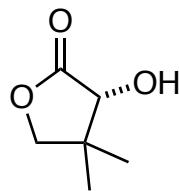
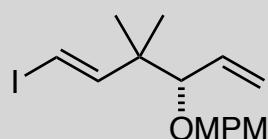


Total Syntheses of (+)-Aquatolide and Related Humulanolides

Takao, K.-i.; Kai, H.; Yamada, A.; Fukushima, Y.; Komatsu, D.; Ogura, A.; Yoshida, K.
Angew. Chem. Int. Ed. 2019, **58**, 9851–9855



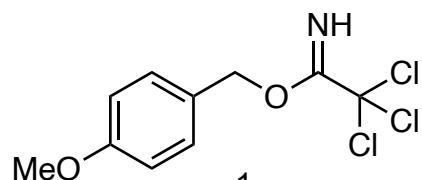
1-5



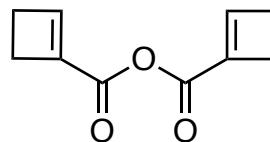
A

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



1



2

- 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?

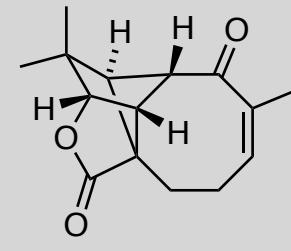
D-(-)-pantolactone

5) What is the name of the reaction?
 Propose a mechanism and geometry?
Takai-Utimoto olefination

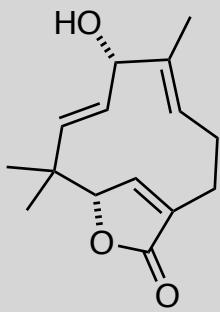
8) Propose a mechanism

*Hint: it is a cascade of three reactions.
 Only one ring in the final product*

9) What is the name reaction?
intramolecular Nozaki-Hiyama-Takai-Kishi olefination



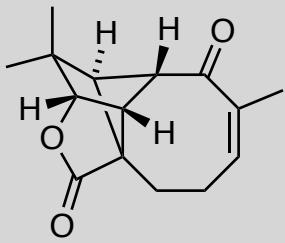
(+)-aquatolide



B

10-13

14-20



(+)-aquatolide

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

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

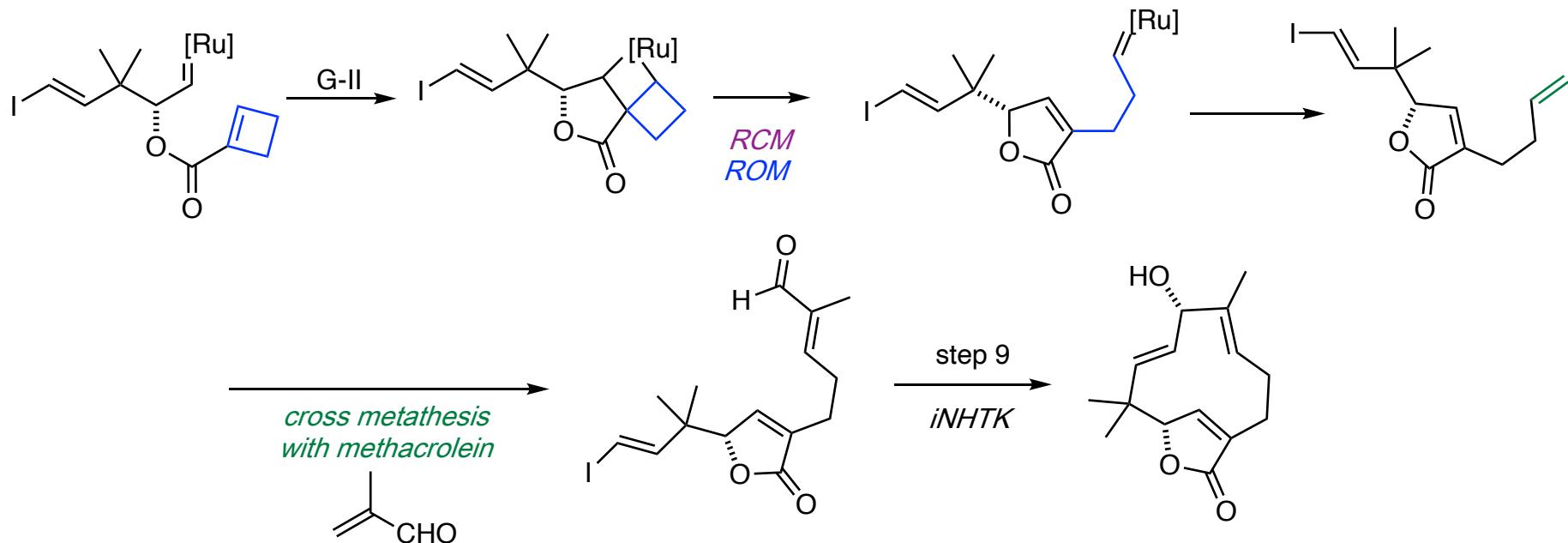
originally proposed
structure of aquatolide

11 and 15) 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?

13) *Hint: Isomerization only*

Step 8 mechanism: ROM-RCM-CM cascade



Step 11 and 15: Photochemical [2+2] cycloaddition regioselectivity

