150 Years of Strecker Reaction

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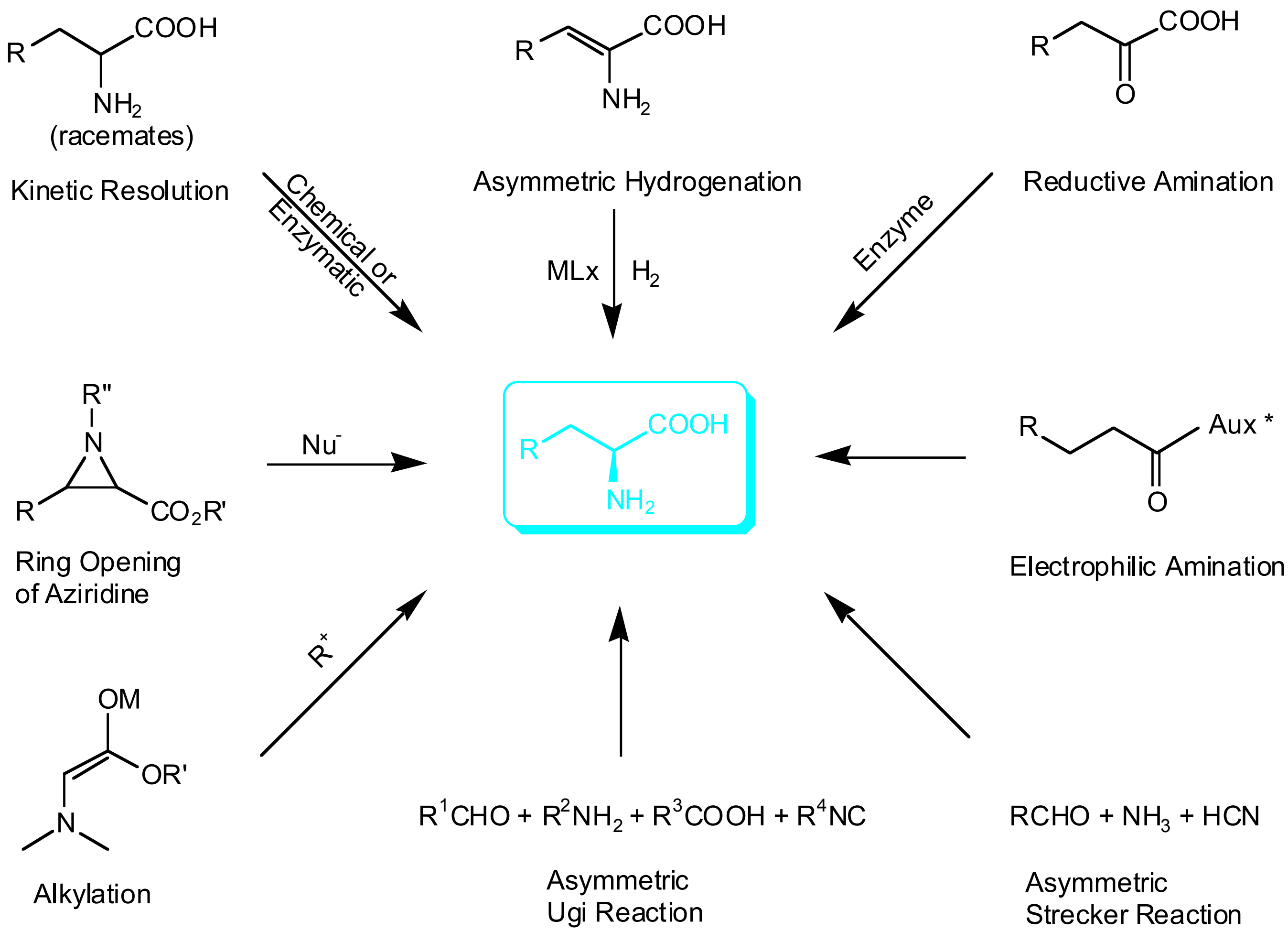
Michigan State University

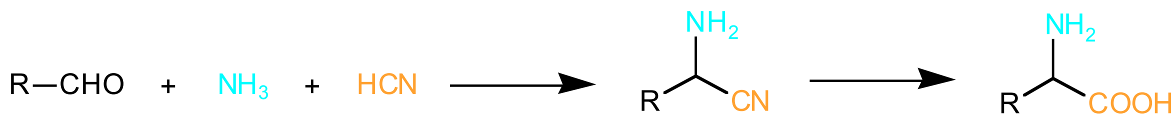
Different Methods of Preparation of Chiral α-amino acids



Duthaler, R. *Tetrahedron*. **1994**, *50*, 1539

Introduction to Strecker Reaction

♦ Classical Strecker synthesis of α-amino acids



"A completely different compound was formed upon the bring together of the aldehyde-ammonia adduct and hydrocyanic acid in the presence of acids."

In addition of chemical analysis of the new compound, characterized it physically:
"The larger crystals of alanine are mother-of-pearl-shiny, hard and crunch between the teeth."

-- Strecker, 1850

♦ Why Strecker reaction?

* Simple starting material, three components, efficient reaction.
* Catalytic asymmetric Strecker reaction still a new and hot area.
* Possibly the prebiotic process which produced amino acids on the primitive earth!

Strecker, A. *Ann. Chem. Pharm.* **1850**, *75*, 27
Miller, S. L. *Science*, **1953**, *117*, 528

Strecker Reaction - An Outline

I. Mechanism study of Strecker reaction.

II. Asymmetric Strecker reaction using chiral auxiliaries

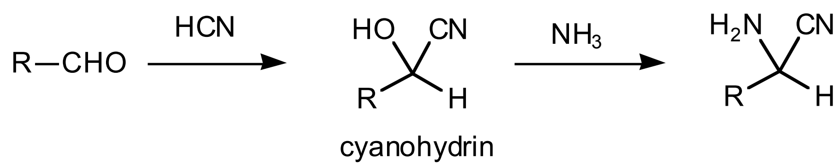
III. Catalytic asymmetric Strecker reaction

IV. Future work

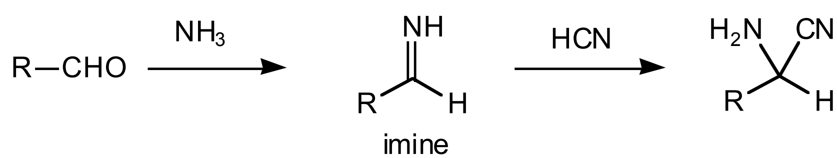
V. Conclusions

Mechanism Study of Strecker Reaction

♦ Cyanohydrin pathway



♦ Imine pathway



♦ The argument began around early 20th century.

-- Snyesarev vs. Stadnikov, 1907 - 1914

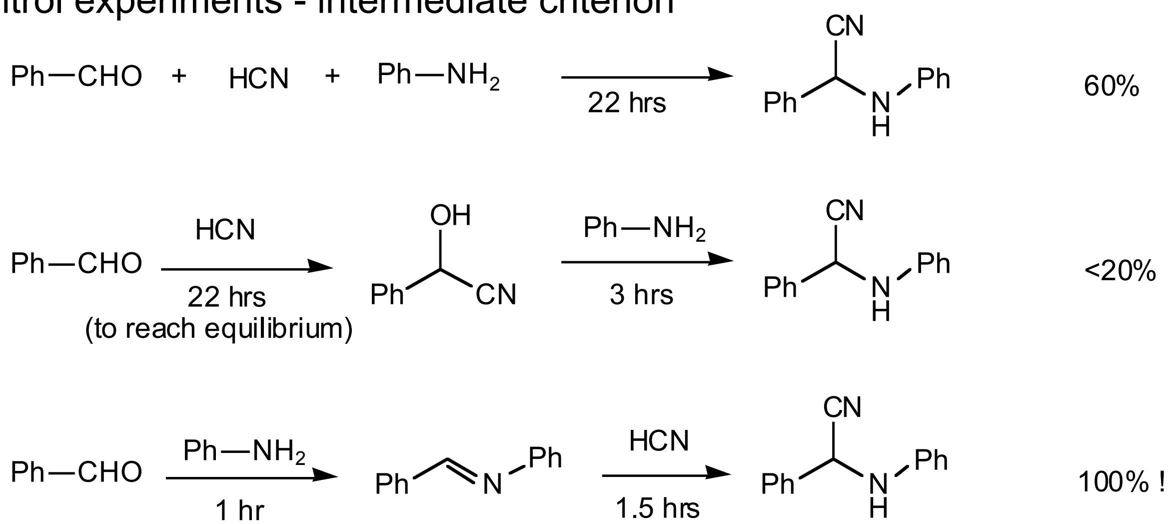
Ogata, Y.; Kawasaki, A. *J. Chem. Soc. B* **1971**, 325-329.

Stadnikoff, G. *Ber.* **1907**, *40*, 1014-19; *J. Russ. Phys. Chem. Soc.* **1914**, *46*, 1201-15.

Snyesarev, A. P. *J. Russ. Phys. Chem. Soc.* **1914**, *46*, 217-23.

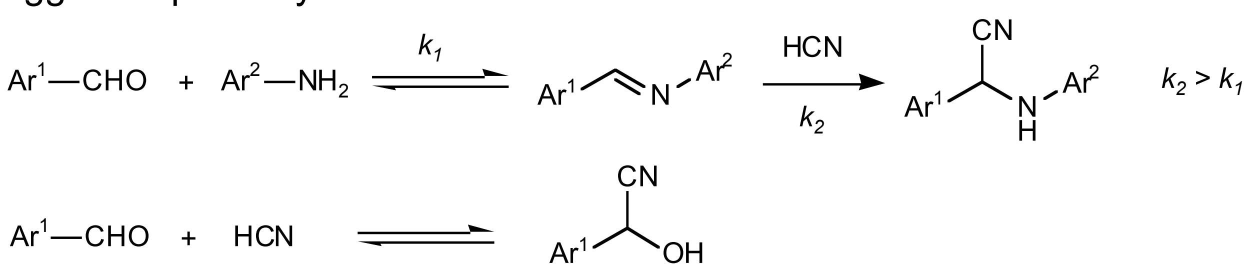
Mechanism Study of Strecker Reaction

♦ Control experiments - intermediate criterion



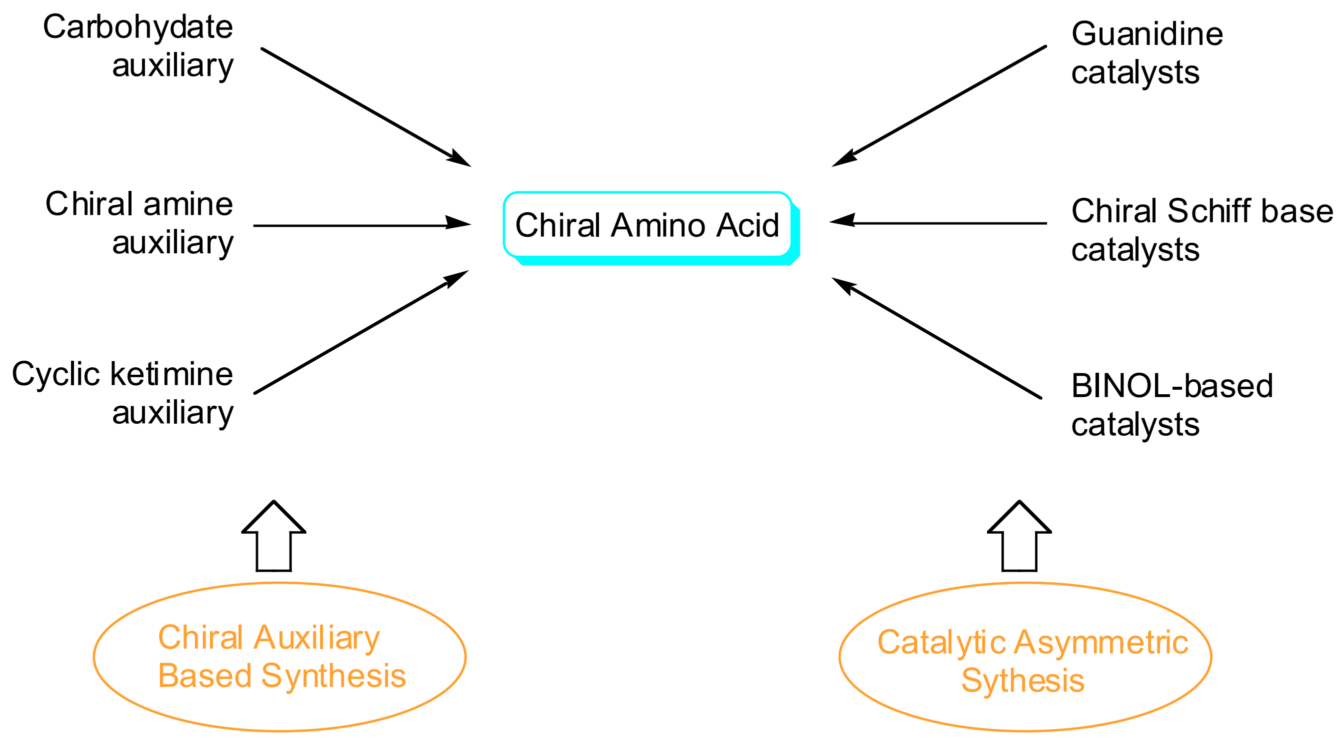
♦ Kinetic study also showed that in the presence of excess CN^- the rate-determining step is imine formation.

♦ Suggested pathways in Strecker reaction



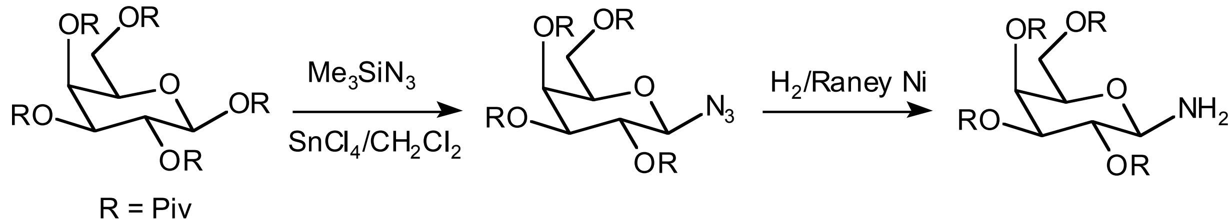
Ogata, Y.; Kawasaki, A. *J. Chem. Soc. B* **1971**, 325-329.
Taillade, J.; Commeyras, A. *Tetrahedron* **1974**, *30*, 2493-2501

Asymmetric Strecker Reaction - An Overview

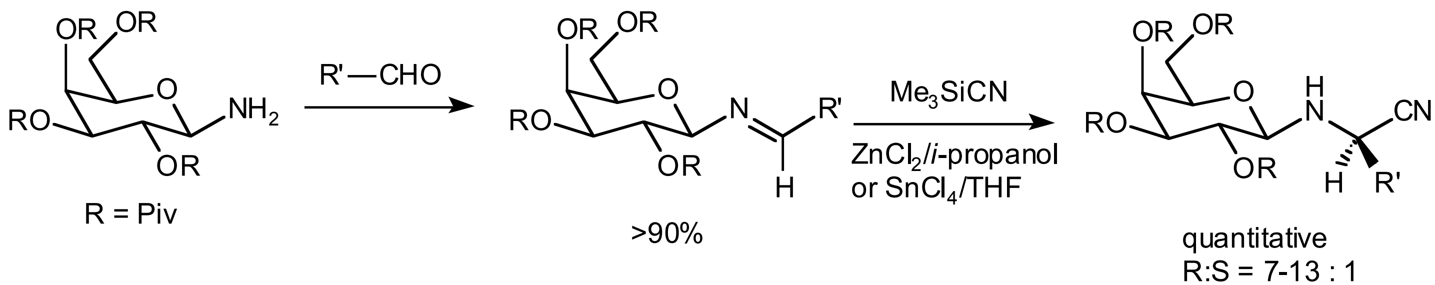


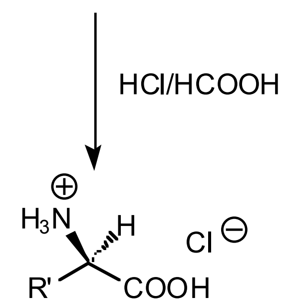
Asymmetric Strecker Reaction Using Carbohydrate Auxiliary

♦ Preparation of carbohydrate templates

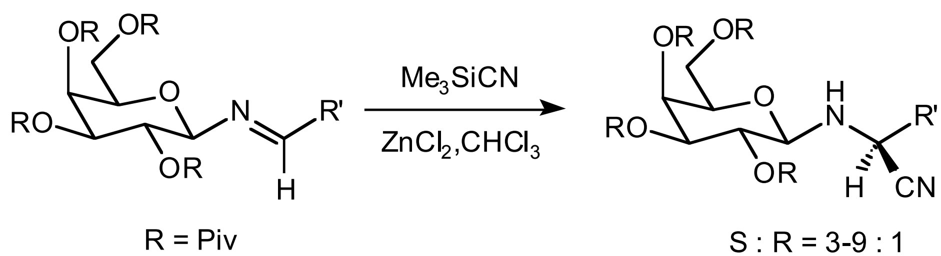


♦ Asymmetric Strecker Reaction Using Carbohydrate



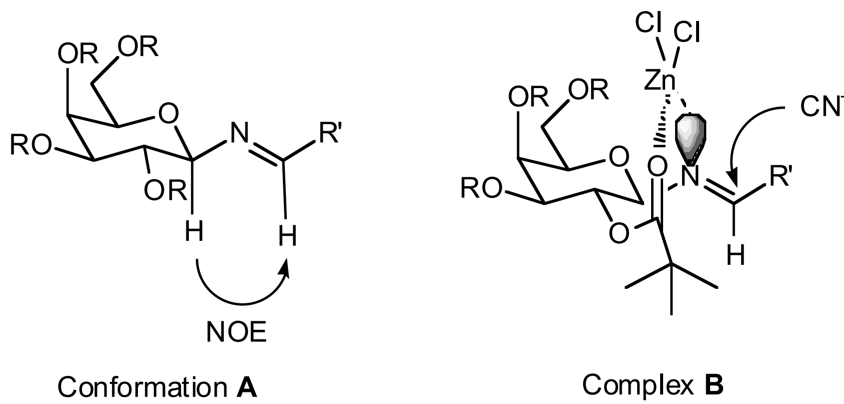


♦ Reversed Asymmetric Induction of Strecker Reaction:



Kunz, H.; Sager, W. *Angew. Chem. Int. Ed.* **1987**, *26*, 557-559.
Kunz, H.; Sager, W.; Pfrengle, W.; Schanzenbach, D. *Tetrahedron Lett.* **1988**, *29*, 4397-4400.

Asymmetric Strecker Reaction Using Carbohydrate Auxiliary

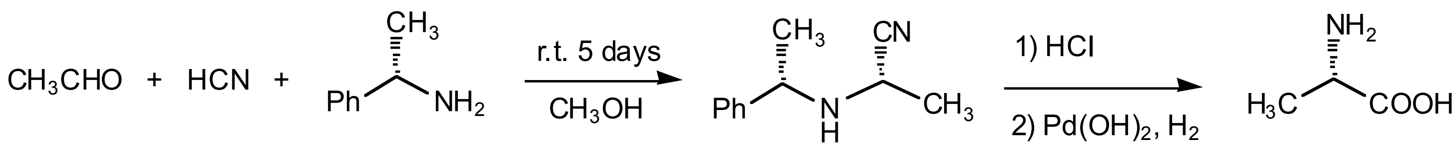


Rationale of stereoselectivity in asymmetric Strecker reaction

Kunz, H.; Sager, W. *Angew. Chem. Int. Ed.* **1987**, *26*, 557-559.
Kunz, H.; Sager, W.; Schanzenbach, D.; Decker, M. *Liebigs Ann. Chem.* **1991**, 649-654.

Asymmetric Strecker Reaction Using Chiral Amine Auxiliary

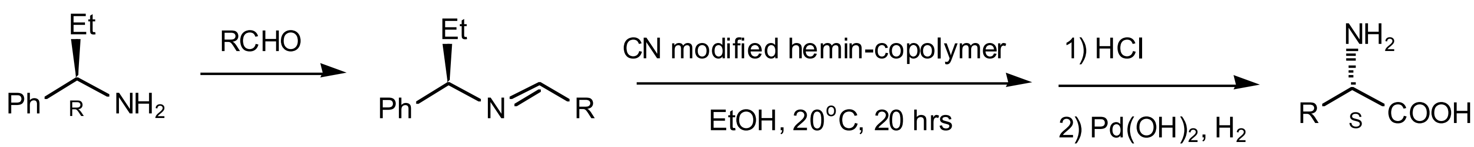
♦ First example of asymmetric Strecker reaction

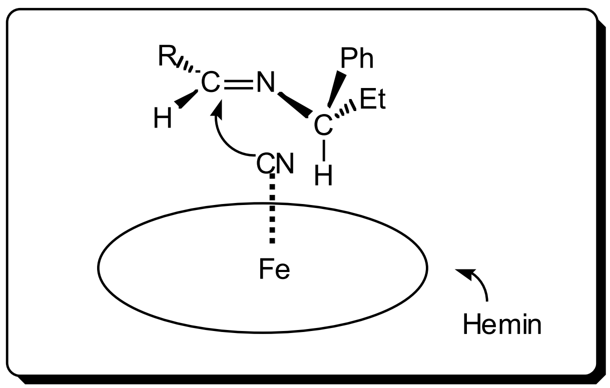


(*S*) - methylbenzylamine

(*S*) - Alanine
17% yield, 90% ee

♦ Asymmetric Strecker reaction using chiral amine and cyanide-modified hemin-copolymer

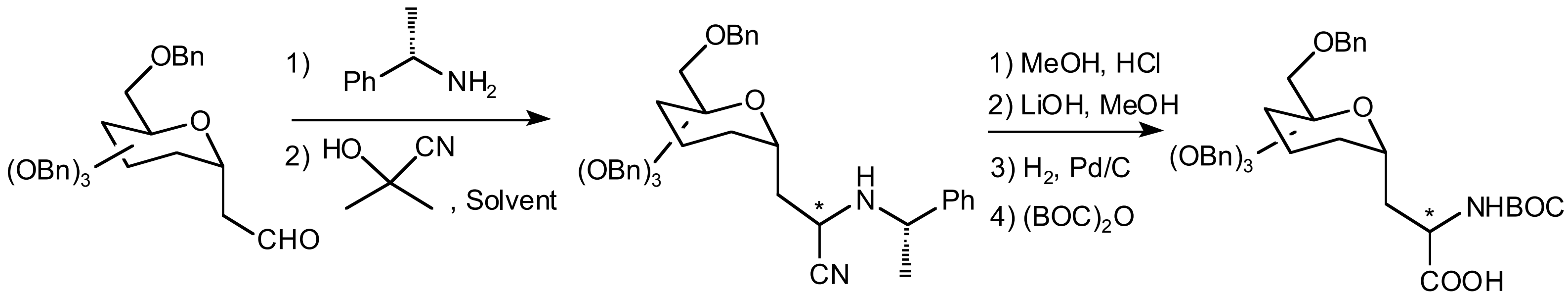




RCHO	ee %	Yield
CH_3CHO	92	57
C_2H_5CHO	96	46
$PhCH_2CHO$	99	41

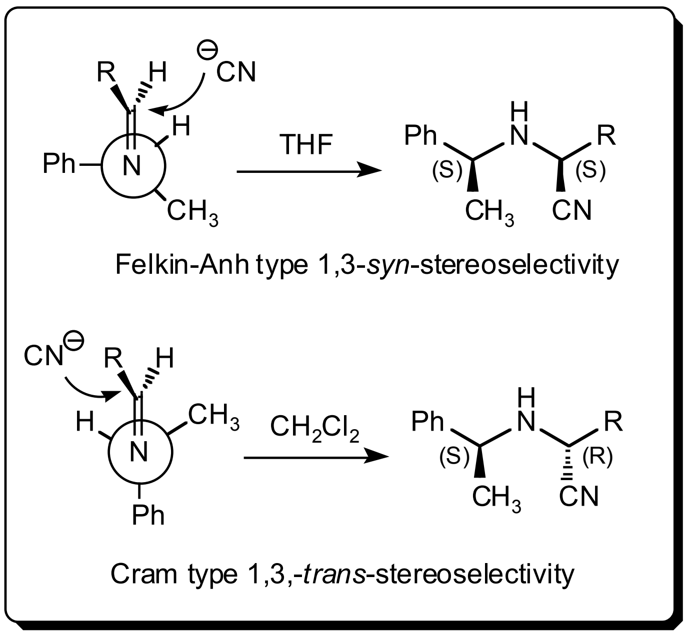
Harada, K. *Nature* **1963**, *200*, 1201.
Harada, K.; Saito, K. *Tetrahedron Lett.* **1989**, *30*, 4535-4538.

Asymmetric Strecker Reaction Using Chiral Amine Auxiliary



A

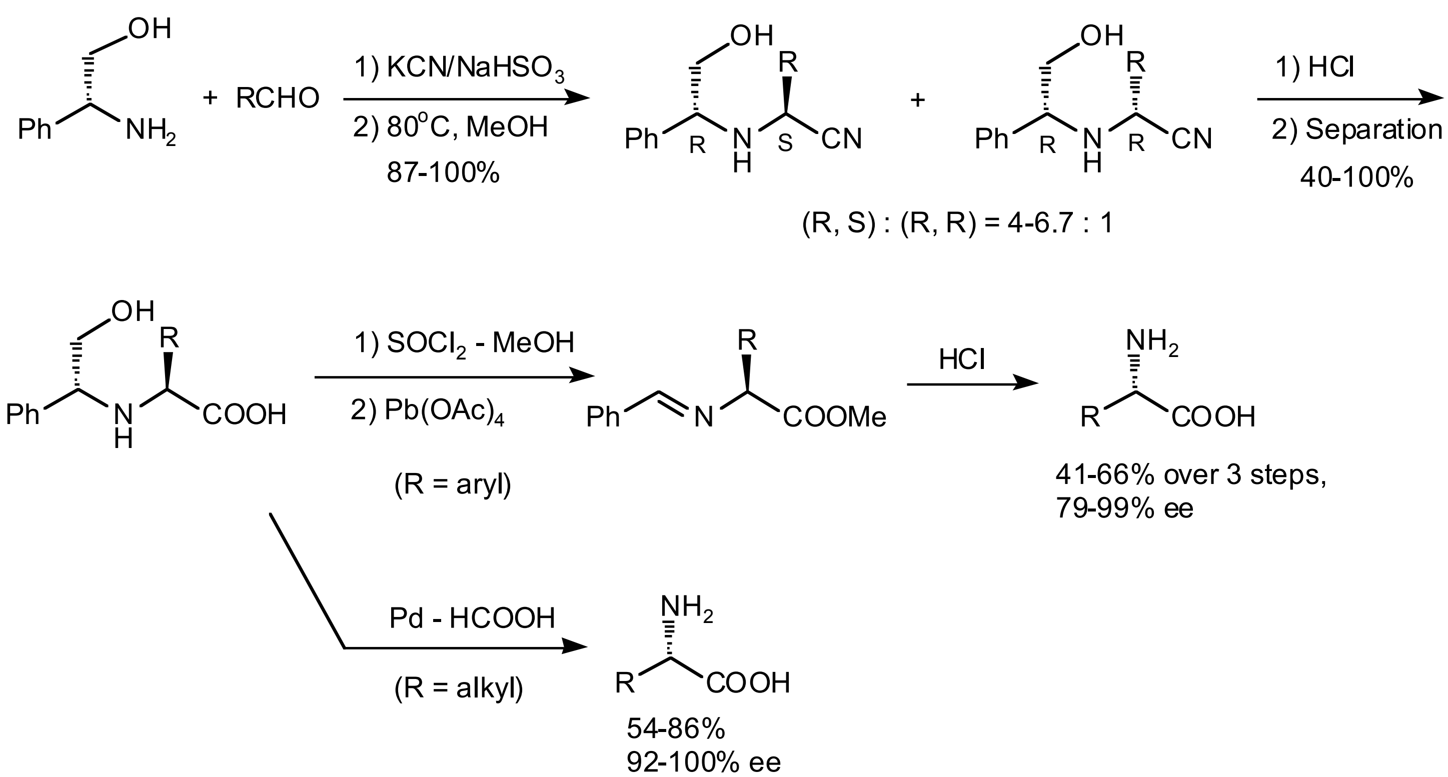
C-gluco-alanine analogue



Solvent	*R/S* of **A**	Yield of **A**
THF	1:3.5	82
CH_2Cl_2	7:1	69

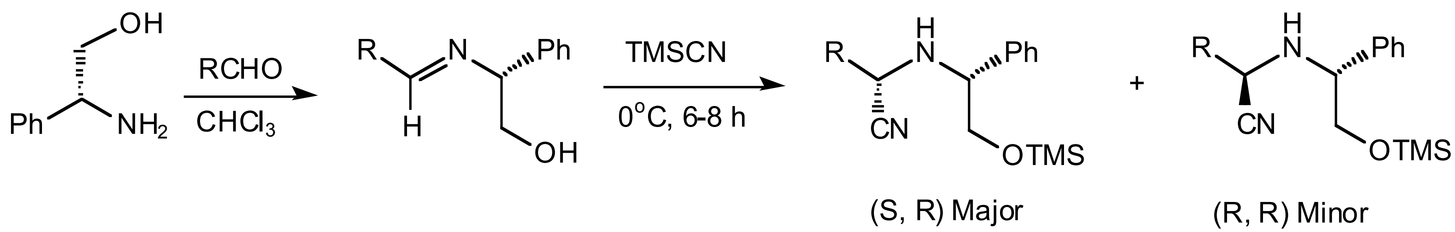
Vincent, S. P.; Schleyer, A.; Wong, C.-H. *J. Org. Chem.* **2000**, *65*, 4440-4443.

Asymmetric Strecker Reaction Using (*R*)-Phenylglycinol Auxiliary

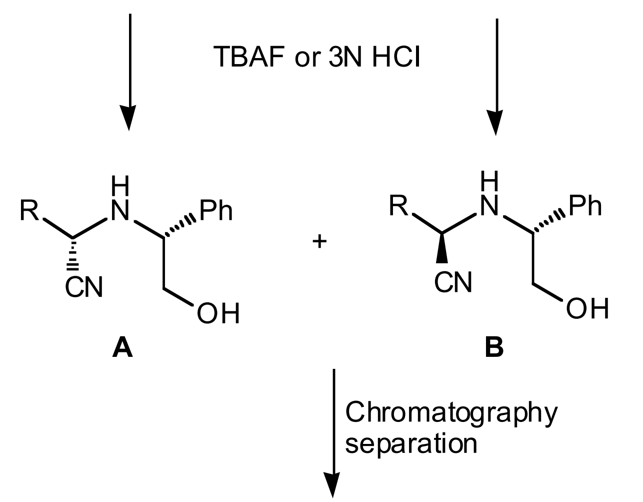


Inaba, T.; Kozono, I.; Fujita, M.; Ogura, K. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2359-2365.

Asymmetric Strecker Reaction Using (*R*)-Phenylglycinol Auxiliary



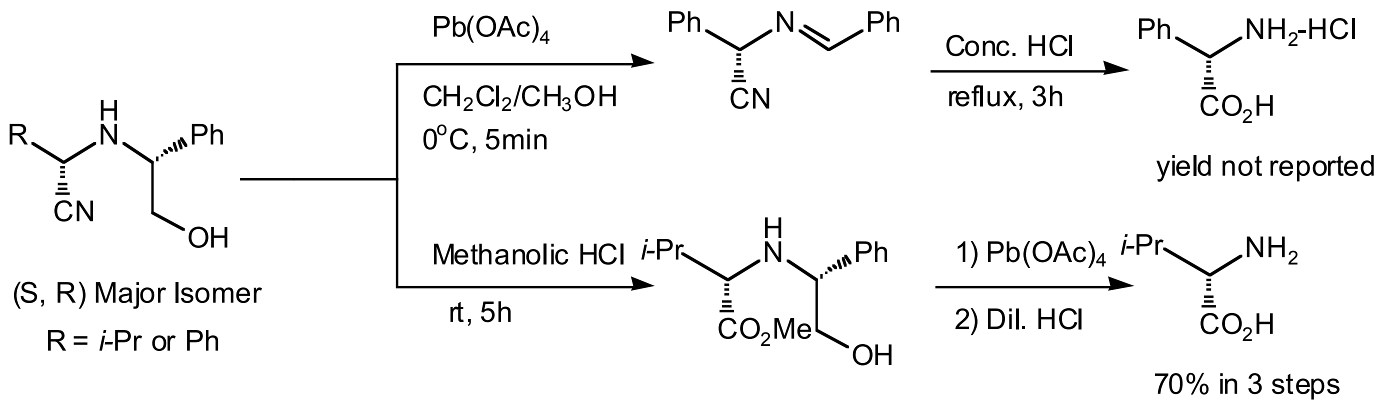
R	Diastereoselectivity (S, R)-**A** : (R, R)-**B**	Total Yield (**A**+**B**), %
Ph	82:18	92
p-MeO-Ph	90:10	95
$PhCH_2CH_2$	54:46	87
i-Bu	84:16	95
t-Bu	88:12	92



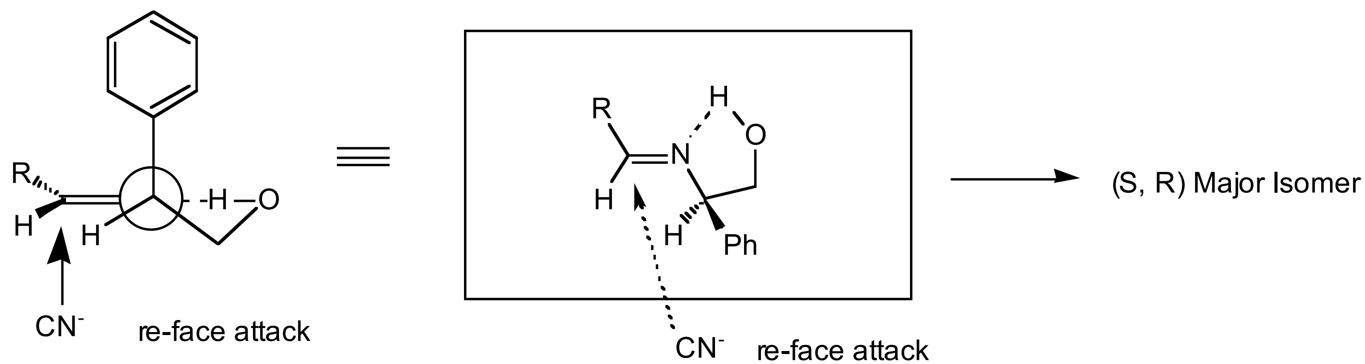
Chakraborty, T. K.; Hussain, K. A.; Reddy, G. V. *Tetrahedron* **1995**, *51*, 9179-9190.

Asymmetric Strecker Reaction Using (*R*)-Phenylglycinol Auxiliary

♦ Removal of chiral auxiliary

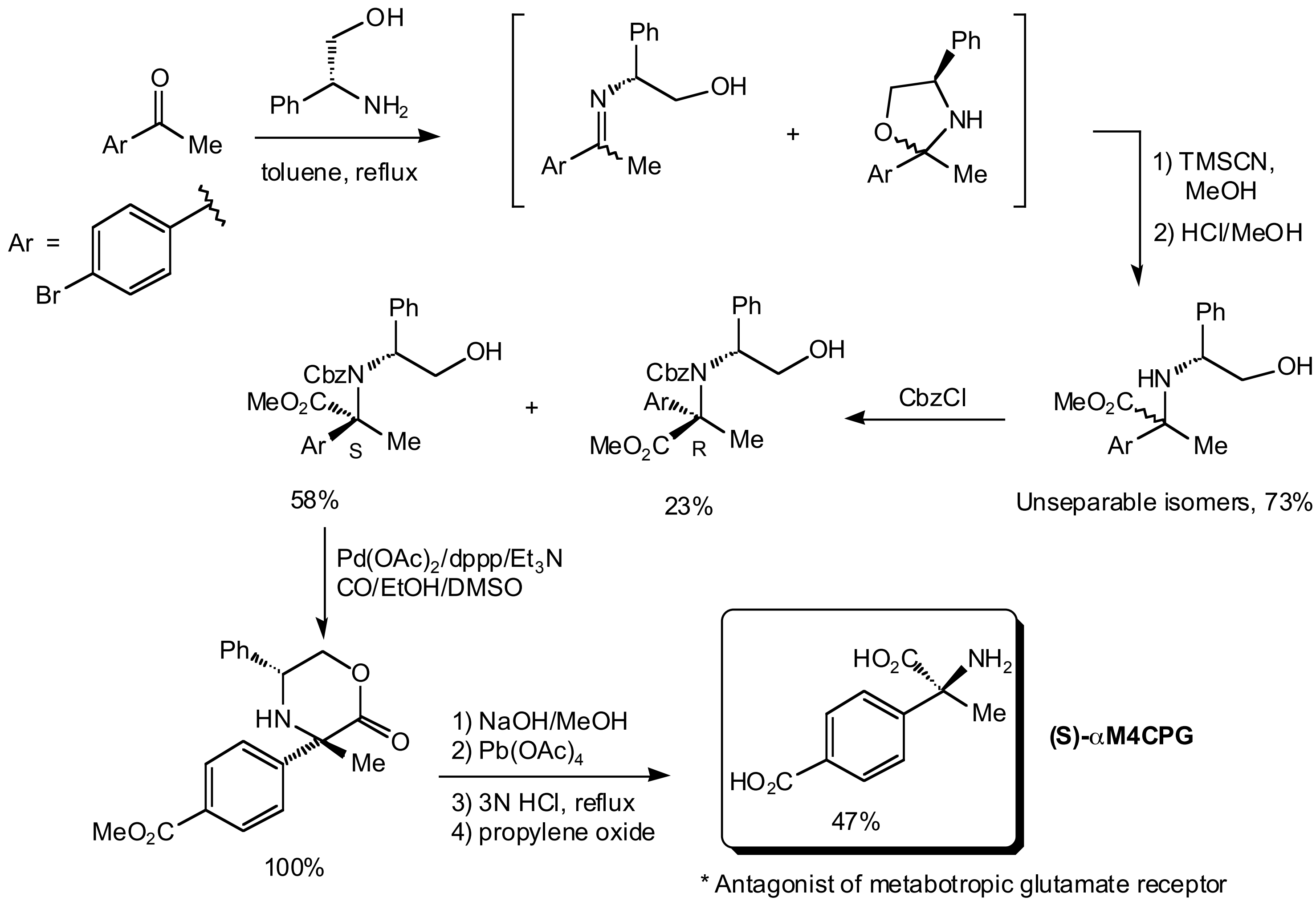


♦ Rationale of diastereoselectivity



Chakraborty, T. K.; Hussain, K. A.; Reddy, G. V. *Tetrahedron* **1995**, *51*, 9179-9190.
Hosangadi, B.; Dave, R. *Tetrahedron Lett.* **1999**, 11295.

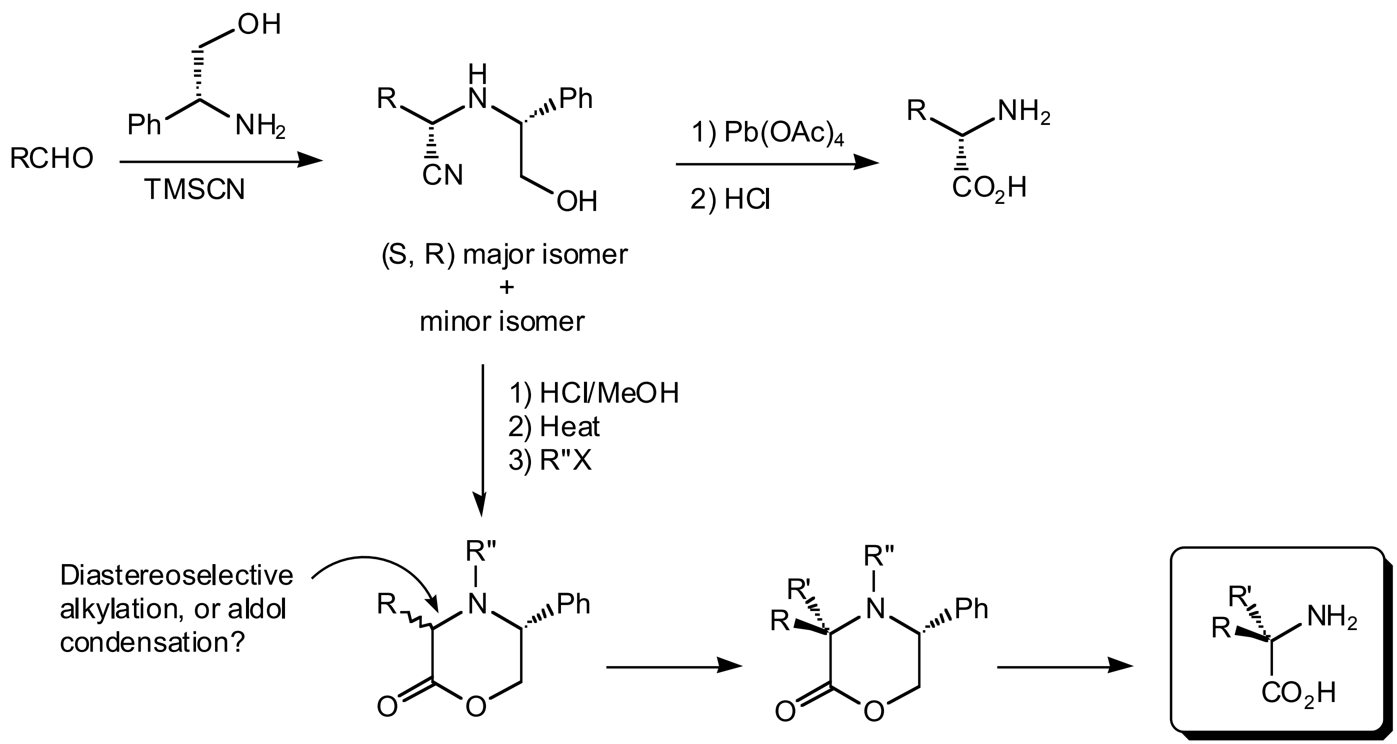
Synthesis of α,α-Disubstituted Amino Acids Using (*R*)-Phenylglycinol Auxiliary



Ma, D.; Tian, H.; Zou, G. *J. Org. Chem.* **1999**, *64*, 120-125.

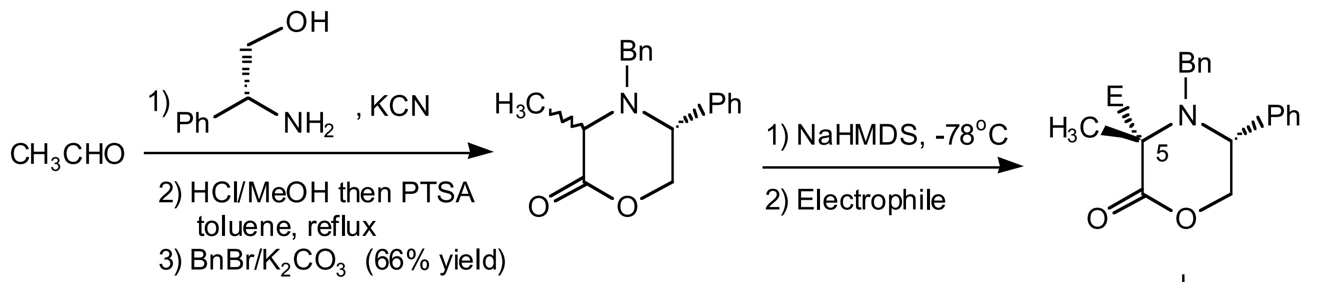
Synthesis of α,α-Disubstituted Amino Acids Using (*R*)-Phenylglycinol Auxiliary

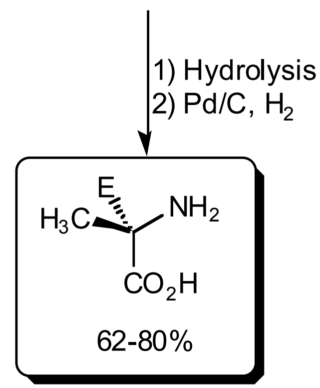
♦ Synthesis of α,α-disubstituted amino acid -- the idea



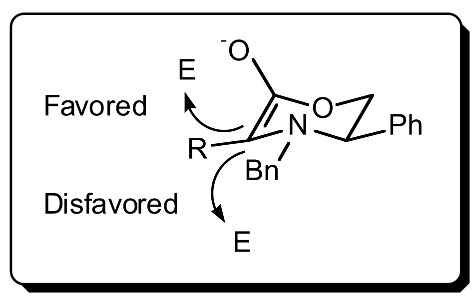
Ma, D.; Ding, K. *Org. Lett.* **2000**, *2*, 2515-2517.

Synthesis of α,α-Disubstituted Amino Acids Using (*R*)-Phenylglycinol Auxiliary



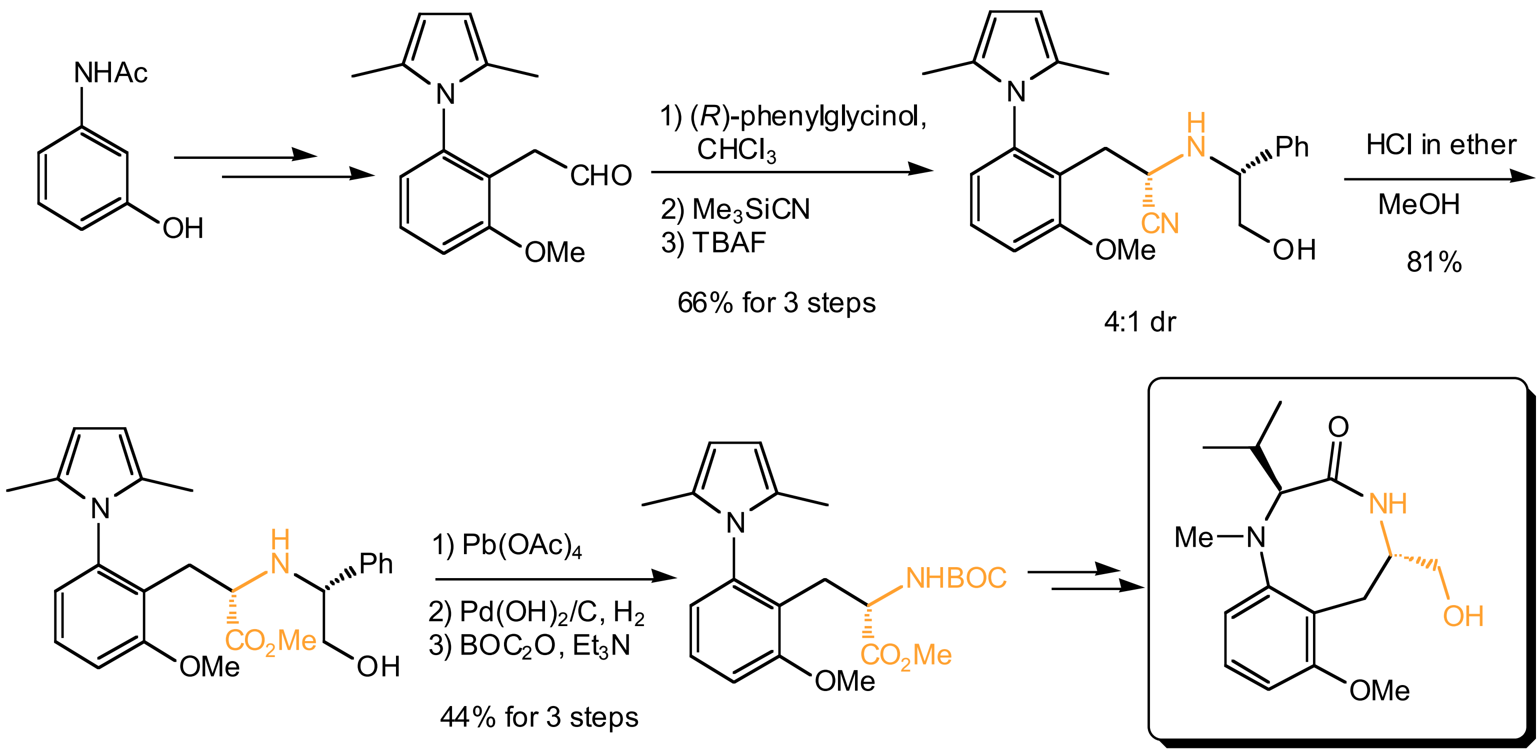


Electophile	Yield	dr of C5	Configuration of C-5
BnBr	90	> 200:1	S
EtI	50	> 200:1	S
n-PrCHO	80	8:1	S (E = (S)-CH(OH)Pr)
$BrCH_2CO_2Me$	87	> 200:1	R



Ma, D.; Ding, K. *Org. Lett.* **2000**, *2*, 2515-2517.

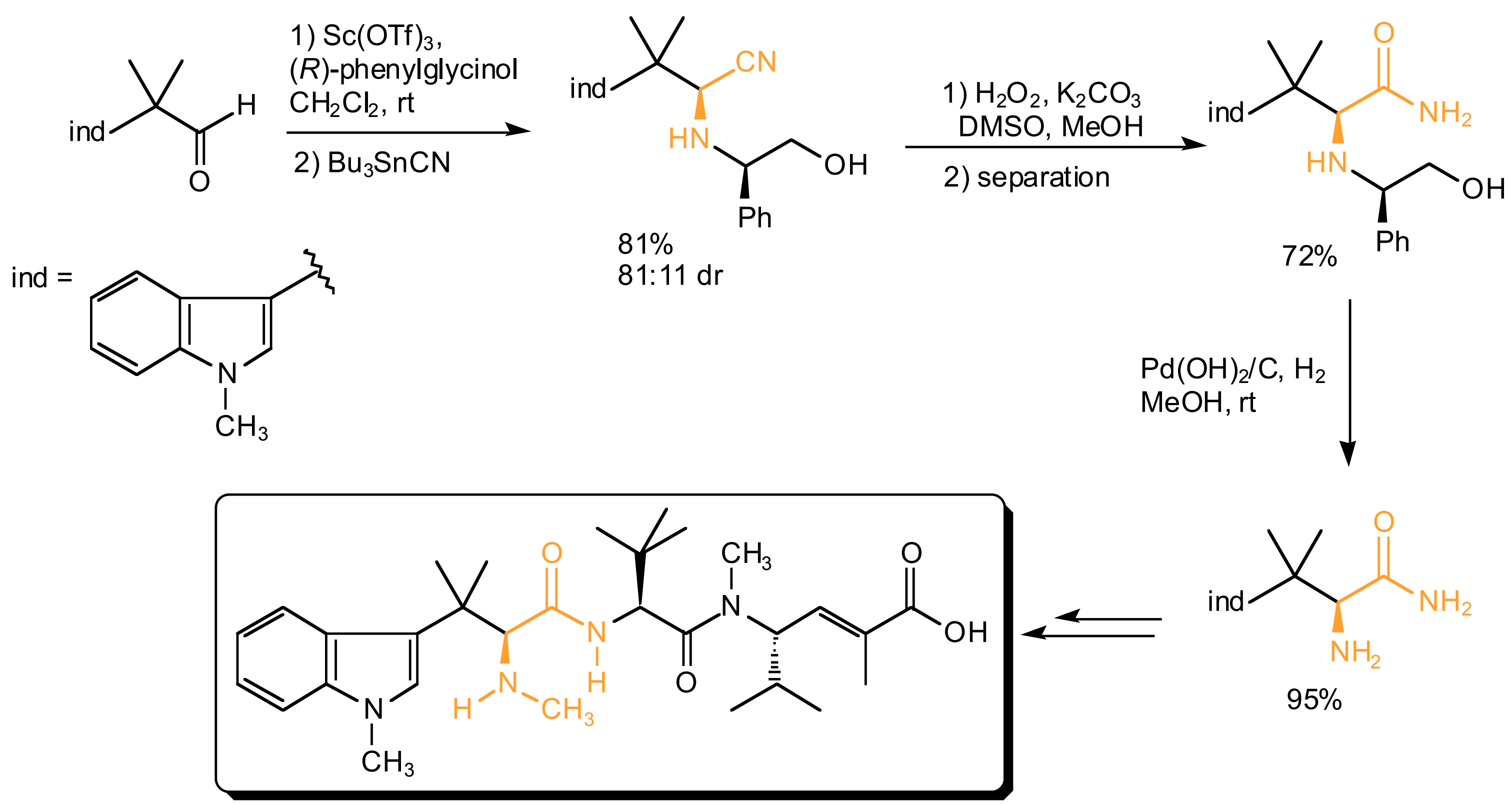
Application of (*R*)-Phenylglycinol Auxiliary in Total Synthesis



7-methoxybenzolactam-V8
Intermediate of potent activator of protein kinase C

Sakamuri, S.; Kozikowski, A. P. *Chem. Commun.* **2001**, 475-476.

Application of (*R*)-Phenylglycinol Auxiliary in Total Synthesis

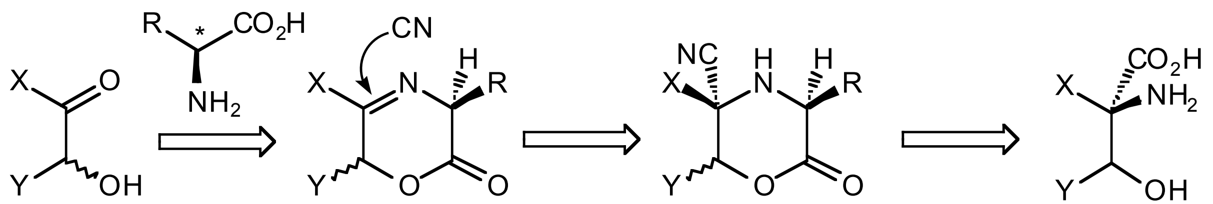


(-)-Hemiasterlin cytotoxin and mitosis inhibitor

Vedejs, E.; Kongkittingam, C. *J. Org. Chem.* **2001**, *66*, 7355-7364.
Reddy, R.; Jaquith, J.; Neelagiri, V.; Saleh-Hanna, S.; Durst, T. *Org. Lett.* **ASAP**, Feb 2, 2002

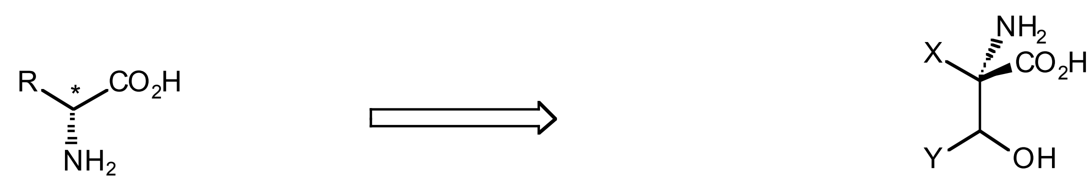
Asymmetric Strecker Reaction Using Chiral Cyclic Ketimine

♦ Asymmetric Strecker reaction using chiral cyclic ketimine -- the idea



X = alkyl or aryl,
Y = H or alkyl or aryl

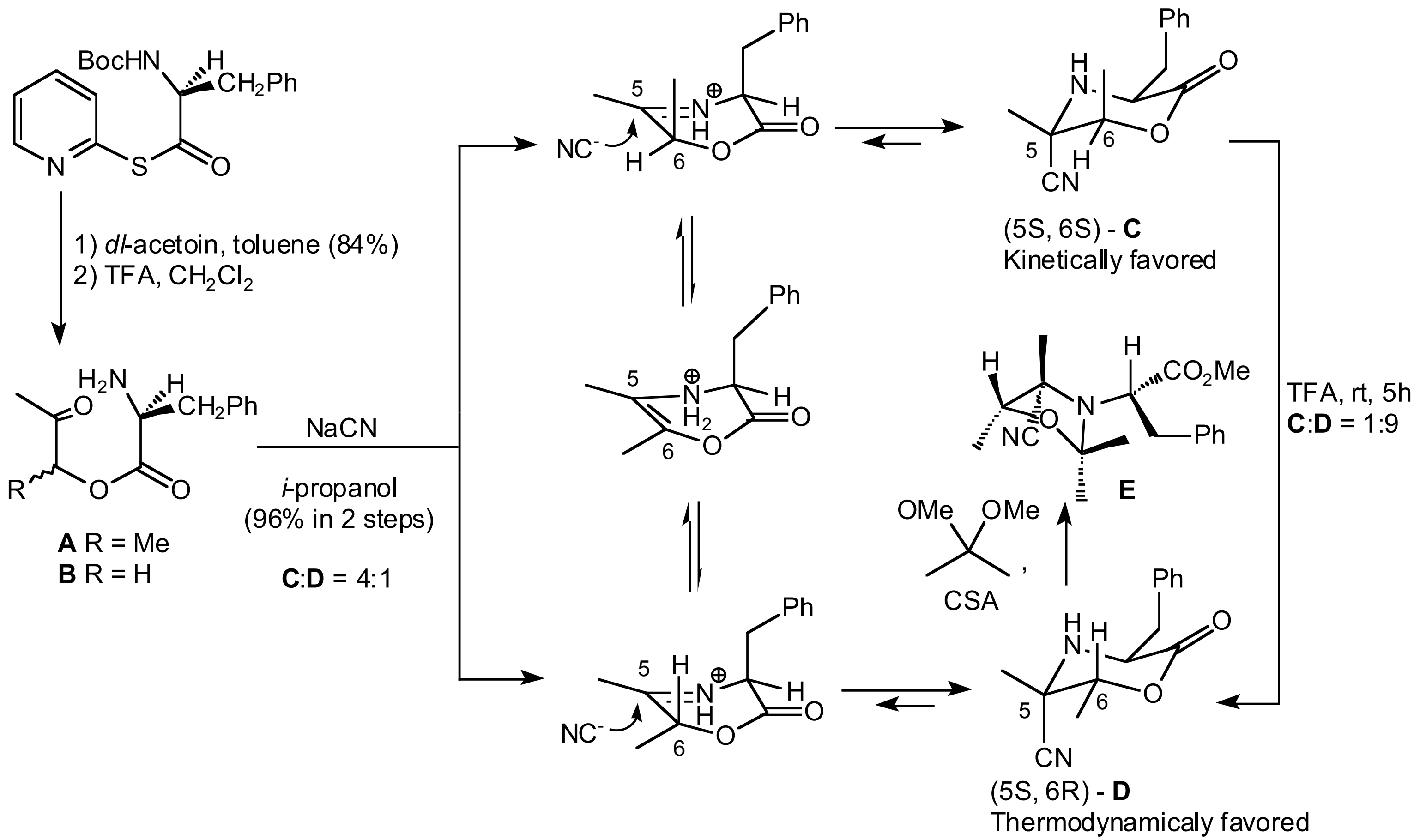
or use:



Moon, S.-H.; Ohfune, Y. *J. Am. Chem. Soc.* **1994**, *116*, 7405-7406.

Asymmetric Strecker Reaction Using Chiral Cyclic Ketimine

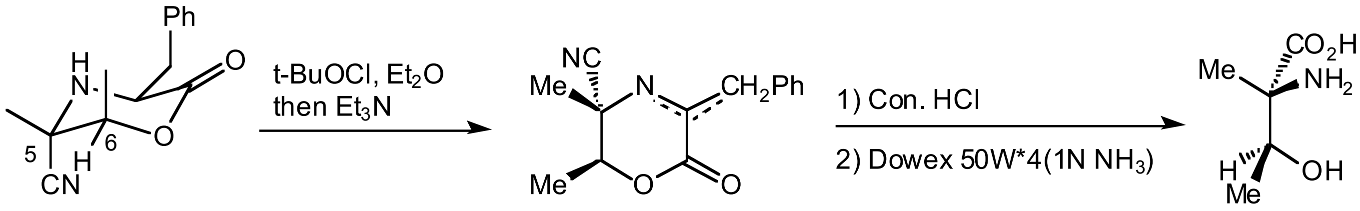
♦ Preparation of intermediate **C** and **D**



Moon, S.-H.; Ohfune, Y. *J. Am. Chem. Soc.* **1994**, *116*, 7405-7406.

Asymmetric Strecker Reaction Using Chiral Cyclic Ketimine

♦ Removal of phenylalanyl moiety and preparation of amino acid.

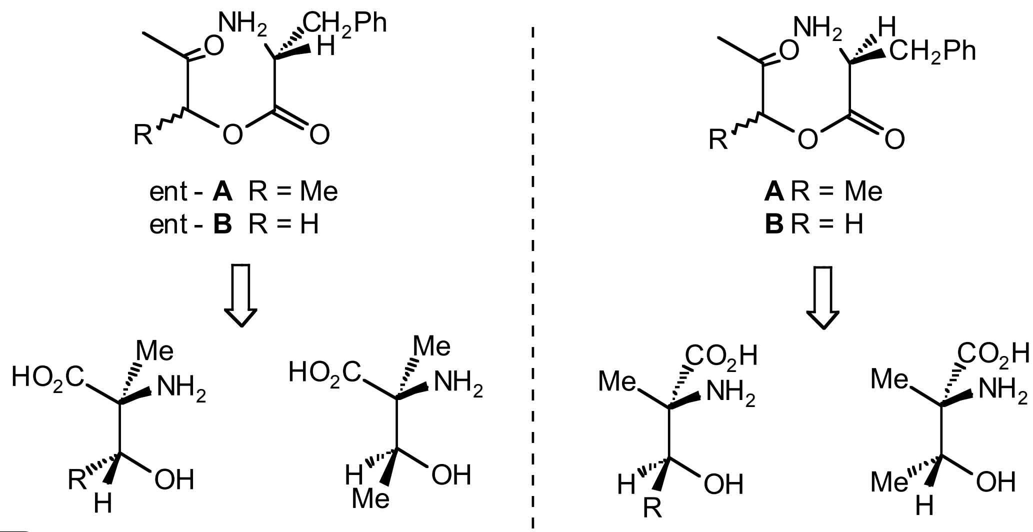


(5S, 6S) - **C**

exo/endo = 2.4:1

1c 84%

♦ Four enantiomers and diastereomers of α-methylthreonine and two enaniomers of α-methylserine were synthesized using the same methodology.

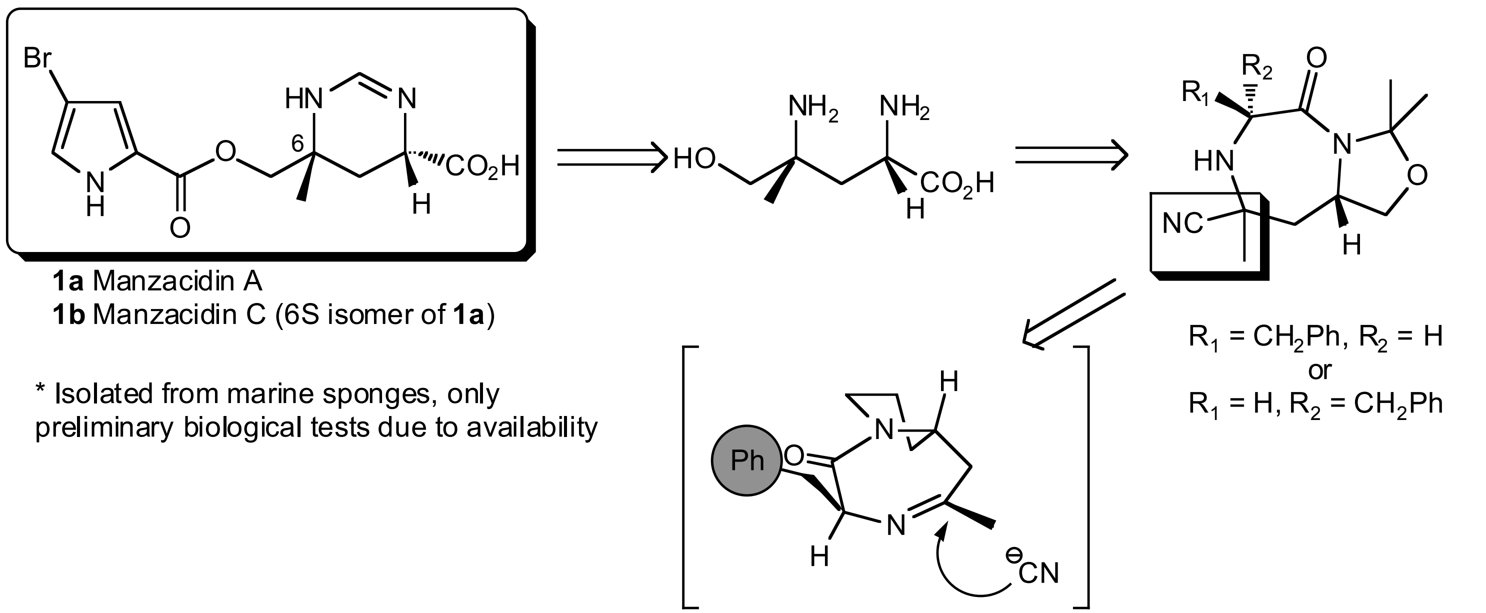


α-methylthreonine α-methylserine	**1a** R = Me **2a** R = H	**1b**	**1c** R = Me **8b** R = H	**1d**

Moon, S.-H.; Ohfune, Y. *J. Am. Chem. Soc.* **1994**, *116*, 7405-7406.

Asymmetric Strecker Reaction Using Chiral Cyclic Ketimine - Application in Total Synthesis

♦ Total synthesis of Manzacidin A and C -- idea and retrosynthesis



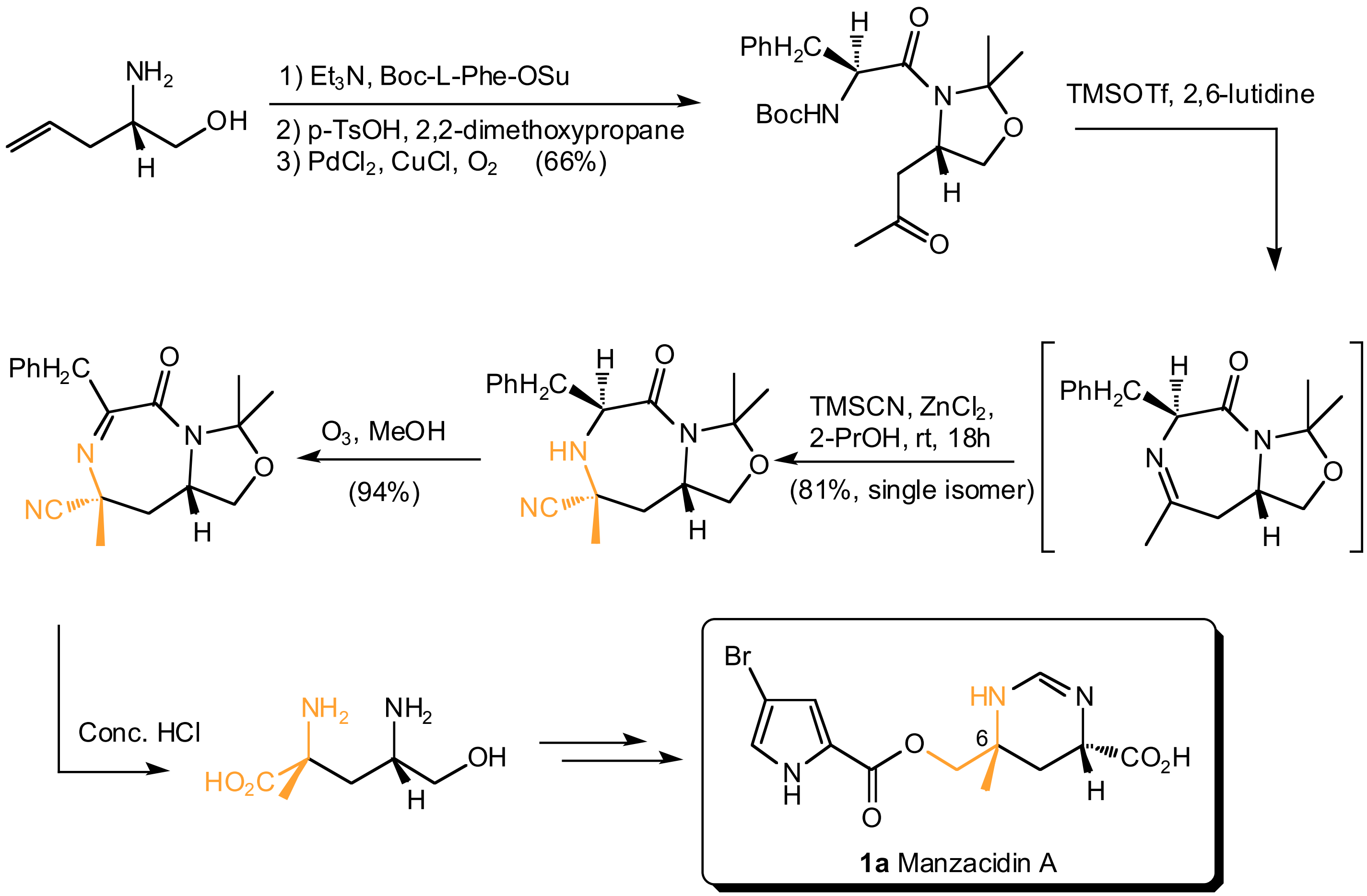
1a Manzacidin A
1b Manzacidin C (6S isomer of **1a**)

$R_1 = CH_2Ph$, $R_2 = H$
or
$R_1 = H$, $R_2 = CH_2Ph$

* Isolated from marine sponges, only preliminary biological tests due to availability

Namba, K.; Shinada, T.; Teramoto, T.; Ohfune, Y. *J. Am. Chem. Soc.* **2000**, *122*, 10708-10709.

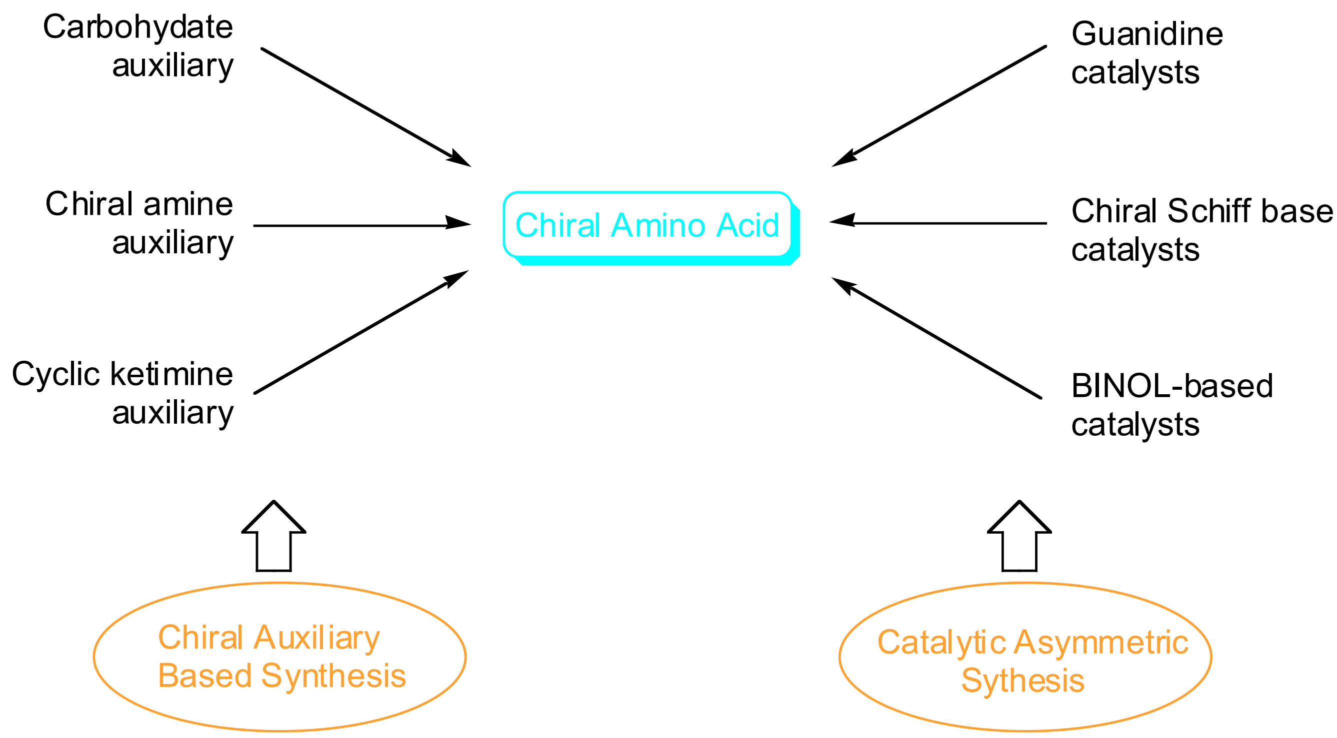
Asymmetric Strecker Reaction Using Chiral Cyclic Ketimine - Application in Total Synthesis



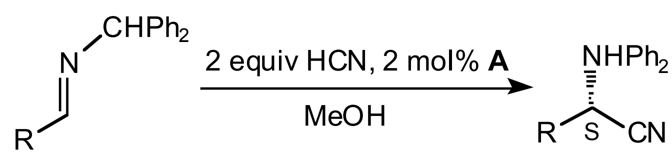
* **1b** Manzacidin C (6S isomer of **1a**) was synthesized using same methodology.

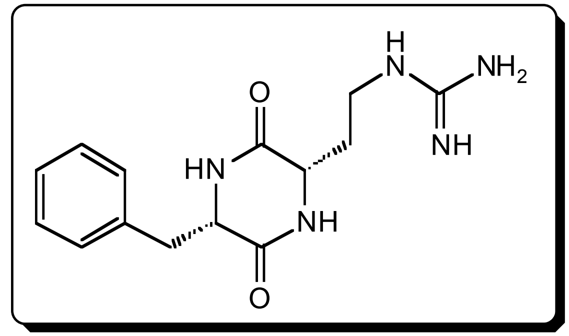
Namba, K.; Shinada, T.; Teramoto, T.; Ohfune, Y. *J. Am. Chem. Soc.* **2000**, *122*, 10708-10709.

Asymmetric Strecker Reaction - Halfway Overview



Catalytic Asymmetric Strecker Reaction Using Chiral Guanidine Catalyst





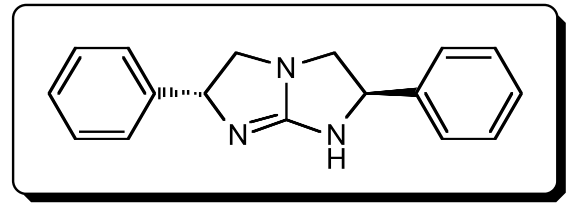
Lipton's Cyclic Dipeptide catalyst **A**

Entry	R	Temp (°C)	Yield (%)	ee (%)
1	C_6H_5	-25	97	>99
2	*p*-ClC_6H_4	-75	97	>99
3	*p*-$OMeC_6H_4$	-75	90	96
4	*m*-$NO_2C_6H_4$	-75	71	<10
5	3-pyridyl	-75	86	<10
6	*i*-Pr	-75	81	<10
7	*t*-Bu	-75	80	17

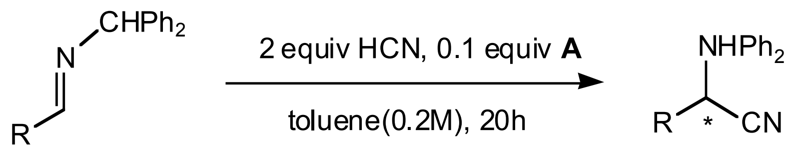
♦ Pros: The first successful example of catalytic asymmetric Strecker reaction
Good for some aromatic imines
Low catalyst loading
♦ Cons: Narrow substrate range

Iyer, M. S.; Gigstad, K. M.; Namdev, N. D.; Lipton, M. *J. Am. Chem. Soc.* **1996**, *118*, 4910-4911.

Catalytic Asymmetric Strecker Reaction Using Chiral Guanidine Catalyst



Corey's bicyclic guanidine catalyst **A**



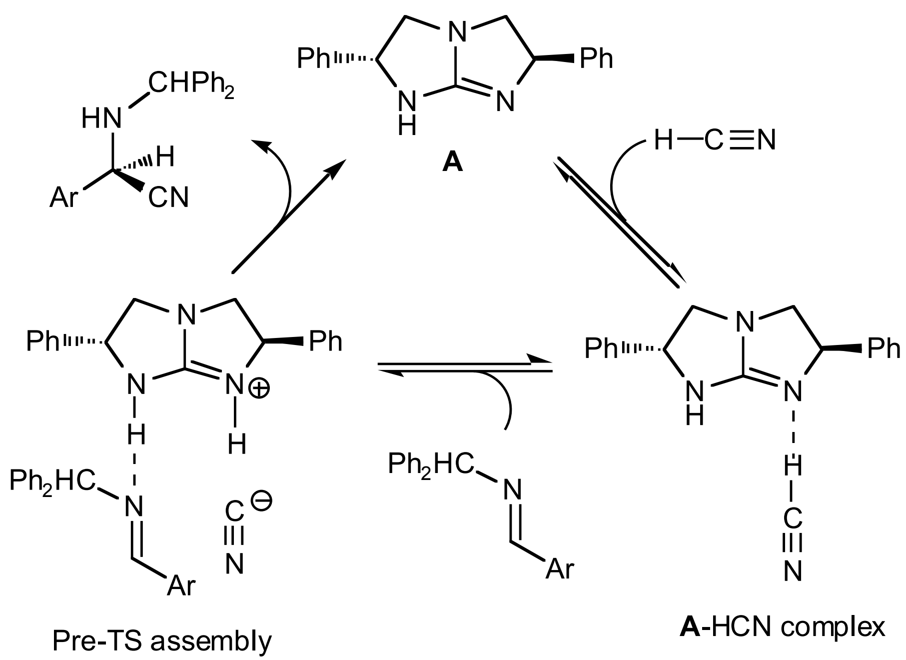
(R) - product when R = Aryl
(S) - product when R = Alkyl

Entry	R	Temp (^{o}C)	Yield (%)	ee (%)
1	C_6H_5	-40	96	86
2	*p*-ClC_6H_4	-20	88	81
3	*p*-$MeOC_6H_4$	-40	99	84
4	*o*-$CH_3C_6H_4$	-20	88	50
5	*i*-Pr	-40	~95%	84
6	*n*-Hex	-40	~95%	63

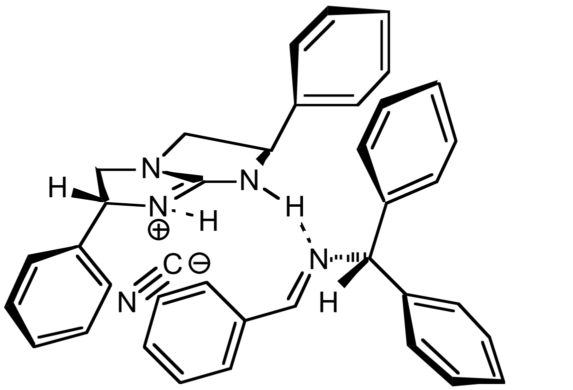
♦ Pros: Improved results for some aliphatic imines
♦ Cons: Narrow substrate range
ee not so great

Corey, E. J.; Grogan, M. J. *Org. Lett.* **1999**, *1*, 157-160.

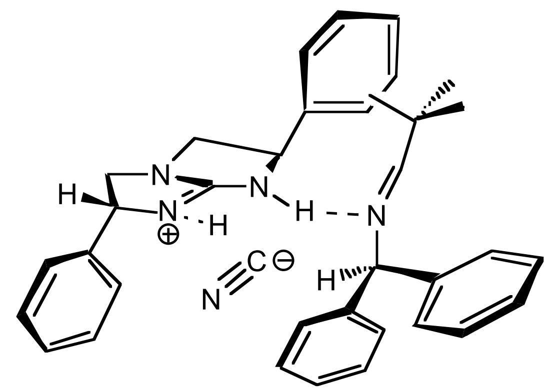
Mechanism of Strecker Reaction Catalyzed by Chiral Guanidine



♦ Catalytic cycle of Guanidine catalyzed Strecker reaction

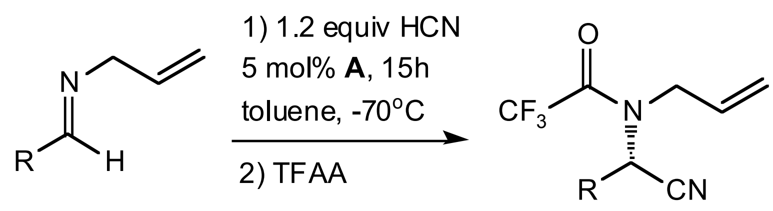


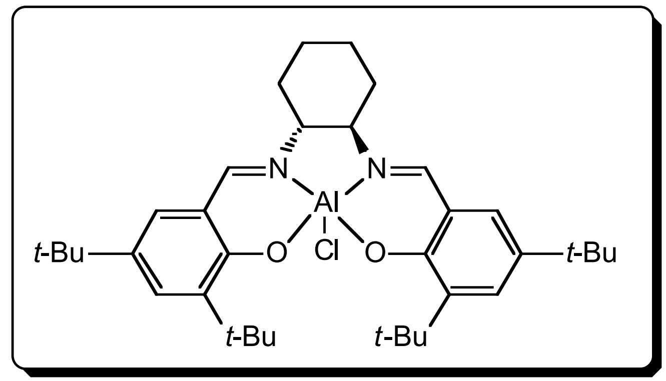
♦ Pre-transition-state assemblies for the Strecker reactions of
N-benzhydryl benzaldimine (above) and
N-benzhydryl pivalaldimine (below).



Corey, E. J.; Grogan, M. J. *Org. Lett.* **1999**, *1*, 157-160.

Catalytic Asymmetric Strecker Reaction Using Chiral(Salen) Al(III) Complex





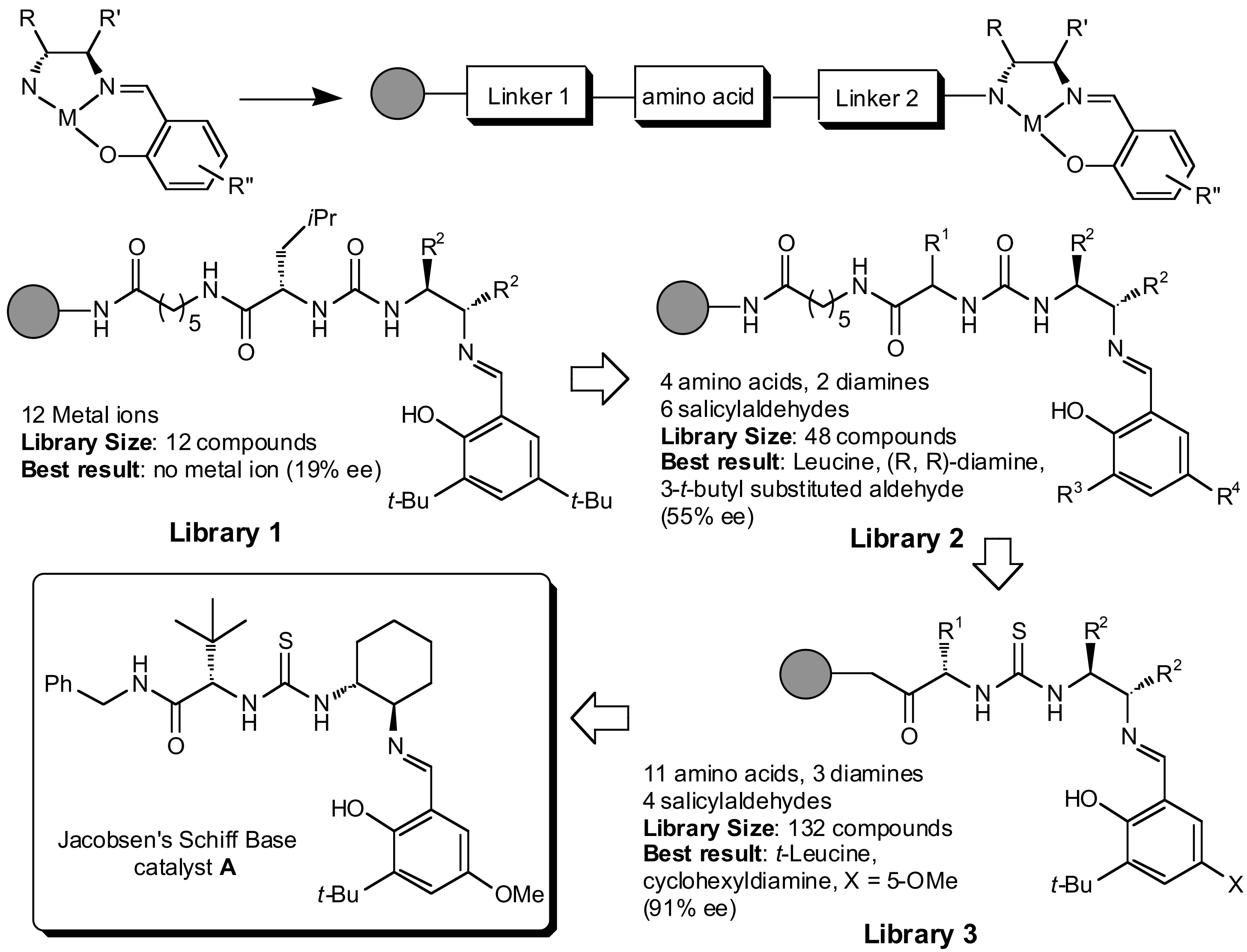
Jacobsen's chiral (salen)Al(III) complex **A**

Entry	R	Yield (%)	ee (%)
1	C_6H_5	91	95
2	*p*-ClC_6H_4	92	81
3	*p*-$OMeC_6H_4$	93	91
4	2-Naphthyl	93	99
5	cyclohexyl	77	57
6	*t*-Bu	69	37

- ♦ Pros: Good results for some aromatic imines
- ♦ Cons: Narrow substrate range

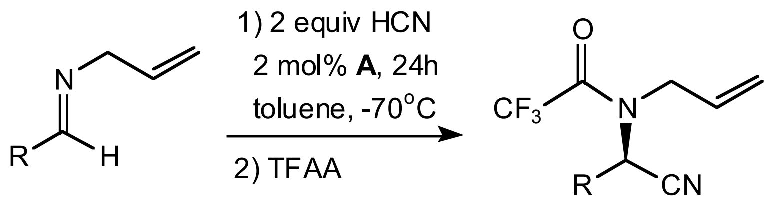
Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 5315-5316.

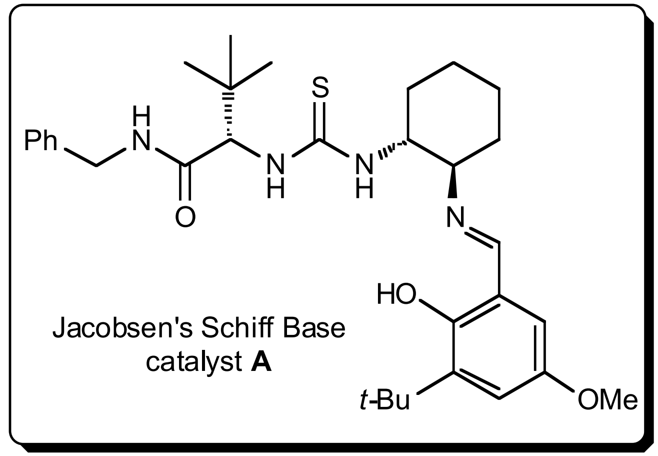
Asymmetric Strecker Reaction Using Chiral Schiff Base Catalyst



Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 4901-4902.

Asymmetric Strecker Reaction Using Chiral Schiff Base Catalyst



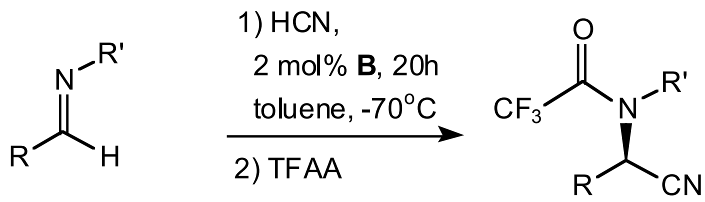


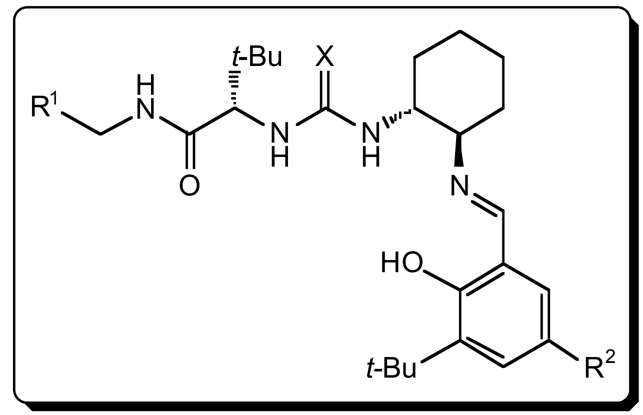
Entry	R	Yield (%)	ee (%)
1	C_6H_5	78	91
2	*p*-BrC_6H_4	65	86
3	*p*-MeOC_6H_4	92	91
4	2-Naphthyl	88	88
5	cyclohexyl	77	83
6	*t*-Bu	70	85

♦ Pros: Good results for most aromatic and aliphatic imines
Low catalyst loading
♦ Cons: No mechanism proposed

Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 4901-4902.

Asymmetric Strecker Reaction Using Chiral Schiff Base Catalyst





A: R^1 = polystyrene, X = S, R^2 = OCO(*t*Bu)
B: R^1 = Ph, X = O, R^2 = OCO(*t*Bu)

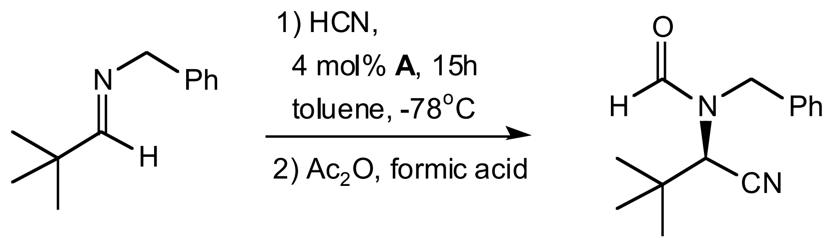
Entry	R	R'	Yield (%)	ee (%)
1	C_6H_5	allyl	74	95
2	*o*-BrC_6H_4	allyl	88	95
3	*m*-BrC_6H_4	allyl	87	90
4	*p*-BrC_6H_4	allyl	89	89
5	*p*-$OCH_3C_6H_4$	allyl	98	95
6	*o*-$OCH_3C_6H_4$	allyl	93	77
7	*t*-Bu	allyl	75	95(91)
8	*t*-Bu	benzyl	88	96(93)
9	$CH_3(CH_2)_4$	benzyl	69	78

- ♦ Pros: Good results for most imines
  Low catalyst loading
- ♦ Cons: No mechanism proposed

Sigman, M. S.; Vachal, P.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2000**, *39*, 1279-1281.

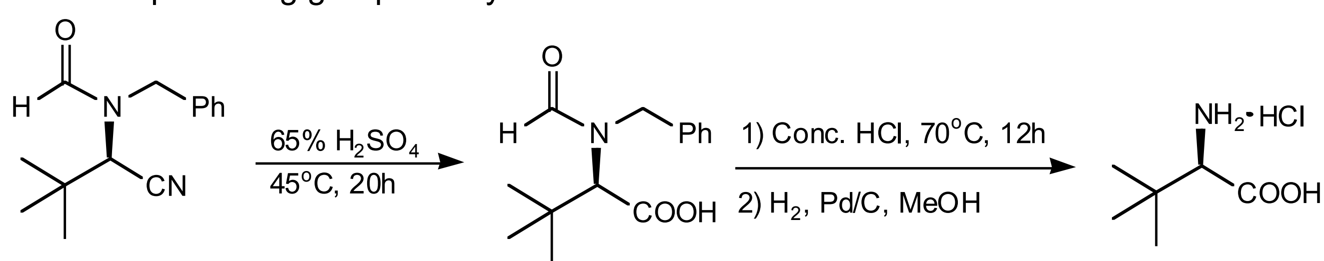
Asymmetric Strecker Reaction Using Chiral Schiff Base Catalyst

♦ Catalytic asymmetric Strecker reaction using polymer-supported catalyst
-- Easy to remove, no loss of reactivity after recycle, but displays slightly lower enantioselectivity,



Cycle	Yield (%)	ee (%)
1	97	92
5	97	92
10	98	93

♦ Removal of protecting group and synthesis of D-*tert*-leucine



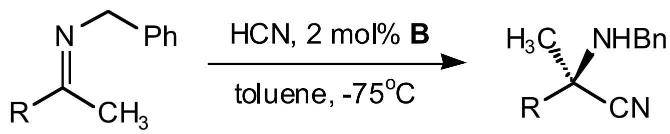
Recrystalized
> 99% ee

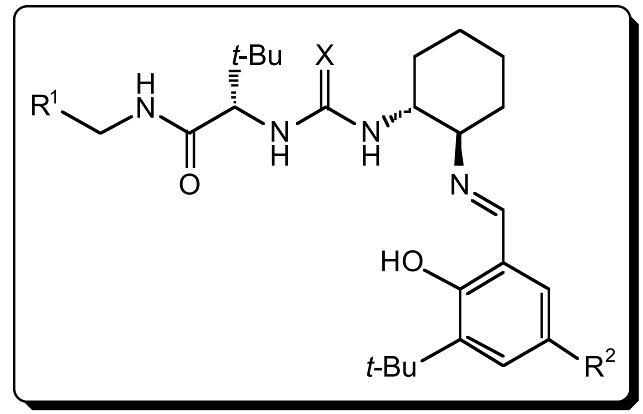
99% yield

D-*tert*-leucine, >$100/g
quant. yield, >99% ee
(84% yield from imine)

Sigman, M. S.; Vachal, P.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2000**, *39*, 1279-1281.

Synthesis of Quaternary Amino Acids Using Chiral Schiff Base Catalyst





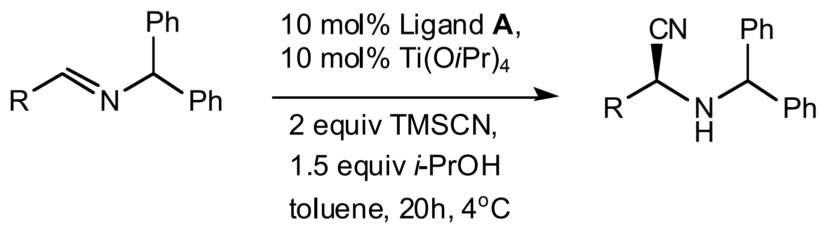
A: R^1 = polystyrene, X = S, R^2 = OCO(*t*Bu)
B: R^1 = Ph, X = O, R^2 = OCO(*t*Bu)

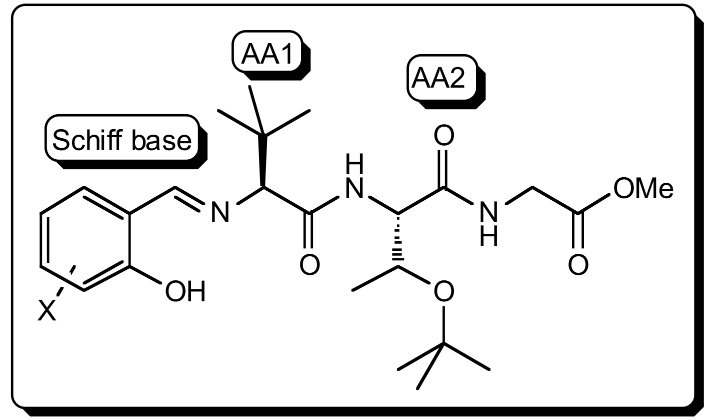
Entry	R	t (h)	Yield (%)	ee (%)
1	C_6H_5	24	97	90
2	*o*-BrC_6H_4	90	45	42
3	*m*-BrC_6H_4	60	97	91
4	*p*-BrC_6H_4	80	quant	93
5	*p*-$CH_3OC_6H_4$	60	98	88
7	*t*-Bu	15	98	70
8	$C_6H_5CH_2CH_2$	17	98	41

- ♦ Pros: Good results for some aromatic imines.
- ♦ Cons: Low ee for some substrates.

Vachal, P.; Jacobsen, E. N. *Org. Lett.* **2000**, *2*, 867-870.

Asymmetric Strecker Reaction Using Chiral Schiff Base Catalyst





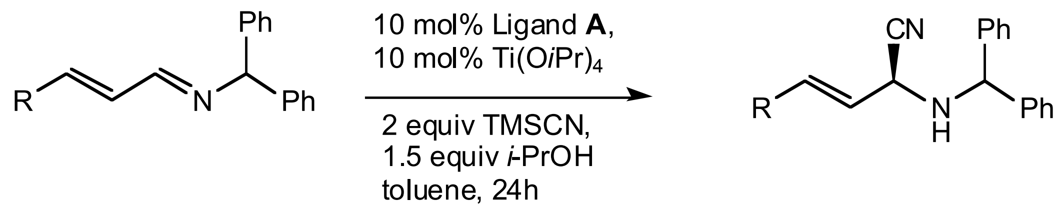
Snapper & Hoveyda's Schiff base Ligand **A**

Entry	R	X	Yield (%)	ee (%)
1	C_6H_5	X = 5-OMe	82	97
2	*o*-ClC_6H_4	X = 3,5-DiCl	85	93
3	*o*-BrC_6H_4	X = 3,5-DiCl	93	94
4	*p*-$CH_3OC_6H_4$	X = 3,5-DiCl	99	94
5	2-naphthyl	X = 5-OMe	80	93
7	*t*-Bu	X = 3,5-DiBr	97	85

♦ Pros: Good results for most imines.
♦ Cons: High catalyst loading

Krueger, C. A.; Kuntz, K. W.; Dzierba, C. D.; Wirschun, W. G.; Gleason, J. D.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 4284-4285.

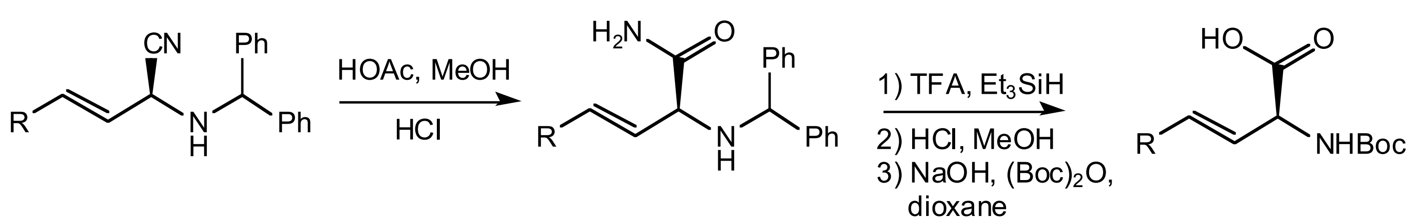
Synthesis of Unsaturated α-Amino Acids Using Chiral Schiff Base Catalyst



Entry	R	X	Yield (%)	ee (%)
1	C_6H_5	X = 1-naphthyl	80	84
2	*o*-$MeOC_6H_4$	X = 1-naphthyl	61	78
3	*p*-$NH_2C_6H_4$	X = 3,5-DiBr	93	76
4	Me	X = 3,5-DiBr	84	85
5	Me-CH=CH-	X = 5-OMe	95	89

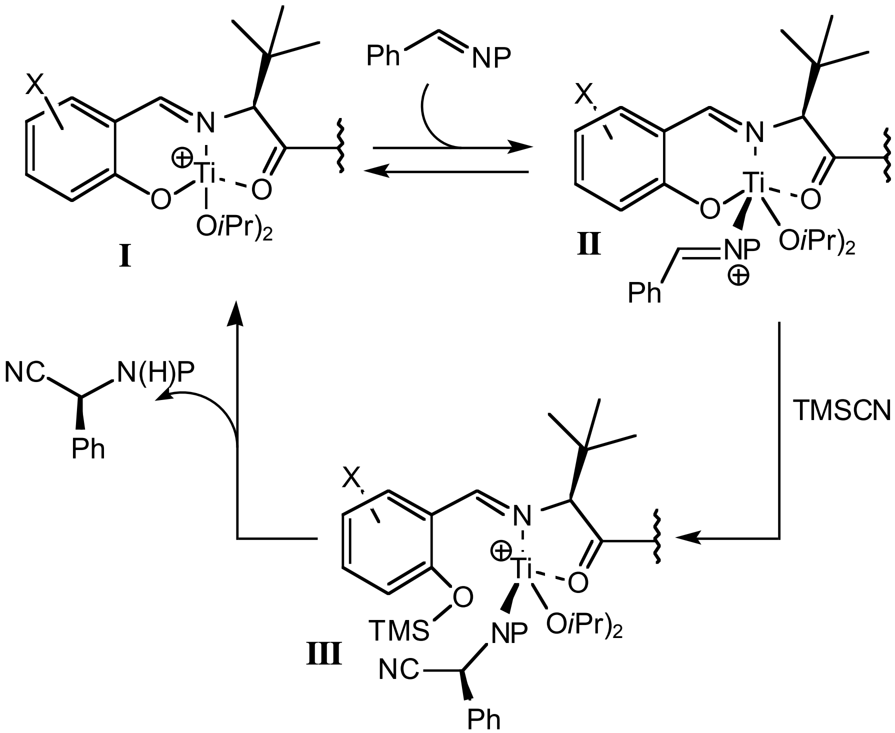
- ♦ Pros: Good results for most imines.
- ♦ Cons: Hydrolysis of product difficult.

♦ Conversion of aminonitriles to Boc-protected amino acids.

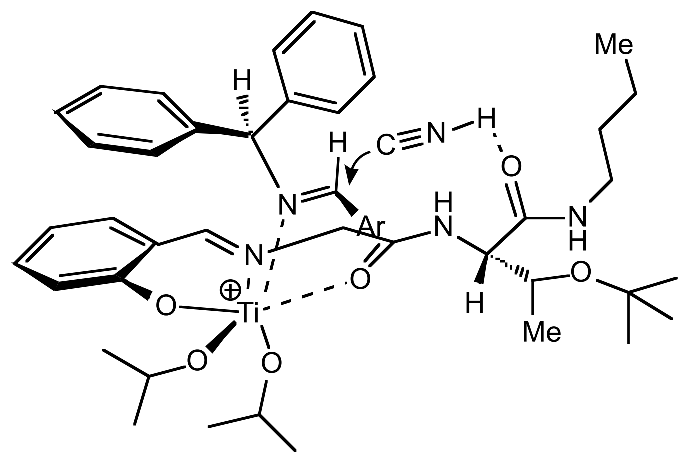


Porter, J. R.; Wirschun, W. G.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 2657-2658.

Proposed Mechanism of Chiral Schiff Base Catalyzed Strecker Reaction



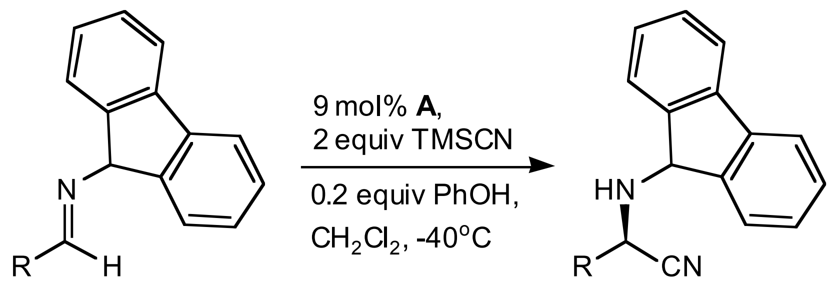
♦ Suggested transition-state of Strecker reaction by molecular modeling and calculation (Below)

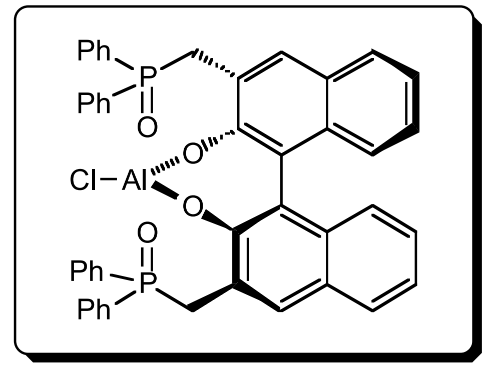


♦ Proposed Mechanism of Schiff base catalyzed Strecker reaction (Above)

Josephsohn, N. S.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2001**, *123*, 11594-11599.

Asymmetric Strecker Reaction Using Bifunctional Catalyst





Shibasaki's bifunctional catalyst **A**

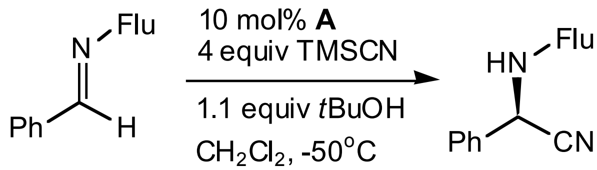
Entry	R	Yield (%)	ee (%)
1	C_6H_5	92	95
2	*p*-ClC_6H_4	92	95
3	*trans*-$CH_3(CH_2)_3CH{=}CH_2$	66	86
4	*n*-Hexyl	80	80
5	*t*-Bu	97	78

♦ Pros: Good results for most imines.
♦ Cons: Polymer-supported bifunctional catalyst works not well.

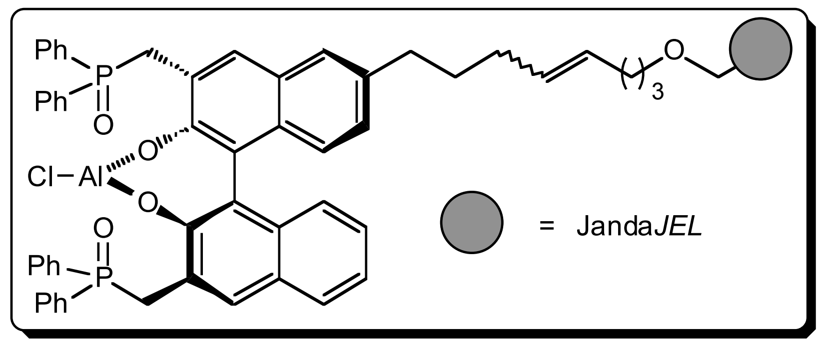
Takamura, M.; Hamashima, Y.; Usuda, H.; Kanai, M.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 1650-1652.
Nogami, H.; Matsunaga, S.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2001**, *42*, 279-283.

Asymmetric Strecker Reaction Using Bifunctional Catalyst

♦ Strecker reaction using polymer-supported bifunctional catalyst

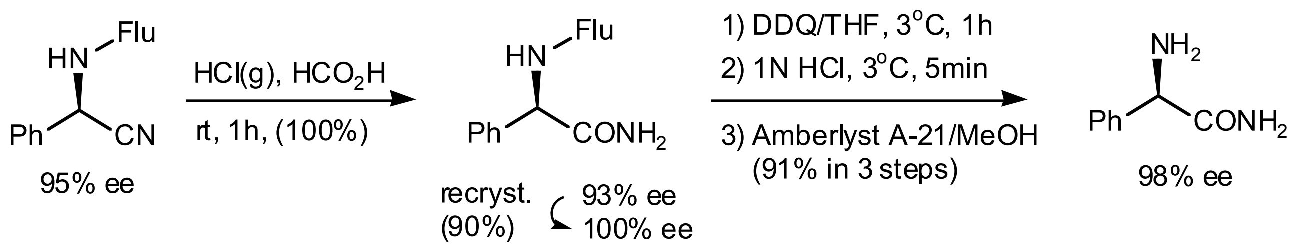


Cycle	Time(h)	Yield (%)	ee (%)
1	60	98	87
3	44	78	83
5	204	83	77



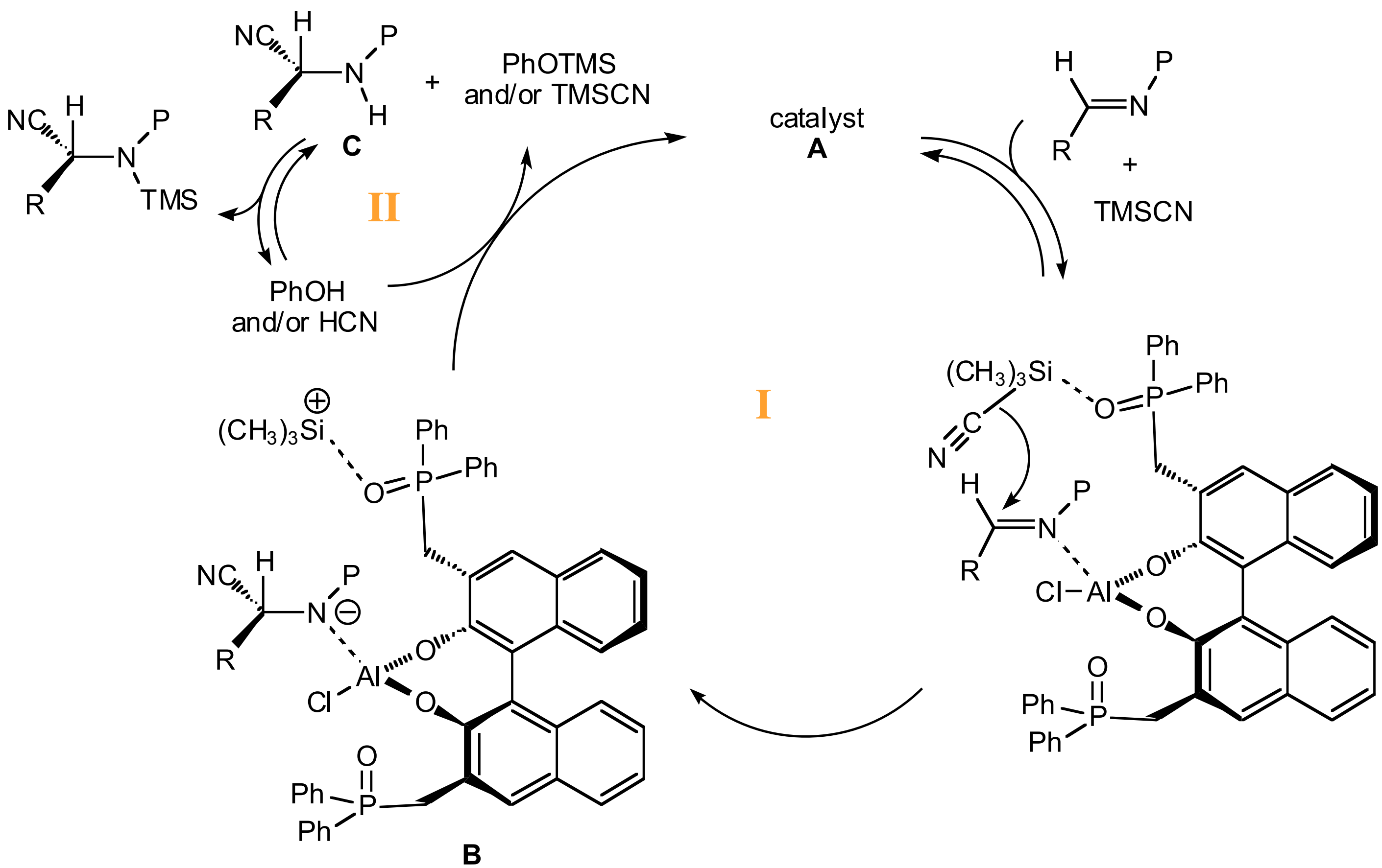
Shibasaki's bifunctional catalyst **A**

♦ Conversion of aminonitriles to amino acid derivatives.



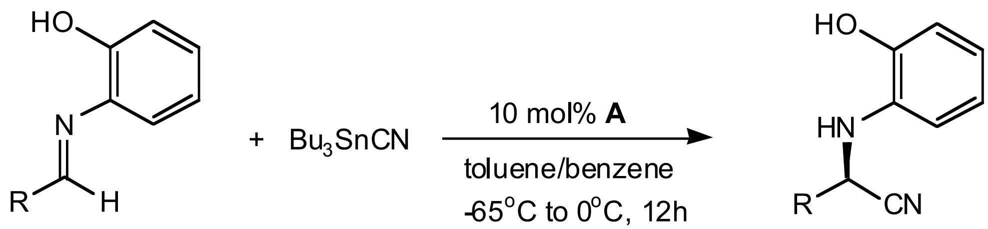
Takamura, M.; Hamashima, Y.; Usuda, H.; Kanai, M.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 1650-1652.
Nogami, H.; Matsunaga, S.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2001**, *42*, 279-283.

Proposed Mechanism of Strecker Reaction Catalyzed by Bifunctional Catalyst

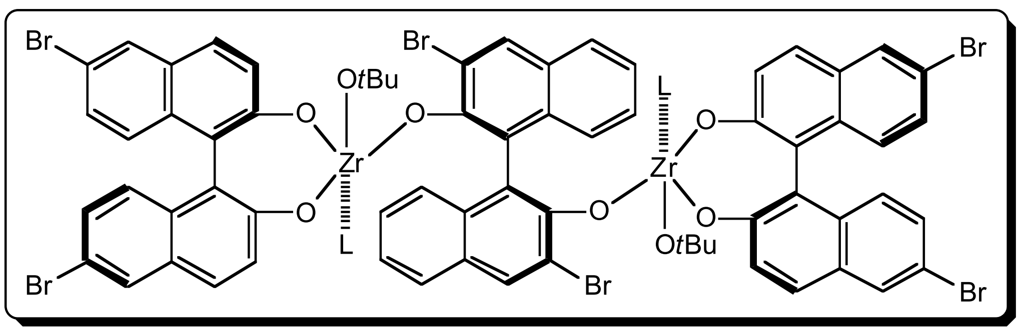


Takamura, M.; Hamashima, Y.; Usuda, H.; Kanai, M.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 1650-1652.

Asymmetric Strecker Reaction Using Chiral Zirconium Catalyst



Entry	R	Yield (%)	ee (%)
1	C_6H_5	92	91
2	*p*-ClC_6H_4	90	88
3	*o*-MeOC_6H_4	96	89
4	*p*-MeOC_6H_4	97	76
5	$C_6H_5(CH_2)_2$	55	83
6	*i*Bu	79	83
7	C_8H_{17}	72	84

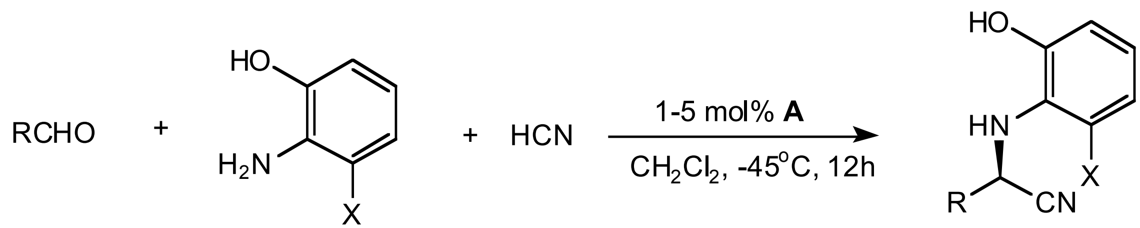


L = NMI Kobayashi's Chiral Zirconium Catalyst **A**

- ♦ Pros: Catalysts commercially available, good for most aromatic imines.
- ♦ Cons: Not so good for aliphatic imines.

Ishitani, H.; Komiyama, S.; Kobayashi, S. *Angew. Chem., Int. Ed.* **1998**, *37*, 3186-3188.

Catalytic Three-Component Strecker Reaction Using Chiral Zirconium Catalyst



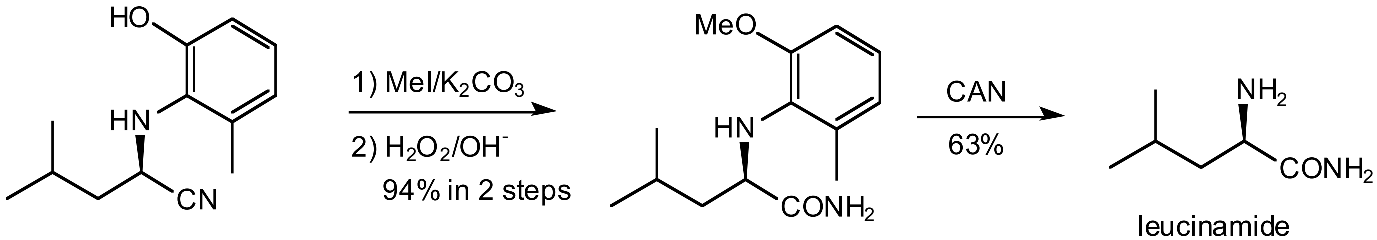
Entry	R	X	Yield (%)	ee (%)
1	C_6H_5	H	80	86
2	$C_6H_5(CH_2)_2$	CH_3	85	94
3	C_8H_{17}	CH_3	83	90
4	cyclohexyl	CH_3	95	94
5	*i*Bu	CH_3	94	91
6	*t*Bu	CH_3	quant	88

- ♦ Pros: First catalytic three-component Strecker reaction;
  Good results for most imines;
  Low catalyst loading
  Catalysts commercially available.
- ♦ Cons: Still need protecting group;
  No mechanism discussion.

Ishitani, H.; Komiyama, S.; Hasegawa, Y.; Kobayashi, S. *J. Am. Chem. Soc.* **2000**, *122*, 762-766.

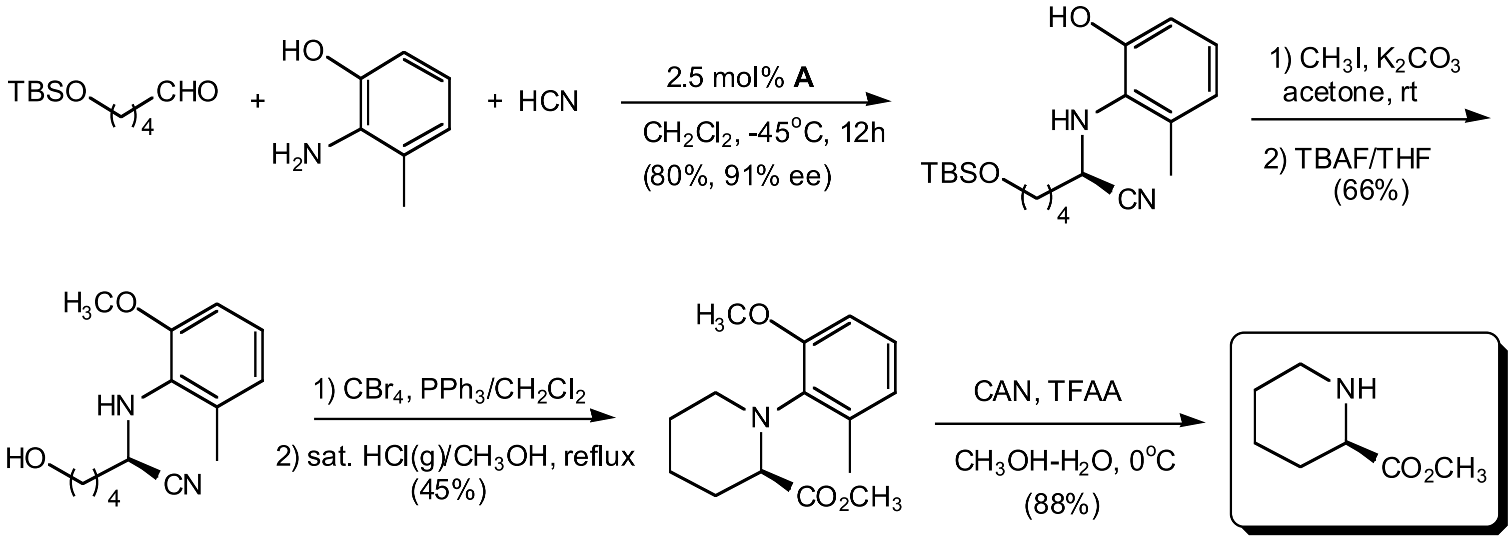
Catalytic Three-Component Strecker Reaction Using Chiral Zirconium Catalyst

♦ Conversion of aminonitriles to amino acid derivatives.



leucinamide

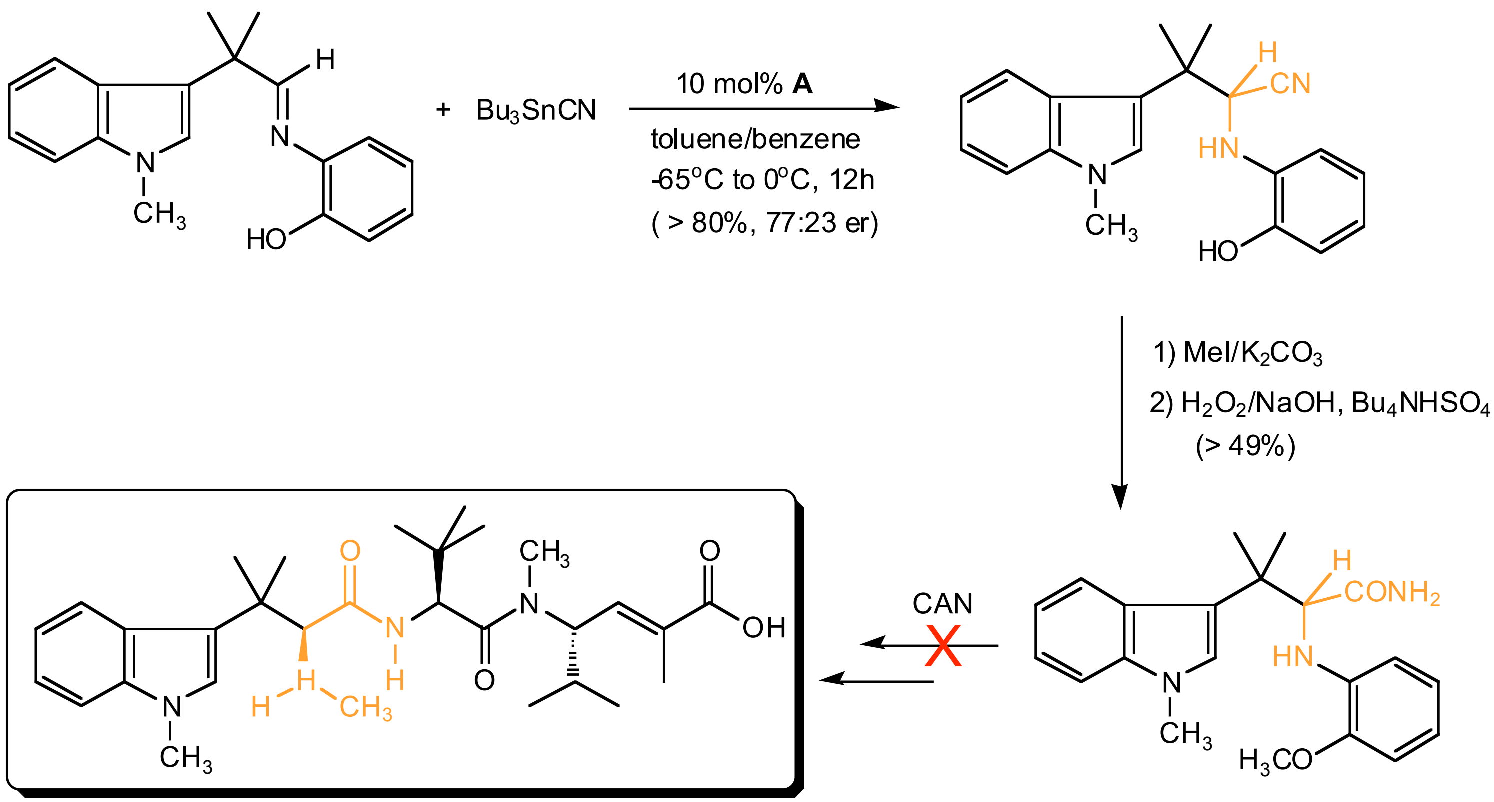
♦ Synthesis of D-pipecolic acid methyl ester.



D-pipecolic acid methyl ester

Ishitani, H.; Komiyama, S.; Hasegawa, Y.; Kobayashi, S. *J. Am. Chem. Soc.* **2000**, *122*, 762-766.

Attempted Application of Catalytic Asymmetric Strecker Reaction



(-)-Hemiasterlin

Vedejs, E.; Kongkittingam, C. *J. Org. Chem.* **2001**, *66*, 7355-7364.

Asymmetric Strecker Reaction - Future Work

♦ Further development of chiral auxiliary methods, more applications in total synthesis.

♦ Successful application of catalytic asymmetric process in synthesis of large molecules.

♦ Better understanding of mechanism of catalytic asymmetric process.

♦ Development of more practical asymmetric catalytic systems toward commercial process.
- higher yield & ee; higher turnover; easier separation… ...

Asymmetric Strecker Reaction - Conclusions

♦ 150 years after discovery of Strecker reaction, asymmetric Strecker reaction has been a real highlight in synthesis of α-amino acids.

♦ After 20 years' development, Strecker reaction using chiral auxiliaries has been proved an efficient method for the preparation of simple amino acids and total synthesis of large molecules.

♦ Catalytic asymmetric Strecker reaction achieved great advance in last 5 years. Although an efficient method for preparation of simple amino acids, its application in synthesis of large molecules and commercial production still needs further development.