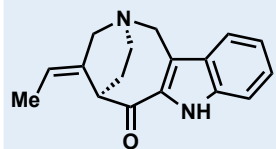
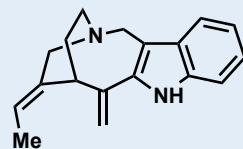
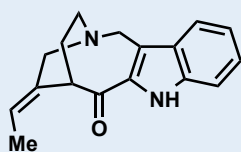


Conolidine

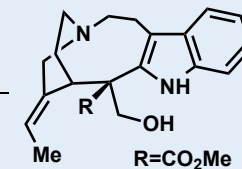
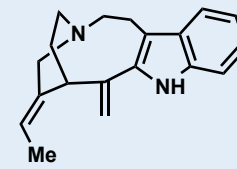
Ibogan and Vallesamine Alkaloids



conolidine



apparicine

stemmadenine
R=CO₂Me

pericine

Isolation:

Kam, T. S. *et al.*, *Chem. Biodivers.*, **2004**, 1, 646.

- Isolated from stem bark of *Tabernaemontana divaricata*
- 1 kg broth yielded 1.3 mg

Biological activity:

Prachayasakul, W. *et al.* *Ind. J. Med. Res.*, **2008**, 127, 317.

- Non-opioid analgesic
- No/low affinity for μ , κ , or δ -opioid receptors
- Formalin test (ED₅₀, mg/kg): 5.6 (morphine 4.6)
- Primary MOA remains unknown



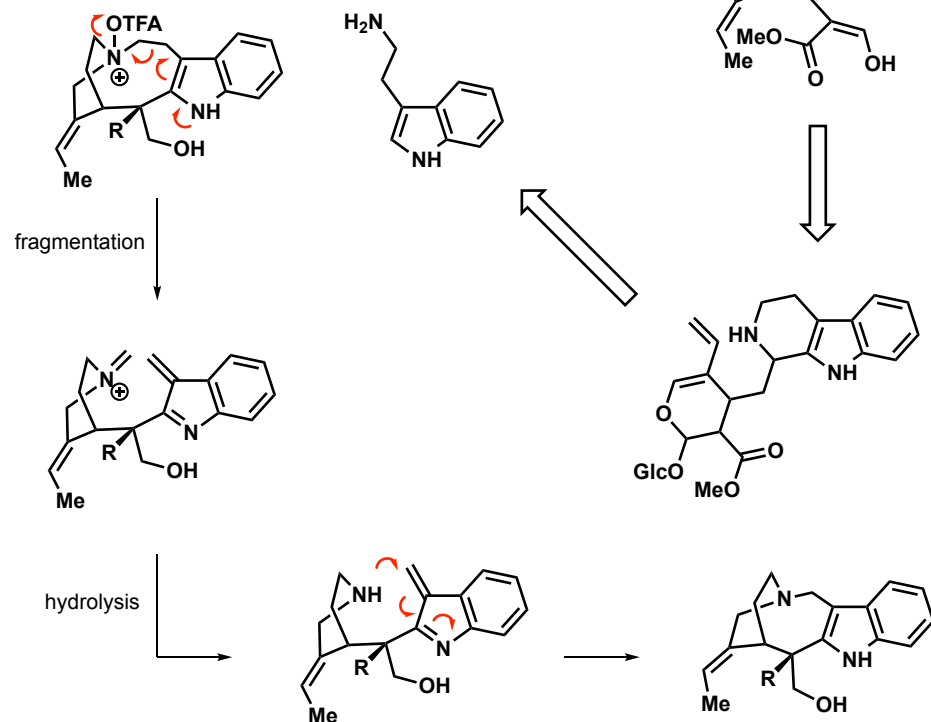
<https://florafaunaweb.nparks.gov.sg/special-pages/plant-detail.aspx?id=4773>

Structure:

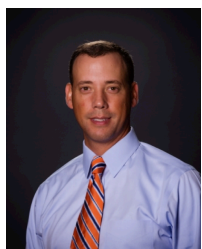
- Indole alkaloid
- 1-azabicyclo[4.2.2] core
- β,γ unsaturated ketone/ exocyclic, trisubstituted olefin

Biosynthesis

- H₂O₂
- (CF₃CO)₂ then NaOH



Scott, A. I. *et al.* *J. Chem. Soc. Chem. Commun.*, **1978**, 947.



Glenn Micalizio

Additional references

Indole alkaloid biosynthesis:

J. Chem. Soc. Chem. Commun., **1970**, 517.

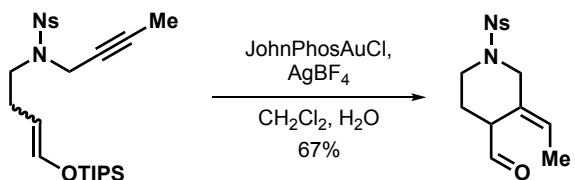
A_{1,3} strain in control of stereoselectivity:

Chem. Rev. **1989**, 89, 1841.

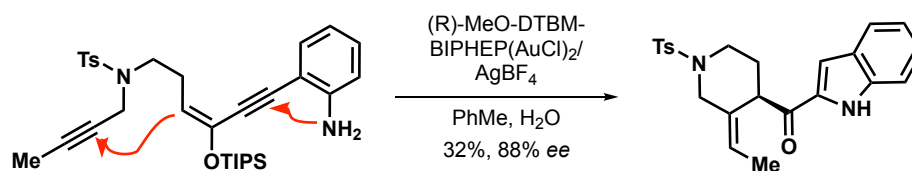
Conolidine

Selected synthetic approaches

Takayama, H. *et al. Tet. Lett.* **2016**, 57, 375.
Key Step: 6-exo-dig [Au] cyclization



Ohno, H. *et al. J. Org. Chem.*, **2016**, 81, 5690.
Key Step: enantioselective 6-exo-dig [Au] cascade/indole synthesis



Total synthesis

Micalizio, G. C. *et al. Nat. Chem.* **2011**, 3, 449.

