Å

b = 14.967 Å

c = 10.7528 Å

β = 98.52°

Cell volume 1031.71 Å³



Photoproduct Recrystallized ($P2_1$)

a = 8.5684 Å

b = 12.8865Å

c = 9.8260 Å

β = 107.98°

Cell volume 1031.99(30) Å³

A crystal is a chemical cemetery

Reactions in the solid state take place with minimum atomic movements.

The next decade will surely see ----- large-amplitude molecular motions in the solid state

Acknowledgements

National Science Foundation
WHERE DISCOVERIES BEGIN