Total Synthesis of the Putative Structure of Stemonidine

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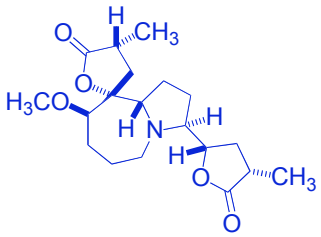
Org. Lett. **2007** ASAP.

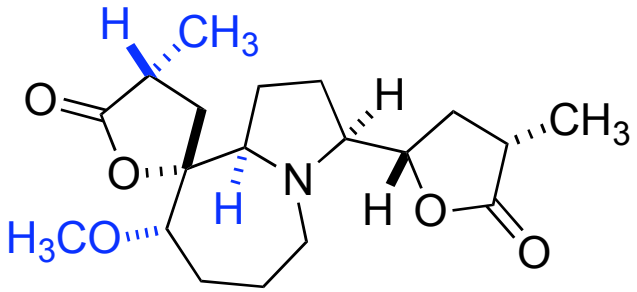
Presented by:

Salvatore J. Spagna

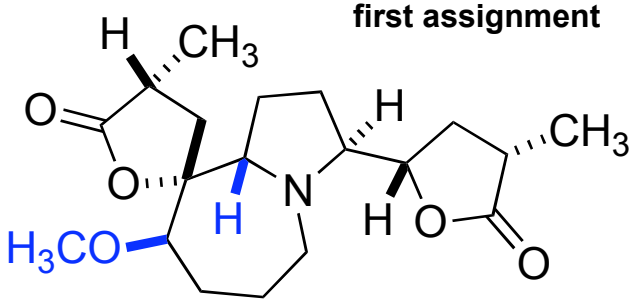


The Background:

Isolated from the roots of *Stemona tuberosa*, initial structure assigned by Xu and co-workers in 1982.



first assignment



second assignment

Used in traditional Chinese and Japanese medicines to treat respiratory disorders and antihelmintics; as well as working as an insecticide

The structure features a pyrolloazepine core and a spirocyclic methyl butrylactone moiety.

Pilli, R. A.; Rosso, G. B.; de Oliveira, M. C. F. In *The Alkaloids*; Cordell, G. A., ed.; Elsevier: New York, **2005** (62) 77.

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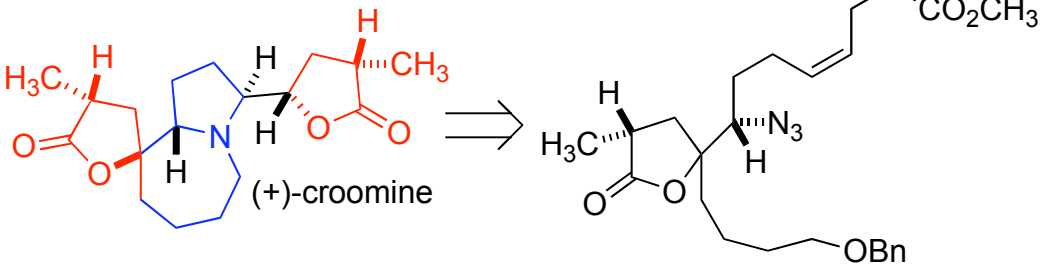
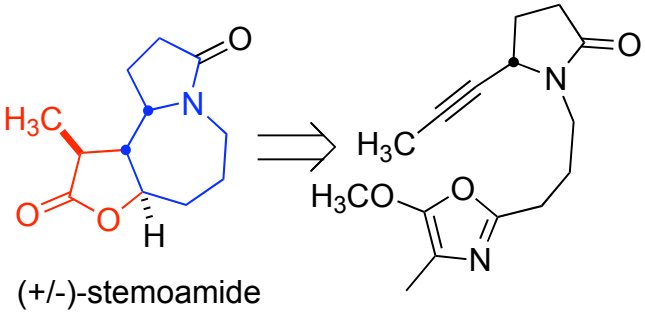
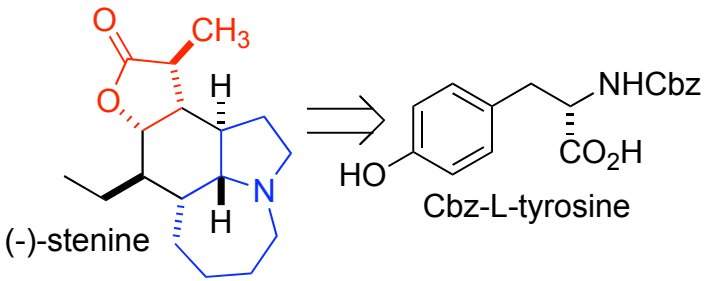
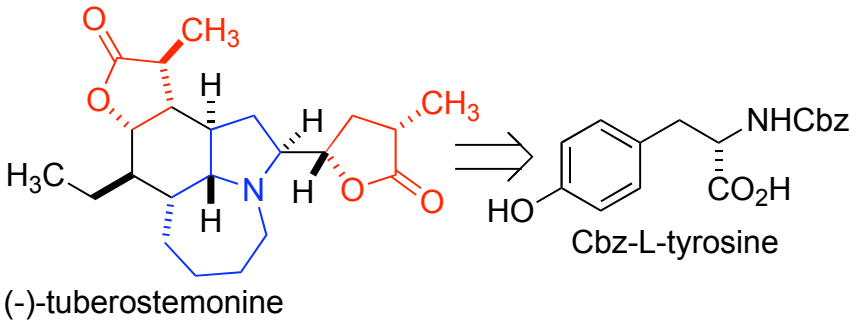
Some Recent Alkaloid Syntheses







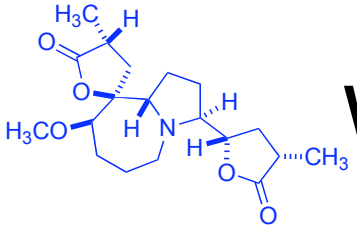


Wipf, P.; Kim, Y.; Goldstein, D. M. *J. Am. Chem. Soc.* **1995** (117) 11106.

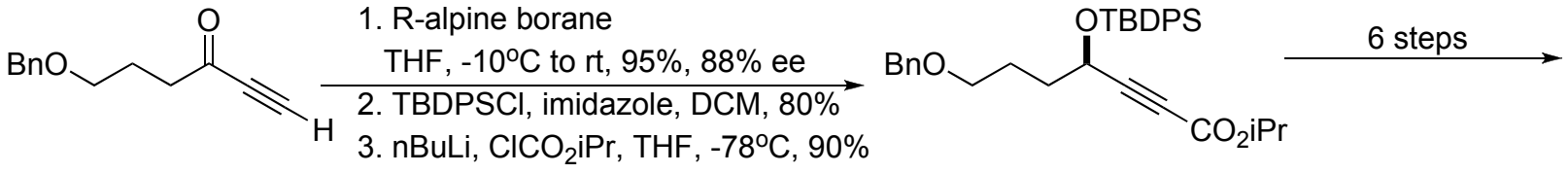
Jacobi, P. A.; Lee, K. *J. Am. Chem. Soc.* **2000** (43) 295.

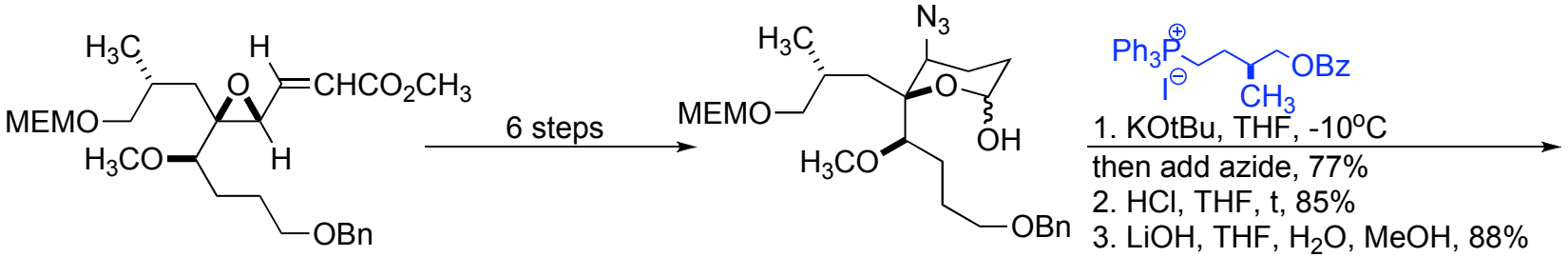
Williams, D. R.; Brown, D. L.; Benbow, J. W. *J. Am. Chem. Soc.* **1989**, (111) 1923.

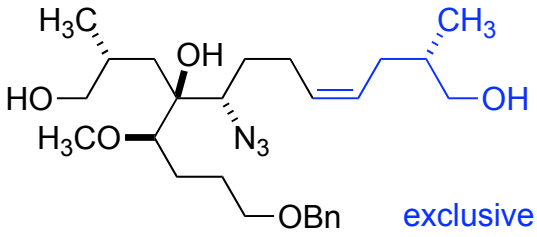
Wipf, P.; Rector, S. R.; Takahashi, H. *J. Am. Chem. Soc.* **2002** (124) 14848.



Williams Synthesis of Stemospironine

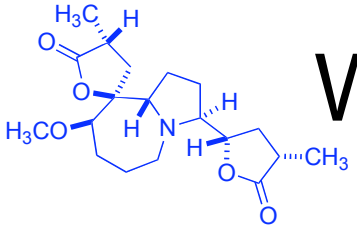




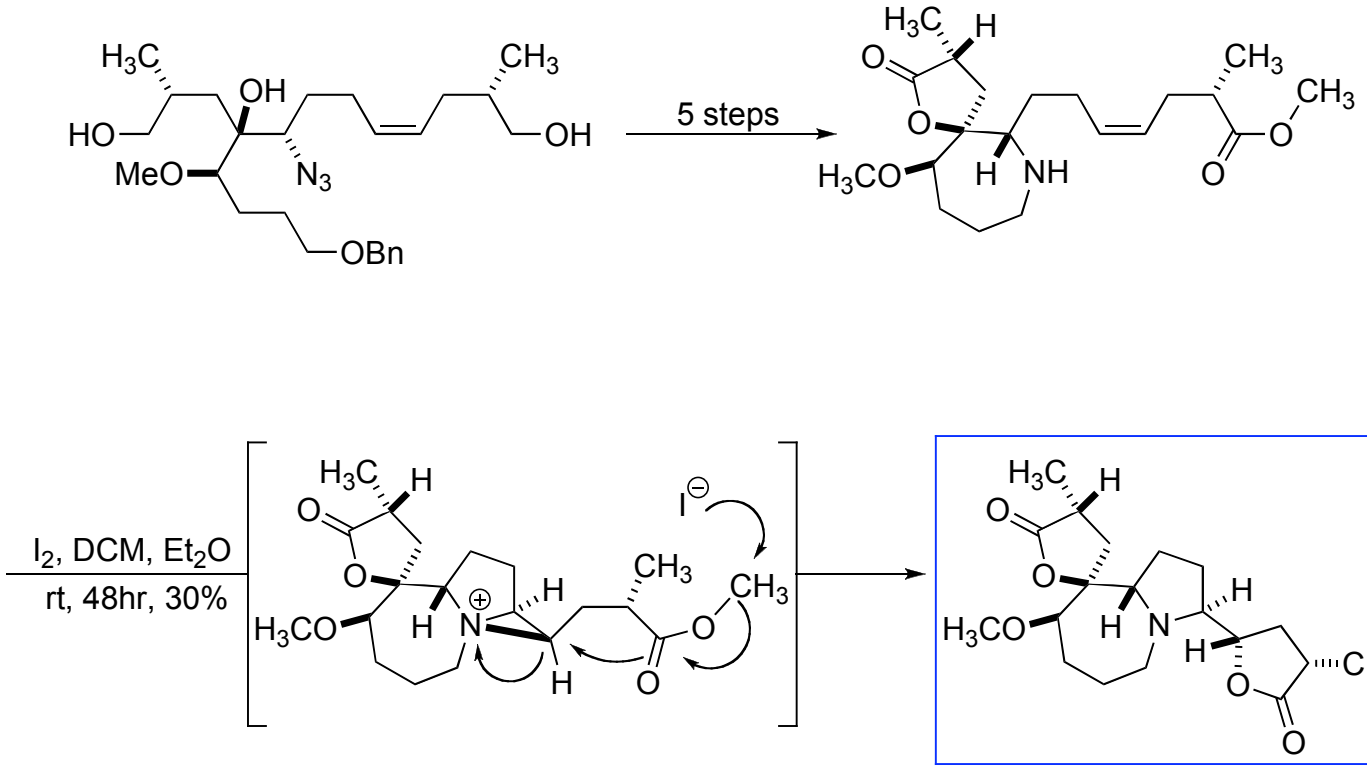


exclusive *Z*-selectivity

Williams, D. R.; Fromhold, M. G.; Early, J. D. *Org. Lett.* **2001** (3) 2721.



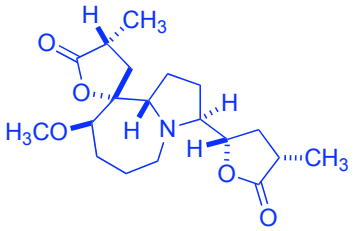
Williams Synthesis of Stemospironine:

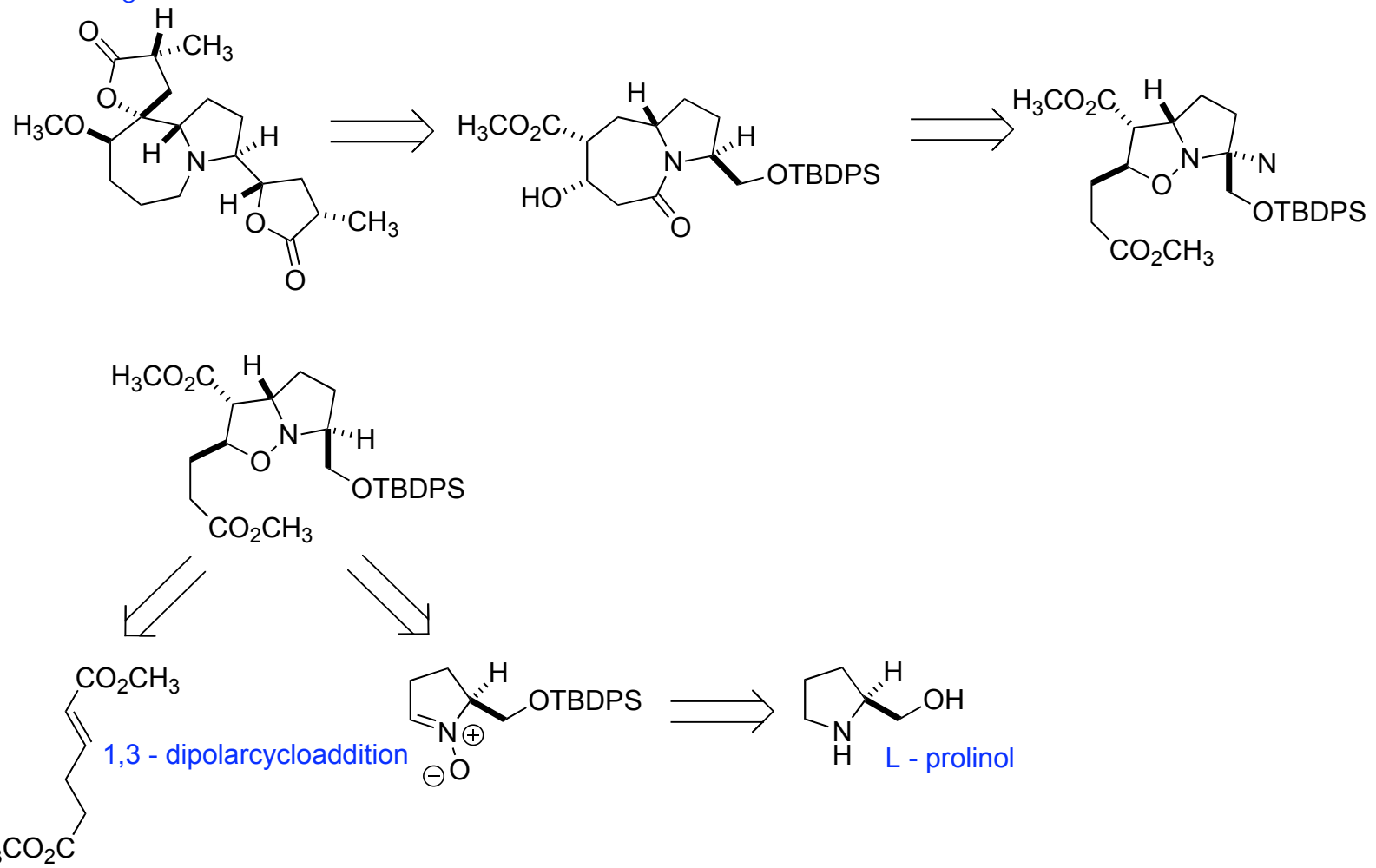


24 step synthesis, 0.38% overall yield

Williams, D. R.; Fromhold, M. G.; Early, J. D. *Org. Lett.* **2001** (3) 2721.

Retrosynthetic Analysis of Stemonidine:





Cid, P.; Closa, M.; de March, P.; Figueredo, M.; Font, J.; Sanfeliu, E.; Soria, A. Eur. *J. Org. Chem*. **2004**, 4215.
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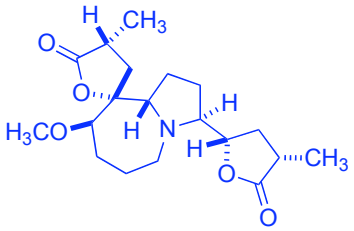
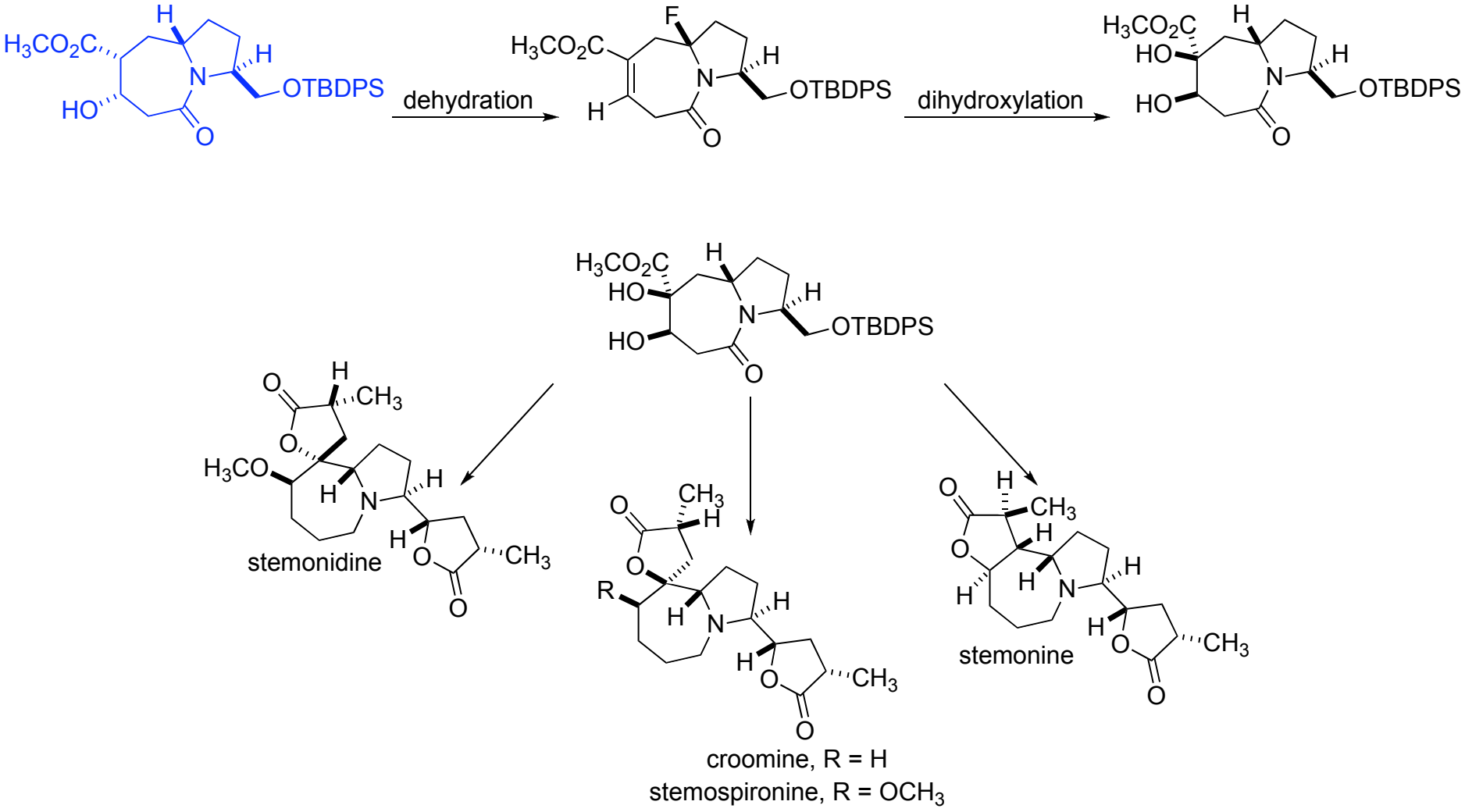
Closa, M.; de March, P.; Figueredo, M.; Font, J. *Tetrahedron: Asymmetry* **1997** (8) 1031.
Busque´, F.; de March, P.; Figueredo, M.; Font, J.; Gallagher, T.; Milán, S. *Tetrahedron: Asymmetry* **2002** (13) 437.

A Key Intermediate





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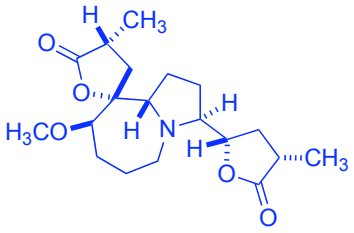
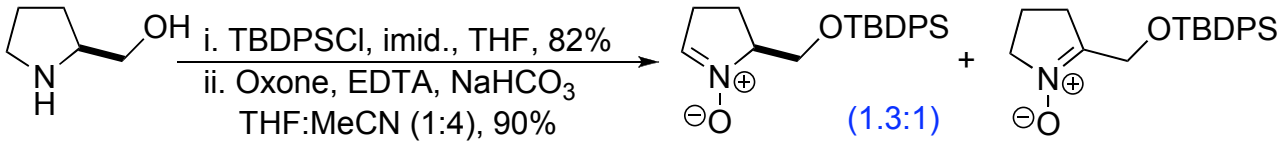
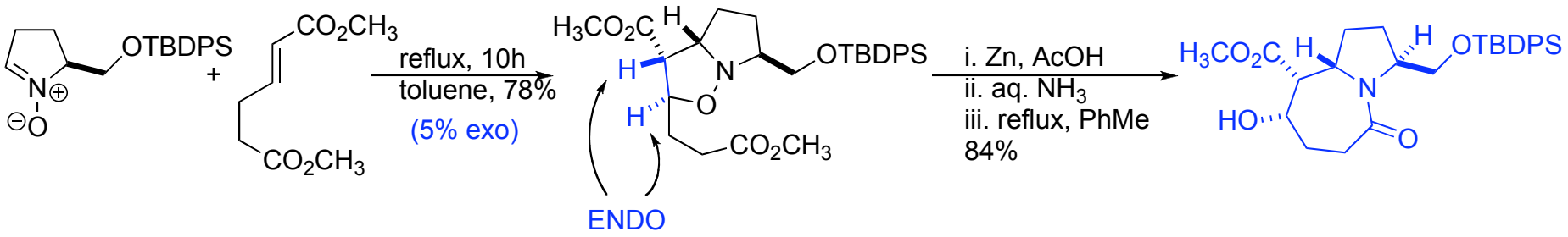
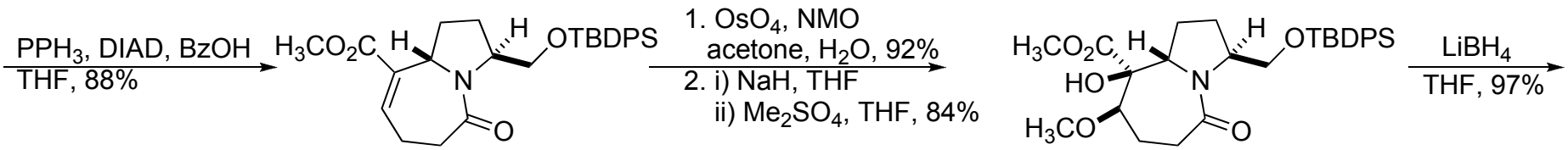
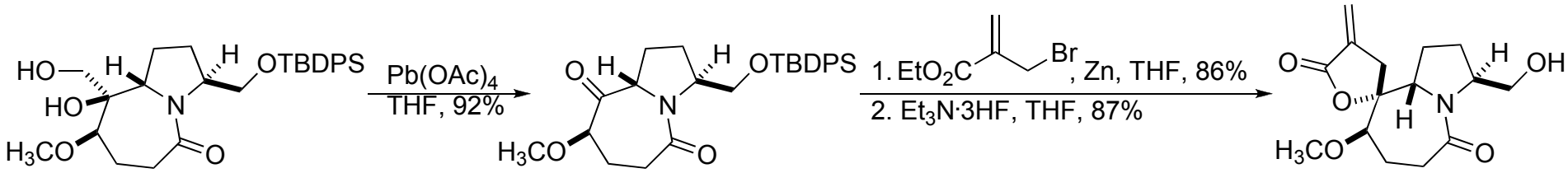
The Synthesis:



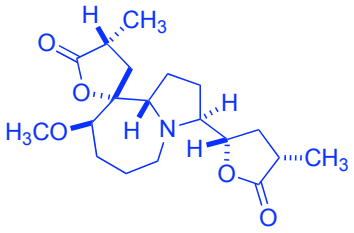


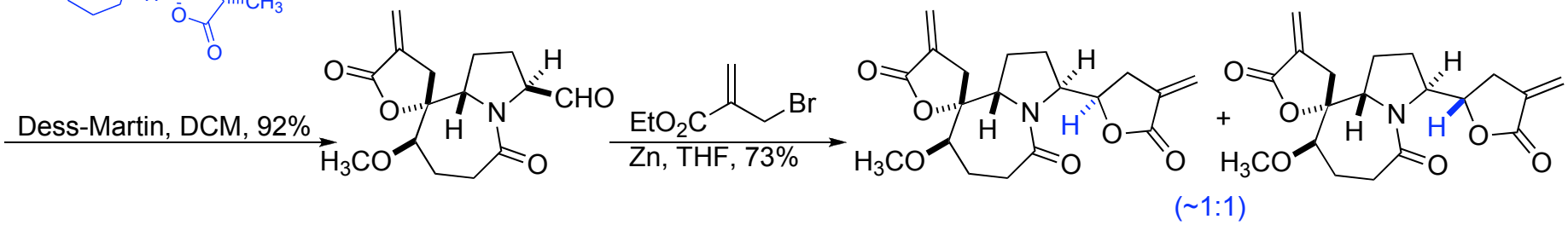


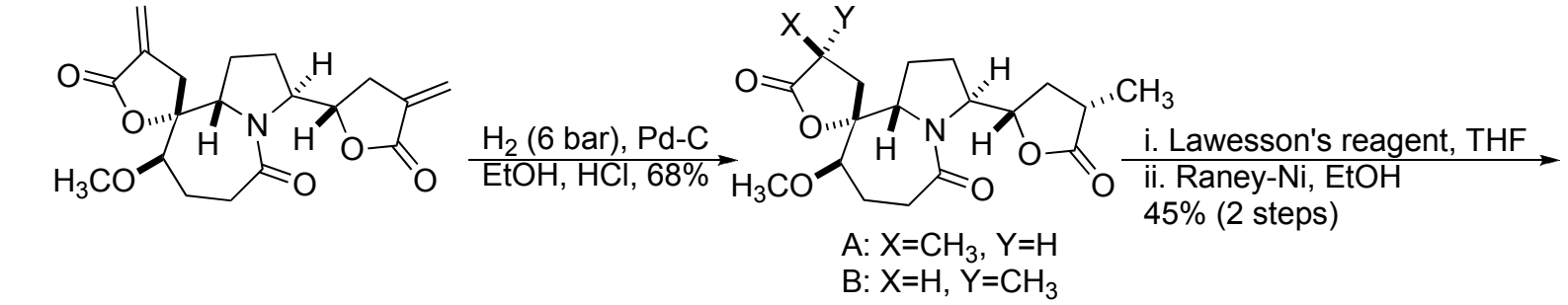


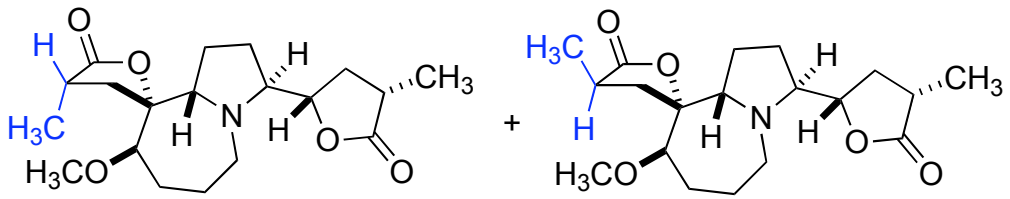


The Synthesis:

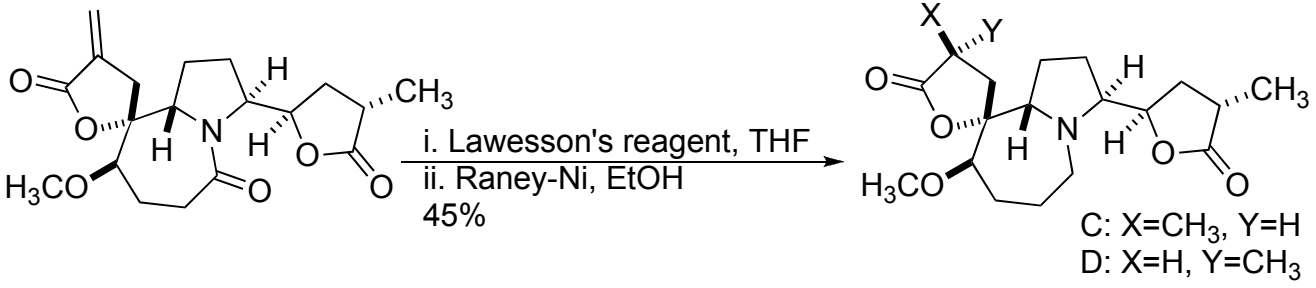


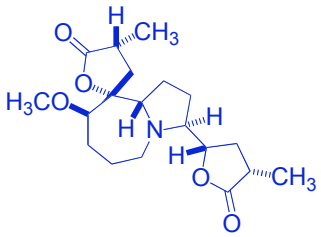






(-)-stemonidine **(-)-11-epi-stemonidine**





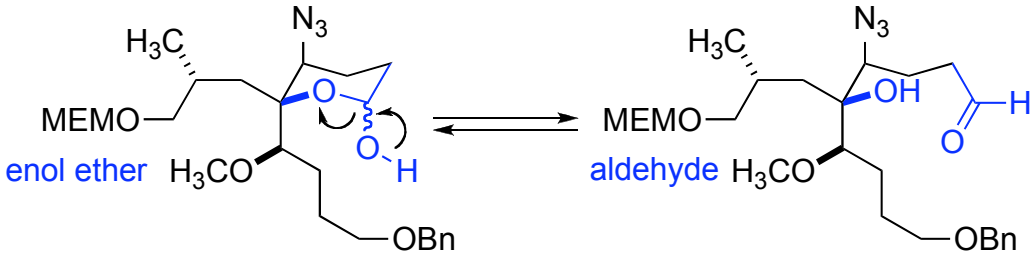
Conclusions:

Stemonidine and its C_{11}-epimer were successfully synthesized from the amino acid proline in 15 steps; with a 4.51% overall yield.

A key intermediate in Stemonidine's synthesis allows the structures of several other alkaloids to be accessed.

Construction of the pyrolloazepine core is cleverly achieved through the use of a 1,3-dipolar cycloaddition.

NMR data from the Williams groups' synthesis of stemospironine, along with NMR data from this stemonidine synthesis suggest an initial incorrect assignment of stemonidine's structure.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H3C
MEMO
O
O
H
enol ether
H3CO
OBn
N3
H3C
MEMO
OH
H
O
aldehyde
H3CO
OBn