

Total Synthesis of the Norcembranoid Scabrolide B and Its Transformation into Sinuscalide C, Ineleganolide, and Horiolide

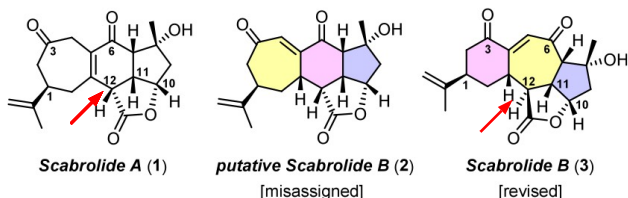
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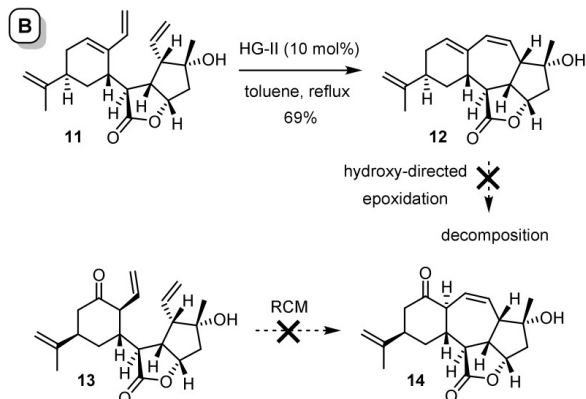
a challenging intramolecular alkenylation of a ketone

a lanthanide catalyzed Mukaiyama-Michael addition

norcembranoid derived from soft corals

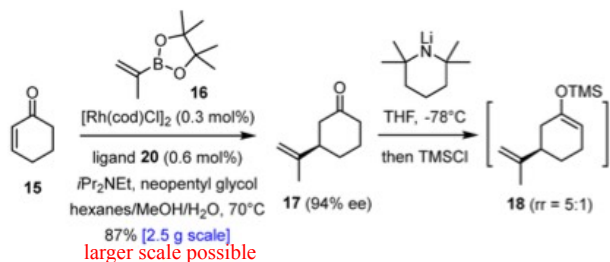


fairly straightforward adjustments of our successful route to scabrolide A (1)

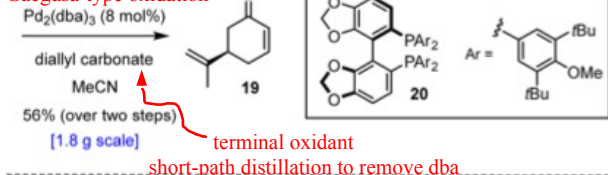


traces of 4-epi-14 had been formed by epimerization of 13 prior to RCM, suggesting that a cis-annulated ring system is less strained

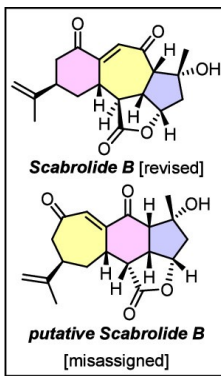
Scheme 2. Preparation of the Building Blocks



Saegusa-type oxidation



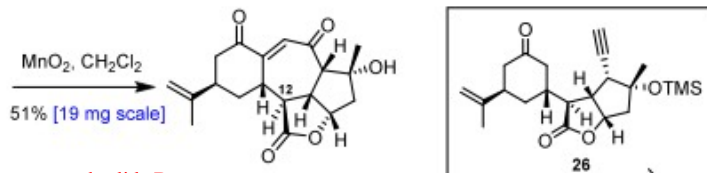
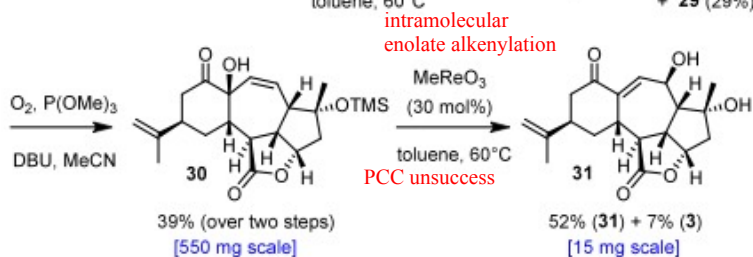
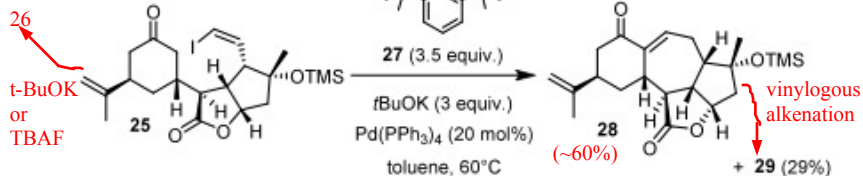
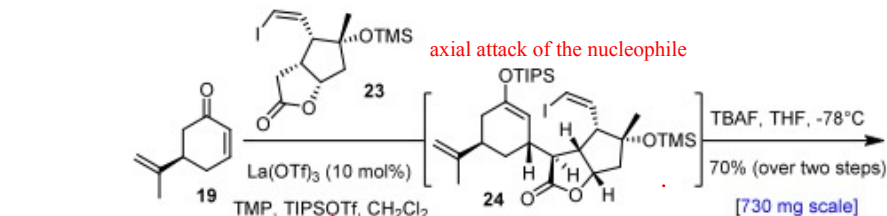
the bulky silyl ether thwarted the end game



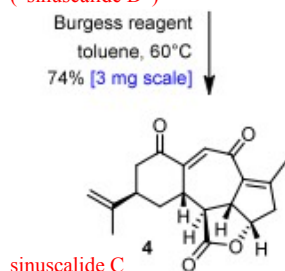
- revised structure of scabrolide B confirmed
- formation of congested central cycloheptene by Pd-catalyzed intramolecular ketone alkenylation
- fragment coupling by lanthanide catalyzed Mukaiyama-Michael addition to norcarvone
- shortcut synthesis of norcarvone by asymmetric Rh catalysis
- late-stage air oxidation/allylic transposition to install the dissonant 1,4-dicarbonyl motif
- elaboration into three sister compounds in one step each with biosynthetic implications

Scheme 3. Completion of the Total Synthesis

Mukaiyama Michael addition



scabrolide B ("sinuscalide D") (-)-3 19 steps



Scheme 4. Syntheses of Ineleganolide and Horiolide

epimerization of the C12

