Absolute Asymmetric Synthesis [AAS] by Photochemistry on Solid-State

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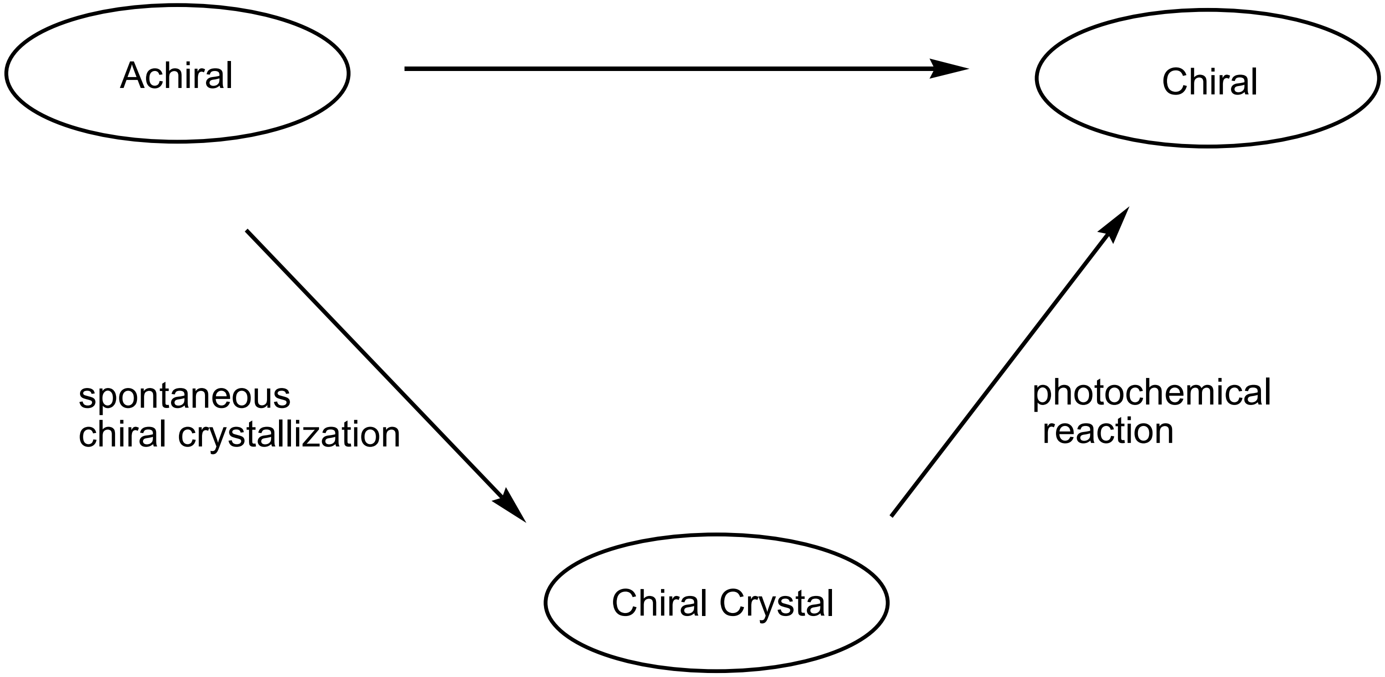
Supergroup Meeting
Sept. 28, 2005

What is an absolute asymmetric synthesis?

Absolute asymmetric synthesis: An asymmetric synthesis starting from
an achiral reagent and
in the absence of any external chiral agent



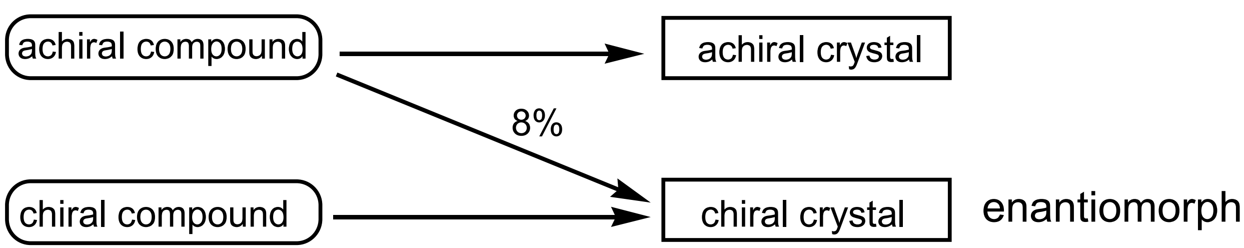
Chiral Crystal

A crystal lacking both a center of symmetry and a glide plane is defined as chiral. Such a chiral crystal must belong to a chiral space group.

Space group: 230 Chiral Space Group: 65

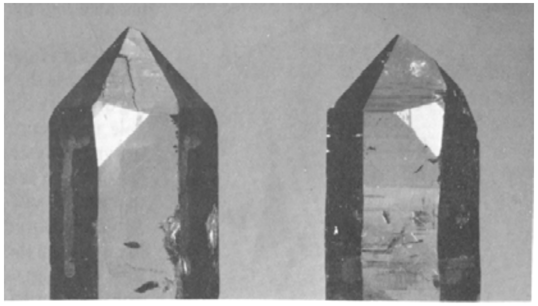
Table: The 10 most common space groups:

Order	Space group	%	Order	Space group	%
1	$P2_1/c$	36.0	6	*Pbca*	4.3
2	$P\bar{1}$	13.7	7	*Pnma*	1.9
3	$P2_12_12_1$	11.6	8	$Pna2_1$	1.8
4	$P2_1$	6.7	9	*Pbcn*	1.2
5	$C2/c$	6.6	10	$P1$	1.1



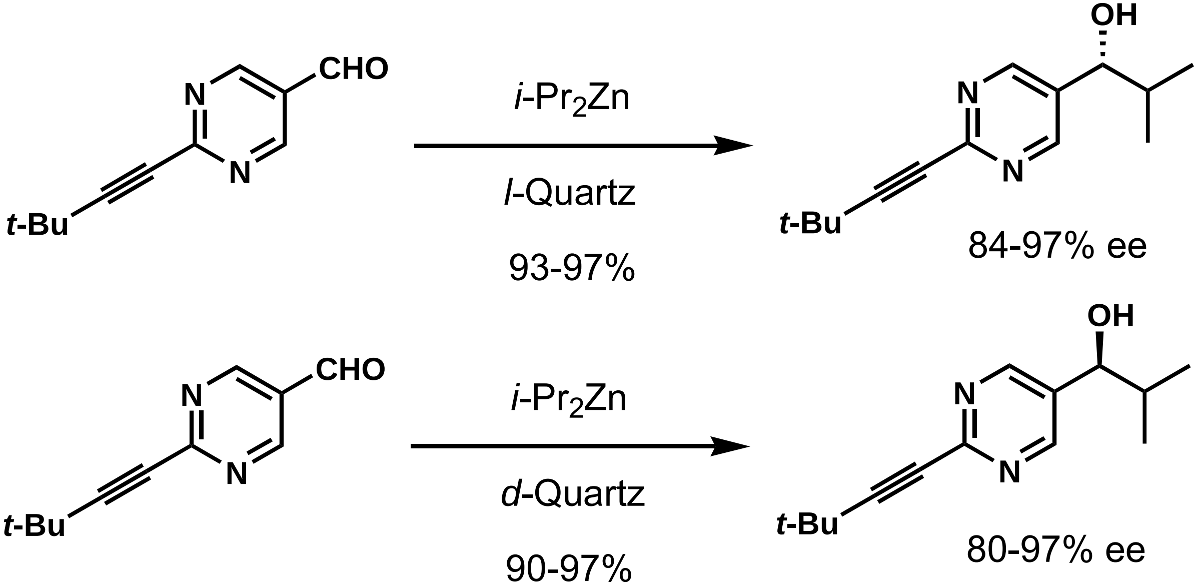
Sakamoto, M. In *Molecular and Suparamolecular Photochemistry: vol 11, Chiral Photochemistry*; Inoue, Y.; Ramamurthy, V. Eds; Marcel Dekker: New York; 2004, p415-461

Asymmetric Induction by Chiral Quartz



l- and *d*-quartz

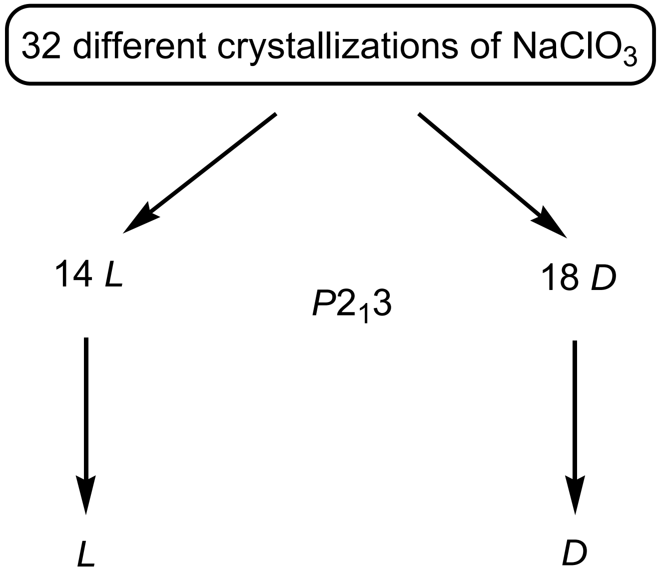
Flack, H. D. www.flack.ch/howard/cristallo/publcns.html



Soai, K.; Osanai, S.; Kadowaki, K.; Yonekubo, S.; Shibata, T.; Sato, I. *J. Am. Chem. Soc.* **1999**, *121*, 11235.

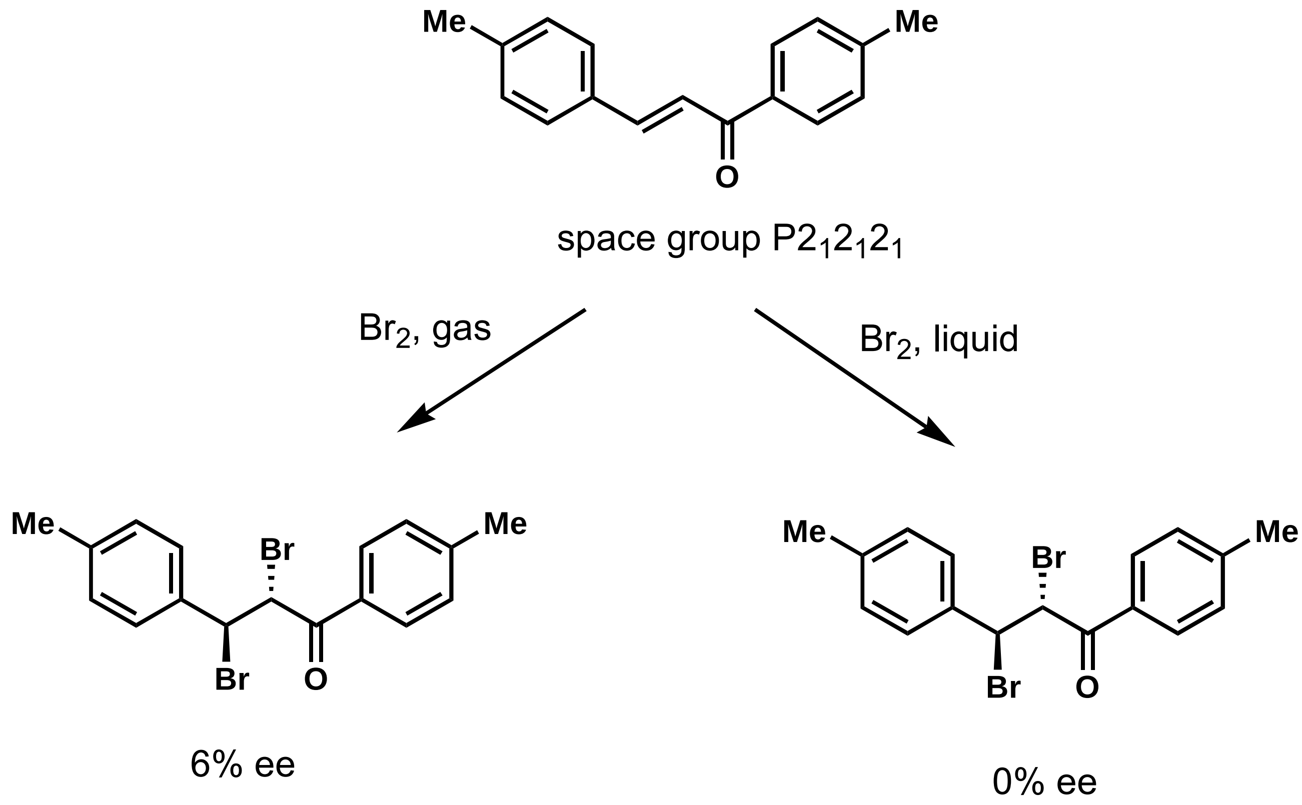
Forming Desired Chiral Crystal

Spontaneous Chiral Crystallization: Equal chance to form *D* or *L* Crystal



Kondepudi, D. K.; Kaufman, R. J.; Singh, N. *Science* **1990**, *250*, 975.

The First Absolute Asymmetric Synthesis Using Crystals

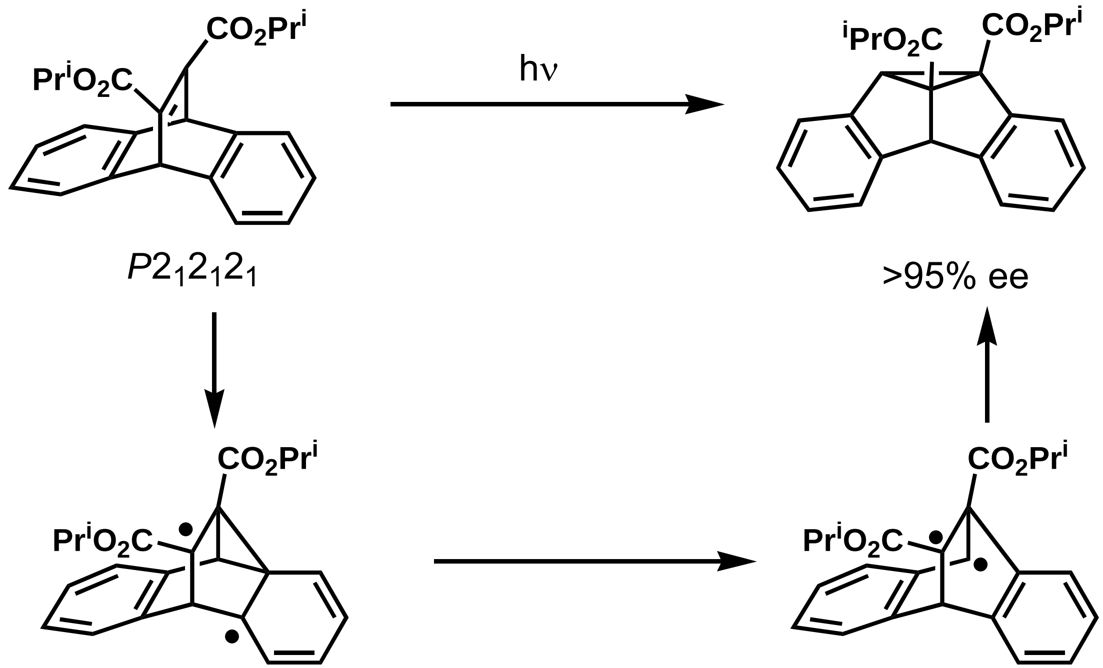


Penzien, K.; Schmidt, G. M. J. *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 608

Absolute Asymmetric Photochemistry on Solid-State

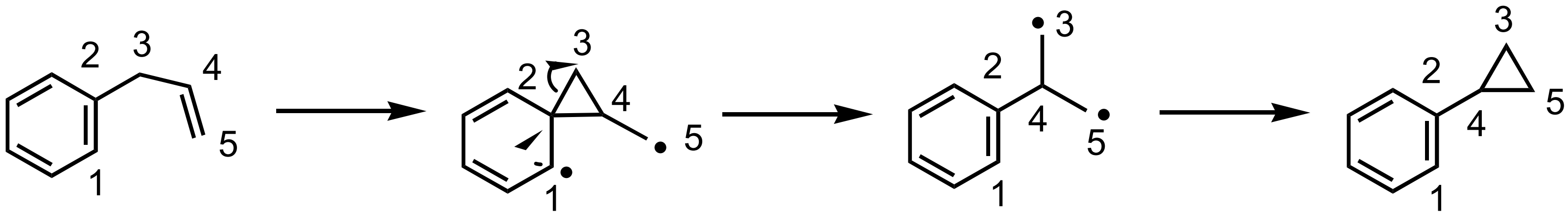
- Unimolecular
  - Di-π-Methane Photorearrangement
  - Electrocyclization
  - [2+2], [4+4]
  - Hydrogen Abstraction Followed by Cyclization
  - Migration and Radical Pair
- Intermolecular
  - Single Component Crystal
  - Cocrystal
- Racemic-to-Chiral

Di-π-Methane Photorearrangement



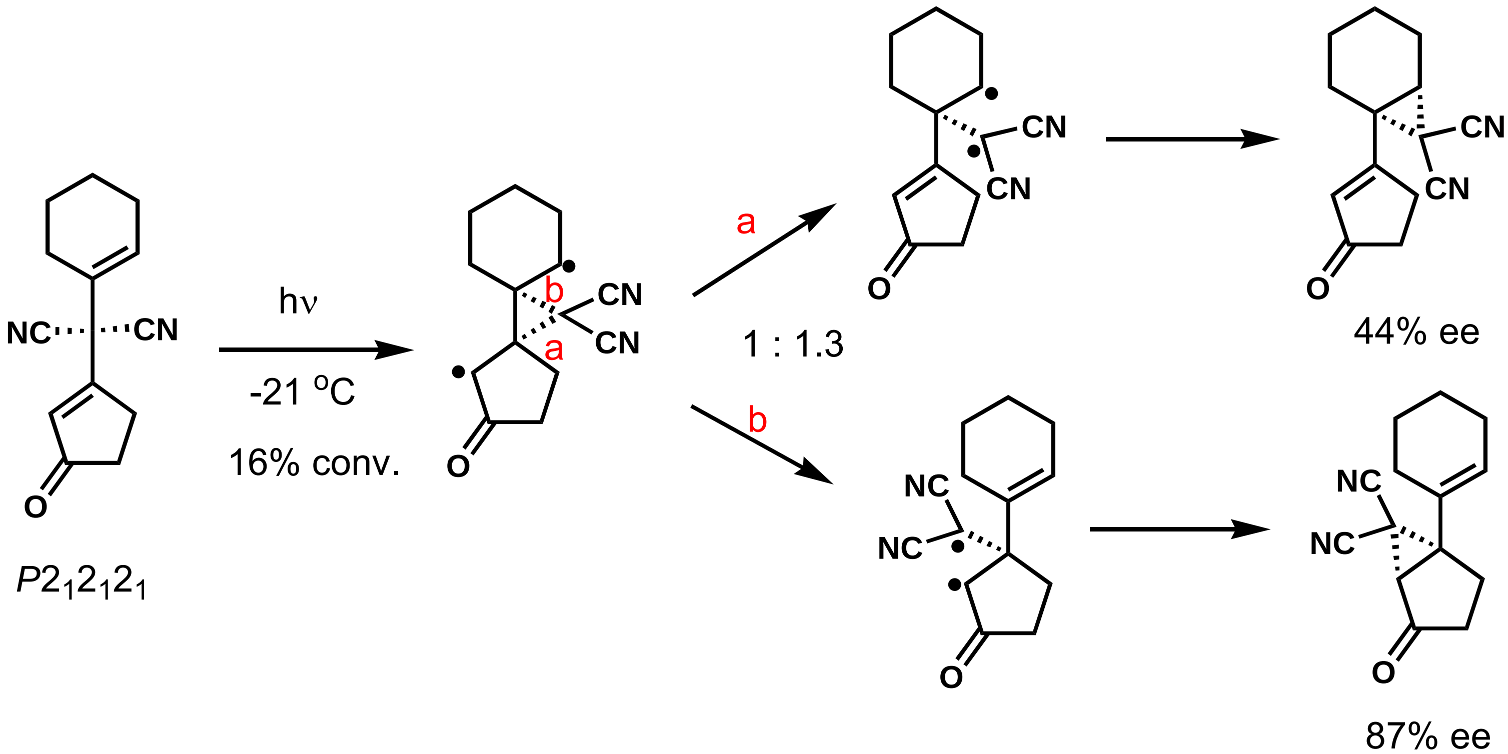
Evans, S. V.; Garcia-Garibay, M.; Omkaram, N,; Scheffer, J. R.; Trotter, J.; Wireko, F. *J. Am. Chem. Soc.* **1986**, *108*, 5648.

Di-π-methane photorearrangement



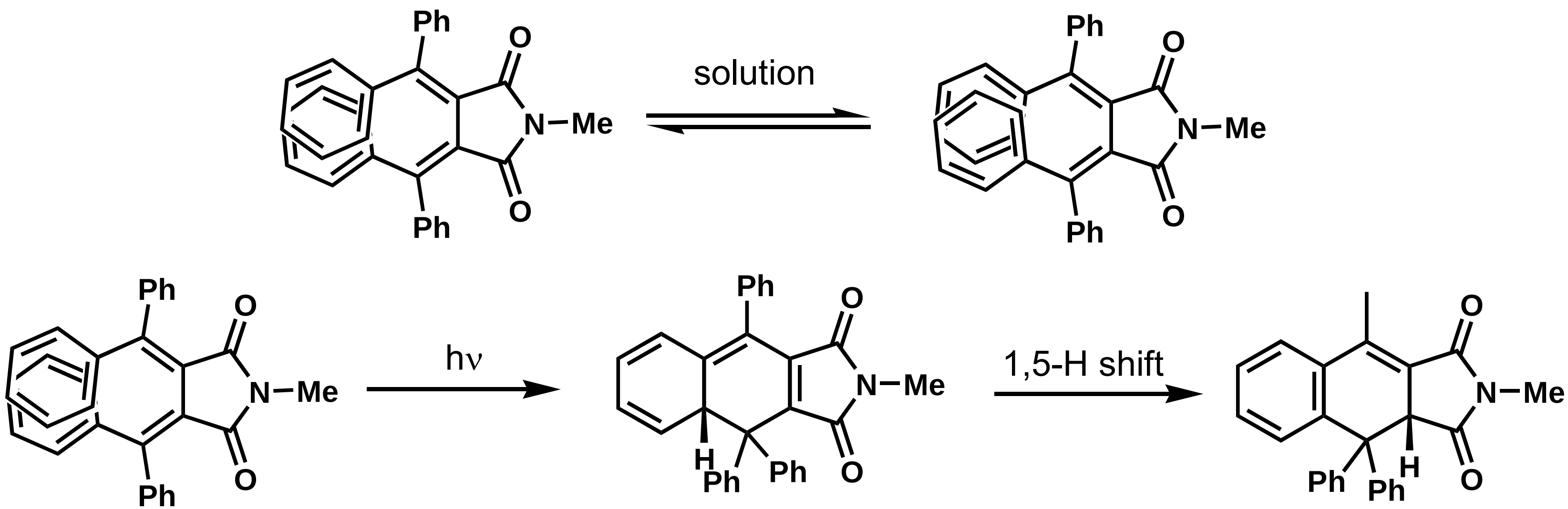
Zimmerman, H. E.; Armesto, D. *Chem. Rev.* **1996**, *96*, 3065.

Di-π-Methane Photorearrangement

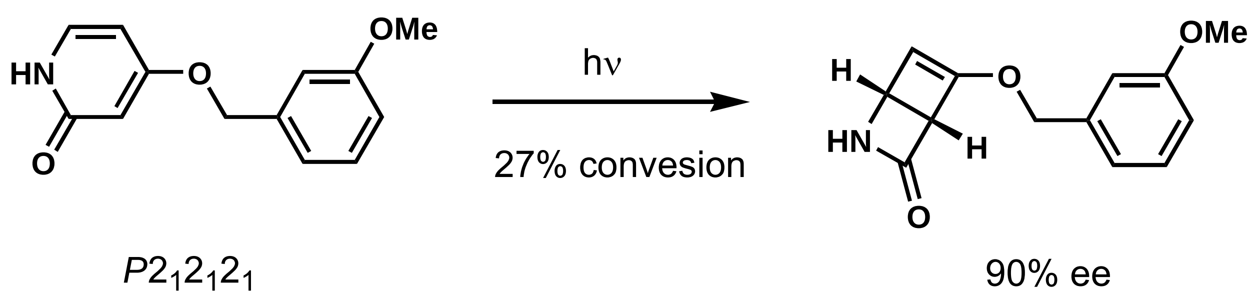


Roughton, A. L.; Muneer, M.; Demuth, M.; Klopp, I.; Kruger, C. *J. Am. Chem. Soc.* **1993**, *115*, 2085.

Photo Electrocyclization

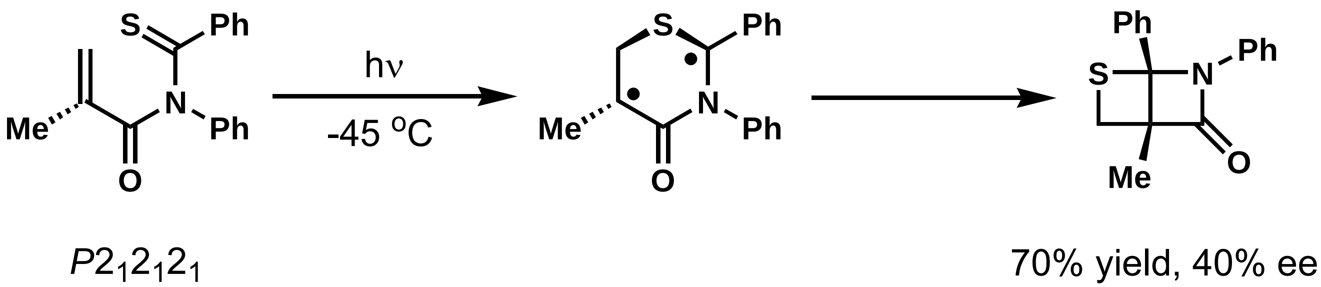


Toda, F.; Tanaka, K. *Superamol. Chem.* **1994**, *3*, 87.

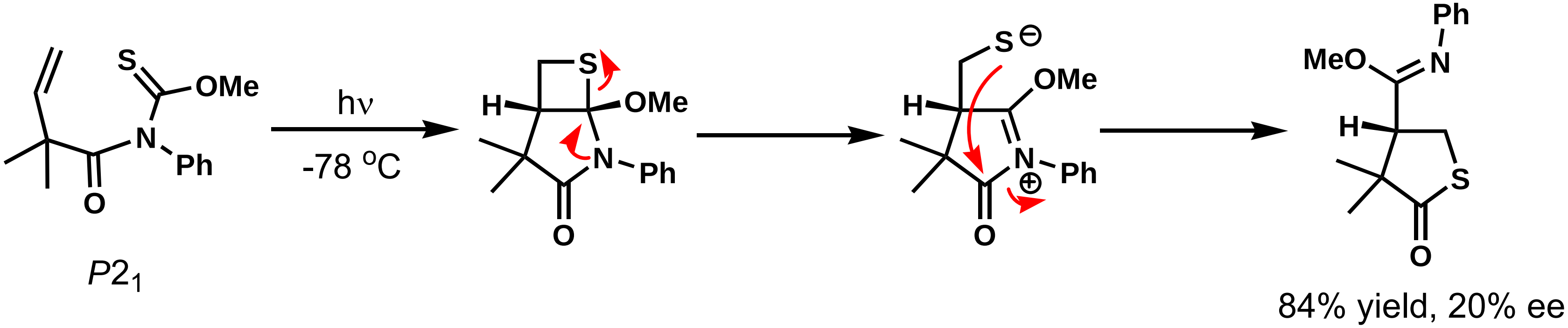


Wu, L.-C.; Cheer, C. J.; Olovsson, G.; Scheffer, J. R.; Trotter, J.; Wang, S.-L.; Liao, F.-L. *Tetrahedron Lett.* **1997**, *38*, 3135.

[2+2] Cycloaddition

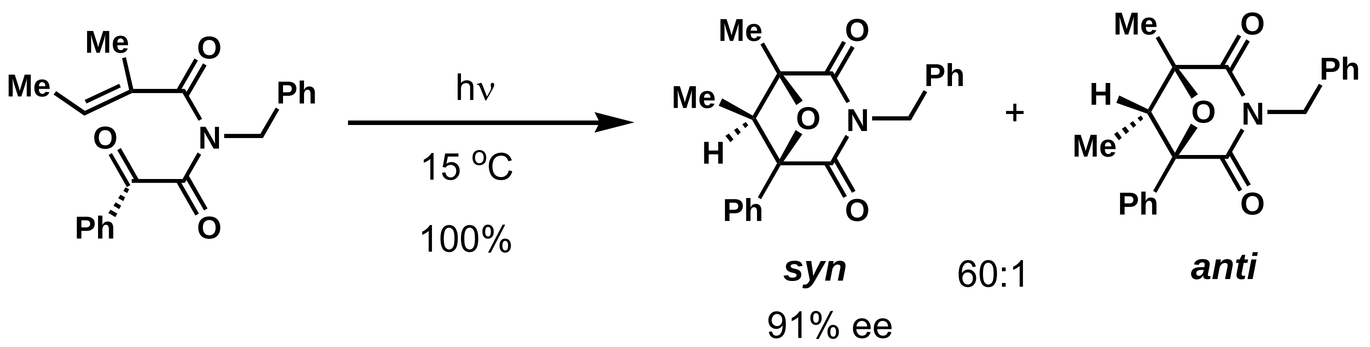


Sakamoto, M.; Hokari, N.; Takahashi, M.; Fujita, T.; Watanabe, S.; Iida, I.; Nishio, T. *J. Am. Chem. Soc.* **1993**, *115*, 818.
Sakamoto, M.; Takahashi, M.; Mino, T.; Fujita, T. *Tetrahedron* **2001**, *57*, 6713.

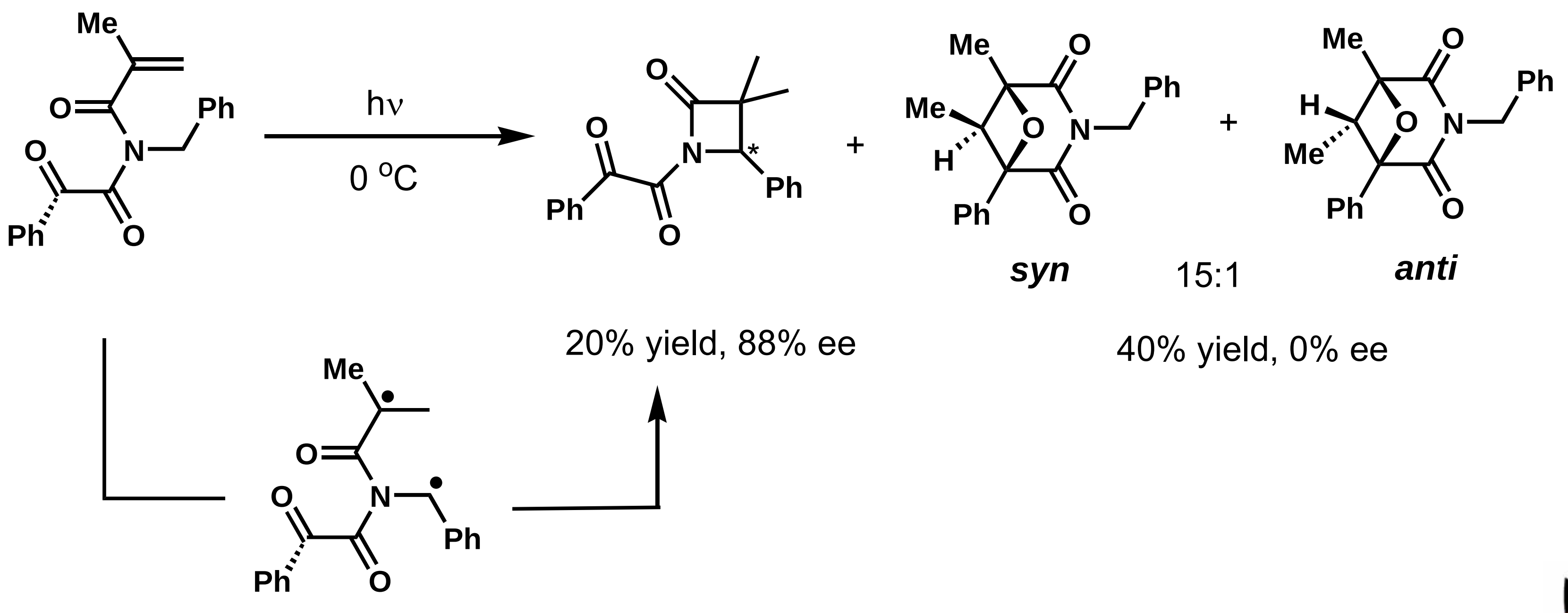


Sakamoto, M.; Takahashi, M.; Arai, T.; Shimizu, M.; Yamaguchi, K.; Mino, T.; Watanabe, S.; Fujita, T. *Chem. Commun.* **1998**, 2315.

[2+2] Cycloaddition

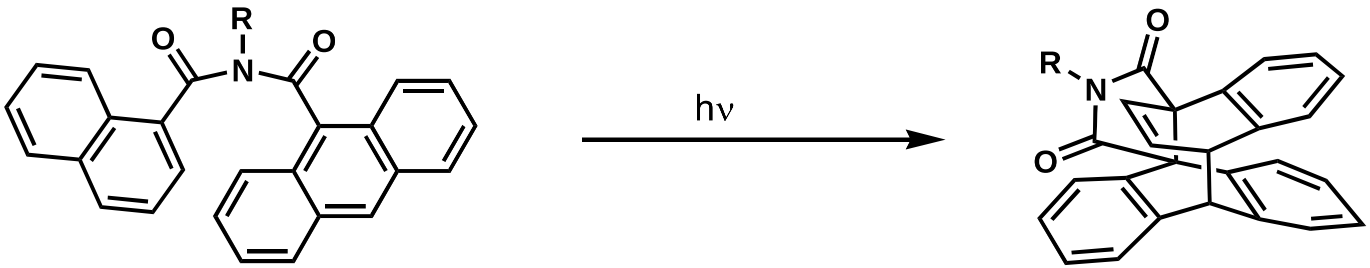


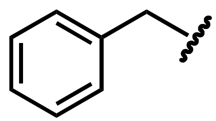
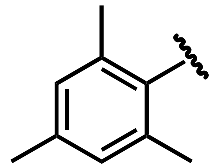
Sakamoto, M.; Takahashi, M.; Arai, T.; Fujita, T.; Watanabe, S.; Iida, I.; Nishio, T.; Aoyama, H. *J. Org. Chem.* **1993**, *58*, 3476.



Sakamoto, M.; Takahashi, M.; Fujita, T.; Watanabe, S.; Nishio, T.; Iida, I.; Aoyama, H. *J. Org. Chem.* **1997**, *62*, 6298.

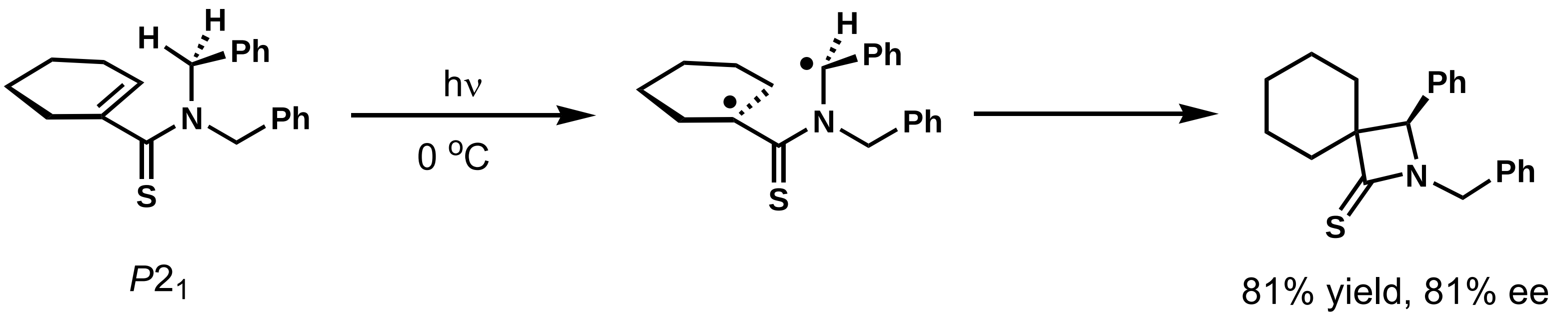
[4+4] Cycloaddition



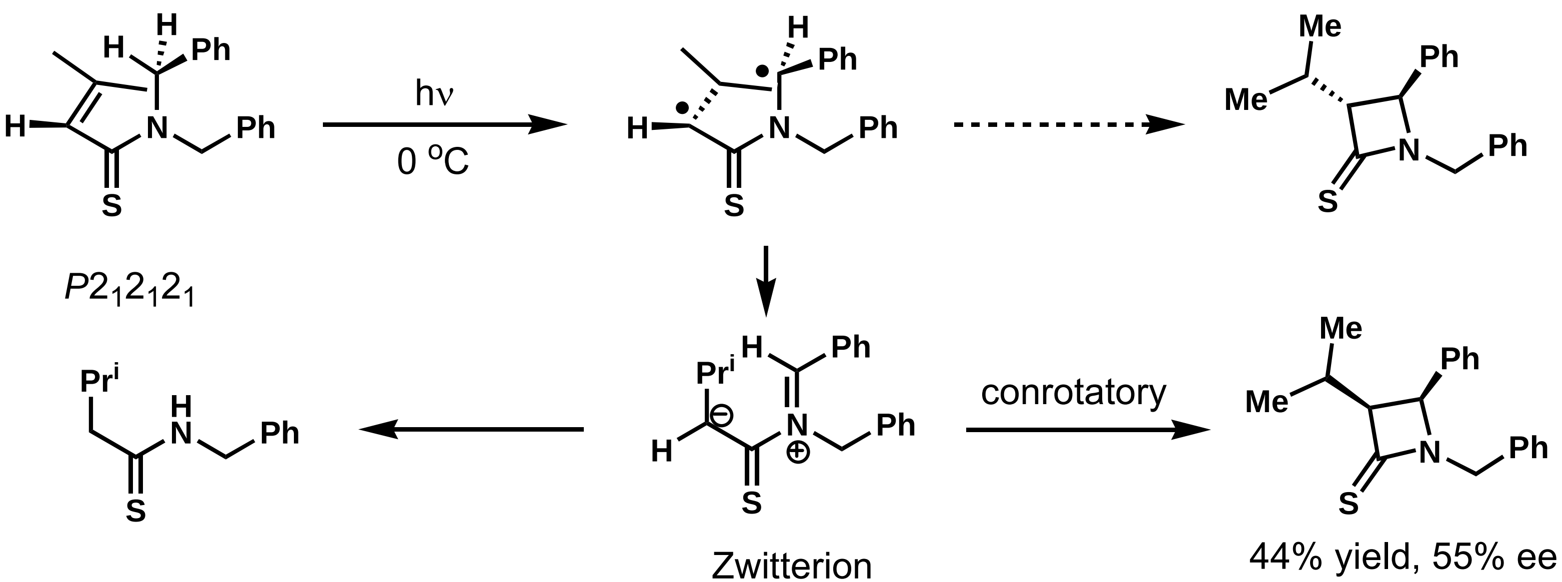
R		Yield, %	ee, %
	$P2_12_12_1$	quantitative	82
	$P2_1$	quantitative	>99

Kohmoto, S.; Ono, Y.; Masu, H.; Yamaguchi, K.; Kishikawa, K.; Yamamoto, M. *Org. Lett.* **2001**, *3*, 4153.

H Abstraction and Cyclization

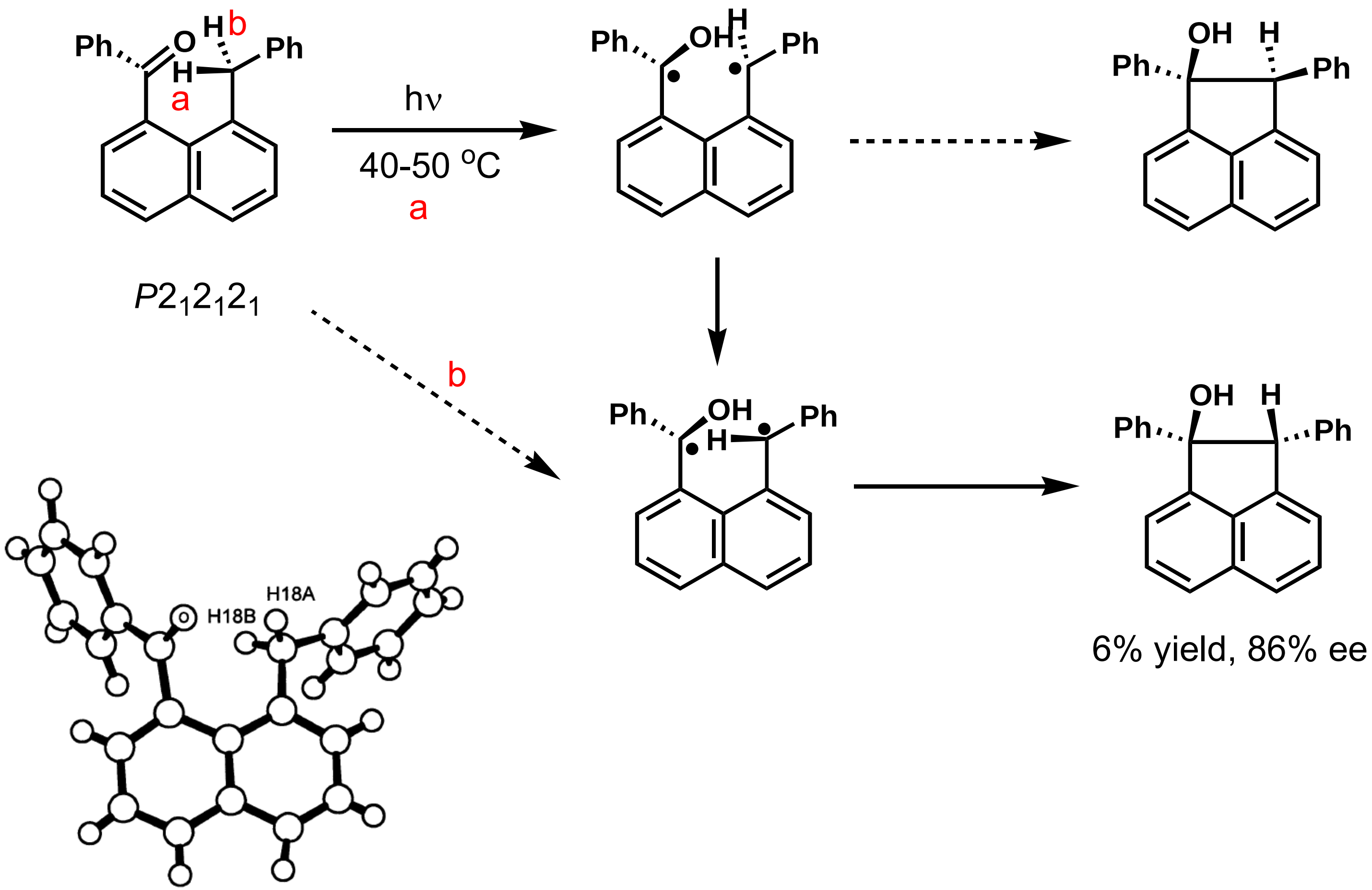


Sakamoto, M.; Takahashi, M.; Kamiya, K.; Yamaguchi, K.; Fujita, T.; Watanabe, S. *J. Am. Chem. Soc.* **1996**, *118*, 10664.



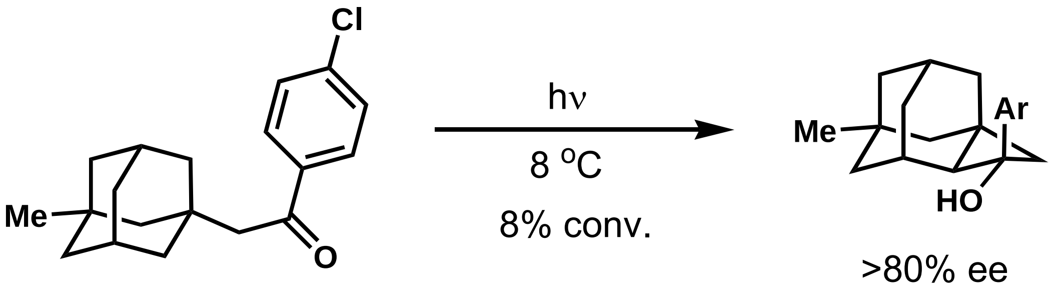
Sakamoto, M.; Takahashi, M.; Arai, W.; Nino, T.; Yamaguchi, K.; Watanabe, S.; Fujita, T. *Tetrahedron* **2000**, *56*, 6795.

H Abstraction and Cyclization



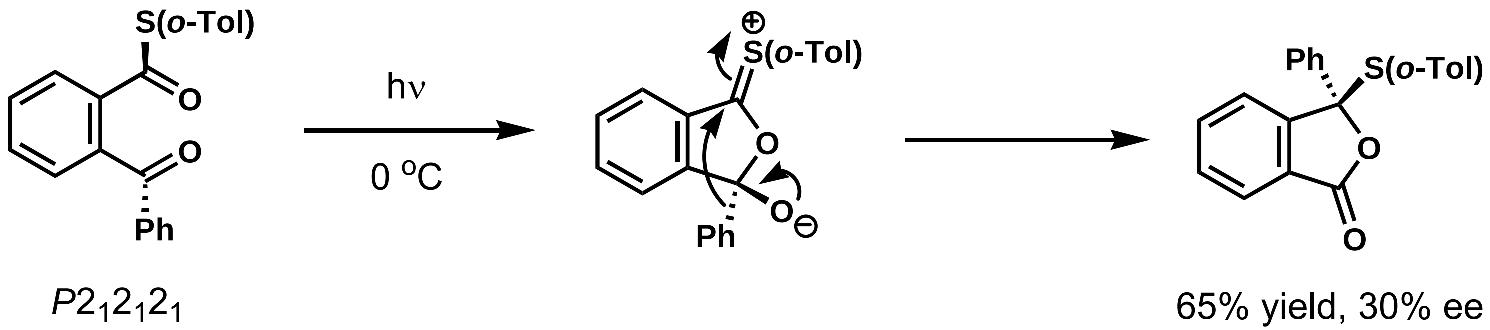
Irngartinger, H.; Fettel, P. W.; Siemund, V. *Eur. J. Org. Chem.* **1998**, 2079.

H Abstraction and Cyclization

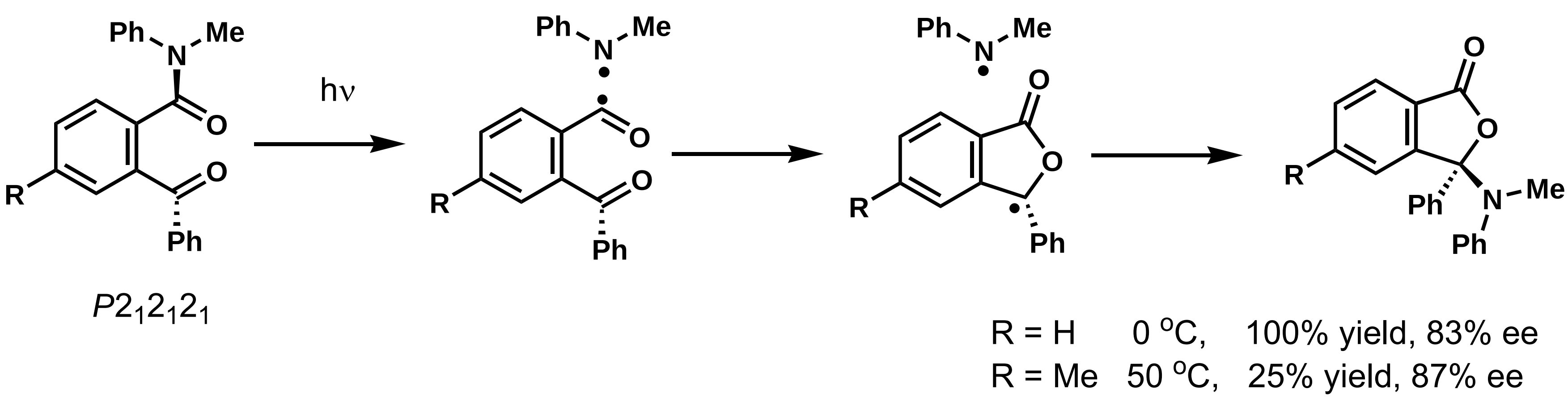


Evans, S. V.; Garcia-Garibay, M.; Omkaram, N,; Scheffer, J. R.; Trotter, J.; Wireko, F. *J. Am. Chem. Soc.* **1986**, *108*, 5648.

Migration of Radical Pair

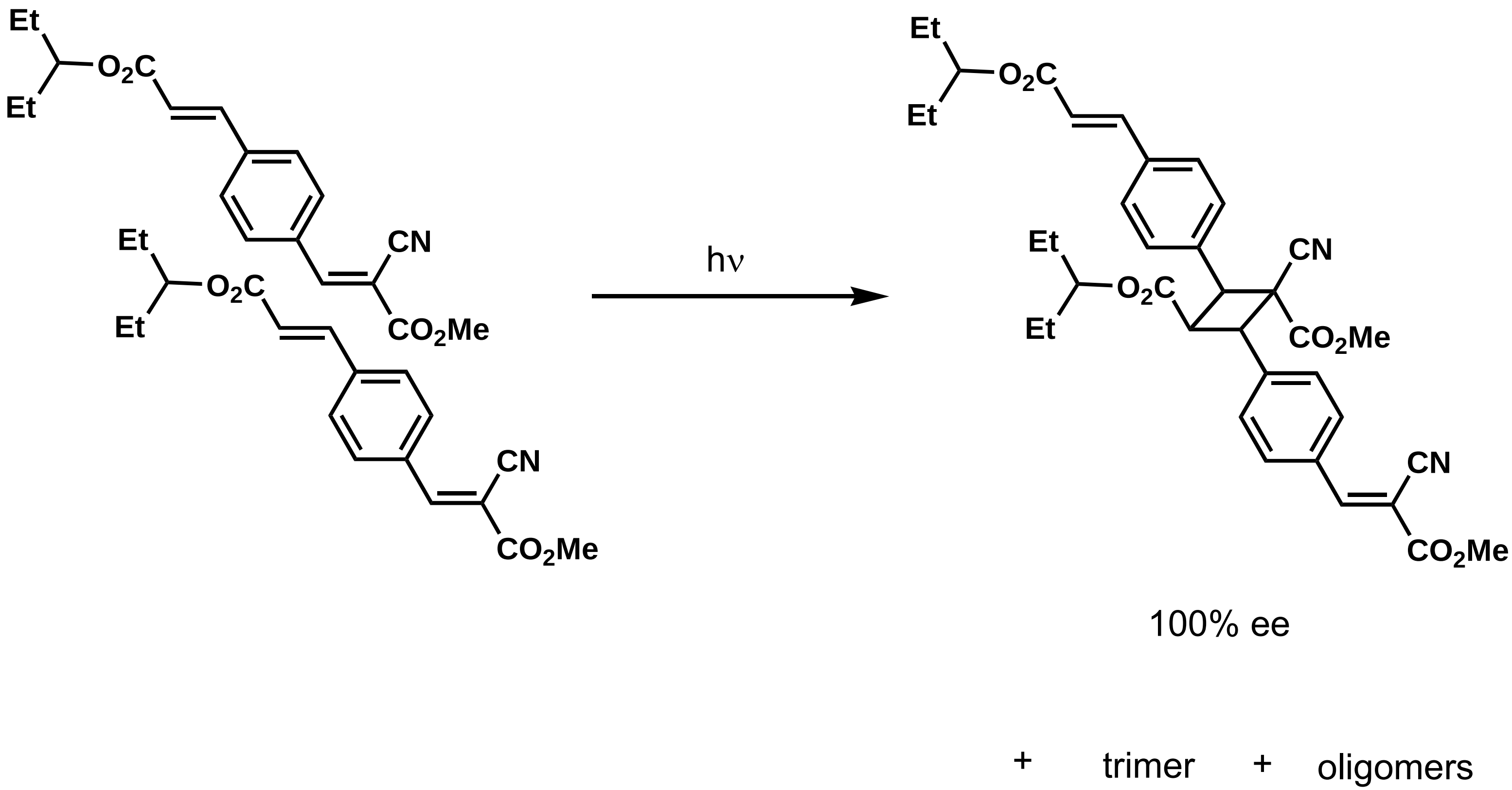


Sakamoto M.; Takahashi, M.; Moriizumi, S.; Yamaguchi, K.; Fujita, T.; Watanabe, S. *J. Am. Chem. Soc.* **1996**, *118*, 8183.



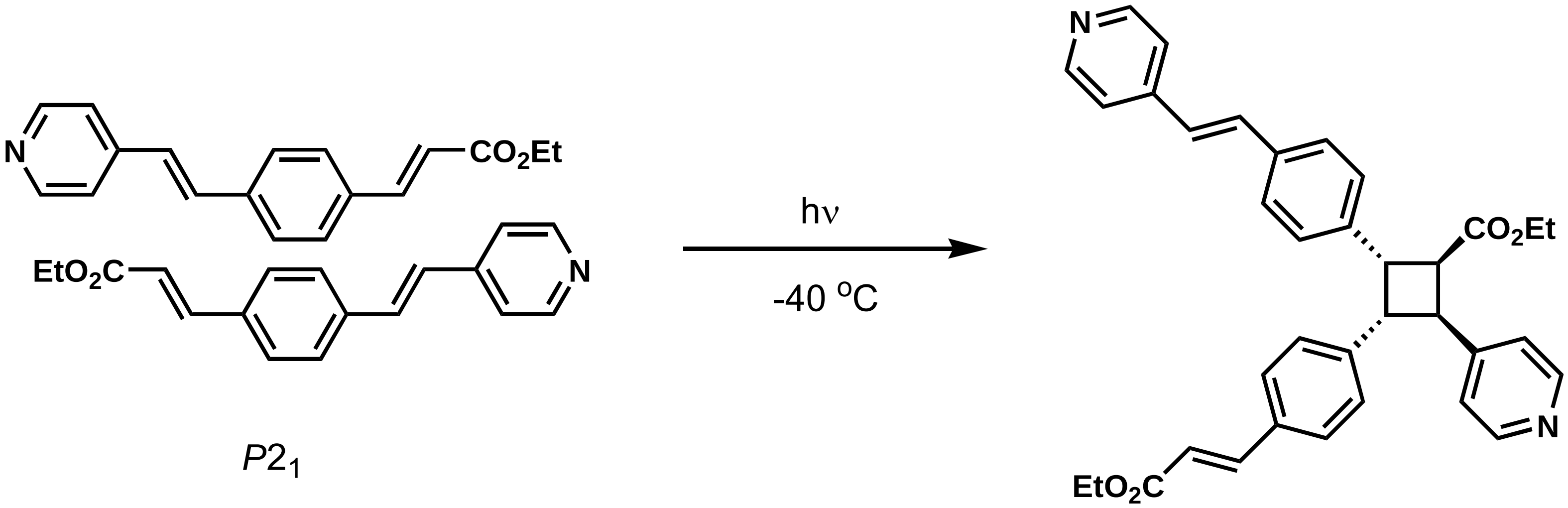
Sakamoto M.; Seikine, N.; Miyoshi, H.; Mino, T.; Fujita, T. *J. Am. Chem. Soc.* **2000**, *122*, 10210.

Intermolecular [2+2]



Addadi, L.; van Mil, J.; Lahav, M. *J. Am. Chem. Soc.* **1982**, *104*, 3422.

Intermoleculer [2+2]

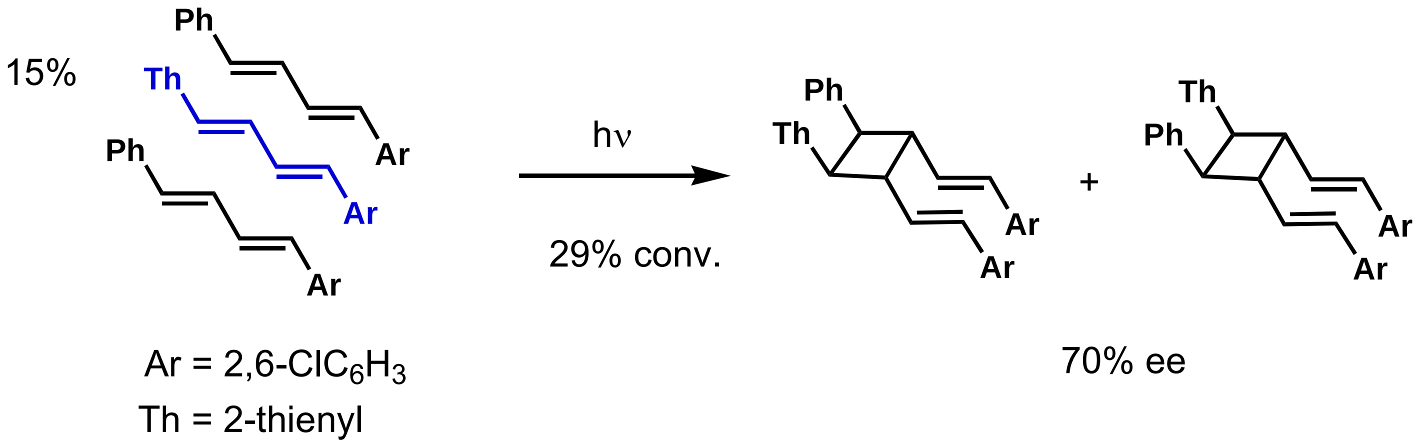


*P*2$_1$

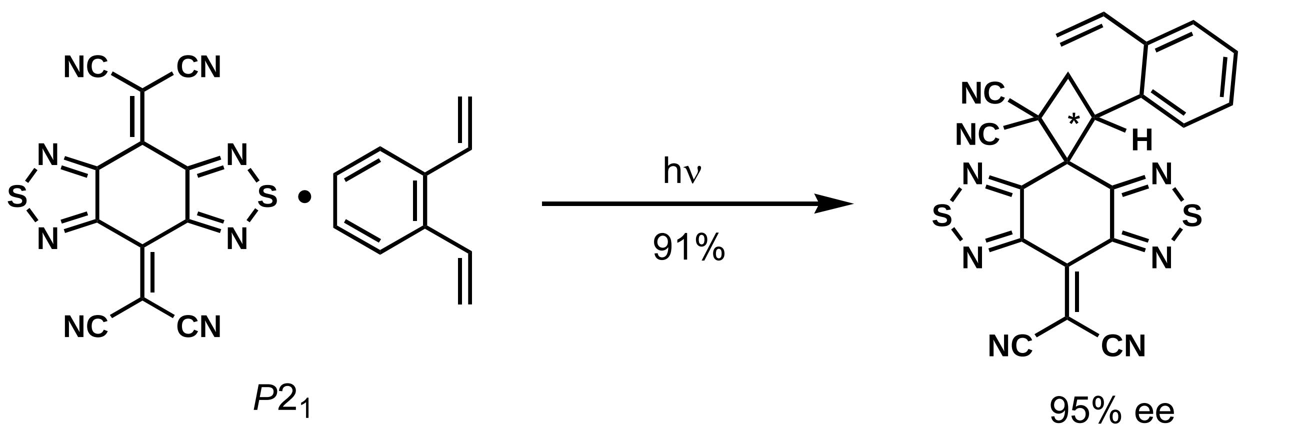
45% yield, 95% ee

Hasegawa, M.; Chung, C.-M.; Muro, N.; Maekawa, Y. *J. Am. Chem. Soc.* **1990**, *112*, 5676.

Intermolecular [2+2]: Cocrystal

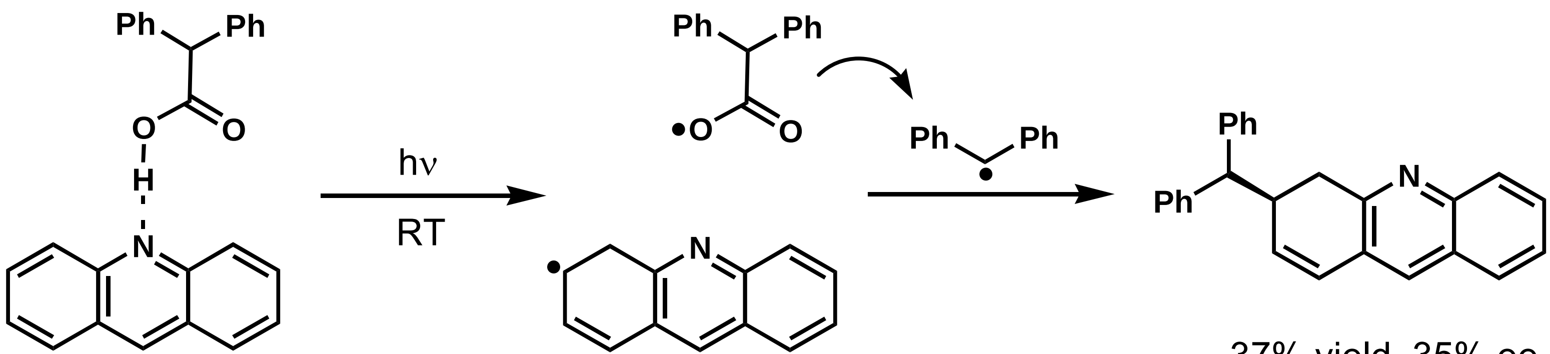


Elgavi, A.; Green, B. G.; Schmidt, G. M. J. *J. Am. Chem. Soc.* **1973**, *95*, 2058.



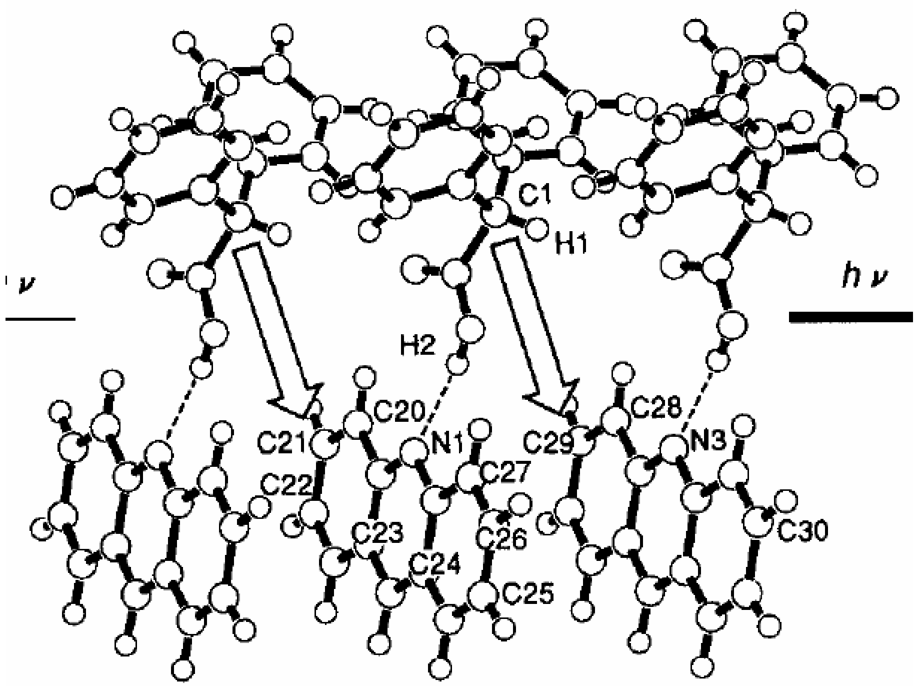
Suzuki, T.; Fukushima, T.; Yamashita, Y.; Miyashi, T. *J. Am. Chem. Soc.* **1994**, *116*, 2793.

Cocrystal For AAS



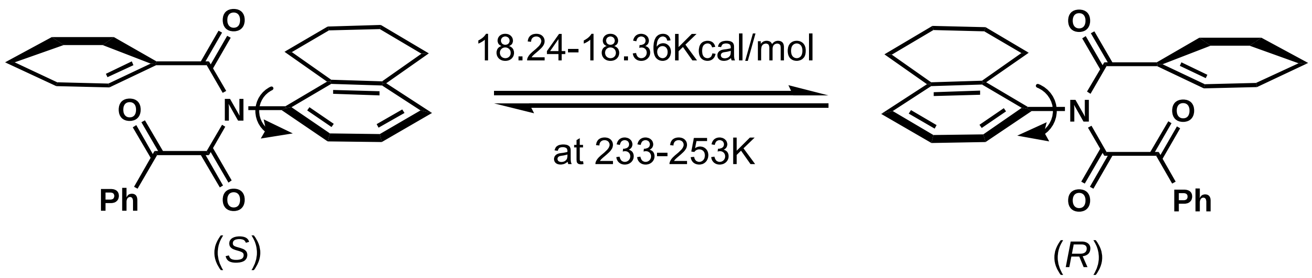
37% yield, 35% ee

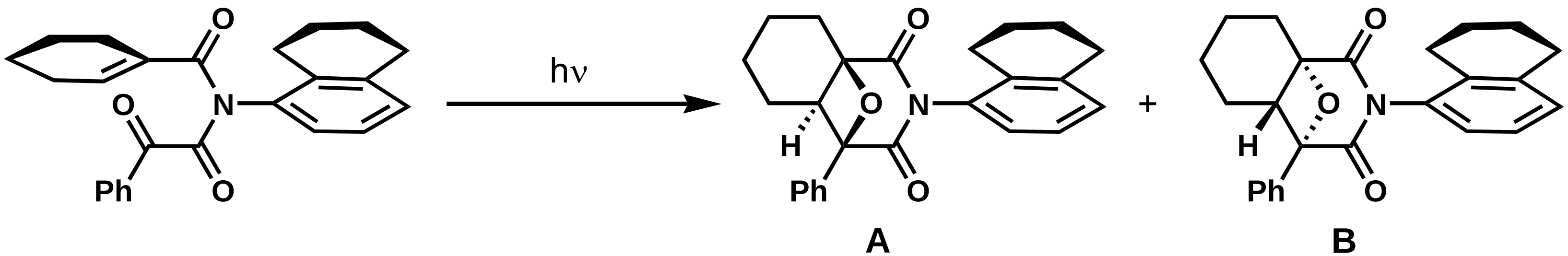
$P2_12_12_1$



Koshima, H.; Ding, K.; Chisaka, Y.; Matsuura, T. *J. Am. Chem. Soc.* **1996**, *118*, 12059.

Frozen Molecular Chirality Memorized by Chiral Crystallization

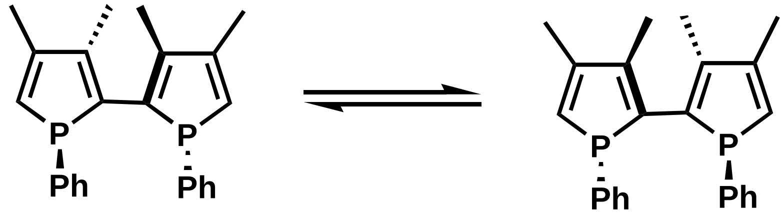




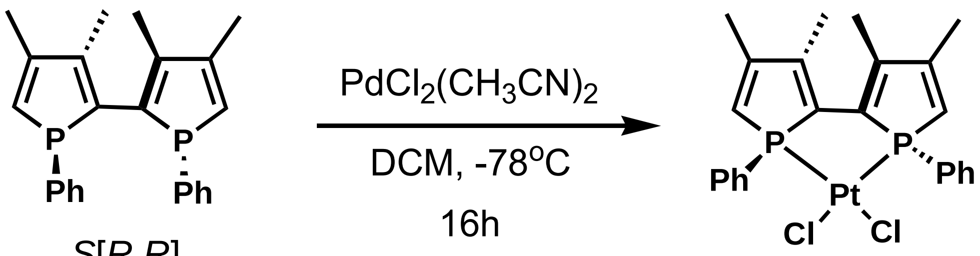
T, °C	Conditions	Yield, %	**A** : **B**	**A**, ee, %	**B**, ee, %
15	Solid State	100	95:5	>99	-
0	THF	-	67:33	0	0
–20	THF	-	68:32	51	31
–60	THF	-	81:19	87	79

Sakamoto, M.; Iwamoto, T.; Nono, N.; Ando, M.; Arai, W.; Mino, T.; Fujita, T. *J. Org. Chem.* **2003**, *68*, 942.

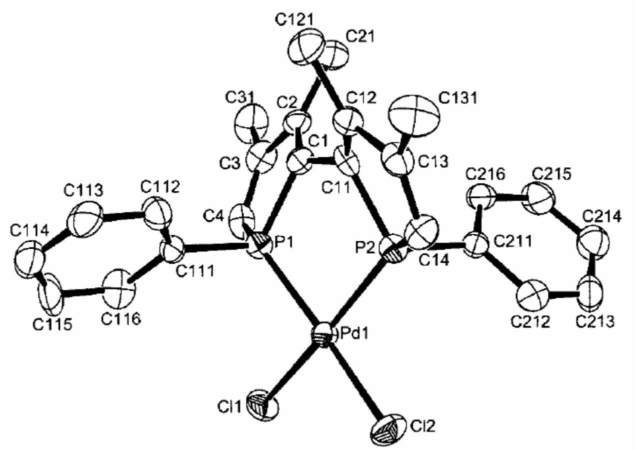
Chirality Retention: From Solid-State to Homogenous Solution

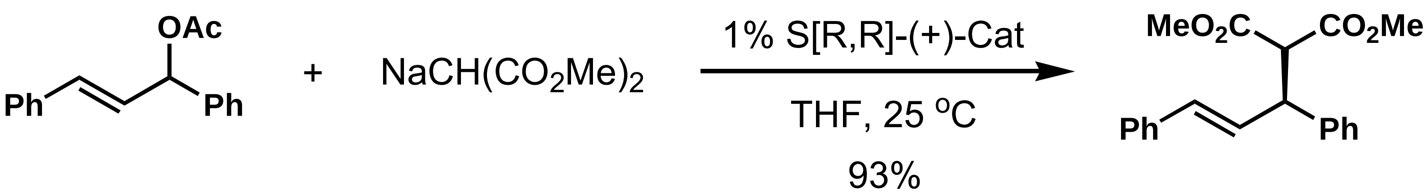


S[*R*,*R*]   *R*[*S*,*S*]



S[*R*,*R*]   *S*[*R*,*R*]-(+)-Cat

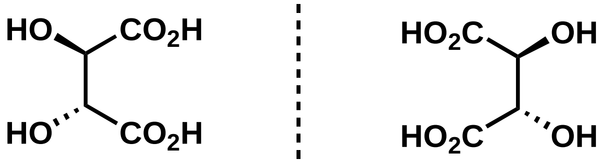




80% ee

Tissot, O.; Gouygou, M.; Dallemer, F.; Daran, J.-C.; Balavoin, G. G. A. *Angew. Chem. Int. Ed.* **2001**, *40*, 1076.

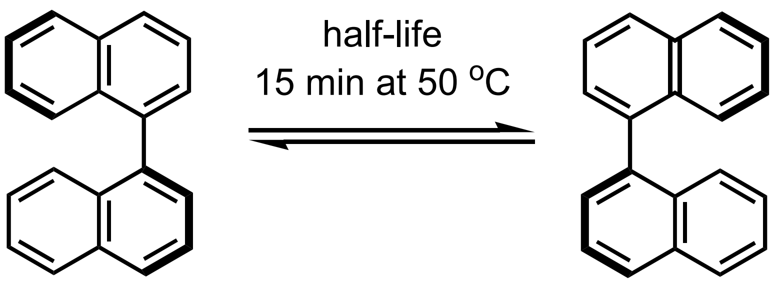
Racemic-to-Chiral: Optical Activity Generated by Crystallization



L-(+)-tartaric acid D-(-)-tartaric acid

Louis Pasteur, 1947

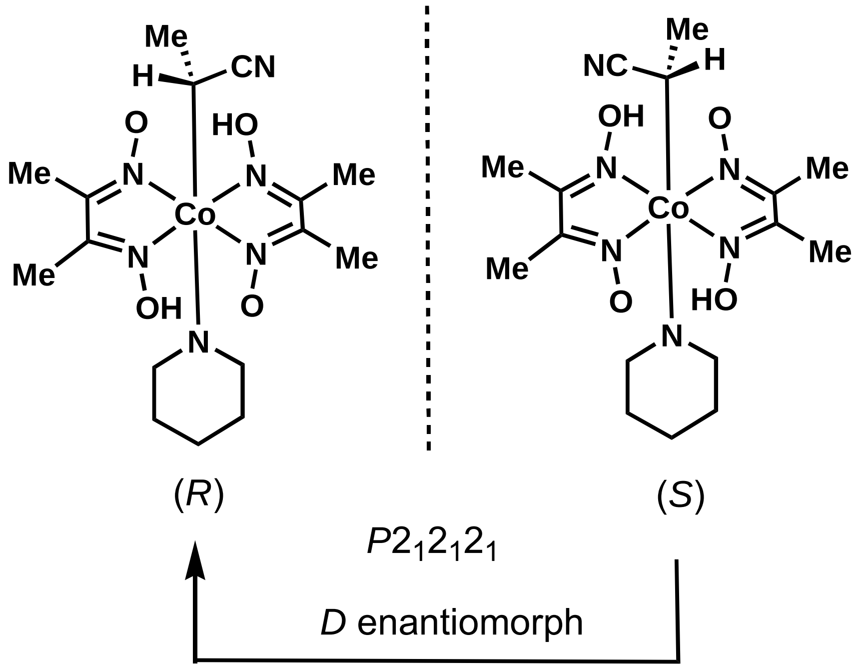
Spontaneous Solid-State Resolution:



S-(+) *R*-(-)

Pincock, R. E.; Wilson, K. R. *J. Am. Chem. Soc.* **1970**, *93*, 1291.

Optical Enrichment of a Racemic Chiral Crystal by X-ray Irradiation



Volumn of reaction cavity: R 7.49 Χ

S 11.57 Χ

Required volume for the racemization: 11.5 Χ

Osano, Y. T.; Uchida, A.; Ohashi, Y. *Nature* **1991**, *352*, 510.