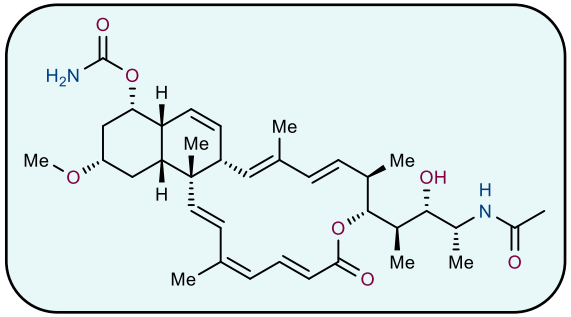
Superstolide A (Roush, 2008)

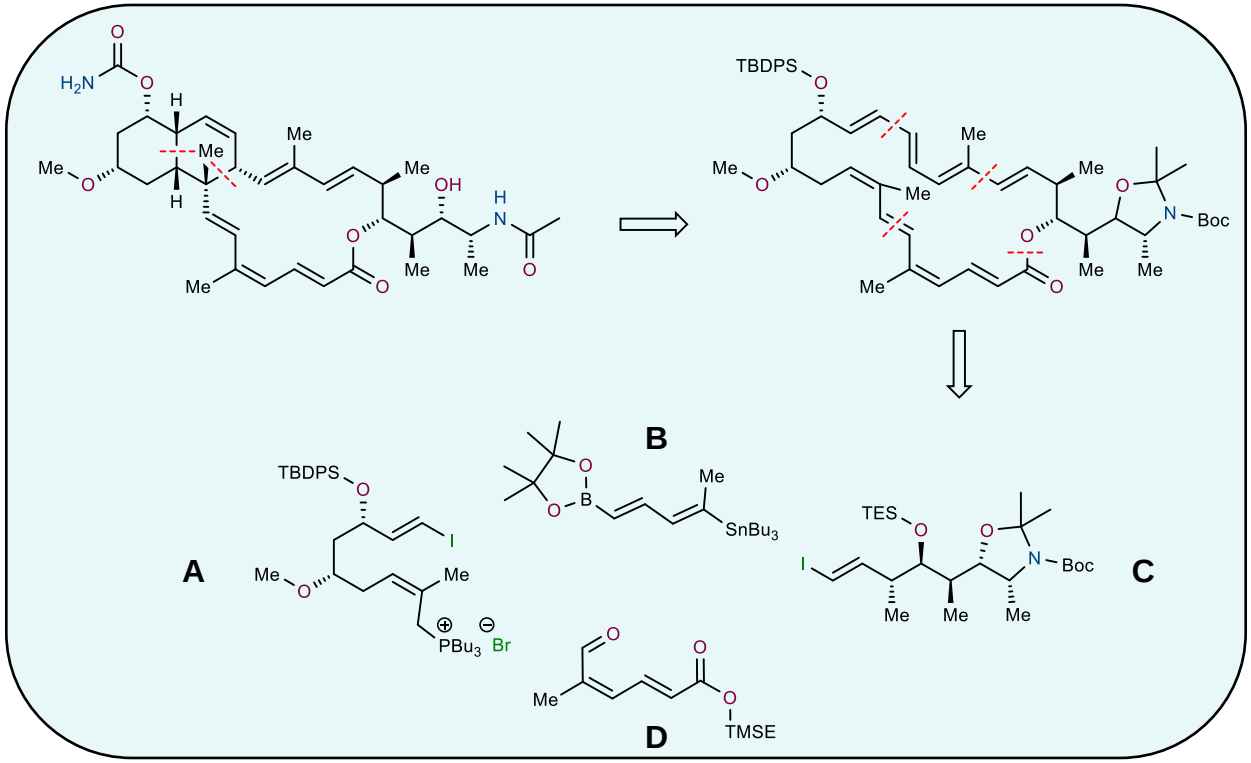
superstolide A



- First isolated in 1994 from *Neosiphonia superstes,* a New Caledonian sponge by D'Auria et. al.
- This molecule along with other members of its respective macrolide family demonstrate potent cytotoxicity against several cancer cell lines.
- Exhibits an IC_{50} of 5ng/mL against murine P388 leukemia cells, 5mg/mL against human nasopharyngeal cells, and 4mg/mL against non-small-cell lung carcinoma cell lines.
- This was the first synthesis of *superstolide A*, which features an elegant transannular Diels-Alder reaction to form a 24-membered octaene and cis-fused dealin system in a single step.

William Roush

Retrosynthetic Analysis

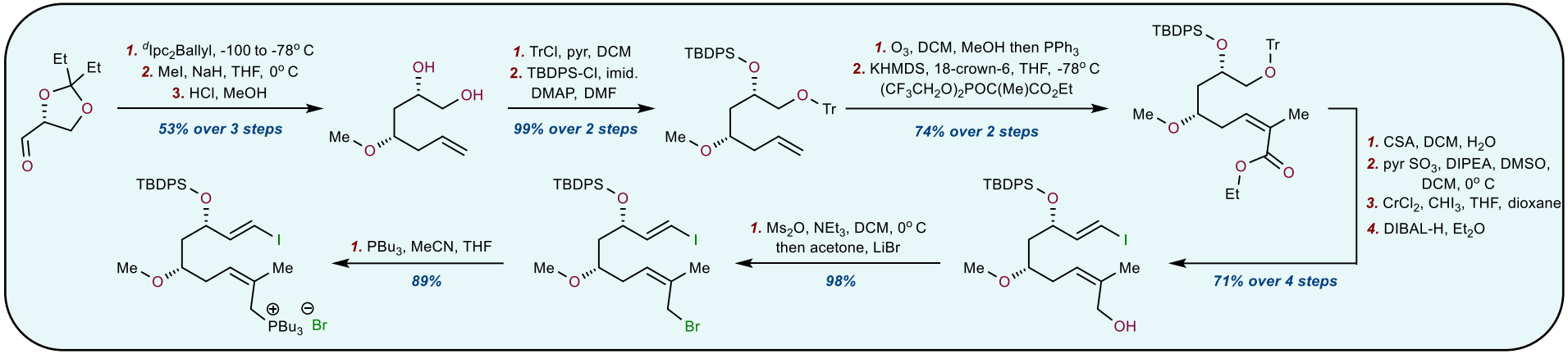


- Strategy breaks the molecule down into 4 simplified building blocks, depicted as A, B, C, and D.
- An alternatively explored route featured a Diels-Alder with a linear precursor that failed to undergo subsequent macrolactonization to forge the octaene macrocycle.
- Using this previous insight on the Diels-Alder, a method of macrocyclization through such chemistry was developed.

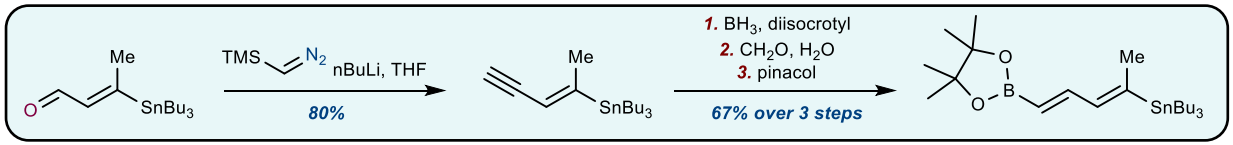
Roush, W. *J. Am. Chem. Soc.* **2008**, *130, 9, 2722-2723* https://doi.org/10.1021/ja710238h.

Superstolide A (Roush, 2008)

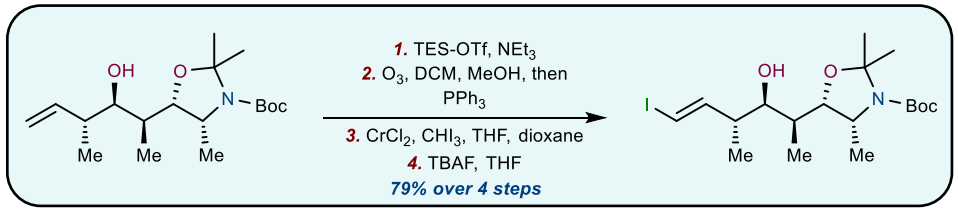
Synthesis of Fragment A



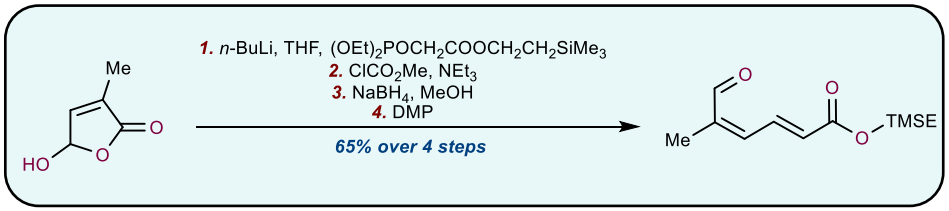
Synthesis of Fragment B



Synthesis of Fragment C



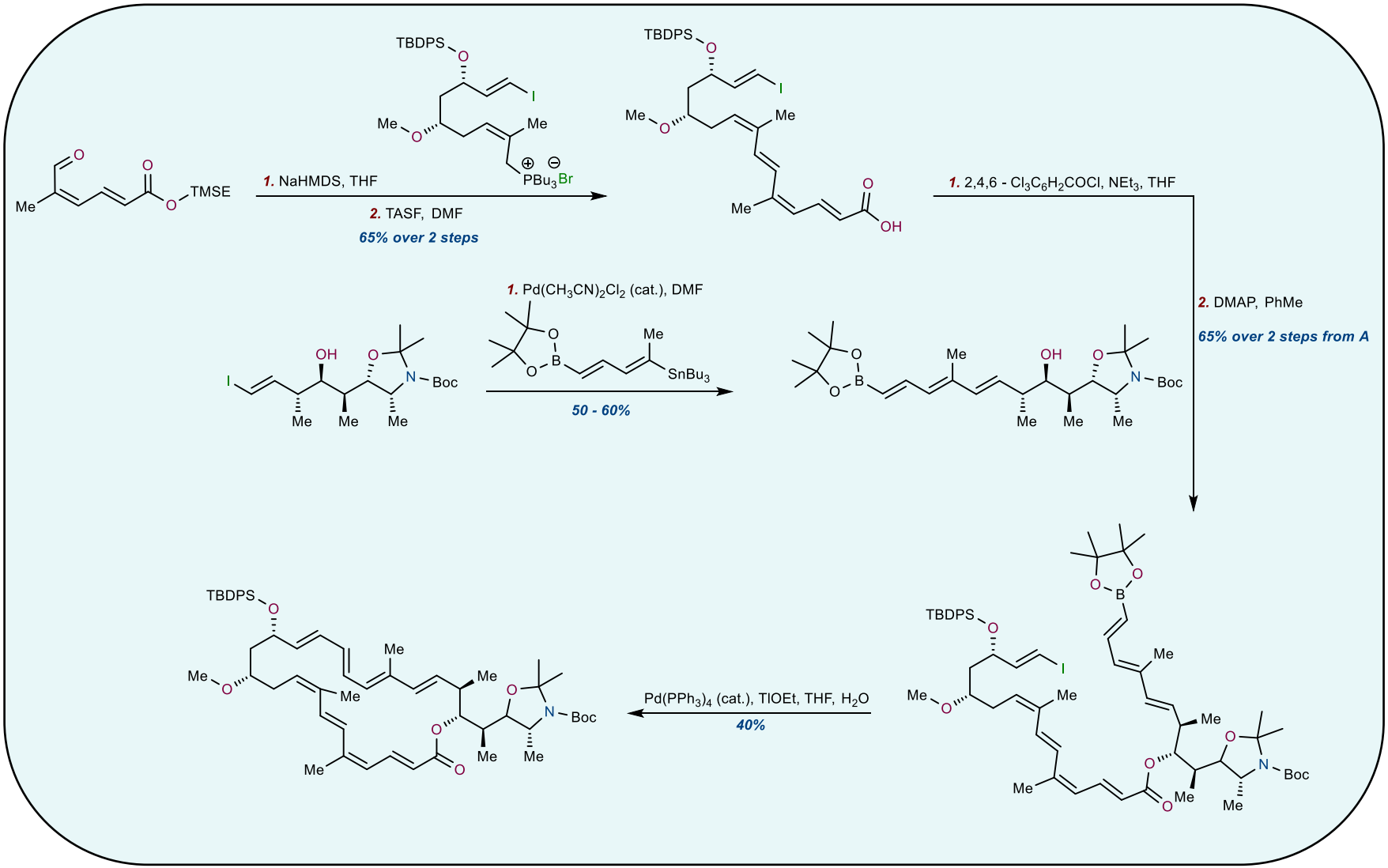
Synthesis of Fragment D



Roush, W. *J. Am. Chem. Soc.* **2008**, *130, 9, 2722-2723* https://doi.org/10.1021/ja710238h.

Superstolide A (Roush, 2008)

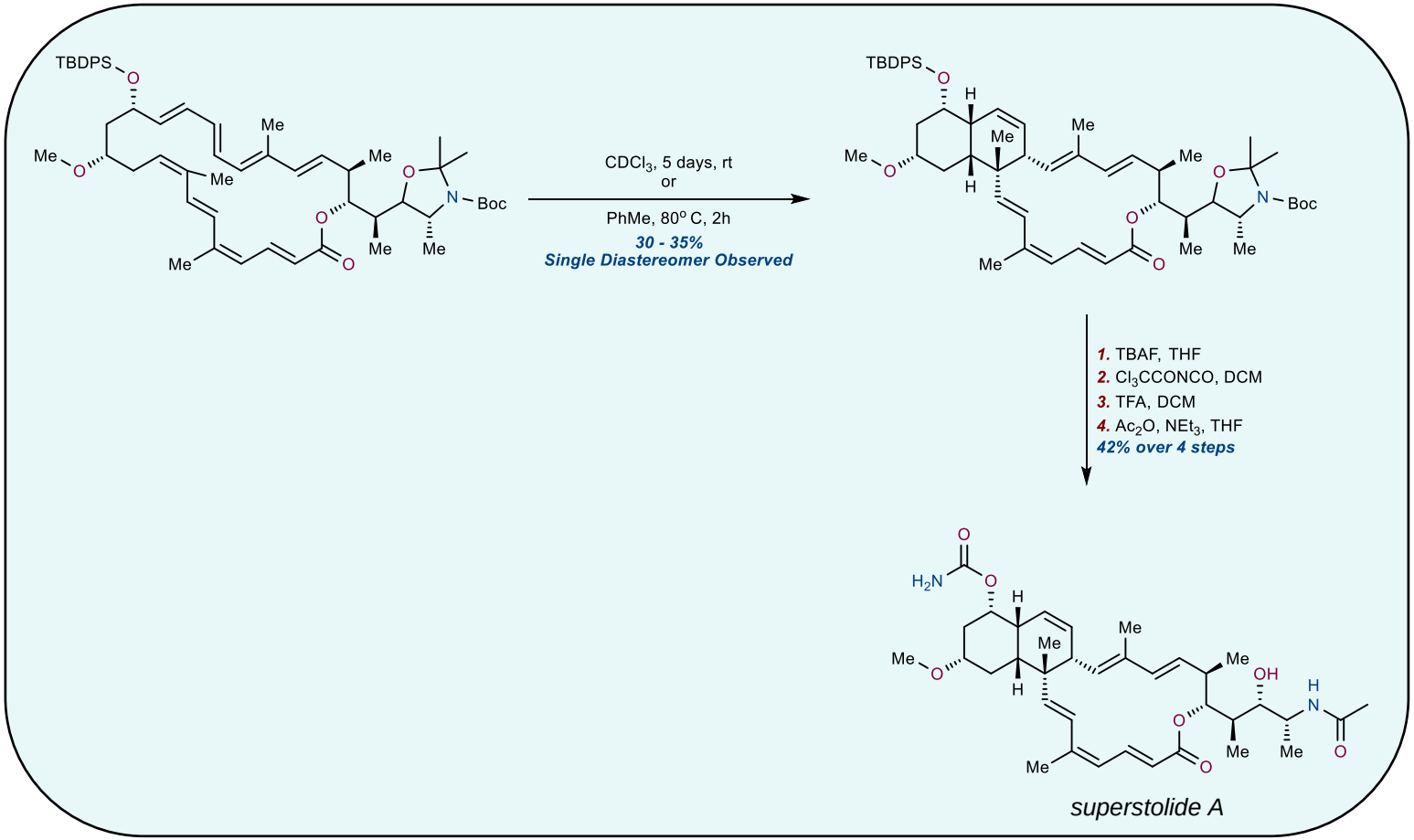
Combining Fragments



Roush, W. *J. Am. Chem. Soc.* **2008**, *130, 9, 2722-2723* https://doi.org/10.1021/ja710238h.

Superstolide A (Roush, 2008)

Finishing the Synthesis



Roush, W. *J. Am. Chem. Soc.* **2008**, *130, 9, 2722-2723* https://doi.org/10.1021/ja710238h.