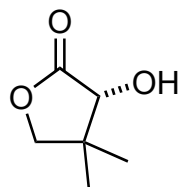


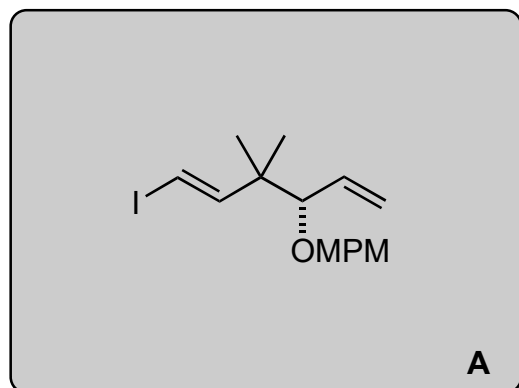
Total Syntheses of (+)-Aquatolide and Related Humulanolides

Takao, K.-i.; Kai, H.; Yamada, A.; Fukushima, Y.; Komatsu, D.; Ogura, A.; Yoshida, K.

Angew. Chem. Int. Ed. **2019**, *58*, 9851–9855

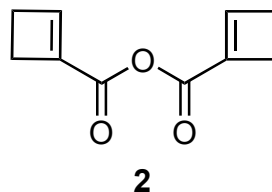
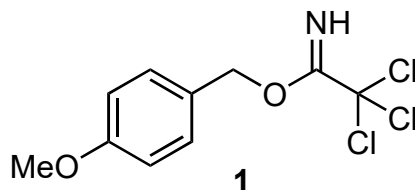


1-5



6-9

- 1) **1**, TfOH
- 2) DIBAL-H, $-78\text{ }^{\circ}\text{C}$
- 3) $[(\text{Ph}_3\text{P})\text{CH}_3]\text{Br}$, $\text{KO}t\text{-Bu}$
- 4) DMP, NaHCO_3
- 5) CrCl_3 , LiAlH_4 , CHI_3



- 6) DDQ
- 7) LiHMDS , **2**, $-78\text{ }^{\circ}\text{C}$
- 8) Grubbs 2nd gen, Methacrolein
- 9) NiCl_2 , CrCl_2

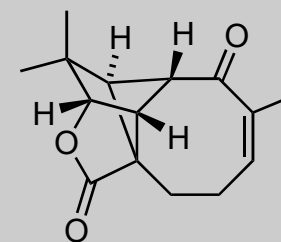
What is the name of the starting material?

D-($-$)-pantolactone

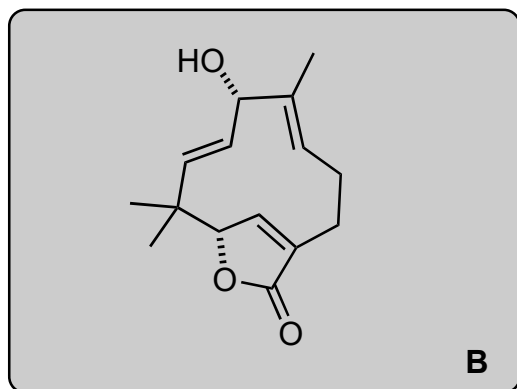
5) What is the name of the reaction? Propose a mechanism and geometry?
intramolecular Nozaki-Hiyama-Takai-Kishi olefination

8) Propose a mechanism
Hint: it is a cascade of three reactions. Only one ring in the final product

9) What is the name reaction?
Takai-Utimoto olefination



(+)-aquatolide

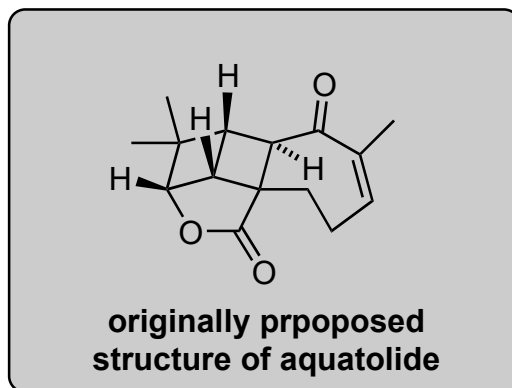
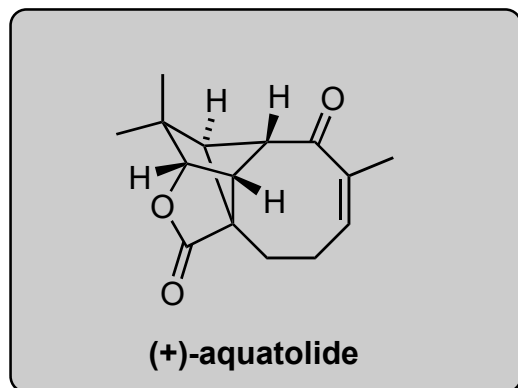


- 10) DMP
- 11) $\text{BF}_3 \cdot \text{OEt}_2$, MeOH
- 12) $h\nu$, Hg lamp
- 13) $\text{BF}_3 \cdot \text{OEt}_2$

- 14) $h\nu$, Hg lamp
- 15) *m*-CPBA
- 16) $h\nu$, Hg lamp
- 17) DMP, NaHCO_3
- 18) NaI, TFA
- 19) TFAA, Et_3N
- 20) NaI, DMF, 60 °C

10-13

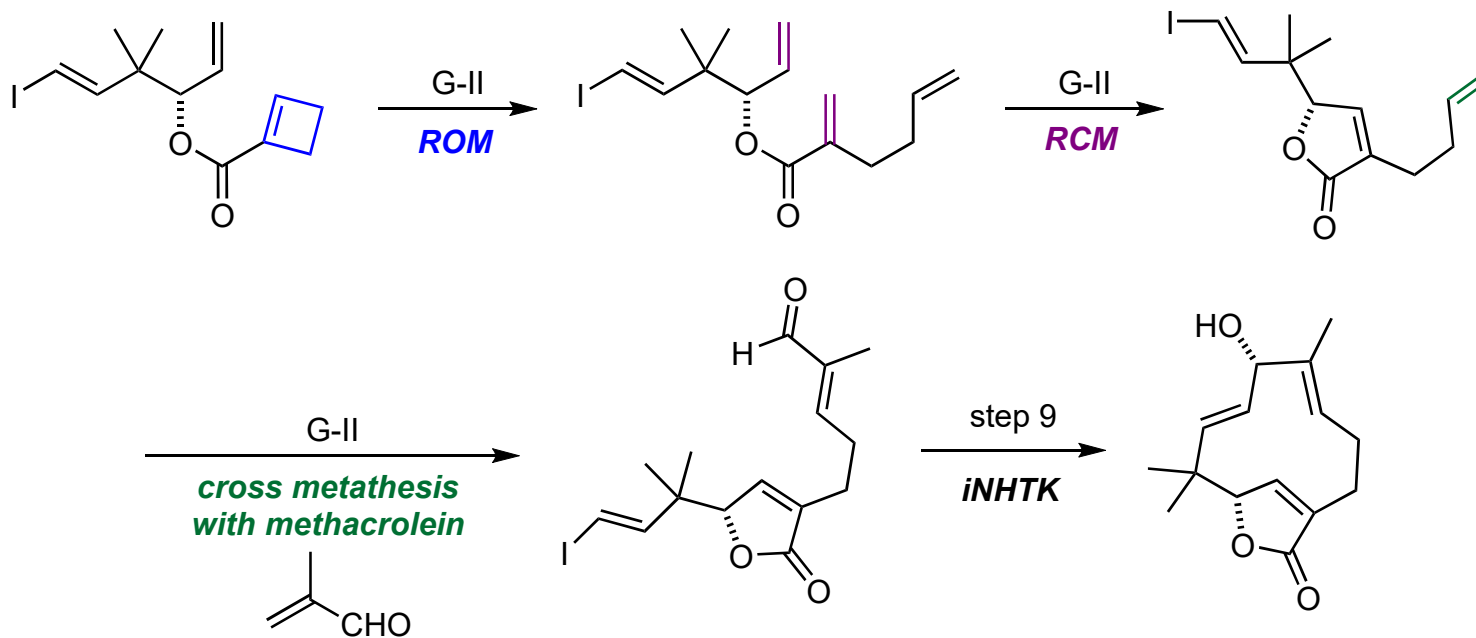
14-20



12 and 16) How would you classify these two photochemical reactions?
Hint: step 11 and step 15 are same class of reaction but the product is different. What is the difference?

14) *Hint: Isomerization only*

Step 8 mechanism: ROM-RCM-CM cascade



Step 12 and 16: Photochemical [2+2] cycloaddition regioselectivity

