FCF 101-2020 Química Orgânica II

Reações nos carbonos α de compostos carbonílicos

Enois e enolatos

Adição/condensação aldólica

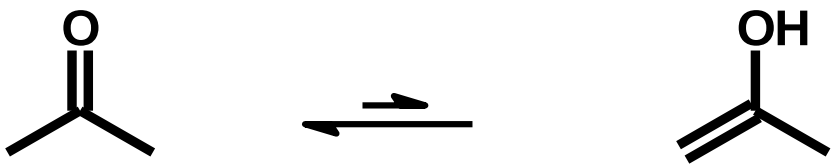
Condensação de Claisen

Reações nos carbonos de α-compostos carbonílicos

1. Acidez dos hidrogênios α
2. Tautomeria ceto-enólica
3. Halogenação de carbonos α de aldeídos e cetonas
4. Alquilação nos carbonos α
5. Reação de Michael (adições conjugadas aos compostos carbonílicos α,β-insaturados
6. Adição de aldol
7. Condensação de Claisen
8. Condensações Intramoleculares

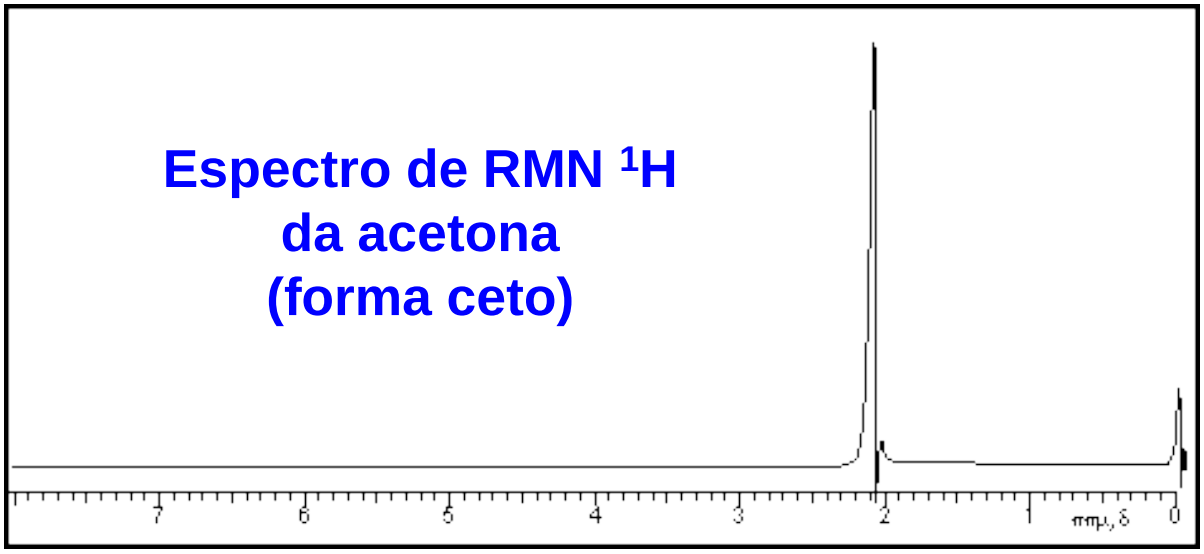
Tautomeria ceto-enólica em compostos carbonílicos

forma ceto **forma enólica**

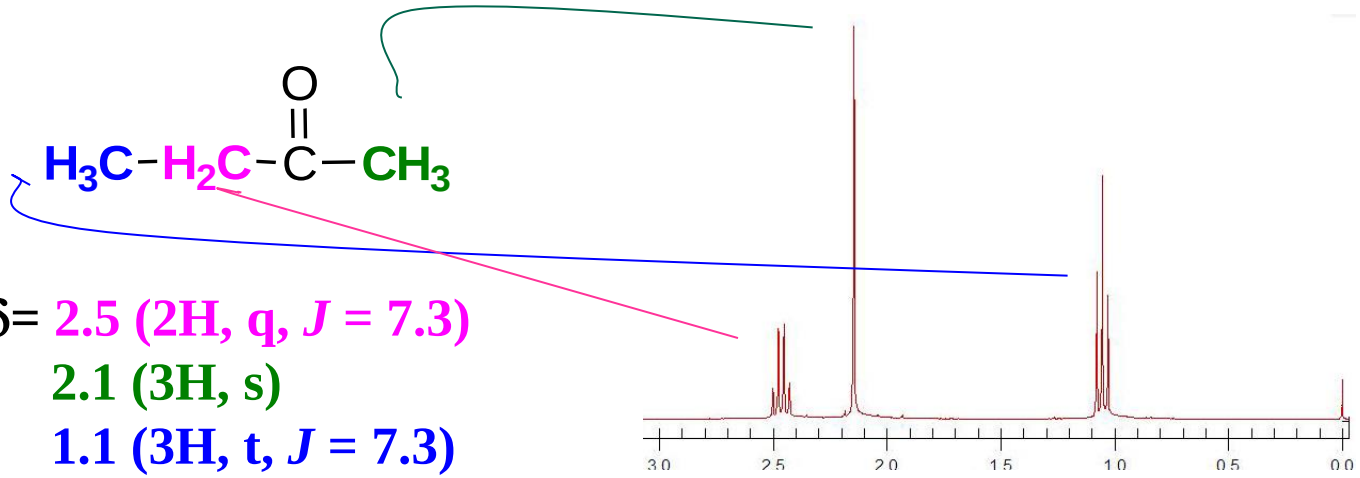


>99.9% **<0.1**

Espectro de RMN ^{1}H da acetona (forma ceto)



A RMN de ^{1}H fornece evidências indiretas da presença da função carbonila e de maior acidez de α-hidrogênios

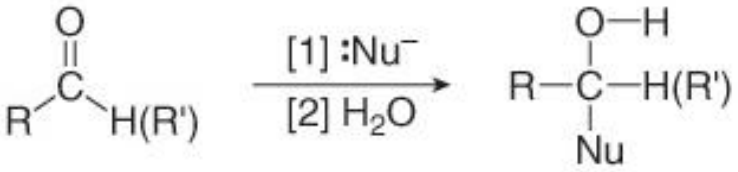


δ= 2.5 (2H, q, *J* = 7.3)
2.1 (3H, s)
1.1 (3H, t, *J* = 7.3)

desprotegido
(menor densidade de elétrons)

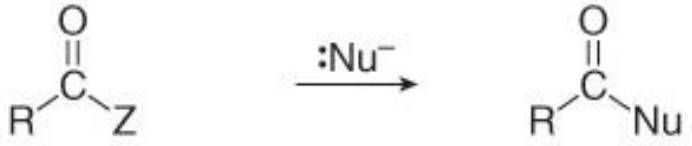
Reações características de compostos carbonílicos

Nucleophilic addition—General reaction



H and Nu are added.

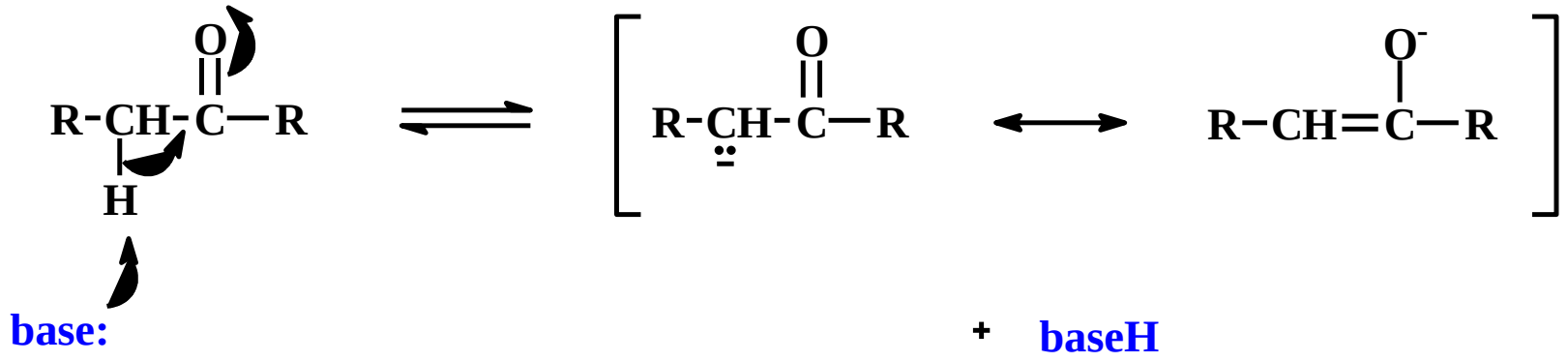
Nucleophilic substitution—General reaction



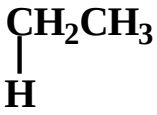
Nu replaces Z.

Z = OH, Cl, OR, NH_2

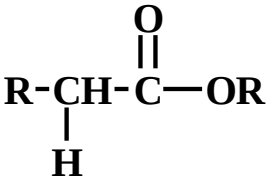
Uma outra possibilidade de reação na posição alfa de compostos carbonílicos:



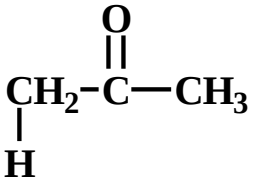
Acidez de hidrogênios α–carbonílicos



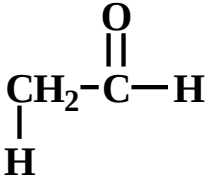
pKa 50



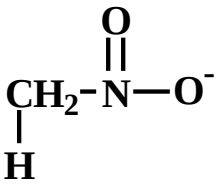
25



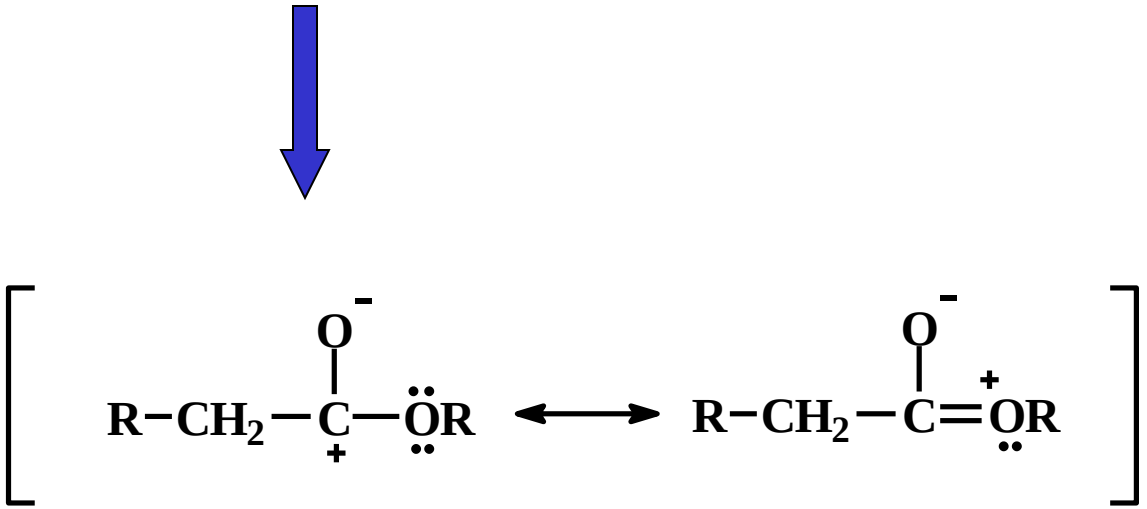
20



17



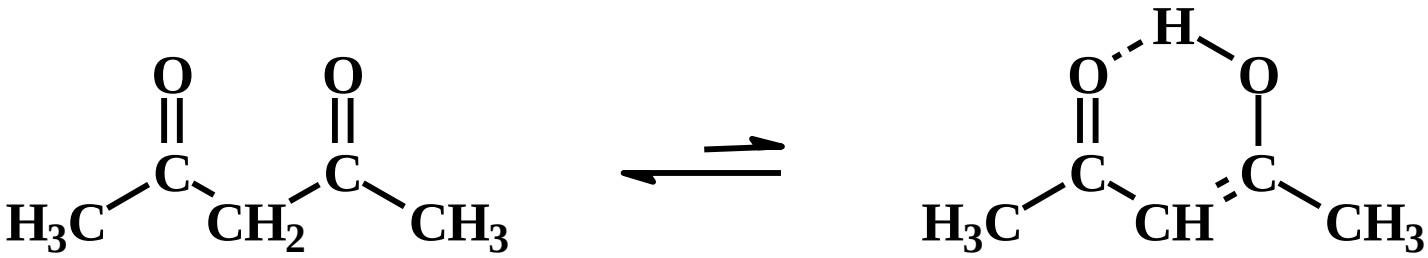
8,6



Tautomeria ceto-enólica

> 99,9%

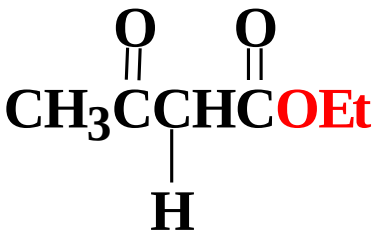
< 0,01%



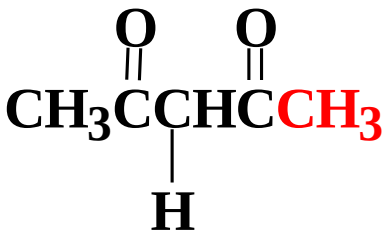
85%

15%

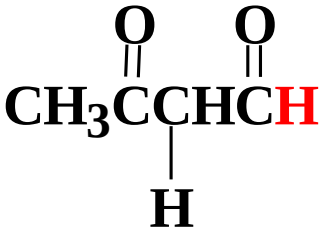
Acidez dos hidrogênios α de compostos β-dicarbonílicos



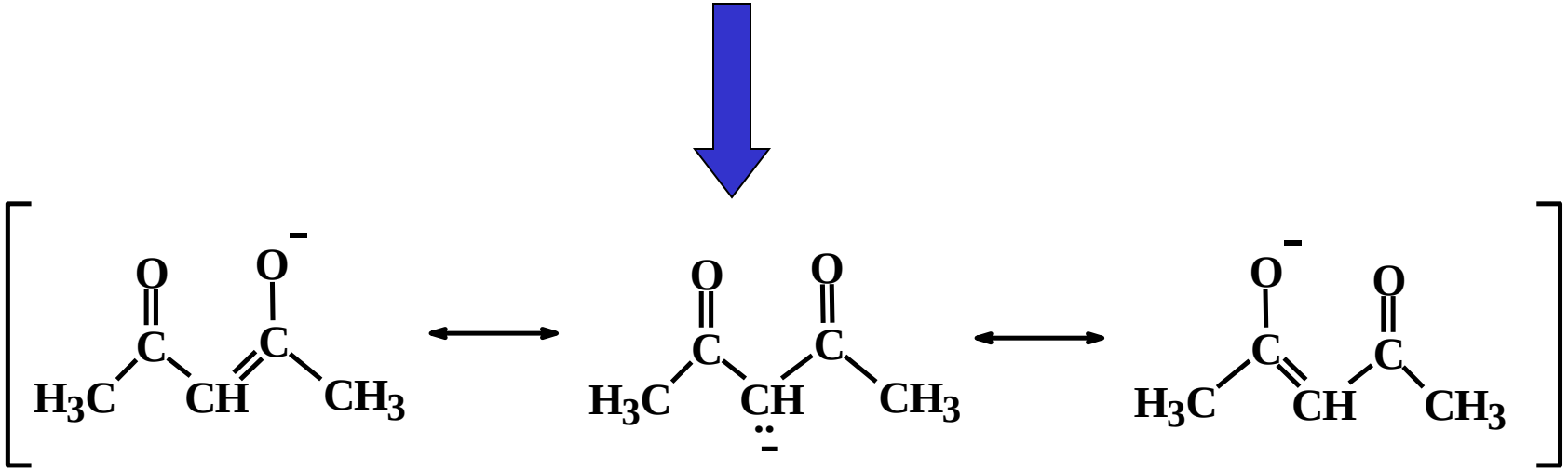
pKa 10,7

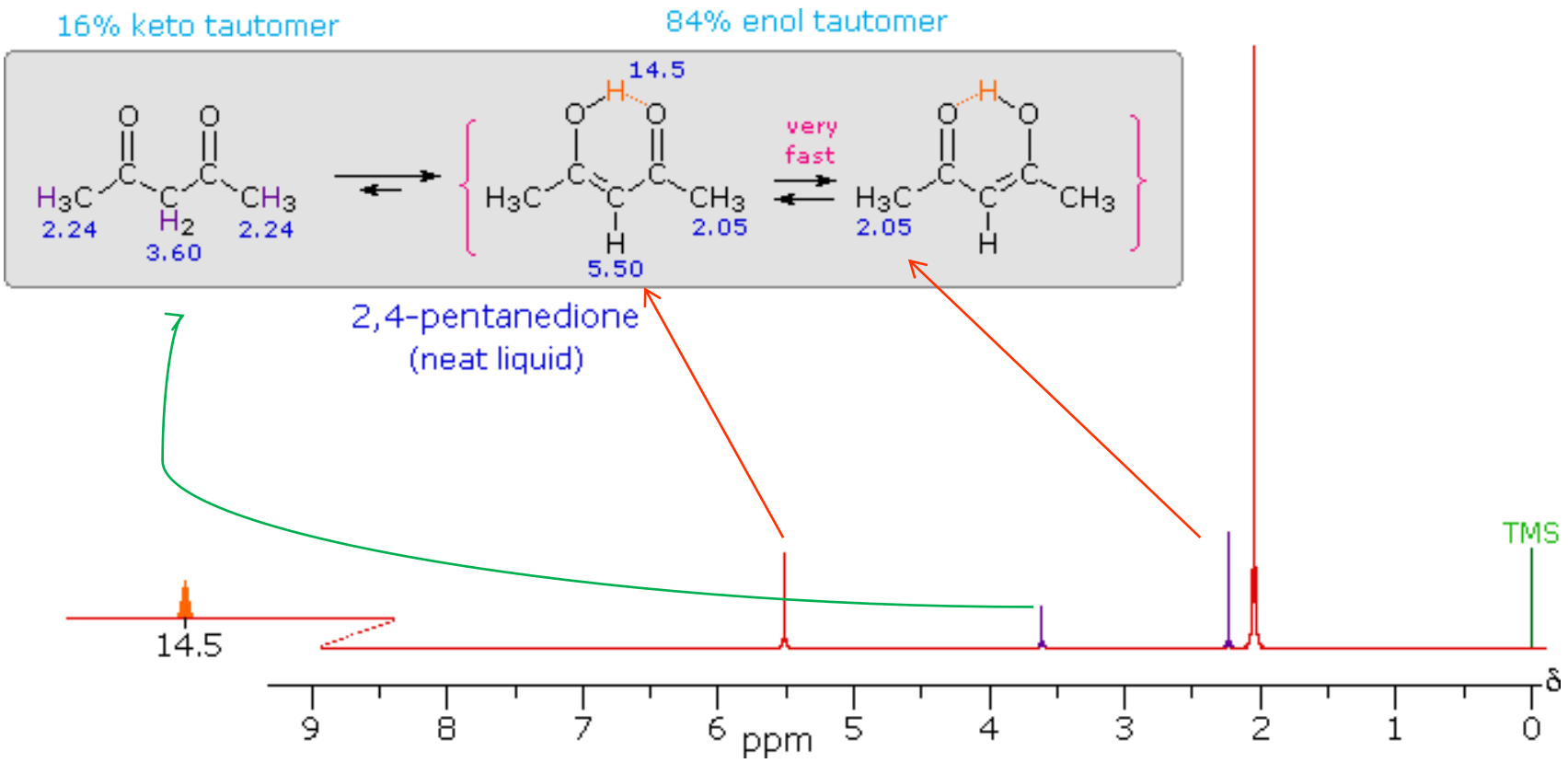


8,9

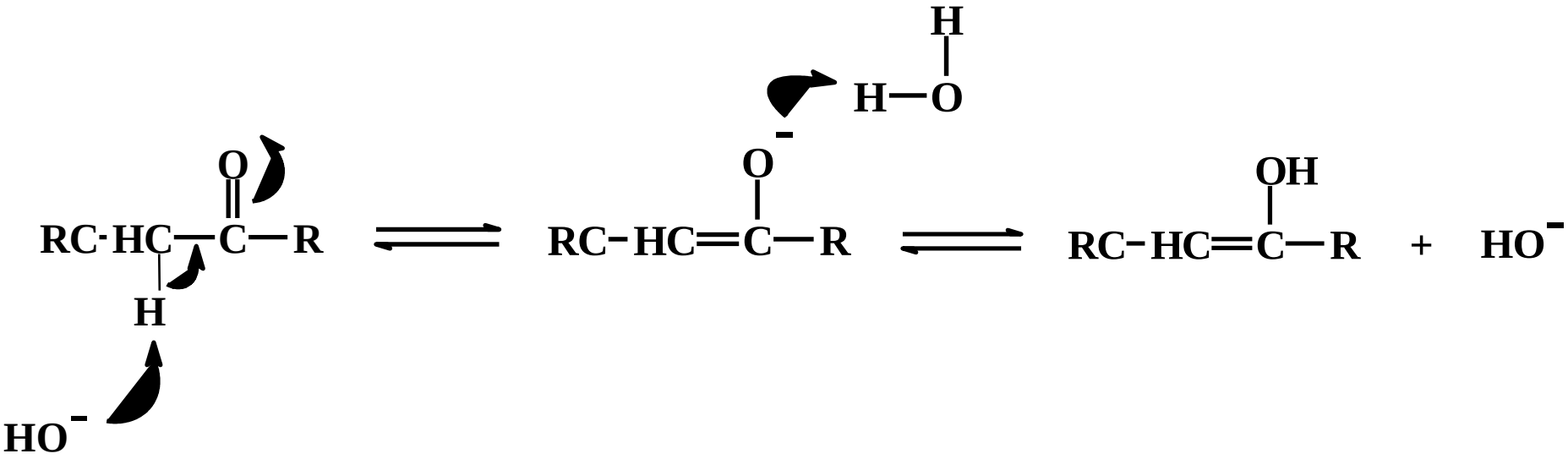


5,9

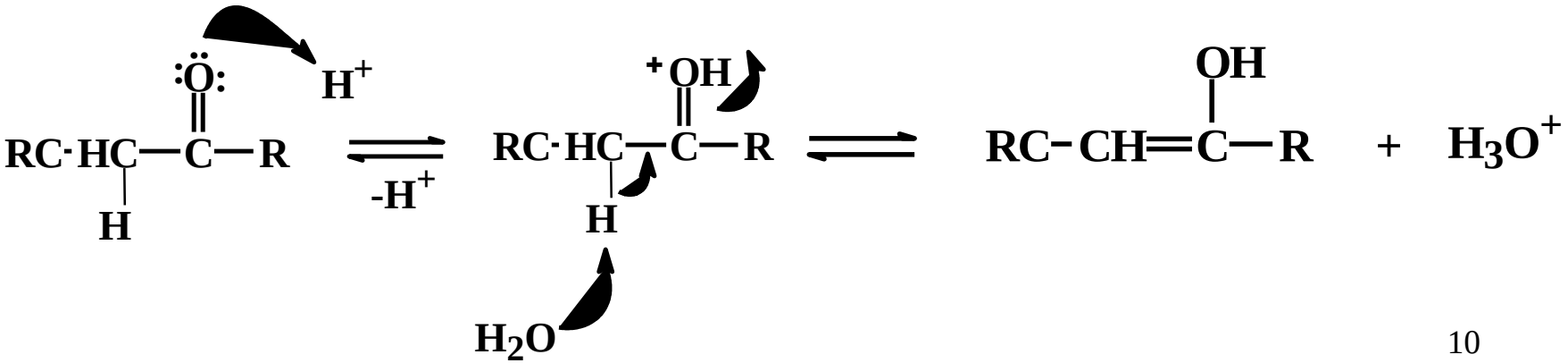



16% keto tautomer
84% enol tautomer
14.5
very
fast
2.24
2.24
3.60
2.05
2.05
5.50
2,4-pentanedione
(neat liquid)
TMS
14.5
9
8
7
6
ppm
5
4
3
2
1
0
δ

Interconversão ceto-enólica catalisada por base

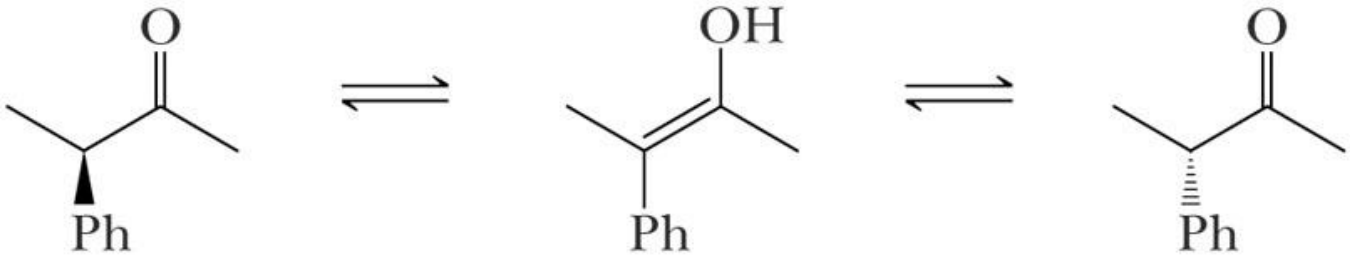


Interconversão ceto-enólica catalisada por ácido



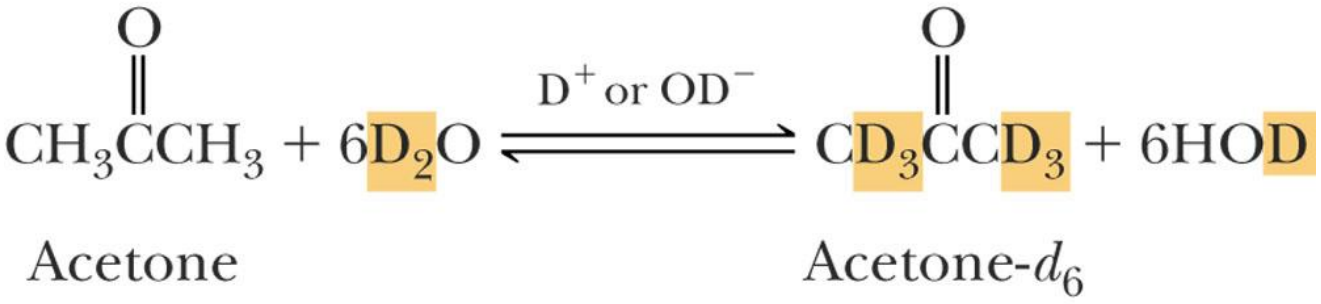
Reações resultants da acidez de hidrogênios na posição α

Racemization



(*R*)-3-Phenyl-2-butanone An achiral enol (*S*)-3-Phenyl-2-butanone

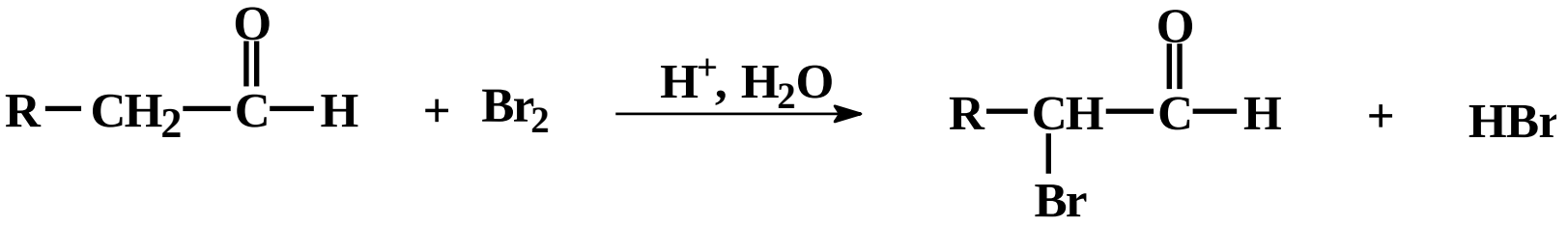
Troca

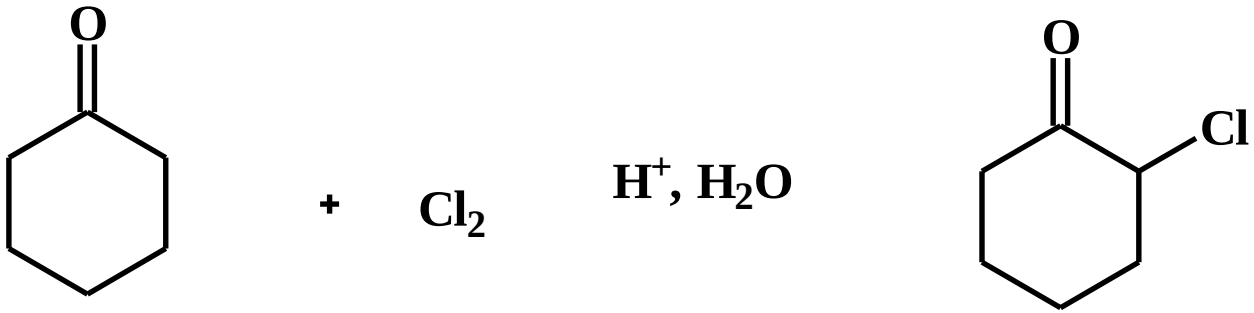


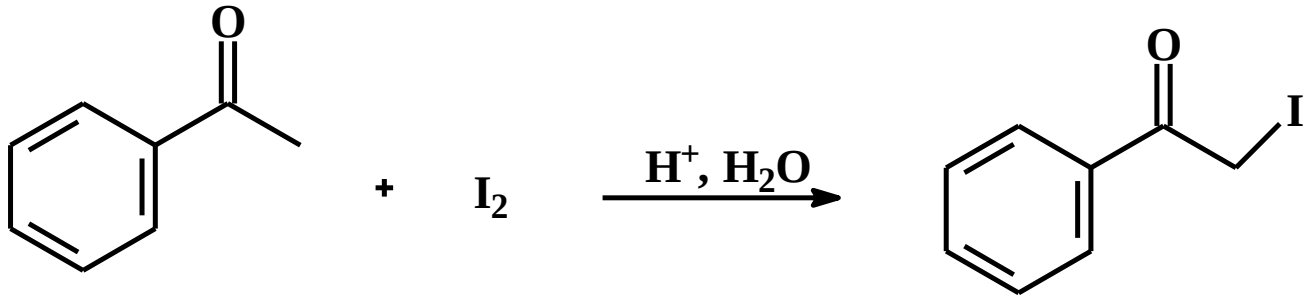
Acetone Acetone-d_6

Halogenação de carbonos α de aldeídos e cetonas

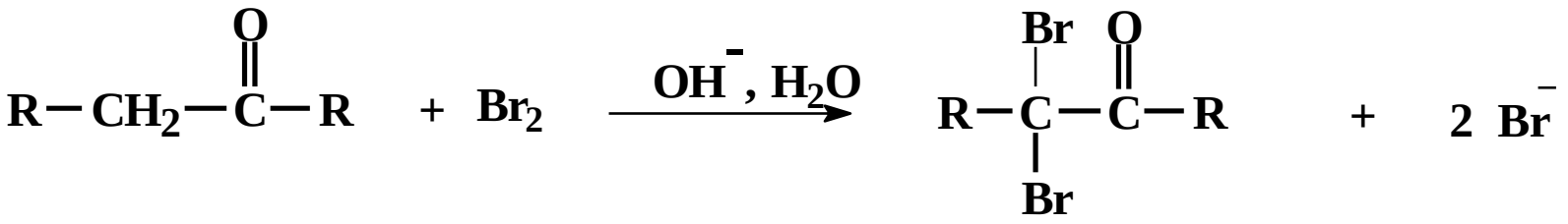
Em meio ácido

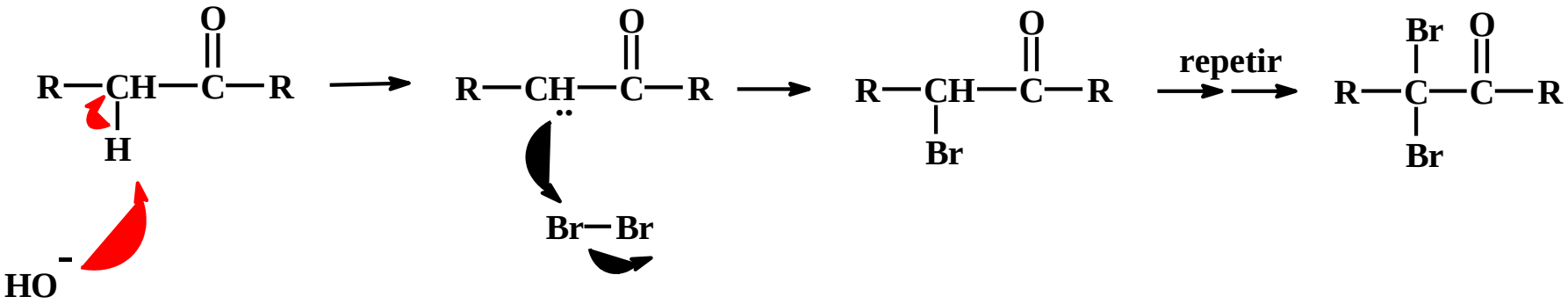






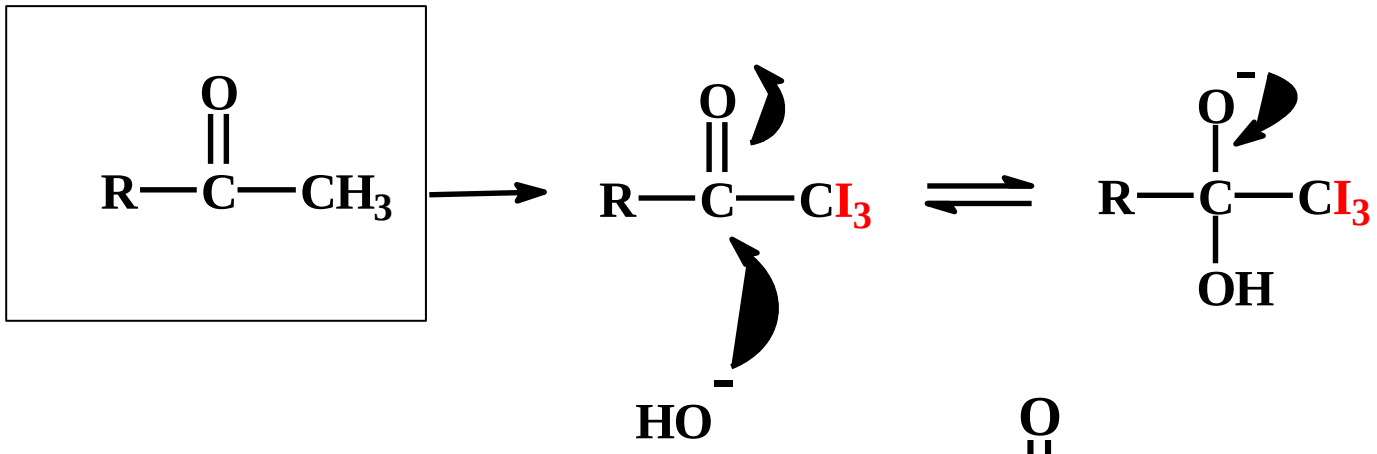
Adição de excesso de halogênio em meio básico





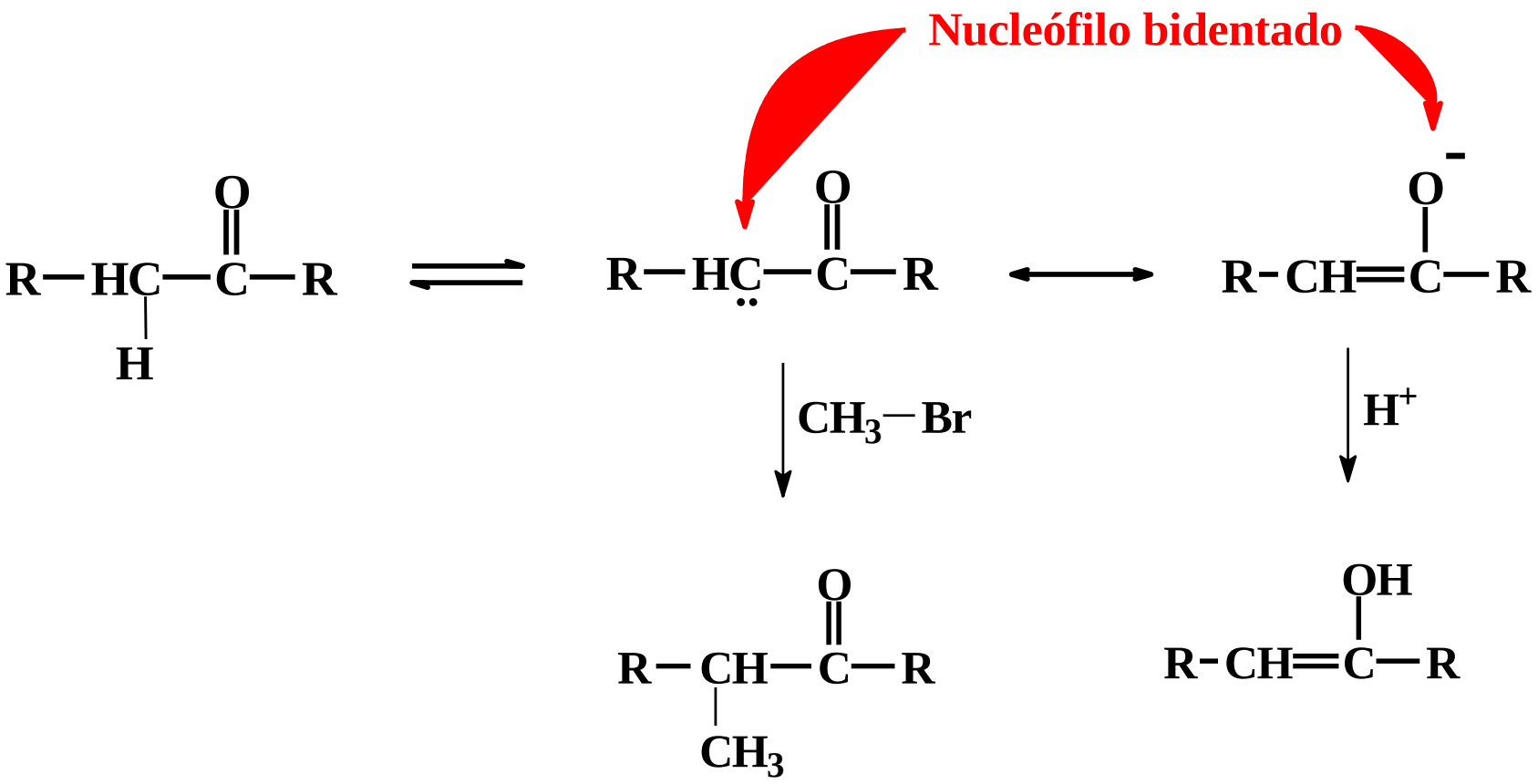
Não há controle das halogenações !!!

Reação de halofórmio

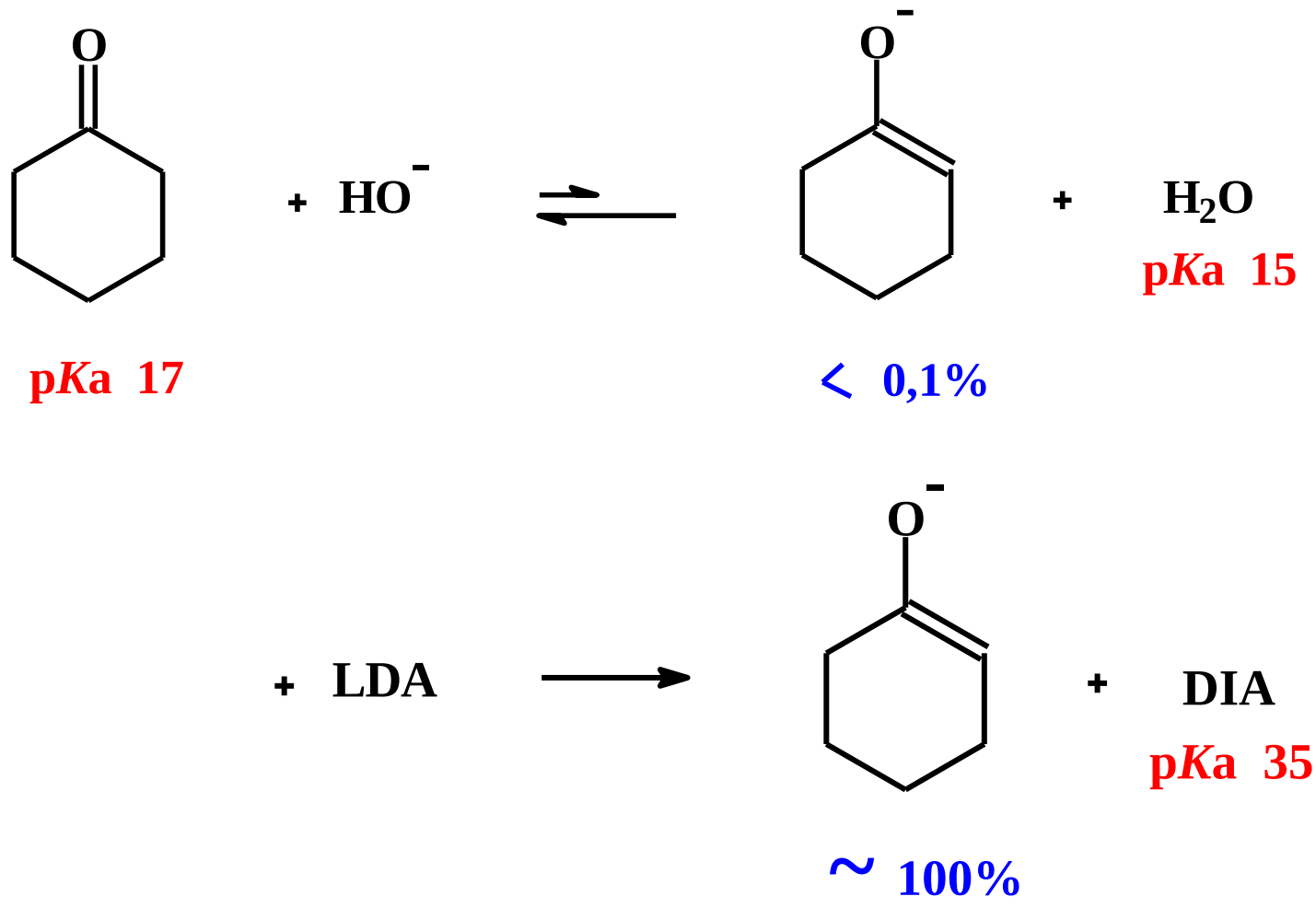


Teste de caracterização de metilcetonas !!!

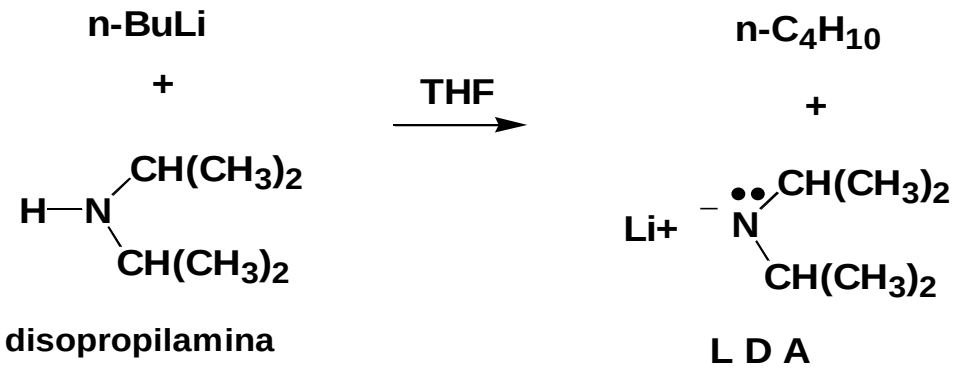
Reações de alquilações nas posições α de compostos carbonílicos



Reações de alquilações no carbono α de compostos carbonílicos

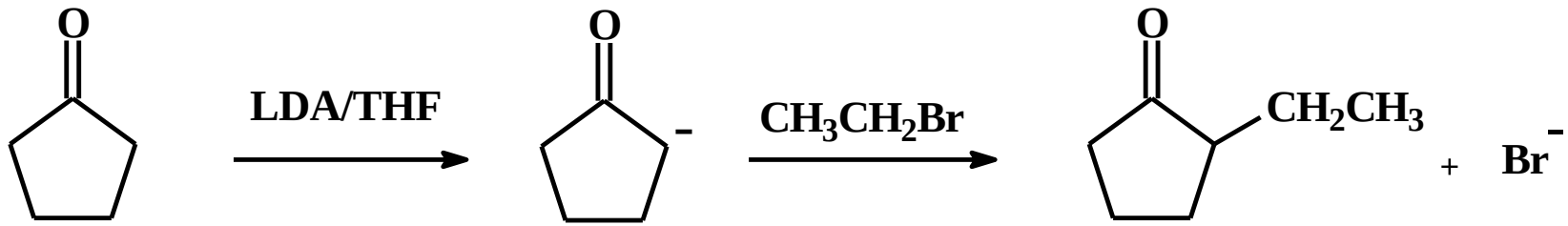


Formação de enolatos usando LDA (diisopropil amideto de lítio)

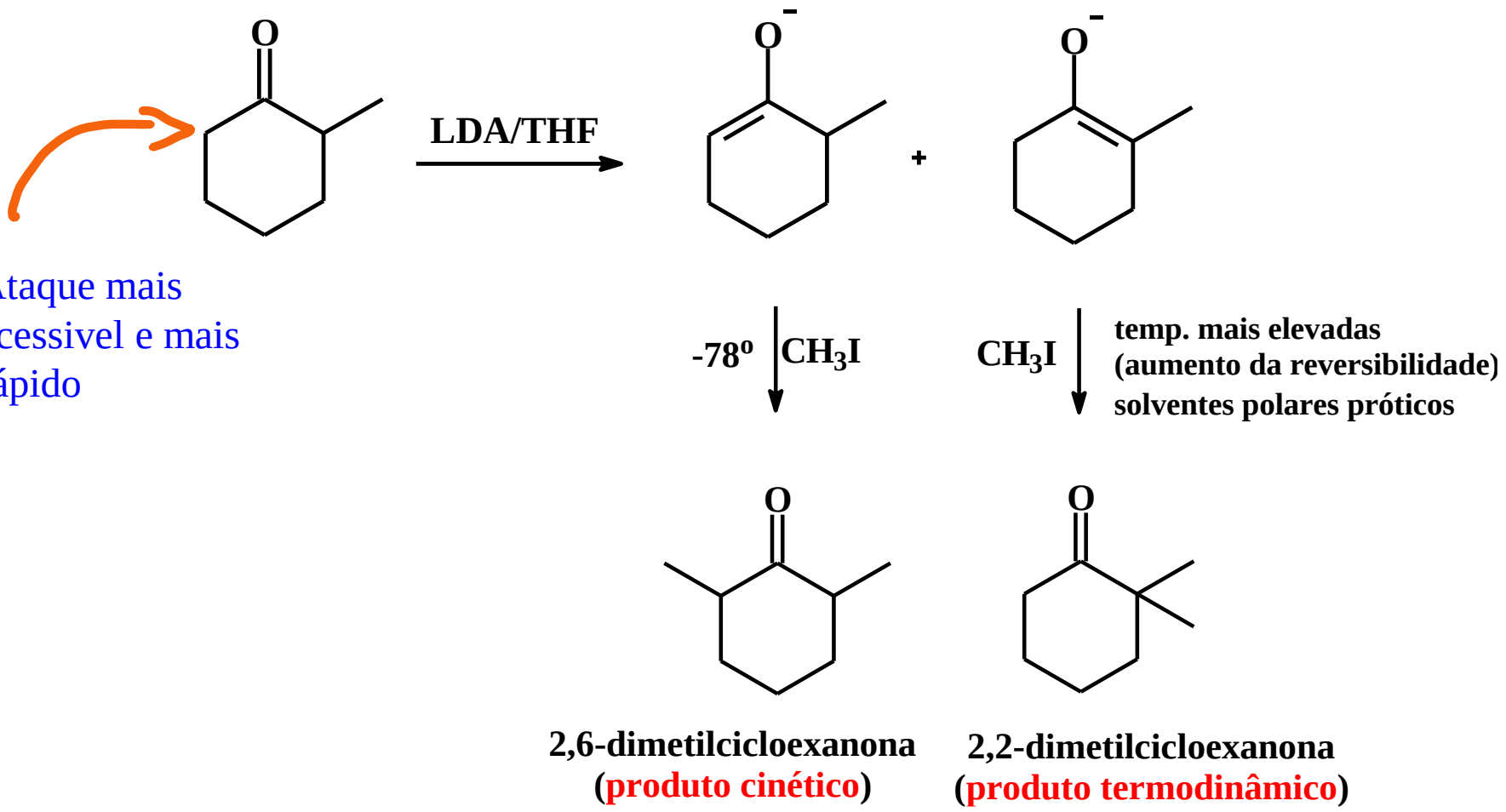


pka 35

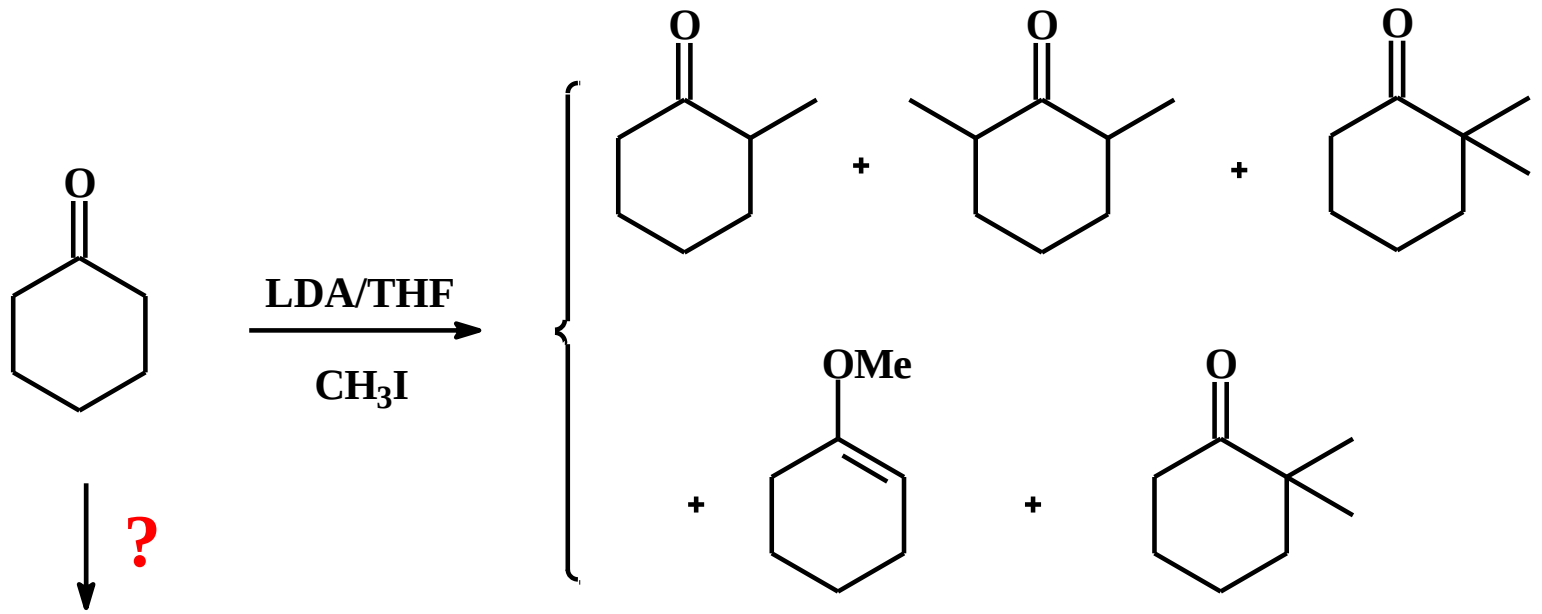
Base forte, mas volumosa (pouco nucleofílica)



Controle de alquilações em carbonos α de cetonas



Controle de alquilações em carbonos α de cetonas

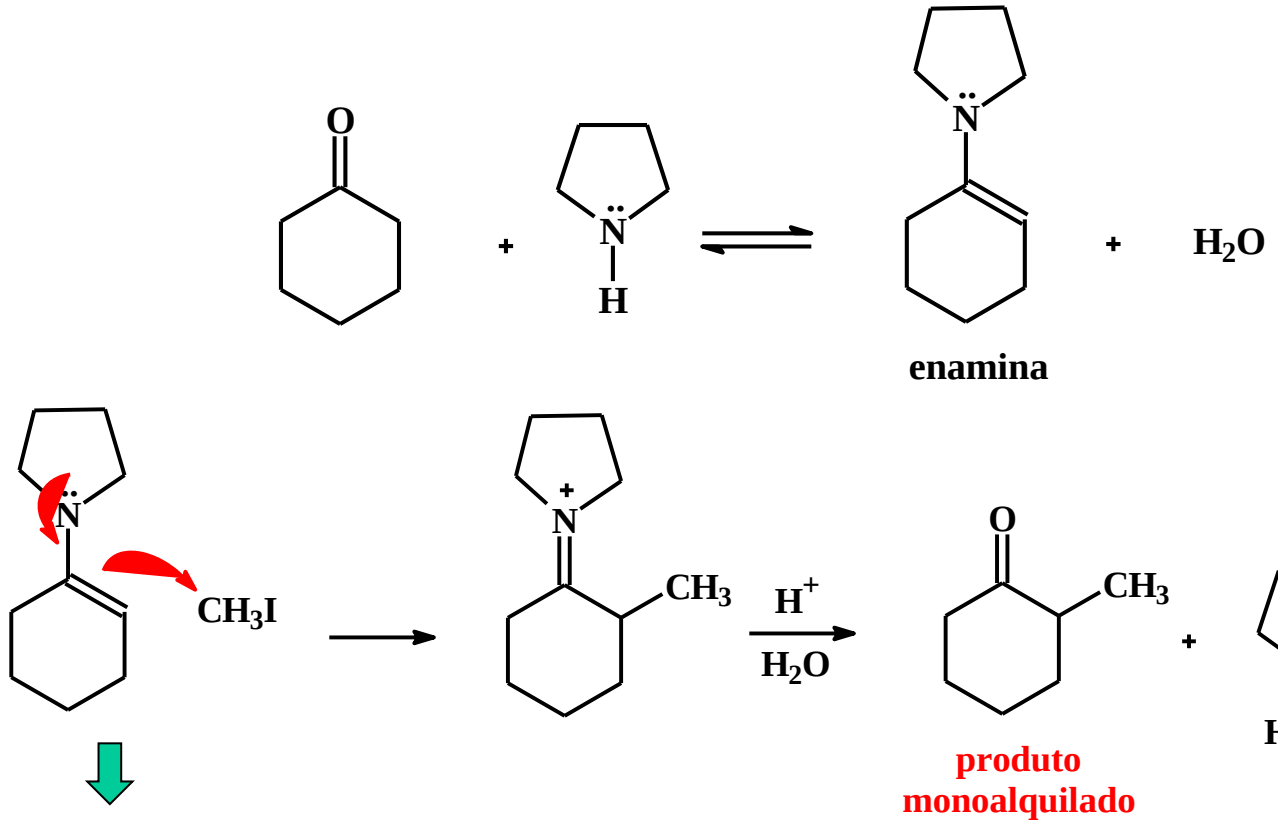


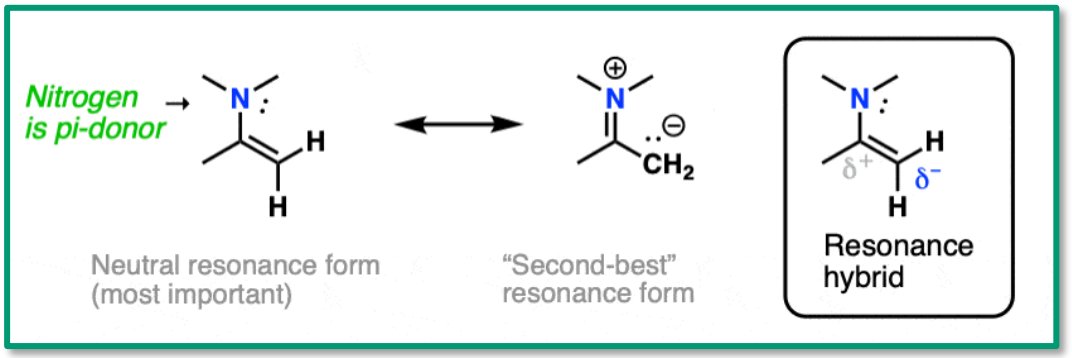
produto monoalquilado

Apesar do rendimento das alquilações empregando como base o LDA, se for fornecido muito CH_3I, ocorrem várias metilações.

Então como fazer para se obter um produto monoalquilado?

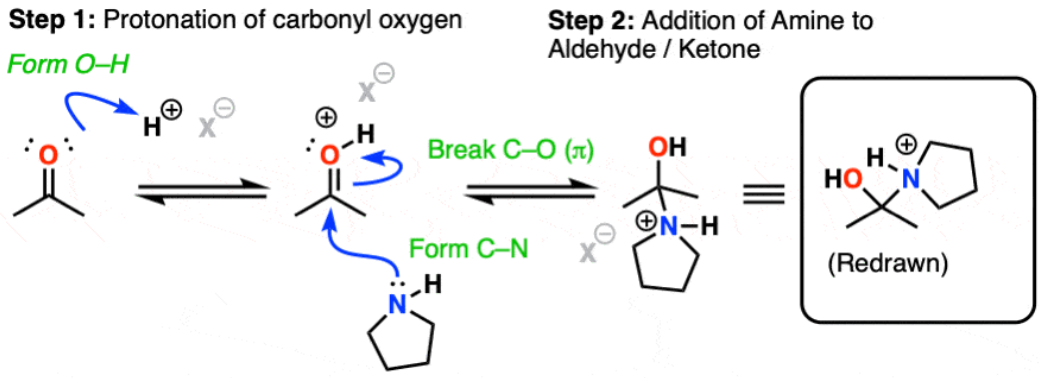
Uso de enaminas em alquilações de cetonas

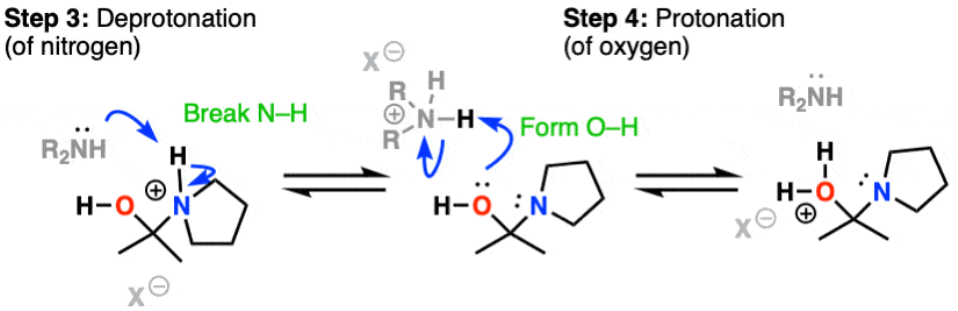




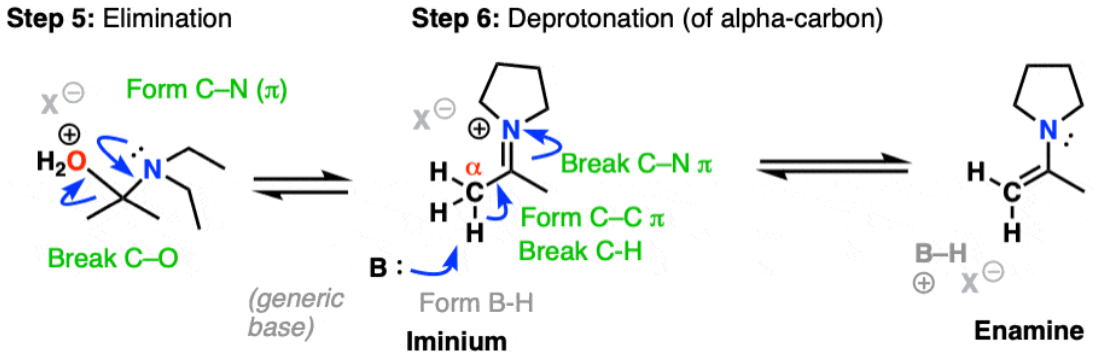
Estruturas de ressonância de uma enamina mostrando a capacidade nucleofílica do carbono conjugado, cujo culmina por atacar o iodometano ou outro carbono eletrofílico.

Mecanismo de formação de enaminas

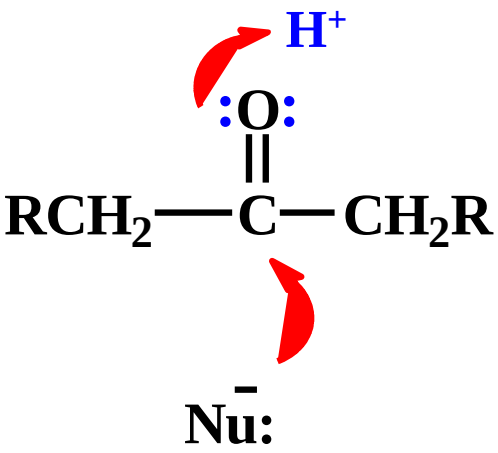




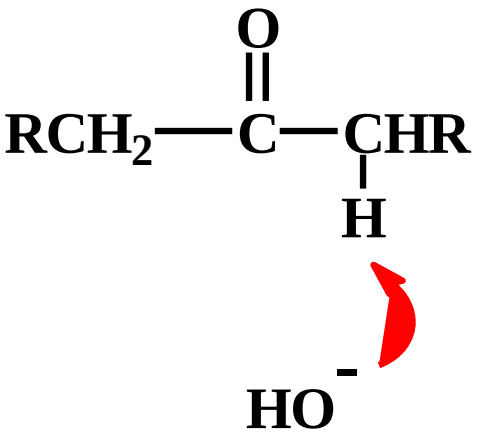
Together, steps 3 and 4 are generically called “proton transfer”. The specific identity of the base (in step 3) and acid (in step 4) is generally not crucial, so it’s OK to write B and B-H.



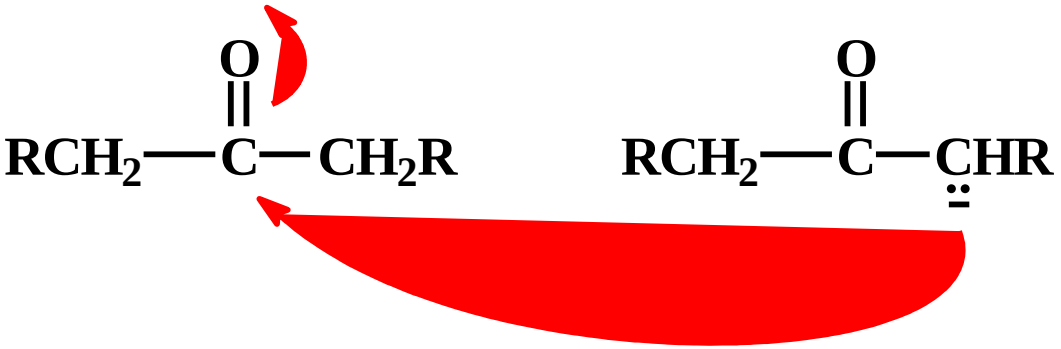
Reações típicas de carbonilas



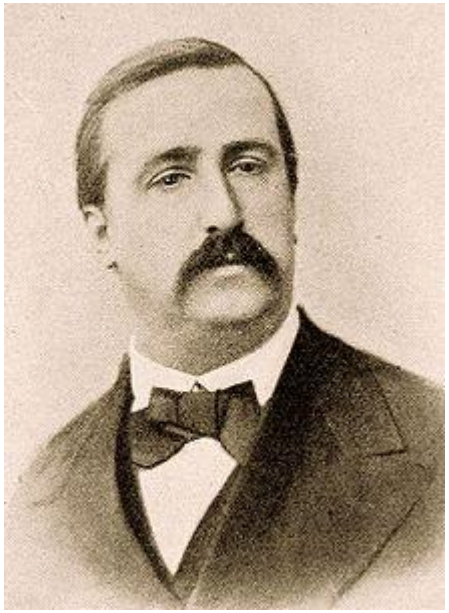
ou



A reação de Aldol envolve ambos processos



Adição de ALDOL



Simultaneous discovery of aldol reaction

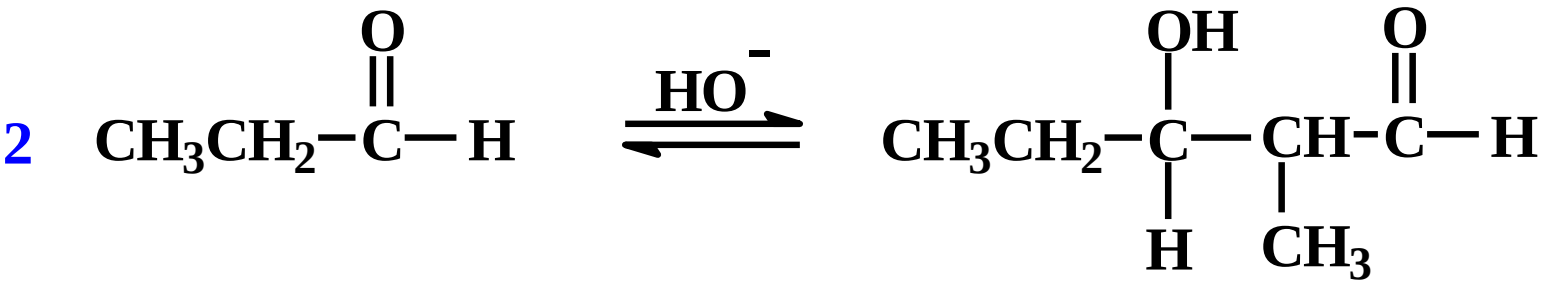
Aleksandr Borodin
Composer and chemist
12 November 1833 - 27 February 1887
Saint Petersburg (Russian)

Charles-Adolphe Wurtz
Chemistry
November 26, 1817- May 10, 1884
France

Borodin "Polovtsian Dances" from the opera "Prince Igor" only children choir

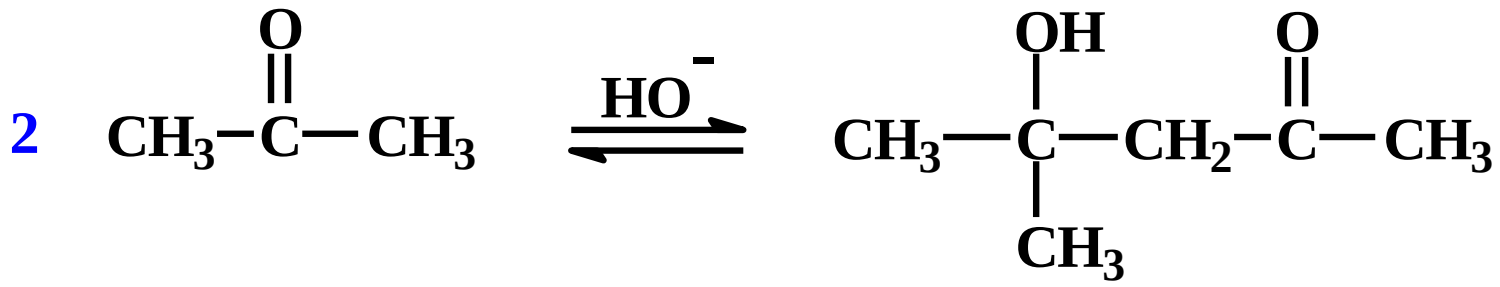
https://www.youtube.com/watch?v=jml39FZ4yns

Exemplos de adição aldólica



β-hidroxialdeido

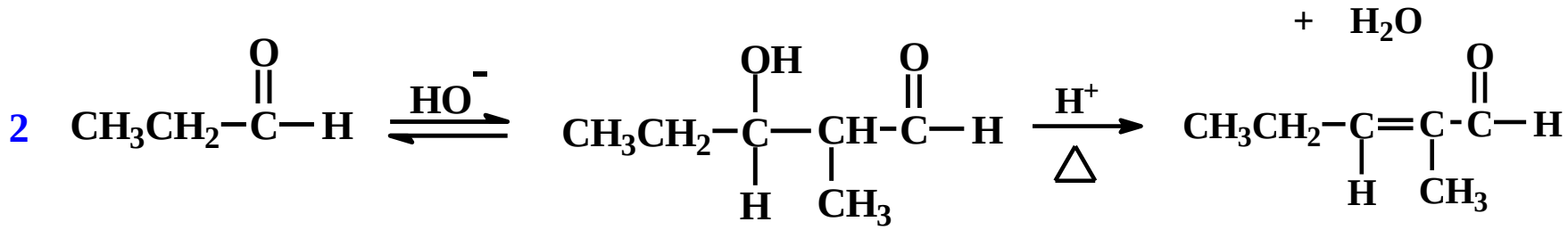
aldeído + **álcool** = **aldol**

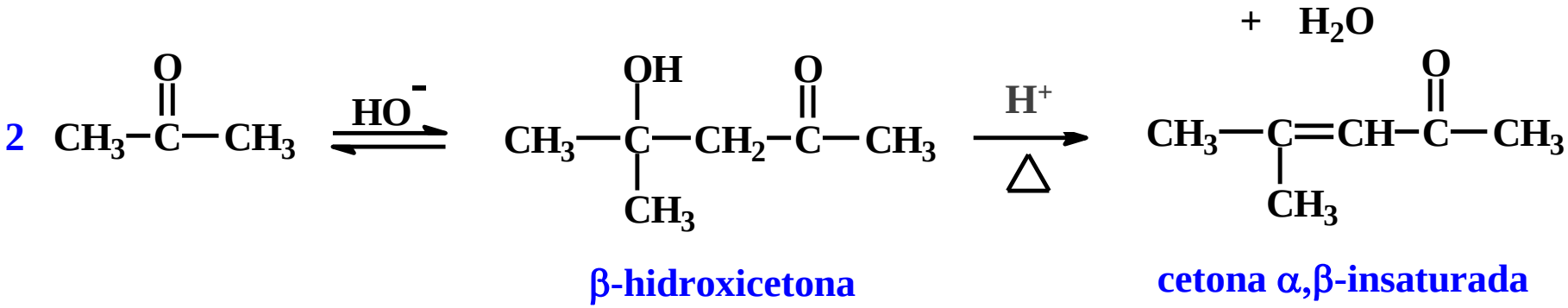


β-hidroxicetona

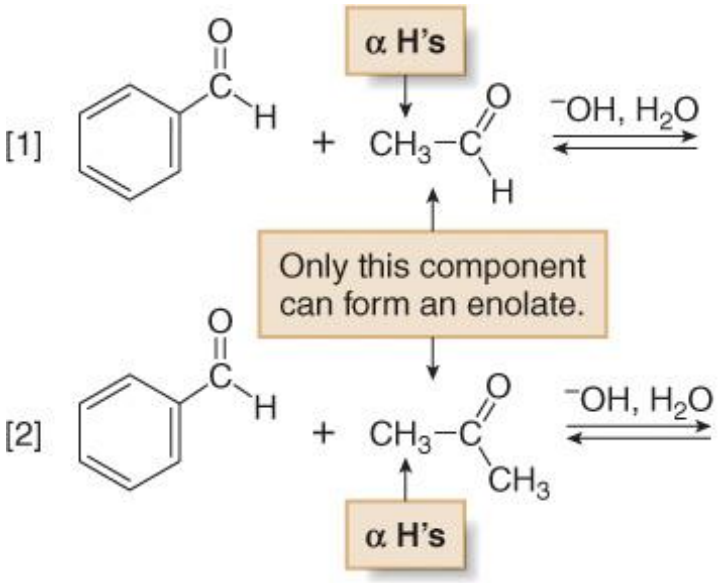
Reação de condensação aldólica

Obtenção de aldeídos α,β-insaturados

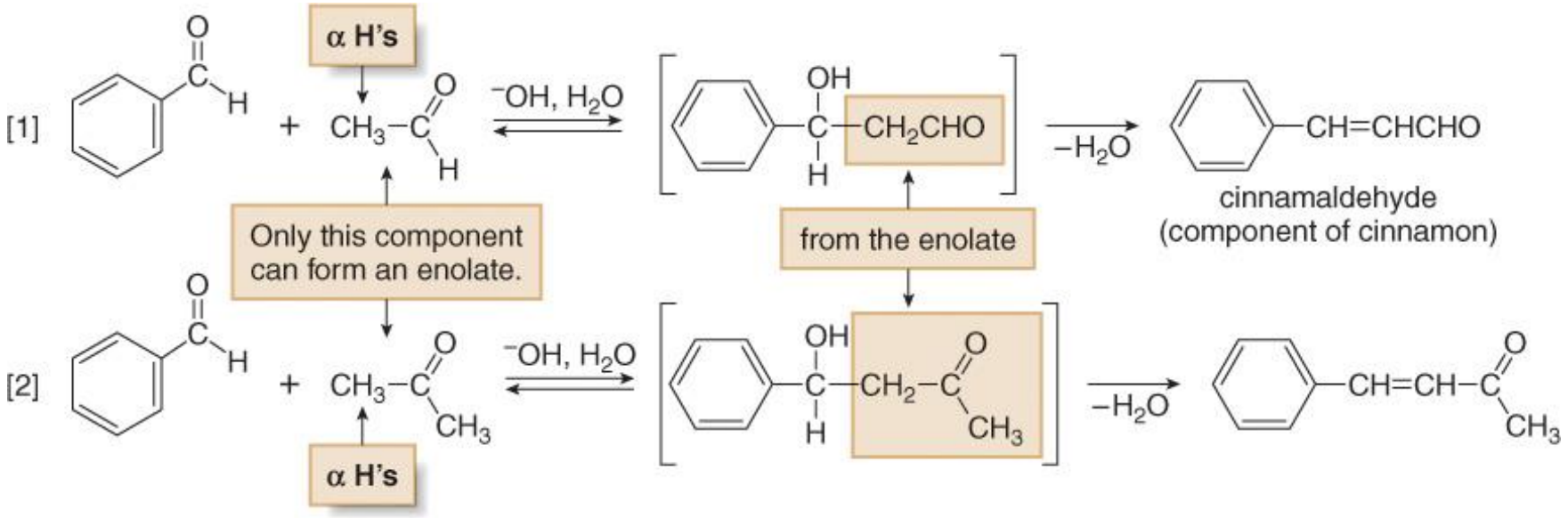




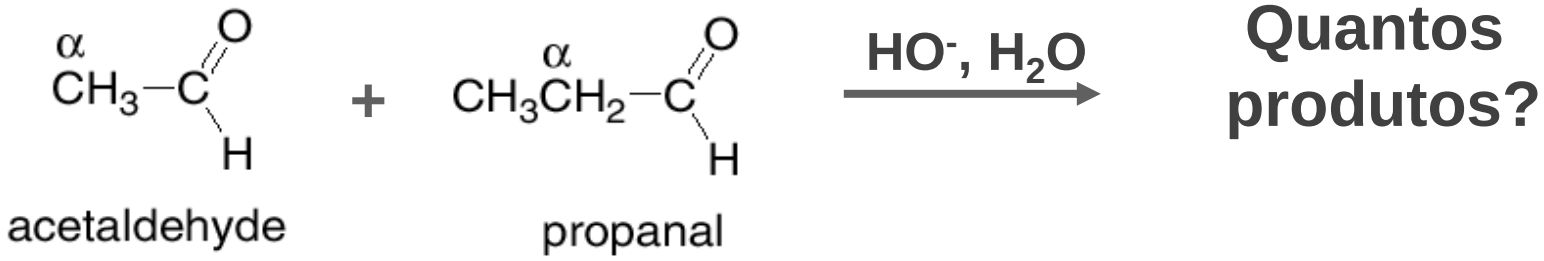
Aldol entre diferentes compostos carbonílicos



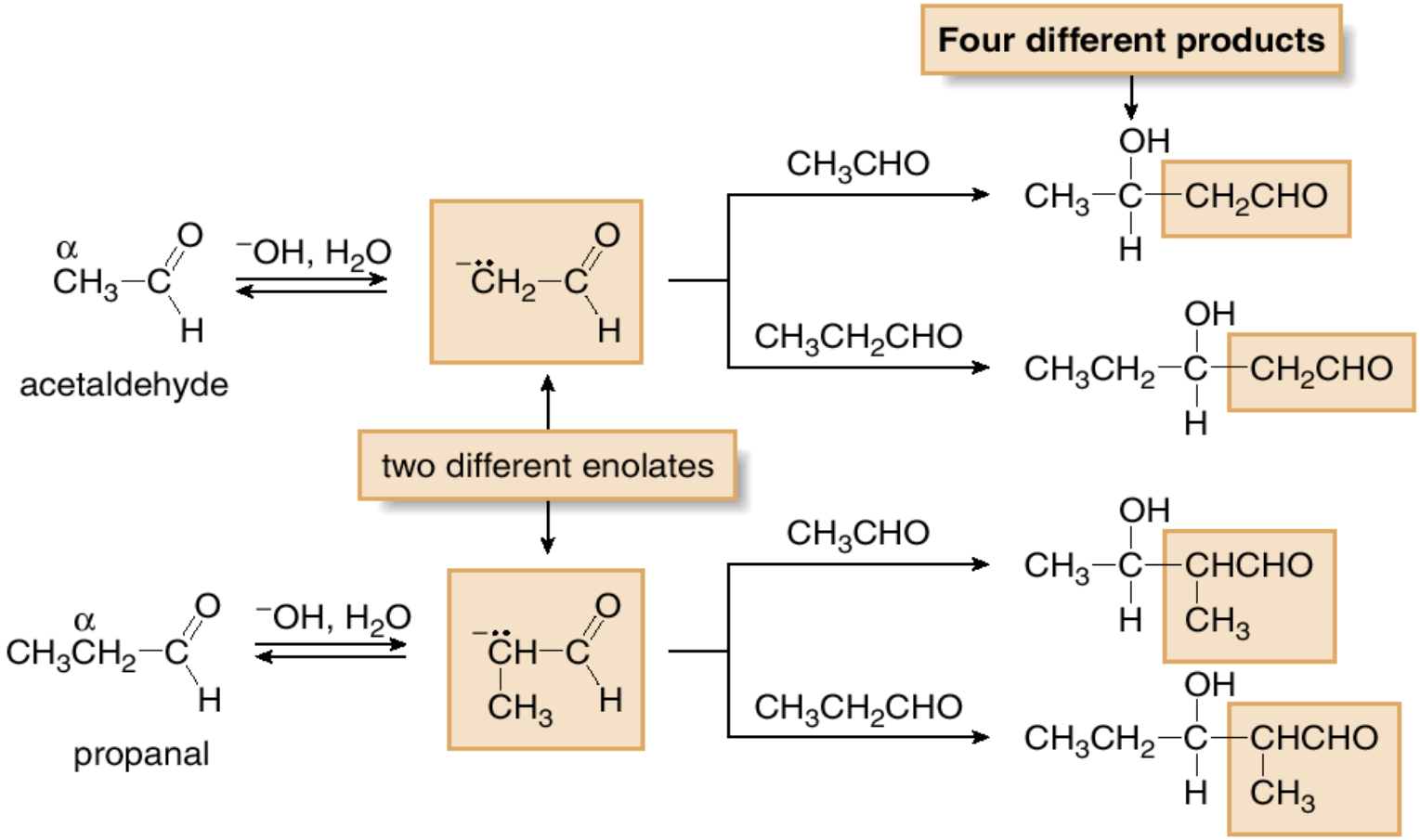
Aldol entre diferentes compostos carbonílicos



Aldol entre diferentes compostos carbonílicos

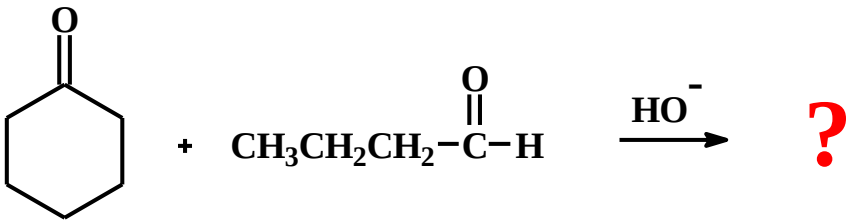


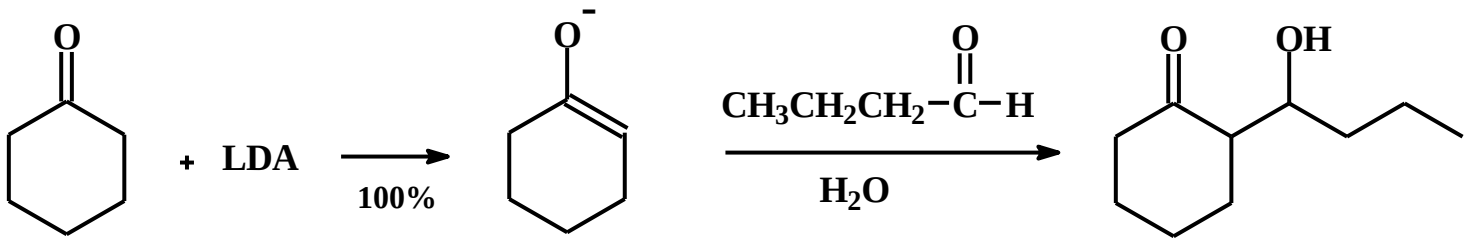
Reações de aldol mistas ou cruzadas



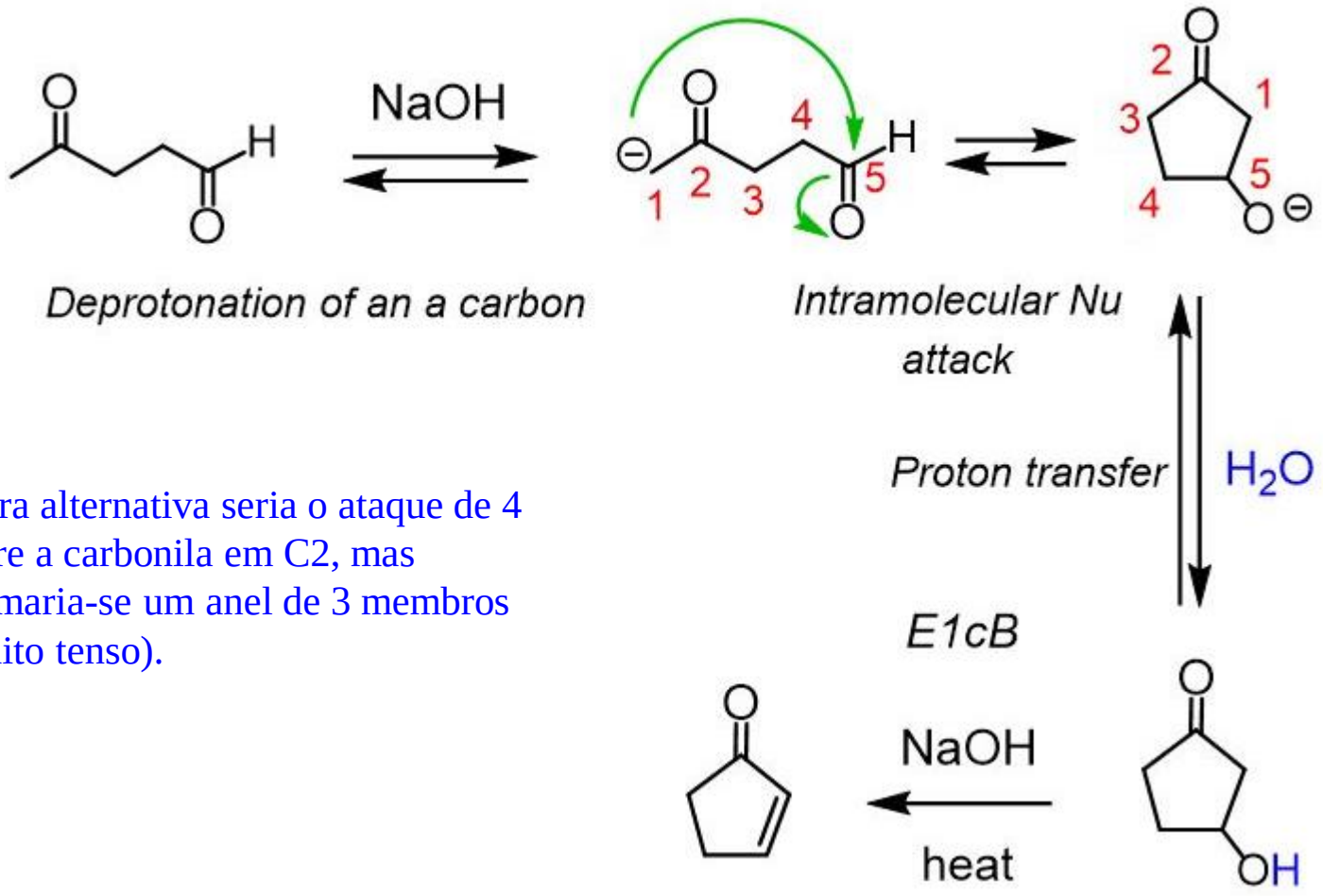
Pouca utilidade sintética!!!

Aldol entre diferentes compostos carbonílicos



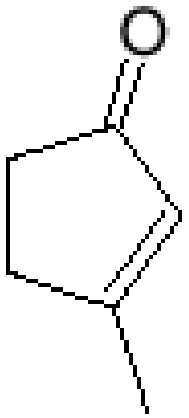


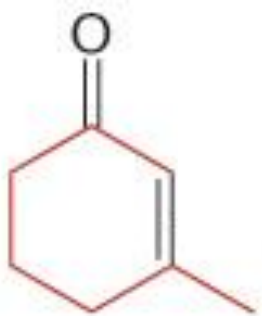
Condensações aldólicas intramoleculares



Outra alternativa seria o ataque de 4 sobre a carbonila em C2, mas Formaria-se um anel de 3 membros (muito tenso).

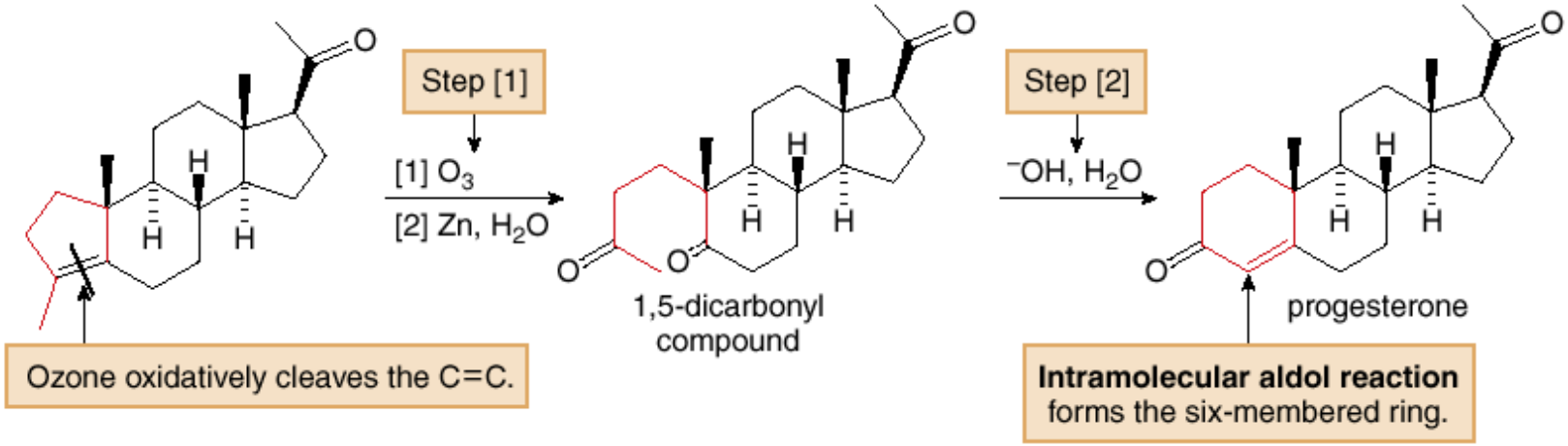
Quais são as estruturas do material de partida de compostos dicarbonílicos para uma reação aldólica intramolecular?



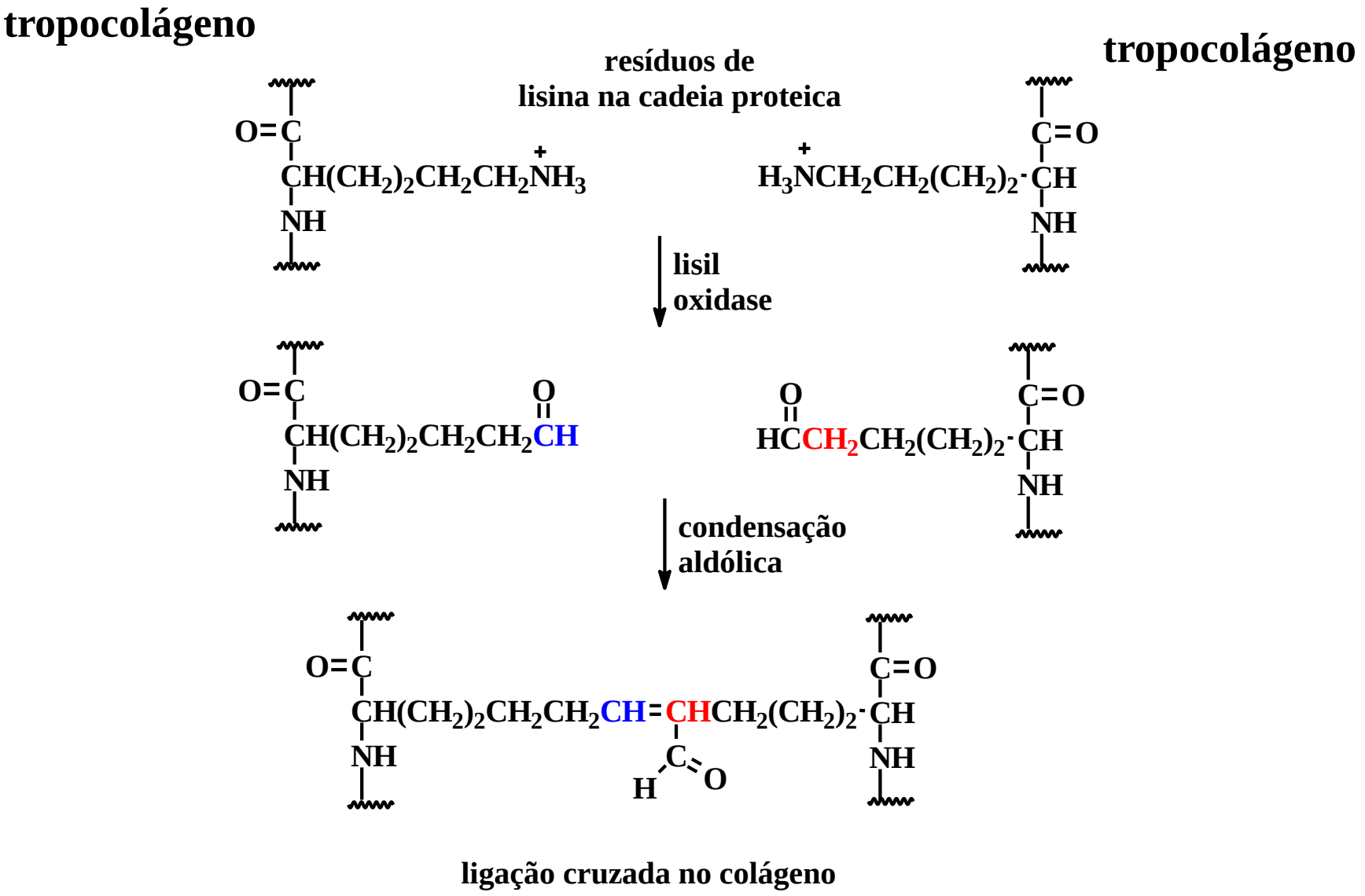


Reação aldólica intramolecular

A síntese do hormônio sexual feminino progesterona envolve uma reação aldólica intramolecular.

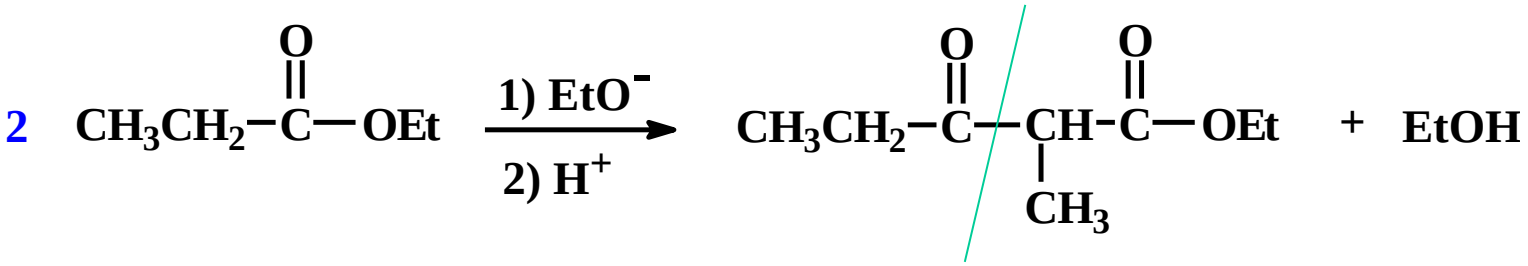


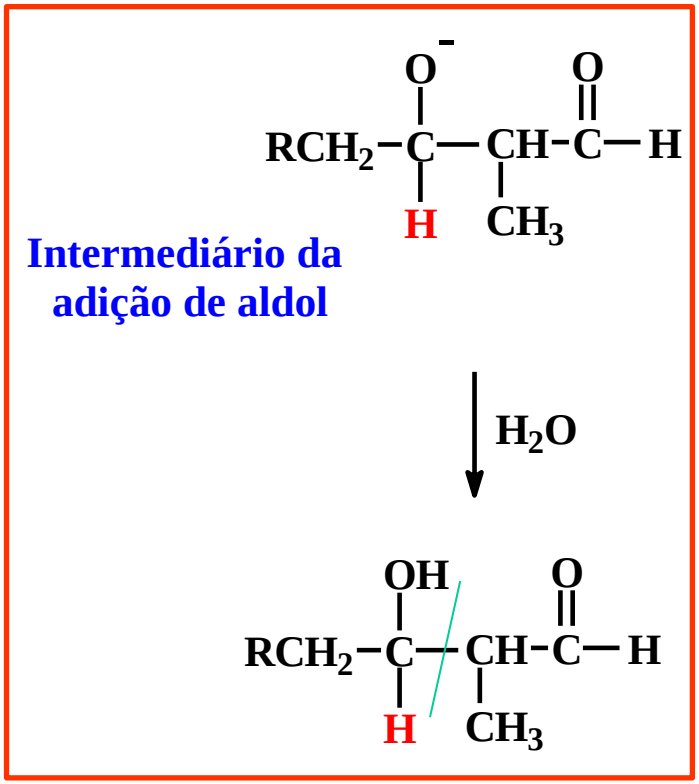
Reação de condensação aldólica em sistemas biológicos



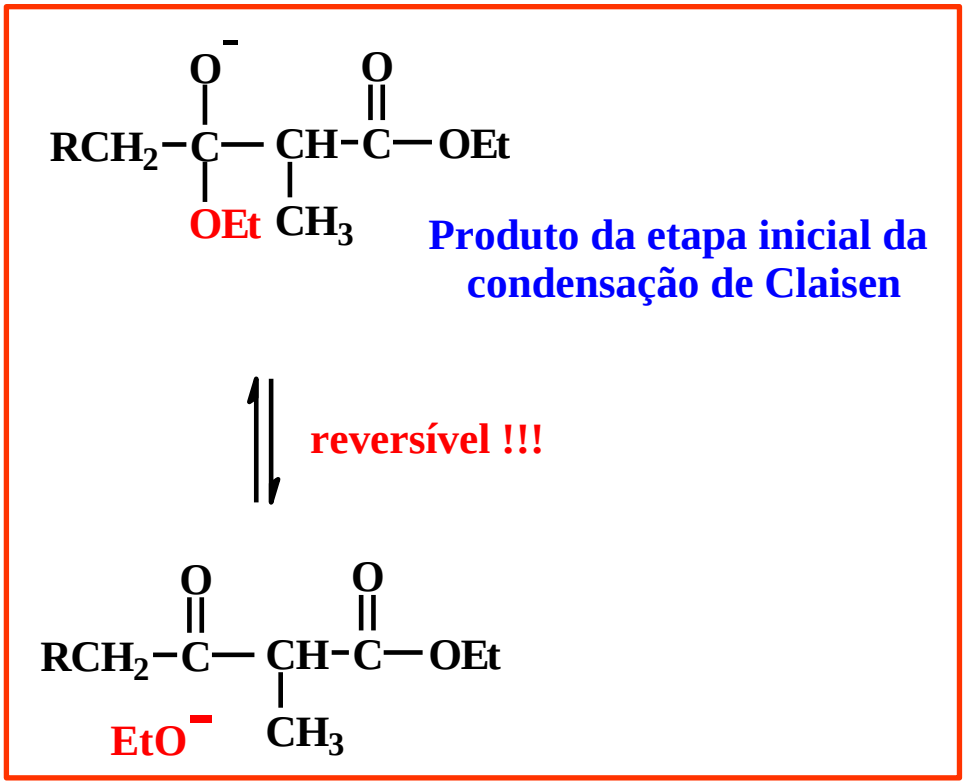
ligação cruzada no colágeno

Reações de condensação de Claisen versus aldol



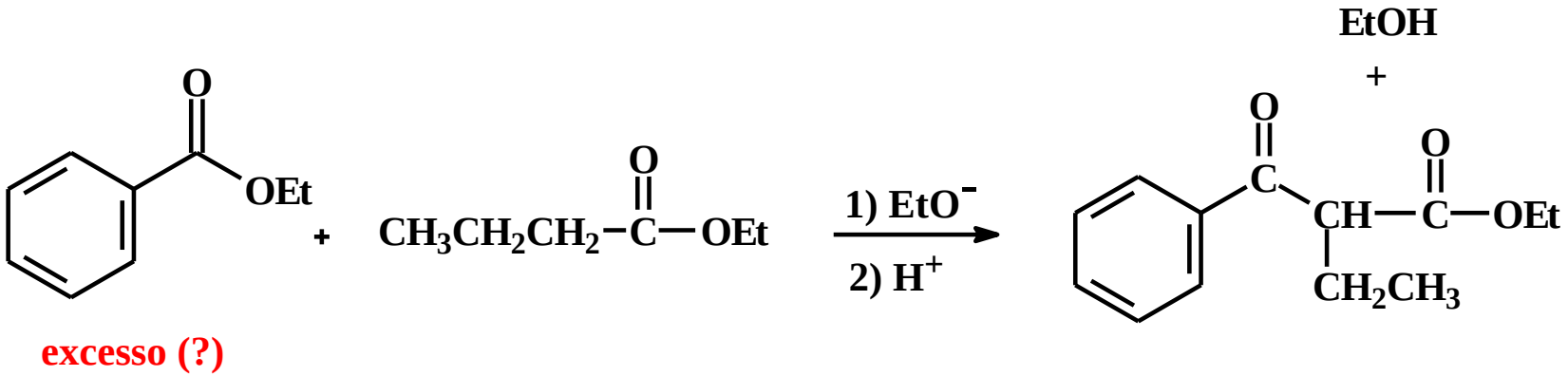


Produto de adição

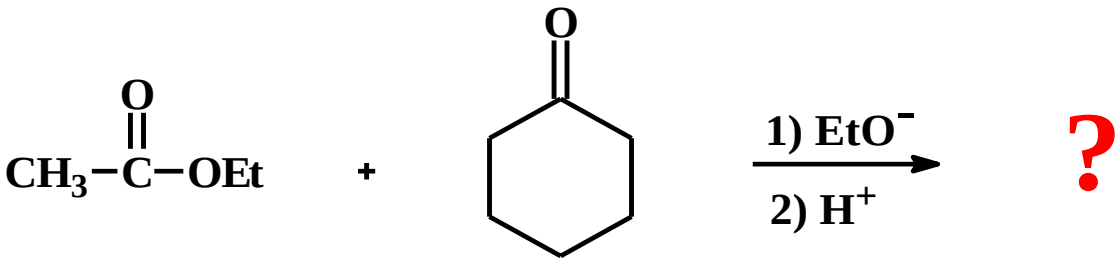


Produto de substituição

Condensação de Claisen cruzada



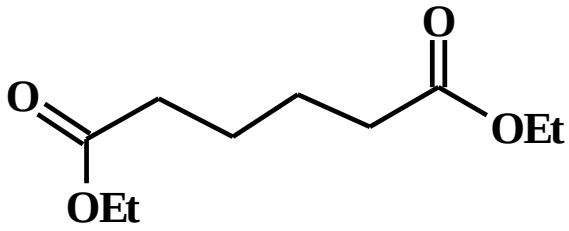
excesso (?)



Qual a sequência da adição dos reagentes para se obter o produto indicado?

Condensações de Claisen intramoleculares

Condensações de Dieckmann (1869-1925)

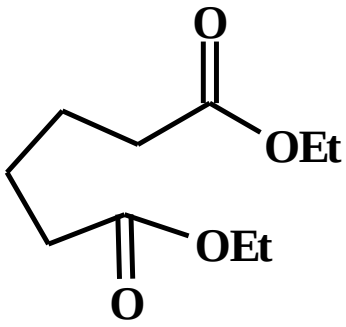


1,6-diéster

1) CH_3O^-

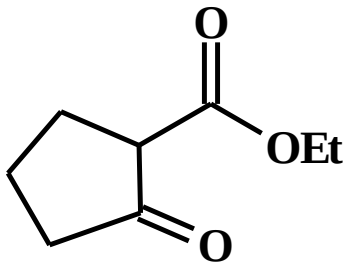
2) H^+

?



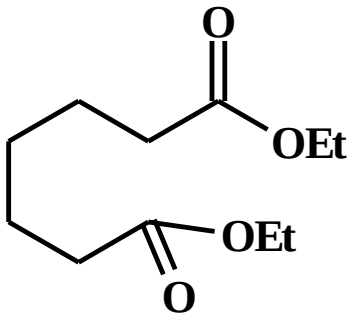
1) CH_3O^-

2) H^+



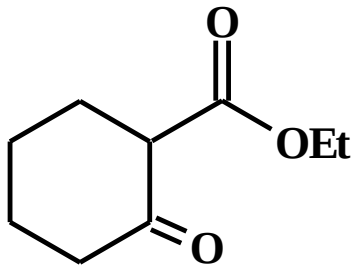
+

CH_3OH



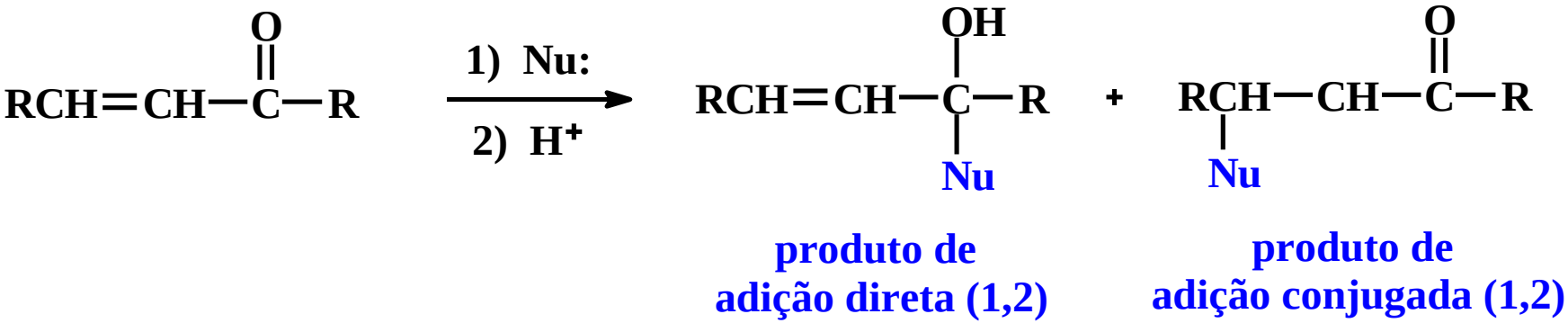
1) CH_3O^-

2) H^+

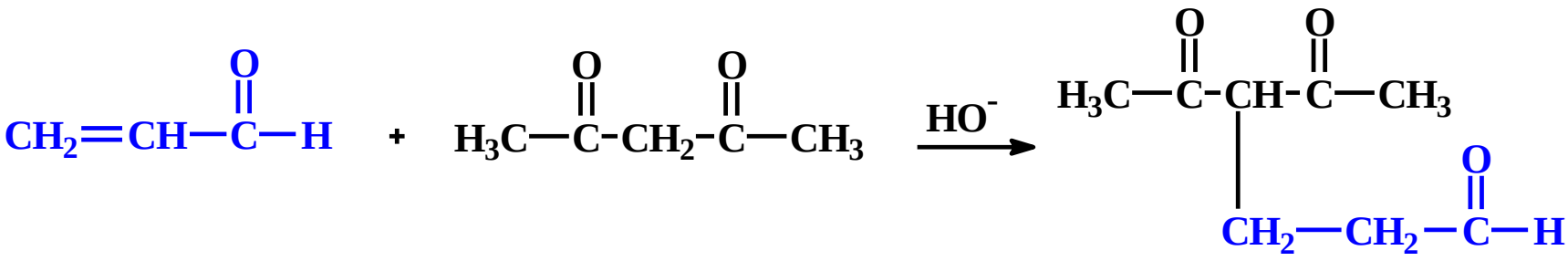


+ CH_3OH

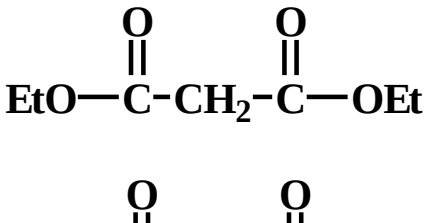
Reações de adições conjugadas a compostos carbonílicos α,β-insaturadas **(Reações de Michael)**

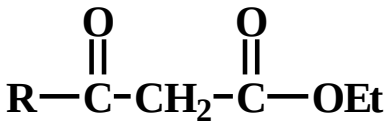


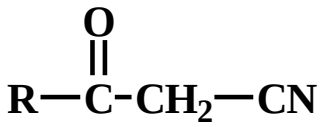
Se Nu: é um enolato → **Reação de Michael**

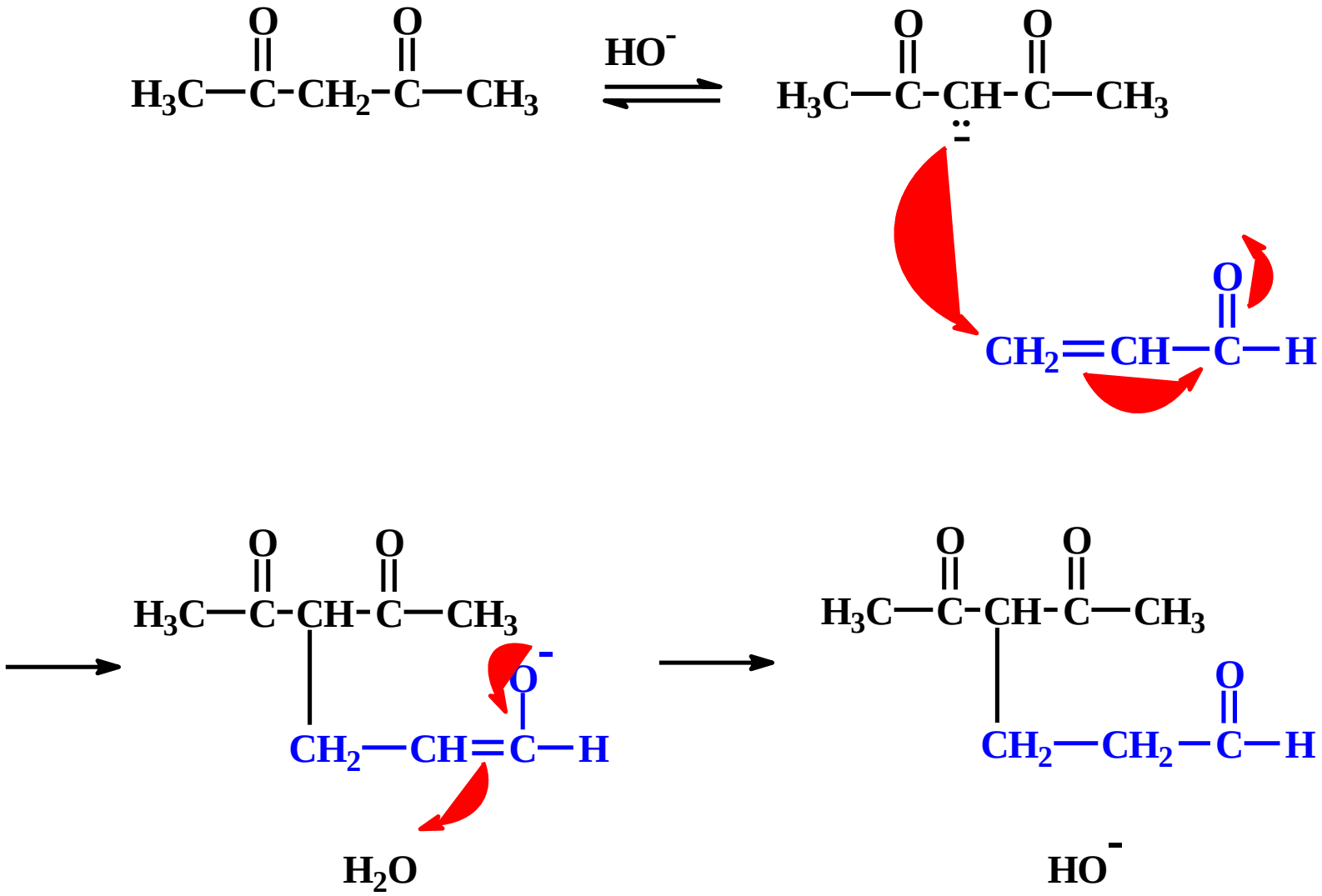


Outros compostos β-dicarbonílicos cujos enolatos que podem fazer o mesmo tipo de ataque:

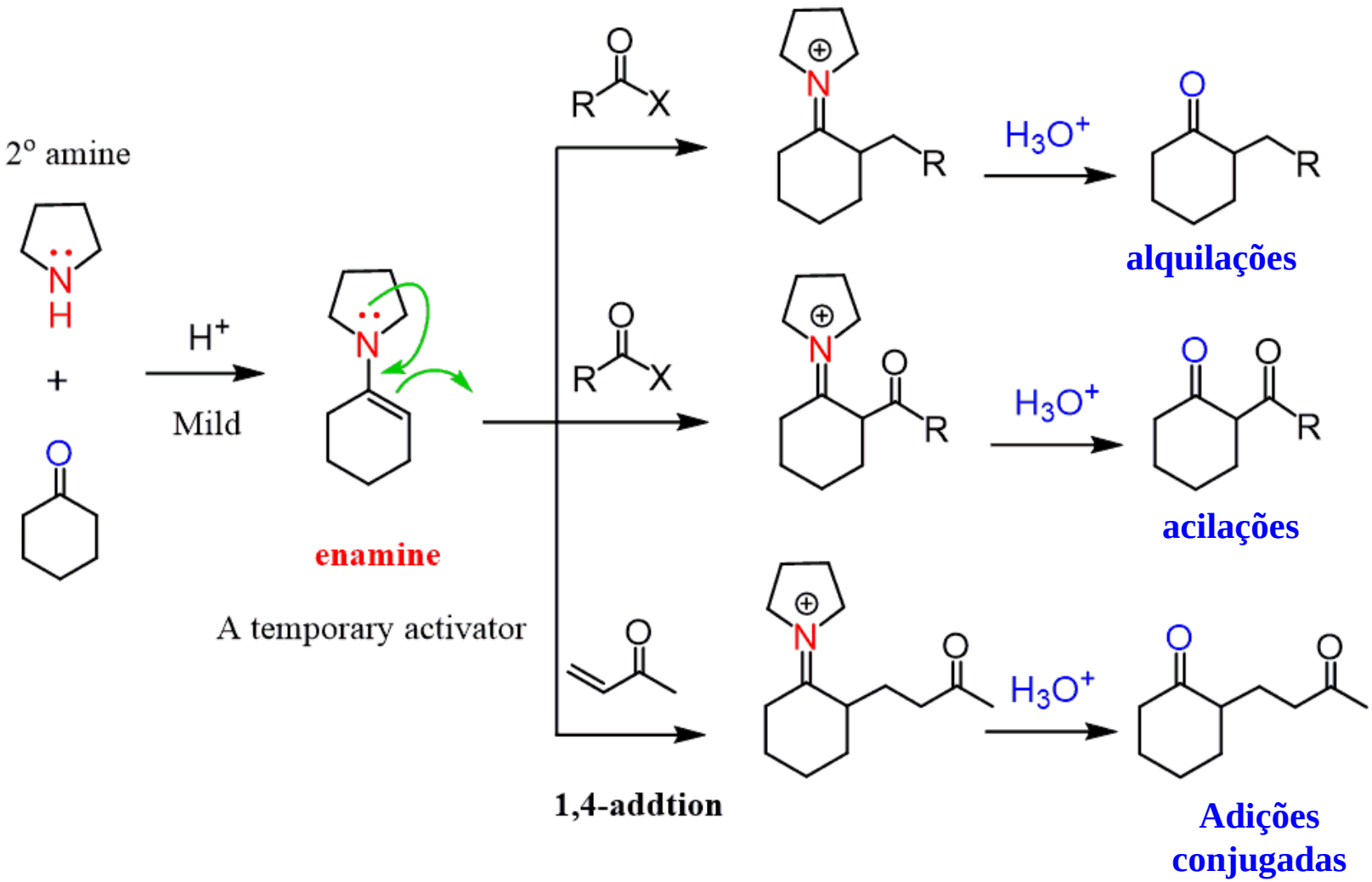




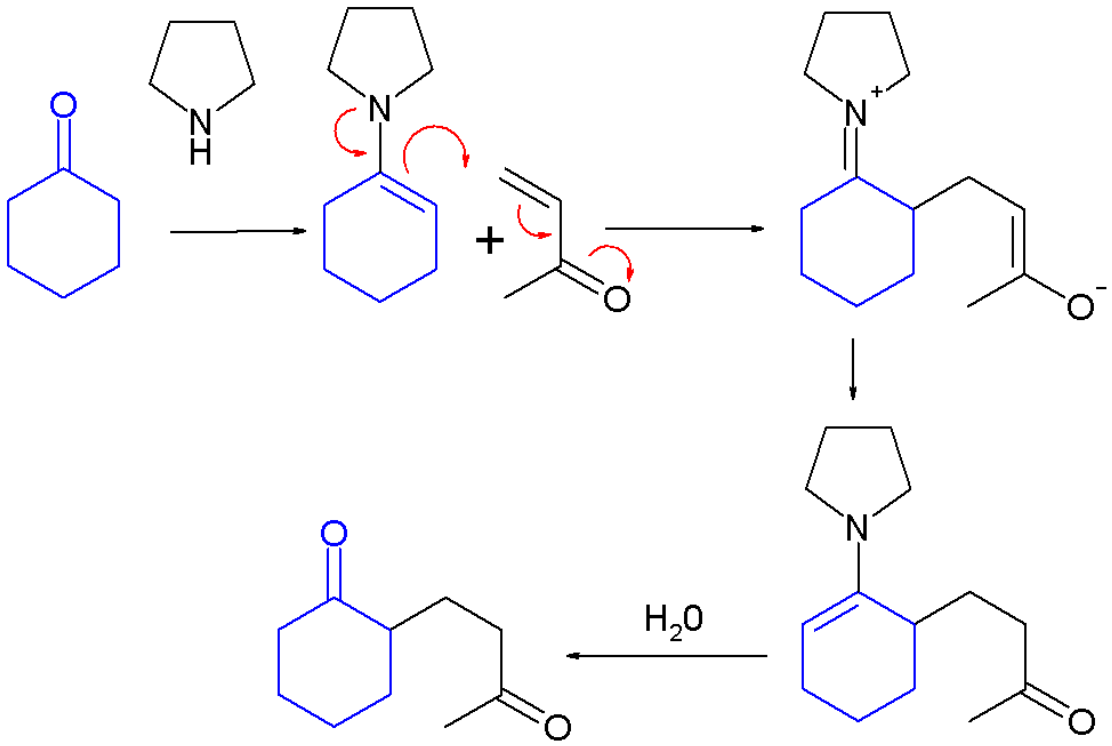



O
O
H3C—C-CH2-C—CH3
HO-
O
O
H3C—C-CH-C—CH3
CH2=CH—C—H
O
O
H3C—C-CH-C—CH3
O-
CH2—CH=C—H
H2O
O
O
H3C—C-CH-C—CH3
O
CH2—CH2—C—H
HO-

Reação de Stork

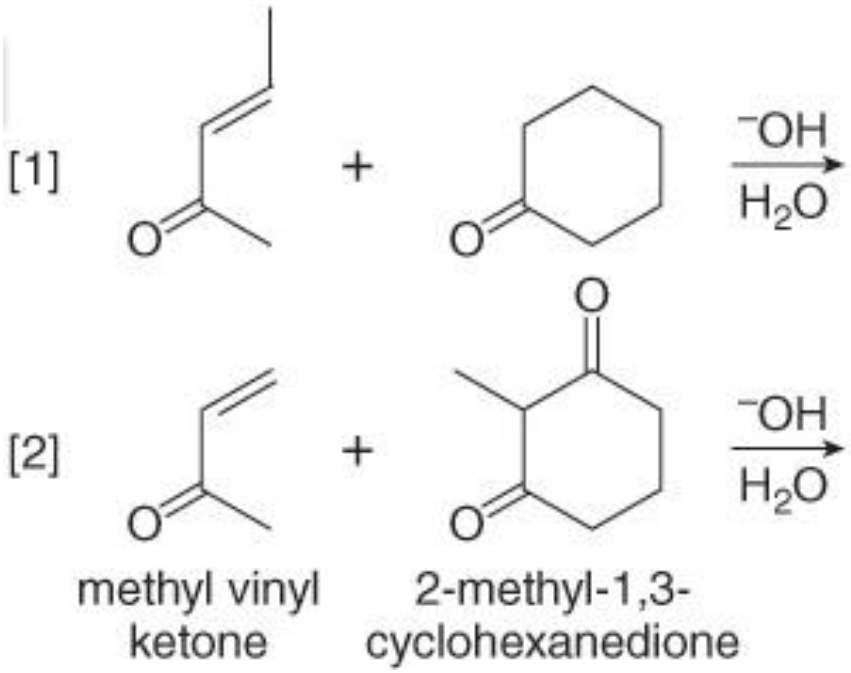


Reação de Stork

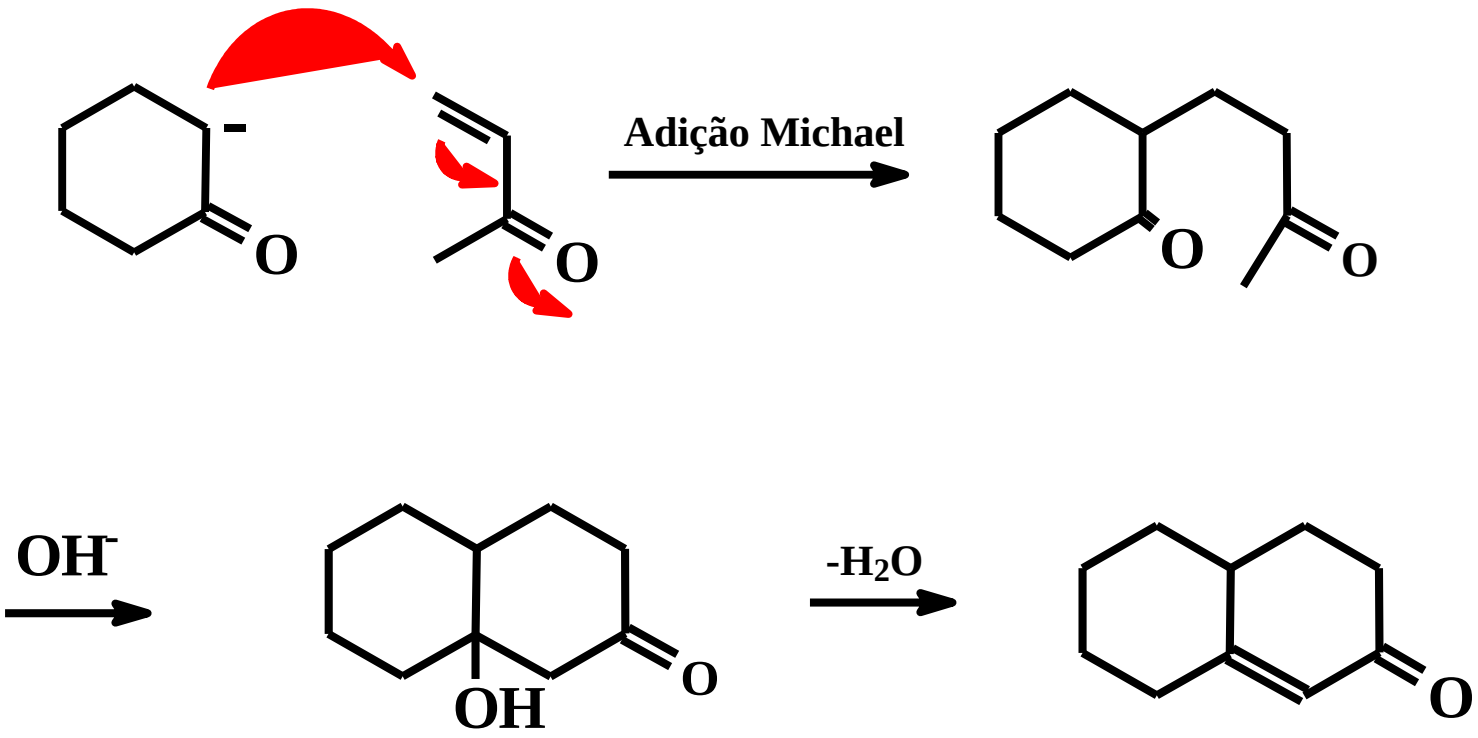


Reações de anelação de Robinson

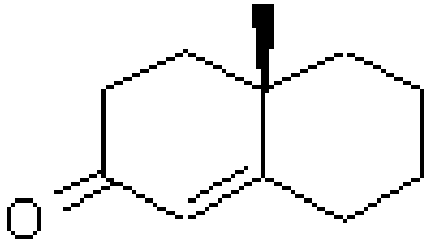
- A reação de anelação de Robinson forma um anel de seis membros e três novas ligações C—C – duas ligações σ e uma ligação π.O produto contém uma cetona α,β-insaturada em um anel ciclohexano – ou seja, uma 2-ciclohexenona.
- Para gerar o componente enolato da anulação de Robinson, normalmente são usados $^{-}$OH em H2O ou $^{-}$OEt em EtOH.



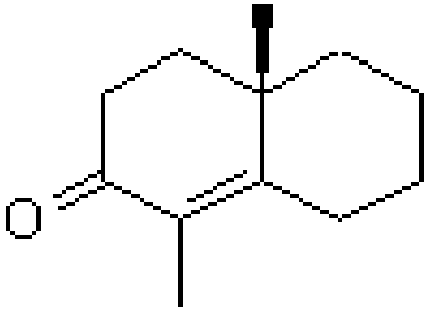
Anelações de Robinson (1886-1975)



Quais seriam os materiais de partida para a preparação das cetonas abaixo ? (via anelações de Robinson)

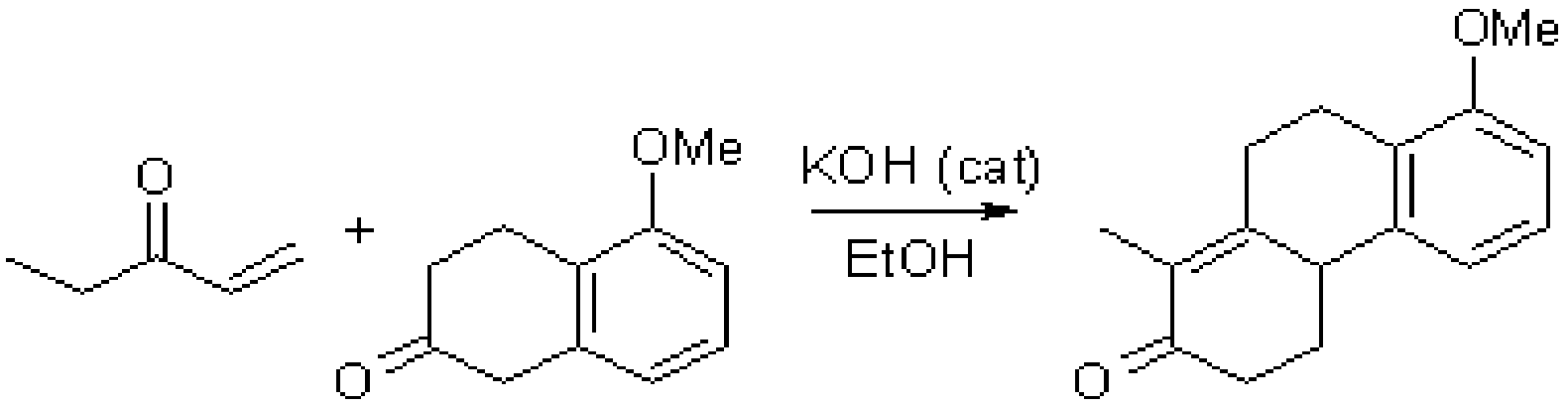


(a)

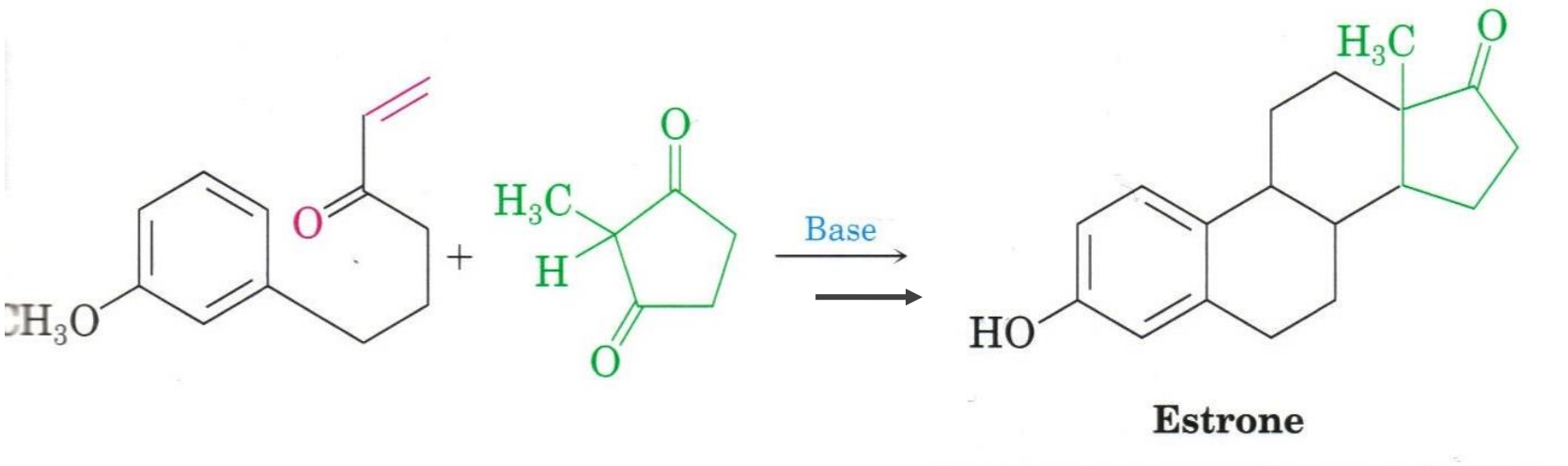


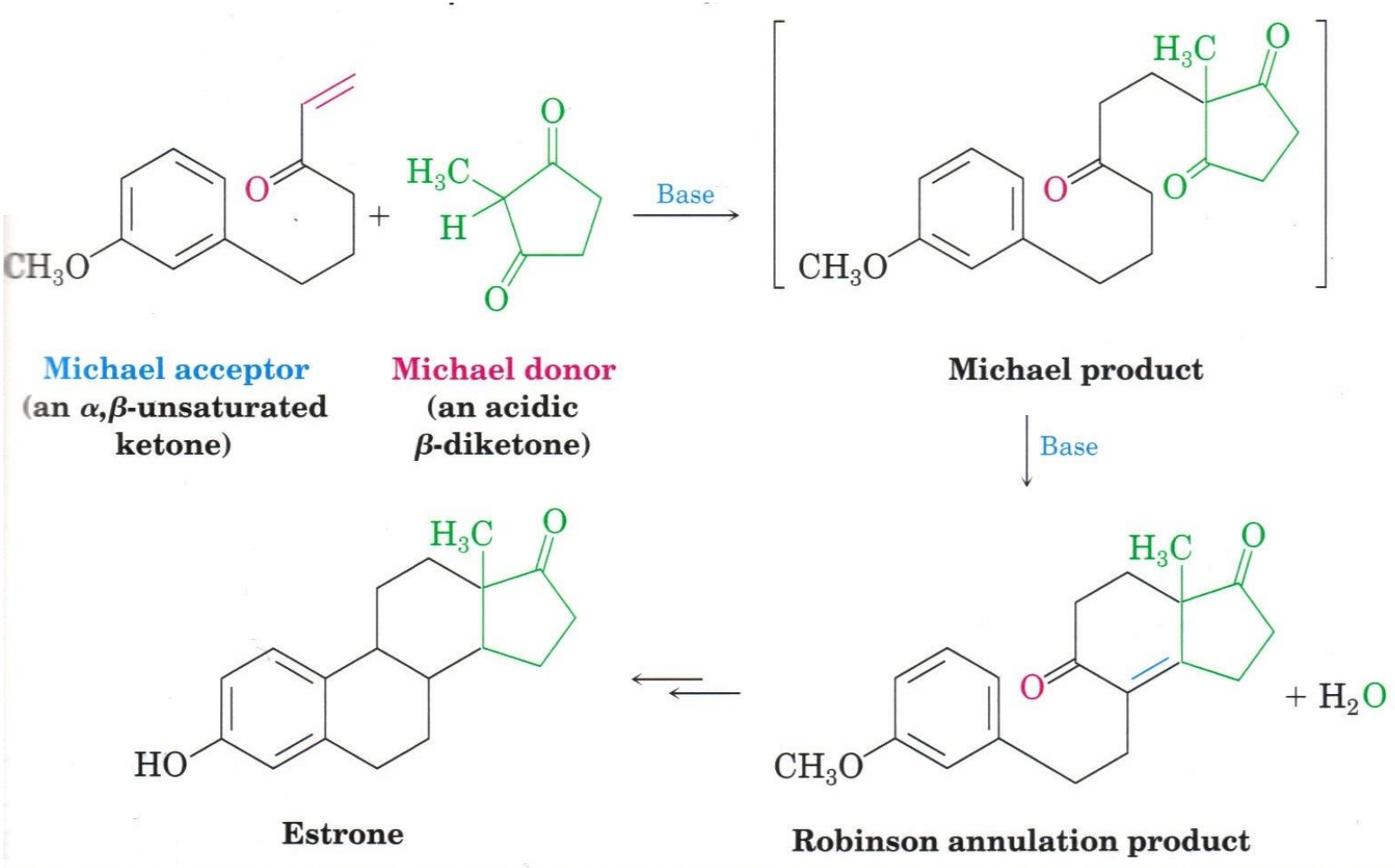
(b)

Qual seria o mecanismo para a reação de anelação de Robinson abaixo?



Qual seria o mecanismo para a reação de anelação de Robinson abaixo?




CH3O
O
+
H3C
H
O
O
Base
H3C
O
O
O
CH3O
Michael acceptor
(an α,β-unsaturated
ketone)
Michael donor
(an acidic
β-diketone)
Michael product
Base
H3C
O
HO
Estrone
H3C
O
O
CH3O
+ H2O
Robinson annulation product