

Literature Report 2012-11-20

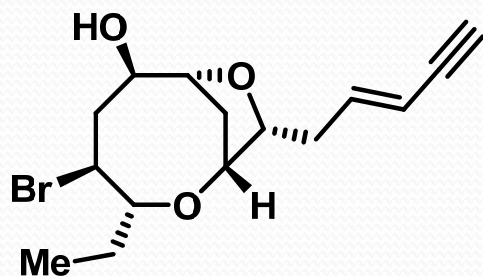
Duan, Y. Checker: Ye, Z.-S.

Concise Synthetic Approaches for the Laurencia Family: Formal Total Syntheses of (\pm)-Laurefucin and (\pm)-*E*- and (\pm)-*Z*-Pinnatifidenyne

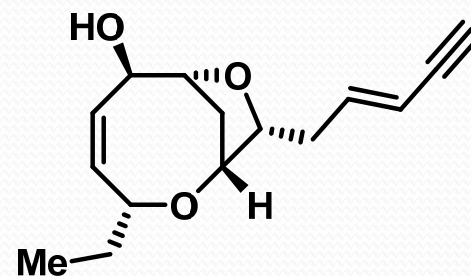
Snyder, S. A. *et al*

J. Am. Chem. Soc. 2012, 134, 17714–17721

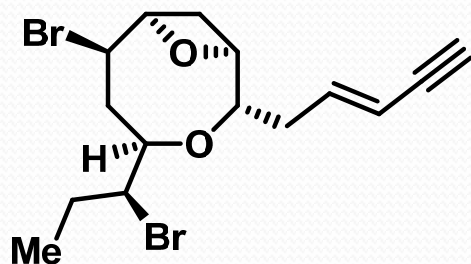
Structures of selected Lauroxocane natural products



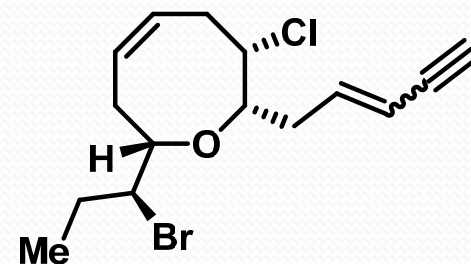
1: Laurefucin



2: 3E-dehydrobromolaurefucin

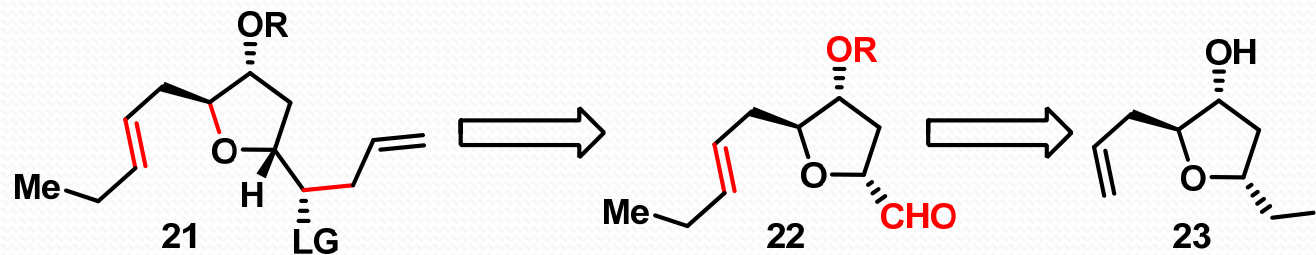
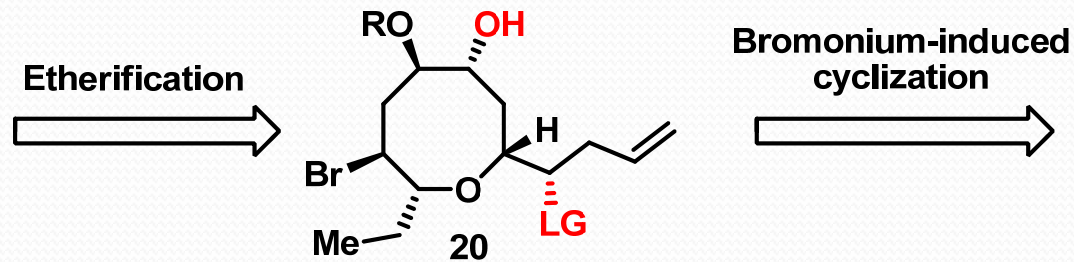
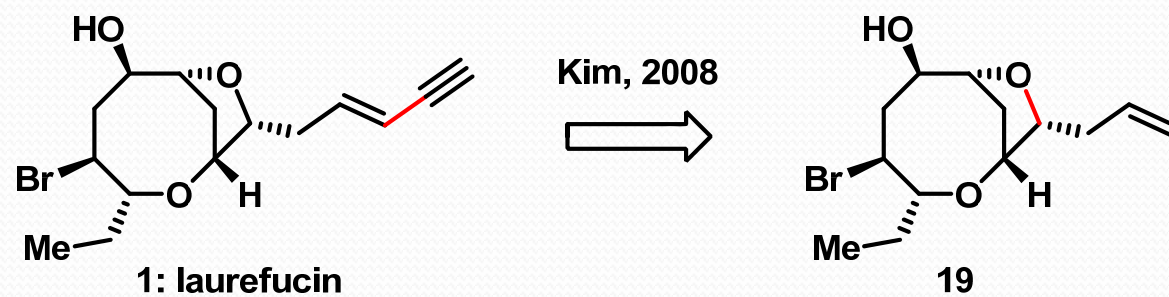


3: 3E-Laurefucin

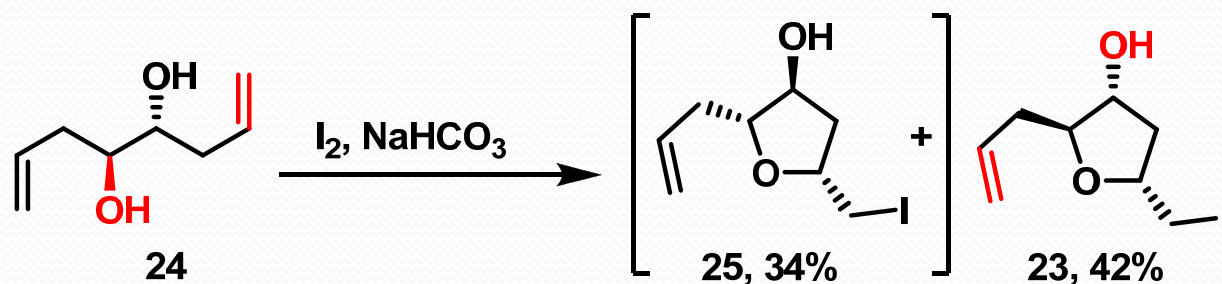


4: E-pinnatifidenyne
5: Z-pinnatifidenyne

Retrosynthesis of Laurefucin (1)

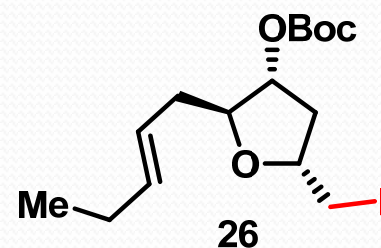


Racemic formal total synthesis of Laurefucin (1) using the BDSB ring-expansion method to access bromoether 19



1) 3-hexene, Hoveyda-Grubbs II, 78%

2) Boc_2O , 87%

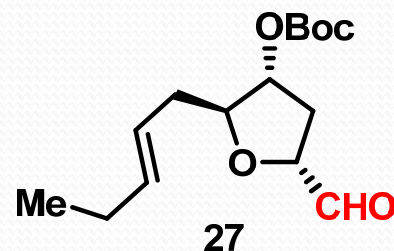


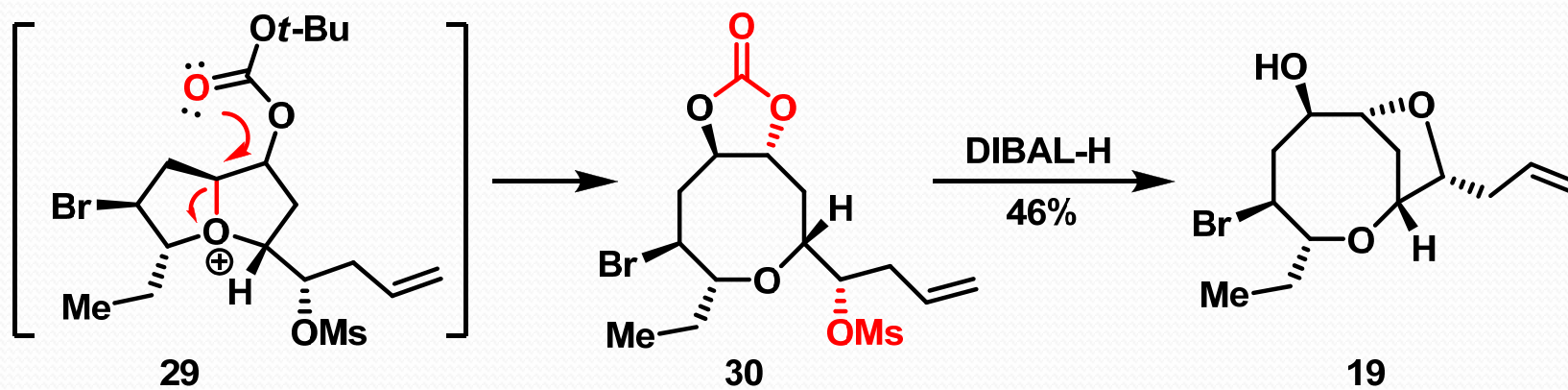
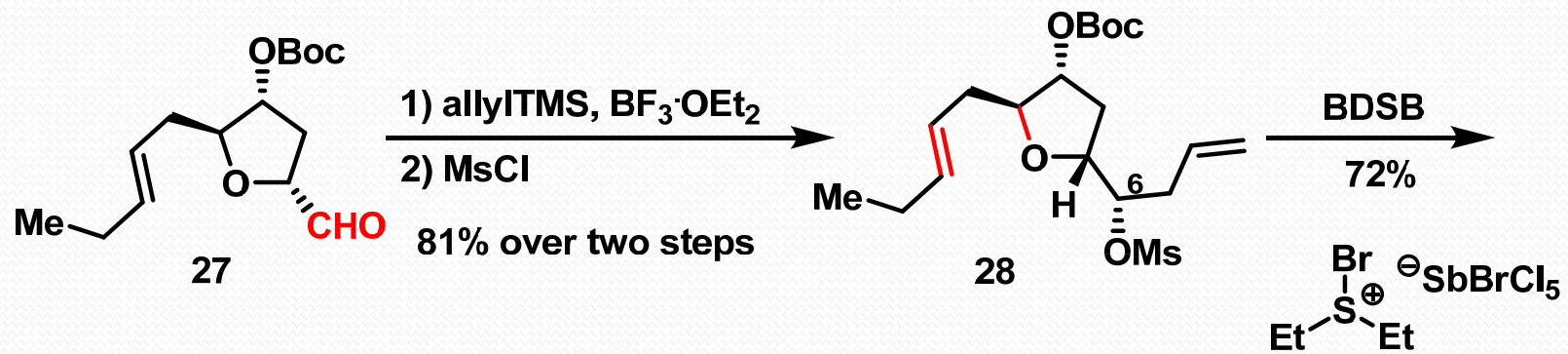
1) NaSPh

2) NCS, H_2O

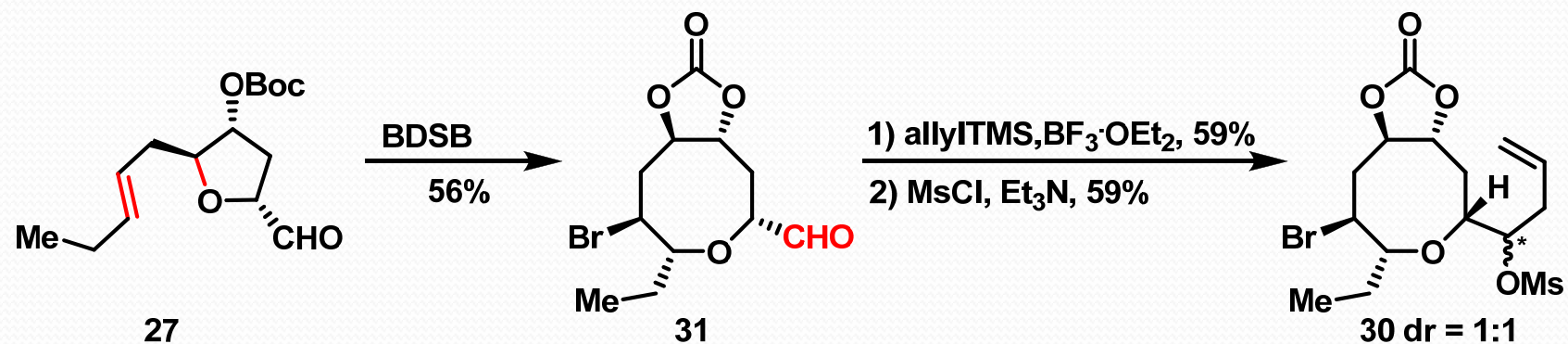
3) TFAA, $NaHCO_3$

60% over three steps

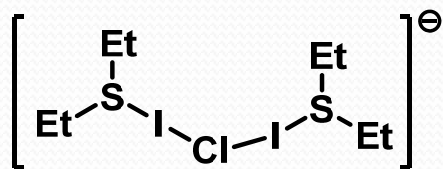
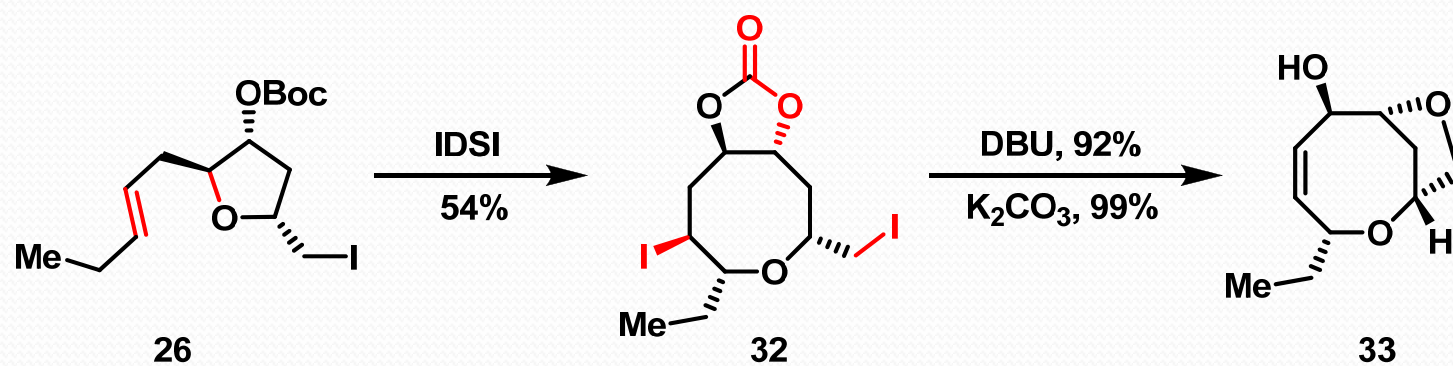




Alternate sequence to generate key intermediate 30

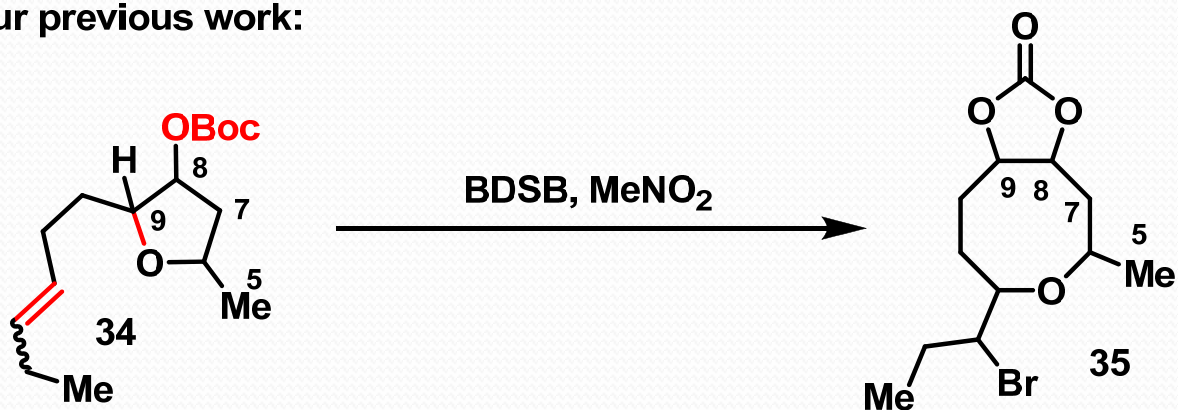


IDSI-Promoted ring expansion and elimination

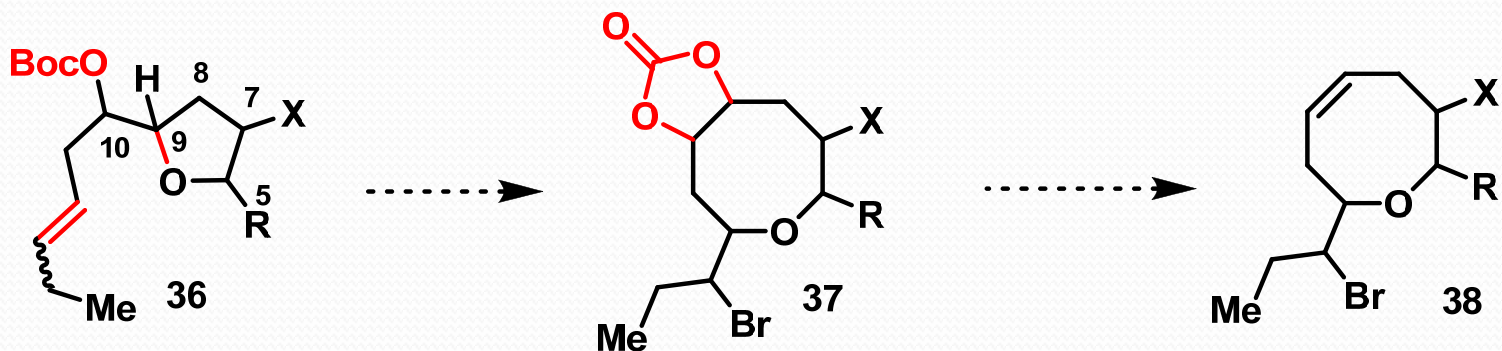


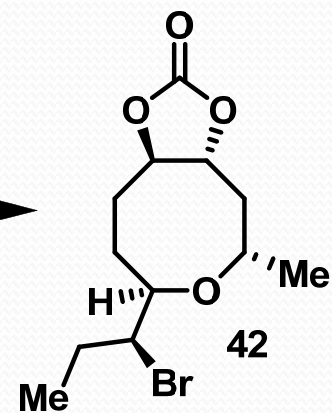
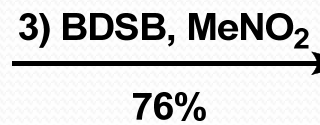
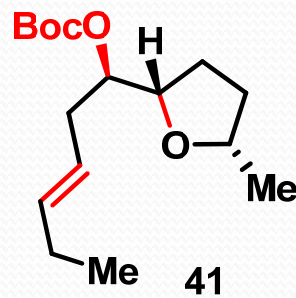
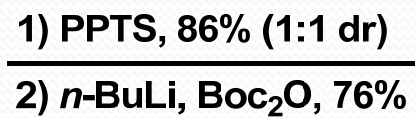
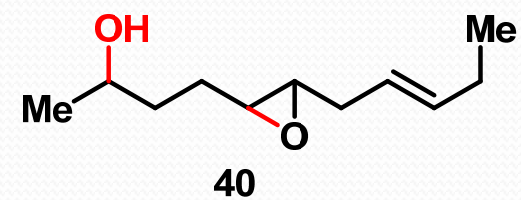
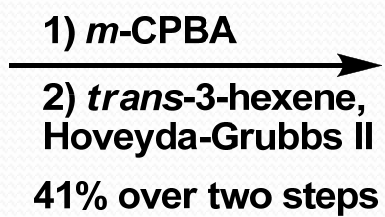
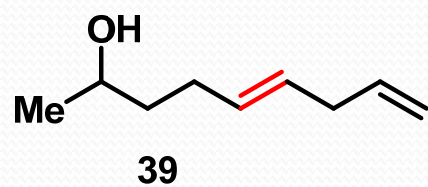
Changing the site of the nucleophilic trap to access alternate functionalization patterns for the Laurencia class

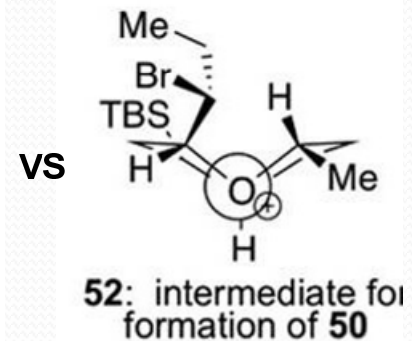
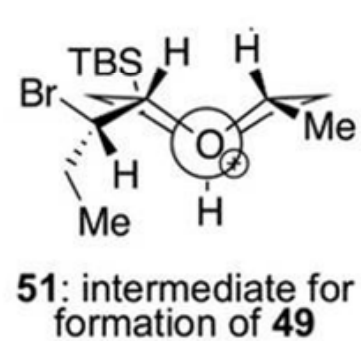
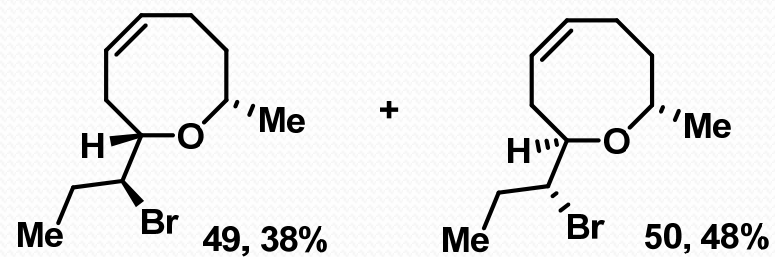
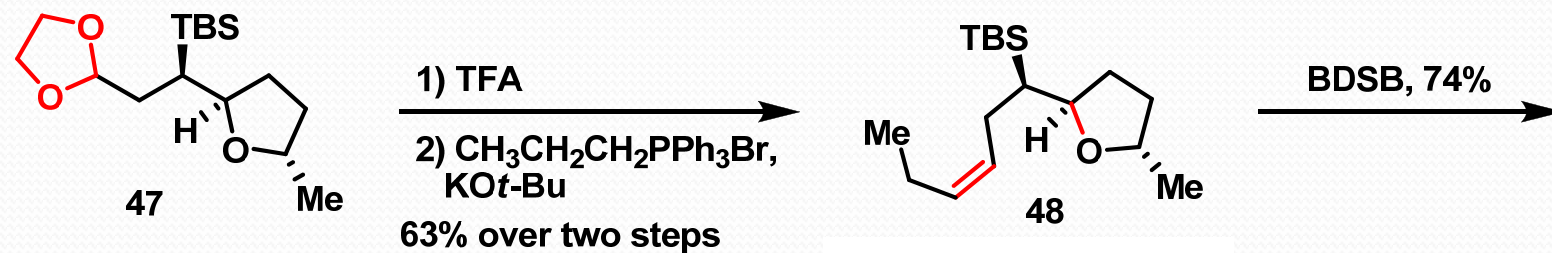
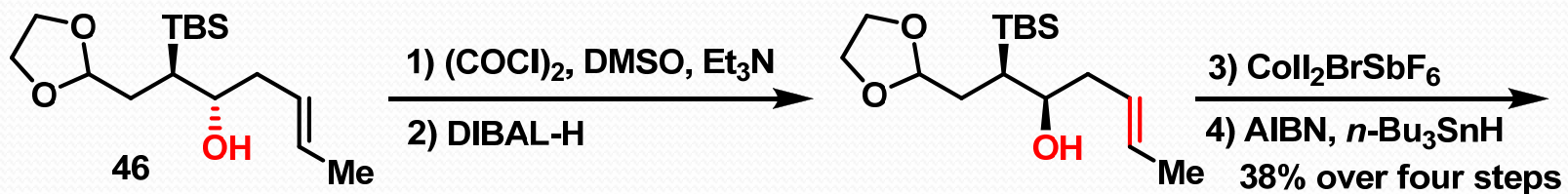
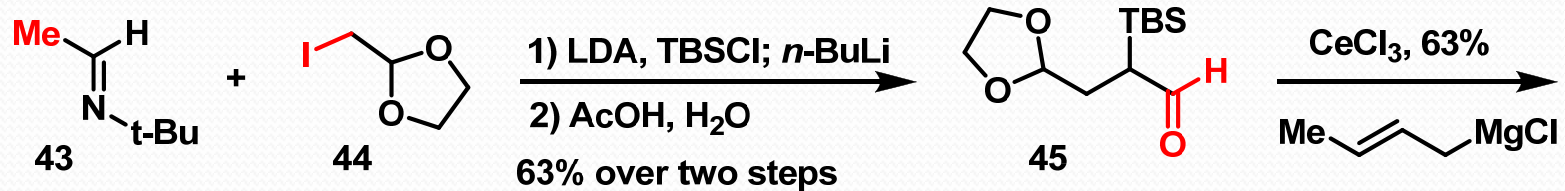
Our previous work:

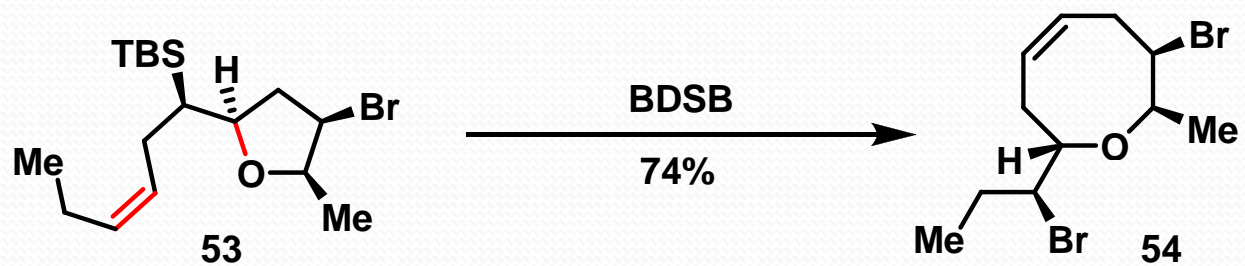


New approach changing the site of nucleophilic trap:

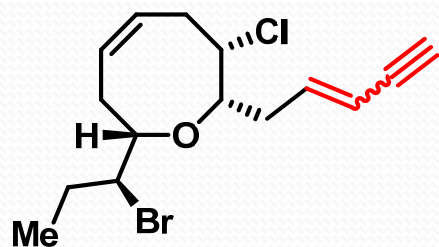




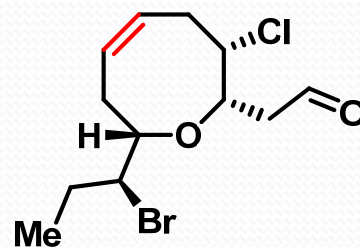




Retrosynthetic analysis for the Pinnatidienynes

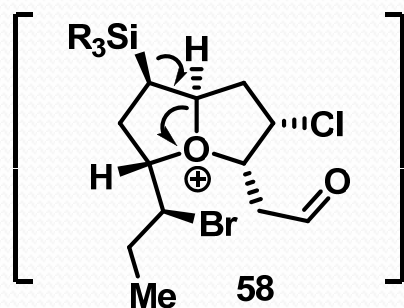
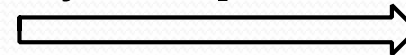


4: *E*-pinnatidienyne
5: *Z*-pinnatidienyne

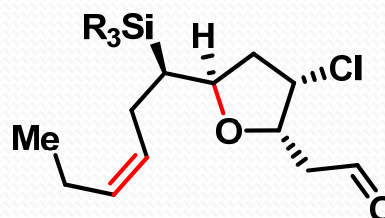


57

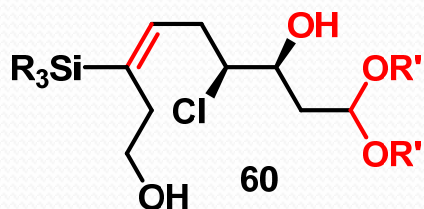
[Bromonium-induced
cyclization]



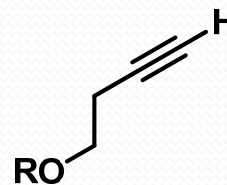
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59

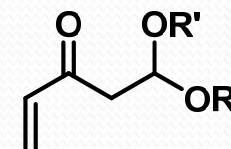


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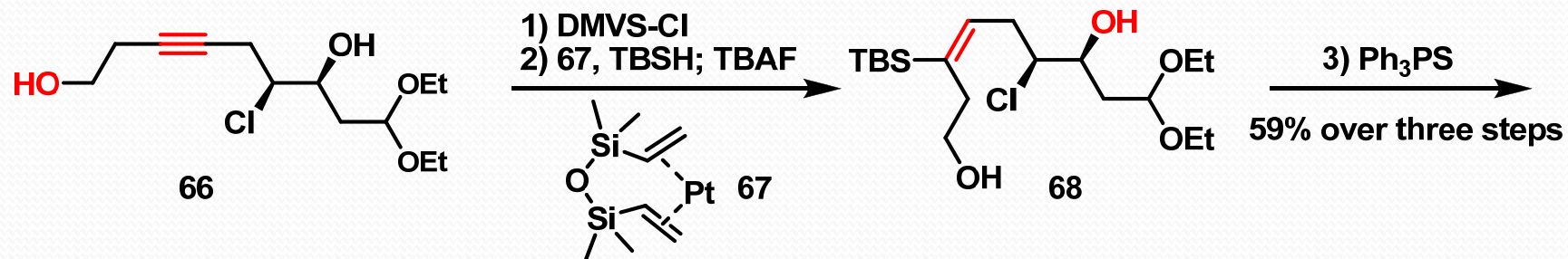
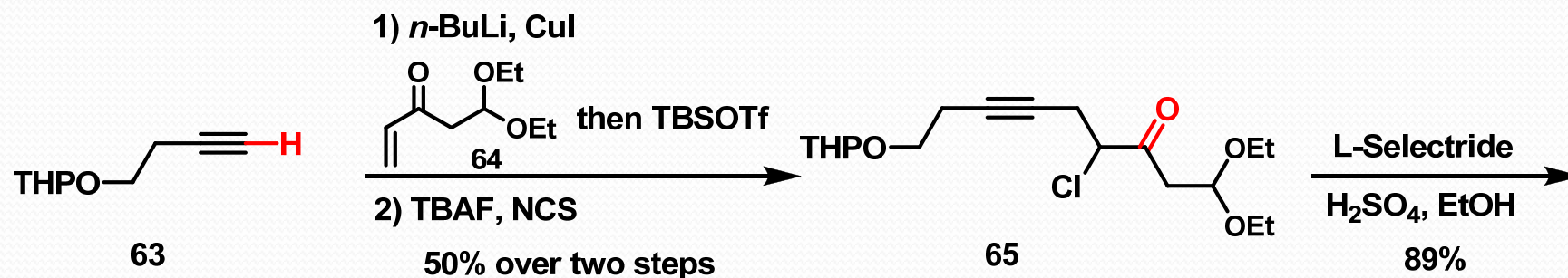
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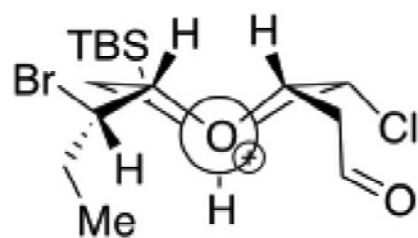
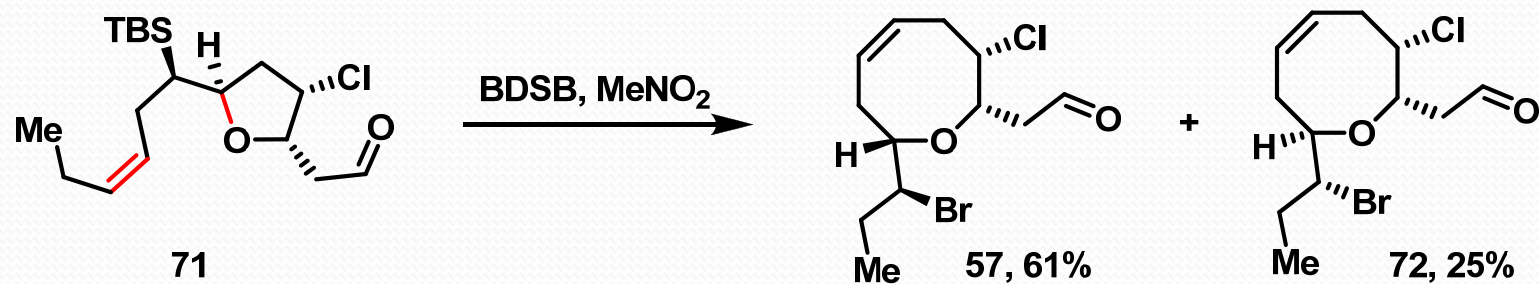
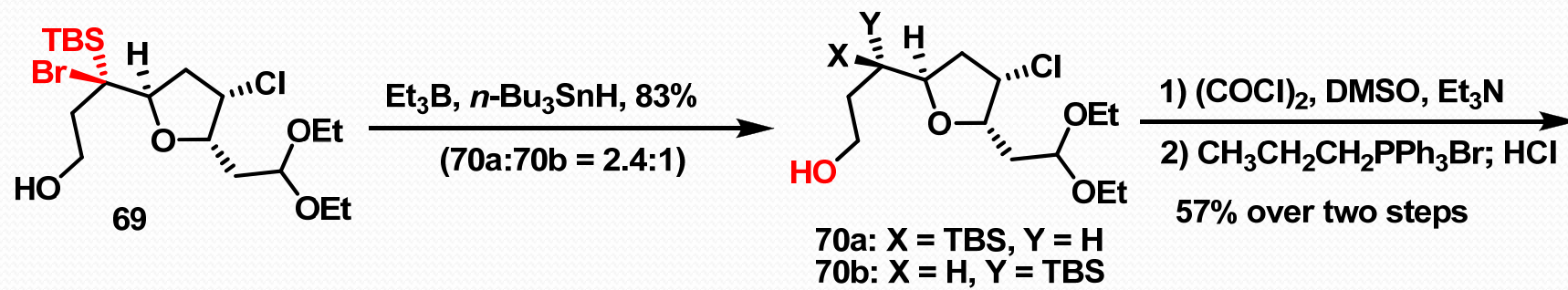
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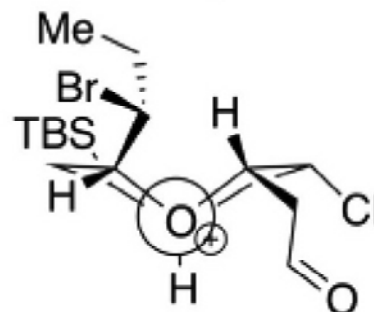
Racemic formal total synthesis of the Pinnatifidenynes using a BDSB initiated ring expansion of an alkylsilane






73: intermediate for formation of 57

vs.



74: intermediate for formation of 72



The lauroxocane natural products (including 1–5, Figure 1), a significant subset of the Laurencia class of haloethers, have been the subject of much experimental interest in recent years. Whether as a testing ground to evaluate strategies for the preparation of stereochemically rich medium-sized rings or as an arena to explore biogenetic hypotheses, numerous discoveries continue to be made in connection with these molecules. For example, we recently developed a stereocontrolled ring-expanding bromoetherification, empowered by a unique bromonium source (BDSB, $\text{Et}_2\text{SBr}\cdot\text{SbBrCl}_5$), which proved capable of forging a diverse array of products reflective of the class.

We have developed sequences capable of rapidly delivering three natural products within the Laurencia family alongside several other congeners that reflect the core functionalization patterns of the class. These syntheses are the most expedient to date in terms of step count, a feature we believe derives from: (1) the relative ease of fashioning complex, stereochemically dense tetrahydrofurans, (2) the diverse range of highly stereoselective ring-expanding bromoetherifications that have been developed, with alterations in the nature and position of the terminating nucleophilic trap providing distinct functional arrays, and (3) examples of modifying eight-membered ring backbone functionality without initiating rearrangements. Overall, we expect that the approach delineated in this Article should afford expedient syntheses of other lauroxocanes as well. As a final note, given the overall range of substrates for which our key ring-expanding bromoetherification process succeeds, both as reported here and in our previous work, it would seem reasonable to presume that such a rearrangement process may have biogenetic relevance given its overall facility and generally high levels of diastereocontrol.