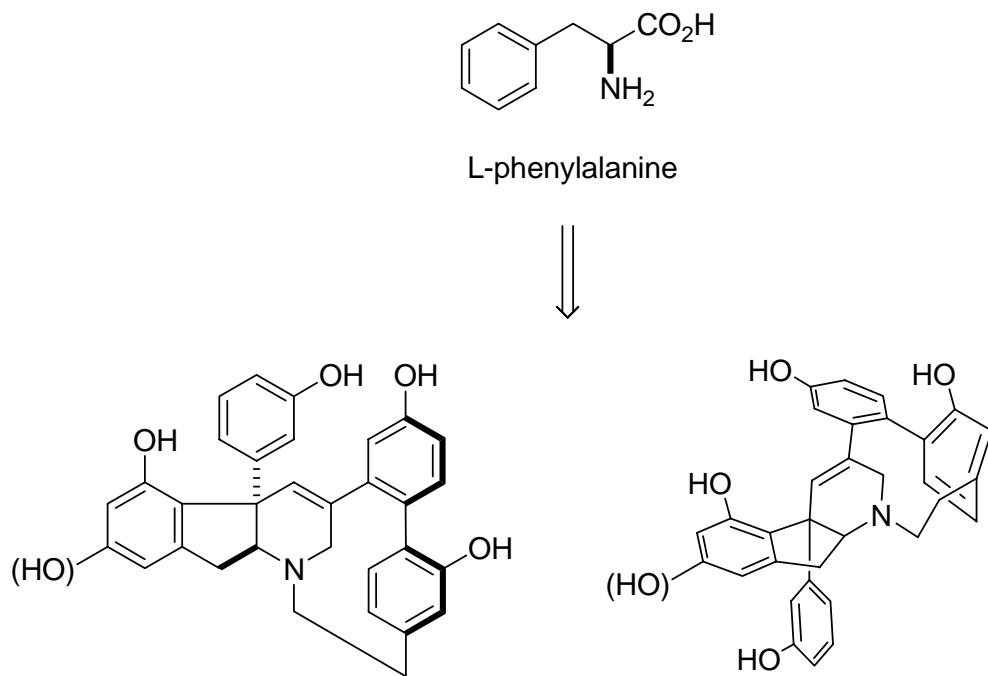
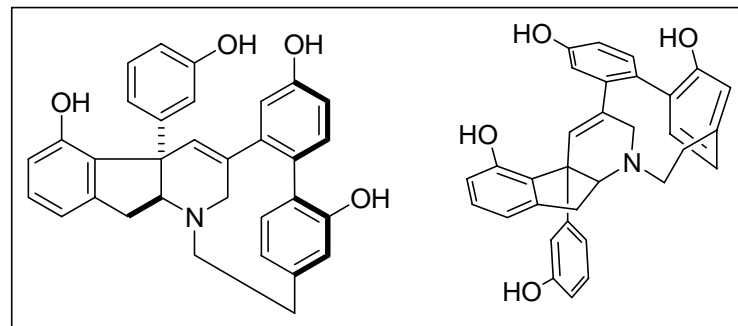


# Biogenetic hypothesis and first steps towards a biomimetic synthesis of haouamines

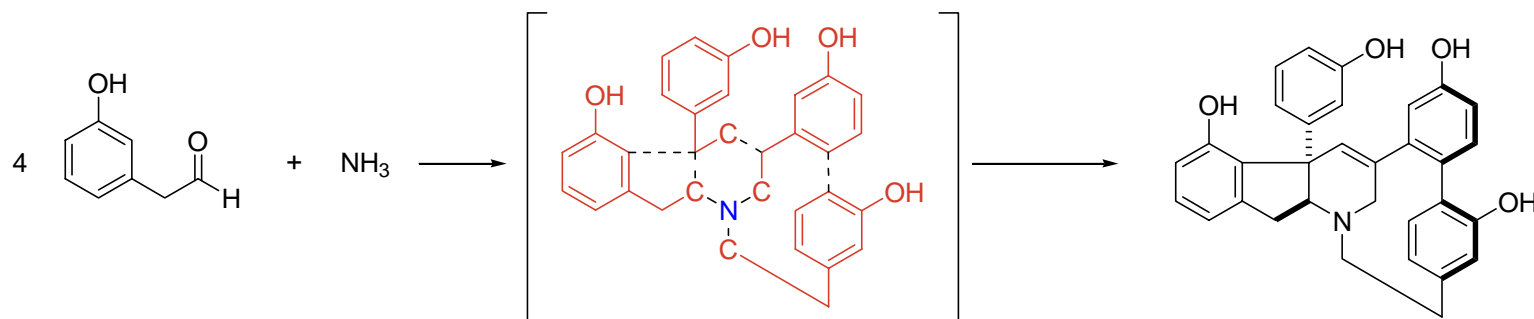
Gravel, E.; Poupon, E. and Hocquemiller, R. *Chem. Commun.*, **2007**, 719.



# Previously Proposed Biosynthetic Pathways of the Haouamines



## Baran's Proposed Biosynthesis



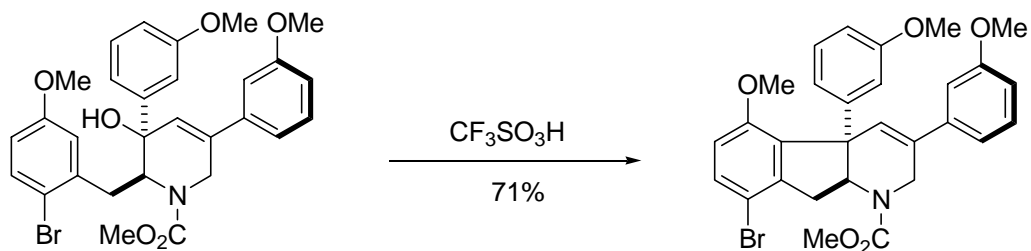
-Condensation events on ammonia equivalent

-Oxidative events forming remaining bonds

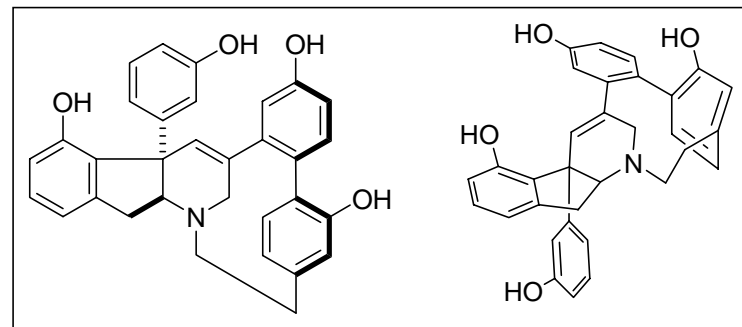
*-Experimental attempts failed.*

Baran and Burns *J. Am. Chem. Soc.* **2006**, 128, 3908

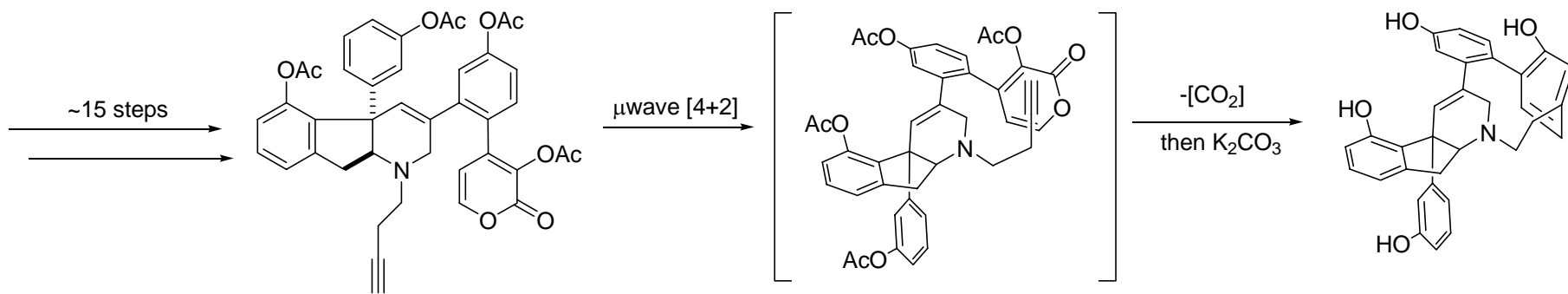
-Only convincing empirical evidence for formation of C24-C26 bond.



## Previous Syntheses of the Haouamines

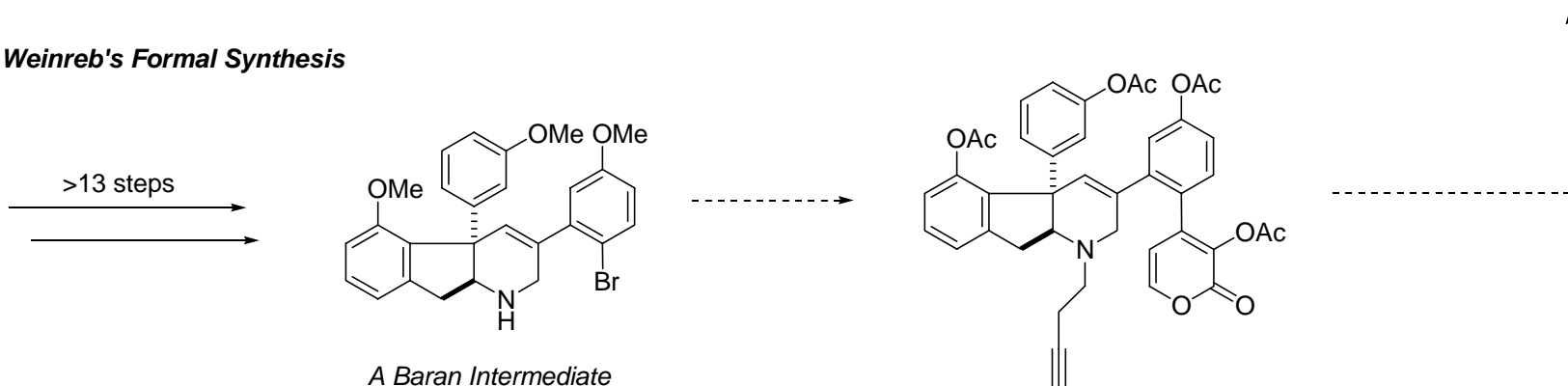


### The Baran Route

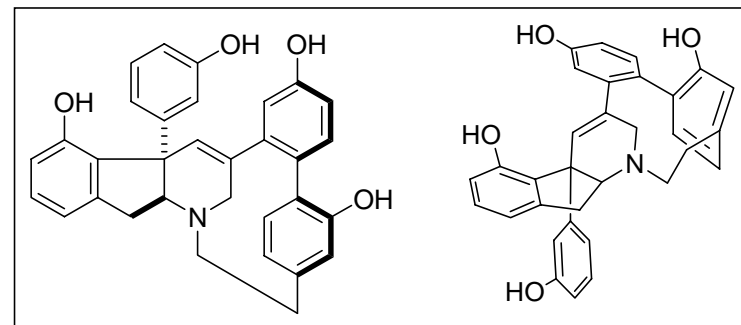
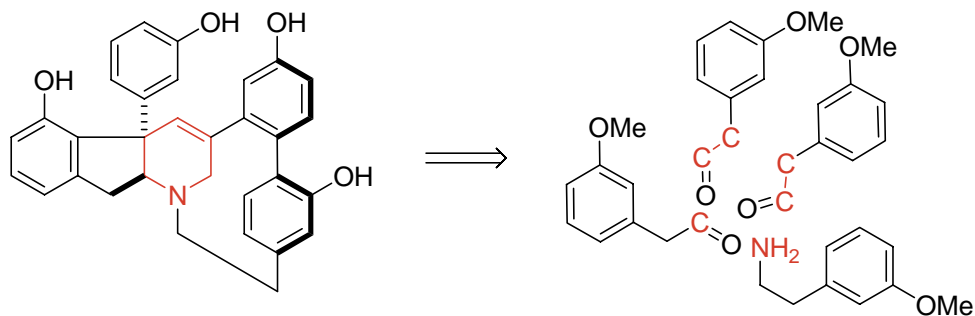


Baran and Burns *J. Am. Chem. Soc.* **2006**, *128*, 3908

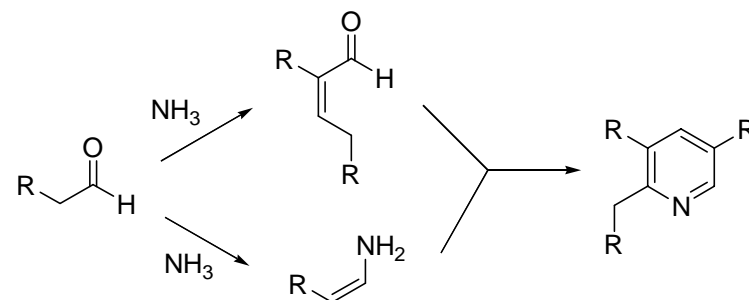
### Weinreb's Formal Synthesis



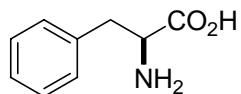
## Revised biosynthesis of the hauouamines



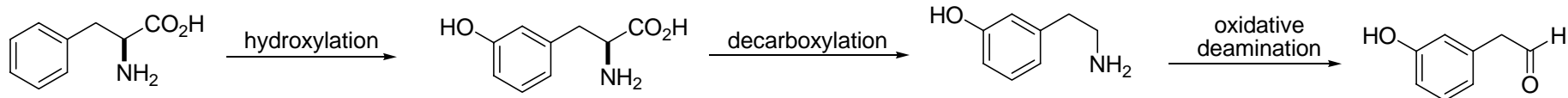
## Chichibabin (Tschitschibabin)-type pyridine synthesis



-Fundamental building block =

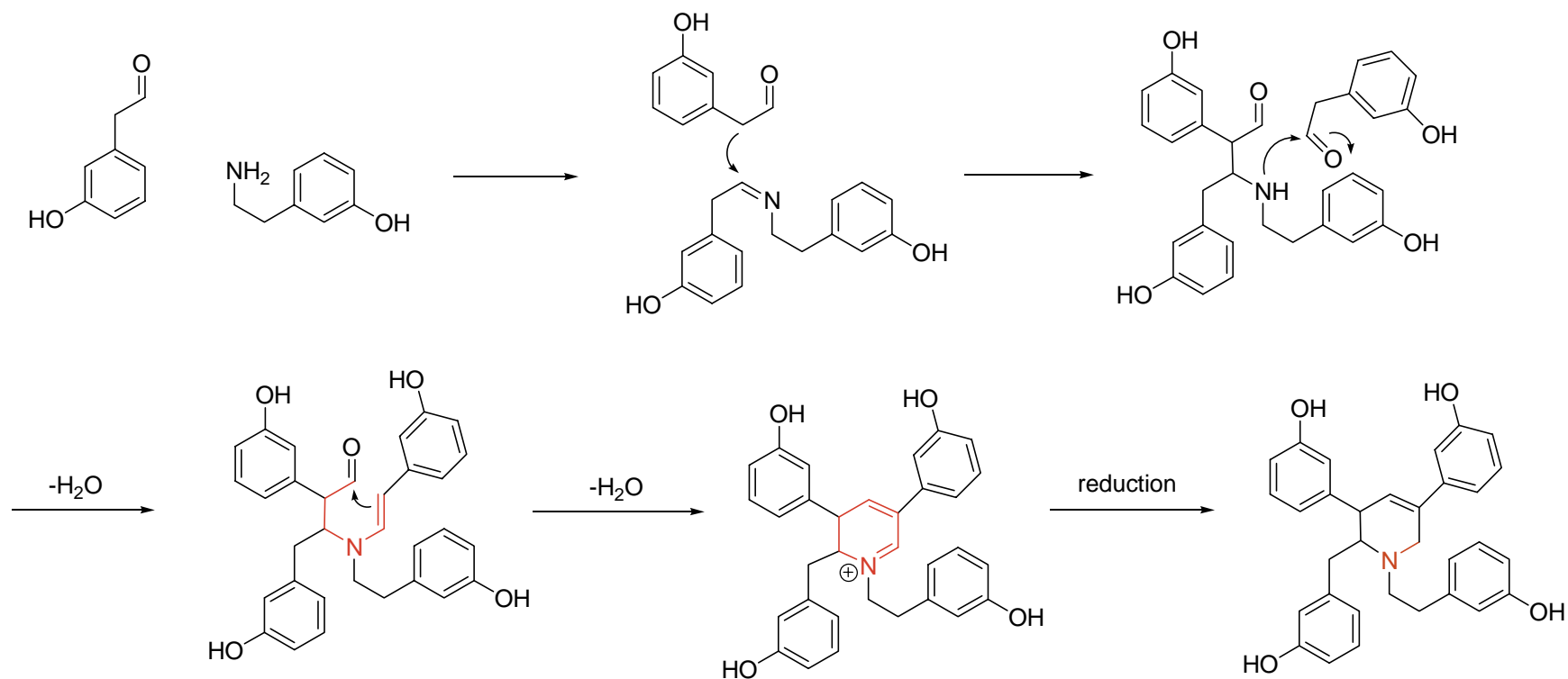
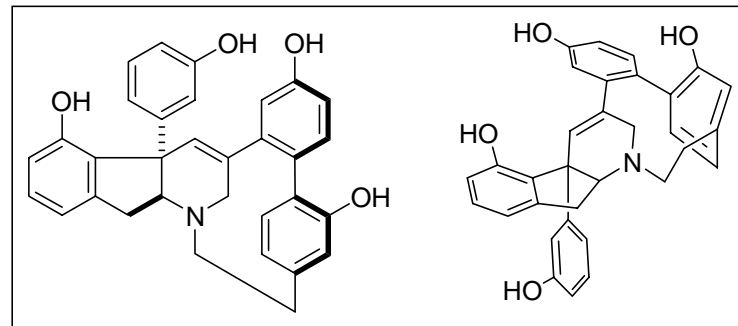


L-phenylalanine

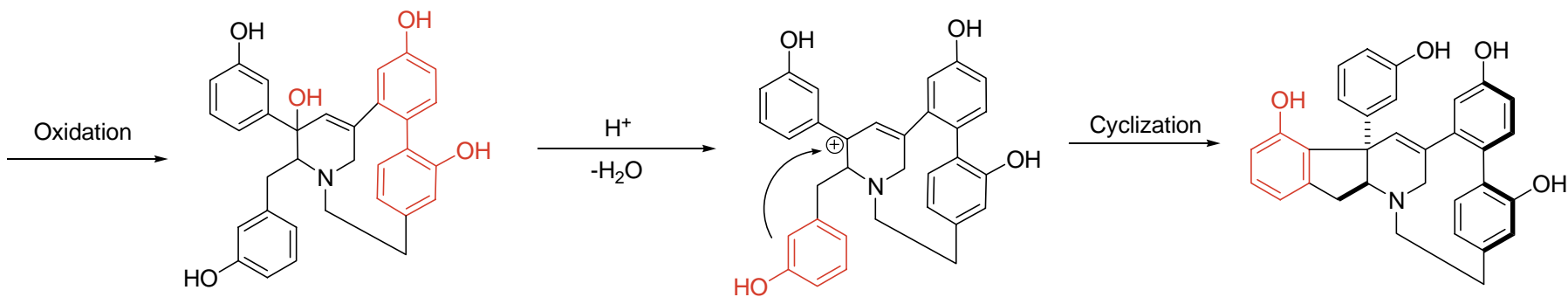
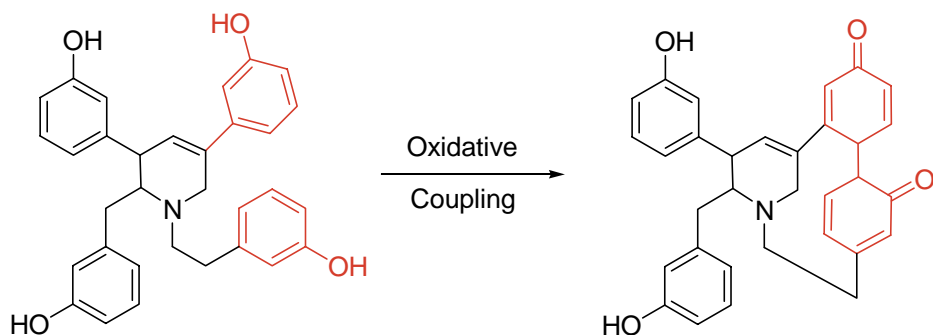
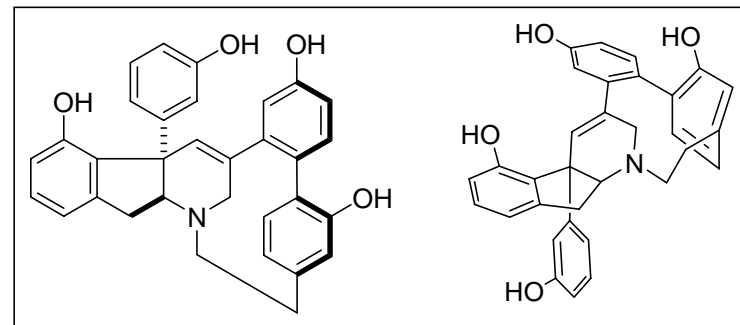


hydroxyl radical attack or  
by-product of tyr-hydroxylase

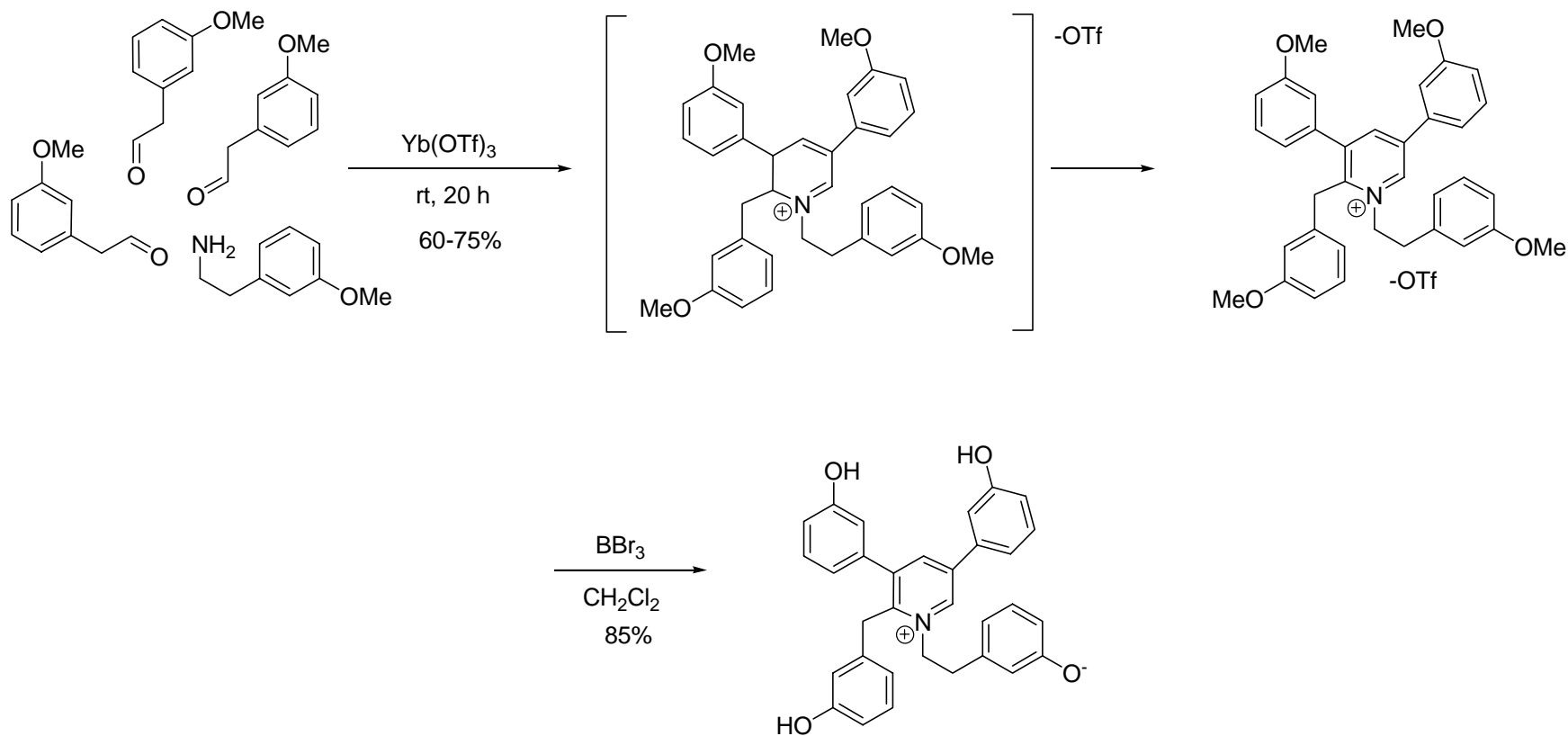
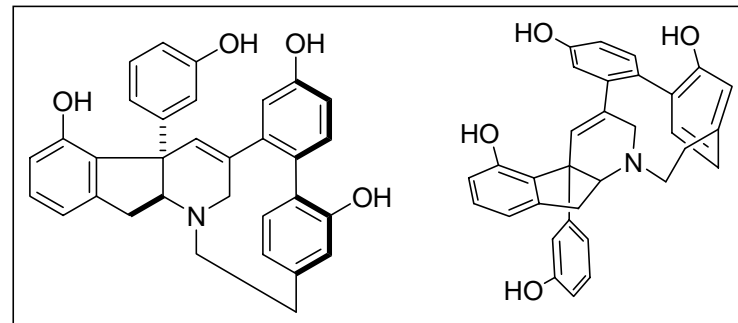
# Complete proposed biosynthesis of the hauuamines



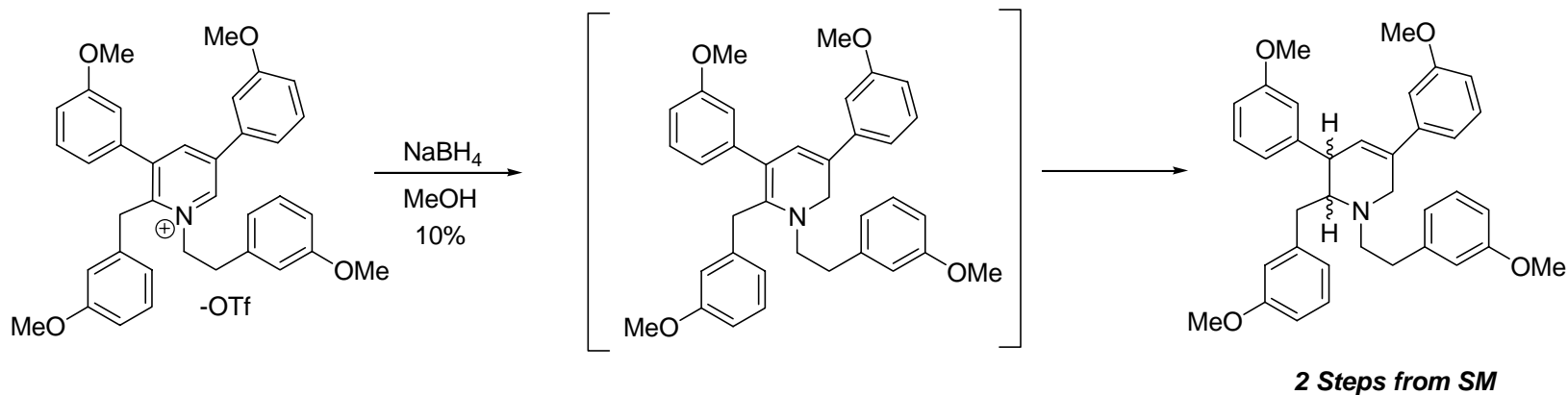
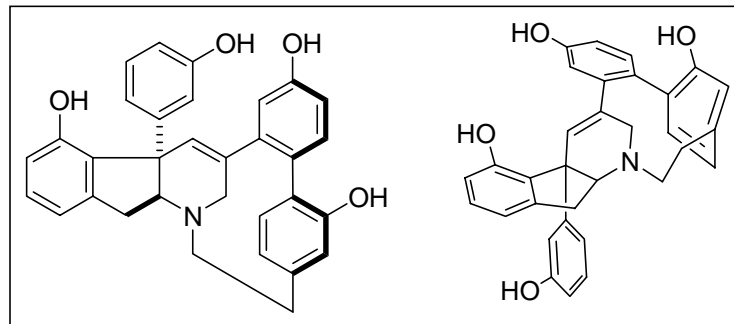
# Complete proposed biosynthesis of the haouamines



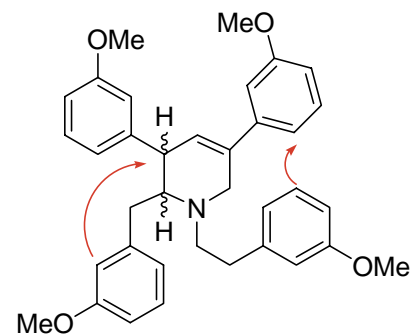
# Testing the biosynthetic hypothesis



## Testing the biosynthetic hypothesis

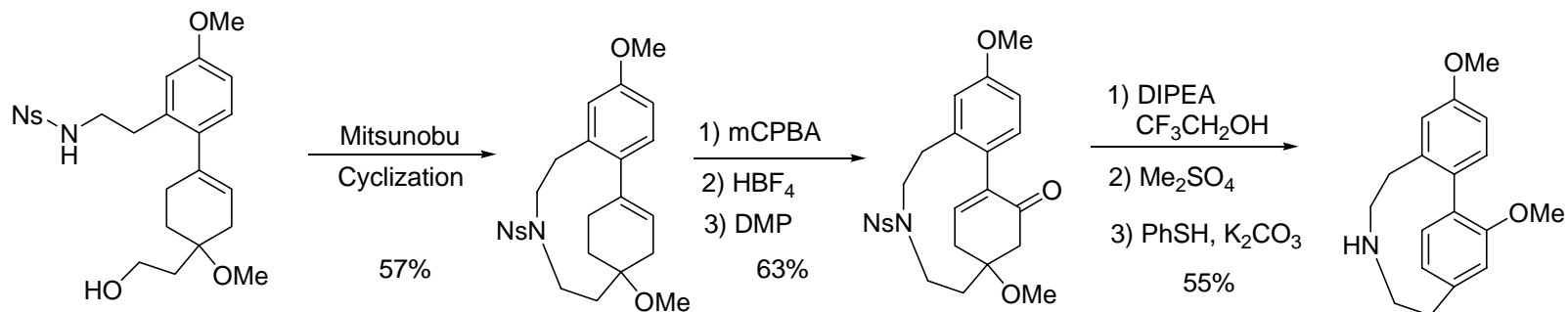
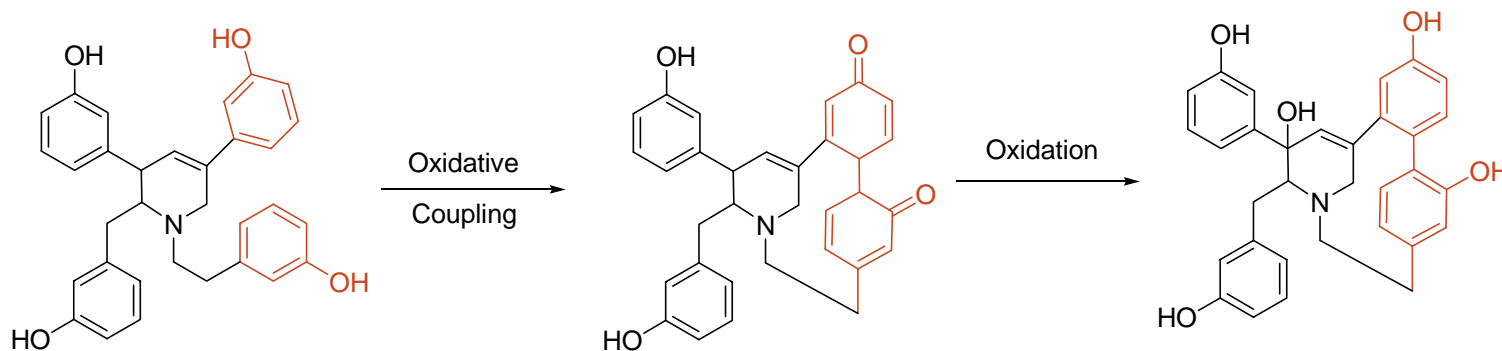
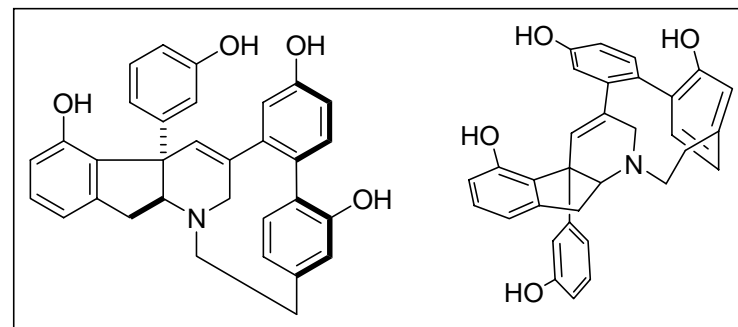


-The reason for such low yields.....likely to be an issue of pseudo-dimerizations through Diels-Alder type cycloadditions of the [intermediate] and [product]."

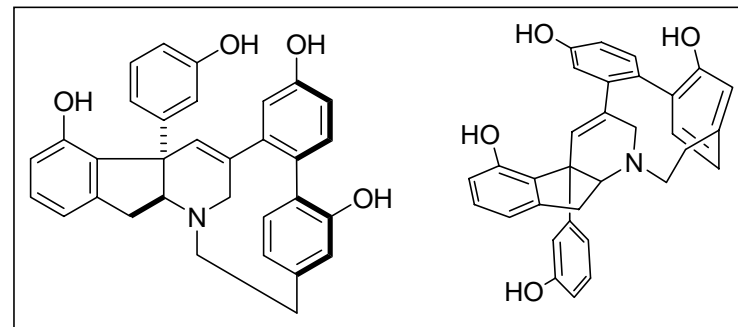
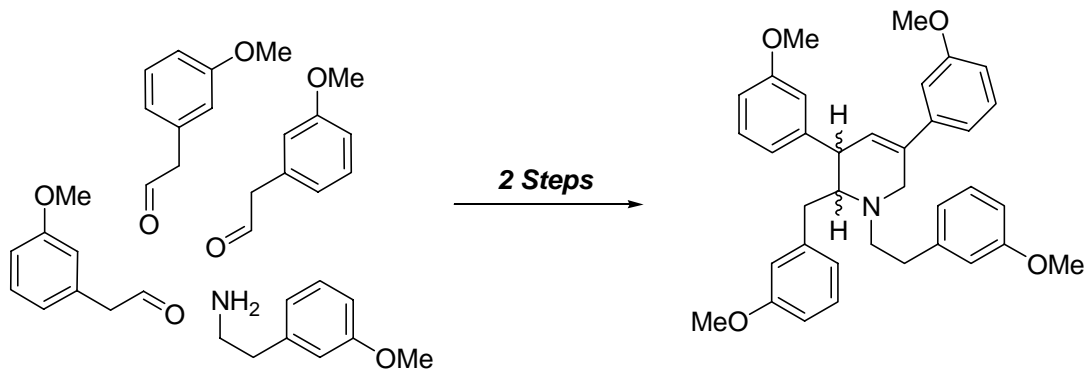




## Our Strategy to access the Haouamines



## Concluding Remarks



***-Revised biosynthesis for the haouamines was propose involving Chichibabin-type cyclization of four Phe-derived aldehydes and a stepwise oxidative coupling.***

***-Execution of part of this proposal generates an advanced intermediate on the way to the haouamines via a 2 step process.***

***-The proposed biosynthesis appears to be a likely pathway based on empirical evidence.***