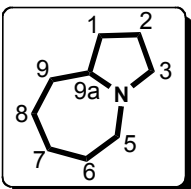
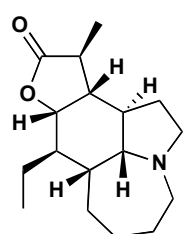
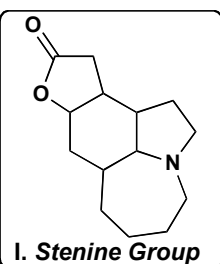


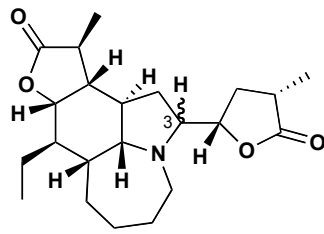
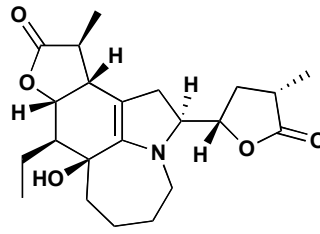
## I. Introduction



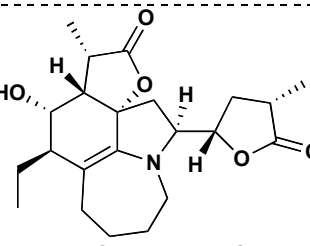
- The *Stemonaceae* plant family, which comprises over 30 species, produces a large class of structurally diverse alkaloids featuring a conserved pyrrolo [1,2-a] azepine = perhydroazaazulene = 4-azazulene nucleus
- Their roots have been used for centuries in traditional chinese medicine for a variety of purposes including (but not limited to): treatment of bronchitis, tuberculosis, pertussis, as well as anti-parasitic agents
- Over 80 members have been discovered and many more are likely to be isolated (restriction is limited to only 8 species, mostly from the *Stemona* genus)



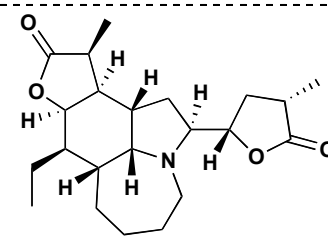
stenine

tuberostemonine ( $H_3 = \alpha$ )  
tuberostemonine A ( $H_3 = \beta$ )

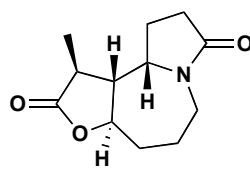
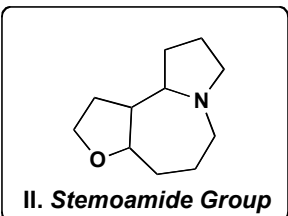
tuberostemonol



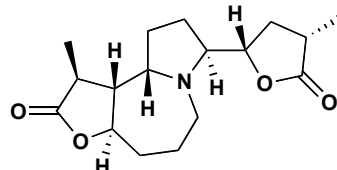
oxotuberostemonine



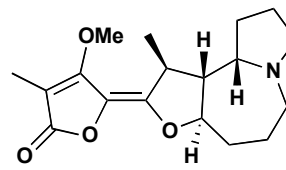
neotuberostemonine



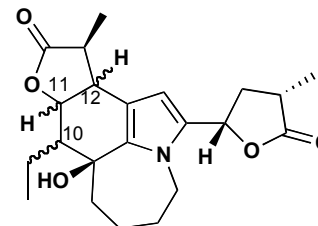
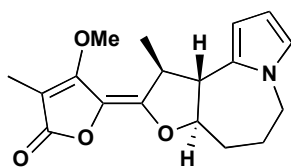
stemoamide



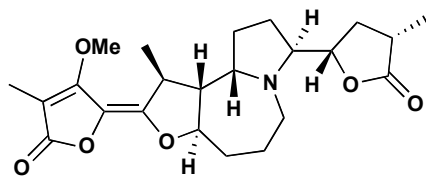
stemonine



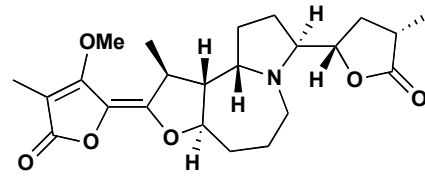
neostemonine

didehydrotuberostemonine ( $H_{11} = \beta, H_{12} = \beta, Et = \beta$ )  
bisdehydroneotuberostemonine ( $H_{11} = \alpha, H_{12} = \alpha$ )

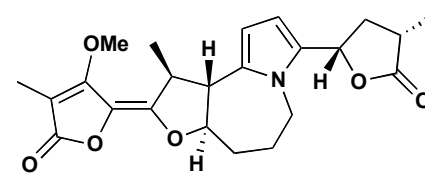
bisdehydroneostemonine



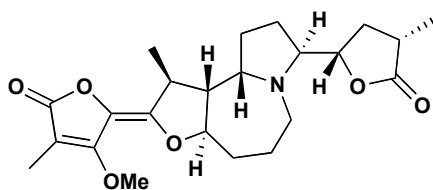
protostemonine



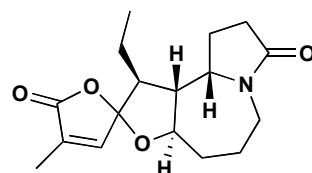
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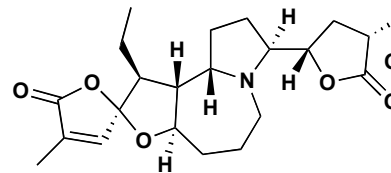
didehydroprotostemonin



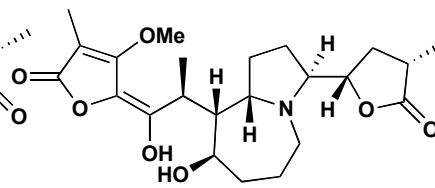
isoprotostemonine



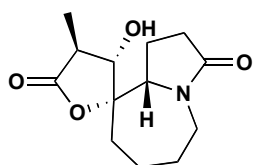
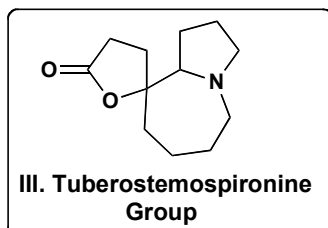
tuberstemoamide



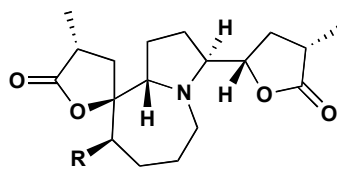
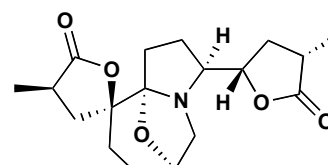
stemoninine



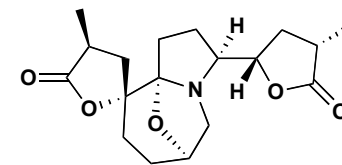
stemodiol



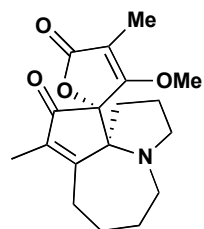
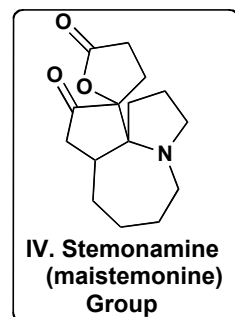
tuberstemospirone

croomine (R = H)  
stemospirone (R = OMe)

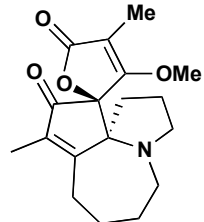
stemotinine



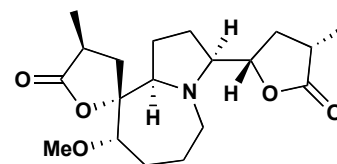
isostemotinine



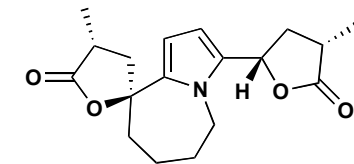
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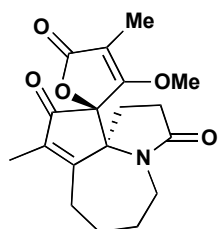
isostemonamine



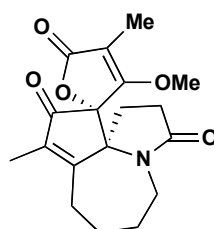
stemonidine



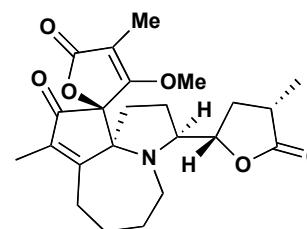
didehydrocroomine



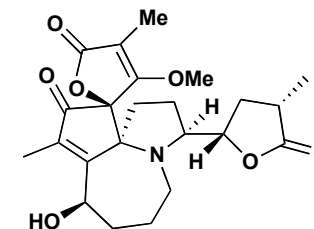
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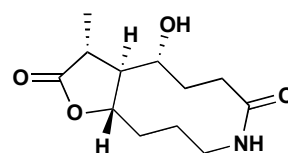
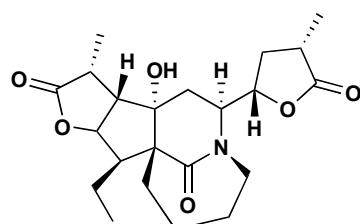
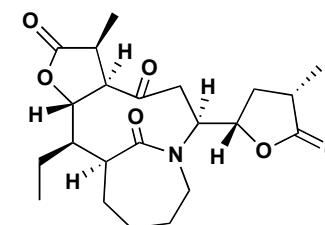
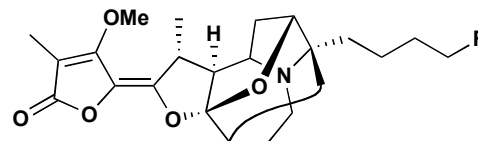
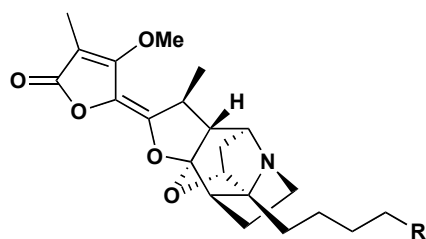
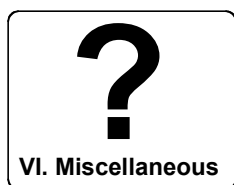
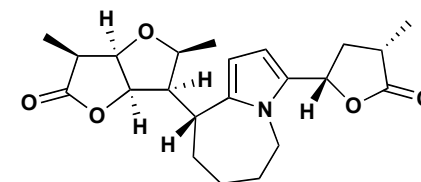
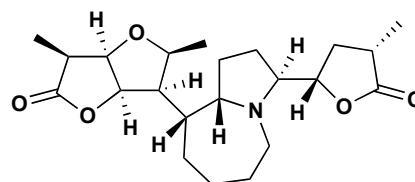
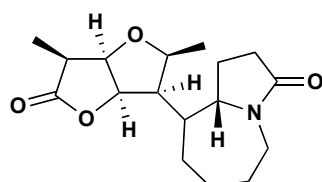
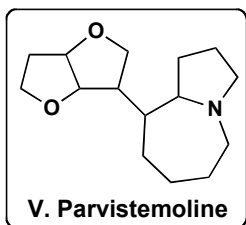
stemonamide



maistemone

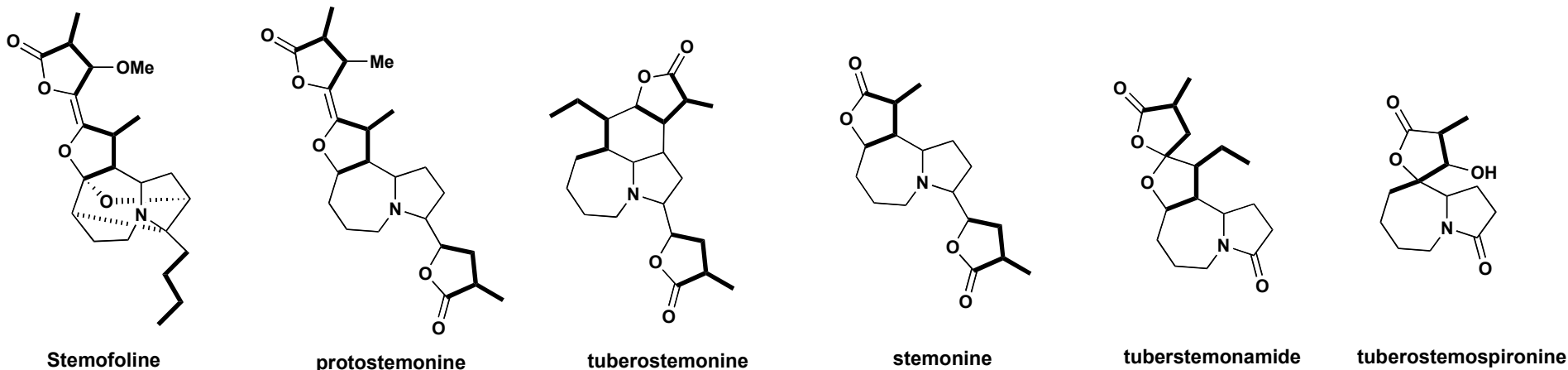


oxymaistemone

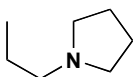


## II. Biosynthetic Considerations

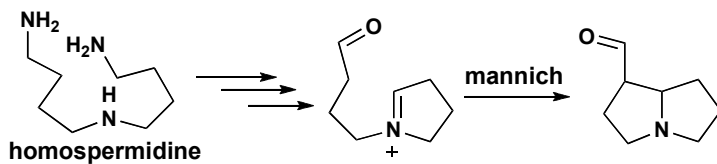
Consider the following carbocyclic skeletons where the C<sub>5</sub> units of presumed terpene origin are drawn in bold:



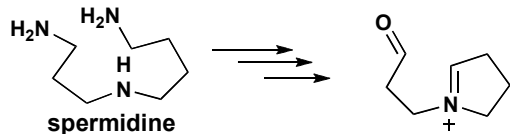
This leaves the following fragment unaccounted for:



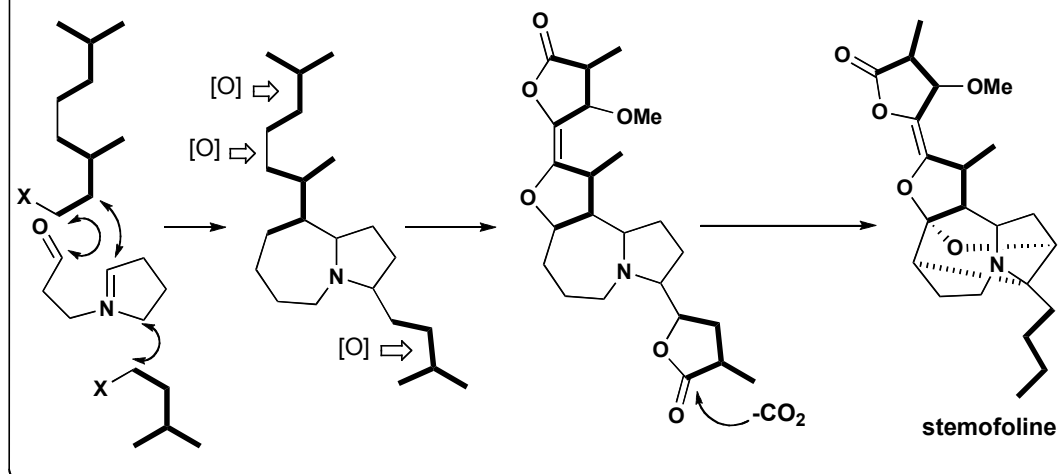
Recall pyrrolizidine biosynthesis:



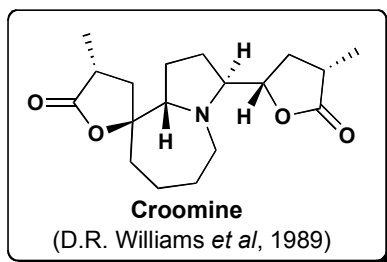
An analogous pathway could produce the stemona alkaloids



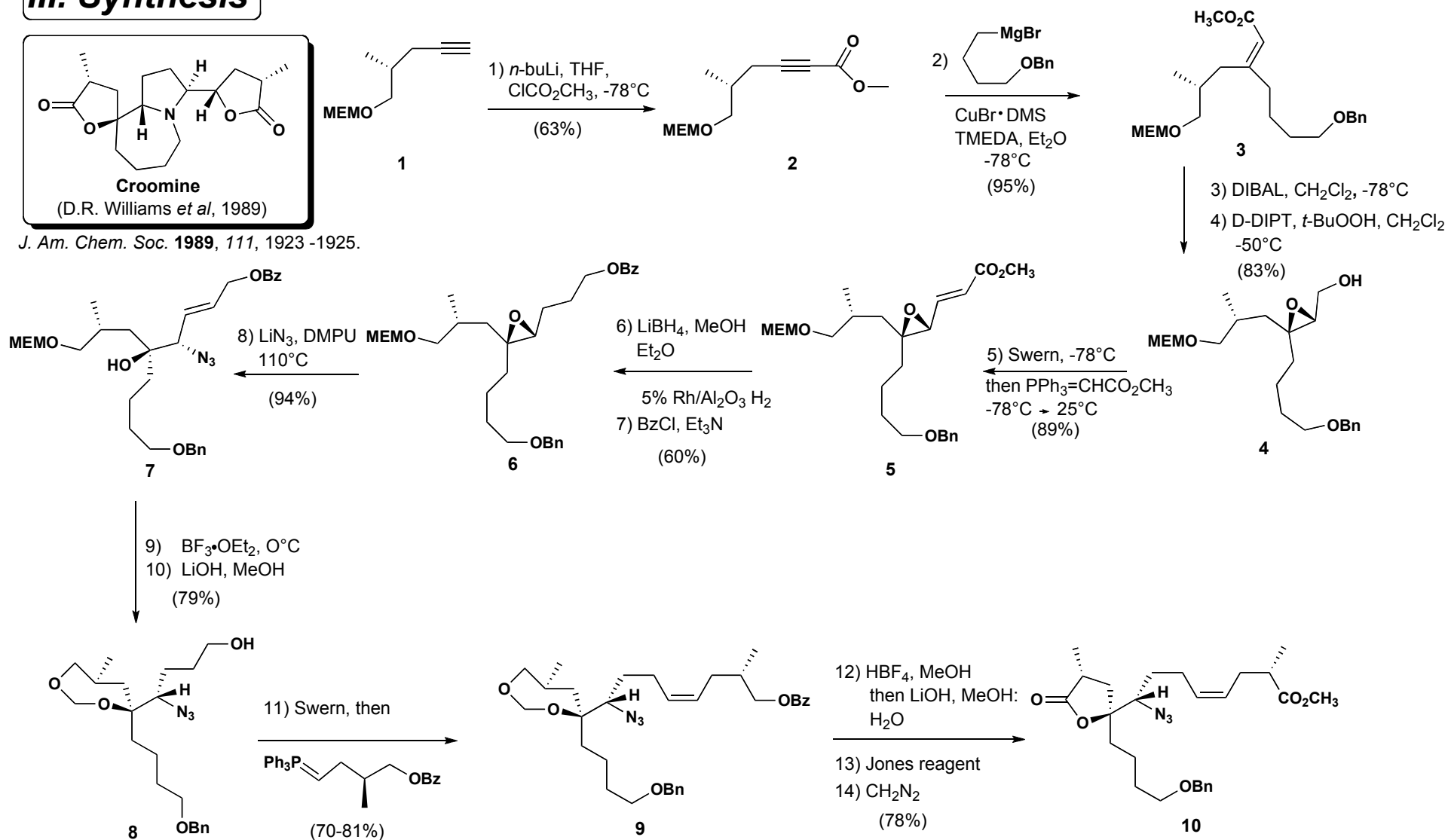
Thus the following biosynthetic picture emerges:

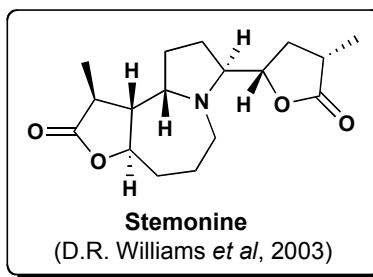
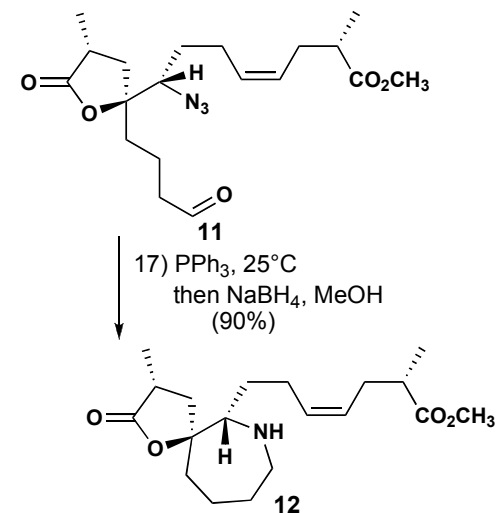
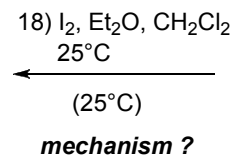
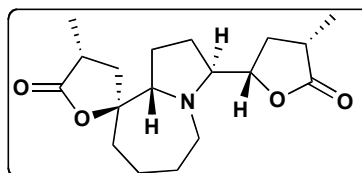
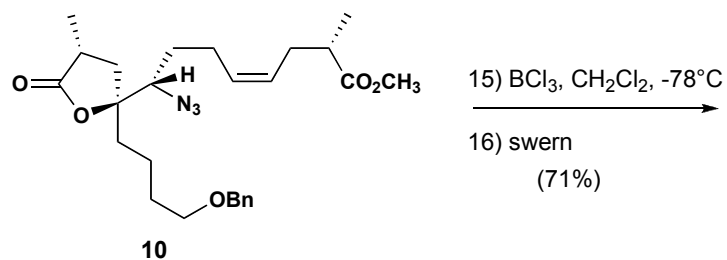
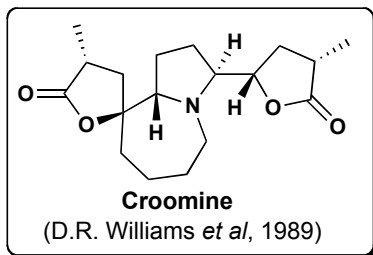


## III. Synthesis



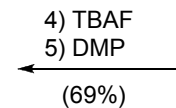
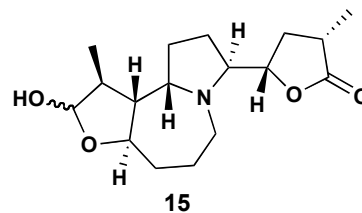
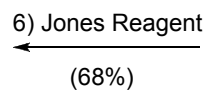
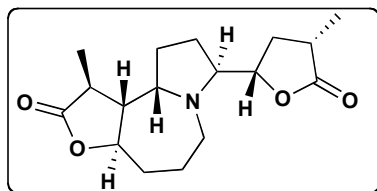
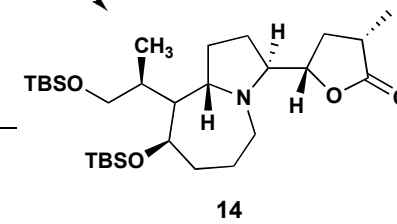
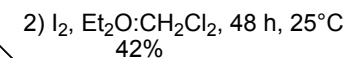
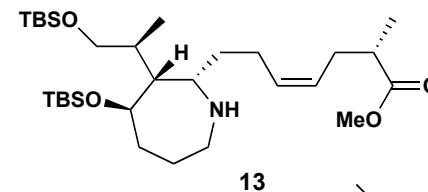
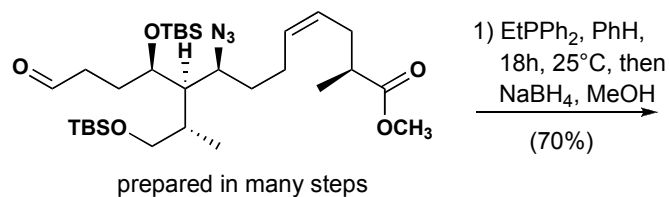
*J. Am. Chem. Soc.* **1989**, *111*, 1923-1925.

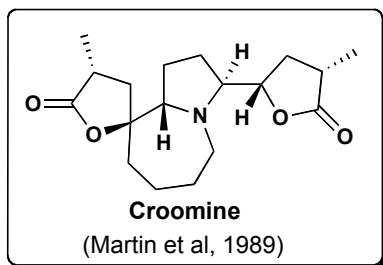




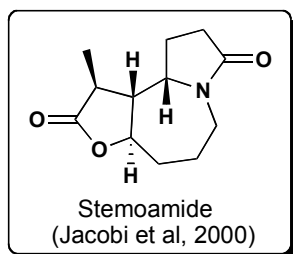
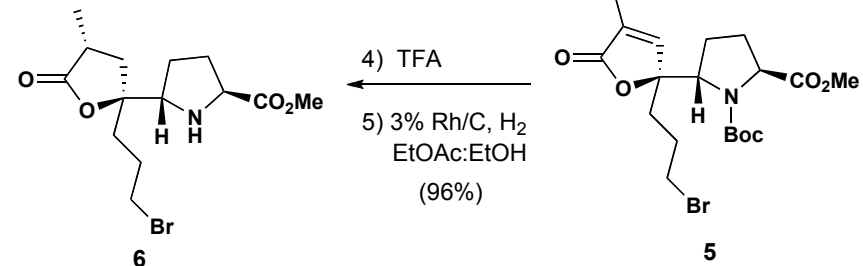
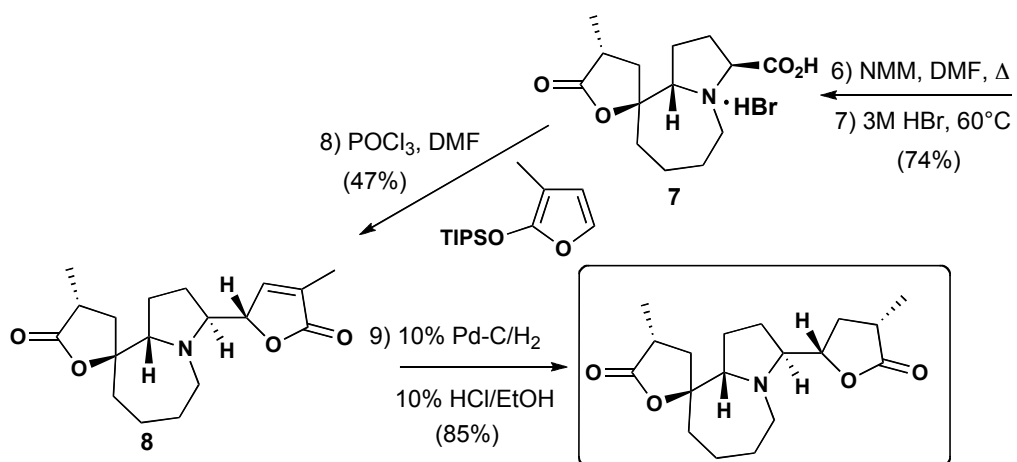
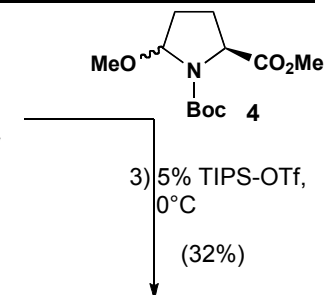
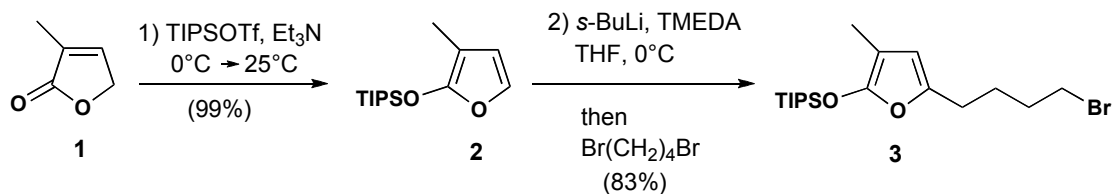
*Org. Lett.* **2003**, 5, 3361-3364

A similar iodination cascade was used here as well

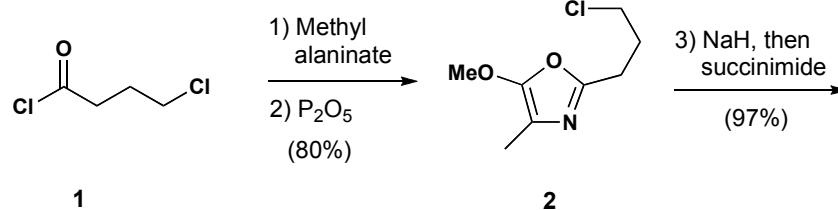




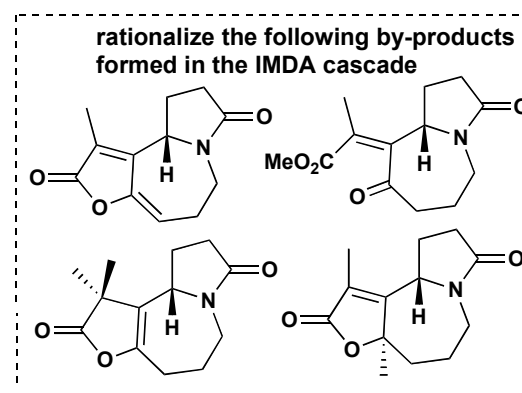
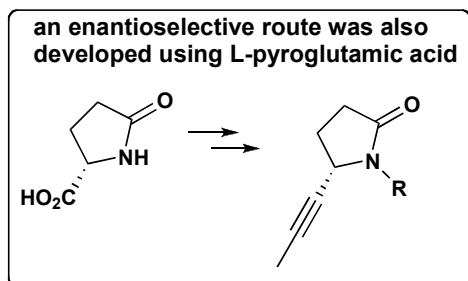
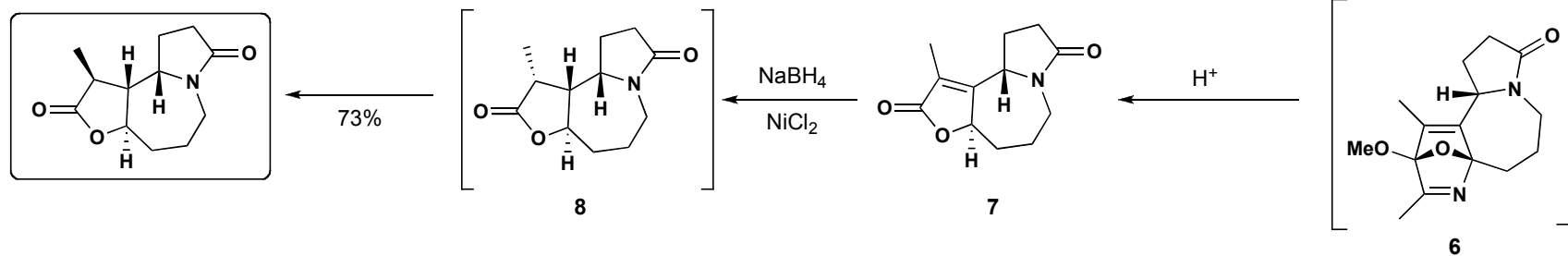
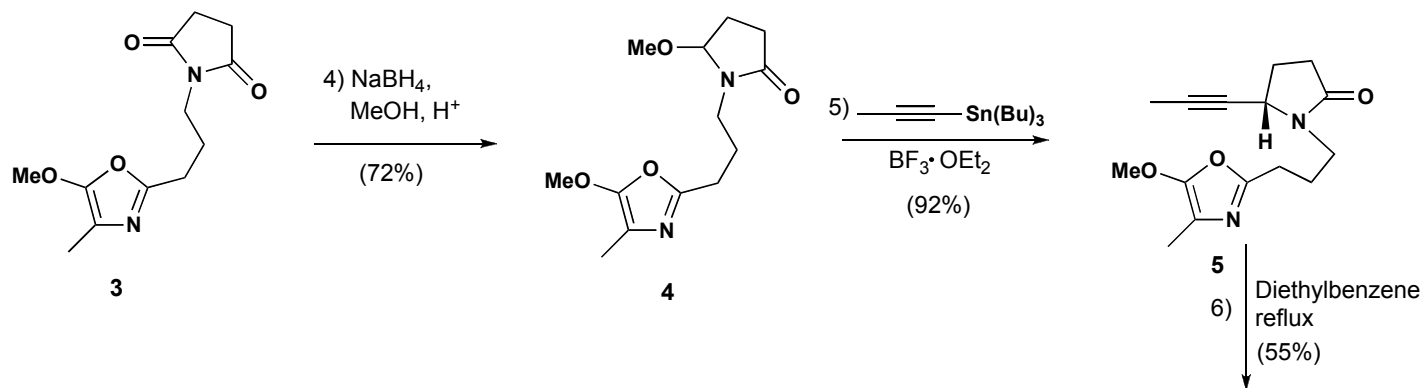
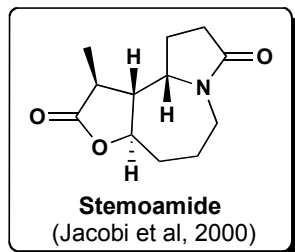
*J. Am. Chem. Soc.* **1996**, 118, 3299-3300.

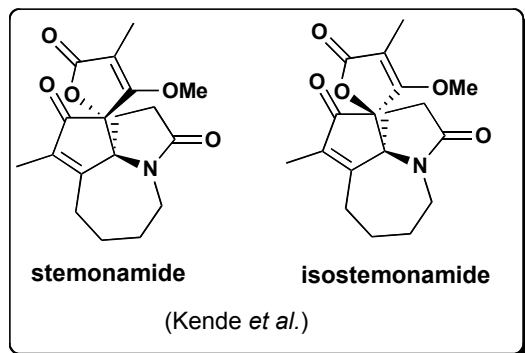


racemic synthesis:

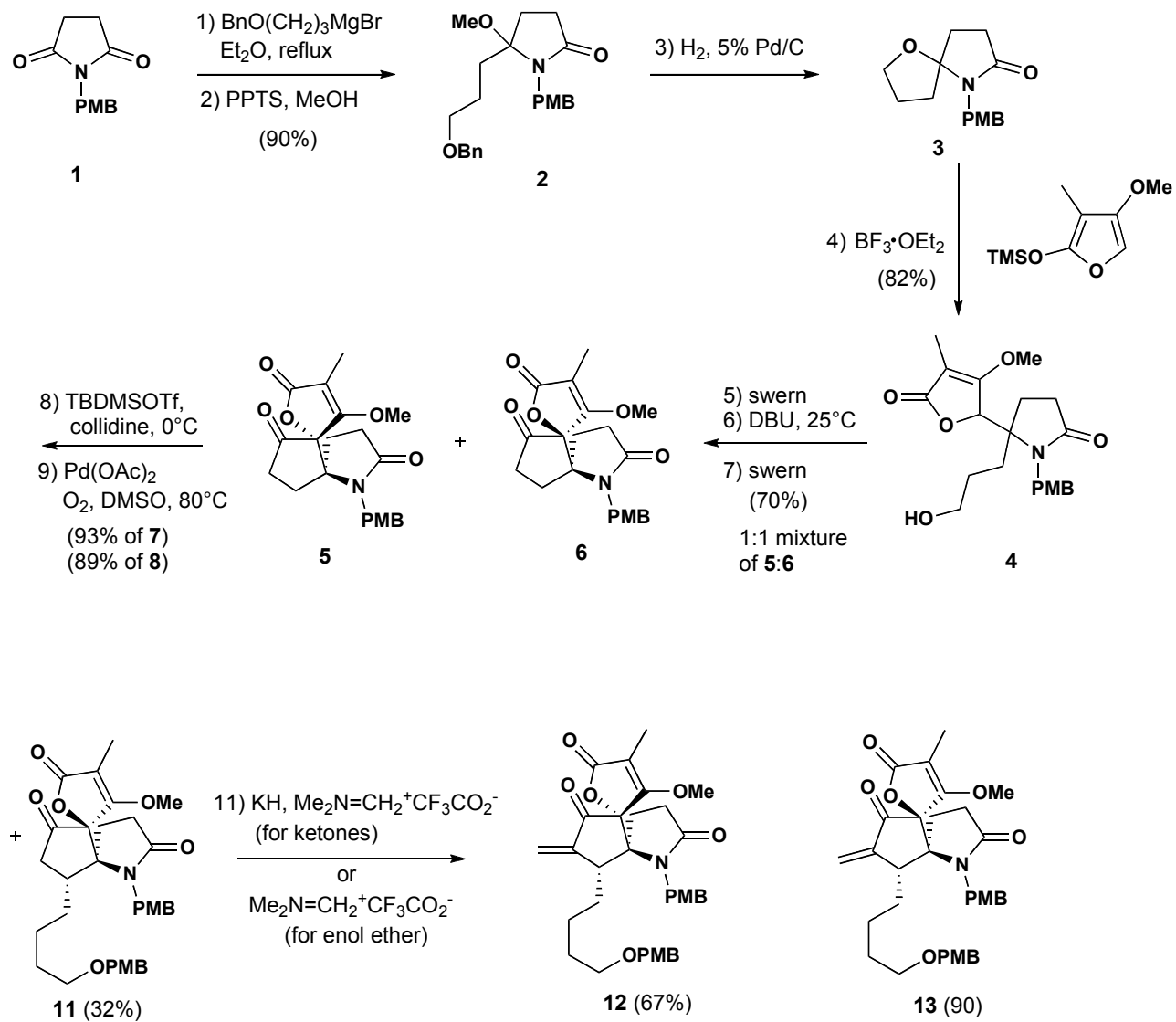


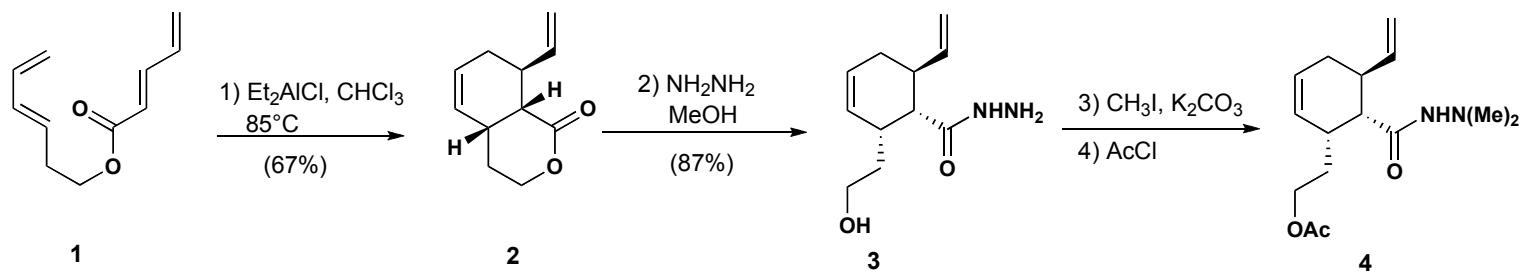
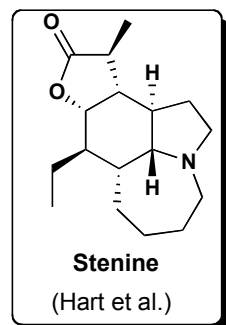
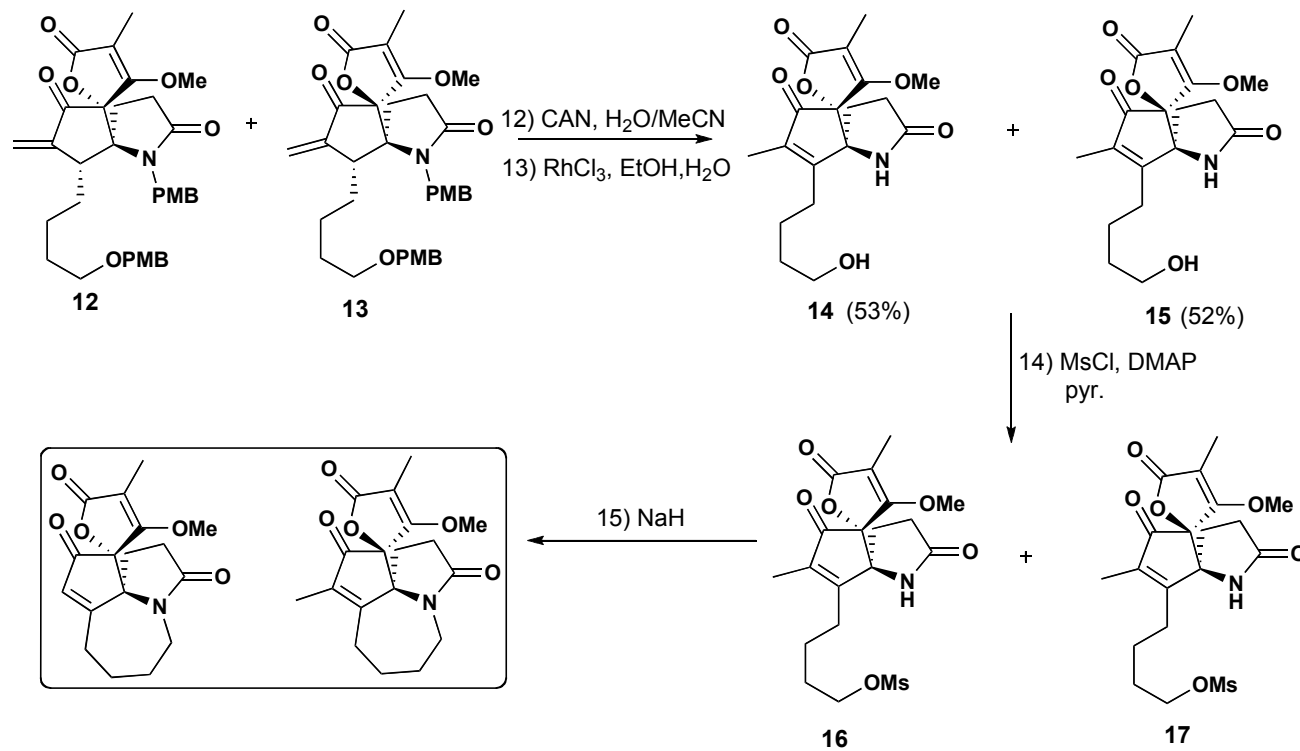
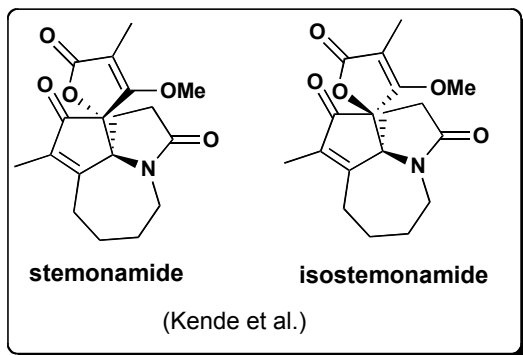
*J. Am. Chem. Soc.* **2000**, 122, 4295-4303

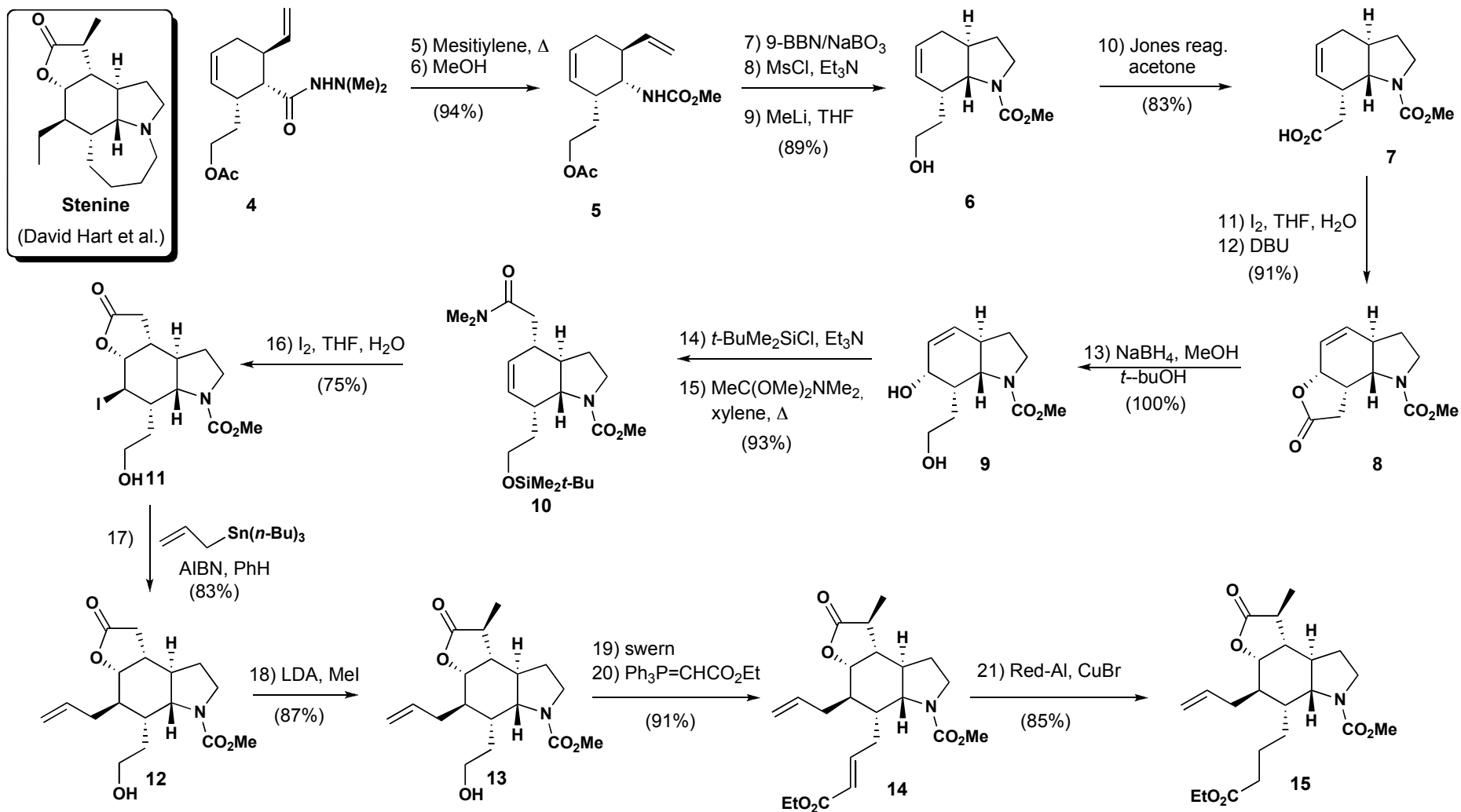


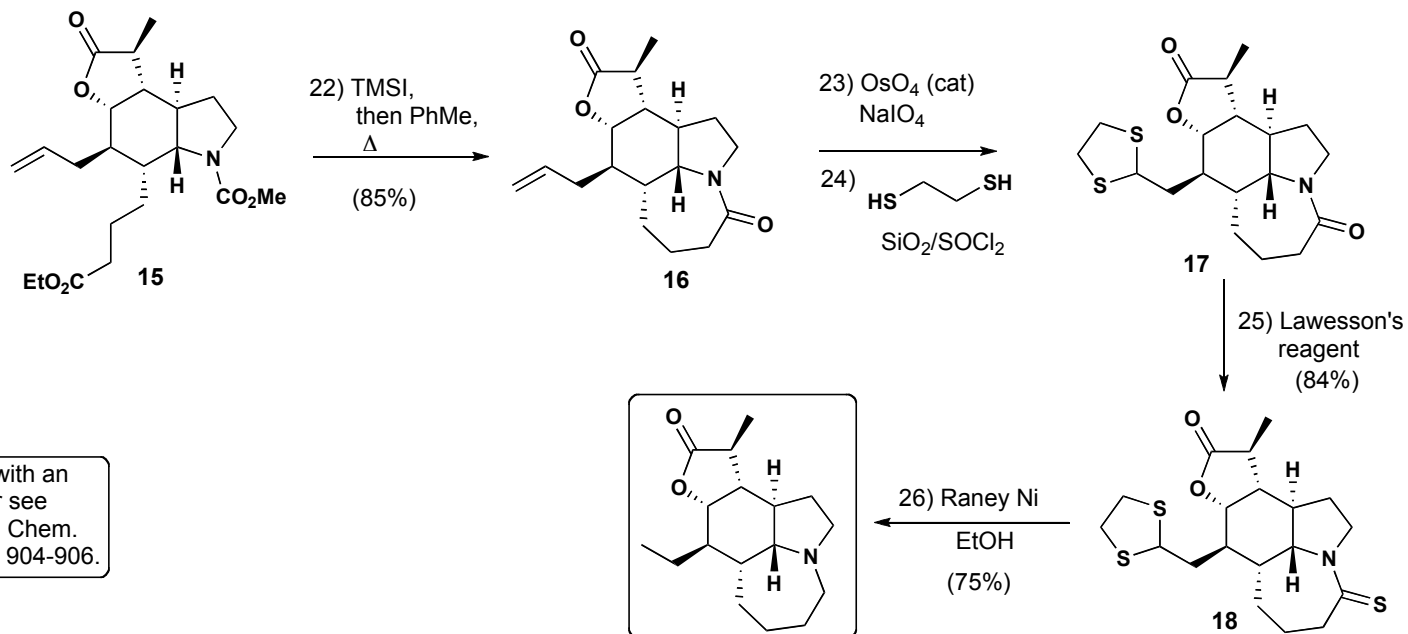
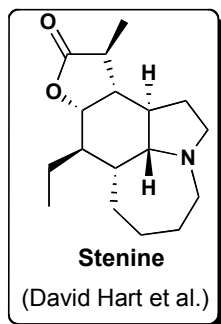


*Org. Lett.* 2001. 16, 2505-2508

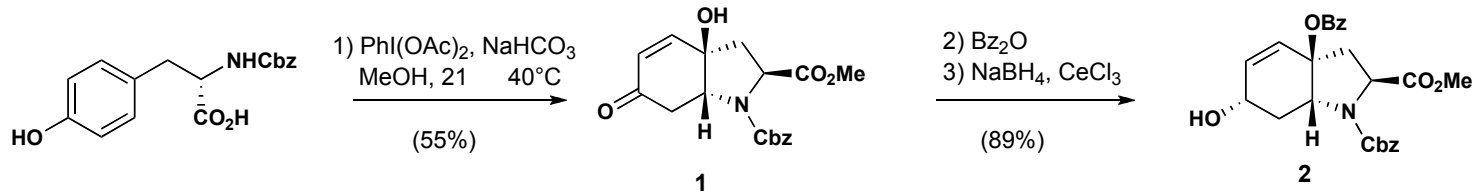
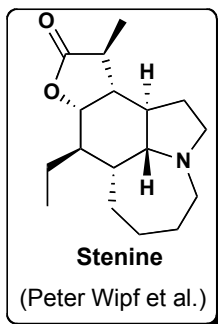




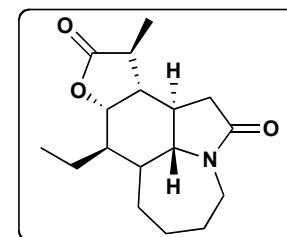
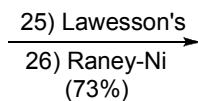
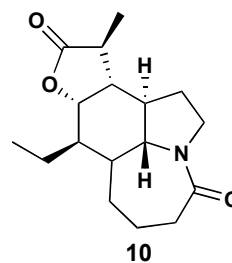
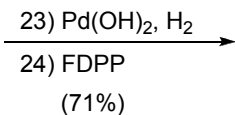
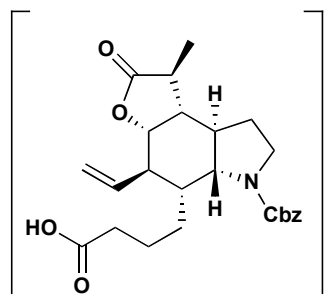
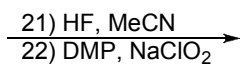
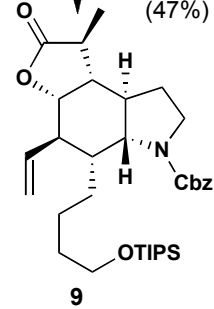
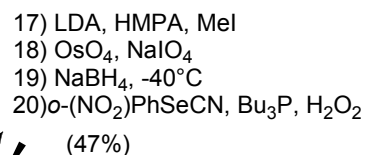
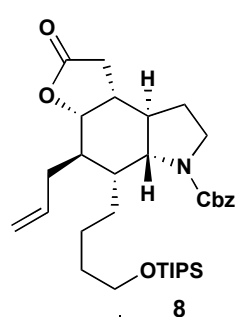
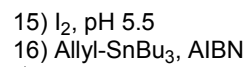
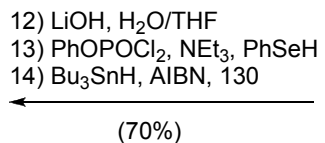
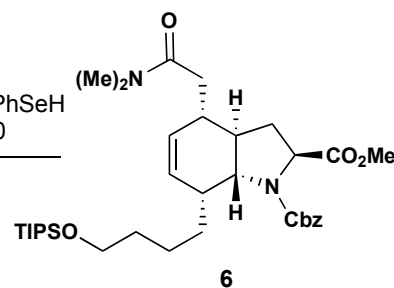
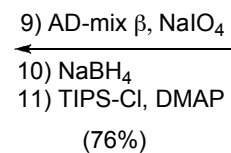
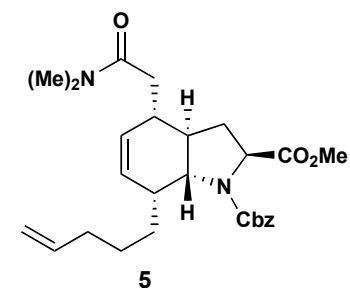
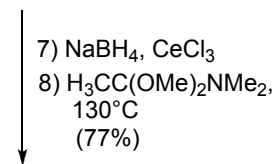
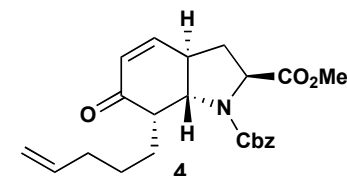
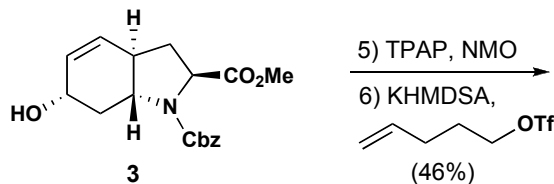
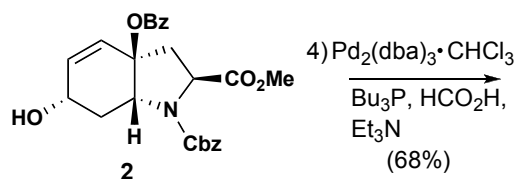
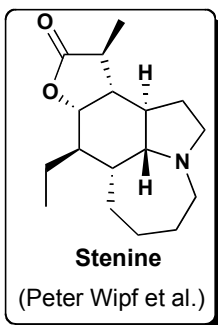


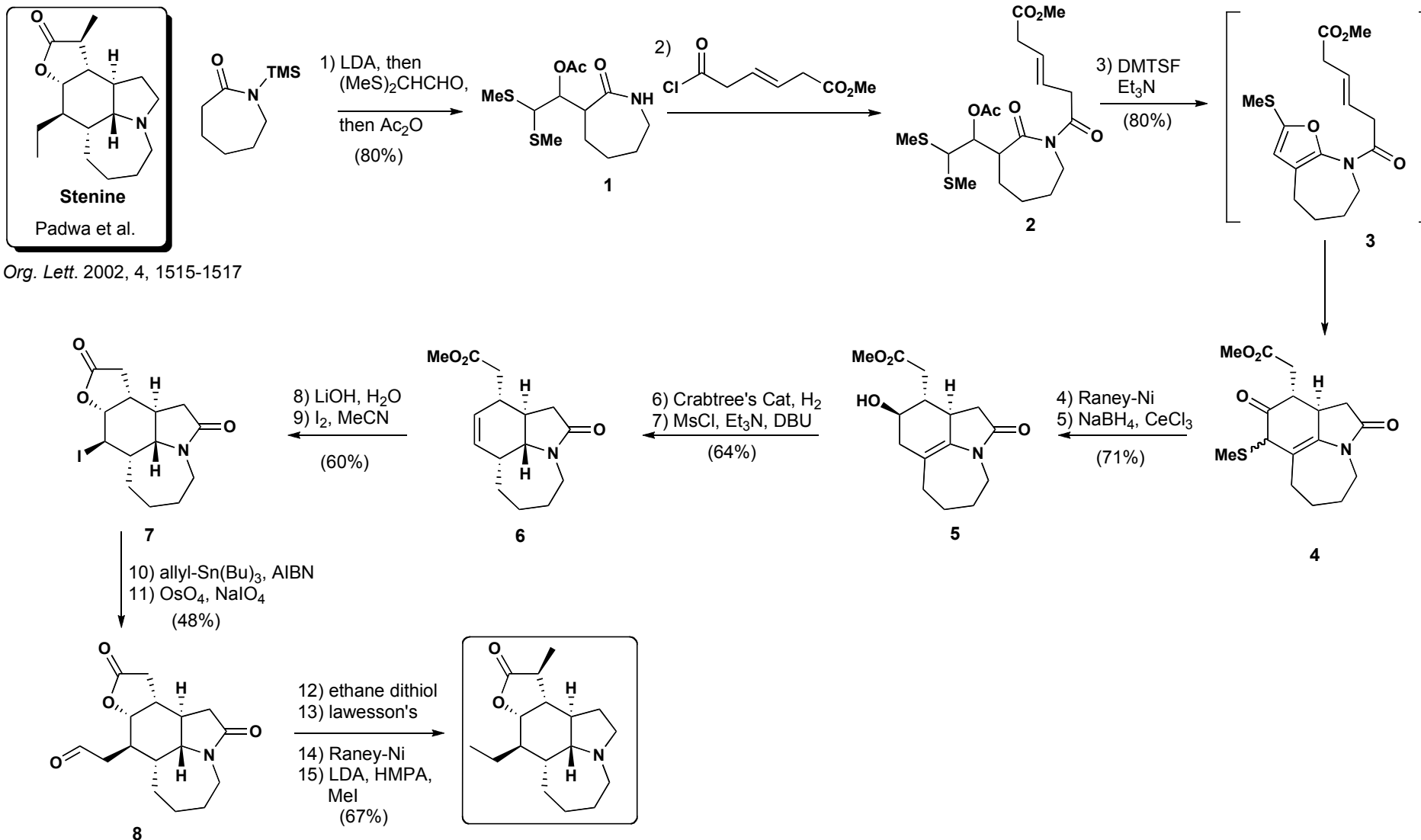


for a similar synthesis with an asymmetric Diels-Alder see Morimoto et al. *Angew. Chem. Int. Ed. Engl.* 1996, 35, 904-906.

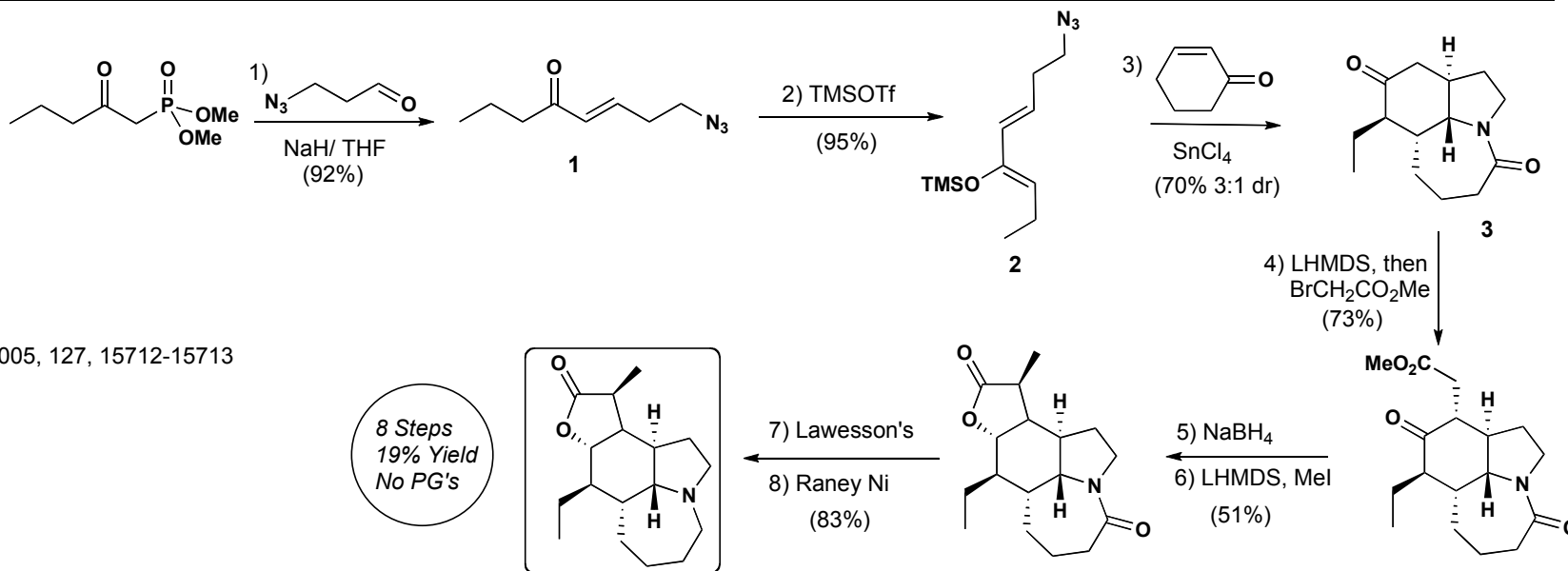
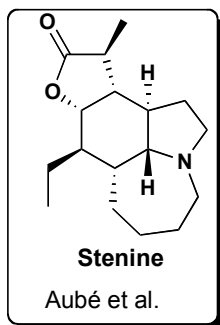


*J. Am. Chem. Soc.* 1995, 117, 11106-11112

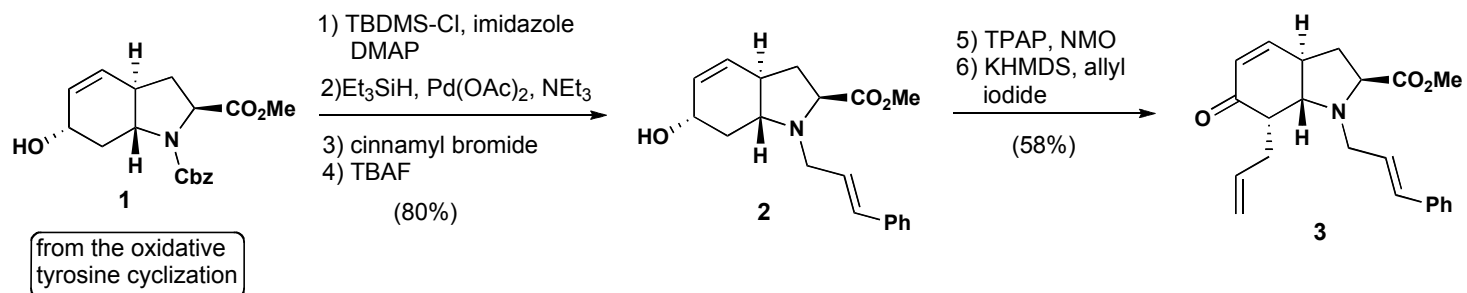
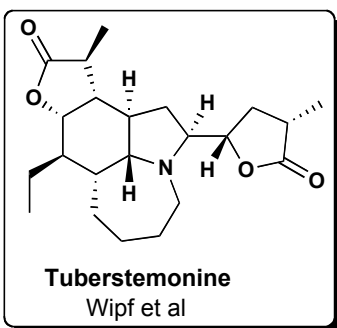


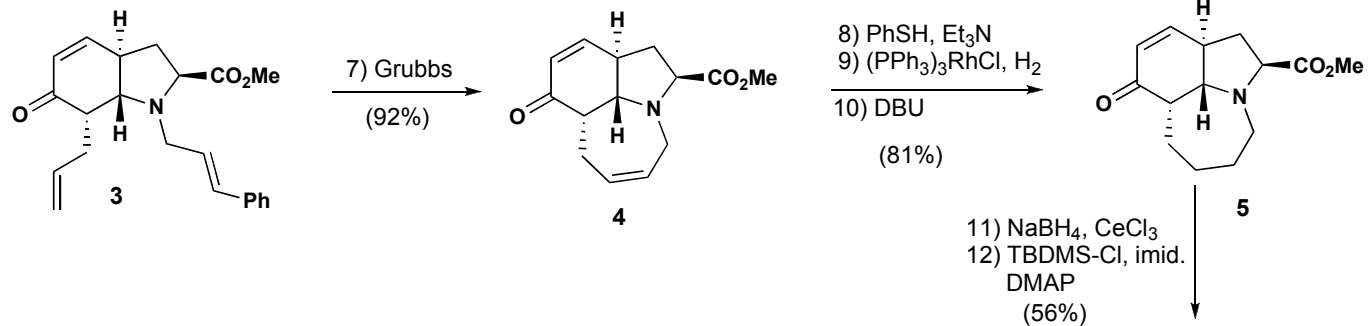
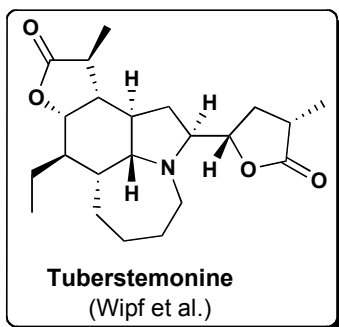


Org. Lett. 2002, 4, 1515-1517

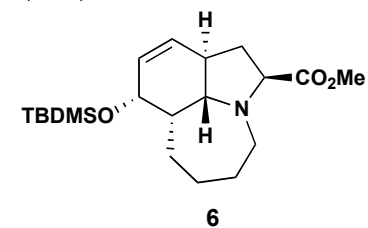


*J. Am. Chem. Soc.* 2005, 127, 15712-15713





11) NaBH<sub>4</sub>, CeCl<sub>3</sub>  
12) TBDMS-Cl, imid.  
DMAP  
(56%)

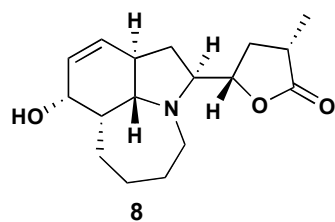


13) (Me)(OMe)NH HCl  
Me<sub>2</sub>AlCl

14) LiDBB  
Br (89%)

15) L-selectride, -78°C

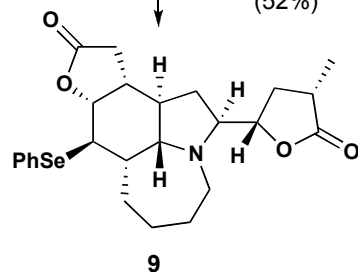
16) TsOH, MeOH  
(56%)



8

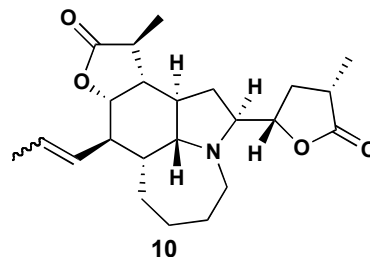
8

17) MeC(OMe)<sub>2</sub>NMe<sub>2</sub>,  
xylene, Δ  
18) PhSeCl, MeCN/H<sub>2</sub>O  
(52%)



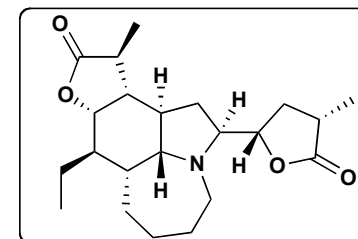
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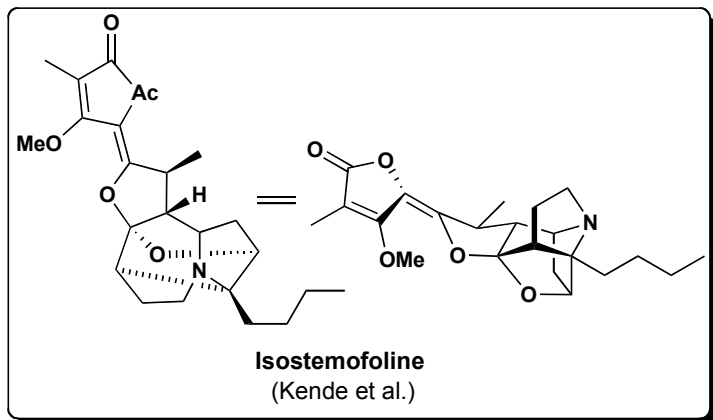
19) allyl-SnPh<sub>3</sub>  
20) LDA, HMPA, MeI  
21) allyltritylamine, DIEA,  
toluene, 110°C  
(45%)



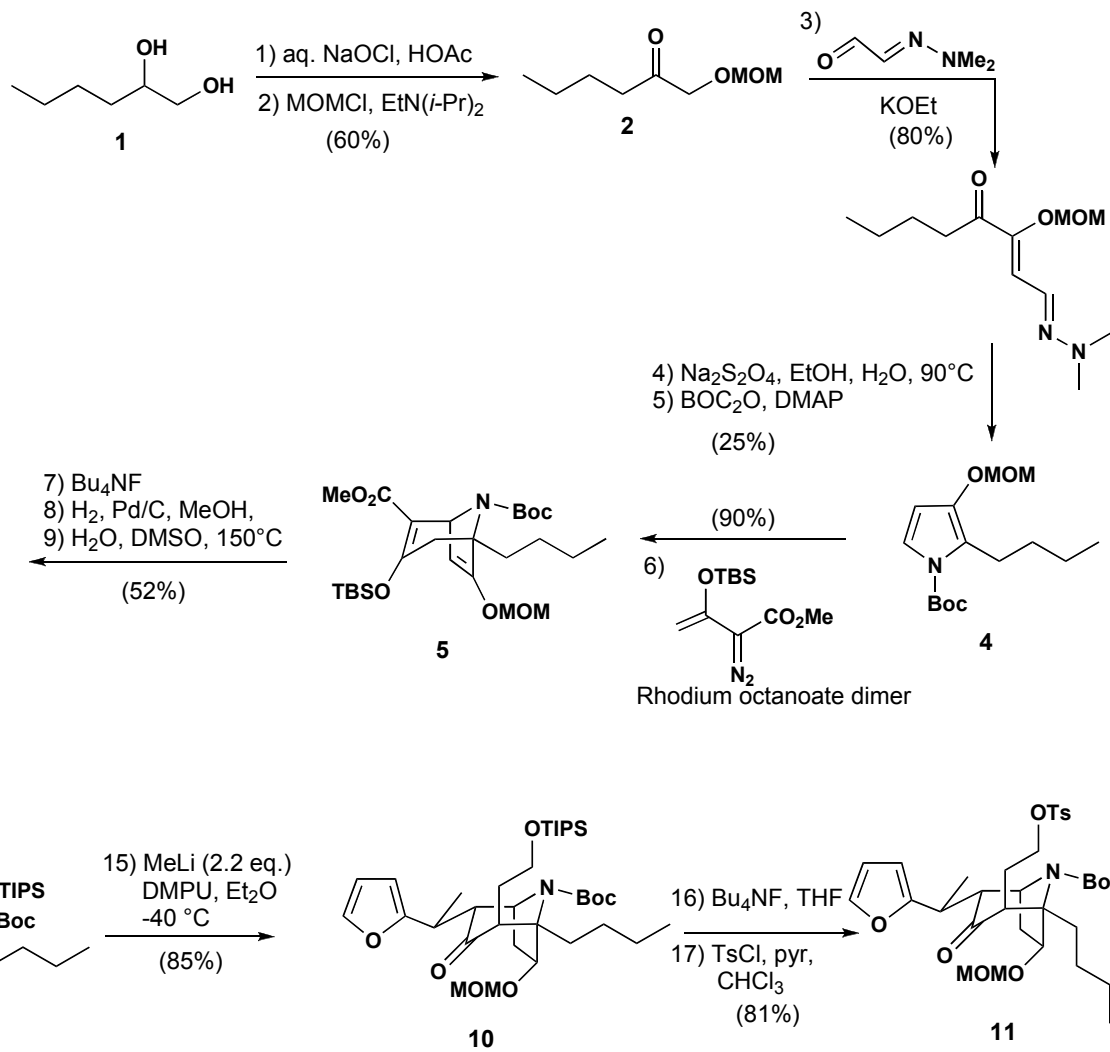
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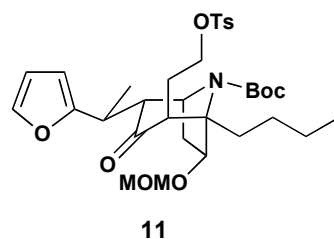
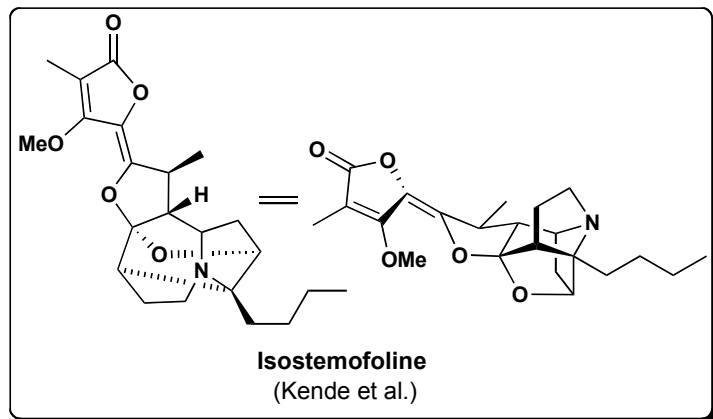
22) Grubbs, TsOH,  
ethylene  
23) Pd/C, H<sub>2</sub>



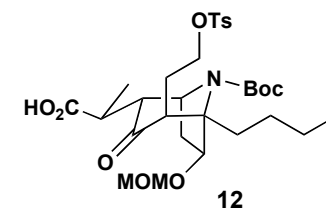


*J. Am. Chem. Soc.* 1999, 121, 7431-7432

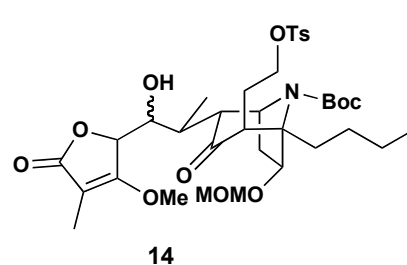




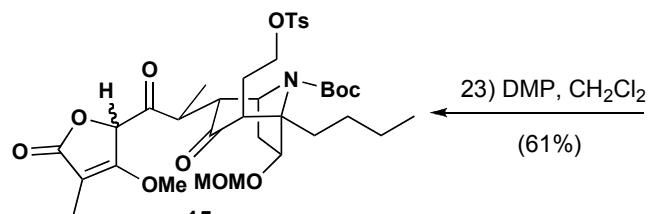
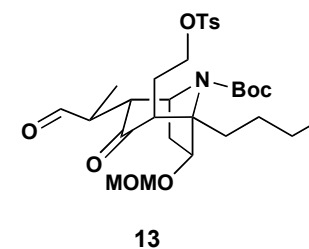
18) O<sub>3</sub>, DMS  
(65%)



19) *i*-BuOCOCI, NMM  
20) NaBH<sub>4</sub>, MeOH  
21) DMP

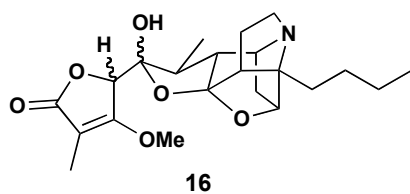


22)   
LiO  
(56%)

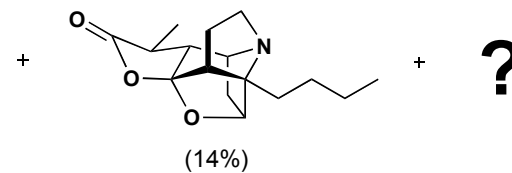
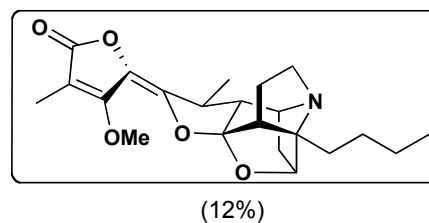


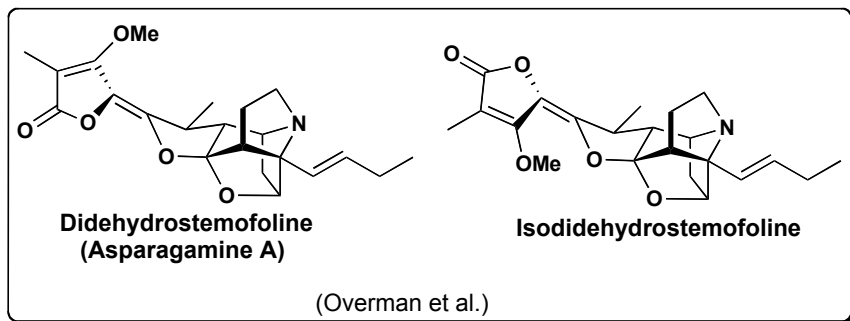
23) DMP, CH<sub>2</sub>Cl<sub>2</sub>  
(61%)

24) CF<sub>3</sub>CO<sub>2</sub>H  
then NaHCO<sub>3</sub>  
(67%)



25) Tf<sub>2</sub>O





*J. Am. Chem. Soc.* 2003, 125, 15284-15285

