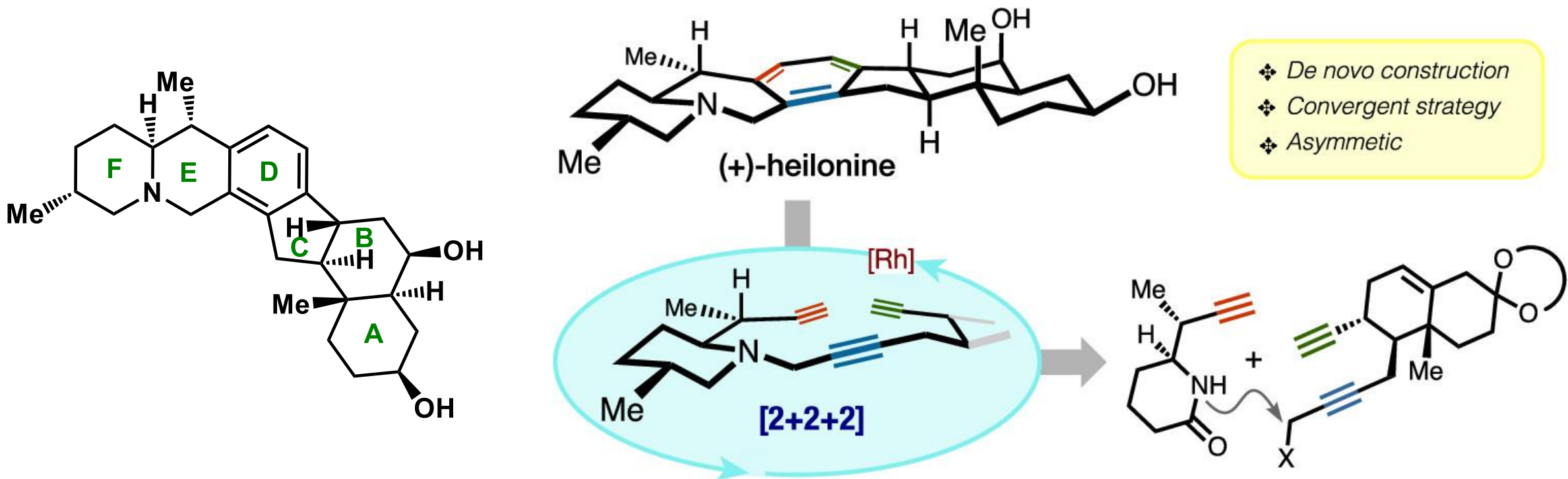


Enantioselective Total Synthesis of (+)-Heilonine

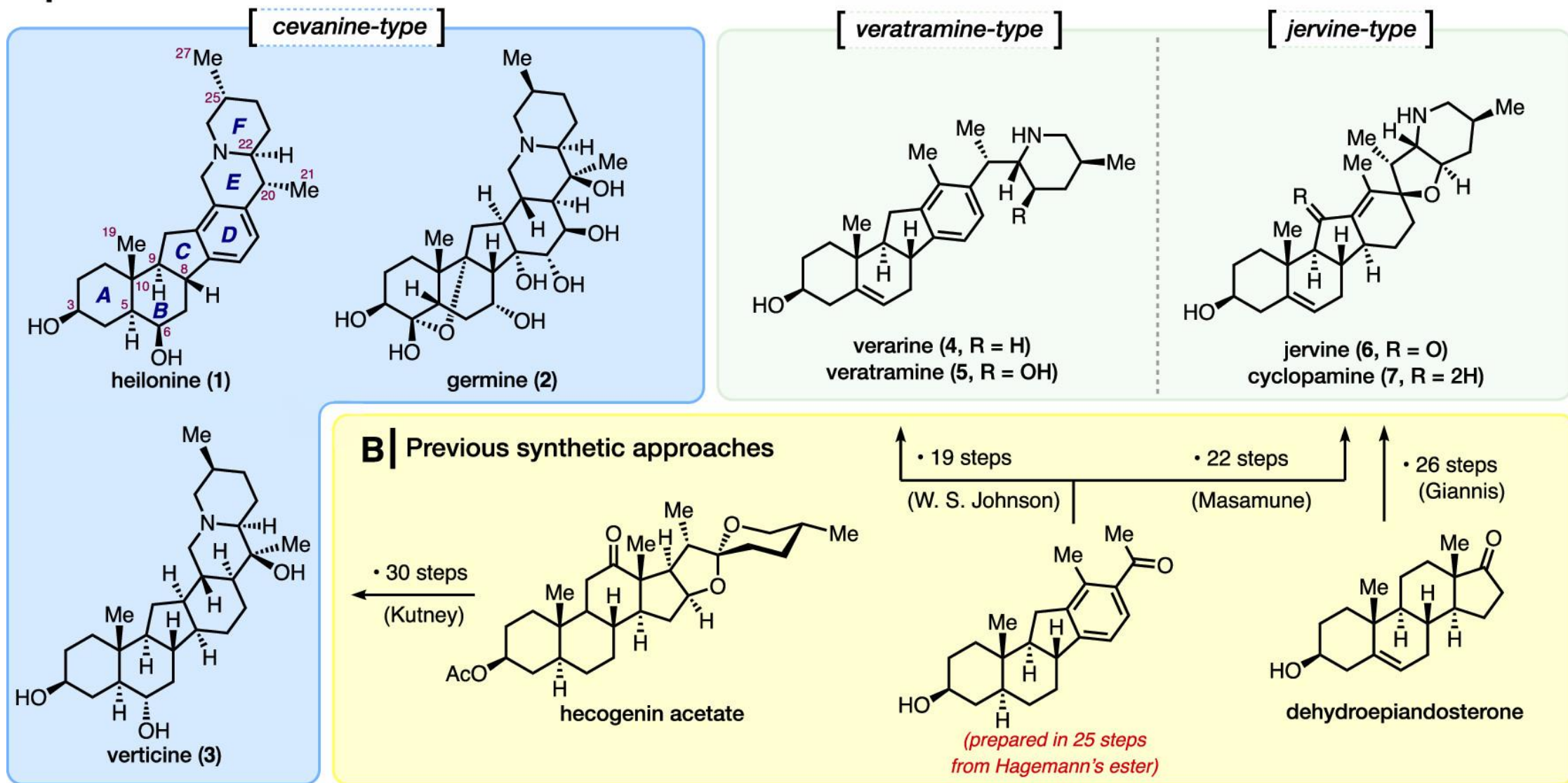
Kyle J. Cassaidy and Viresh H. Rawal



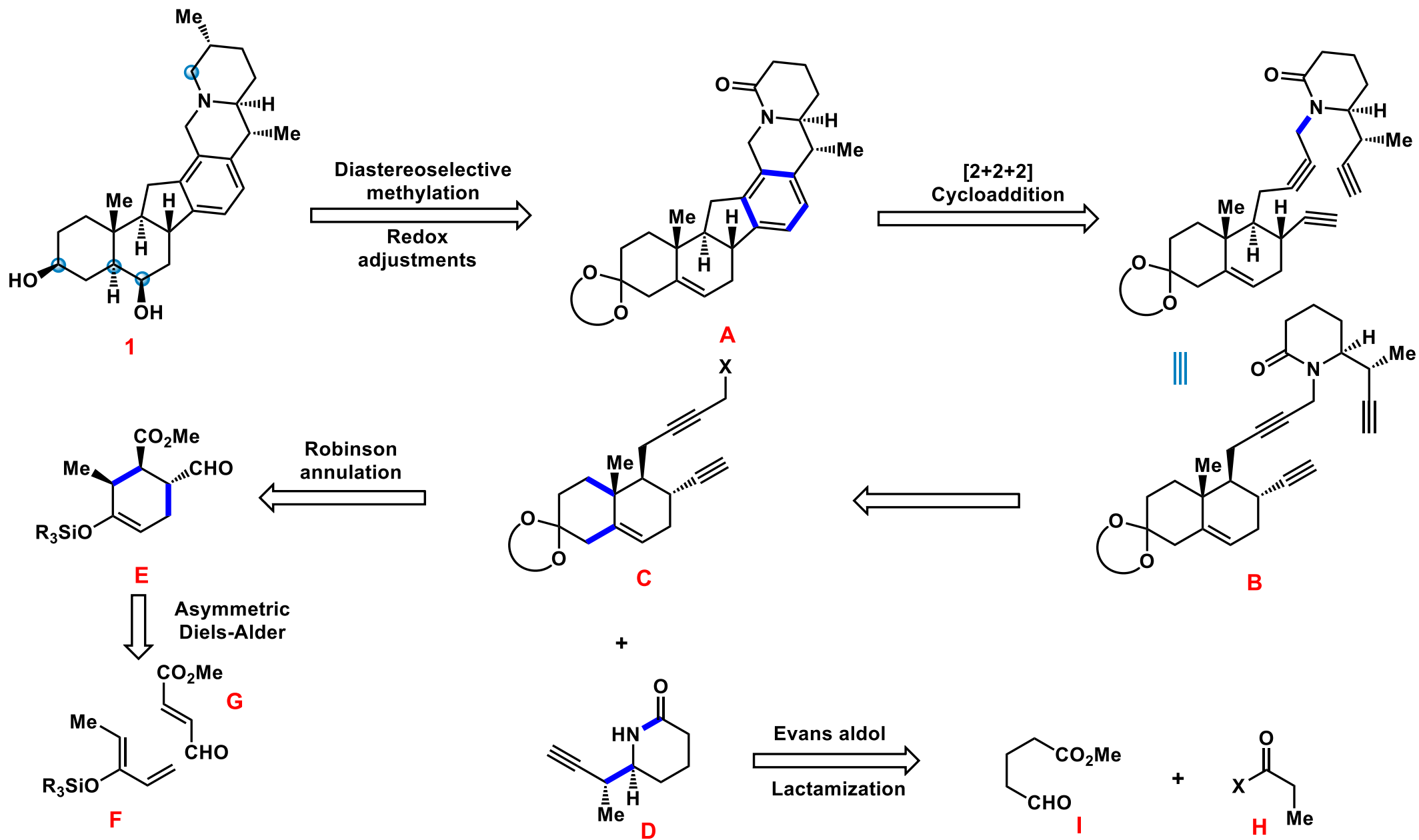
J. Am. Chem. Soc. **2021**, *143*, 16394.

**(A) Representative members of the Veratrum alkaloids of the three structural subtypes and
(B) Previous total syntheses of the Veratrum alkaloids.**

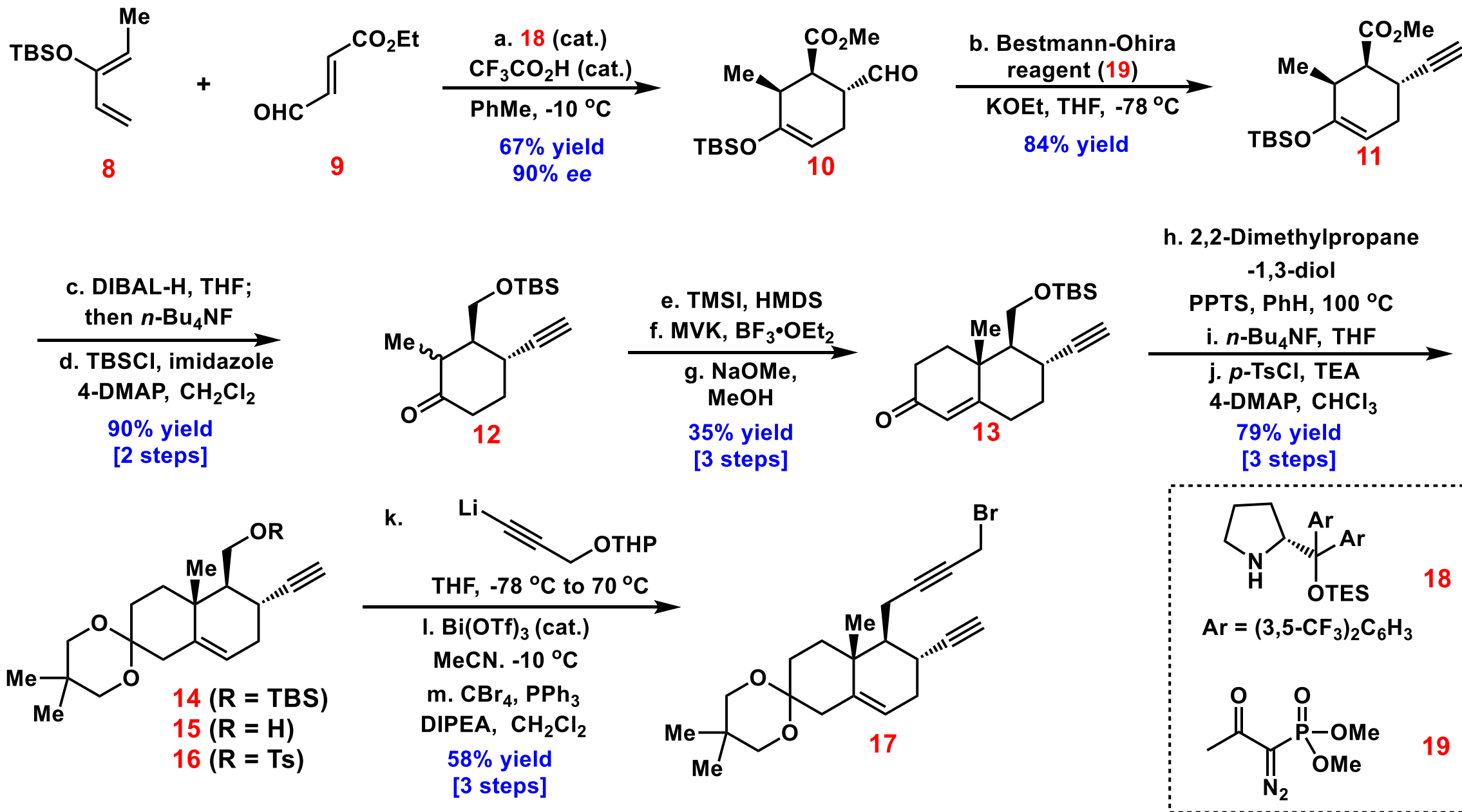
A | Subfamilies of *Veratrum* alkaloids



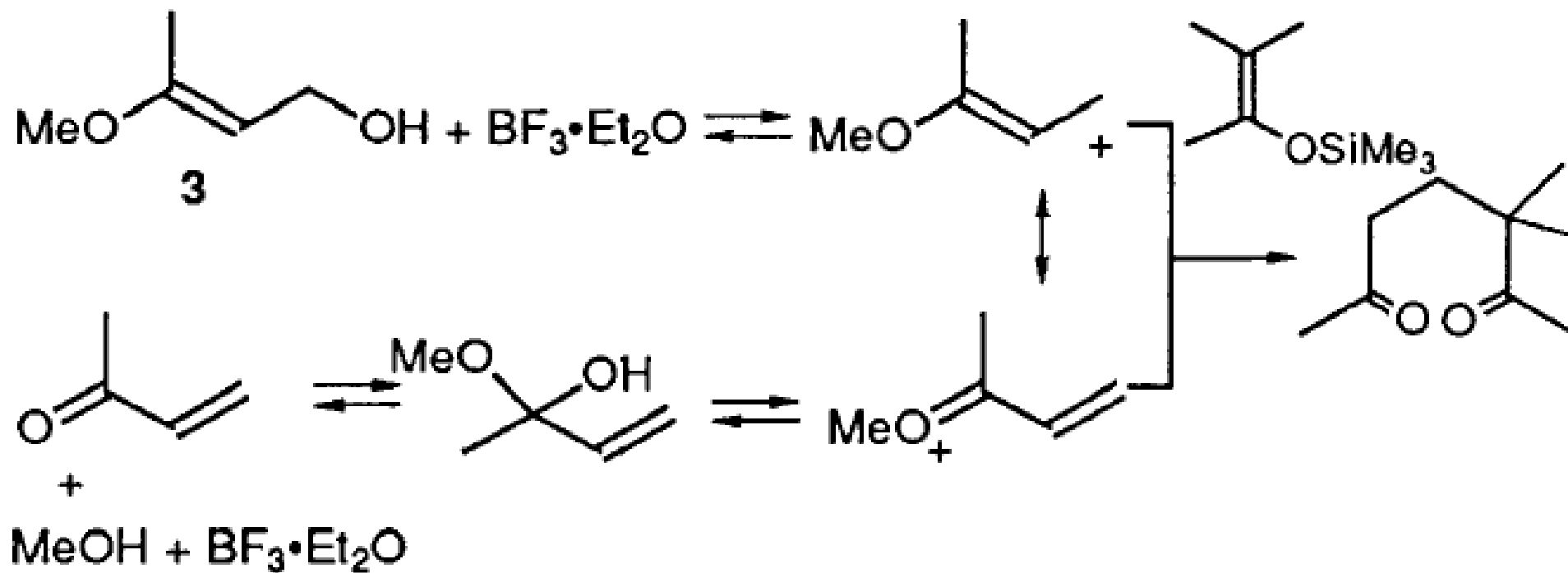
Retrosynthetic Strategy to Heilonine (1) Utilizing a Convergent Fragment Coupling and [2 + 2 + 2] Cycloaddition



Synthesis of Propargyl Bromide Fragment (17)

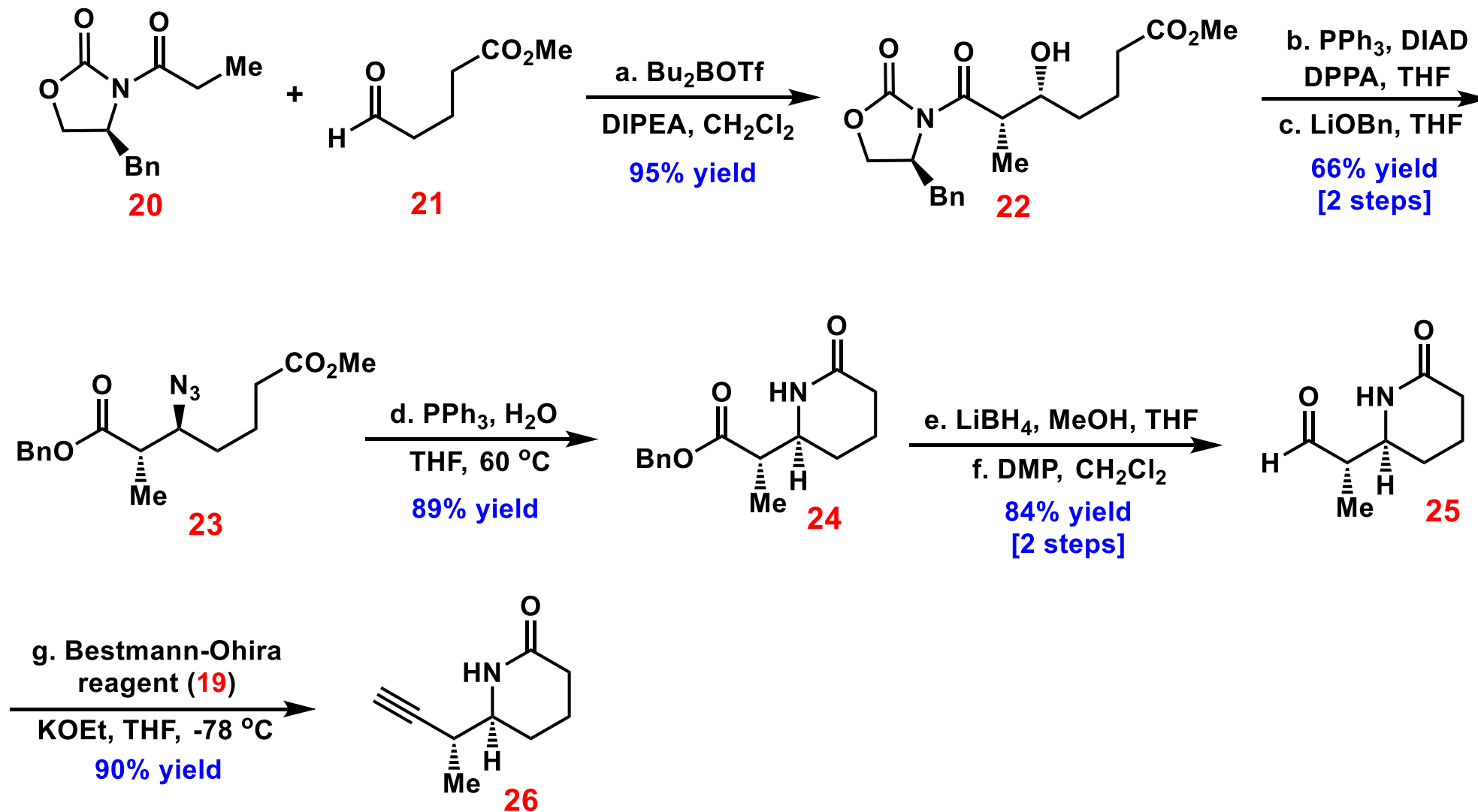


Mukaiyama–Michael reaction with MVK ($\text{BF}_3 \cdot \text{OEt}_2$, *i*-PrOH)

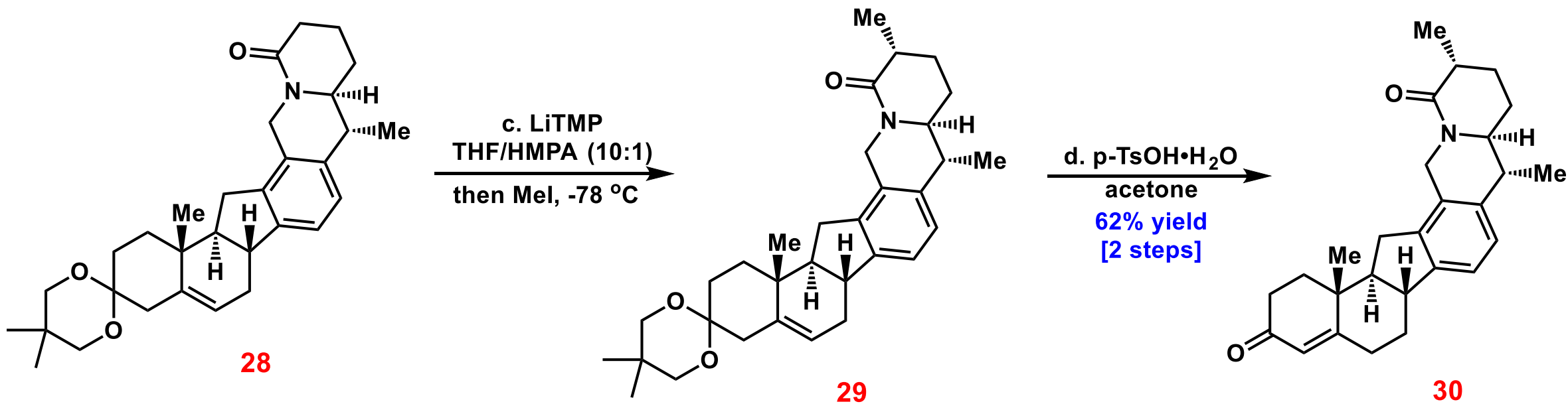
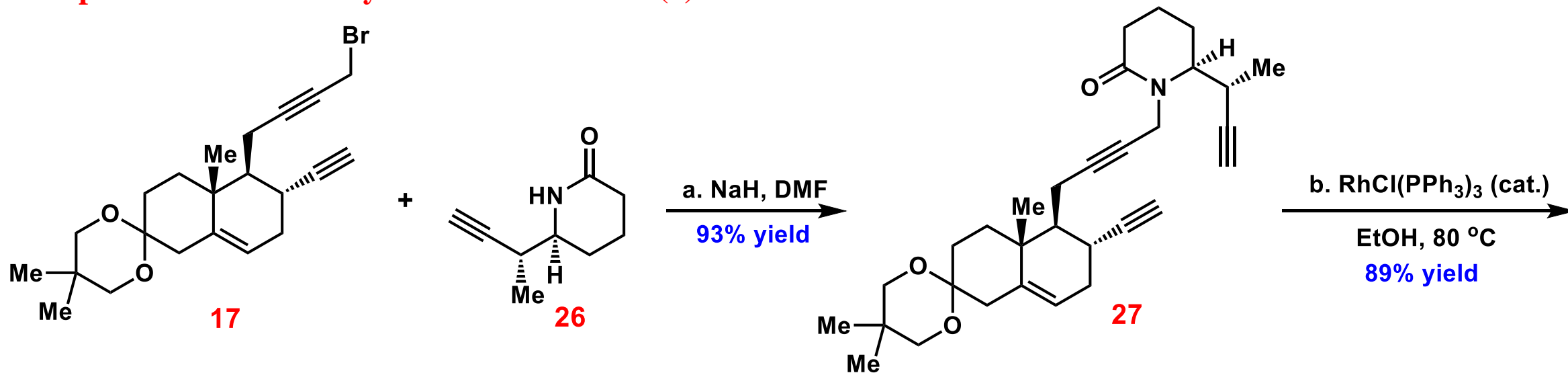


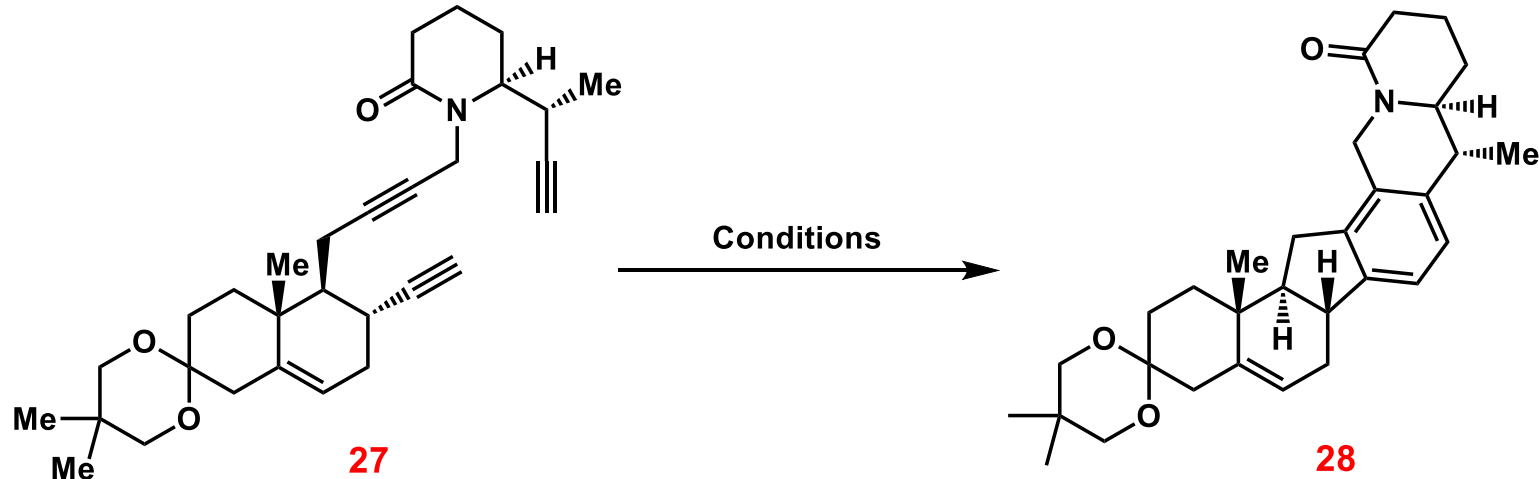
J. Chem. Soc., Perkin Trans. 1, 1992, 387.

Synthesis of Piperidinone Fragment (26)

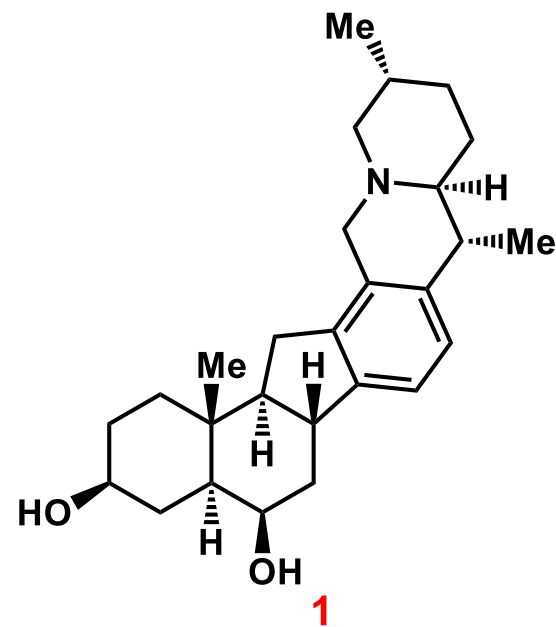
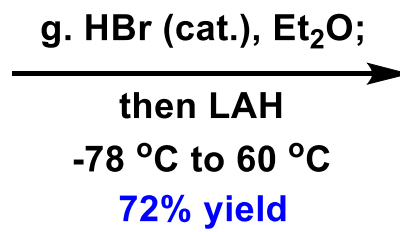
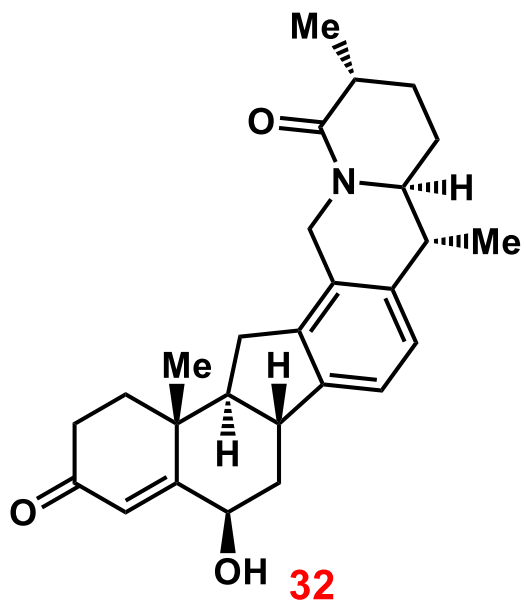
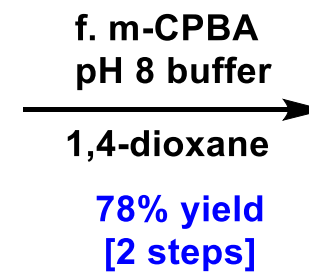
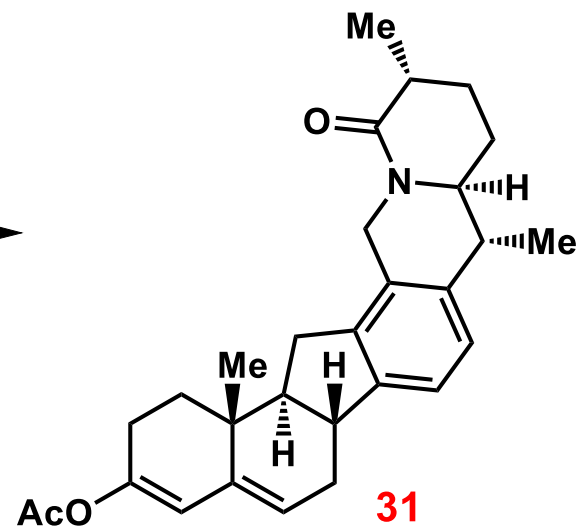
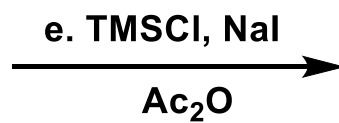
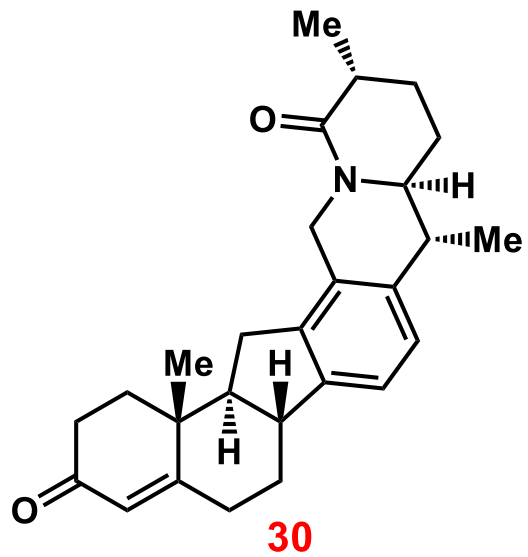


Completion of the Total Synthesis of Heilonine (1)





<i>Entry</i>	<i>Conditions</i>	<i>Result</i>
1.	RhCl(PPh ₃) ₃ (5 mol%) CH ₂ Cl ₂ , RT	18% yield
2.	RhCl(PPh ₃) ₃ (5 mol%) DCE, 80 °C	43% yield
3.	RhCl(PPh ₃) ₃ (5 mol%) EtOH, 80 °C	57% yield
4.	RhCl(PPh₃)₃ (10 mol%) EtOH, 80 °C	89% yield
5.	Cp* ⁺ Ru(cod)Cl (20 mol%) DCE, 80 °C	67% yield



- intramolecular [2 + 2 + 2] cycloisomerization**
- organocatalytic enantioselective Diels–Alder reaction**
- late-stage diastereoselective methylation of a
heptacyclic intermediate**
- one-pot acid-catalyzed isomerization–global reduction**