

## ***Chapter 33 — Stereoselective reactions of cyclic compounds: Part B***

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- Iodolactonizations and stereoselectivity
- Baldwin's rules for ring closure
- Epoxidations and stereoselectivity

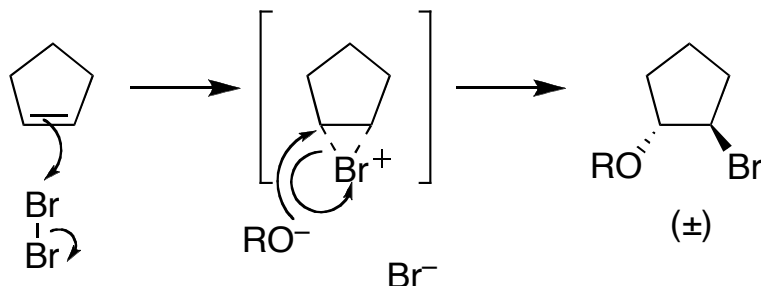
### **Reading guide:**

**Ch. 18** Read only pages 457–474

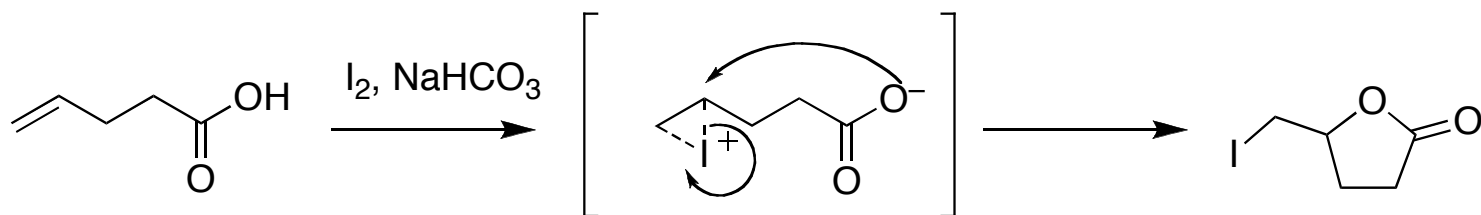
**Ch. 33** Skip section on unsaturated 6-membered rings (858–861)

# ***A new reaction for making cyclic compounds: Iodolactonization***

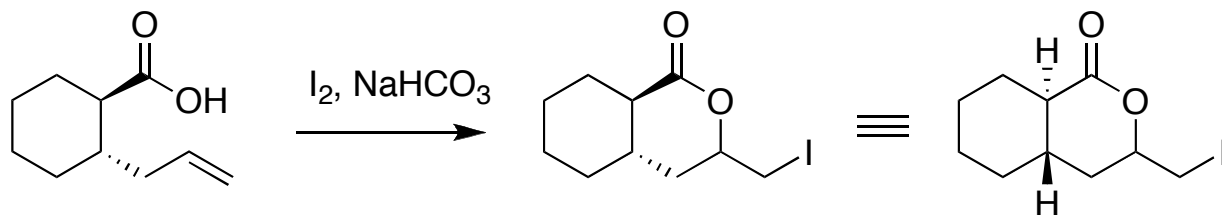
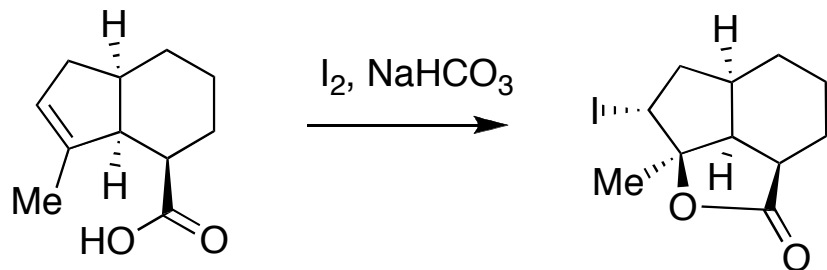
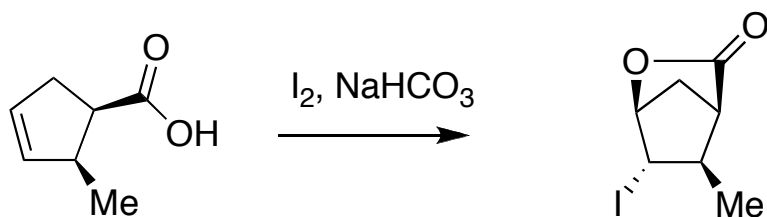
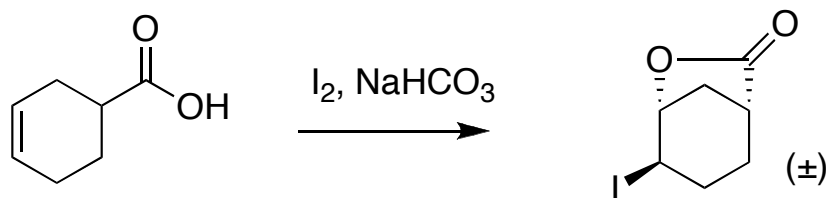
Remember reactions of alkenes through bromonium ion intermediates?



Iodine reacts with alkenes to make “iodonium ions” in the same way... and an internal carboxylate the right number of atoms away can attack to give a 5, 6, or 7-membered cyclic ester (“lactone”).



## Two points on the stereoselectivity of iodolactonizations

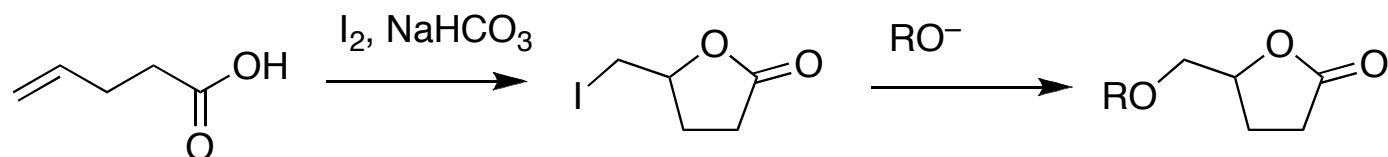


Because this is an  $S_N2$ -like reaction proceeding through a iodonium intermediate, the attacking oxygen and the iodine *must* end up on opposite sides of the alkene.

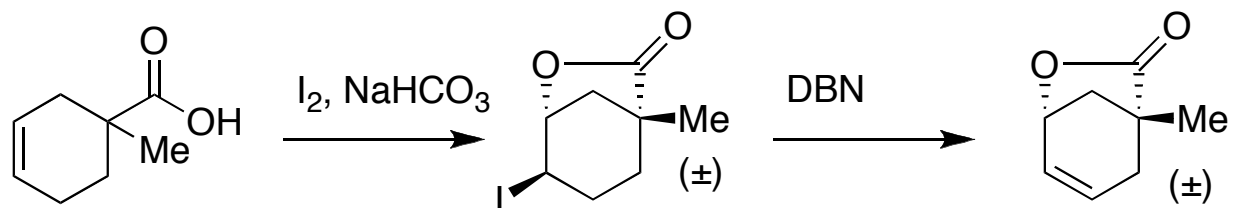
In a cyclic starting material, the carboxylate is “tethered” to one side; it can only reach one face of the alkene, so that’s the face that ends up with the oxygen atom.

# What can you do with an iodolactone?

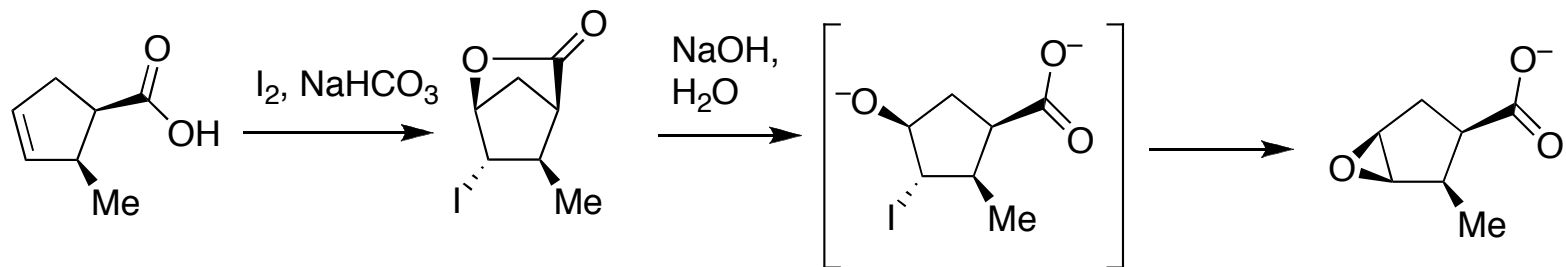
1) Use the iodoalkyl part as an alkylating agent



2) Eliminate the iodine atom to give an alkene (DBN is a non-nucleophilic base)



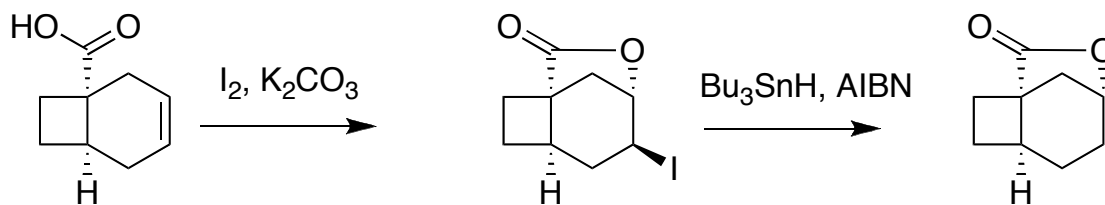
3) Hydrolyze the ester, and then use the resulting hydroxy-iodo compound to form an epoxide



## What can you do with an iodolactone?

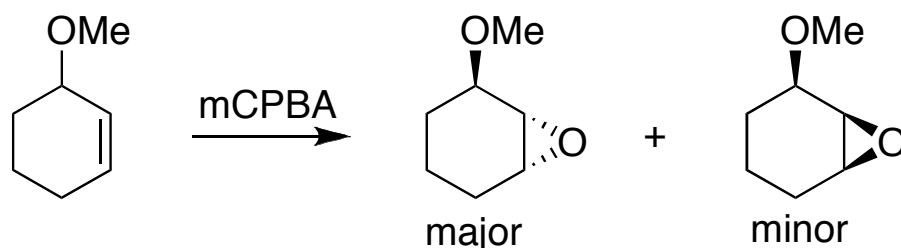
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4) Reduce away the iodine atom via a free-radical methodology.

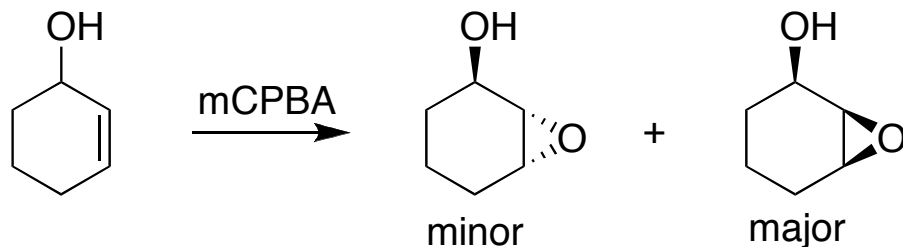


## ***An example of stereoselectivity that is not based on steric repulsion***

As expected, epoxidation by a peracid such as mCPBA normally chooses the side of the alkene with a minimum of steric hindrance...



... but this can be reversed when a neighbouring alcohol is present in the allylic position. The alcohol, by *hydrogen bonding to the peracid*, can direct the reagent to the same face of the alkene as the alcohol.

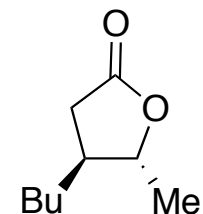
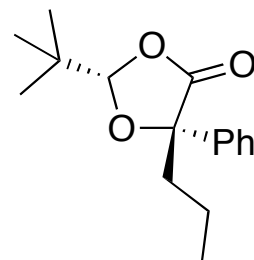
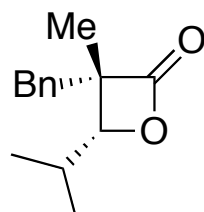
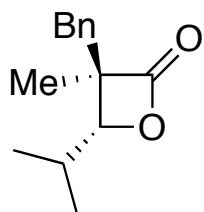
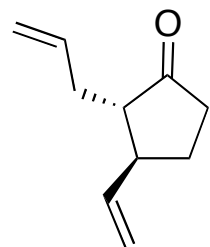


VO(acac)<sub>2</sub>, *t*-BuOOH also makes epoxides from alkenes, and is directed even more strongly to the same face as a neighbouring alcohol (CGWW pg. 877–888)

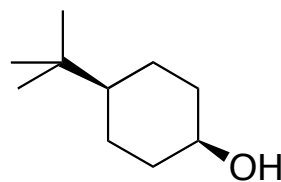
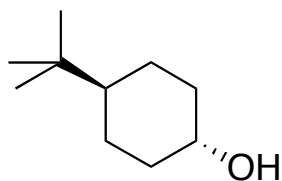
# *I can make that! (Ch. 33)*

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## 4- and 5-membered rings with stereochemistry

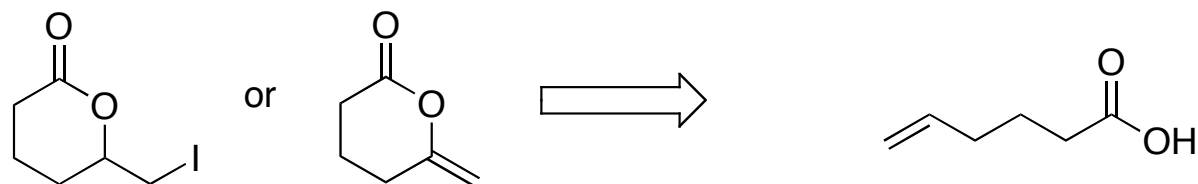


## 6-membered rings with stereochemistry



## *I can make that! (Ch. 33)*

**Iodolactones/Lactones in general** (with or without subsequent iodine elimination)



**Epoxides** — using mCPBA, VO(acac)<sub>2</sub>/t-BuOOH, or two-step methods that rely on bromoalcohol or iodoalcohol intermediates

To pick the right epoxidation method, pay attention to starting material and product stereochemistry!

