

- Isolated in 1975 from *Euphorbia resinifera*, a species of spurge native to the Atlas Mountains in Morocco.
- Resiniferatoxin belongs to the daphnane diterpene orthoesters (DDOs) family of natural products (5,7,6-fused ring system with an orthoester)
- It is a TRPV1 (capsaicin receptor) activator and potential analgesic.
- Three total syntheses have been completed so far by: Wender (1997), Inoue (2017, 2022) and Maimone (2022).

Isolation: Hecker, A. E. et al. *Tetrahedron Letters*, **1975**, 16, 1595 [https://doi.org/10.1016/S0040-4039\(00\)72207-6](https://doi.org/10.1016/S0040-4039(00)72207-6)

**Total syntheses:**

Wender, P. A. et al. *J. Am. Chem. Soc.*, **1997**, 119, 12976 <https://doi.org/10.1021/ja972279y>

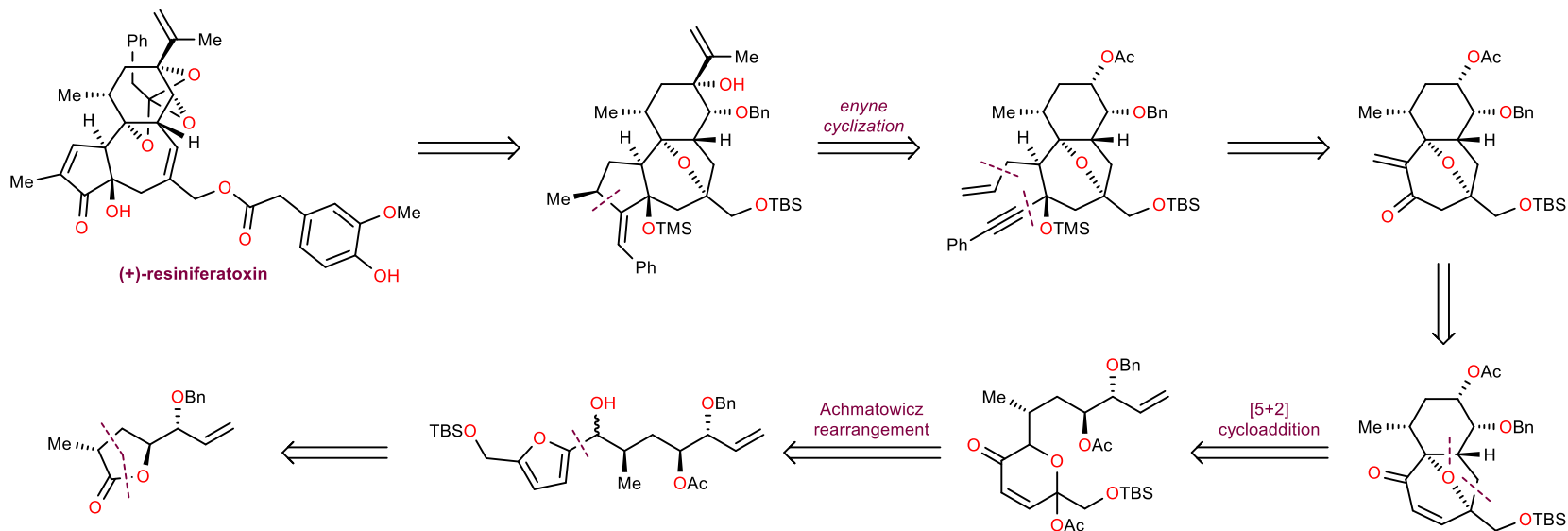
Inoue, M. et al. *J. Am. Chem. Soc.*, **2017**, 139, 16420 <https://doi.org/10.1021/jacs.7b10177>

Inoue, M. et al. *J. Am. Chem. Soc.*, **2021**, 143, 12387 <https://doi.org/10.1021/jacs.1c06450>

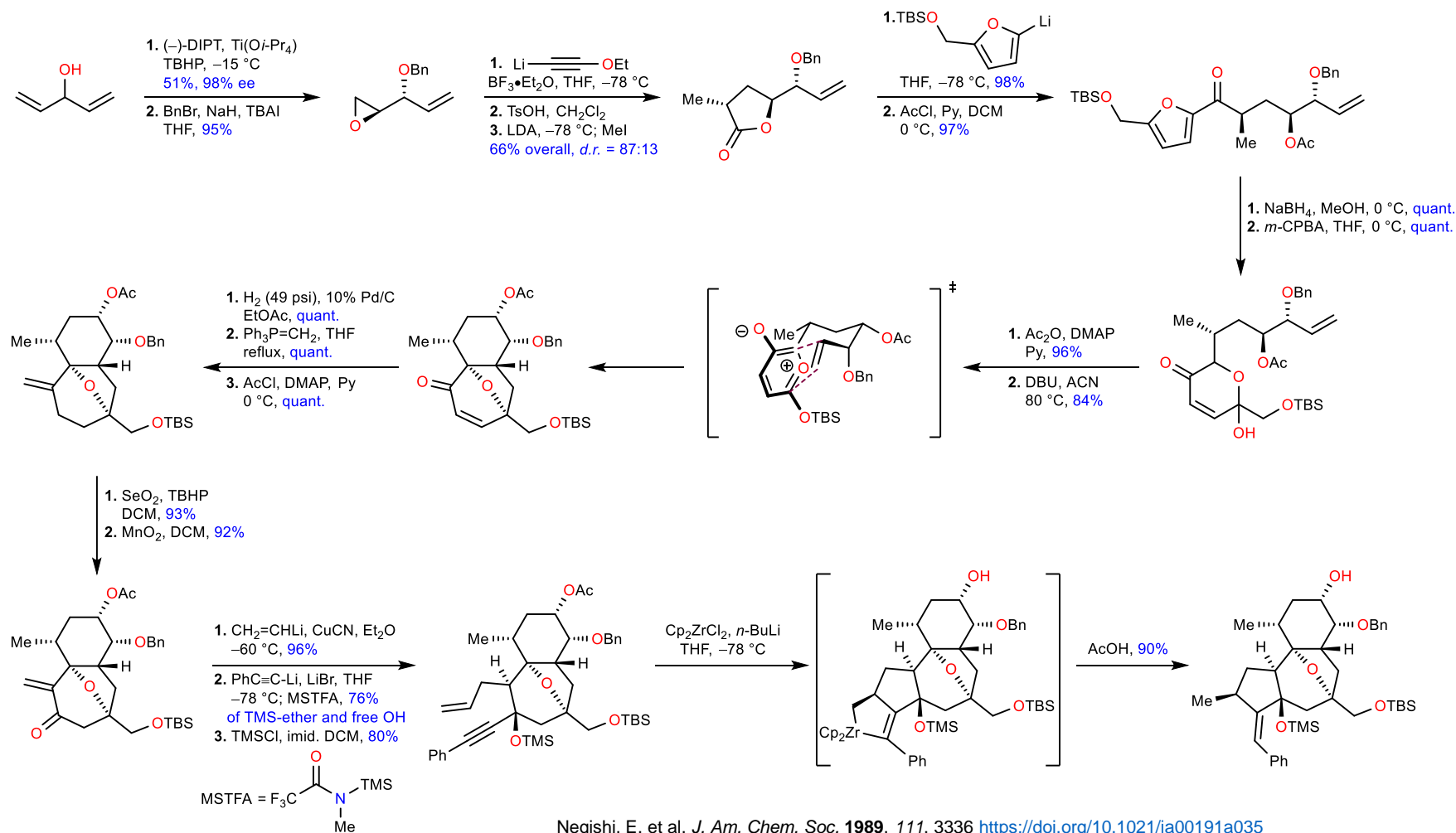
Inoue, M. et al. *Org. Lett.*, **2022**, 24, 929 <https://doi.org/10.1021/acs.orglett.1c04286>

Maimone, T. J. et al. *J. Am. Chem. Soc.*, **2022**, 144, 16332 <https://doi.org/10.1021/jacs.2c08200>

## Retrosynthetic Analysis:



## Forward Synthesis:



Negishi, E. et al. *J. Am. Chem. Soc.* **1989**, *111*, 3336 <https://doi.org/10.1021/ja00191a035>

**Endgame:**

