

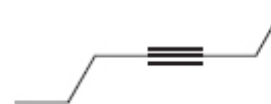
# Alchini - Acetileni



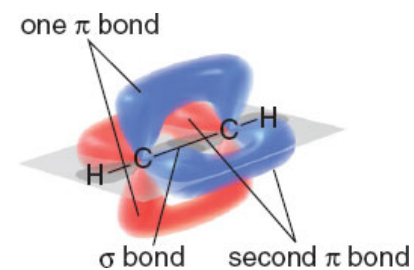
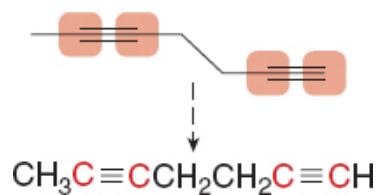
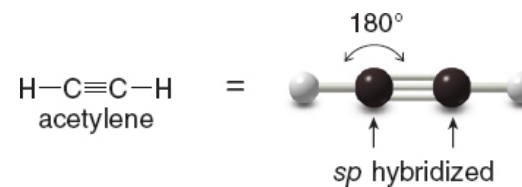
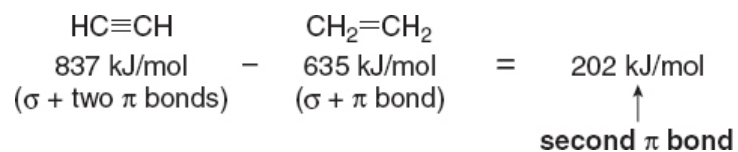
alkyne



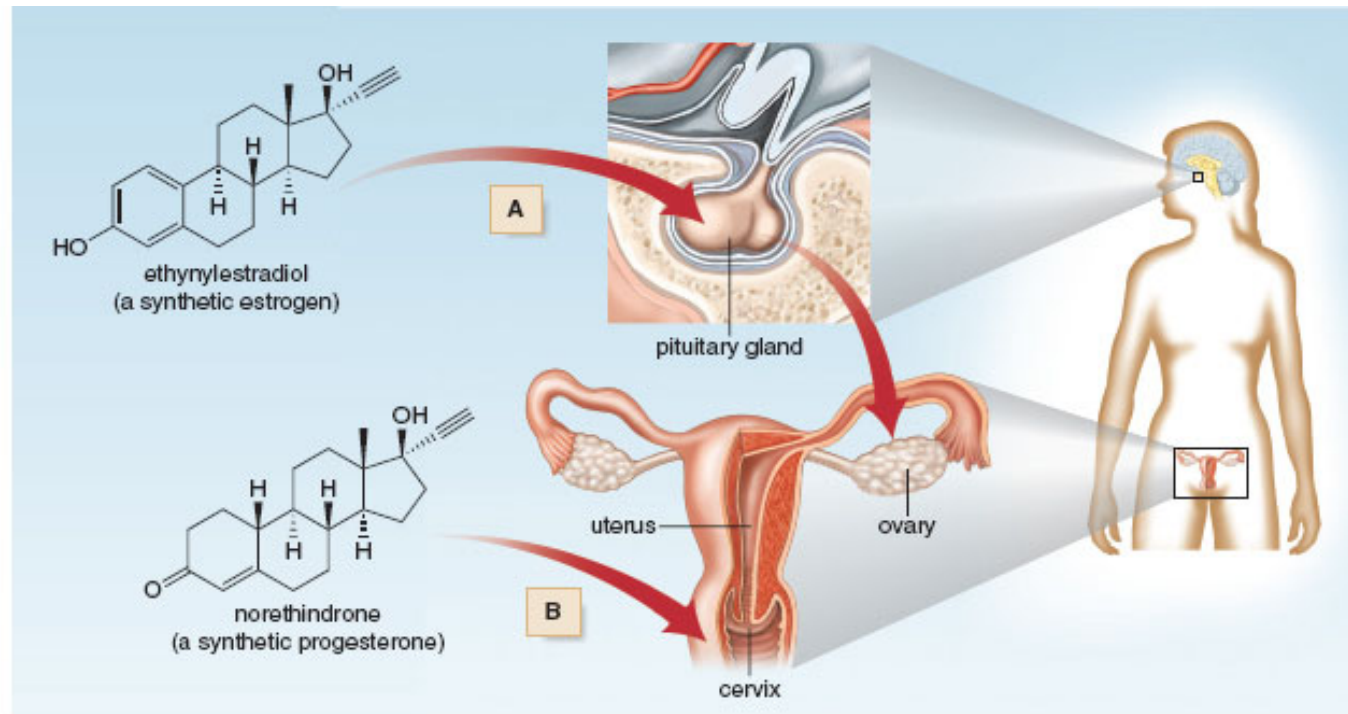
terminal alkyne



internal alkyne



## Alchini Interessanti – anticontraccettivi orali

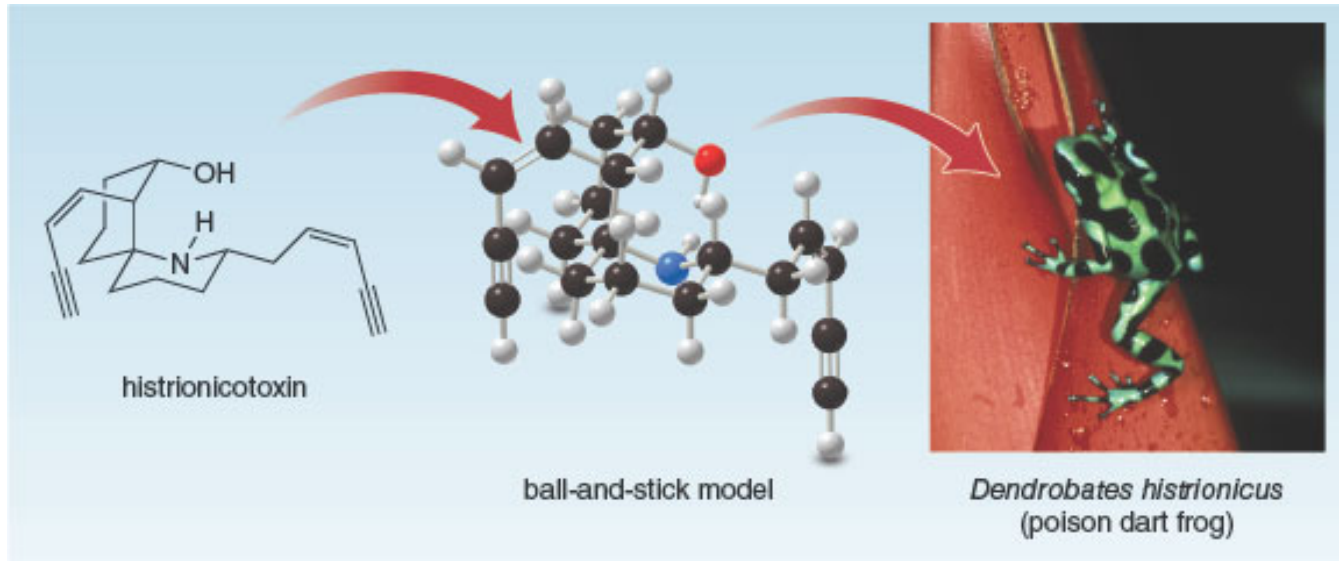


Monthly cycles of hormones from the pituitary gland cause ovulation, the release of an egg from an ovary. To prevent pregnancy, the two synthetic hormones in many oral contraceptives have different effects on the female reproductive system.

**A:** The elevated level of **ethynylestradiol**, a synthetic estrogen, “fools” the pituitary gland into thinking a woman is pregnant, so ovulation does not occur.

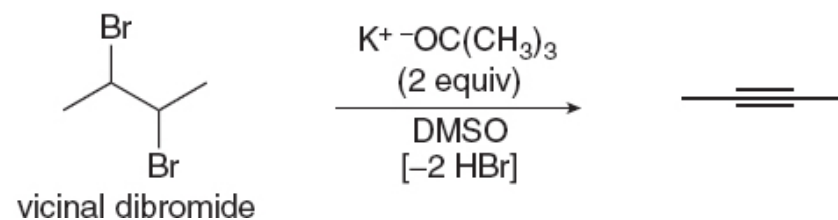
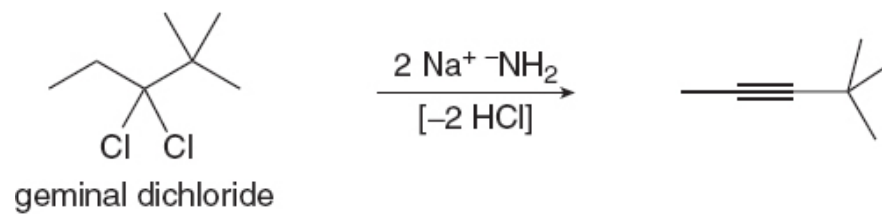
**B:** The elevated level of **norethindrone**, a synthetic progesterone, stimulates the formation of a thick layer of mucus in the cervix, making it difficult for sperm to reach the uterus.

## Alcheni in natura - tossine

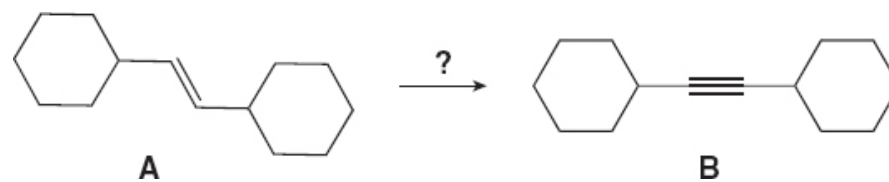


- Histrionicotoxin is a defensive toxin that protects *Dendrobates histrionicus* from potential predators. These small “poison dart” frogs inhabit the moist humid floor of tropical rainforests, and are commonly found in western Ecuador and Colombia. Histrionicotoxin acts by interfering with nerve transmission in mammals, resulting in prolonged muscle contraction.

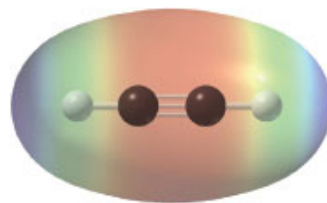
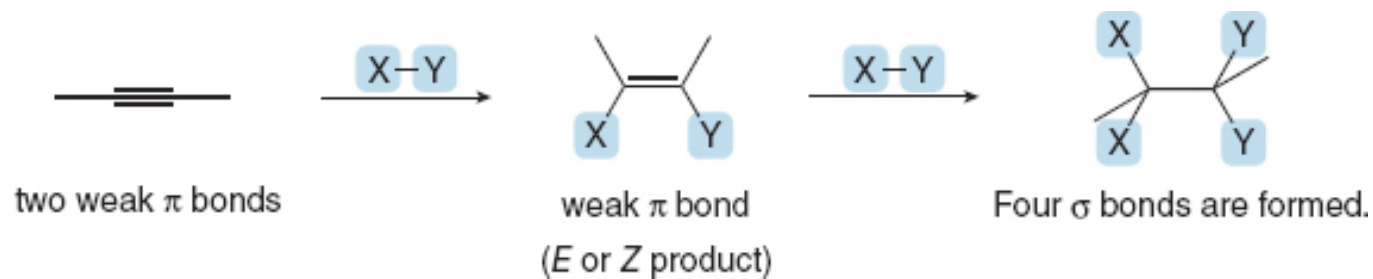
## Sintesi alchini – reazioni di eliminazione



Come faccio a convertire A in B?

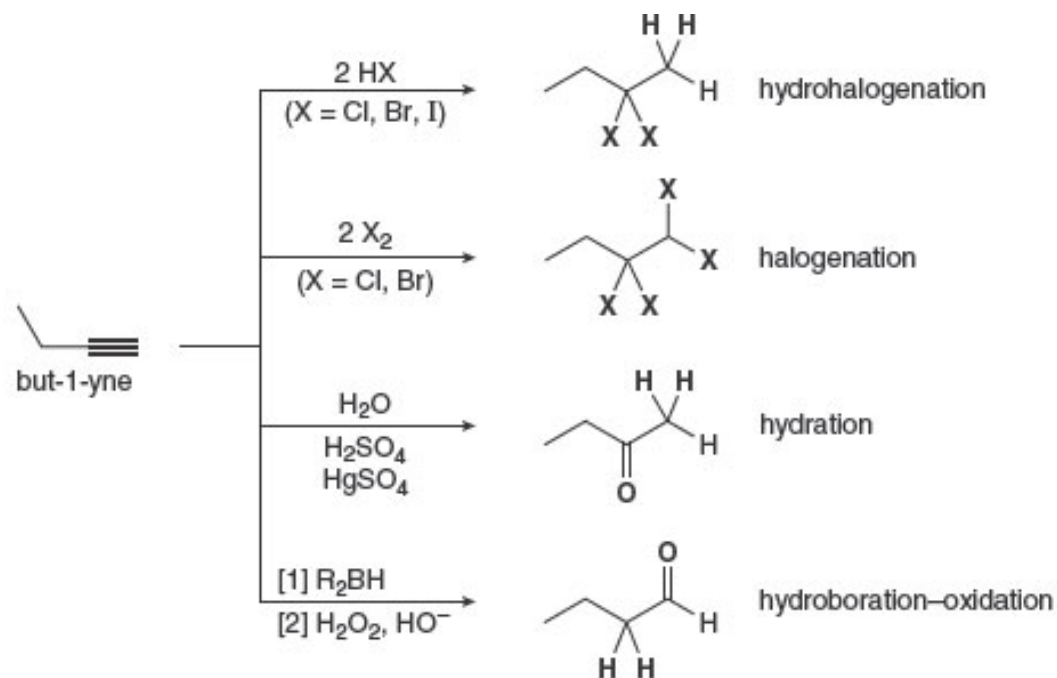


## Reattività: reazioni di addizione



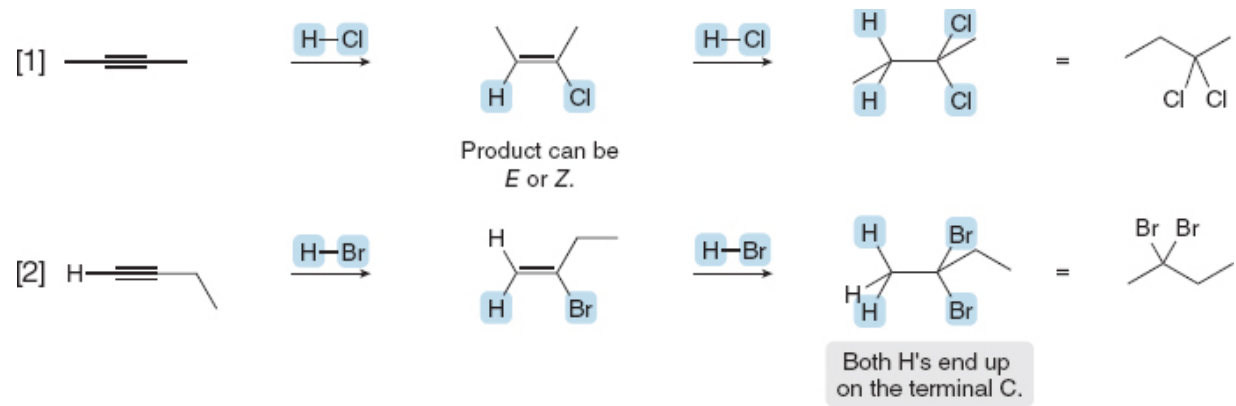
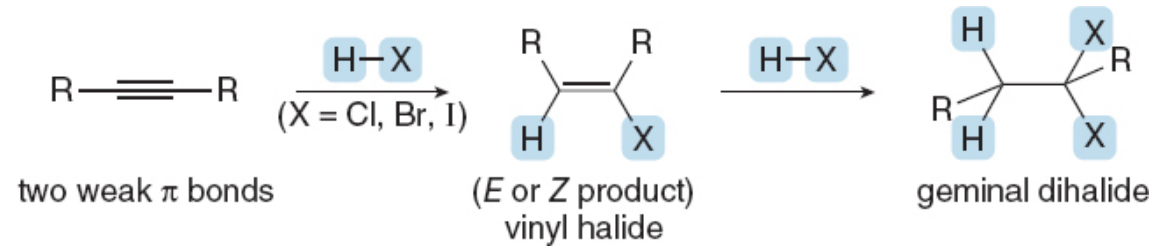
**Gli alcheni sono elettron-ricchi per cui reagiscono con elettrofili**  
**addizione elettrofila**

## Reazioni di addizione – formazione di composti carbonilici/alogeno derivati



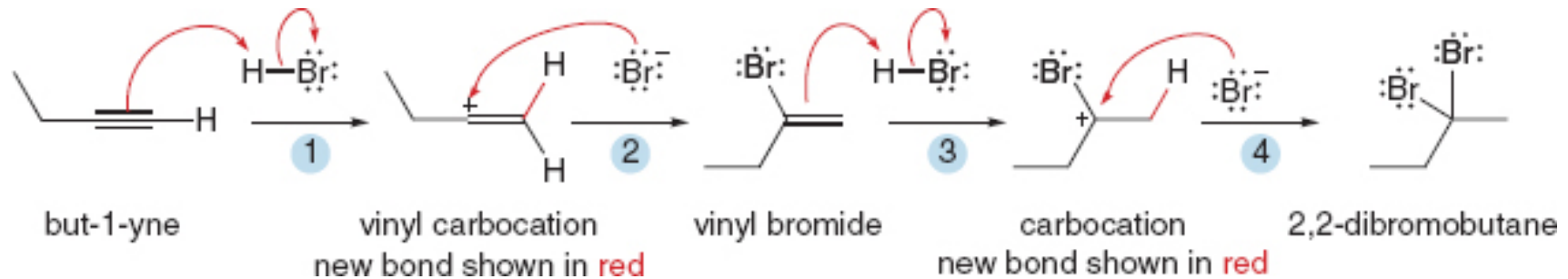
- In each addition, both  $\pi$  bonds of the triple bond are broken, and four new bonds are formed.

## Addizione elettrofila di HX: Idroalogenazioni

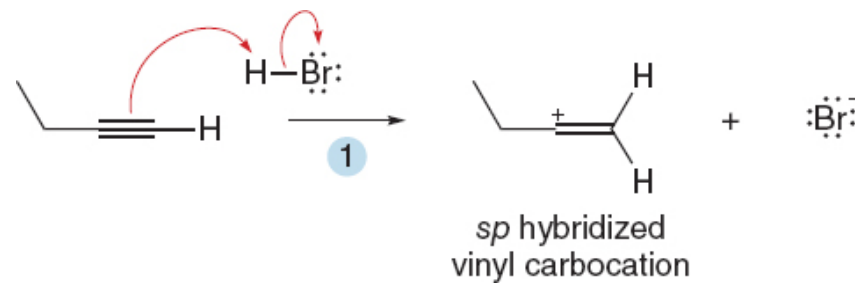


- Con 2 equivalenti di HX si forma il dihalogeno geminale
- L'idroalogenazione ha regiochimica Markovnikov
- Con un equivalente di HX si forma il vinyl-alogeno

## Meccanismo a più stadi via carbocatione



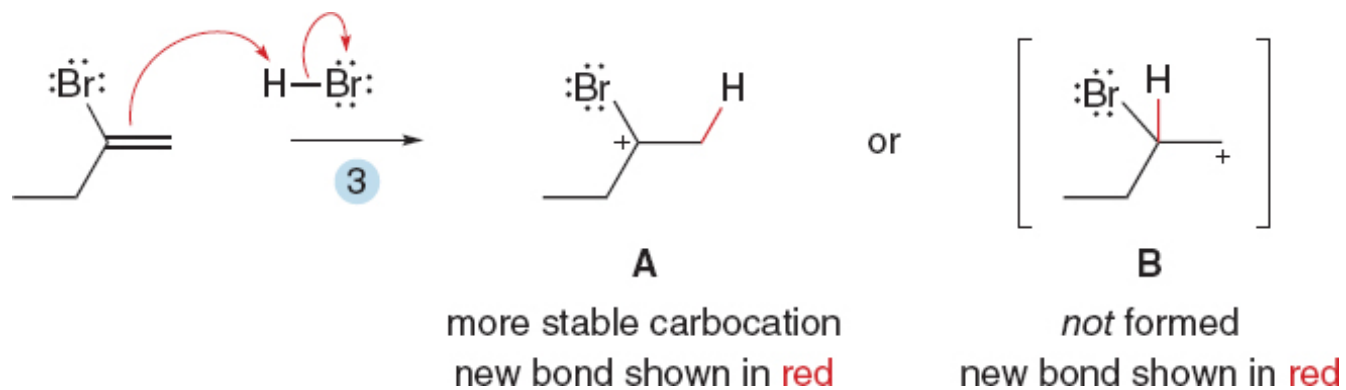
## Carbocatione vinilico



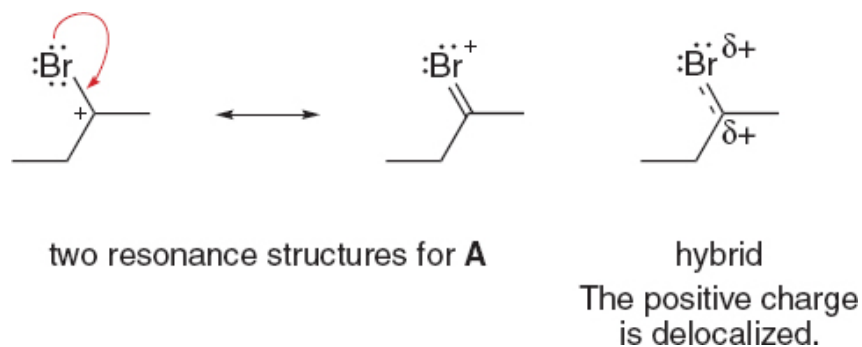
Il carbocatione vinilico (Step [1]) è ibridizzato *sp* quindi è meno stabile di un carbocatione *sp*<sup>2</sup>. Pertanto le addizioni elettrofile di HX saranno più lente rispetto ad un alchene, anche se gli alchini sono più polarizzabili e hanno elettroni  $\pi$  meno trattenuti



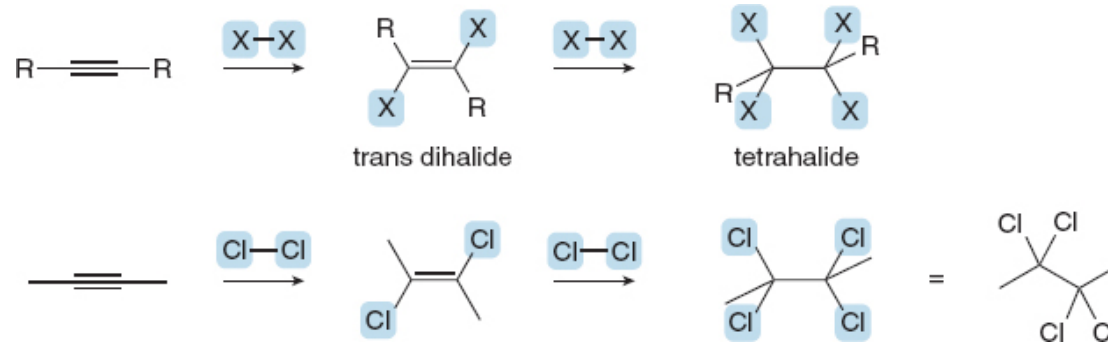
## Reattività vinil bromuro - regiochimica



Si forma il carbocatione A perchè è stabilizzato per risonanza (anche se il Br è più elettronegativo dell'H)

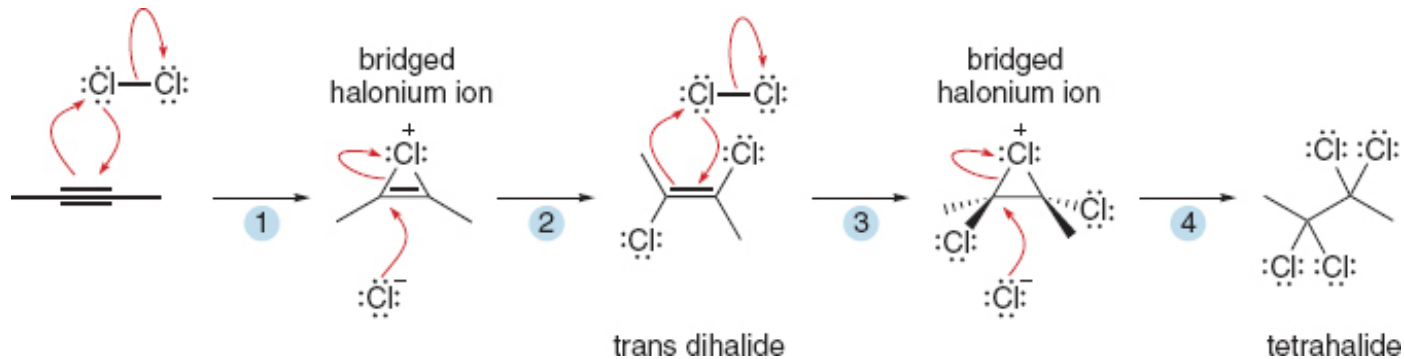


## Reazioni di addizione di alogeni

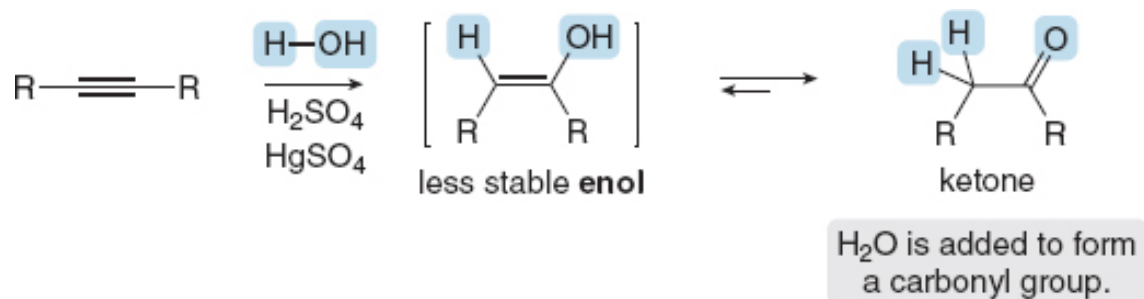


### Formazione di alcheni dialogenati (trans) e alcani tetraalogenati

#### Meccanismo (via ponti alonio)

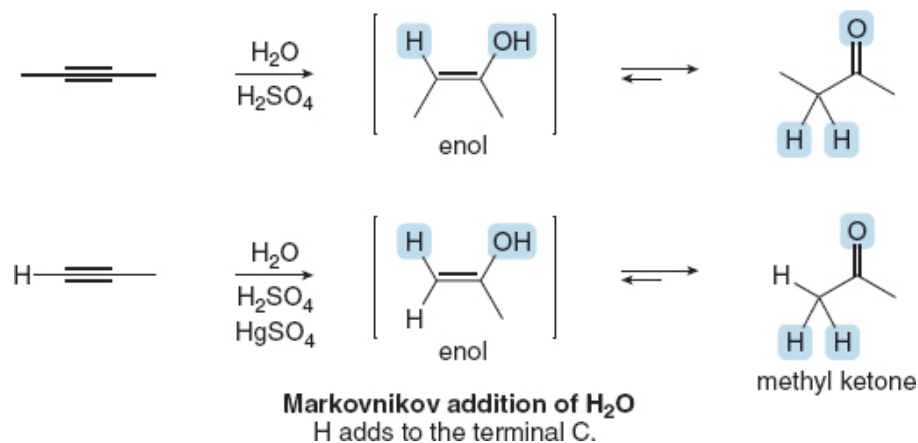


## Reazioni di addizione di acqua (in acido)

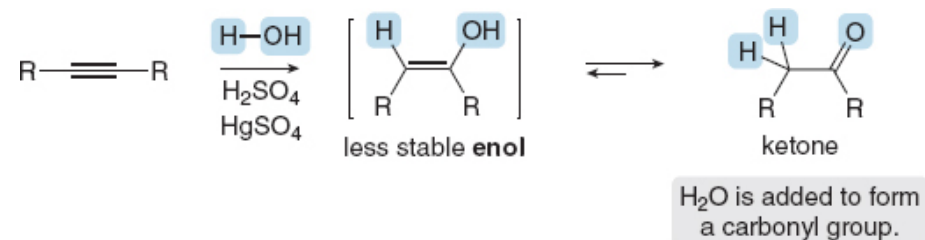


Si forma un composto carbonilico o intermedio enolo.

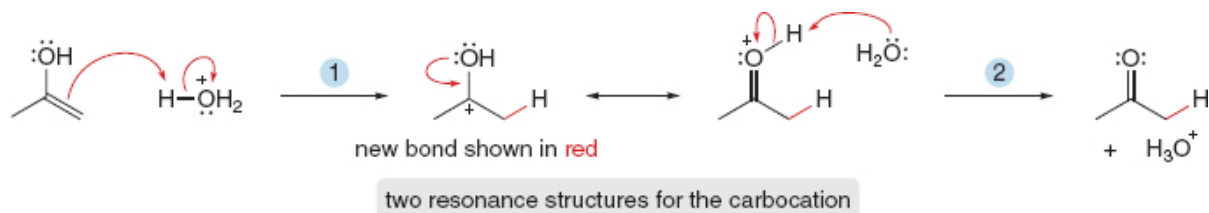
Alchini terminali richiedono la presenza di HgSO<sub>4</sub>. Addizione secondo Markovnikov



## Reazioni di addizione di acqua (in acido)

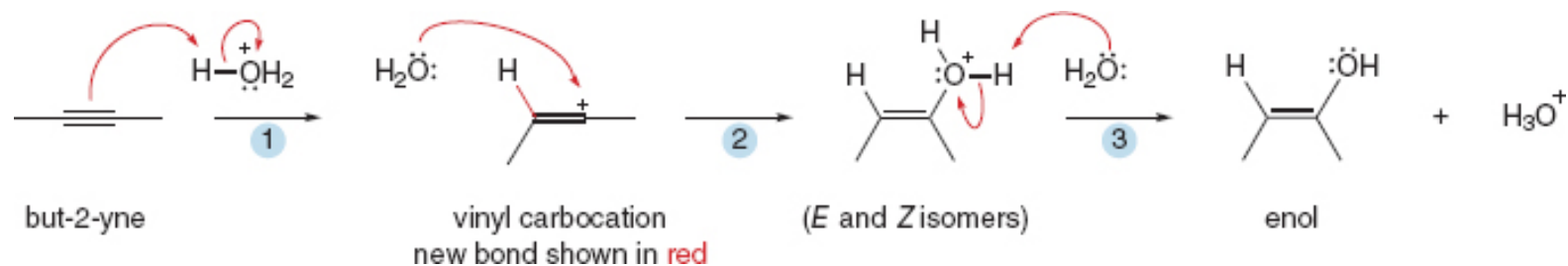


## Tautomeria cheto- enolica (acido catalizzata)

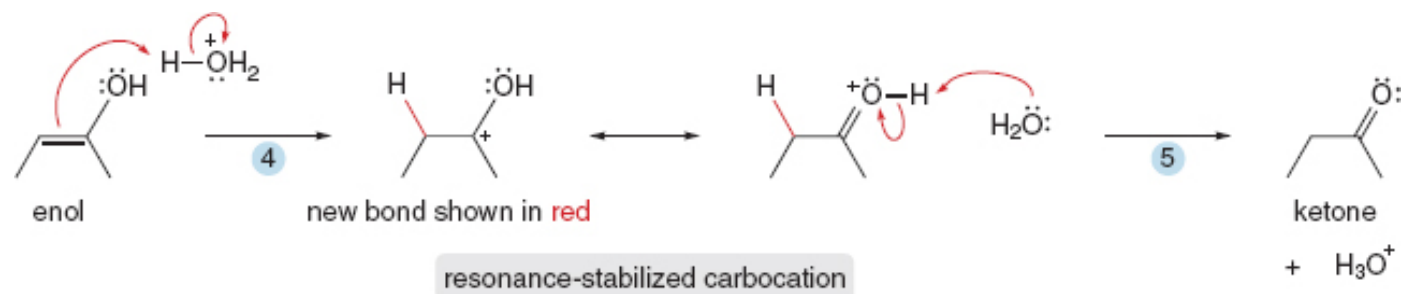


## Idratazione di alchini – meccanismo

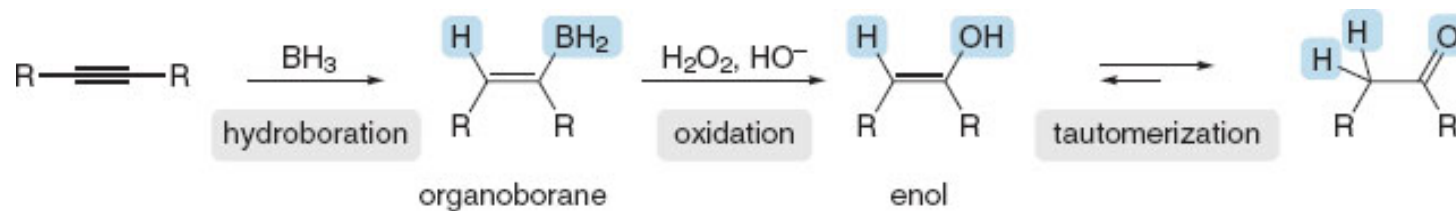
### Idratazione a enolo



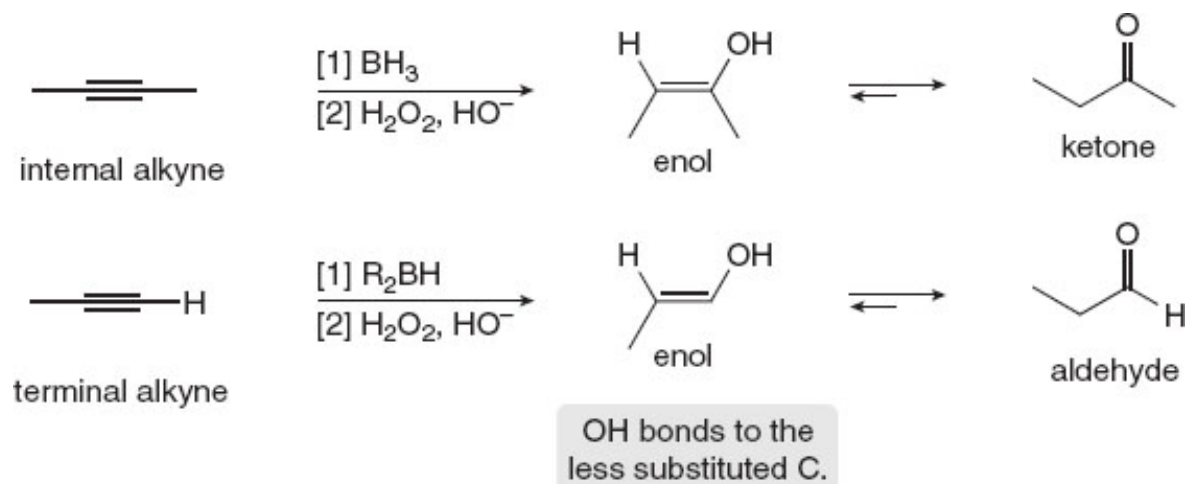
### Tautomeria cheto- enolica (acido catalizzata)



## Idroborazione/ossidazione di alchini

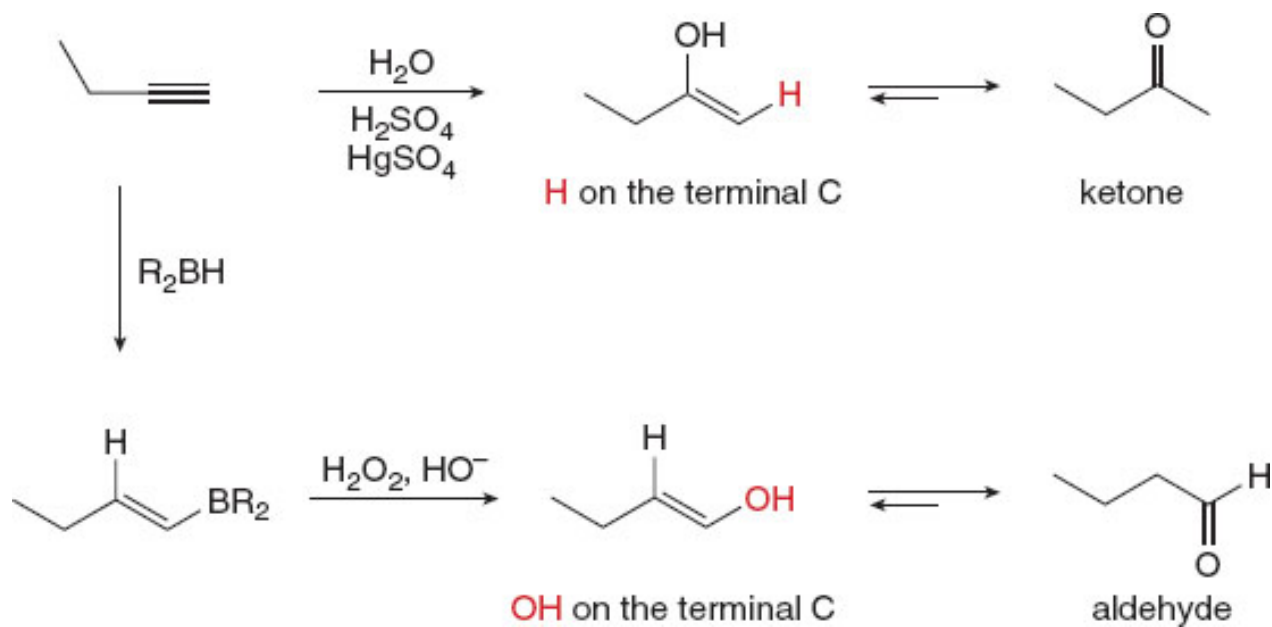


## Regiochimica (anti Markovnikov)



# Conversione alchini – composti carbonilici

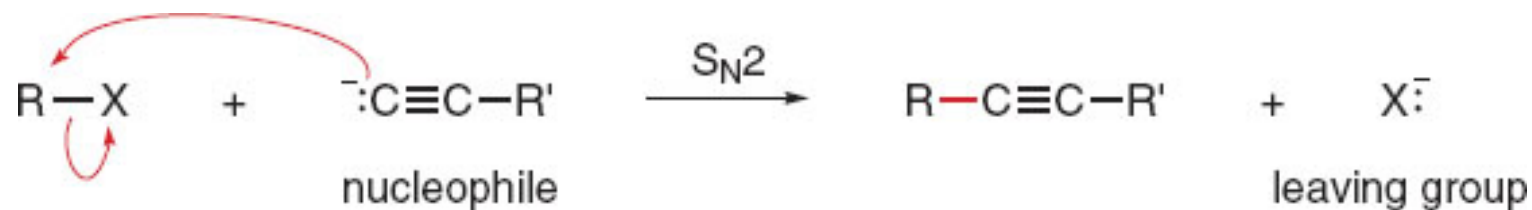
## Controllo regiochimico:



## Reazioni di anioni acetiluro



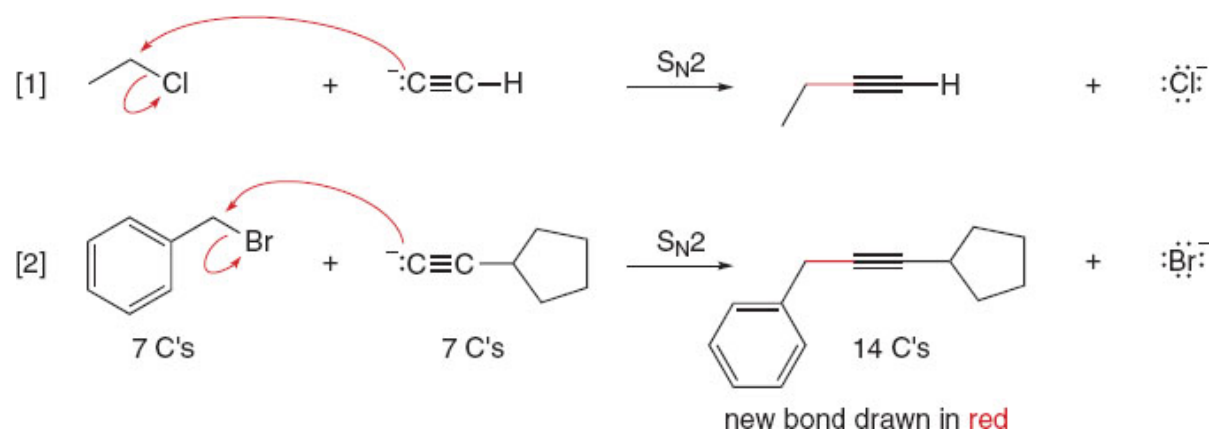
## Reazioni con alogenuri alchilici ( $S_N2$ ) formazione legami C-C con $\text{CH}_3\text{X}$ e alogenuri primari





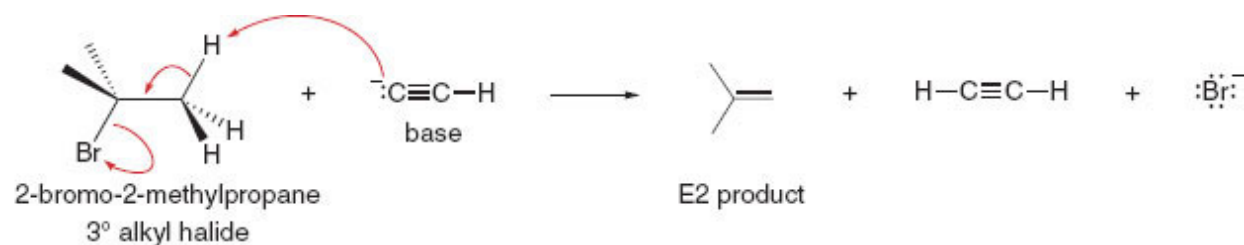
# Reazioni con alogenuri alchilici (S<sub>N</sub>2)

formazione legami C-C con CH<sub>3</sub>X e alogenuri primari

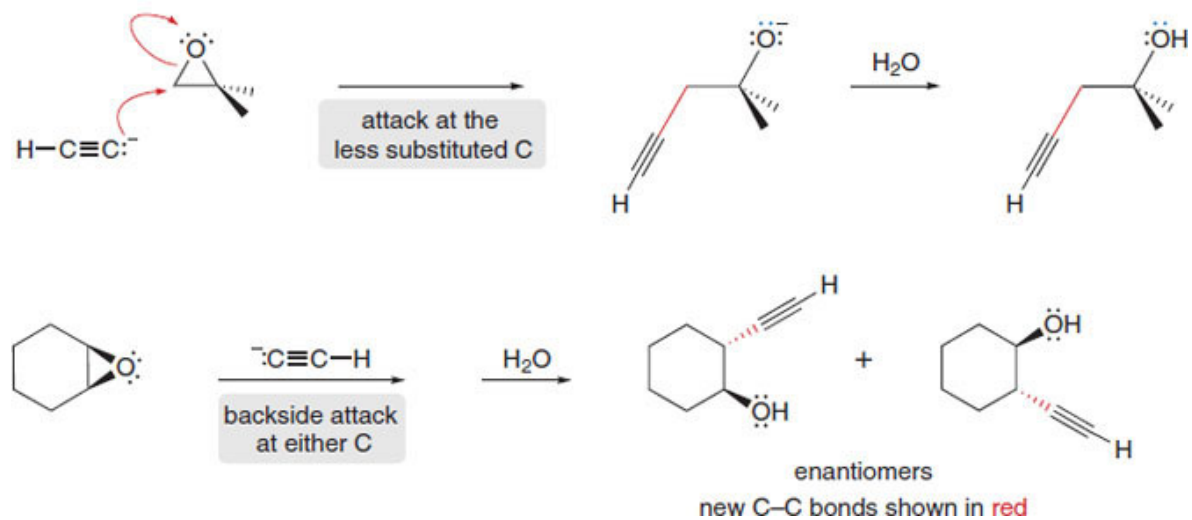


## Reazioni con alogenuri terziari ingombrati: E2

Steric hindrance prevents an S<sub>N</sub>2 reaction.



## Reazioni di anioni acetiluro con epossidi



## Reazione stereospecifica e regioselettiva

Quali sono i prodotti delle seguenti reazioni?



## Gli alchini

Gli alchini contengono un triplo legame carbonio-carbonio costituito da un legame  $\sigma$  forte e due legami  $\pi$  deboli. Ogni carbonio è ibridizzato  $sp$  e lineare

Gli alchini sono denominati usando il suffisso -ino

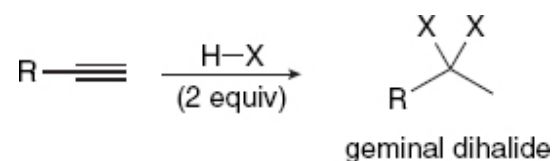
Gli alchini hanno forze intermolecolari deboli, che danno loro mp e bp bassi e li rendono insolubili in acqua

Poiché i suoi legami  $\pi$  più deboli rendono li rendono elettrone-ricchi subiscono facilmente reazioni di addizione con elettrofili

## Reazioni di addizione ad alchini

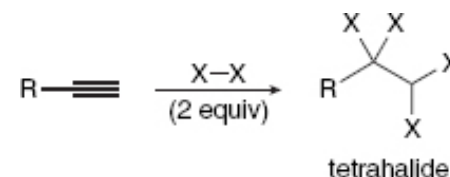
### Idroalogenazione (addizione di HX)

Regiochimica secondo Markovnikov:  
si forma il carbocatione più stabile.



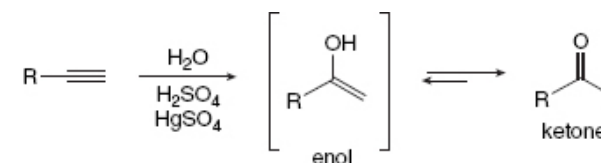
### Alogenazione – Addizione X<sub>2</sub>

Si forma un intermedio ione alonio a ponte.  
L'addizione di X<sub>2</sub> è anti



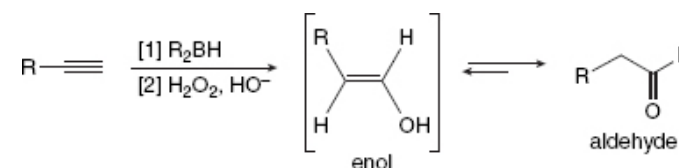
### Idratazione - Addizione di H<sub>2</sub>O

Regiochimica secondo Markovnikov.  
Si forma l'enolo che riarrangia al chetone corrispondente.



### Idroborazione - Ossidazione - Addizione di H<sub>2</sub>O

Regiochimica anti-Markovnikov.  
L'enolo riarrangia al composto carbonilico corrispondente



## Reazioni con ioni acetiluro

### Sintesi di Acetiluri

Regiochimica secondo Markovnikov:  
si forma il carbocatione più stabile.



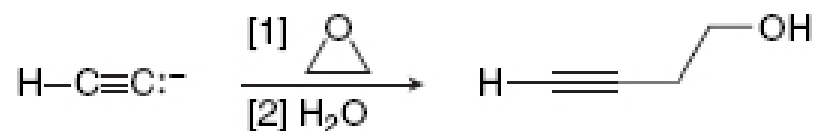
### Reazione con alchilogenuri

S<sub>N</sub>2- formazione di legami C-C,  
meglio con metil e alogenuri primari



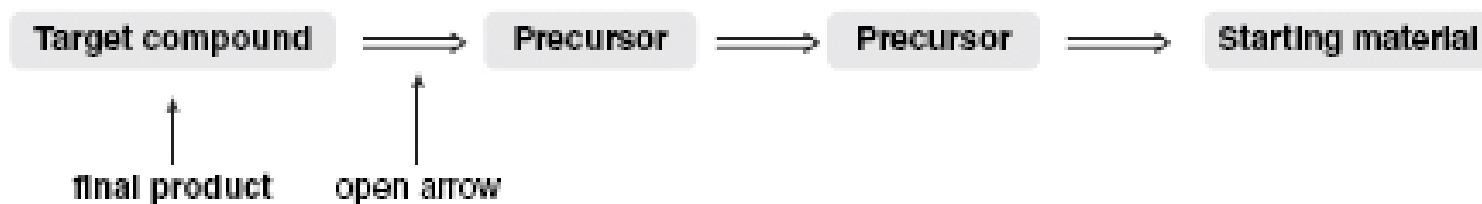
### Reazione con epossidi

S<sub>N</sub>2- formazione di legami C-C,  
Formazione di un beta-alcol,  
attacco al carbonio meno sostituito



# Sintesi organica: Approccio Razionale

**Analisi retrosintetica:** sintesi a ritroso dal prodotto finale al substrato di partenza



Nella progettazione di una sintesi possiamo suddividere le reazioni in:

- Reazioni che portano alla formazione di nuovi legami C-C
- Reazioni che interconvertono gruppi funzionali

# Sintesi organica: Approccio Razionale

## Analisi retrosintetica: sintesi a ritroso dal prodotto finale al substrato di partenza

### How To Develop a Retrosynthetic Analysis

**Step [1]** Compare the carbon skeletons of the starting material and product.

- If the product has more carbon-carbon  $\sigma$  bonds than the starting material, the synthesis must form one or more C-C bonds. If not, only functional group interconversion occurs.
- Match the carbons in the starting material with those in the product, to see where new C-C bonds must be added or where functional groups must be changed.

**Step [2]** Concentrate on the functional groups in the starting material and product and ask:

- What methods introduce the functional groups in the product?
- What kind of reactions does the starting material undergo?

**Step [3]** Work backwards from the product and forwards from the starting material.

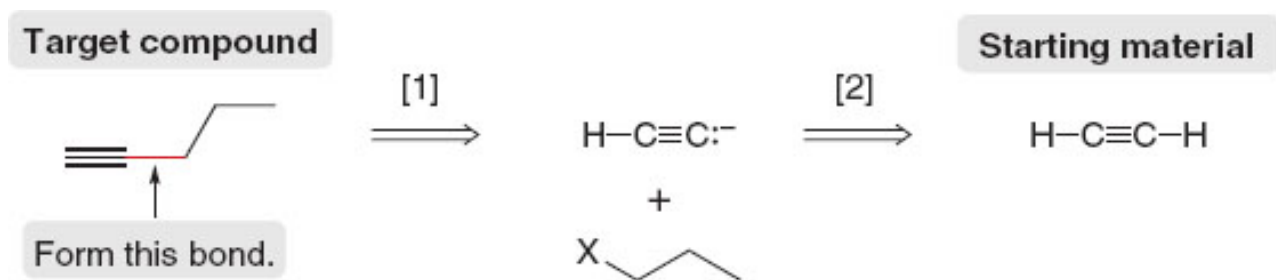
- Ask: What is the immediate precursor of the product?
- Compare each precursor to the starting material to determine if there is a one-step reaction that converts one to the other. Continue this process until the starting material is reached.
- Always generate simpler precursors when working backwards.
- Use fewer steps when multiple routes are possible.
- Keep in mind that you may need to evaluate several different precursors for a given compound.

**Step [4]** Check the synthesis by writing it in the synthetic direction.

- To check a retrosynthetic analysis, write out the steps beginning with the starting material, indicating all necessary reagents.

## Analisi Retrosintetica

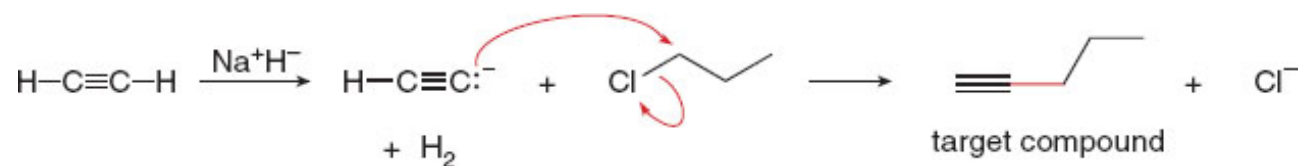
Proporre una sintesi di  $\text{HC}\equiv\text{C}-\text{CH}_2-\text{CH}_2-\text{CH}_3$  da  $\text{HC}\equiv\text{CH}$  e qualsiasi altro reagente organico/inorganico



[1] Formo un nuovo legame C-C usando un anione acetiluro e un alogenuro alchilico primario

[2] Preparo l'acetiluro dall'acetilene mediante trattamento con una base

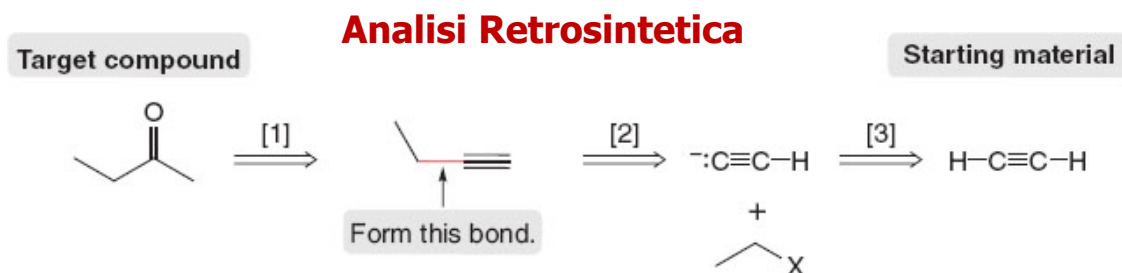
## Sintesi proposta



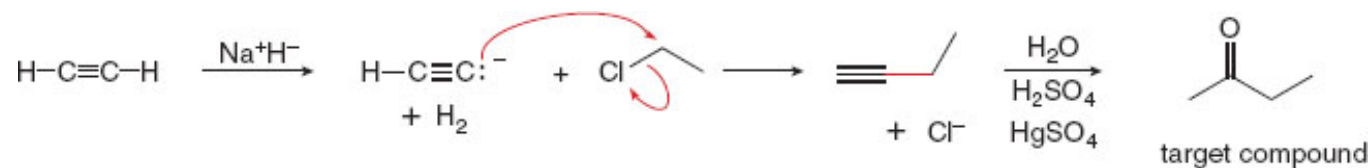


## Esercizio

Proporre una sintesi di  $\text{CH}_3\text{CH}_2\text{C(O)CH}_3$  da un qualsiasi reagente organico con 2 atomi di carbonio

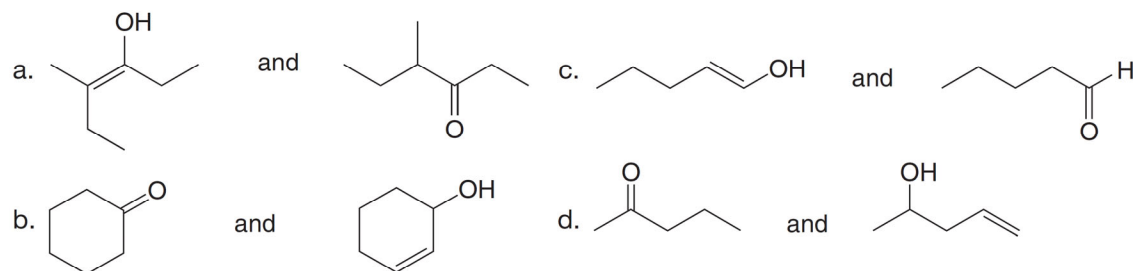


### Sintesi proposta

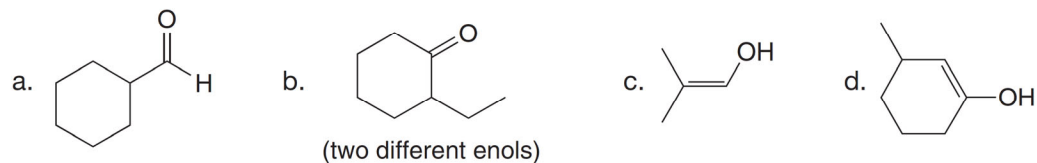


Proporre una sintesi di  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CHO}$  da qualsiasi reagente con 2 atomi di carbonio

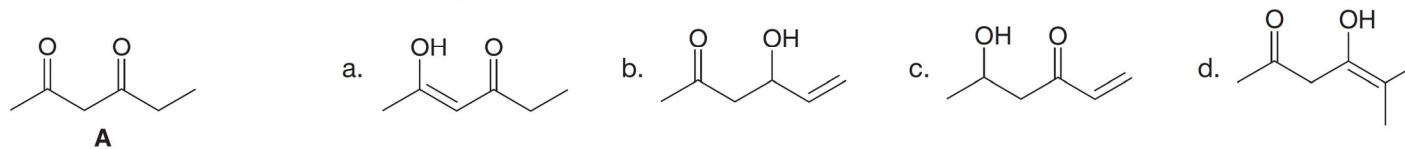
11.28 Which of the following pairs of compounds represent keto–enol tautomers?



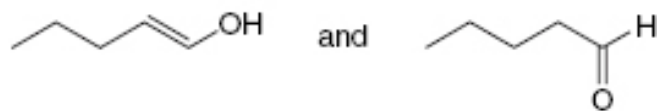
11.29 Draw the enol form of each keto tautomer in parts (a) and (b), and the keto form of each enol tautomer in parts (c) and (d).



11.30 How is each compound related to **A**? Choose from tautomers, constitutional isomers but not tautomers, or neither.



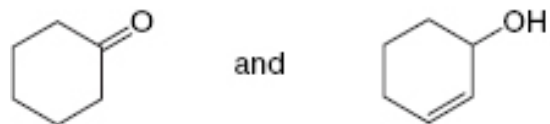
11.31 Ignoring stereoisomers, draw the two possible enols for butan-2-one ( $\text{CH}_3\text{COCH}_2\text{CH}_3$ ), and predict which one is more stable.



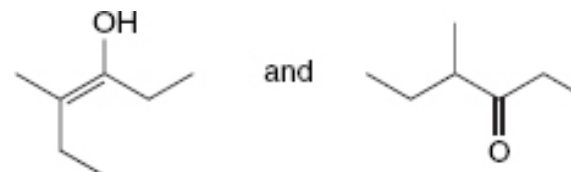
**A**



**B**



**C**



**D**

**11.33** Draw the products formed when hex-1-yne is treated with each reagent.

a. HCl (2 equiv)

d.  $\text{H}_2\text{O} + \text{H}_2\text{SO}_4 + \text{HgSO}_4$

g. [1]  $\text{NH}_2^-$ ; [2]  $\text{CH}_3\text{CH}_2\text{Br}$

b. HBr (2 equiv)

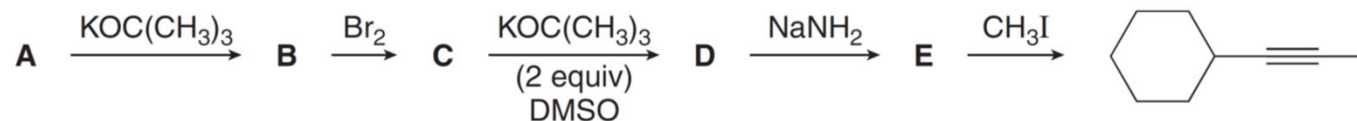
e. [1]  $\text{R}_2\text{BH}$ ; [2]  $\text{H}_2\text{O}_2, \text{HO}^-$

h. [1]  $\text{NH}_2^-$ ; [2] ; [3]  $\text{H}_2\text{O}$

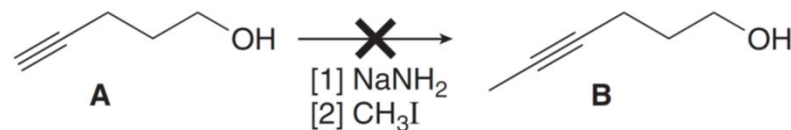
c.  $\text{Cl}_2$  (2 equiv)

f. NaH

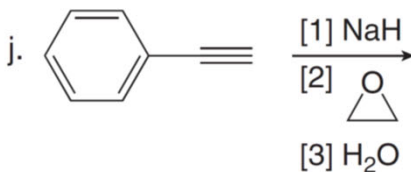
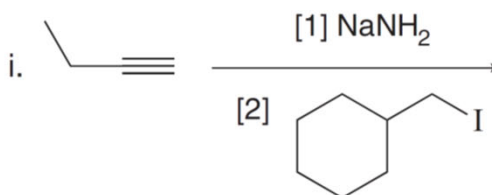
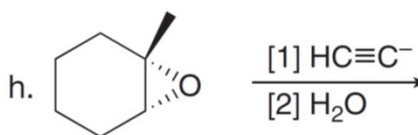
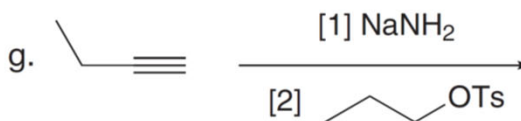
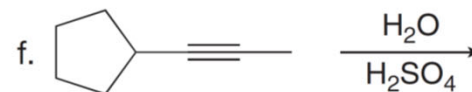
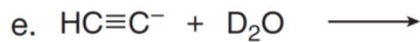
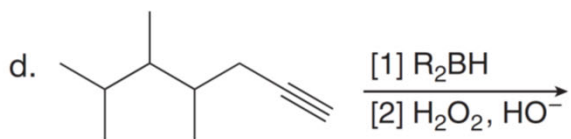
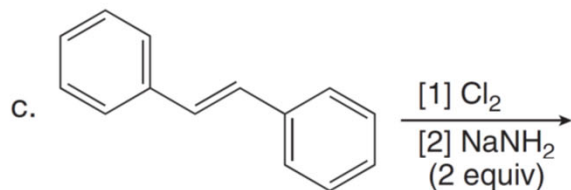
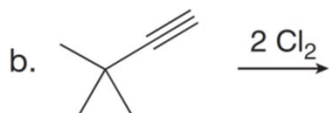
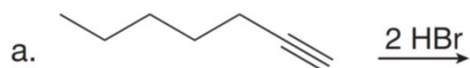
**11.39** Draw the structure of compounds **A–E** in the following reaction scheme.



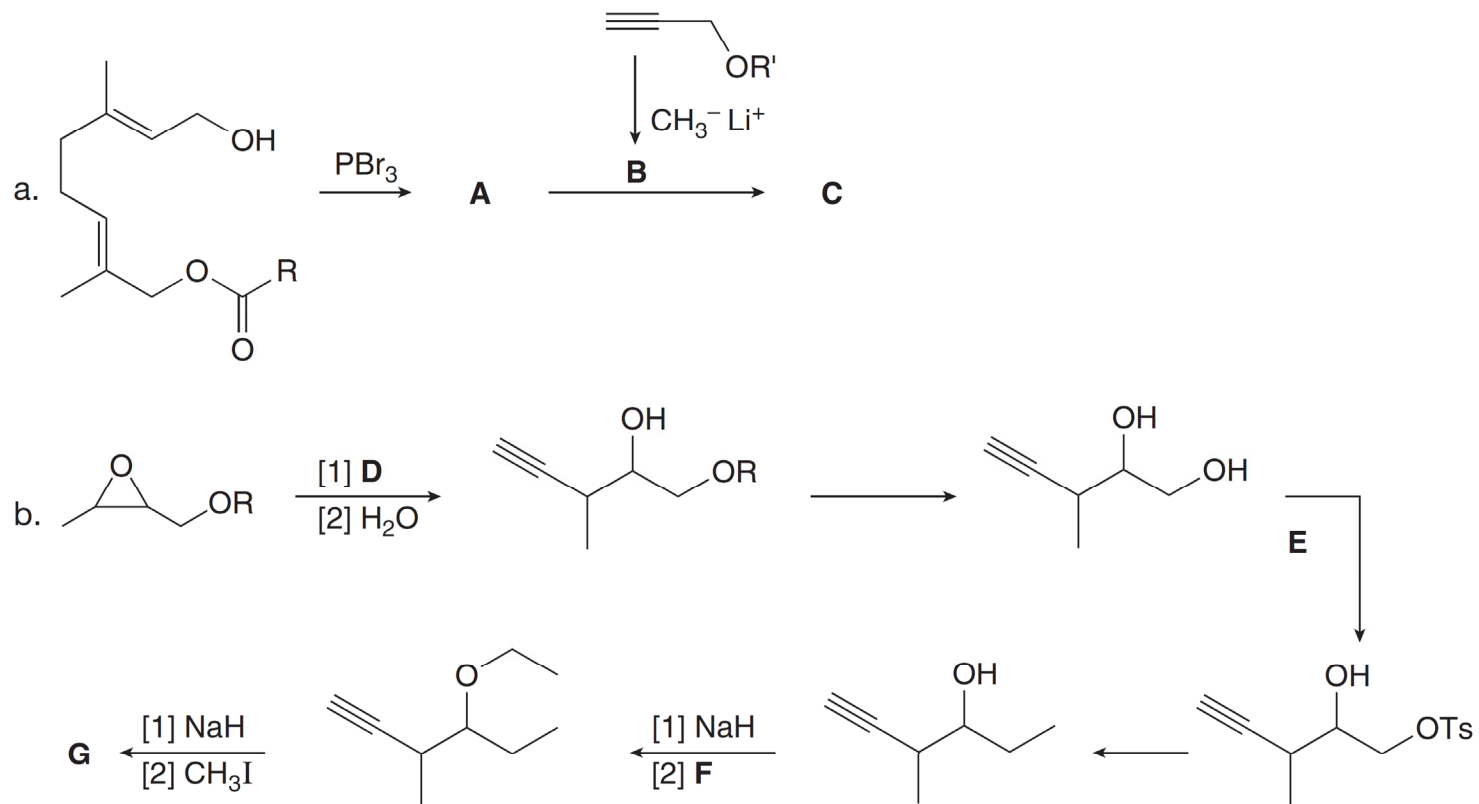
**11.40** When alkyne **A** is treated with  $\text{NaNH}_2$  followed by  $\text{CH}_3\text{I}$ , a product having molecular formula  $\text{C}_6\text{H}_{10}\text{O}$  is formed, but it is *not* compound **B**. What is the structure of the product and why is it formed?



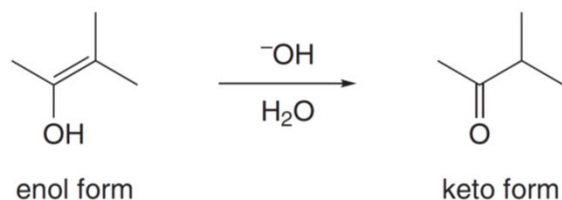
11.38 Draw the organic products formed in each reaction.



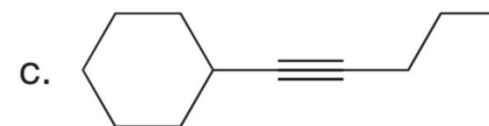
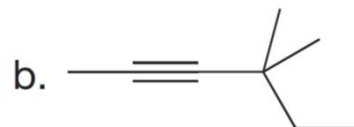
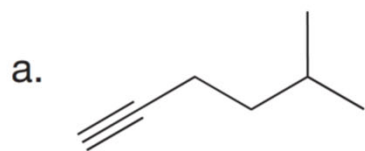
**11.43** Identify the lettered compounds in the following reaction schemes. Each reaction sequence was used in the synthesis of a natural product.



- 11.46** Tautomerization in base resembles tautomerization in acid, but deprotonation precedes protonation in the two-step mechanism. (a) Draw a stepwise mechanism for the following tautomerization. (b) Then draw a stepwise mechanism for the reverse reaction, the conversion of the keto form to the enol.

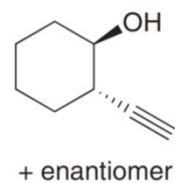


- 11.50** What acetylide anion and alkyl halide are needed to synthesize each alkyne?

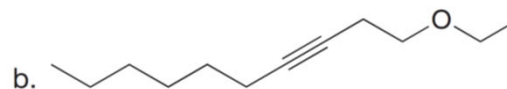
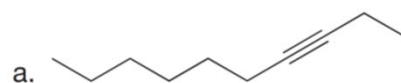


- 11.58** Explain why the C=C of an enol is more nucleophilic than the C=C of an alkene, despite the fact that the electronegative oxygen atom of the enol inductively withdraws electron density from the carbon-carbon double bond.

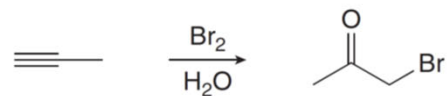
- 11.53** Devise a synthesis of the following compound from cyclohexene and acetylene. You may use any other inorganic reagents.



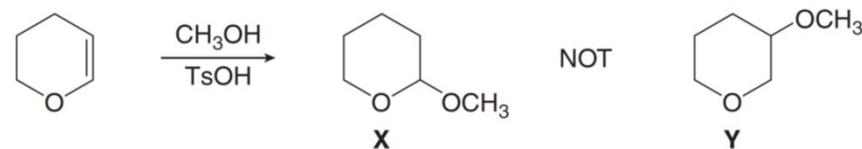
- 11.54** Devise a synthesis of each compound. You may use  $\text{HC}\equiv\text{CH}$ , ethylene oxide, and alkyl halides as organic starting materials and any inorganic reagents.



- 11.61** Draw a stepwise mechanism for the following reaction.

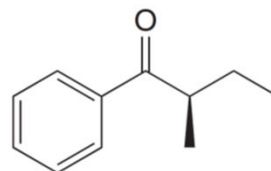


- 11.62** Why is compound **X** formed in the following reaction, instead of its constitutional isomer **Y**?





- 11.65** Explain why an optically active solution of (*R*)- $\alpha$ -methylbutyrophenone loses its optical activity when dilute acid is added to the solution.



(*R*)- $\alpha$ -methylbutyrophenone

- 11.52** Devise a synthesis of each compound using  $\text{CH}_3\text{CH}_2\text{CH}=\text{CH}_2$  as the starting material. You may use any other organic compounds or inorganic reagents.

