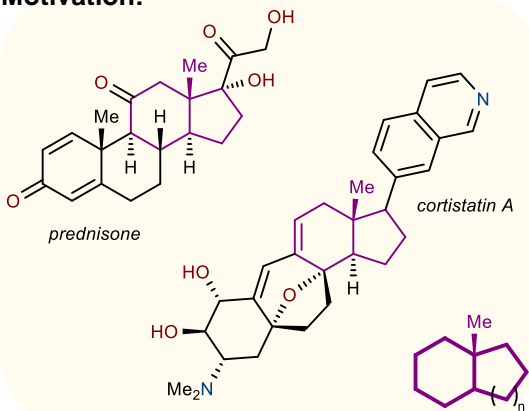
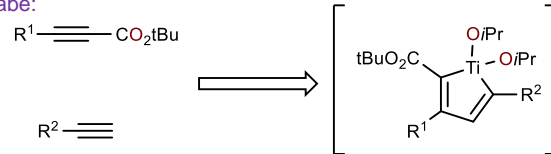


Motivation:

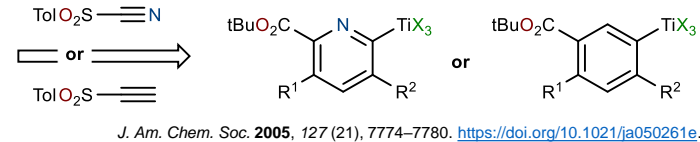


2+2+2 annulation with aromatization

Urabe:

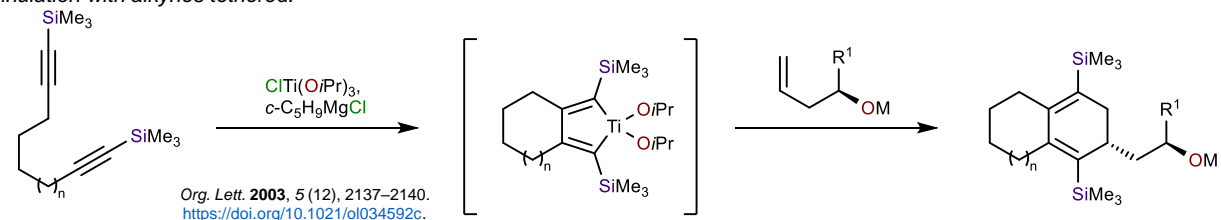


Prior work:



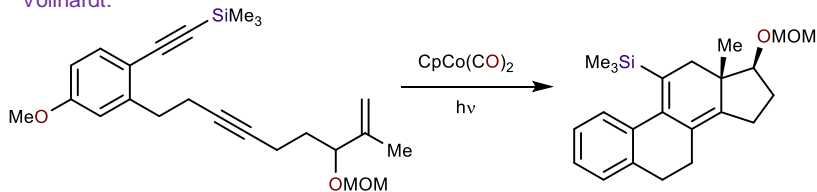
2+2+2 annulation with alkynes tethered:

Cha:

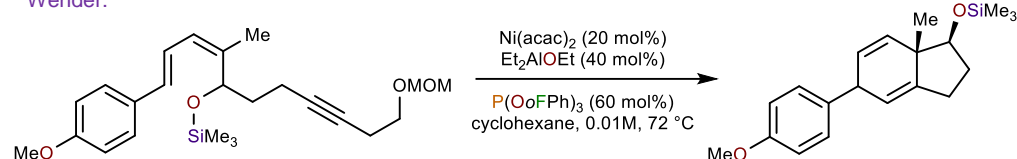


2+2+2 annulation with alkynes + alkene tethered:

Vollhardt:

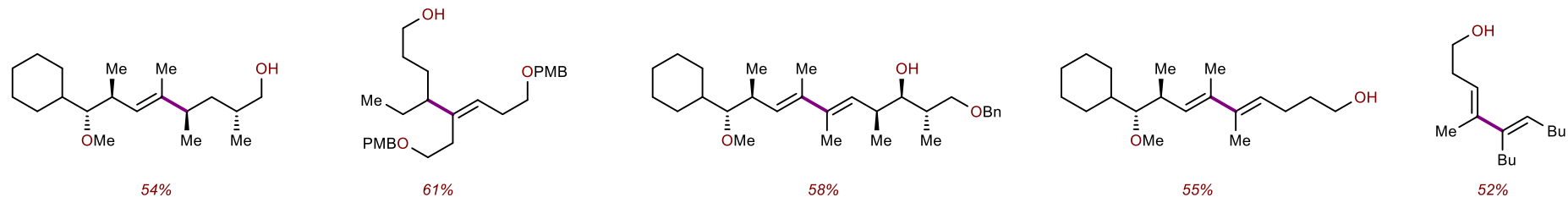
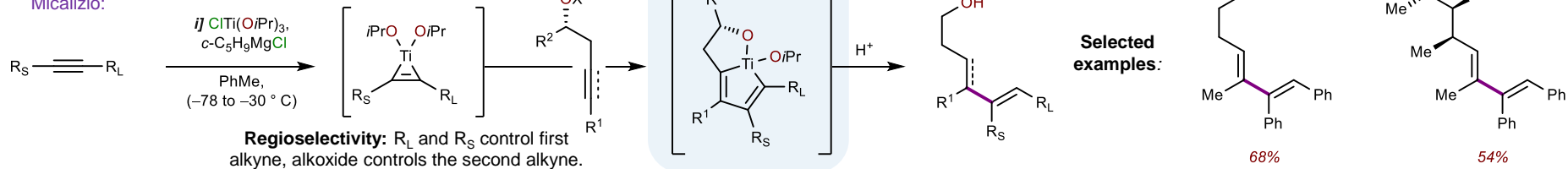


Wender:

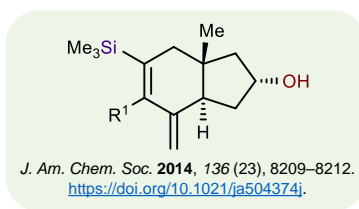
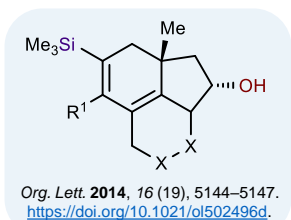
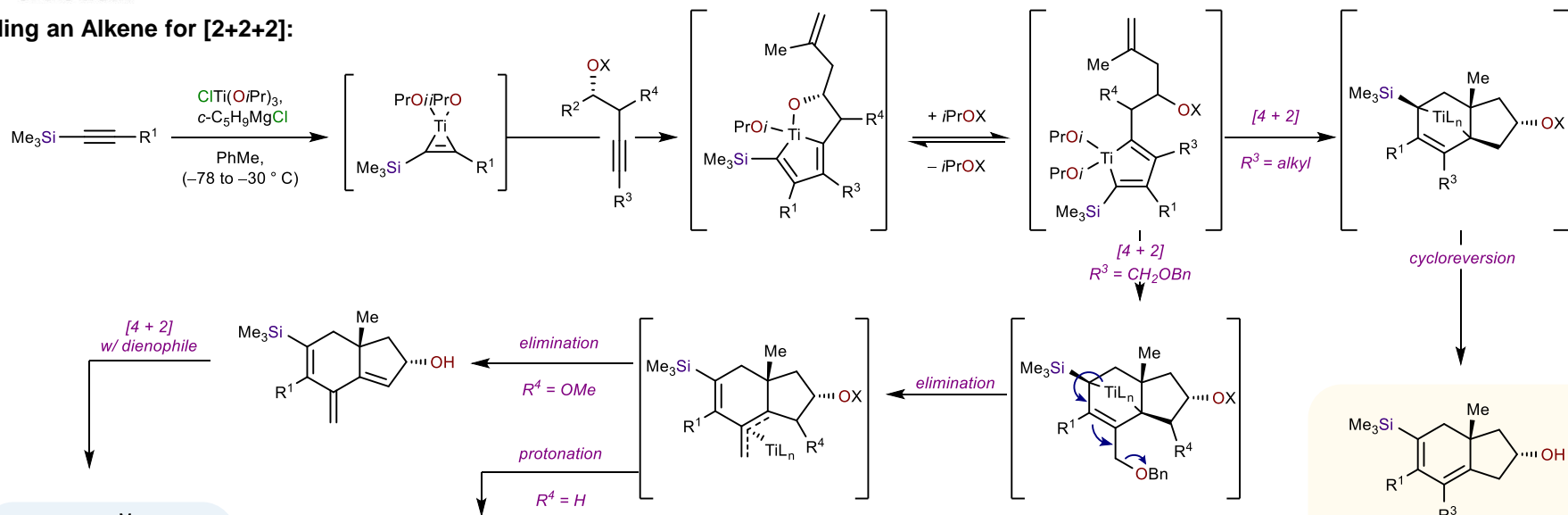


This work:

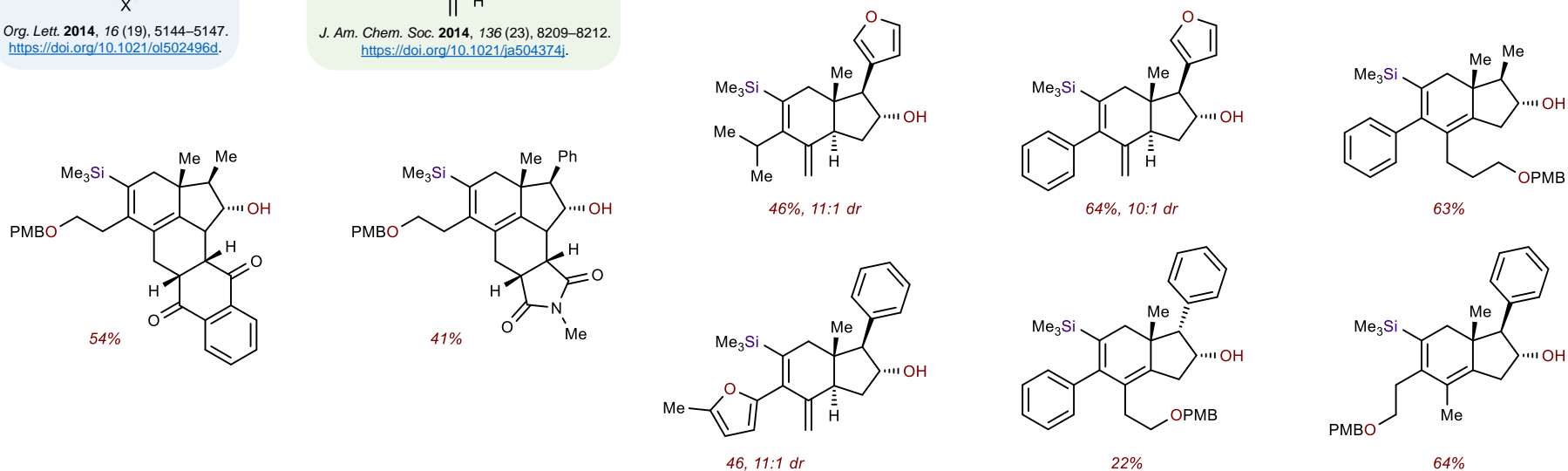
Micalizio:



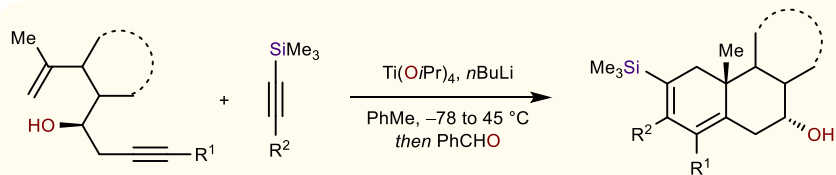
Adding an Alkene for [2+2+2]:



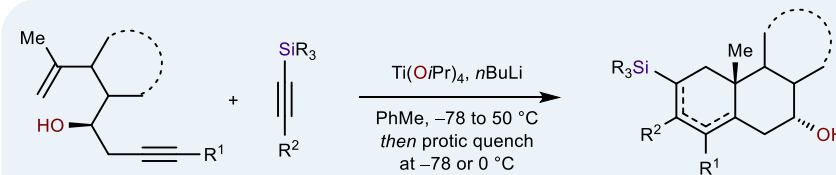
Selected examples:



6-6 fused rings:

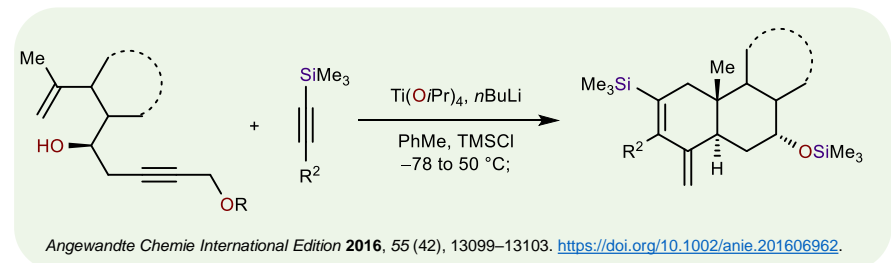
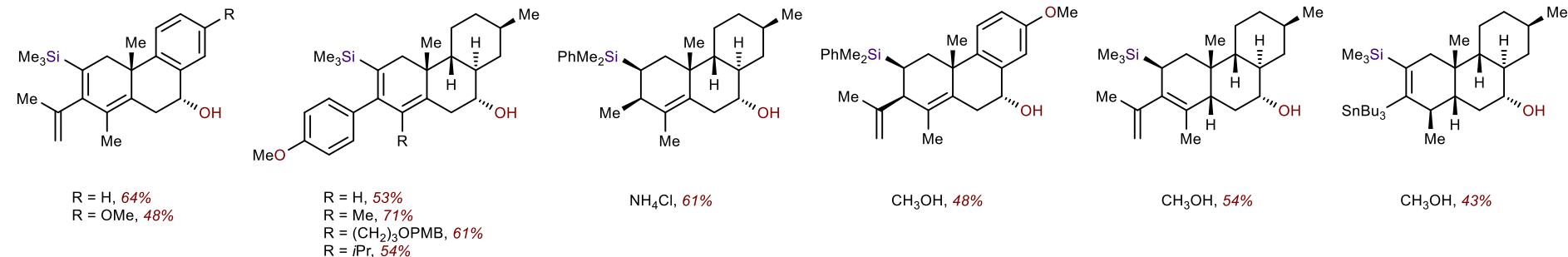


J. Am. Chem. Soc. **2015**, *137* (20), 6624–6628. <https://doi.org/10.1021/jacs.5b02107>.

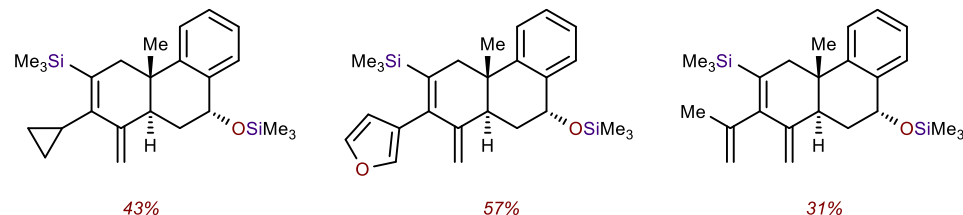


J. Am. Chem. Soc. **2015**, *137* (20), 6624–6628. <https://doi.org/10.1021/jacs.5b02107>.

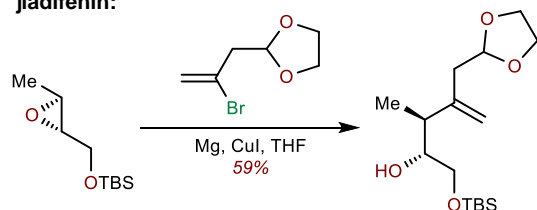
Selected examples:



Angewandte Chemie International Edition **2016**, *55* (42), 13099–13103. <https://doi.org/10.1002/anie.201606962>.

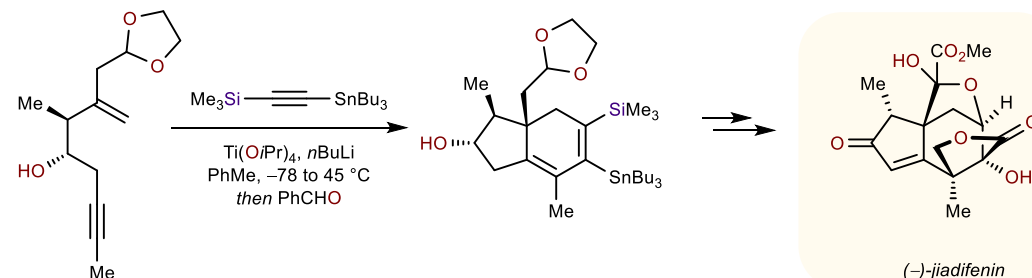


Total synthesis of jiadifenin:



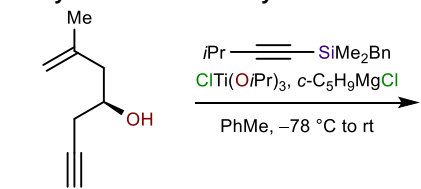
J. Am. Chem. Soc. **2016**, *138* (4), 1150–1153. <https://doi.org/10.1021/jacs.5b12694>.

Applications:

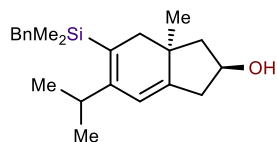


(-)-jiadifenin

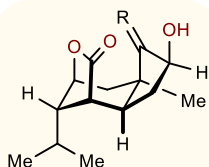
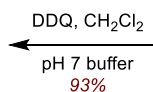
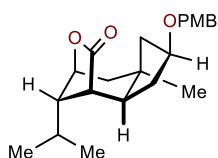
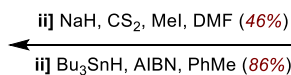
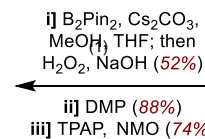
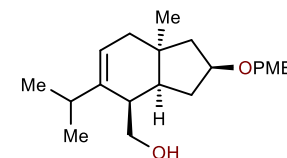
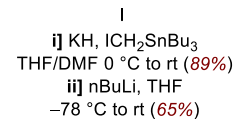
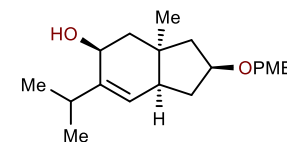
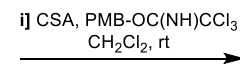
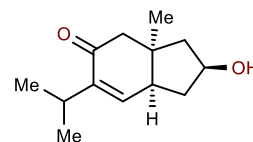
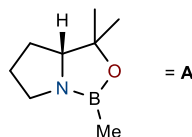
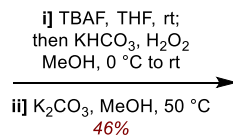
Total synthesis of desmethylene corialactone D:



three steps from epichlorohydrin



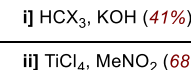
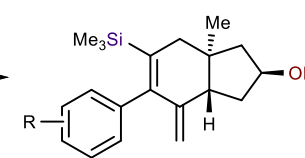
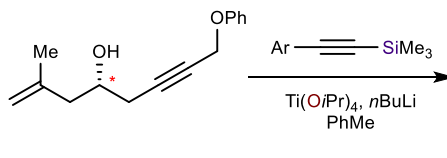
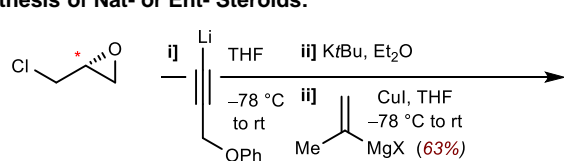
Applications (cont.):



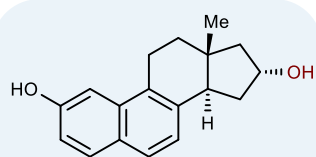
(+)-C₁₄-desmethylene corialactone D
R = H, H vs CH₂

Org. Lett. 2019, 21 (9), 3193–3197. <https://doi.org/10.1021/acs.orglett.9b00921>. For the synthesis of Cortistatin Pentacyclic Core see: Org. Lett. 2016, 18 (11), 2624–2627. <https://doi.org/10.1021/acs.orglett.6b01048>.

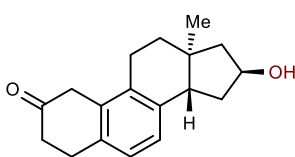
Synthesis of Nat- or Ent- Steroids:



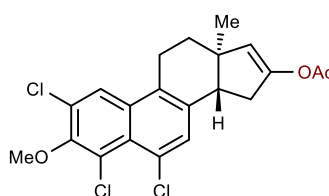
Selected examples:



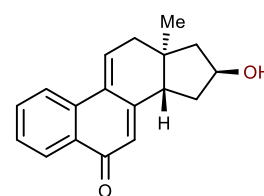
GI₅₀ = 0.2 μg/mL (800 nM)
MDA-MB-231
human breast cancer cells



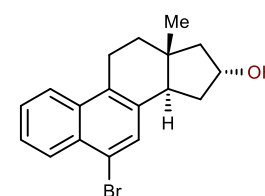
• Birch Reduction
• hydrolysis



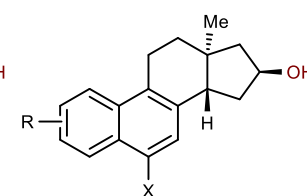
selective enolization



• borylation/oxidation
• oxidation



20% yield from epichlorohydrin



5 or 6 steps from epichlorohydrin

Nature Chemistry 2018, 10 (1), 70–77. <https://doi.org/10.1038/nchem.2865>; Org. Lett. 2018, 20 (19), 6220–6224. <https://doi.org/10.1021/acs.orglett.8b02689>.