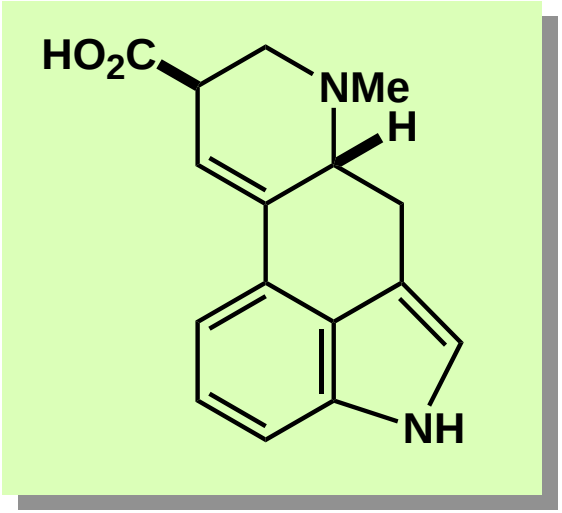
1 Synthetic Studies on (+)-Lysergic Acid



Isolation

L. Craig *et al.*, *J. Biol. Chem.*, 104, 547 (1934)

Structure Determination

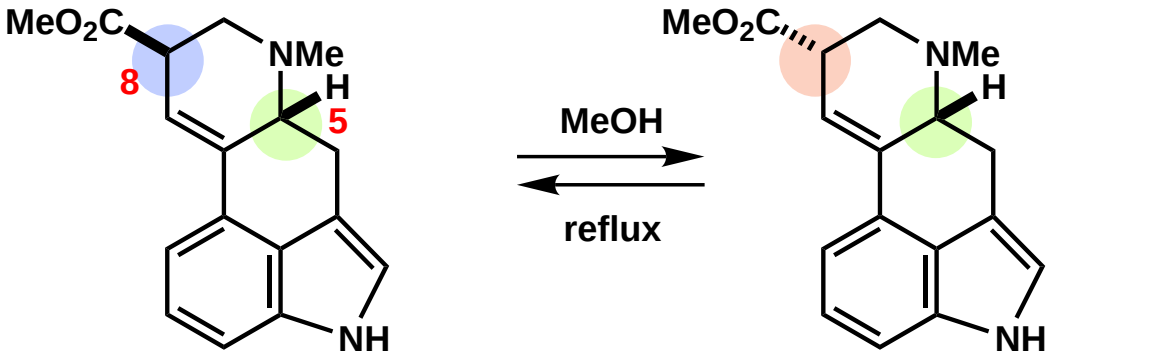
A. Stoll *et al.*, *Helv. Chim. Acta,* 37, 2039 (1954)

Total Syntheses (Racemic Form)

R. B. Woodward *et al.*, *J. Am. Chem. Soc.*, 76, 5256 (1954); 78, 3087 (1956)
M. Julia *et al.*, *Tetrahedron Lett.*, 1569 (1969)
V. W. Armstrong *et al.*, *ibid.*, 4311 (1976)
W. Oppolzer *et al.*, *Helv. Chim. Acta*, 64, 478 (1981)
R. Ramage *et al.*, *Tetrahedron*, 37, Suppl. 9, 157 (1981)
J. Rebek, Jr. *et al.*, *J. Am. Chem. Soc.,* 106, 1813 (1984)
I. Ninomiya *et al.*, *J. Chem. Soc., Perkin Trans. 1*, 941 (1985)
T. Kurihara *et al.*, *Chem. Pharm. Bull.*, 34, 442 (1986)

2

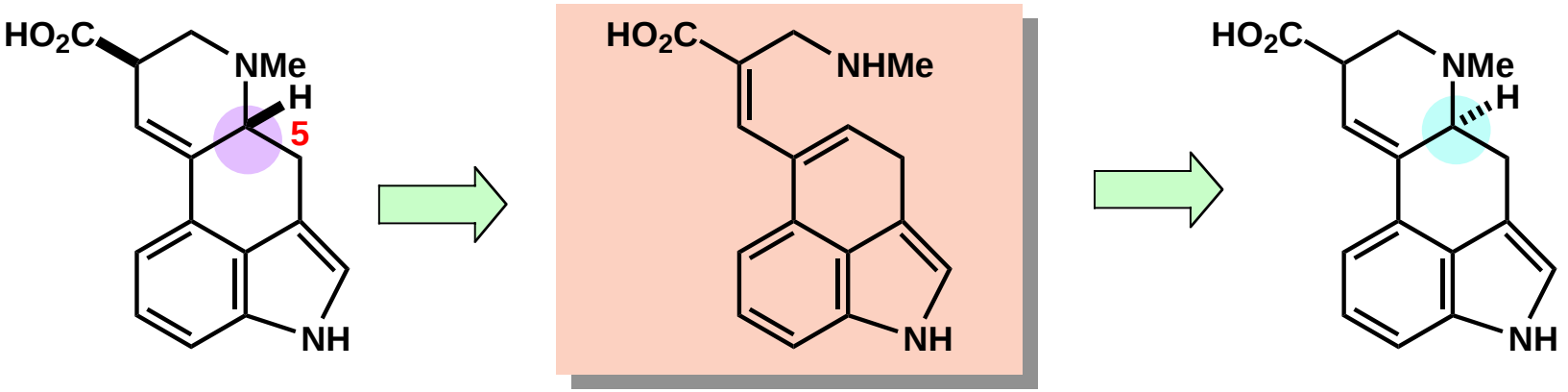
Lysergic Acid is Easily Epimerized



(±)-Methyl lysergate : (±)-Methyl isolysergate

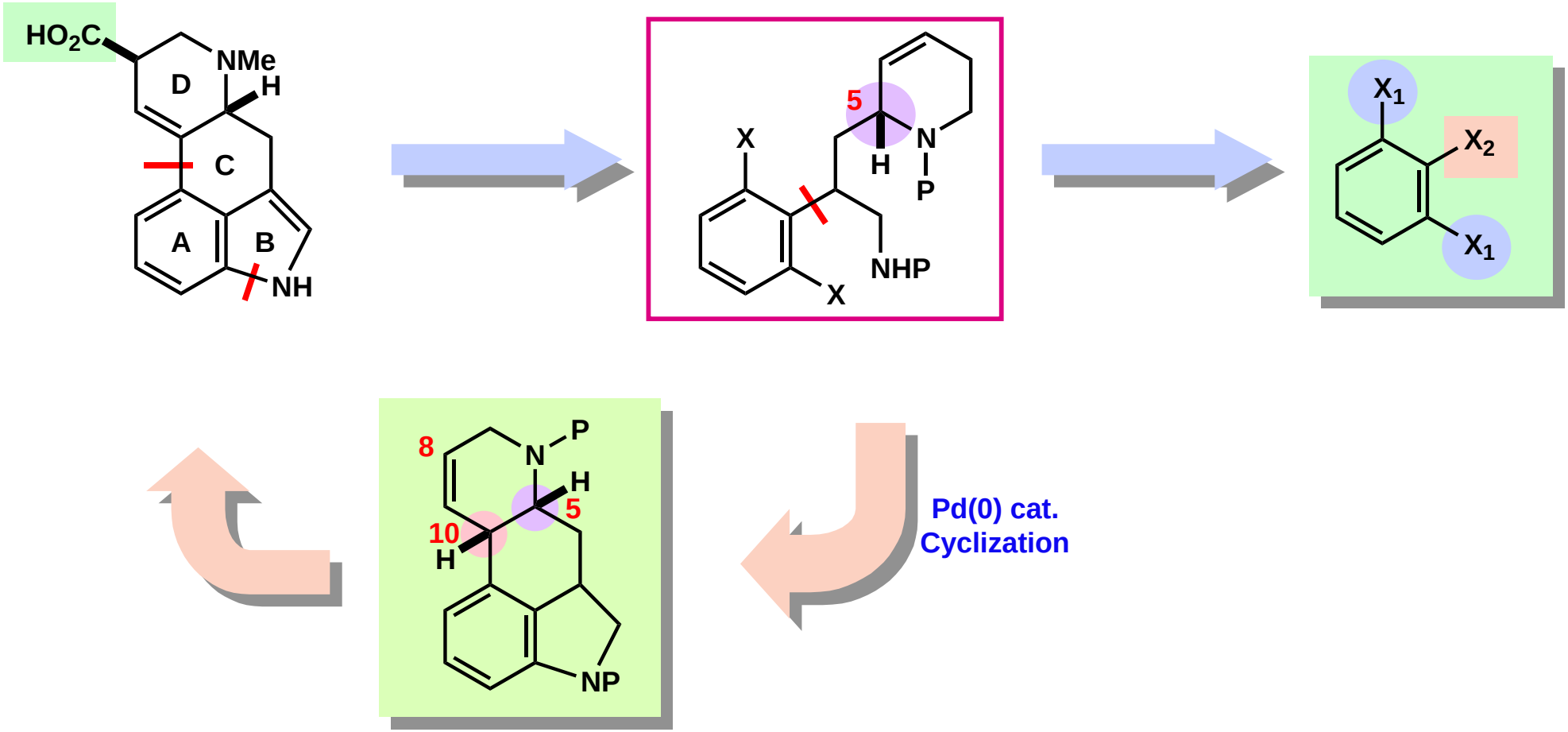
3 : 2

I. Ninomiya *et al.*, *J. Chem. Soc., Perkin Trans. 1*, 941 (1985)

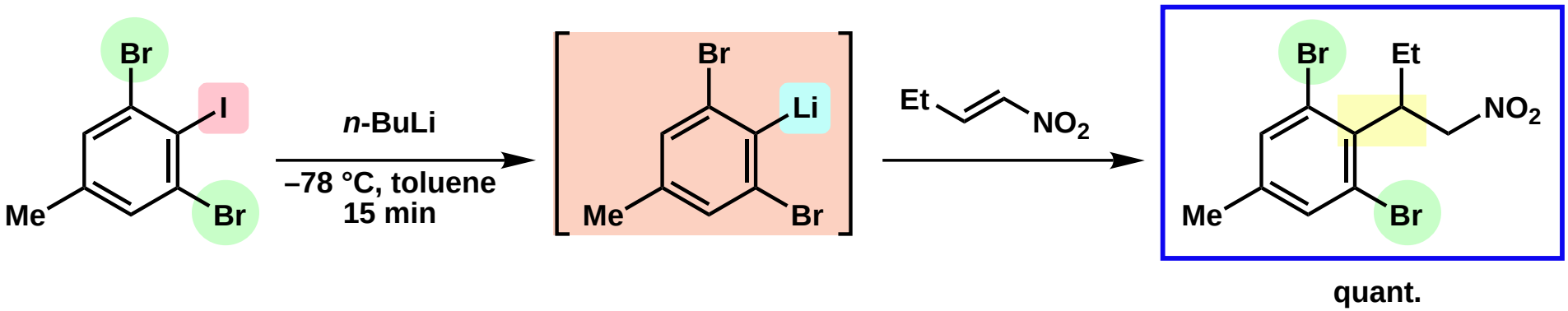


R. Ramage *et al.*, *Tetrahedron*, 37, Suppl. 9, 157 (1981)

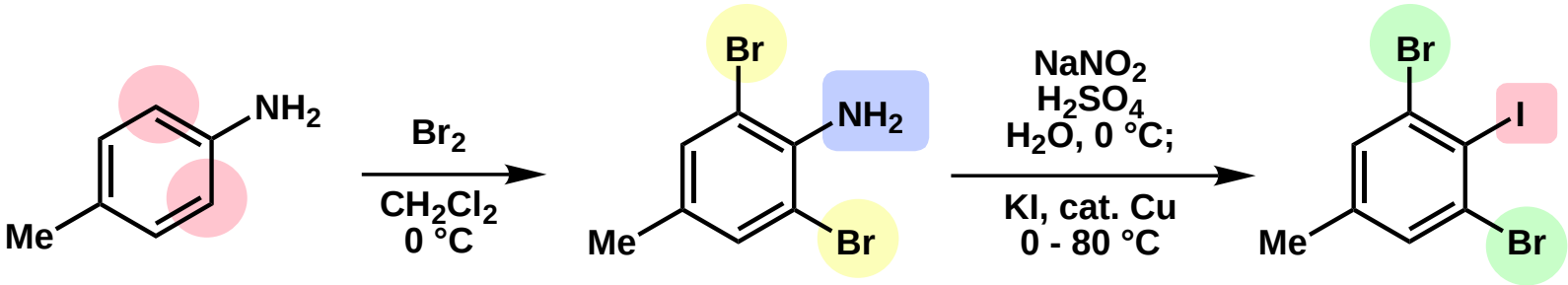
Key Disconnection



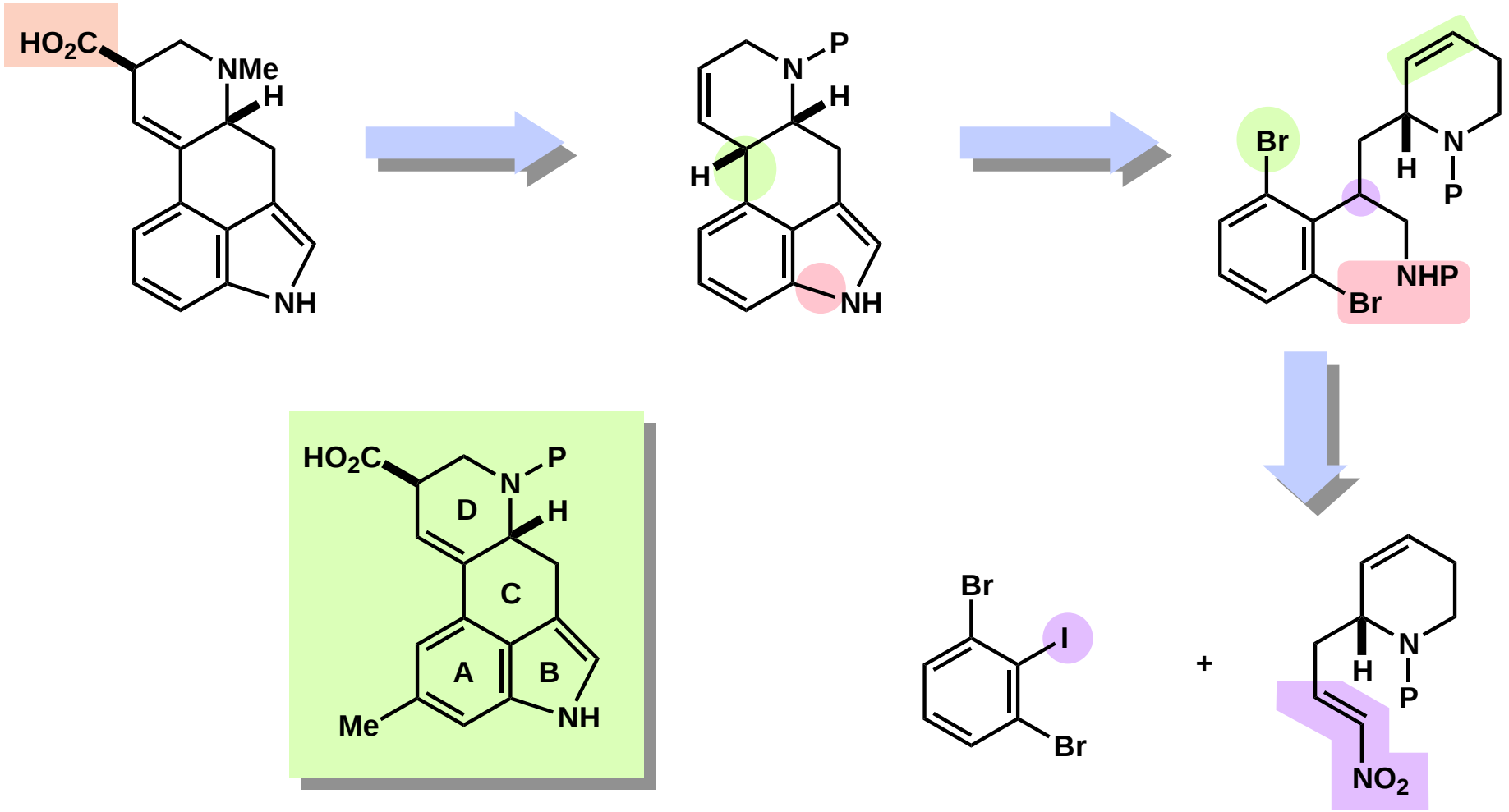
Novel Method of the Connection



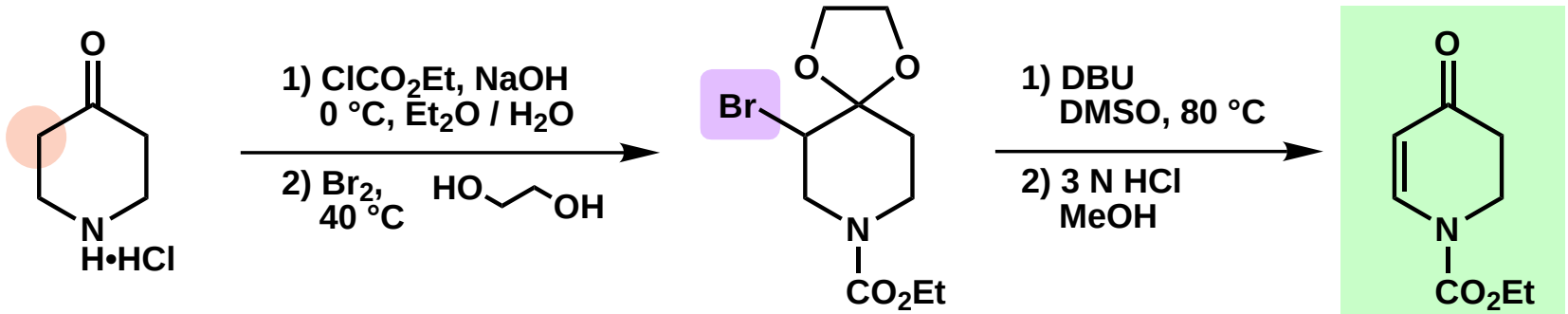
quant.



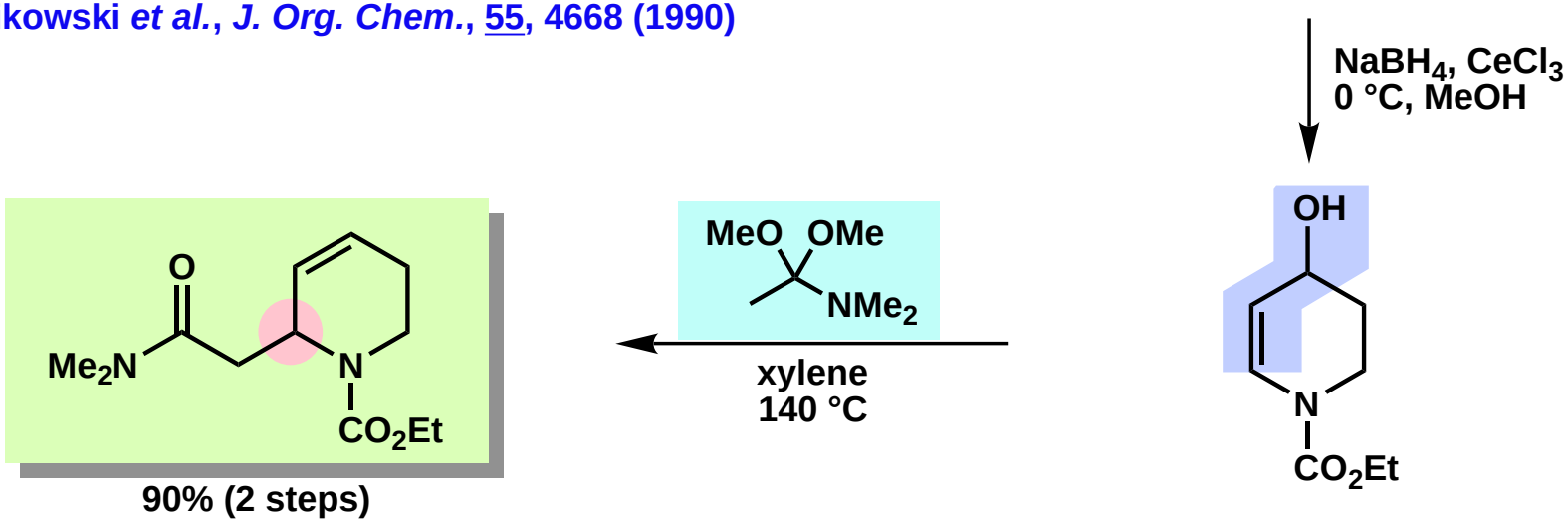
Retrosynthetic Analysis



Model Study

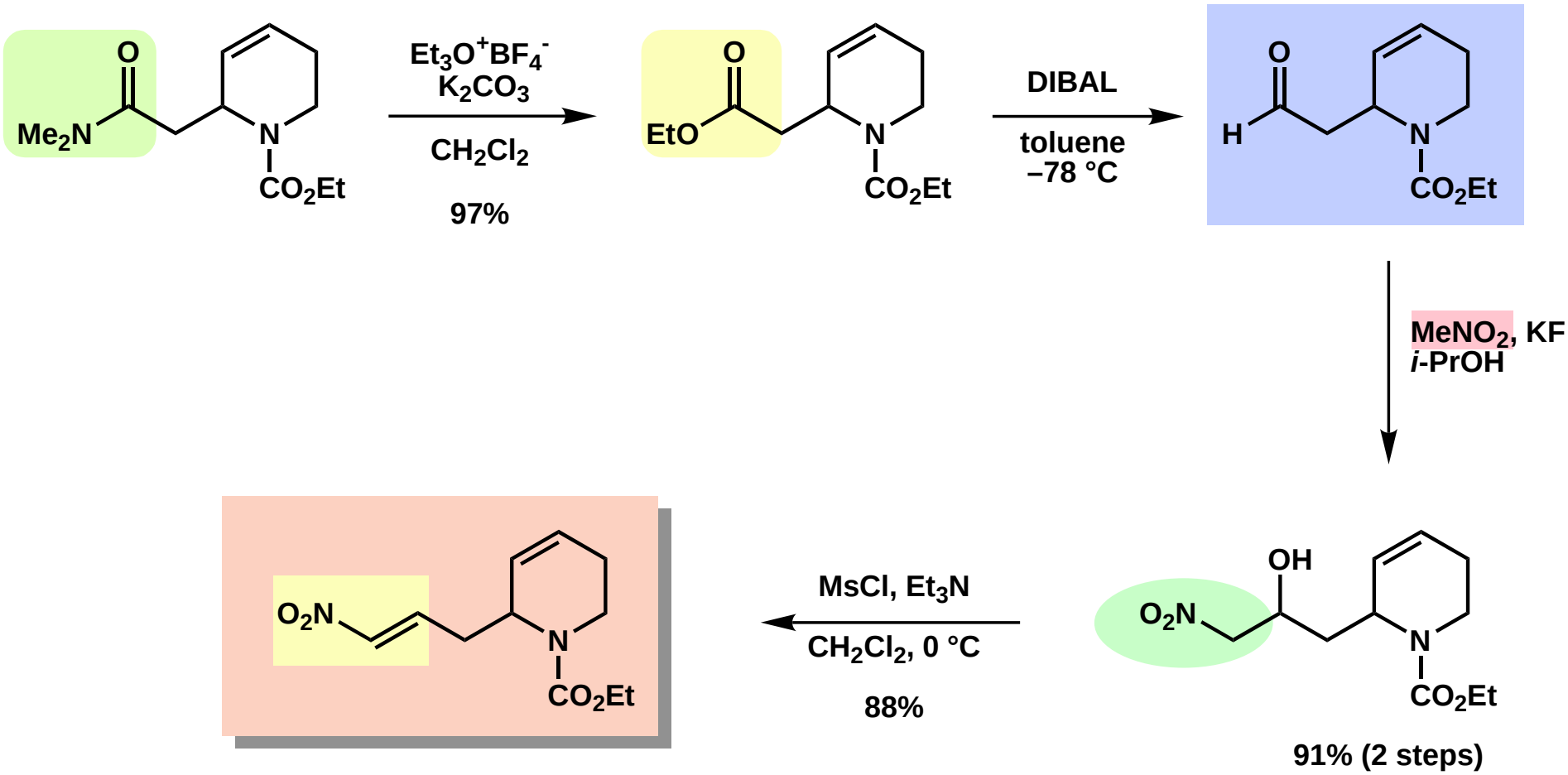


A. P. Kozikowski *et al.*, *J. Org. Chem.*, 55, 4668 (1990)

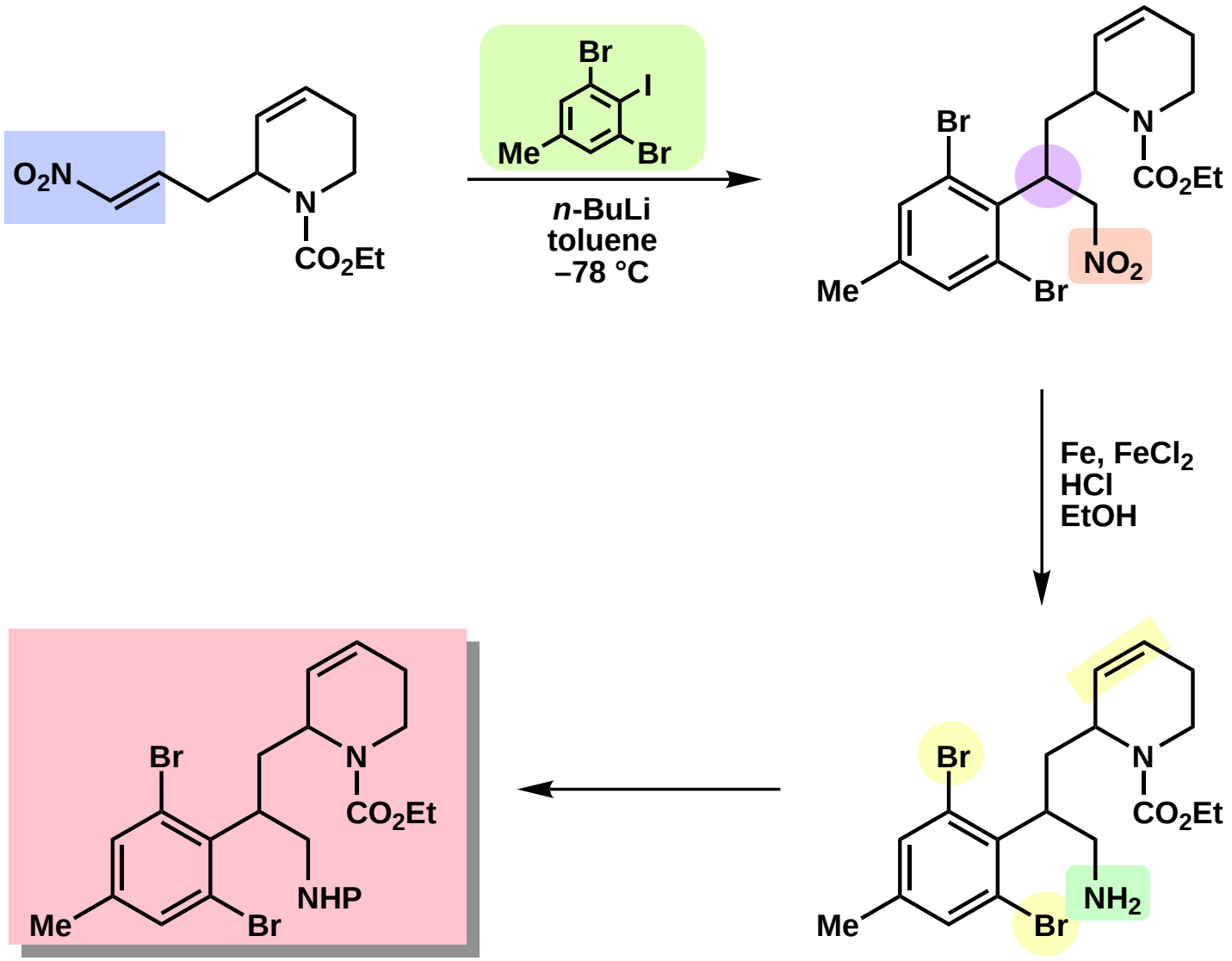


90% (2 steps)

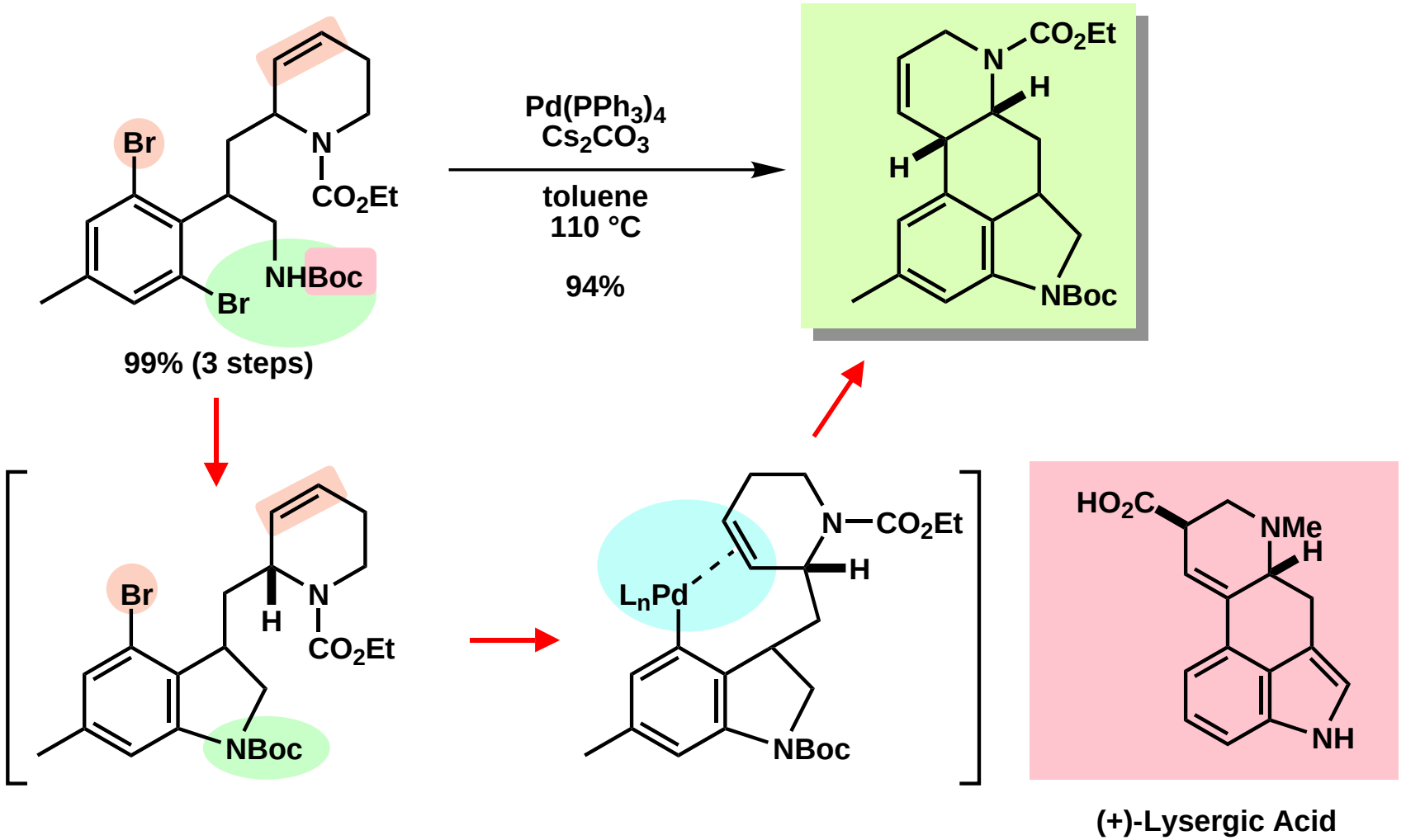
Synthesis of α-Nitroalkene



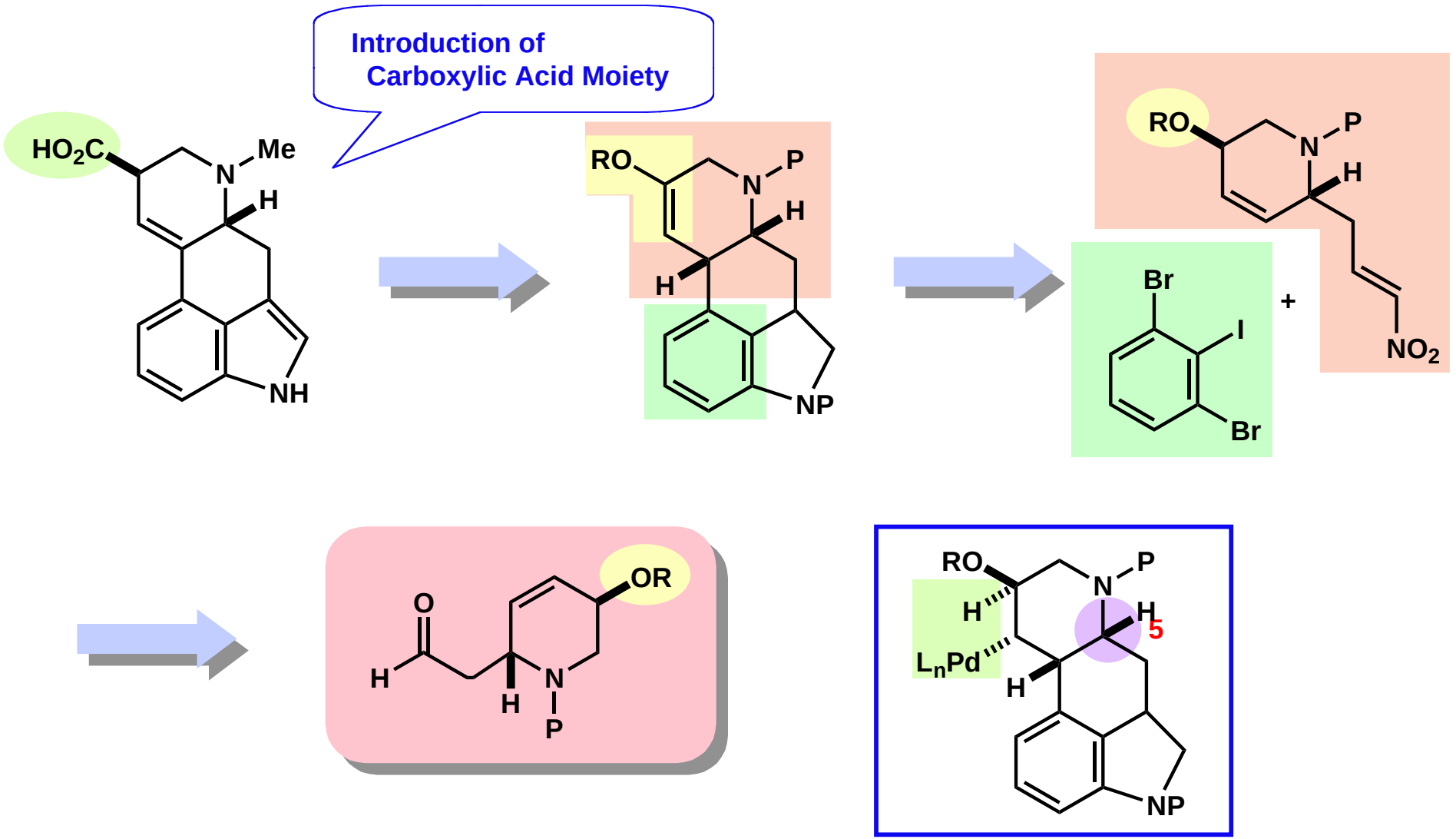
Preparation of Cyclization Precursors



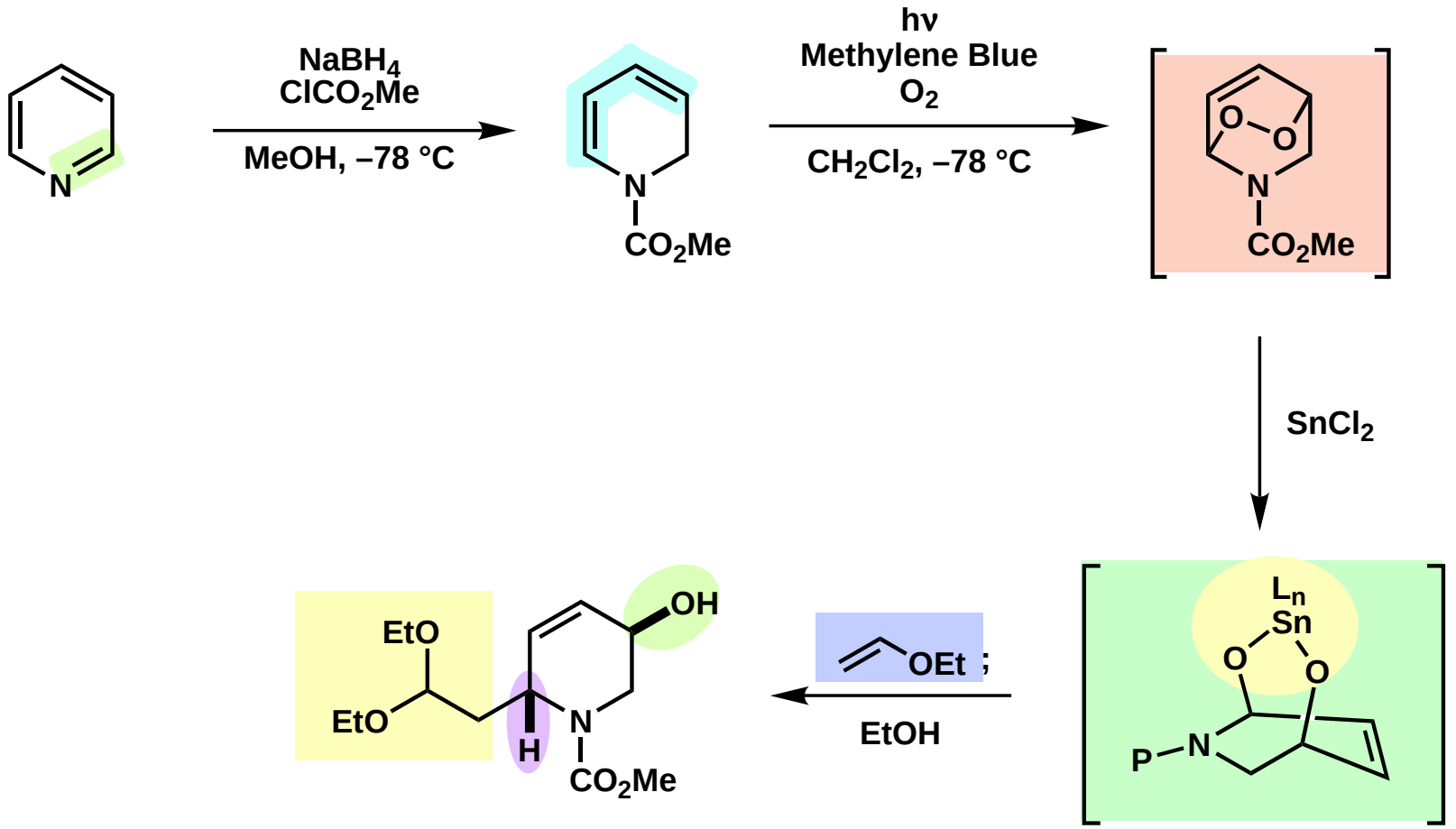
Double Cyclization Succeeded !



Modified Retrosynthetic Analysis

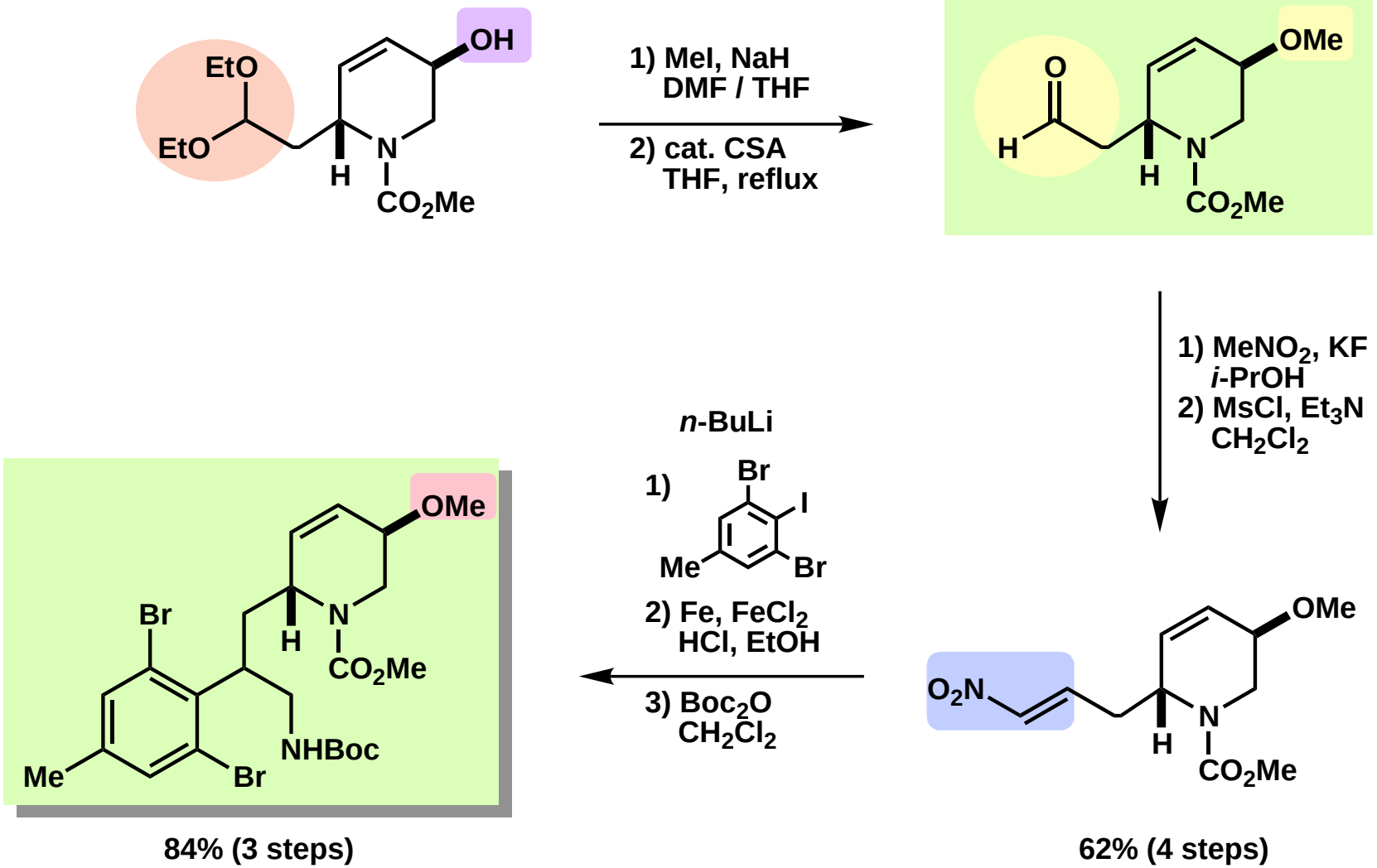


Synthesis of D Ring Unit

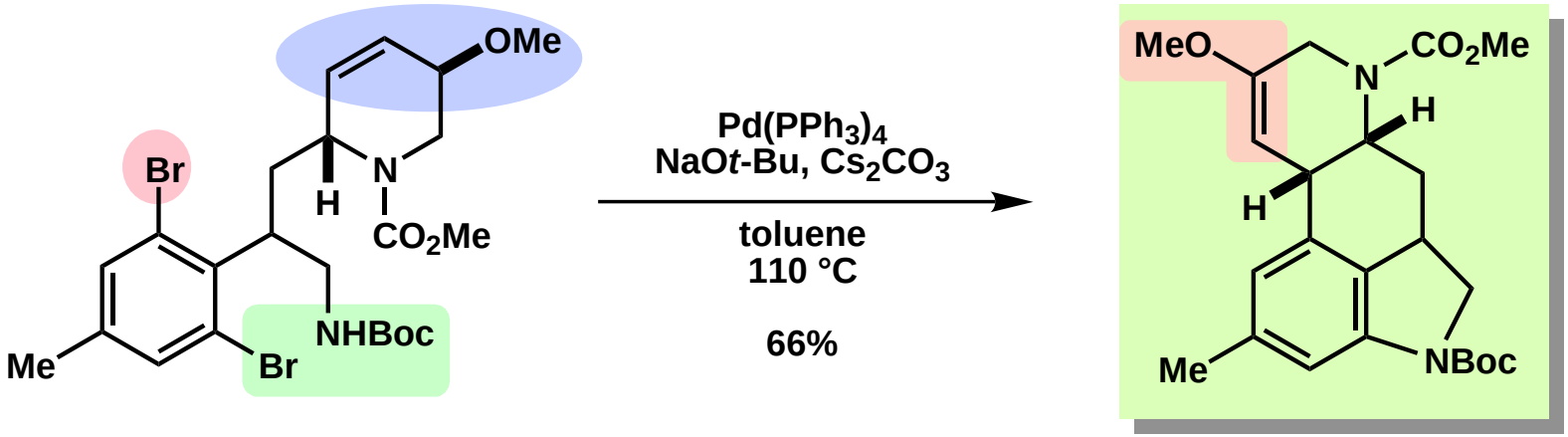


M. Natsume *et al.*, *Tetrahedron Lett.*, 36, 3473 (1979)

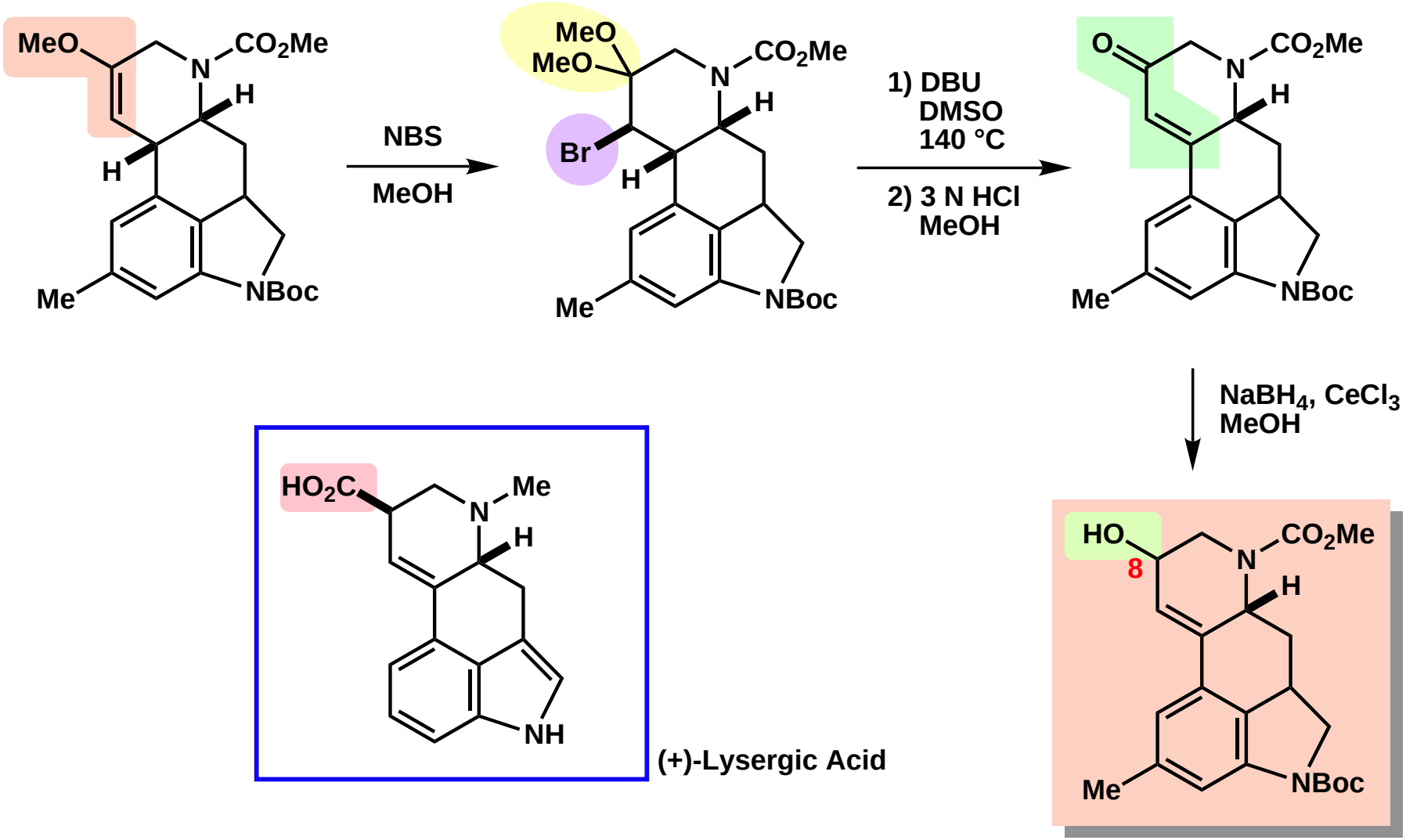
Conversion to Cyclization Precursor



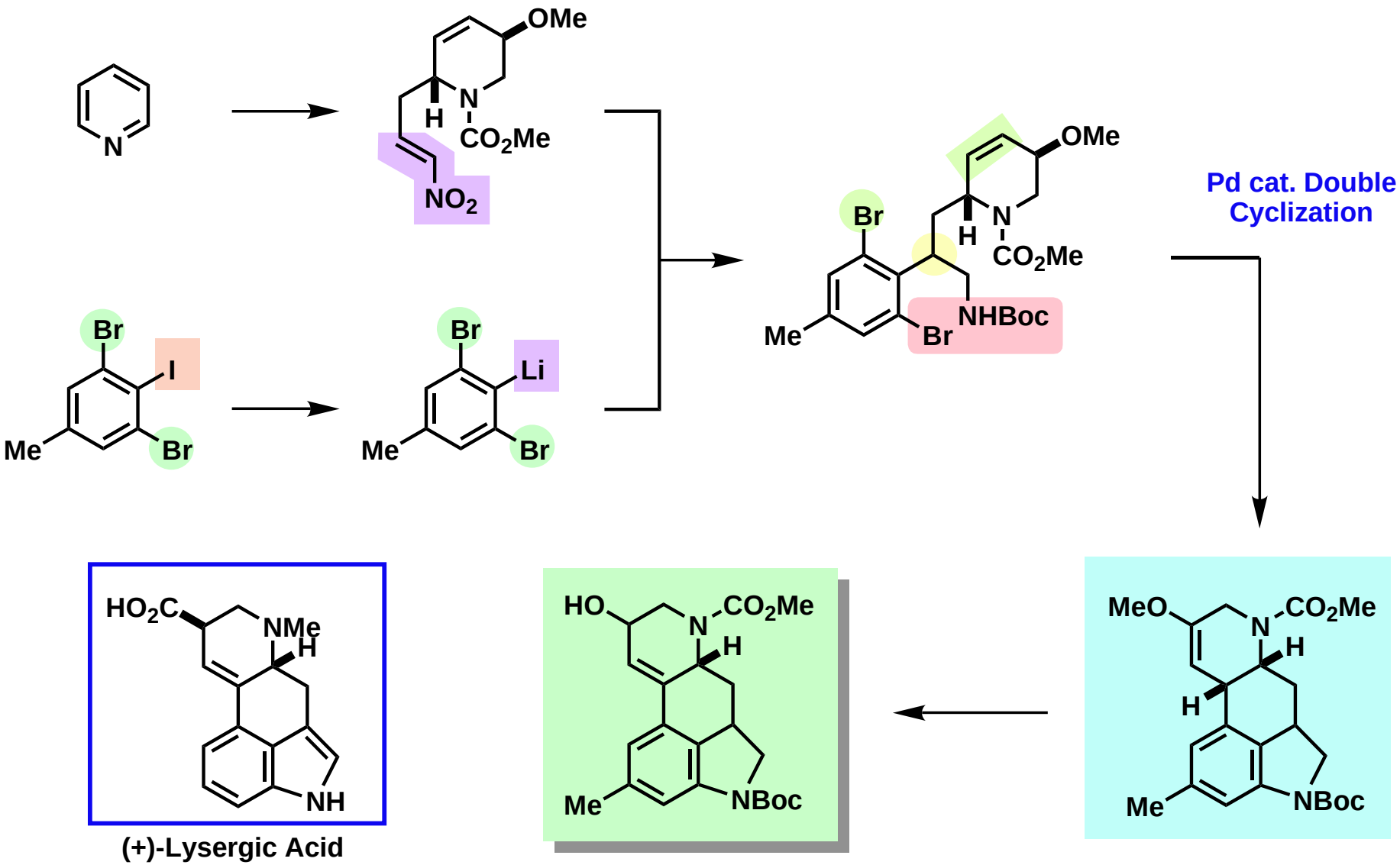
Construction of the Tetracyclic Skeleton



Latest Results



Summary


OMe
N
H
CO2Me
NO2
Br
I
Me
Br
Li
Me
Br
OMe
Br
N
H
CO2Me
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Me
Br
Pd cat. Double
Cyclization
MeO
N
CO2Me
H
H
Me
NBoc
HO
N
CO2Me
H
Me
NBoc
HO2C
NMe
H
NH
(+)-Lysergic Acid