

Progress Toward the Total Synthesis of Ergot Alkaloids:

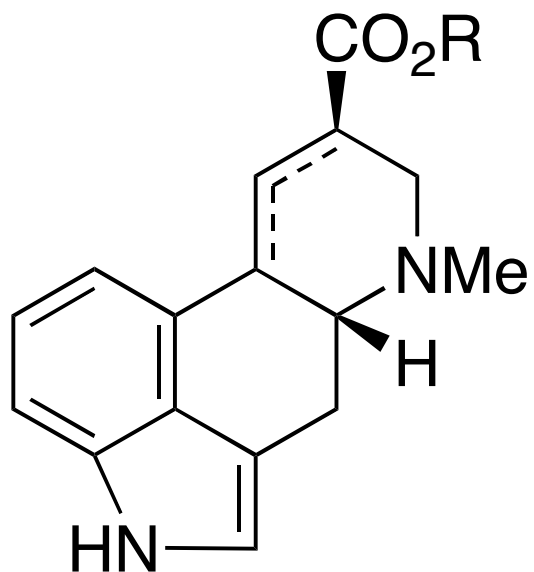
Cody Timmons

Wipf Group

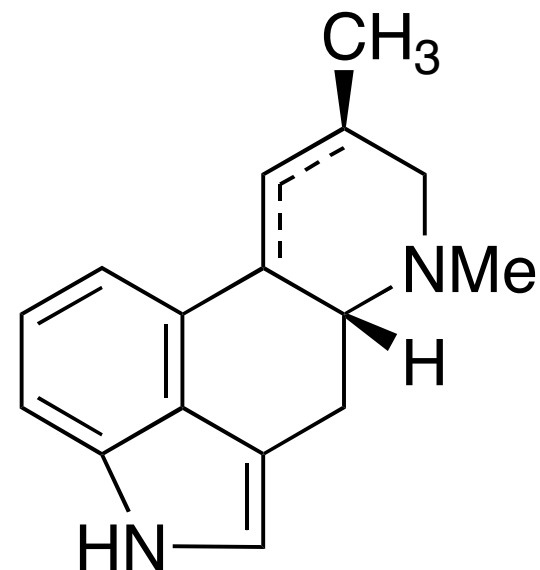
12/23/2006

University of Pittsburgh

Ergot Alkaloids

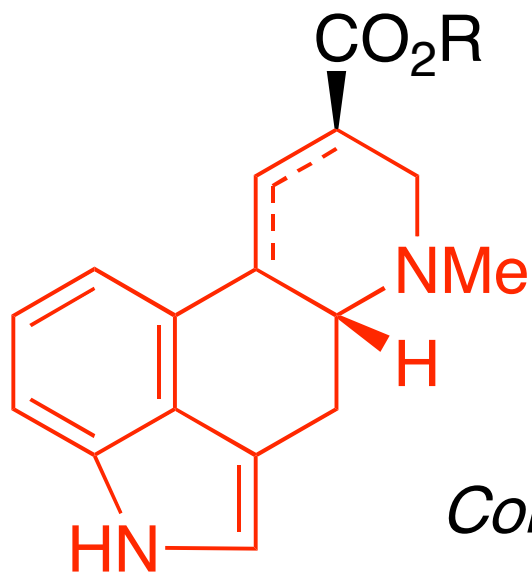


Lysergic acid subclass



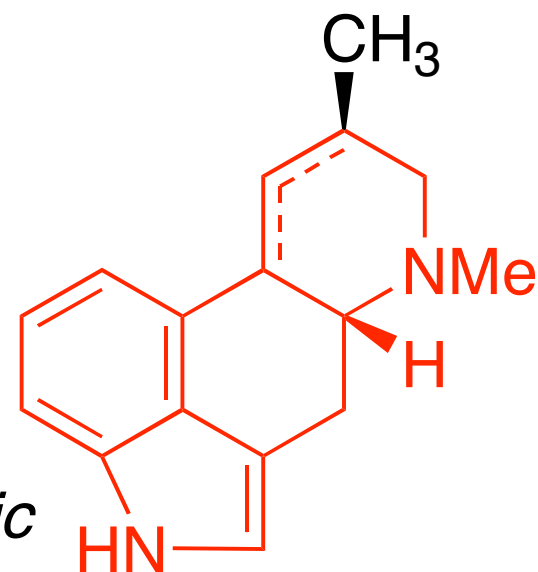
Clavine subclass

Ergot Alkaloids



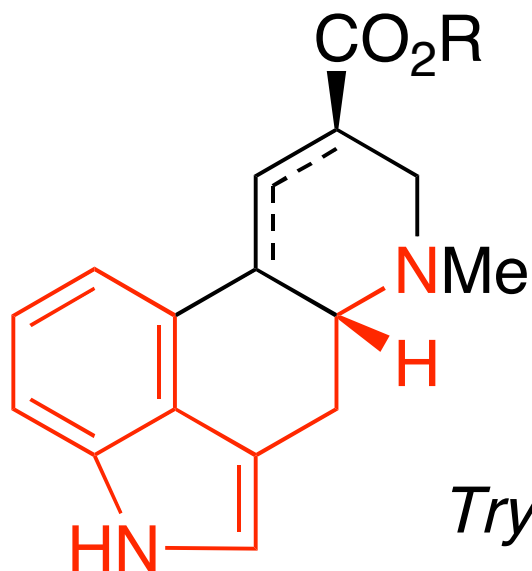
Lysergic acid subclass

*Common tetracyclic
core*



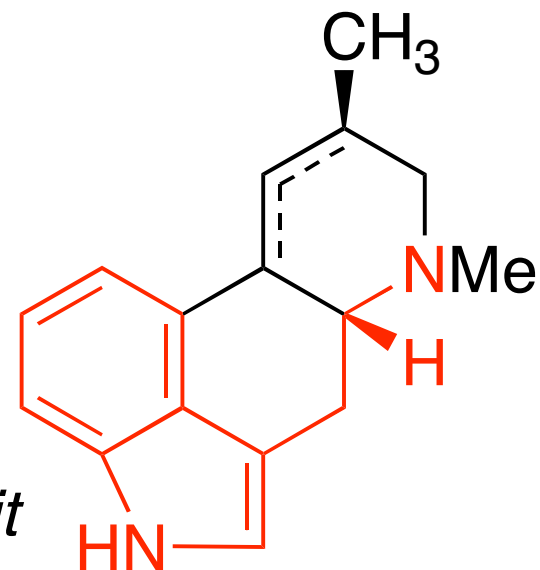
Clavine subclass

Ergot Alkaloids



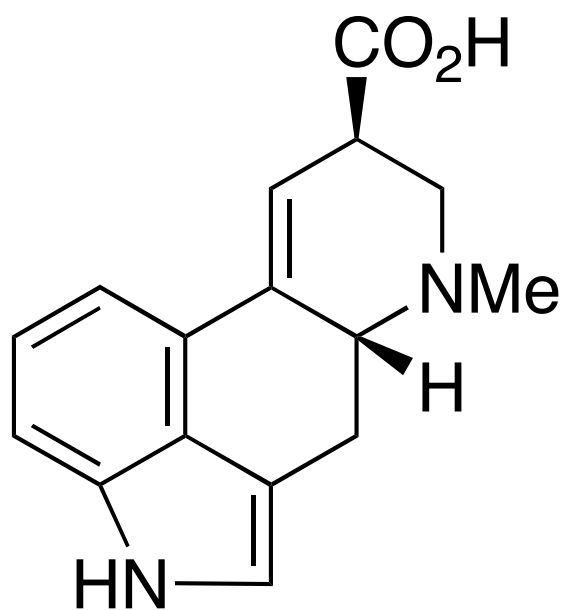
Tryptophan subunit

Lysergic acid subclass

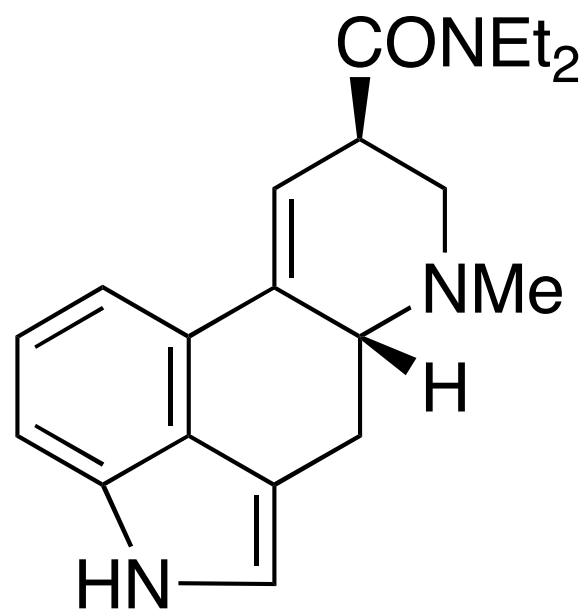


Clavine subclass

Lysergic Acid Compounds

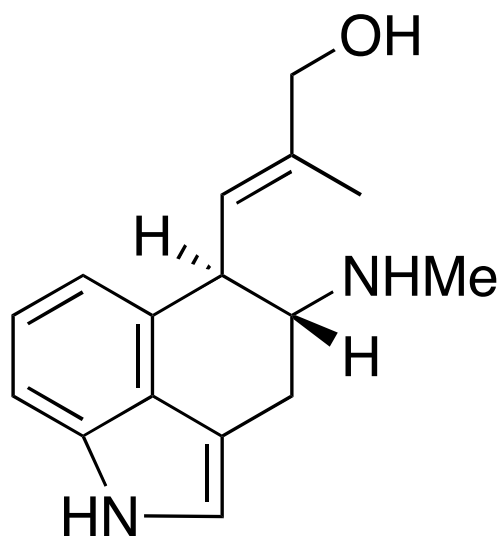


Lysergic acid

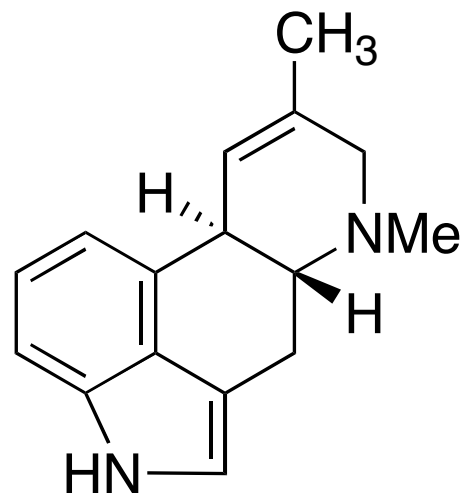


Lysergic acid diethylamide (LSD)

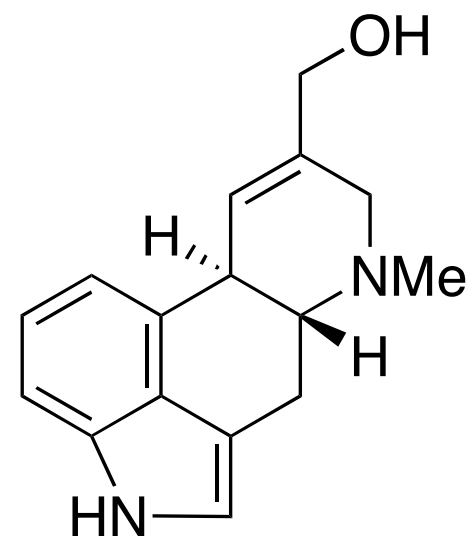
Clavine Compounds



Chanoclavine-I



Agroclavine



Elymoclavine

History

Ergotism

(aka St. Anthony's Fire)

Disease resulting from eating cereal grains (esp. rye) infected with ergot fungus

Ergot on a head of grain



History

Ergotism

(aka St. Anthony's Fire)

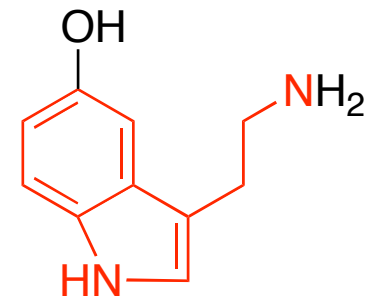
Symptoms include: convulsions, vomiting, hallucinations, gangrene, insanity, and death

Last epidemic: 2001-Ethiopia

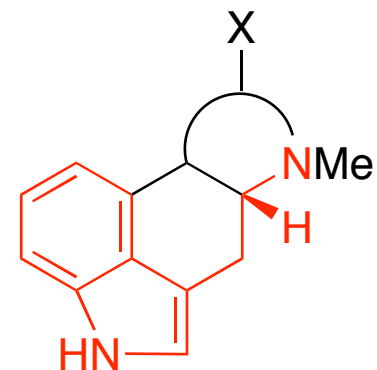
Cause of Salem Witch Trials?

Physiological Effects

- Ergolines: bind serotonin receptors...induce mood swings, vomiting, vasoconstriction, gangrene, convulsions
- Historical uses: abortive agent, controlling maternal bleeding, hallucinogen, treatment of Parkinson's disease, migraine



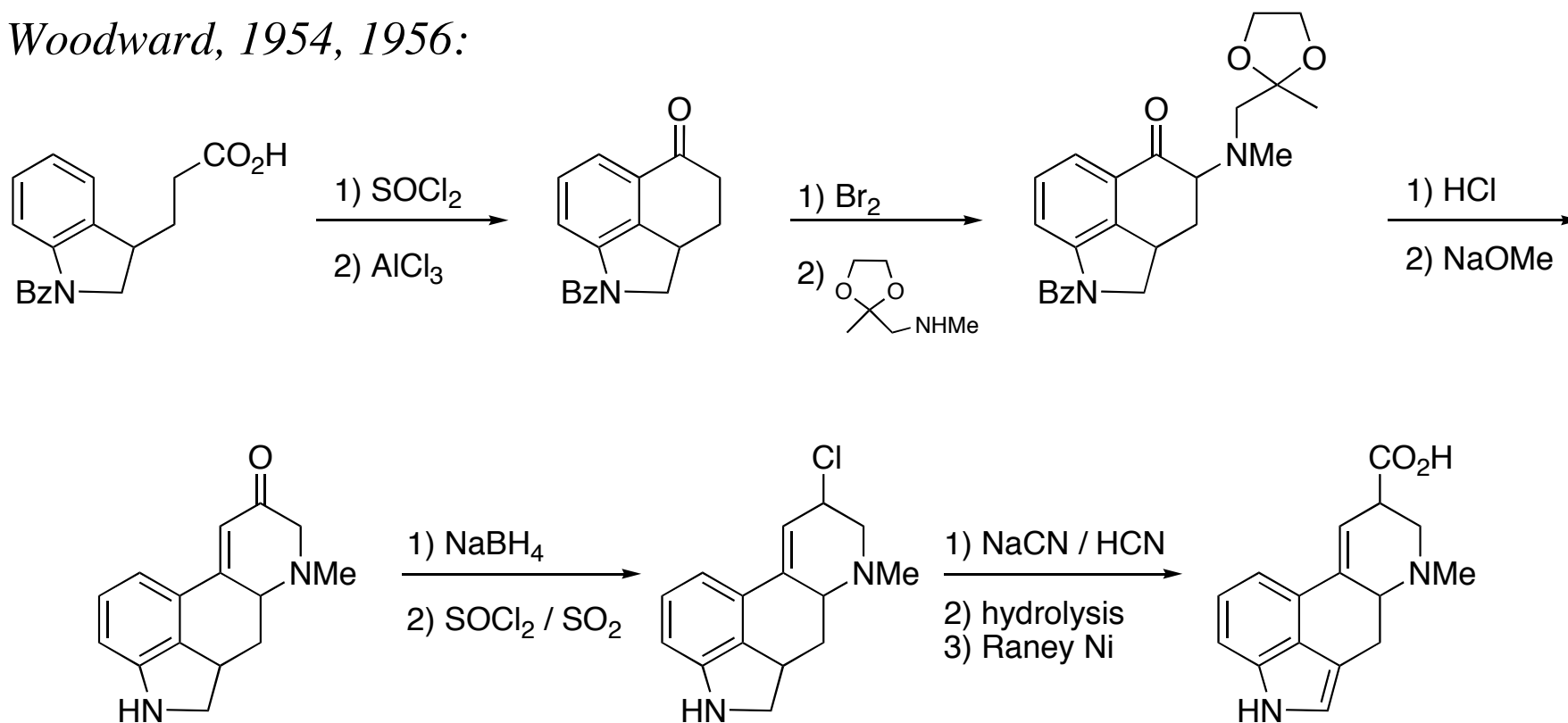
Serotonin
(5-hydroxytryptamine)



Ergoline Skeleton

Literature Highlights: Lysergic Acid

Woodward, 1954, 1956:

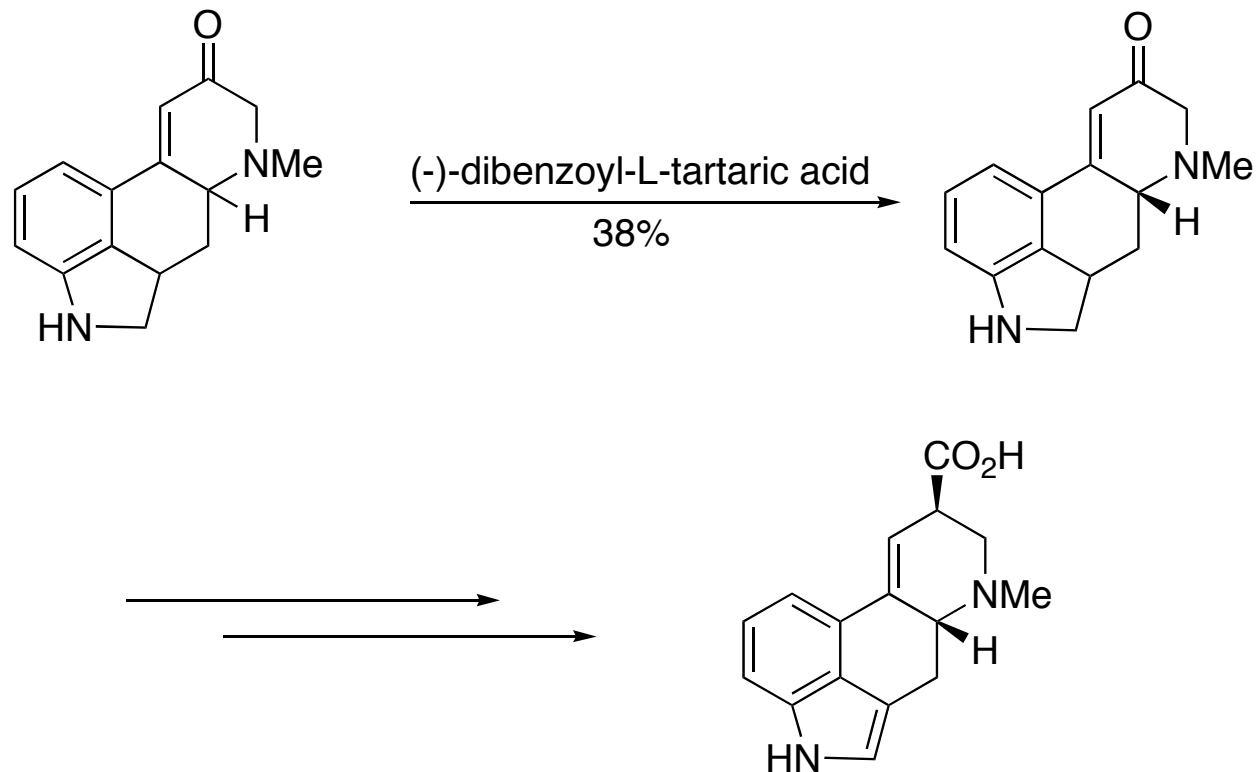


JACS, **1954**, 76, 5256.

JACS, **1956**, 78, 3087.

Literature Highlights: Lysergic Acid

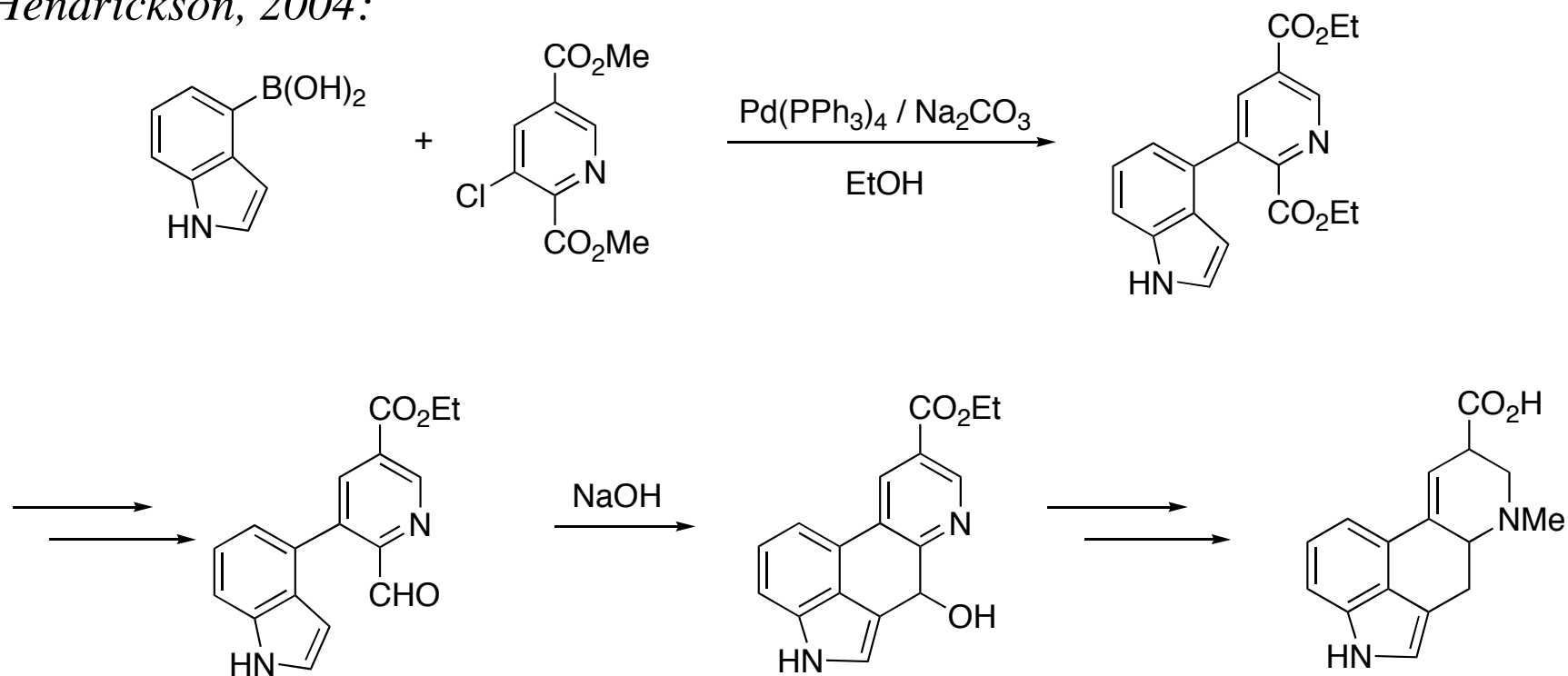
Szantay, 2004 (resolution of Uhle's ketone):



JOC, 2004, 69, 5993.

Literature Highlights: Lysergic Acid

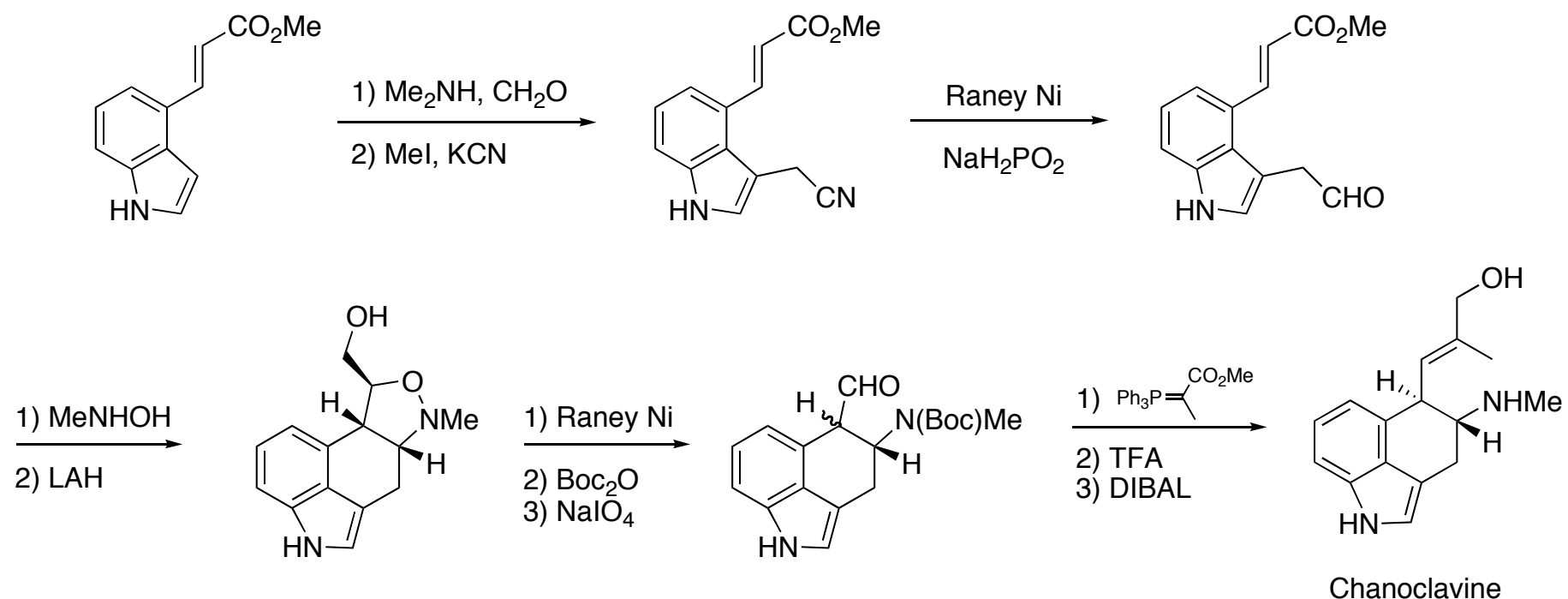
Hendrickson, 2004:



OL, 2004, 6, 3.

Literature Highlights: Clavine Alkaloids

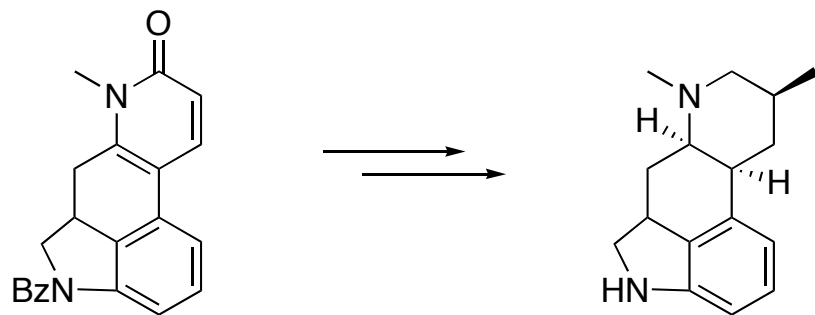
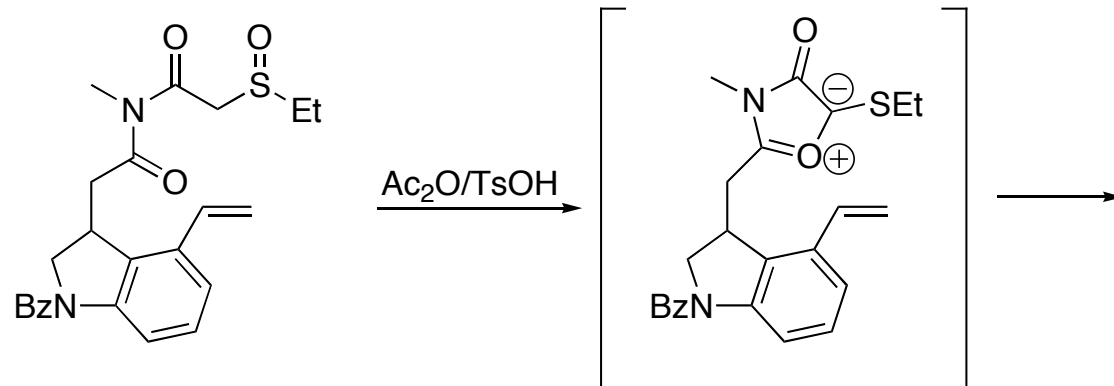
Oppolzer, 1983:



Tet., **1983**, 39, 3695.

Literature Highlights: Clavine Alkaloids

Padwa, 2000:

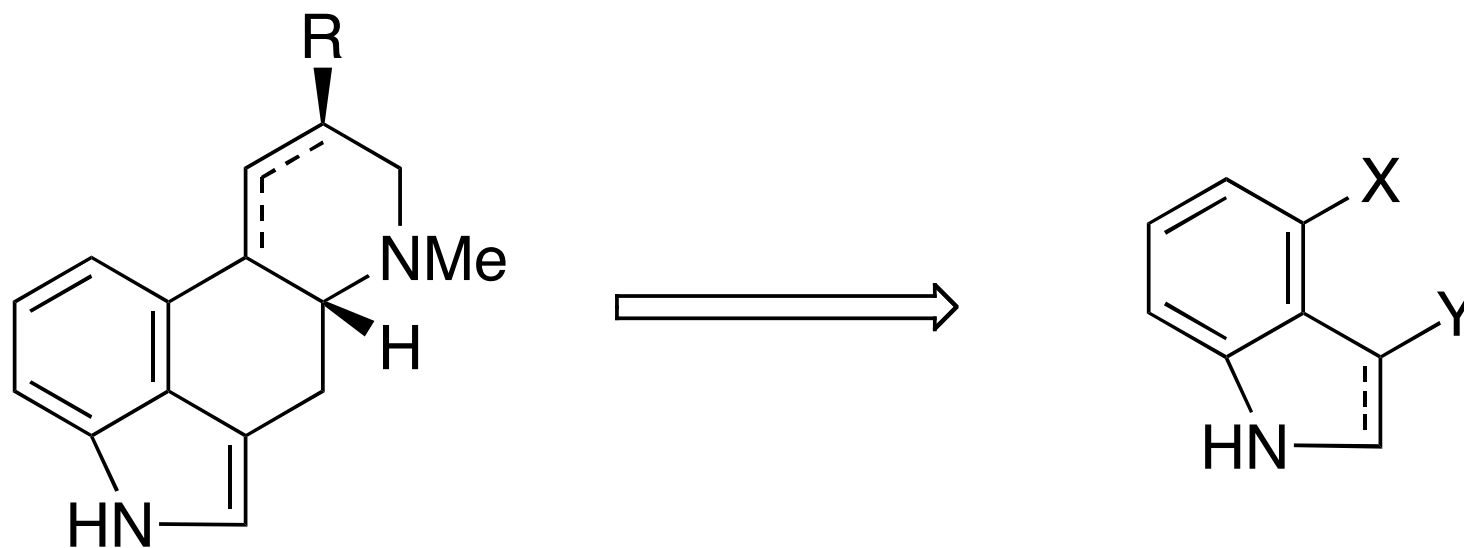


Costaclavine

JOC, 2000, 65, 2368.

Synthetic Trend

Indole core present in starting materials



Acknowledgments

- Prof. Peter Wipf
- Dr. Anthony Cuzzupe
 - (synthesis of D-A precursor, initial D-A studies)
- Wipf Group members