

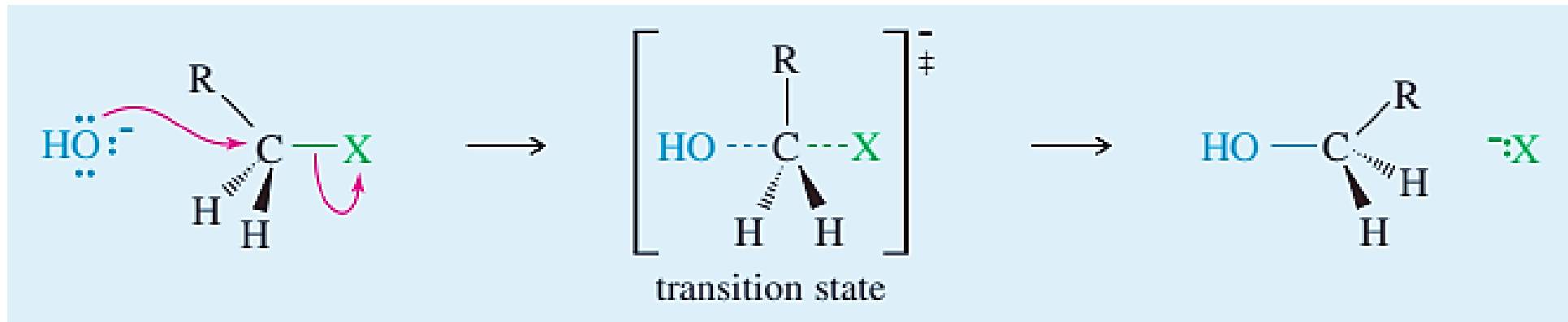
# دوره الكل ها: ساختار و سنتز شیمی آلی فصل دوم: سنتز الكل ها

مدرس: امیرمهدی ایمان زاده

۱۴۰۱-۱۴۰۲

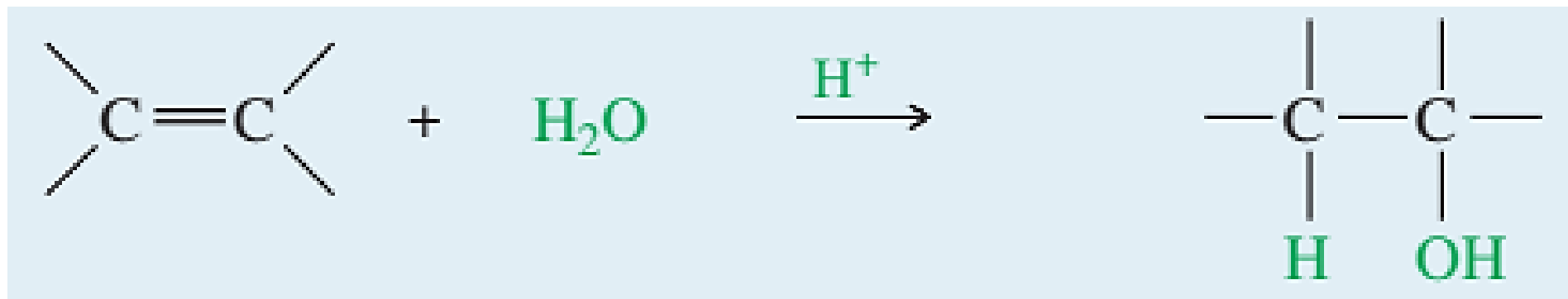
# جایگزینی نولکئوفیلی روی آلکیل هالید

- دو مولکولی تک مرحله ای (SN2)
- جابجا شدن یک نوکلئوفیل با یک نوکلئوفیل دیگر
- روی کربن  $sp^3$



# هیدراسیون کاتالیز شده با اسید آلکن ها

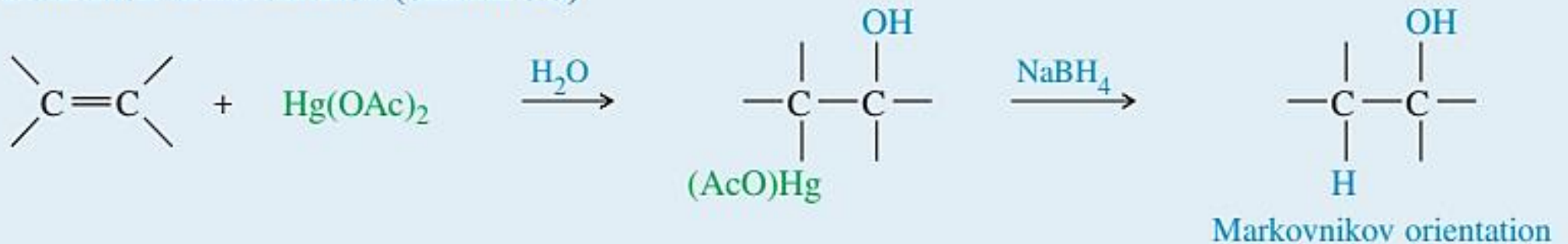
- قاعده پایه ای مارکونیکوف



# اکسی مرکوراسیون-دمرکوراسیون آلکن ها

• تشکیل الکل نوع ...

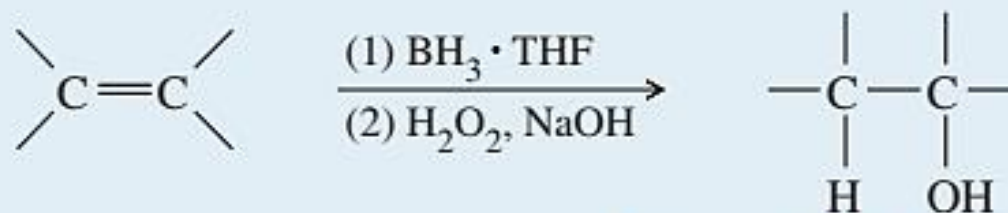
## 2. Oxymercuration–demercuration (Section 8-5)



# هیدروبوراسیون-اکسیداسیون آلکن ها

• آنتی و الکل نوع پایین تر

## 3. Hydroboration-oxidation (Section 8-7)

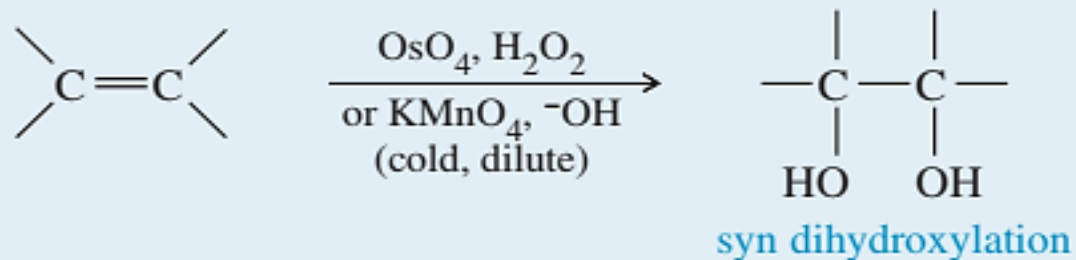


syn addition, anti-Markovnikov orientation

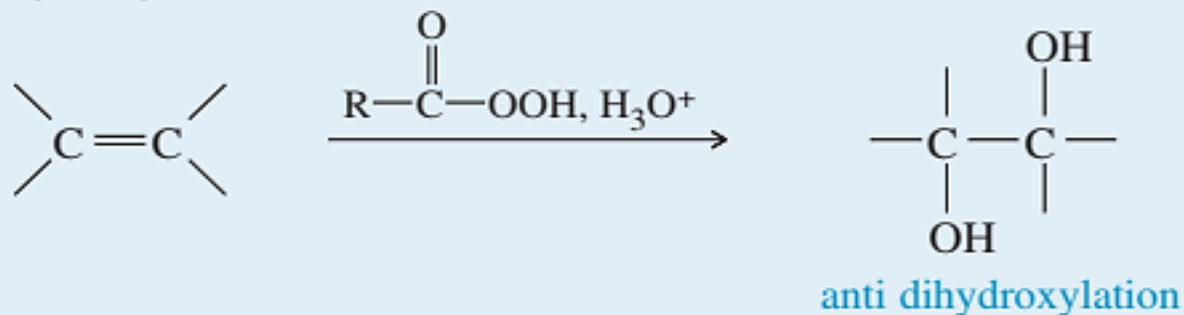
# دی هیدروکسیلاسیون و سنتز دی آل از آلکن ها

• بصورت سین و یا آنتی

## *Syn Dihydroxylation*



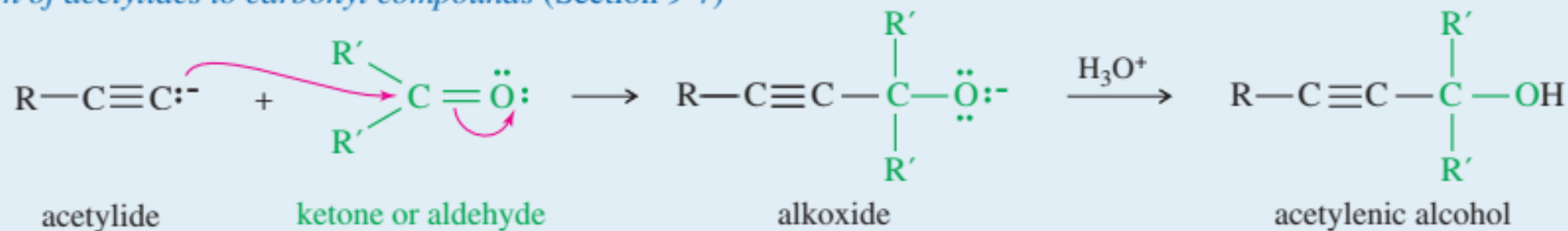
## *Anti Dihydroxylation*



# افزودن استیلید به ترکیبات کربونیلی

• مکانیسم پایه ای

## 5. Addition of acetylides to carbonyl compounds (Section 9-7)

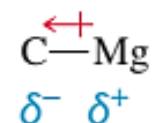
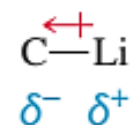


# واکنش گر های ارگانو متالیک برای سنتز الکل ها

- تعریف ارگانومتالیک: وجود پیوند کوالان بین اتم فلز و کربن
- مقایسه با آلکیل هالید ها
- گرینیارد ها و ارگانولیتیم ها
- از بهترین راههای تشکیل پیوند کربن-کربن

Electronegativities					
Li	1.0				C 2.5
Na	0.9	Mg	1.3	Al	1.6
K	0.8				

C—M bond



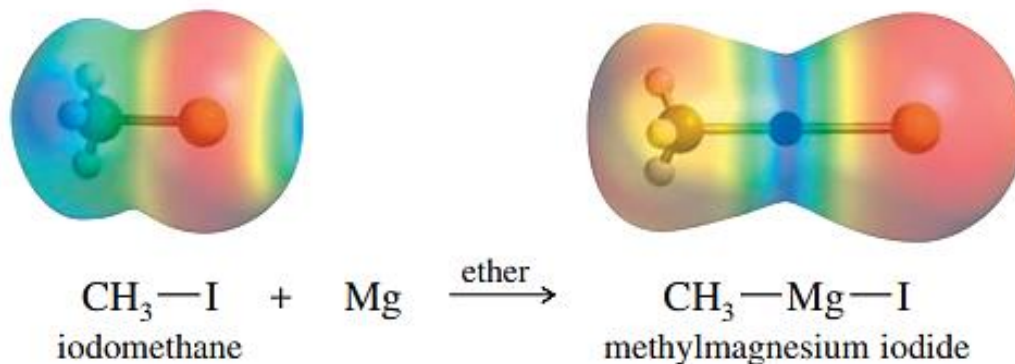


# واکنش گر های ارگانو متالیک برای سنتز الکل ها

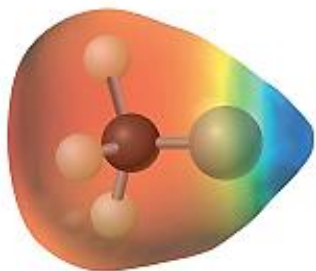
- واکنش گر گرینیارد چیست؟
- شرایط محیط واکنش (دی اتیل اتر)

reactivity:  $R-I > R-Br > R-Cl \gg R-F$

The following reactions show the formation of some typical Grignard reagents.

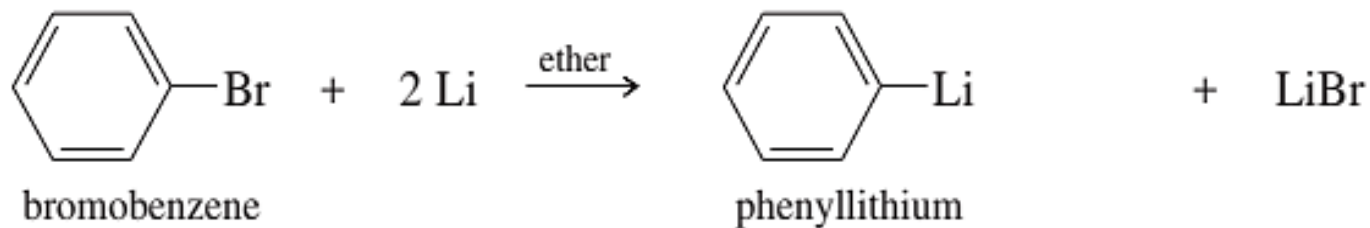
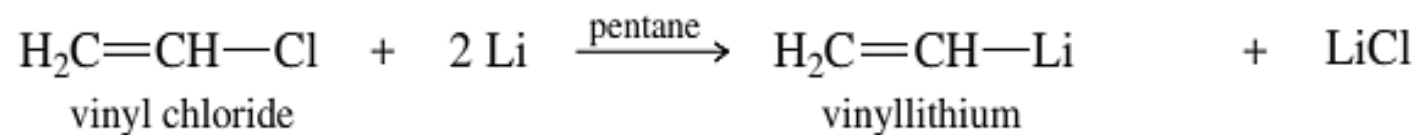
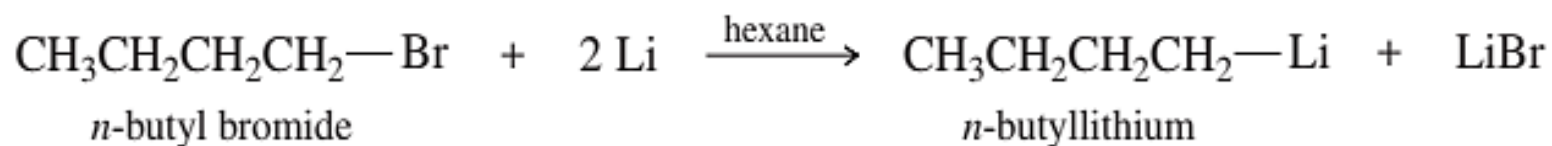


# واکنش گر های ارگانو متالیک برای سنتز الکل ها



EPM of CH<sub>3</sub>Li

- ارگانولیتیم چیست؟
- تفاوت در محیط واکنش

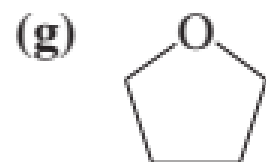


# واکنش گر های ارگانو متالیک برای سنتز الکل ها

• کدام حلال زیر برای تشکیل واکنش گر گرینیارد نمی تواند استفاده شود؟

(a) *n*-hexane

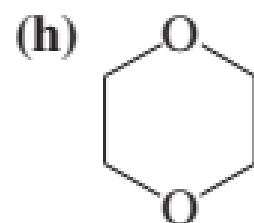
(d) cyclohexane



THF  
(tetrahydrofuran)

(b)  $\text{CH}_3 - \text{O} - \text{CH}_3$

(e) benzene



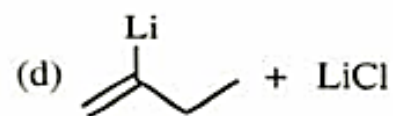
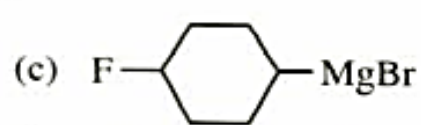
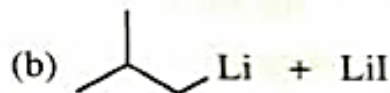
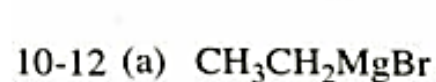
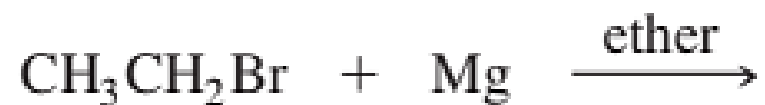
1,4-dioxane

(c)  $\text{CHCl}_3$

(f)  $\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_3$

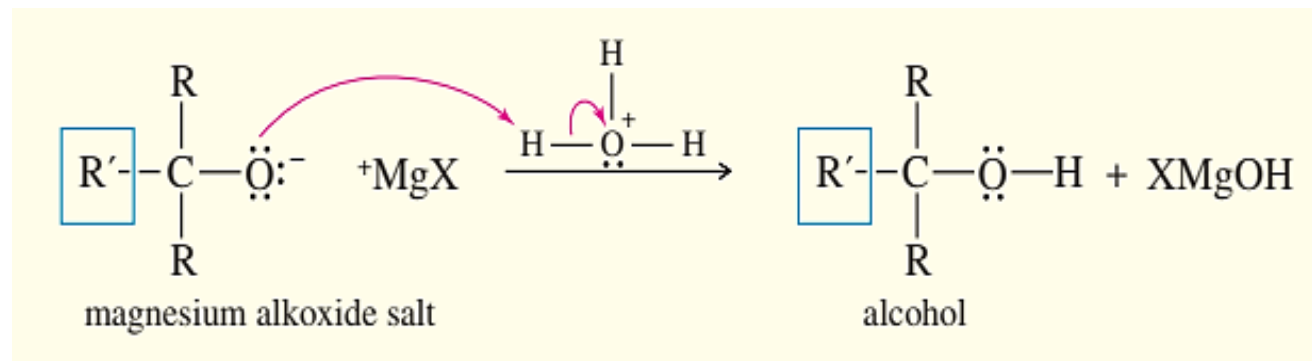
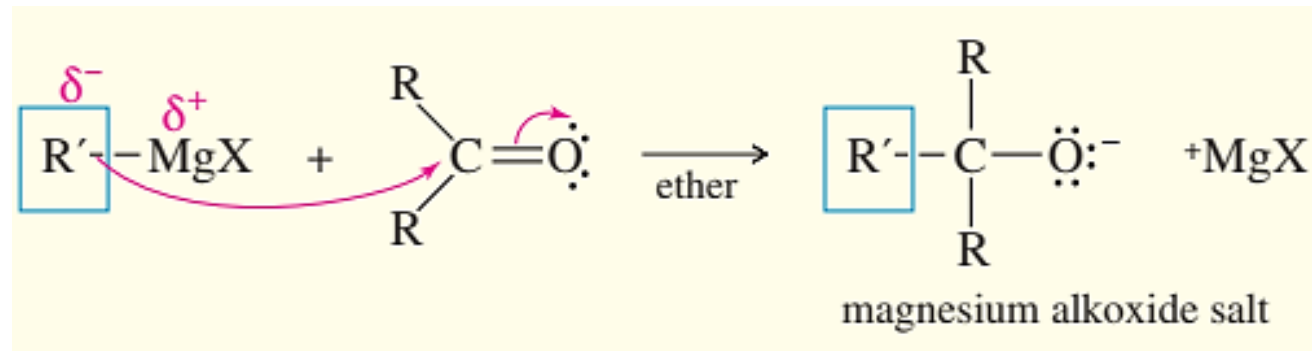
10-11 The Grignard reaction needs a solvent containing an ether functional group: (b), (f), (g), and (h) are possible solvents. Dimethyl ether, (b), is a gas at room temperature, however, so it would have to be liquefied at low temperature for it to be a useful solvent.

## واکنش گرهای ارگانو متالیک برای سنتز الکل ها



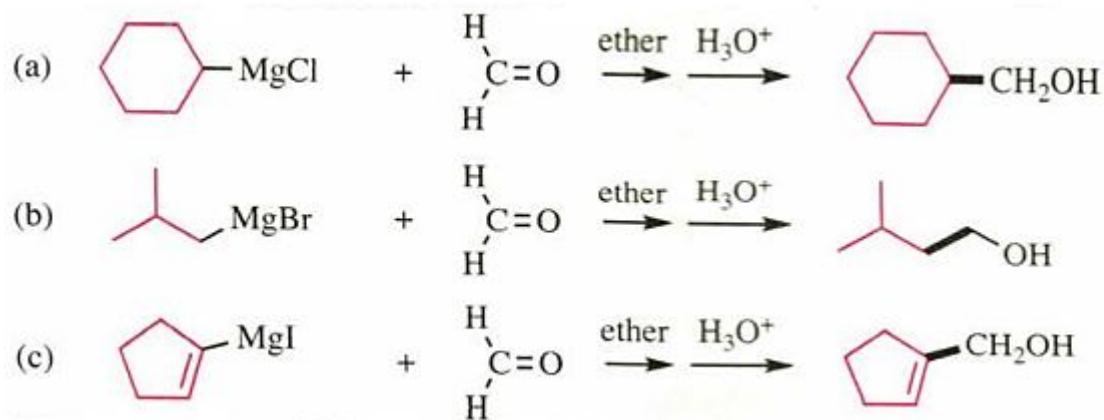
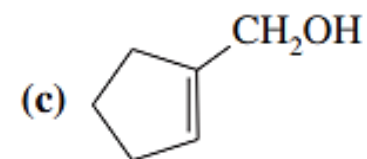
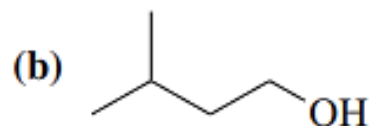
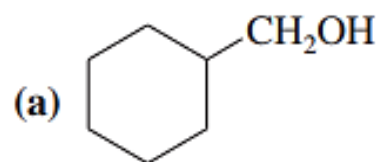
# واکنش های ترکیبات ارگانو متالیک

- فرقی نمیکند چه ارگانولیتیم باشد، چه گرینارد



# افزودن واکنش گر گرینیارد به فرمالدهید

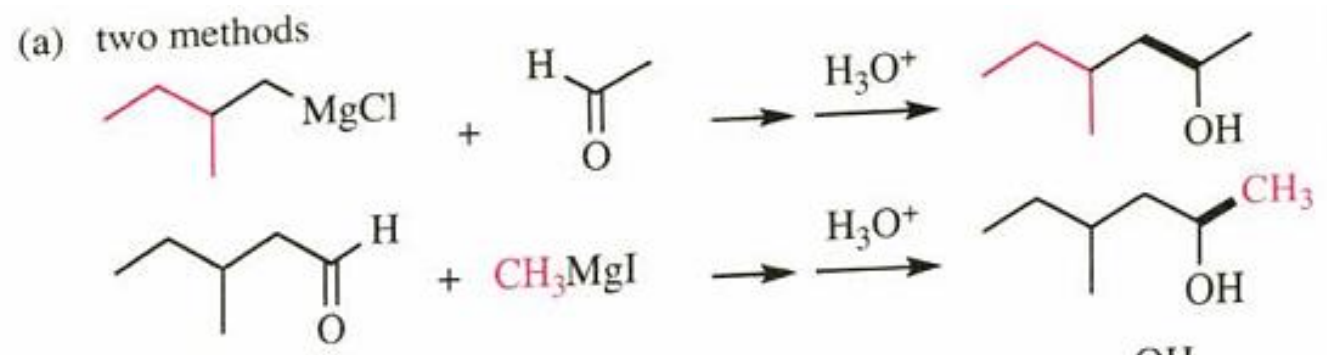
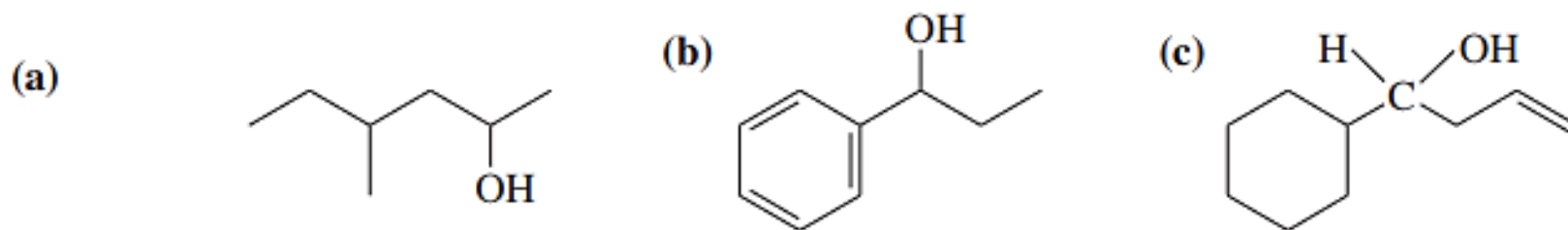
- ترکیبات زیر را با افزودن واکنش گر گرینیارد مناسب به فرمالدهید، سنتز کنید؟



In this solution, the portion of the product that came from the Grignard reagent is shown in red.

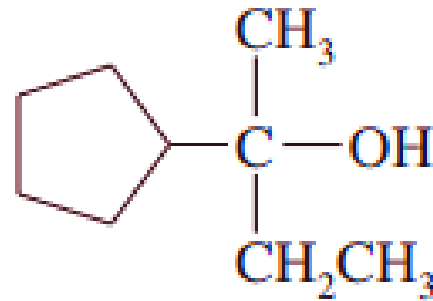
# افزودن واکنش گر گرینیارد به آلدهید

• برای ترکیبات زیر دو روش سنتز پیشنهاد کنید؟



# افزودن واکنش گر گرینیارد به کتون

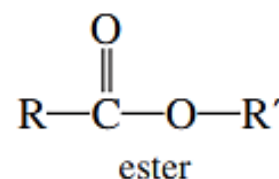
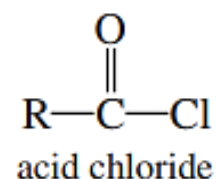
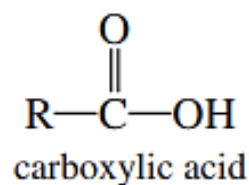
- ترکیب زیر را با واکنش گرهای گرینیاردی سنتز کنید که بیشتر از ۵ کربن نداشته باشند؟





# افزودن واکنش گر گرینیارد به اسید کلرید و استر

• اسید کلرید و استر مشتقات اسید کربوکسیلیک هستند

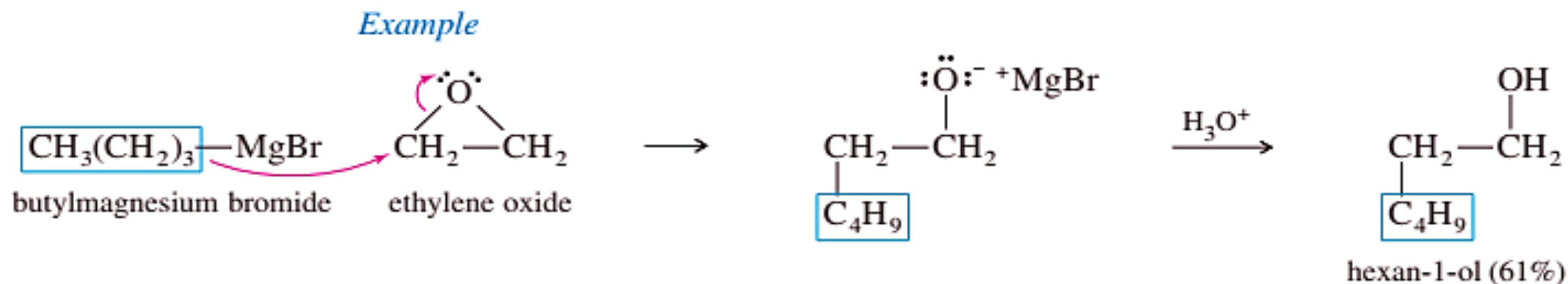


## 3-ethyl-2-methylpentan-3-ol



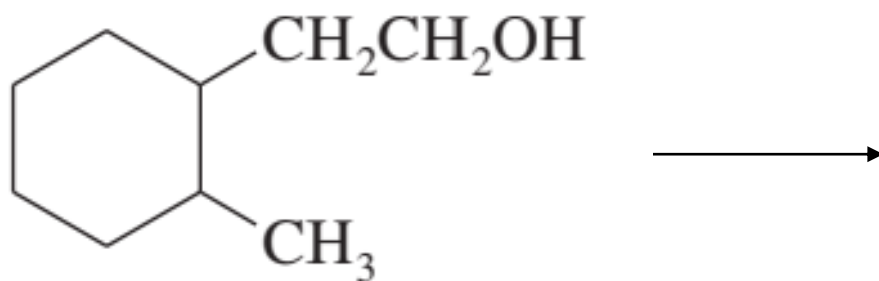
# بازشدن حلقه با اتیلن اکساید

- حمله نوکلئوفیلی به حلقه اپوکسایدی توسط واکنش گر گرینیار
- تخفیف فشار زاویه ای (بایر) اپوکساید
- واکنش پذیری: اپوکساید << اترهای خطی



# بازشدن حلقه با اتیلن اکساید

ترکیبات زیر را با تأیید دادن واکنش گر گرینارد روی اتیلن اکساید سنتز کنید؟



2-phenylethanol  $\longrightarrow$

# لیتیم دی آلکیل کوپرات

- یک ارگانومتالیک دیگر
- یا همان واکنش گر گیلمن

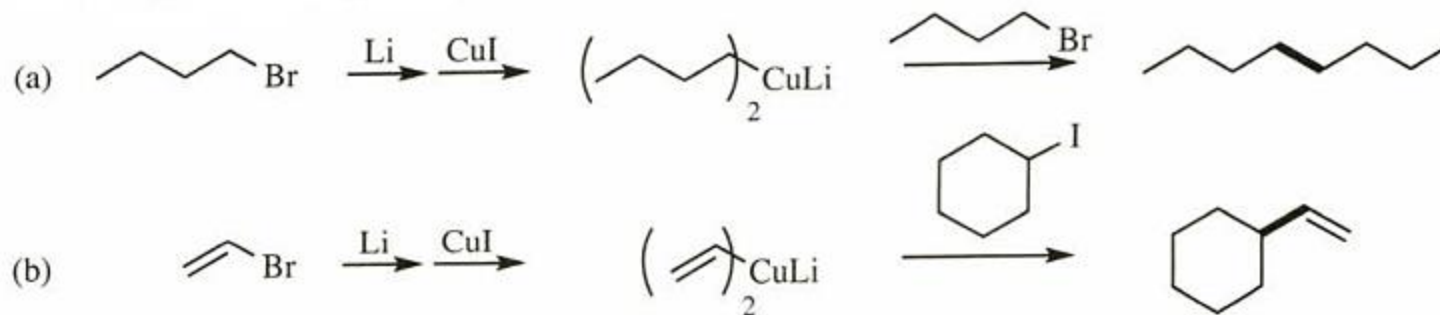
Show how you would synthesize the following compounds from alkyl halides, vinyl halides, and aryl halides containing no more than six carbon atoms.

(a) octane

(b) vinylcyclohexane

(c) *trans*-oct-3-ene

(d) cyclopentyl propyl ketone

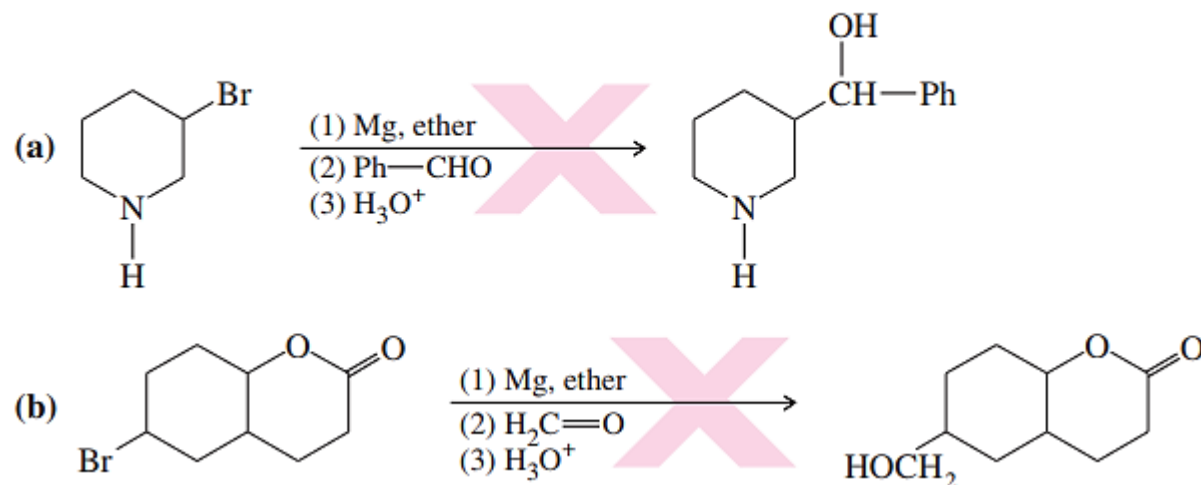


# واکنش با باند های چندگانه الکتروفیل

Protonate the Grignard or organolithium:  $\text{O}-\text{H}$ ,  $\text{N}-\text{H}$ ,  $\text{S}-\text{H}$ ,  $\text{C}\equiv\text{C}-\text{H}$

Attacked by the Grignard or organolithium:  $\text{C}=\text{O}$ ,  $\text{C}=\text{N}$ ,  $\text{C}\equiv\text{N}$ ,  $\text{S}=\text{O}$ ,  $\text{N}=\text{O}$

Point out the flaws in the following incorrect Grignard syntheses.

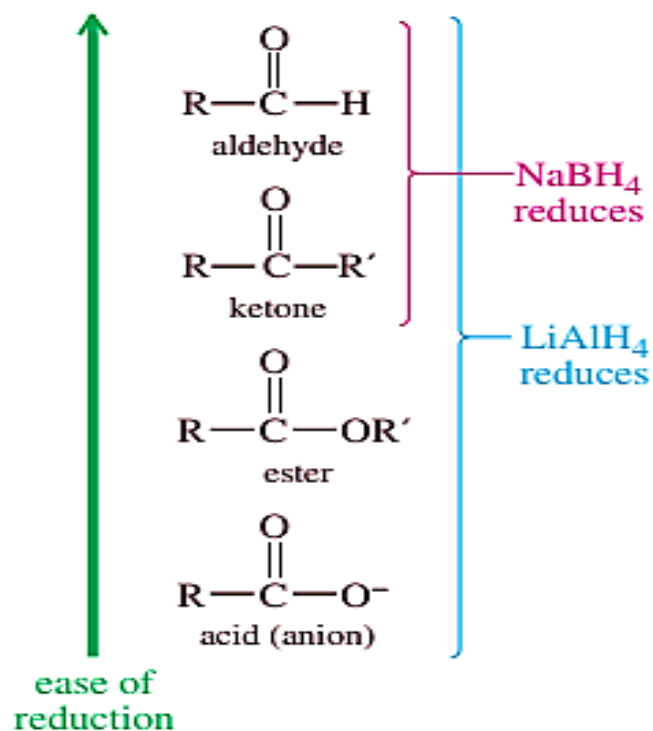


(a) As the Grignard reagent is formed, it would instantaneously be protonated by the  $\text{N}-\text{H}$  present in other molecules of the same substance.

(b) As the Grignard reagent is formed, it would immediately attack the ester functional group present in other molecules of the same substance.

# احیای گروه کربونیل: سنتز الکل نوع یک و دو

به این دو تصویر که خلاصه تمام احیاست دقت کنید



		$\text{NaBH}_4$	$\text{LiAlH}_4$
aldehyde	$\text{R}-\text{C}(=\text{O})-\text{H}$	$\text{R}-\text{CH}_2-\text{OH}$	$\text{R}-\text{CH}_2-\text{OH}$
ketone	$\text{R}-\text{C}(=\text{O})-\text{R}'$	$\text{R}-\text{CH}(\text{OH})-\text{R}'$	$\text{R}-\text{CH}(\text{OH})-\text{R}'$
alkene	$>\text{C}=\text{C}<$	no reaction	no reaction
acid anion	$\text{R}-\text{C}(=\text{O})-\text{O}^-$ anion in base	no reaction	$\text{R}-\text{CH}_2-\text{OH}$
ester	$\text{R}-\text{C}(=\text{O})-\text{OR}'$	no reaction	$\text{R}-\text{CH}_2-\text{OH}$

Note: The products shown are the final products, after hydrolysis of the alkoxide.

# احیای گروه کربونیل: سنتز الکل نوع یک و دو

کاربرد های لیتیم آلومینیوم هیدرید:

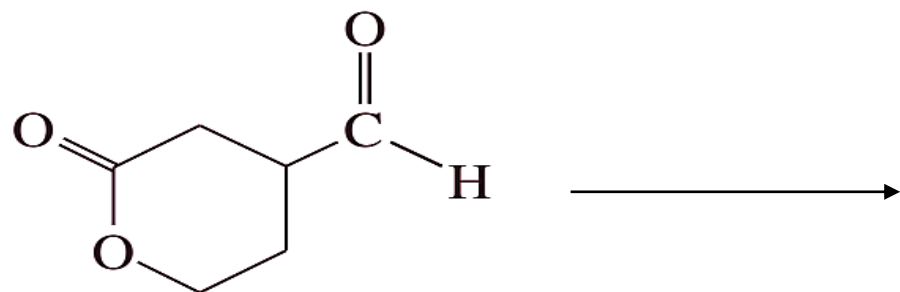
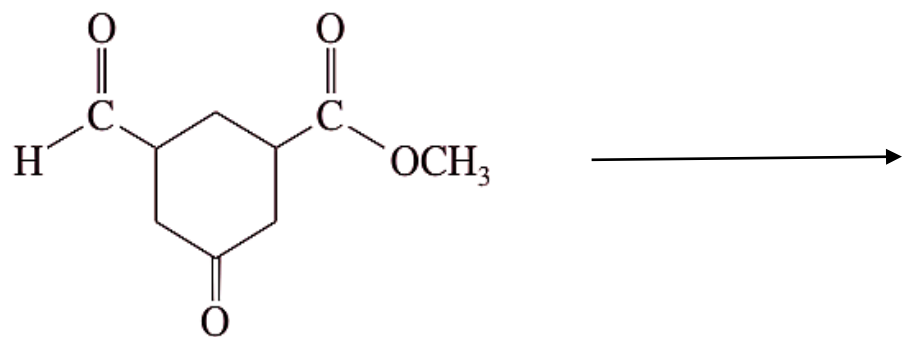
LAH >> NaBH<sub>4</sub> ✓

✓ خلاصه کار :

- کتون >--- الکل نوع دوم
- استر، آلدهید و کربوکسیلیک اسید >--- الکل نوع اول
- ابتدا یون آلکوکسید و بعد از آن پروتوناسیون و الکل نوع اول و دوم

# احیای گروه کربونیل: سنتز الکل نوع یک و دو

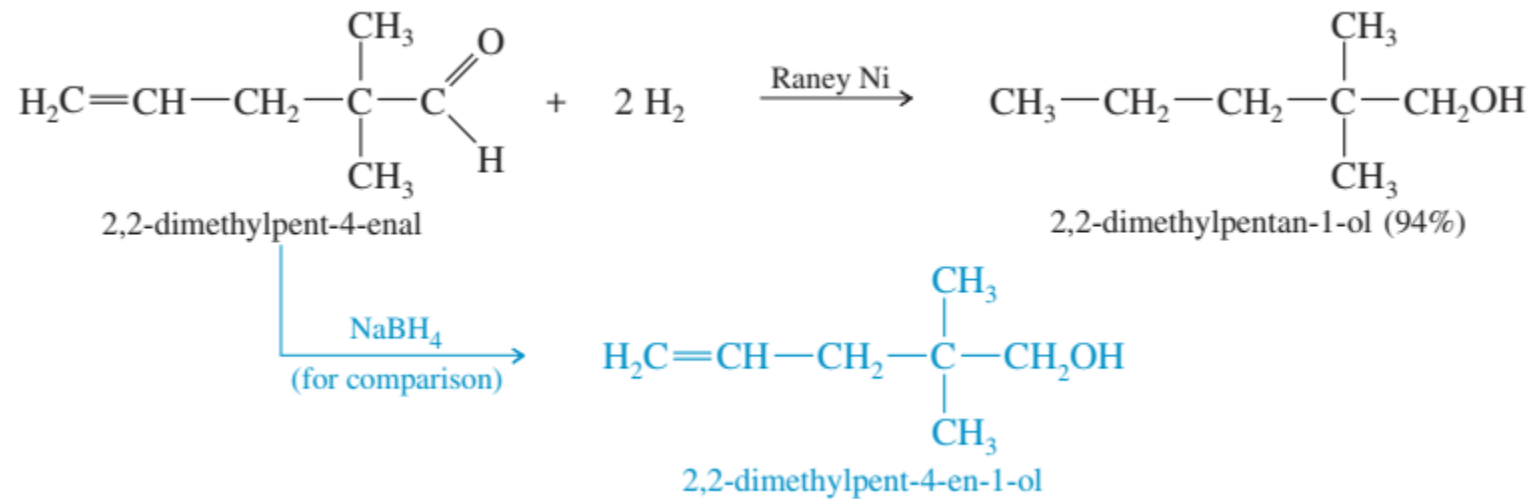
تمرین (با هردو احیاگر و مرور مکانیسم)





# هیدروژناسیون کاتالیتیک کتون و آلدهید

- با استفاده از رانی نیکل هیدروژناسیون انجام میشود



## مباحث تدریس نشده

۲-۹- واکنش های جانبی ارگانومتالیک : احیای آلکیل هالید ها

۲-۹-۱- واکنش با ترکیبات اسیدی

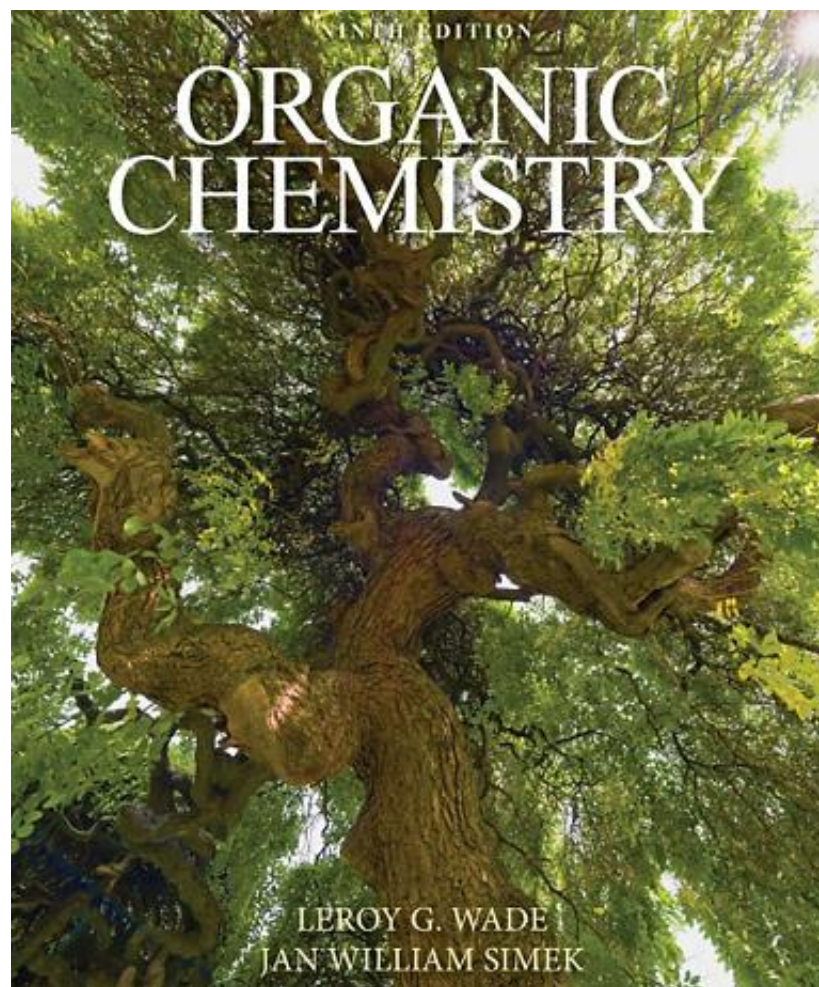
۲-۱۱- تیولها (مرکاپتان ها)

# مهارتهای مورد انتظار = نتیجه دوره

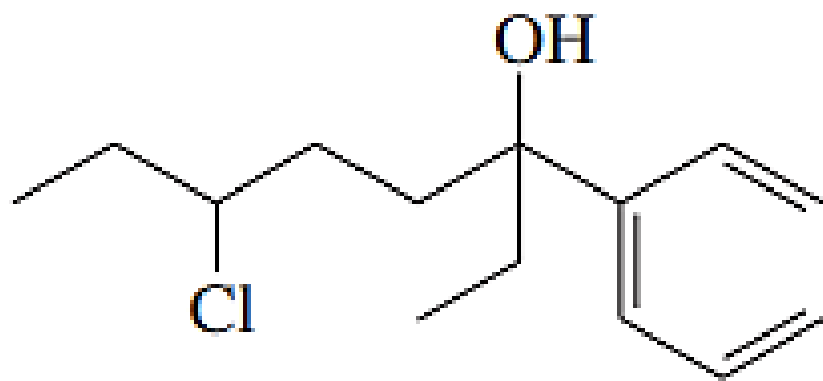
Each skill is followed by problem numbers exemplifying that particular skill.

- 1 Draw structures and assign names for alcohols, phenols, diols, and thiols.
- 2 Predict relative boiling points, acidities, and solubilities of alcohols.
- 3 Show how to convert alkenes, alkyl halides, and carbonyl compounds to alcohols.
- 4 Predict the alcohol products of the hydration, hydroboration, and dihydroxylation of alkenes.
- 5 Use Grignard and organolithium reagents to synthesize primary, secondary, and tertiary alcohols with the required carbon skeletons.
- 6 Propose syntheses and oxidation products for simple thiols.

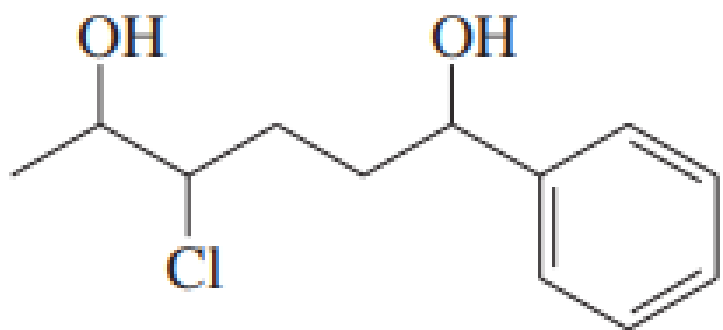
منابع تمام اسلاید ها (هر دو فصل)



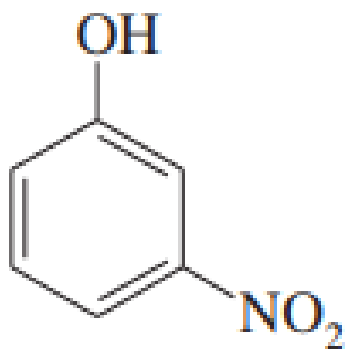
## حل تمرین و آزمون (نمونه سوالات)، پروژه



6-chloro-3-phenyloctan-3-ol; 3°



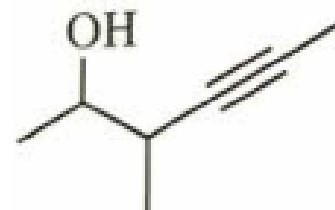
4-chloro-1-phenylhexane-1,5-diol  
3-nitrophenol



*meso*-2,4-pentanediol



3-methylhex-4-yn-2-ol



Predict which member of each pair has the higher boiling point, and explain the reasons for your predictions.

- |  |                               |
|--|-------------------------------|
| (a) hexan-1-ol or 3,3-dimethylbutan-1-ol | (b) hexan-2-one or hexan-2-ol |
| (c) hexan-2-ol or hexane-1,5-diol        | (d) pentan-2-ol or hexan-2-ol |

Predict which member of each pair is more acidic, and explain the reasons for your predictions.

- |  |  |
|--|--|
| (a) cyclopentanol or 3-chlorophenol            | (b) cyclohexanol or cyclohexanethiol     |
| (c) cyclohexanol or cyclohexanecarboxylic acid | (d) butan-1-ol or 2,2-dichlorobutan-1-ol |

Predict which member of each group is most soluble in water, and explain the reasons for your predictions.

- (a) butan-1-ol, pentan-1-ol, or propan-2-ol
- (b) chlorocyclohexane, cyclohexanol, or cyclohexane-1,2-diol
- (c) phenol, cyclohexanol, or 4-methylcyclohexanol



10-33

(a) Hexan-1-ol will boil at a higher temperature as it is less branched than 3,3-dimethylbutan-1-ol.

(b) Hexan-2-ol will boil at a higher temperature because its molecules hydrogen bond with each other, whereas molecules of hexan-2-one have no intermolecular hydrogen bonding.

(c) Hexane-1,5-diol will boil at a higher temperature as it has two OH groups for hydrogen bonding. Hexan-2-ol has only one group for hydrogen bonding.

(d) Hexan-2-ol will boil at a higher temperature because it has a higher molecular weight than pentan-2-ol. All other structural features of the two molecules are the same, so they should have the same intermolecular forces.

10-34 Refer to Table 10-4 to compare acidities of different functional groups. The strength of an acid is determined by the stability of its conjugate base.

(a) 3-Chlorophenol is more acidic than cyclopentanol. In general, phenols are many orders of magnitude more acidic than alcohols because phenoxide anions are stabilized by resonance.

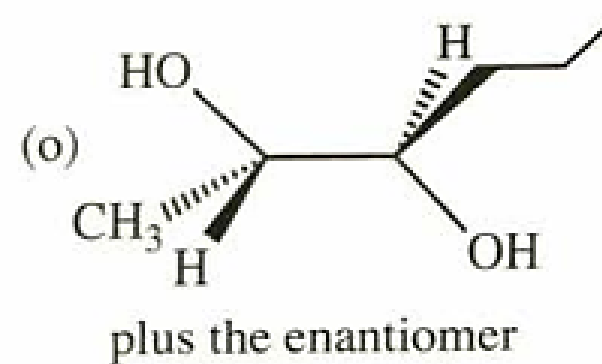
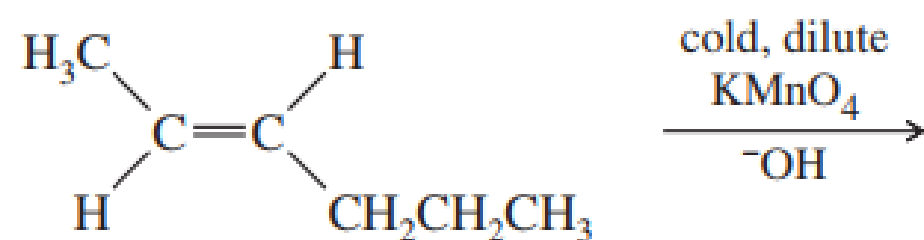
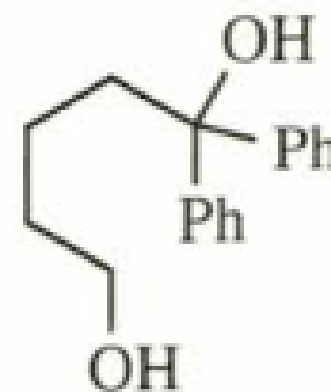
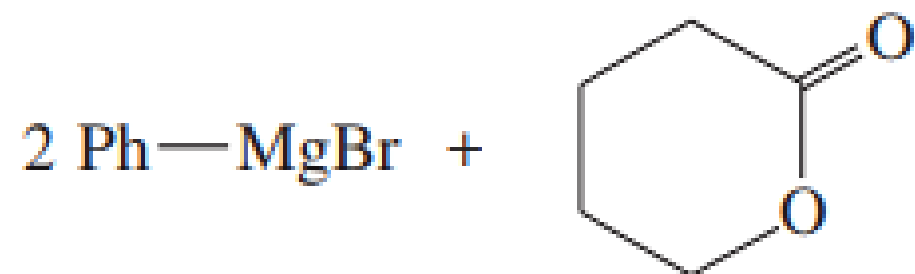
(b) Cyclohexanethiol is more acidic than cyclohexanol. S is beneath O on the periodic table, and acidity increases down the periodic table. Larger anions are more stable because a negative charge on a larger atom is distributed over a larger volume, with lower electron density and greater delocalization of the negative charge.

(c) Cyclohexanecarboxylic acid is more acidic than cyclohexanol. In general, carboxylic acids are many orders of magnitude more acidic than alcohols because carboxylate anions are stabilized by resonance.

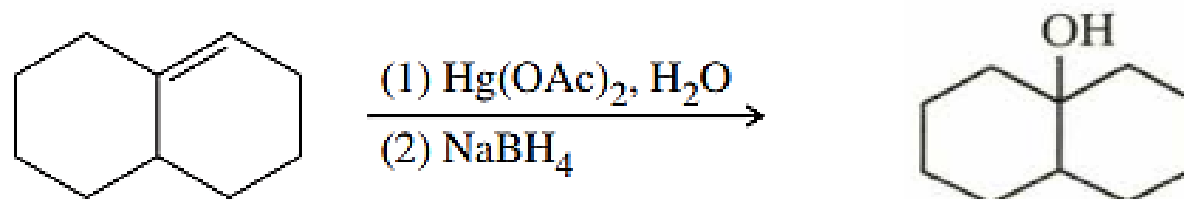
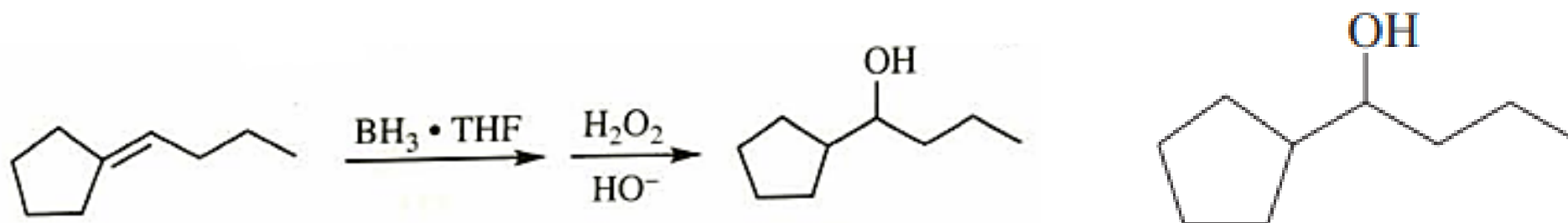
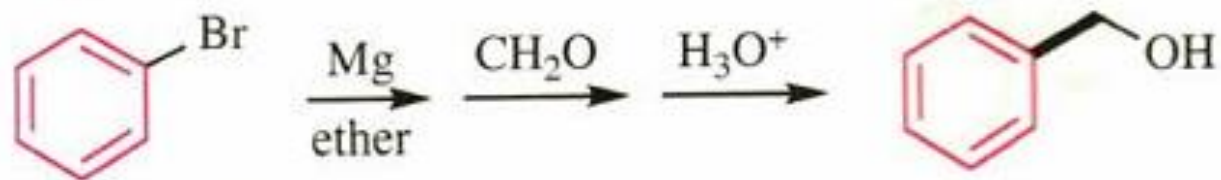
(d) 2,2-Dichlorobutan-1-ol is more acidic than butan-1-ol because of the two electron-withdrawing substituents near the acidic functional group.

10-35

- (a) Propan-2-ol is the most soluble in water as it has the fewest carbons and the most branching.
- (b) Cyclohexane-1,2-diol is the most soluble as it has two OH groups for hydrogen bonding. Cyclohexanol has only one OH group; chlorocyclohexane cannot hydrogen bond and is the least soluble.
- (c) Phenol is the most soluble as it can hydrogen bond better than cyclohexanol. Phenol is a stronger acid and will be ionized to a greater extent than cyclohexanol. Cyclohexanol has low solubility, and 4-methylcyclohexanol has the added hydrophobic methyl group, decreasing its water solubility.



benzyl alcohol ( $\text{Ph}-\text{CH}_2-\text{OH}$ ) from bromobenzene ( $\text{Ph}-\text{Br}$ )



Starting from bromobenzene and any other reagents and solvents you need, show how you would synthesize the following compounds. Any of these products may be used as starting materials in subsequent parts of this problem.

(a) 1-phenylpropan-1-ol

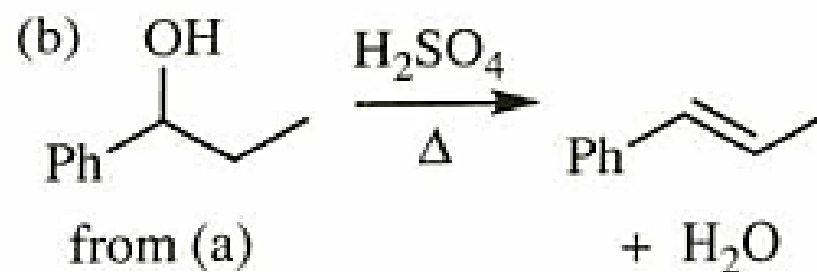
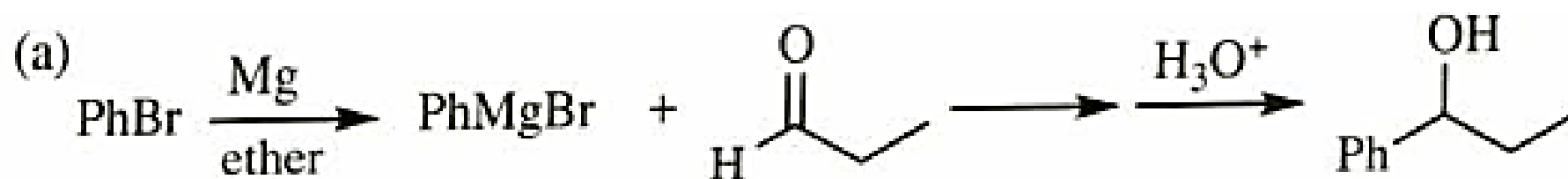
(b) 1-phenylpropene

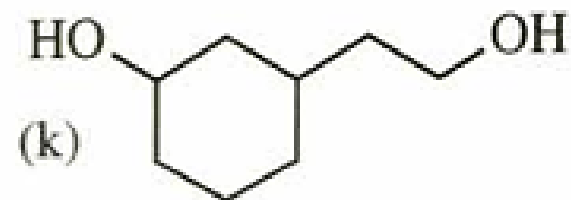
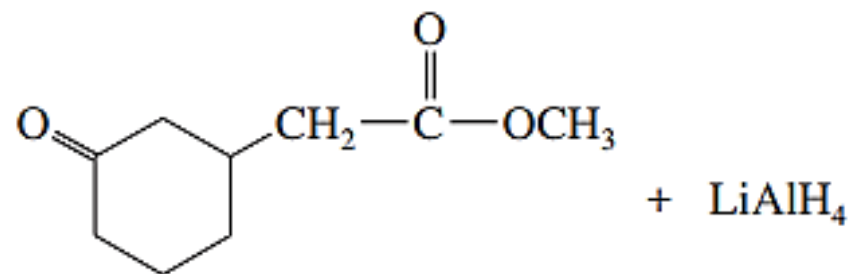
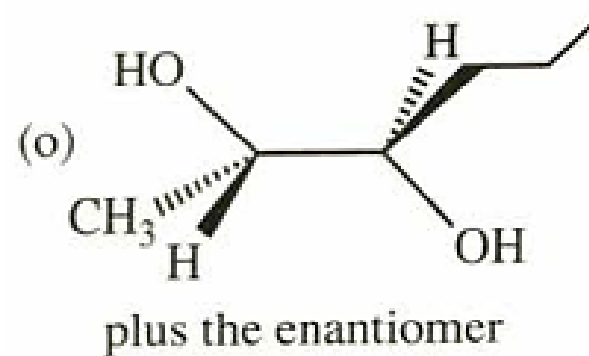
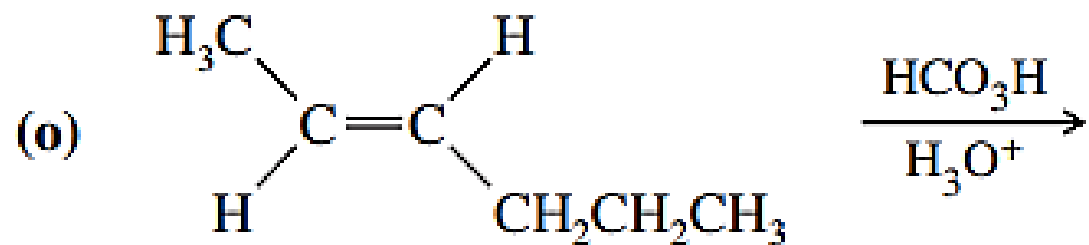
(c) 1-phenylpropan-2-ol

(d) 3-phenylprop-2-en-1-ol

(e) 2-phenylbutan-2-ol

(f) 2-phenylbut-2-ene

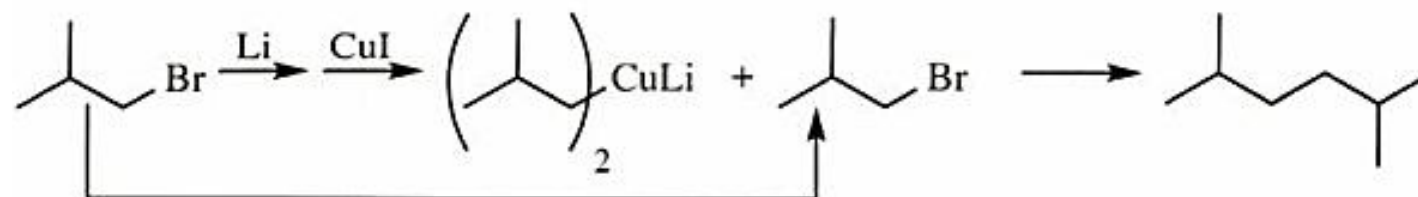
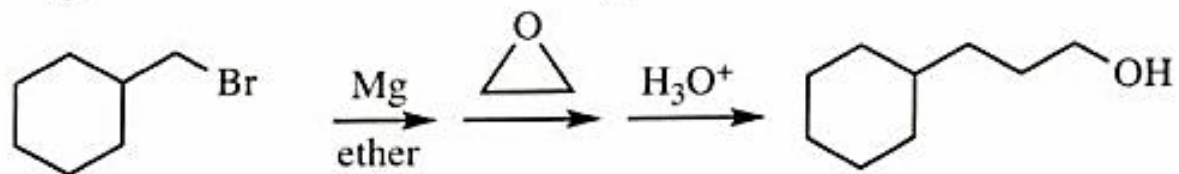
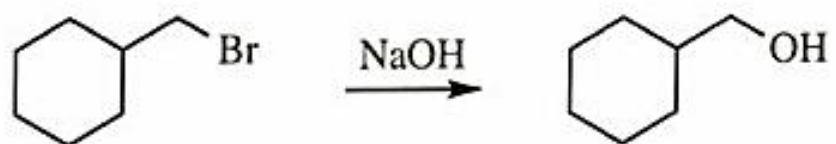
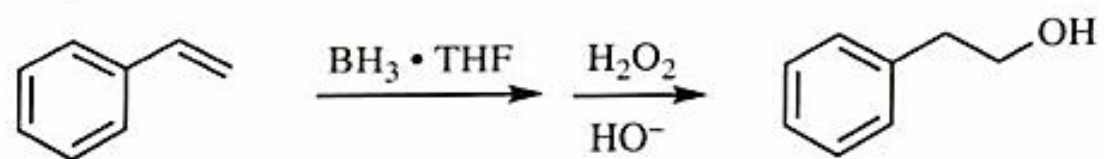
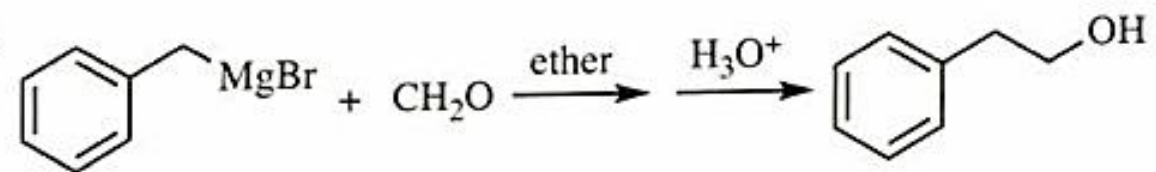




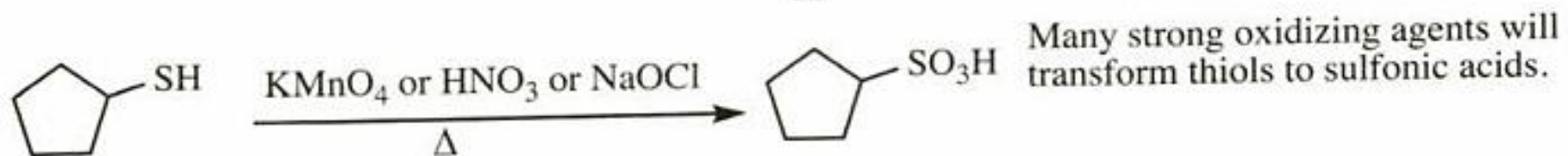
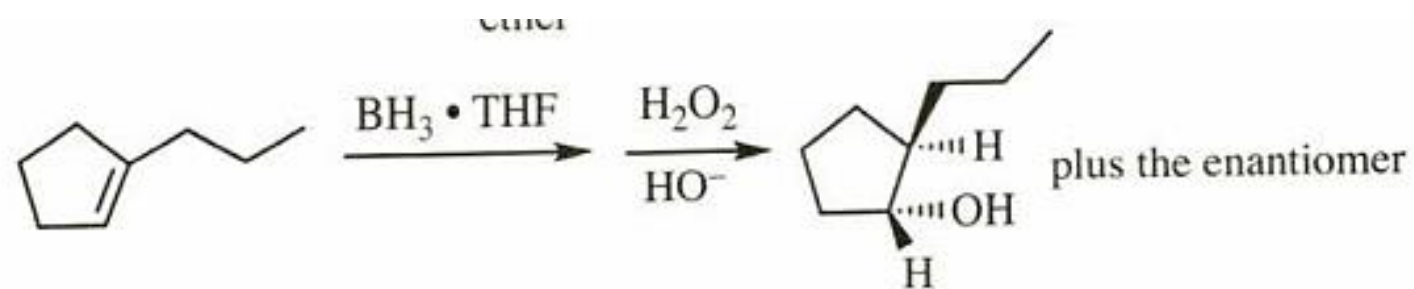
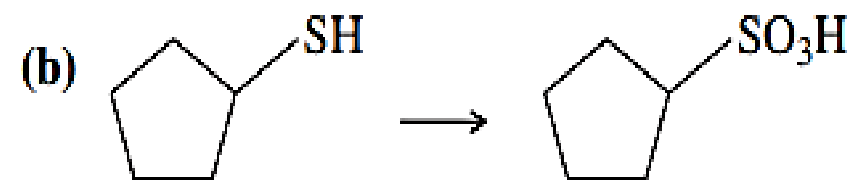
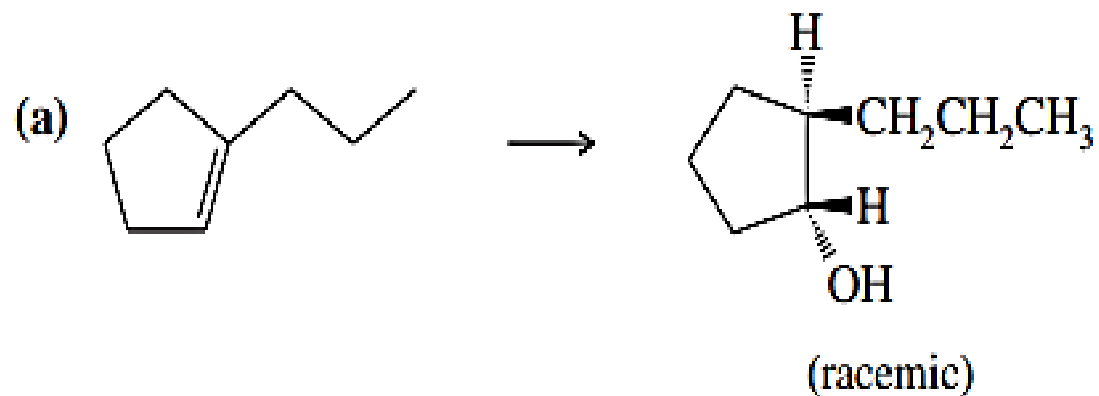
Show how you would synthesize the following:

- (a) 2-phenylethanol by the addition of formaldehyde to a suitable Grignard reagent
- (b) 2-phenylethanol from a suitable alkene
- (c) cyclohexylmethanol from an alkyl halide using an  $S_N2$  reaction
- (d) 3-cyclohexylpropan-1-ol by the addition of ethylene oxide to a suitable Grignard reagent
- (e) *cis*-pent-2-en-1-thiol from a suitable alkenyl halide
- (f) 2,5-dimethylhexane from a four-carbon alkyl halide



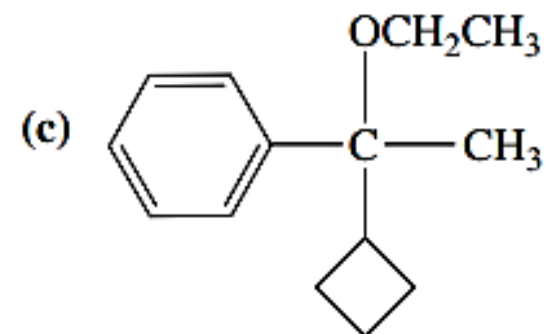
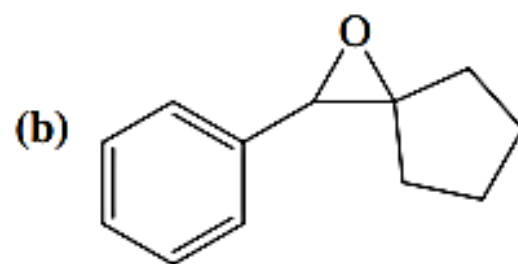
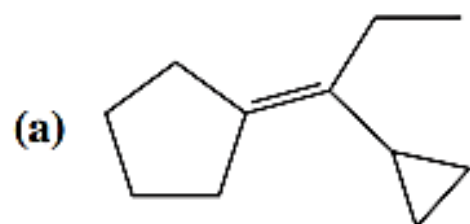






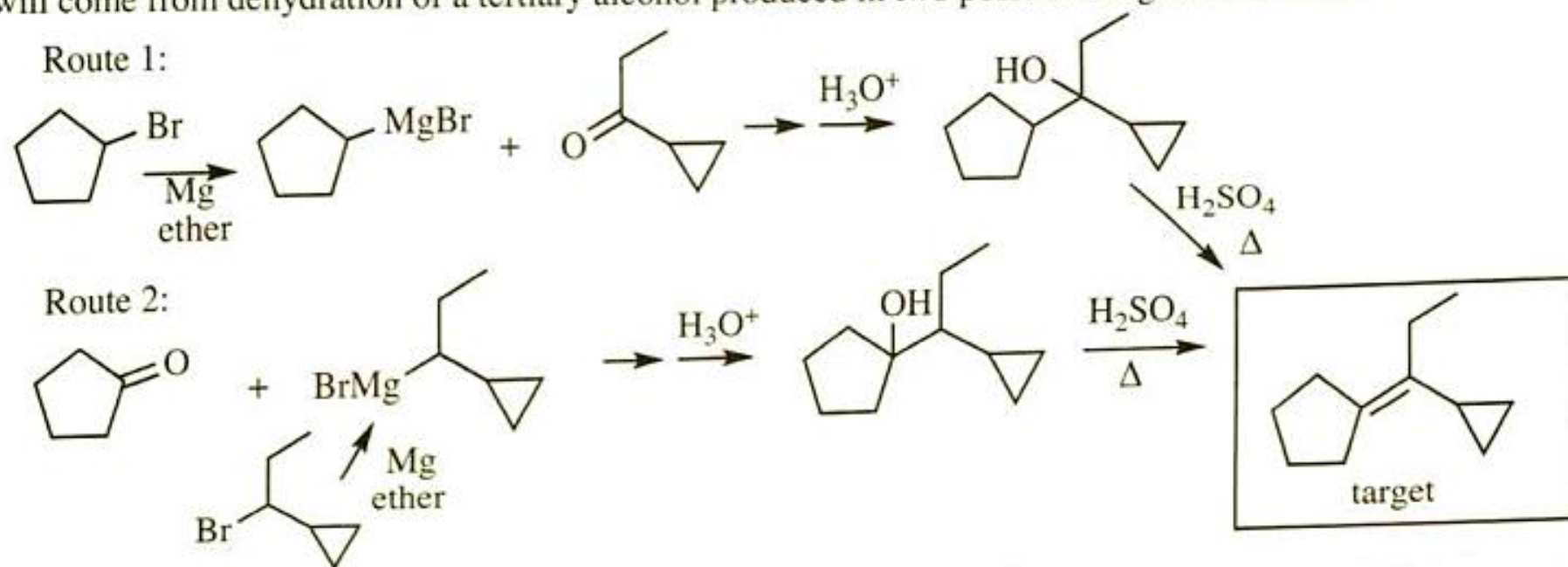
## پروژه

Show how you would synthesize the following compounds from any starting materials containing no more than six carbon atoms.



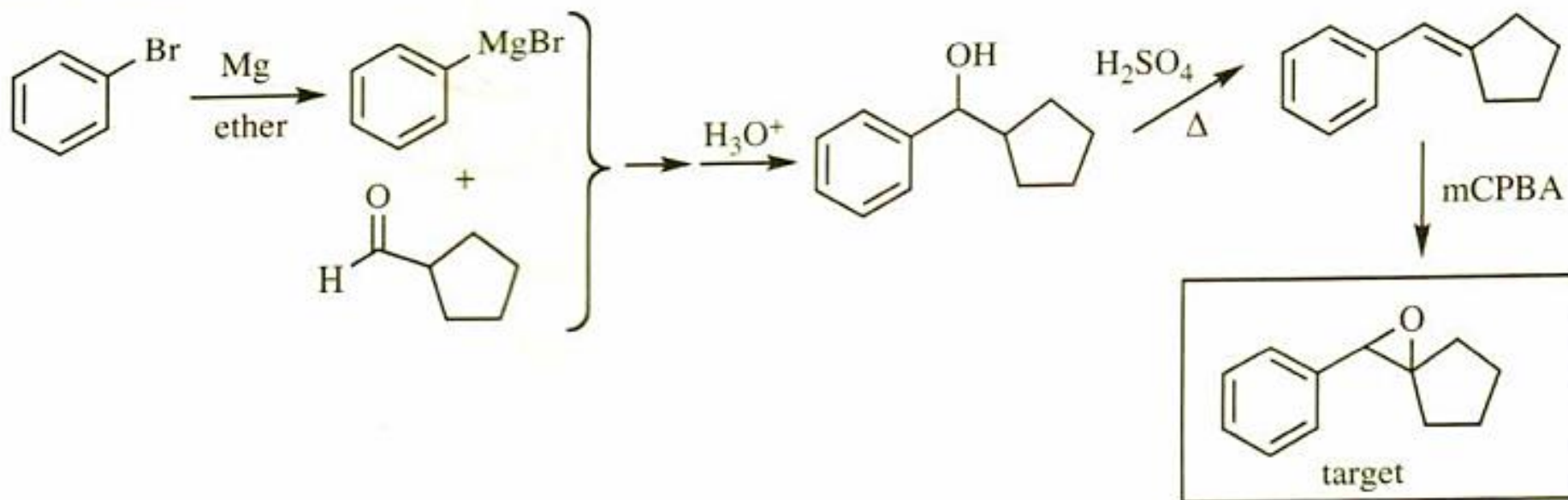
# پاسخ ها

(a) The goal is to synthesize the target compound (boxed) from starting materials of six carbons or fewer. The product has 11 carbons, so the logical "disconnection" in working backwards is one six-carbon fragment and the cyclopentane ring that could be joined in a Grignard reaction. The tetrasubstituted  $C=C$  will come from dehydration of a tertiary alcohol produced in two possible Grignard reactions.



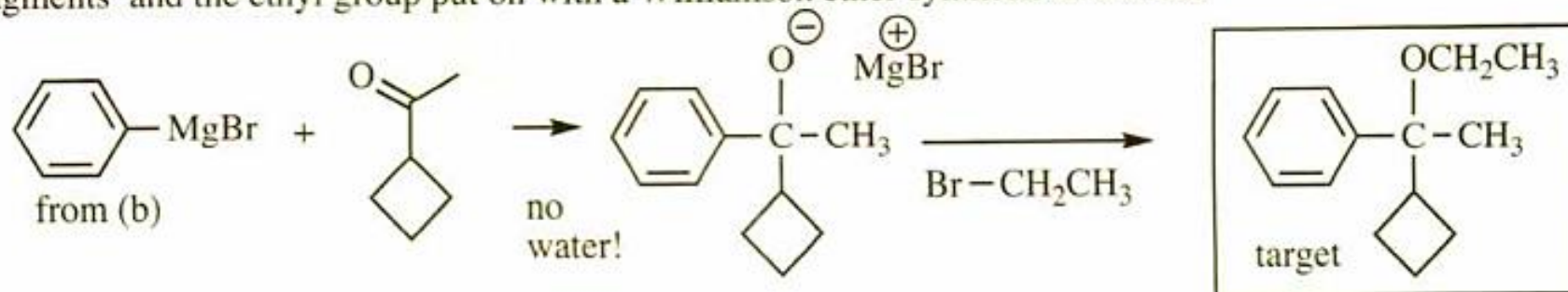
# پاسخ ها

(b) The goal is to synthesize the target compound (boxed) from starting materials of six carbons or fewer. The product has 12 carbons, so the logical "disconnection" in working backwards is two six-carbon fragments which could be joined in a Grignard reaction. The best way to make epoxides is from the double bond, and double bonds are made from alcohols which are the products of Grignard reactions.

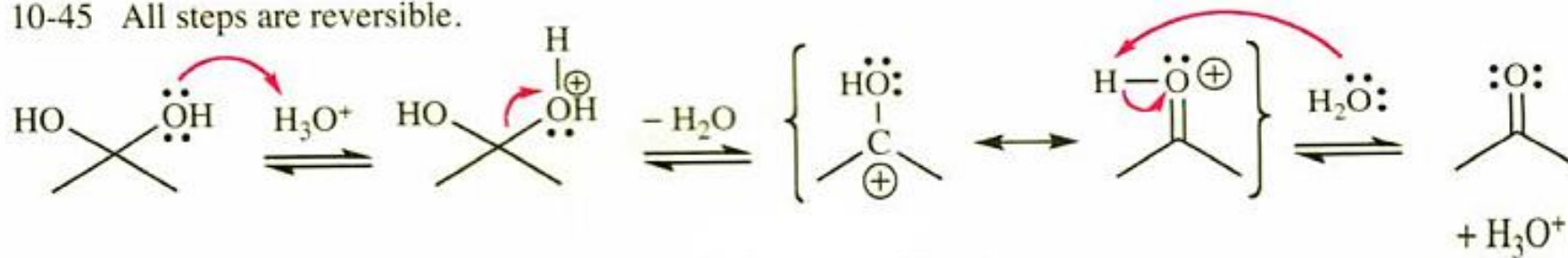


# پاسخ ها

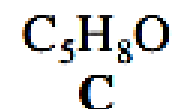
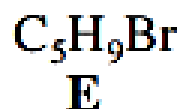
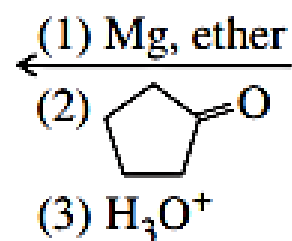
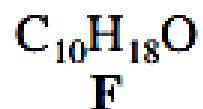
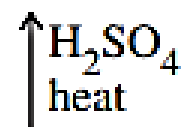
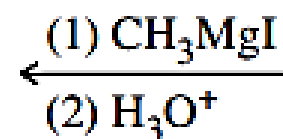
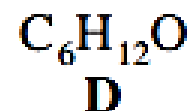
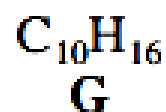
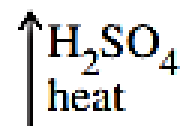
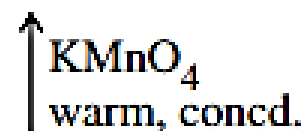
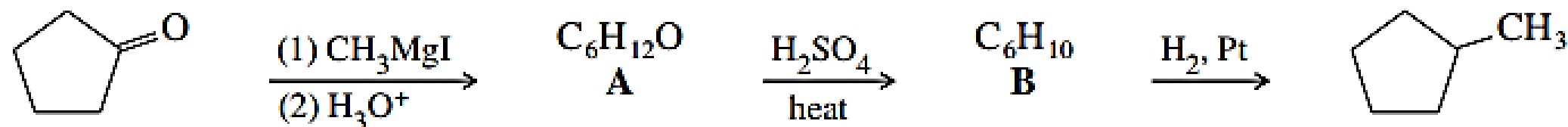
(c) The goal is to synthesize the target compound (boxed) from starting materials of six carbons or fewer. The product has 14 carbons, so the logical "disconnection" in working backwards is two six-carbon fragments and the ethyl group put on with a Williamson ether synthesis at the end.



10-45 All steps are reversible.

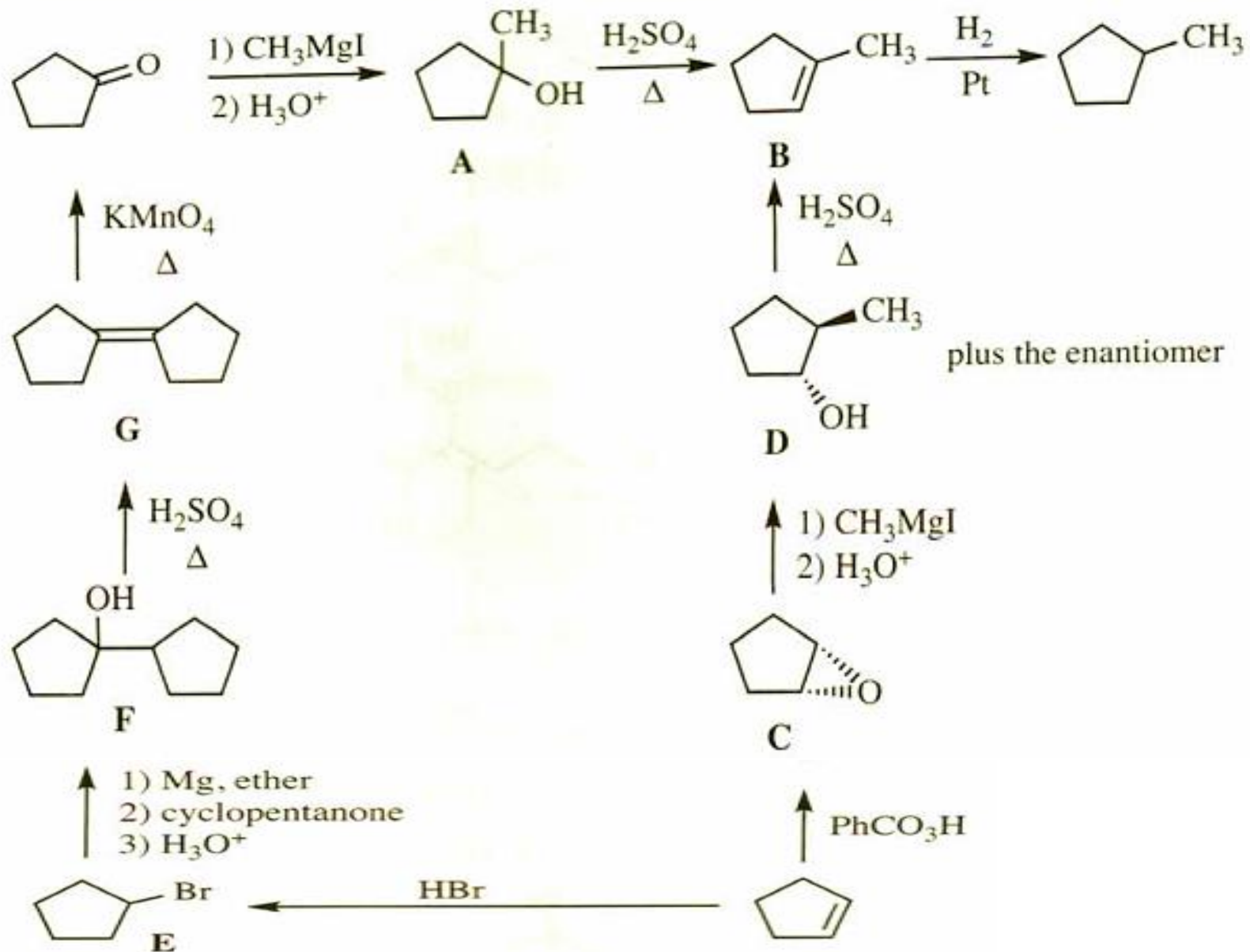


Determine the structures of compounds **A** through **G**, including stereochemistry where appropriate.

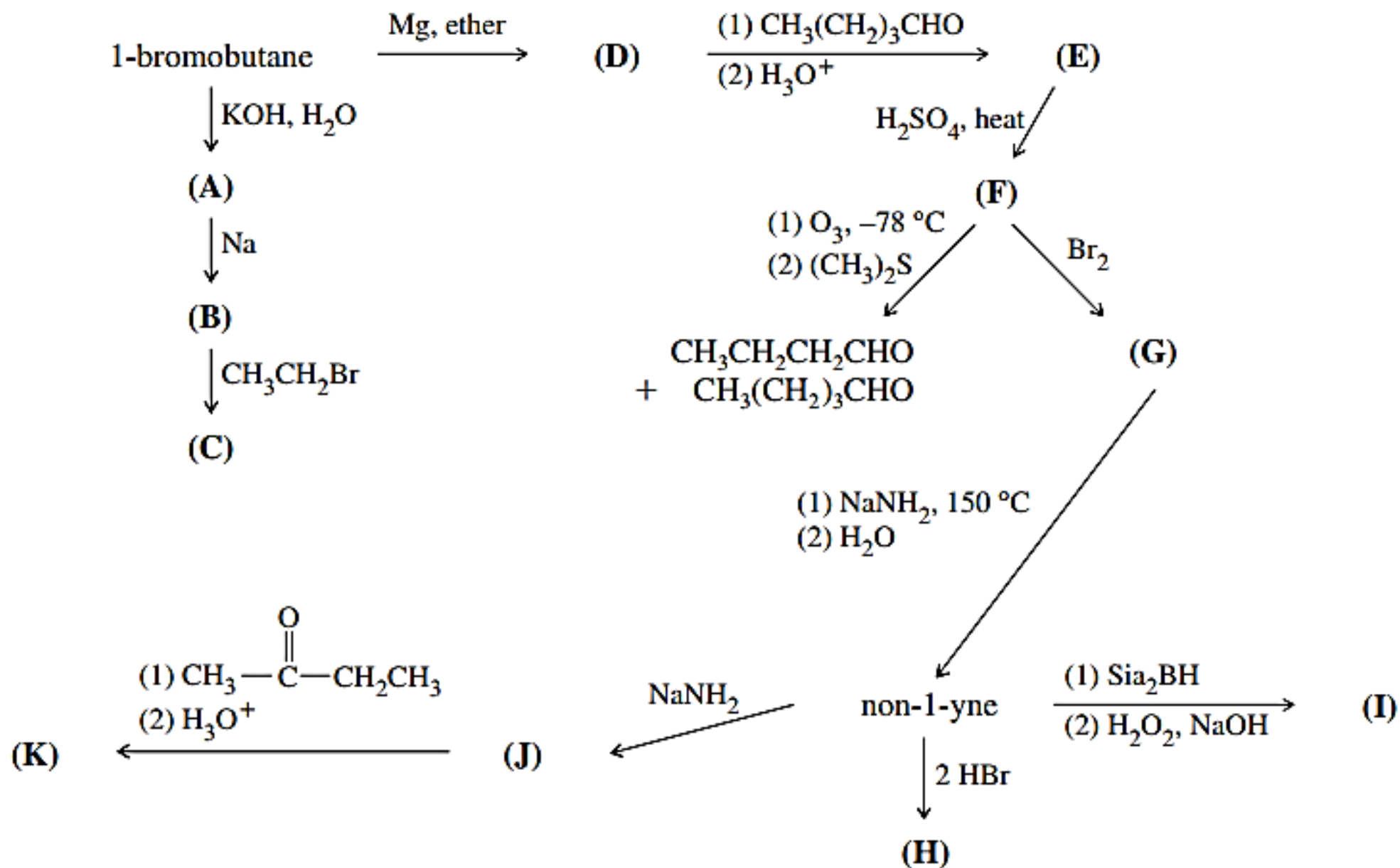




10-49 When mixtures of isomers can result, only the major product is shown.

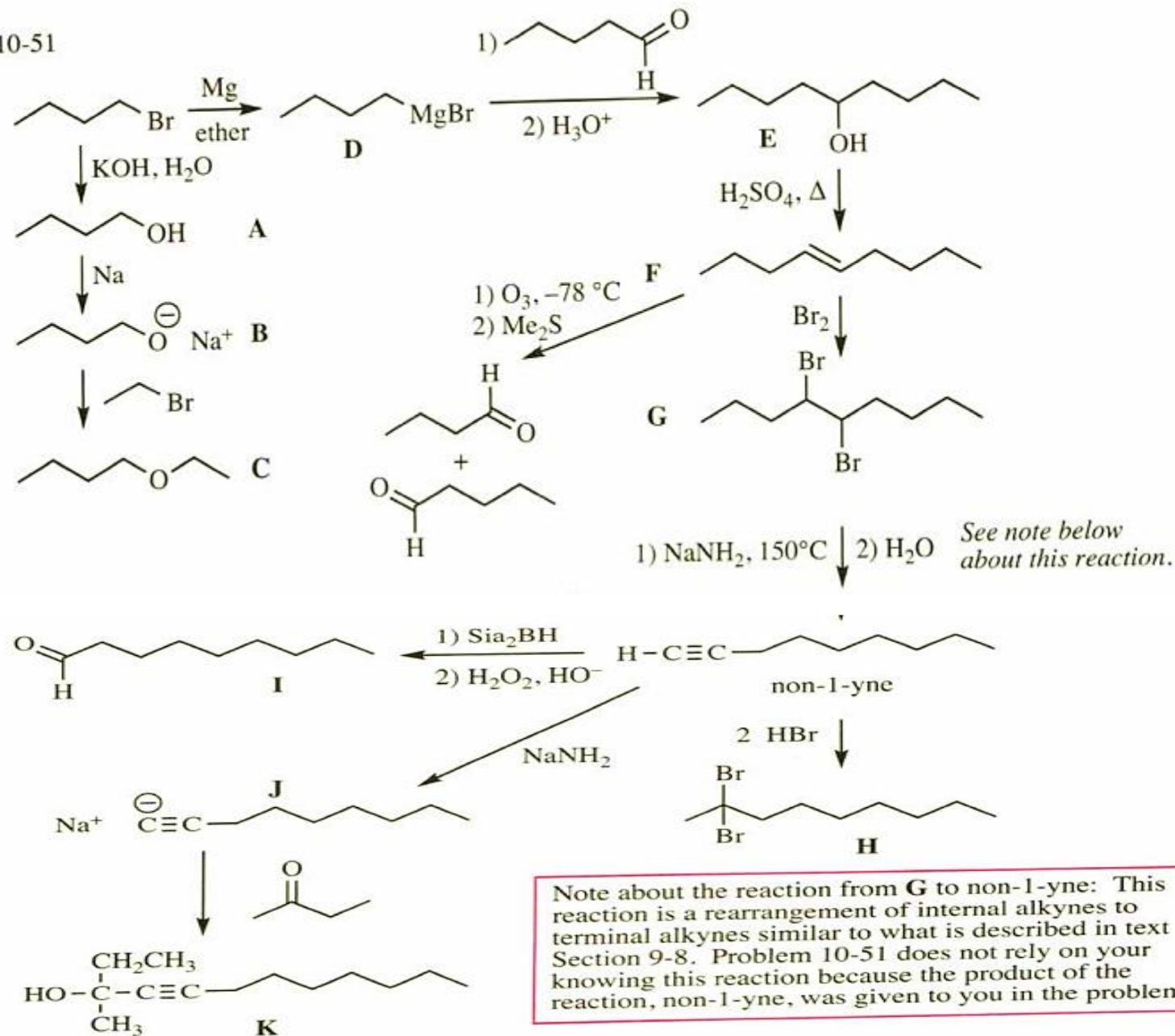


پاسخ  
اسلاید  
قبلی





10-51



پاسخ  
اسلاید  
قبلی

Thanks for your attention  
Any comments? Questions?