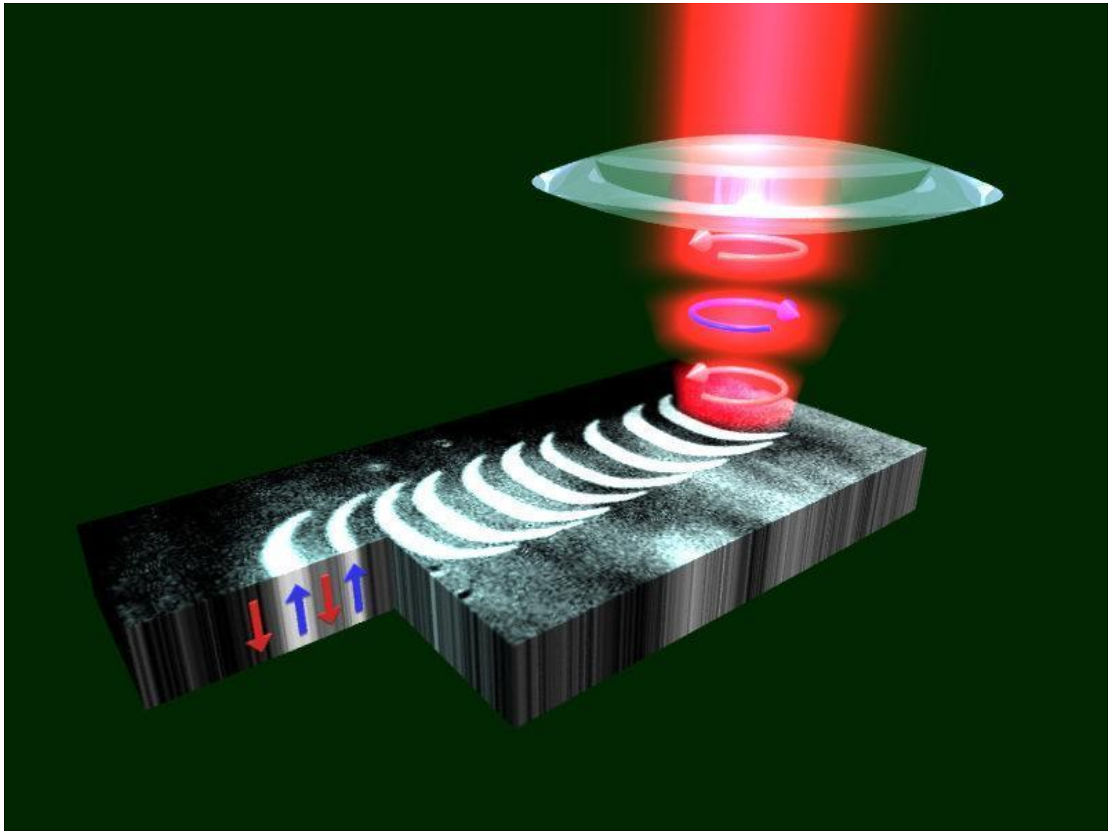
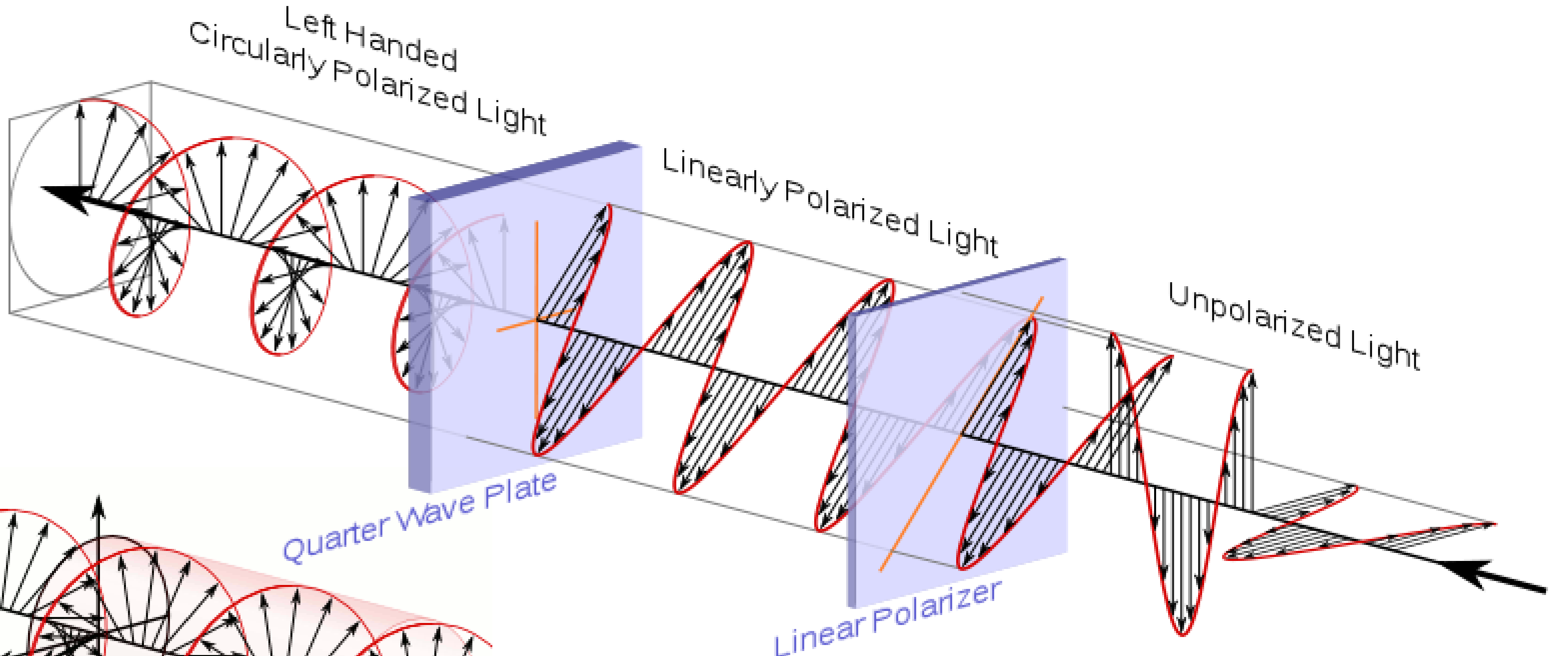
Enantioselective photochemistry

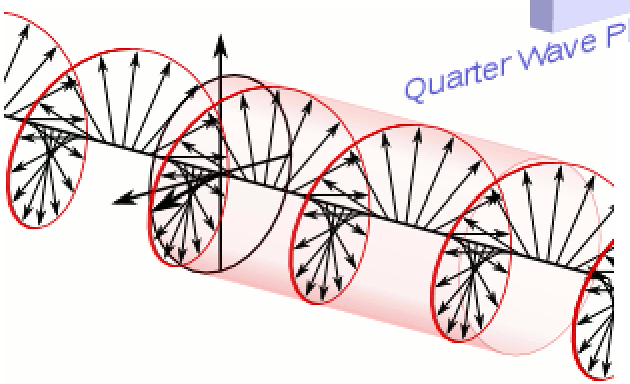


Zhe Dong

2014-01-15

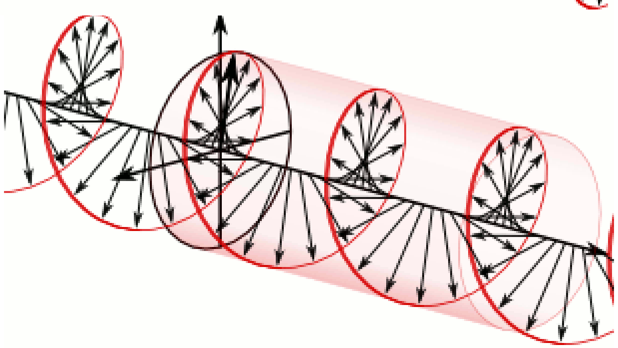
Introduction of Circular Polarization Light





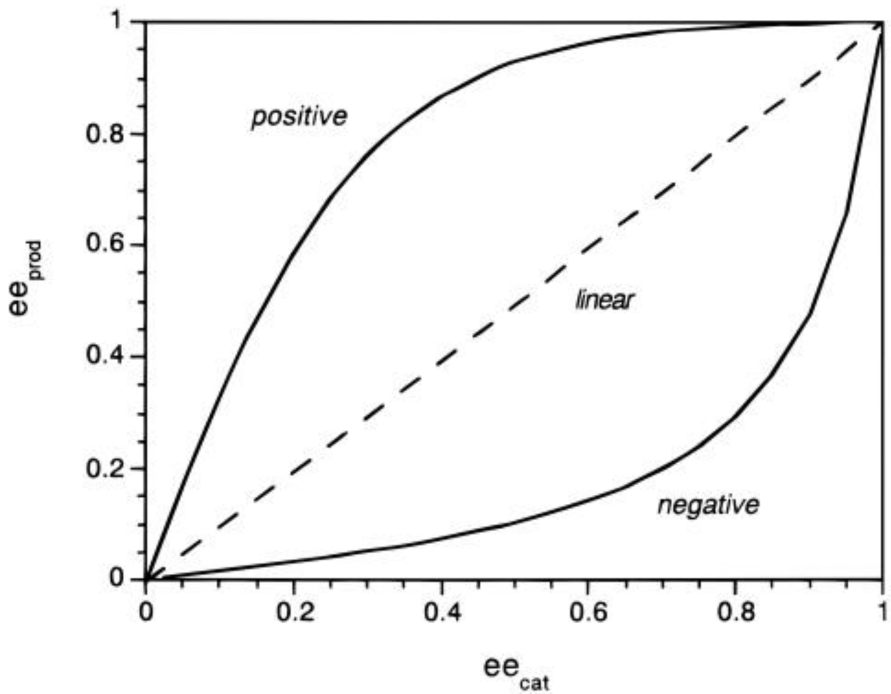
Left-CPL-’S’ light

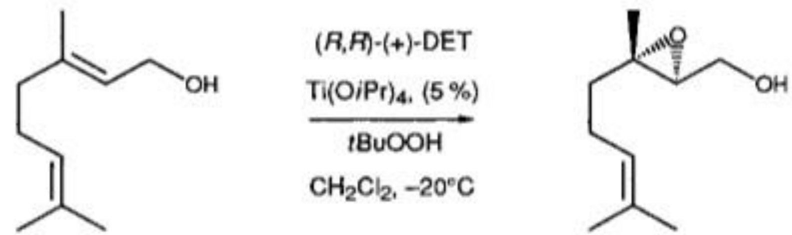
Chiral light -> Chiral Product?



Right-CPL-’R’ light

Introduction of Non-Linear Effects

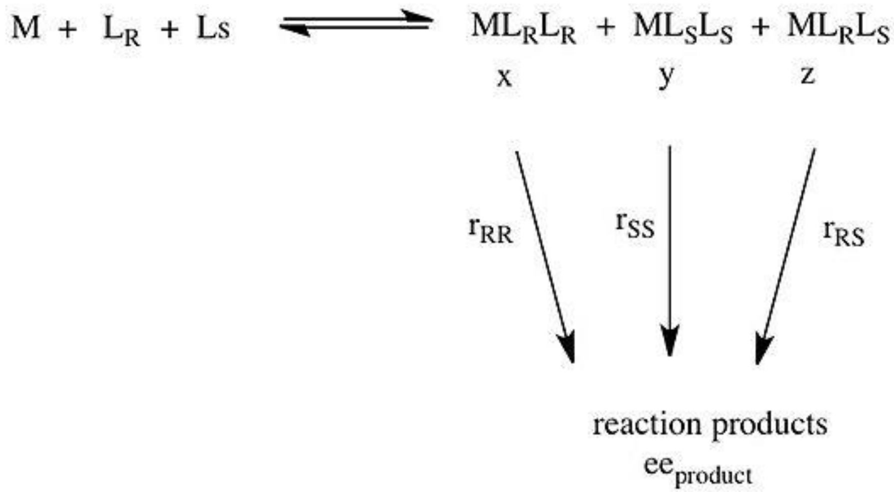




20%ee of DET
45%ee of Product

How can this happen?
Chiral Lignand Self-assembly -> diastereoselectivity
For transition metal catalysis usually means multi-metal in T.S.

Introduction of Non-Linear Effects



Concentrations: x, y, z

Rates: r_{RR}, r_{SS}, r_{RS}

Equilbrium constant:
$K = \frac{z^2}{xy}$

$$ee_{\mathrm{product}} = ee_{\mathrm{max}} ee_{\mathrm{auxiliary}} (1+\beta)/(1+g\,\beta)$$

$$\beta = z/x + y$$

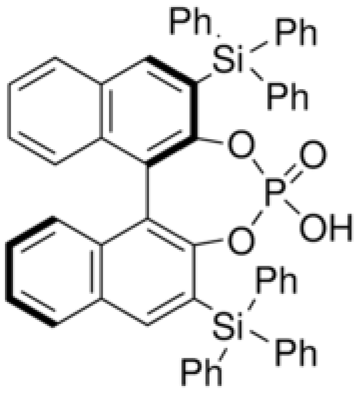
$$g = r_{rs}/r_{rr}$$

General Way for enatioselective synthesis

Photochemistry | Normal chemistry

chiral auxiliary (chiral SET) → Kinetic resolution (by light!) → Enatioselective catalyst (chiral molecule or chiral light)

chiral auxiliary (chiral arrow pushing) → Kinetic resolution (by chiral molecule) → Enatioselective catalyst (chiral molecule)



Chiral light- just need electricity and glass

100mg 300 dollar F.W. 870

Introduction

- The direct CPL introduce the ee:
- The Soai reaction combine CPL and auto-tamden-catalysis
- Diastereoseletive Photoreactions with Chiral Auxiliaries
- Enantioselective Photoreactions with Chiral catalyst

Direct CPL introduce the ee

- The direct CPL introduce the ee:
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Direct CPL introduce the ee

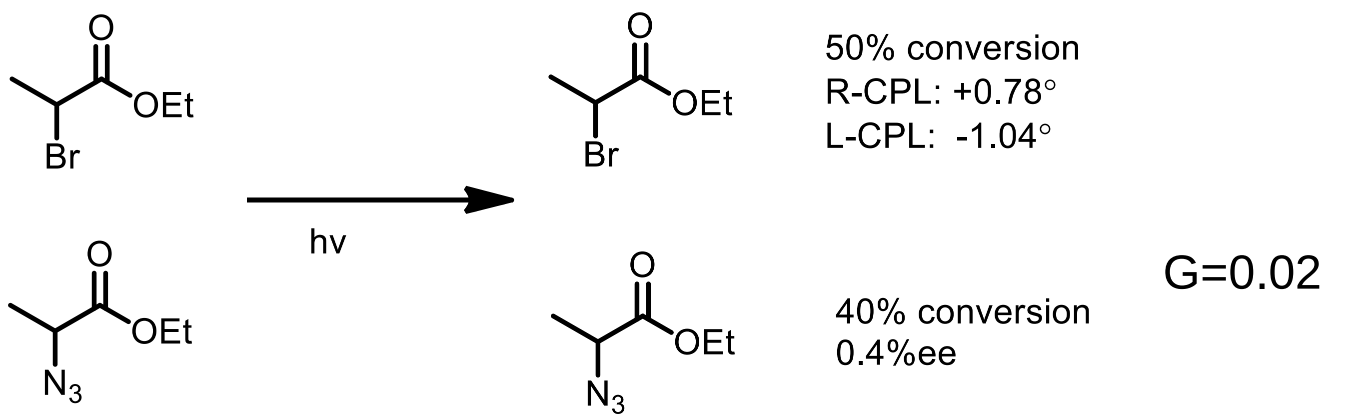
Early development :

1.This possibility was well illustrated by *van't Hoff* in 1894.

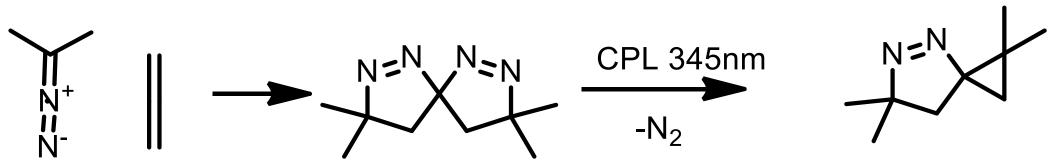
2. The detection of CD by Cotton in 1896 further corroborated that CPL could induce optical activity in chemical systems. But just Point CPL has a different influence on the reaction.

3.W. Kuhn first succeed in 1929 to get some enatiopure product.

4.The interest in CPL induced photochemistry peaked again in the 1970s, when reliable spectropolarimeters for CD measurements became commercially available.



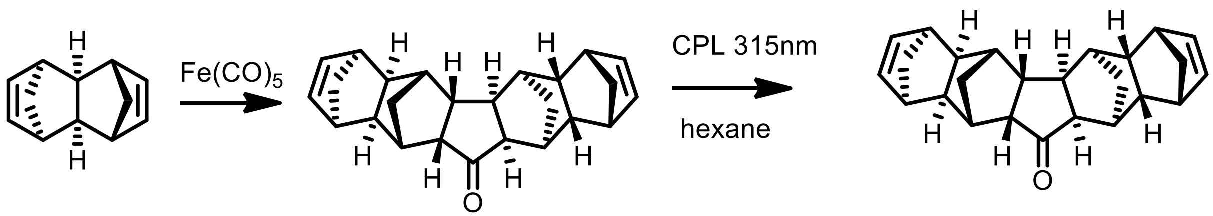
Direct CPL introduce the ee



59%conversion
4.8%ee
84%conversion
8.3%ee

g=0.1

Blume, R.; Rau, H.; Schuster, O. *J. Am. Chem. Soc.* **1976**, *98*, 6583.



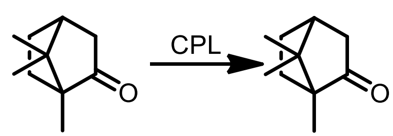
racemic

60%conversion 3.0%ee g=0.06

chiral

<40% yield

Computation show
g=0.80 show get 38% ee



racemic camphor

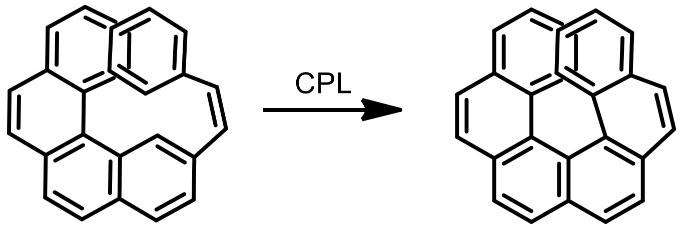
chiral product

20%ee

>98% conversion
1% yield

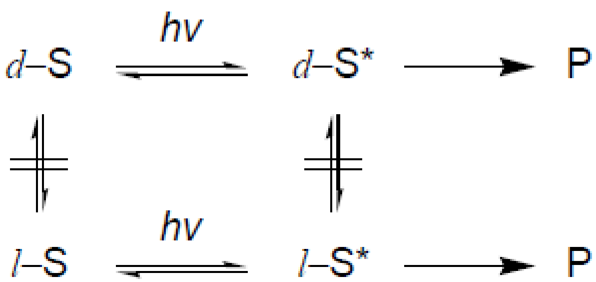
Nicoud, J. F.; Eskenazi, C.; Kagan, H. B. *J. Org. Chem.* **1977**, *42*, 4270.

Direct CPL introduce the ee



0.5%ee by Kagan

Eskenazi, C.; Kagan, H. B *Tetrahedron,* **1975**, 31, 2139



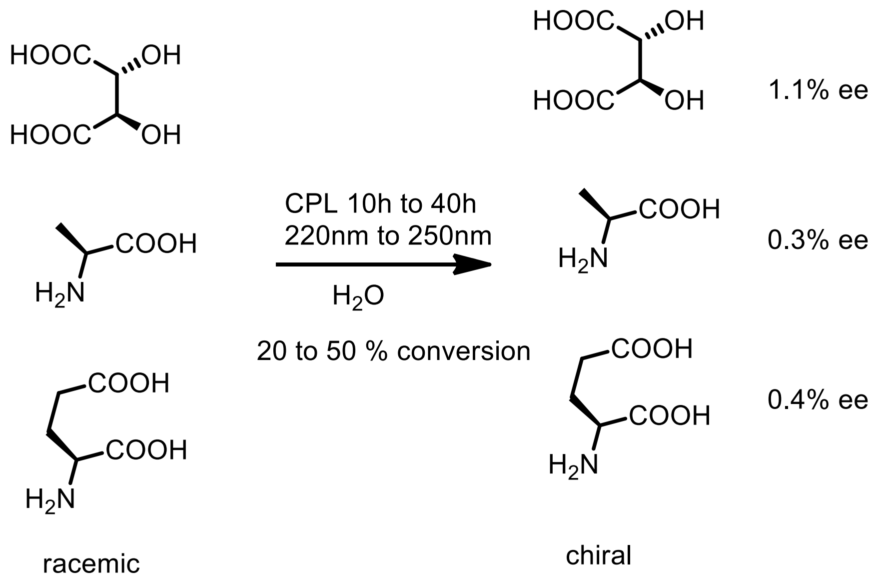
$$g = \frac{\Delta\varepsilon}{\varepsilon}$$

$$\Delta\varepsilon = \varepsilon_R - \varepsilon_S$$

$$\mathrm{ee} = \frac{C_R - C_S}{C_R + C_S} = \frac{\varepsilon_R - \varepsilon_S}{\varepsilon_R + \varepsilon_S} = \frac{\Delta\varepsilon}{2\varepsilon} = \frac{g}{2}$$

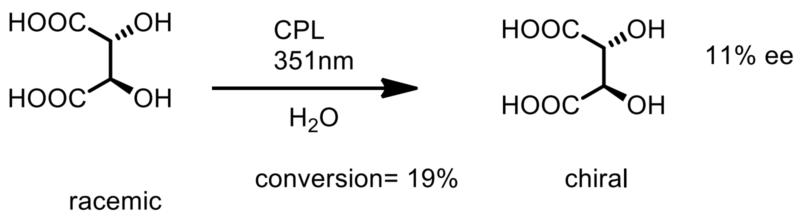
Balavoine, G.; Moradpour, A.; Kagan, H. B. *J. Am. Chem. Soc.* **1974**, *96*, 5152.

Focused Laser Induced Enantioenrichment



Is this one origin of the Chirality and life?

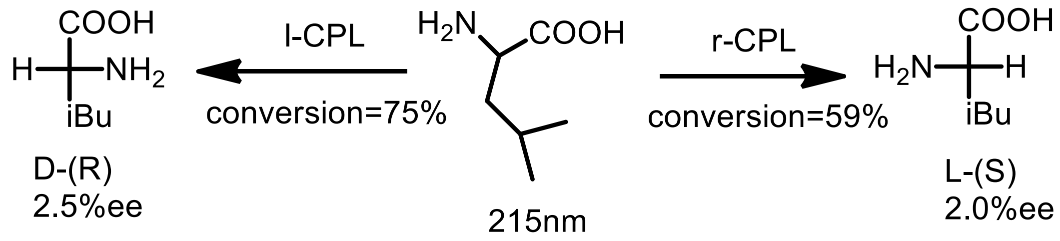
Norden, B. *Nature* **1977**, *266*, 567



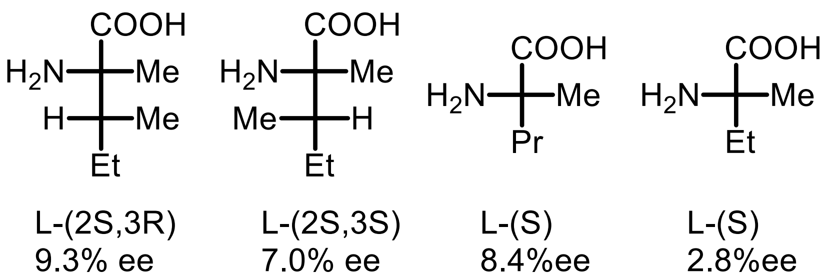
Highly intense CPL is from an XeF (351nm) excimer laser.

Shimizu, Y. *J. Chem. Soc. Perkin Trans. 1* **1997**, 1275.

CPL react with amino acid



Flores, J. J.; Bonner, W. A.; Massey, G. A. *J. Am. Chem. Soc.* **1977**, *99*, 3622.



Cronin, J. R.; Pizzarello, S. *Science* **1997**, *275*, 951..

Soai reaction

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Soai reaction

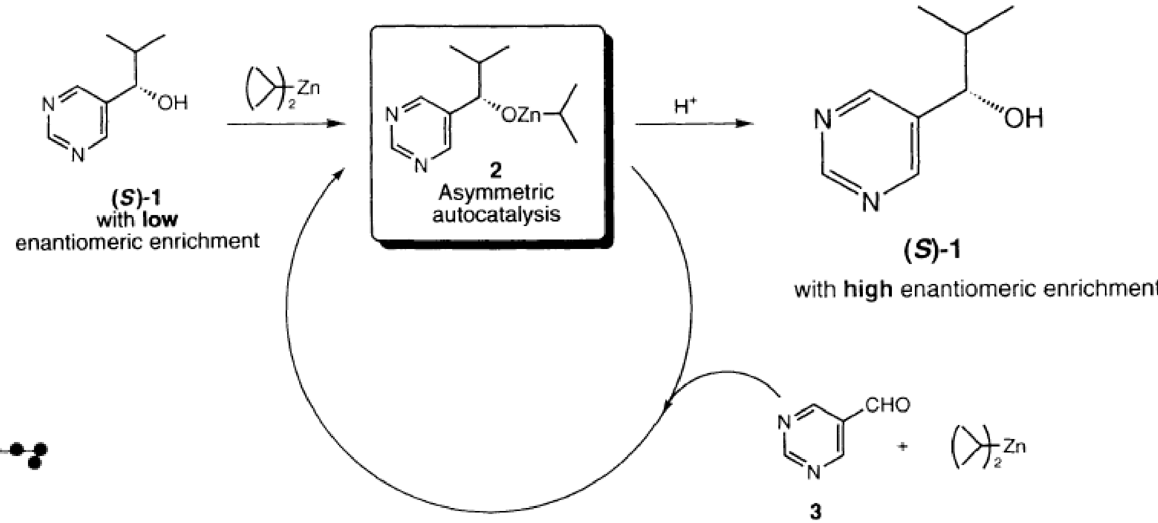
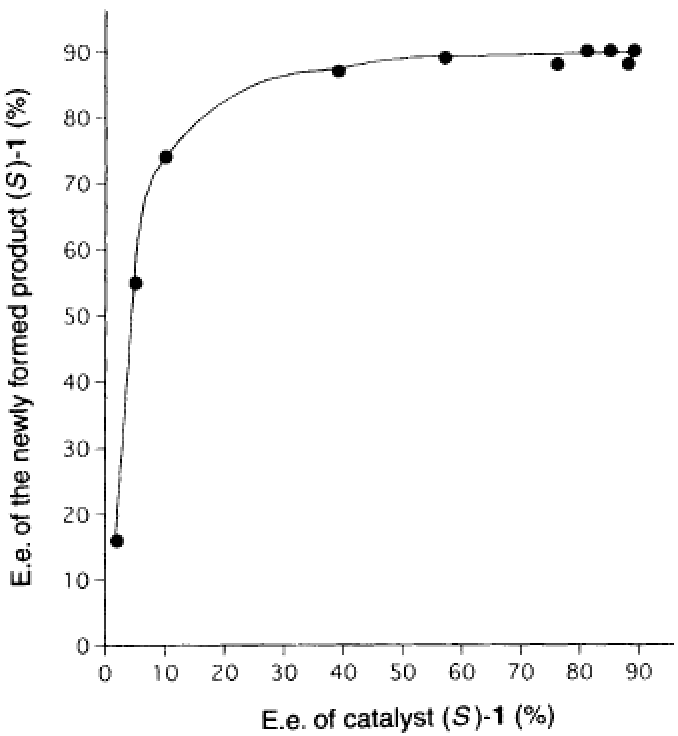


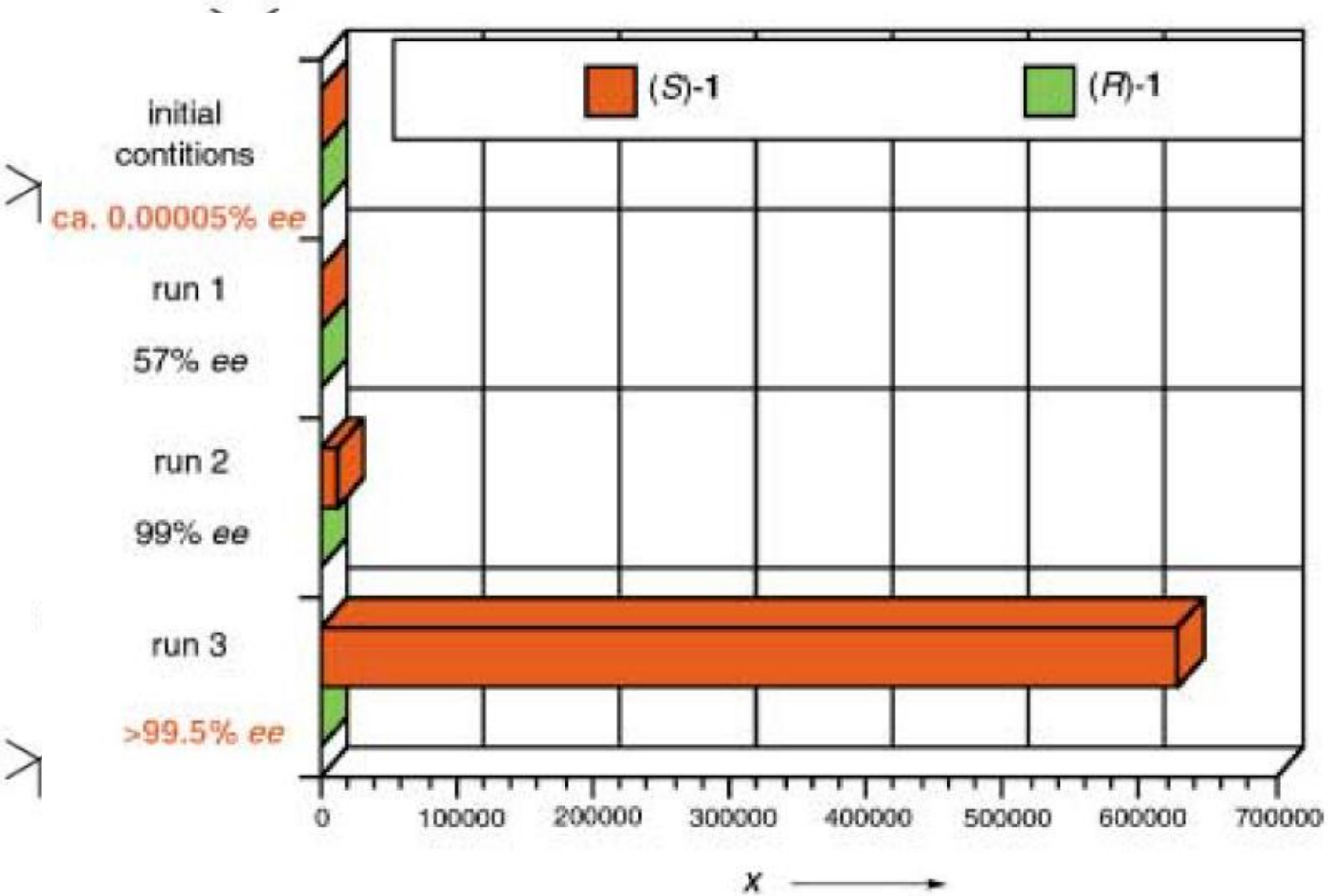
FIG. 2 Proposed reaction scheme of asymmetric autocatalysis of (S)-**1**.

767



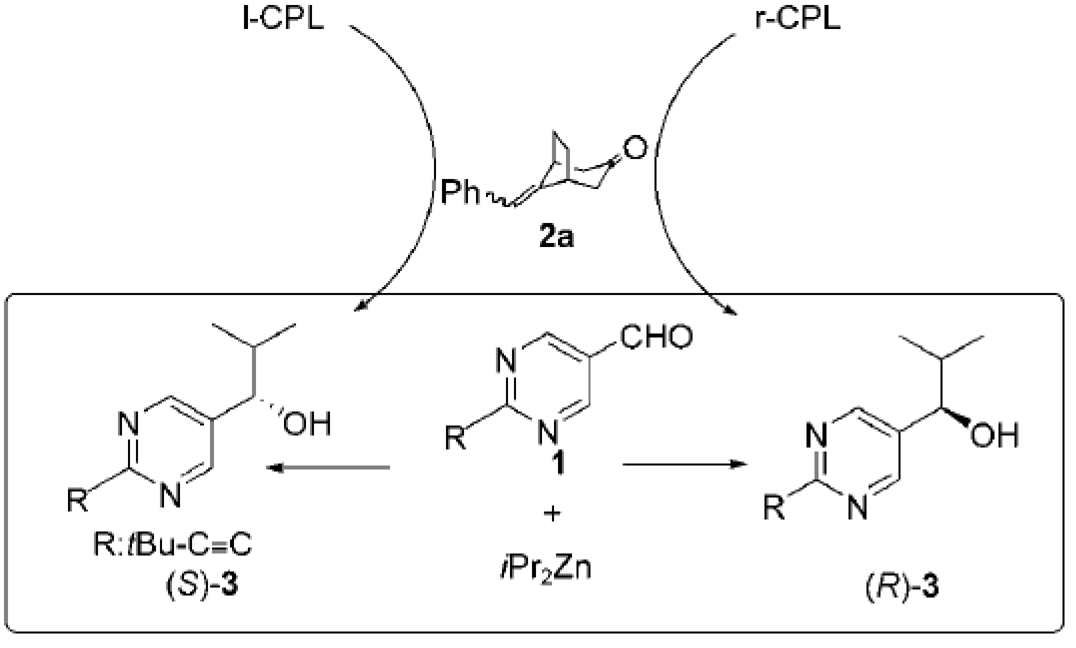
K. Soai, T. Shibata, H. Morioka and K. Choji Nature, **1995**, *378, 767-768.*

Soai reaction



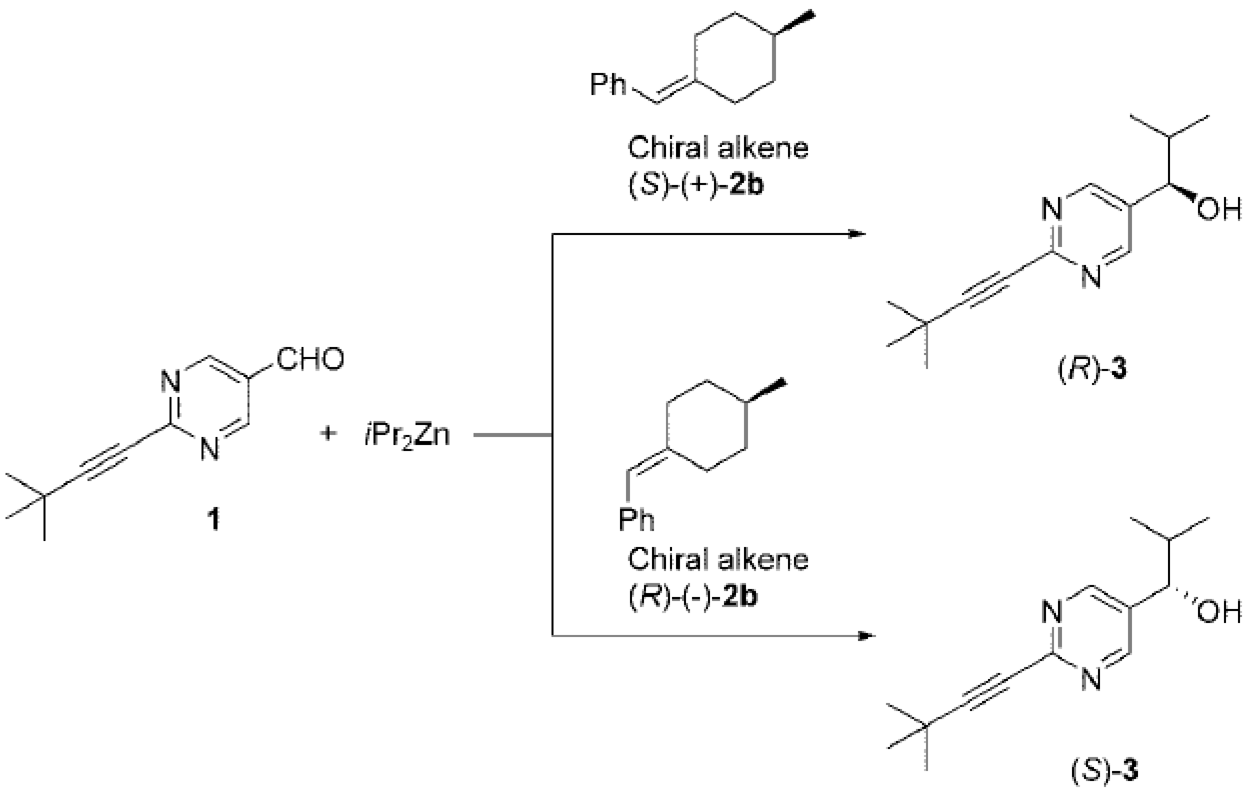
Sato, I.; Urabe, H.; Ishiguro, S.; Shibata, T.; Soai, K.
Angew. Chem. Int. Ed. **2003**, *42*, 315.

Soai reaction



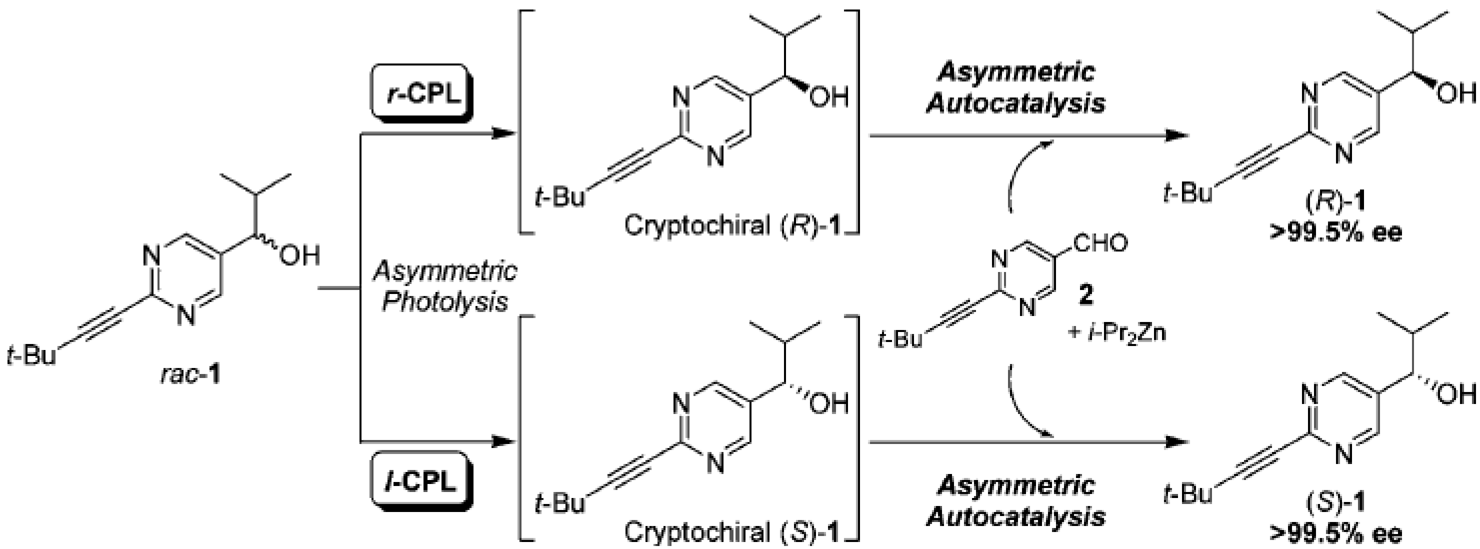
Sato, I.; Sugie, R.; Matsueda, Y.; Furumura, Y.; Soai, K.
Angew. Chem. Int. Ed. **2004**, *43*, 4490.

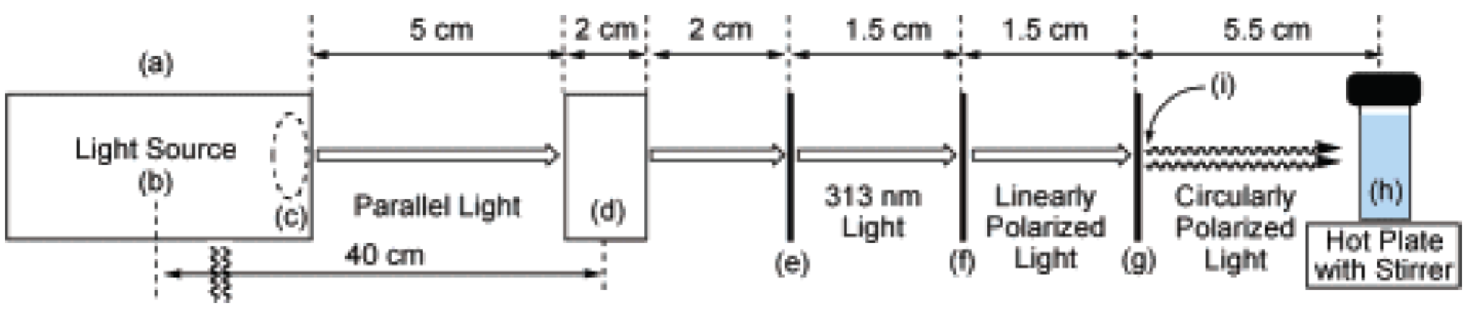
Soai reaction



Sato, I.; Sugie, R.; Matsueda, Y.; Furumura, Y.; Soai, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 4490.

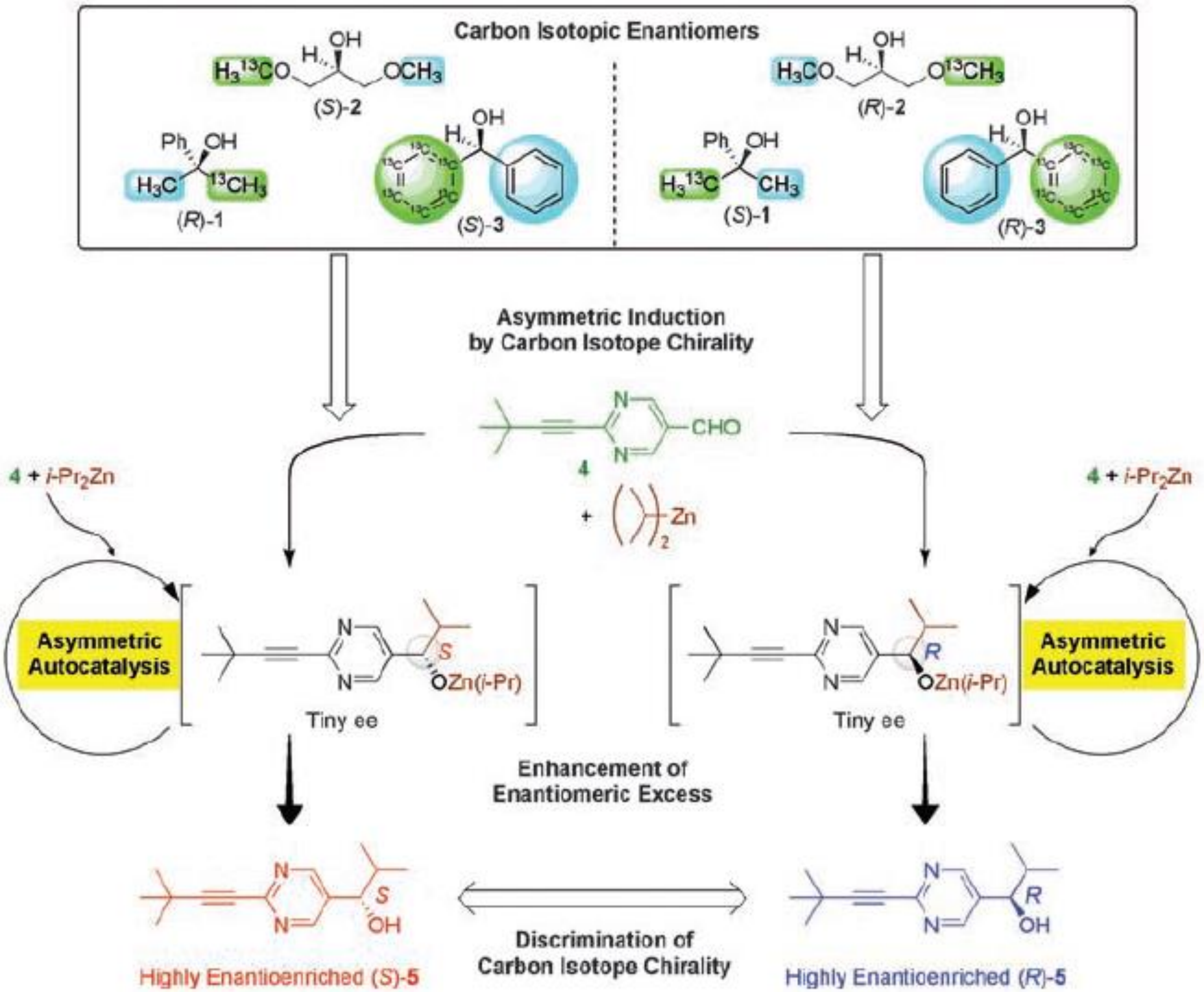
Soai reaction





Kawasaki, T.; Sato, M.; Ishiguro, S.; Saito, T.; Morishita, Y.; Sato, I.; Nishino, H.; Inoue, Y.; Soai, K. *J. Am. Chem. Soc.* **2005**, *127*, 3274.

Soai reaction



Kawasaki, T.; Sato, M.; Morishita, Y.; Sato, I.; Inoue, Y.; Soai, K. *Science.* **2009**, *324*, 492.

Diastereoseletive Photoreactions with Chiral Auxiliaries

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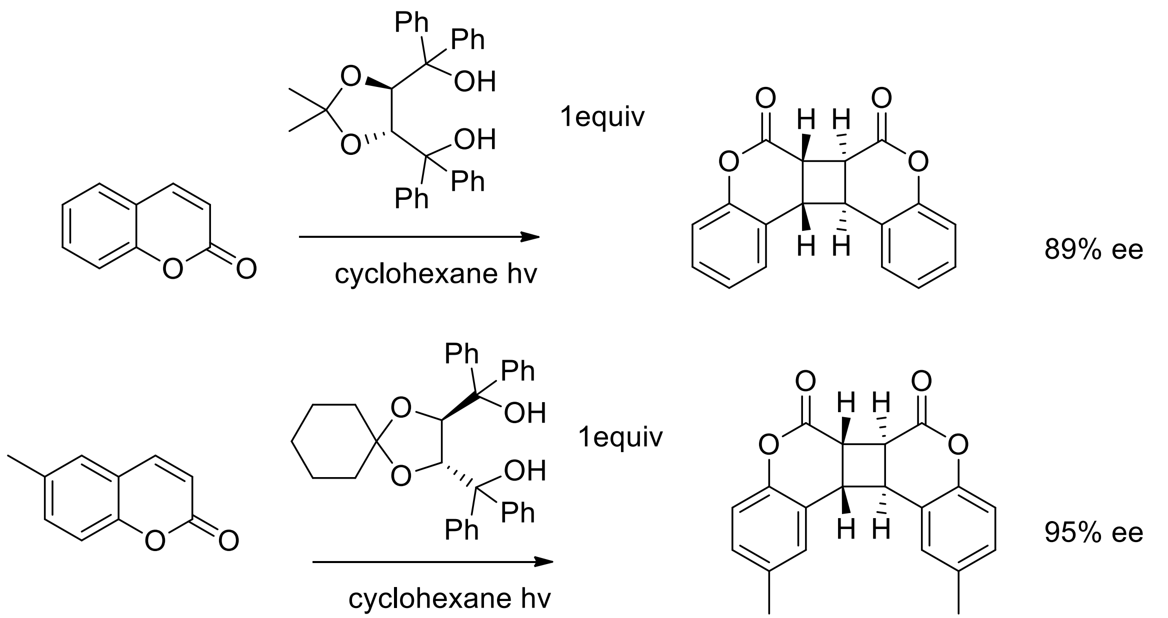
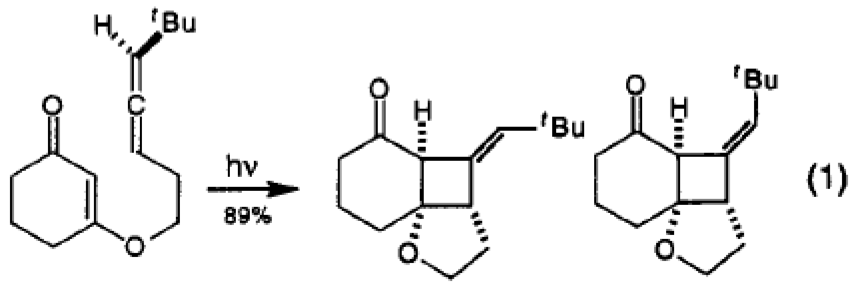
Diastereoseletive Photoreactions with Chiral Auxiliaries



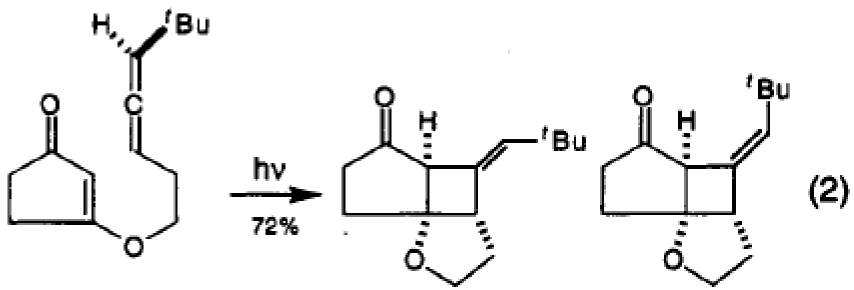
Tanaka, K.; Fujiwara, T. *Org. Lett.* **2005**, *7*, 1501.

Diastereoseletive Photoreactions with Chiral Auxiliaries



18 (92% ee) **19** (91% ee) **20** (92% ee)

Asymmetric induction 99% 100%

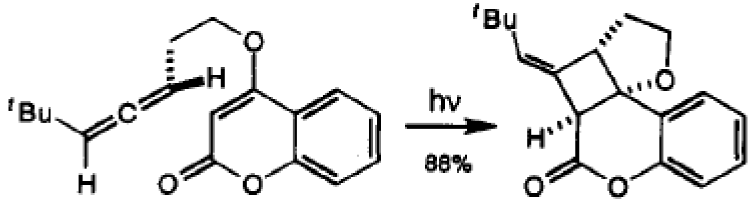


21 (89% ee) **22** (78% ee) **23** (74% ee)

Asymmetric induction 88% 83%

Carreira, E. M.; Hastings, C. A.; Shepard, M. S.; Yerkey, L. A.;Millward, D. B. *J. Am. Chem. Soc.* **1994,** *116*, 6622–6630.

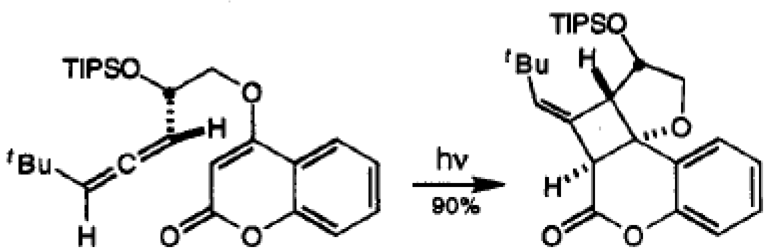
Diastereoseletive Photoreactions with Chiral Auxiliaries



(3)

24 (92% ee) **25** (92% ee)

Asymmetric induction 100%



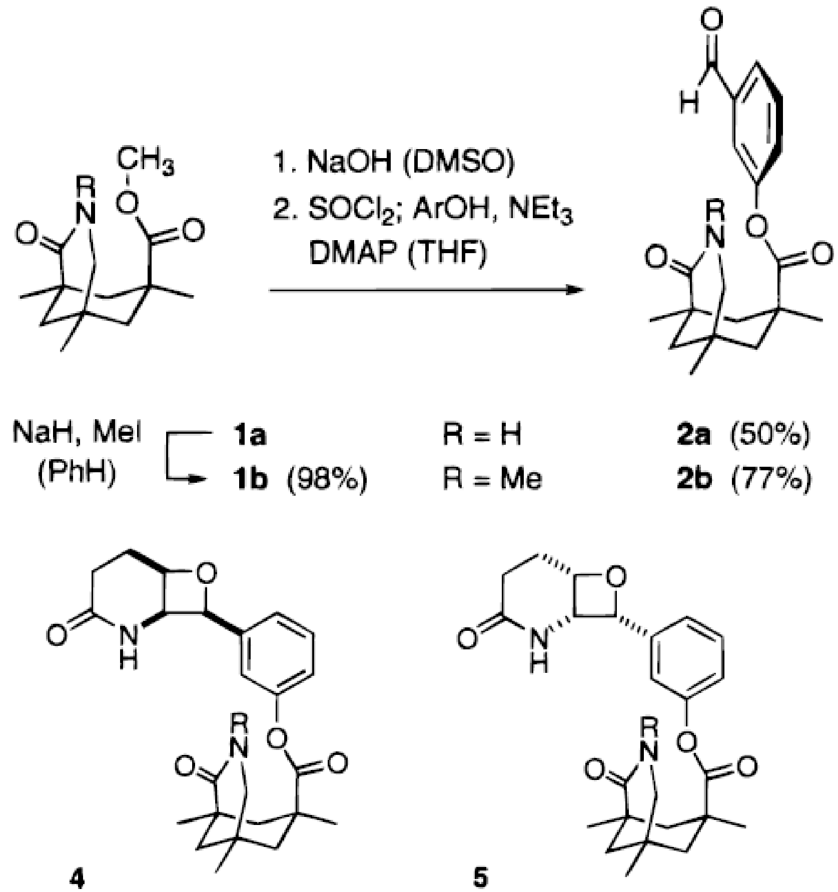
(4)

26 **27**

Diastereoselection 100%

Carreira, E. M.; Hastings, C. A.; Shepard, M. S.; Yerkey, L. A.;Millward, D. B. *J. Am. Chem. Soc.* **1994,** *116*, 6622–6630.

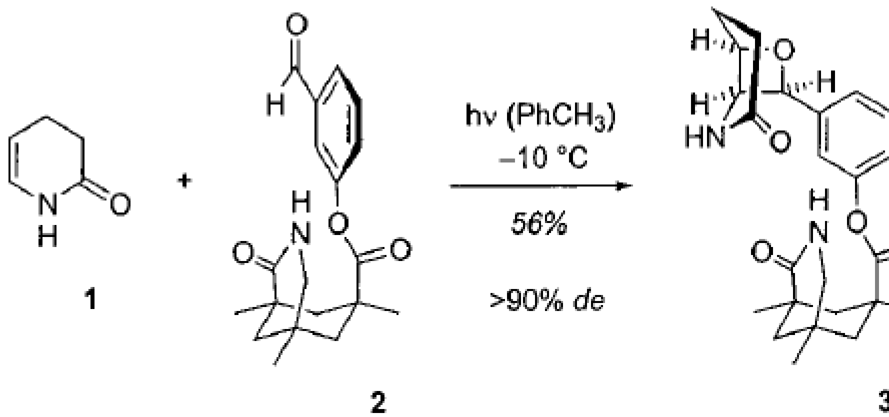
Diastereoseletive Photoreactions with Chiral Auxiliaries

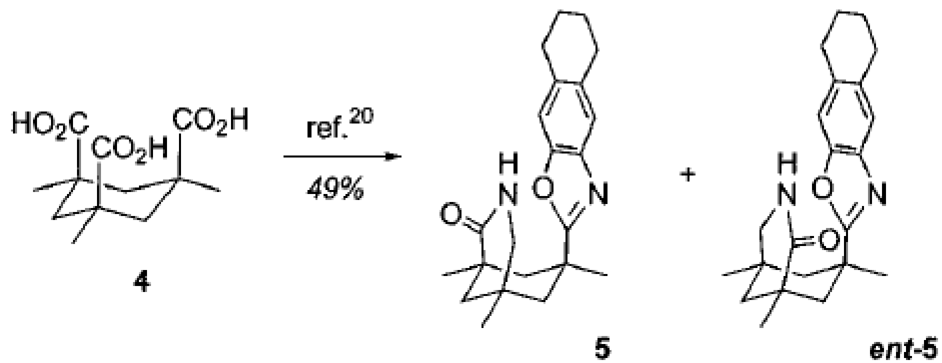


de > 19:1

T. Bach, H. Bergmann, K. Harms, *J. Am. Chem. Soc.* **1999**, *121*, 10650-10651.

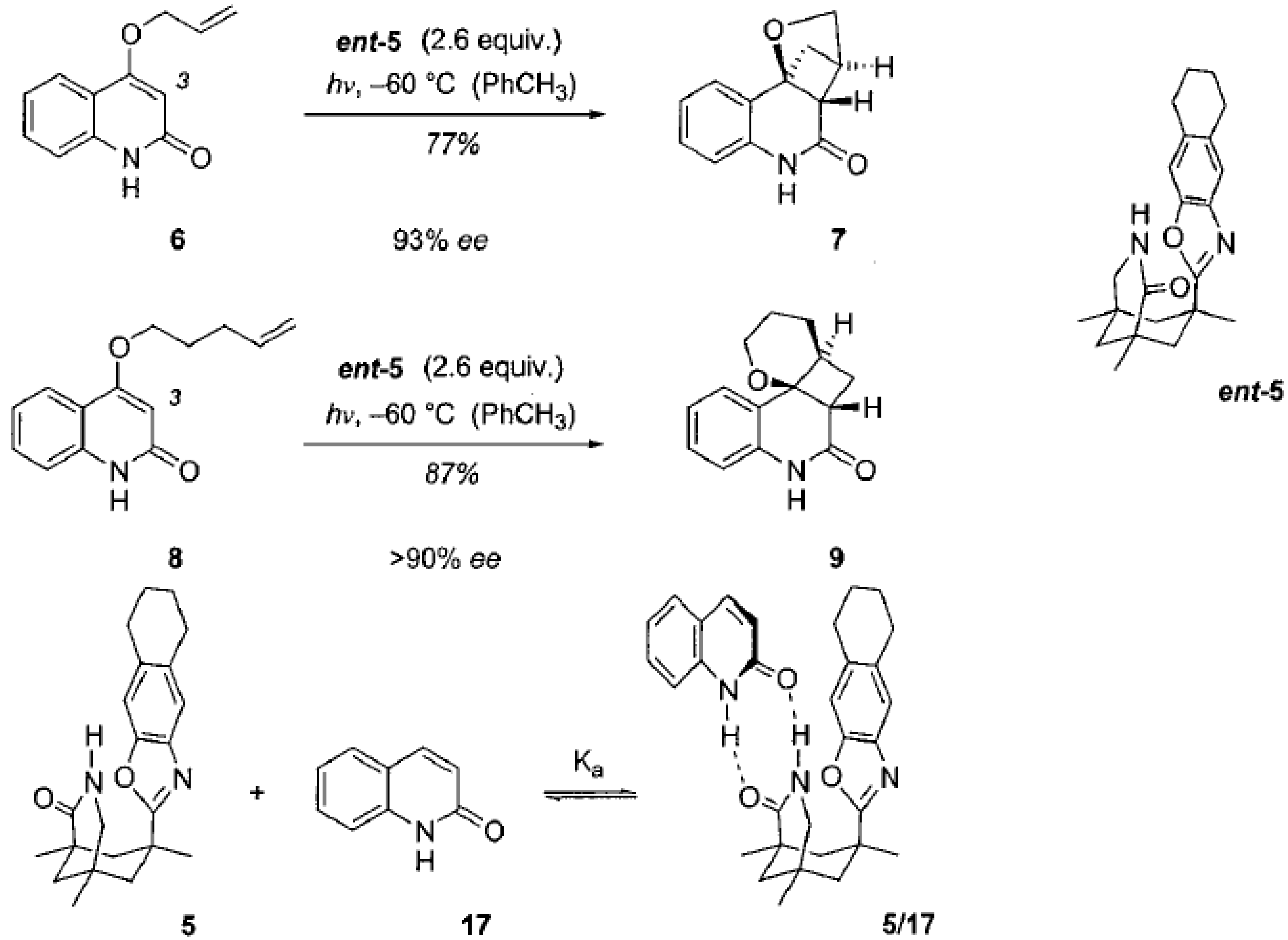
Diastereoseletive Photoreactions with Chiral Auxiliaries





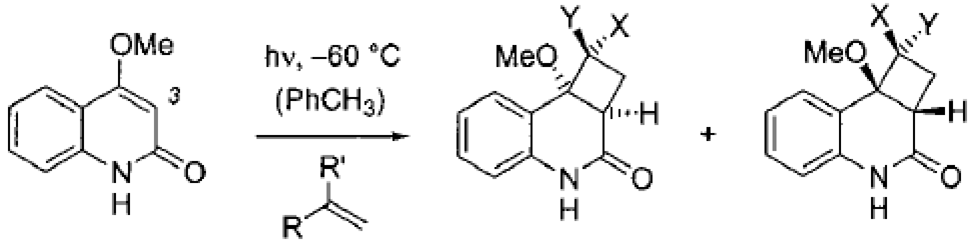
Bach, T.; Bergmann, H.; Grosch, B.; Harms, K. *J. Am. Chem. Soc.* **2002**, *124*, 7982.

Diastereoseletive Photoreactions with Chiral Auxiliaries



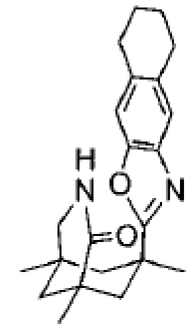
Bach, T.; Bergmann, H.; Grosch, B.; Harms, K. *J. Am. Chem. Soc.* **2002**, *124*, 7982.

Diastereoseletive Photoreactions with Chiral Auxiliaries



12 **13**

13a	R = $CH_2CH_2CH_2OH$	R' = H	**14**	X = R, Y = H	*ent*-**14**
13b	R = CH_2OAc	R' = H			
13c	R = OAc	R' = H	**15**	X = H, Y = R	*ent*-**15**
13d	R = Ph	R' = H			
13e	R = COOMe	R' = H			
13f	R = CH_2CH_3	R' = CH_2CH_3	**14f**		*ent*-**14f**

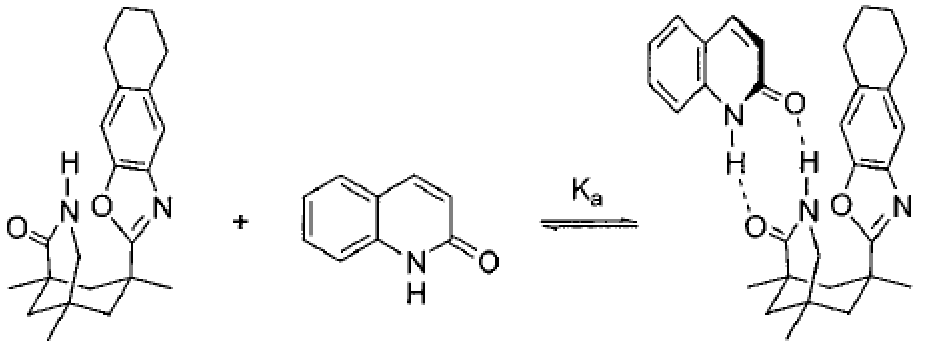


ent-**5**

entry	substrate	host	dr[a] (**14/15**)	yield [%][b]	product	ee [%][c]
1	**13a**	**5**	> 95/5	80	**14a**	81
2	**13b**	**5**	> 95/5	80	**14b**	92
3	**13b**	*ent*-**5**	> 95/5	81	*ent*-**14b**	91
4	**13c**	*ent*-**5**	63/27	89	*ent*-**14c**	93
					ent-**15c**	98
5	**13d**	**5**	< 5/95	29[d]	**15d**	83
6	**13e**	**5**	90/10	84	**14e**	82
7	**13f**	**5**	–	61	**14f**	92

Bach, T.; Bergmann, H.; Grosch, B.; Harms, K. *J. Am. Chem. Soc.* **2002**, *124*, 7982.

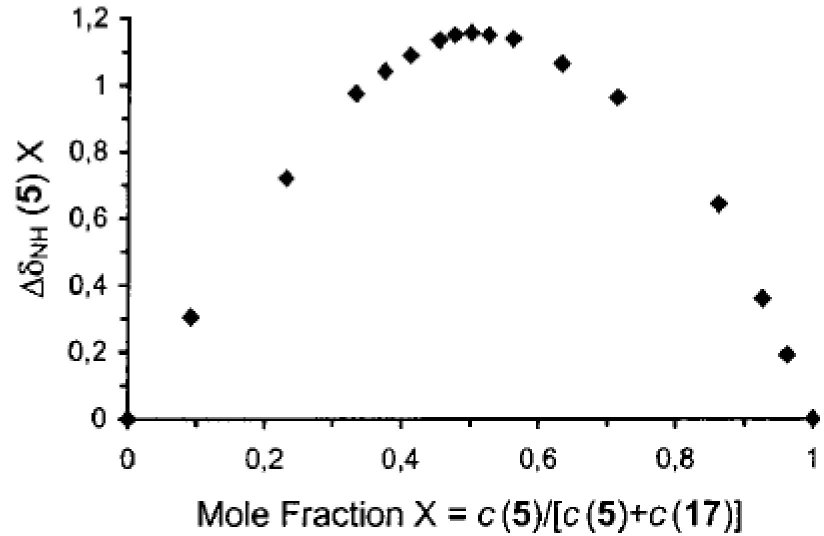
Diastereoseletive Photoreactions with Chiral Auxiliaries



5 17 5/17

$$\Delta H = -11.8\,\frac{kJ}{\text{mol}}$$

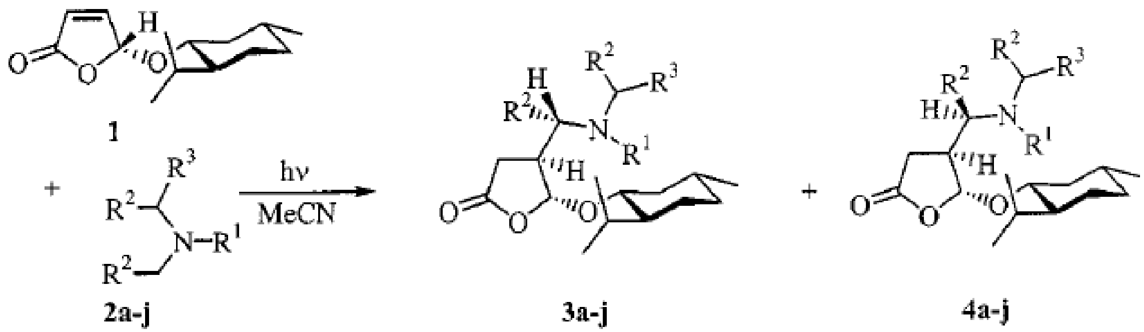
$$\Delta G = -13.5\,\frac{kJ}{\text{mol}}$$

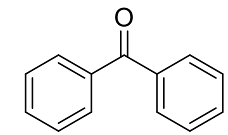


Urea ketone model:
Has homo dimer problem.
ΔH around 8kj/mol

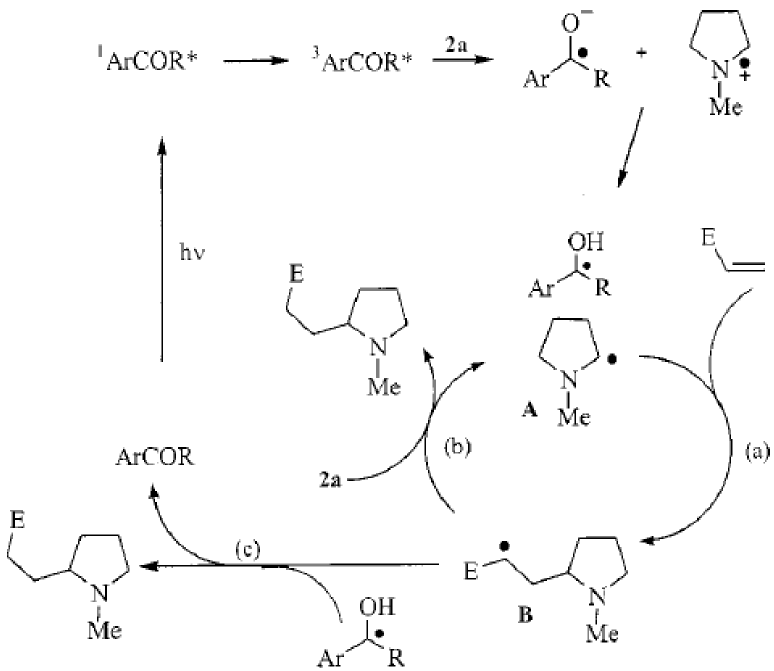
Bach, T.; Bergmann, H.; Grosch, B.; Harms, K. *J. Am. Chem. Soc.* **2002**, *124*, 7982.

Diastereoseletive Photoreactions with Chiral Auxiliaries



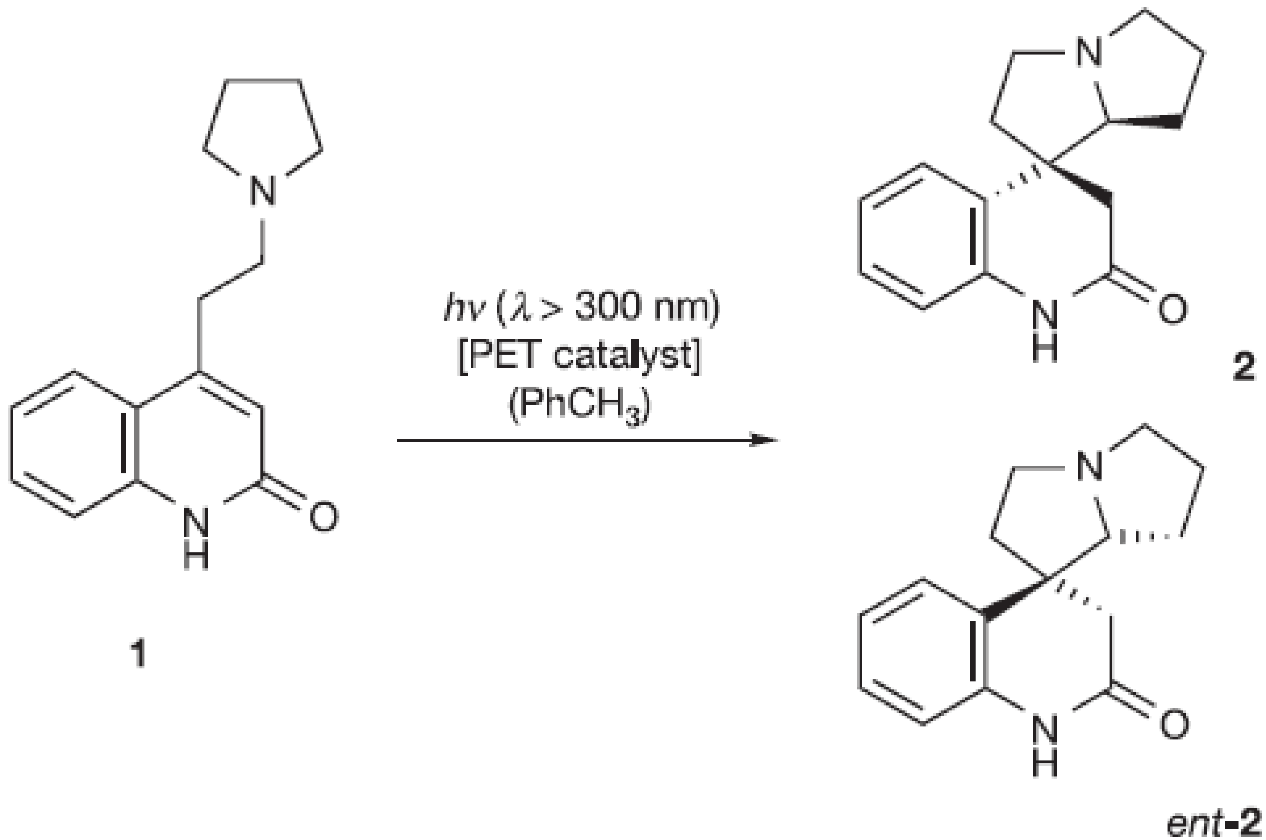


cataylst



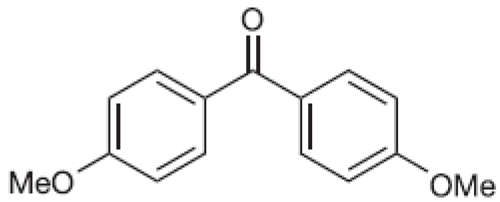
Bertrand, S.; Hoffmann, N.; Pete, J. *Eur. J. Org. Chem.* **2000**, 2227.

Enantioselective Photoreactions with Chiral catalyst

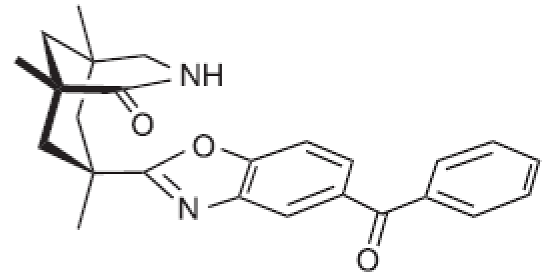


Bauer, A.; Westkamper, F.; Grimme, S.; Bach, T. *Nature* **2005**, *436*, 1139.

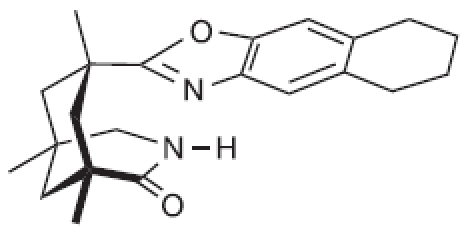
Enantioselective Photoreactions with Chiral catalyst



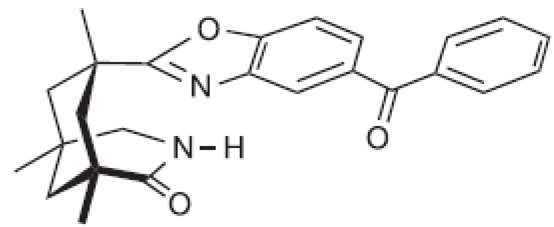
3



4



5

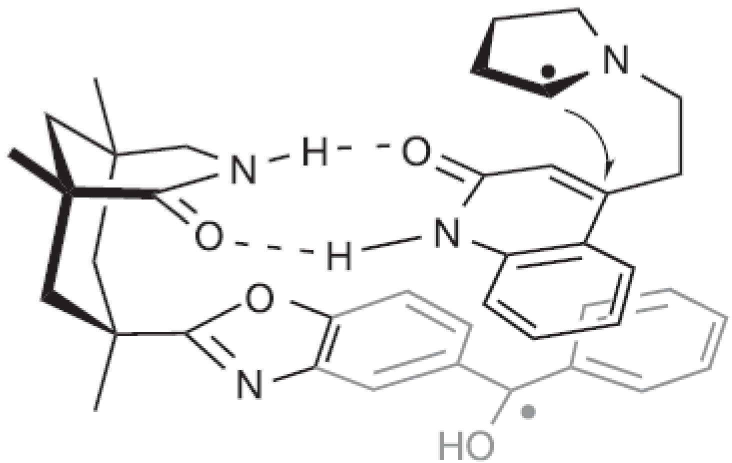


ent-**4**

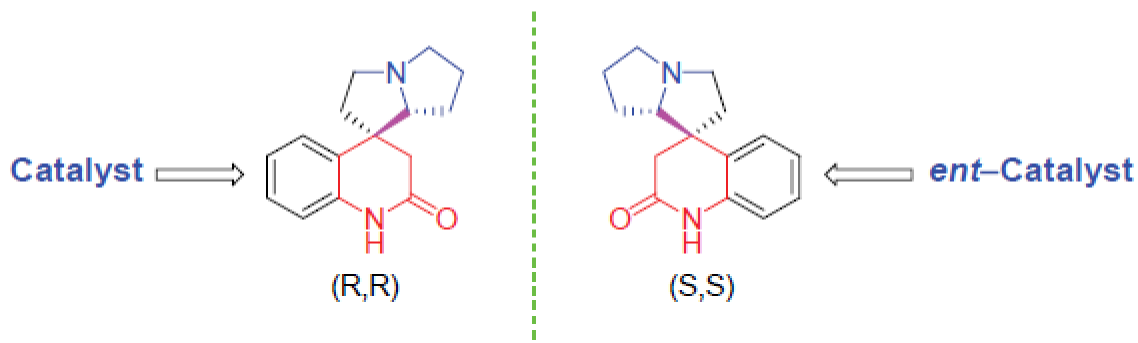
Entry no	Catalyst	Equiv.*	Time (h)	Product	e.r.†	e.e.‡ (%)	Yield§ (%)
1	**3**	0.1	3.5	**2**/*ent*-**2**	50/50	–	71
2	**4**	0.05	5	**2**	60/40	20	61
3	**4**	0.1	2.5	**2**	69/31	38	55
4	*ent*-**4**	0.1	3	*ent*-**2**	31/69	38	52
5	**4**	0.2	2	**2**	77/23	54	57
6	**4**	0.3	1	**2**	85/15	70	64
7	**3**/**5**‖	0.1/1.2	2	*ent*-**2**	14/86	72	39

Bauer, A.; Westkamper, F.; Grimme, S.; Bach, T. *Nature* **2005**, *436*, 1139.

Enantioselective Photoreactions with Chiral catalyst



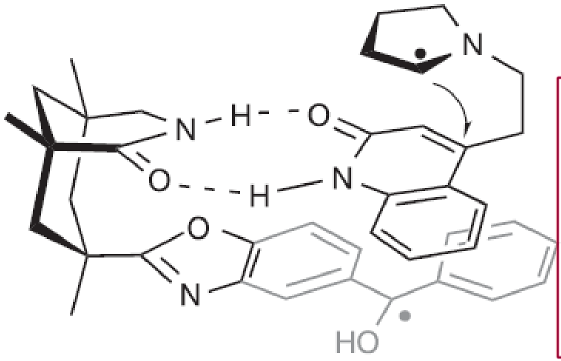
6

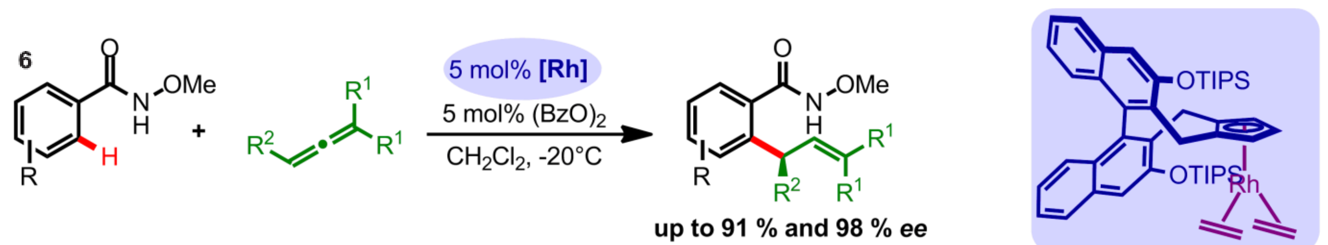


How to obtain (R,S) or (S,R)?

Bauer, A.; Westkamper, F.; Grimme, S.; Bach, T. *Nature* **2005**, *436*, 1139.

Enantioselective Photoreactions with Chiral catalyst

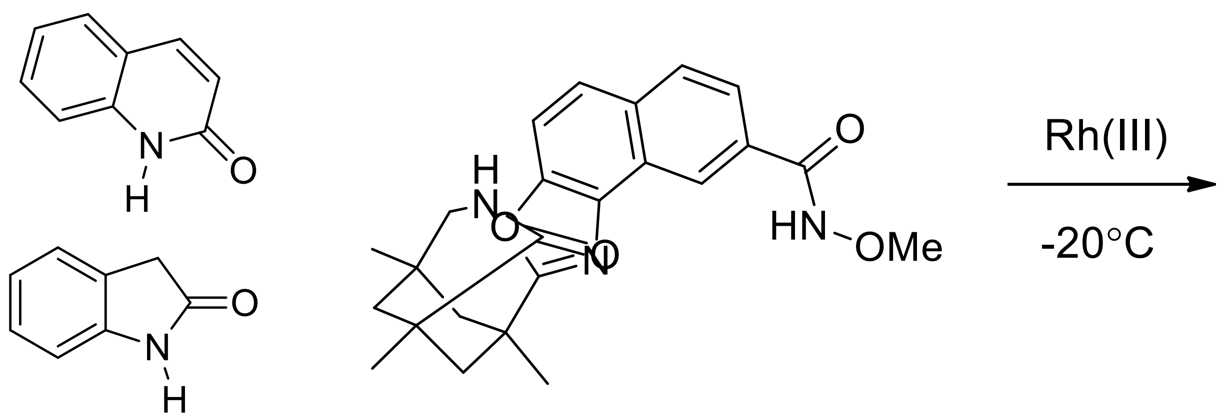




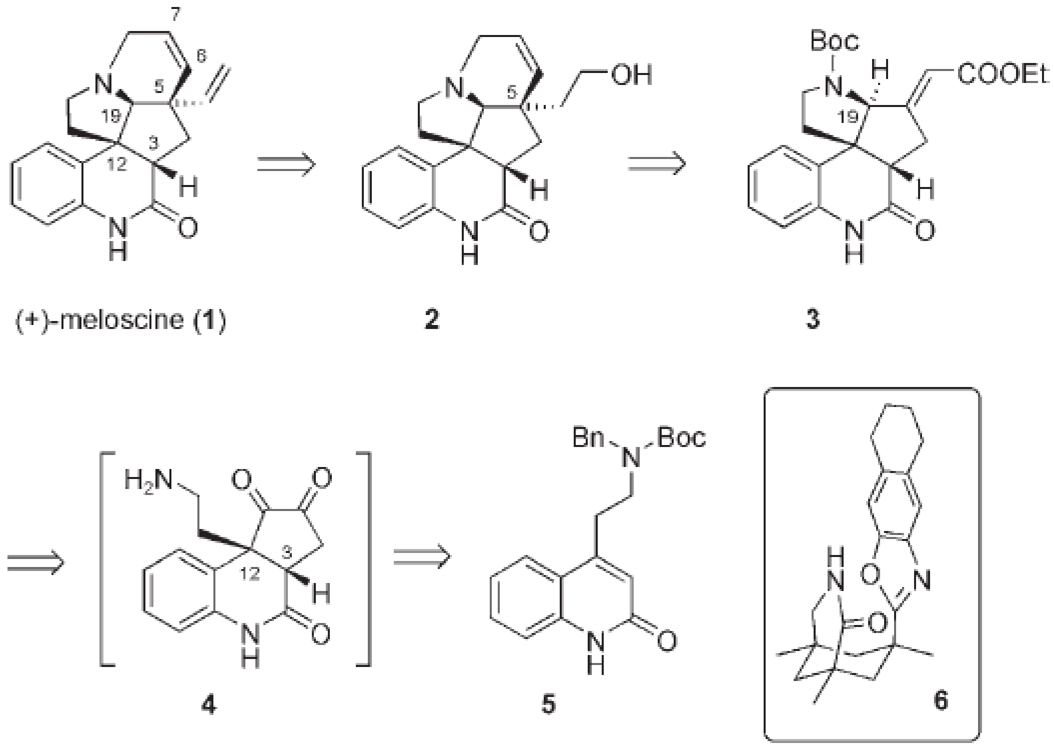
Bauer, A.; Westkamper, F.; Grimme, S.; Bach, T. *Nature* **2005**, *436*, 1139.

B. Ye, N. Cramer, *J. Am. Chem. Soc.* **2013**, *135*, 636-639

What will happen if we combine this template and directing group ?

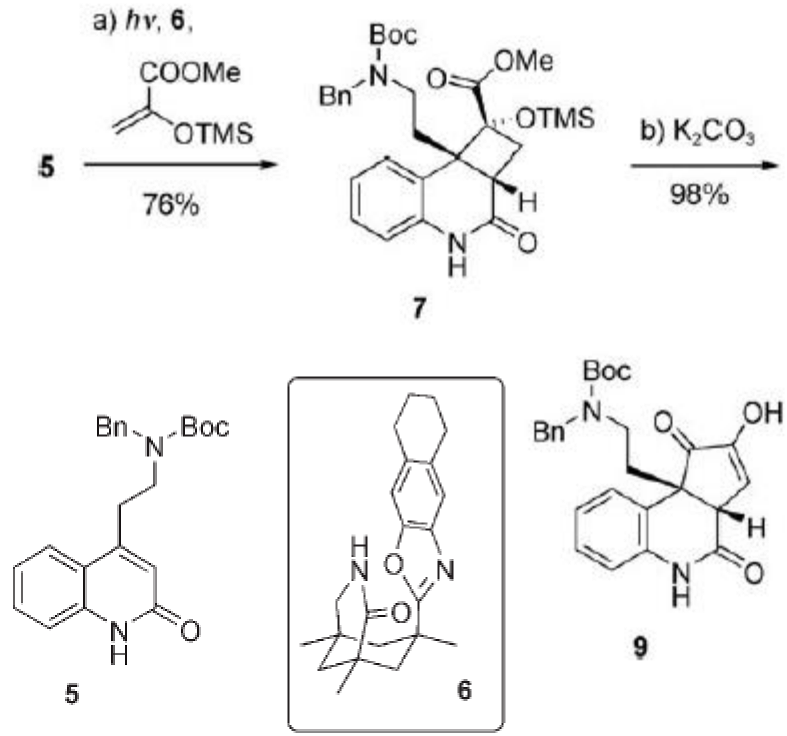


Enantioselective Photoreactions with Chiral catalyst



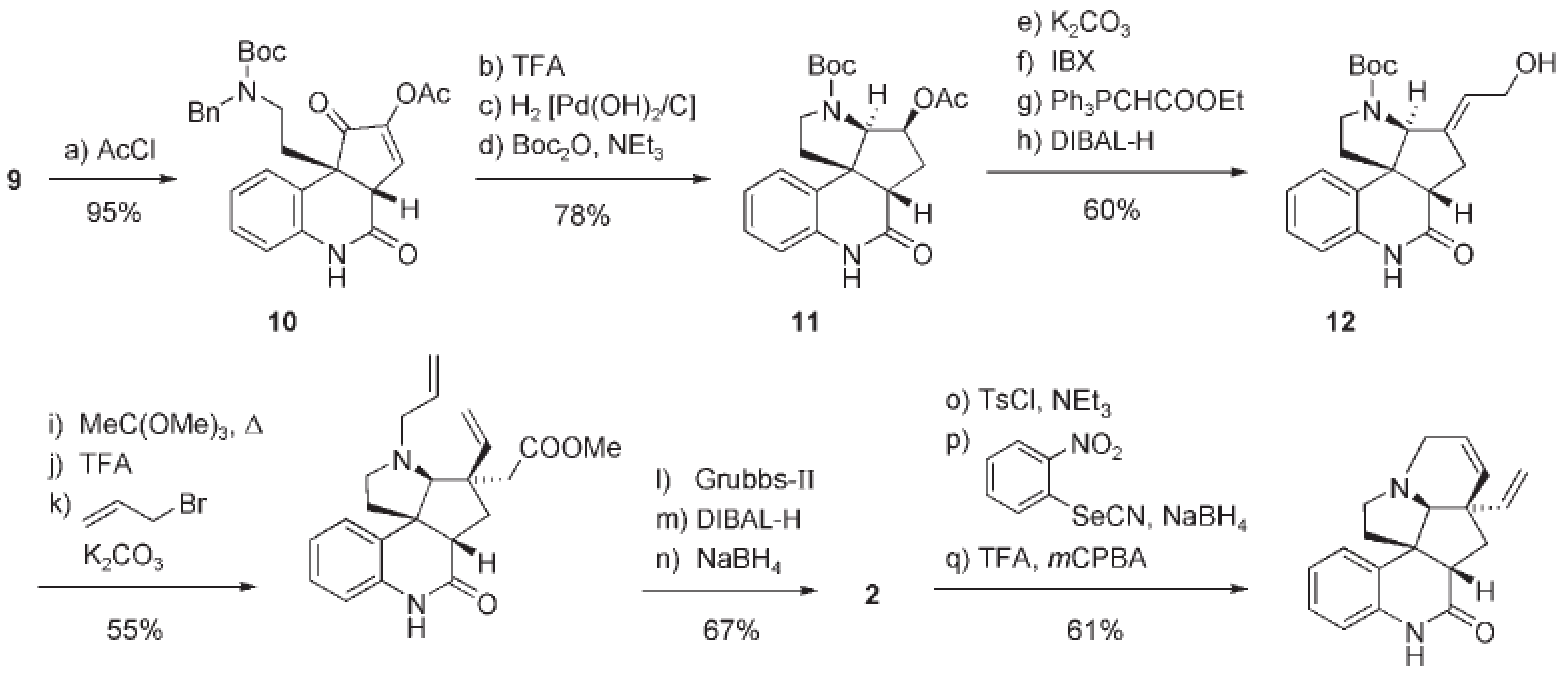
P. Selig, T. Bach, *Angew. Chem. Int. Ed.* **2008**, *47*

Enantioselective Photoreactions with Chiral catalyst



P. Selig, T. Bach, *Angew. Chem. Int. Ed.* **2008**, *47*

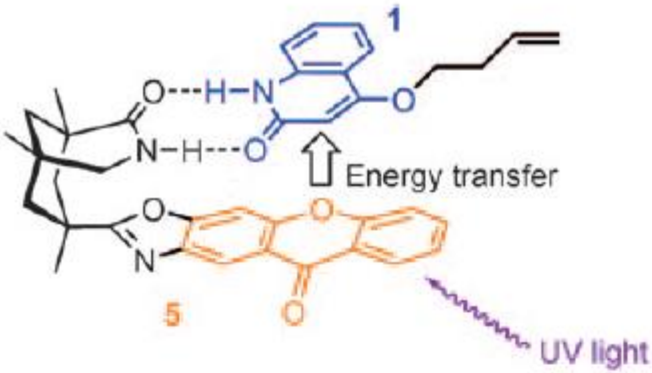
Enantioselective Photoreactions with Chiral catalyst

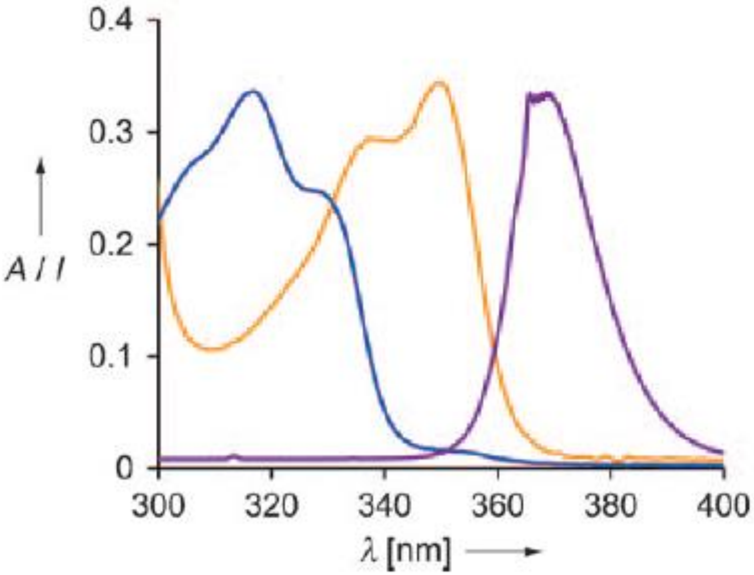


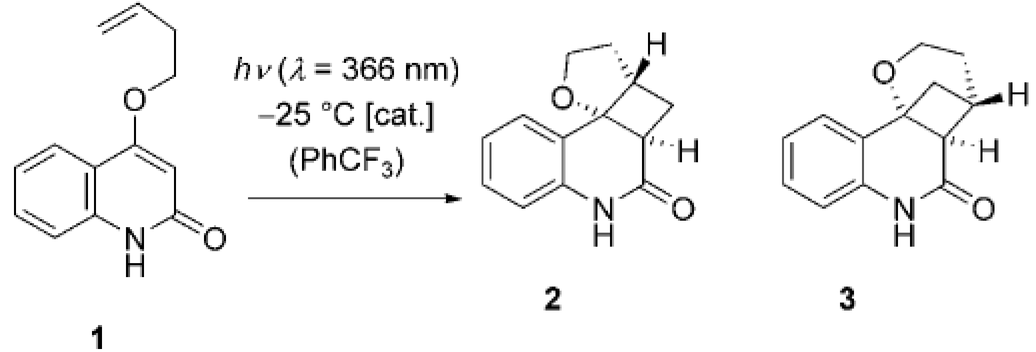
15 steps from 5， 7% overall yield (Overman racemic 24 steps)

P. Selig, T. Bach, *Angew. Chem. Int. Ed.* **2008**, *47*

Enantioselective Photoreactions with Chiral catalyst



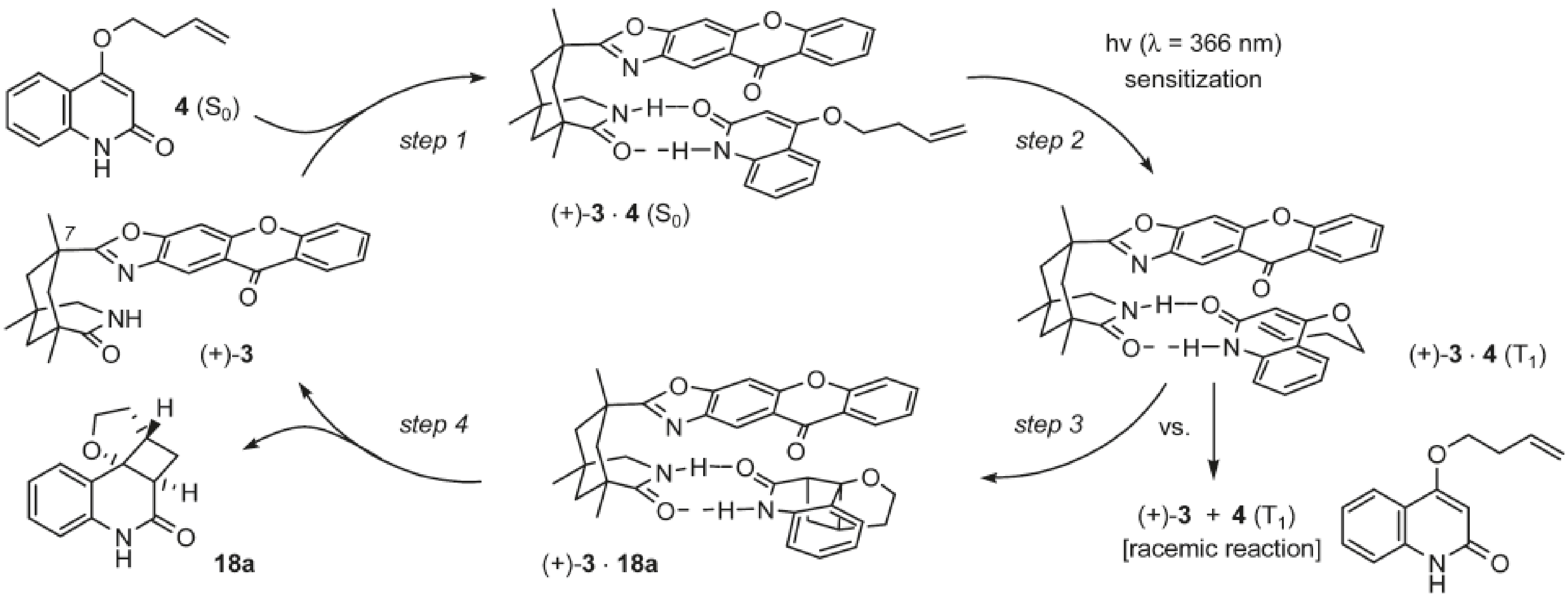




5% **5** conv=50% brsm=98% **2**/**3**=78/22 90%ee
20% **5** conv=73% brsm=78% **2**/**3**=79/21 94%ee

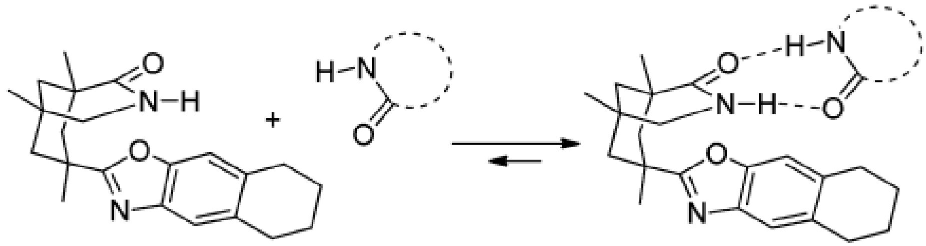
C. Muller. A. Bauer, T. Bach. *Angew. Chem. Int. Ed.* ***2009****, 48, 6640 –6642*

Enantioselective Photoreactions with Chiral catalyst

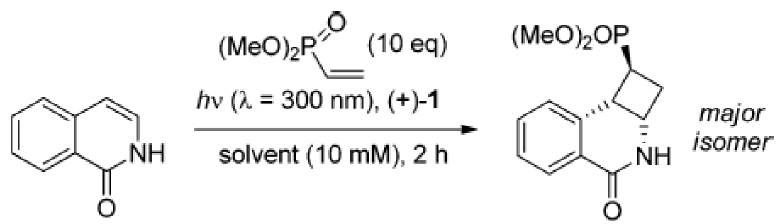


C. Müller, A. Bauer, M. M. Maturi, M. C. Cuquerella, M. A. Miranda, T. Bach, *J. Am. Chem. Soc.* **2011**, *133*, 16689–16697.

Enantioselective Photoreactions with Chiral catalyst



(+)-1

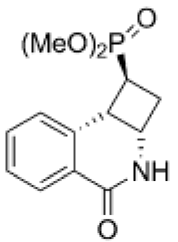


2 3a

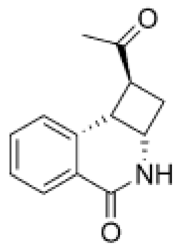
entry	T (°C)	solvent	(+)-1 (equiv)	yield (%)[a]	isomer ratio[b]	ee (%)[c]
1	rt	PhMe	–	75	3:1[d]	–
2	rt	PhMe	2.5	78	5:1[d]	26
3	rt	$PhCF_3$	2.5	74	5:1[d]	36
4	0	$PhCF_3$	2.5	83	4:1[d]	62
5	−20	$PhCF_3$	2.5	86	5:1[d]	70
6	−40	$PhCF_3$	2.5	95	5:1[d]	80
7	−40	PhMe	2.5	95	12:1[d]	72
8	−60	PhMe	2.5	97	12:1	90
9	−60	PhMe	1.5	99	12:1	84
10	−75	PhMe	2.5	93	16:1	93
11	−75	PhMe	1.5	95	16:1	86

S. C. Coote, T. Bach, *J. Am. Chem. Soc.* **2013**, *135*, 14948-14951.

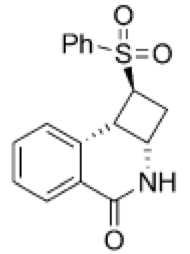
Enantioselective Photoreactions with Chiral catalyst



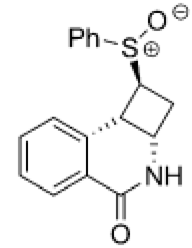
3a
93% (i.r. 16:1)
93% ee



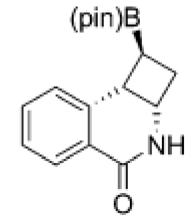
3b
90% (i.r. >20:1)
96% ee



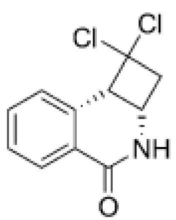
3c
98% (i.r. >20:1)
99% ee



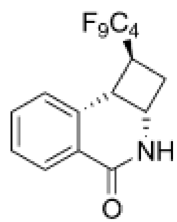
3d
95% (i.r. >20:1)[a]
96% ee[a]



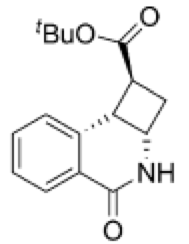
3e
86% (i.r. >20:1)[b]
98% ee[b]



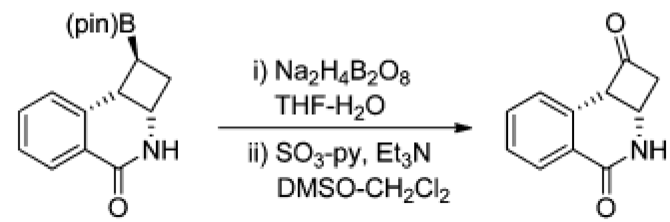
3f
92% (i.r. >20:1)
98% ee



3g
93% (i.r. >20:1)
88% ee



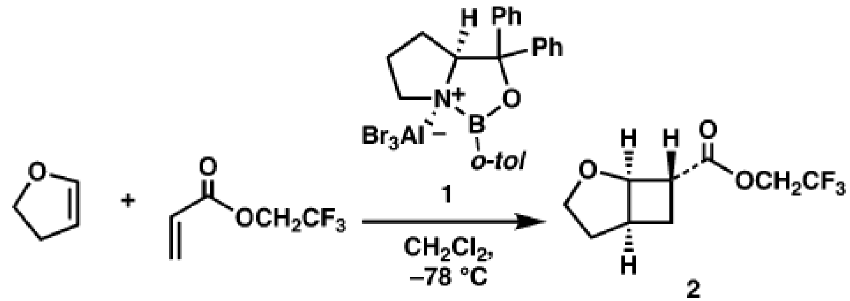
3h
93% (i.r. >20:1)
98% ee

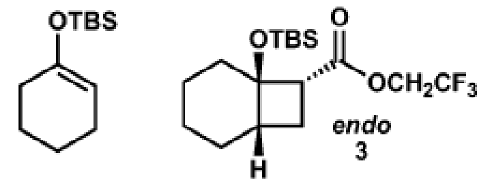
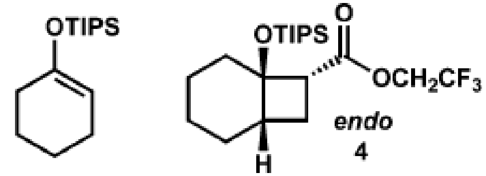
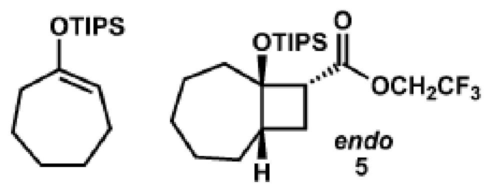
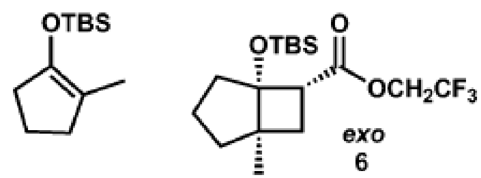


3e → **5**
81% (3 steps)
r.r. >20:1, 98% ee

S. C. Coote, T. Bach, *J. Am. Chem. Soc.* **2013**, *135*, 14948-14951.

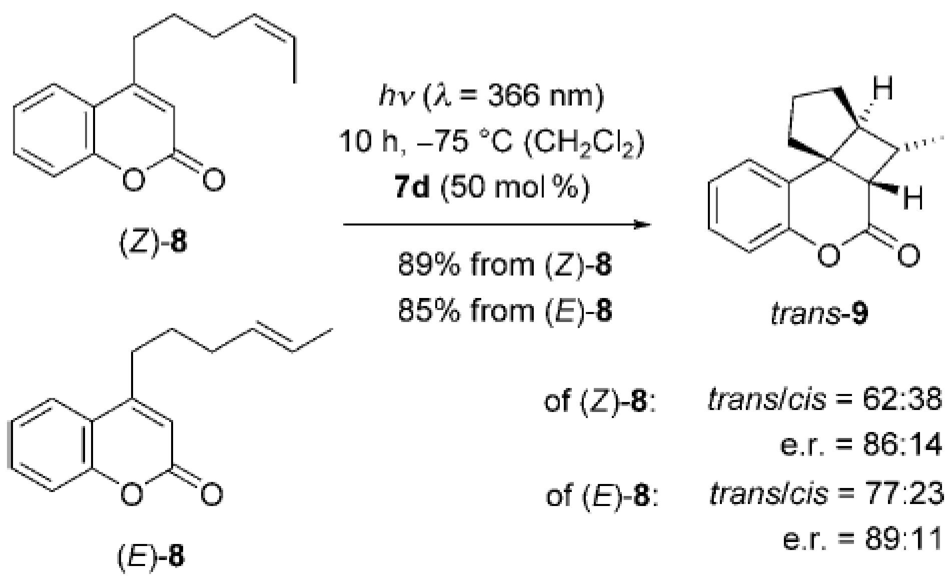
Enantioselective Photoreactions with Chiral catalyst

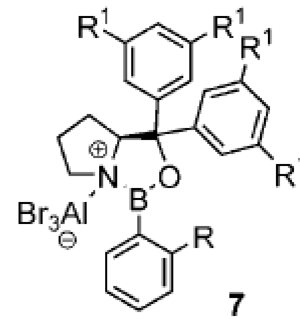


(2)	 endo 3	6	97 (82:18)	92[a]
(3)	 endo 4	12	99 (97:3)	92[b]
(4)	 endo 5	6	99 (99:1)	99[b]
(5)	 exo 6	0.5	99 (1:99)	98[a]

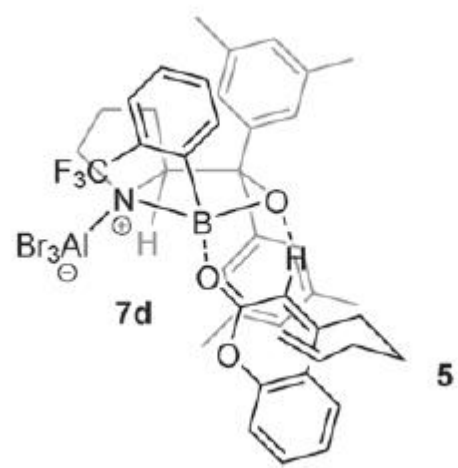
E. Canales. E. J. Corey *J. Am. Chem. Soc*. **2007**, *129,* 12686-12687

Enantioselective Photoreactions with Chiral catalyst



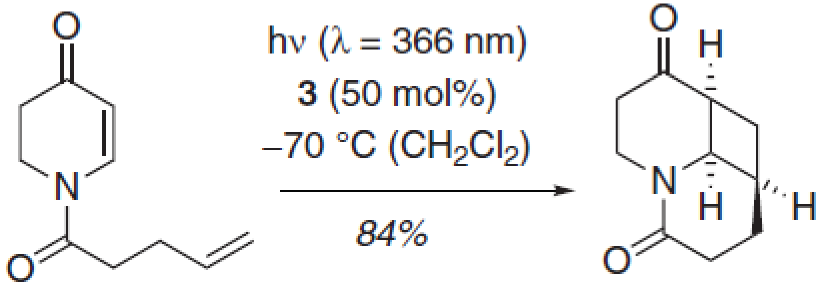


7d: R=CF_3 R1=Me

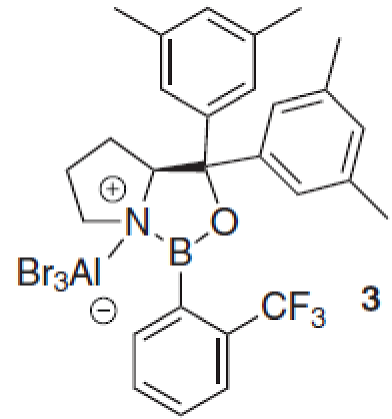


H. Guo, E. Herdtweck T. Bach. *Angew. Chem. Int. Ed.* ***2010****, 49, 7782 – 7785*

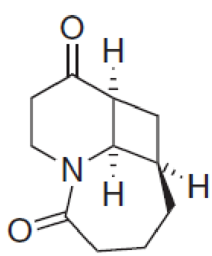
Enantioselective Photoreactions with Chiral catalyst



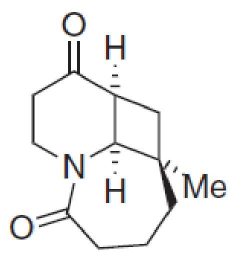
1 → **2** (88% *ee*)



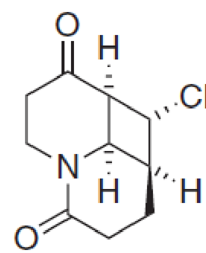
3



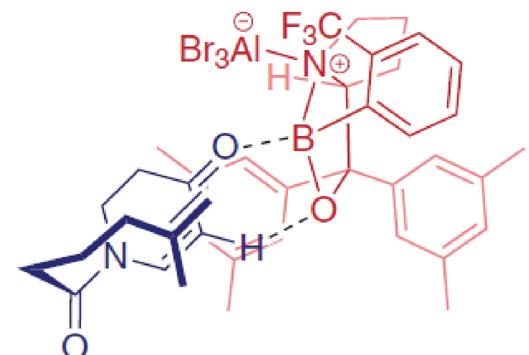
7
84% (90% *ee*)



8
83% (81% *ee*)



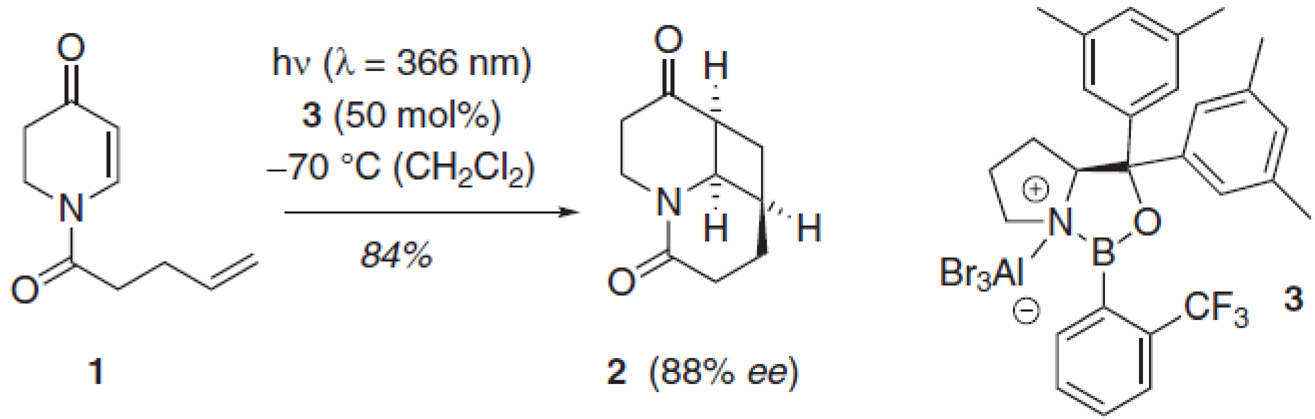
9
83% (82% *ee*)

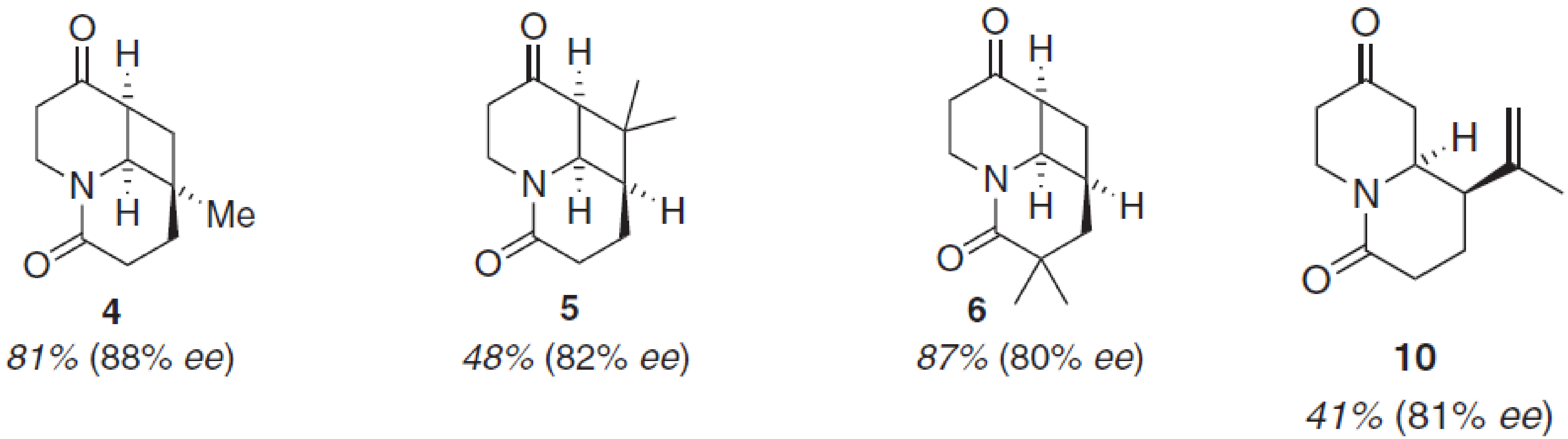


12·3

R. Brimioulle, T. Bach, *Science* **2013**, *342*, 840-843

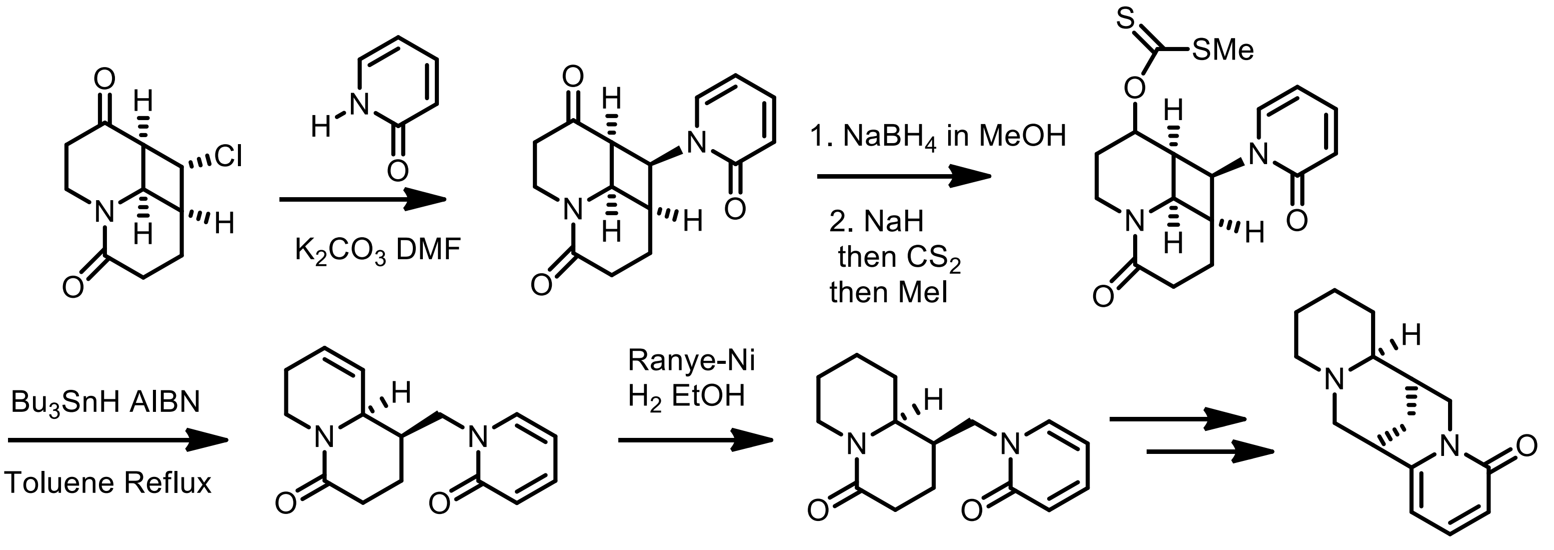
Enantioselective Photoreactions with Chiral catalyst





R. Brimioulle, T. Bach, *Science* **2013**, *342*, 840-843

Enantioselective Photoreactions with Chiral catalyst



R. Brimioulle, T. Bach, *Science* **2013**, *342*, 840-843

Conclusion

- The direct CPL introduce the ee: Low yield and low ee.
- The Soai reaction combine CPL and auto-tamden-catalysis: very Limited substrate
- Diastereoseletive Photoreactions with Chiral Auxiliaries : Not effective compared with Macmillan's SOMO system.
- Enantioselective Photoreactions with Chiral catalyst: Extremely High loading and limited substrate.

All in all there is a great potential room to be improved!