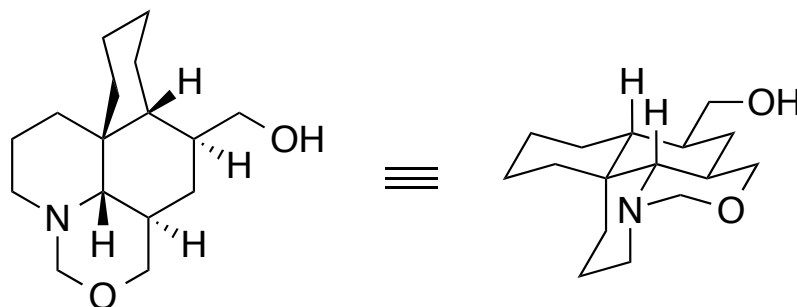


Total Synthesis of the Tetracyclic Antimalarial Alkaloid (\pm)-Myrioneurinol

Anthony J. Nocket and Steven M. Weinreb

Angew. Chem. Int. Ed. **2014**, *53*, 1 – 5



Ruiting Liu

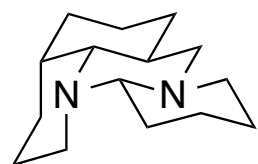
Wipf Group Current Literature

11/08/2014

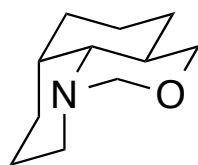
The Myrioneuron alkaloid

1

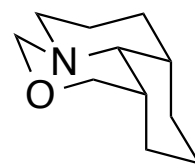
- Isolated from southeast asian plant *Myrioneuron nutans*, Schoberine, Mytioxazine A, Mytioxazine B have been synthesized by Bernard Bodo



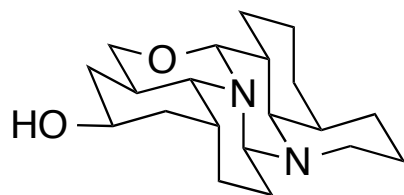
Schoberine



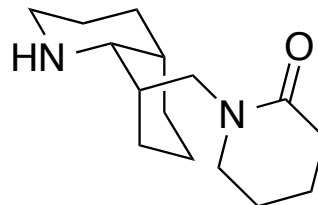
Mytioxazine A



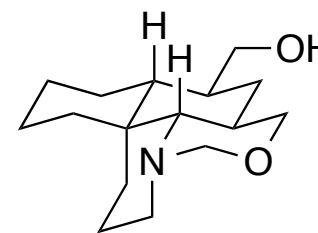
Mytioxazine B



Myrobotinol



Myrionine



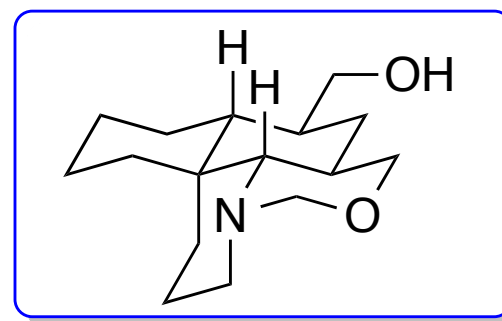
Myrioneurinol

The Myrioneuron alkaloid

Myrioneurinol

2

- New member of the Myrioneuron alkaloid, isolated from leaves of *Myrioneuron nutans*
- significant antimalarial activity against *Plasmodium falciparum* (IC₅₀: 11 mg/mL)
- Four tightly fused, rigid array of chair six-membered rings



Myrioneurinol

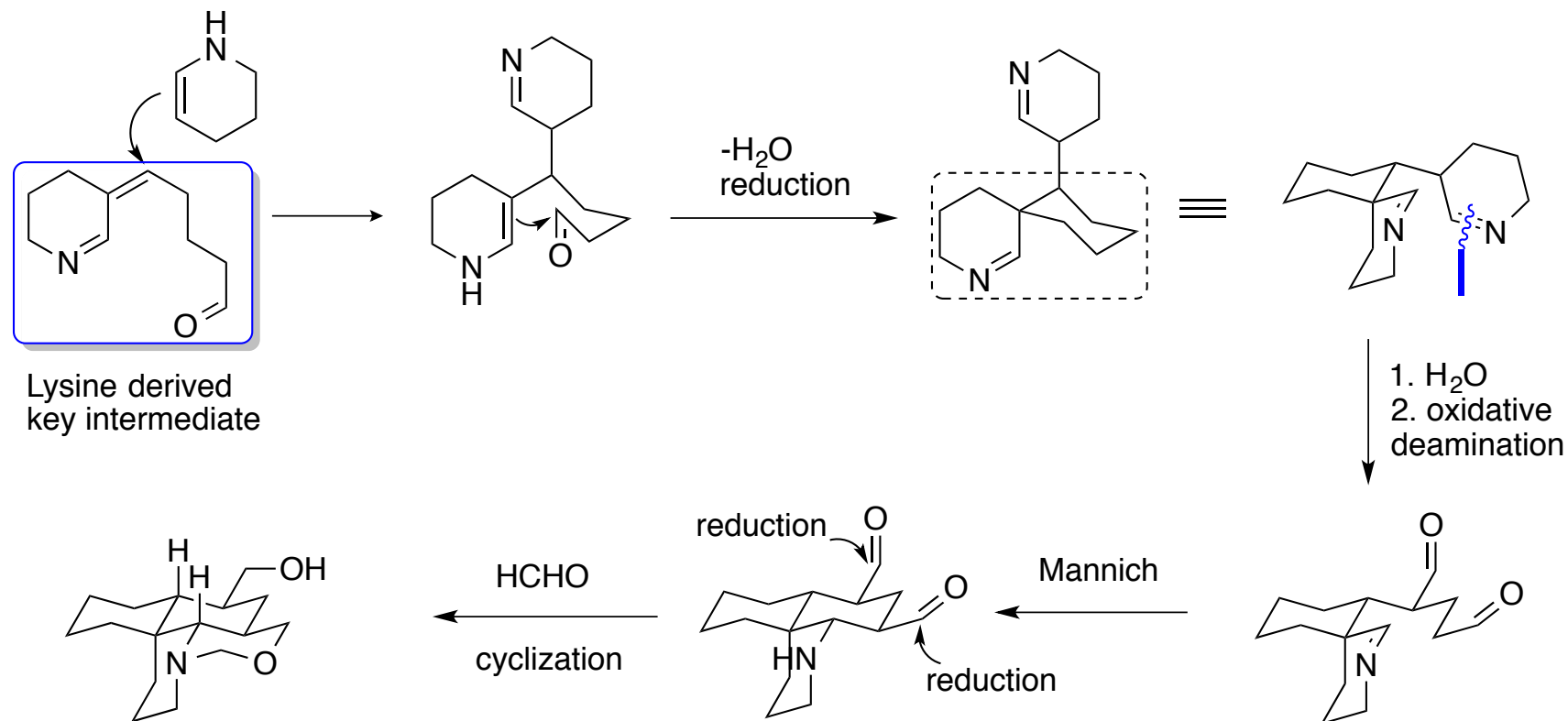
Tetrahedron 63 (2007) 11244–11249

Tetrahedron Letters 43 (2002) 7565–7568

J. Org. Chem. 2008, 73, 7565–7573

Biosynthesis

3

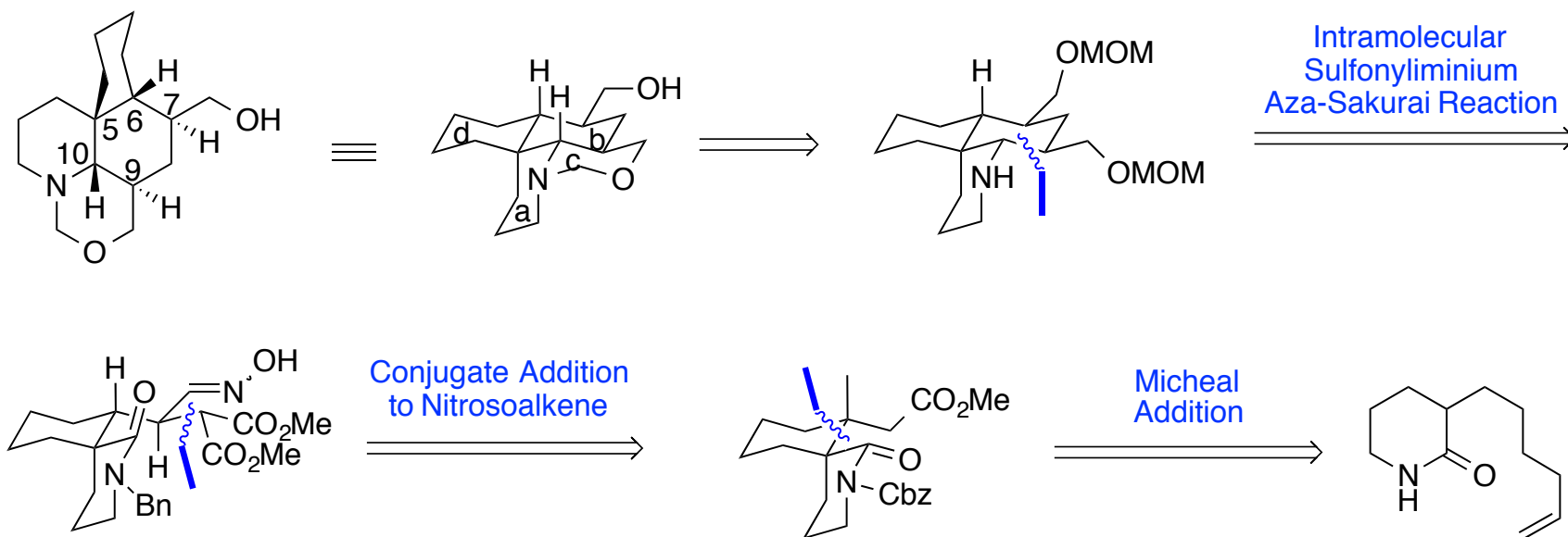


Plausible biosynthetic pathway to myrioneurinol

Nat. Prod. Rep., **2010**, *27*, 32–56

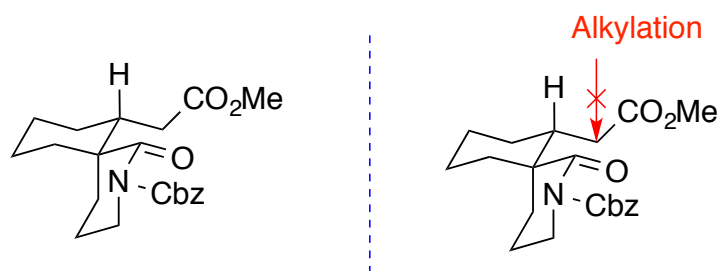
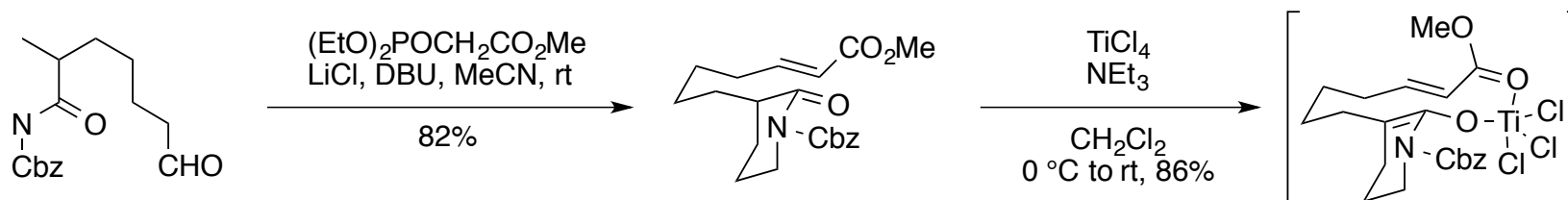
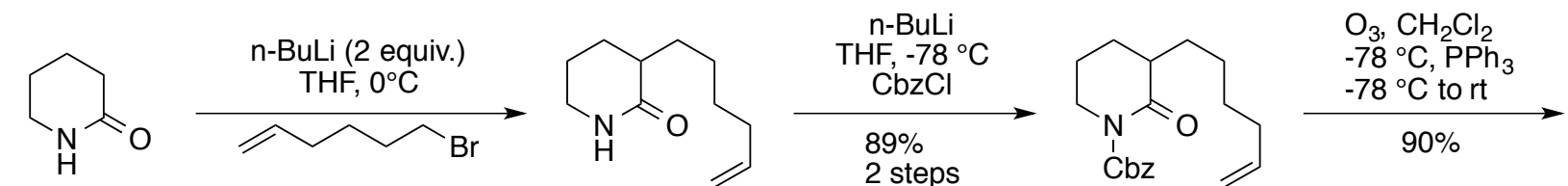
Retrosynthesis

4



a/d Ring – Michael addition

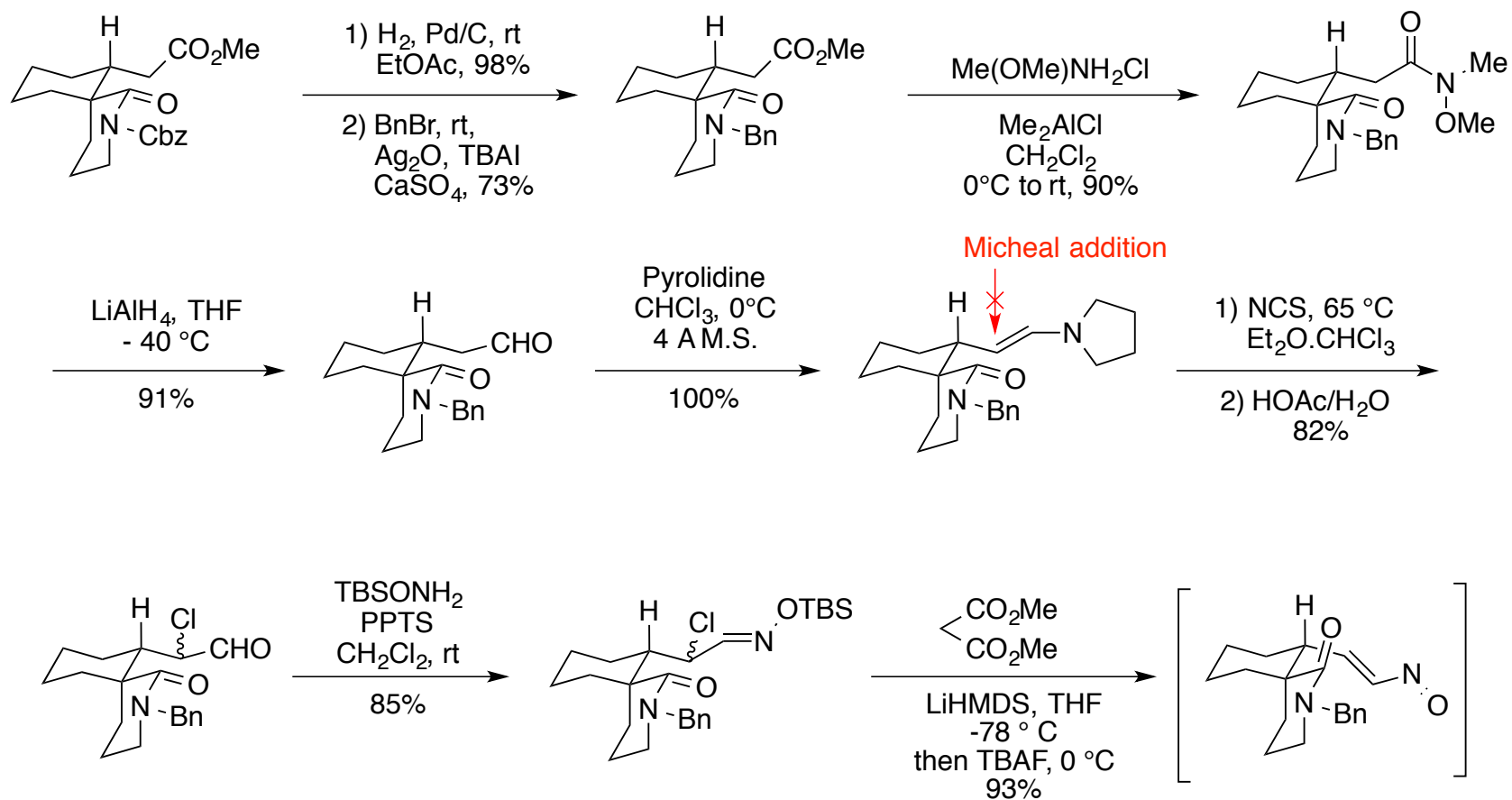
5



J. Org. Chem. **1991**, *56*, 5750
Tetrahedron Lett. **1989**, *30*, 6511

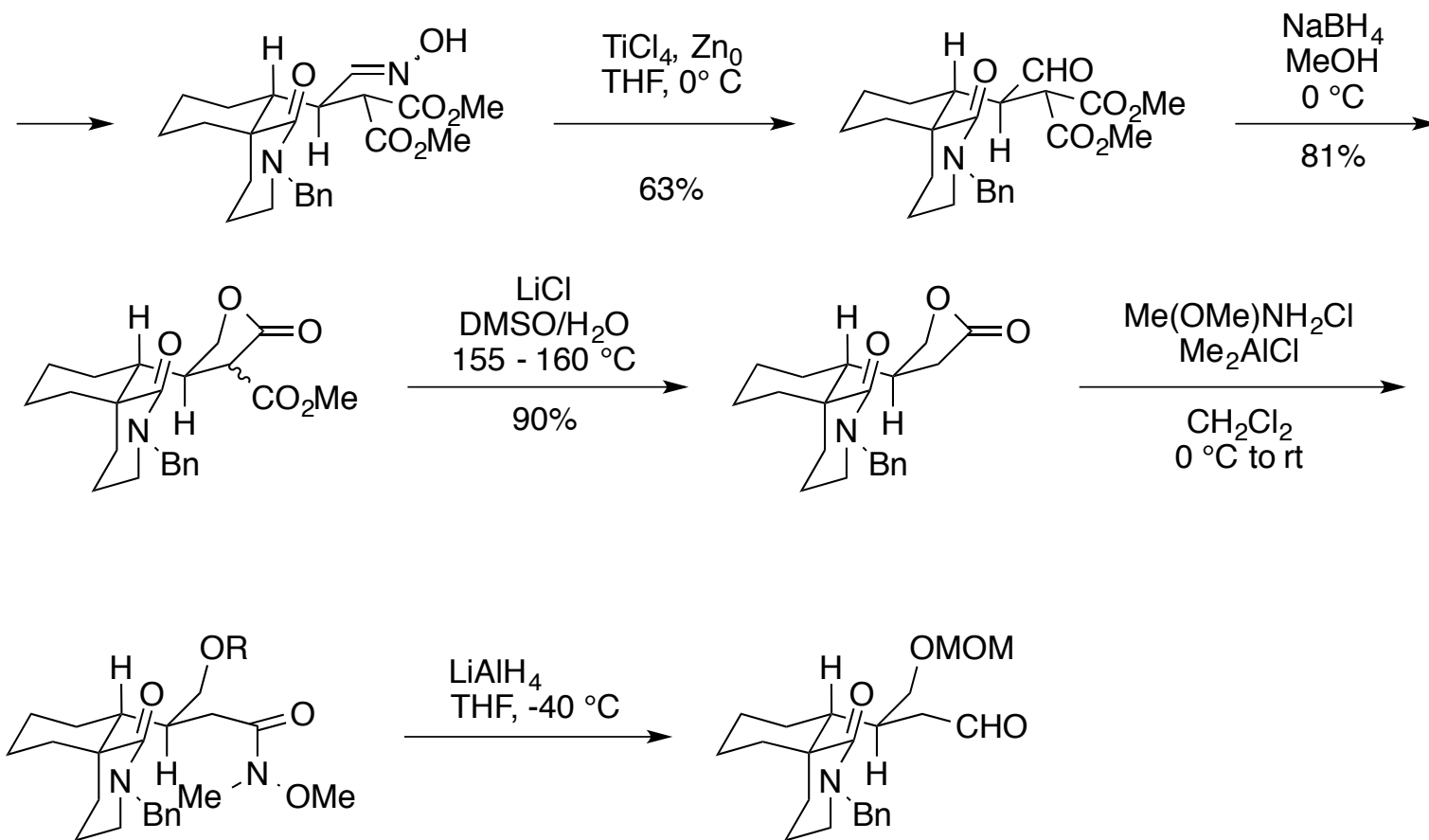
C7-Pains and gains

6



Conjugate Addition to a Nitrosoalkene

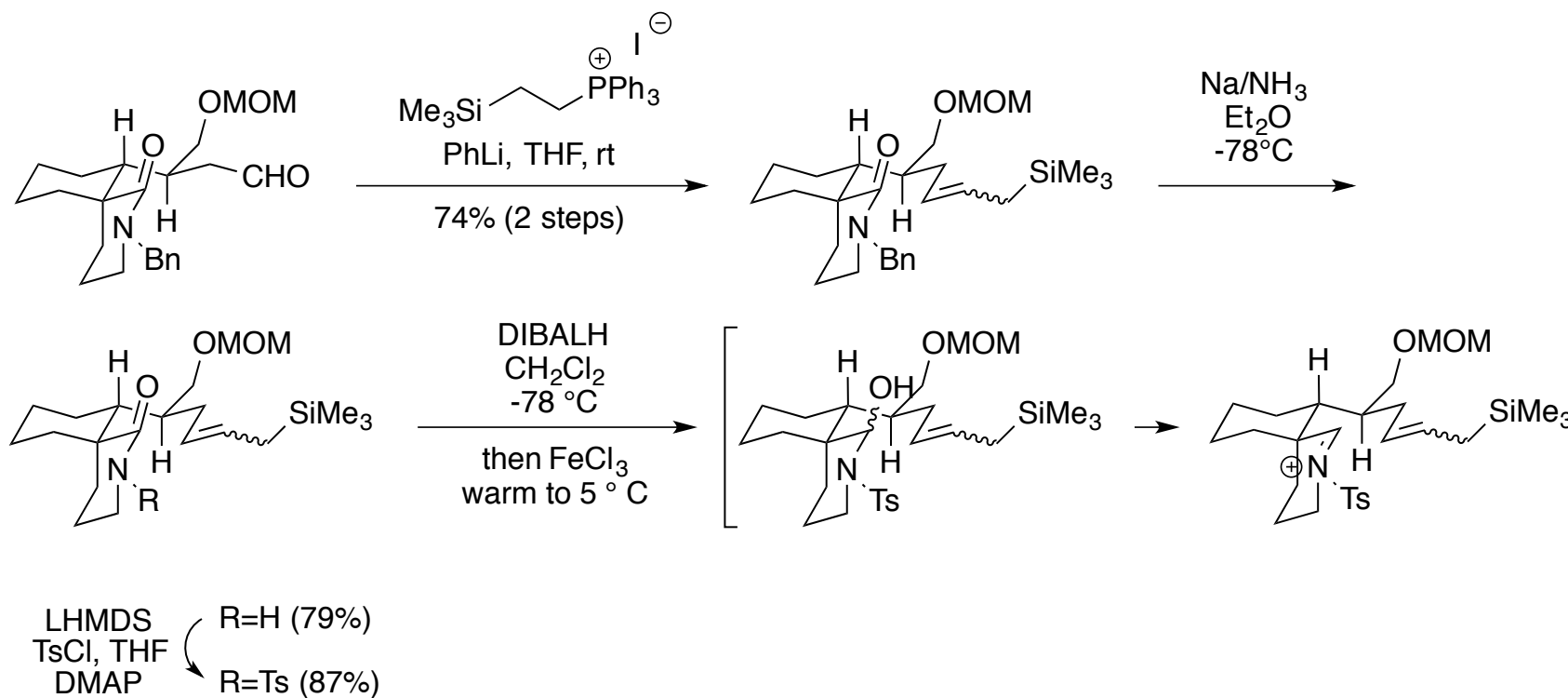
7



Tetrahedron Lett. **2010**, 51, 2032
Org. Lett. **2011**, 13, 1258.

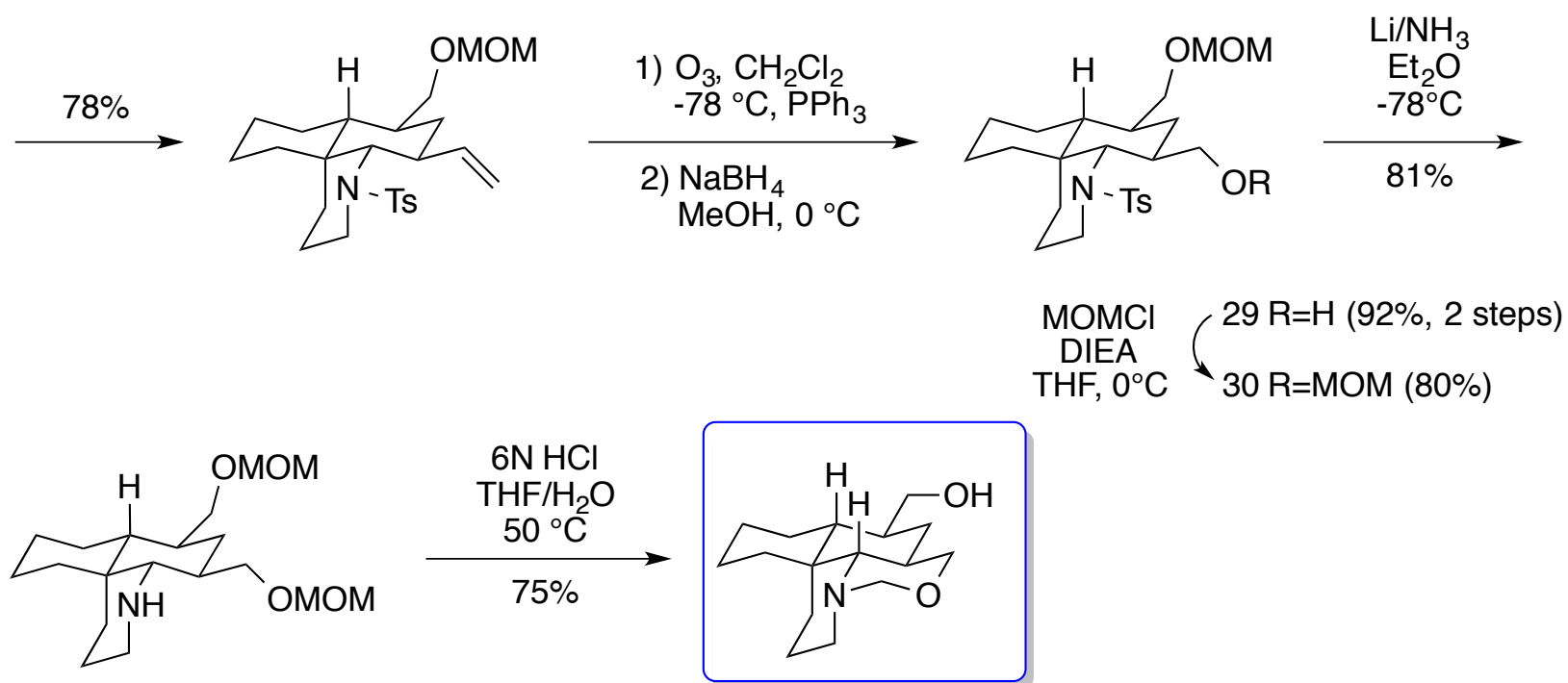
Sulfonyliminium Sakurai Reaction

8



J. Organomet. Chem. **1979**, 181, 293.

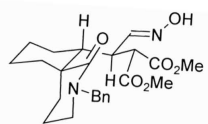
J. Org. Chem. **2006**, 71, 2078



Conclusion



- First total synthesis (\pm)-Myrioneurinol
- 28 steps, 1.8% yield
- Three highly diastereoselective reactions to install the correct configuration at the C5/C6, C7, C9/C10 configuration



(E)-16

