Some Approaches to Synthesis of Marine Natural Products Containing Medium-Sized Rings

Literature Presentation
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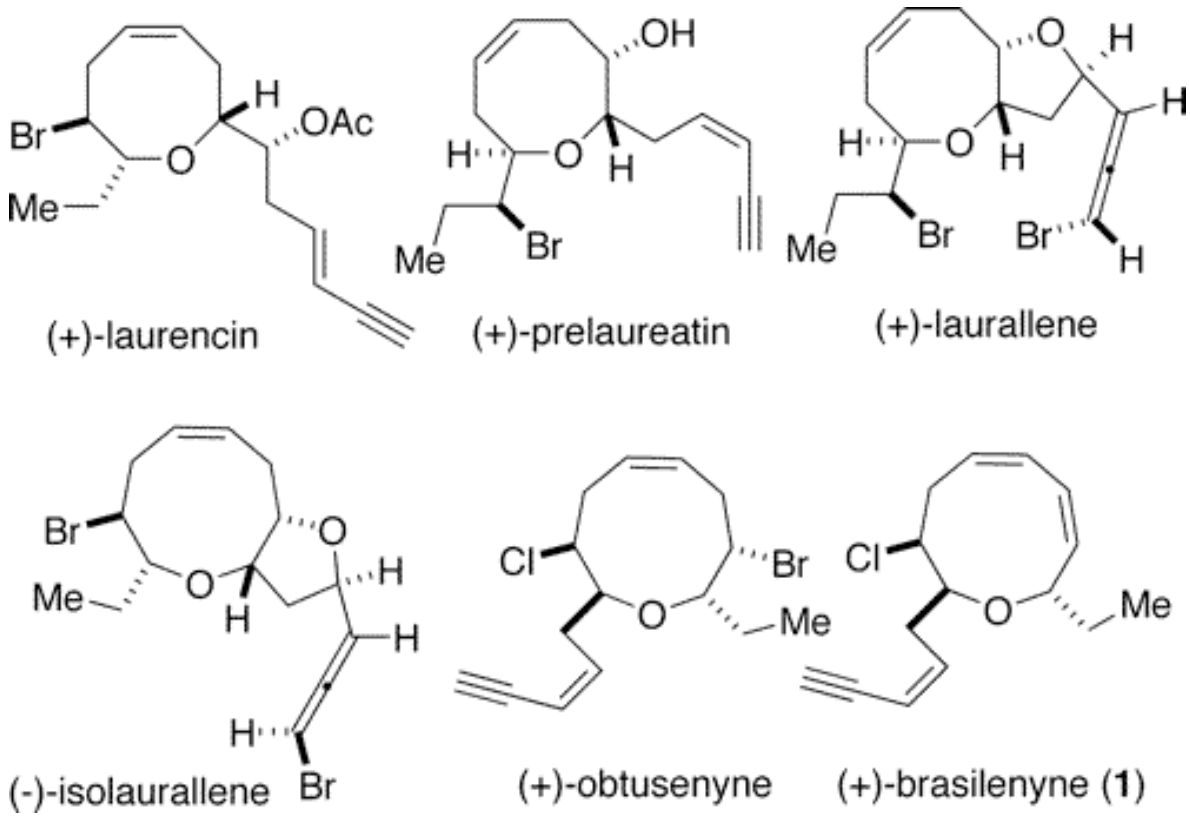
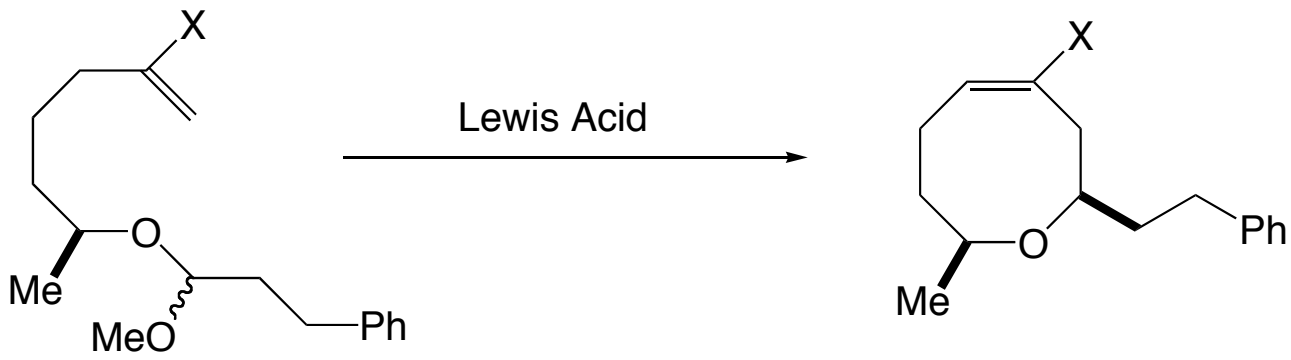
Denmark, S.E.; Yang, S.-M. *J. Am. Chem. Soc.* **2004**, *126*, 12432-12440
Crimmins, M.T.; Tabet, E.A. *J. Am. Chem. Soc.* **2000**, *122*, 5473-5476
Bratz, M.; Bullock, W.H.; Overman, L.E.; Takemoto, T. *J. Am. Chem. Soc.* **1995**, *117*, 5985-5966

Representative C15 Medium-Sized Ring Ether Marine Metabolites



1.Total Synthesis of (+)-Laurencin: The Key Reaction



31%, X = Me_3Si ($SnCl_4$, CH_2Cl_2, -60 to -20^oC)
78%, X = PhS (BF_3*Et_2O, t-BuOMe, -78 to -30^oC)

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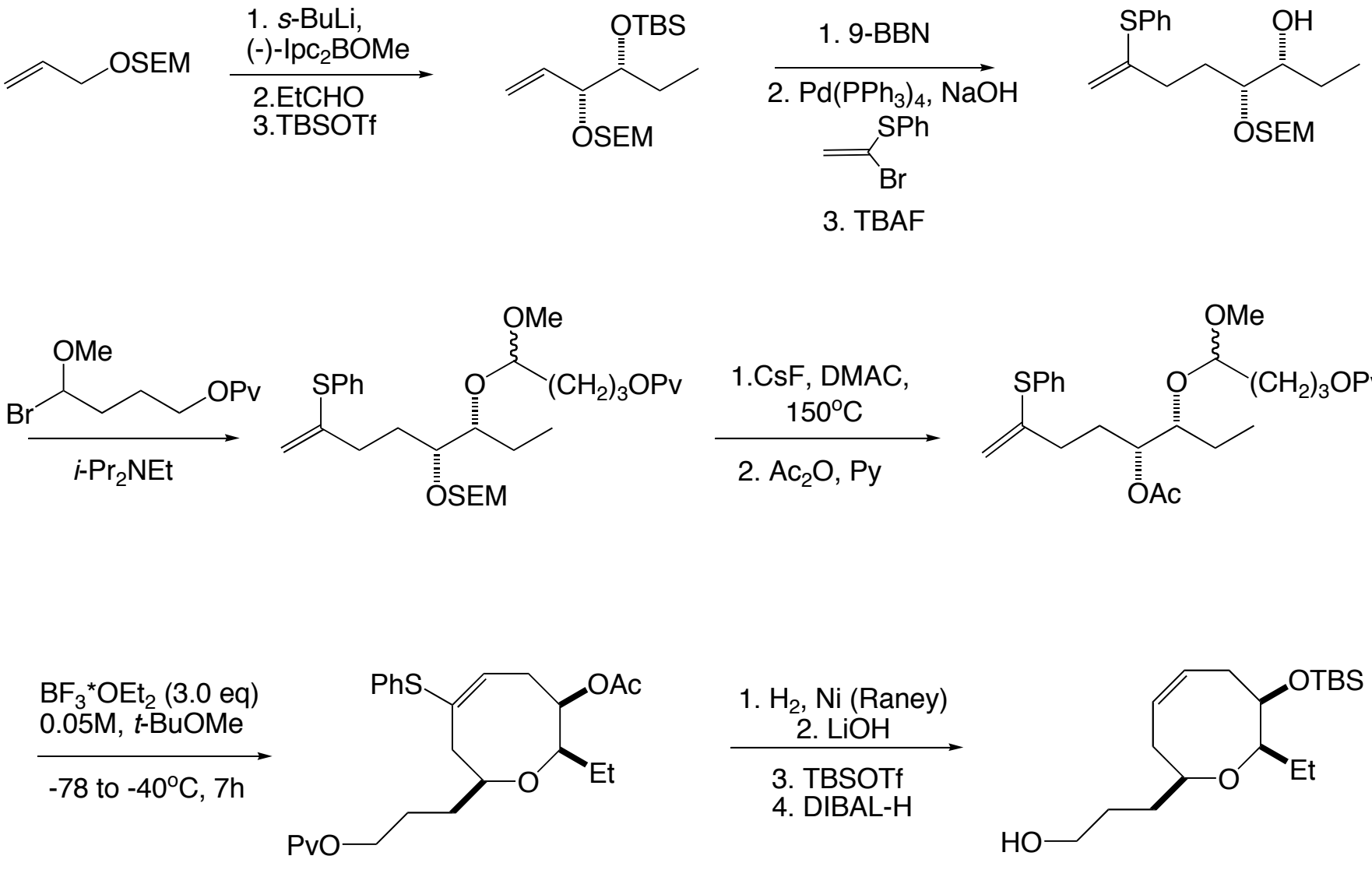
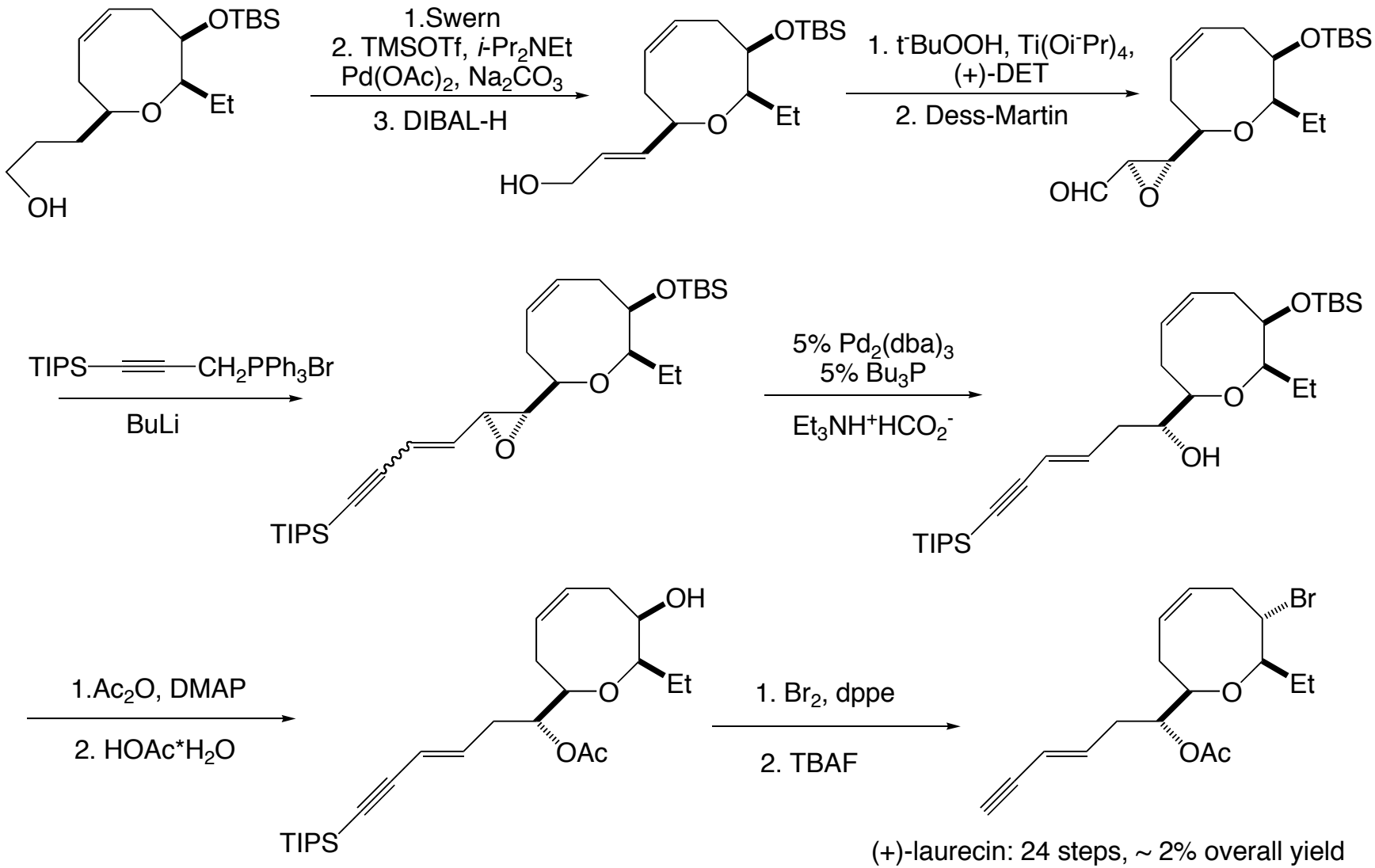
1.Total Synthesis of (+)-Laurencin: Cyclization

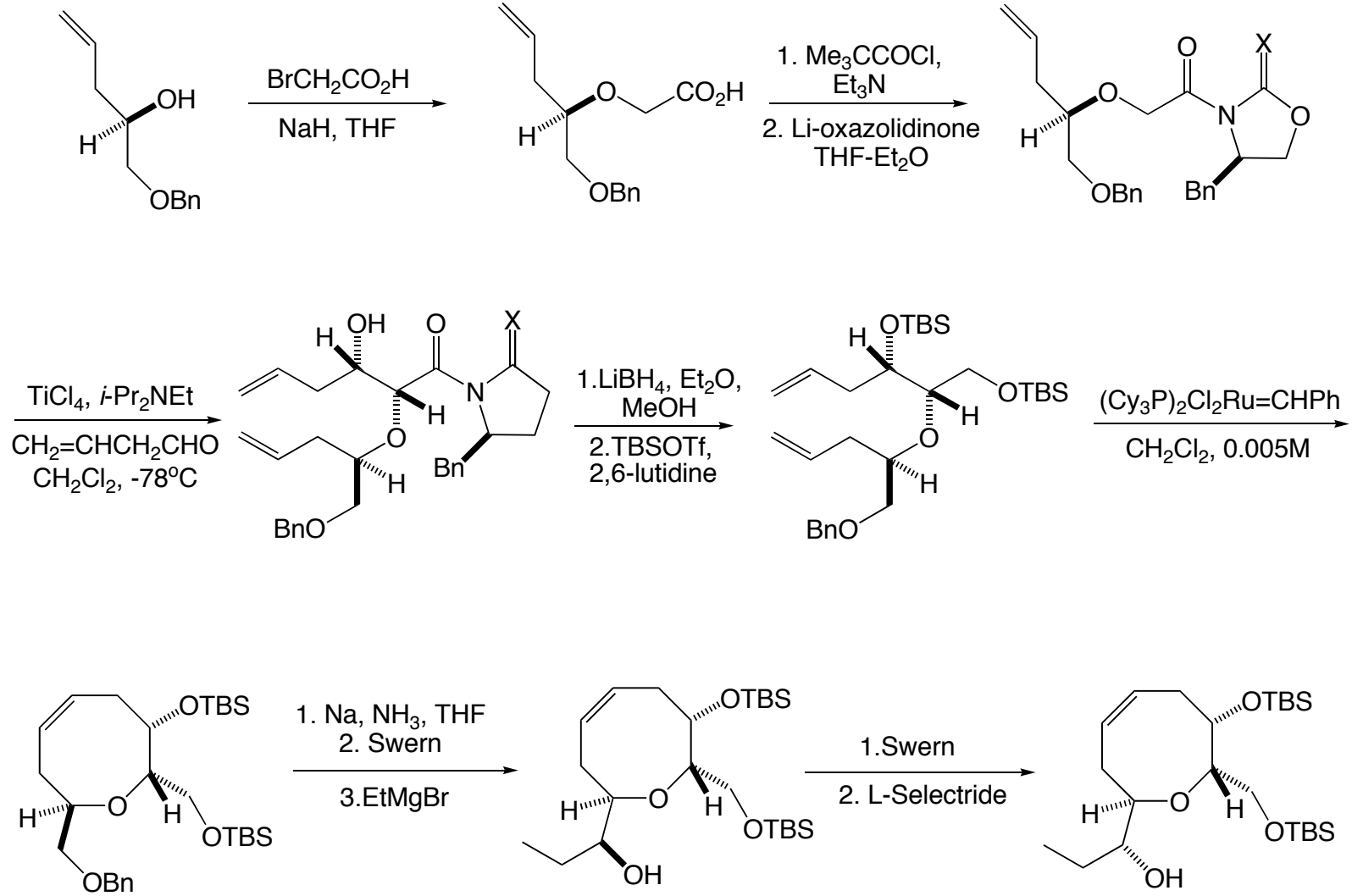


1.Total Synthesis of (+)-Laurencin: Final Steps



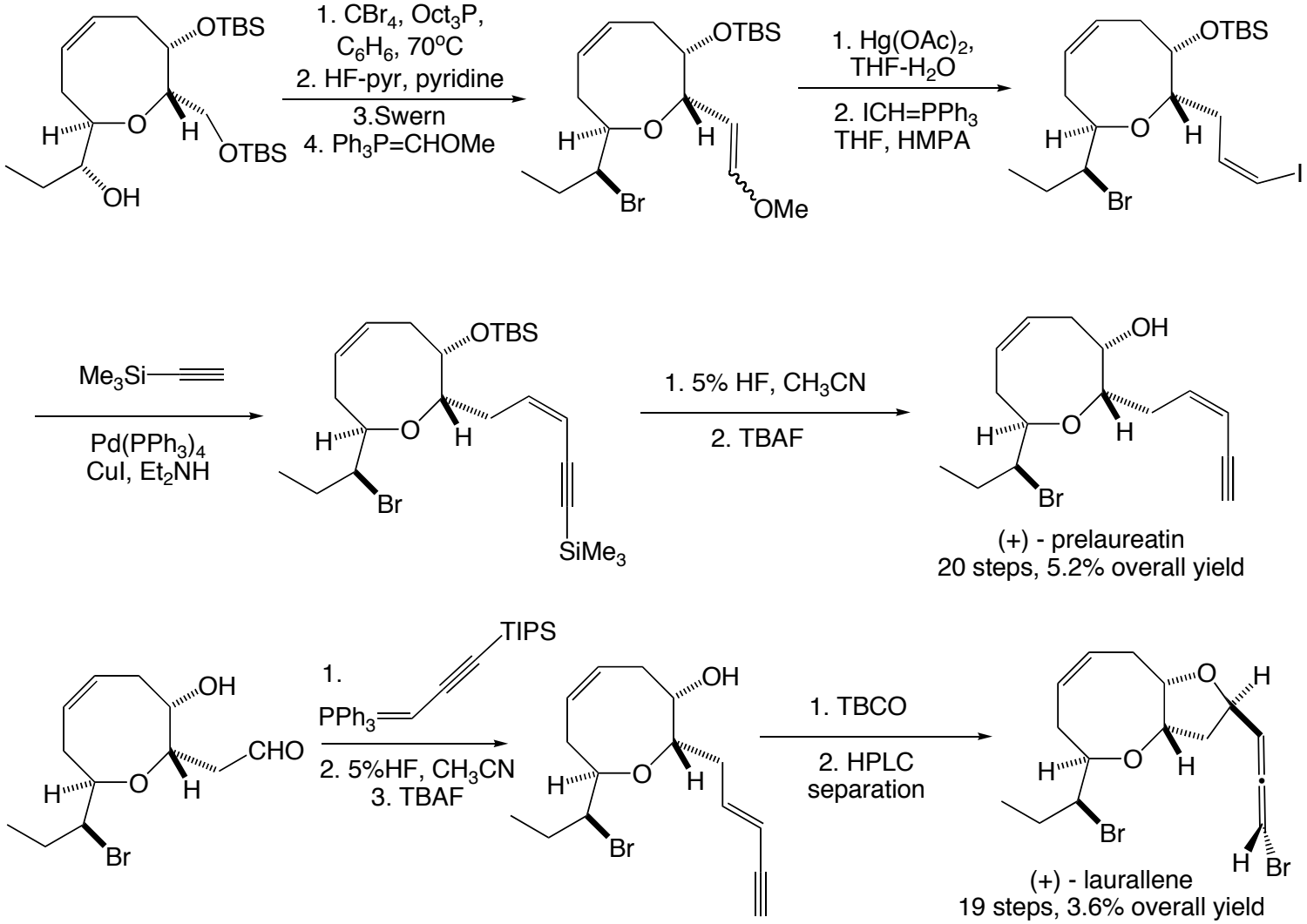
(+)-laurecin: 24 steps, ~ 2% overall yield

2.Total Synthesis of (+)-Prelaureatin and (+)-Laurallene: The Key Step and The Ring Closure

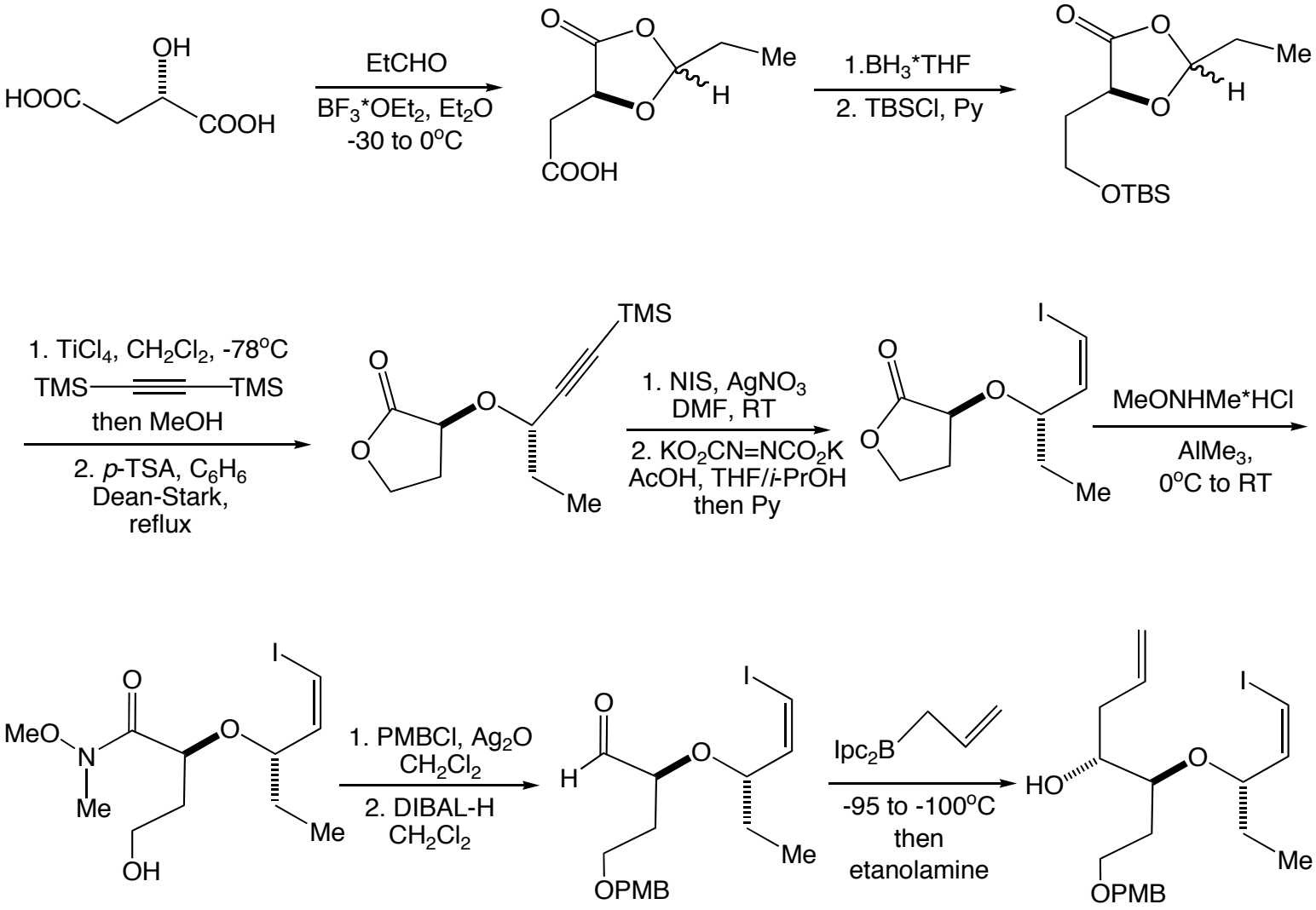


Crimmins, M.T.; Tabet, E.A. *J. Am. Chem. Soc.* **2000**, *122*, 5473-5476

2.Total Synthesis of (+)-Prelaureatin and (+)-Laurallene: Finishing Steps



3.Total Synthesis of (+)-Brasilenyne: Beginning



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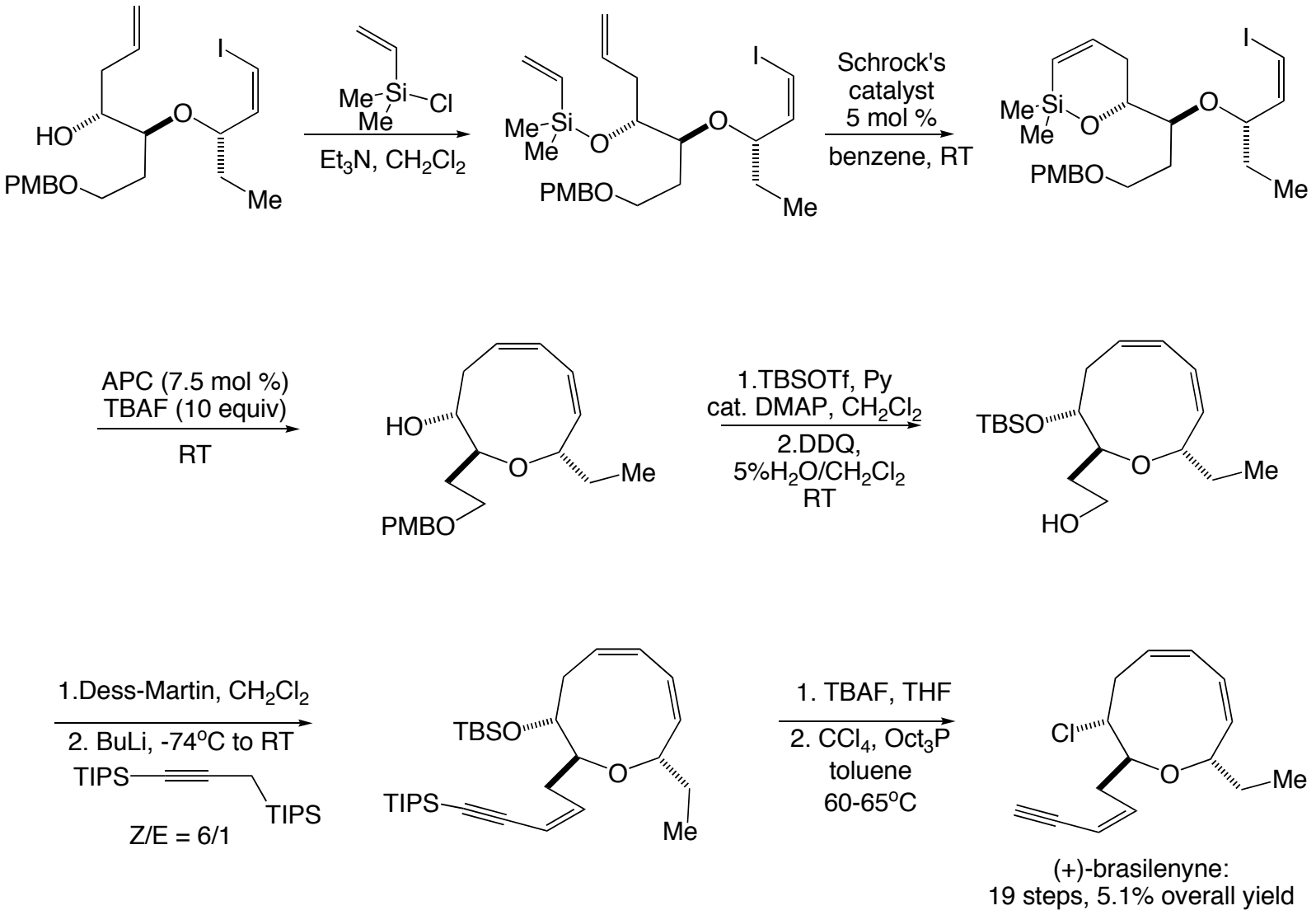
3.Total Synthesis of (+)-Brasilenyne: The End



(+)-brasilenyne:
19 steps, 5.1% overall yield

Conclusions:

- Medium-sized rings are very common to many classes of natural products, especially marine metabolites
- Even relatively simple natural products, containing medium-sized rings, are challenging synthetic targets, requiring individual approach
- Among others, metathesis and coupling reactions are most popular means of medium size ring construction