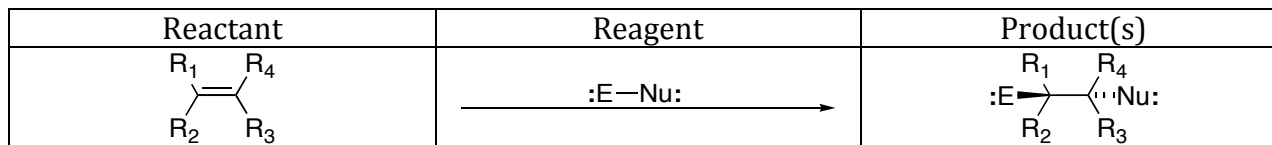


## REACTION STUDY SHEET

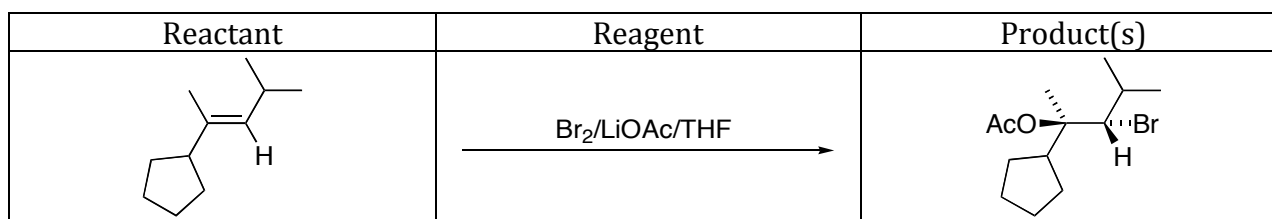
NAME OF REACTION: **Antarafacial (*anti*) Addition of an Electrophile (:E—Nu:) to an Alkene**

Important feature of this reaction: the electrophilic atom carries a non-bonding pair of electrons.

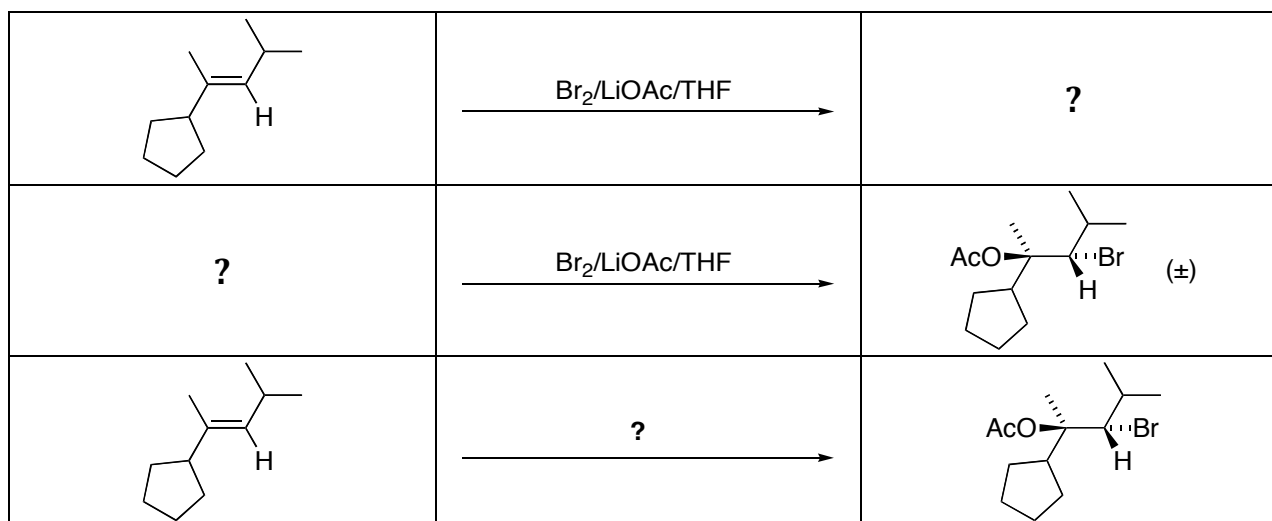
**General form of the reaction:**



**A specific example**



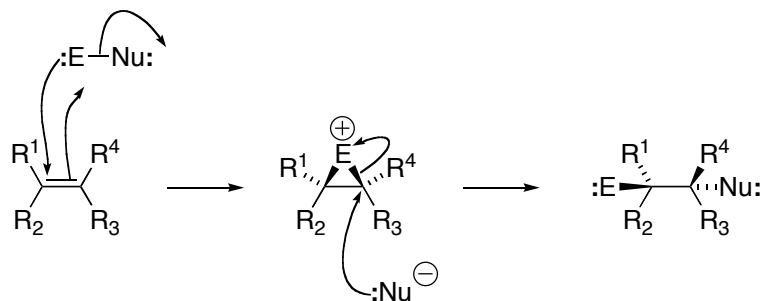
**What ways can this specific example be asked on an exam (i.e. what flash cards do I need?)**



**What does this reagent do?**

It adds :E—Nu: across a  $\pi$  bond of an alkene to give a bromohydrin. The addition is stereospecific to give the antarafacial (*anti*) adduct. This stereochemistry is a direct result of the involvement of a three-membered cyclic onium ion intermediate, which is made possible by the lone pair on the electrophilic atom. *Without this lone pair, the stereospecificity is lost because the three-membered cyclic onium ion becomes impossible to form.*

### What is the mechanism of this reaction?



**What is the stereochemistry of this reaction?** The addition is stereospecific. It occurs with antarafacial (*anti*) addition of the two groups to the  $\pi$  bond (i.e. the electrophilic atom, :E, and the nucleophilic atom, Nu:, are added to opposite faces of the  $\pi$  bond).

**What is the regiochemistry of this reaction?** The addition occurs with Markovnikov regiochemistry: the :E atom becomes bonded to the end of the  $\pi$  bond that is less able to carry a positive charge (i.e. would make the less stable carbocation), and the Nu: atom becomes bonded to the end of the  $\pi$  bond that is better able to support a positive charge (i.e. would be the more stable carbocation)

**Is there an intermediate involved in this reaction?** There is a three-membered cyclic onium ion intermediate. This intermediate has every atom with a complete outer-shell octet, which makes it lower energy than a simple carbocation (stabilized by hyperconjugation or conjugation with a  $\pi$  bond), which has one carbon atom that is electron deficient (i.e. lacks a complete octet).

**Does this intermediate lead to any special reactivity or observations?** Yes: this three-membered ring must open *anti*, so the overall addition is always antarafacial. When the double bond is part of a cyclohexene ring, the E and Nu groups both end up axial, although the ring may then flip to make them both equatorial. Antarafacial addition will supersede the regiochemical preference for Markovnikov addition.

### What reagent or combinations of reagents can be used to make the active reagent in this reaction?

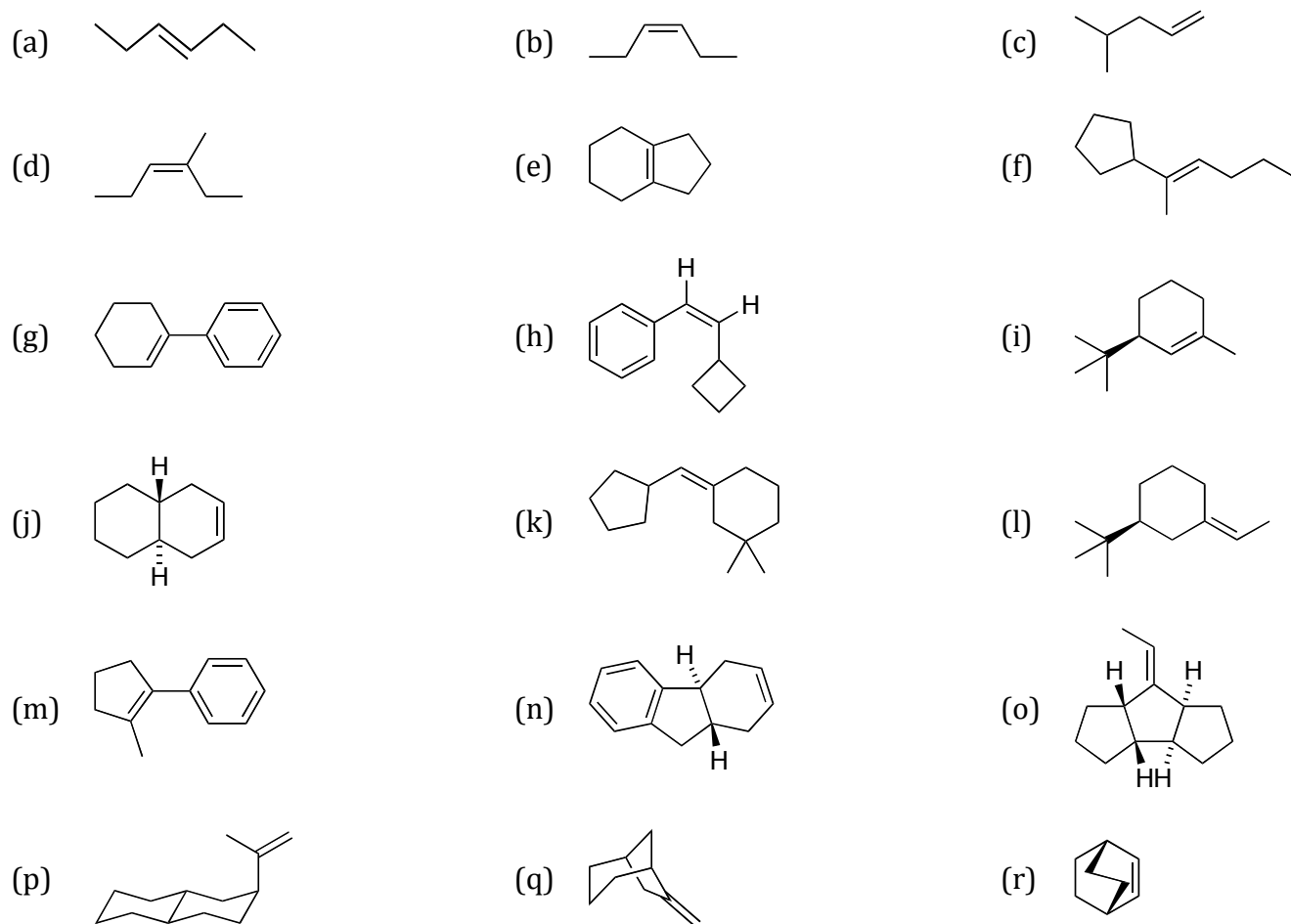
All reagents are separated into the E—Nu segments.

- Adding X—OH: X<sub>2</sub>/H<sub>2</sub>O; Br<sub>2</sub>/KBr/H<sub>2</sub>O; I<sub>2</sub>/KI/H<sub>2</sub>O; NaBrO<sub>3</sub>/NaHSO<sub>3</sub>/H<sub>2</sub>SO<sub>4</sub>/H<sub>2</sub>O; NaOCl/H<sub>2</sub>O; Hg(OAc)<sub>2</sub>/H<sub>2</sub>O/THF; etc.
- Adding X—OR: Br<sub>2</sub>/ROH; Hg(OCOFCF<sub>3</sub>)<sub>2</sub>/ROH; etc.
- Adding X—OCOR [this reaction is especially useful in an intramolecular version because it gives cyclic esters, or lactones]: I<sub>2</sub>/RCO<sub>2</sub>Li/THF; Hg(OAc)<sub>2</sub>/THF; Hg(OAc)<sub>2</sub>/EtOH; etc.
- Adding I—N<sub>3</sub>: IN<sub>3</sub>/CH<sub>2</sub>Cl<sub>2</sub>
- Adding RS(e)—X: PhSCl/CH<sub>2</sub>Cl<sub>2</sub>; PhSeBr/CH<sub>2</sub>Cl<sub>2</sub>; etc.
- Adding X—Y: Br<sub>2</sub>/LiCl/MeCN; ICl/CH<sub>2</sub>Cl<sub>2</sub>; etc.
- Adding X—NHCO<sub>2</sub>R [this reaction is most useful in the intramolecular version]: Br<sub>2</sub>/ROCONH<sub>2</sub>; Hg(OCOFCF<sub>3</sub>)<sub>2</sub>/ROCONH<sub>2</sub>; etc.

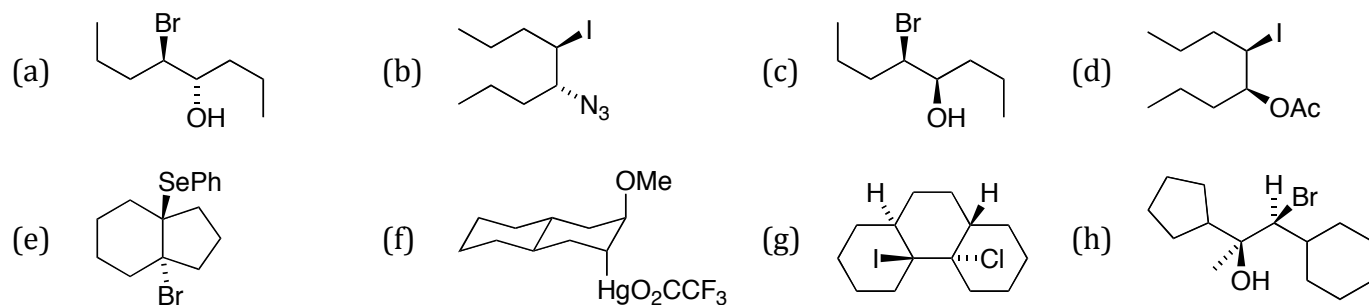
**Practice Problems:**

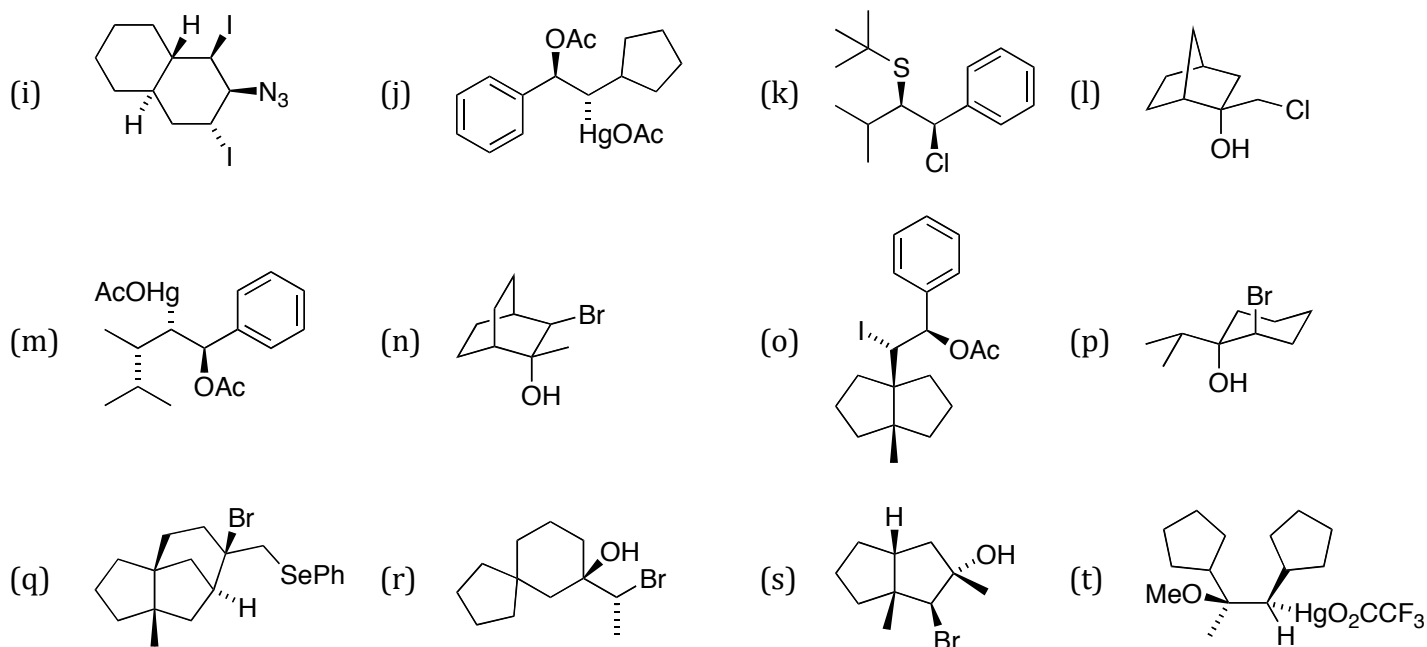
**What is the major organic product formed from each of the following alkenes with the reagent specified?**

- (1)  $\text{Br}_2/\text{H}_2\text{O}$       (2)  $\text{Hg}(\text{OCOCF}_3)_2/\text{THF}/\text{MeOH}$       (3)  $\text{C}_6\text{H}_5\text{SeCl}/\text{CH}_2\text{Cl}_2$   
 (4)  $\text{I}_2/\text{LiOCOCH}_3/\text{THF}$       (5)  $\text{IN}_3/\text{CH}_2\text{Cl}_2$       (6)  $\text{CH}_3\text{SBr}/\text{CH}_2\text{Cl}_2$



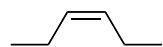
**What alkene and reagent combination should be used to prepare each of the following addition products? [Only one enantiomer is shown, although some products may be racemic] If more than one diastereoisomer or regioisomer will be formed as a major product, give the structure of that other product.**





## SELECTED ANSWERS

What is the major organic product formed from each of the following alkenes with the reagent specified?



(b) The starting alkene is symmetrical and not chiral; the product is racemic, but there is no regiochemistry involved in this addition. The antarafacial addition may result in addition of the electrophilic atom to the top face or the bottom face of the double bond with equal facility, but note how the two new chiral centers have stereochemistry that reflects the stereochemistry of the original double bond (*Z*).

(1)

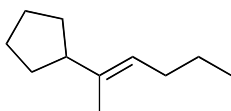
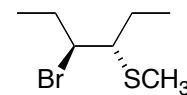
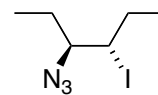
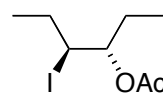
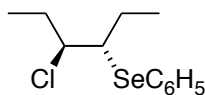
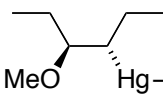
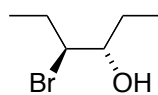
(2)

(3)

(4)

(5)

(6)

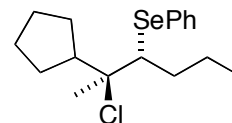
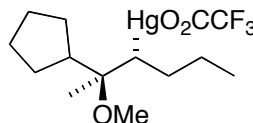
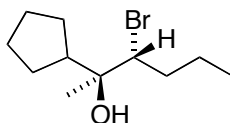


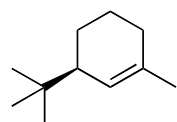
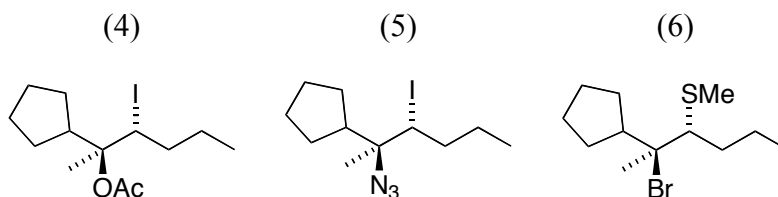
(f) The starting alkene is not symmetrical and not chiral; the product is racemic, and this addition will occur with Markovnikov regiochemistry. The antarafacial addition may result in addition of the electrophilic atom to the top face or the bottom face of the double bond with equal facility, but note how the two new chiral centers have stereochemistry that reflects the *E* stereochemistry of the original double bond.

(1)

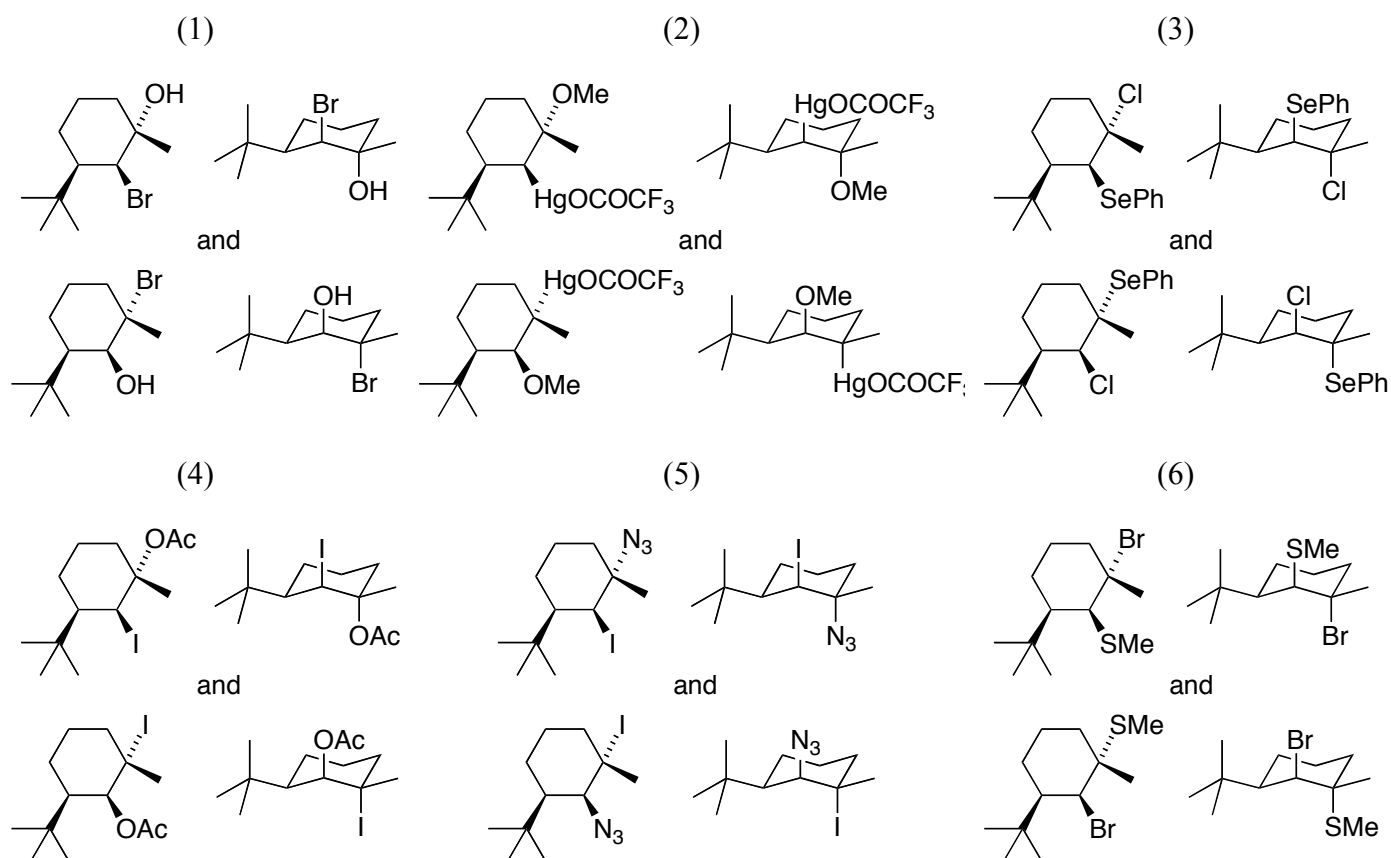
(2)

(3)

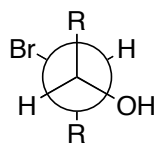
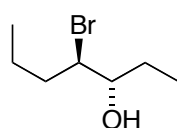




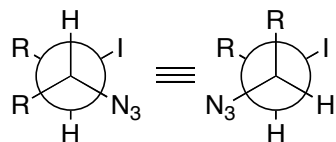
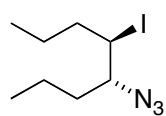
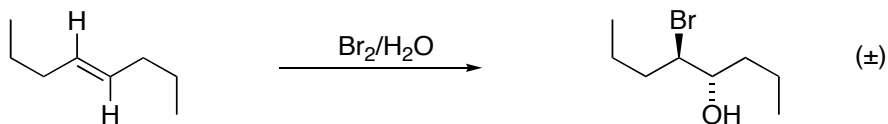
(i) The starting alkene is not symmetrical and is chiral, and the *tert*-butyl group prevents the ring from inverting. Antarafacial addition in cyclohexanes forces the two new  $\sigma$  bonds to be formed in a *trans*-diaxial relationship. This supersedes the Markovnikov rule for regiochemistry of the addition. The upper product results from initial addition of the electrophilic atom to the top face of the  $\pi$  bond; the lower product results from initial addition of the electrophilic atom to the bottom face of the  $\pi$  bond. The products are regioisomers, but are both *E* isomers. The result of the reaction may be better understood and seen in the chair projection formulas.



**What alkene and reagent combination should be used to prepare each of the following addition products? [Only one enantiomer is shown, although some products may be racemic]**

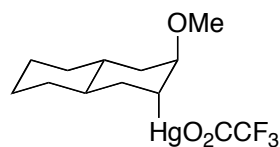
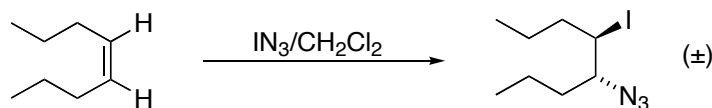


(a) The functional groups in this molecule are the bromine and the hydroxy groups, which are on adjacent carbon atoms. This locates the position of the double bond; these groups can be incorporated into a molecule by the antarafacial addition of HO—Br to an alkene through a three-membered cyclic bromonium ion intermediate. When we examine the Newman projection of this product, we see that when the bromine and the hydroxy groups are *anti* to each other, so are the hydrogen atoms and the alkyl groups. This means that in the starting alkene, the alkyl groups must be *anti* to each other, and so must the hydrogen atoms. The starting alkene is therefore *E*-4-octene.



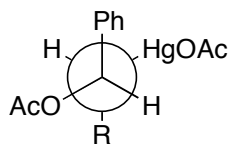
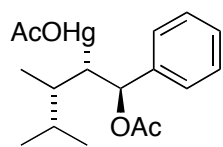
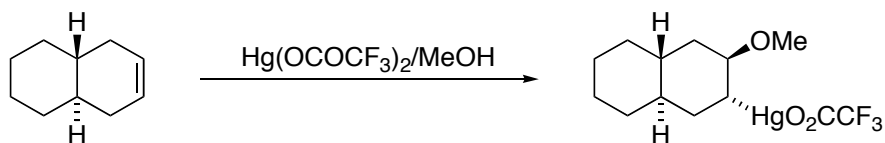
(b) The functional groups in this molecule are the iodine and the azide groups, which are on adjacent carbon atoms. This locates the position of the double bond; these groups can be incorporated into a molecule by the antarafacial

addition of I—N<sub>3</sub> to an alkene through a three-membered cyclic iodonium ion intermediate. When we examine the Newman projection of this product, we see that when the iodine and the azide group are *syn* to each other, so the first thing we must do is to re-write the Newman projection so that these two groups are *anti* to each other. In this conformation, the two alkyl groups are *syn* to each other, and so are the hydrogen atoms. This means that in the starting alkene, the alkyl groups must be *syn* to each other, and so must the hydrogen atoms. The starting alkene is therefore *Z*-4-octene.



(f) The functional groups in this molecule are the methoxy group and the mercury group, which are on adjacent carbon atoms. This locates the position of the double bond. They are both axial, which places them in an *anti* relationship; they can be incorporated into a molecule by the antarafacial addition of MeO—HgOCOCF<sub>3</sub> to

an alkene in methanol solvent through a three-membered cyclic mercurinium ion intermediate. The reagent itself is formed by using mercury (II) trifluoroacetate in methanol.



(m) The functional groups in this molecule are the acetate and the mercuriacetate groups, which are on adjacent carbon atoms. This locates the position of the double bond; these groups can be incorporated into a molecule by the antarafacial addition of AcOHg—OAc to an alkene through a three-membered cyclic mercurinium ion intermediate. The mercury

atom is attached to a secondary carbon, and the acetate is secondary and benzylic, which corresponds to Markovnikov regiochemistry in the addition. When we examine the Newman projection of this product, we see that the bromine and sulfur atoms are *anti* to each other, as are the two alkyl groups and the two hydrogen atoms. This means that in the starting alkene, the alkyl groups must be *anti* to each other, and so must the hydrogen atoms. The starting alkene is therefore the *E* isomer. The other chiral center present in the product is not affected during the reaction, so it must have been present already in the starting alkene.

