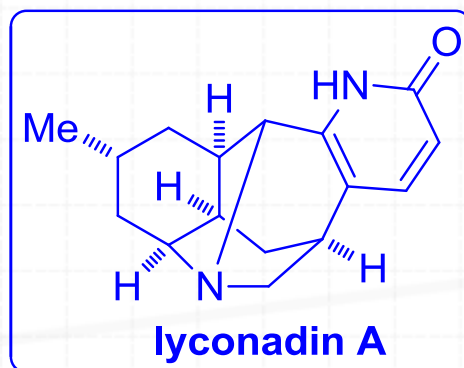


Total Syntheses of Lyconadins A–C



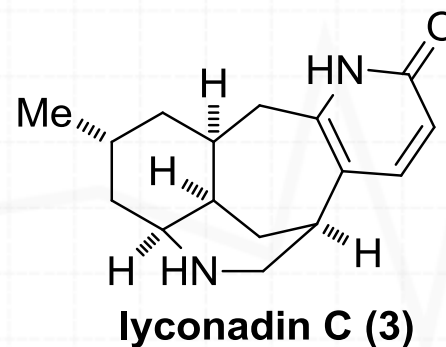
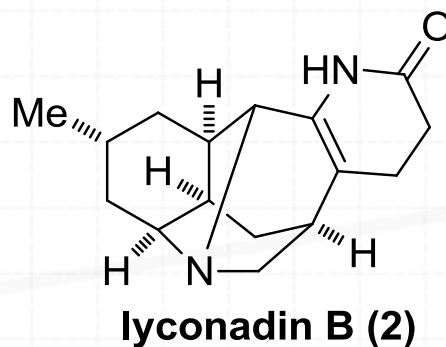
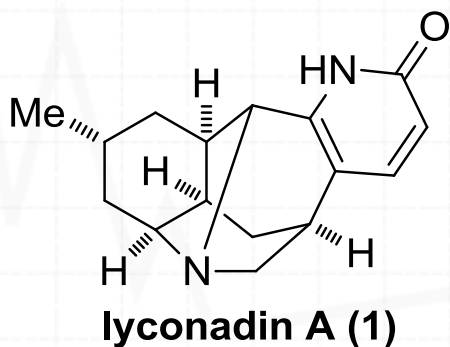
Nishimura, T.; Unni, A. K.; Yokoshima, S.; **Fukuyama**, T.
J. Am. Chem. Soc. **2013**, *135*, 3243-3247.



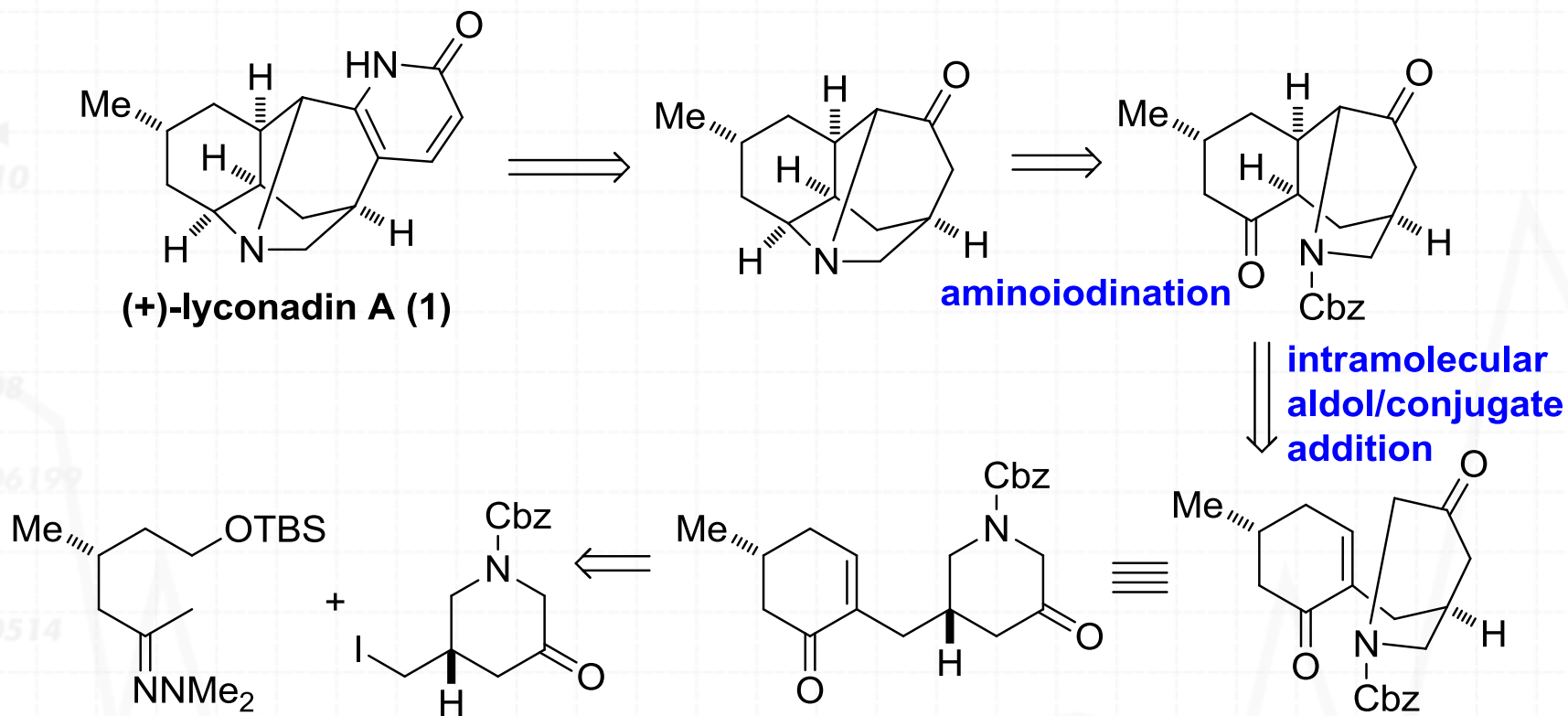
Current literature
Gong Xu
2013-06-13

About Lyconadin A and related alkaloids

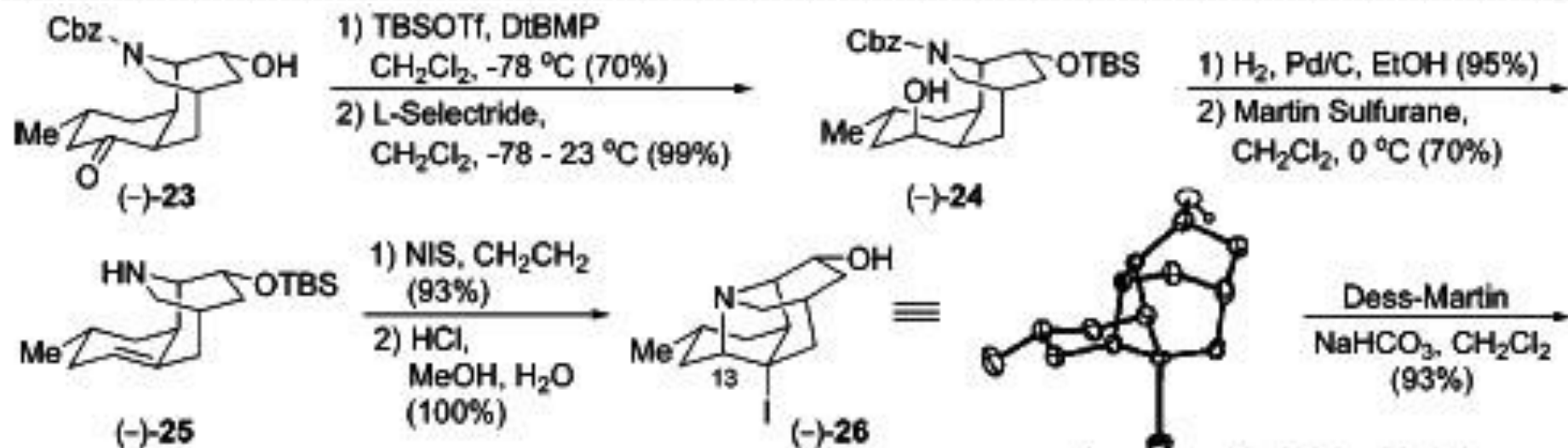
- Lycopodium alkaloids;
- Isolated from **Lycopodium complanatum** in 2001 by Kobayashi et al;
- **Pentacyclic** skeleton: including a **2-pyridone ring**, **six** stereogenic centers, and a **tertiary amine** at a bridgehead.



First total synthesis of (+)-Lyconadin A by Smith



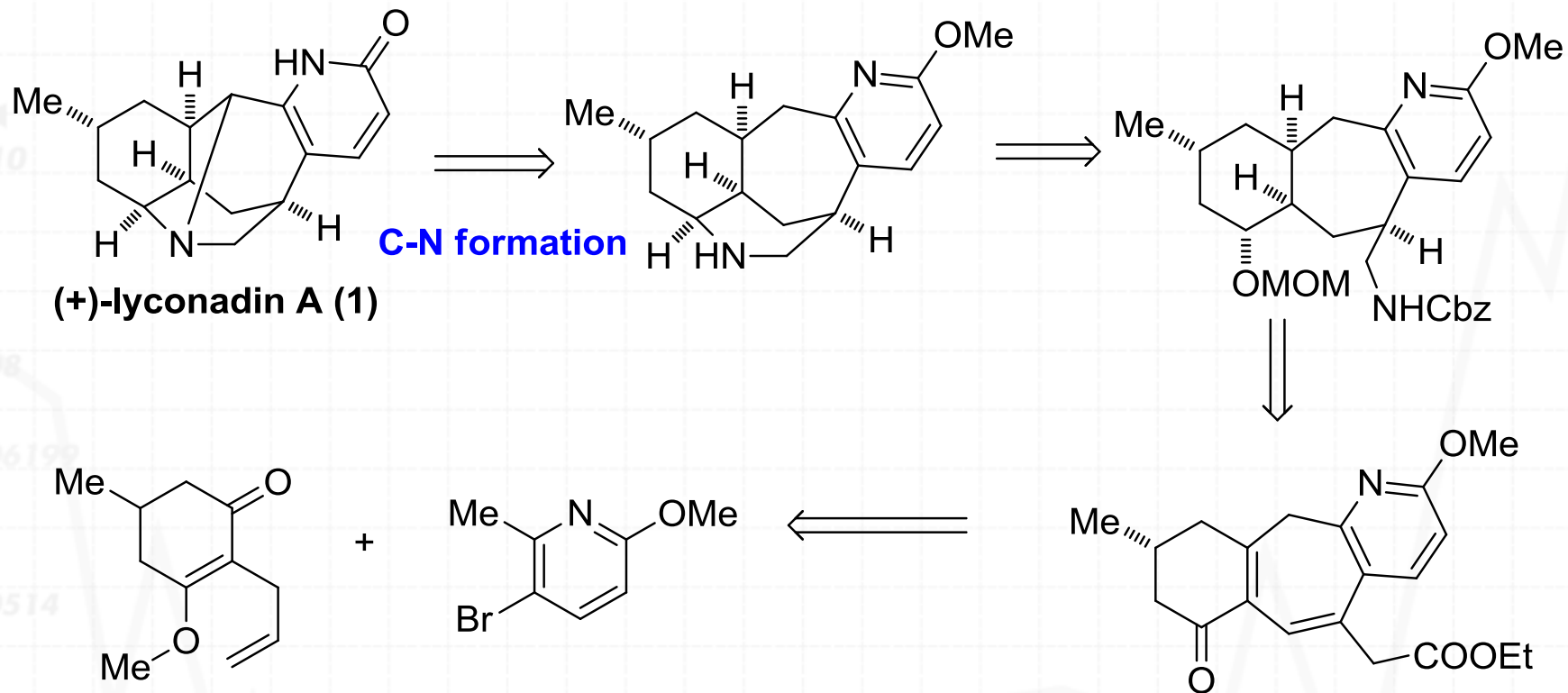
Generation of the C(13)-N bond



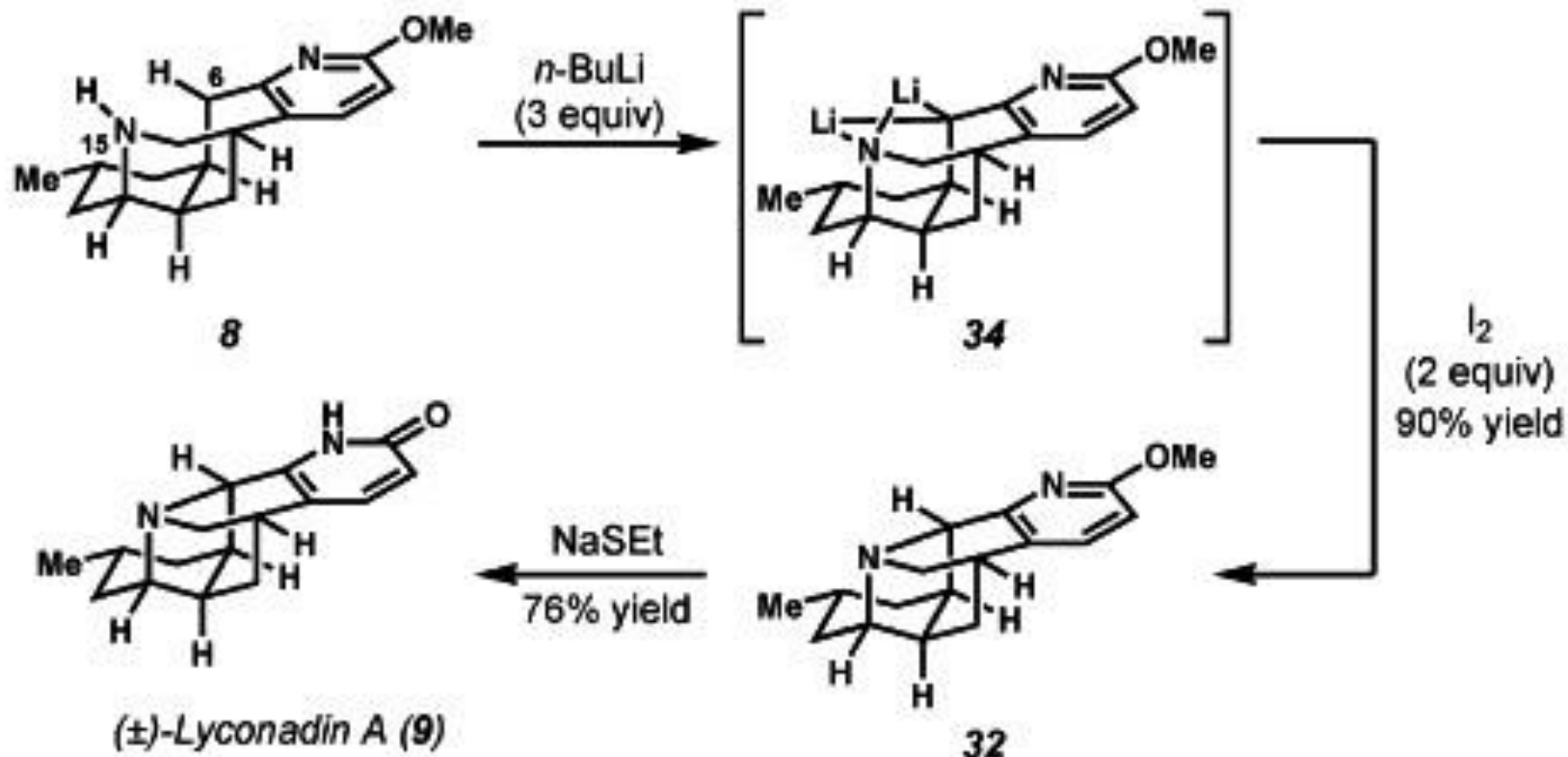
0.0514

0.02

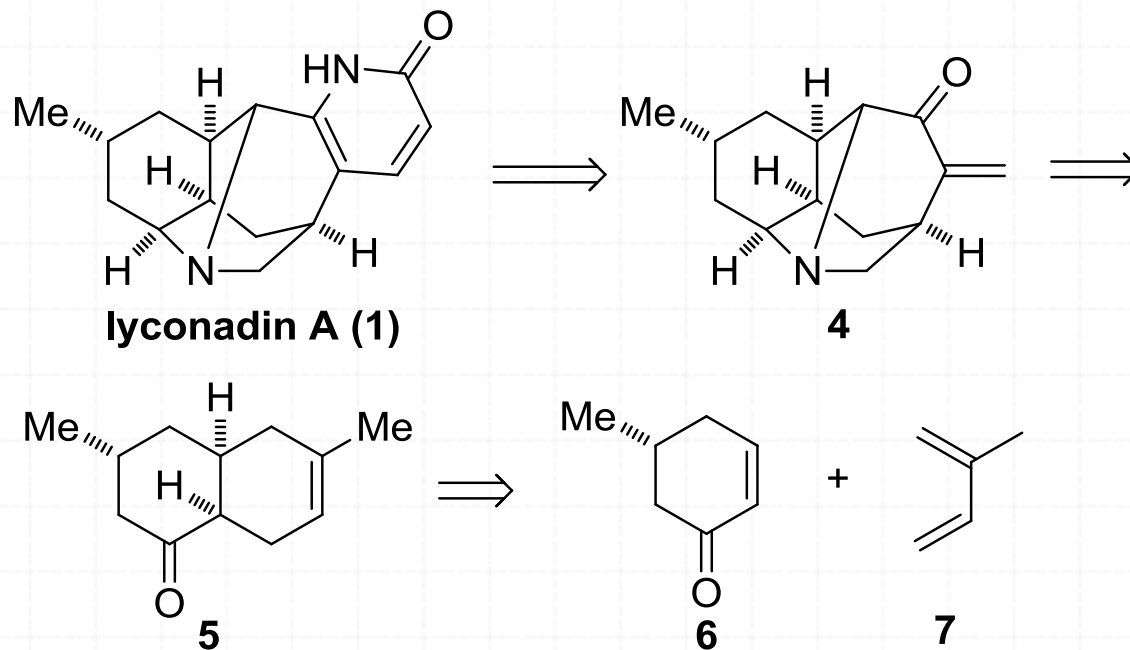
Total synthesis of (+)-Lyconadin A by Sarpong



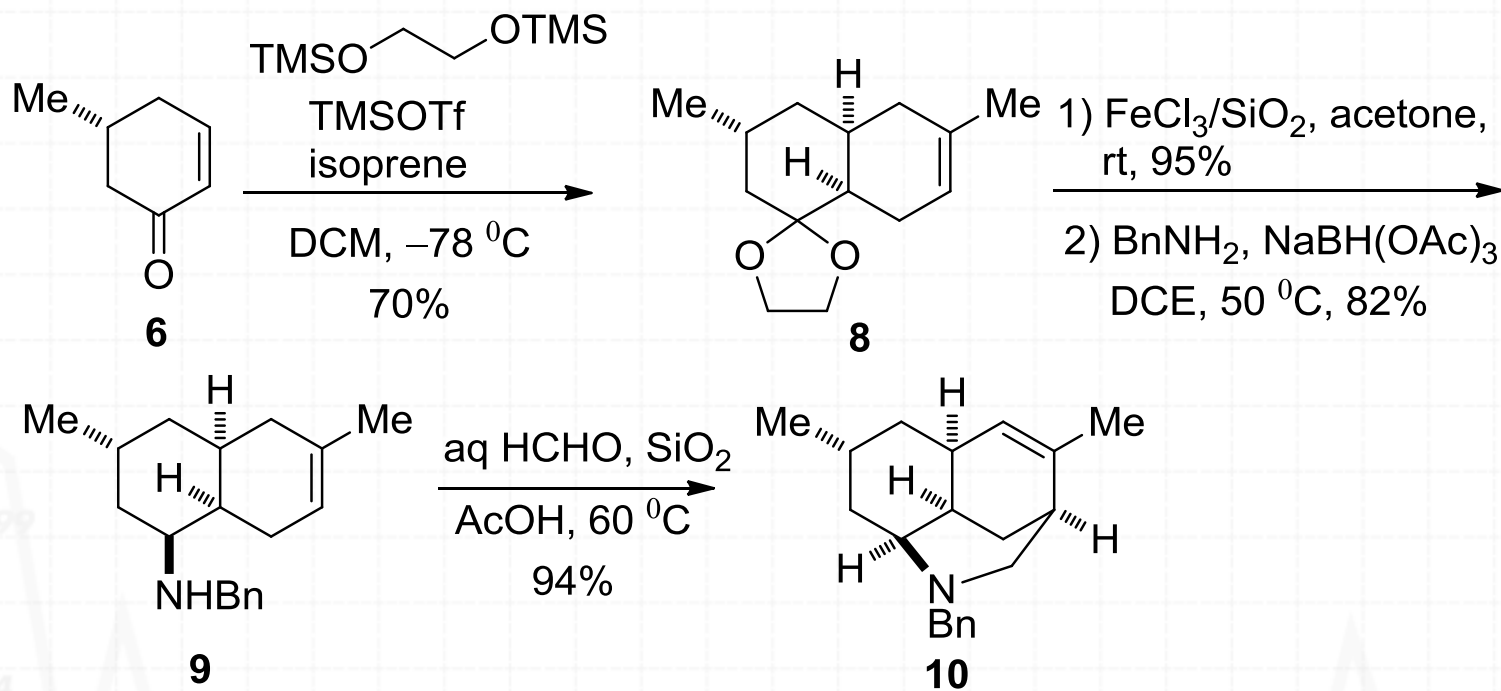
Direct C-N bond forming approach



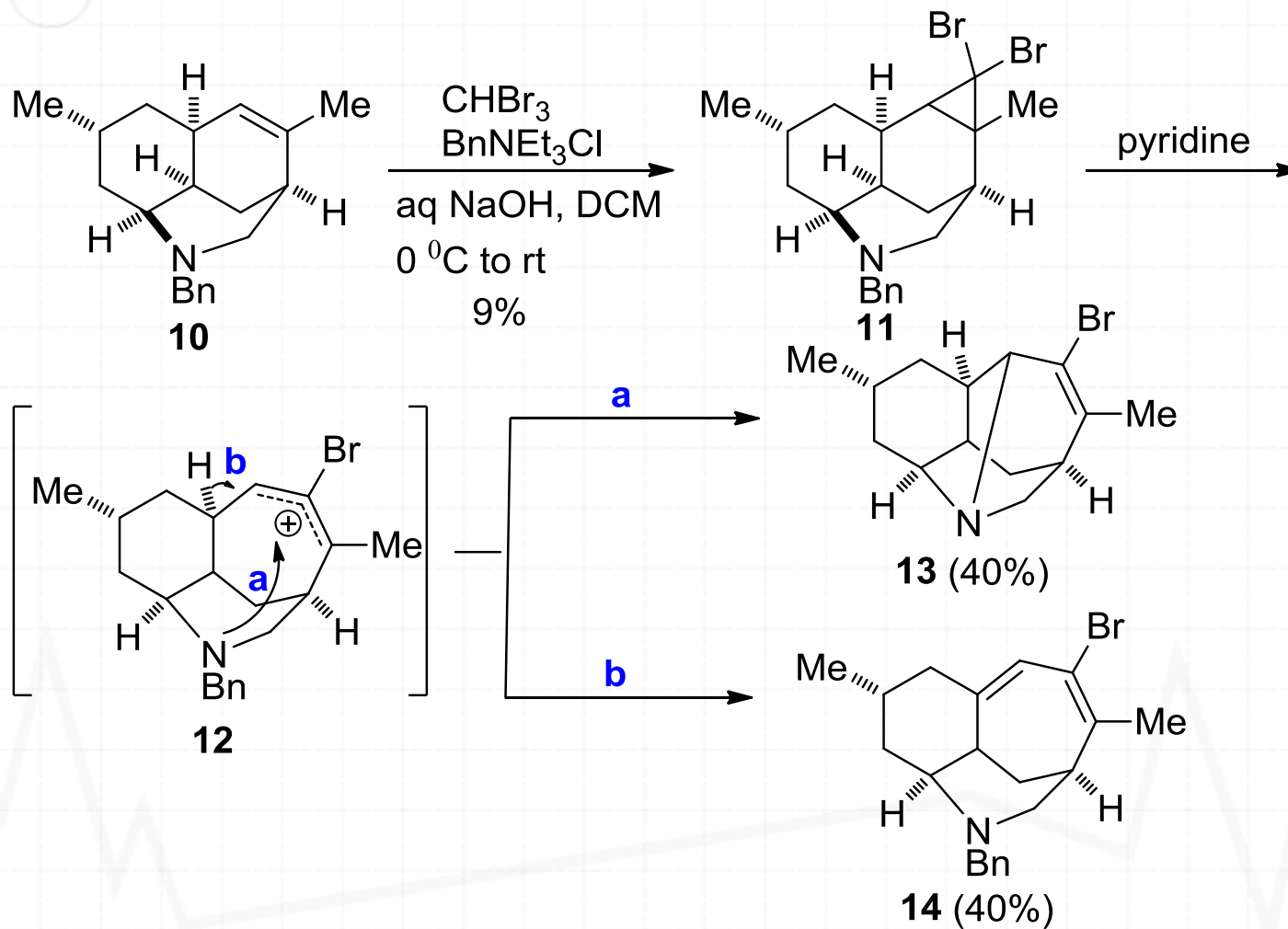
Fukuyama's retrosynthesis



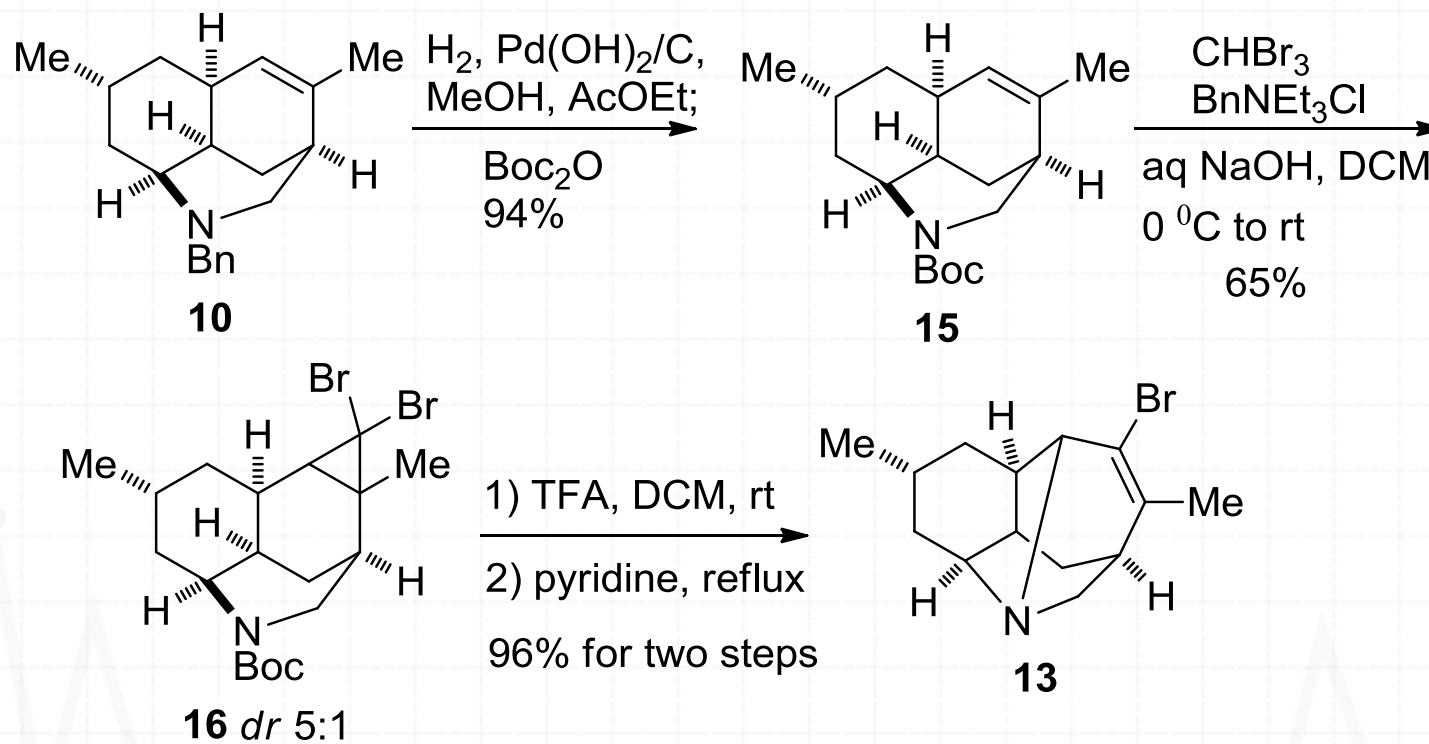
Diels-Alder Reaction and Aza-Prins Reaction



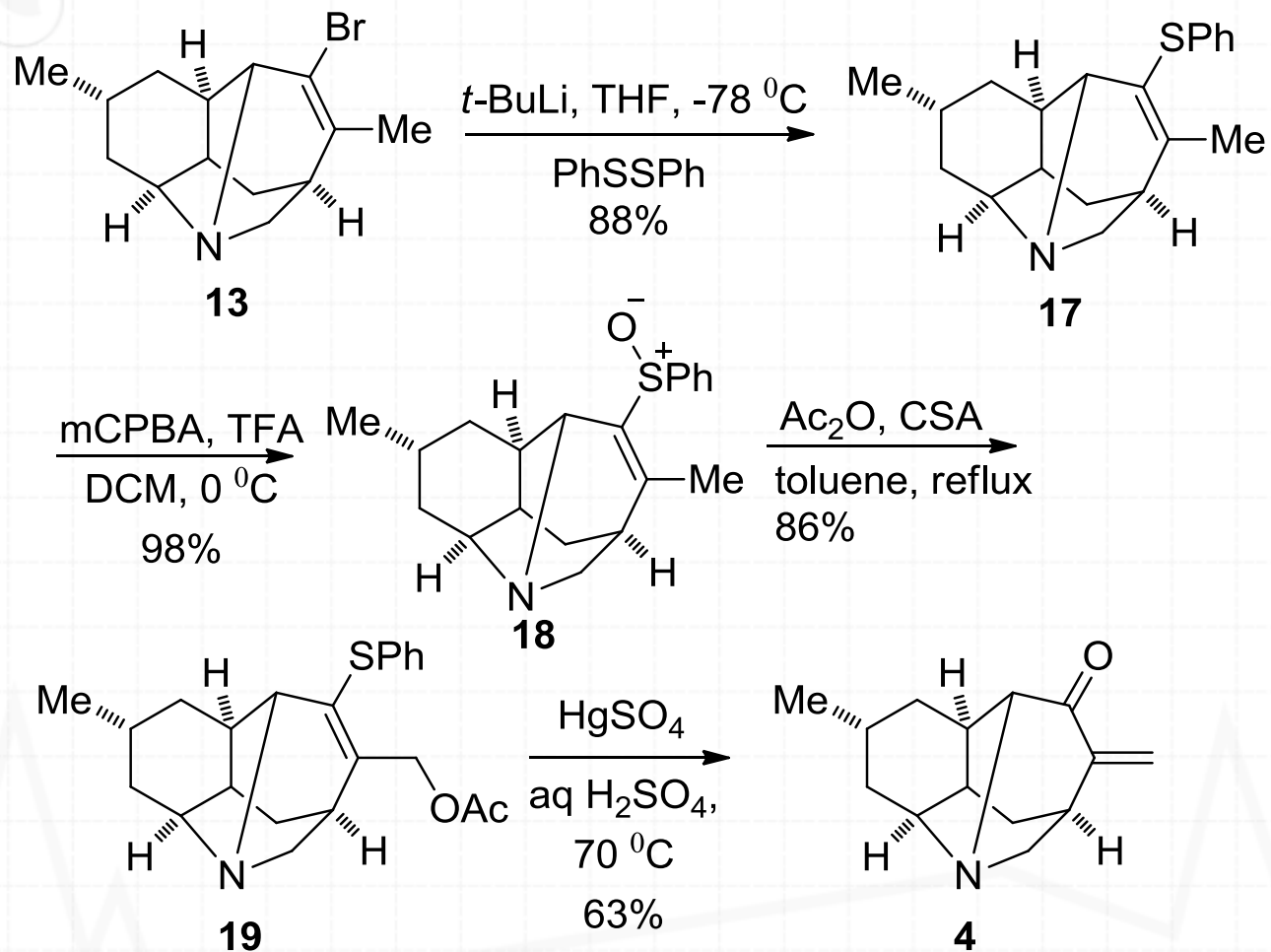
Attempted Formation of Tetracyclic Core



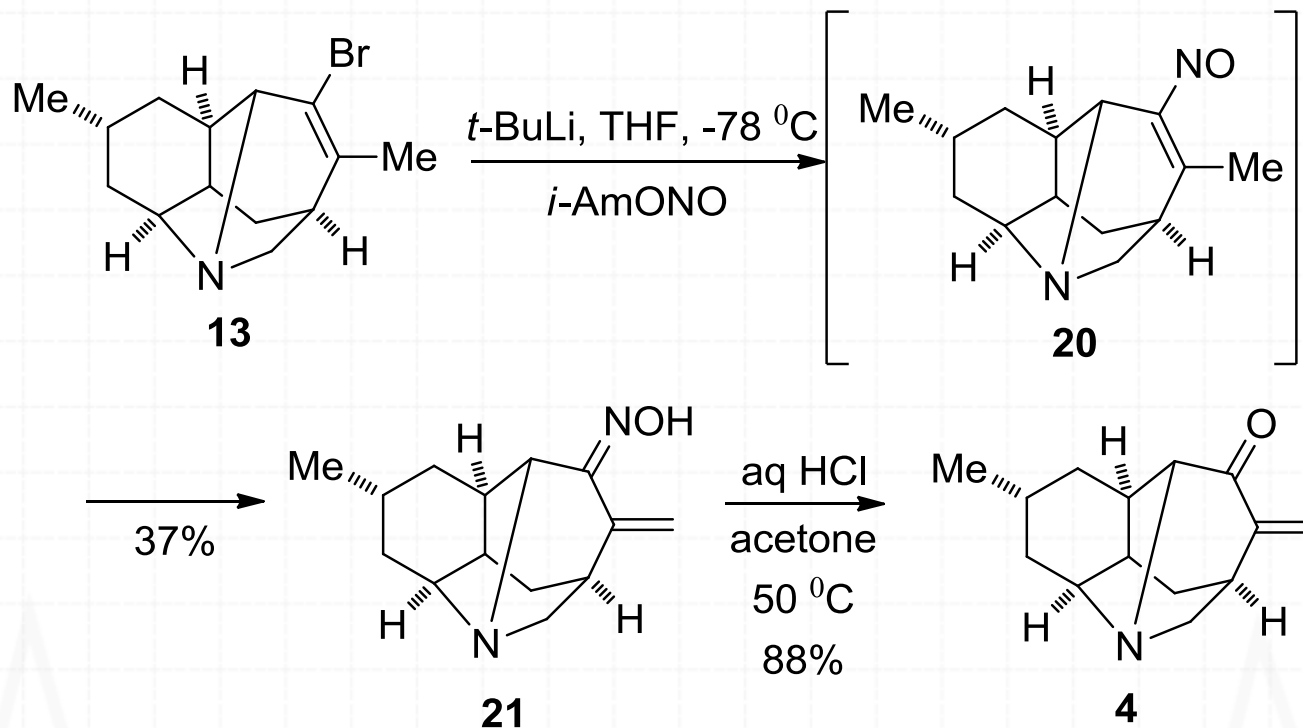
Construction of Tetracyclic Skeleton



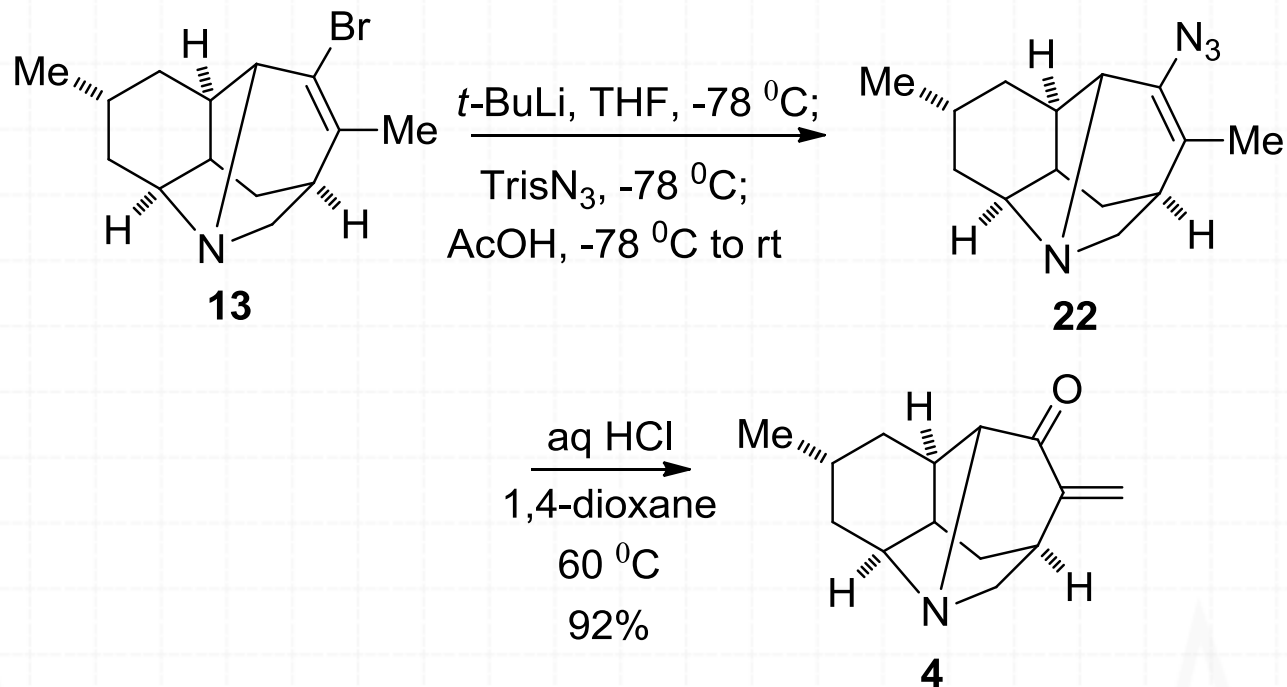
Transformation into Enone via Vinylogous Pummerer Rearrangement



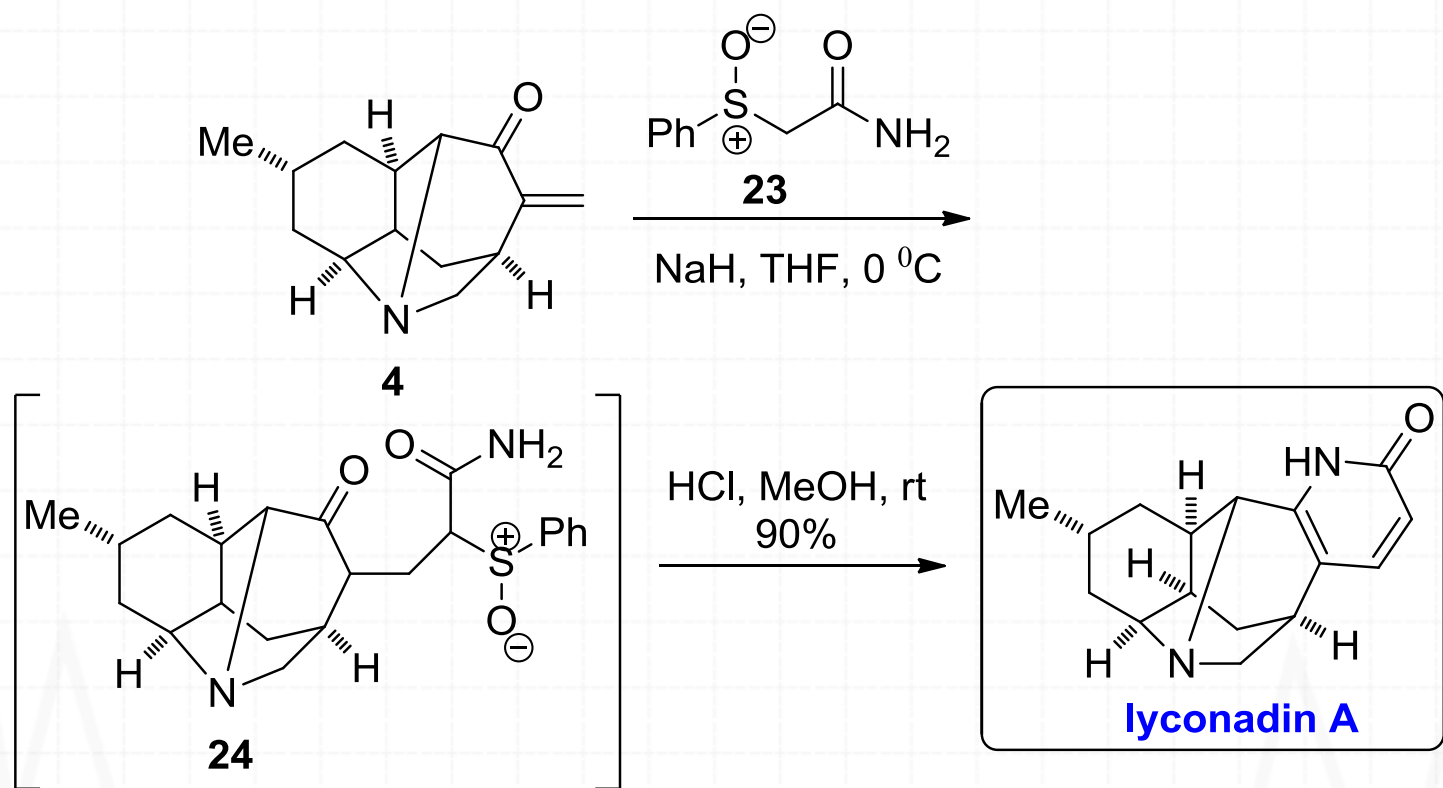
Transformation into Enone through an Oxime



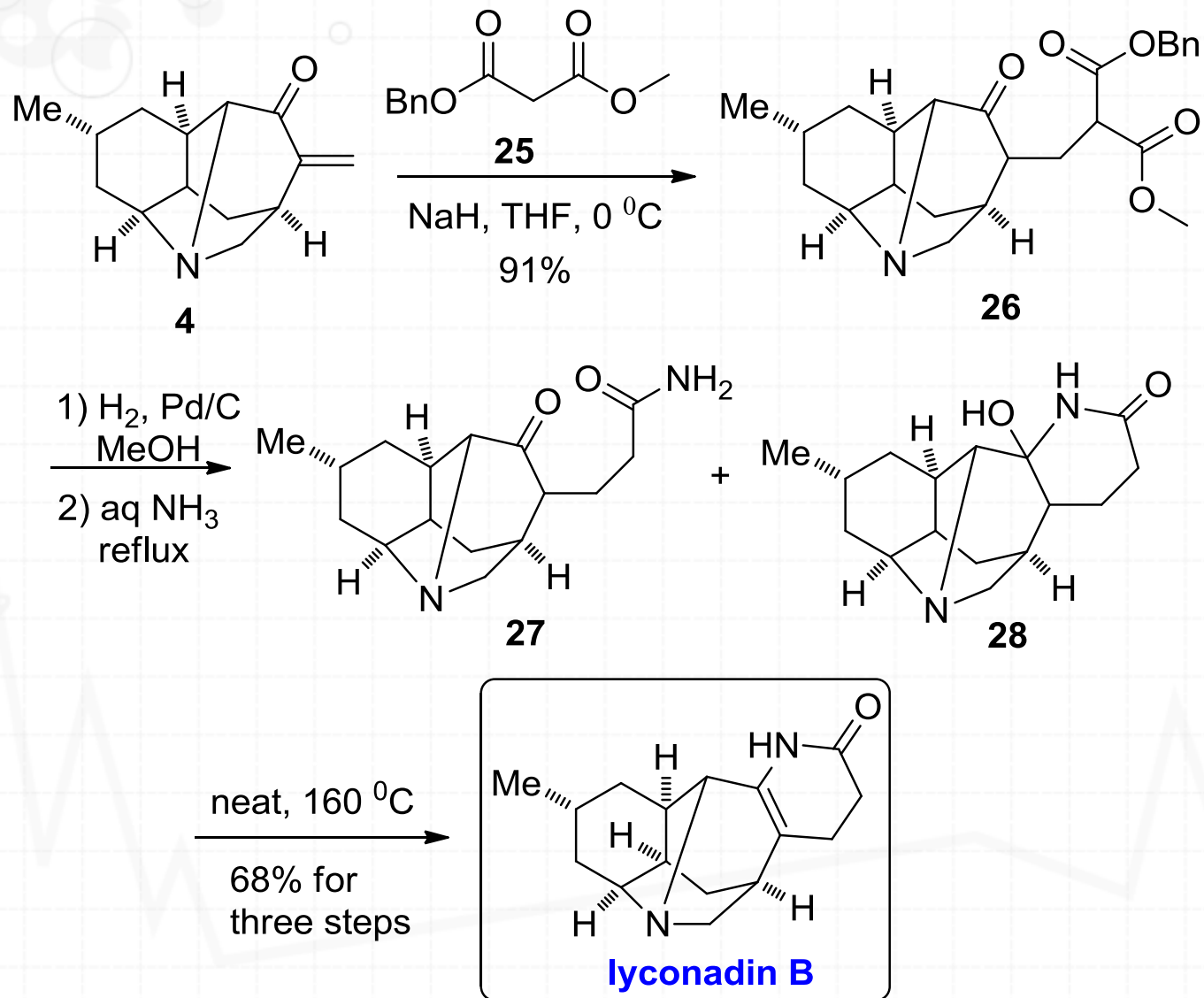
Transformation into Enone through an Azide



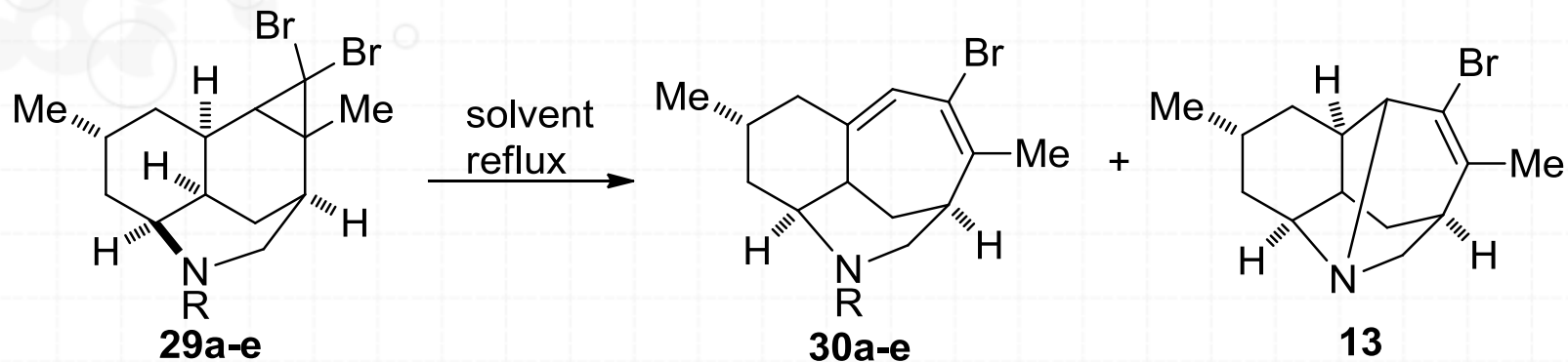
Completion of Synthesis of Lyconadin A



Synthesis of Lyconadin B



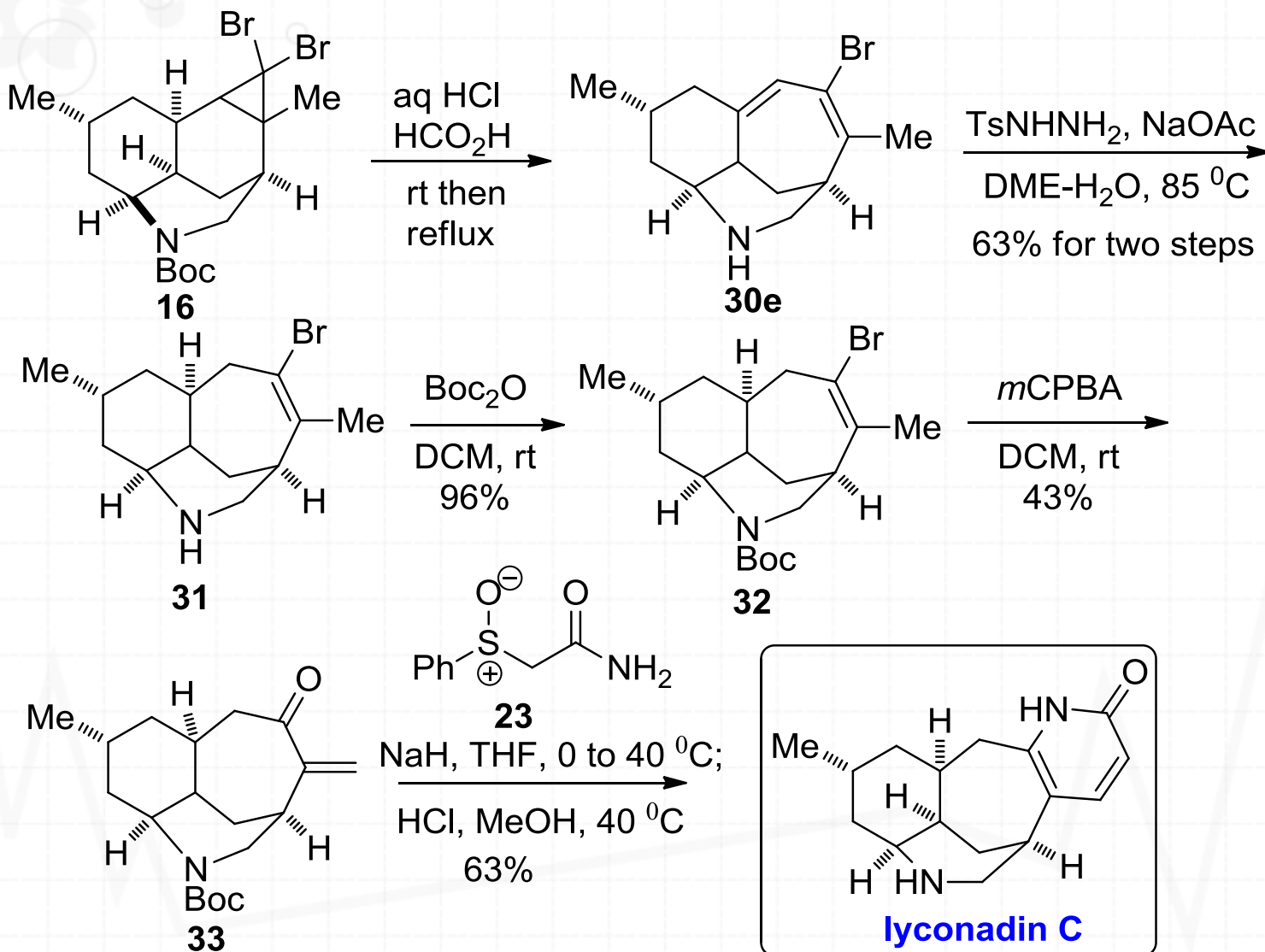
Synthesis of Lyconadin C - Cleavage of Dibromocyclopropane Ring



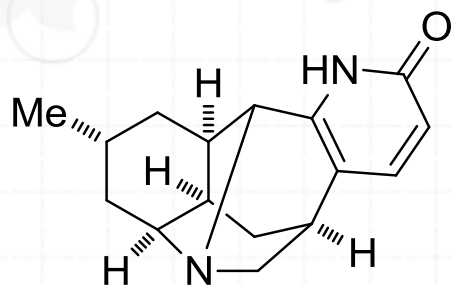
entry	R	substrate	solvent	yield ^a (%)	
				30a-e	13
1	Boc	29a	pyridine	20	46
2	Ts	29b	AcOH	43	51
3	<i>p</i> -Ns	29c	AcOH	51	42
4	<i>o</i> -Ns	29d	AcOH	89	trace
5	H	29e·HCl	AcOH	62	20
6	H	29e·HCl	HCO ₂ H	74	<i>b</i>

^aIsolated yields. ^bCompound 13 could not be detected.

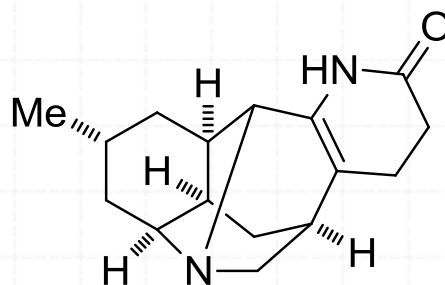
Synthesis of Lyconadin C



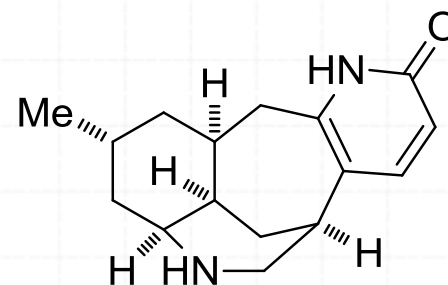
Summary



lyconadin A (1)



lyconadin B (2)



lyconadin C (3)

Features:

A facile construction of the highly fused tetracyclic skeleton through a combination of an **aza-Prins reaction** and an **electrocyclic ring opening**, followed by formation of a C–N bond.



Thank you!