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# Problems Answers

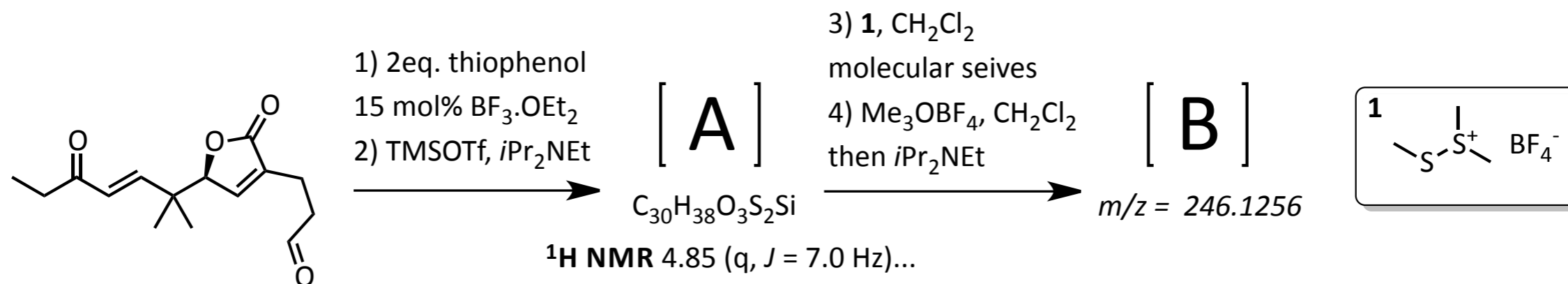
Johannes Walker

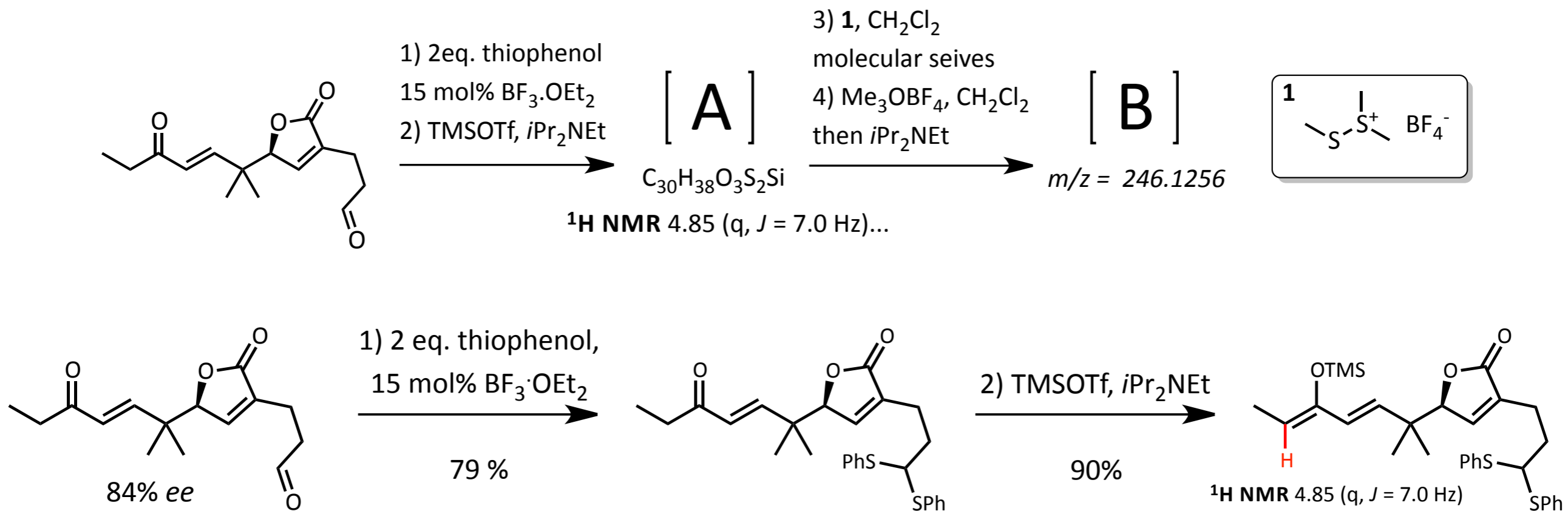
19/11/13

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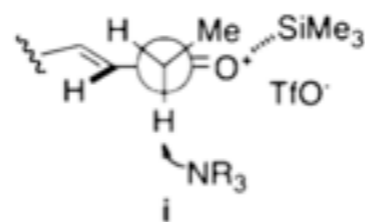
Trost, B.M.; *J. Am. Chem. Soc.*, **2012**, *134*, 1474–1477

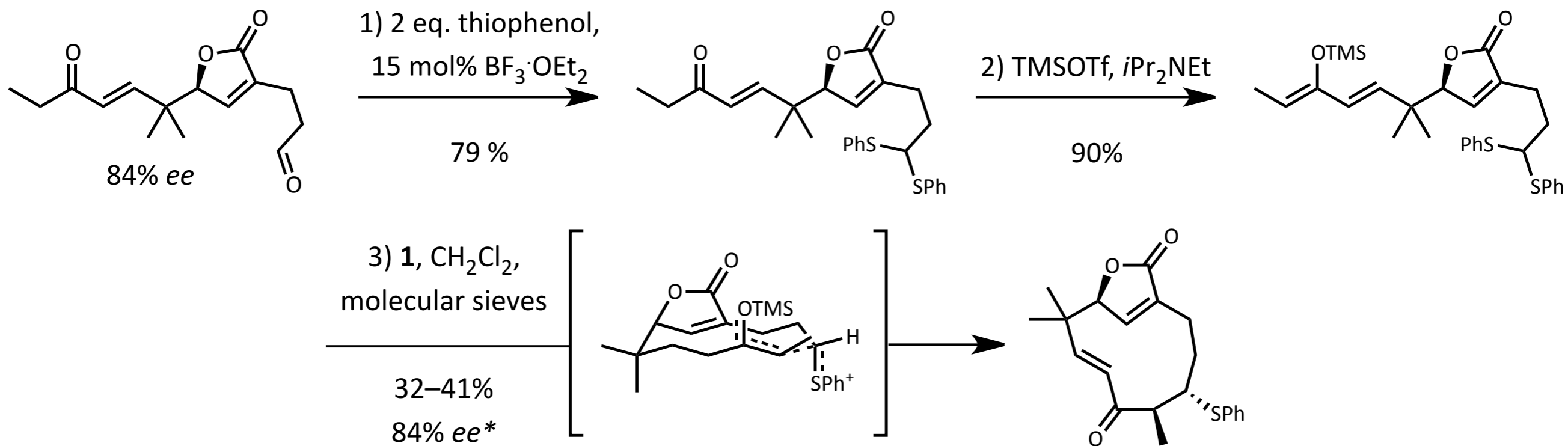
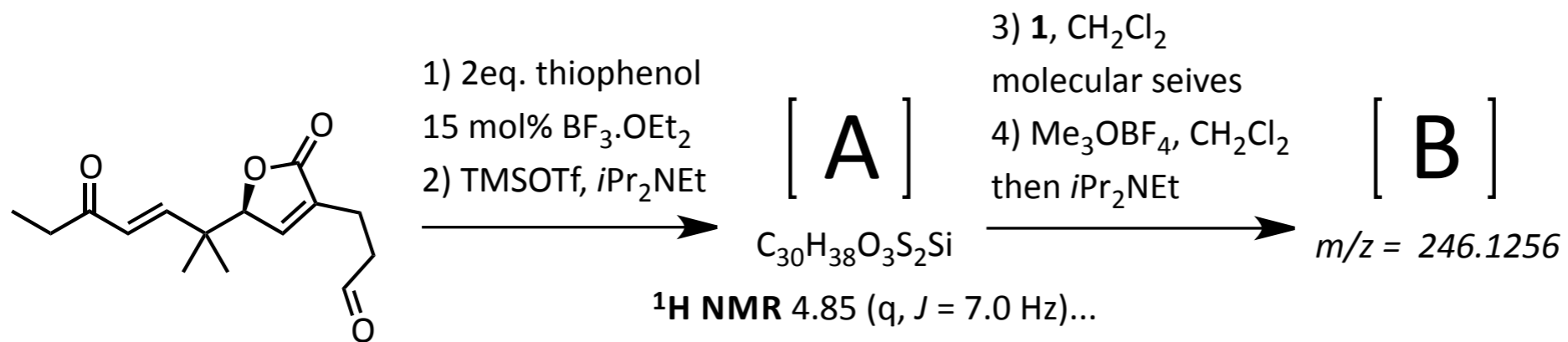
### Thionium Ion initiated Medium-Sized Ring Formation: The Total Synthesis of Asteriscunolide D



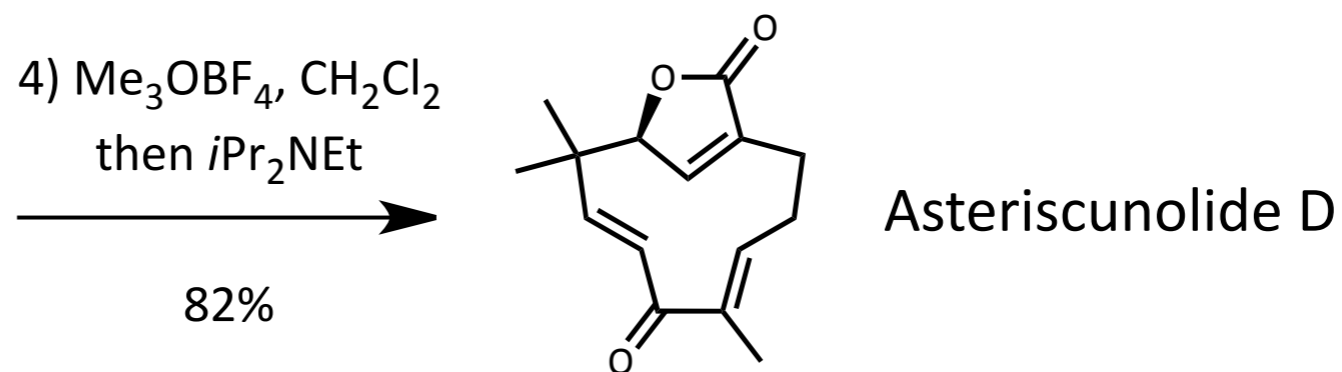


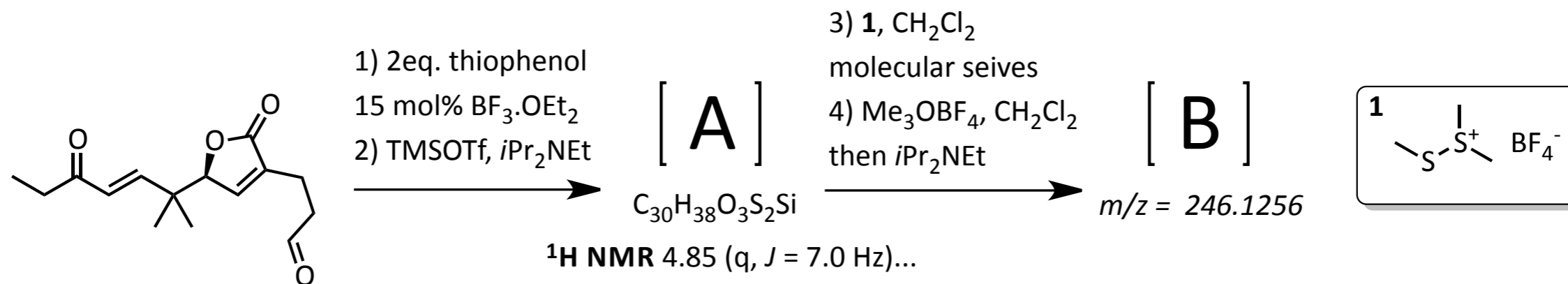
(19) An enolization model consistent with the observed *Z*-selectivity avoids steric interaction of the methyl group with the nearly coplanar vinyl hydrogen atom compared to a lone pair of electrons on oxygen as depicted in **i**.





\*Could be improved to >98% *ee* on recrystallisation



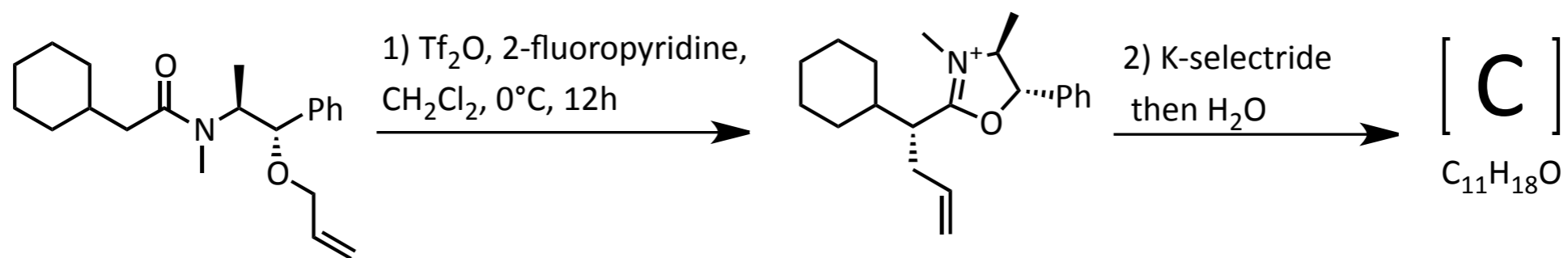


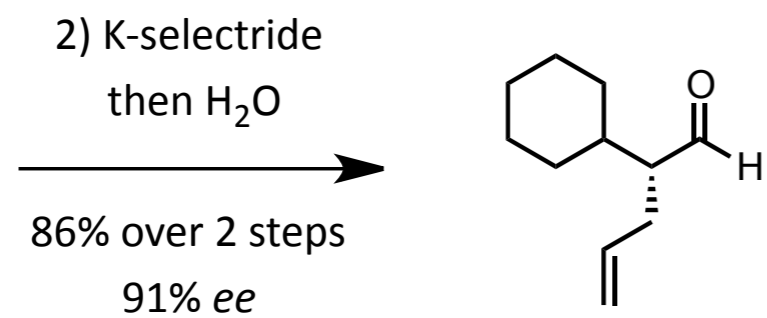
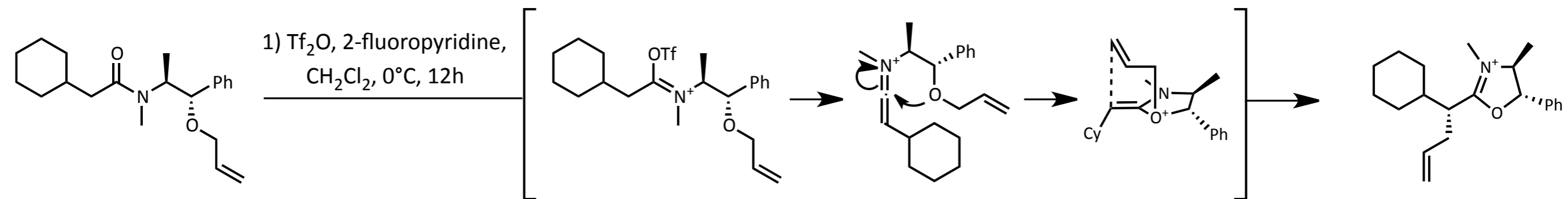
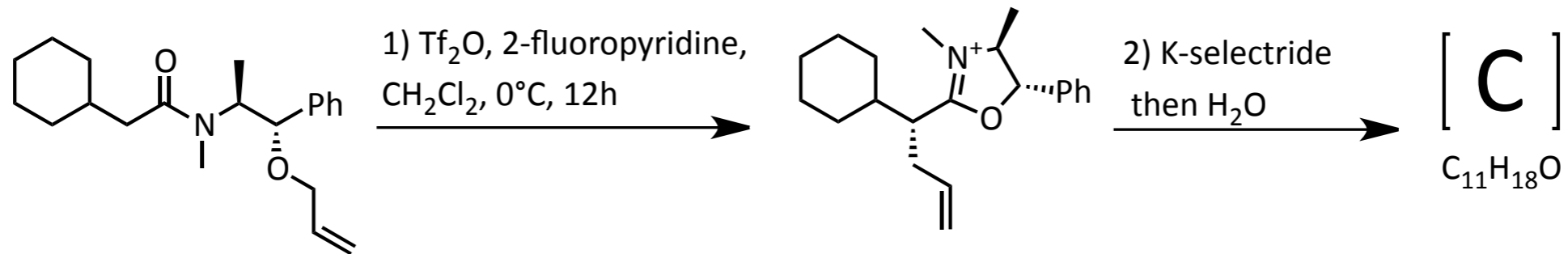
Points to note:

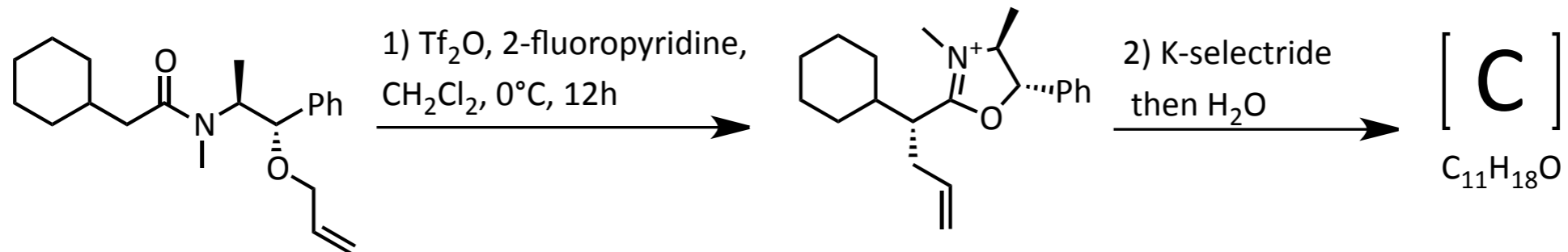
- 1) Use of thionium ions as ‘super-carbonyls’
- 2) DMTSF has also shown remarkably chemoselective activator for the thioacetal moiety in some acid sensitive compounds
- 3) Diastereoselective macrocyclisation to give usually difficult to form medium-sized ring
- 4) Stereoselective (*E*) olefin formation in final product, in accordance with the Hofmann elimination rule

Maulide, N.; *J. Am. Chem. Soc.*, **2013**, *135*, 14968–14971

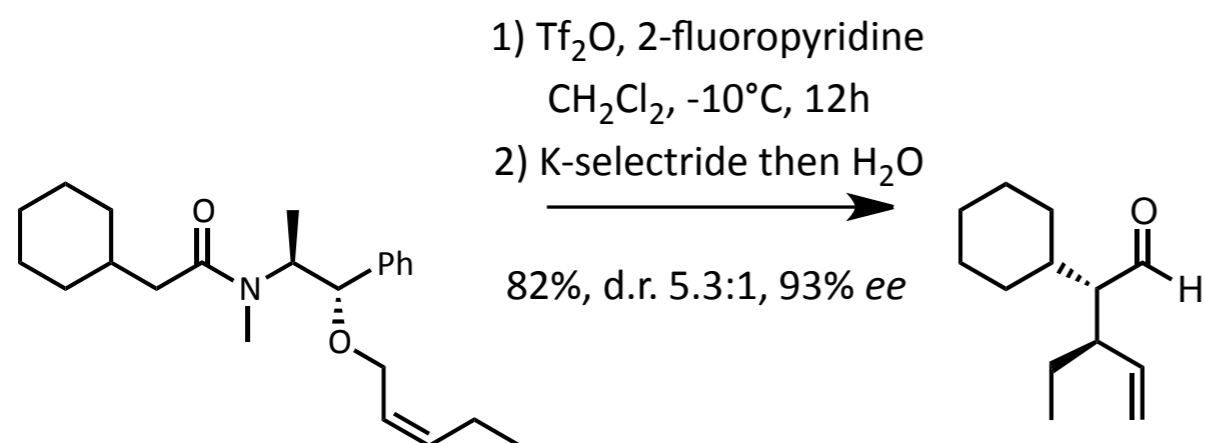
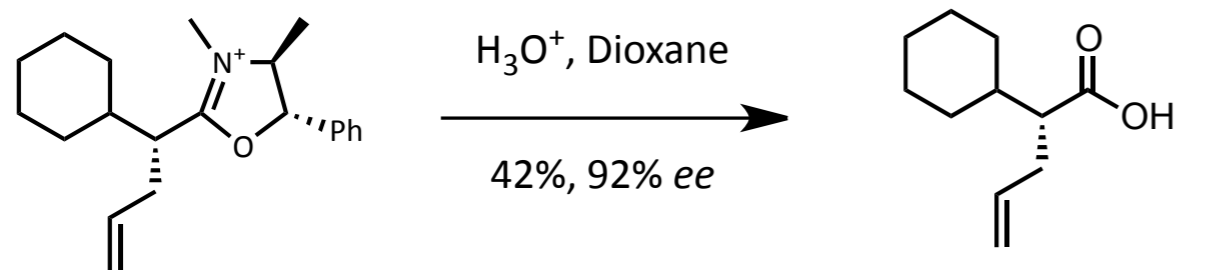
Electrophilic Rearrangements of Chiral Amides: A Traceless Asymmetric  $\alpha$ -Allylation



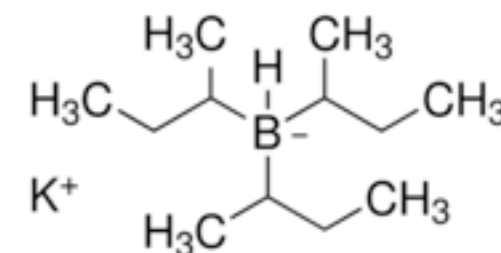




### Extensions to the methodology:



### K-Selectride:

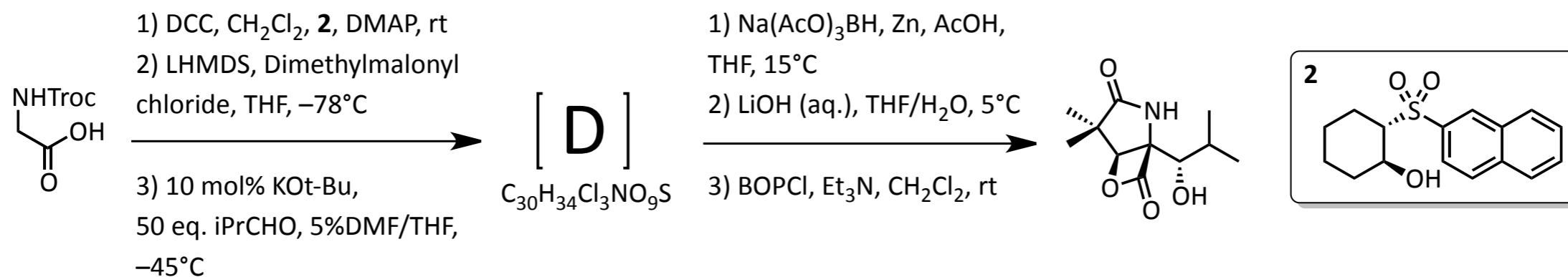


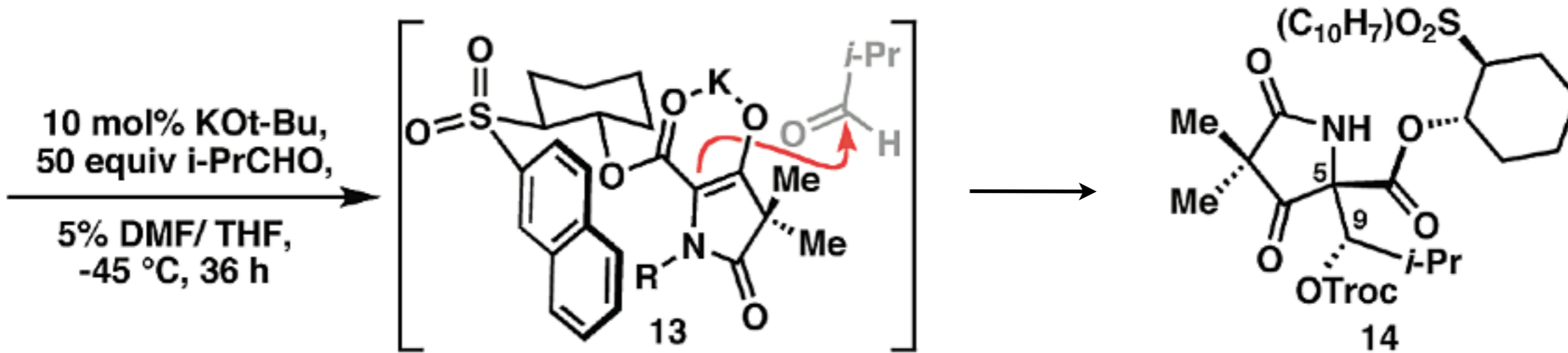
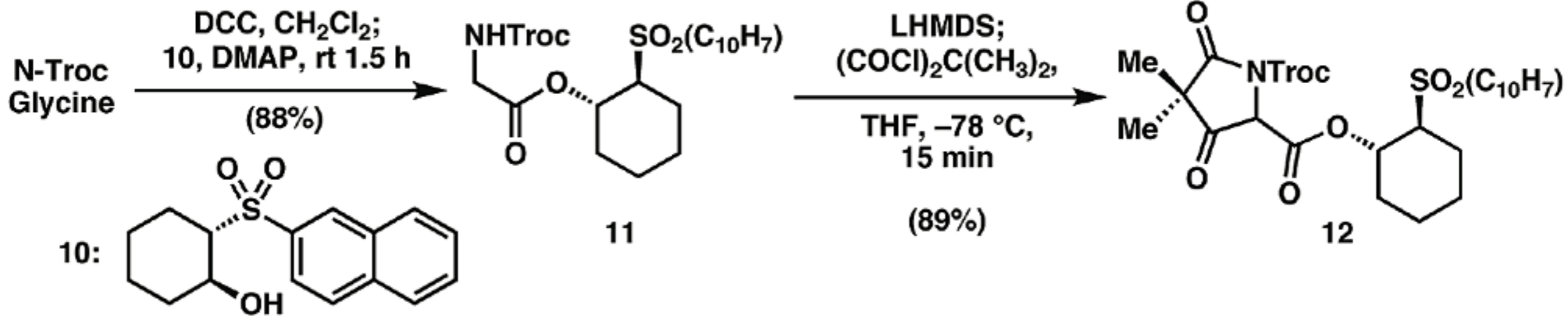
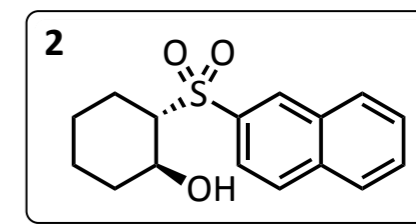
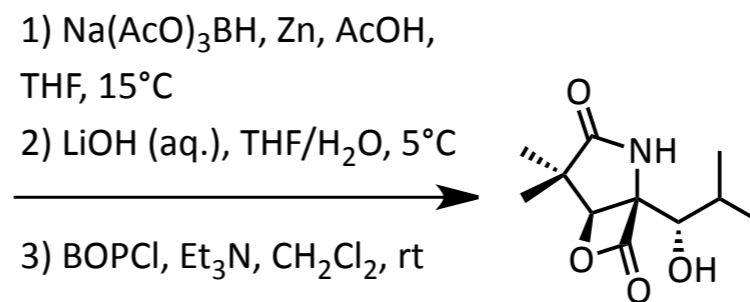
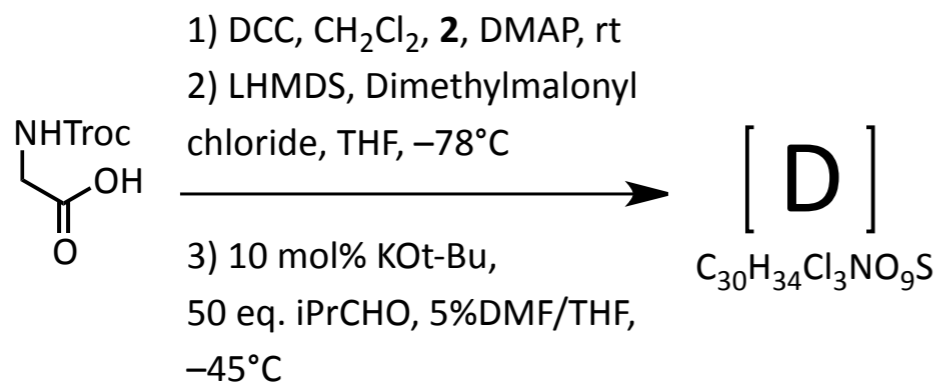
- Borohydride reducing agent
- N- (Sodium) and L- (Lithium) reagents are also available (Sigma)
- May be used for stereoselective conjugate hydride reductions and carbonyl 1,2 reductions due to steric bulk
- Also known to reduce imides, lactams and oxazolines in high yield, hence use here

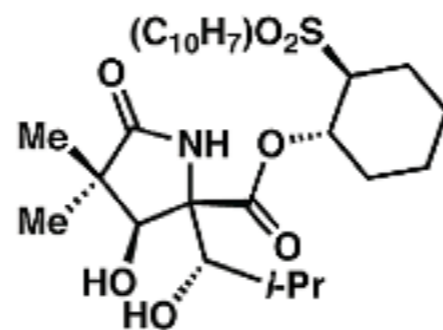
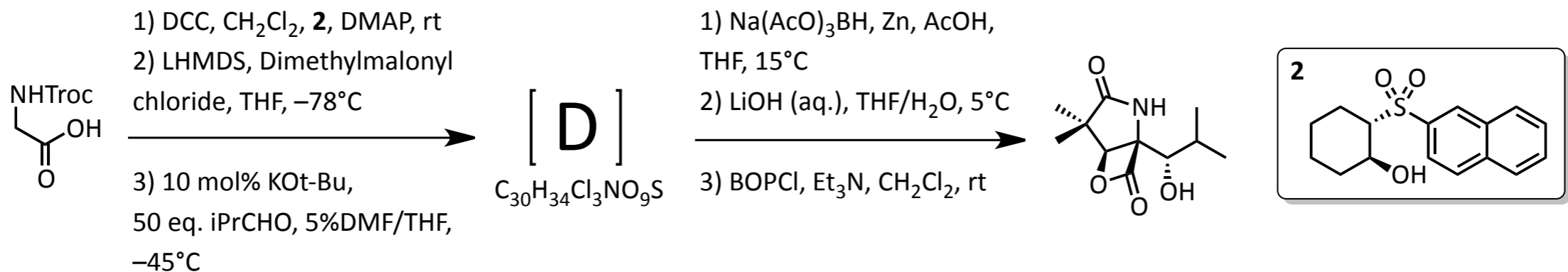


Corey, E.J.; *J. Am. Chem. Soc.*, **2009**, *131*, 5746–5747

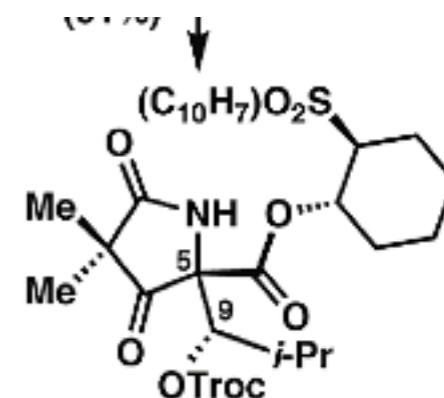
## A Short and Efficient Synthesis of (–)-7-Methylomuralide, a Potent Proteasome Inhibitor



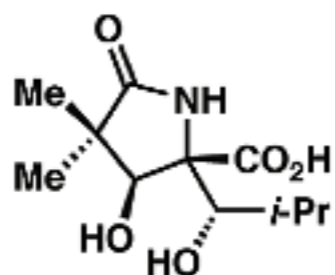




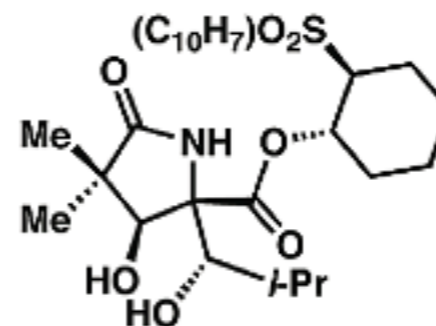
15



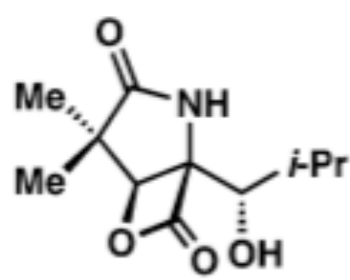
14



(-)-16

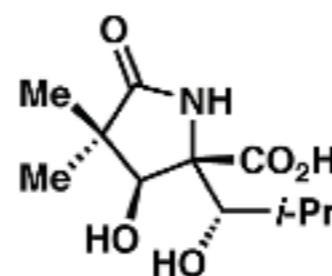


15



3

$\xrightarrow{\begin{array}{l} \text{BOPCl, Et}_3\text{N,} \\ \text{CH}_2\text{Cl}_2, \text{ rt, 1 h} \end{array}}$ 
  
 (80% over 2 steps)



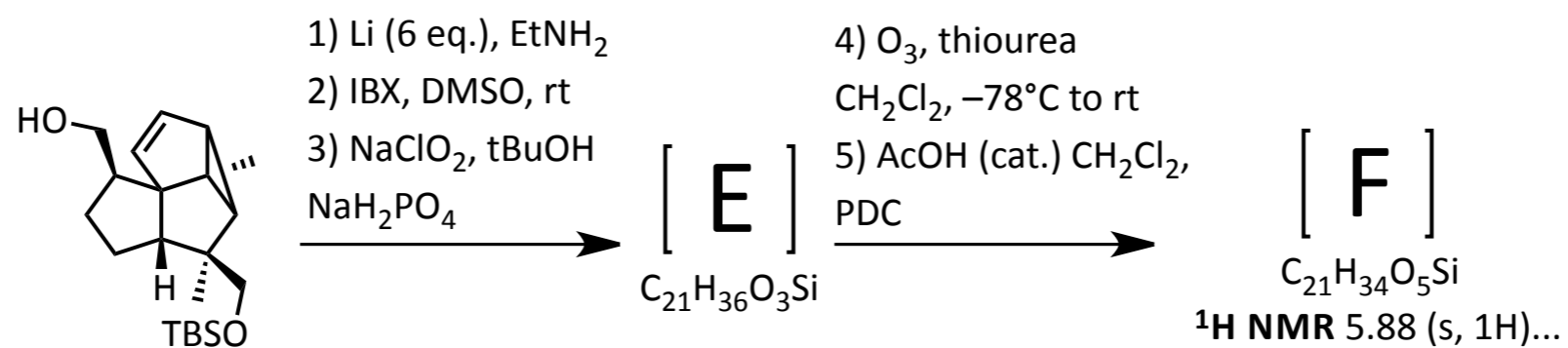
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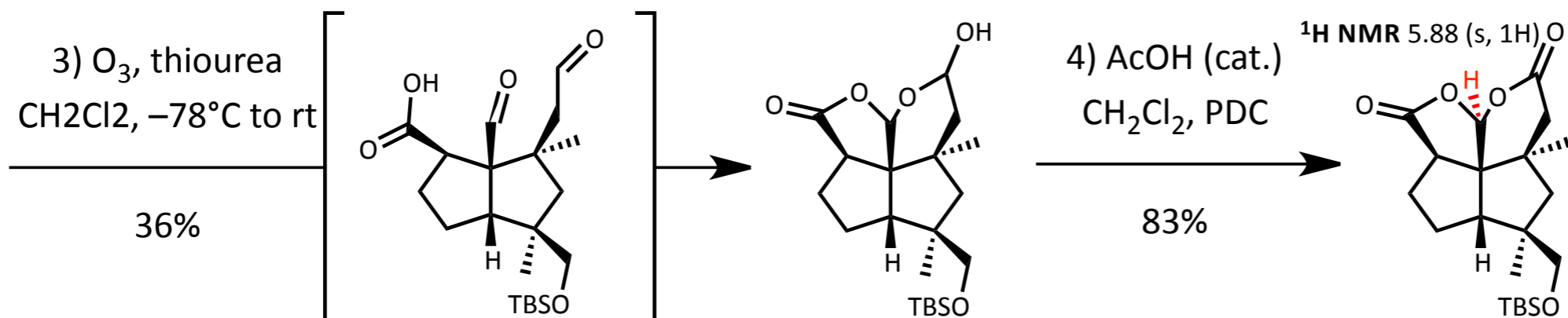
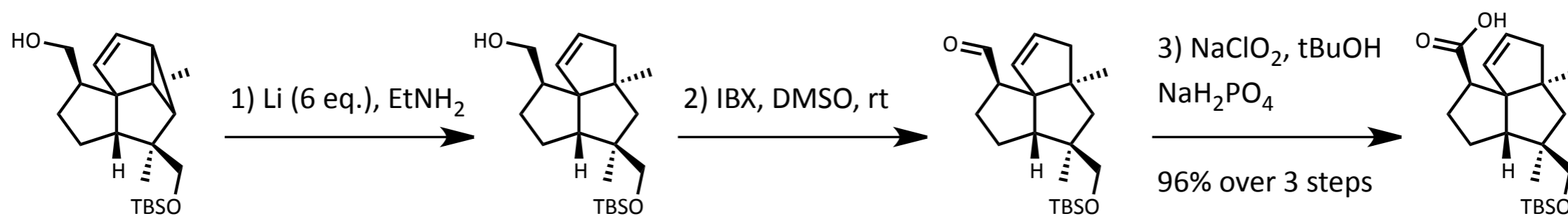
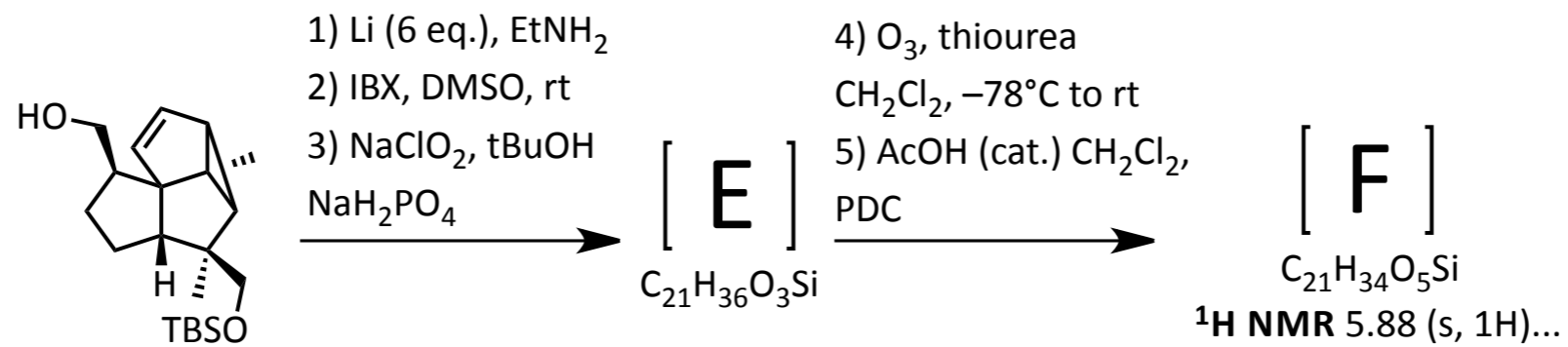
Points to note:

1) Use of chiral sulfone as an alternative chiral auxiliary

Mulzer, J.; *Org. Lett.*, **2010**, *12*, 272–275

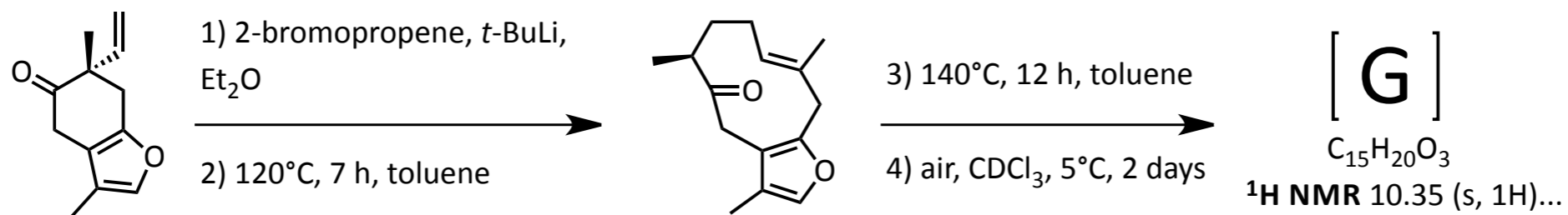
From Silphinenes to Penifulvins: A Biomimetic Approach to Penifulvins B and C

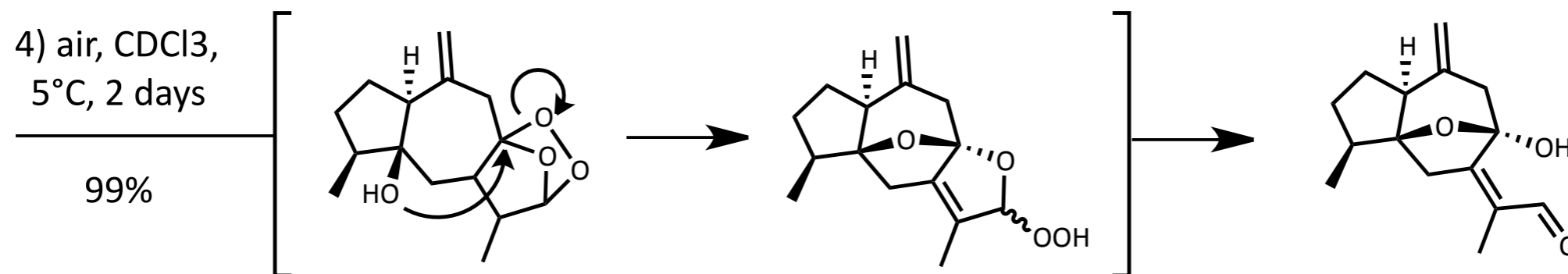
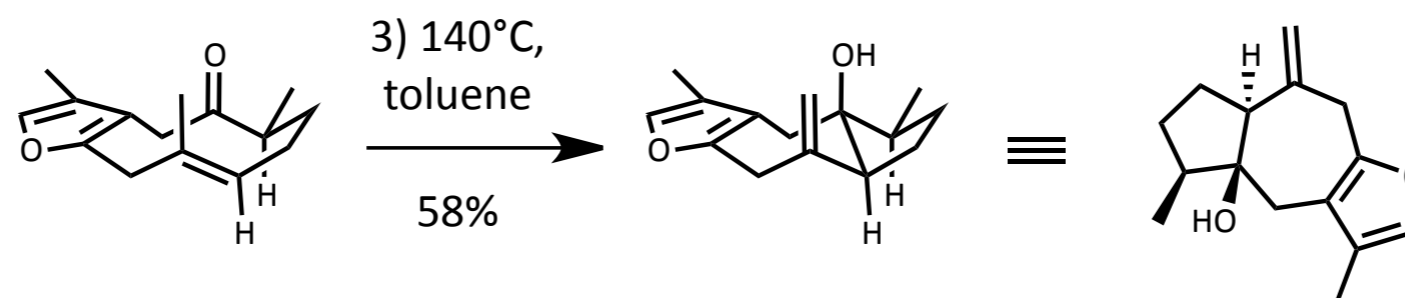
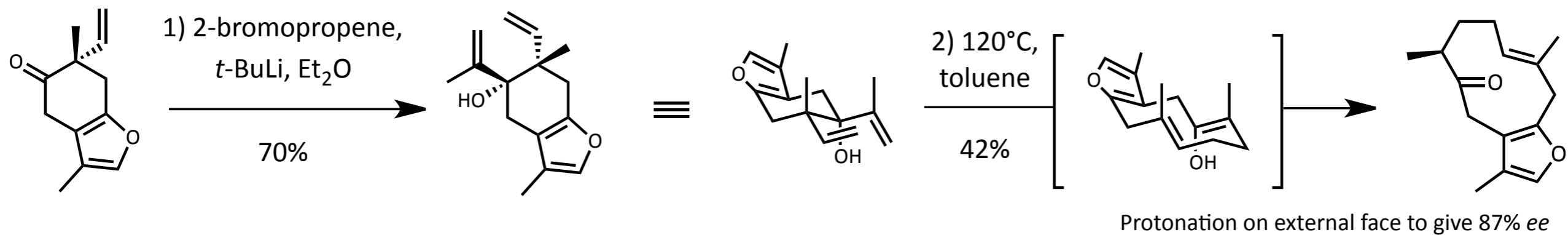
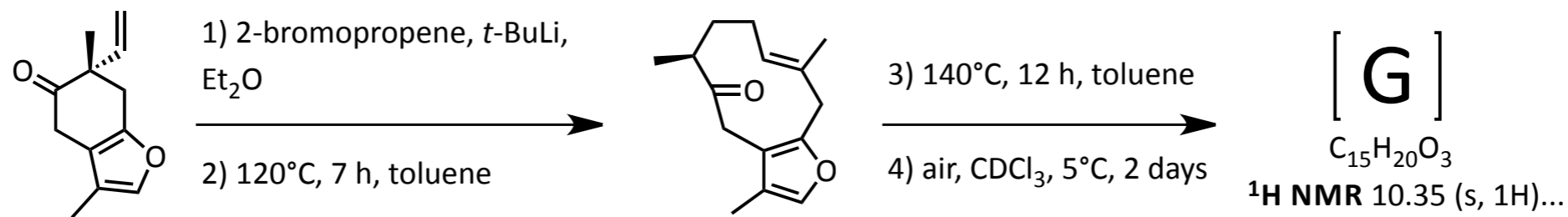




Zografos, A.; *Org. Lett.*, **2013**, *15*, 152–155

Non-natural Elemene as the “Stepping Stone” for the synthesis of Germacrane and Guaiane Sesquiterpenes





Things to note:

- 1) Rearrangement to give usually difficult to form medium-sized ring
- 2) Change in 10-membered ring conformation between Cope and ene reactions