Recent Advances in the Total Synthesis of Natural Products Containing Eight-Membered Carbocycles (2009-2019)
Li et al. Chem. Rev. 2020, 120, 5910-5953

"The more there are methods to access a certain scaffold, more it is difficult to make that scaffold"
-> 8-membered rings

Strain energy = 14 kcal/mol (cyclohexane: 1 kcal/mol)
Multiple conformations because flexible --> stereoselectivity is challenging
BC is generally favoured but depends on substituion pattern
Challenge in TS: bridged, fused polycycles, FG tolerance

(+)-aquatolide (Takao et al. Angew. Chem. Int. Ed, 2019, 58, 9851-9855)

D-(-)-pantolactone

1. NiCl₂, CrCl₂
2. DMP, NaHCO₃

1. hv
2. BF₃·OEt₂, MeOH

(+)-aquatolide


1. DMP
2. Sml₂
3. Na, EtOH

1. TFA-imidazole
2. EDC, DMAP
3. Et₂Zn then HCl

(+)-12-epi-mutilin

SOLUTIONS
(-)-6-epi-ophiobolin N (Maimone et al. Science, 2016, 352, 1078-1082)
(±)-aquatolide (Takao et al. Angew. Chem. Int. Ed, 2019, 58, 9851-9855)

[Chemical reaction diagram]
