

How Is Chemotherapy Used to Treat Cancer?

Chemotherapy is the use of any drug to treat any disease. But to most people, the word chemotherapy means drugs used for cancer treatment. It's often shortened to "chemo."

Surgery and radiation therapy remove, kill, or damage cancer cells in a certain area, but chemo can work throughout the whole body. This means chemo can kill cancer cells that have spread (metastasized) to parts of the body far away from the original (primary) tumor.

Goals of chemotherapy treatment

If your doctor has recommended chemotherapy to treat your cancer, it's important to understand the goals of treatment when making treatment decisions. There are three main goals for chemotherapy (chemo) in cancer treatment:

1. Cure
2. Control
3. Palliation

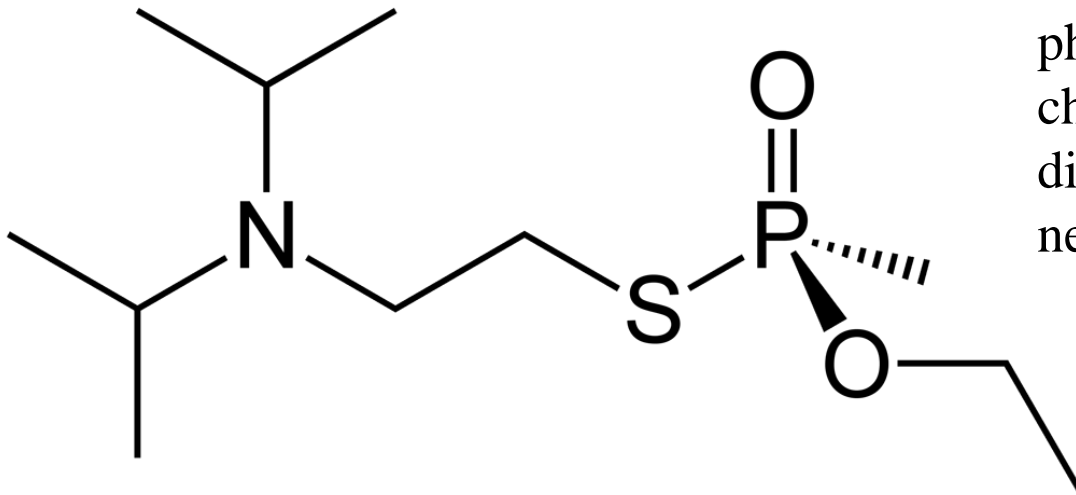
Chemist/pharmacist/drugstore

ASIA PACIFIC

Is it a good way to use chemical?

Kim Jong-nam Was Killed by VX Nerve Agent, Malaysians Say

By RICHARD C. PADDOCK and CHOE SANG-HUN FEB. 23, 2017



VX (nerve agent)
10 mg is enough to kill a
person through skin contact

Nerve agents are a class of phosphorus-containing organic chemicals (organophosphates) that disrupt the mechanisms by which nerves transfer messages to organs.

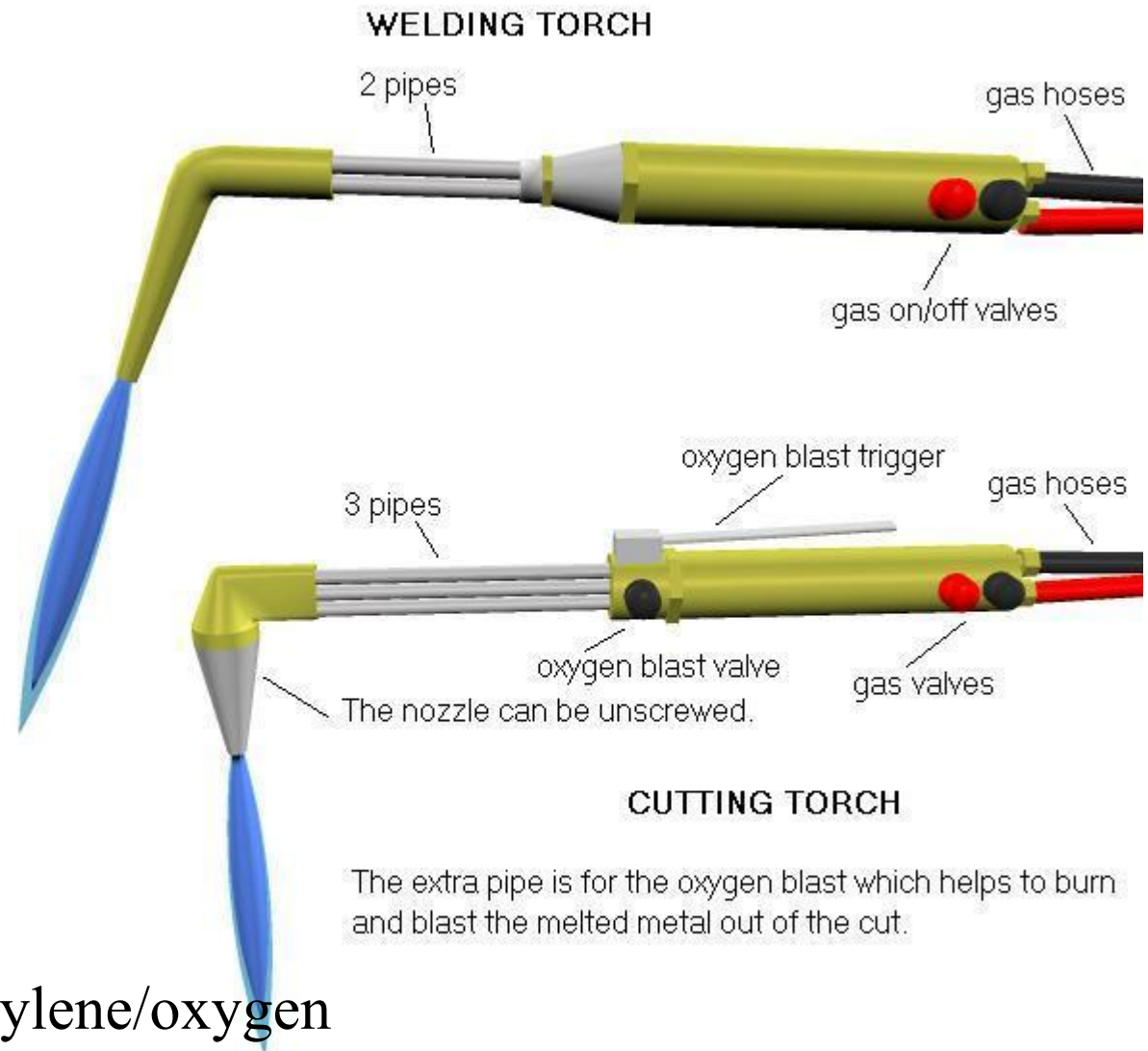


Organic Chemistry

CHE 203

Lecture 9: Alkynes

Le Quoc Chon – Duy Tan University

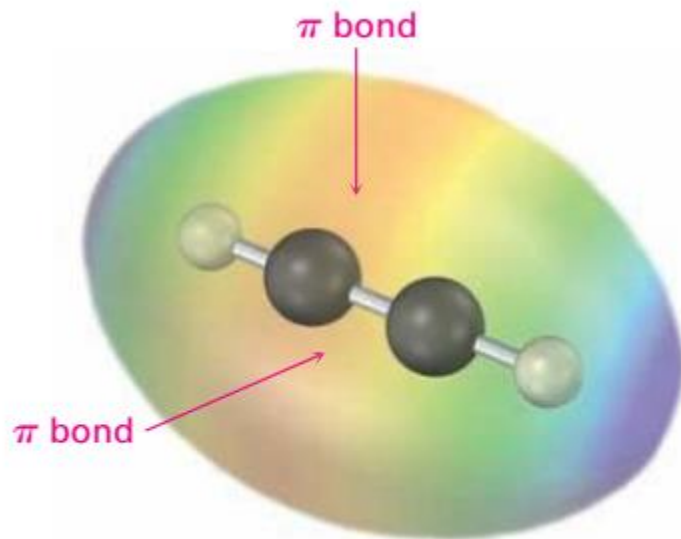


Nhiệt độ ngọn lửa acetylene/oxygen

Flame of **Acetylene**/oxygen: 3330 °C

Oxy-fuel welding and cutting

Alkyne

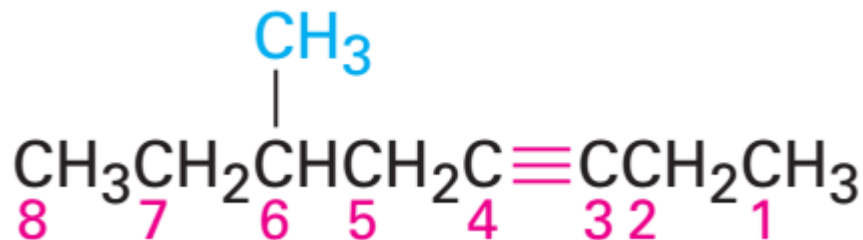


sp

Naming Alkynes

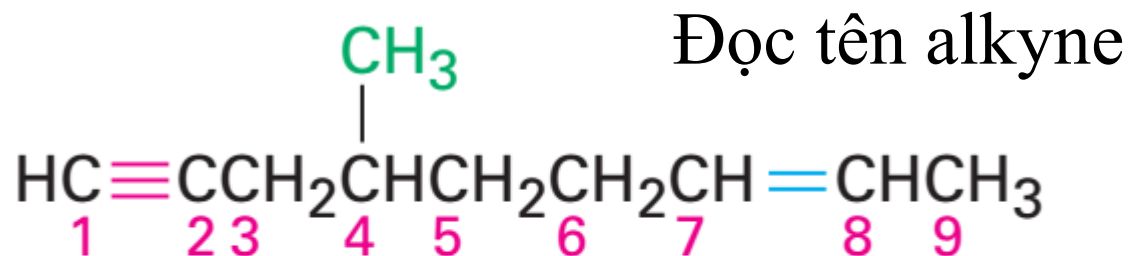
Đọc tên alkyne

Numbering at the end nearer to the triple bond. (đánh số sao cho liên kết ba ở vị trí thấp nhất có thể)

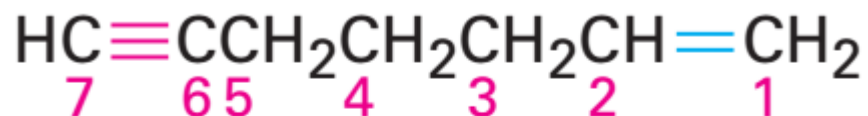


6-Methyl-3-octyne
(New: **6-Methyloct-3-yne**)

Naming Alkynes



4-Methyl-7-nonen-1-yne
(New: **4-Methylnon-7-en-1-yne**)



(ưu tiên
nội đôi vị
trí thấp)

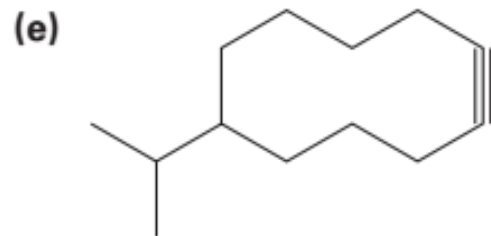
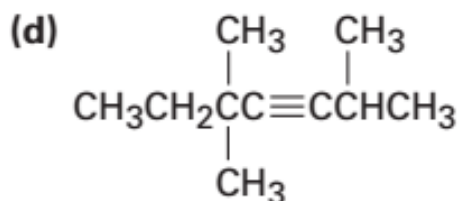
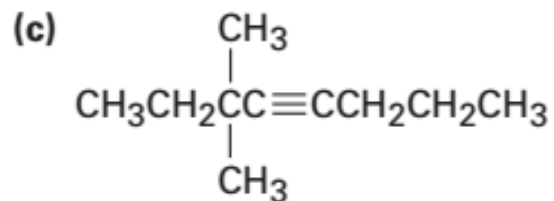
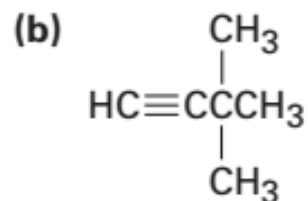
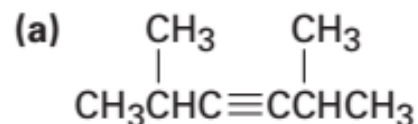
1-Hepten-6-yne
(New: **Hept-1-en-6-yne**)

Naming Alkynes

Đọc tên alkyne

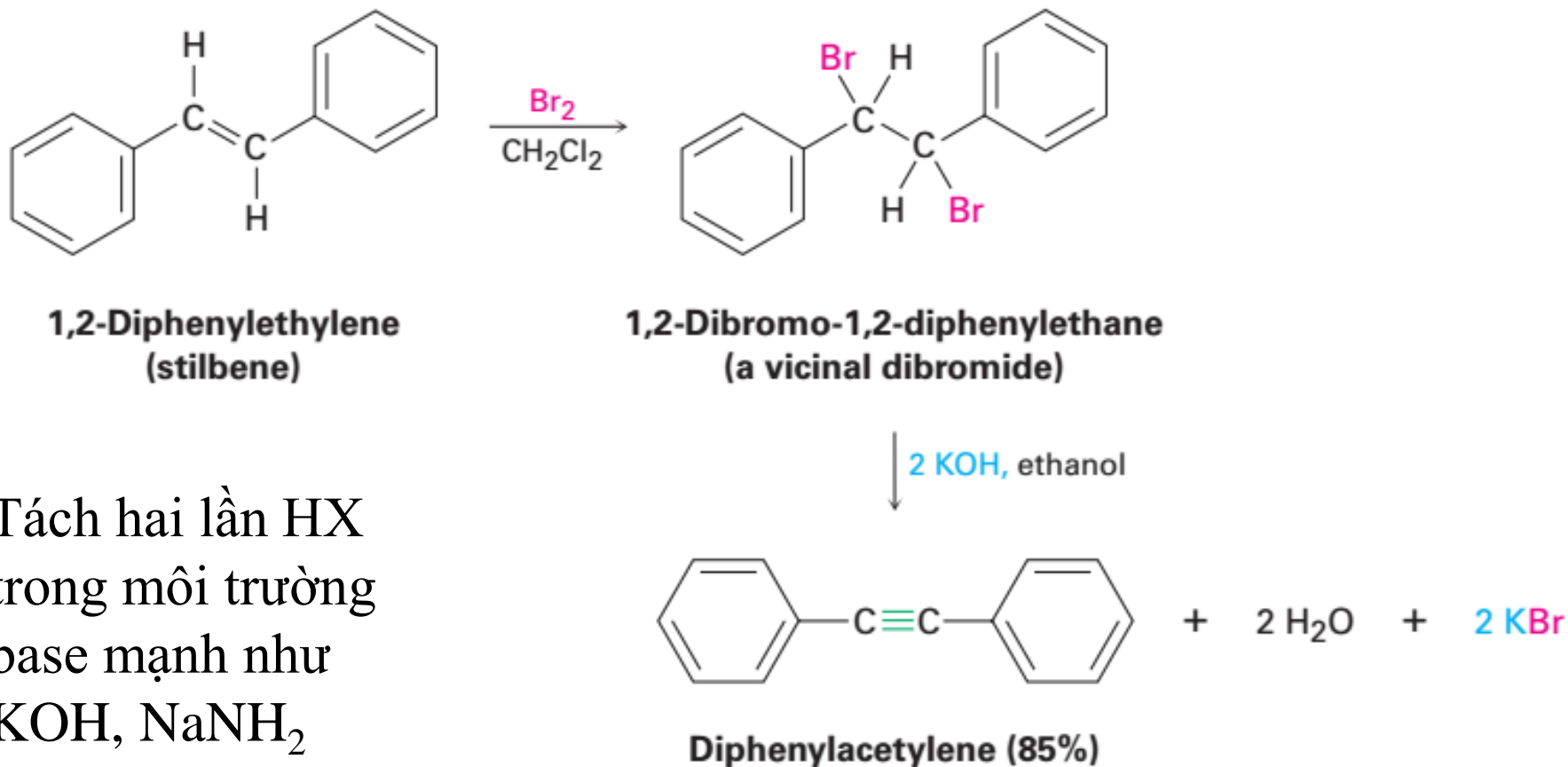
PROBLEM 9-1

Name the following alkynes:



Preparation of Alkynes

Điều chế alkyne



Tách hai lần HX
trong môi trường
base mạnh như
KOH, NaNH₂

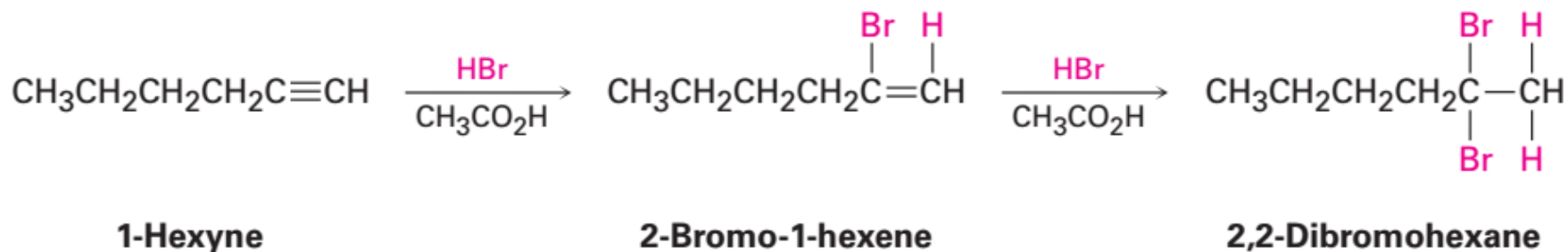
Phản ứng của alkyne

Reactions of Alkynes

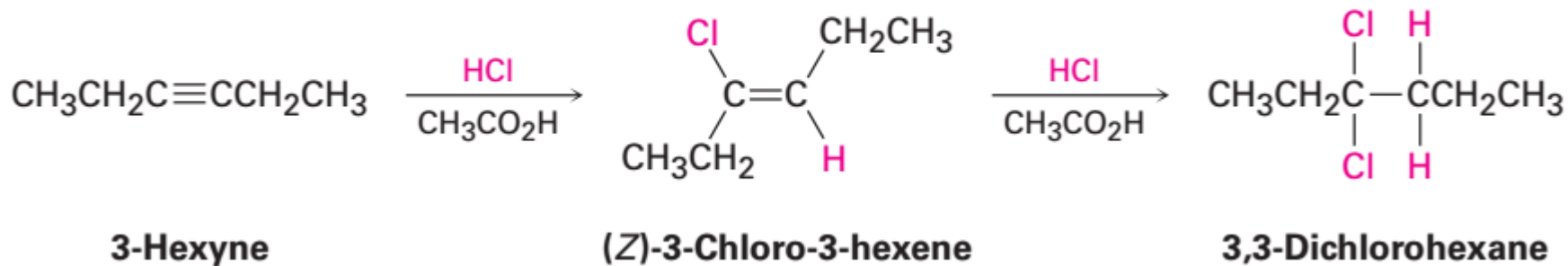
Markovnikov's rule

Cộng HX

HBr addition



HCl addition



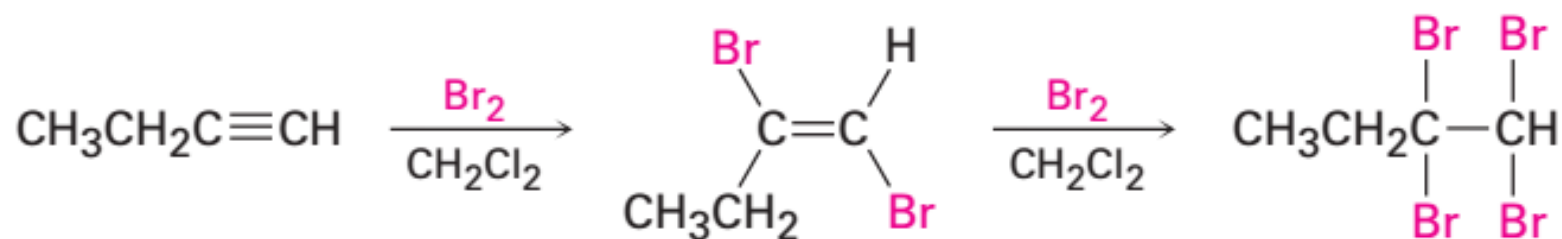
(trans stereochemistry)

Reactions of Alkynes

Phản ứng của alkyne

Cộng X_2

Br_2 addition



1-Butyne

(*E*)-1,2-Dibromo-1-butene

1,1,2,2-Tetrabromobutane

(trans stereochemistry)

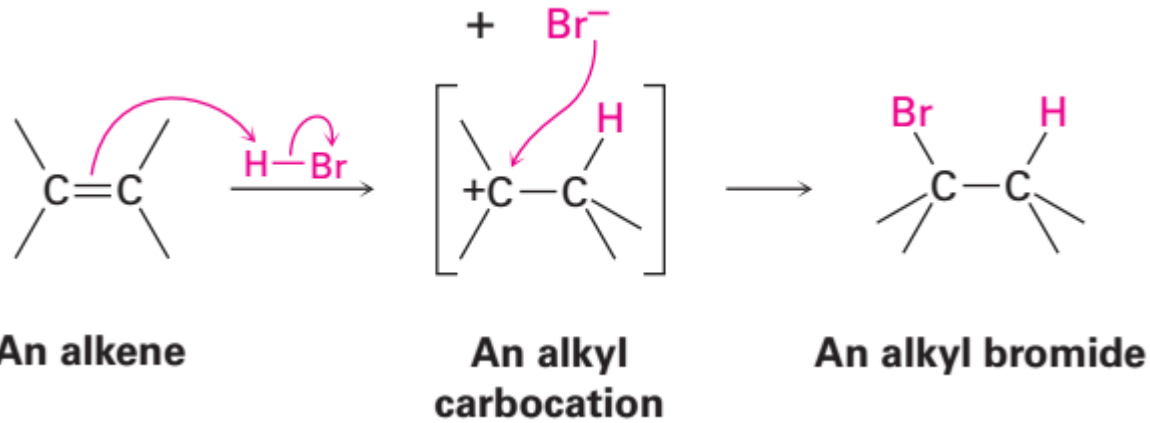
Remind (nhớ lại)

E, Z configuration?

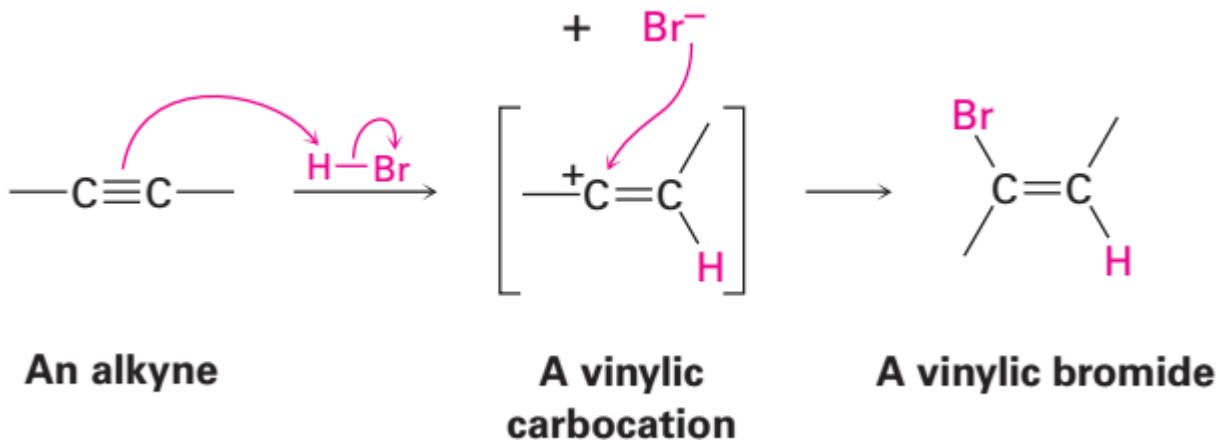
Cis-trans configuration?

Mechanism of addition reactions

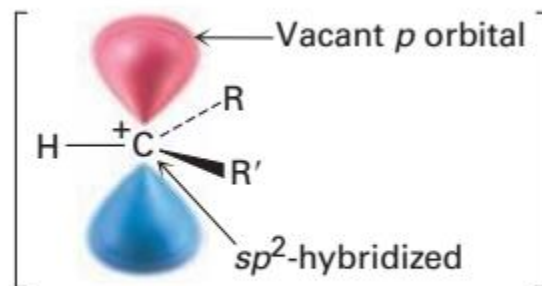
(cơ chế của phản ứng cộng)



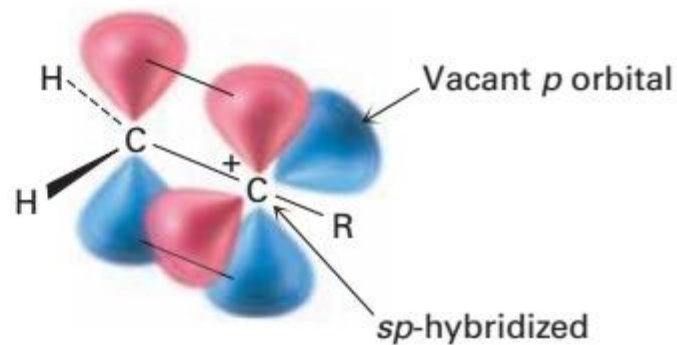
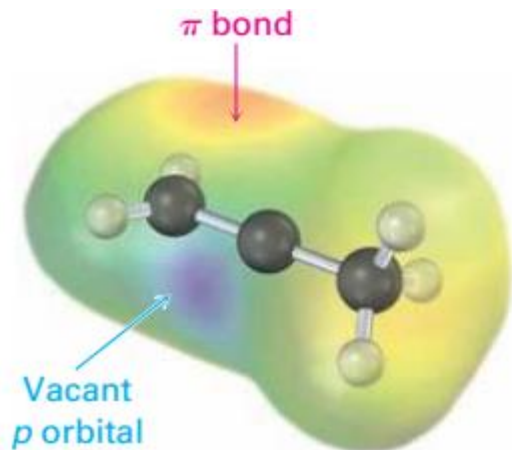
So sánh
alkene và
alkyne



Structure of carbocation (cấu trúc của carbocation)



A 2° alkyl carbocation



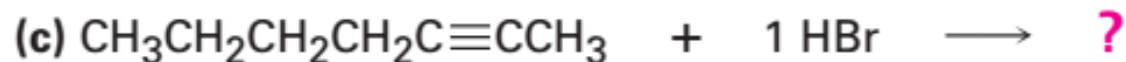
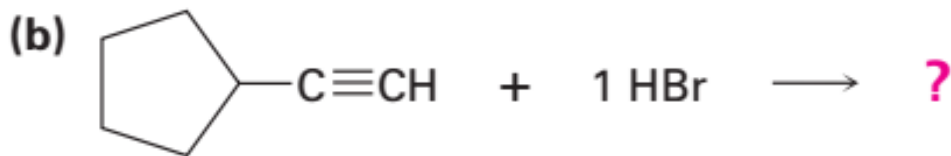
A 2° vinylic carbocation

Problem

Dự đoán sản phẩm của các phản ứng sau

PROBLEM 9-3

What products would you expect from the following reactions?



(hydrate hóa alkyne)

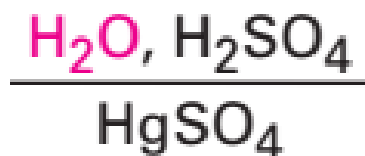
Hydration of alkynes

2 methods (hai phương pháp)



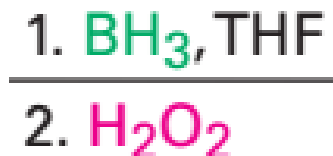
Catalyzed by Mercury (II) ion

=> Results in Markovnikov products

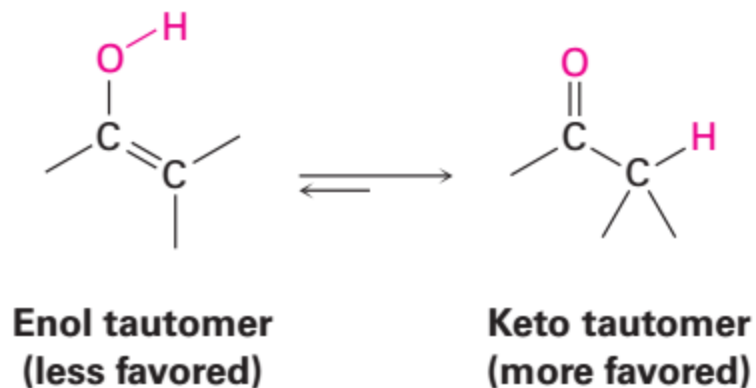
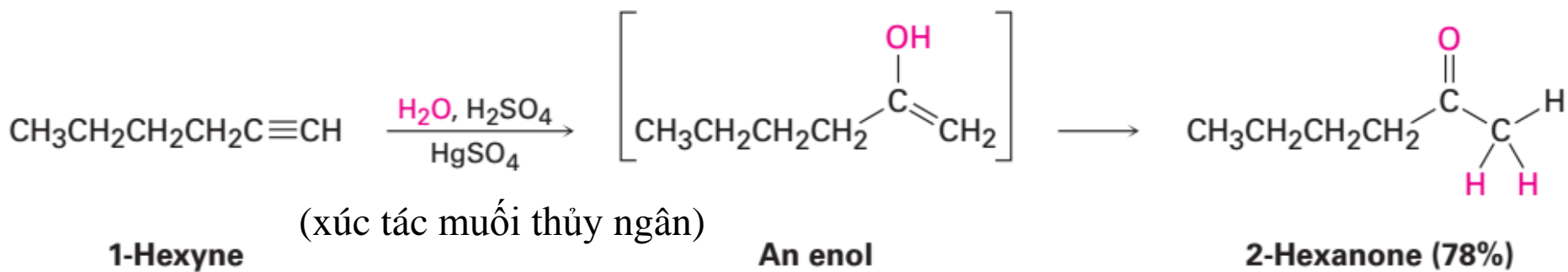


Hydroboration-oxidation

=> Results in non-Markovnikov products



Hydration of Alkynes



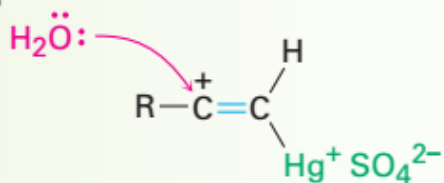
(giai đoạn này gọi là keto-enol tautomerism)



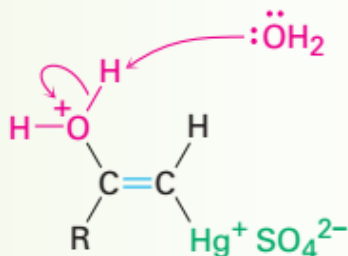
1



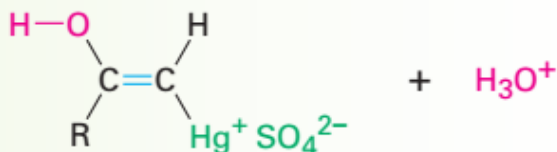
Mechanism (cơ chế)



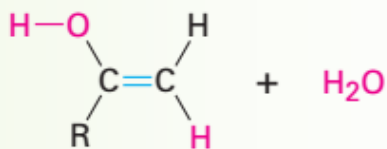
2



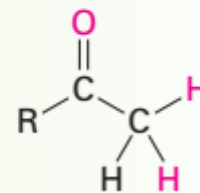
3



4



5

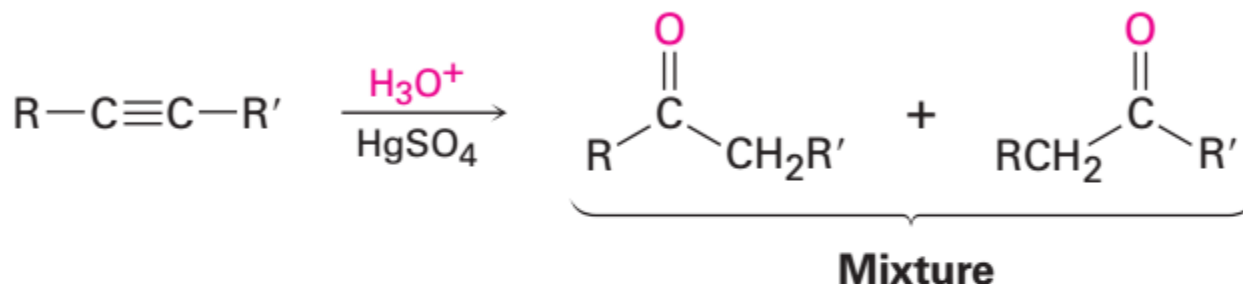


Hydration of Alkynes

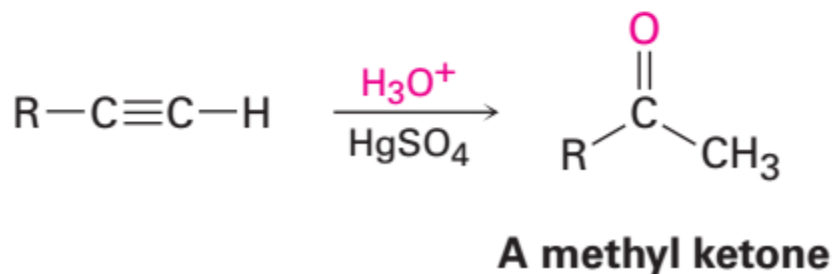
(tạo hỗn hợp hay đơn chất)

Tạo hỗn hợp hay chỉ một sản phẩm tùy thuộc vào alkyne ban đầu

An internal alkyne



A terminal alkyne

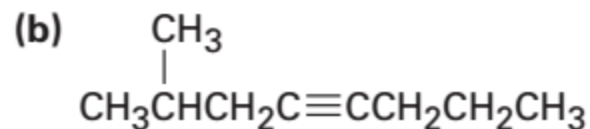
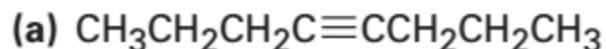


Phản ứng này
không tạo ra hỗn
hợp.

Problems

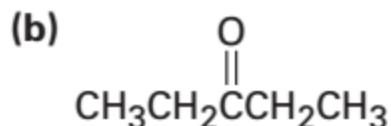
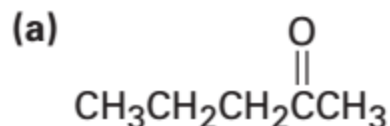
PROBLEM 9-4 (hydration các alkynes sau tạo sản phẩm nào)

What products would you obtain by hydration of the following alkynes?

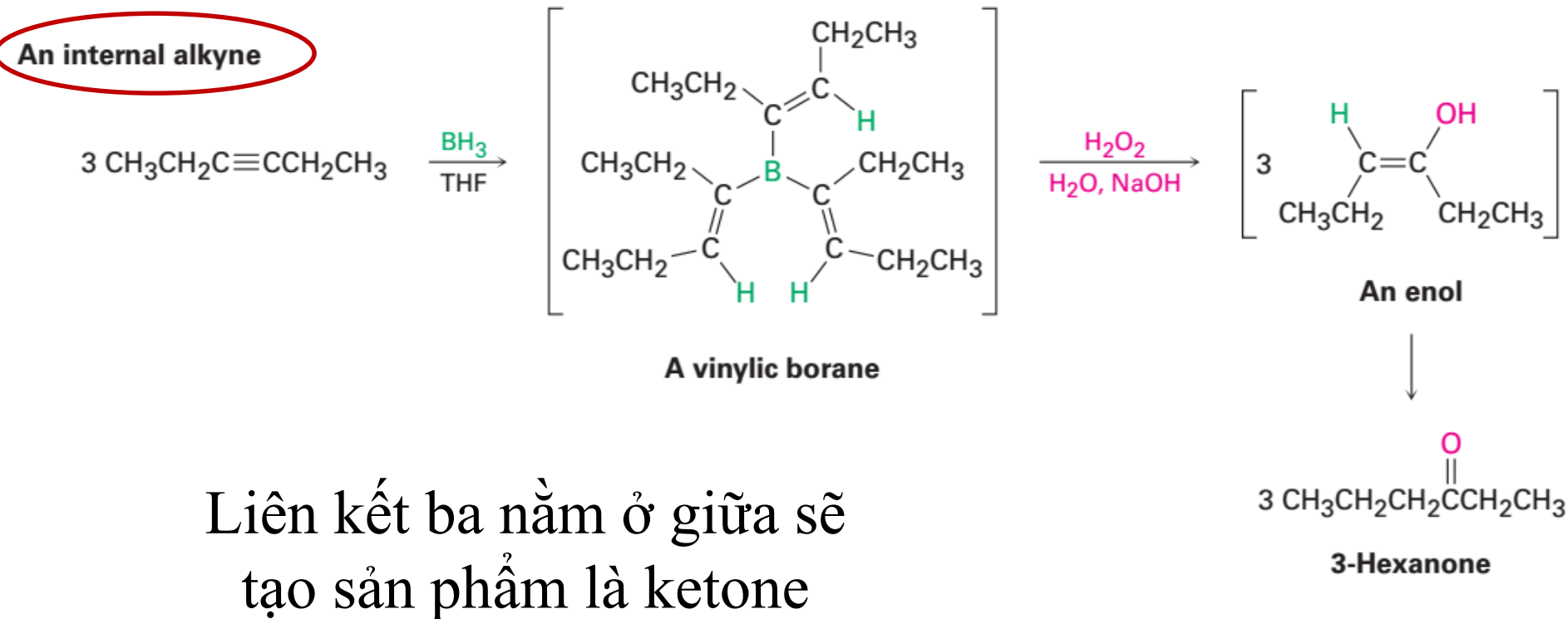


PROBLEM 9-5 (bắt đầu từ alkyne nào để tạo ra các ketone sau)

What alkynes would you start with to prepare the following ketones?



Hydroboration-oxidation of alkynes

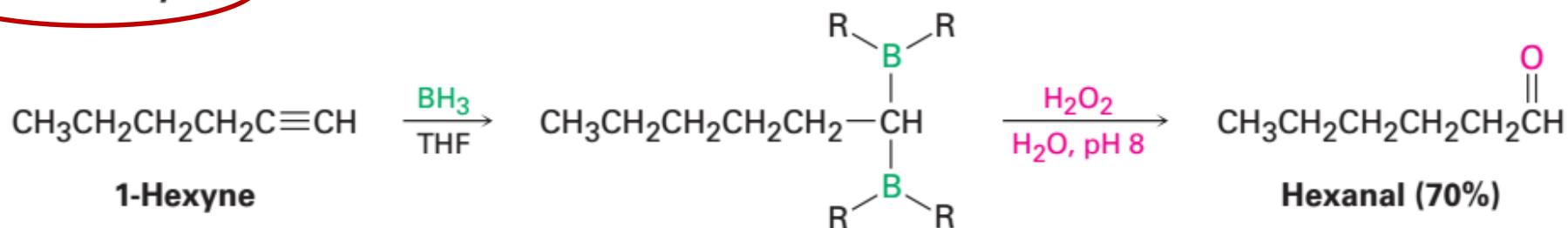


Liên kết ba nằm ở giữa sẽ
tạo sản phẩm là ketone

Tạo ketone

Hydroboration-oxidation of alkynes

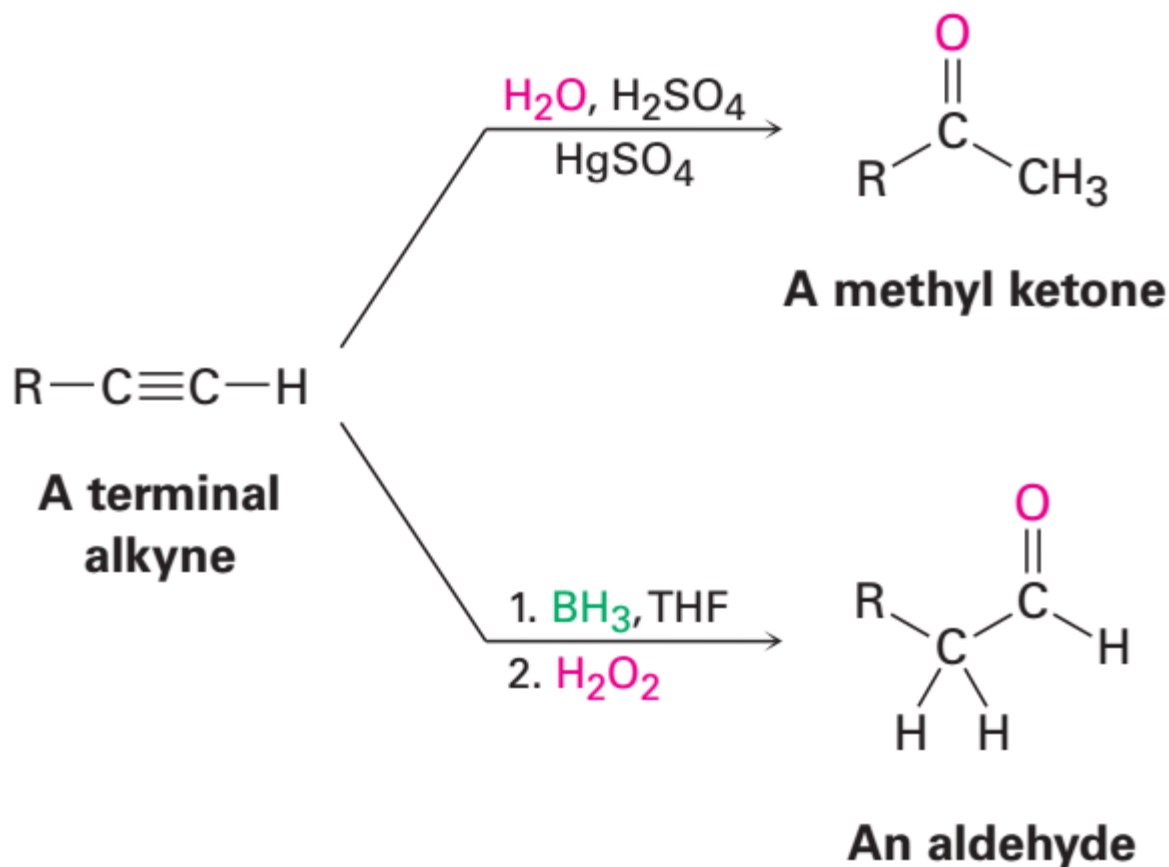
A terminal alkyne



Liên kết ba nằm ở cuối mạch sẽ tạo sản phẩm là aldehyde.

Tạo aldehyde

Compare two reactions

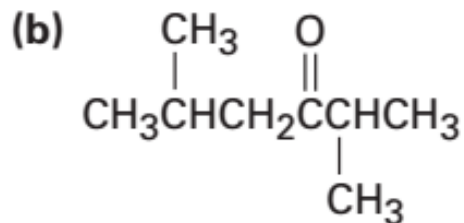
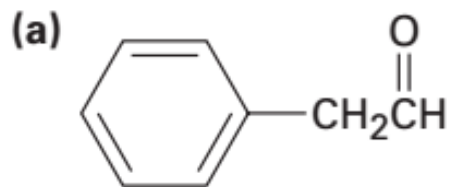


Different conditions generate different products.
Thay đổi điều kiện phản ứng sẽ thay đổi sản phẩm phản ứng.

Problem

PROBLEM 9-6

What alkyne would you start with to prepare each of the following compounds by a hydroboration–oxidation reaction?



Problem

PROBLEM 9-7

How would you prepare the following carbonyl compounds starting from an alkyne (reddish brown = Br)?

(a)



(b)

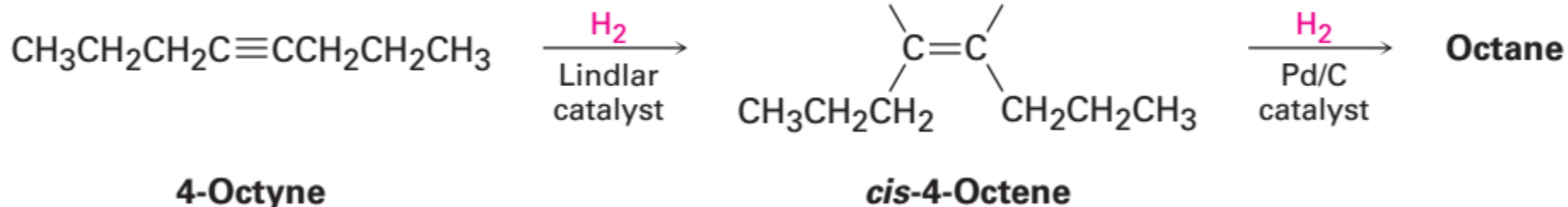


Reduction of alkynes (phản ứng khử)

(hai giai đoạn, khử hoàn toàn)



(khử có thể dừng lại ở alkene)

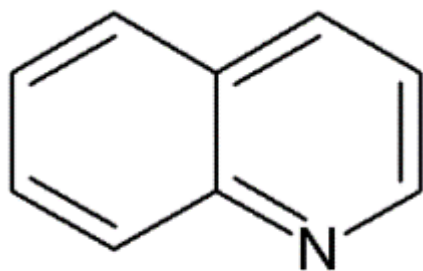


5% Pd-CaCO₃

+

Pb(OCOCH₃)₂

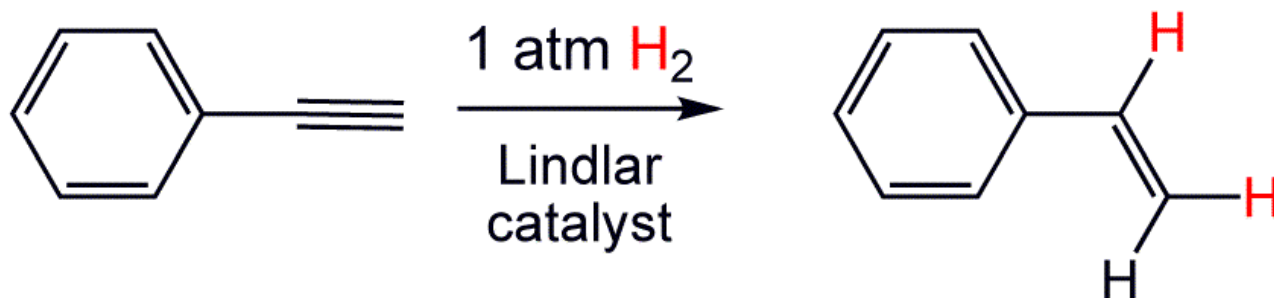
+



Quinoline

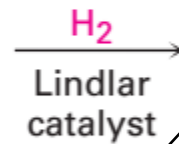
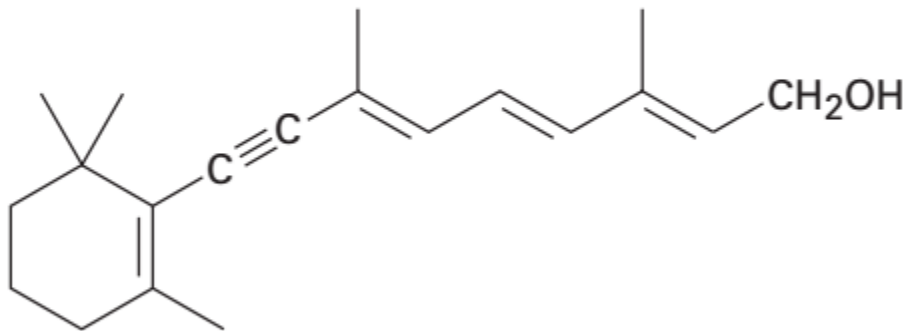
Lindlar catalyst

Dừng lại ở alkene

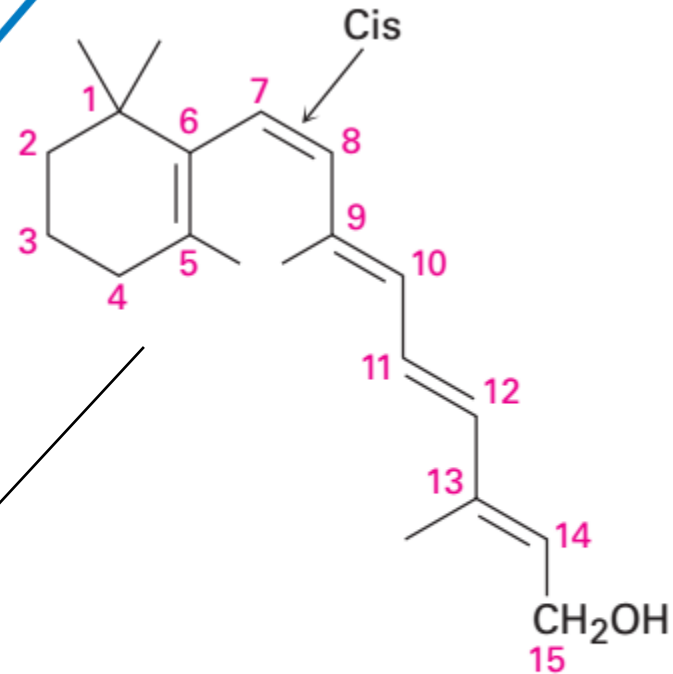


Example in Pharma

F. Hoffmann-La Roche AG is a Swiss multinational healthcare company that operates worldwide under two divisions: Pharmaceuticals and Diagnostics.



heat

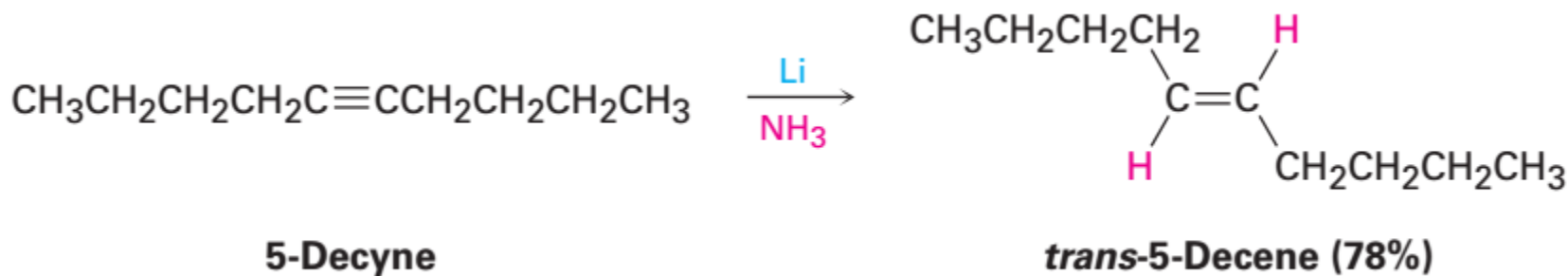


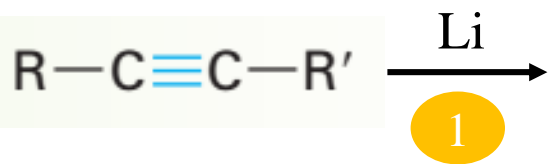
7-cis-Retinol
(7-cis-vitamin A; vitamin A has a trans double bond at C7)

Trans at C7

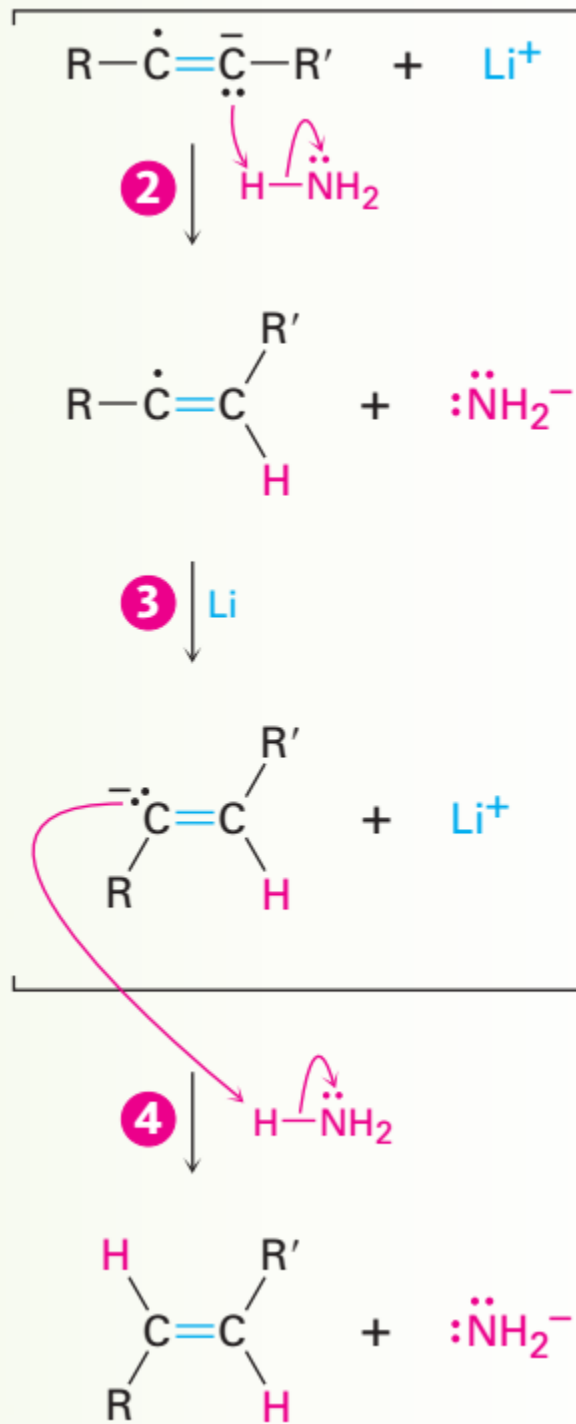
Alternative method: Na or Li in NH₃ liquid as reducing agent

(một phương pháp khác sử dụng kim loại Na, Li trong dung dịch NH₃)





Mechanism



A trans alkene

Problem

PROBLEM 9-8

(Điều chế các chất sau từ alkyne)

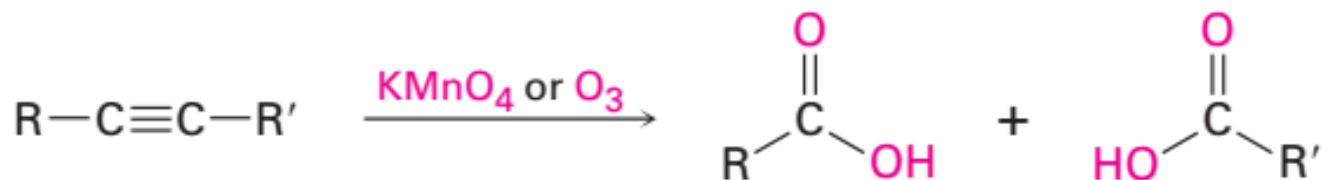
Using any alkyne needed, how would you prepare the following alkenes?

(a) *trans*-2-Octene **(b)** *cis*-3-Heptene **(c)** 3-Methyl-1-pentene

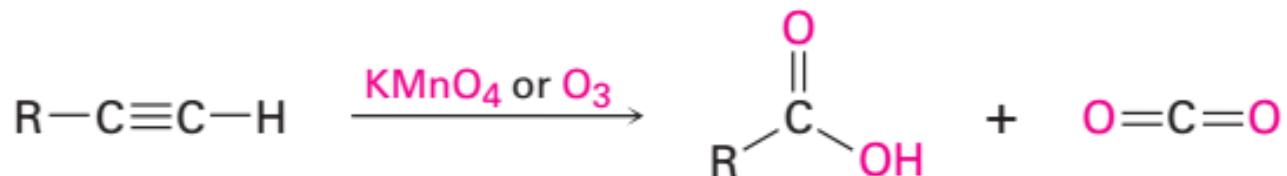
Oxidation of alkynes

(oxy hóa alkyne)

An internal alkyne (nối ba ở giữa)



A terminal alkyne (nối ba ở cuối)



Acidity of alkyne

(tính acid của alkyne)

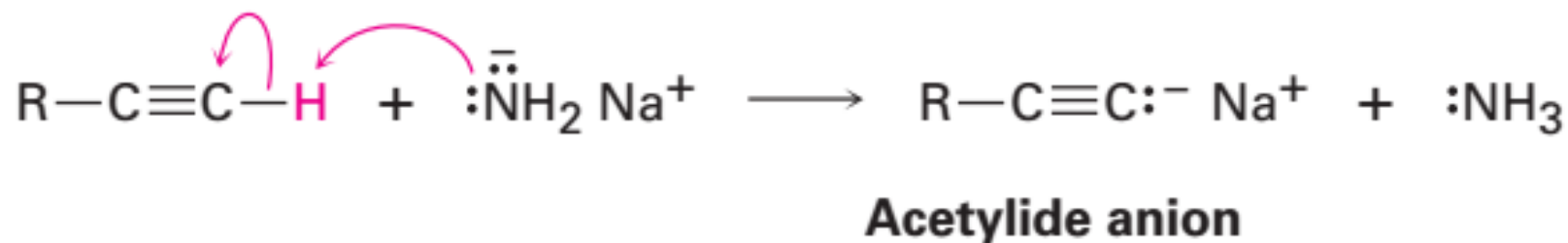



TABLE 9-1 Acidity of Simple Hydrocarbons

Family	Example	K_a	pK_a	
Alkyne	$\text{HC}\equiv\text{CH}$	10^{-25}	25	<p style="text-align: center;">Stronger acid</p>  <p style="text-align: center;">Weaker acid</p>
Alkene	$\text{H}_2\text{C}=\text{CH}_2$	10^{-44}	44	
Alkane	CH_4	10^{-60}	60	

Amonia $pK_a = 35$

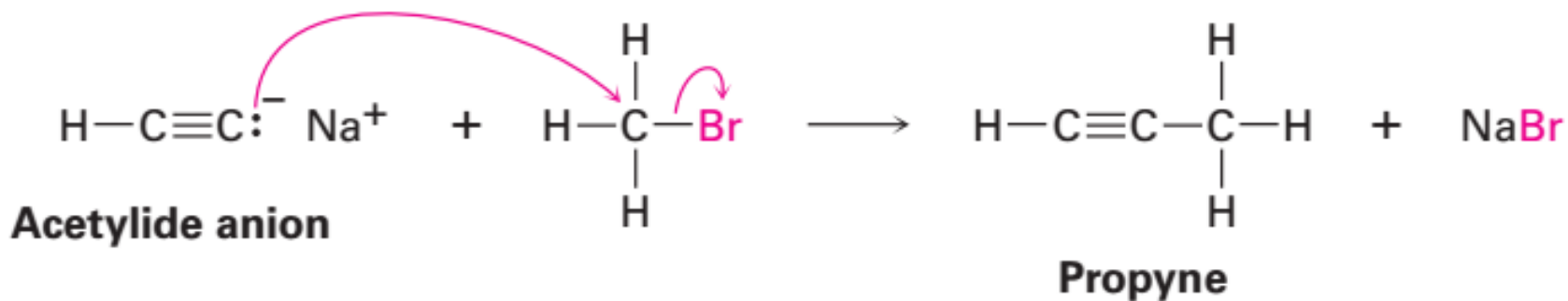
Problem

PROBLEM 9-9 (chất nào có thể deprotonate acetone)

The pK_a of acetone, CH_3COCH_3 , is 19.3. Which of the following bases is strong enough to deprotonate acetone?

- (a) KOH (pK_a of $\text{H}_2\text{O} = 15.7$) (b) $\text{Na}^+ \text{ } ^-\text{C}\equiv\text{CH}$ (pK_a of $\text{C}_2\text{H}_2 = 25$)
(c) NaHCO_3 (pK_a of $\text{H}_2\text{CO}_3 = 6.4$) (d) NaOCH_3 (pK_a of $\text{CH}_3\text{OH} = 15.6$)

Alkylation of acetylide anion

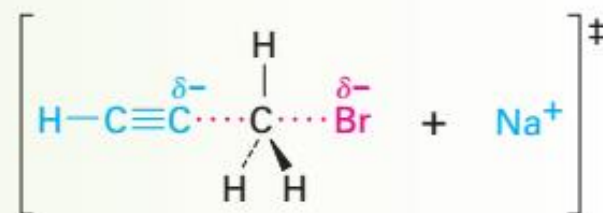


Mechanism

1 The nucleophilic acetylide anion uses its electron lone pair to form a bond to the positively polarized, electrophilic carbon atom of bromomethane. As the new C-C bond begins to form, the C-Br bond begins to break in the transition state.

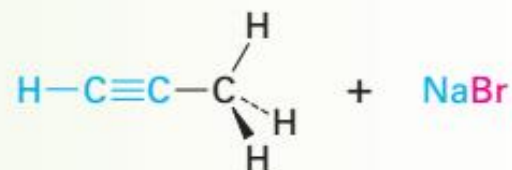


1



Transition state

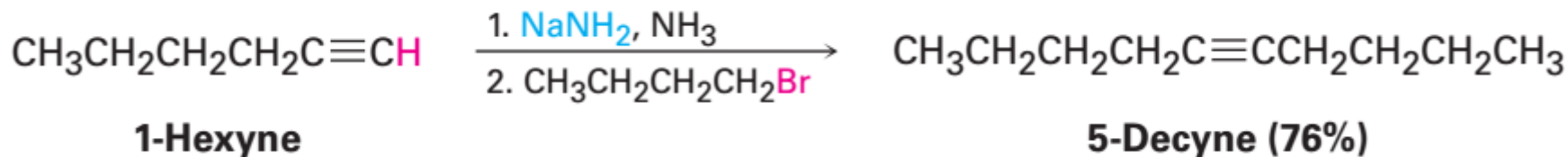
2



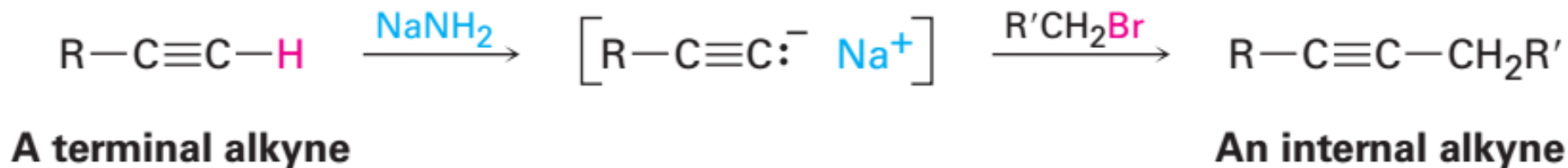
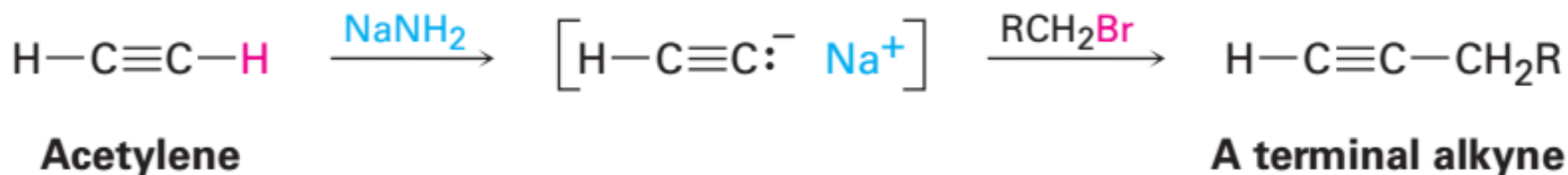
2 The new C-C bond is fully formed and the old C-Br bond is fully broken at the end of the reaction.

Alkylation

(phản ứng alkyl hóa)



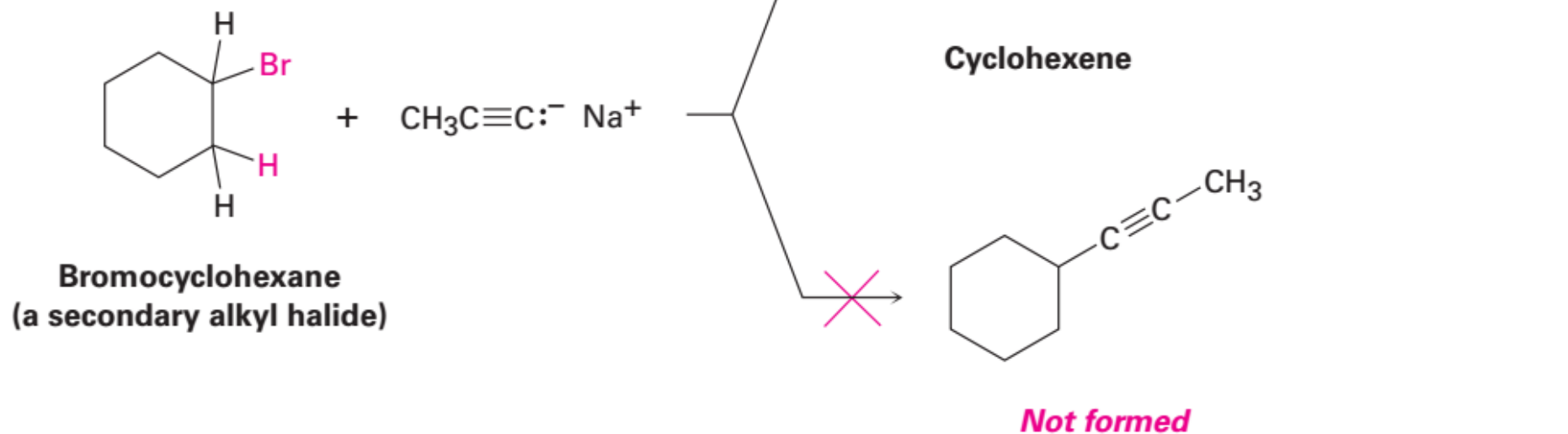
(Dùng để tạo alkyl có mạch dài hơn, nhưng chỉ dùng với alkyne bậc 1)



Alkylation

(phản ứng alkyl hóa)

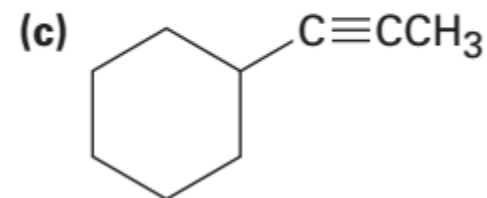
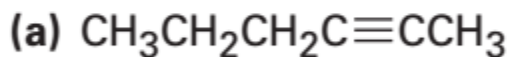
(Đối với alkyne bậc 2, 3 sẽ xảy ra phản ứng tách loại)



Problem

PROBLEM 9-10

Show the terminal alkyne and alkyl halide from which the following products can be obtained. If two routes look feasible, list both.



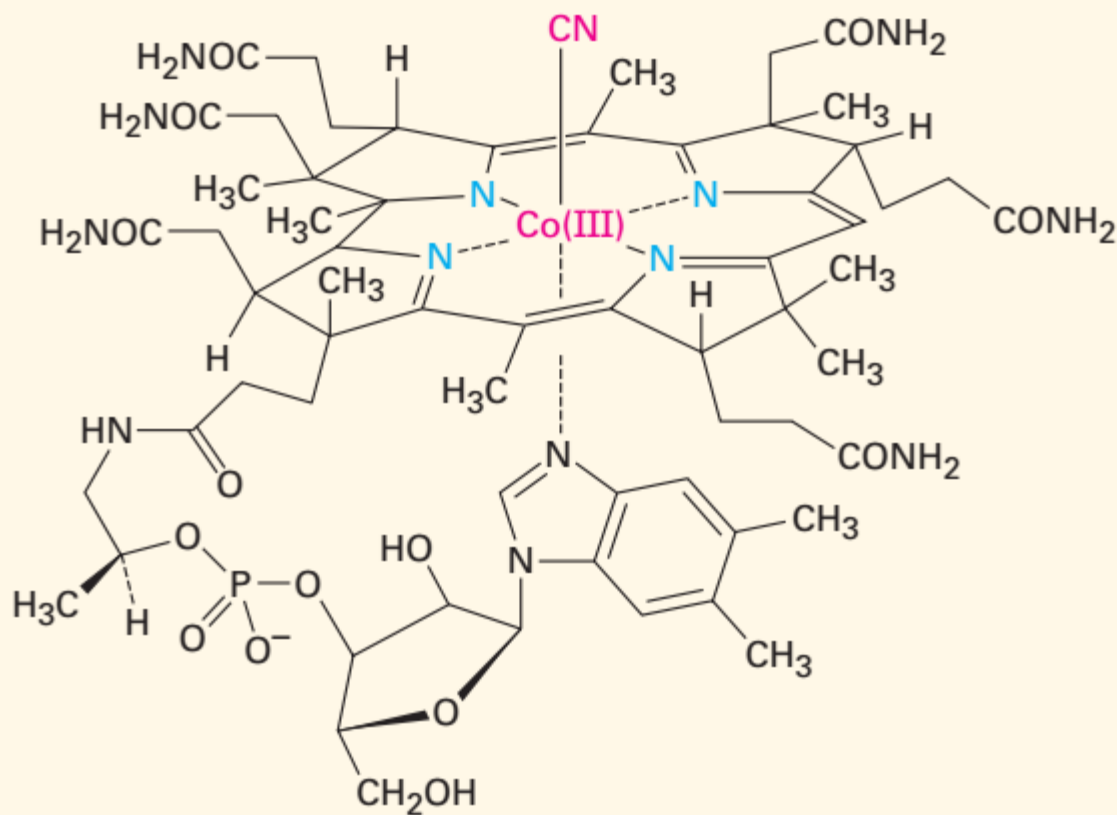
Problem

PROBLEM 9-11

How would you prepare *cis*-2-butene starting from propyne, an alkyl halide, and any other reagents needed? This problem can't be worked in a single step. You'll have to carry out more than one reaction.

The Art of Organic Synthesis

10 year to
synthesize this
with more than
100 graduate
students and
postdocs



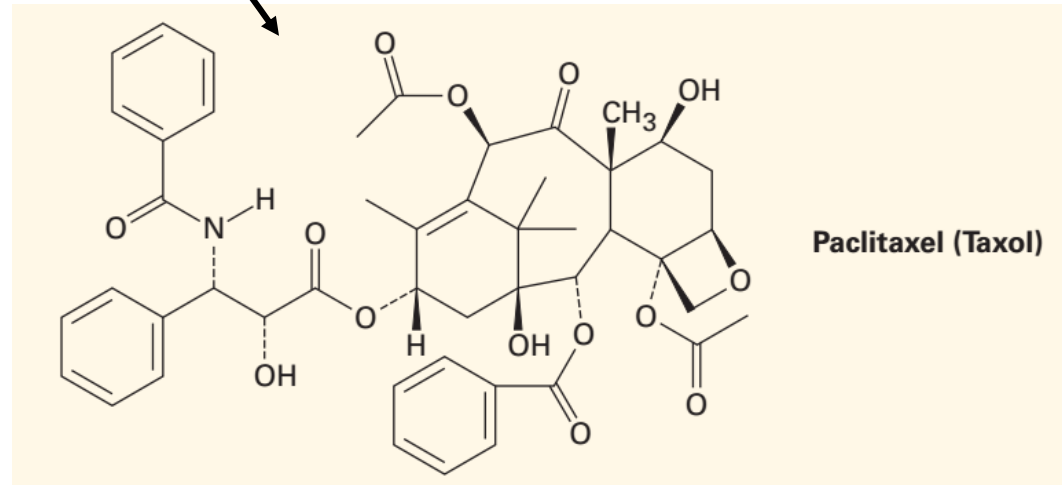
Vitamin B₁₂

Taxol: well-known natural source cancer drug



Pacific yew in North America

(first isolate 1971)



(an anticancer: breast, lung, ovarian cancer)

To date, Taxol is the best-selling cancer drug ever manufactured. Annual sales of the drug peaked in 2000, reaching \$1.6 billion

now synthesis and manufactured by cell culture (good story)

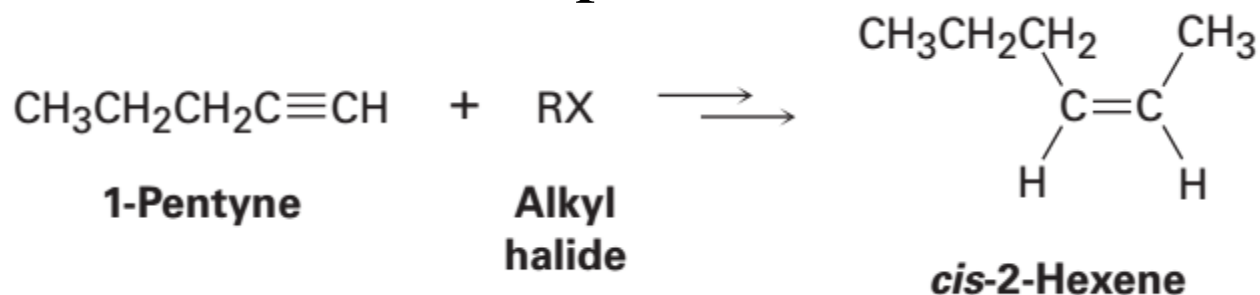
Introduction on Organic Synthesis

(giới thiệu về tổng hợp hữu cơ)

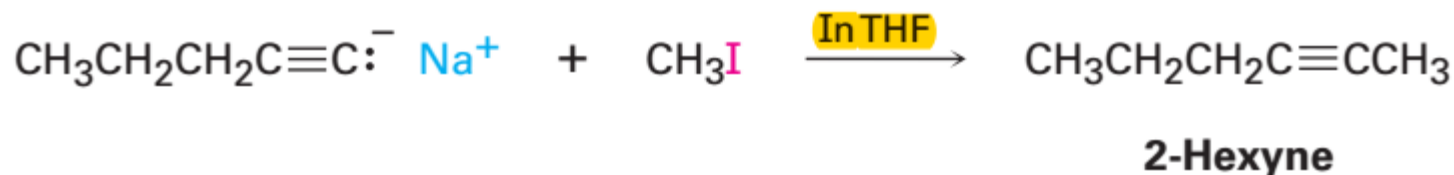
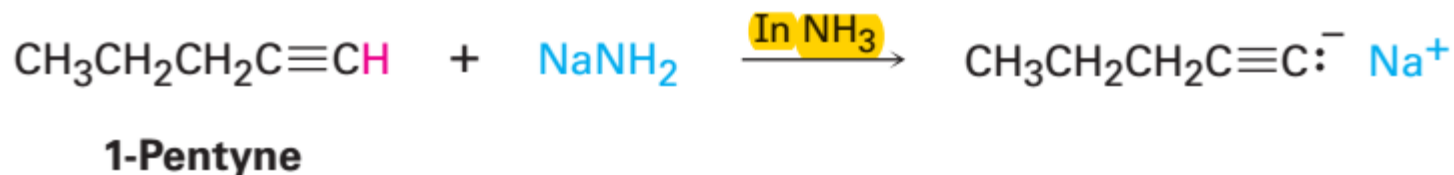
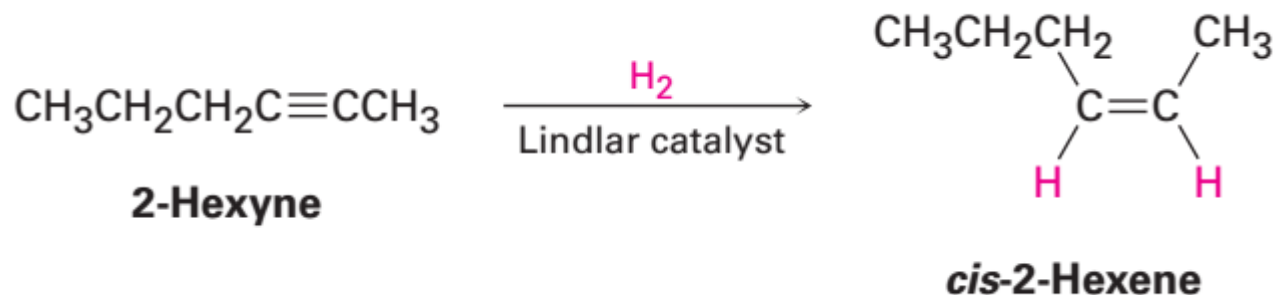
retrosynthetic

(look at final product and work backward)

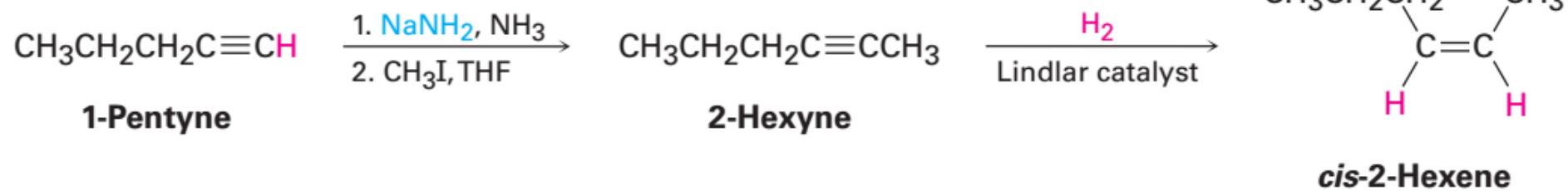
Example: (more than 1 step)



Work backward

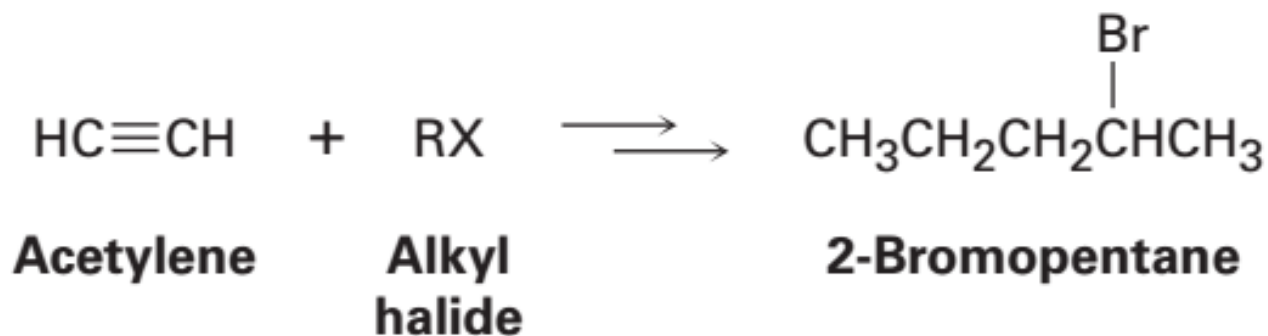


Answer

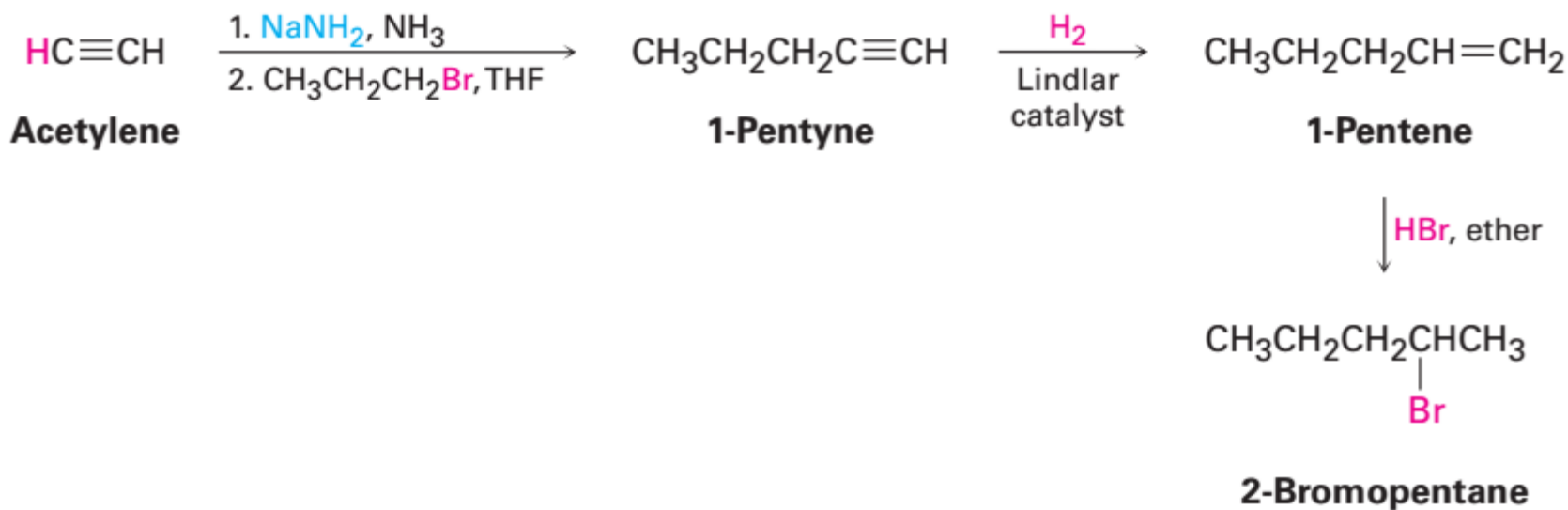


Problem

Synthesize 2-bromopentane from acetylene and an alkyl halide. More than one step is needed.

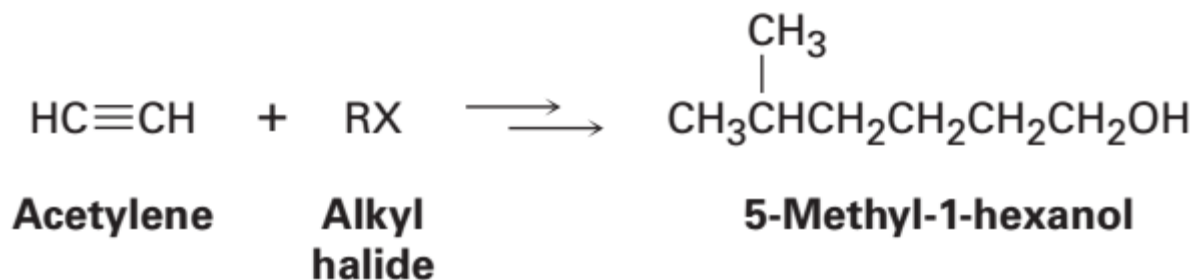


Answer

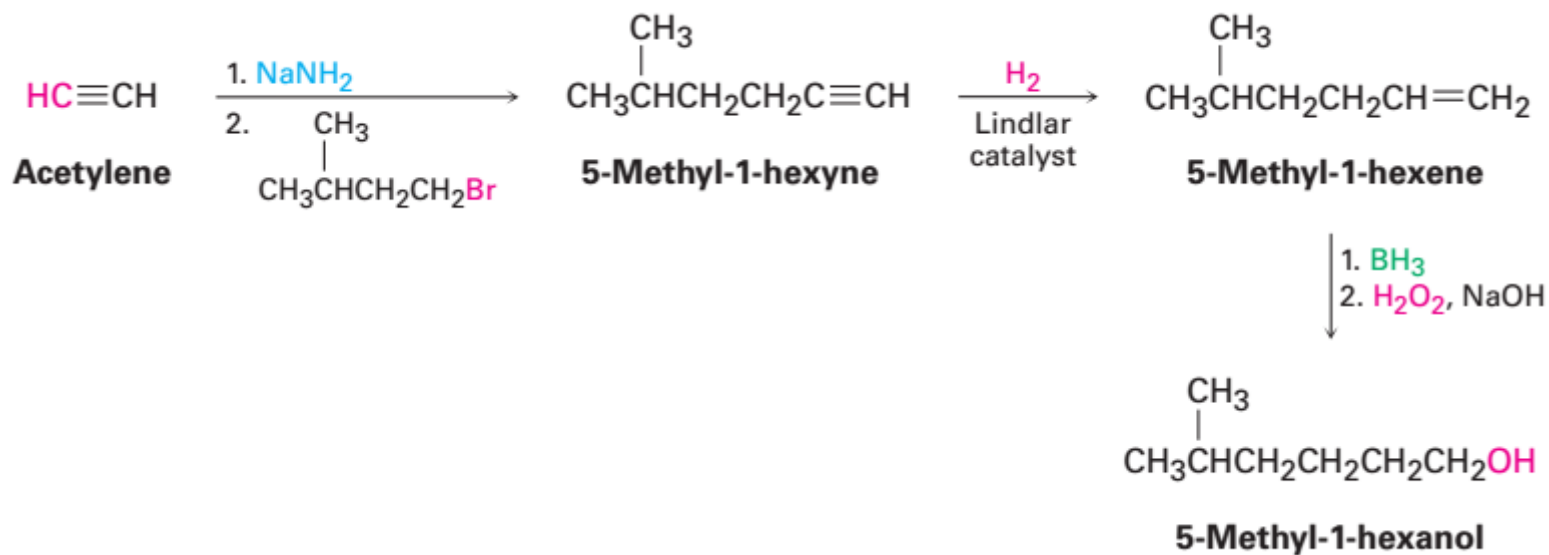


Problem

Synthesize 5-methyl-1-hexanol (5-methyl-1-hydroxyhexane) from acetylene and an alkyl halide.



Answer



Problems

PROBLEM 9-12

Beginning with 4-octyne as your only source of carbon, and using any inorganic reagents necessary, how would you synthesize the following compounds?

- (a) *cis*-4-Octene (b) Butanal (c) 4-Bromooctane
(d) 4-Octanol (e) 4,5-Dichlorooctane (f) Butanoic acid

PROBLEM 9-13

Beginning with acetylene and any alkyl halide needed, how would you synthesize the following compounds?

- (a) Decane (b) 2,2-Dimethylhexane (c) Hexanal (d) 2-Heptanone