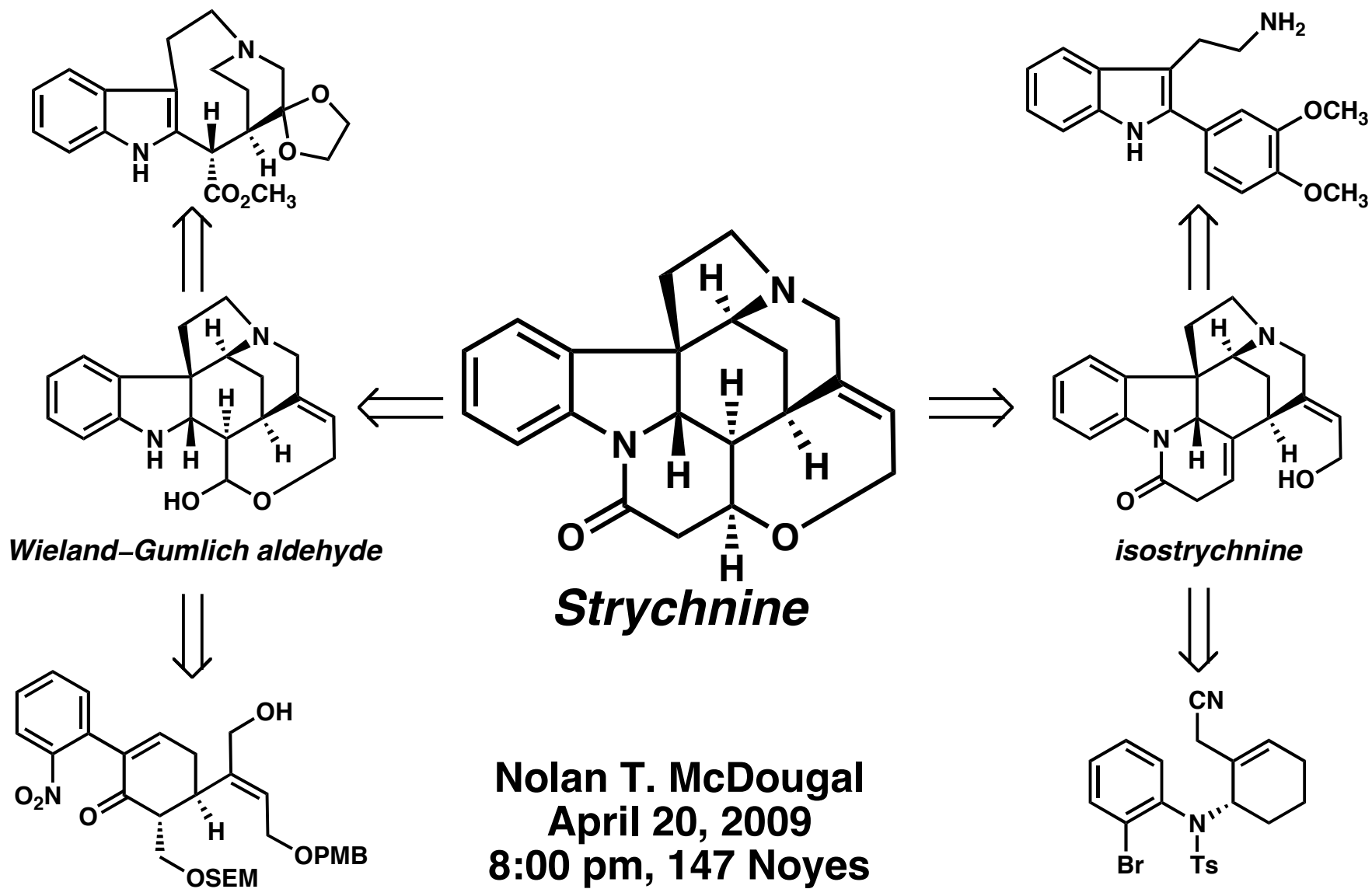
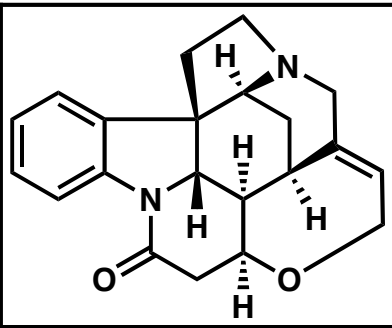


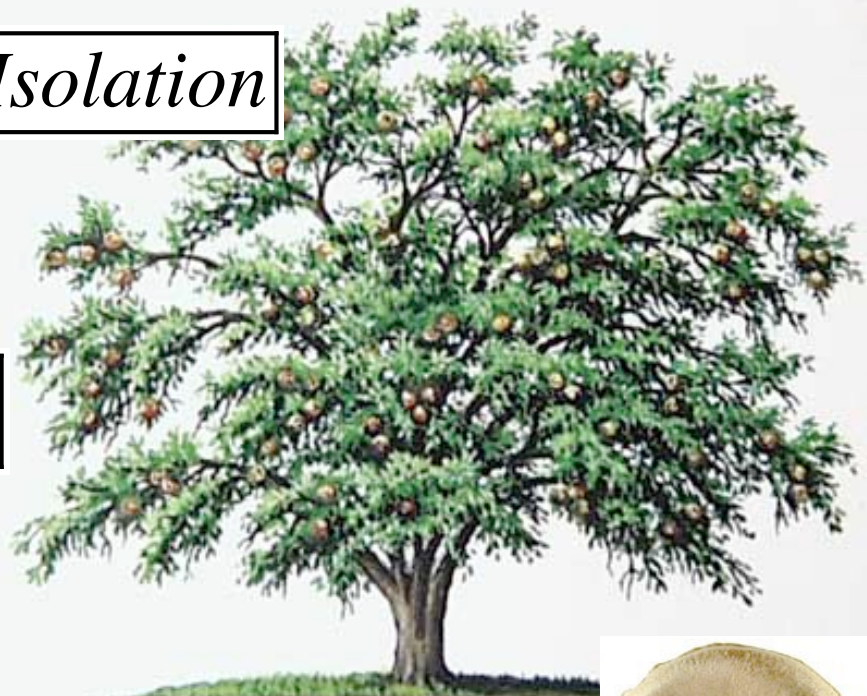
Comparative Total Syntheses of Strychnine





Strychnine – Isolation

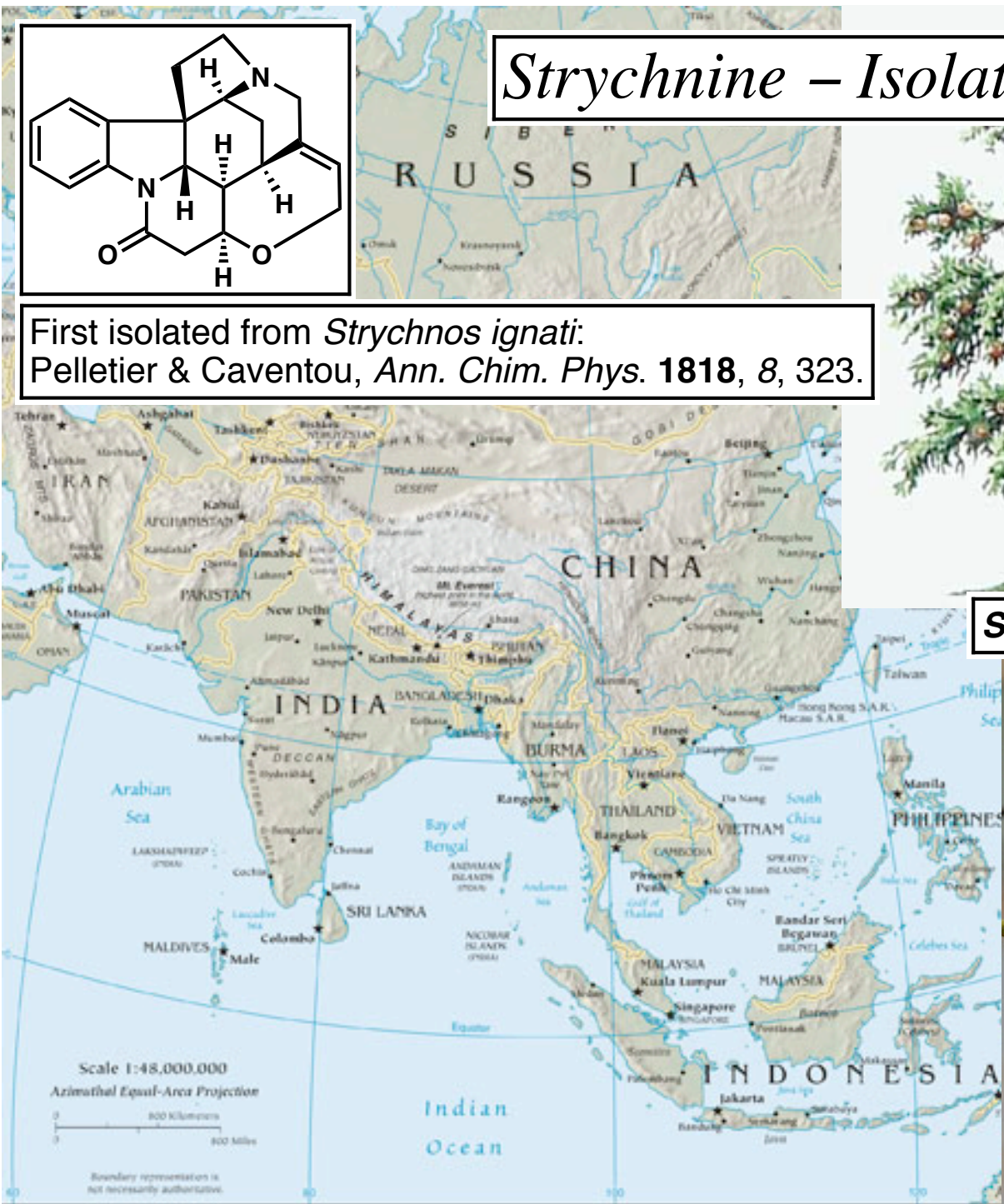
First isolated from *Strychnos ignati*:
Pelletier & Caventou, *Ann. Chim. Phys.* **1818**, 8, 323.



Strychnos nuxvomica



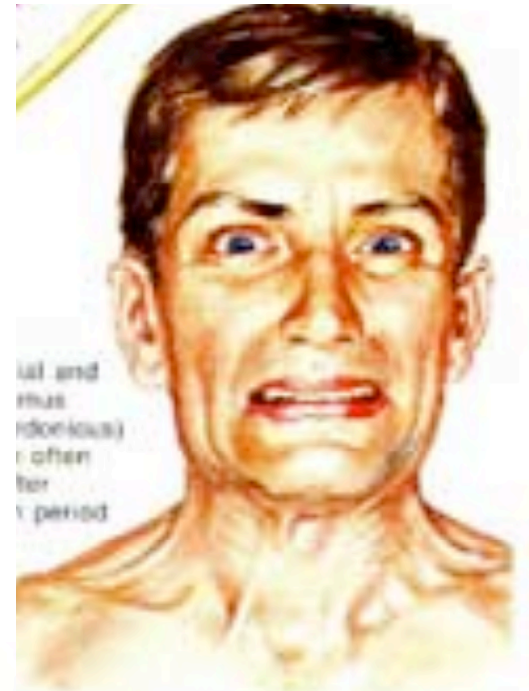
2cm



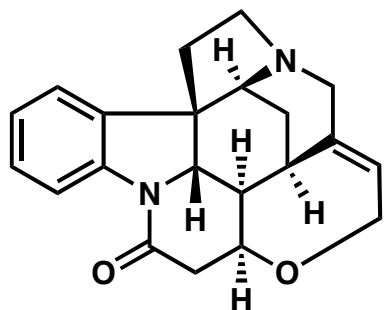
Strychnine Poisoning and Treatment

- **Biological Response** - Blocks postsynaptic inhibition as an antagonist of glycine in the central nervous system, resulting in over-transmission of signals and in reflex arcs, which would normally be suppressed by the postsynaptic action of glycine. i.e. the tiniest sensory stimulus (noises, movement, or light) produces powerful muscular contraction.
- **Symptoms** - Tightness and twitching of the muscles, agitation and hyperreflexia. Stiffness of the body and lockjaw. Nearly continuous convulsions. Cessation of respiration. Death comes from asphyxiation caused by paralysis of the neural pathways that control breathing, or by exhaustion from the convulsions.
The patient never loses consciousness.
- **Treatment** - There is no specific antidote. Oral application of an activated charcoal infusion. Anticonvulsants are administered along with muscle relaxants, and if necessary artificial respiration. Treatment in the late 19th and early 20th centuries was to administer tannic acid which precipitates the strychnine as an insoluble salt, and then to anaesthetise the patient with chloroform until the effects of the strychnine had worn off.

- Dr. Pierre-Eloi Fouquier
- doctor during Napoleonic Wars

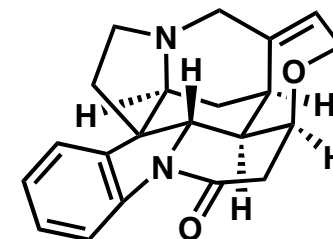


Complete tetanic spasm in advanced disease. Patient rigid in moderate opisthotonos, with arms extended, abdomen boardlike. Respiratory arrest may occur



Structure of Strychnine

"For its molecular size it is the most complex substance known." - Robert Robinson (1952)

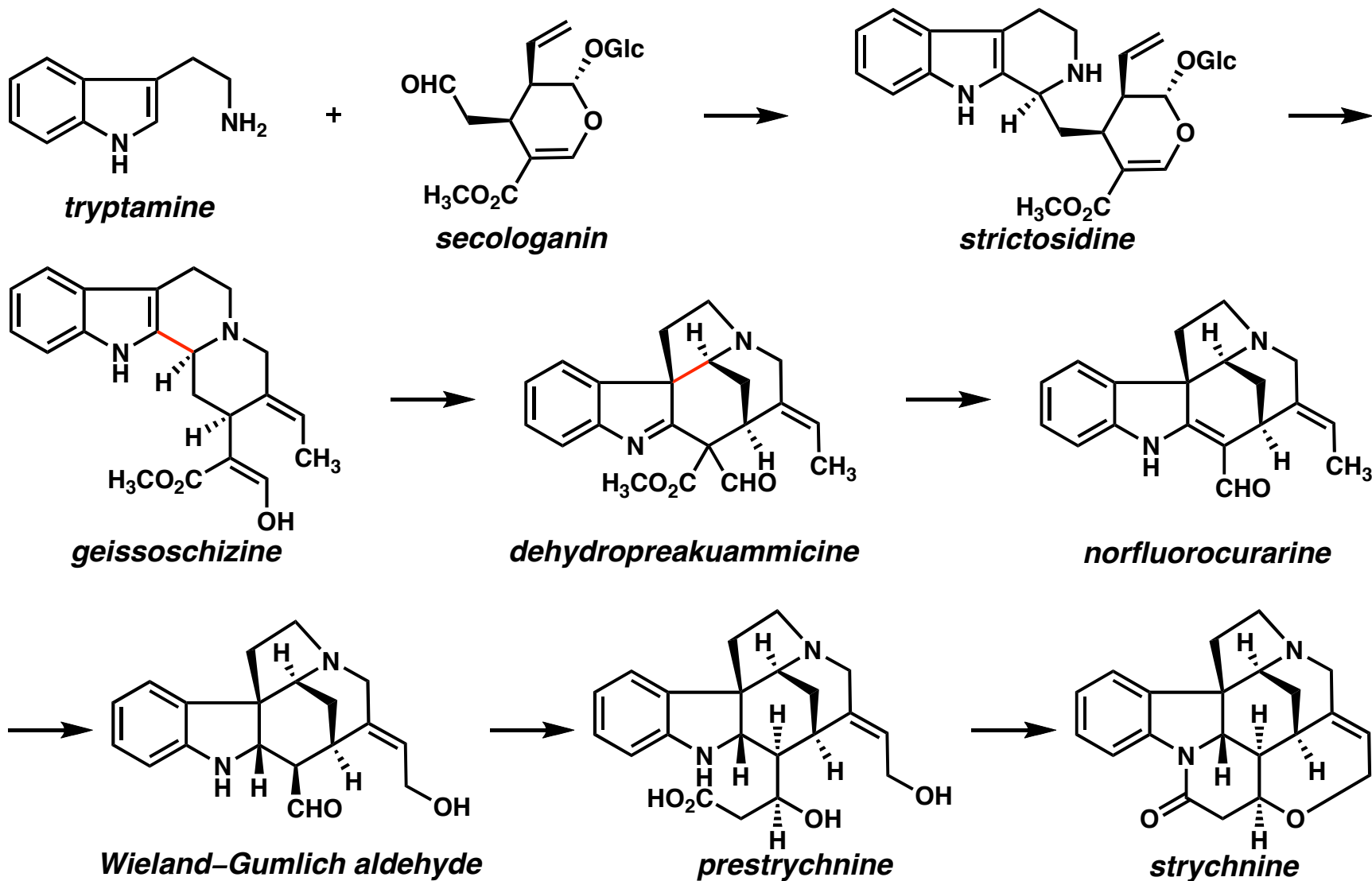


"Admittedly, by one whose special familiarity with the intricacies of its structure and behavior might excuse a certain prejudice, but with six nuclear asymmetric centers and seven rings constituted from only twenty-four skeletal atoms, the case is a good one" - R. B. Woodward (1963)

-
- First isolated in 1818 by Pelletier & Caventou
 - Pelletier & Caventou, *Ann. Chim. Phys.* **1818**, 8, 323.
 - Elemental composition determined in 1838 by Regnault
 - Regnault, *Ann.* **1838**, 26, 35.
 - Degradation studies (1880's-1950's) by Robinson, Leuchs, and Woodward

publications	(~250)	(~125)
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 - Structure defined in 1946 by Robinson and in 1947 by Woodward
 - Openshaw & Robinson, *Nature* **1946**, 157, 438.
 - Woodward *et al.* *J. Am. Chem. Soc.* **1947**, 69, 2250.
 - Woodward & Brehm, *J. Am. Chem. Soc.* **1948**, 70, 2107-2115.
 - Relative stereochemistry defined by X-ray crystal in 1951 by Robertson & Beevers, and Bijvoet
 - Robertson & Beevers, *Nature* **1950**, 165, 690-691.
 - Bijvoet *et al.* *Acta Crystallogr.* **1951**, 4, 275-280.
 - Absolute stereochemistry defined by X-ray crystal in 1956 by Peerdeman
 - Peerdeman, *Acta Crystallogr.* **1956**, 9, 824.
 - Absolute stereochemistry defined by chemical methods in 1963 by Schmid
 - Schmid *et al.* *Helv. Chim. Acta.* **1963**, 46, 1212-1231.

Biosynthesis of Strychnine

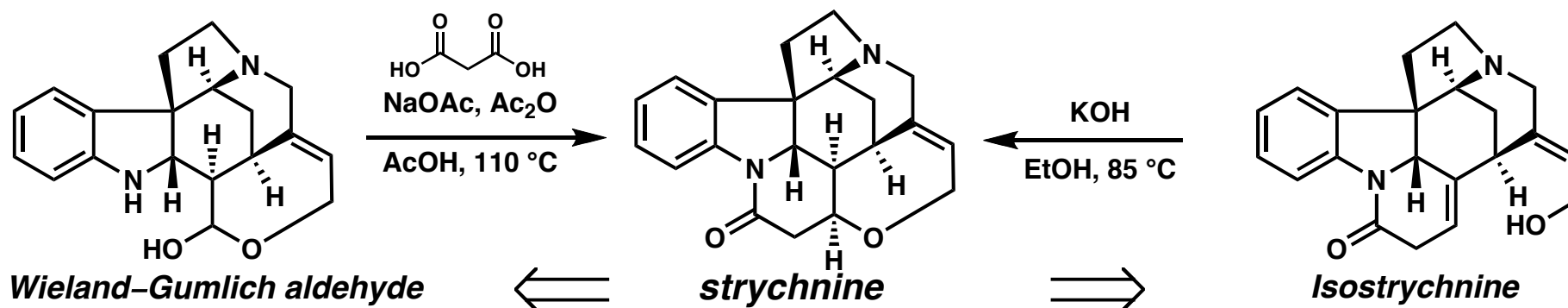


Schmid *et al.* *Helv. Chim. Acta.* **1969**, *52*, 776-789.

Helmberger & Scott, *J. Chem. Soc., Chem. Commun.* **1973**, 217-218.

Syntheses of Strychnine

- **R. B. Woodward** - Harvard University (1954)
- **Philip Magnus** - University of Texas (1992)
- **Gilbert Stork** - Columbia University (1992)
- **Larry E. Overman** - University of California, Irvine (1993)
- **Martin E. Kuehne** - University of Vermont (1993)
- **Viresh H. Rawal** - The Ohio State University (1994)
- **Josep Bonjoch & Joan Bosch** - University of Barcelona (1999)
- **Stephen F. Martin** - University of Texas (1996-2001)
- **Michael J. Eichberg & K. Peter C. Vollhardt** - University of California, Berkeley (2000)
- **Graham J. Bodwell** - Memorial University of Newfoundland (2002)
- **Miwako Mori** - Hokkaido University (2002)
- **Masakatsu Shibasaki** - University of Tokyo (2002)
- **Tohru Fukuyama** - University of Tokyo (2004)
- **Albert Padwa** - Emory University (2007)



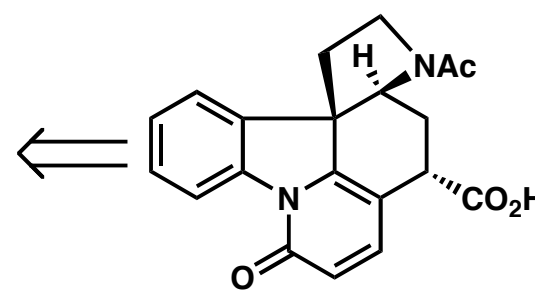
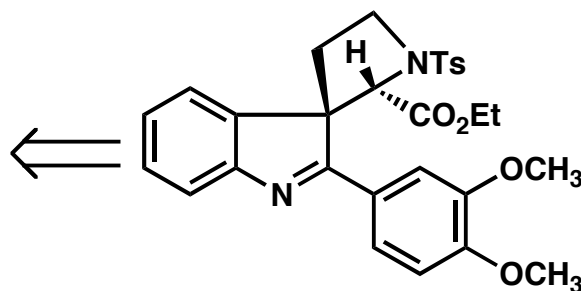
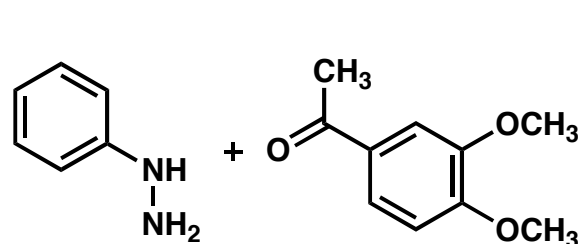
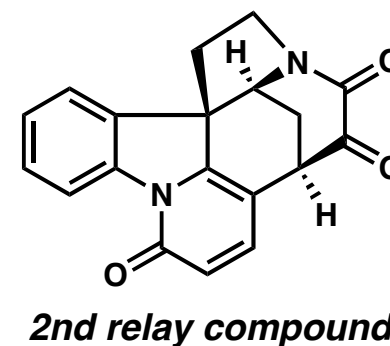
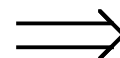
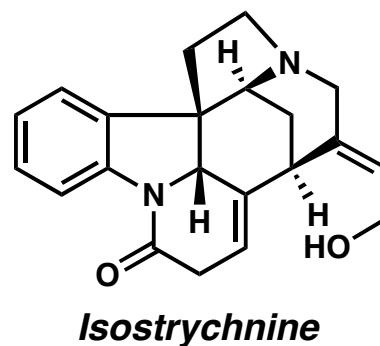
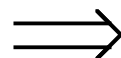
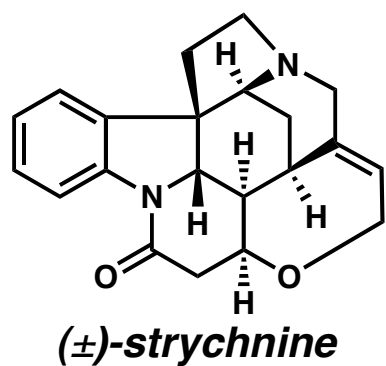
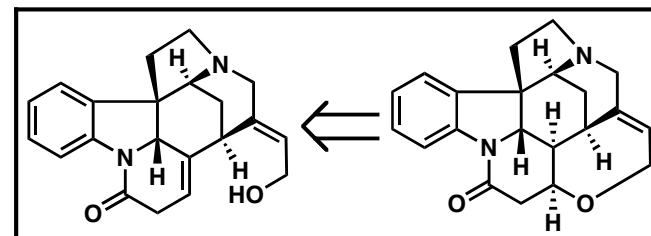
Wieland-Gumlich aldehyde synthesis: Wieland & Gumlich, *Liebigs Ann. Chem.* **1932**, 494, 191-200.

Conversion to strychnine: Anet & Robinson, *Chem. Ind.* **1953**, 245.

Isostrychnine synthesis: Wieland & Jennen, *Liebigs Ann. Chem.* **1940**, 545, 99-112.

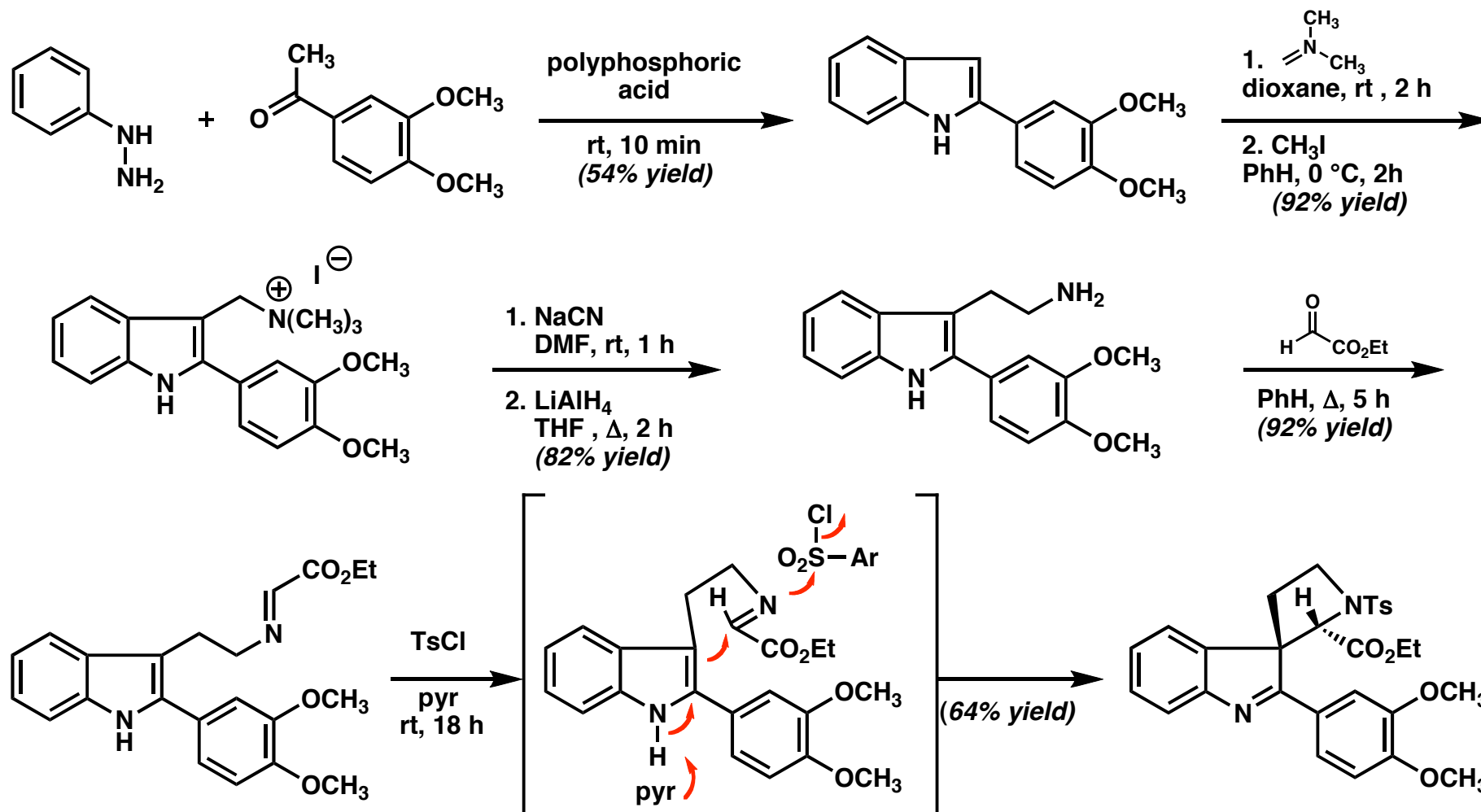
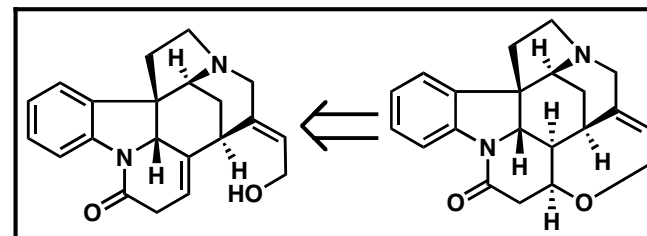
Conversion to strychnine: Prelog *et al.* *Helv. Chim. Acta* **1948**, 31, 2244-2246.

Retrosynthetic Analysis of Woodward's (\pm)-Synthesis (1954)



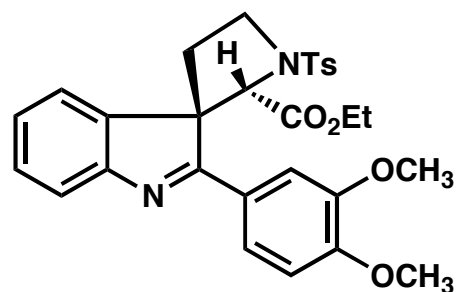
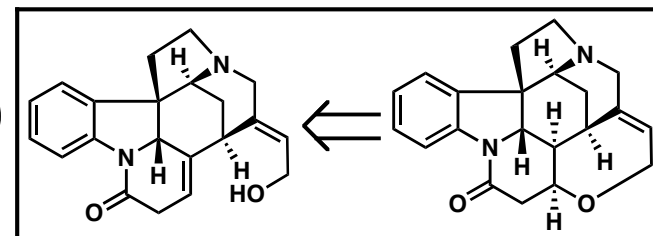
1st relay compound

Woodward's (\pm)-Total Synthesis (1954)

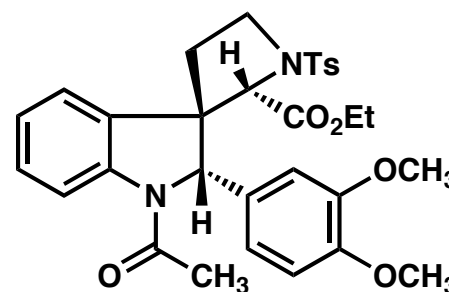


Woodward et al. *J. Am. Chem. Soc.* **1954**, 76, 4749-4751.
 Woodward et al. *Tetrahedron* **1963**, 19, 247-288.

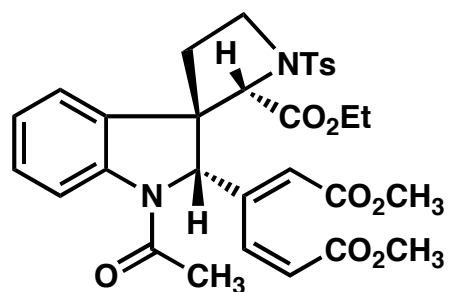
Woodward's (\pm)-Total Synthesis (1954)



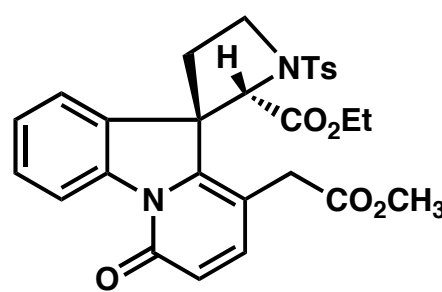
1. NaBH₄
EtOH/H₂O, Δ , 1h
2. Ac₂O, pyr
100 °C, 1 h
(84% yield)



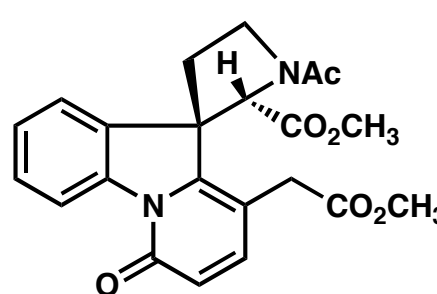
O₃
AcOH/H₂O
rt, 22 min
(29% yield)



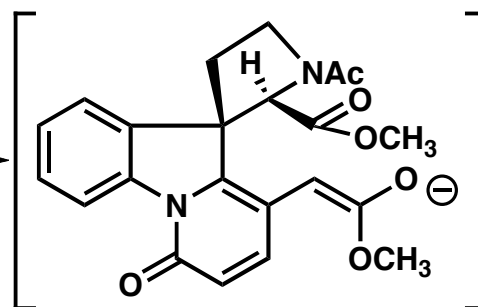
HCl
CH₃OH, Δ , 10 h
(75% yield)



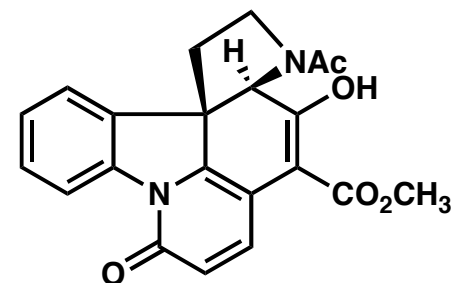
1. HI, red P
AcOH, Δ
2. Ac₂O, pyr
rt, 1 h
3. CH₂N₂
CH₃OH/Et₂O
(57% yield)



NaOCH₃
CH₃OH
 Δ , 20 min

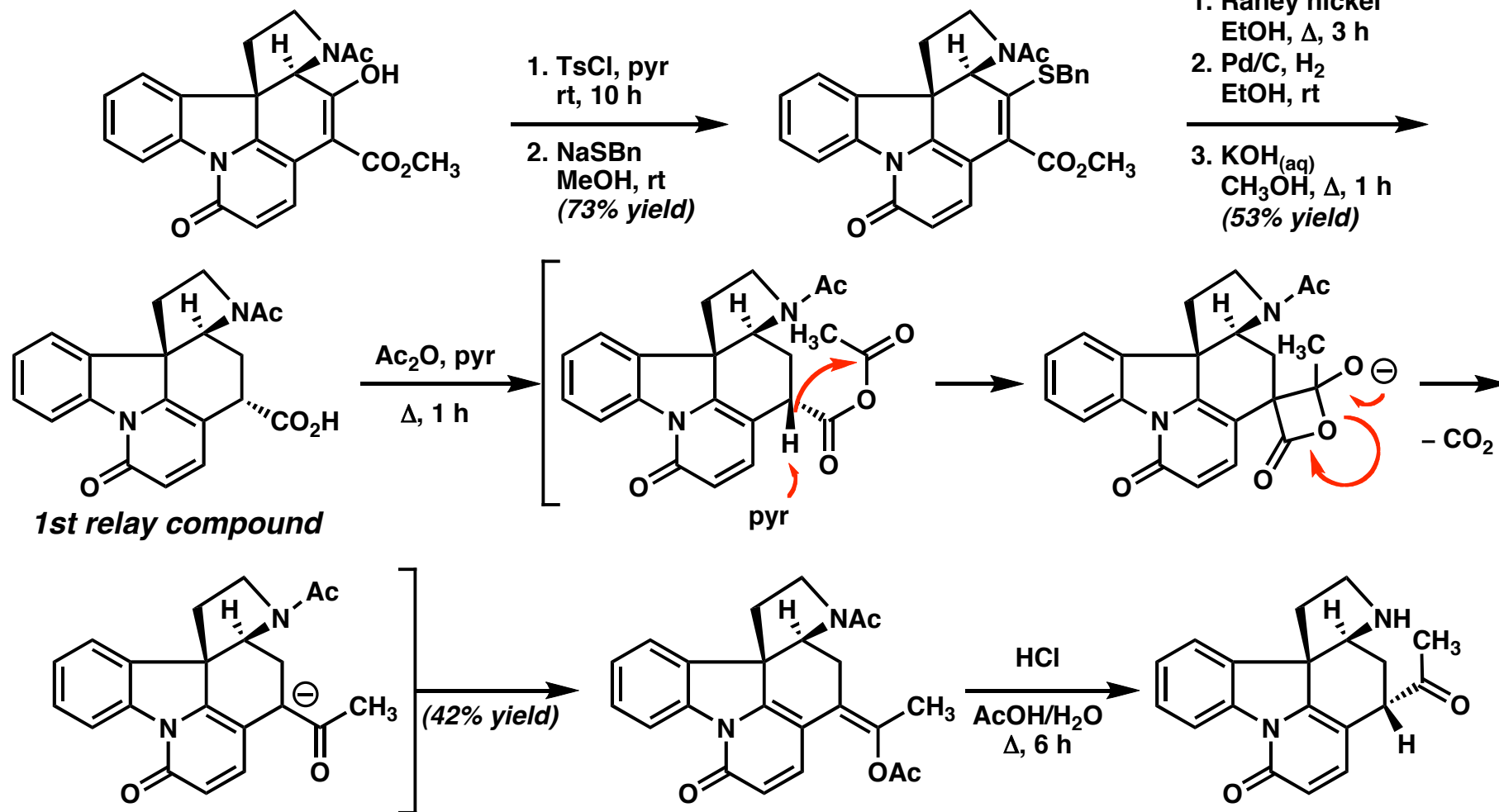
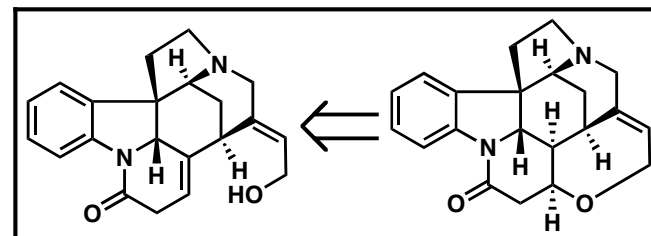


Dieckmann
(88% yield)



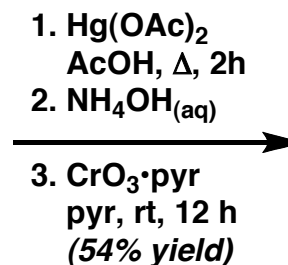
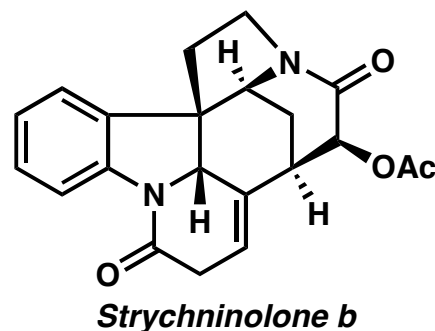
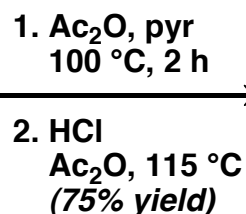
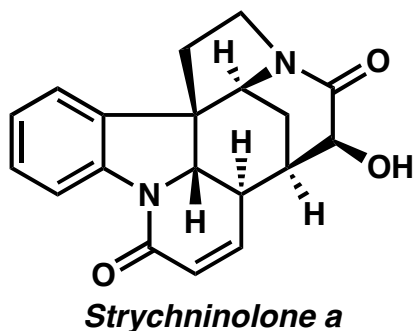
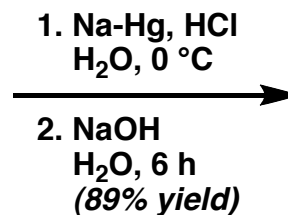
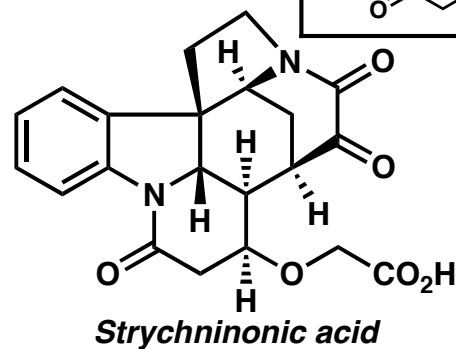
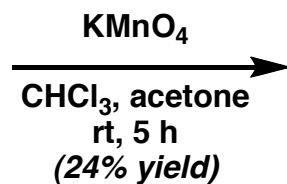
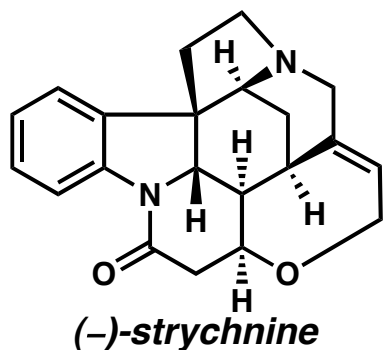
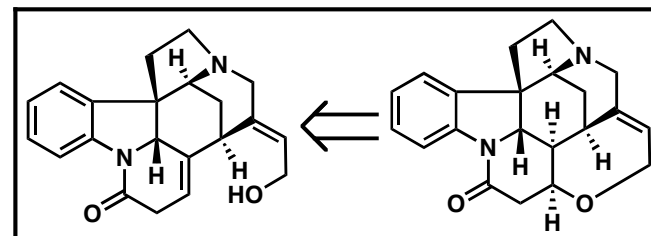
Woodward et al. *J. Am. Chem. Soc.* **1954**, 76, 4749-4751.
Woodward et al. *Tetrahedron* **1963**, 19, 247-288.

Woodward's (\pm)-Total Synthesis (1954)

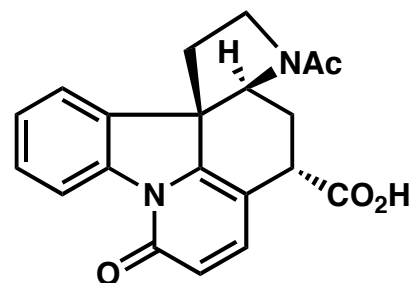
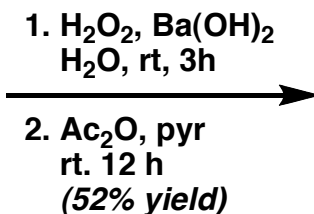
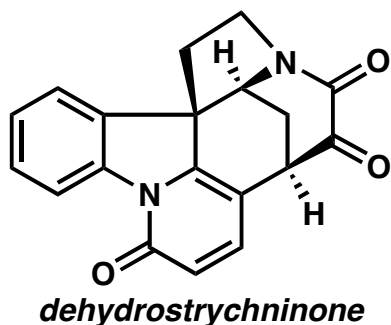


Woodward et al. *J. Am. Chem. Soc.* **1954**, 76, 4749-4751.
 Woodward et al. *Tetrahedron* **1963**, 19, 247-288.

Woodward's (-)-Relay Synthesis (1954)



2nd relay compound



1st relay compound

Leuchs & Schwaebel, *Ber. Dtsch. Chem. Ges.* **1913**, 46, 3693-3699.

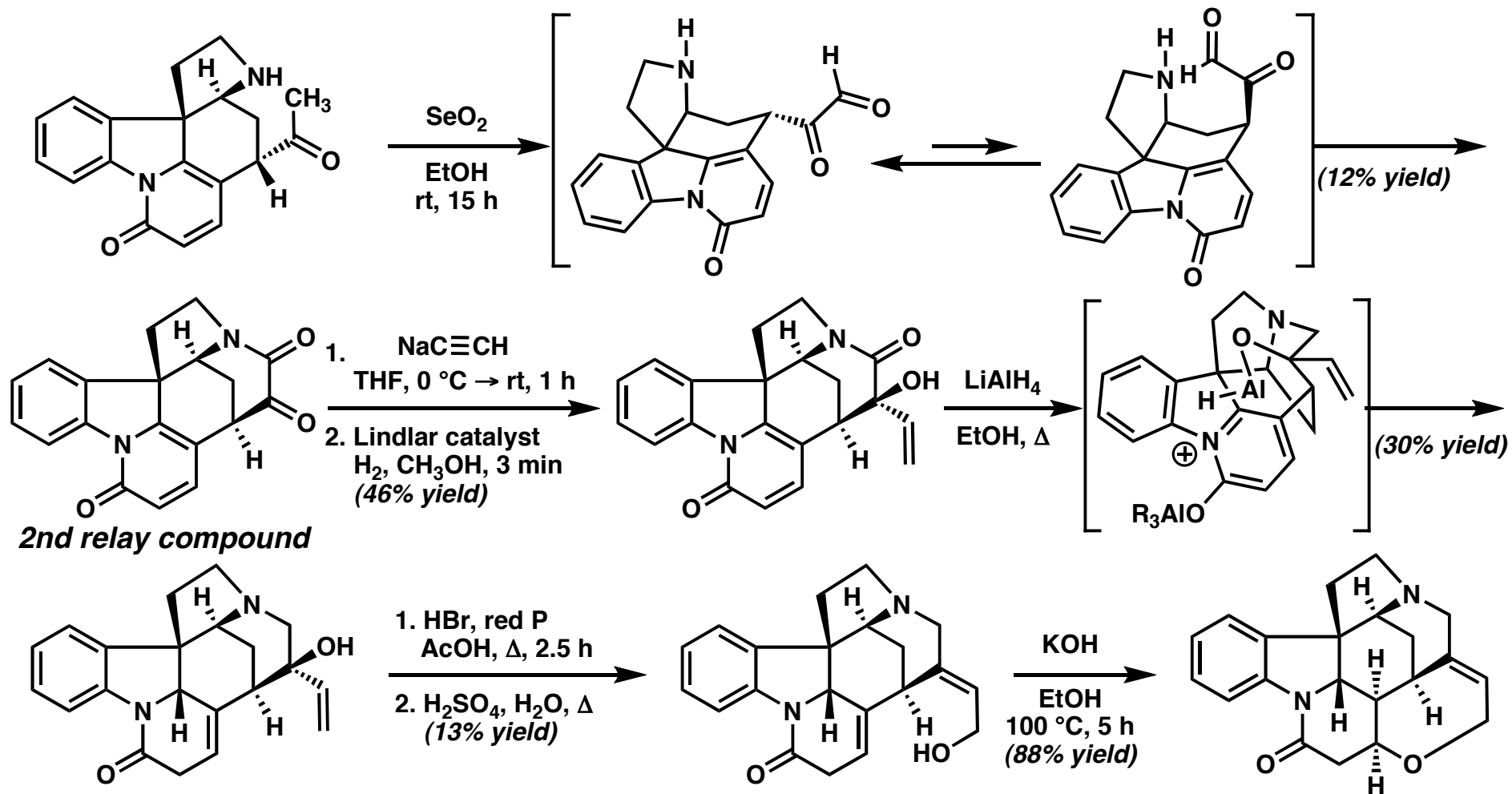
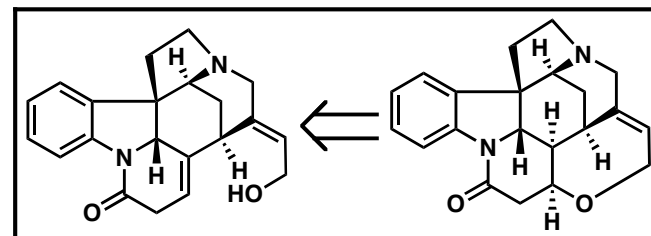
Leuchs & Schwaebel, *Ber. Dtsch. Chem. Ges.* **1914**, 47, 1552-1560.

Leuchs & Schwaebel, *Ber. Dtsch. Chem. Ges.* **1919**, 52, 1443-1453.

Prelog *et al.* *Helv. Chim. Acta* **1949**, 32, 1052-1057.

Woodward *et al.* *J. Am. Chem. Soc.* **1954**, 76, 4749-4751.

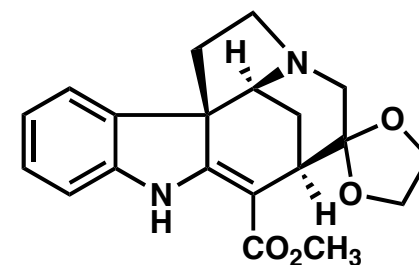
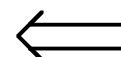
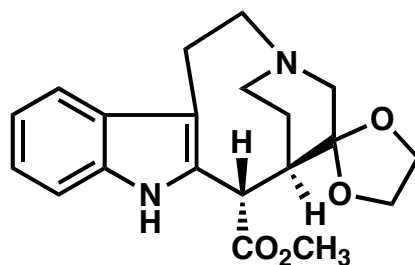
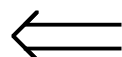
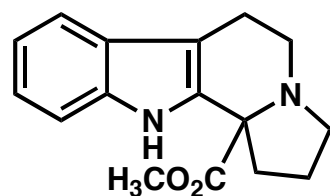
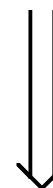
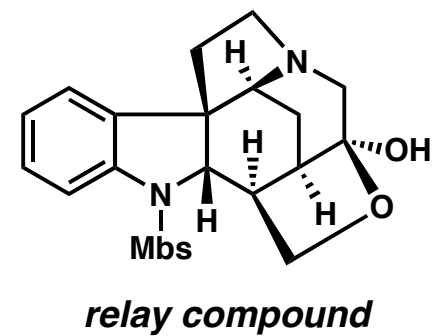
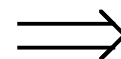
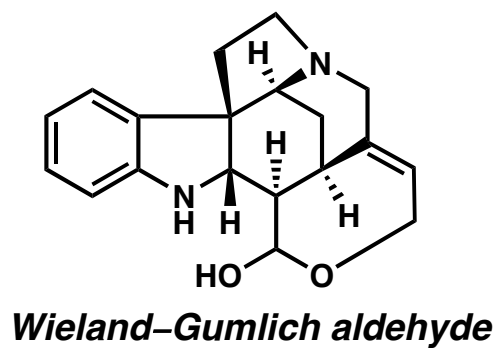
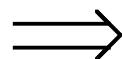
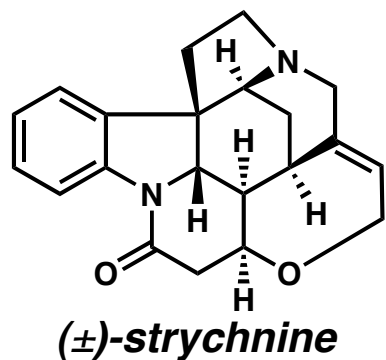
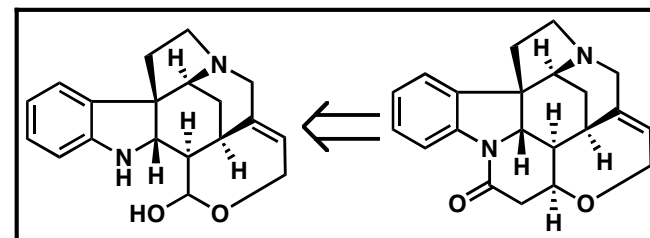
Woodward's (\pm)-Total Synthesis (1954)



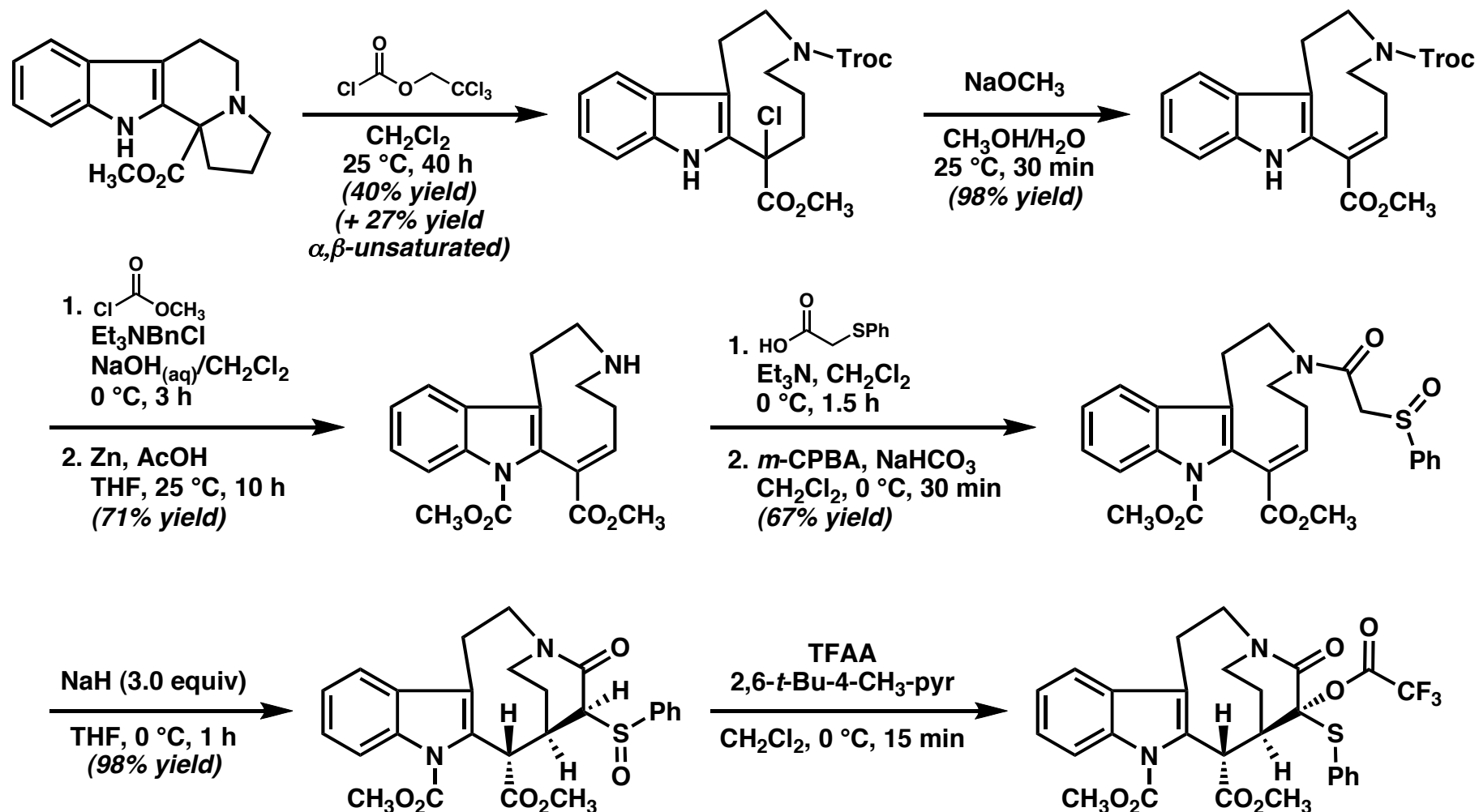
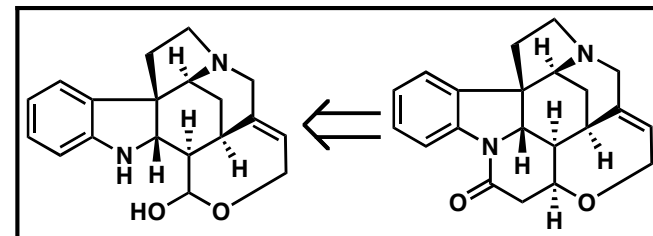
Woodward et al. *J. Am. Chem. Soc.* **1954**, 76, 4749-4751.
Woodward et al. *Tetrahedron* **1963**, 19, 247-288.

(\pm)-strychnine
0.00006% yield
28 steps

Retrosynthetic Analysis of Magnus's (±)-Synthesis (1992)



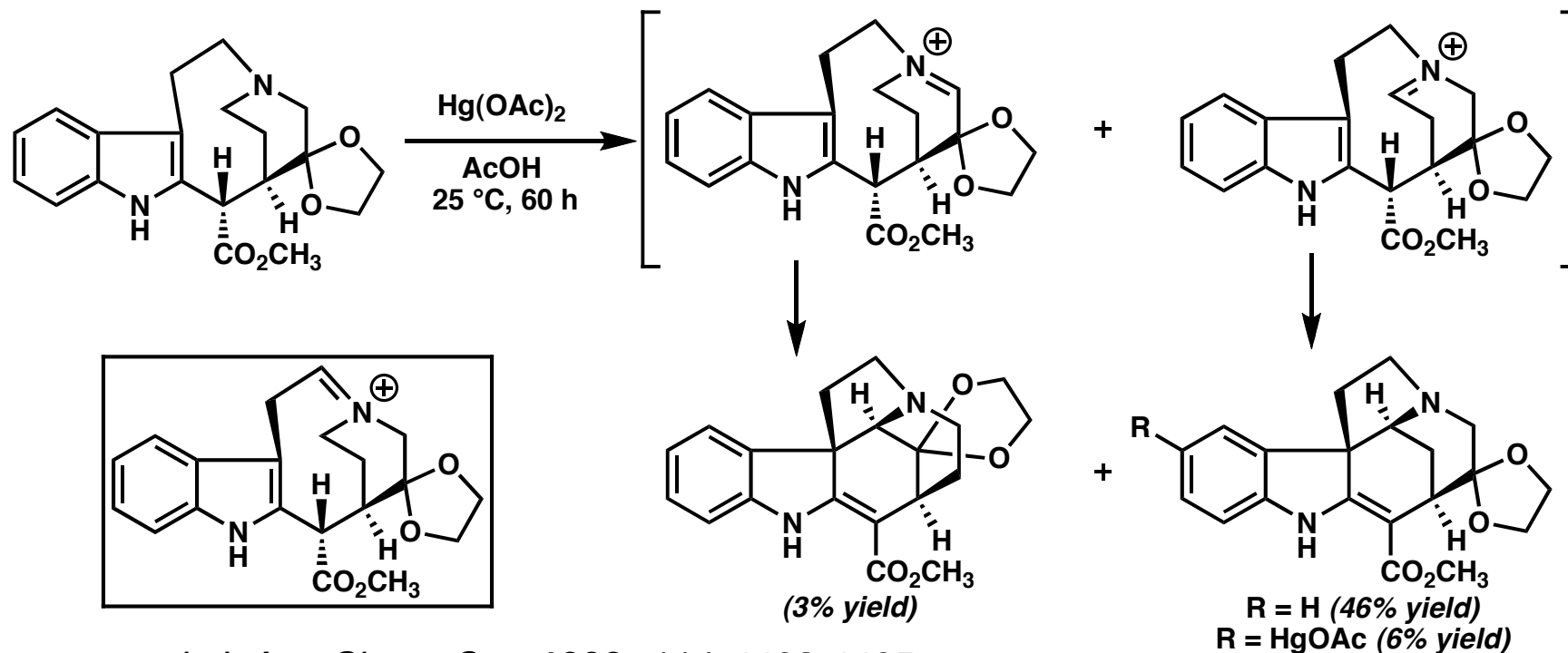
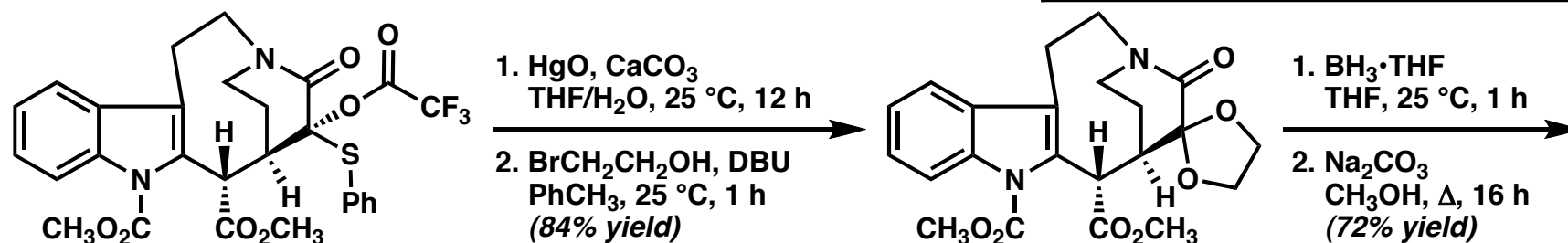
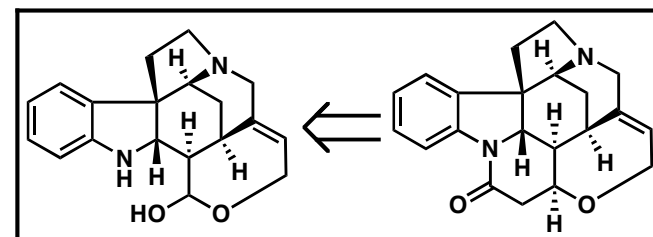
Magnus's (\pm)-Total Synthesis (1992)



Magnus *et al.* *J. Am. Chem. Soc.* **1992**, *114*, 4403-4405.

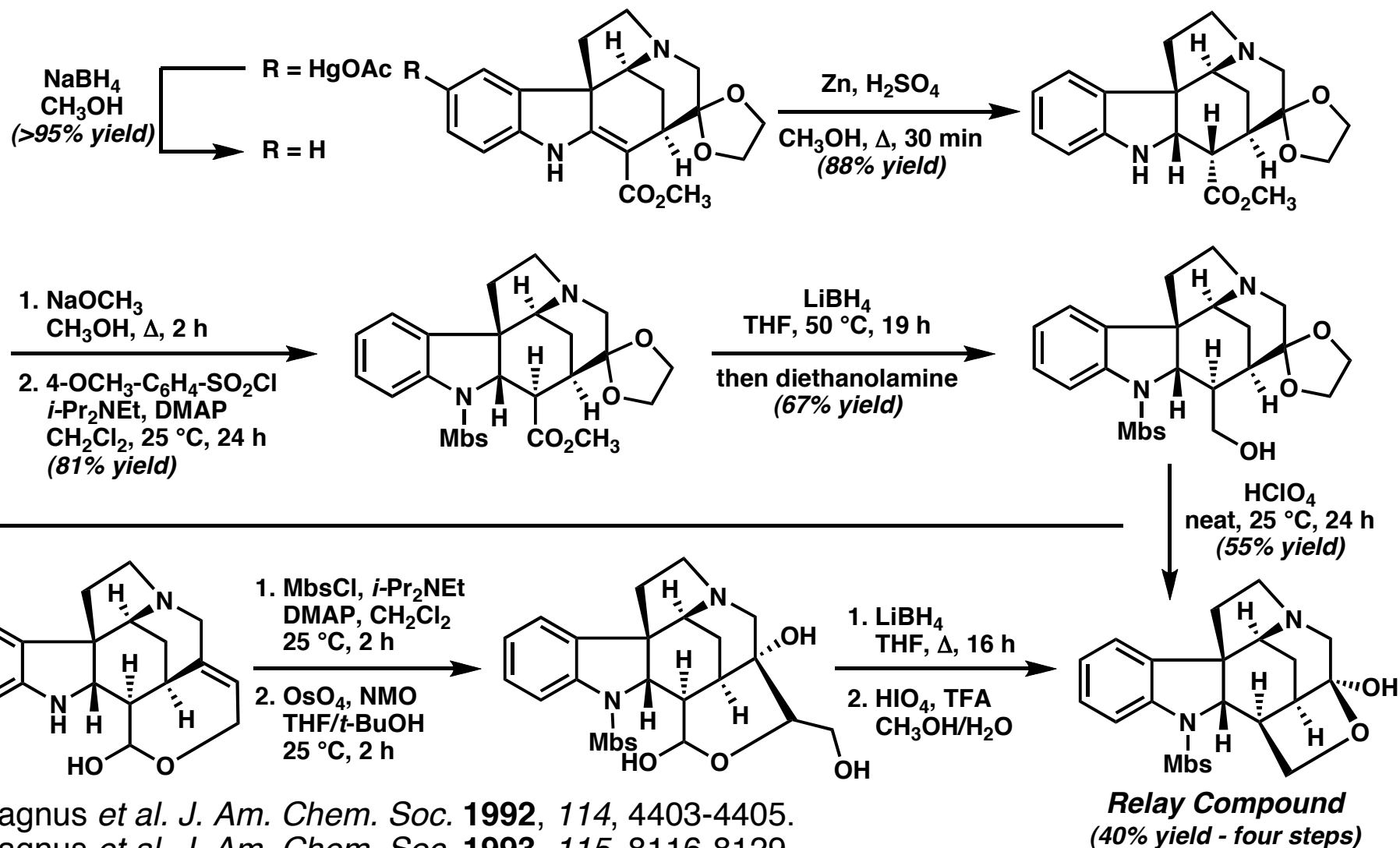
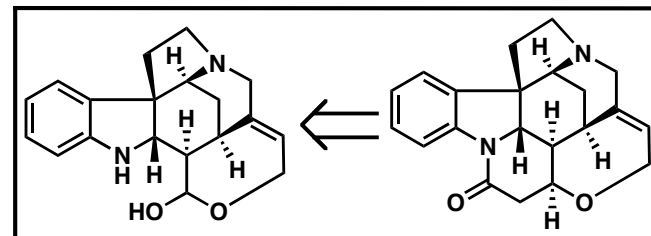
Magnus *et al.* *J. Am. Chem. Soc.* **1993**, *115*, 8116-8129.

Magnus's (\pm)-Total Synthesis (1992)



Magnus *et al.* *J. Am. Chem. Soc.* **1992**, *114*, 4403-4405.
 Magnus *et al.* *J. Am. Chem. Soc.* **1993**, *115*, 8116-8129.

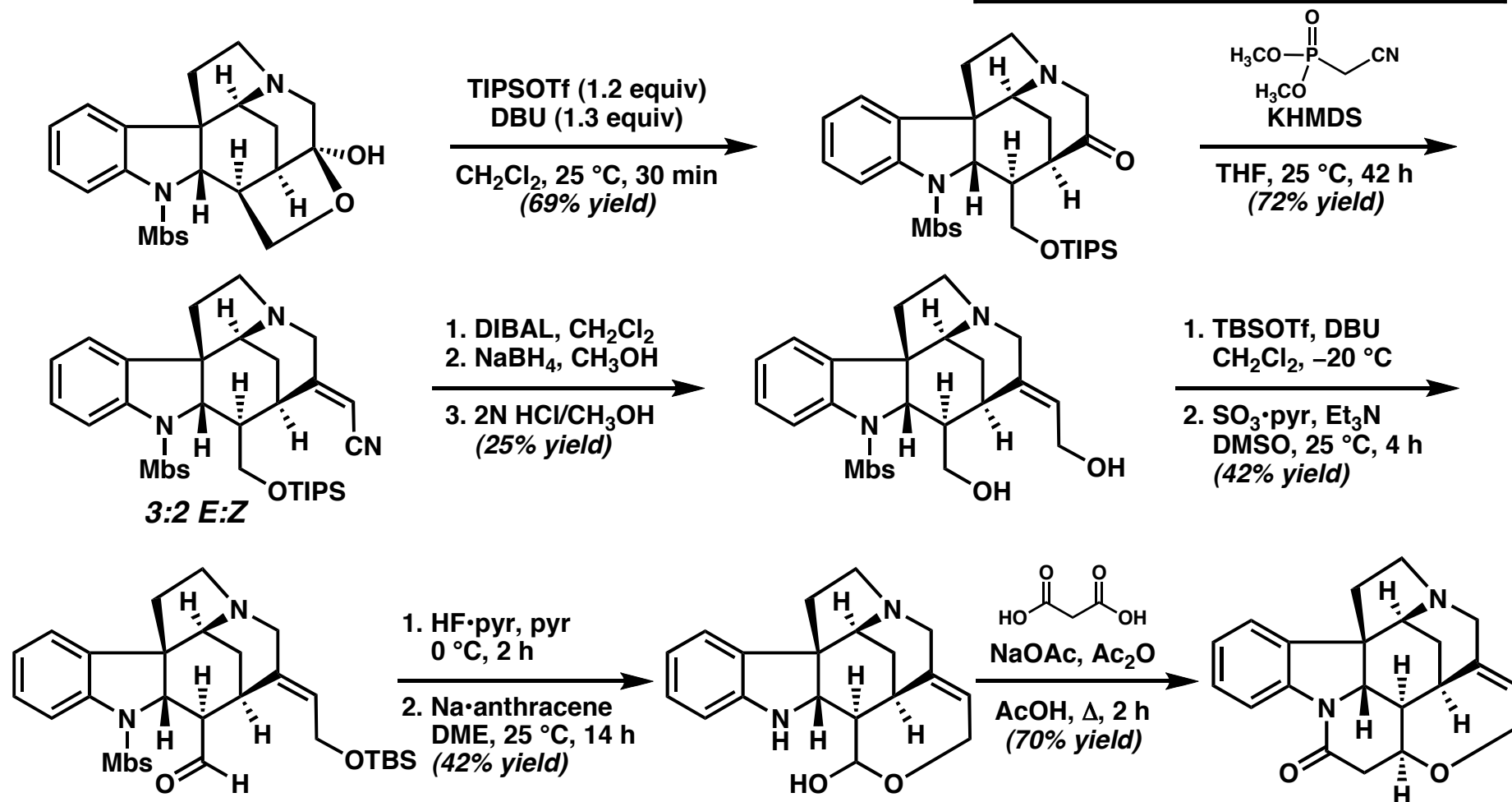
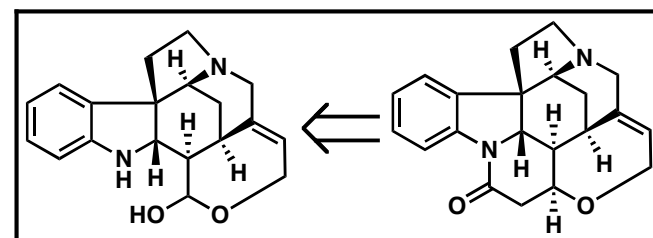
Magnus's (\pm)-Total Synthesis (1992)



Magnus et al. *J. Am. Chem. Soc.* **1992**, *114*, 4403-4405.

Magnus et al. *J. Am. Chem. Soc.* **1993**, *115*, 8116-8129.

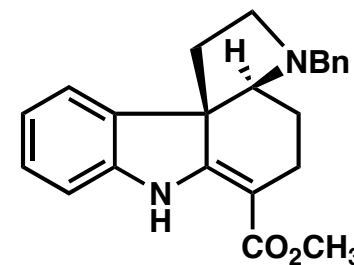
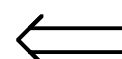
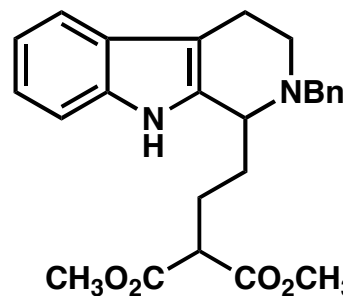
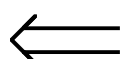
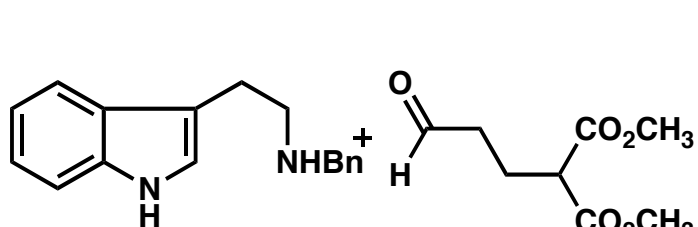
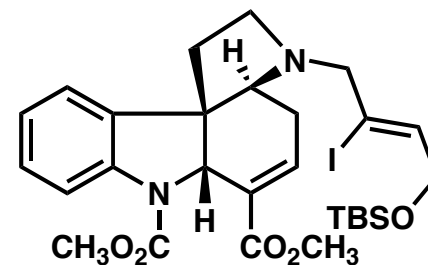
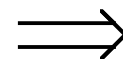
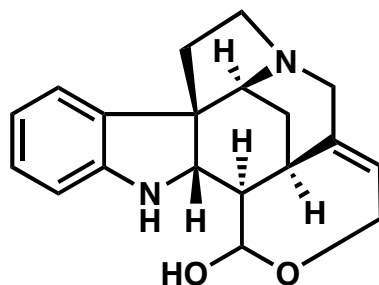
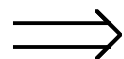
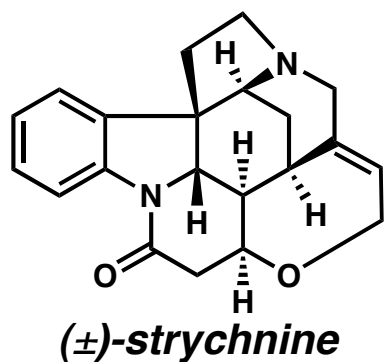
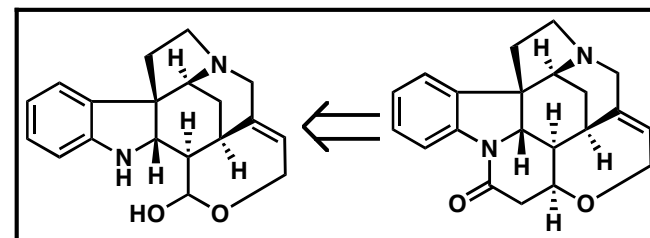
Magnus's (\pm)-Total Synthesis (1992)



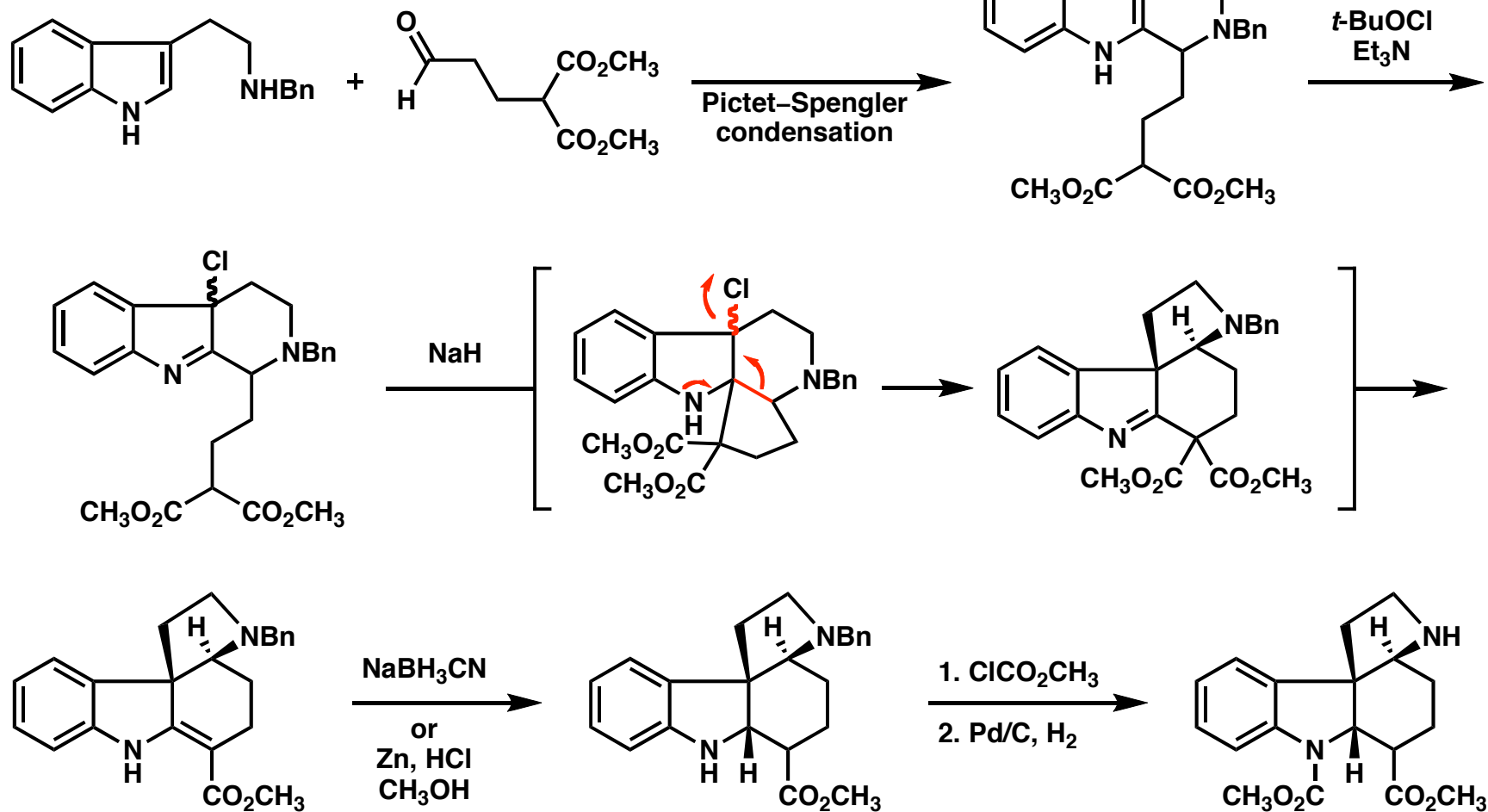
(\pm)-strychnine
0.03% yield
27 steps

Magnus *et al.* *J. Am. Chem. Soc.* **1992**, *114*, 4403-4405.
 Magnus *et al.* *J. Am. Chem. Soc.* **1993**, *115*, 8116-8129.

Retrosynthetic Analysis of Stork's (±)-Synthesis (1992)

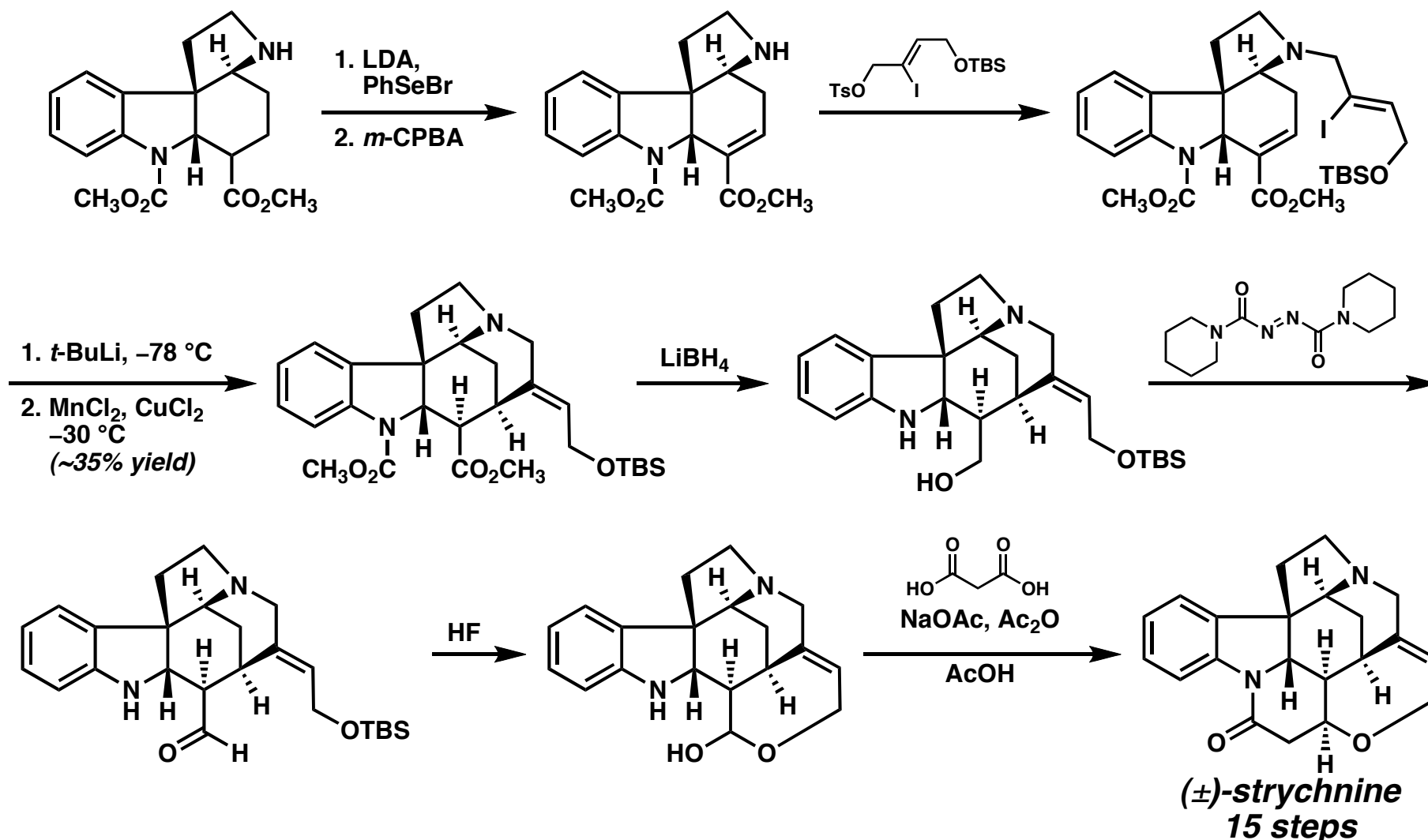
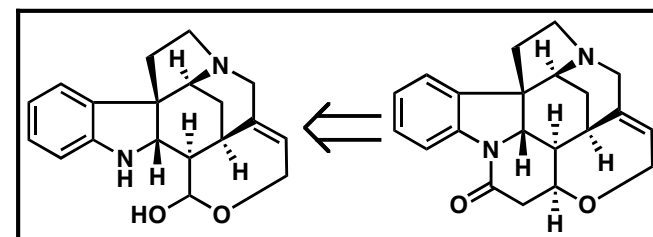


Stork's (\pm)-Total Synthesis (1992)



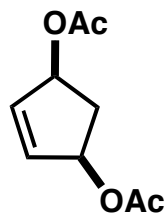
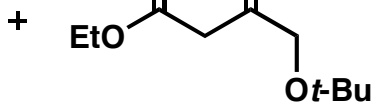
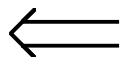
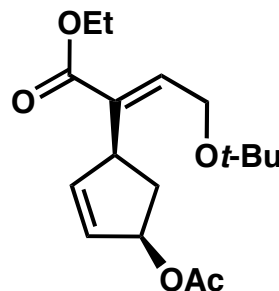
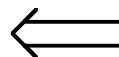
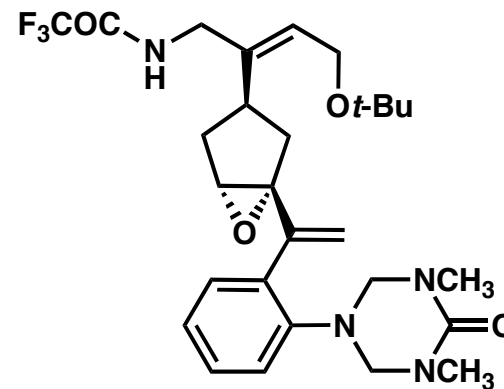
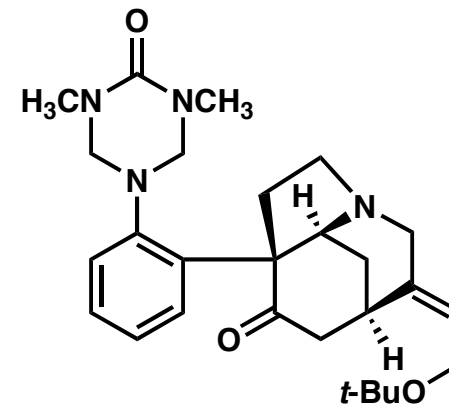
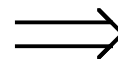
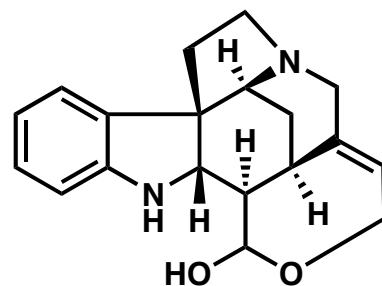
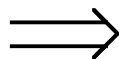
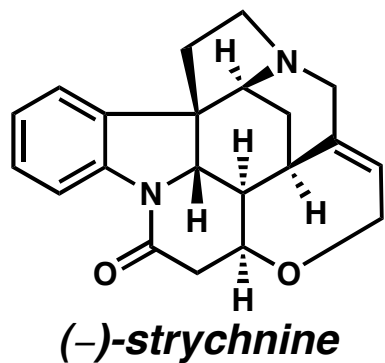
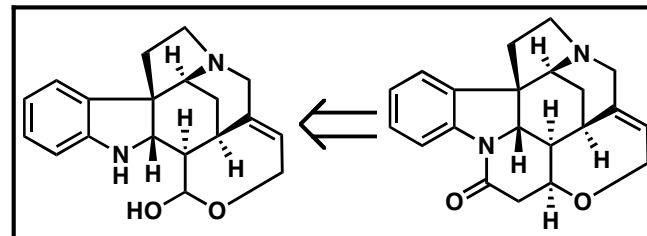
Stork, Disclosed at the Ischia Advanced School of Organic Chemistry, Ischia Porto, Italy, **Sept. 21, 1992.**

Stork's (\pm)-Total Synthesis (1992)

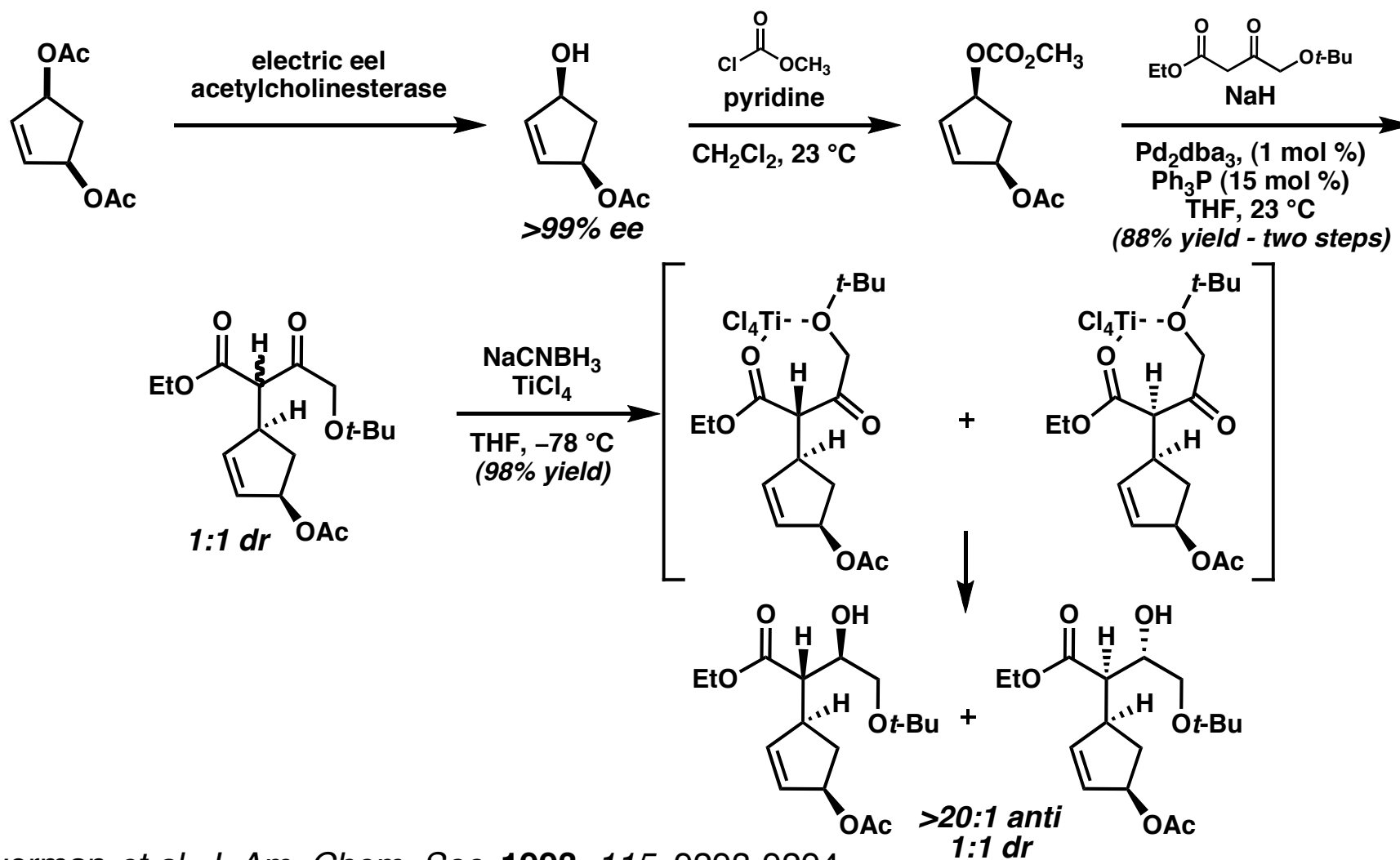
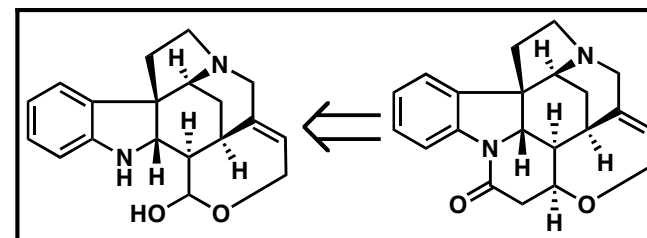


Stork, Disclosed at the Ischia Advanced School of Organic Chemistry, Ischia Porto, Italy, **Sept. 21, 1992.**

Retrosynthetic Analysis of Overman's (-)-Synthesis (1993)

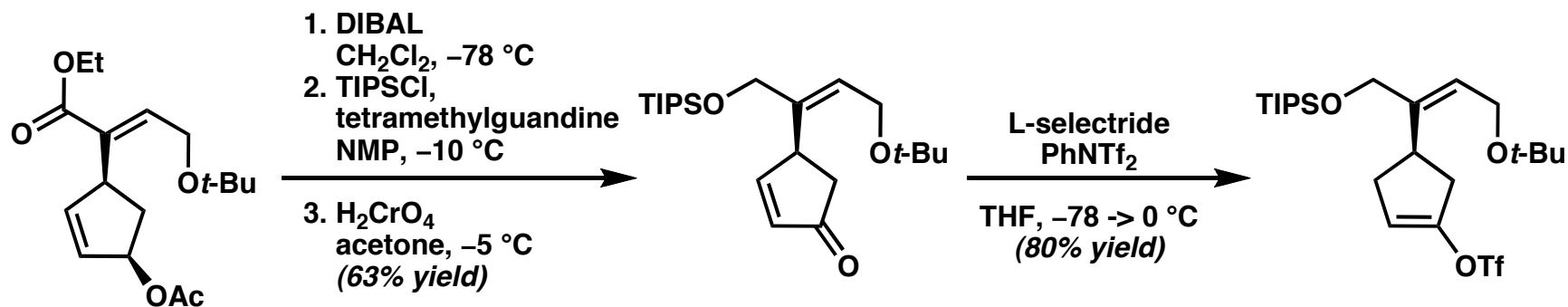
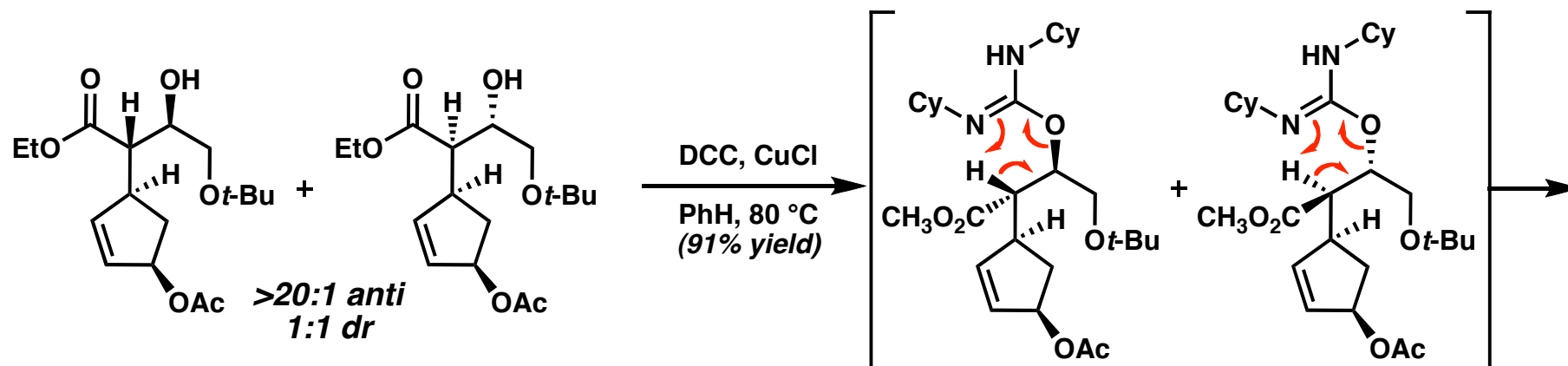
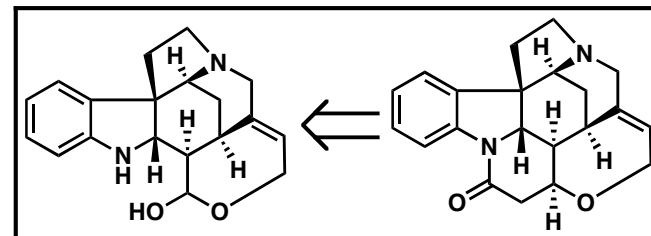


Overman's (-)-Total Synthesis (1993)



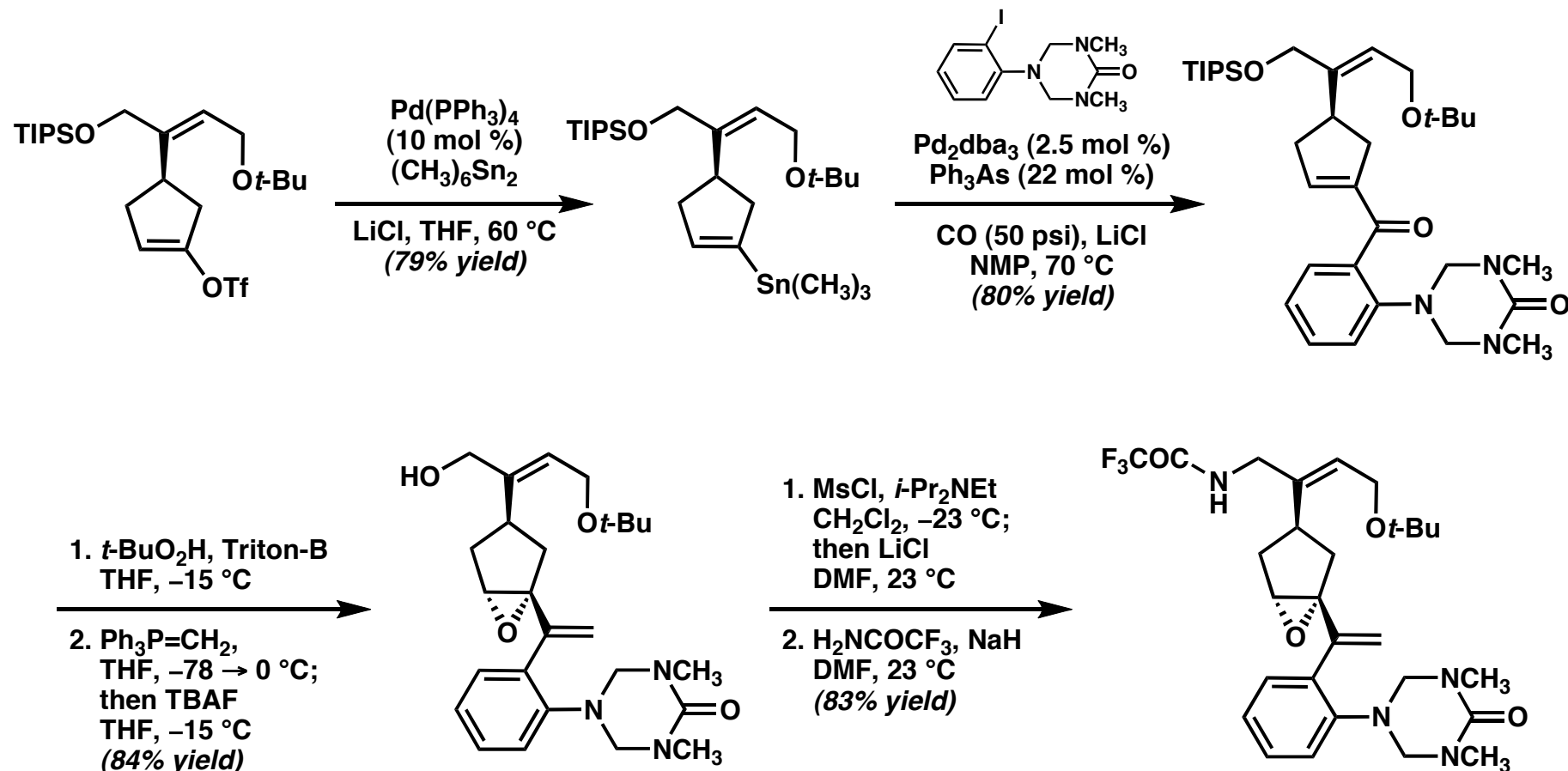
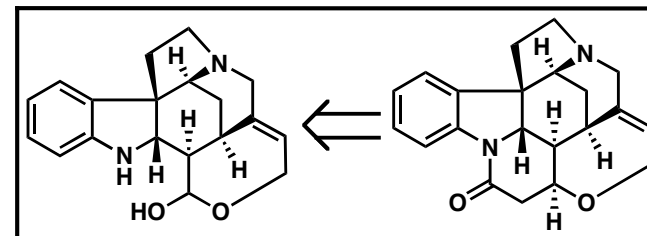
Overman *et al.* *J. Am. Chem. Soc.* **1993**, *115*, 9293-9294.
Overman *et al.* *J. Am. Chem. Soc.* **1995**, *117*, 5776-5788.

Overman's (-)-Total Synthesis (1993)



Overman *et al.* *J. Am. Chem. Soc.* **1993**, *115*, 9293-9294.
Overman *et al.* *J. Am. Chem. Soc.* **1995**, *117*, 5776-5788.

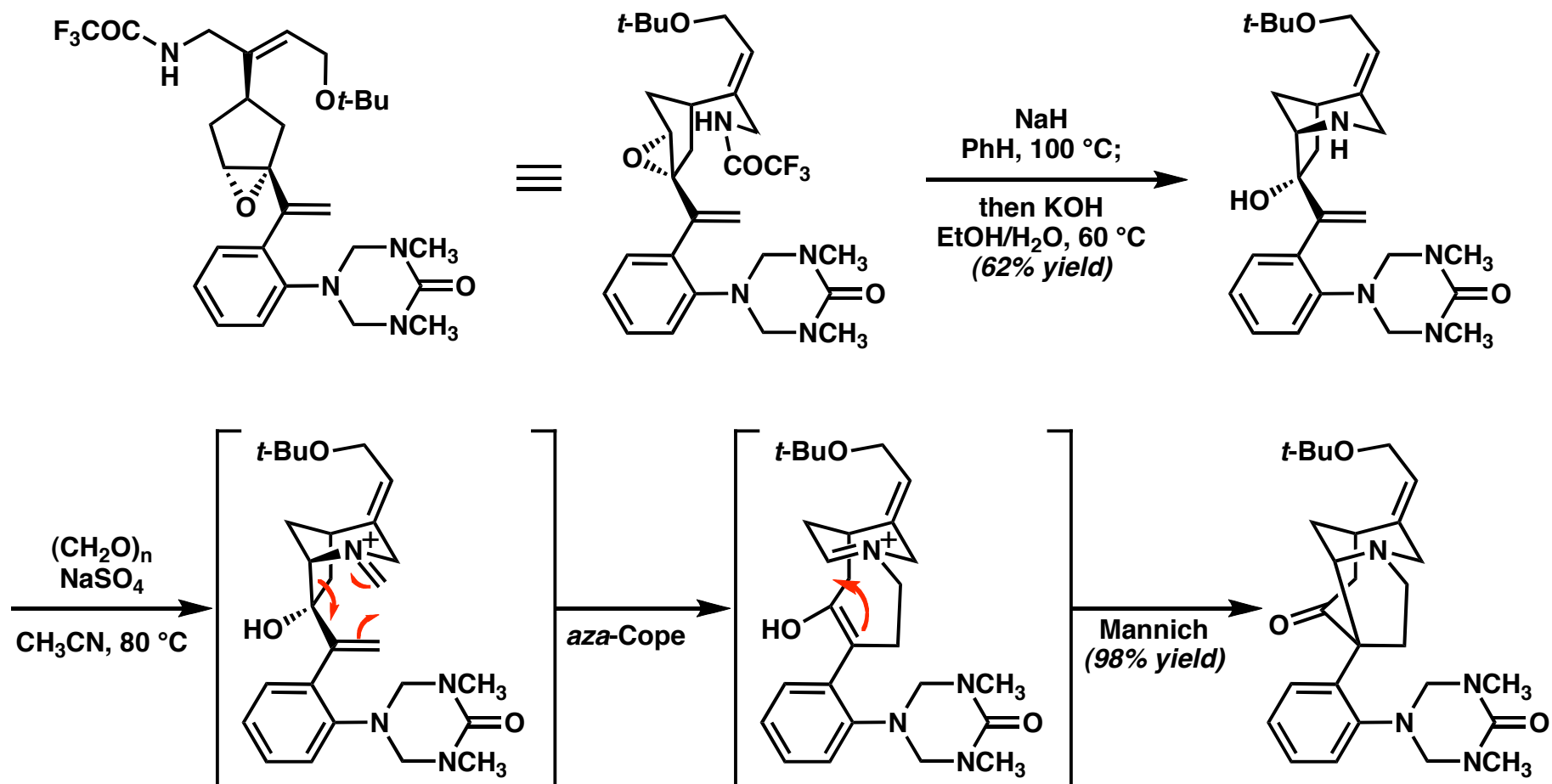
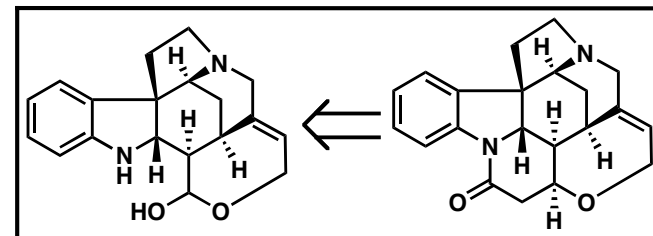
Overman's (-)-Total Synthesis (1993)



Overman *et al.* *J. Am. Chem. Soc.* **1993**, *115*, 9293-9294.

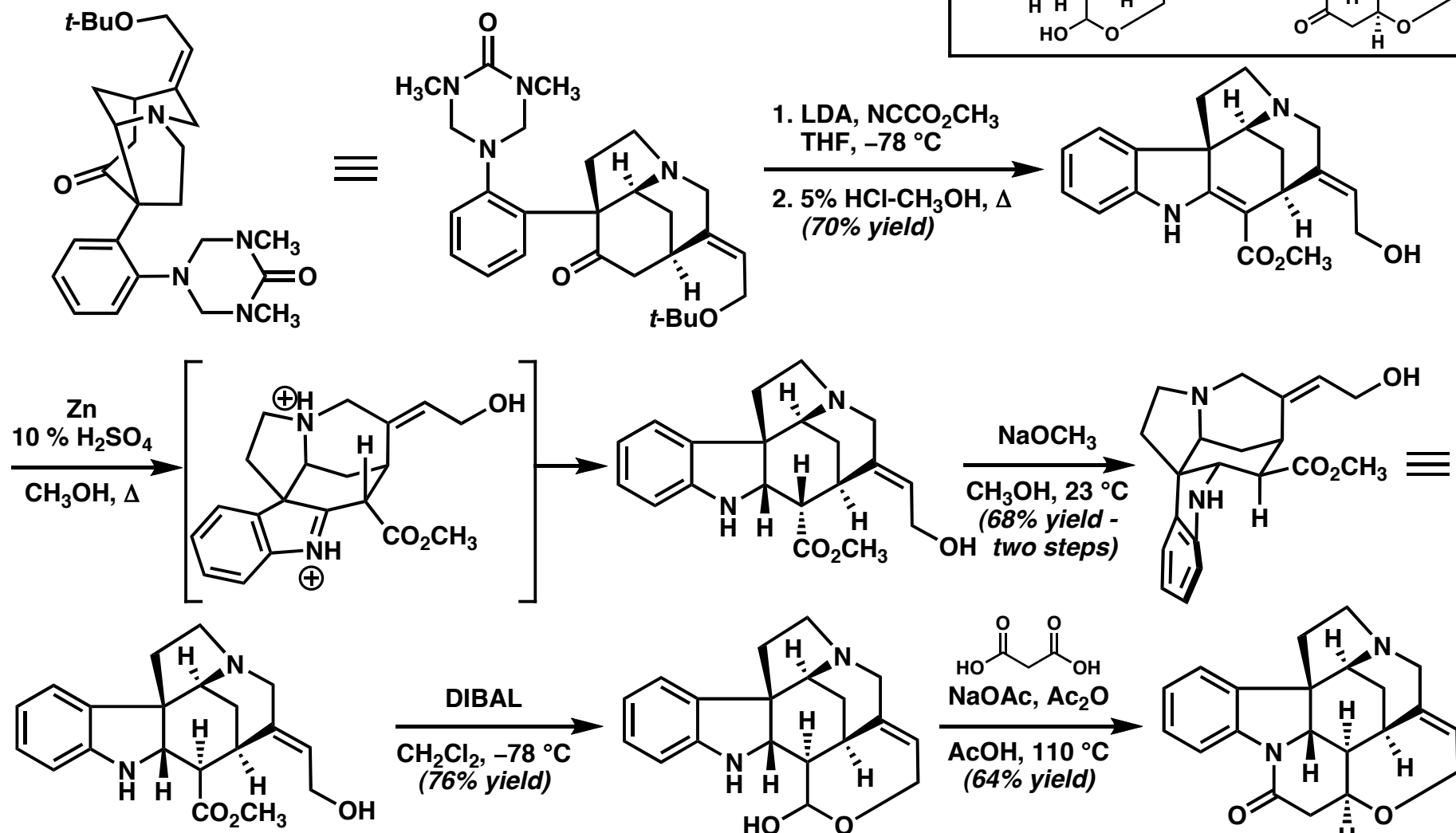
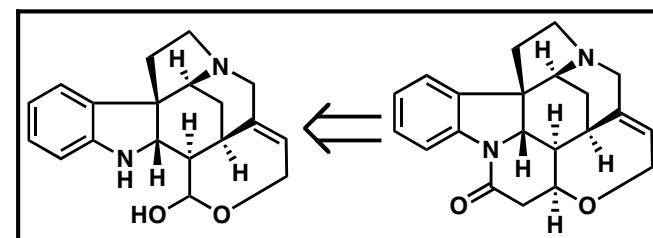
Overman *et al.* *J. Am. Chem. Soc.* **1995**, *117*, 5776-5788.

Overman's (-)-Total Synthesis (1993)



Overman *et al.* *J. Am. Chem. Soc.* **1993**, *115*, 9293-9294.
Overman *et al.* *J. Am. Chem. Soc.* **1995**, *117*, 5776-5788.

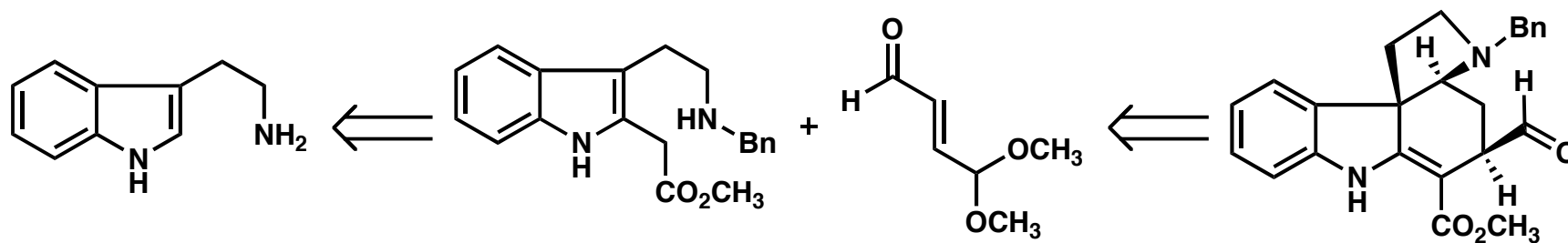
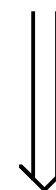
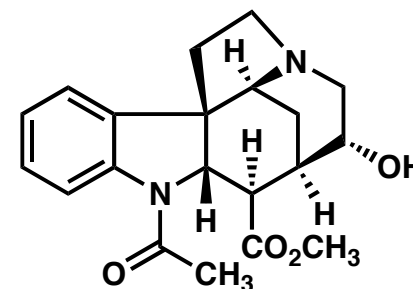
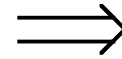
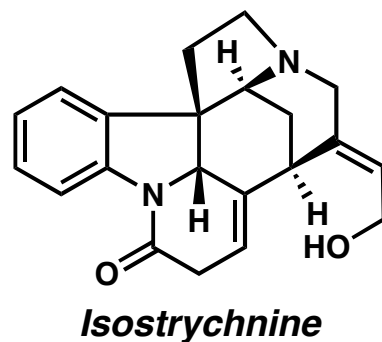
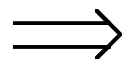
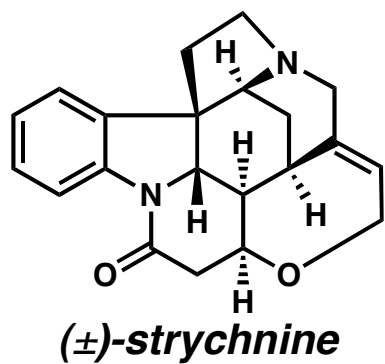
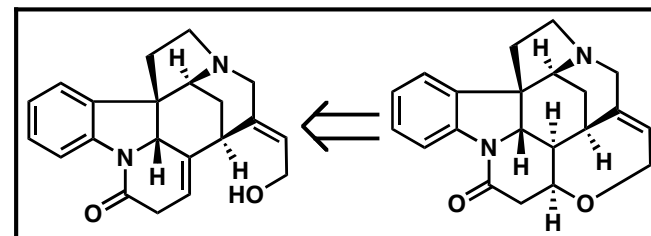
Overman's (-)-Total Synthesis (1993)



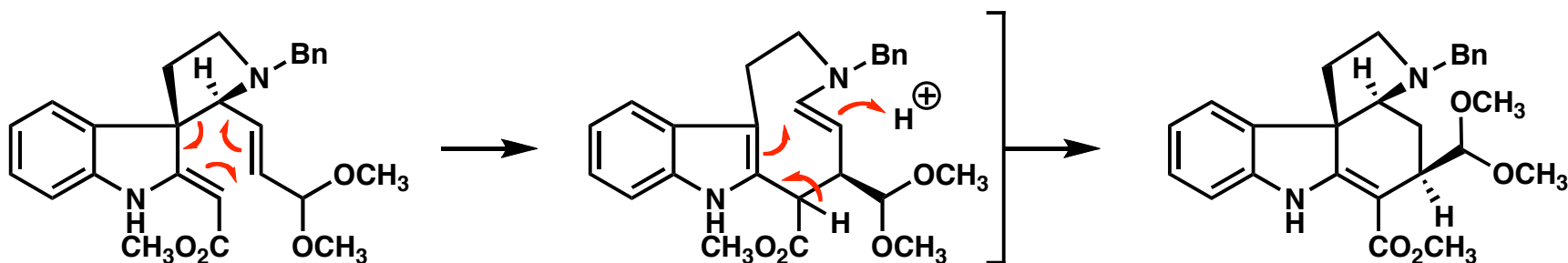
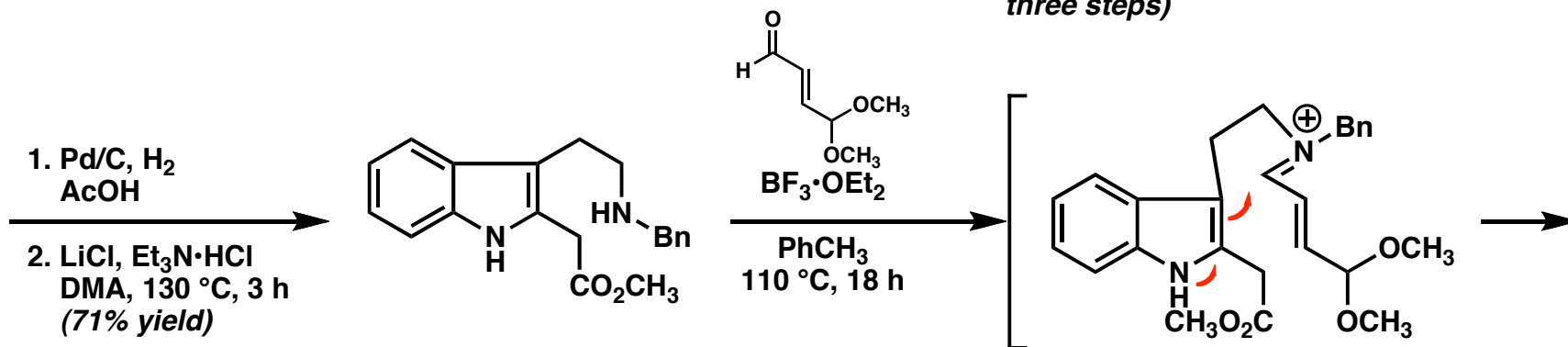
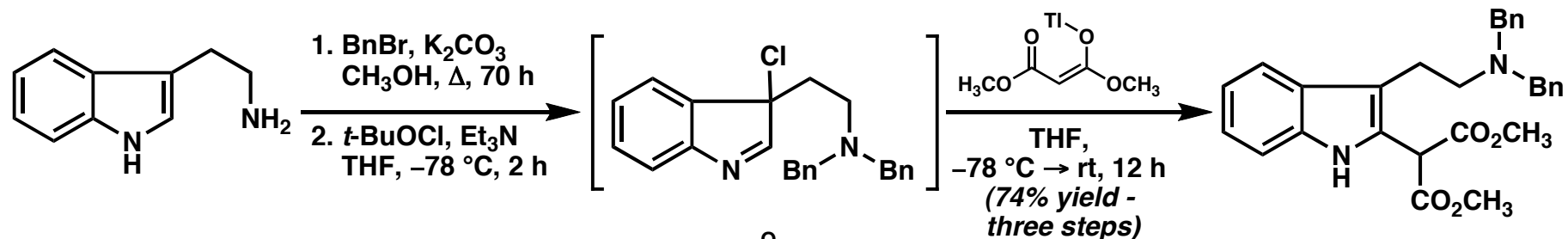
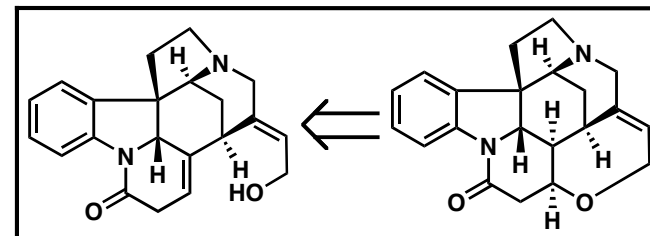
Overman *et al.* *J. Am. Chem. Soc.* **1993**, *115*, 9293-9294.
Overman *et al.* *J. Am. Chem. Soc.* **1995**, *117*, 5776-5788.

(±)-strychnine
3% yield
25 steps

Retrosynthetic Analysis of Kuehne's (±)-Synthesis (1993)

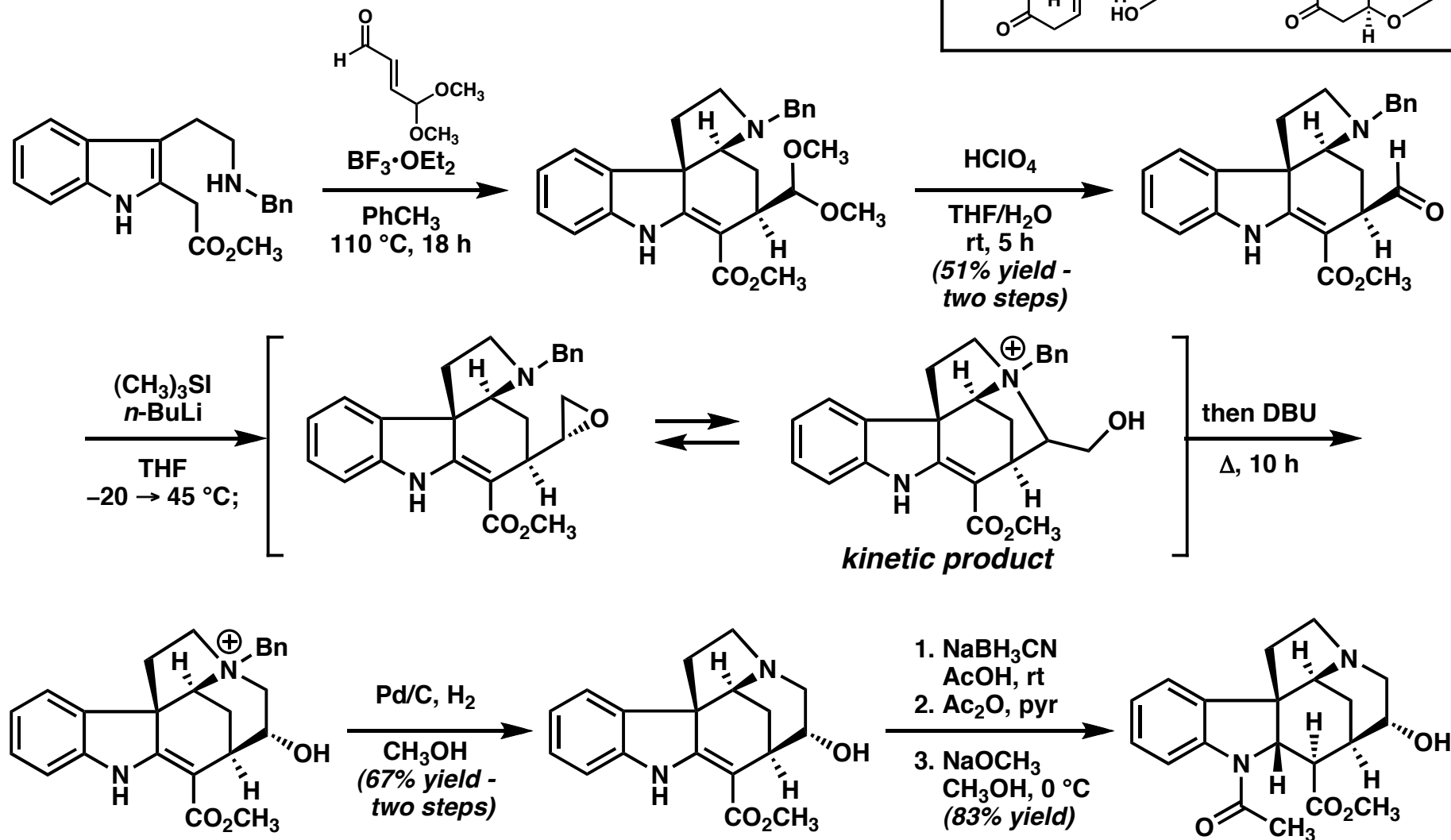
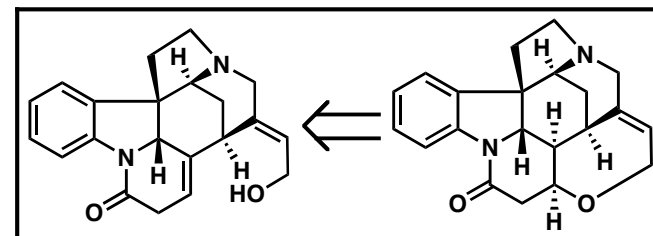


Kuehne's (\pm)-Total Synthesis (1993)



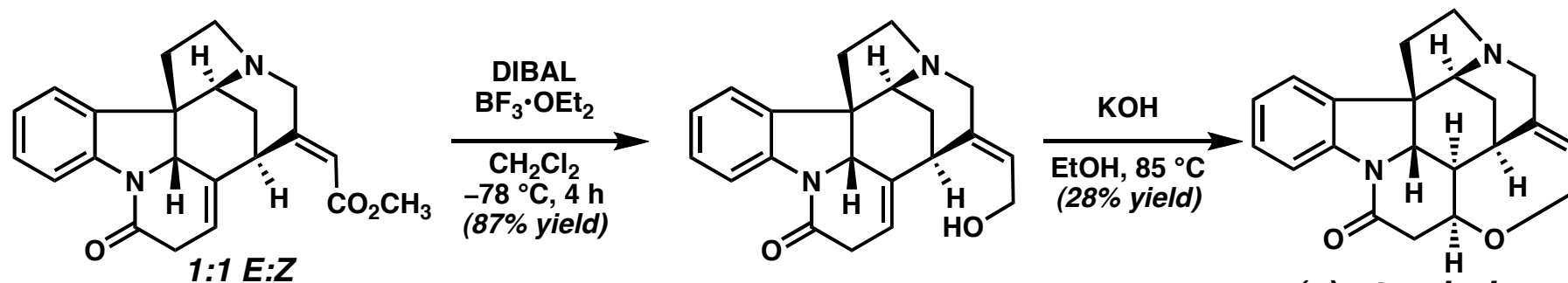
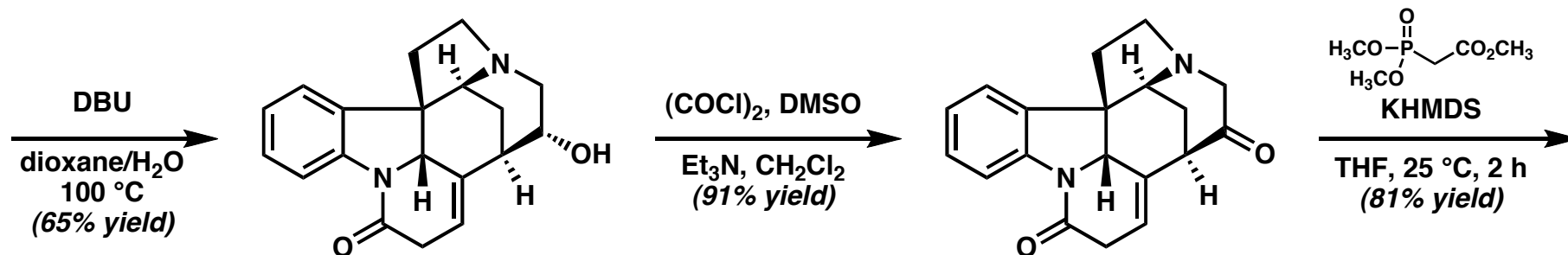
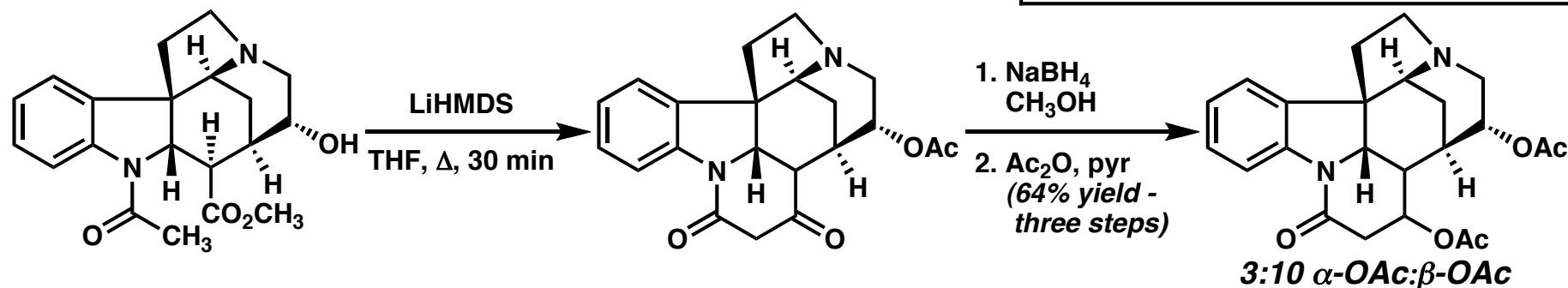
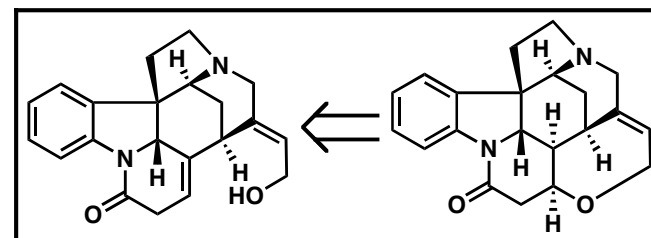
Kuehne & Xu, *J. Org. Chem.* **1993**, *58*, 7490-7497.
Kuehne & Xu, *J. Org. Chem.* **1998**, *63*, 9427-9433.

Kuehne's (\pm)-Total Synthesis (1993)



Kuehne & Xu, *J. Org. Chem.* **1993**, *58*, 7490-7497.
Kuehne & Xu, *J. Org. Chem.* **1998**, *63*, 9427-9433.

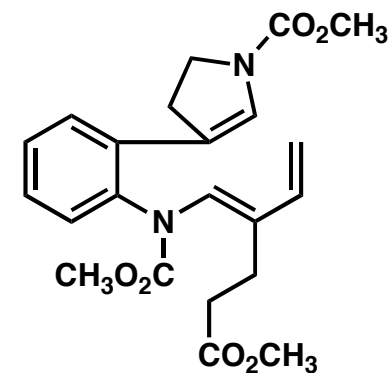
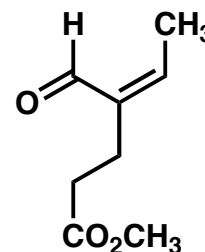
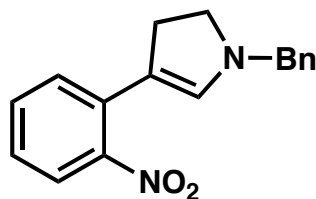
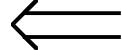
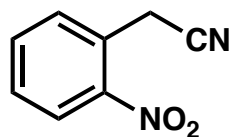
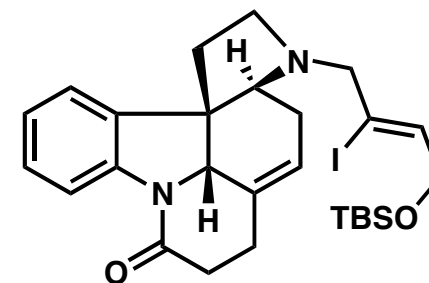
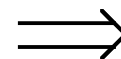
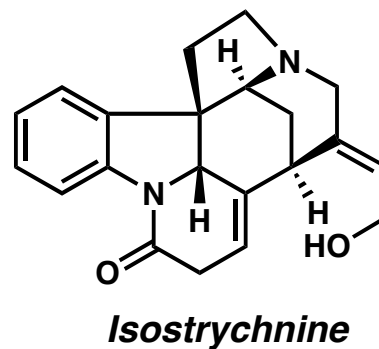
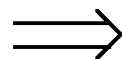
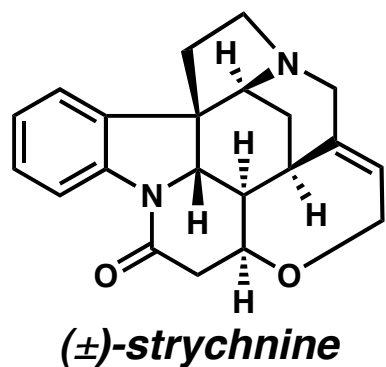
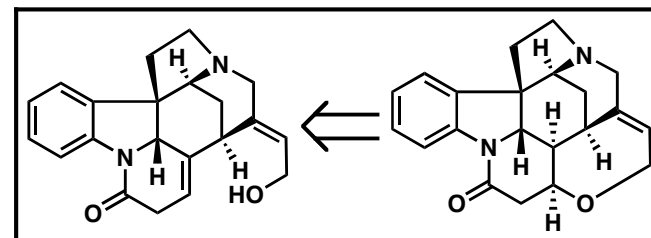
Kuehne's (\pm)-Total Synthesis (1993)



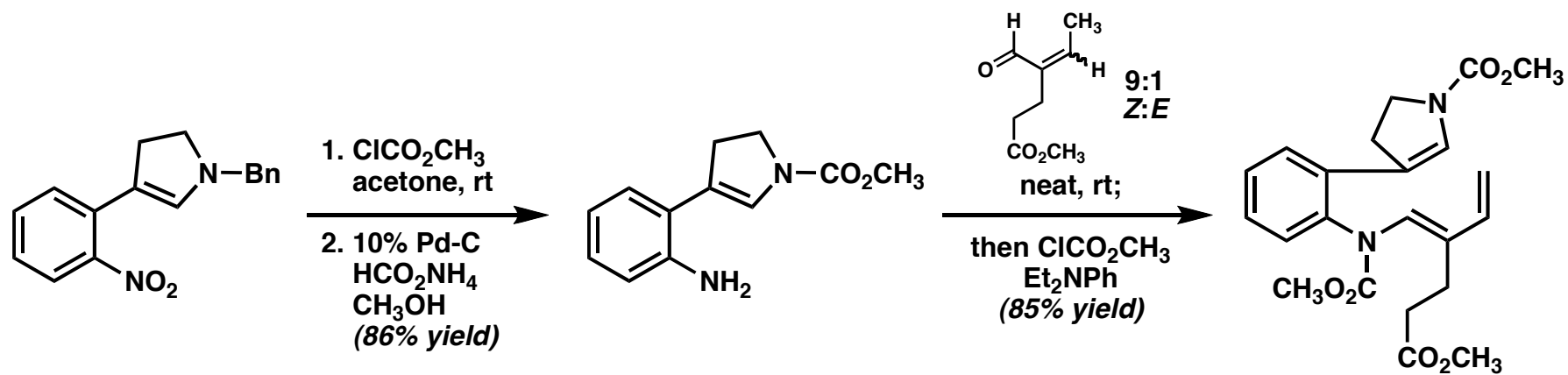
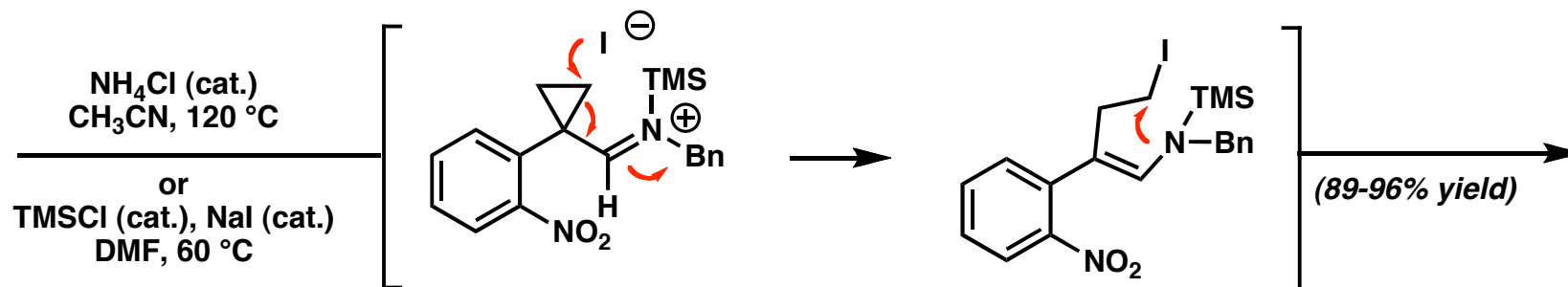
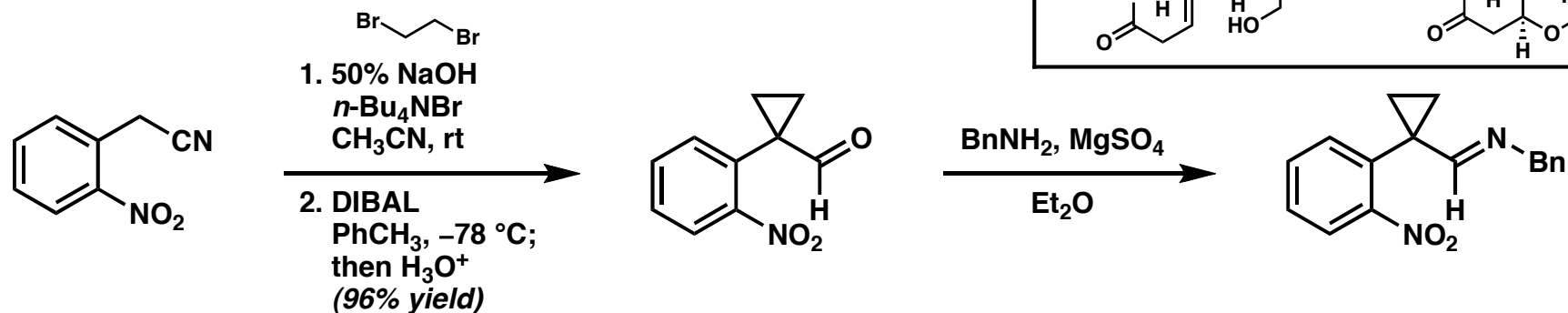
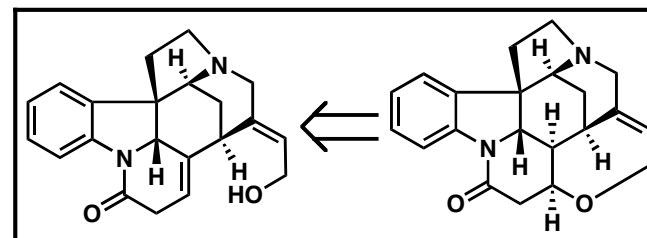
(\pm)-strychnine
1.4% yield
17 steps

Kuehne & Xu, *J. Org. Chem.* **1993**, *58*, 7490-7497.
 Kuehne & Xu, *J. Org. Chem.* **1998**, *63*, 9427-9433.

Retrosynthetic Analysis of Rawal's (±)-Synthesis (1994)

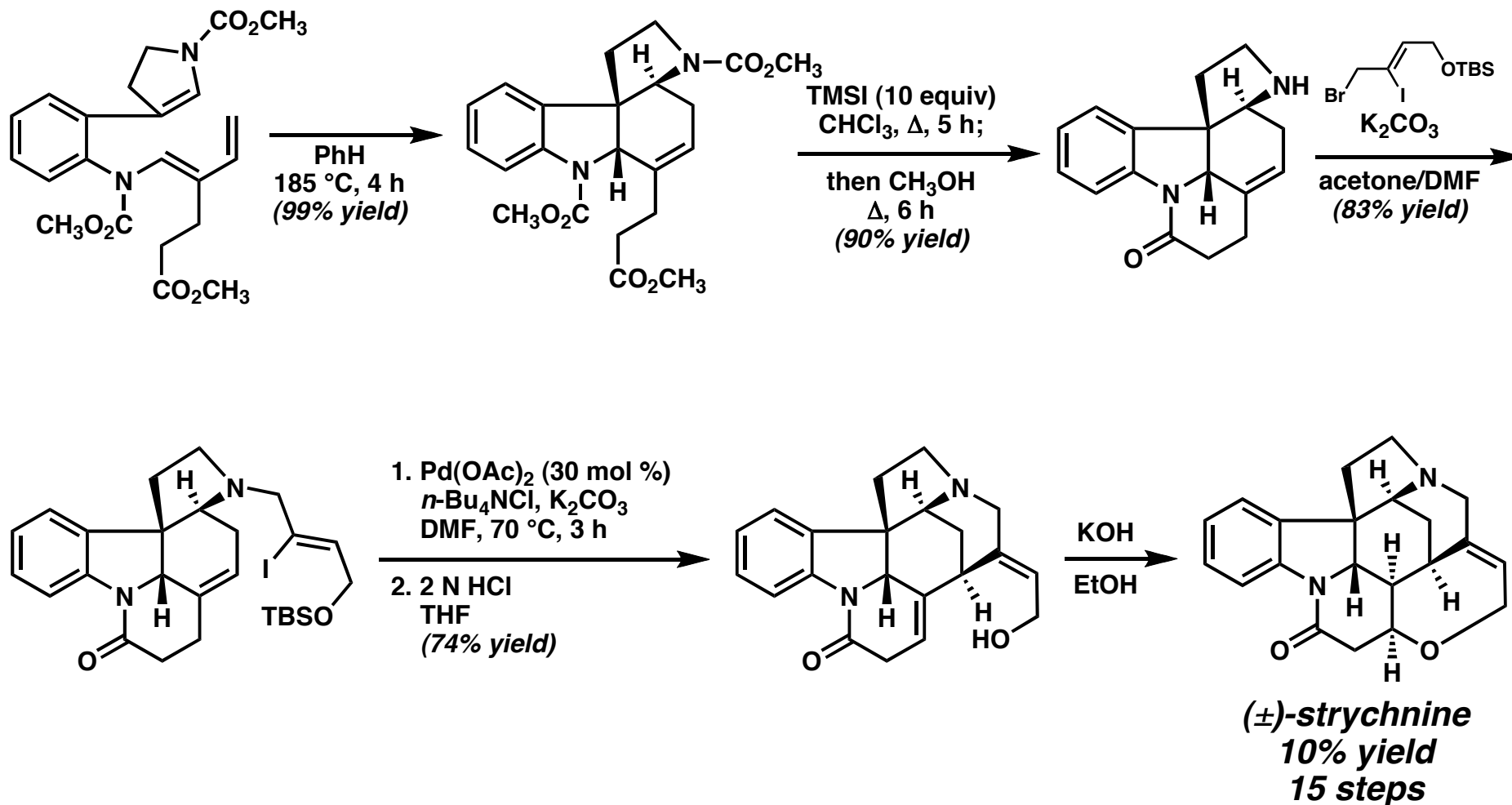
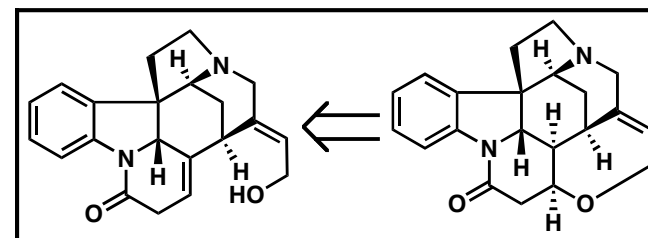


Rawal's (\pm)-Total Synthesis (1994)



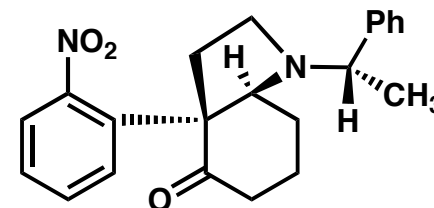
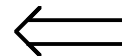
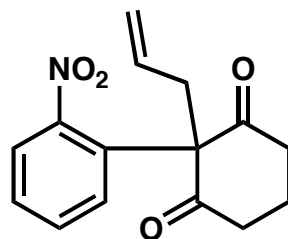
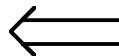
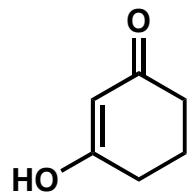
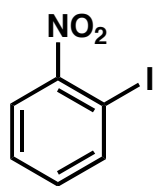
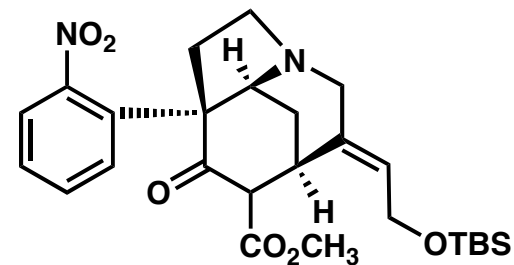
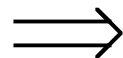
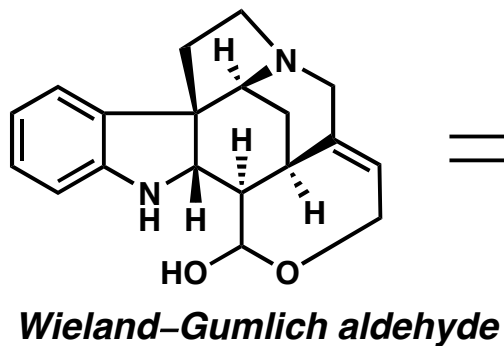
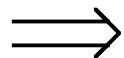
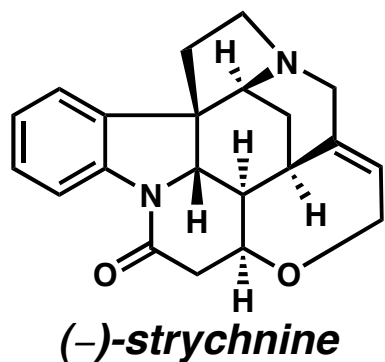
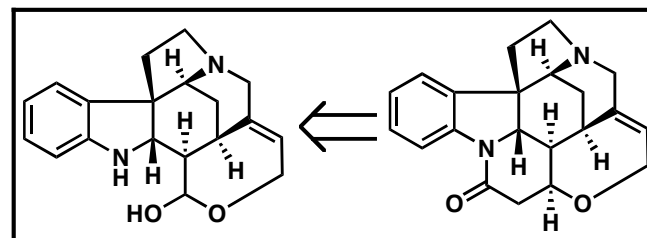
Rawal & Iwasa, *J. Org. Chem.* **1994**, *59*, 2685-2686.

Rawal's (\pm)-Total Synthesis (1994)

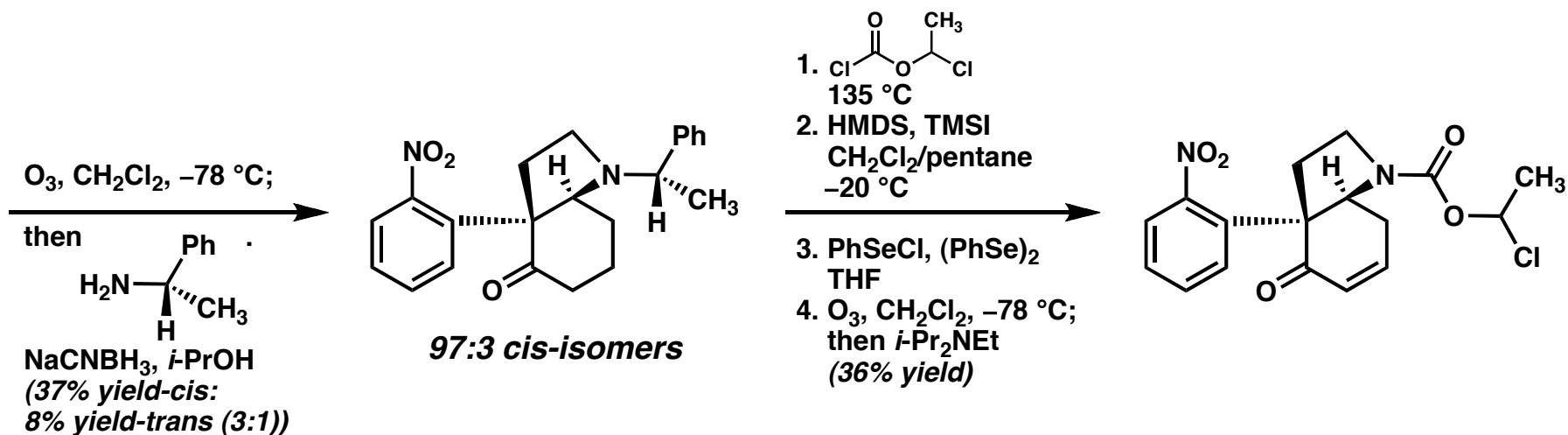
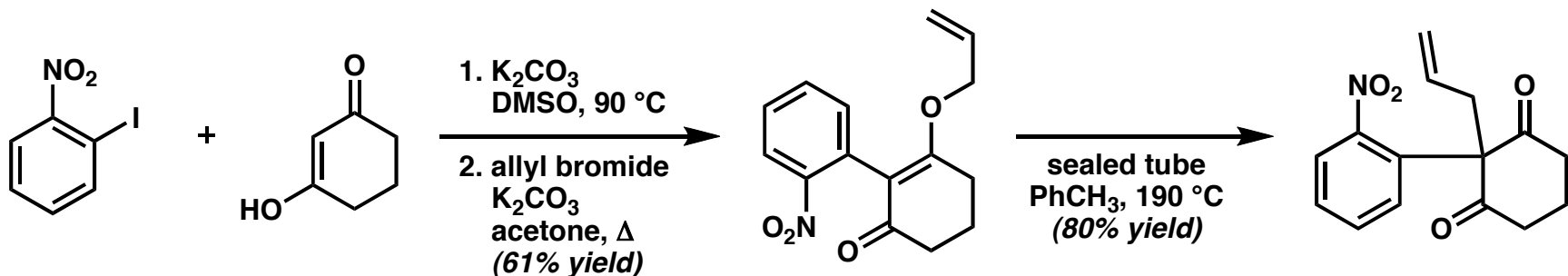
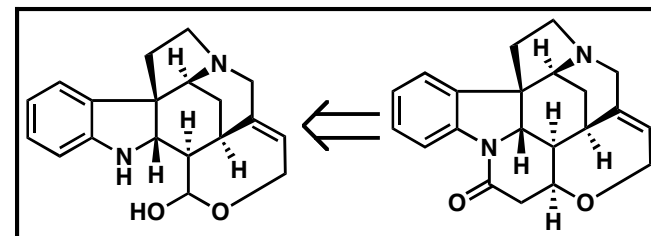


Rawal & Iwasa, *J. Org. Chem.* **1994**, *59*, 2685-2686.

Retrosynthetic Analysis of Bonjoch– Bosch's (–)-Synthesis (1999)

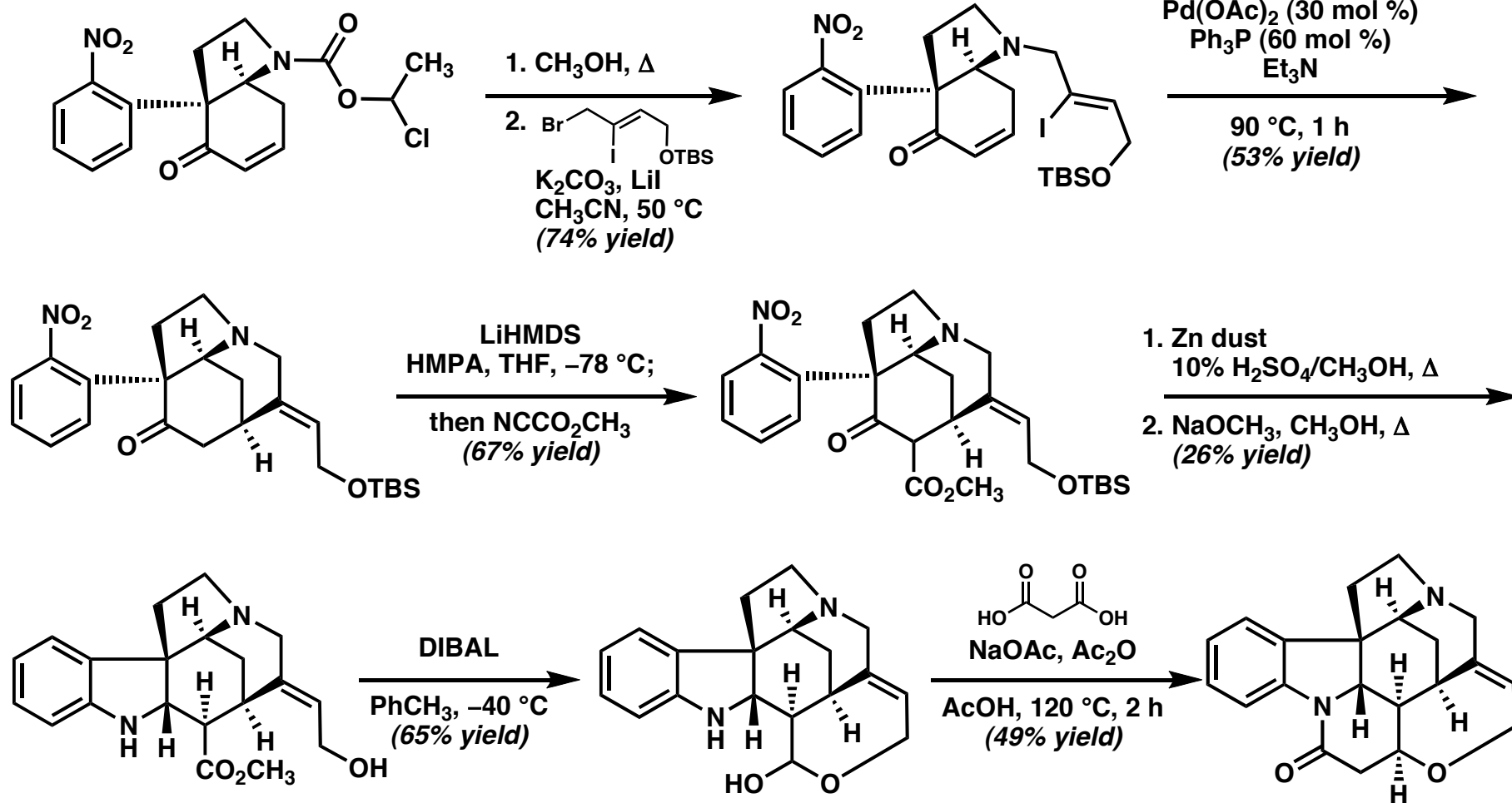
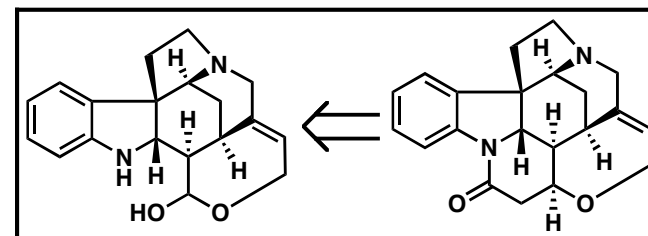


Bonjoch-Bosch's (-)-Synthesis (1999)



Bonjoch, Bosch *et al.* *Angew. Chem. Int. Ed.* **1999**, *38*, 395-397.
 Bonjoch, Bosch *et al.* *Chem. Euro. J.* **2000**, *6*, 655-665.

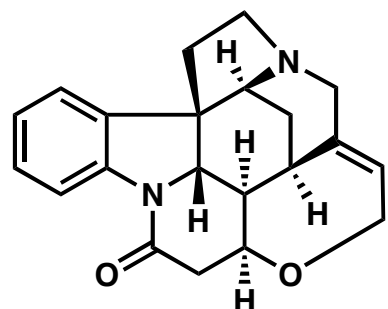
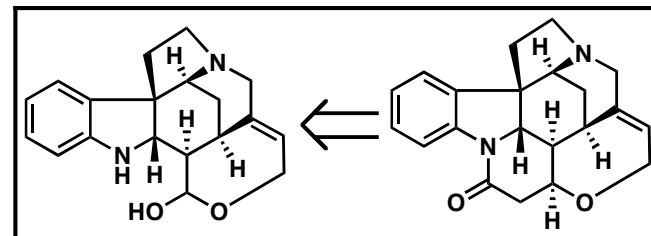
Bonjoch-Bosch's (-)-Synthesis (1999)



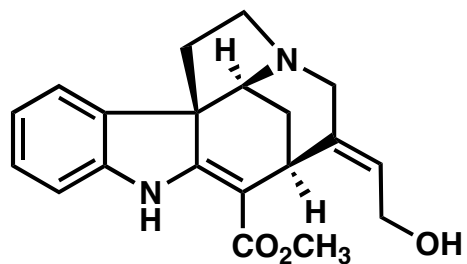
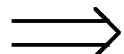
(-)-strychnine
0.15% yield
15 steps

Bonjoch, Bosch *et al.* *Angew. Chem. Int. Ed.* **1999**, *38*, 395-397.
 Bonjoch, Bosch *et al.* *Chem. Euro. J.* **2000**, *6*, 655-665.

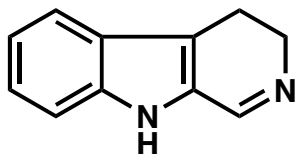
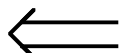
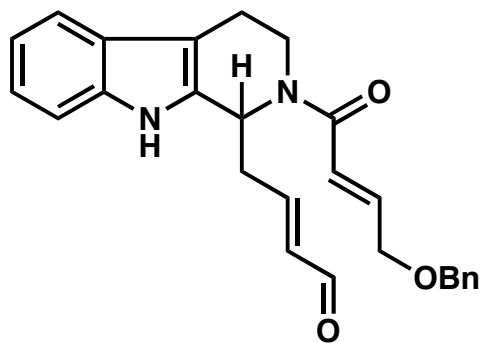
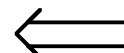
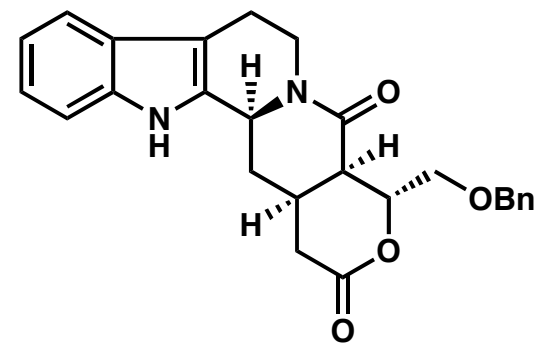
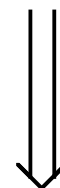
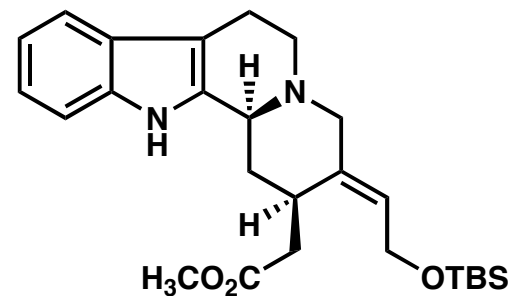
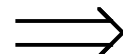
Retrosynthetic Analysis of Martin's (±)-Synthesis (1996-2001)



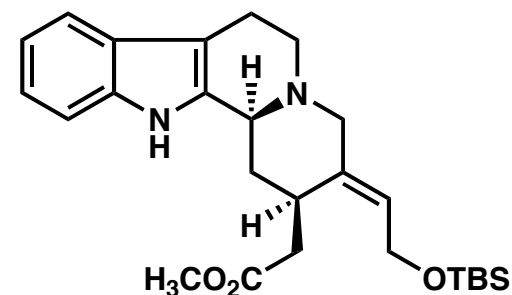
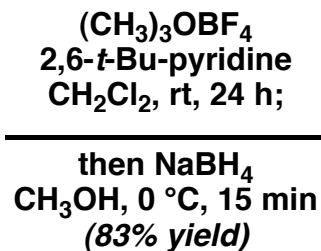
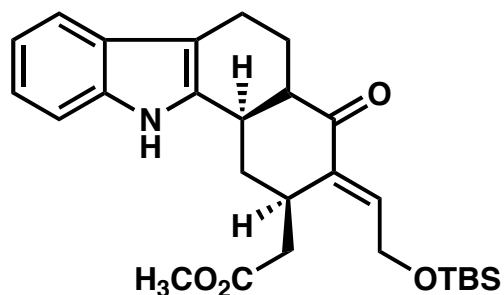
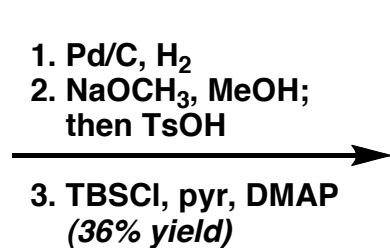
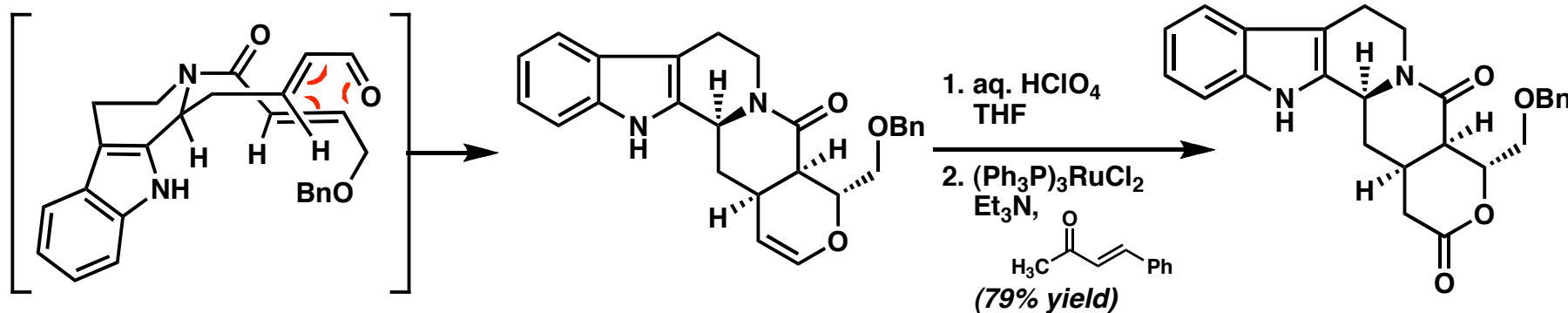
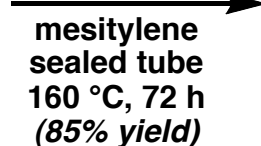
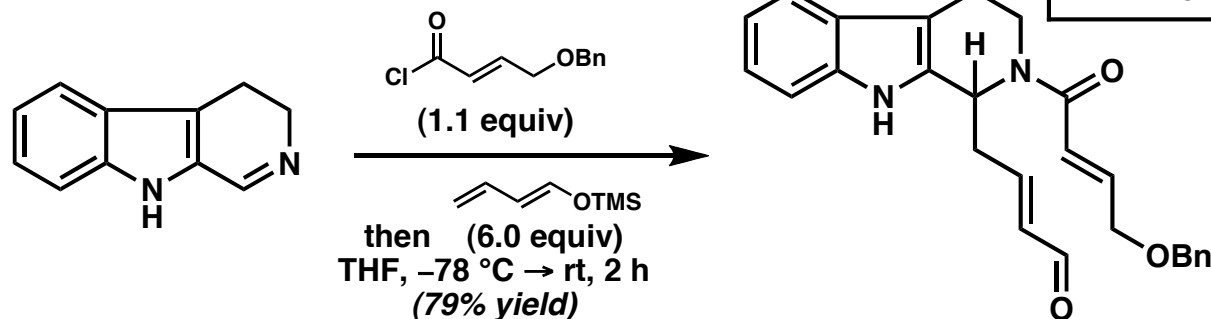
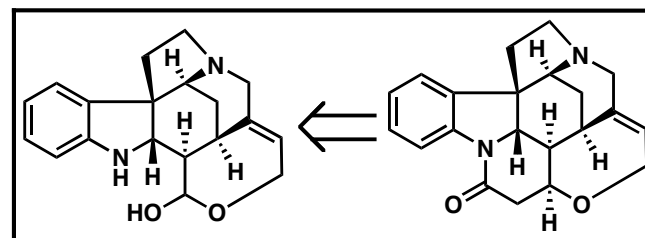
(±)-strychnine



formal synthetic
intermediate of Overman

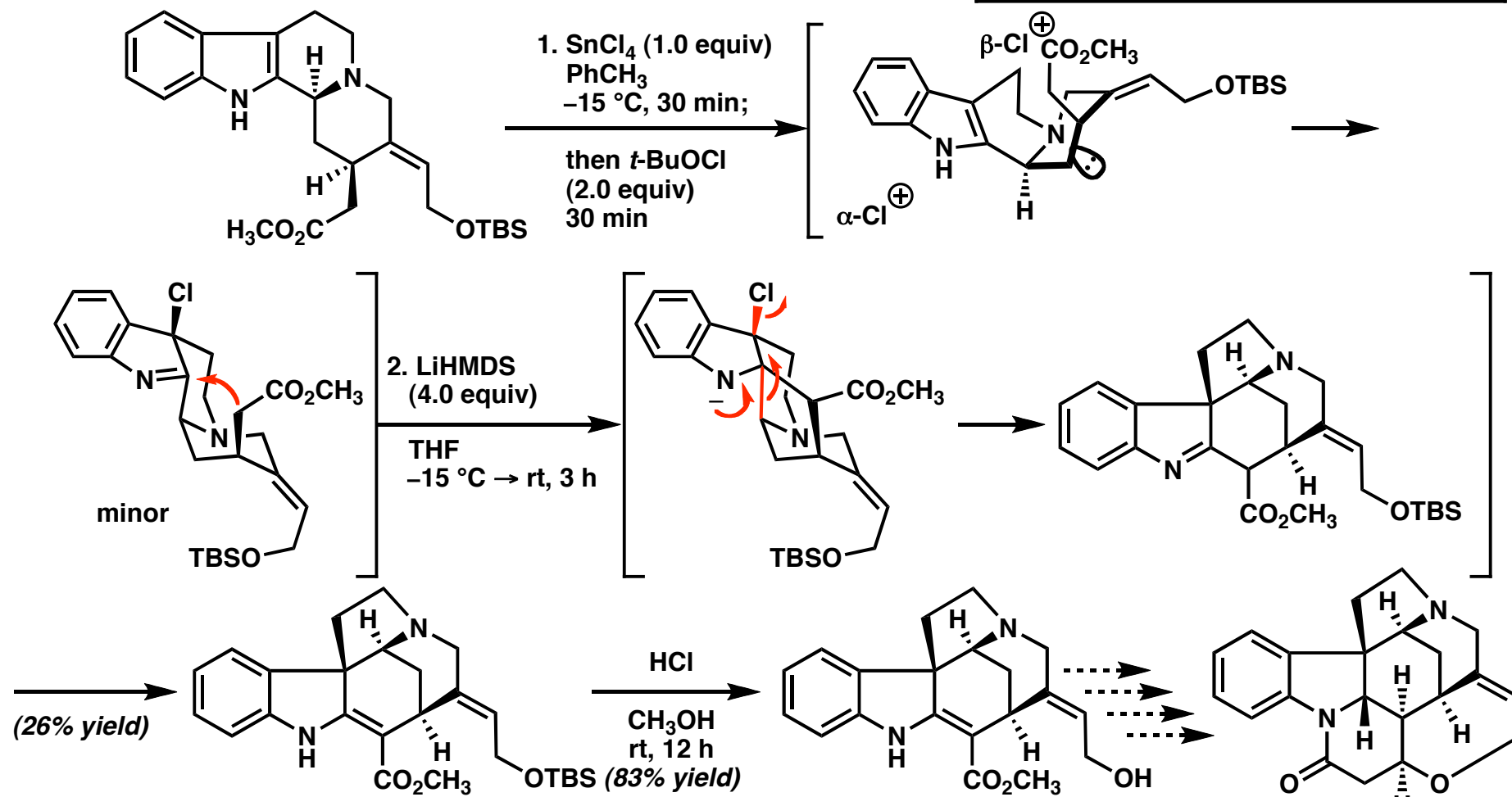
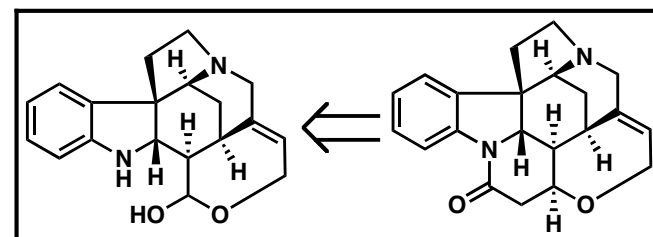


Martin's (\pm)-Formal Synthesis (1996-2001)



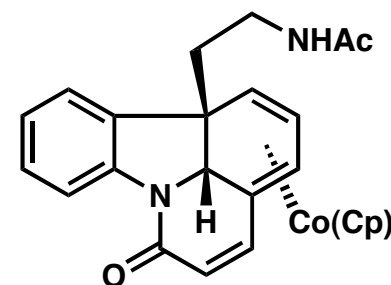
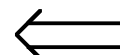
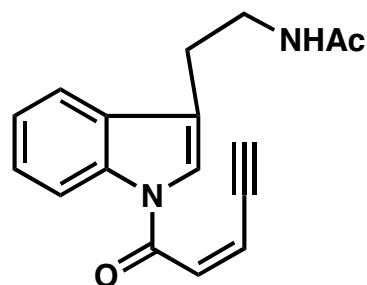
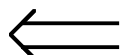
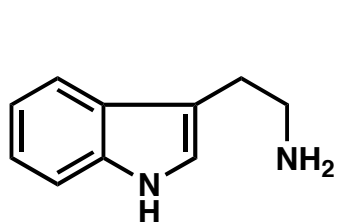
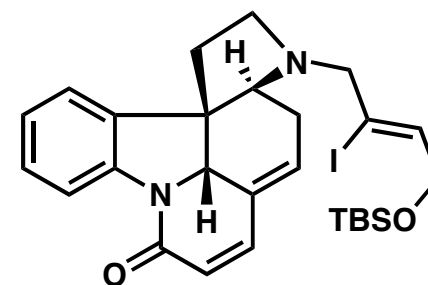
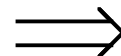
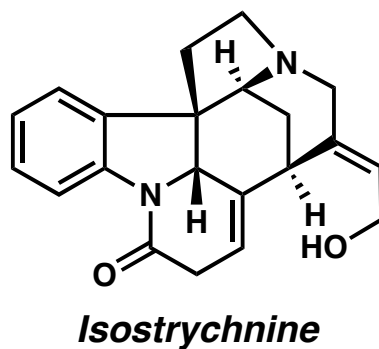
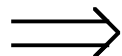
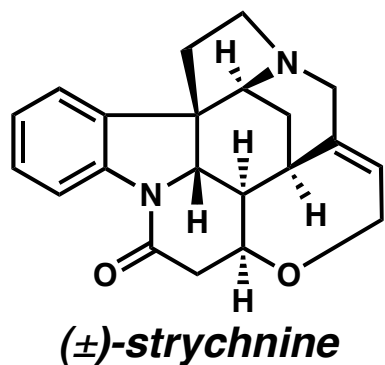
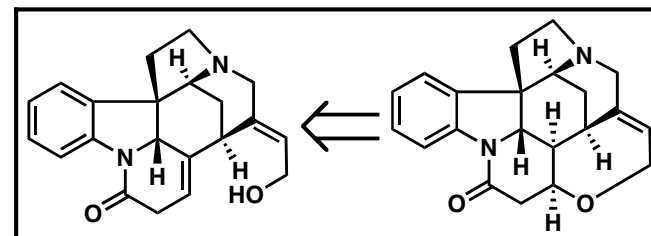
Martin *et al.* *J. Am. Chem. Soc.* **1996**, *118*, 9804-9805.
 Martin *et al.* *J. Am. Chem. Soc.* **2001**, *123*, 8003-8010.

Martin's (\pm)-Formal Synthesis (1996-2001)

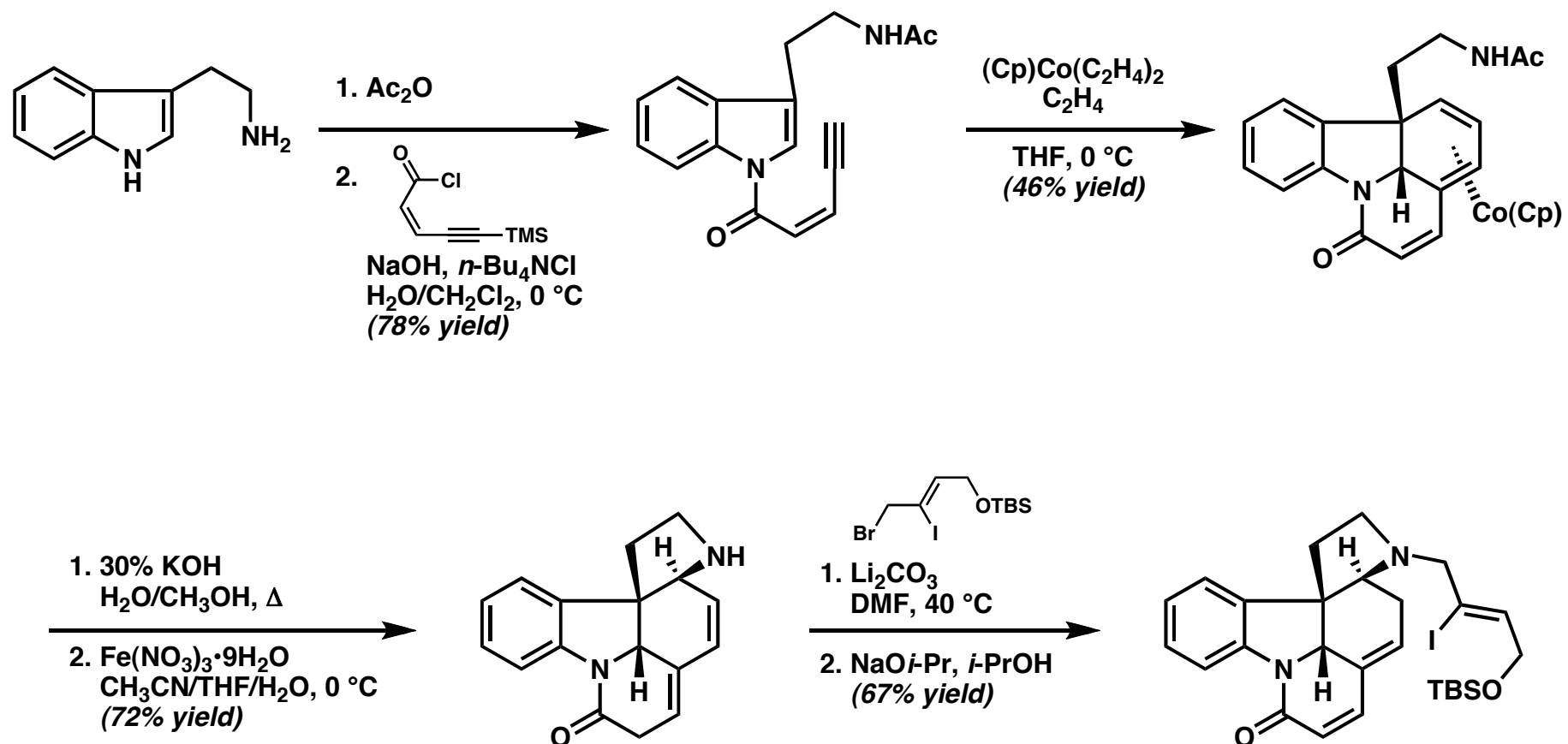
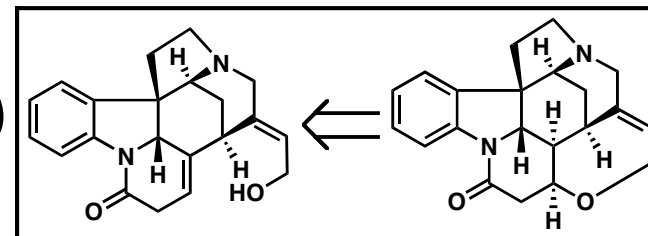


Martin *et al.* *J. Am. Chem. Soc.* **1996**, *118*, 9804-9805.
 Martin *et al.* *J. Am. Chem. Soc.* **2001**, *123*, 8003-8010.

Retrosynthetic Analysis of Eichberg-Vollhardt's (\pm)-Synthesis (2000)

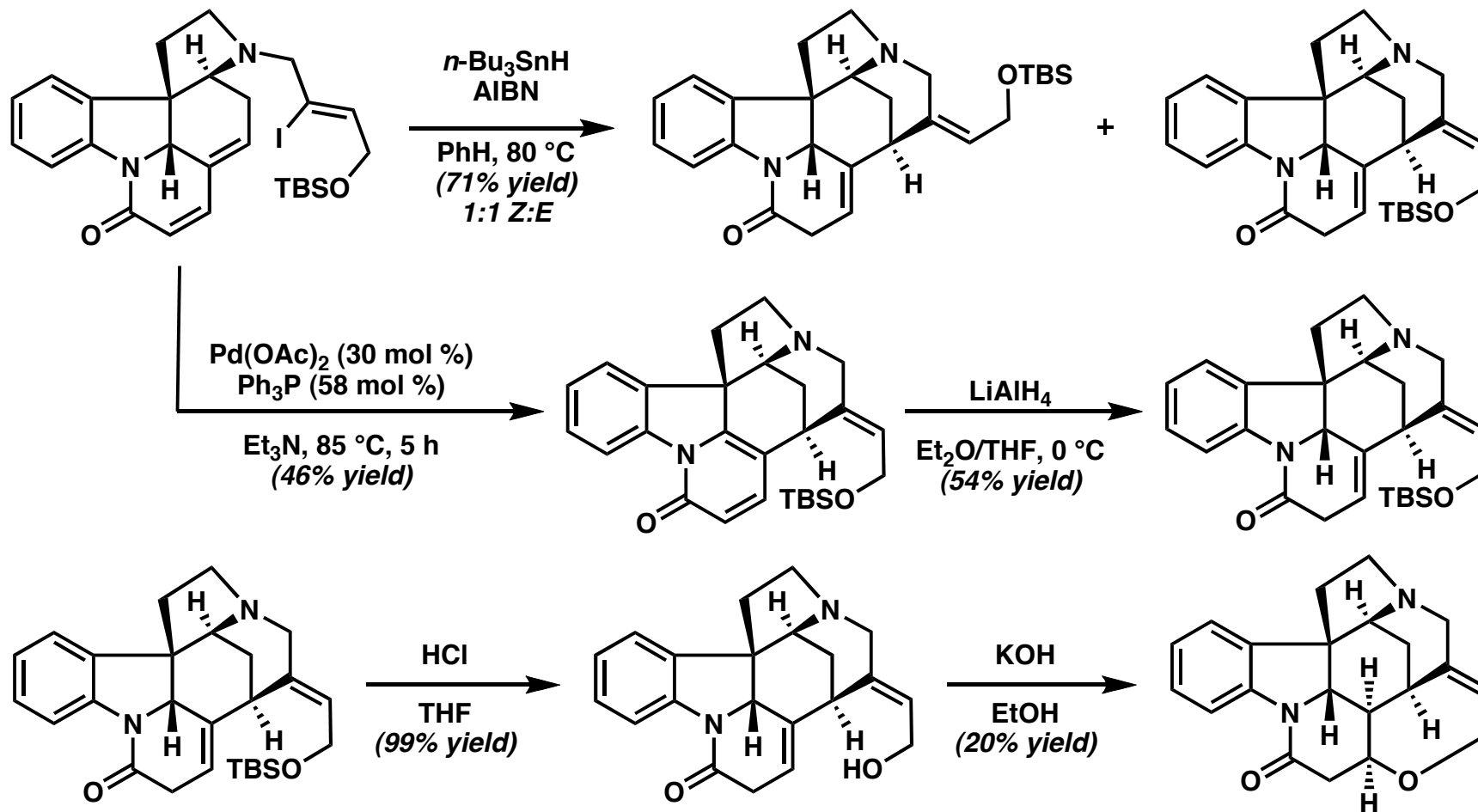
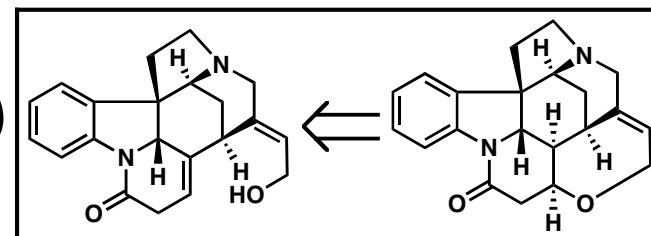


Eichberg-Vollhardt's (\pm)-Synthesis (2000)



Eichberg, Vollhardt *et al.* *Org. Lett.* **2000**, 2, 2479-2481.

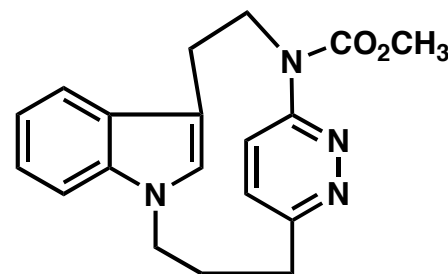
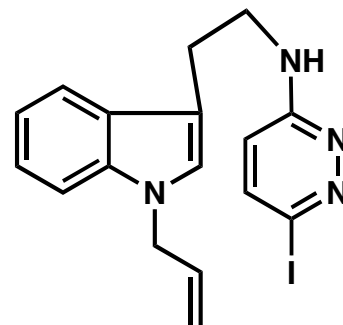
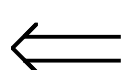
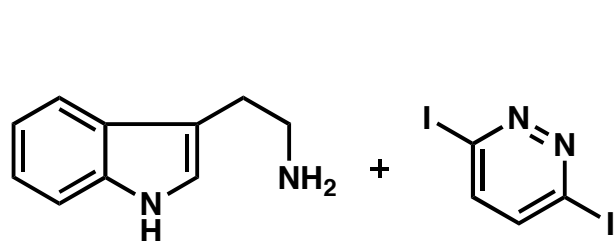
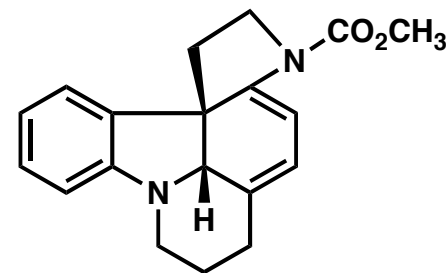
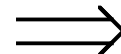
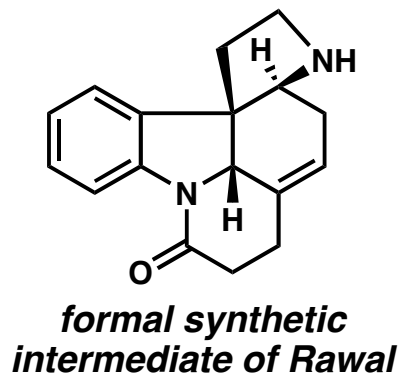
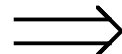
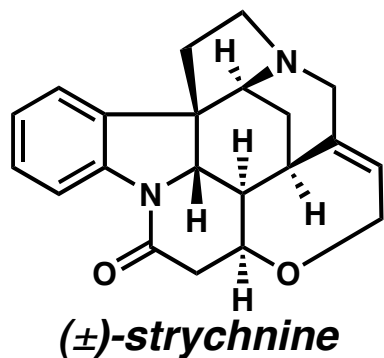
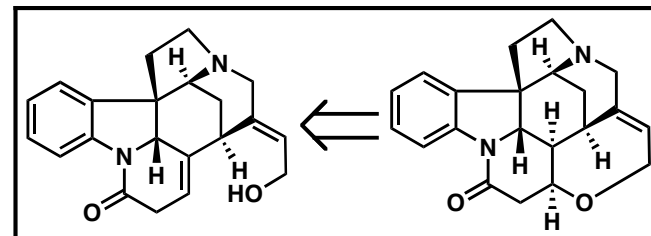
Eichberg-Vollhardt's (\pm)-Synthesis (2000)



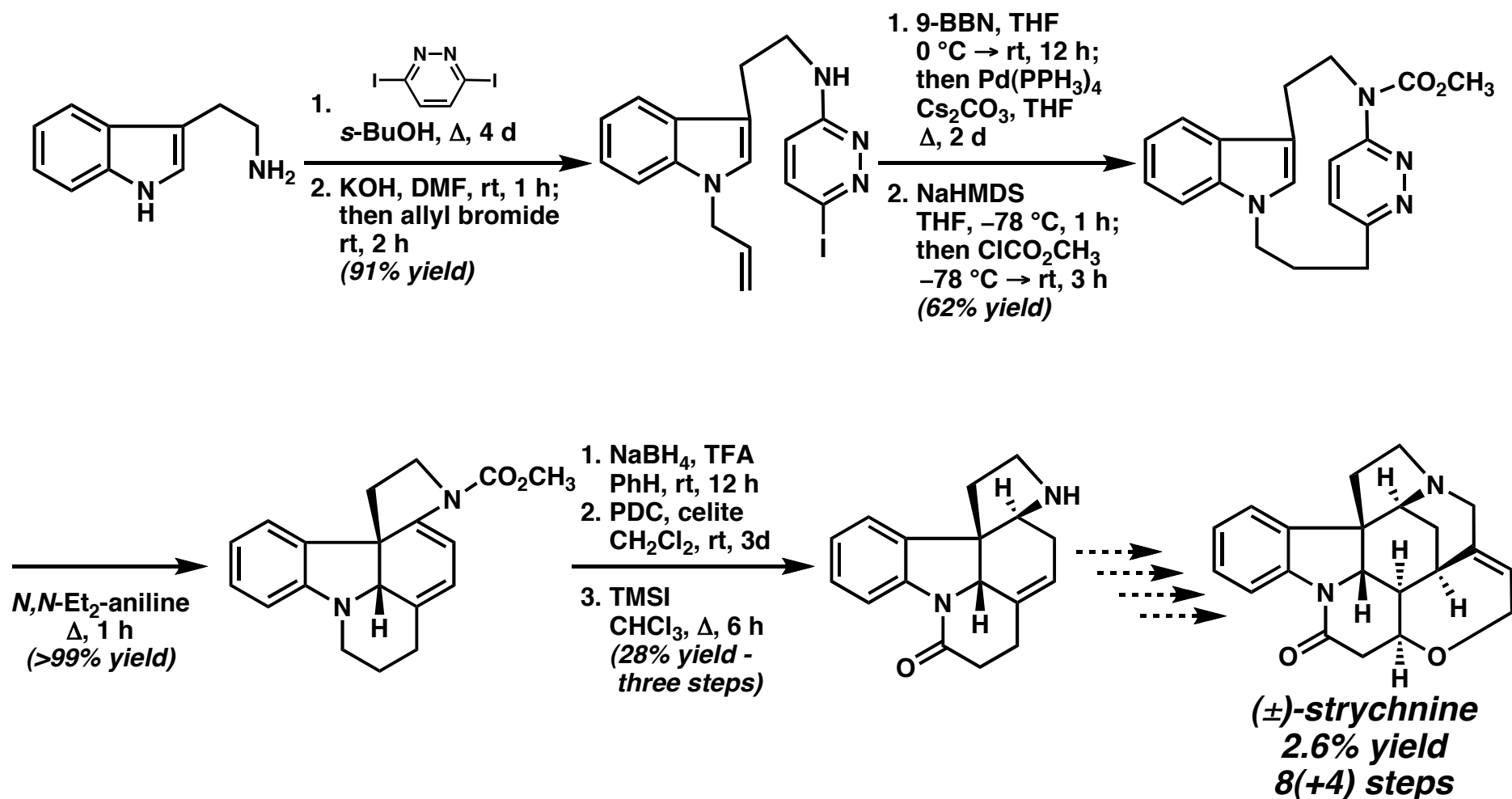
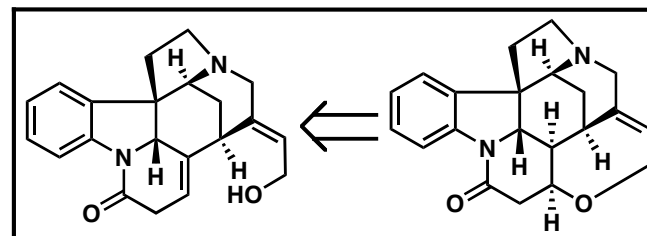
(\pm)-strychnine
0.6% yield
16 steps

Eichberg, Vollhardt *et al.* *Org. Lett.* **2000**, *2*, 2479-2481.

Retrosynthetic Analysis of Bodwell's (±)-Synthesis (2002)

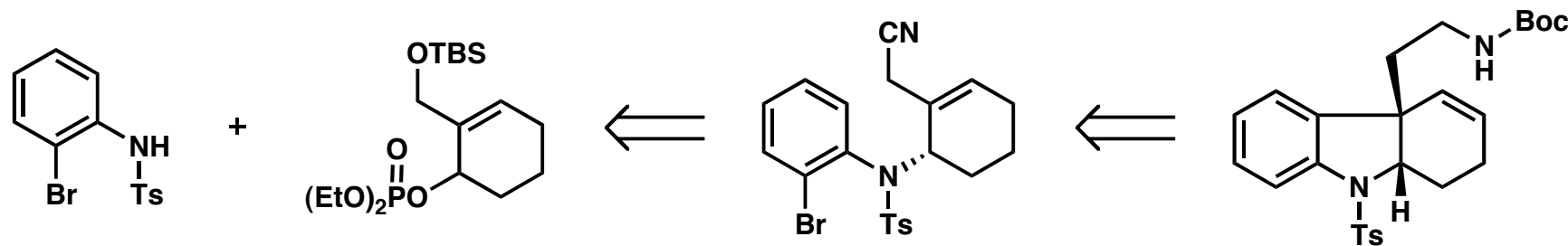
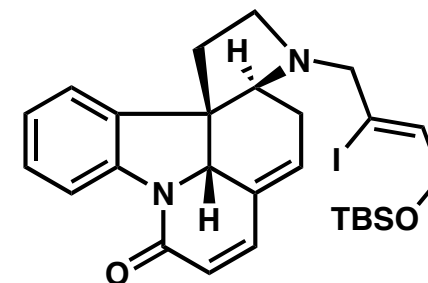
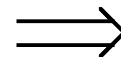
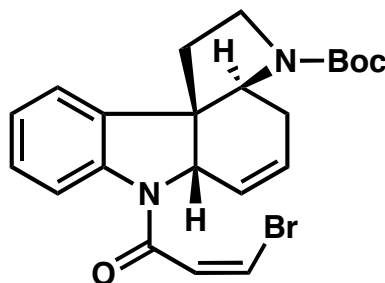
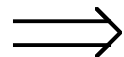
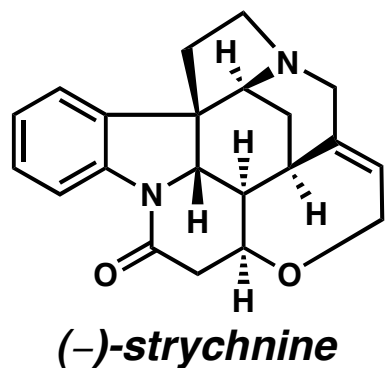
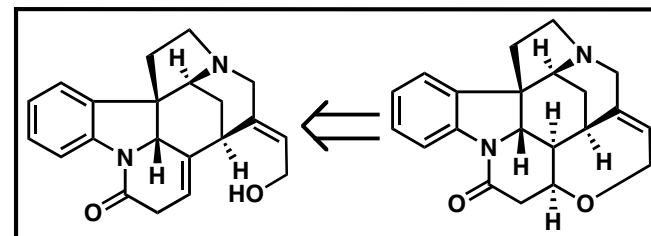


Bodwell's (\pm)-Formal Synthesis (2002)

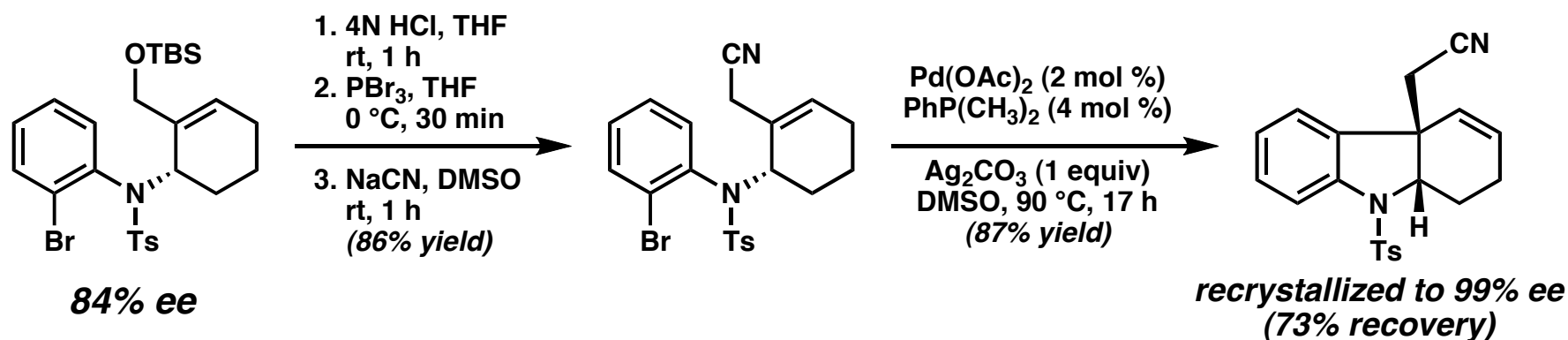
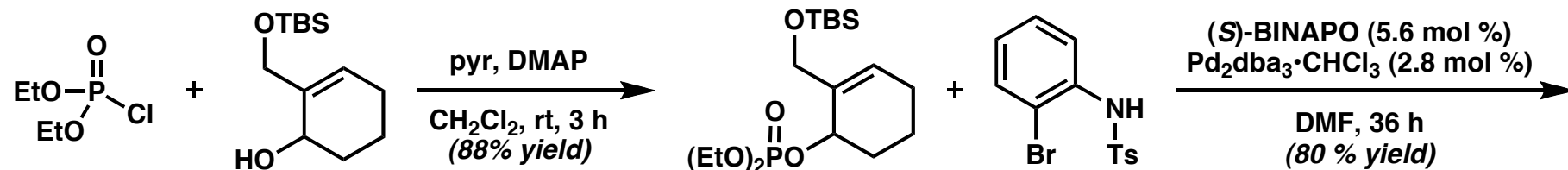
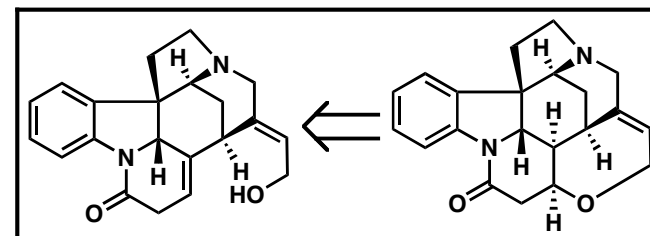


Bodwell & Li, *Angew. Chem. Int. Ed.* **2002**, *41*, 3261-3262.

Retrosynthetic Analysis of Mori's (-)-Synthesis (2002)

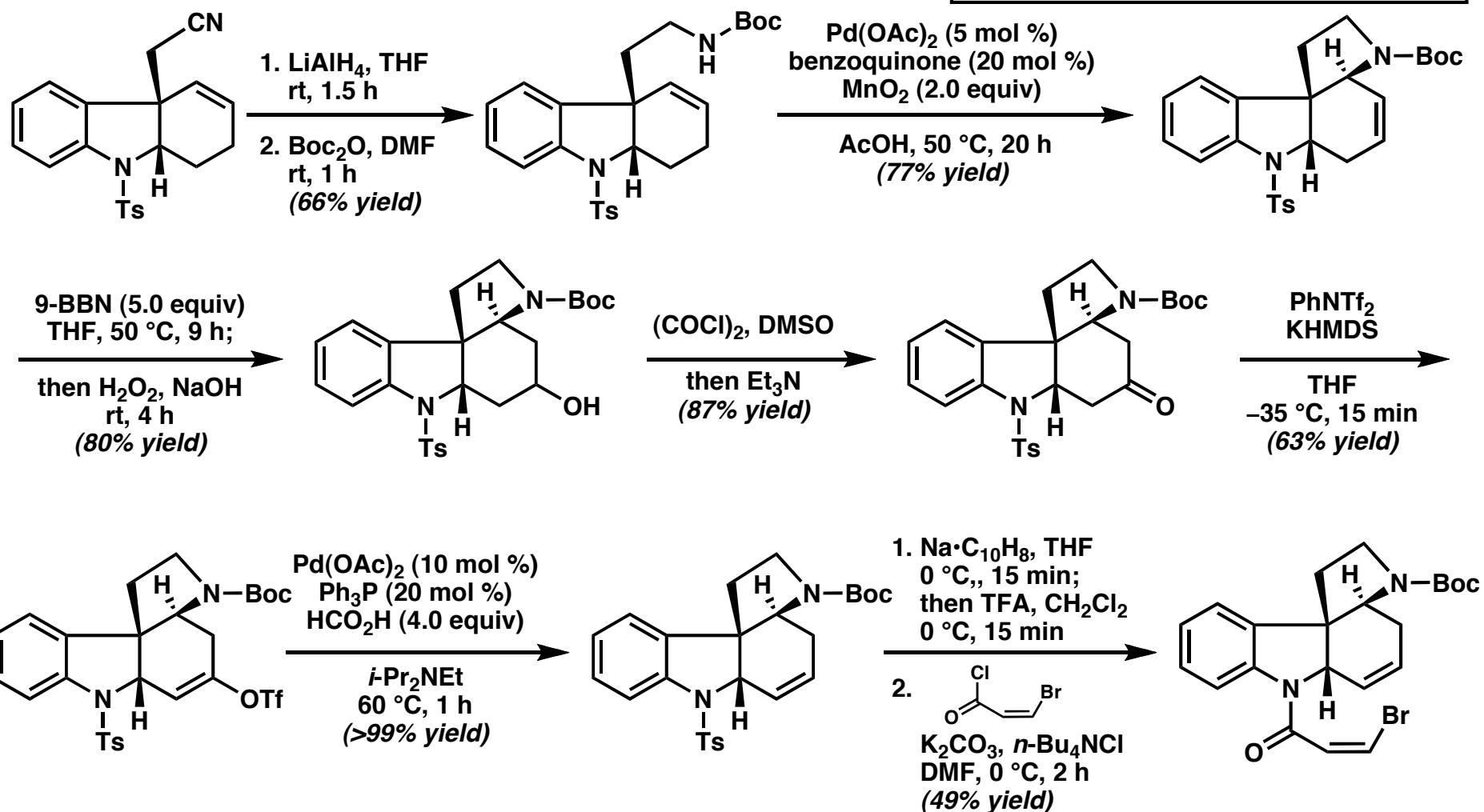
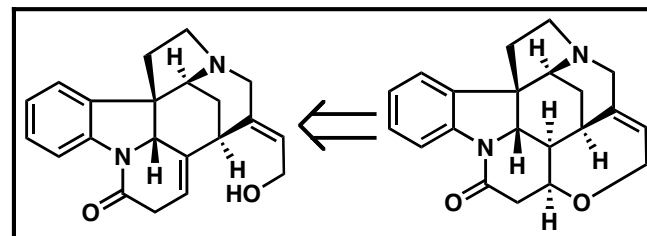


Mori's (-)-Total Synthesis (2002)



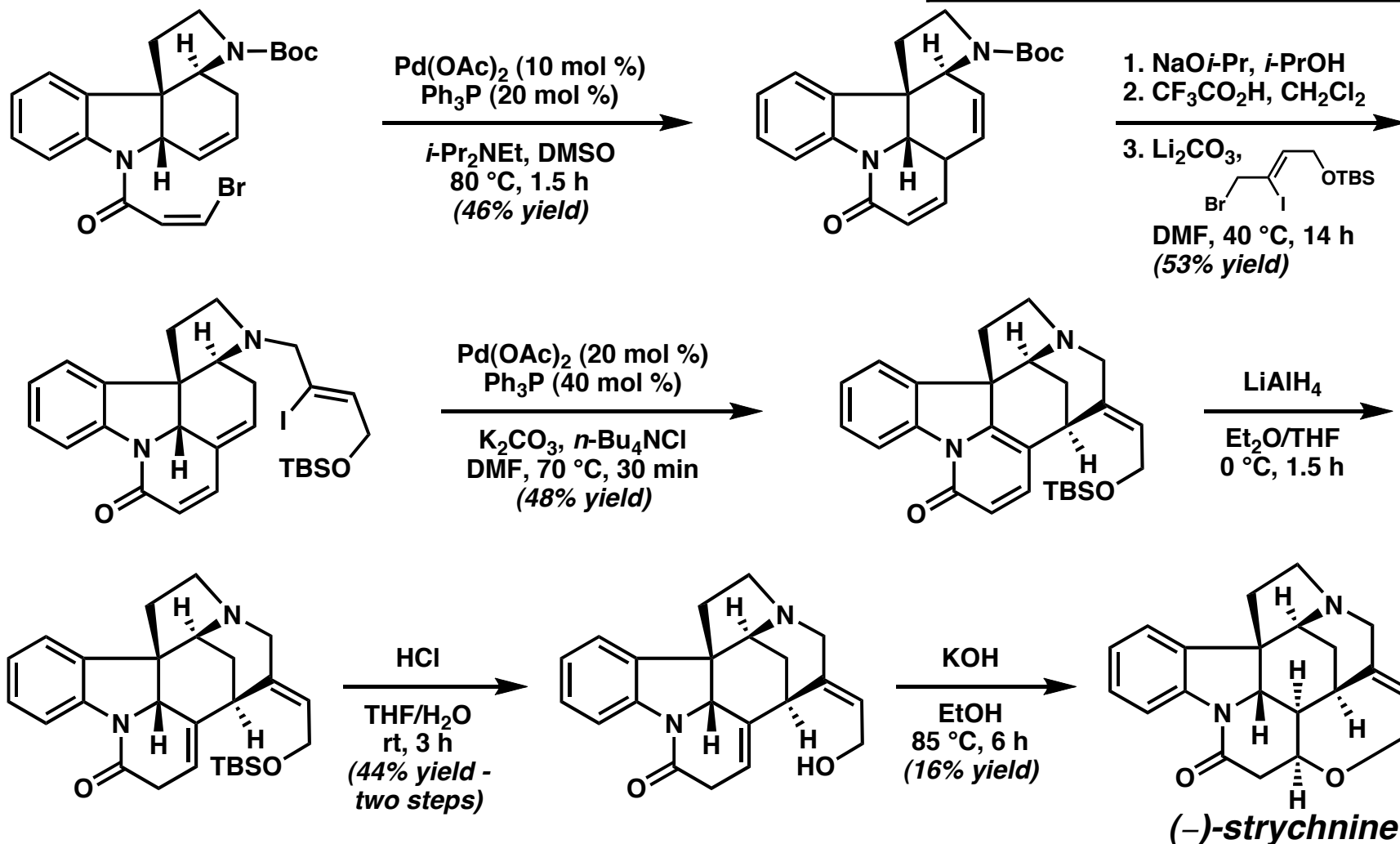
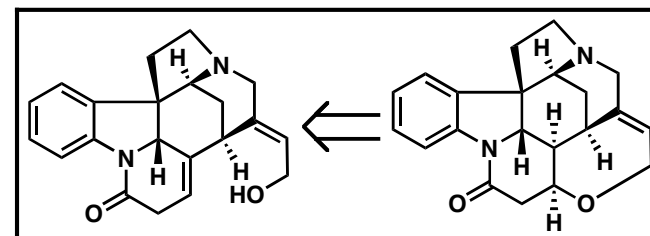
Nakanishi & Mori, *Angew. Chem. Int. Ed.* **2002**, *41*, 1934-1936.
Mori *et al.* *J. Am. Chem. Soc.* **2003**, *125*, 9801-9807.

Mori's (-)-Total Synthesis (2002)



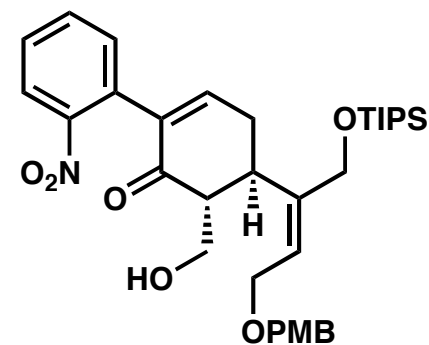
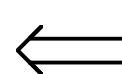
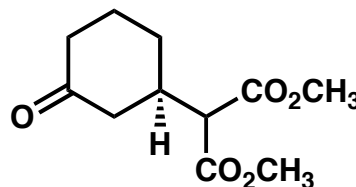
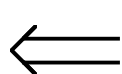
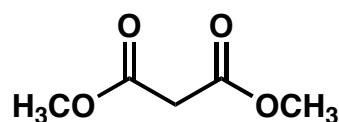
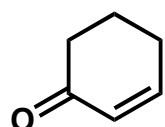
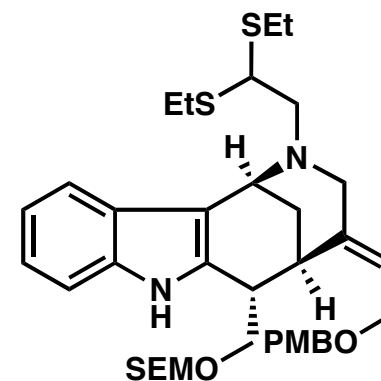
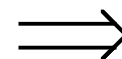
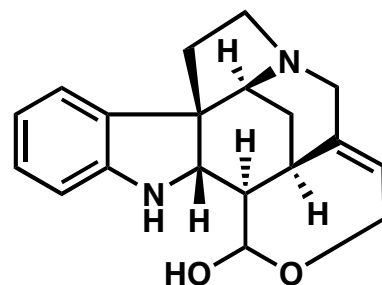
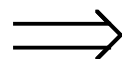
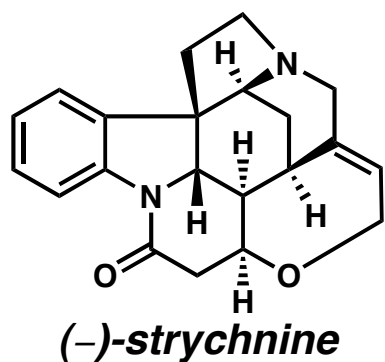
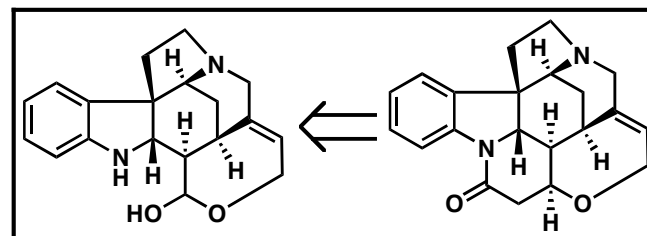
Nakanishi & Mori, *Angew. Chem. Int. Ed.* **2002**, 41, 1934-1936.
 Mori *et al.* *J. Am. Chem. Soc.* **2003**, 125, 9801-9807.

Mori's (-)-Total Synthesis (2002)

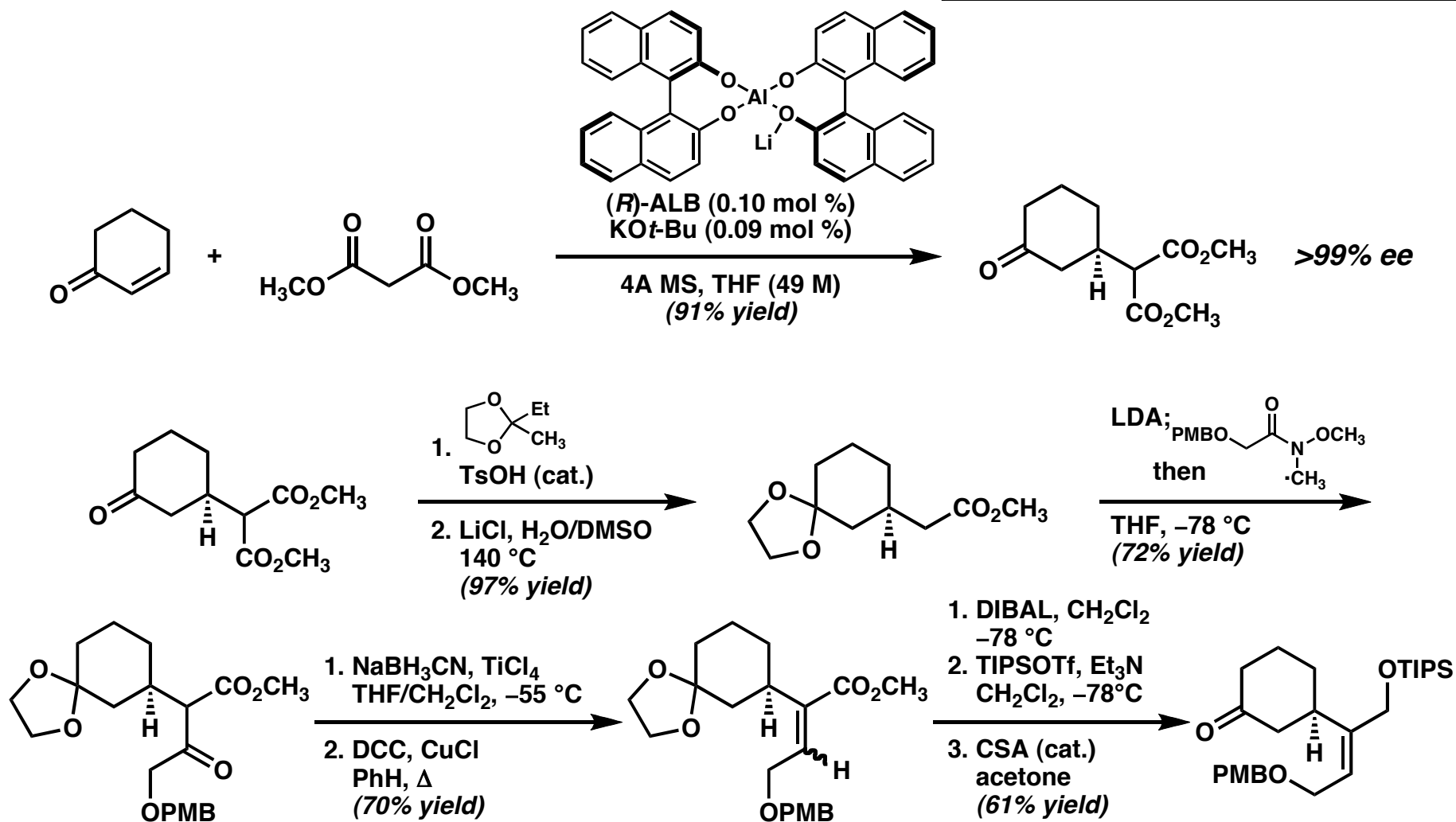
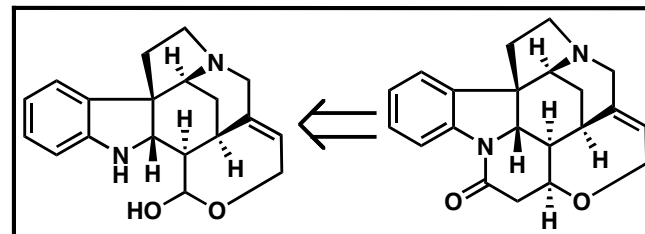


Nakanishi & Mori, *Angew. Chem. Int. Ed.* **2002**, 41, 1934-1936.
 Mori et al. *J. Am. Chem. Soc.* **2003**, 125, 9801-9807.

Retrosynthetic Analysis of Shibasaki's (-)-Synthesis (2002)

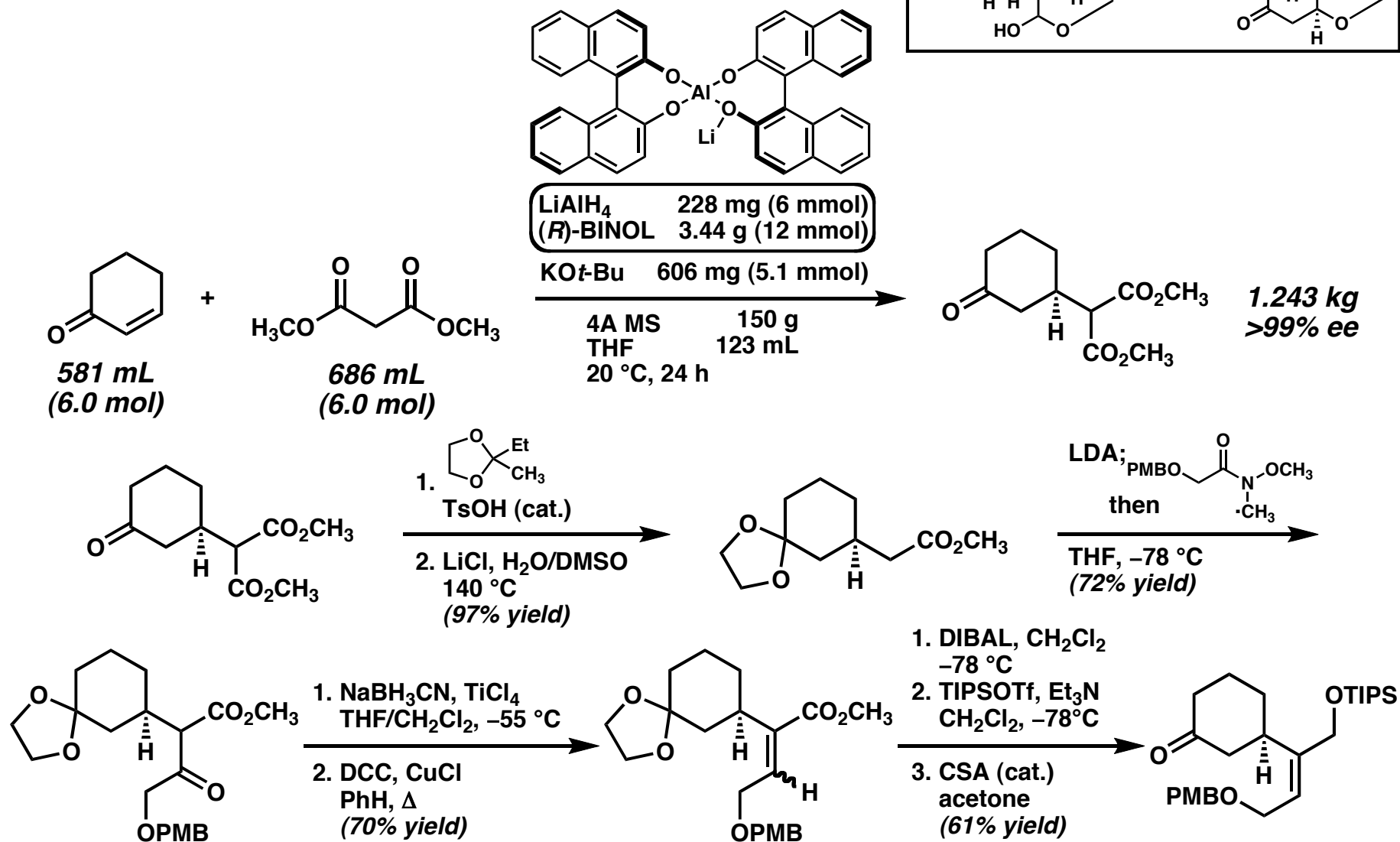
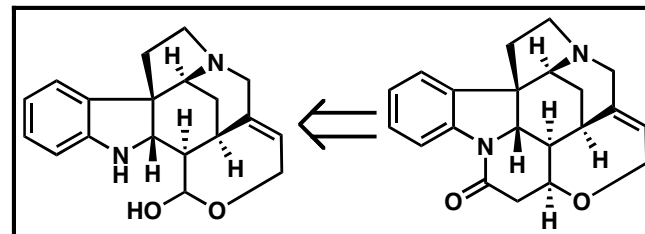


Shibasaki's (-)-Total Synthesis (2002)



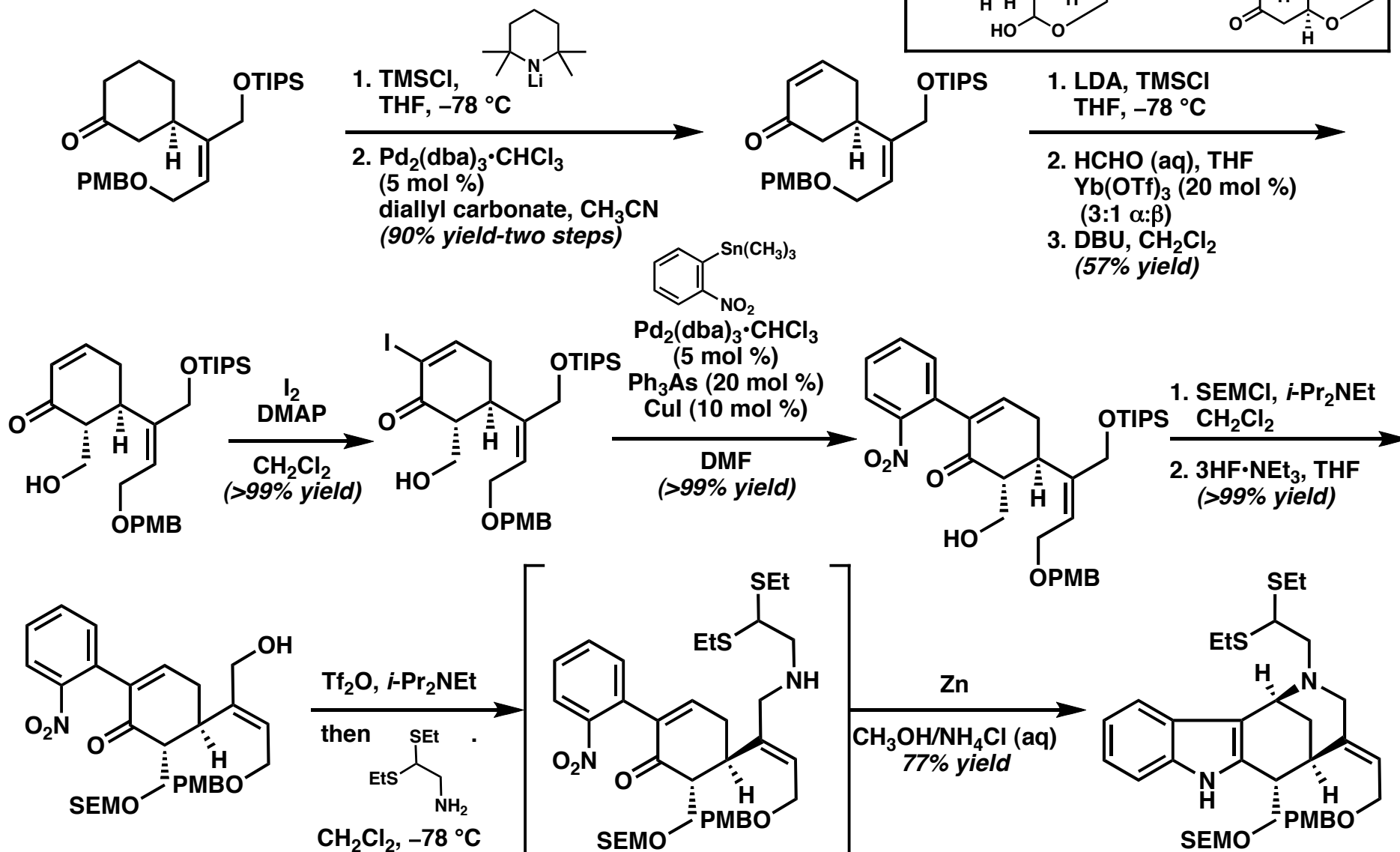
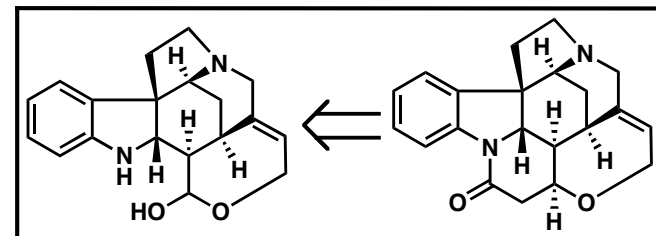
Shibasaki *et al.* *J. Am. Chem. Soc.* **2002**, *124*, 14546-14247.

Shibasaki's (-)-Total Synthesis (2002)



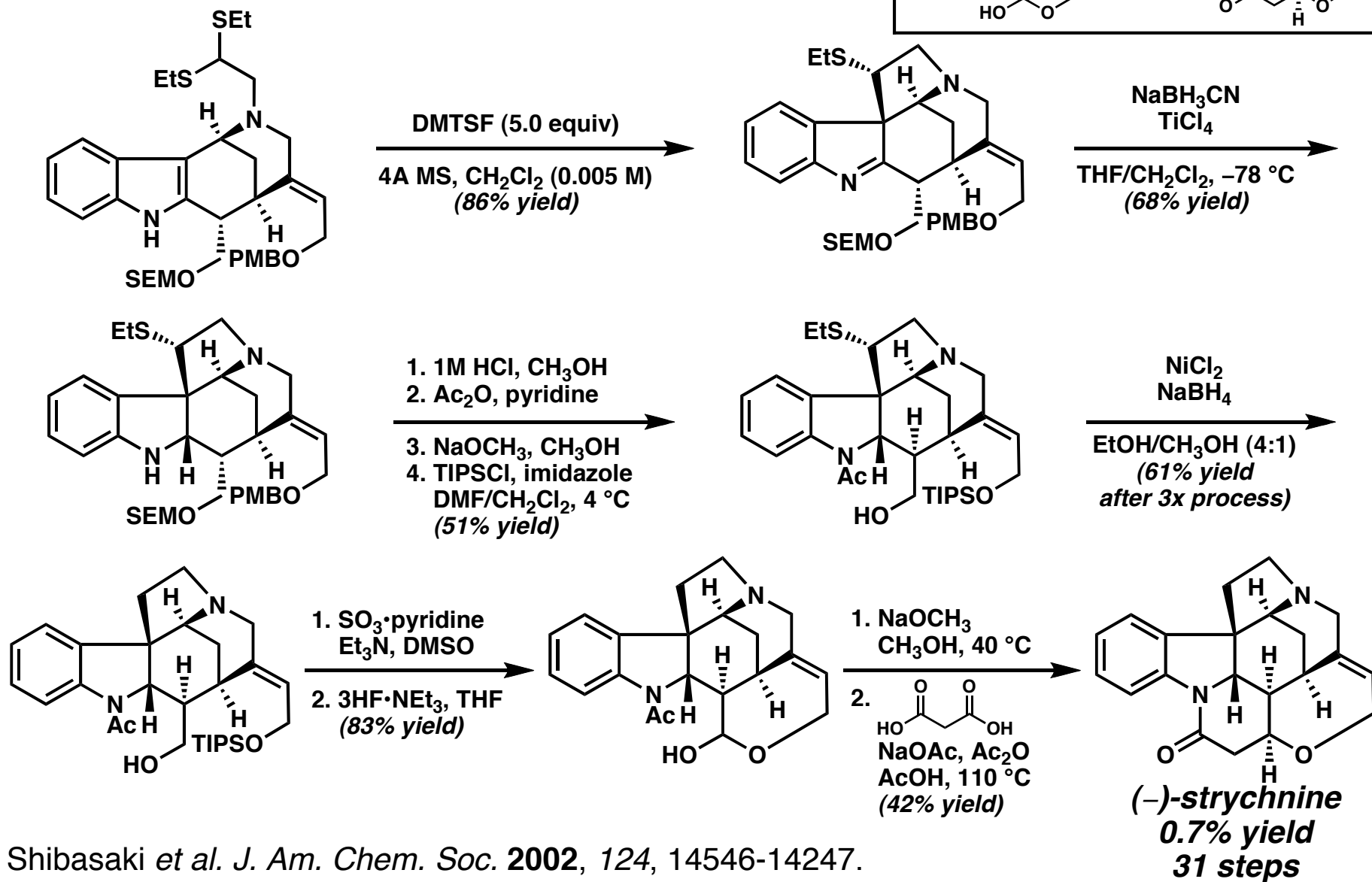
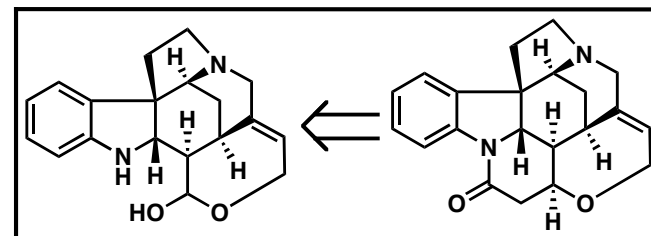
Shibasaki et al. *J. Am. Chem. Soc.* **2002**, *124*, 14546-14247.

Shibasaki's (-)-Total Synthesis (2002)



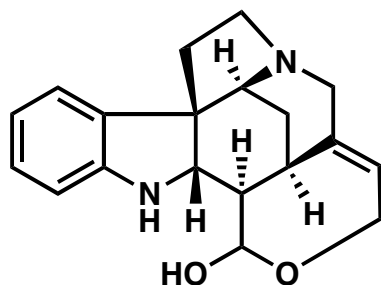
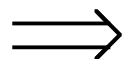
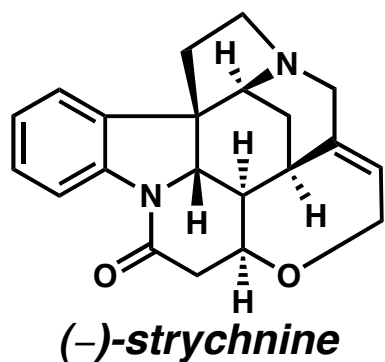
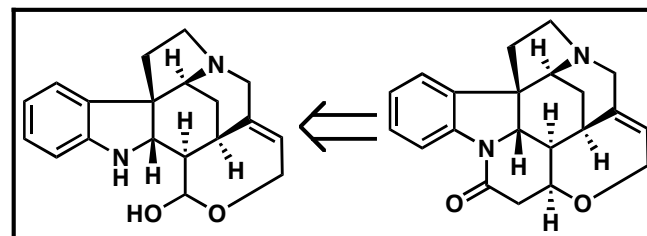
Shibasaki et al. *J. Am. Chem. Soc.* **2002**, *124*, 14546-14247.

Shibasaki's (-)-Total Synthesis (2002)

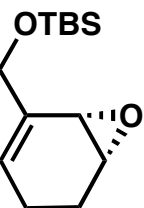
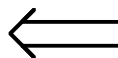
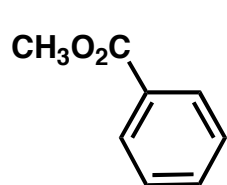
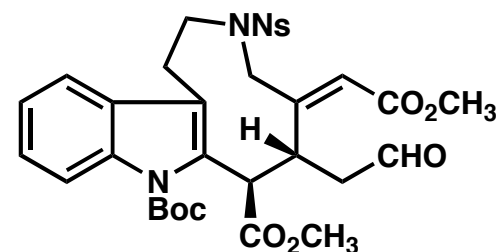
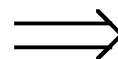


Shibasaki *et al.* *J. Am. Chem. Soc.* **2002**, *124*, 14546-14247.

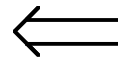
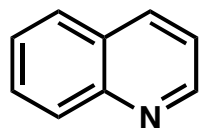
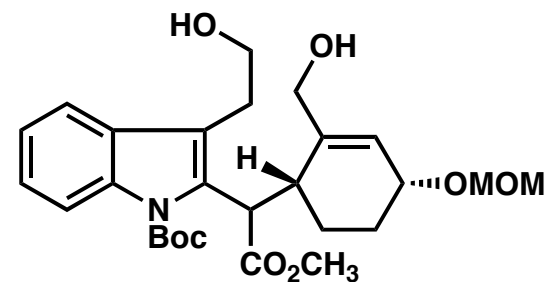
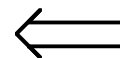
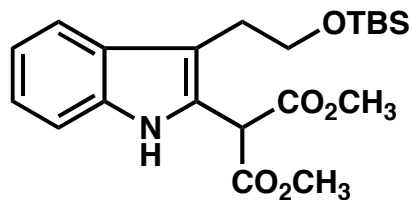
Retrosynthetic Analysis of Fukuyama's (-)-Synthesis (2004)



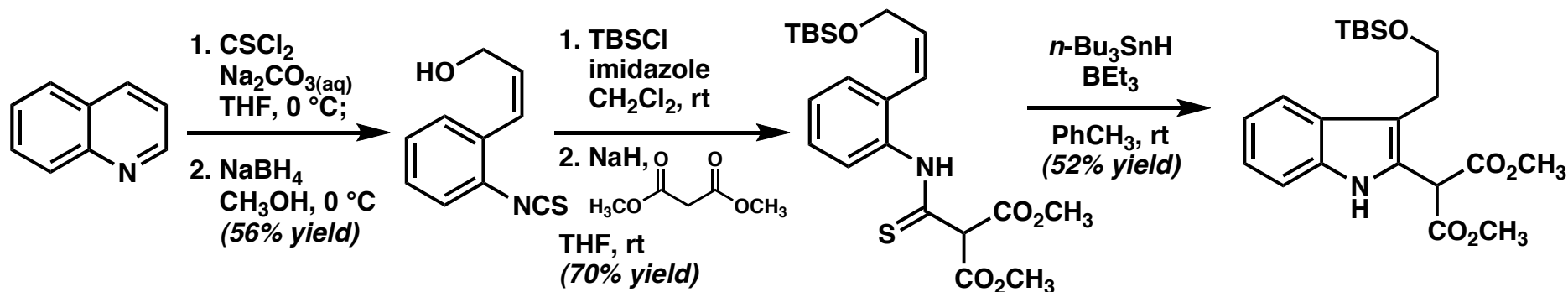
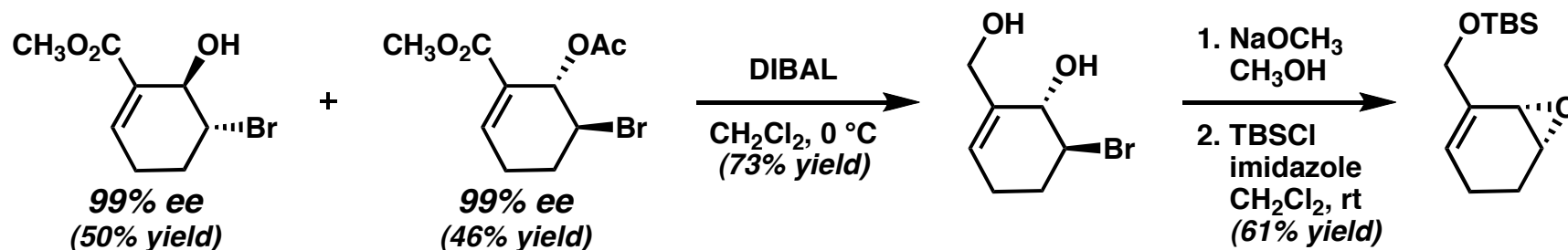
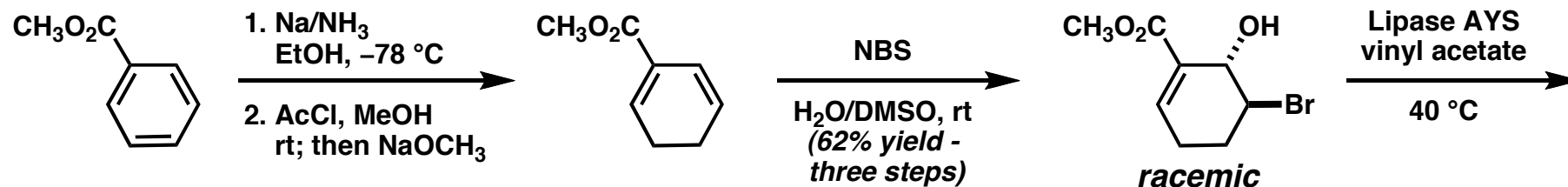
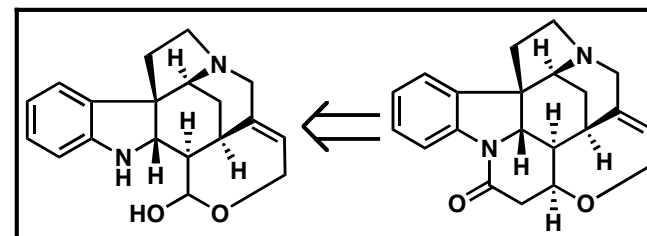
Wieland-Gumlich aldehyde



+

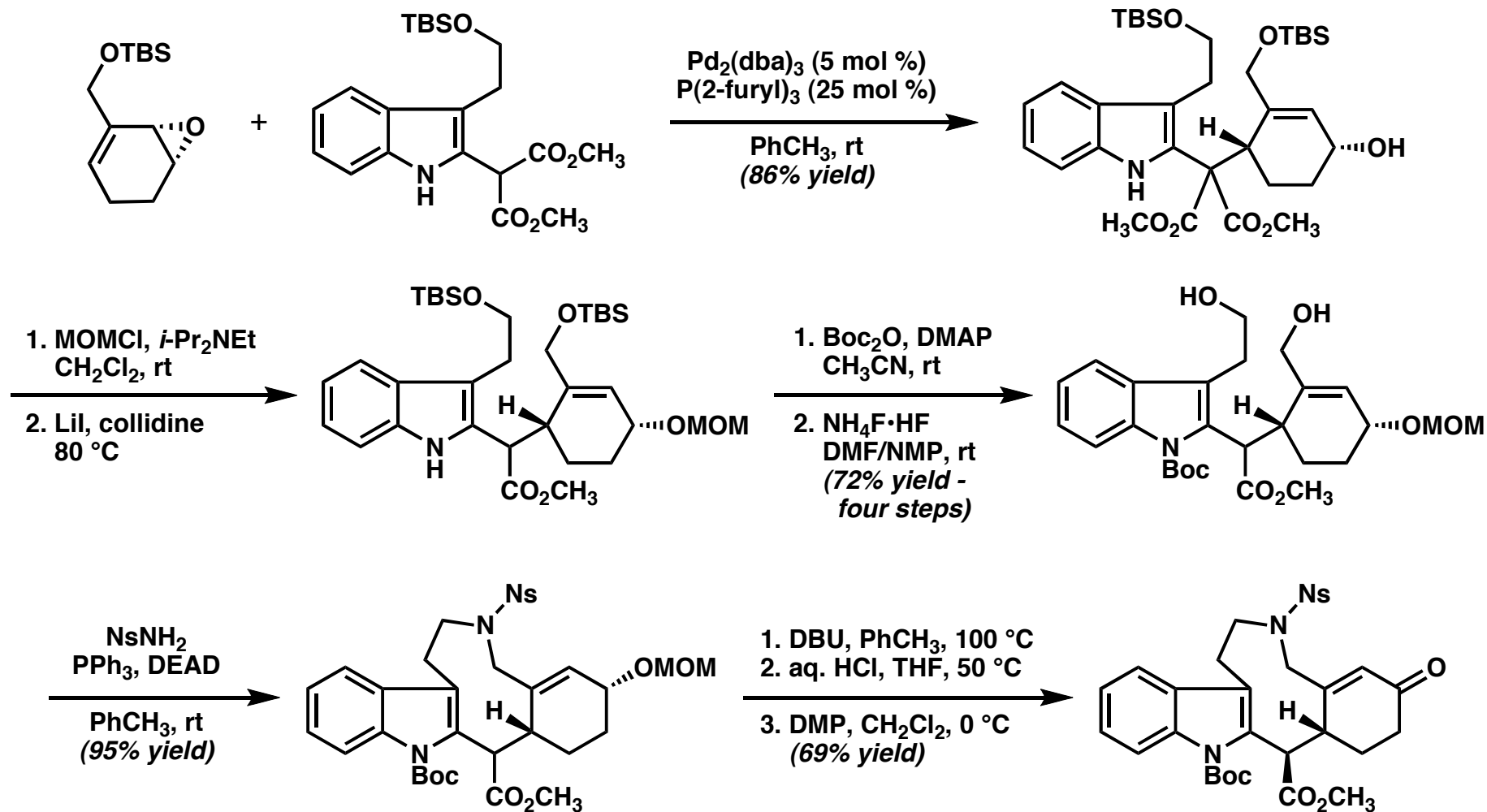
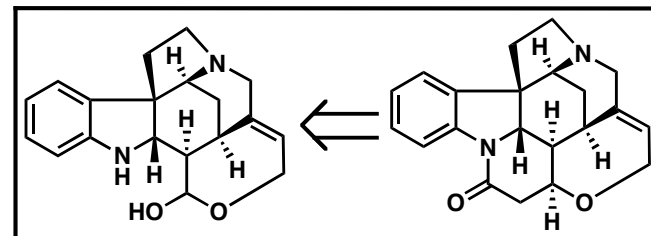


Fukuyama's (-)-Total Synthesis (2004)



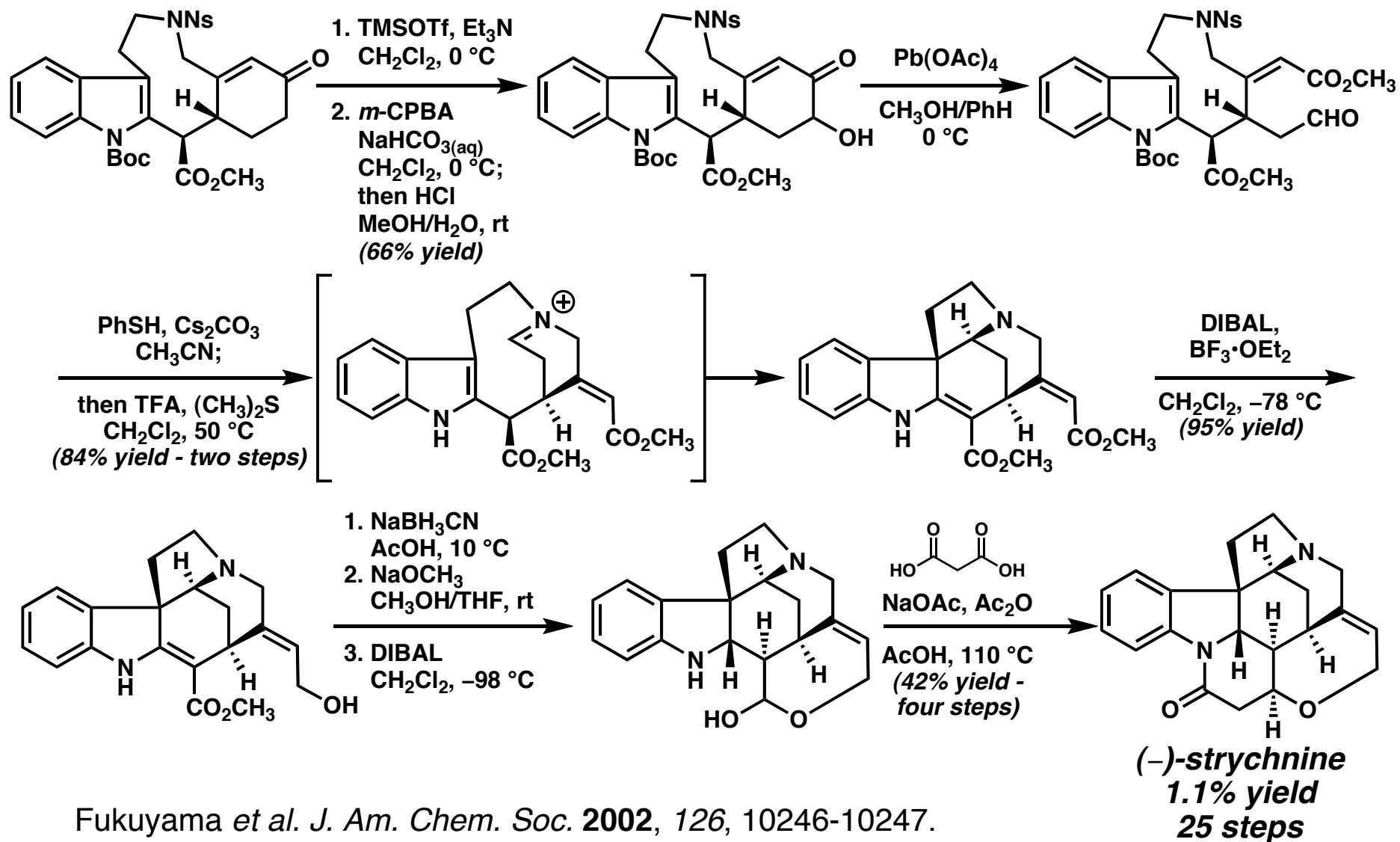
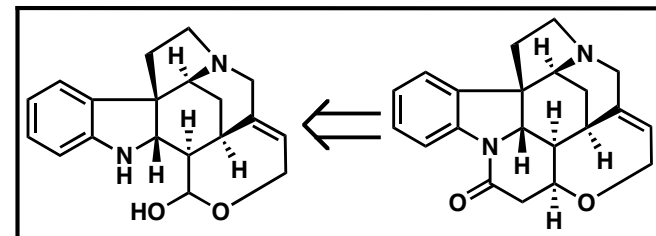
Fukuyama et al. *J. Am. Chem. Soc.* **2002**, *126*, 10246-10247.

Fukuyama's (-)-Total Synthesis (2004)

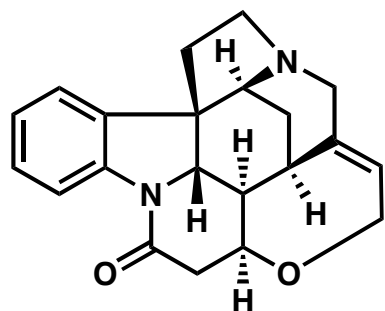
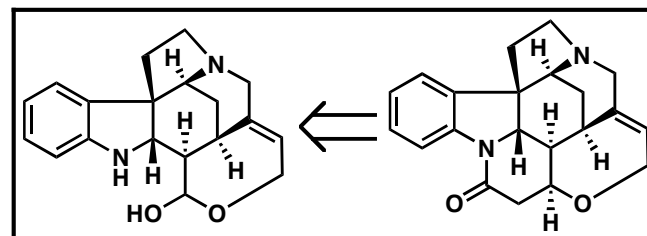


Fukuyama *et al.* *J. Am. Chem. Soc.* 2002, **126**, 10246-10247.

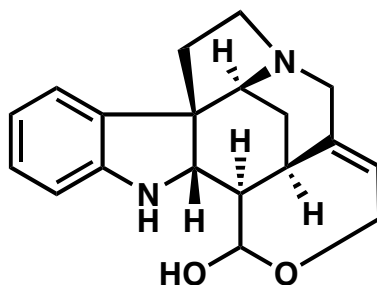
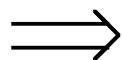
Fukuyama's (-)-Total Synthesis (2004)



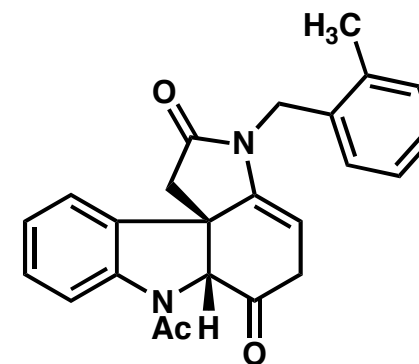
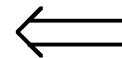
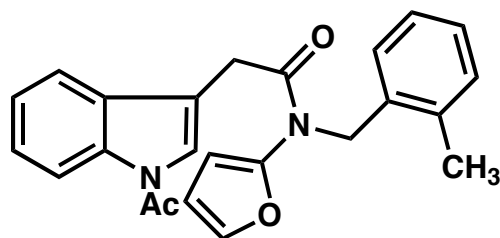
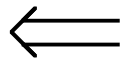
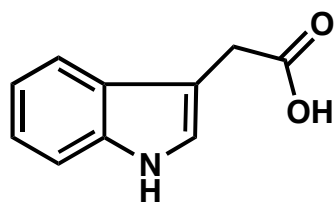
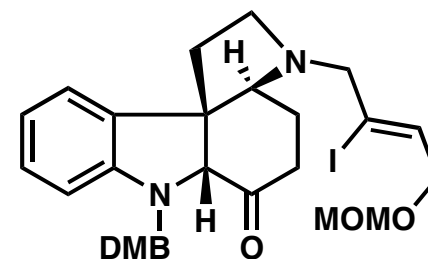
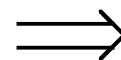
Retrosynthetic Analysis of Padwa's (±)-Synthesis (2007)



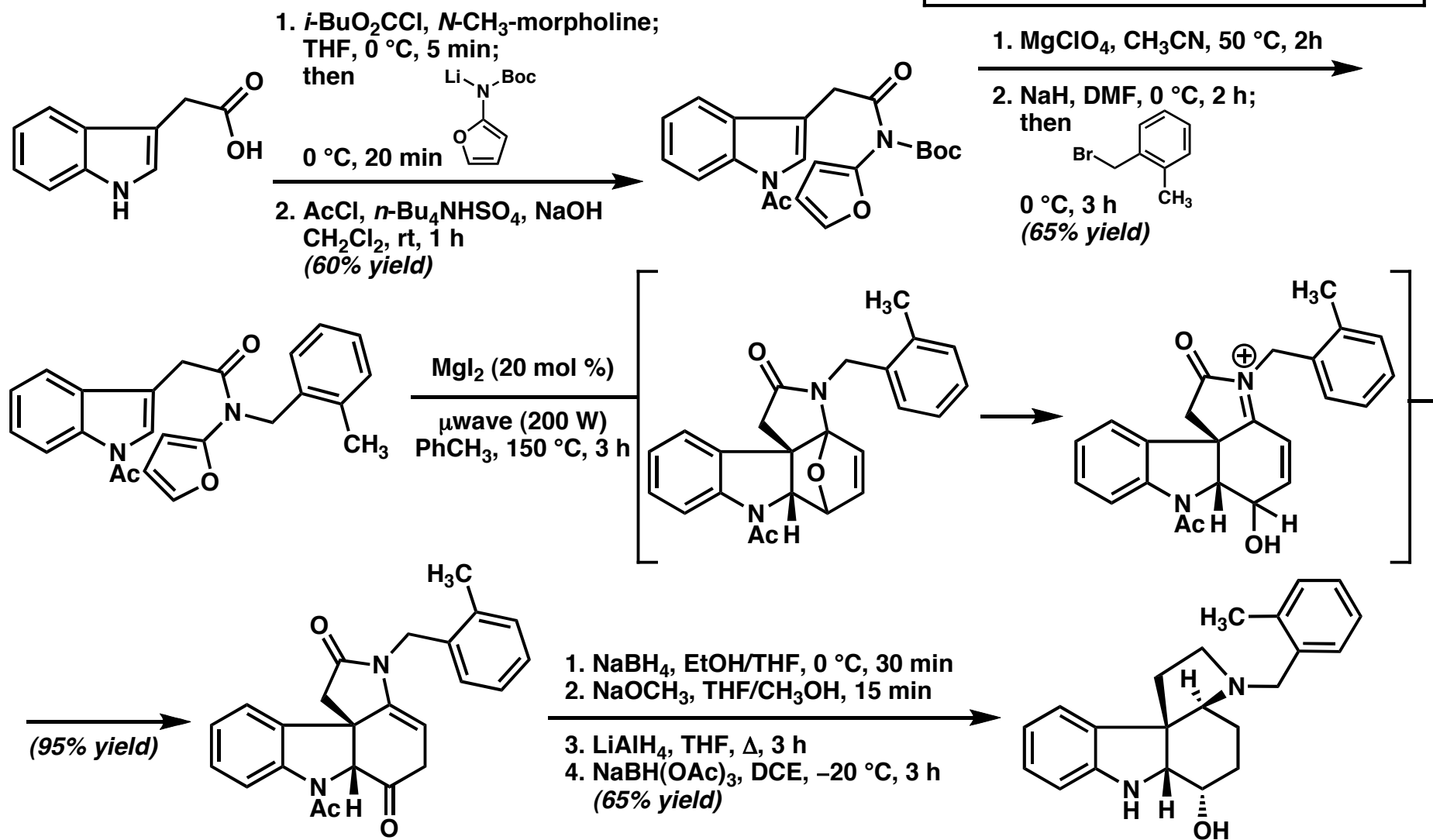
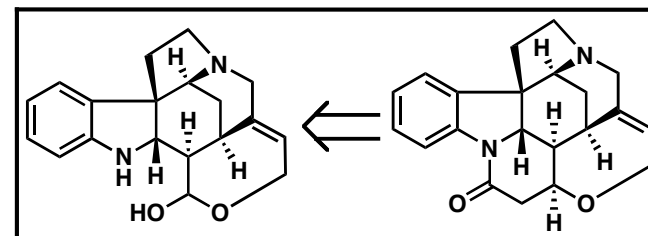
(±)-strychnine



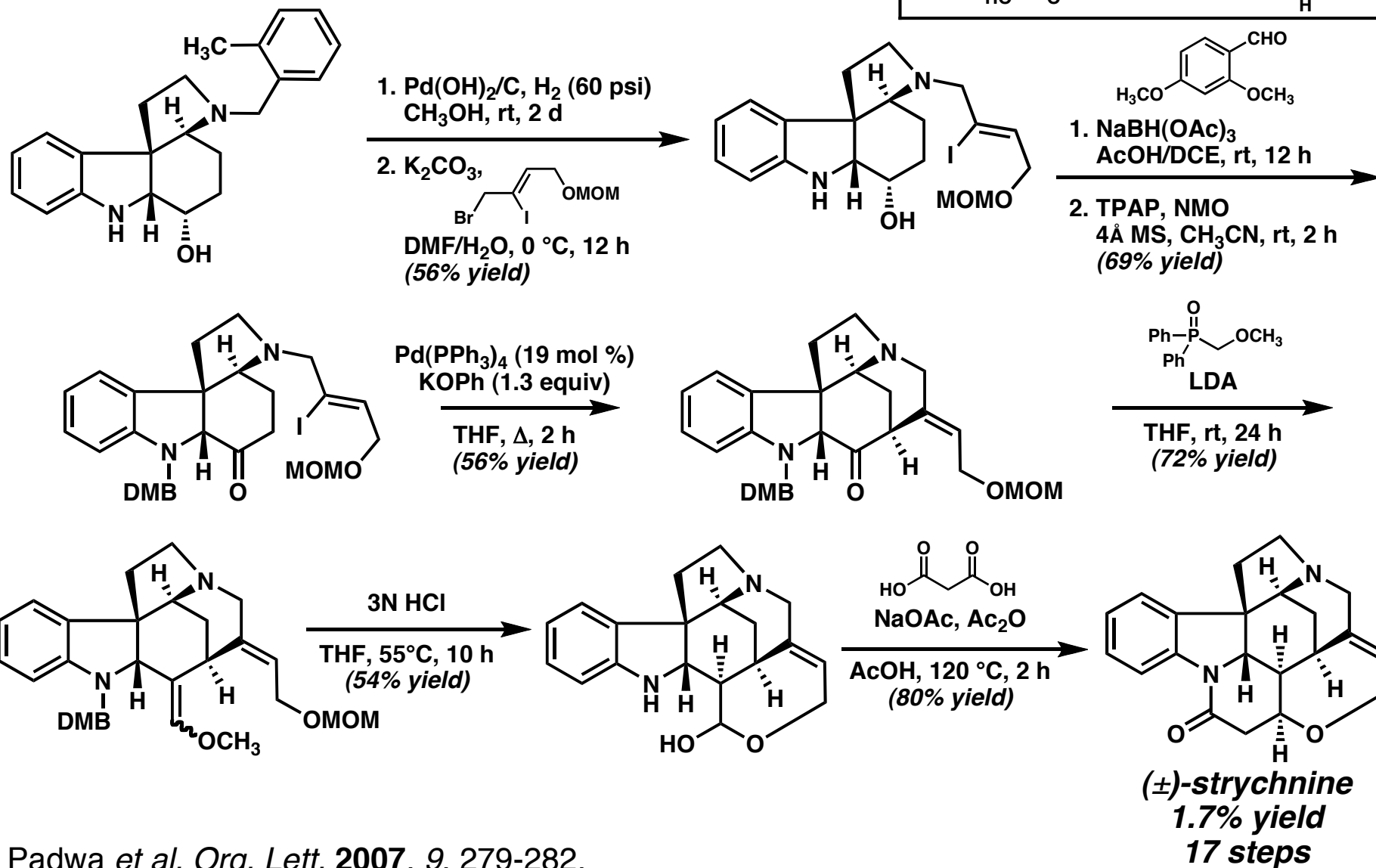
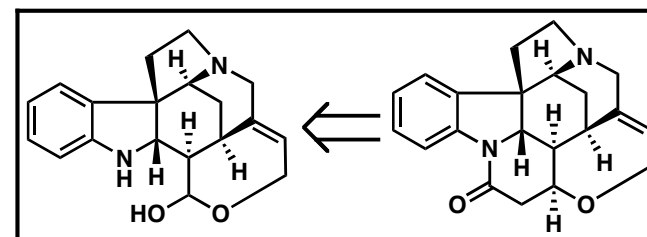
Wieland-Gumlich aldehyde

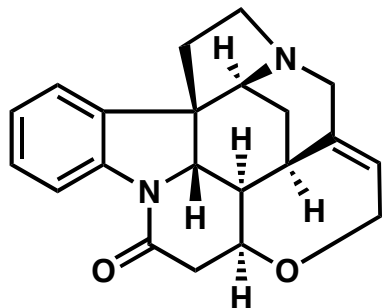


Padwa's (\pm)-Total Synthesis (2007)



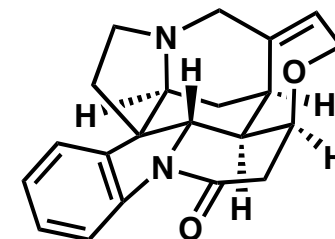
Padwa's (\pm)-Total Synthesis (2007)





Conclusions on Strychnine

"For its molecular size it is the most complex substance known." - Robert Robinson (1952)



14 total syntheses

8 racemic syntheses

6 asymmetric syntheses

2 utilize the chiral pool, 2 utilize enzymatic transformations, 2 utilize an asymmetric method

- **R. B. Woodward - 1954**
- **Philip Magnus - 1992**
- **Gilbert Stork - 1992**
- **Larry E. Overman - 1993**
- **Martin E. Kuehne - 1993**
- **Viresh H. Rawal - 1994**
- **Josep Bonjoch & Joan Bosch - 1999**
- **Stephen F. Martin - 1996-2001**
- **Michael Eichberg & Peter Vollhardt - 2000**
- **Graham J. Bodwell - 2002**
- **Miwako Mori - 2002**
- **Masakatsu Shibasaki - 2002**
- **Tohru Fukuyama - 2004**
- **Albert Padwa - 2007**

\$273 /Kg (Shanghai FWD Chemicals Limited)
approximately 1.4¢ /lethal human dose (~50 mg)