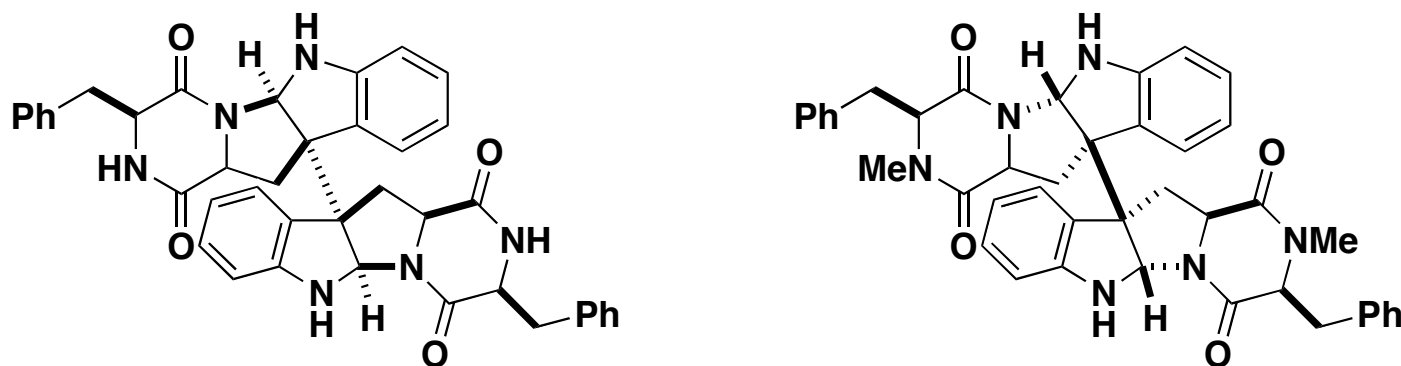


Concise Total Synthesis of (+)-WIN 64821 and (-)-Ditryptophenaline

Movassaghi, M.; Schmidt, M. A.; Ashenhurst, J. A.
Angew. Chem. Int. Ed. **2008**, *47*, 1485-1487



Current Literature

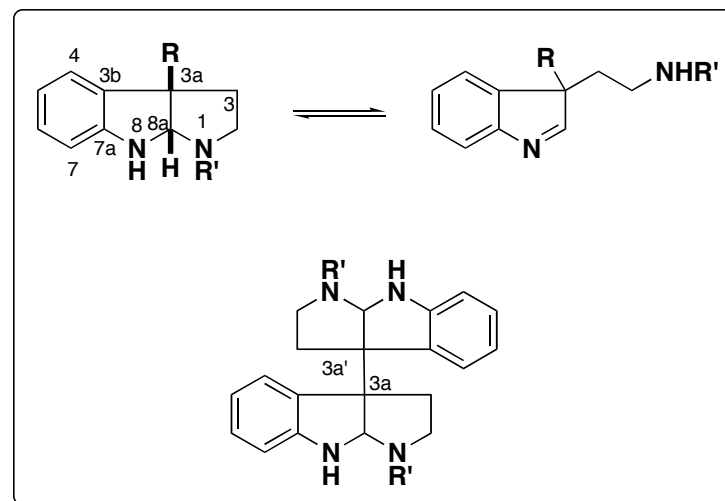
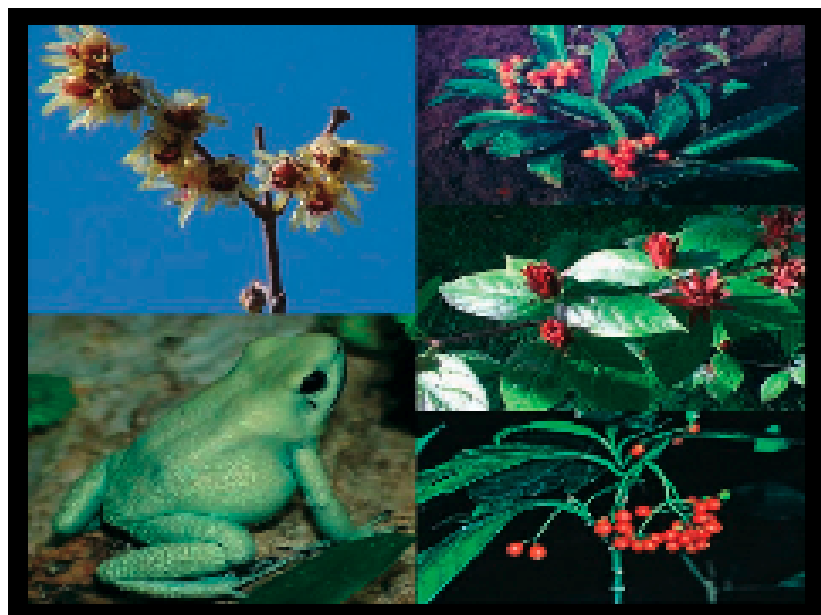
Kalyani Patil

2/16/08

Outline

- Background
- Biosynthetic Proposal
- Synthesis of Calycanthaceous Alkaloids
- Enantioselective Formation of Quaternary Centers: Overman
- Title Paper
- Summary

Alkaloids Containing *cis*-pyrrolidino[2,3-*b*]indolines

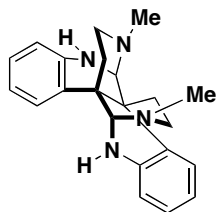


Sources:

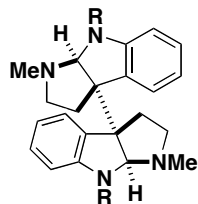
Psychotria oleoides, Calycanthus floridus,
Hodgkinsonia frutescens, Phyllobates terribilis,
Chimonanthus fragrans

Steven, A.; Overman, L. E. *Angew. Chem. Int. Ed.* **2007**, *46*, 5488-5508

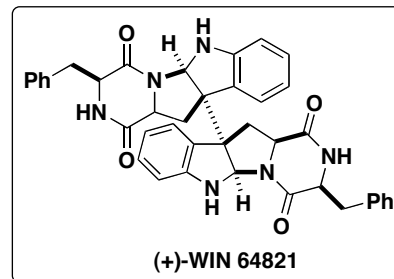
Members of Hexahydropyrroloindole Family



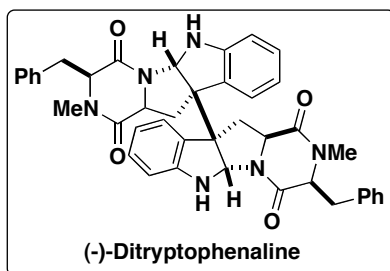
(-)-Calycanthine



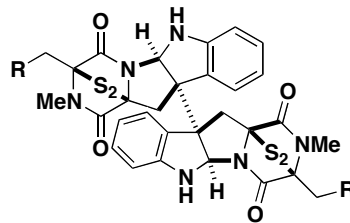
R = H, (+)-Chimonanthine
R = Me, (+)-Folicanthine



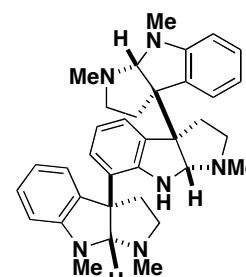
(+)-WIN 64821



(-)-Ditryptophenaline



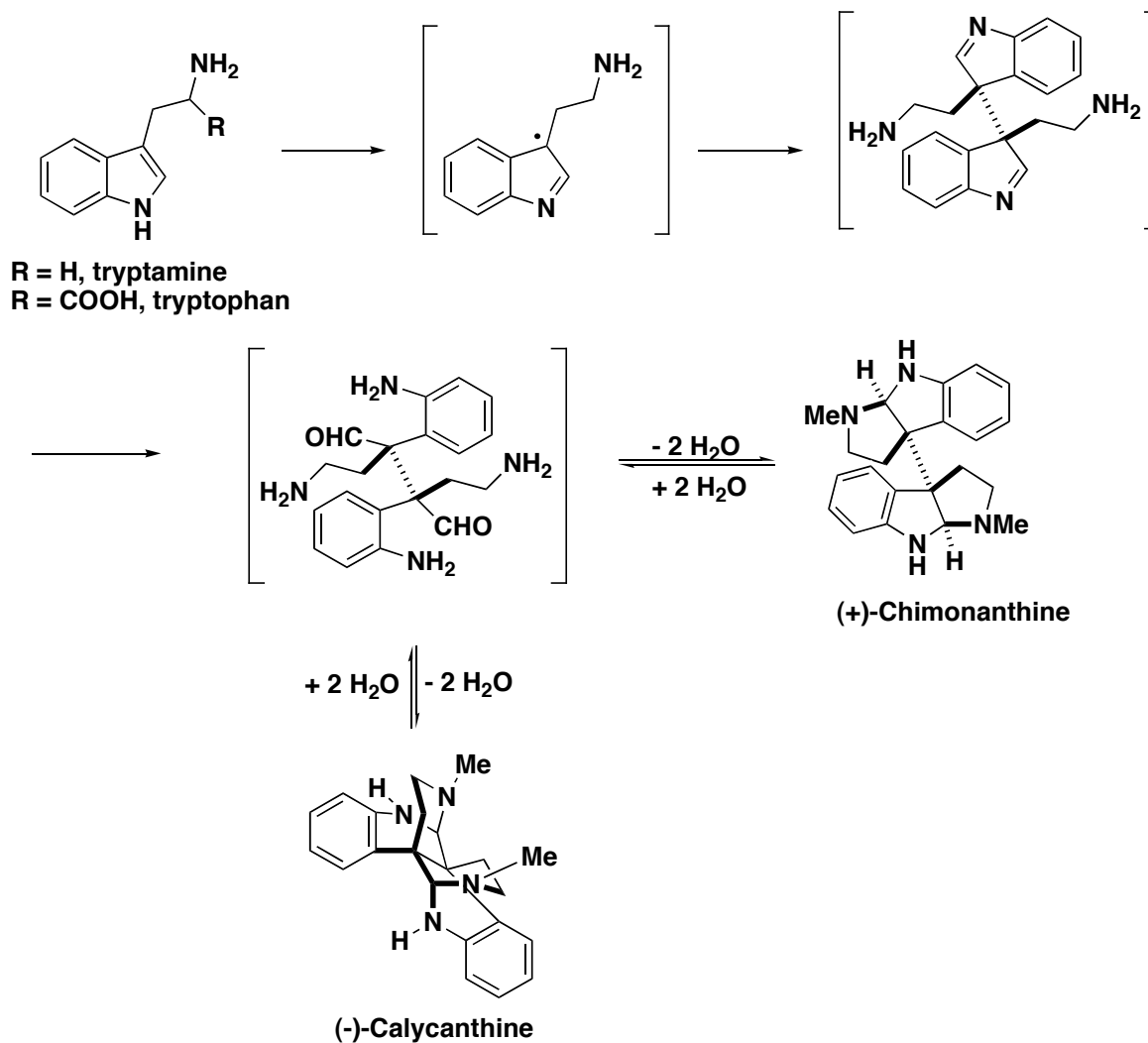
R = OH, (+)-Chaetocin A
R = H, (+)-11,11'-Dideoxyverticillin A



(-)-Idiospermuline

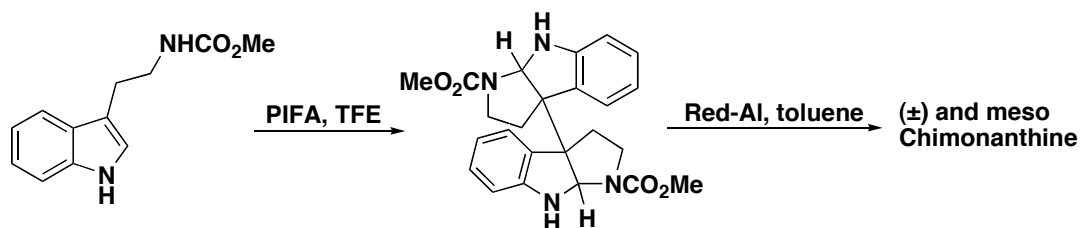
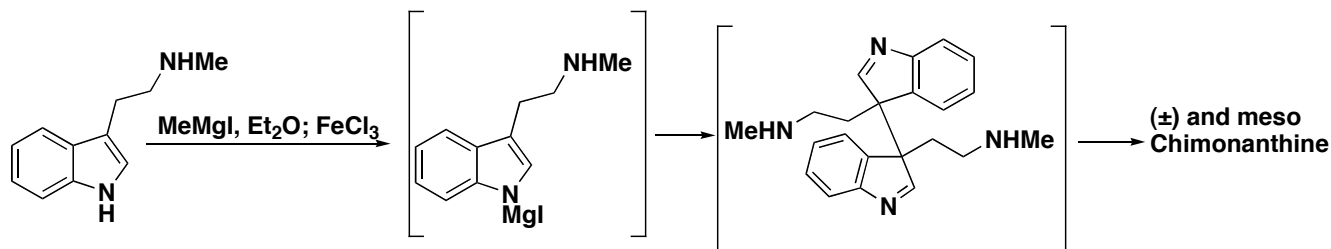
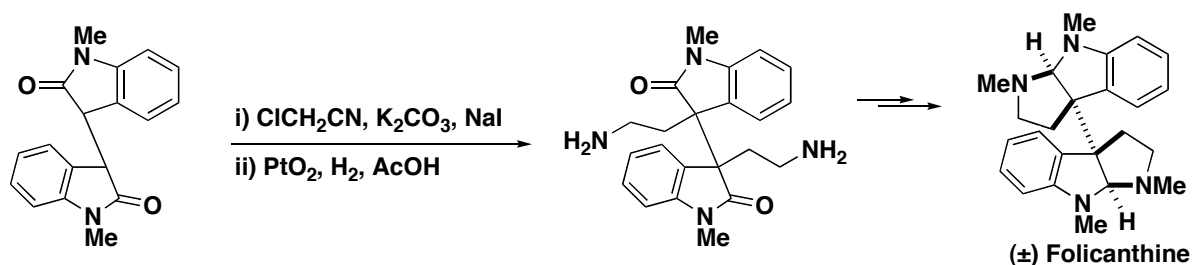
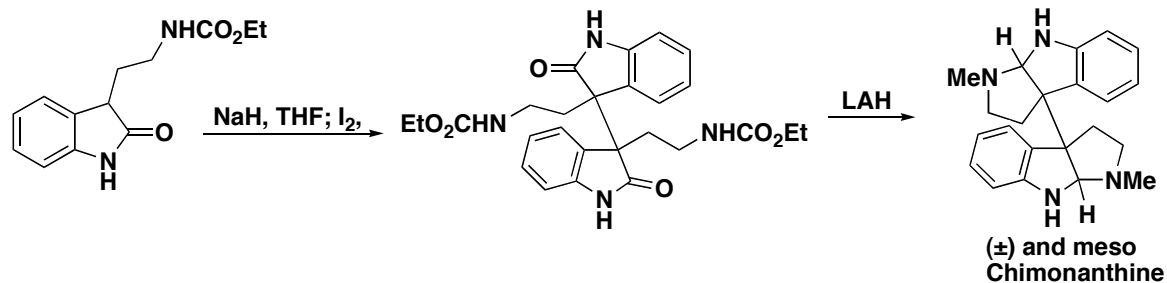
- Isolated from *Aspergillus flavus*; bispyrrolidinoindoline core
- WIN 64821 = Q 20547-A; P antagonist against human NK1 receptor w/ $K_i \sim 230 \pm 30$ nM in human astrocytoma cells
- Potential analgesics and antiinflammatory agents; treatment of arthritis, asthma
- (+)-Chaetocin- isolated from fermentation broth of *Chaetomium minutum*: inhibitor of lysine specific histone methyl transferase
- (+)-11,11'-Deoxyverticillin- isolated from *Shiraia bambusicola*: tyrosine kinase inhibitor

Postulated Biosynthetic Route Toward Calycanthaceous Alkaloids



Schmidt, M. A.; Movassaghi, M. *Synlett* **2008**, 313-324

Previous Syntheses of Chimonanthines/(±)-Folicanthine



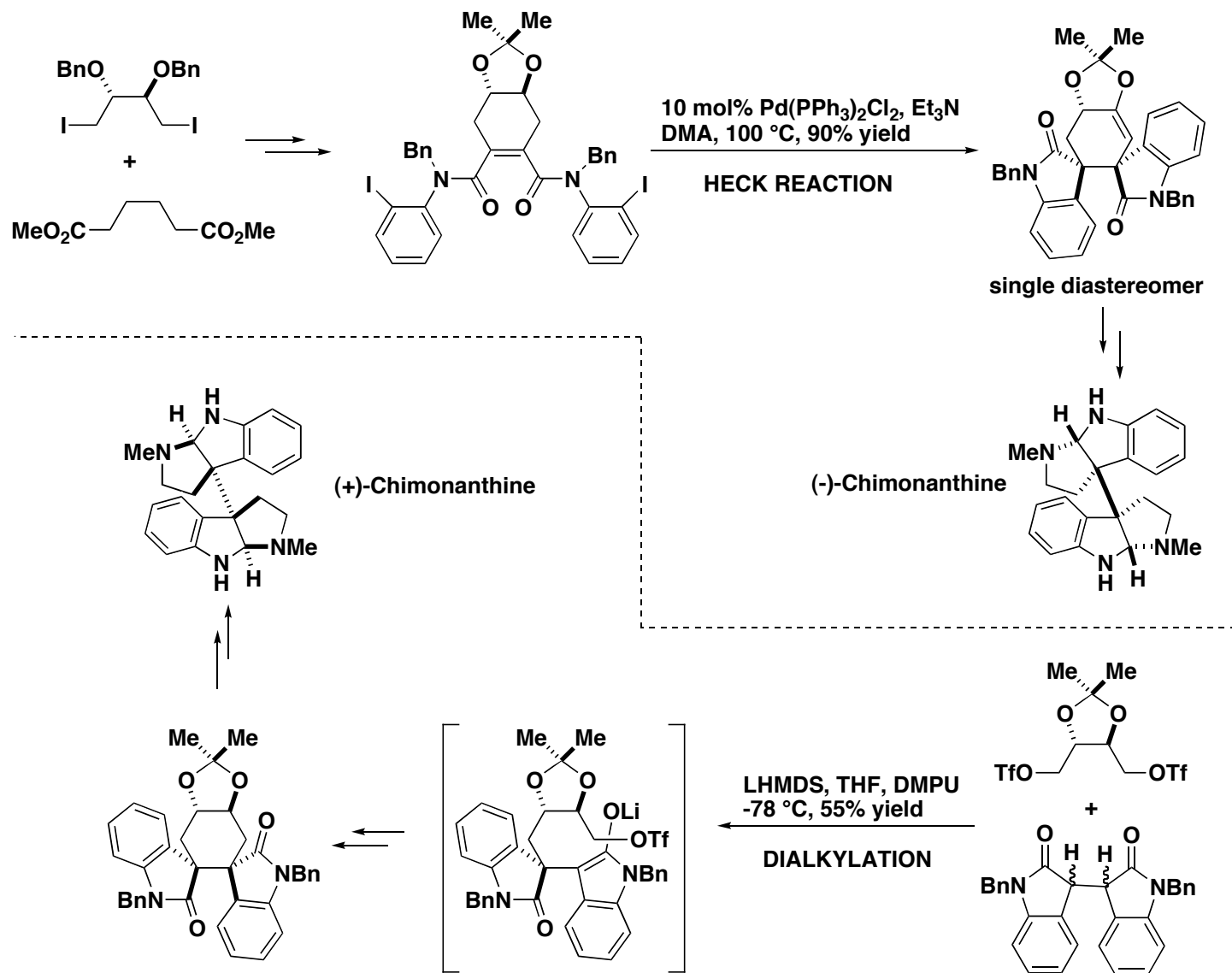
Hendrickson, J. B.; Goschke, R.; Rees, R. *Tetrahedron* **1964**, 20, 565

Hino, T.; Yamada, S. -I. *Tetrahedron Lett.* **1963**, 4, 1757

Scott, A. I.; McCapra, F.; Hall, E. S. *J. Am. Chem. Soc.* **1964**, 86, 302

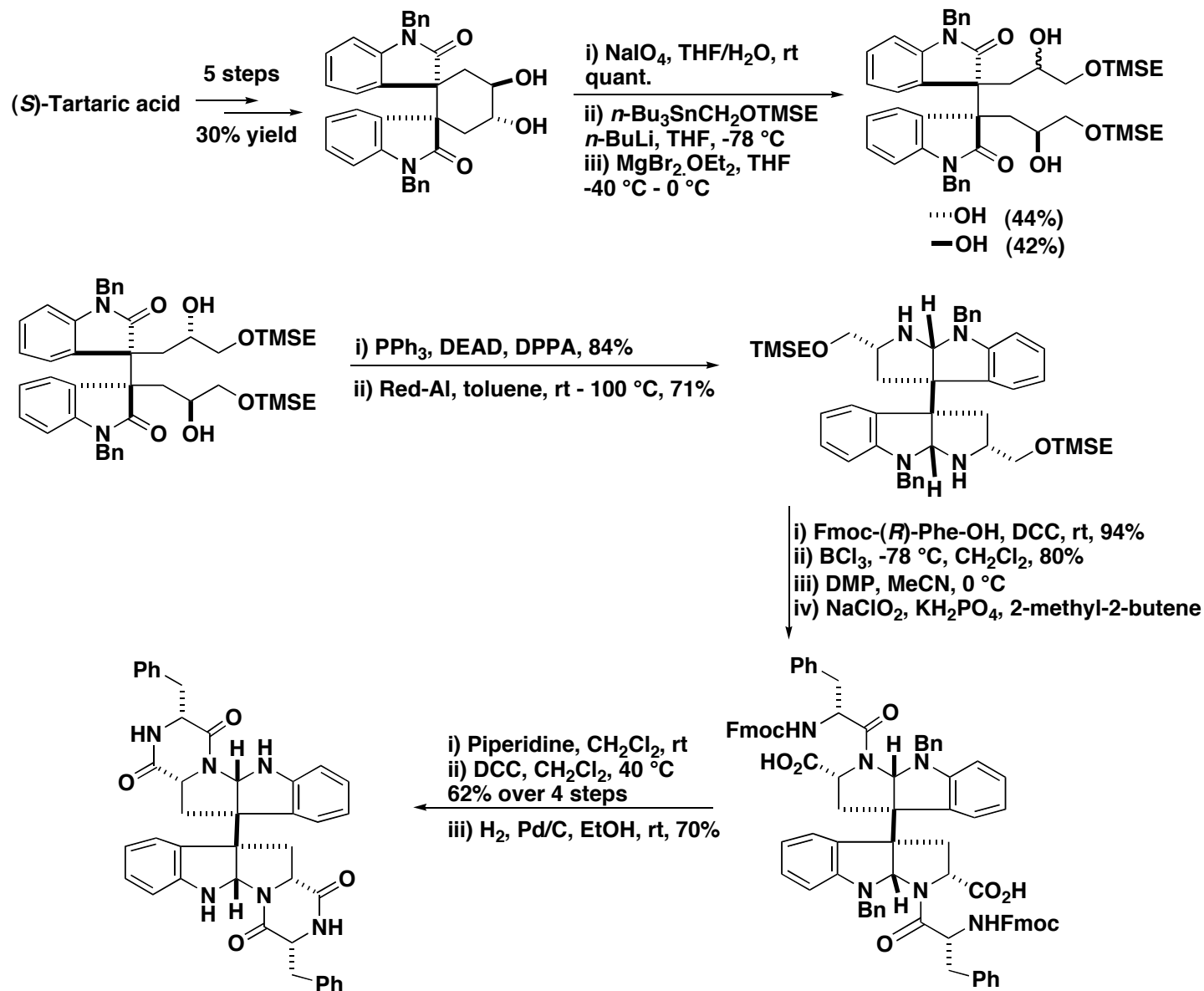
Ishikawa, H.; Takayama, H.; Aimi, N. *Tetrahedron Lett.* **2002**, 43, 5637

Enantioselective Formation of Quaternary Centers: Dialkylation and Heck Reaction



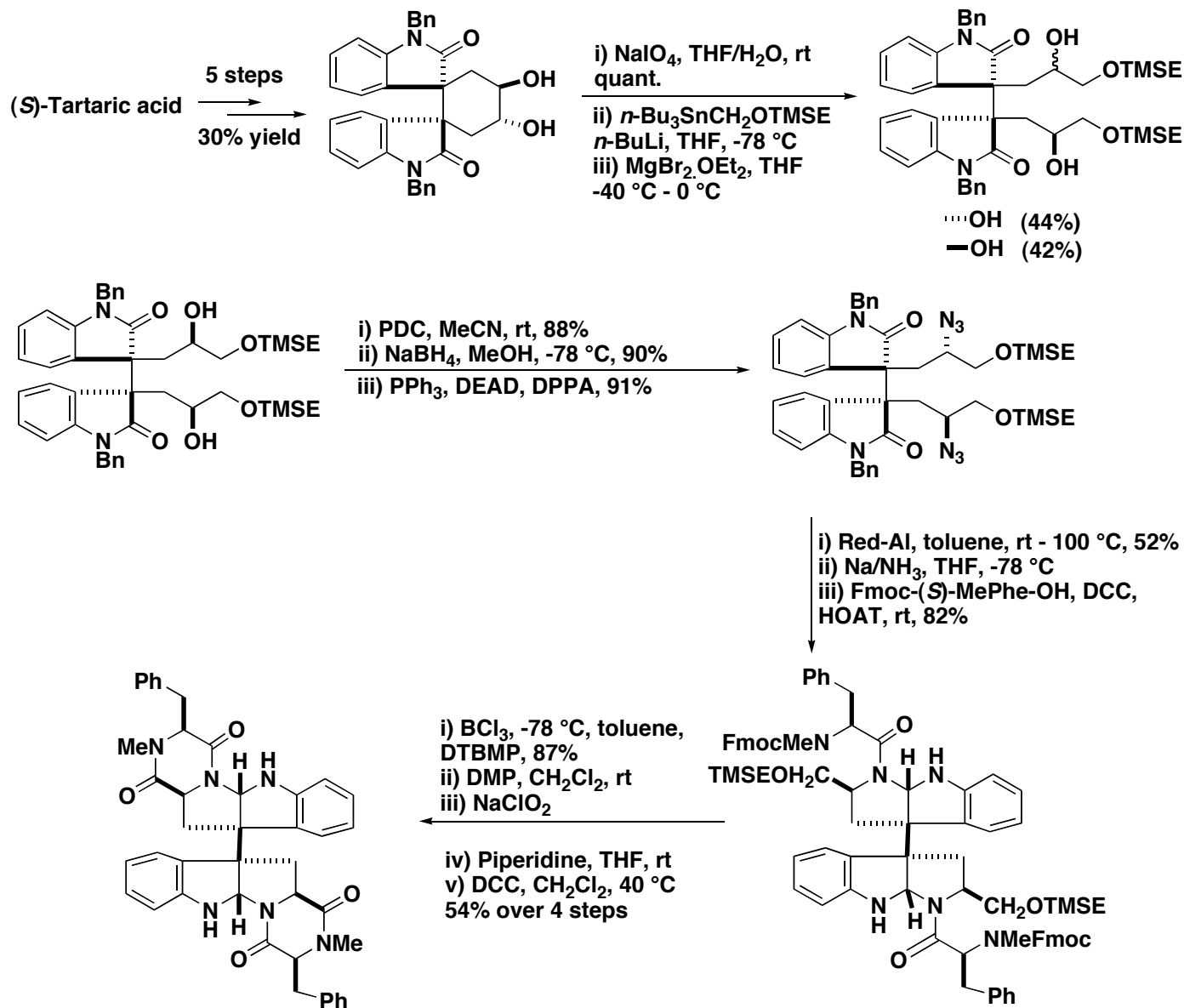
Overman, L. E.; Paone, D. V. *J. Am. Chem. Soc.* **2001**, *123*, 9465-9467

Overman's Synthesis of *ent*-WIN 64821



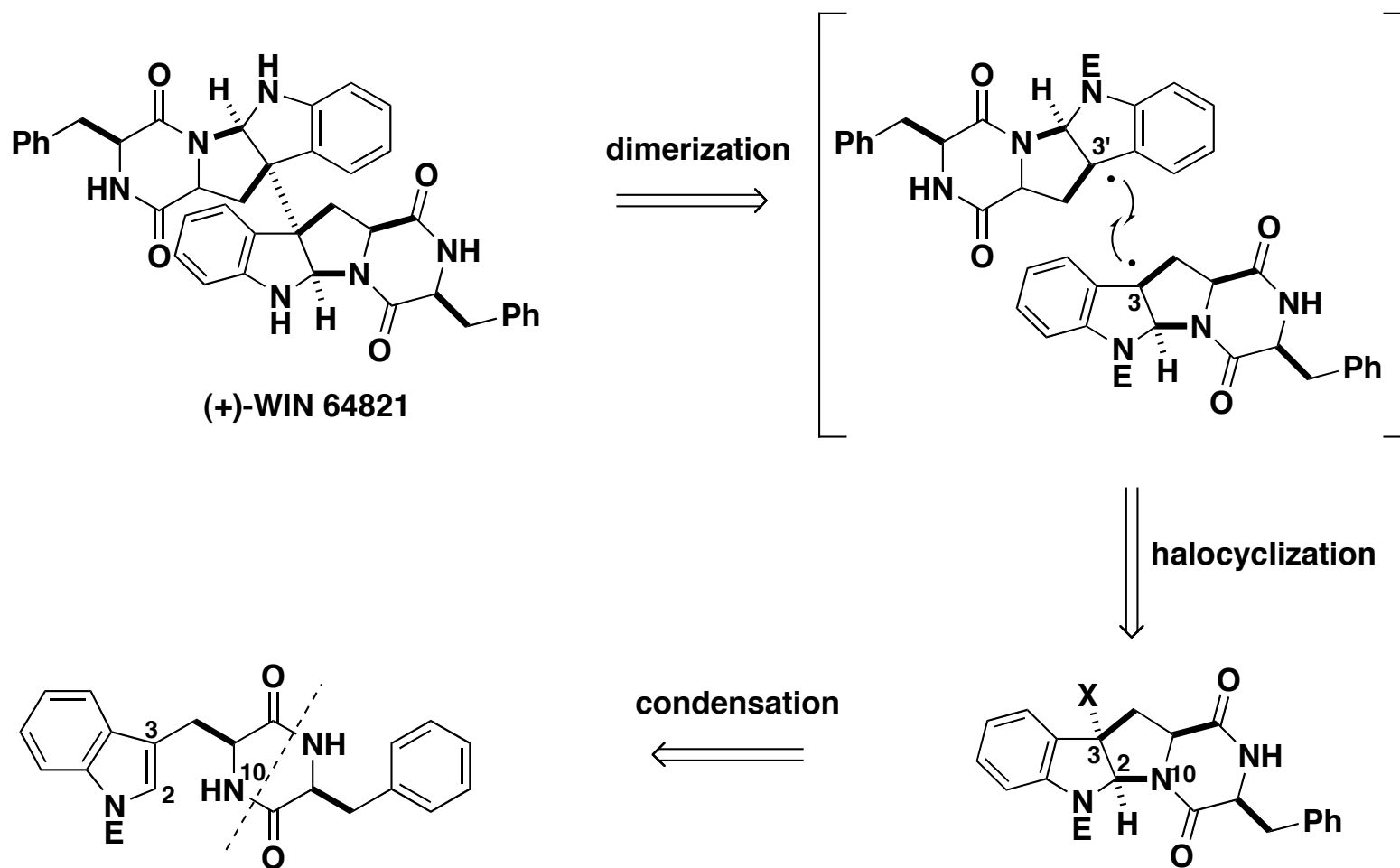
Overman, L. E.; Paone, D. V. *J. Am. Chem. Soc.* **2001**, *123*, 9465-9467

Overman's Synthesis of Dityryptophan



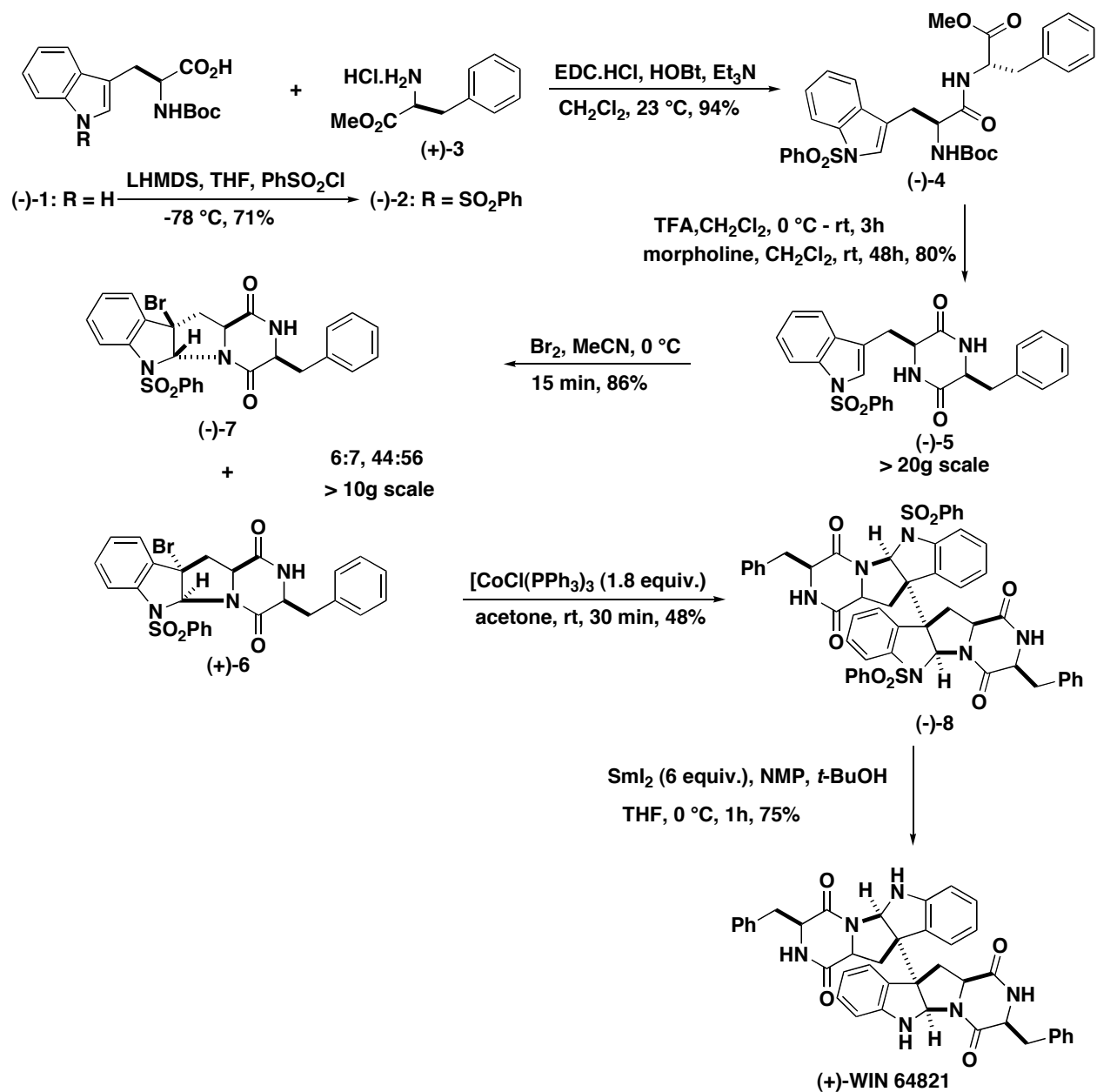
Overman, L. E.; Paone, D. V. *J. Am. Chem. Soc.* **2001**, *123*, 9465-9467

Title Paper: Retrosynthesis of (+)-WIN 64821



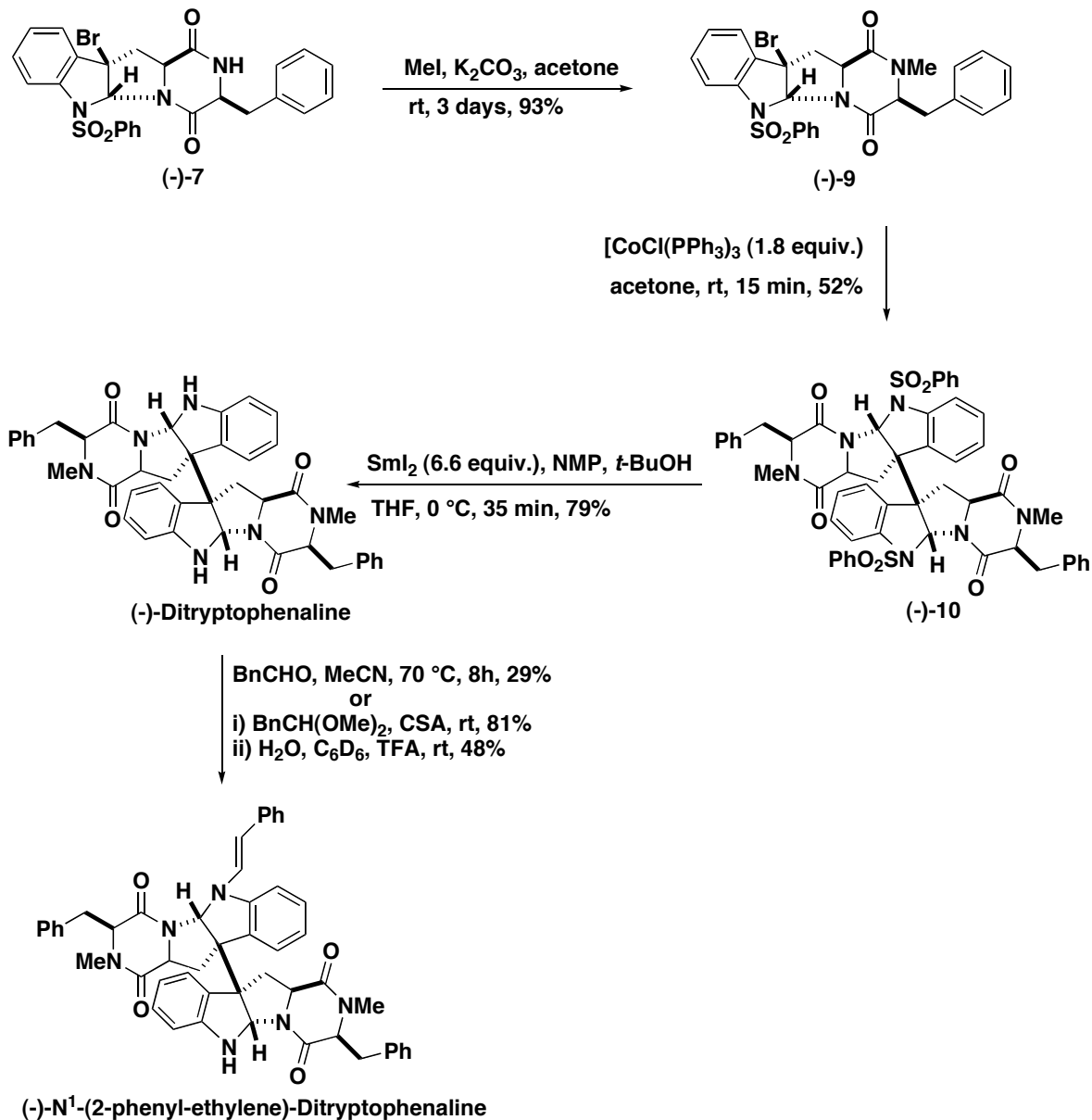
Movassaghi, M.; Schmidt, M. A.; Ashenhurst, J. A. *Angew. Chem. Int. Ed.* **2008**, *47*, 1485-1487

Title Paper: Total Synthesis of (+)-WIN 64821



Movassaghi, M.; Schmidt, M. A.; Ashenurst, J. A. *Angew. Chem. Int. Ed.* **2008**, *47*, 1485-1487

Title Paper: Total Synthesis of (-)-Ditryptophenaline



Movassaghi, M.; Schmidt, M. A.; Ashenurst, J. A. *Angew. Chem. Int. Ed.* **2008**, *47*, 1485-1487

Summary

- Enantioselective synthesis of (+)-WIN 64821 in 6 steps (66% overall yield); (-) Dityryptophenaline in 7 steps (73% overall yield)
- Formation of vicinal quaternary centers by Co catalyzed reductive homodimerization of alkyl bromides
- First synthesis of (+)-WIN 64821