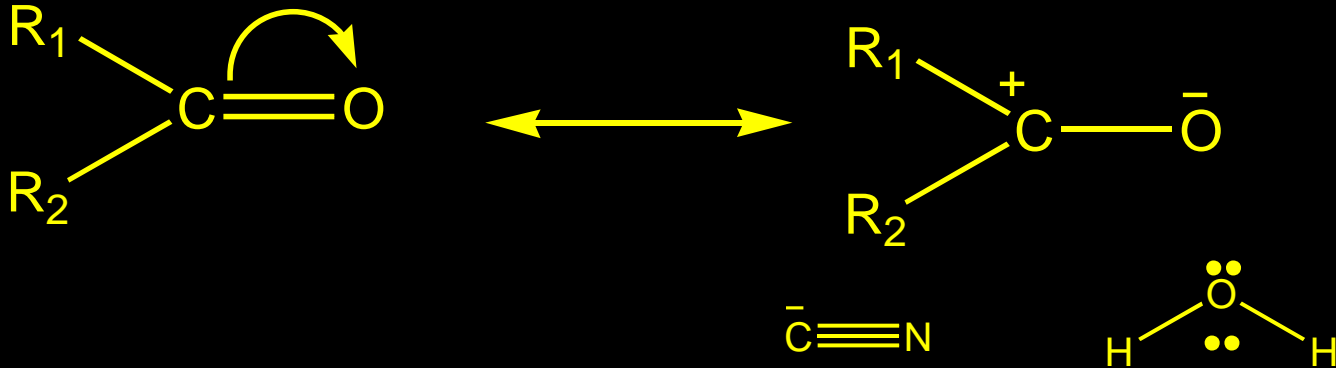


Adição Nucleofílica ao Grupo Carbonila

**Aldeídos e cetonas –
reatividade**

Compostos carbonílicos

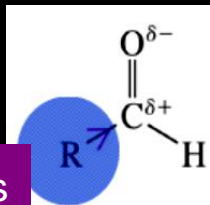
Híbridos de ressonância



- ✓ A carbonila tem caráter polar
- ✓ Pode ser atacada por espécies nucleofílicas
- ✓ Exemplo: CN⁻; H₂O

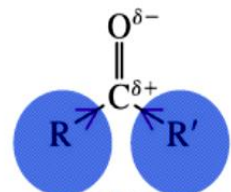
Reatividade de aldeídos e cetonas

aldeídos

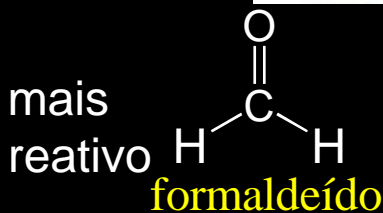
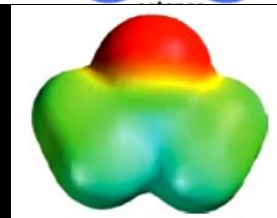
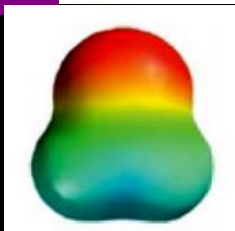


Mais reativos

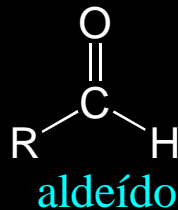
cetonas



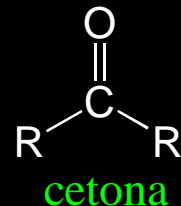
Menos reativos



>



>



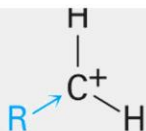
menos reativo

REATIVIDADE

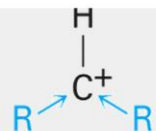


Eletrofilicidade de Aldeídos e Cetonas

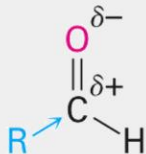
- Aldeído C=O é mais polarizado que cetona C=O
- Como em carbocátions, uma maior quantidade de grupos alquila estabilizam o caráter +
- Cetona tem mais grupos alquílicos, estabilizando o carbono C=O indutivamente



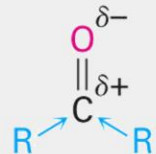
1° carbocation
(less stable, more reactive)



2° carbocation
(more stable, less reactive)



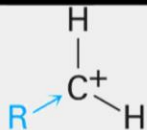
Aldehyde
(less stabilization of $\delta+$, more reactive)



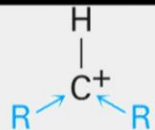
Ketone
(more stabilization of $\delta+$, less reactive)

Reatividade de Aldeídos Aromáticos

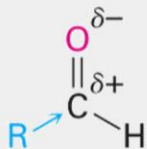
- Menos reativo em reações de adição nucleofílica do que aldeídos alifáticos
- Efeito de ressonância doando elétrons do anel aromático torna a C=O menos atrativa para nucleófilos do que o grupo carbonila de um aldeído alifático



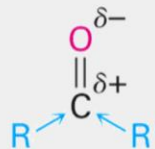
1° carbocation
(less stable, more reactive)



2° carbocation
(more stable, less reactive)



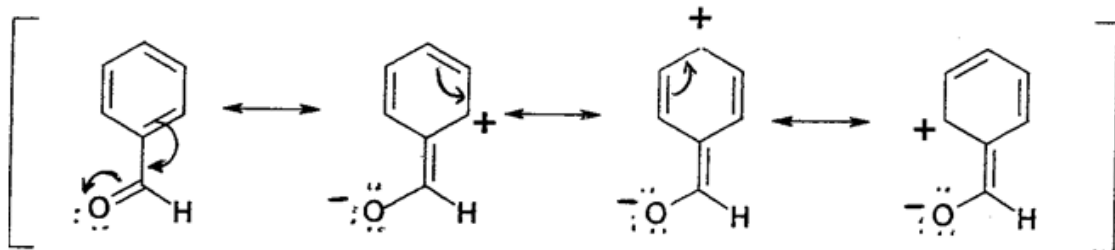
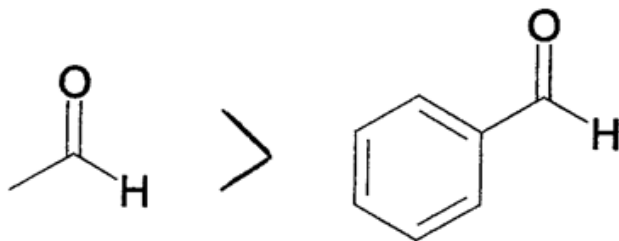
Aldehyde
(less stabilization of δ^+ , more reactive)



Ketone
(more stabilization of δ^+ , less reactive)

CONJUGAÇÃO (EFEITO DE RESSONÂNCIA)

DIMINUIÇÃO DA REATIVIDADE



The reactivity of carbonyl compounds is also related to the basicity of Y⁻:

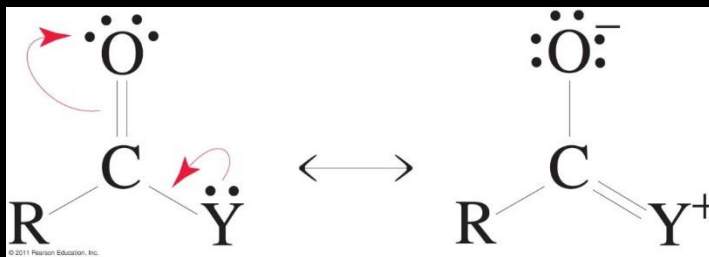
relative reactivities of carbonyl compounds

acyl halide > acid anhydride > aldehyde > ketone > ester ~ carboxylic acid > amide > carboxylate ion

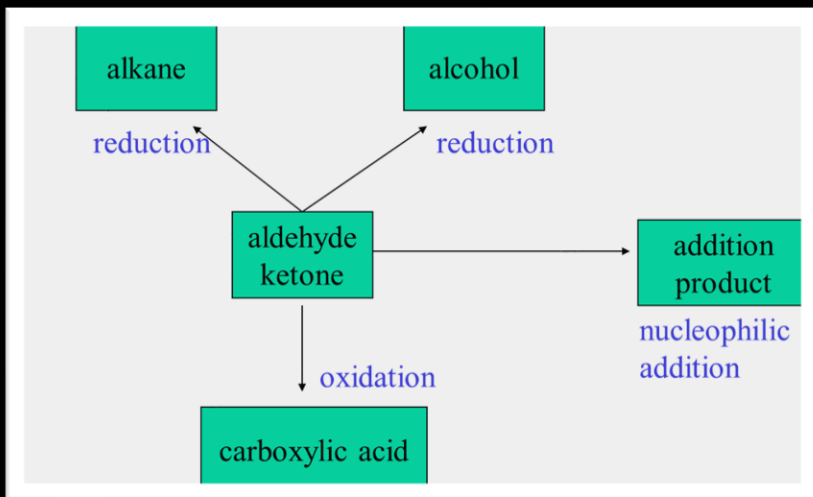
most reactive

least reactive

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Reações de aldeídos e cetonas



- oxidação
- redução

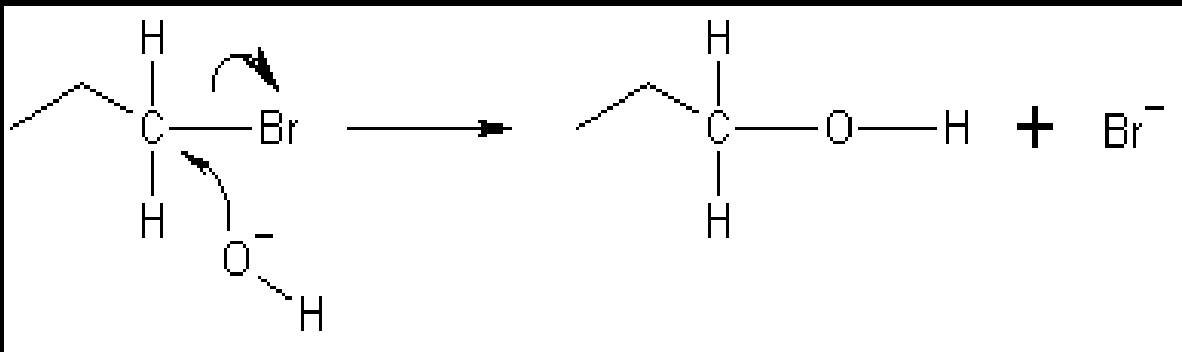
- adição nucleofílica

- Aldeídos são facilmente oxidados, cetonas não.

- Aldeídos são mais reativos em adições nucleofílicas do que cetonas.

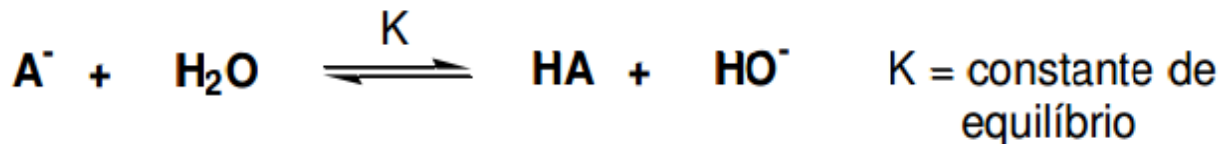
NUCLEÓFILO

- ✓ doa par de elétrons para um eletrófilo para formar uma ligação
- ✓ moléculas ou íons com um par de elétrons livre ou com uma ligação π
- ✓ são bases de Lewis



Basicidade vs nucleofilicidade

Basicidade é uma propriedade termodinâmica:



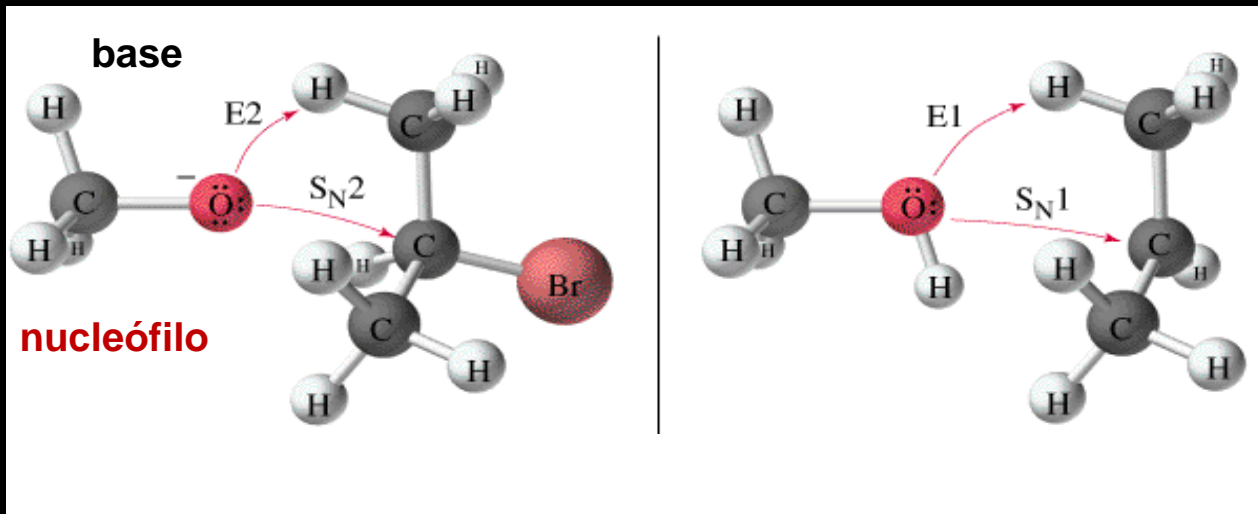
Nucleofilicidade: conceito cinético



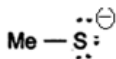
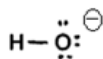
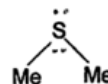
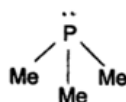
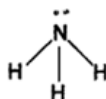
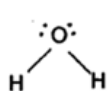
Bases fortes são tipicamente bons nucleófilos

NUCLEÓFILOS VS BASES

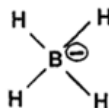
Misturas de produtos são comuns



ESPÉCIES NEUTRAS OU CARREGADAS NEGATIVAMENTE QUE POSSUAM
PAR ELETRÔNICO EM ORBITAL DE ALTA ENERGIA



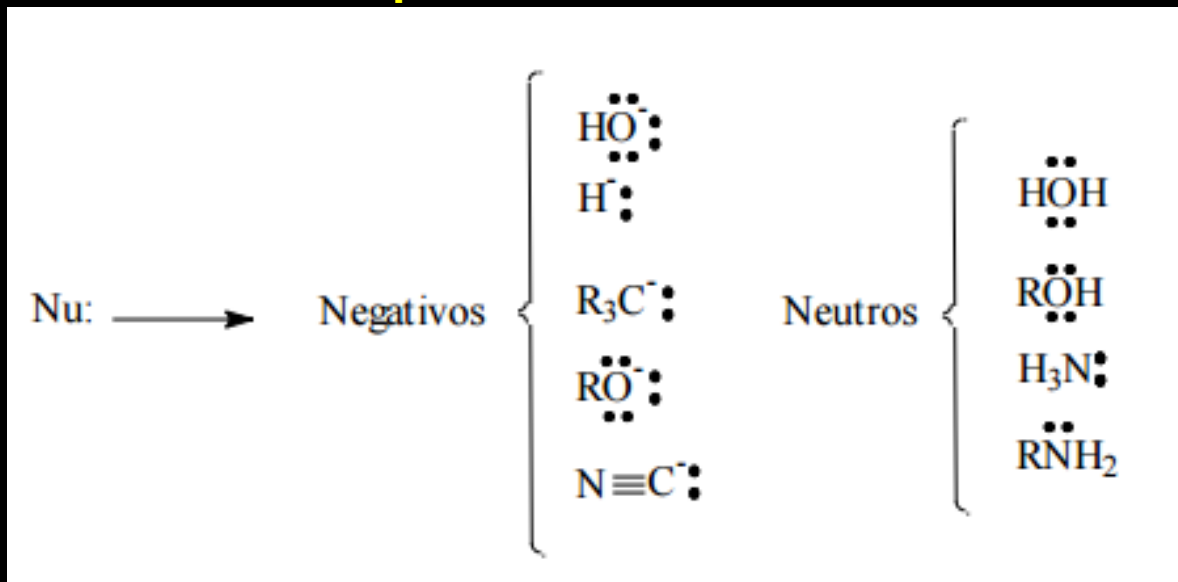
π



σ

Adição nucleofílica a aldeídos e cetonas

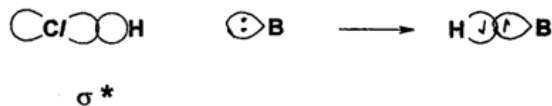
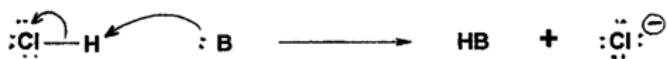
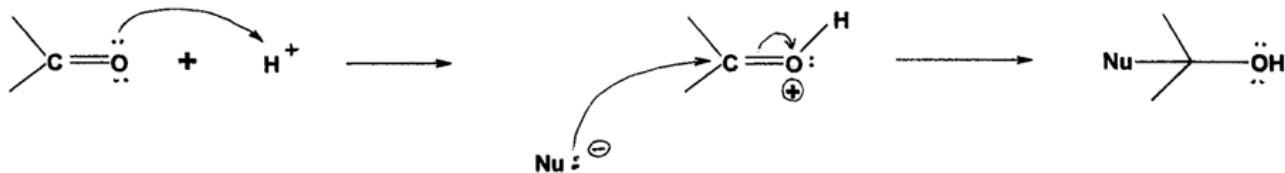
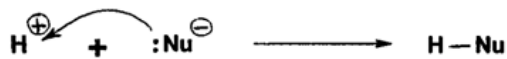
Exemplos de nucleófilos:



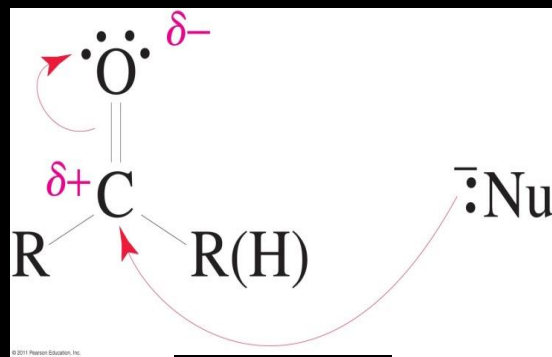
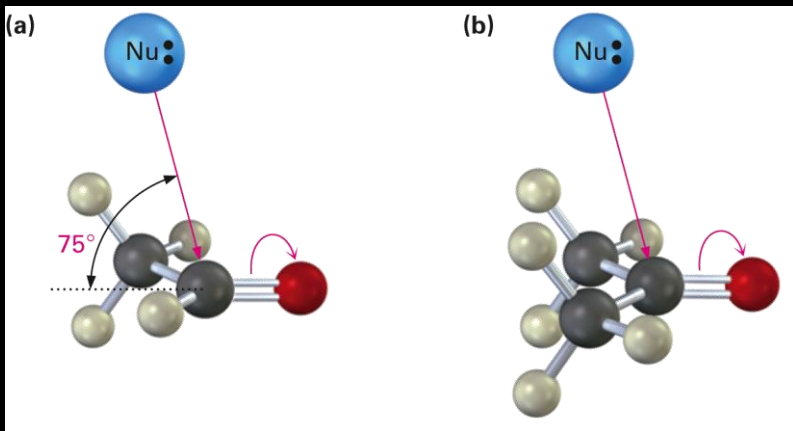
ESPÉCIES NEUTRAS OU CARREGADAS POSITIVAMENTE

COM UM ORBITAL VAZIO OU COM UM

ORBITAL ANTI-LIGANTE DE BAIXA ENERGIA

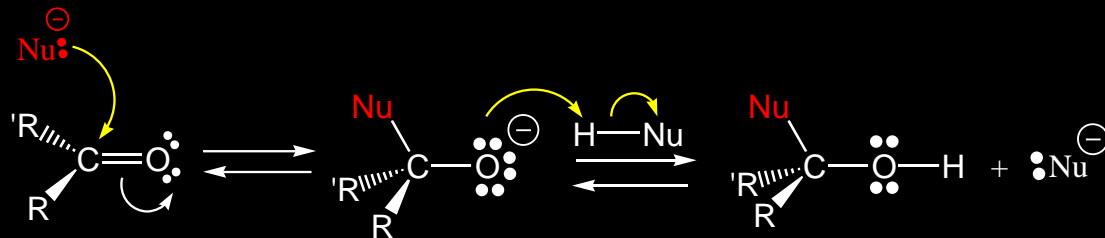


Adição nucleofílica a aldeídos e cetonas



Adição nucleofílica a aldeídos e cetonas

Esquema genérico

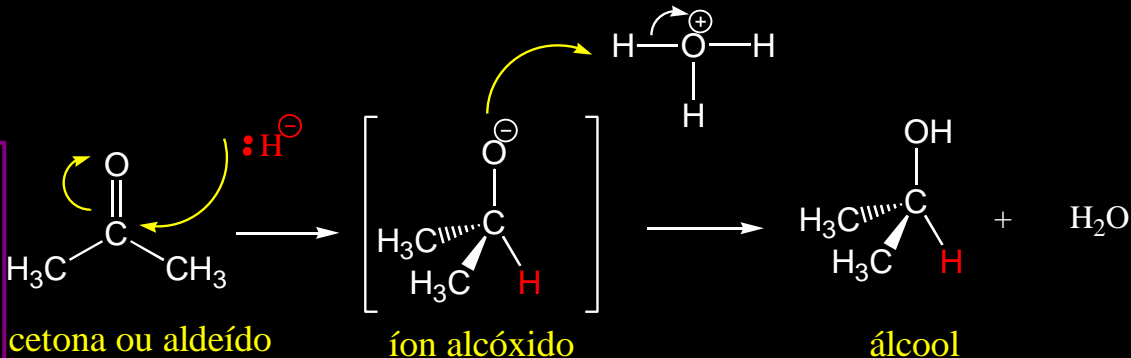


trigonal plano

intermediário tetraédrico

produto tetraédrico

Exemplo:
Reação com Hidreto

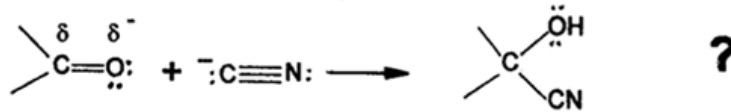


cetona ou aldeído

íon alcóxido

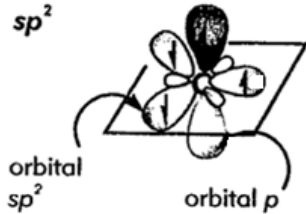
álcool

QUAL O MECANISMO DA REAÇÃO ?

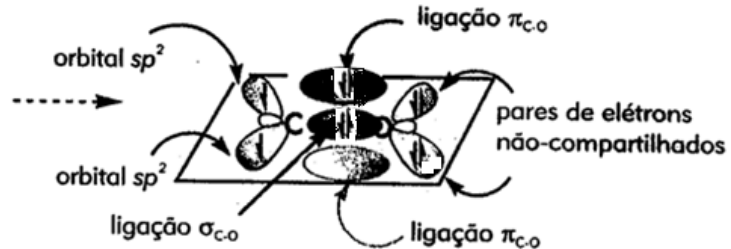
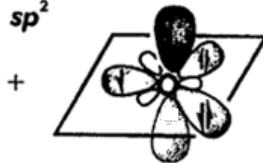


CONSIDEREMOS A ESTRUTURA ELETRÔNICA DO GRUPO CARBONILA

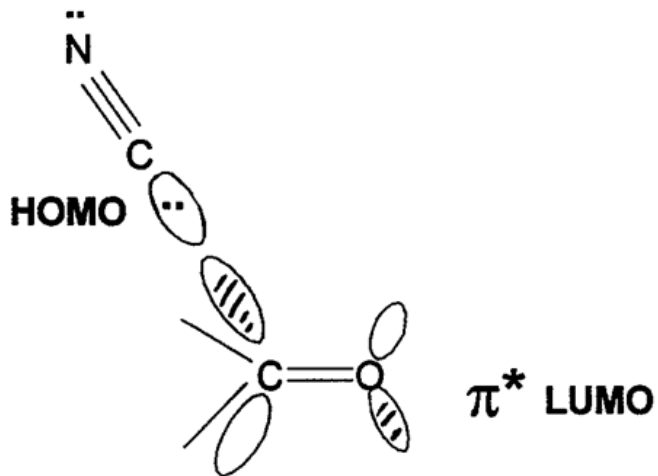
Carbono
 sp^2



Oxigênio
 sp^2

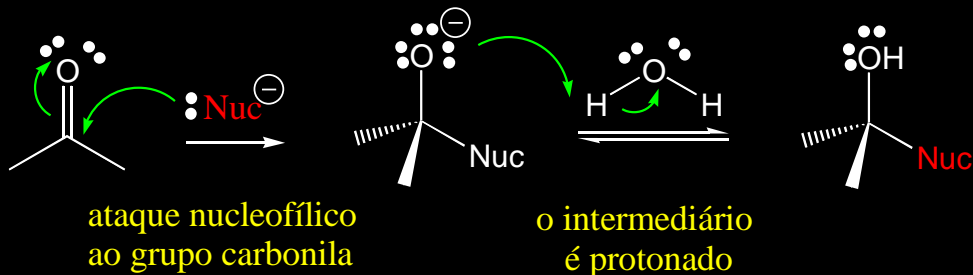


INTERAÇÃO ENTRE O ELETRÓFILO E O NUCLEÓFILO

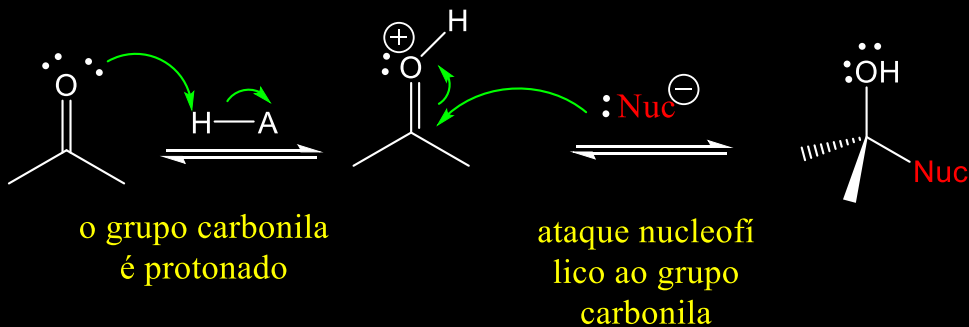


Adição nucleofílica a aldeídos e cetonas

Sob condições básicas

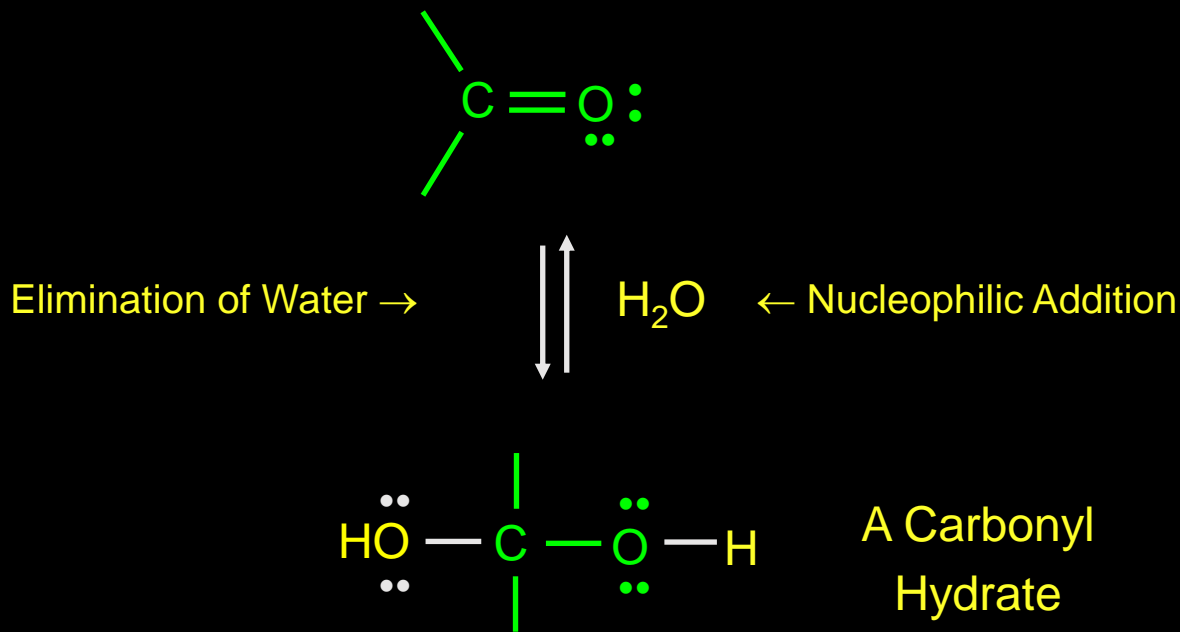


Sob condições ácidas

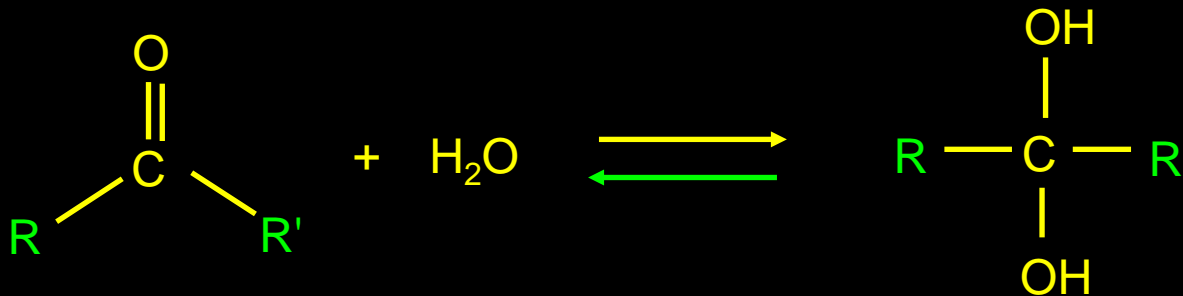


**Princípios da Adição Nucleofílica aos Grupos Carbonila:
Hidratação de Aldeídos e Cetonas**

Hidratação de Aldeídos e Cetonas



Efeito dos substituentes no equilíbrio da hidratação



compared to H

electronic:

alkyl groups stabilize
reactants

steric:

alkyl groups crowd
product

Constantes de Equilíbrio e Taxas Relativas de Hidratação

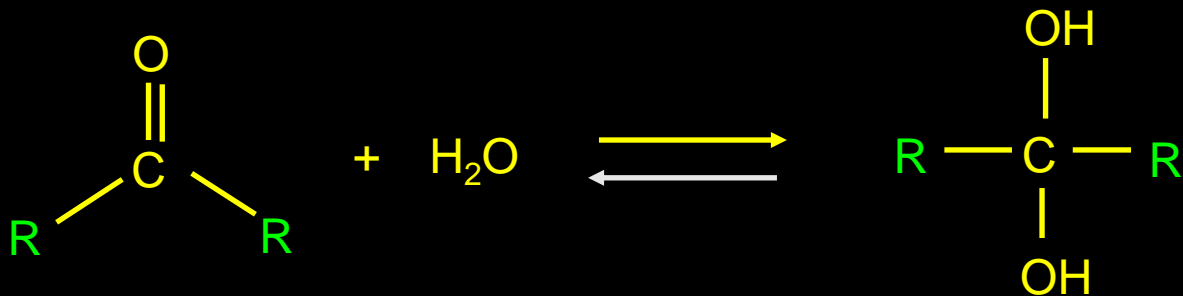
C=O	hydrate	K	%	Relative rate
$\text{CH}_2=\text{O}$	$\text{CH}_2(\text{OH})_2$	2300	>99.9	2200
$\text{CH}_3\text{CH}=\text{O}$	$\text{CH}_3\text{CH}(\text{OH})_2$	1.0	50	1.0
$(\text{CH}_3)_3\text{CCH}=\text{O}$	$(\text{CH}_3)_3\text{CCH}(\text{OH})_2$	0.2	17	0.09
$(\text{CH}_3)_2\text{C}=\text{O}$	$(\text{CH}_3)_2\text{C}(\text{OH})_2$	0.0014	0.14	0.0018

Quando o equilíbrio favorece o hidrato?

when carbonyl group is destabilized

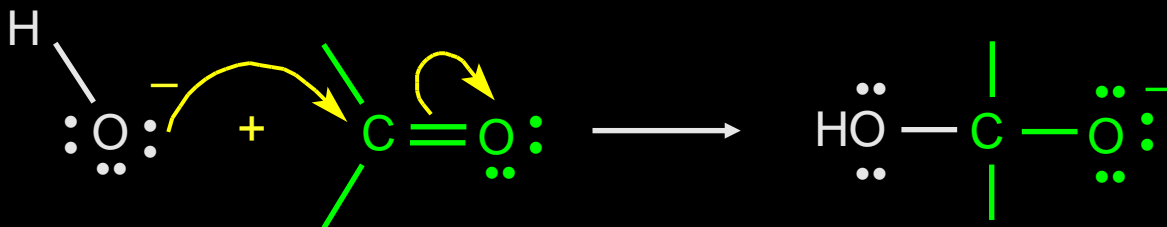
- alkyl groups stabilize C=O
- electron-withdrawing groups destabilize C=O

Efeito dos substituentes no equilíbrio da hidratação



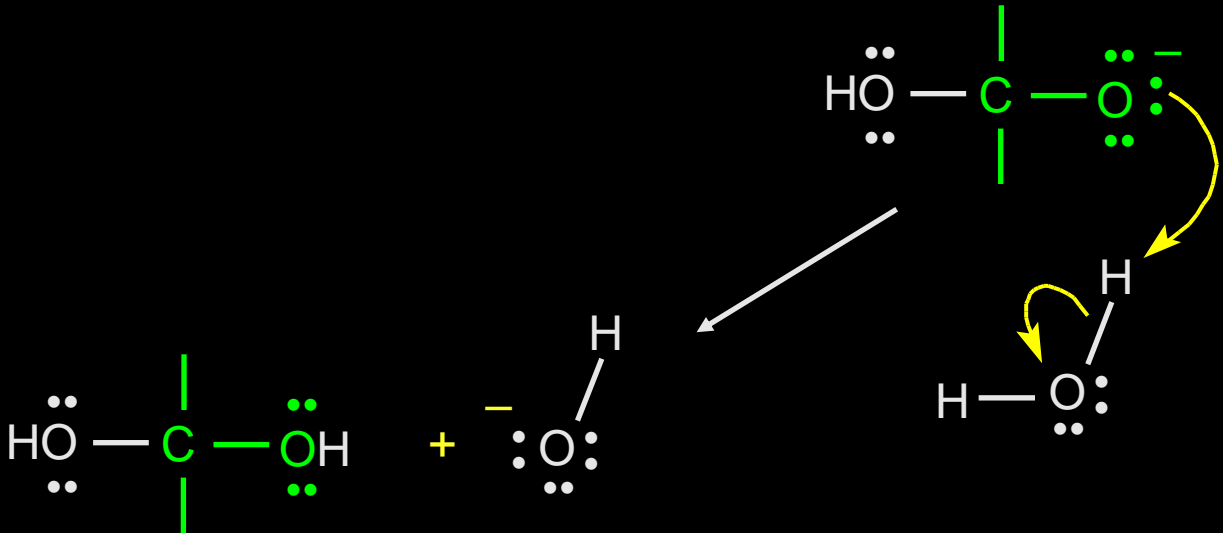
Mecanismo de Hidratação (catalisada por base)

Step 1:



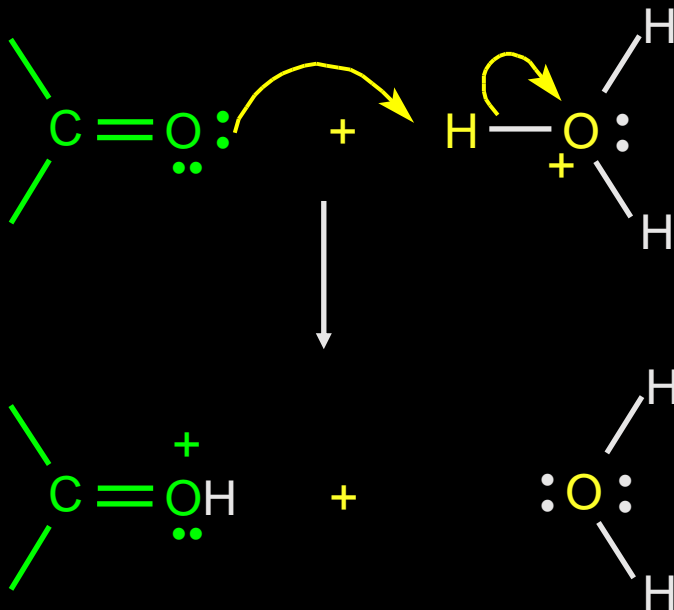
Mecanismo de Hidratação (base)

Step 2:



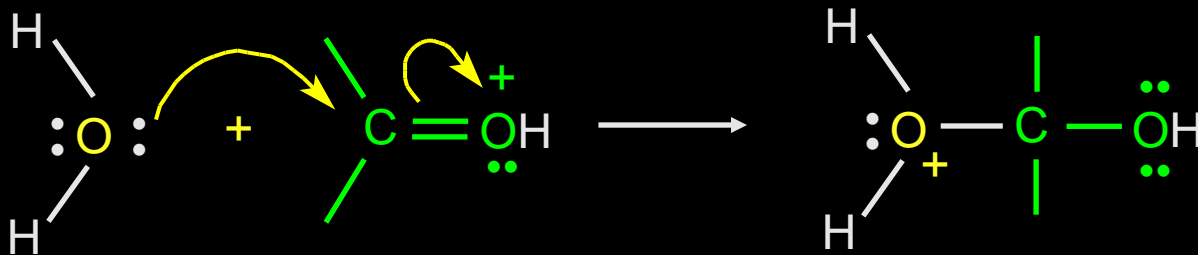
Mecanismo de Hidratação (catalisada por ácido)

Step 1:



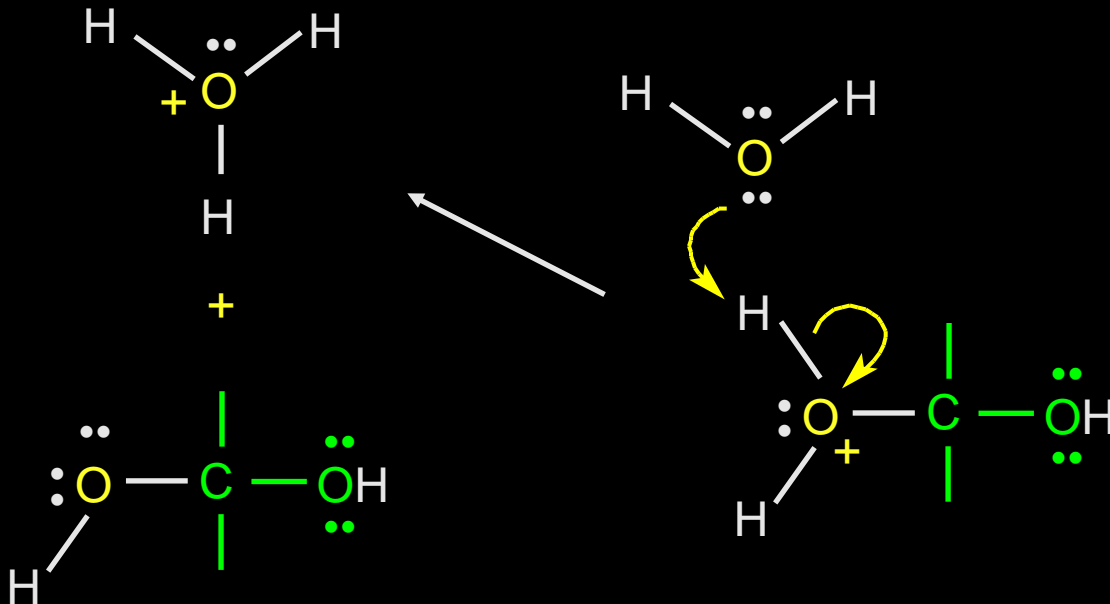
Mecanismo de Hidratação (catalisada por ácido)

Step 2:



Mecanismo de Hidratação (catalisada por ácido)

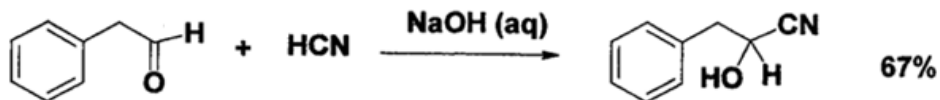
Step 3:



ADIÇÃO NUCLEOFÍLICA A ALDEÍDOS E CETONAS

A1. ADIÇÃO DE NUCLEÓFILOS DE CARBONO

A1.1. ADIÇÃO DE CIANETO



Ciano-hidrina

MECANISMO



GERAÇÃO DO NUCLEÓFILO

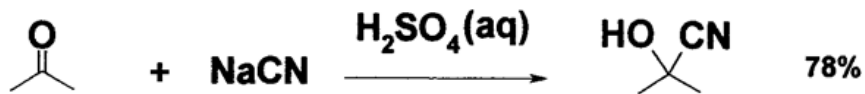


ATAQUE NUCLEOFÍLICO



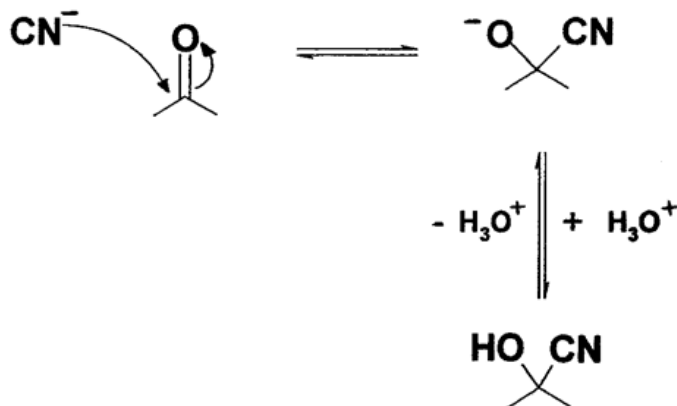
PROTONAÇÃO
REGENERAÇÃO
DA BASE

OUTRA METODOLOGIA

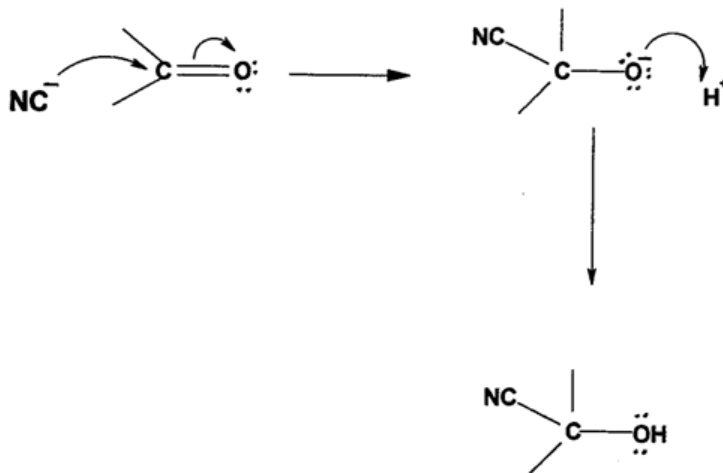


Ciano-hidrina

MECANISMO



OUTRA MANEIRA DE ESCREVER MECANISMOS DE REAÇÃO

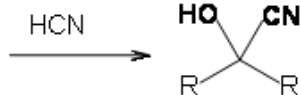
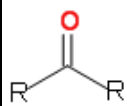


SETAS CURVAS

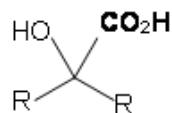
- MOVIMENTO DE ELÉTRONS
- SE DO HOMO PARA O LUMO
- OUTRA SETA PARA QUEBRA DA LIGAÇÃO
- SETA SOBRE O ÁTOMO QUE RECEBERÁ O PAR

IMPORTÂNCIA SINTÉTICA DA ADIÇÃO DE CIANETO A CARBONÍLICOS

Exemplo : Para R=CH₃

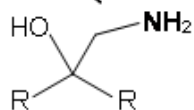


hidrólise

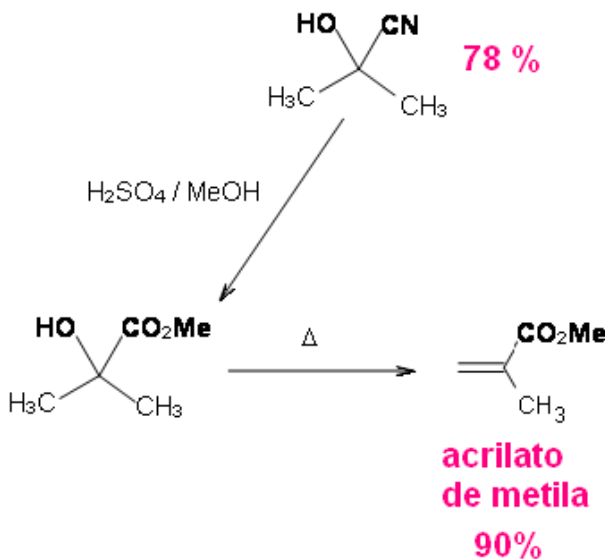


α-hidróxi ácidos

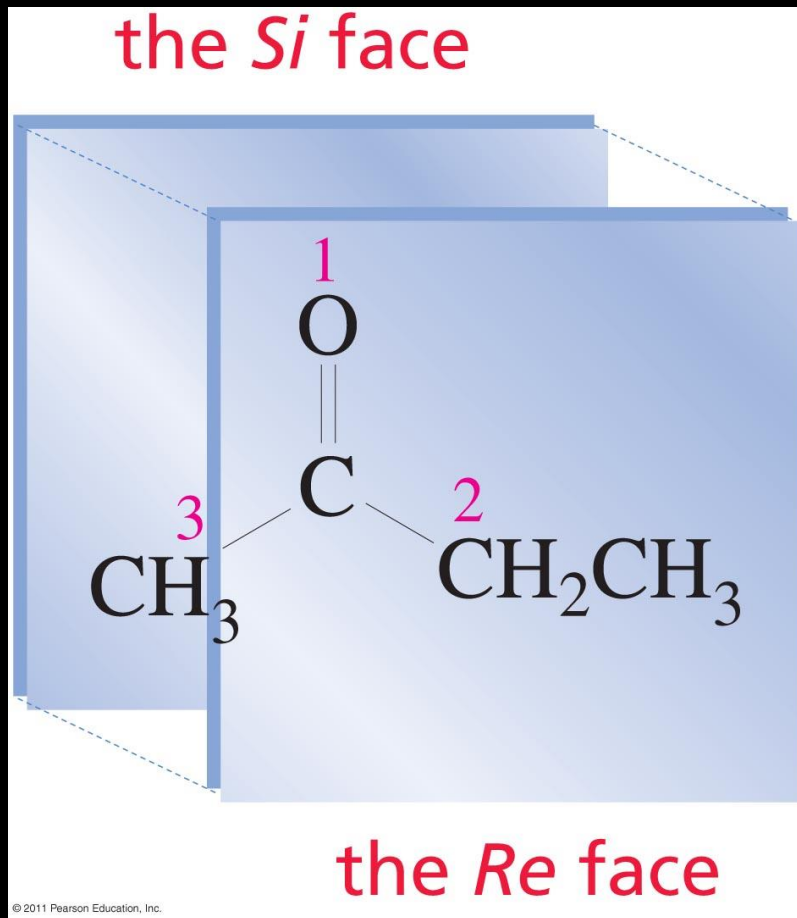
redução



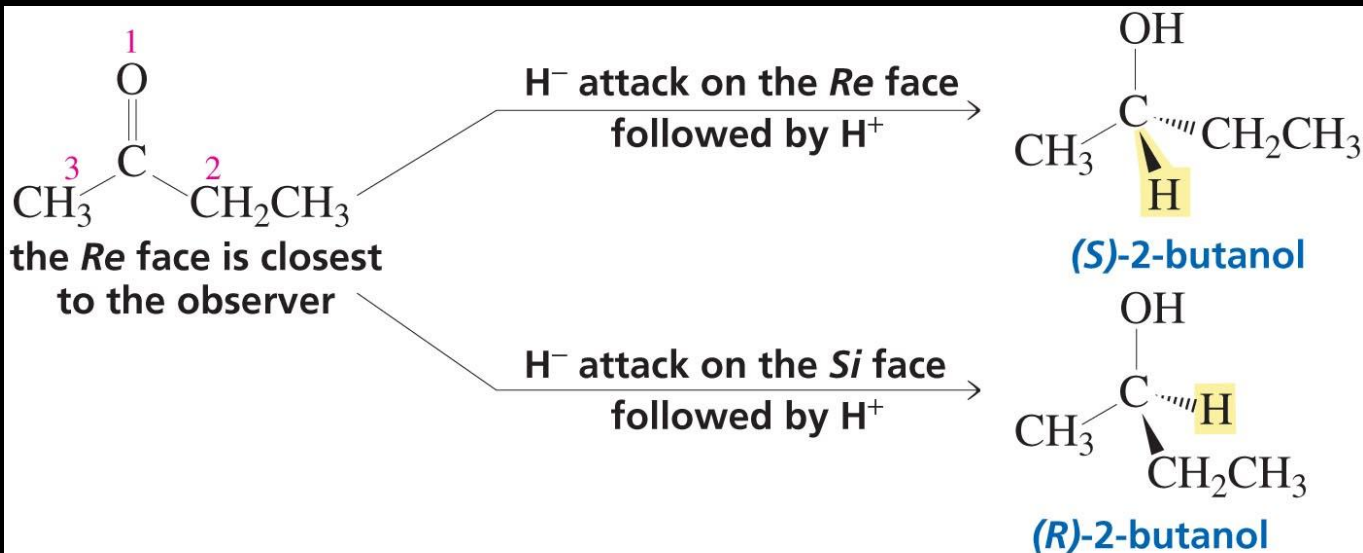
β-aminoálcoois



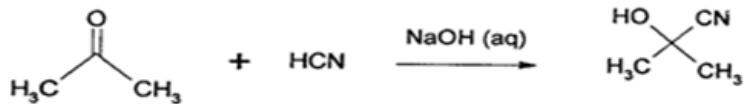
Estereoquímica da Reação de Adição Nucleofílica



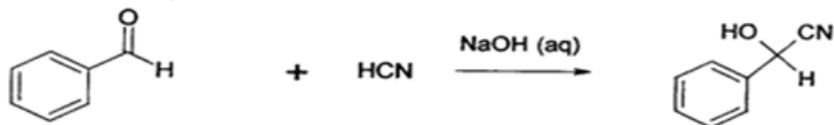
Estereoquímica da Reação de Adição Nucleofílica



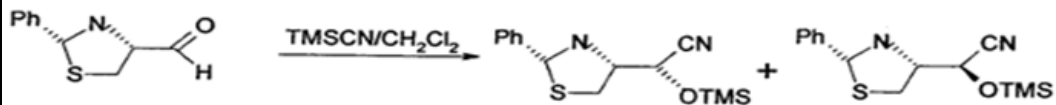
FATOS EXPERIMENTAIS



NÃO HÁ CENTRO ESTEREOGÊNICO



MISTURA RACÊMICA

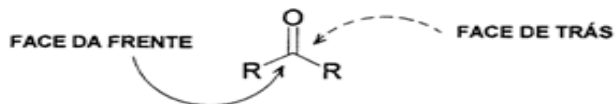


92

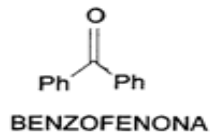
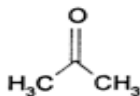
8

MISTURA DE DIASTEREISÔMEROS

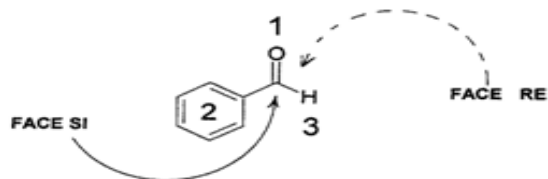
SÍNTESE ESTEREOSSELETIVA - PRINCÍPIOS



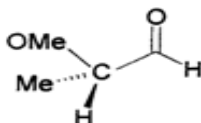
FACES HOMOTÓPICAS

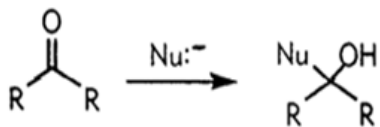


FACES ENANTIOTÓPICAS



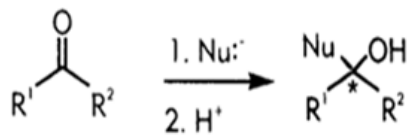
FACES DIASTEREOTÓPICAS





faces homotópicas

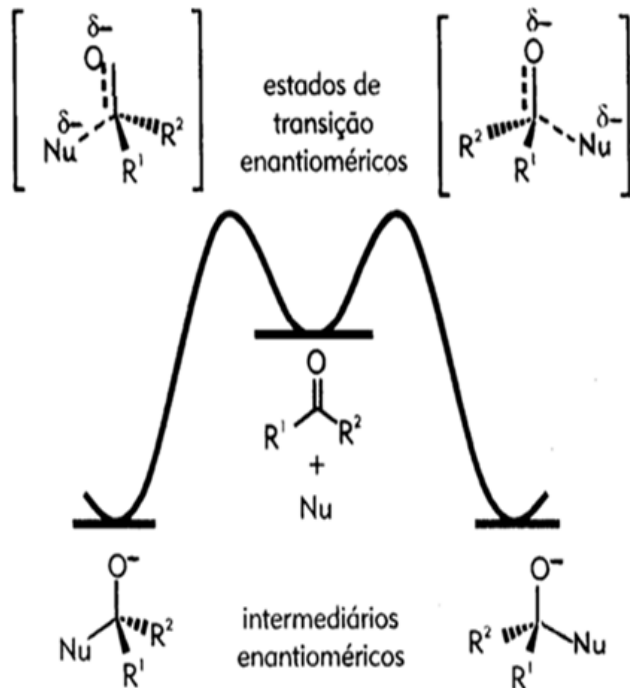
não há formação de centro estereogênico



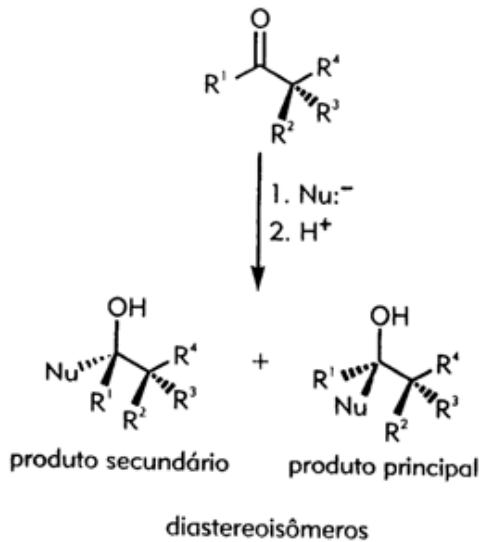
faces proquirais enantiotópicas

há formação de uma mistura racêmica

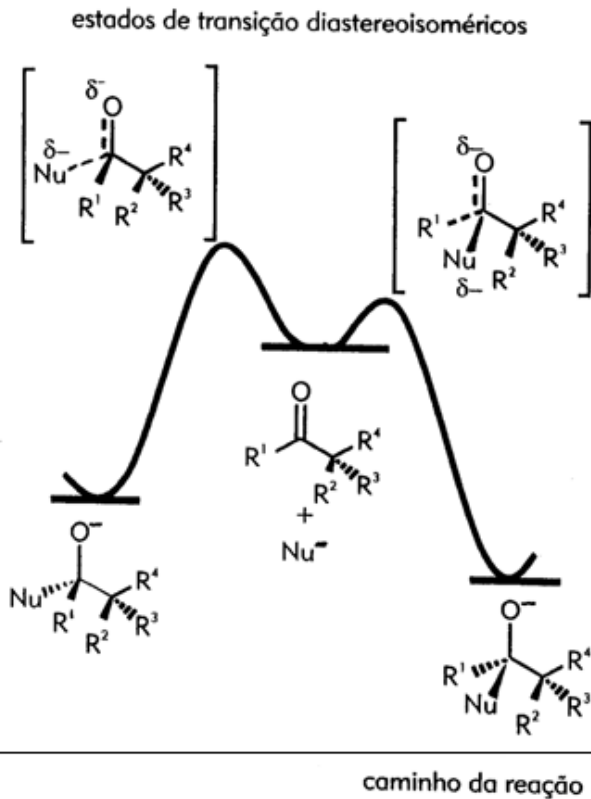
E



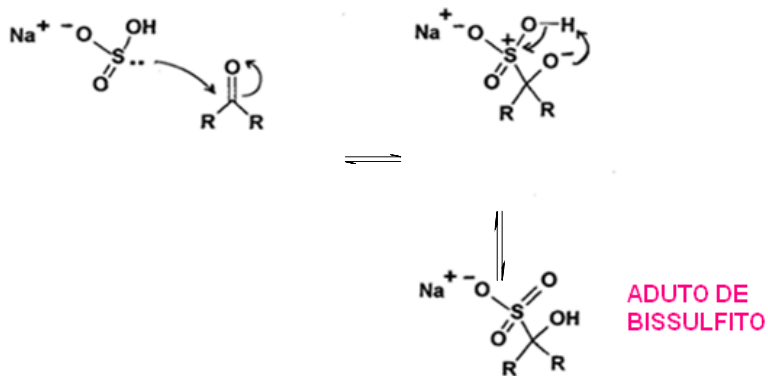
caminho da reação



E



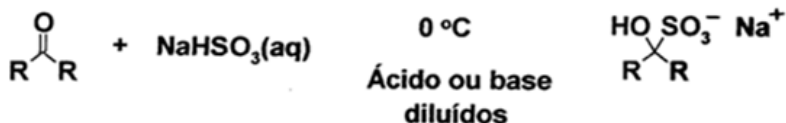
A2. ADIÇÃO DE BISSULFITO A COMPOSTOS CARBONÍLICOS



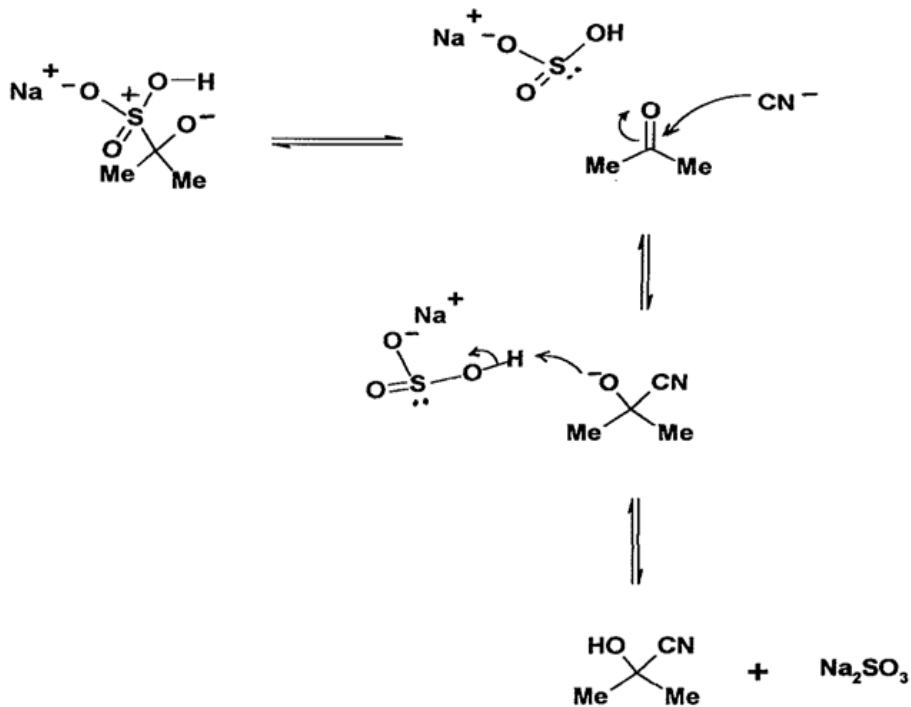
COMPOSTOS BISSULFÍTICOS

FREQUENTEMENTE ESTÁVEIS E CRISTALINOS

UTILIZADOS PARA PURIFICAR ALDEÍDOS



OUTRA UTILIDADE DE COMPOSTOS BISSULFÍTICOS

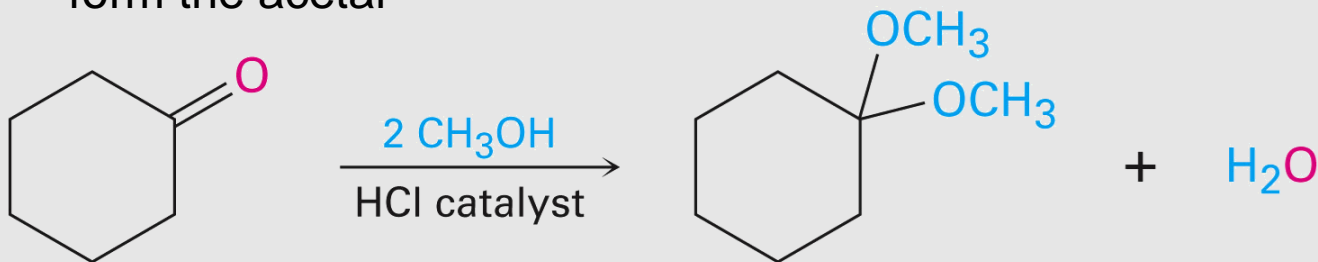


DISPENSA O USO DE ÁCIDO E, PORTANTO, SEM GERAÇÃO DE HCN

Nucleophilic Addition of Alcohols: Acetal Formation



- Alcohols are weak nucleophiles but acid promotes addition forming the conjugate acid of $C=O$
- Addition yields a hydroxy ether, called a hemiacetal (reversible); further reaction can occur
- Protonation of the $-OH$ and loss of water leads to an oxonium ion, $R_2C=OR^+$ to which a second alcohol adds to form the acetal



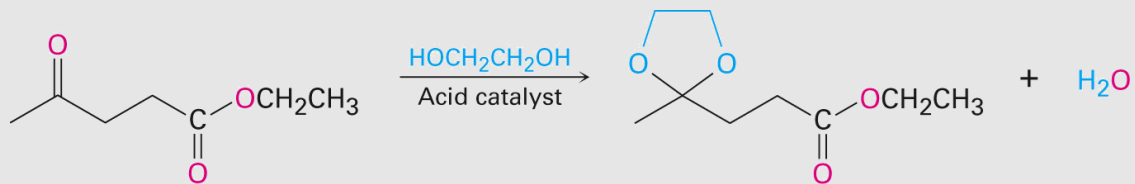
Cyclohexanone

**Cyclohexanone
dimethyl acetal**

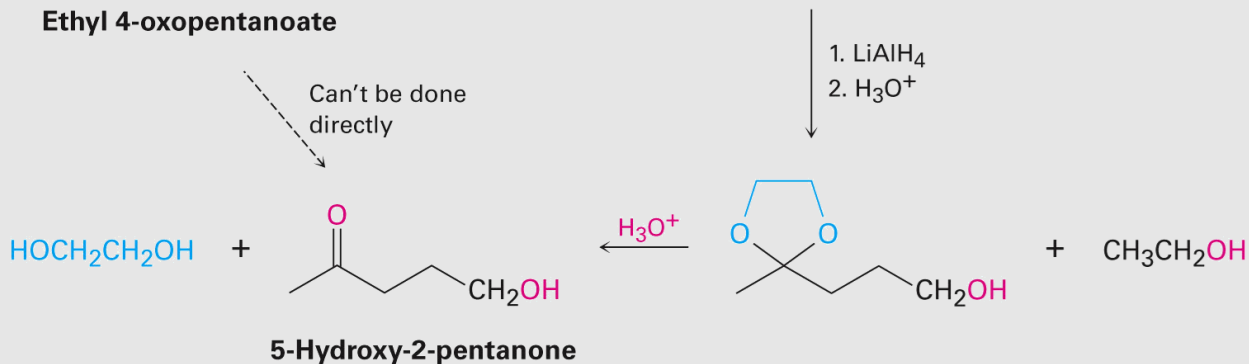


Uses of Acetals

- Acetals can serve as protecting groups for aldehydes and ketones
- It is convenient to use a diol to form a *cyclic* acetal (the reaction goes even more readily)

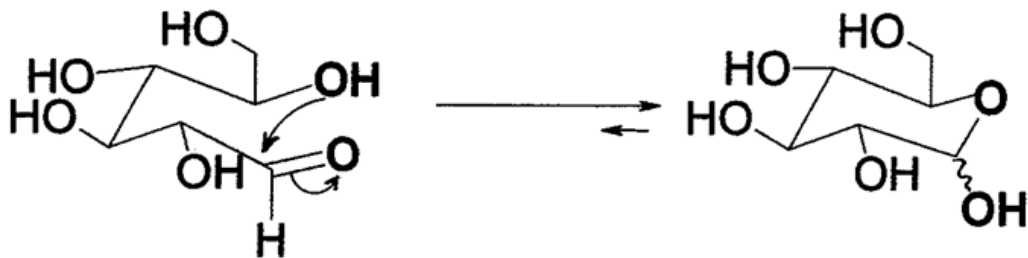


Ethyl 4-oxopentanoate

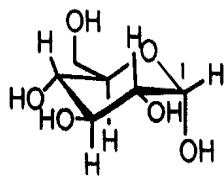
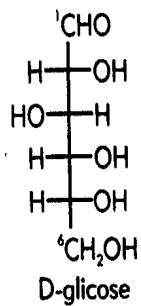


HEMICETAIS CÍCLICOS

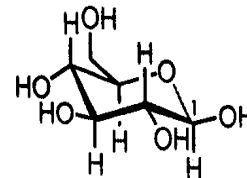
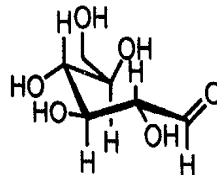
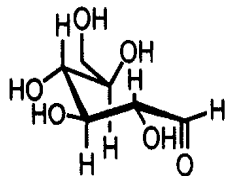
ESTÁVEIS COM ANÉIS DE CINCO OU SEIS MEMBROS



MISTURA DE EPÍMEROS



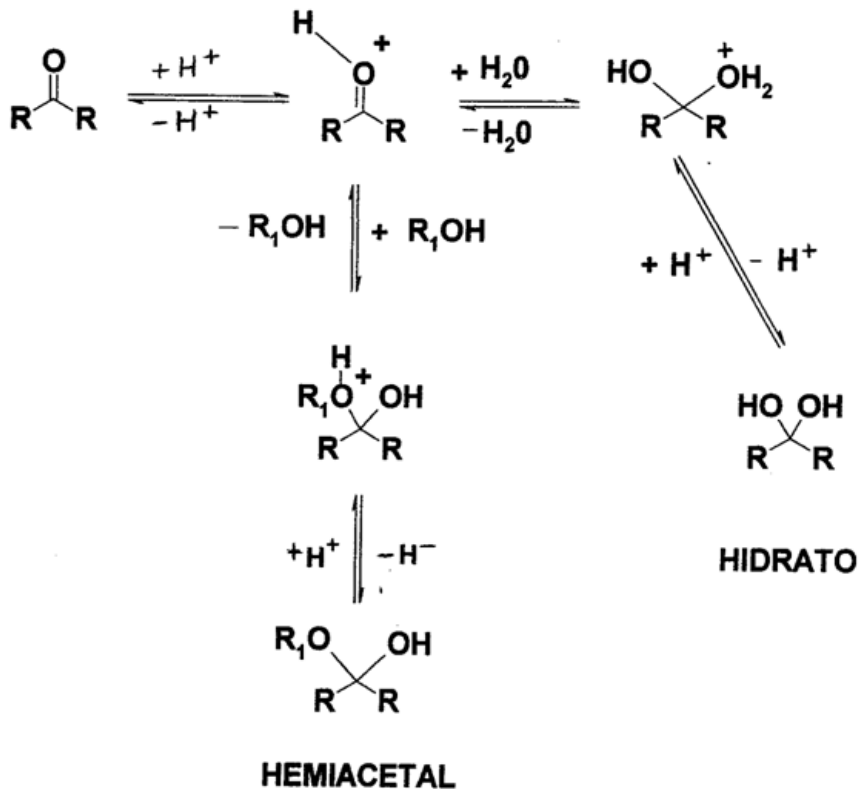
α -D-glicose
 $[\alpha]_D = +112$
 36%



conformeros da D-glicose

β -D-glicose
 $[\alpha]_D = +18,7$
 64%

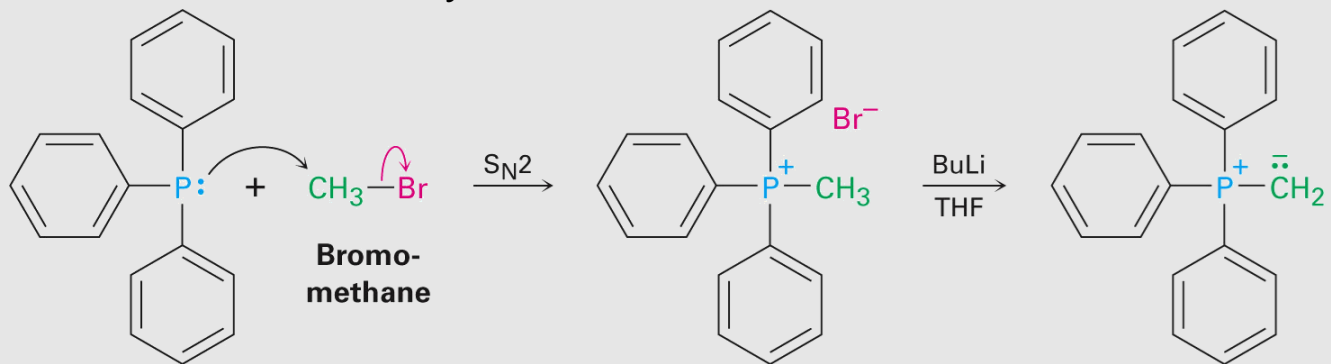
FORMAÇÃO DE HIDRATOS E HEMIIACETAIS SOB CATÁLISE ÁCIDA



Nucleophilic Addition of Phosphorus Ylides: The Wittig Reaction



- The sequence converts $C=O$ to $C=C$
- A phosphorus *ylide* adds to an aldehyde or ketone to yield a dipolar intermediate called a *betaine*
- The intermediate spontaneously decomposes through a four-membered ring to yield alkene and triphenylphosphine oxide, $(Ph)_3P=O$
- Formation of the ylide is shown below



Triphenylphosphine

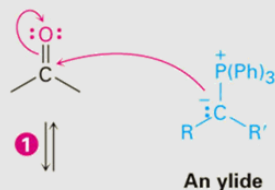
Methyltriphenylphosphonium bromide

Methylenetriphenylphosphorane

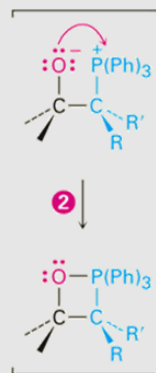
Mechanism of the Wittig Reaction



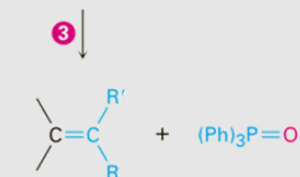
- 1 The nucleophilic carbon atom of the phosphorus ylide adds to the carbonyl group of a ketone or aldehyde to give an alkoxide ion intermediate.



- 2 The alkoxide ion then undergoes intramolecular O-P bond formation to produce a four-membered ring . . .



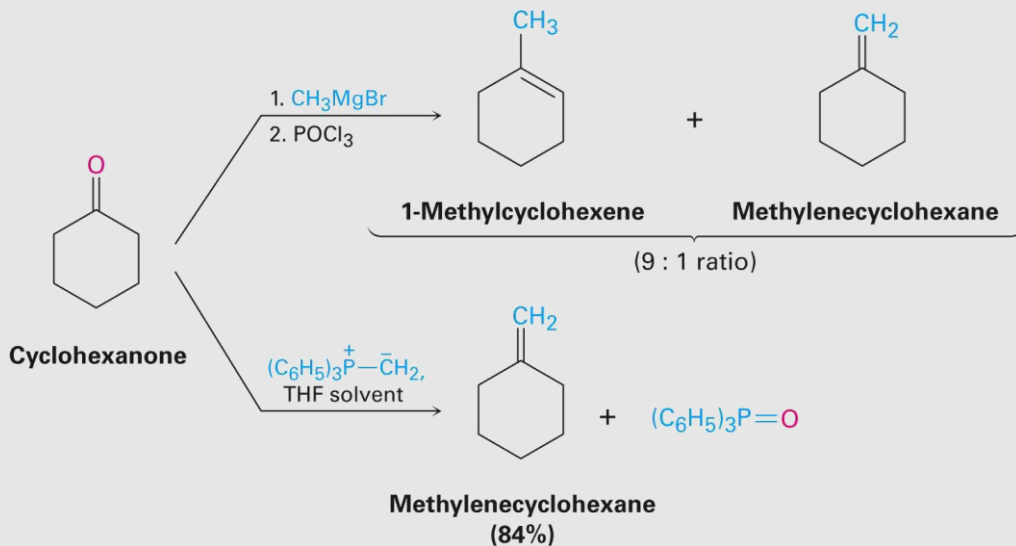
- 3 . . . which spontaneously decomposes to give an alkene and triphenylphosphine oxide.



Uses of the Wittig Reaction



- Can be used for monosubstituted, disubstituted, and trisubstituted alkenes but not tetrasubstituted alkenes
The reaction yields a pure alkene of known structure
- For comparison, addition of CH_3MgBr to cyclohexanone and dehydration with, yields a mixture of two alkenes

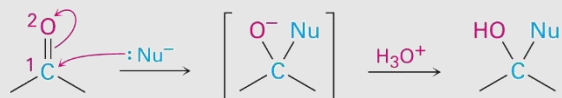


Conjugate Nucleophilic Addition to α,β -Unsaturated Aldehydes and Ketones

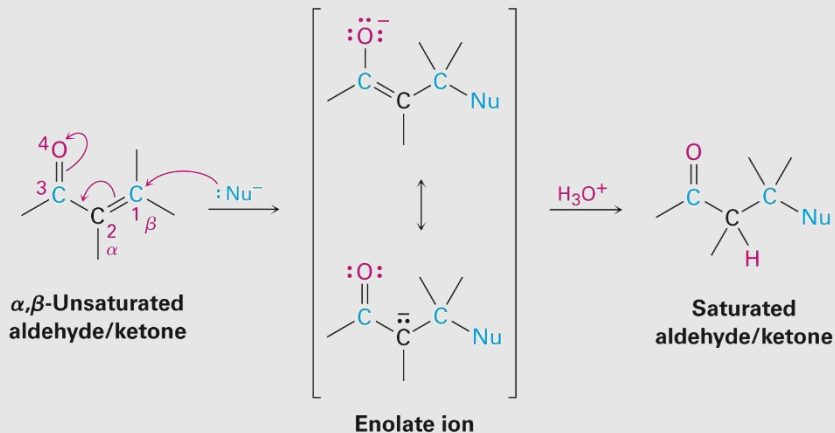


- A nucleophile can add to the $C=C$ double bond of an α,β -unsaturated aldehyde or ketone (conjugate addition, or 1,4 addition)
- The initial product is a resonance-stabilized enolate ion, which is then protonated

Direct (1,2) addition



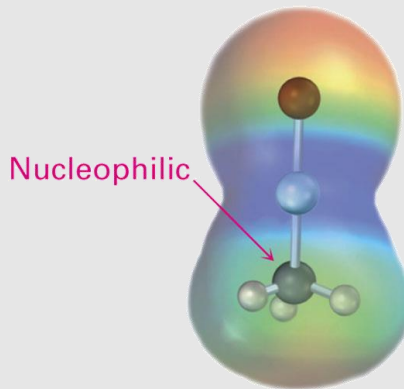
Conjugate (1,4) addition



Nucleophilic Addition of Grignard Reagents and Hydride Reagents: Alcohol Formation



- Treatment of aldehydes or ketones with Grignard reagents yields an alcohol
 - Nucleophilic addition of the equivalent of a *carbon* anion, or **carbanion**. A carbon–magnesium bond is strongly polarized, so a Grignard reagent reacts for all practical purposes as $R: - MgX^+$.



**Methylmagnesium
chloride**

Mechanism of Addition of Grignard Reagents

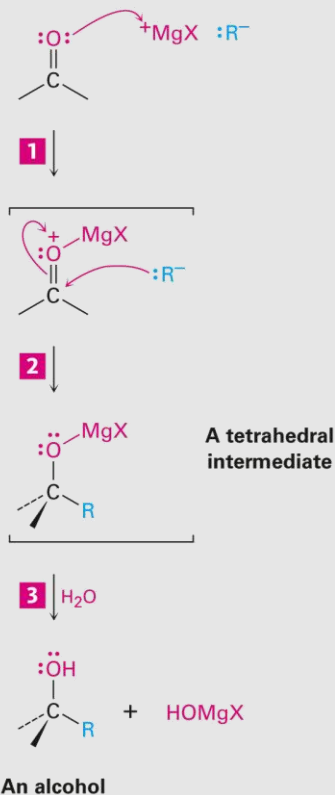


- Complexation of $C=O$ by Mg^{2+} , Nucleophilic addition of R^- , protonation by dilute acid yields the neutral alcohol
- Grignard additions are irreversible because a carbanion is not a leaving group

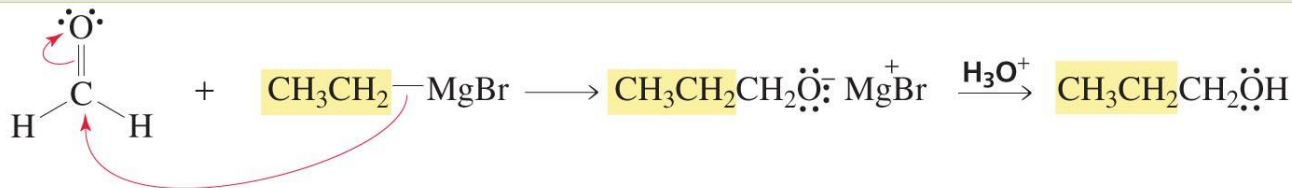
1 The Lewis acid Mg^{2+} first forms an acid-base complex with the basic oxygen atom of the aldehyde or ketone, thereby making the carbonyl group a better acceptor.

2 Nucleophilic addition of an alkyl group R^- to the aldehyde or ketone produces a tetrahedral magnesium alkoxide intermediate . . .

3 . . . which undergoes hydrolysis when water is added in a separate step. The final product is a neutral alcohol.



Grignard reagents are used to prepare alcohols:



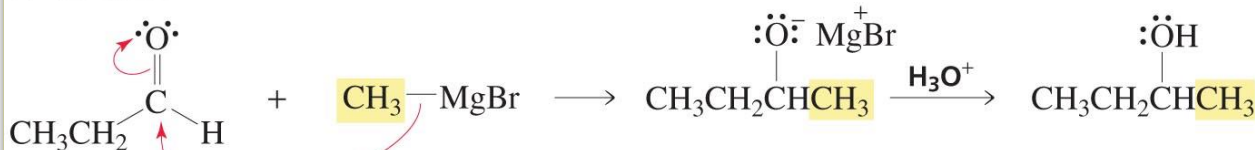
formaldehyde

ethylmagnesium
bromide

an alkoxide ion

1-propanol
a primary alcohol

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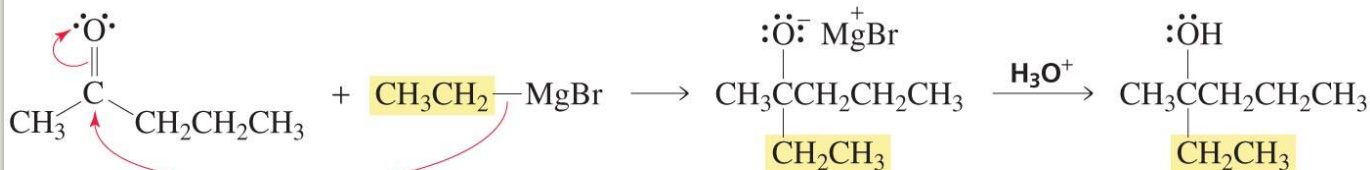


propanal

methylmagnesium
bromide

2-butanol
a secondary alcohol

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2-pentanone

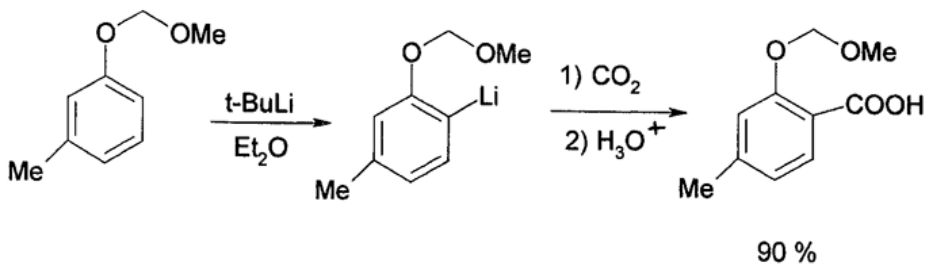
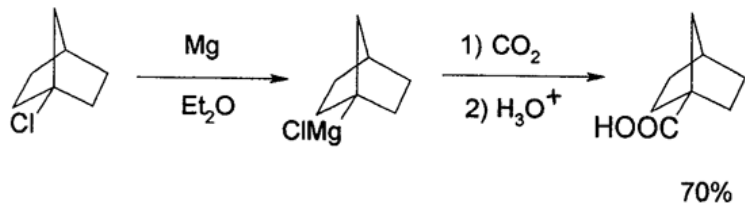
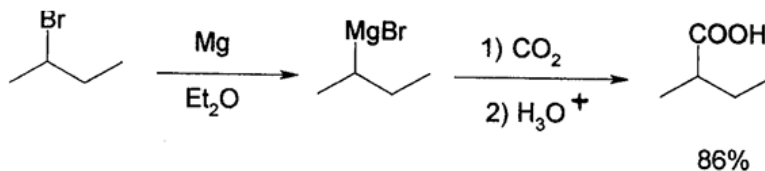
ethylmagnesium
bromide

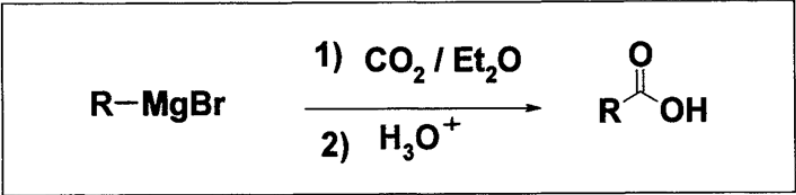
3-methyl-3-hexanol
a tertiary alcohol

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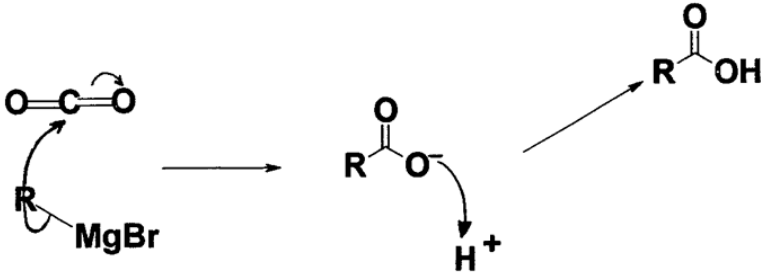
A.6. ADIÇÃO DE COMPOSTOS ORGANOMETÁLICOS A CARBONÍLICOS

PREPARANDO ÁCIDOS CARBOXÍLICOS



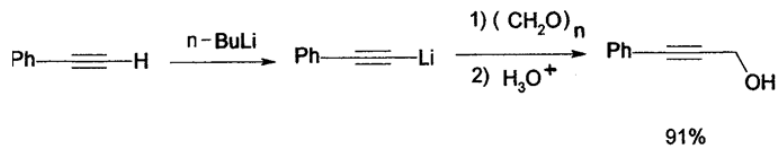
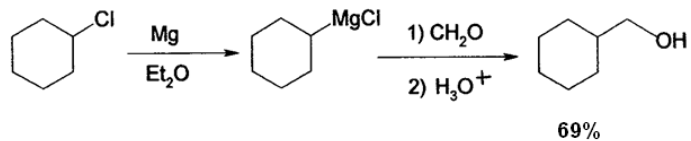


MECANISMO



PREPARANDO ÁLCOOIS PRIMÁRIOS

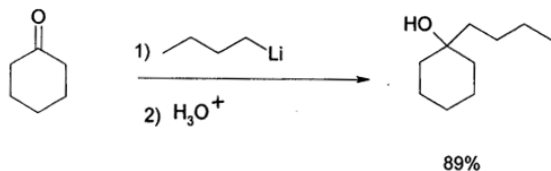
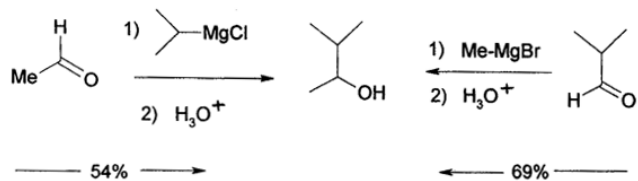
ORGANOMETÁLICO + FORMALDEÍDO



PREPARAÇÃO DE ÁLCOOS SECUNDÁRIOS E TERCIÁRIOS

ORGANOMÉTALICO + ACETALDEÍDO = ÁLCOOL SECUNDÁRIO

ORGANOMÉTALICO + CETONA = ÁLCOOL TERCIÁRIO



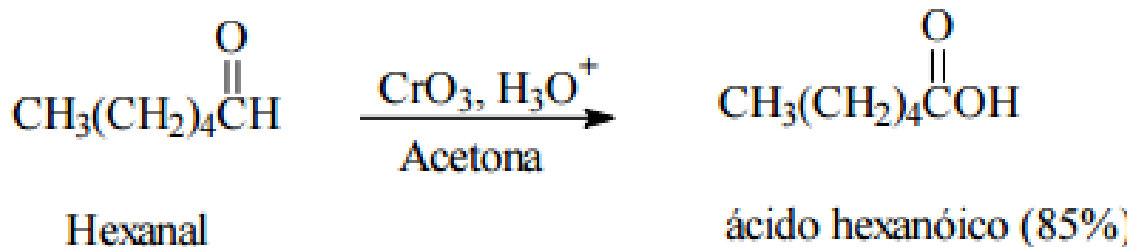
Oxidação de aldeídos e cetonas

Aldeídos: facilmente oxidados para produzir os ácidos carboxílicos

Cetonas: normalmente inertes à oxidação

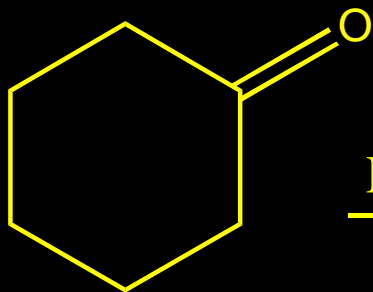
Diferença: **aldeídos** têm um hidrogênio ($-CHO$) que pode ser abstraído como próton durante a oxidação, mas a **cetona** não

Oxidação de aldeídos e cetonas

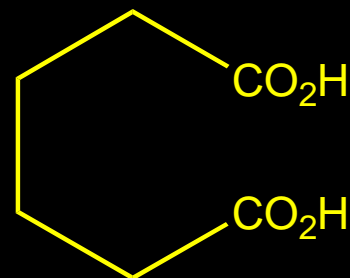
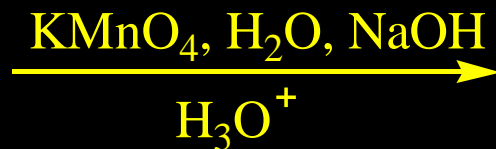


CrO_3 em ácido aquoso: oxidação rápida, à temperatura ambiente e com bom rendimento.

Outros agentes oxidantes: KMnO_4 , HNO_3 a quente



ciclo-hexanona



ácido hexanodióico

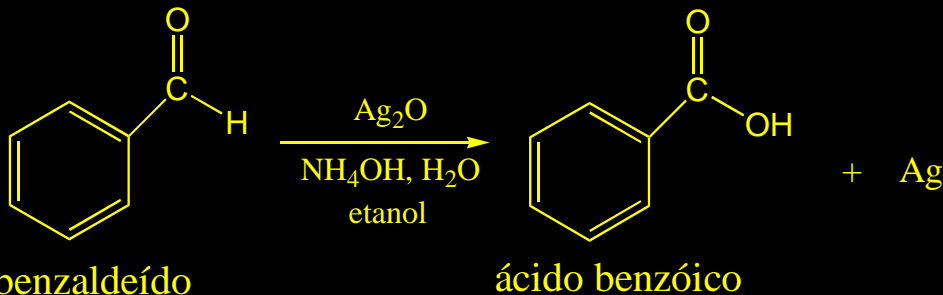
Fonte:

http://www.esalq.usp.br/departamentos/lce/arquivos/aulas/2016/LCE0118/quimica_organica.pdf

Oxidação de aldeídos e cetonas

Desvantagens da oxidação com CrO_3 : condições ácidas, podem ocorrer reações laterais.

Alternativa: óxido de prata, Ag_2O , em amônia aquosa = **reagente de Tollens**.



Espelho de prata