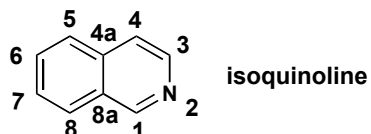
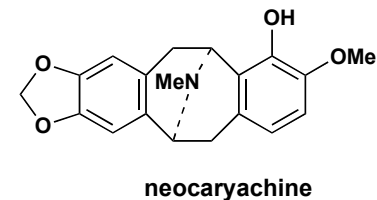
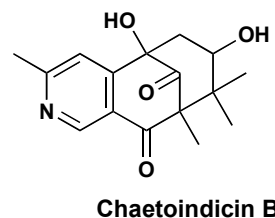
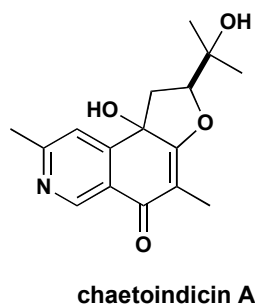
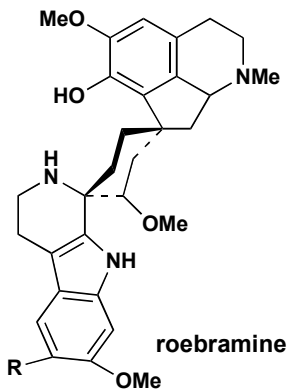
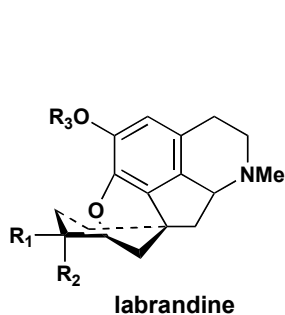
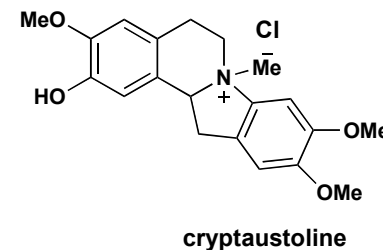
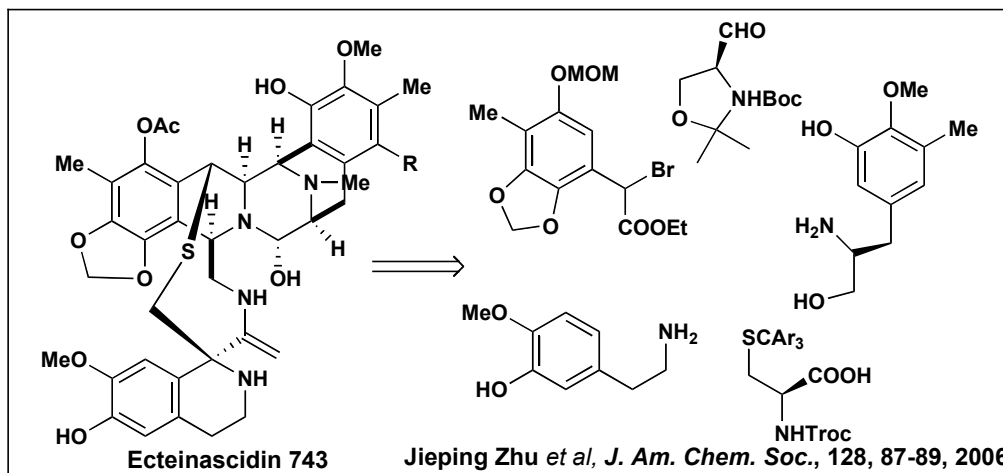
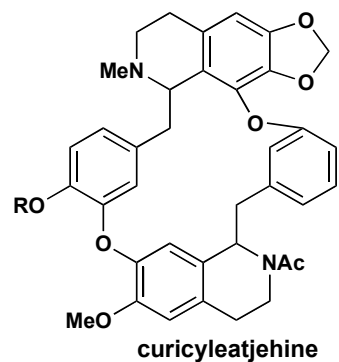
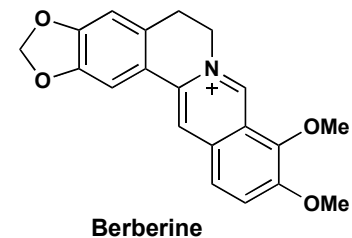
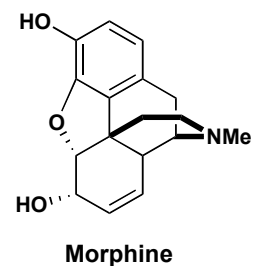
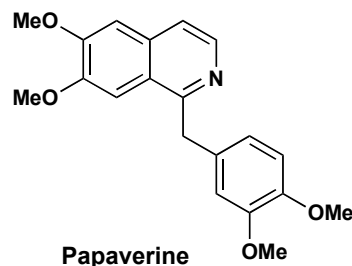


Isoquinoline Alkaloids



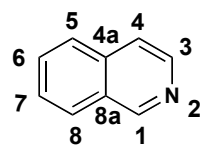
-isoquinoline first isolated from coal tar in 1885, sweetish odour
-isoquinoline alkaloids, large family, until now over 400 members
-Biological activities:

antimalarial, anti-HIV, insect growth retarding
antitumor, antimicrobial, antileukmic
antibacterial, Parkinson's disease



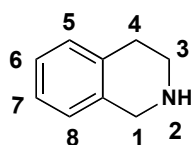
Guo-Lin Zhang *et al.* *Org. Lett.* 2006, 8, 3613-3615

Isoquinoline Alkaloids

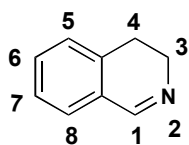


isoquinoline

planar, 10 π electron deficient aromatic system
electrophilic attack: C4 and C8
nucleophilic attack: C1 and C3

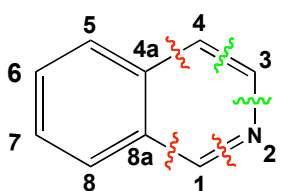


tetrahydroisoquinoline



dihydroisoquinoline

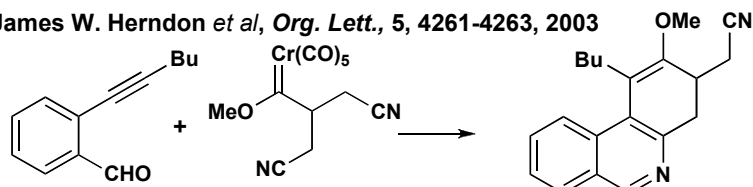
Synthesis of core



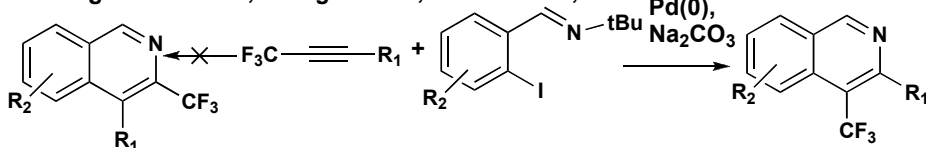
Classic:
C_{8a}-C₁: Bischler-Napieralski reaction
Pictet-Gams reaction
C₁-N₂: Pictet-Spengler reaction
C₄-C_{4a}: Pomeranz-Fritsch reaction

Novel:
Formation of C₃-C₄ and N₂-C₃
Ring expansion of other ring system

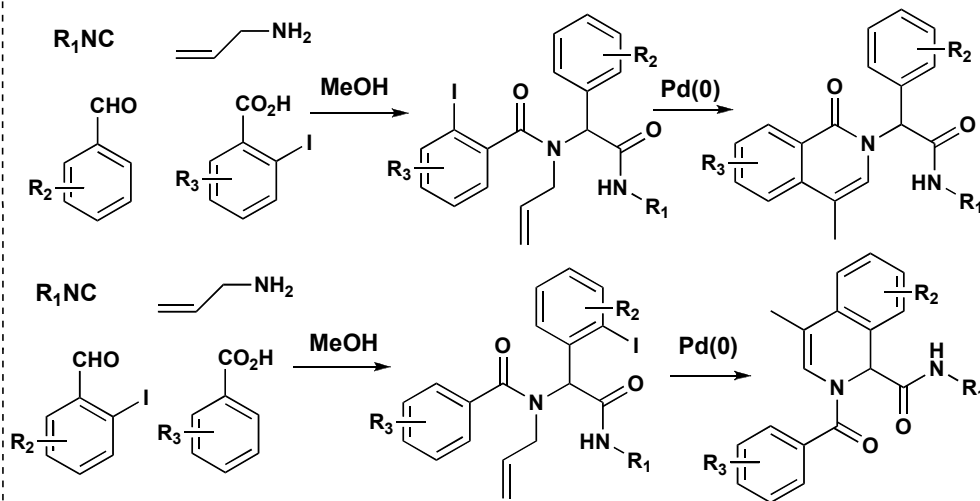
James W. Herndon *et al*, *Org. Lett.*, 5, 4261-4263, 2003



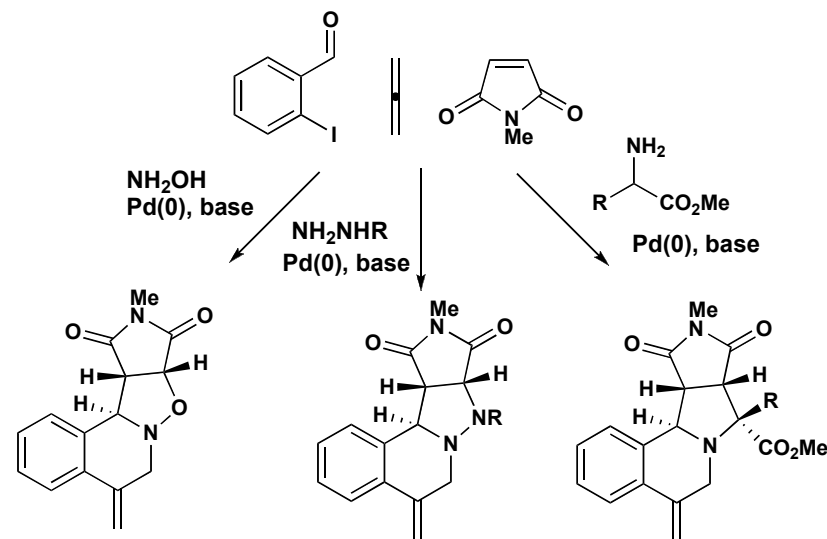
Jungha Chae *et al*, *J. Org. Chem.*, 10172-10174, 2005



Zhen Yang *et al*, *Org. Lett.*, 6, 3155-3158, 2004



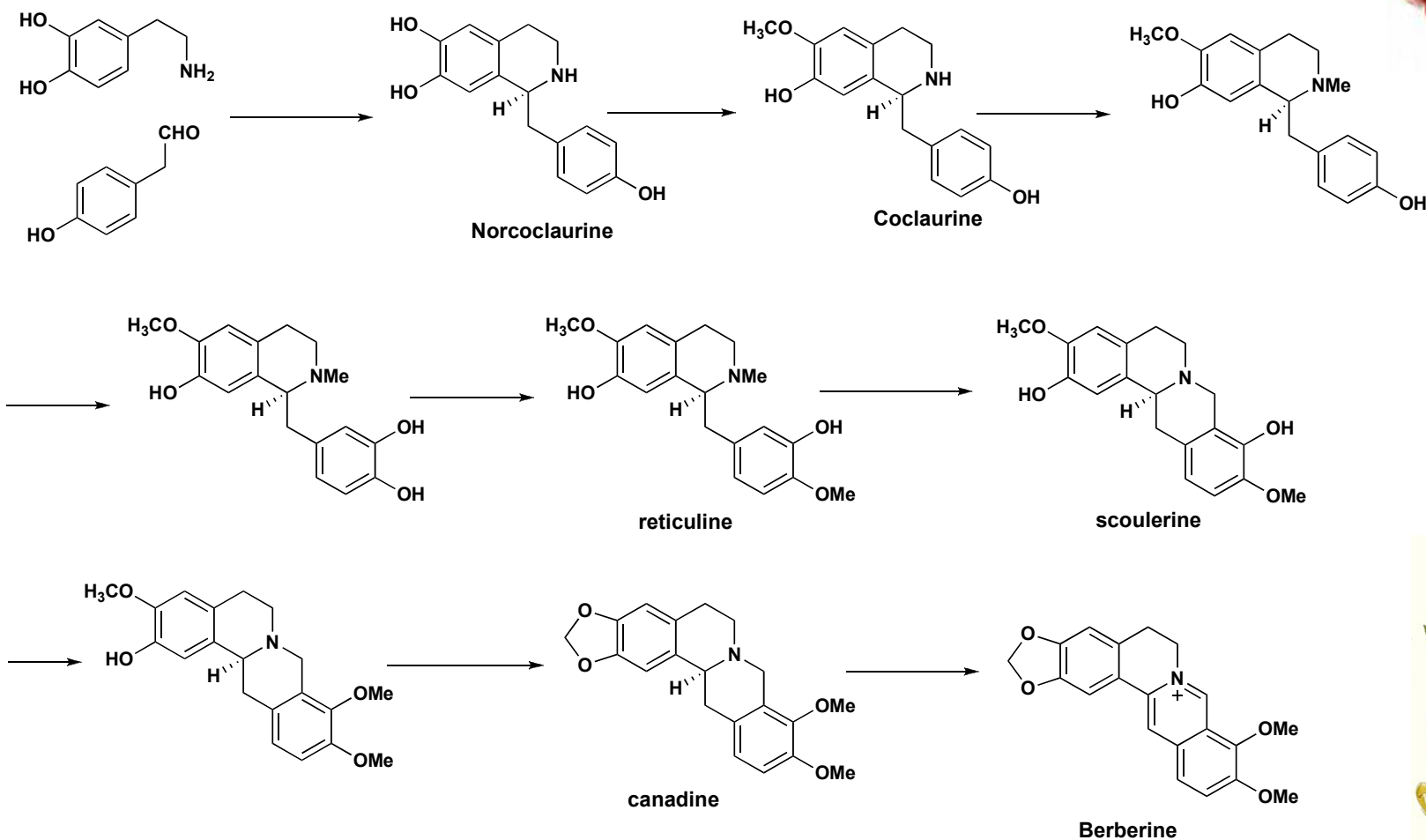
Ronald Grigg *et al*, *Angew Chem Int Ed*, 44, 7570-7574, 2005



Isoquinoline Alkaloids

Biosynthesis of isoquinoline alkaloids

Biosynthesis pathway to berberine in *Berberis* cell cultures



Heinz G. Floss et al, J. Am. Chem. Soc, 117(5), 1995



coclaurine
from zizyphus



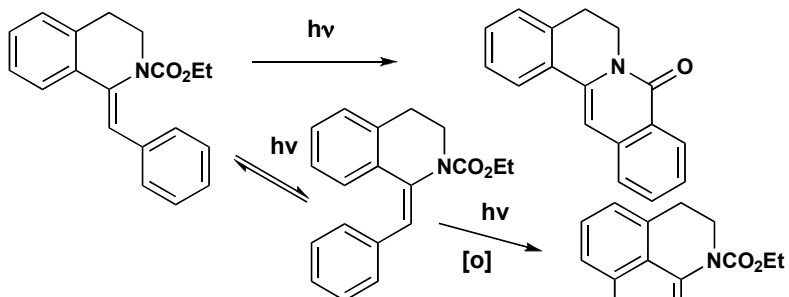
reticuline
from siparuna



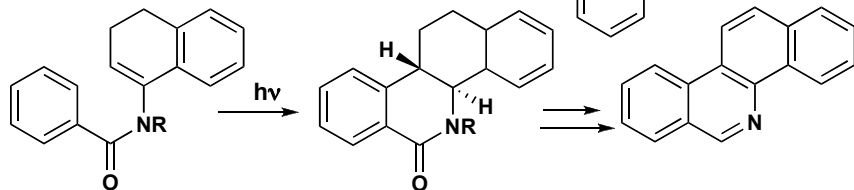
Berberine from
Berberis

Photochemical Synthesis of Isoquinoline alkaloids

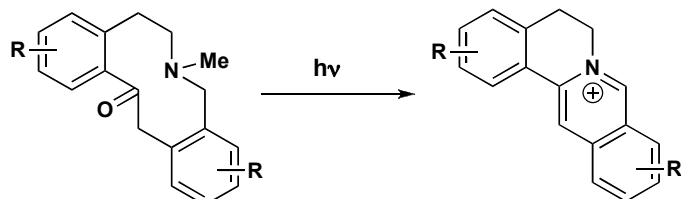
1. G. R. Lenz et al, J. Am. Chem. Soc, 88, 5369, 1966



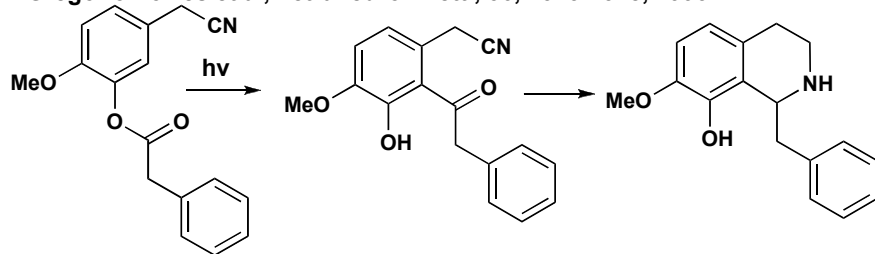
2. T. Mori et al, Tetrahedron Lett., 3643, 1963



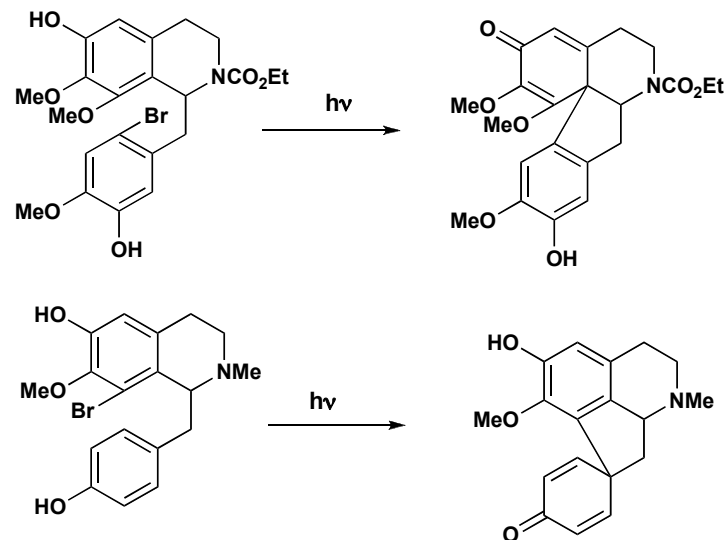
3. P. D. Gardner et al, Tetrahedron Lett., 2493, 1967



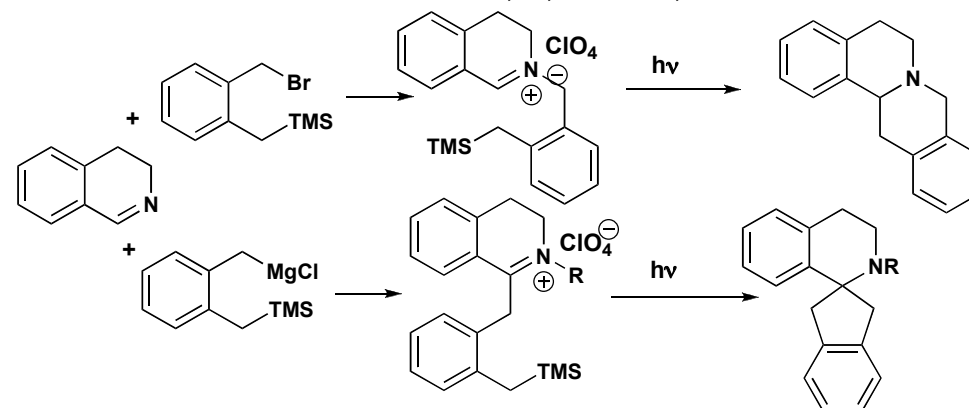
4. Gregorio Torres et al, Tetrahedron Lett., 36, 1315-1318, 1995



5. K. Fukumoto et al, Tetrahedron, 27, 5993, 1971



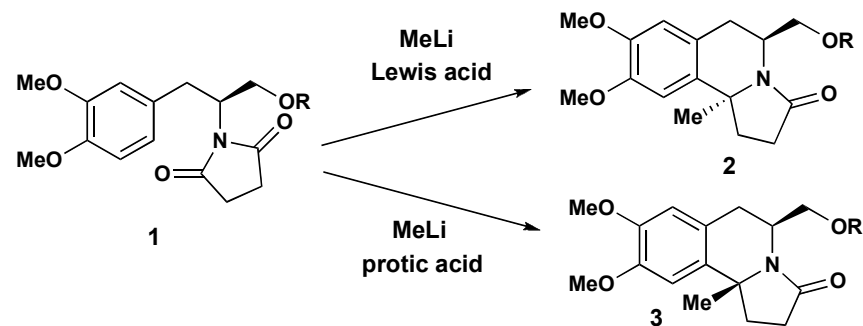
6. Patrick S. Mariano et al Tetrahedron Lett., 26, 5867-5870, 1985



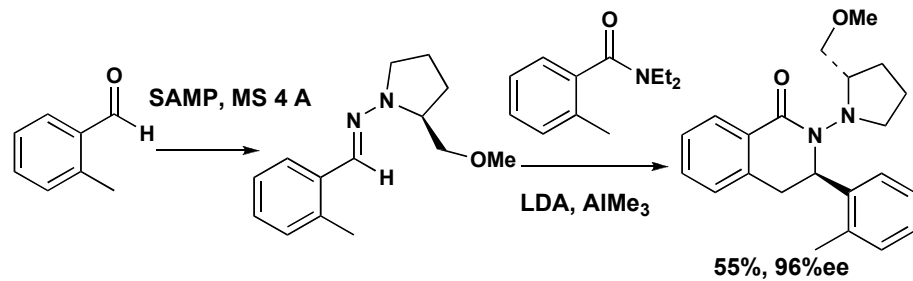
for more see Jeremy's group meeting materials

Asymmetric Synthesis of Isoquinoline Alkaloids

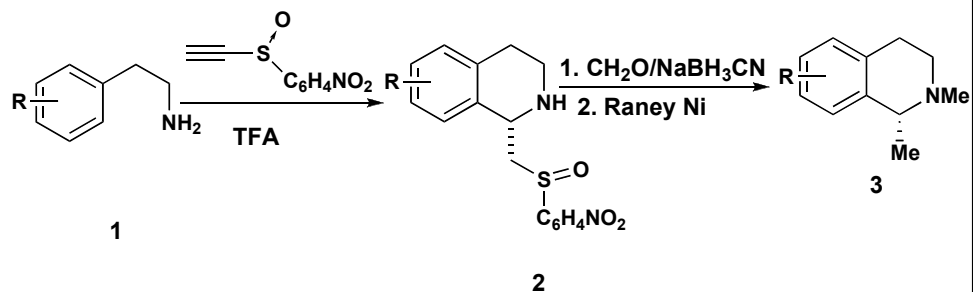
1. Esther Leter *et al*, *J. Org. Chem.* 70, 10368-10374, 2005



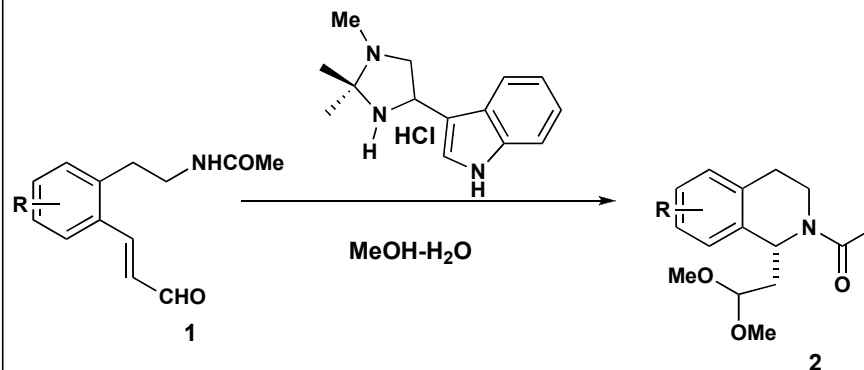
2. Marine Boudou and Dieter Enders, *J. Org. Chem.* 70, 9486-9494, 2005



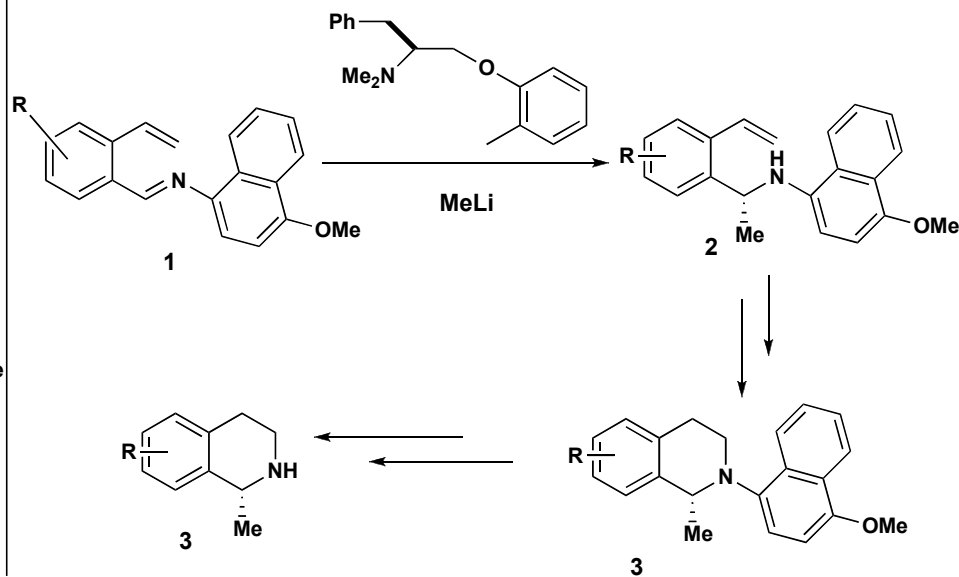
3. Jiang, L *et al*, *Tetrahedron Lett.*, 36, 715, 1995



4. Ihara, M. *Heterocycles*, 59, 51, 2003

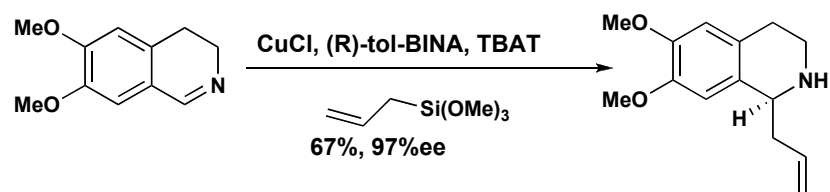


5. Tomioka, K., *Tetrahedron Lett.* 41, 5533, 2000

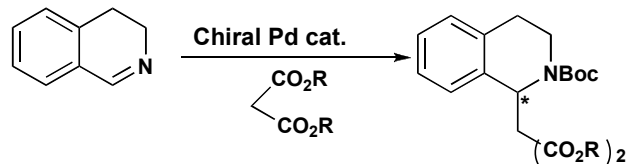


Aymmetric Synthesis of Isoquinoline Alkaloids

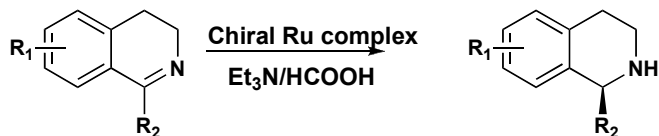
6. Michiko Miyazaki and coworkers, *Org. Lett.*, 8, 1295-1297, 2006



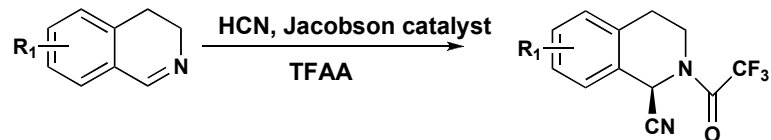
7. Mikiko Sodeoka *et al.*, *J. AM. CHEM. SOC.*, JA065646R, 2006



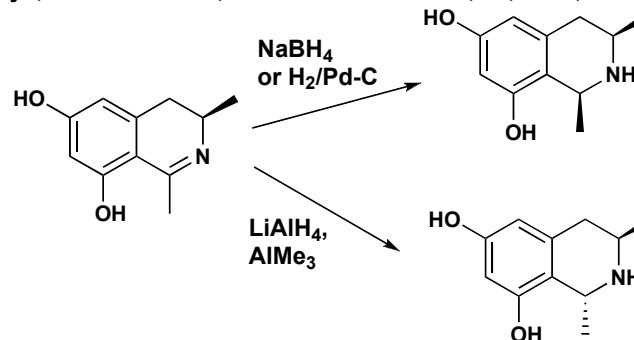
8. Joanna Szawkalo and Zbigniew Czarnocki, *Monatshhefte fur Chemie*, 136, 1619-1627, 2005



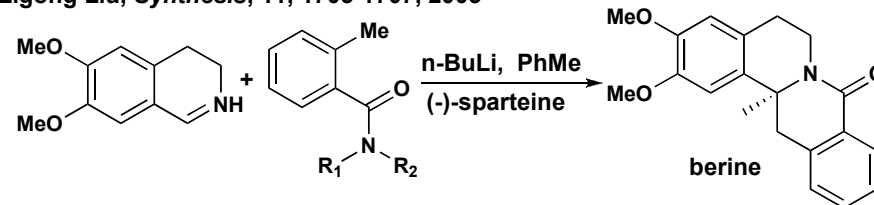
9. Takashi Itoh *et al.*, *Synlett*, 10, 1595-1597, 2006



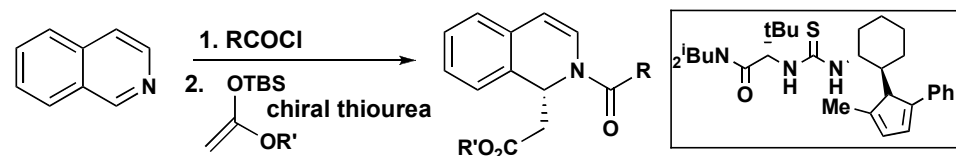
10. Hoye, T. R. and Chen, M. *Tetrahedron Lett.*, 37, 3099, 1996



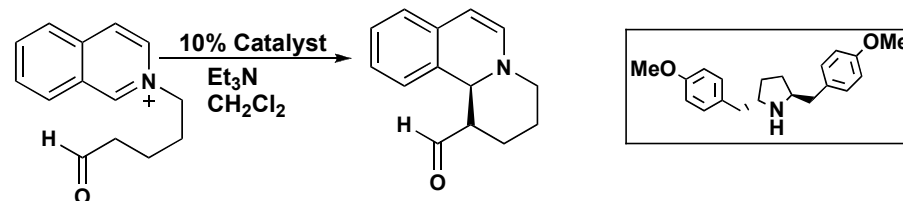
11. Ligong Liu, *Synthesis*, 11, 1705-1707, 2003



12. Eric N. Jacobson *et al.*, *Angew. Chem. Int. Ed.*, 44, 6700-6704, 2005

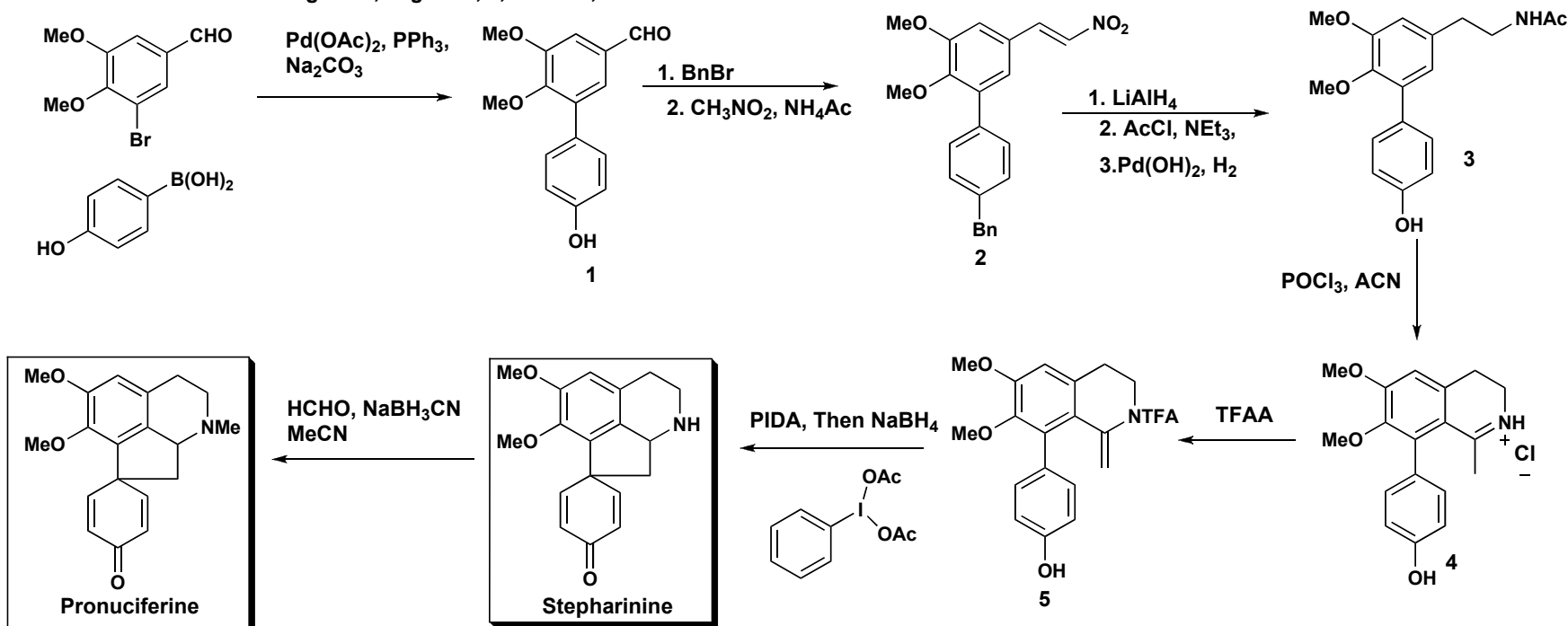


13. Karl Anker Jørgensen *et al.*, *Angew. Chem. Int. Ed.*, 44, 6058-6063, 2005

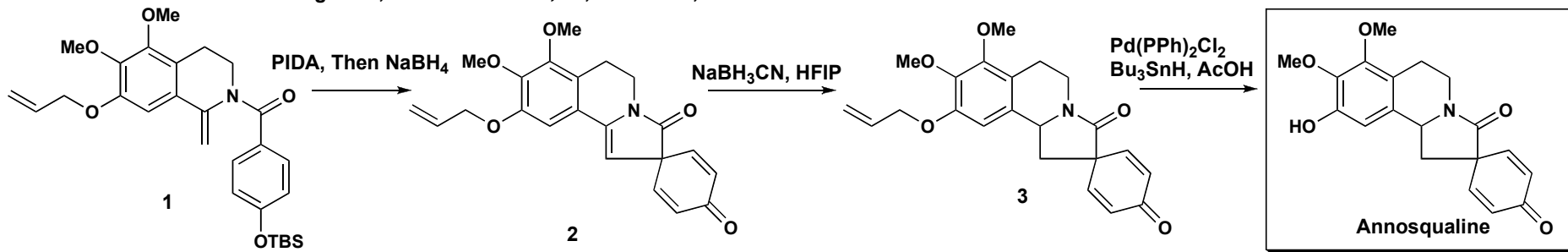


Total synthesis of isoquinoline alkaloids natural product

Toshio Honda and Hiroki Shigehisa, *Org. Lett.* 8, 657-659, 2006

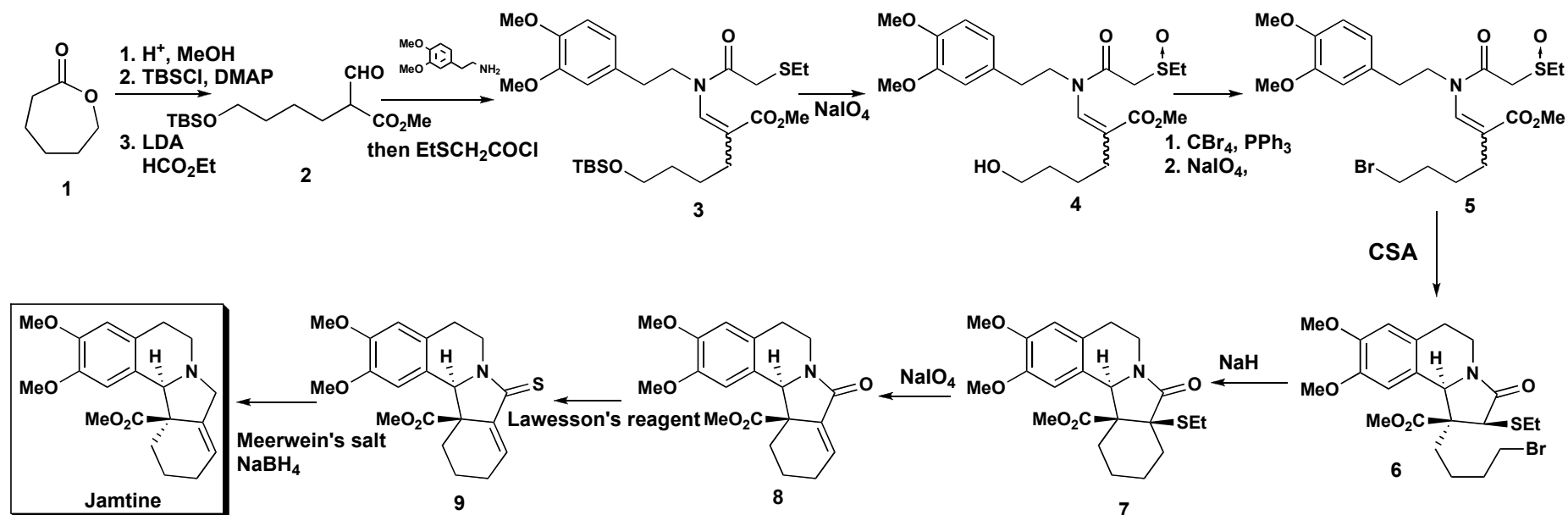


Toshio Honda and Hiroki Shigehisa, *Tetrahedron Lett.* 47, 7301-7306, 2006

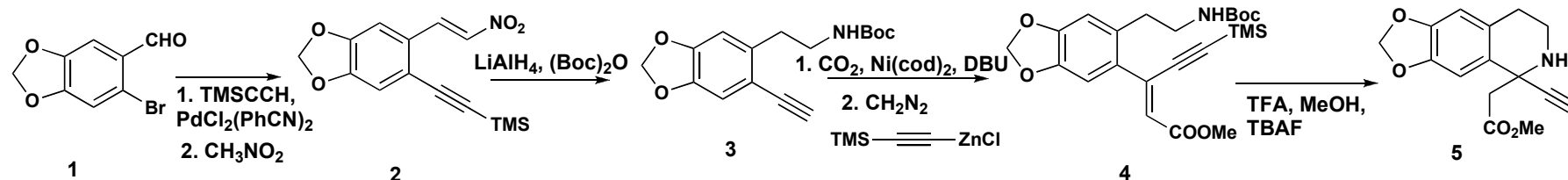


Total synthesis of isoquinoline alkaloids natural product

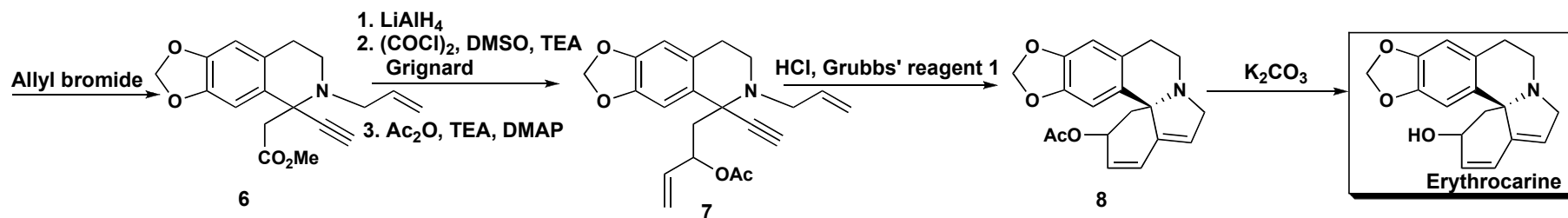
Albert Padwa and M. Diana Danca, *Org. Lett.*, 715-717, 4, 2002



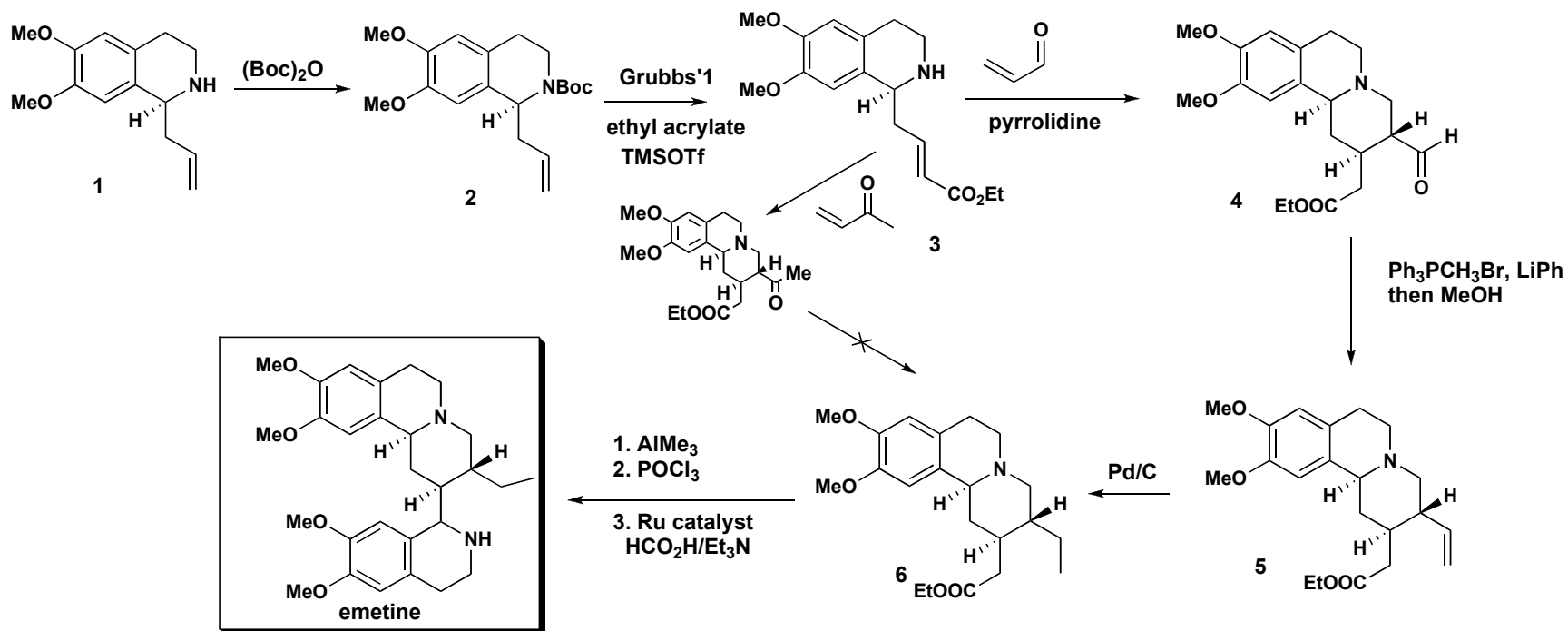
Miwako Mori *et al*, *Org. Lett.*, 5, 2323-2325, 2003



Total synthesis of isoquinoline alkaloids natural product

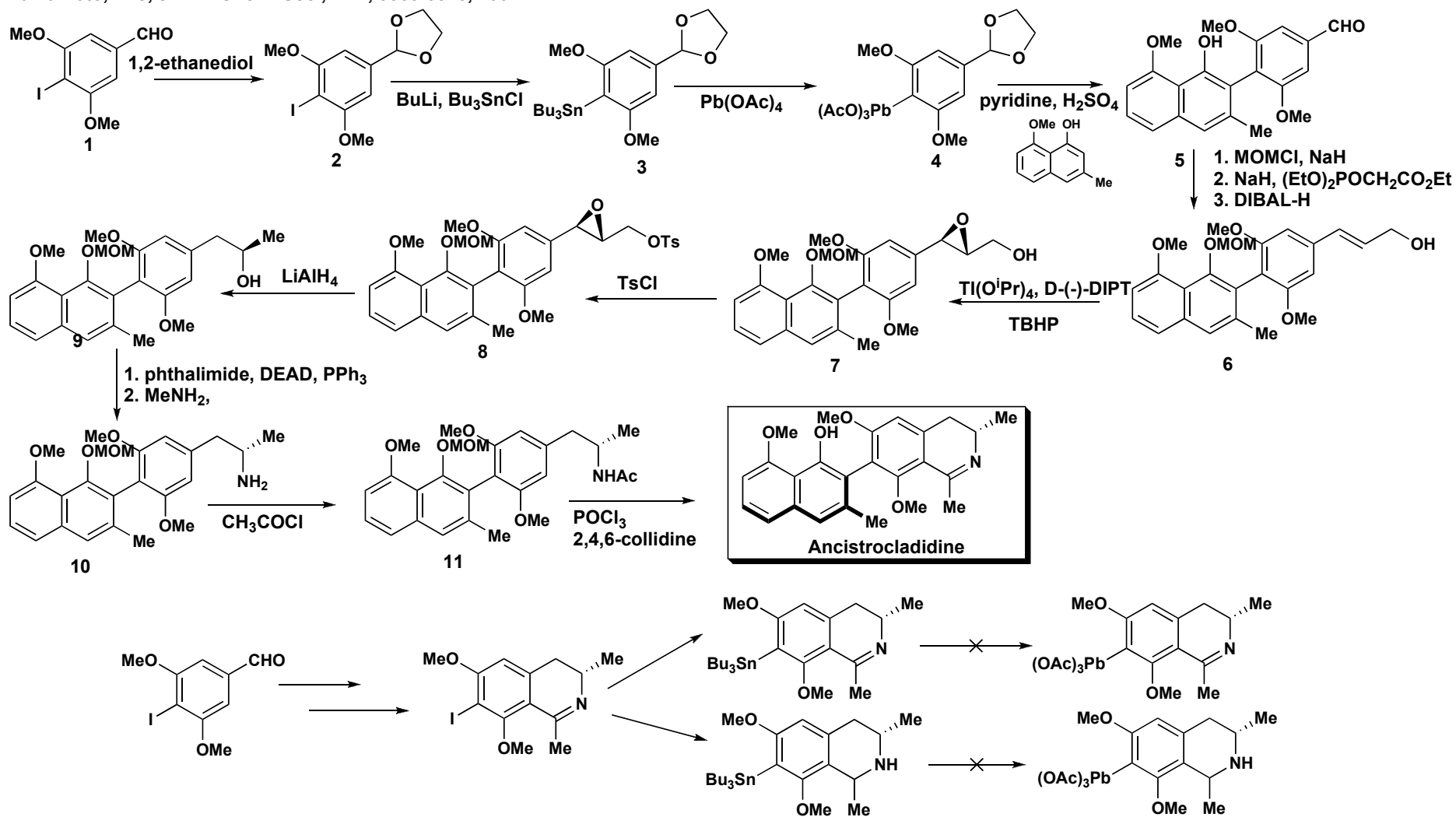


Michiko Miyazaki and coworkers, *Org. Lett.* 8, 1295-1297, 2006;
Tietze, L. F *et al*, *Angew. Chem. Int. Ed.*, 42, 4254, 2003



Total synthesis of isoquinoline alkaloids natural product

Christopher J. Bungard and Jonathan C. Morris, *J. Org. Chem.*, 7345-7363, 2006
Yamamoto, H. J., *J. Am. Chem. Soc.*, 124, 5365-5375, 2002



Total synthesis of isoquinoline alkaloids natural product

Brian M. Stoltz *et al*, *J. Am. Chem. Soc.*, 125, 15000-150001, 2003

