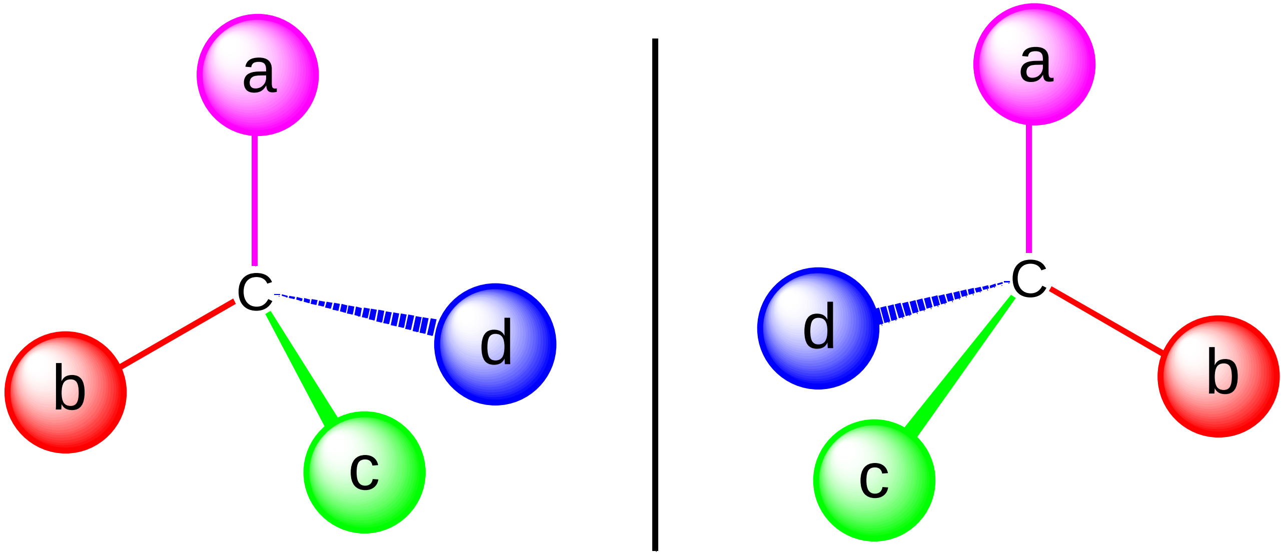
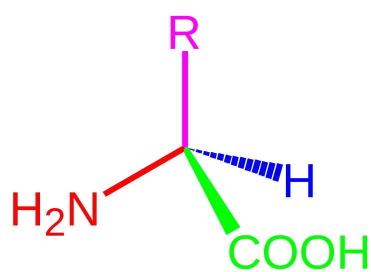
ELSI 1st Symposium
Tokyo Tech, Tokyo
March 27-29, 2013

Asymmetric Autocatalysis and the Origin of Homochirality of Biomolecules

Kenso Soai
Department of Applied Chemistry
Tokyo University of Science
soai@rs.kagu.tus.ac.jp

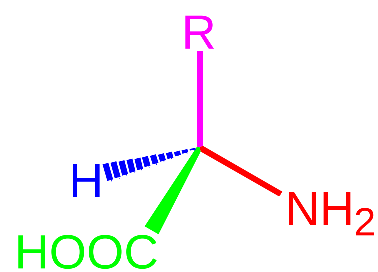
Molecular Asymmetry





L-Amino Acid

Natural



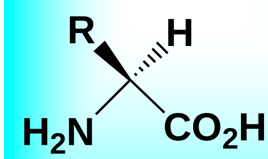
D-Amino Acid

Unnatural

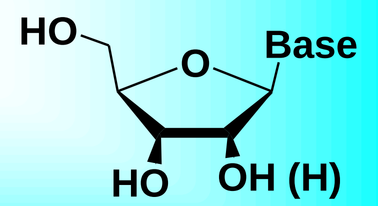
Origins of Chiral Homogeneity of Biomolecules

Why and when did biomolecules become highly enantiomerically enriched ?

Homochirality



L-amino acid



D-sugar

?

Chiral organic compound
with low enantiomeric excess

Asymmetric autocatalysis with amplification of ee

Asymmetric induction

Origins of chirality (proposed)
Circularly polarized light
Chiral inorganic crystal: Quartz

Text books tell:

Without any chiral catalyst or ligand, the probability of the formation of *S* and *R* enantiomers is 1 : 1, the product is racemate containing the equal amounts of *S* and *R* enantiomers.

To synthesize enantioenriched compounds, one needs to use asymmetric (chiral) catalyst or ligand.

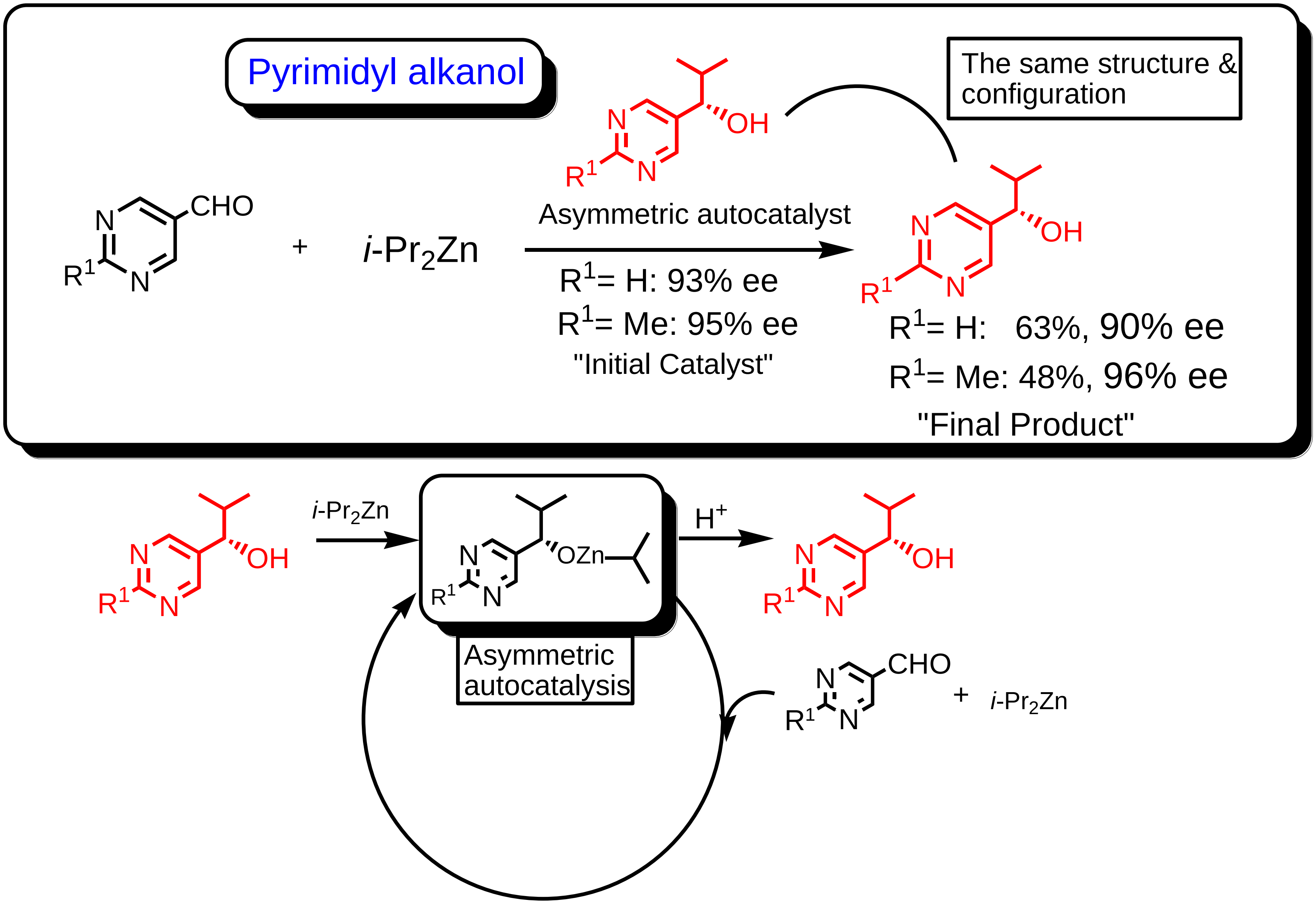
Asymmetric catalysis

$$A + B \xrightarrow[\text{asymmetric cat.}]{C^*} D^*$$

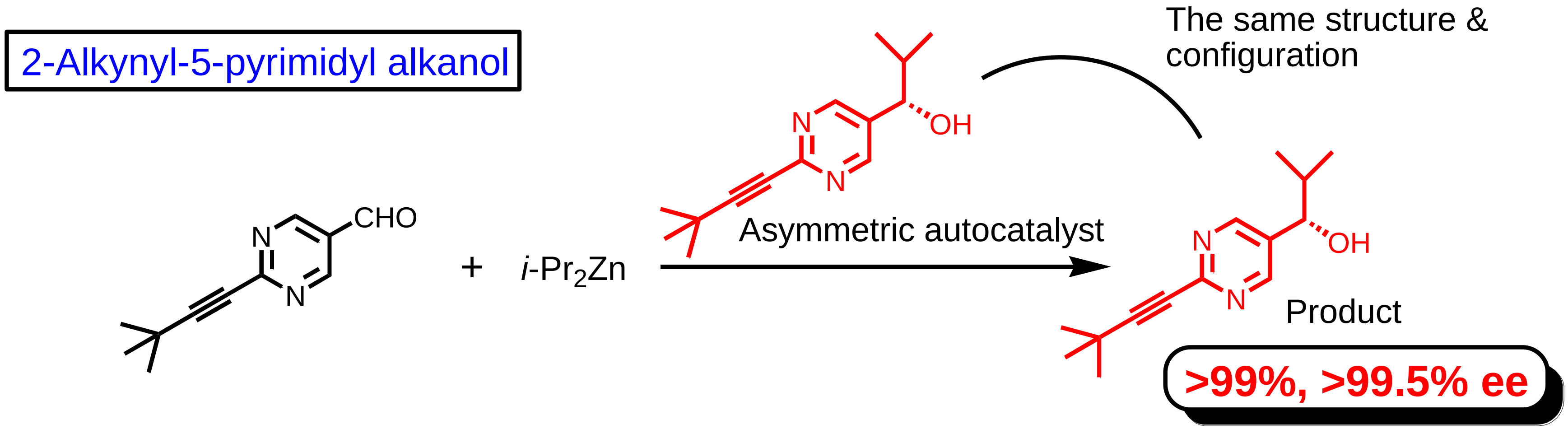
$$\frac{|R - S|}{R + S} \times 100$$

% enantiomeric excess (ee)	Ratio of enantiomers	
99	99.5	0.5
90	95	5
50	75	25
2	51	49
0 (racemate)	50	50

Highly Enantioselective Asymmetric Autocatalysis



Practically Perfect Asymmetric Autocatalysis



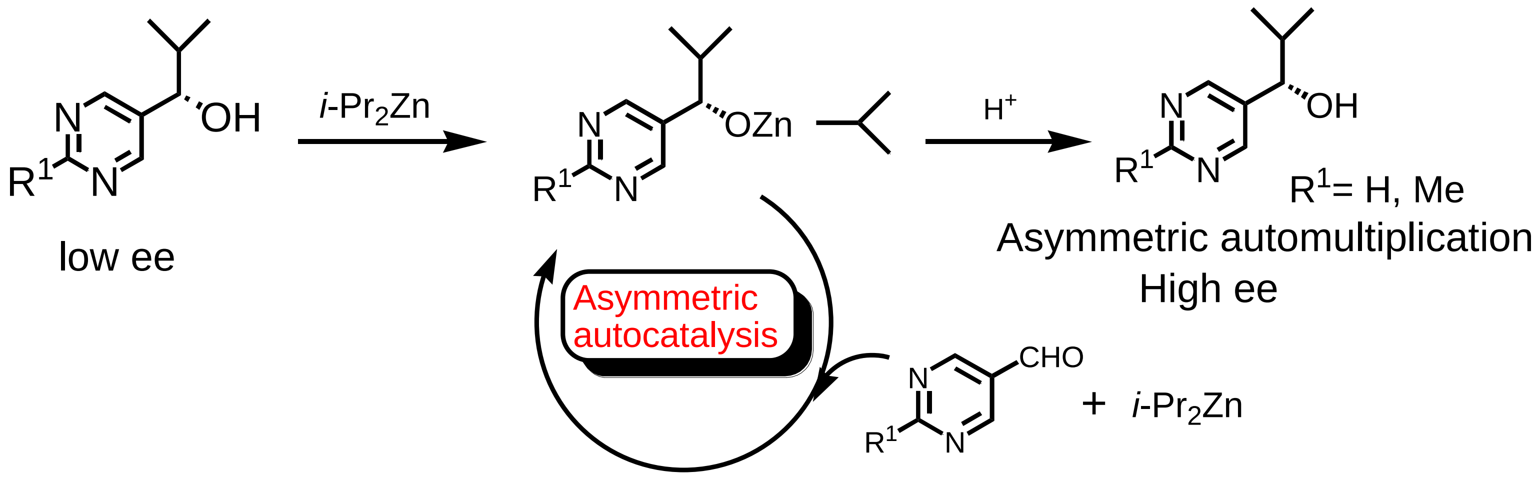
Consecutive Asymmetric Autocatalysis

	Asymm. autocat. (% ee)	Product Yield(%)	Product ee(%)	Factor of multiplication
1	>99.5	>99	>99.5	
2	>99.5	>99	>99.5	
3	>99.5	>99	>99.5	
4	>99.5	>99	>99.5	
5	>99.5	>99	>99.5	
6	>99.5	>99	>99.5	
7	>99.5	>99	>99.5	
8	>99.5	>99	>99.5	
9	>99.5	>99	>99.5	
10	>99.5	>99	>99.5	*ca.* 6×10^7 times

Molar ratio: aldehyde : *i*-Pr_2Zn : catalyst = 1.0 : 1.7 : 0.2

Asymmetric Autocatalysis with Amplification of Enantiomeric Excess

Amplification of ee without the need for any other chiral auxiliary



Consecutive asymmetric autocatalysis with amplification of ee (R1= H)

Run	Asym. autocat. (% ee)	Asym. autocat. & Product Yield (%)	Asym. autocat. & Product (% ee)
1	2	46	10
2	10	75	57
3	57	80	81
4	81	75	88
5	88	79	88

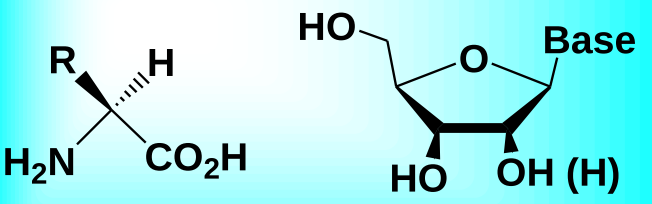
2% ee → 88% ee

Soai, K.; Shibata, T.; Morioka, H.; Choji, K. *Nature*, **1995**, *378*, 767.

Origins of Chiral Homogeneity of Biomolecules

Why and when did biomolecules become highly enantiomerically enriched ?

Homochirality



L-amino acid **D-sugar**

?

Asymmetric autocatalysis with amplification of ee

Chiral organic compound
with low enantiomeric excess

Asymmetric induction

Origins of chirality (proposed)
Circularly polarized light
Chiral inorganic crystal: Quartz

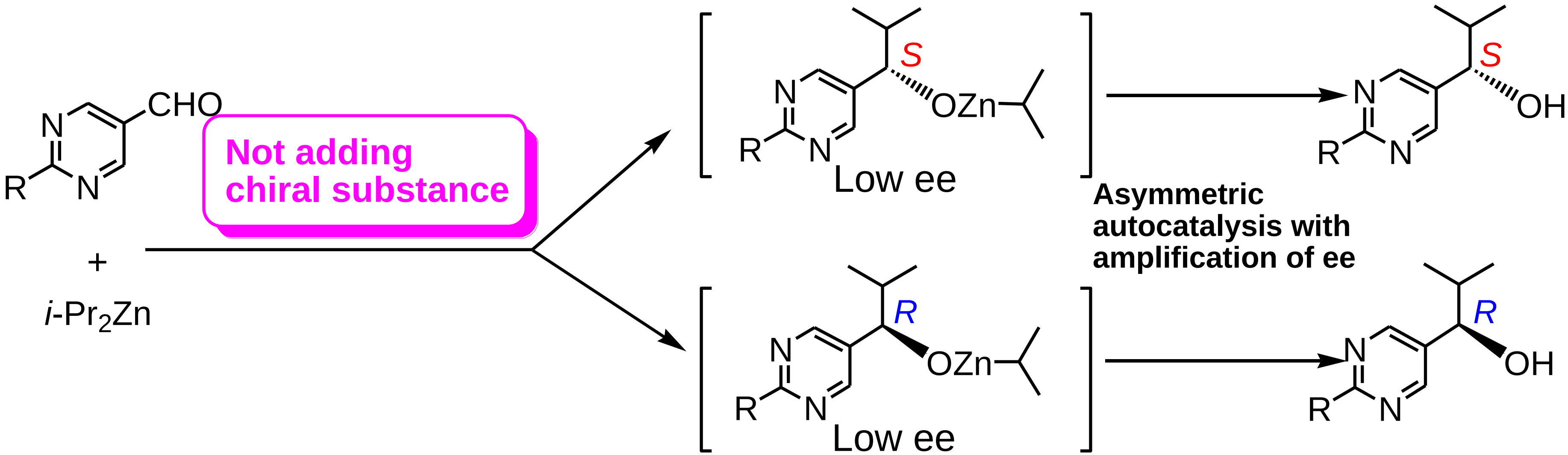
Origins of Homochirality of Organic Compounds

Examination in Conjunction with Asymmetric Autocatalysis

- Circularly polarized light
- Chiral organic crystals formed from achiral compounds
- Achiral organic crystal formed from achiral compound
- Chiral inorganic crystals: Quartz, Sodium chlorate
- Spontaneous absolute asymmetric synthesis

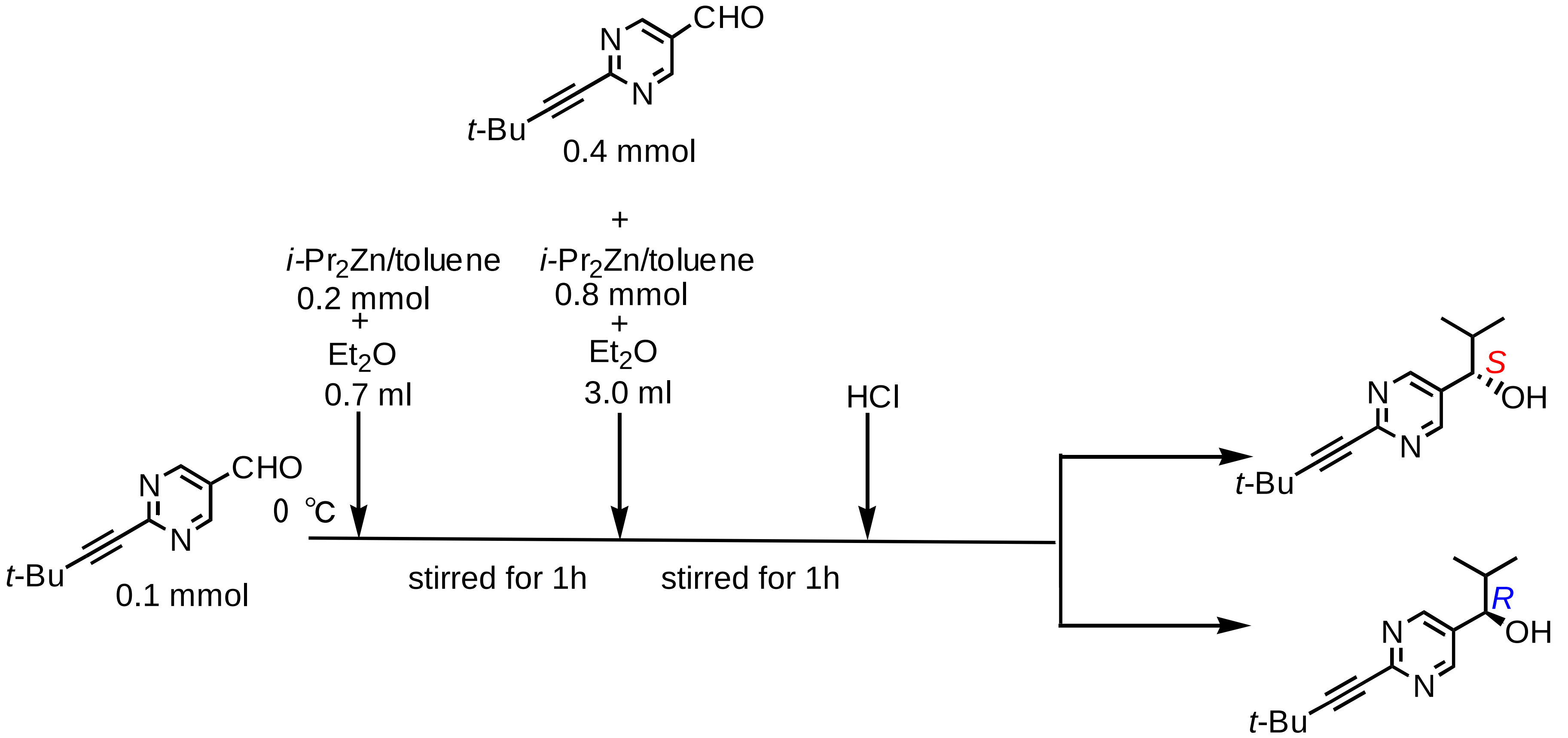
Spontaneous Absolute Asymmetric Synthesis

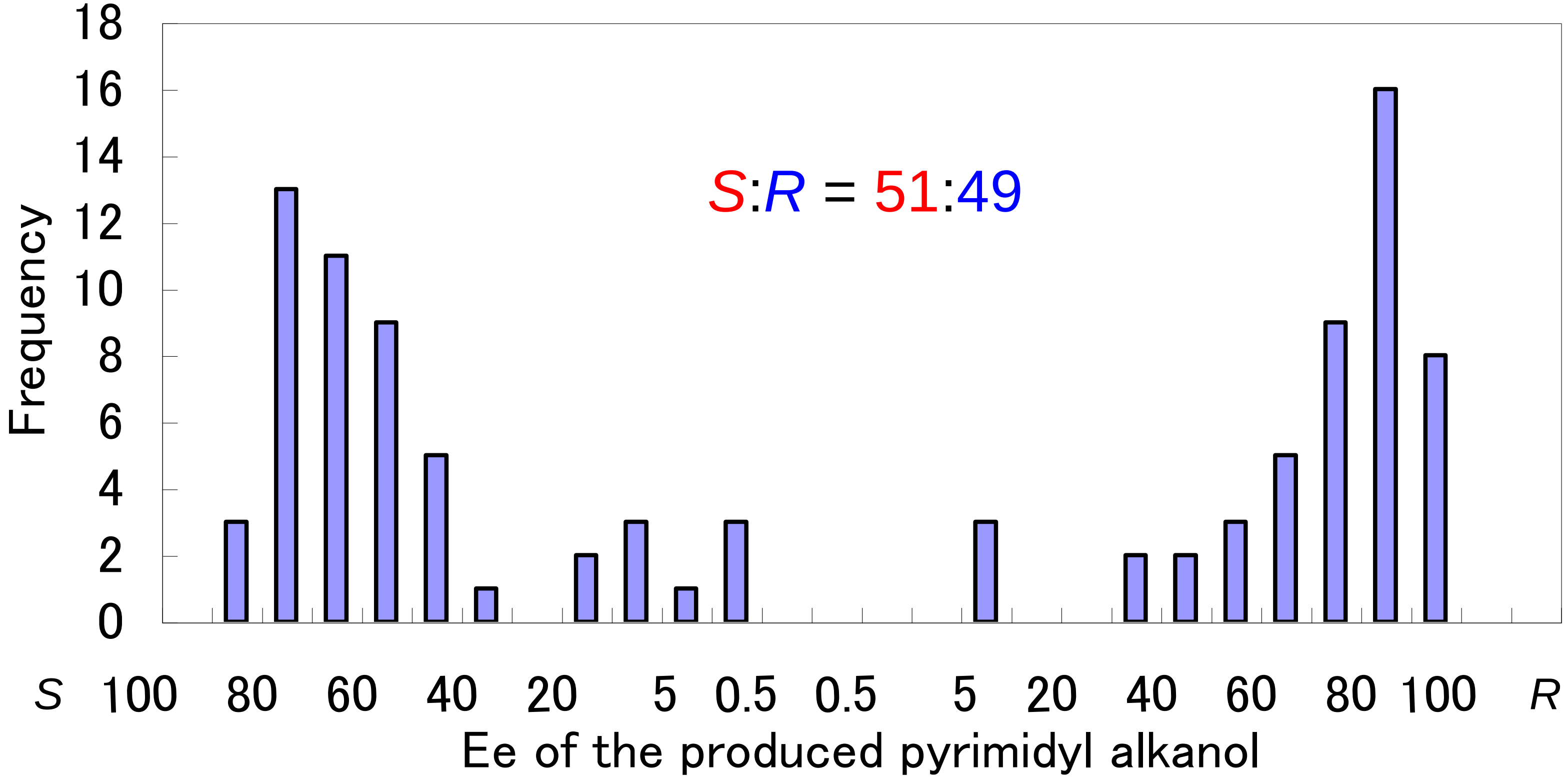
Asymmetric Autocatalysis of Pyrimidyl Alkanol without Adding Chiral Substance



K. Soai, T. Shibata, Y. Kowata, Japanese Patent, (1997) 9268179.

Asymmetric synthesis of Pyrimidyl Alkanol without Adding Chiral Substance in Conjuction with Asymmetric Autocatalysis in a Mixed Solvent of Diethyl Ether and Toluene

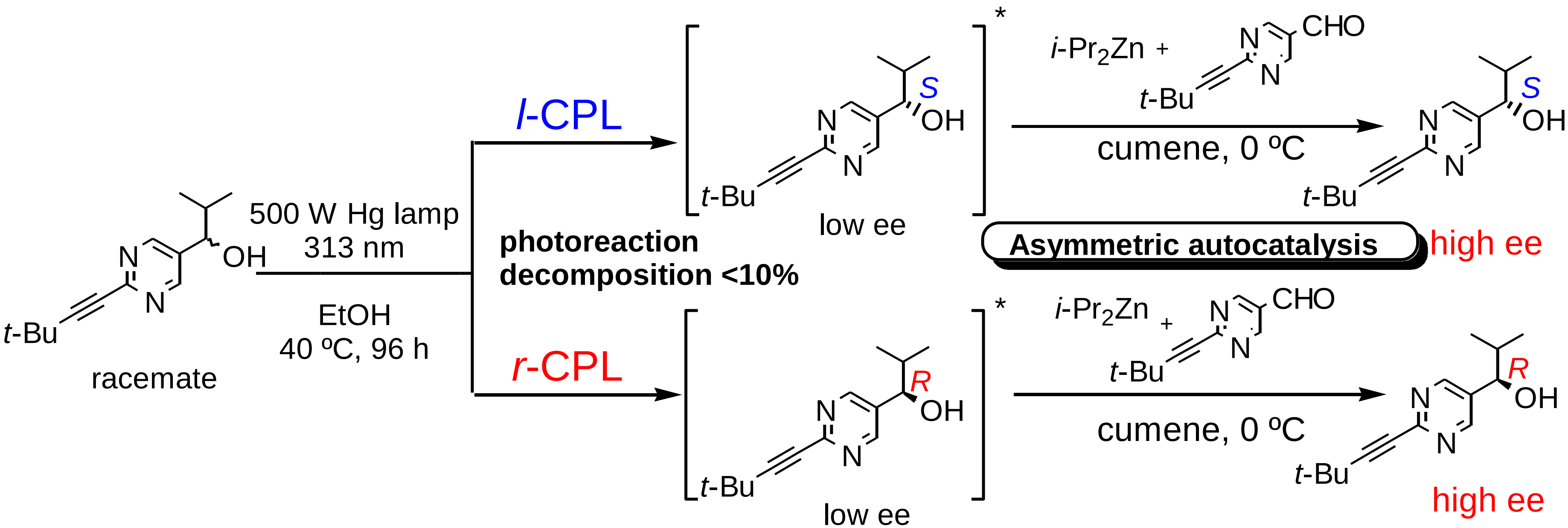




Distribution of (*S*)–and (*R*)–pyrimidyl alkanol is almost stochastic

Direct Irradiation of Circularly Polarized Light to Asymmeric Autocatalysis

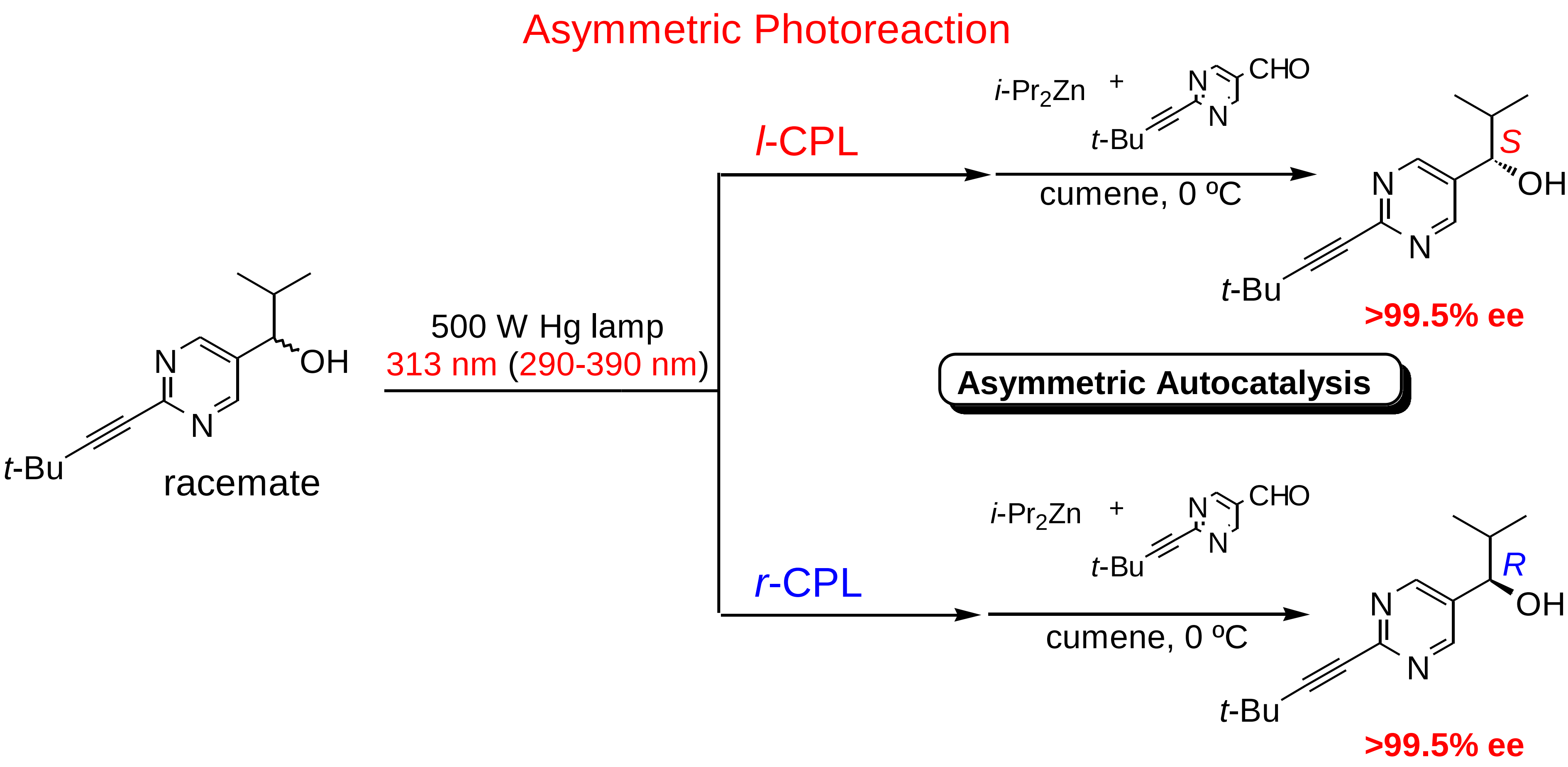
Asymmetric Autocatalysis of Pyrimidyl Alkanol Irradiated with *l*- or *r*-CPL (313 nm)



Entry	CPL	5-pyrimidyl alkanol		
		Yield/ %	ee/ %	config.
1	*l*	95	85	*S*
2	*r*	97	82	*R*
3	*l*	97	60	*S*
4	*r*	98	65	*R*

Entry	CPL	5-pyrimidyl alkanol		
		Yield/ %	ee/ %	config.
5	*l*	92	65	*S*
6	*r*	90	56	*R*
7	*l*	95	62	*S*
8	*r*	94	70	*R*

Direct Relationship Between CPL and Organic Compound with High ee



Enantioselective Synthesis of Pyrimidyl Alkanol in the Presence of *d*- or *l*-Quartz

Run	Quartz		Pyrimidyl alkanol	
			Yield (%)	ee(%)(config.)
Series A				
A1	*d*	(4.4 μm)	90	89 (*S*)
A2	*l*	(7.6 μm)	97	85 (*R*)
A3	*d*		88	86 (*S*)
A4	*l*		96	84 (*R*)
Series B				
B1	*l*		97	95 (*R*)
B2	*l*		97	93 (*R*)
B3	*d*		96	95 (*S*)
B4	*d*		97	95 (*S*)
Series C				
C1	*d*		93	97 (*S*)
C2	*l*		97	97 (*R*)
C3	*l*		95	97 (*R*)
Series D				
D1	*l*	(3.4 μm)	95	93 (*R*)
D2	*d*	(2.9 μm)	95	94 (*S*)

For Series B-D, quartz (SiO_2) : aldehyde :*i*-Pr_2Zn = 1.9 : 1.0 : 2.0. Added in three portions.
For Series A, quartz (SiO_2) : aldehyde :*i*-Pr_2Zn = 8.0 : 1.0 : 2.5. Added in two portions.

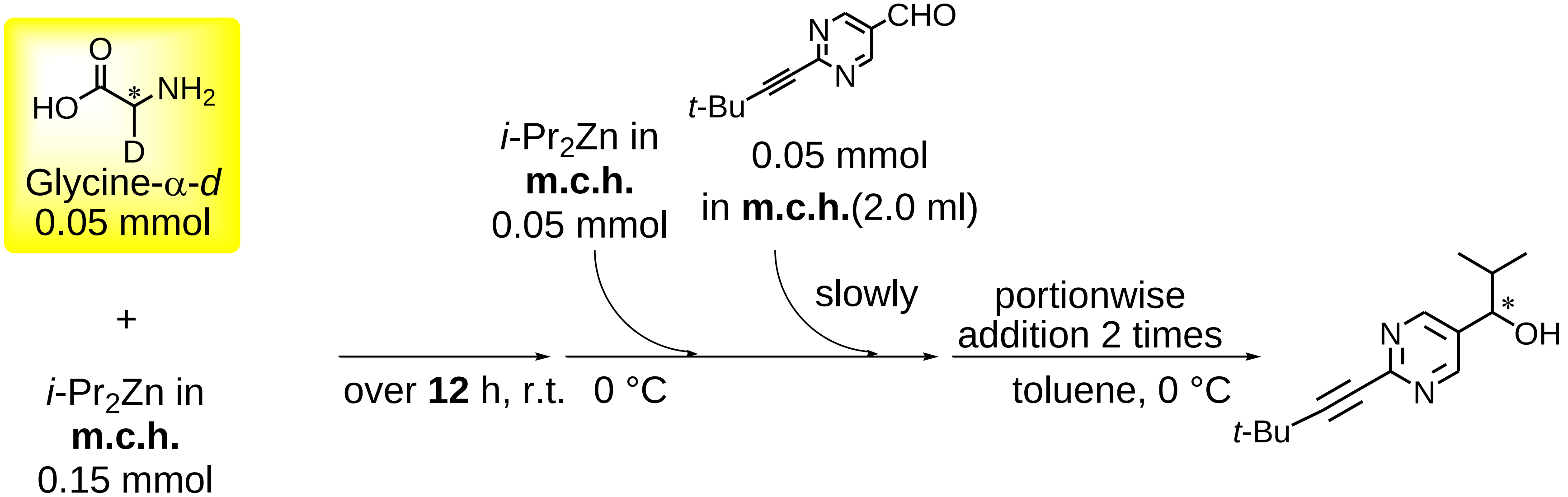
The Deuterium Enrichment of Amino acids in Carbonaceous Meteorites

Amino acid	Murchison δD(‰)	Murray δD(‰)
Glycine	—	399 ± 17
D-Alanine	429 ± 127	614 ± 61
α-Methylalanine	3058 ± 186	3097 ± 86
DL-Isovaline	3419 ± 118	3181 ± 108

δD of terrestrial compound is about 50

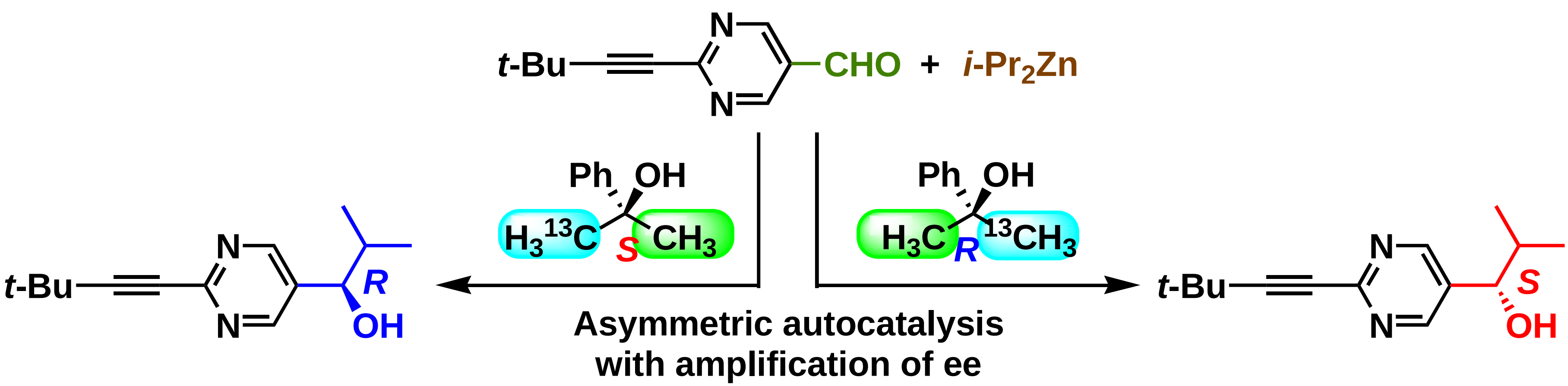
Pizzarello S.; Huang Y. *Geochim. Cosmochim. Acta* **2005**, *69*, 599.

Asymmetric Autocatalysis using Chiral Deuterated Glycine as Chiral Initiator



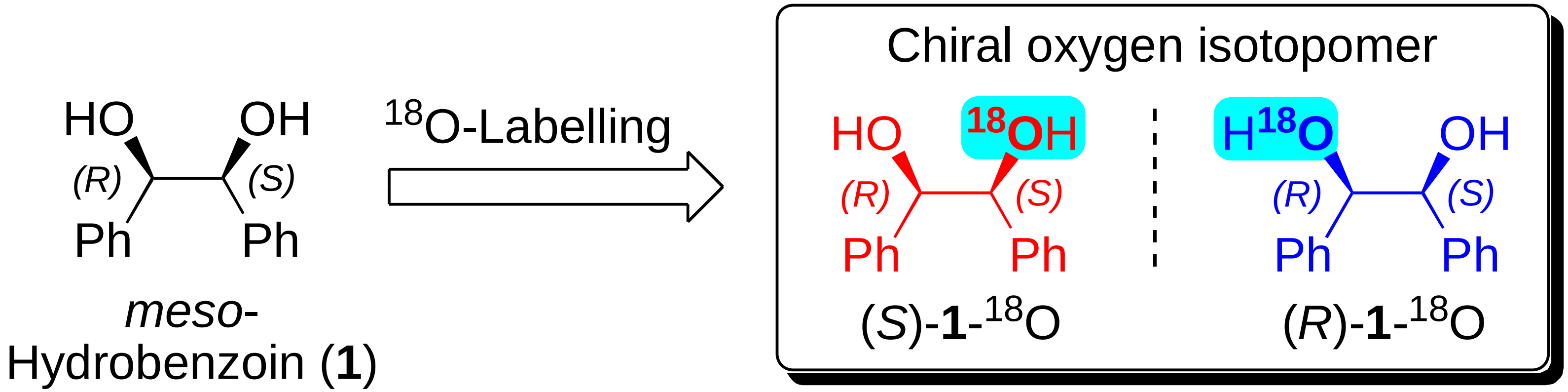
Entry	Glycine-*α*-*d*	Pyrimidyl alkanol		
		Yield(%)	ee(%)	Config.
1	***R***	90	91	***R***
2	***S***	94	96	***S***
3	***R***	94	93	***R***
4	***S***	95	93	***S***
5	***R***	94	91	***R***
6	***S***	94	94	***S***

Asymmetric Autocatalysis Triggered by Carbon Isotopically Chiral Alcohol

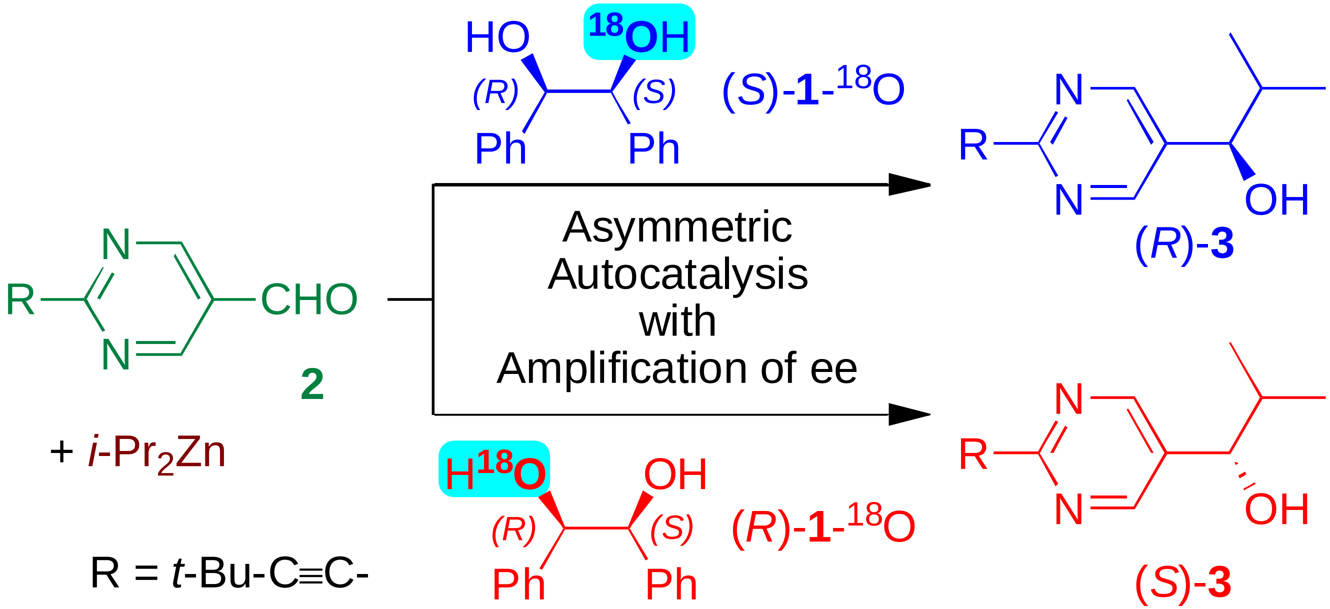


Entry	^{12}C/^{13}C-Chiral Alcohol		Pyrimidyl alkanol		
	Config.	ee (%)	Yield (%)	ee (%)	Config.
1	*R*	89	96	88	*S*
2	*S*	93	92	93	*R*
3	*R*	89	89	85	*S*
4	*S*	93	97	94	*R*
5	*R*	89	94	92	*S*
6	*S*	93	95	96	*R*

Generation of chirality by the oxygen isotope substitution

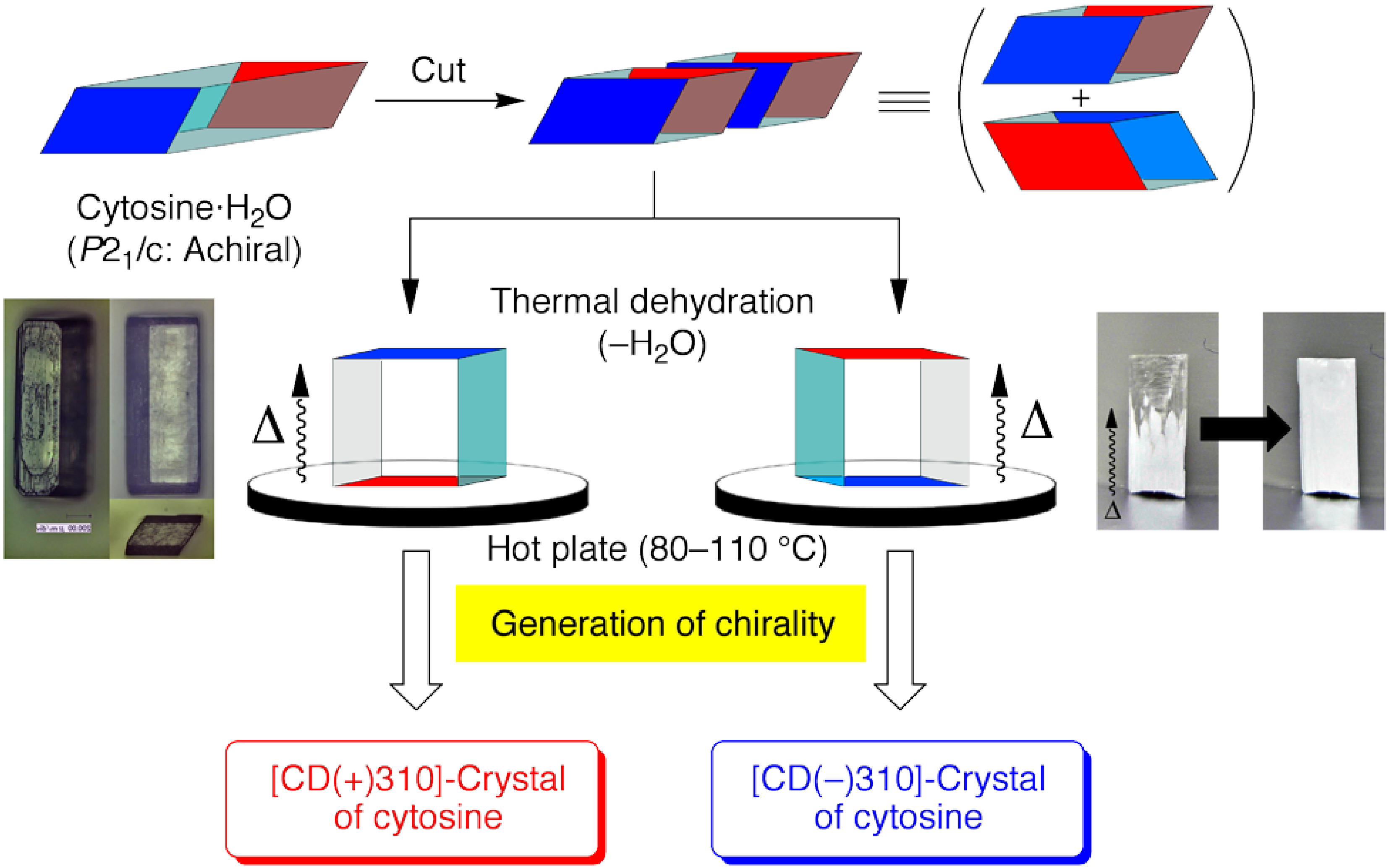


Asymmetric autocatalysis triggered by chiral oxygen isotopomer



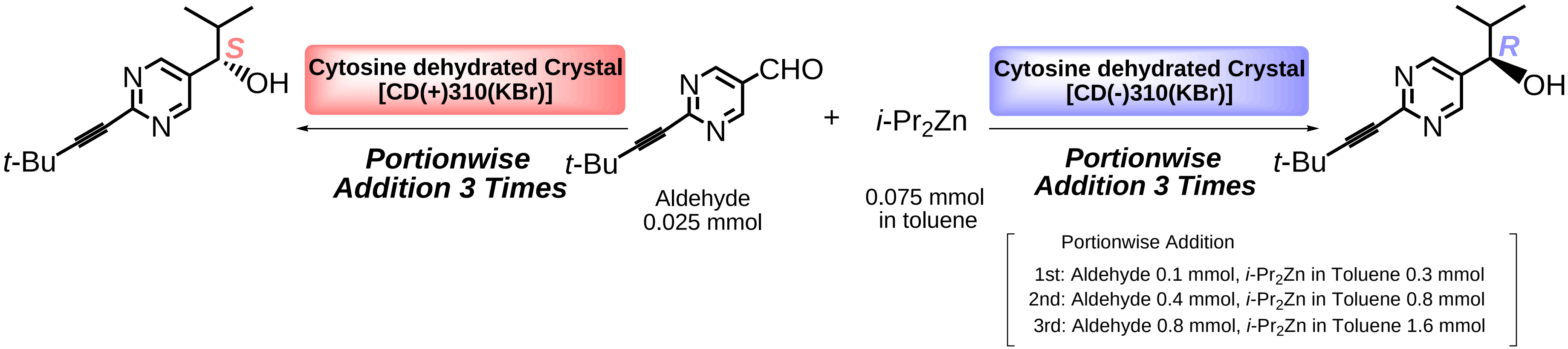
Entry	Chiral trigger		5-Pyrimidyl alkanol **2**		
		Sample#	Yield	ee	config.
1	(*S*)-**1**-^{18}O	#1	97	97	*R*
2	(*R*)-**1**-^{18}O	#2	96	89	*S*
3	(*S*)-**1**-^{18}O	#1	85	93	*R*
4	(*R*)-**1**-^{18}O	#2	93	91	*S*
5	(*S*)-**1**-^{18}O	#3	82	93	*R*
6	(*R*)-**1**-^{18}O	#4	94	96	*S*

Correlation Between Crystal Face and CD



Kawasaki, T.; Hakoda, Y, Mineki, H.; Suzuku, K.; Soai, K. *J. Am. Chem. Soc*. **2010**, *132*, 2874-2875.

Asymmetric Autocatalysis Initiated by Chiral Dehydrated Crystal of Cytosine

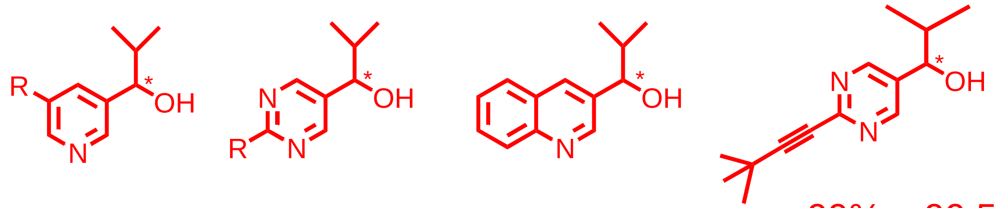


Entry	Chiral Initiator Crystal of Dehydrated Cytosine	Pyrimidyl Alkanol Yield (%)	Ee(%)	Config.
1	CD(+)310(KBr)	88	92	*S*
2	CD(-)310(KBr)	88	94	*R*
3	CD(+)310(KBr)	85	89	*S*
4	CD(-)310(KBr)	88	96	*R*
5	CD(+)310(KBr)	87	96	*S*
6	CD(-)310(KBr)	87	91	*R*
7	CD(+)310(KBr)	95	90	*S*
8	CD(-)310(KBr)	99	96	*R*
9 a)	CD(+)310(KBr)	88	>99.5	*S*
10 b)	CD(-)310(KBr)	90	>99.5	*R*

a) Additional 3 rounds of asymmetric autocatalysis.
b) Additional 4 rounds of asymmetric autocatalysis.

Summary

(I) Asymmetric autocatalysis

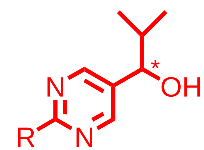


>99%, >99.5% ee

Practically perfect
asymmetric autocatalysis

(II) Asymmetric autocatalysis with amplification of ee

ca. 0.00005% ee —Asymmetric autocatalysis→ >99.5% ee



(III) Origin of homochirality of organic compound

Circularly polarized light → **Chiral compound with high ee**

Spontaneous asymmetric synthesis → Chiral compound with high ee

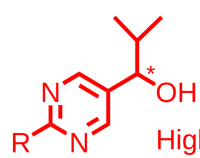
Inorganic chiral crystals → Chiral compound with high ee

d- and *l*-Quartz

d- and *l*-Sodium chlorate

Chiral silica → Chiral compound with high ee

aldehyde + *i*-Pr_2Zn →



High ee