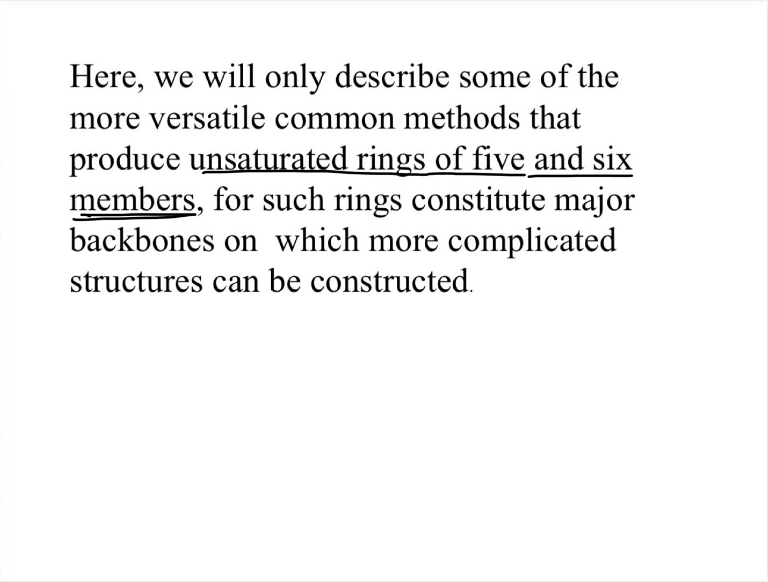
بدنا نصنّع

① unsaturated ② conjugated ← aromatic

cycle فيها hetero cycle ← heterocyclic

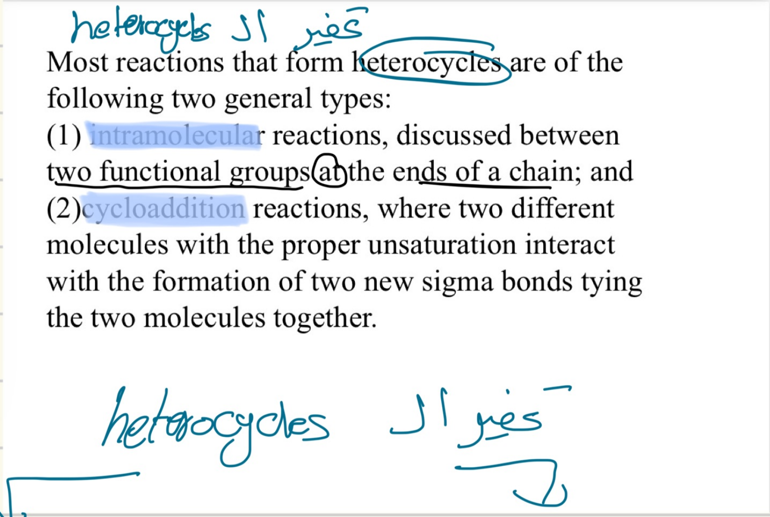


Here, we will only describe some of the more versatile common methods that produce unsaturated rings of five and six members, for such rings constitute major backbones on which more complicated structures can be constructed.

Phile : محب

electrophile : ① محب للـ e^- ② لازم يكون موجب الشحنة

nucleophile : ① محب للنواه والنواه موجبة . ② لازم يكون هوه سالب الشحنة (او) عنده f زواج الكترونات غير رابطه زي ال N



heterocycles تغير ال

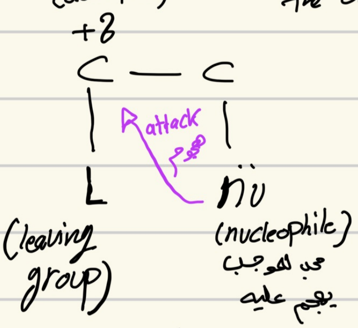
Most reactions that form heterocycles are of the following two general types:
(1) intramolecular reactions, discussed between two functional groups at the ends of a chain; and
(2) cycloaddition reactions, where two different molecules with the proper unsaturation interact with the formation of two new sigma bonds tying the two molecules together.

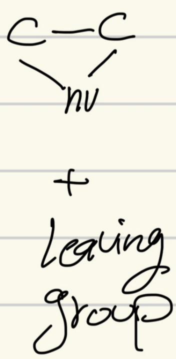
heterocycles تغير ال

فكره عامه نفهم
لازم نفهم
بالتفصيل
في ال chapter

intramolecular rxns : Between Two functional groups at the end of the chain

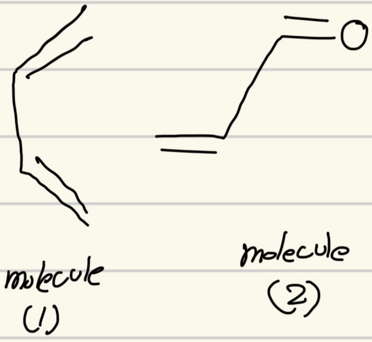
الآلية





cycloaddition rxns : Two different Molecules with unsaturated bonds تتفاعل مع بعض وتكون two new sigma bonds

الآلية



يصير عندي تحرّك لل double bonds

تحول كل الروابط الثنائية إلى روابط sigma (أحادية)

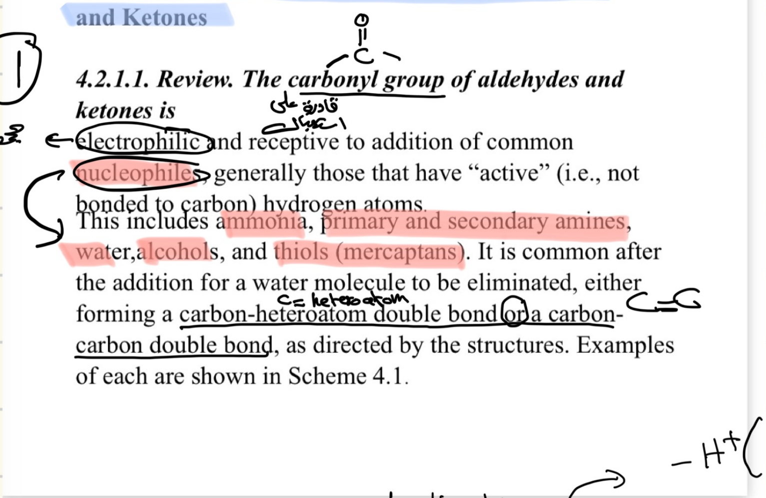
carbonyl group ←

$R\overset{O}{\overset{\|}{C}}R'$

ketone

$R\overset{O}{\overset{\|}{C}}H$ → carbonyl group

تفاعلات ال aldehyde وال ketone



4.2.1. The Use of Familiar Reactions of Aldehydes and Ketones

①

4.2.1.1. Review. The carbonyl group of aldehydes and ketones is electrophilic and receptive to addition of common nucleophiles, generally those that have "active" (i.e., not bonded to carbon) hydrogen atoms. This includes ammonia, primary and secondary amines, water, alcohols, and thiols (mercaptans). It is common after the addition for a water molecule to be eliminated, either forming a carbon-heteroatom double bond or a carbon-carbon double bond, as directed by the structures. Examples of each are shown in Scheme 4.1.

مجموعة كاربونيل ← electrophilic

قادرة على استقبال

C = heteroatom

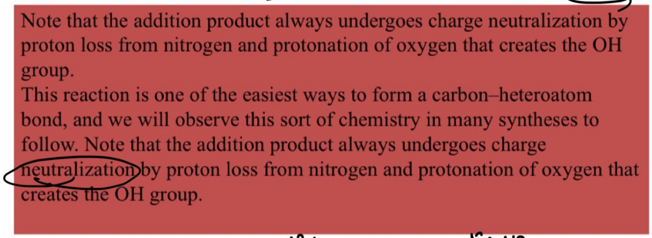
C=C

خطوات ⇒ addition → neutralization

→ −H⁺ (proton loss from electrophile)

→ +H⁺ (protonation of the O⁻) → elimination

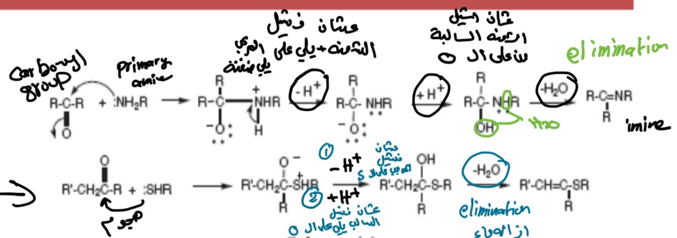
إزالة ماء وعمل رابطة ثنائية بين يلي نشلتهم OH وال H



Note that the addition product always undergoes charge neutralization by proton loss from nitrogen and protonation of oxygen that creates the OH group.
This reaction is one of the easiest ways to form a carbon–heteroatom bond, and we will observe this sort of chemistry in many syntheses to follow. Note that the addition product always undergoes charge neutralization by proton loss from nitrogen and protonation of oxygen that creates the OH group.

example ① →

example ② →



Scheme 4.1

$$\overset{-\delta}{O}\ \|\ \overset{+\delta}{C}$$

carbonyl group

electronegativity: قدرة الذرة على سحب الكترونات الرابطة نحوها.

O > C

أعلى سالبية كهربائية

O — C

nucleophile ← −δ وكأنها كسبت الالكترونات

+δ → electrophile E⁺ وكأنها فقدت الالكترونات

⇒ مجموعة ال carbonyl تعمل تفاعلات addition (إضافة) : من تفكك شكل

رابطة ثلاثية → رابطة ثنائية

رابطة ثنائية → رابطة أحادية

رابطة رباعية → رابطة ثلاثية

carbonyl group (في ال تفاعل) (electrophile) + مركب (nucleophile) → مرتبط مع H

thiols (mercaptans) SH

NH3 ammonia

NH2 (Primary amines)
NH (Secondary amines)

H2O

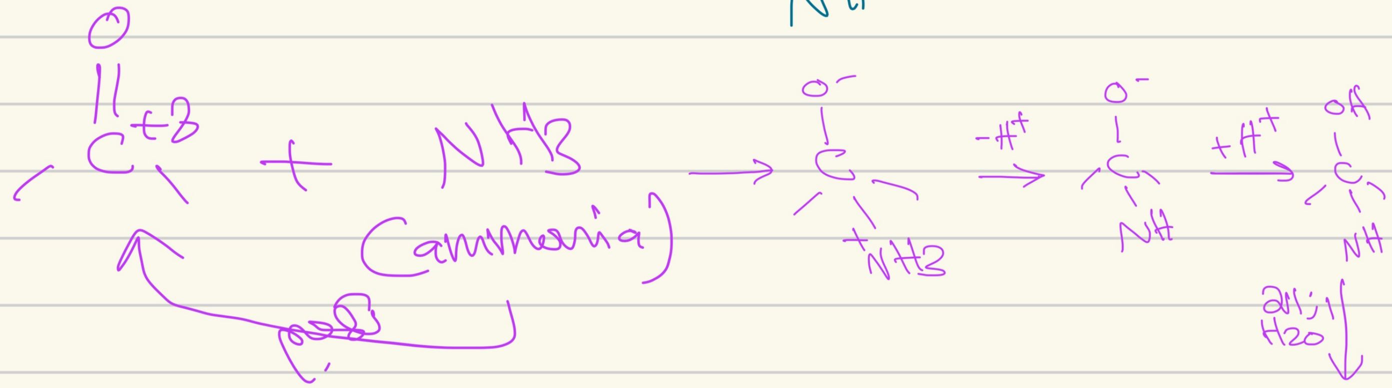
alcohol

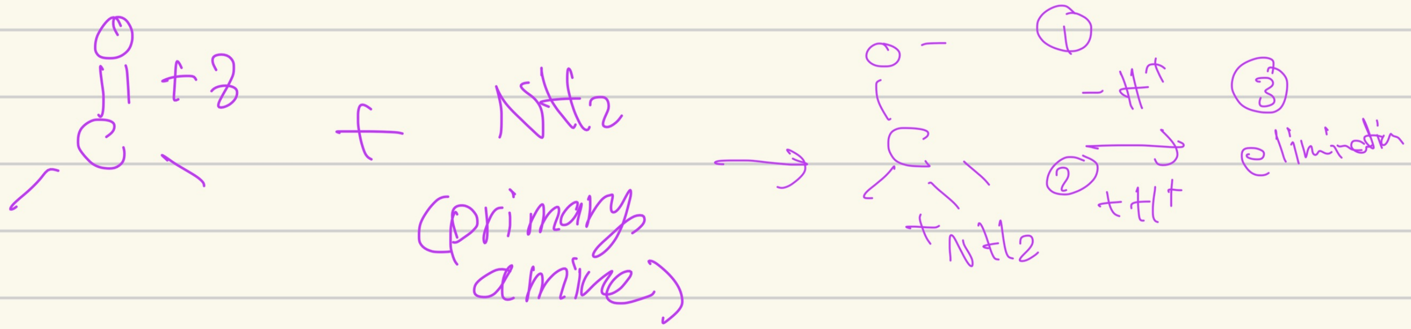
carbonyl carbon E⁺ (electrophile)

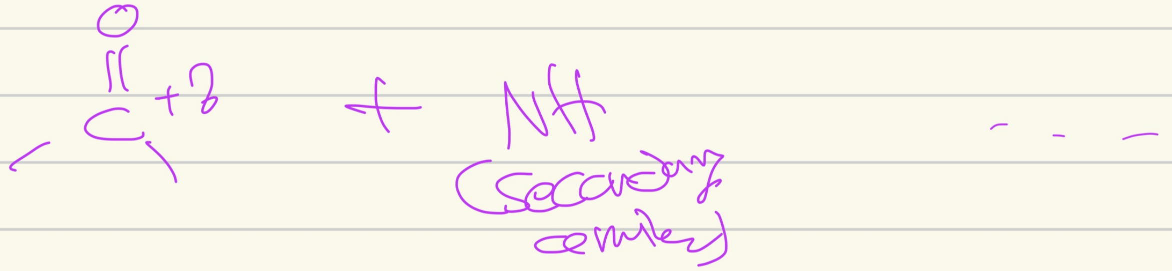
electrophile + nuclephile H (addition) تفاعل

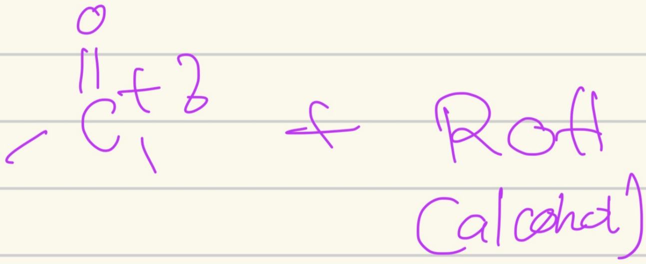
electrophile ⇓ (carbonyl group)

nuclephile ⇓ SH, NH3, NH2 / NH, alcohol, H2O

①


②


③


④


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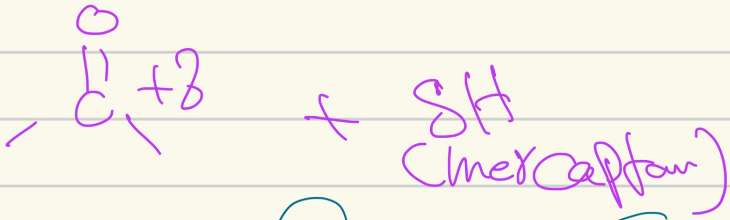
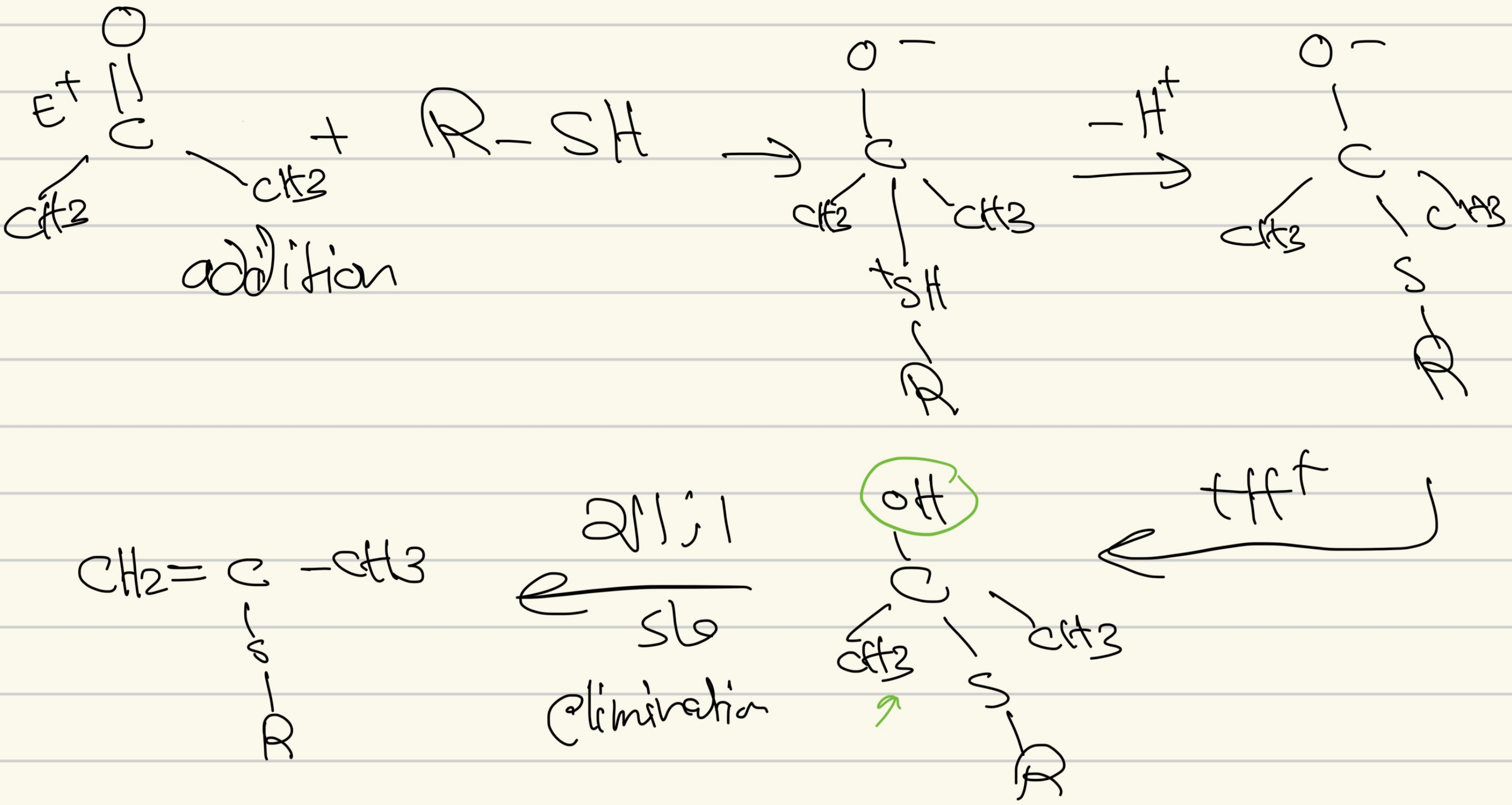


① بعدما أضفنا ال electrophile ← ② - H⁺ عشان نشيل الشحنة الموجبة ← ③ + H⁺ عشان نشيل الشحنة السالبة ← ④ elimination ازالة ماء وعمل رابطة ثنائية (ونضع الرابطة بين الذرتين يلي وقفنا عندهم C H و OH

ملخص الفكرة بمثال :



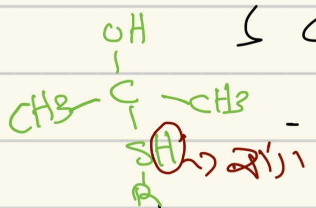
بالنسبة لموضوع ال elimination :

أنا بعمل إزالة لل H_2O بشيل OH من

كربونة الكربونيل OH C بشيل وال H من

أشباهها ؟ ال H الها أولويات

① اذا كانت ال heteroatom < N ---
< S

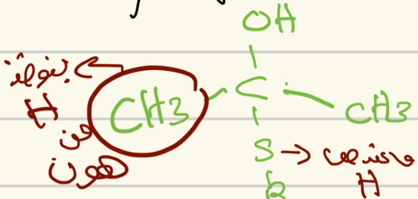


بس هاد H نزل ال H منها .

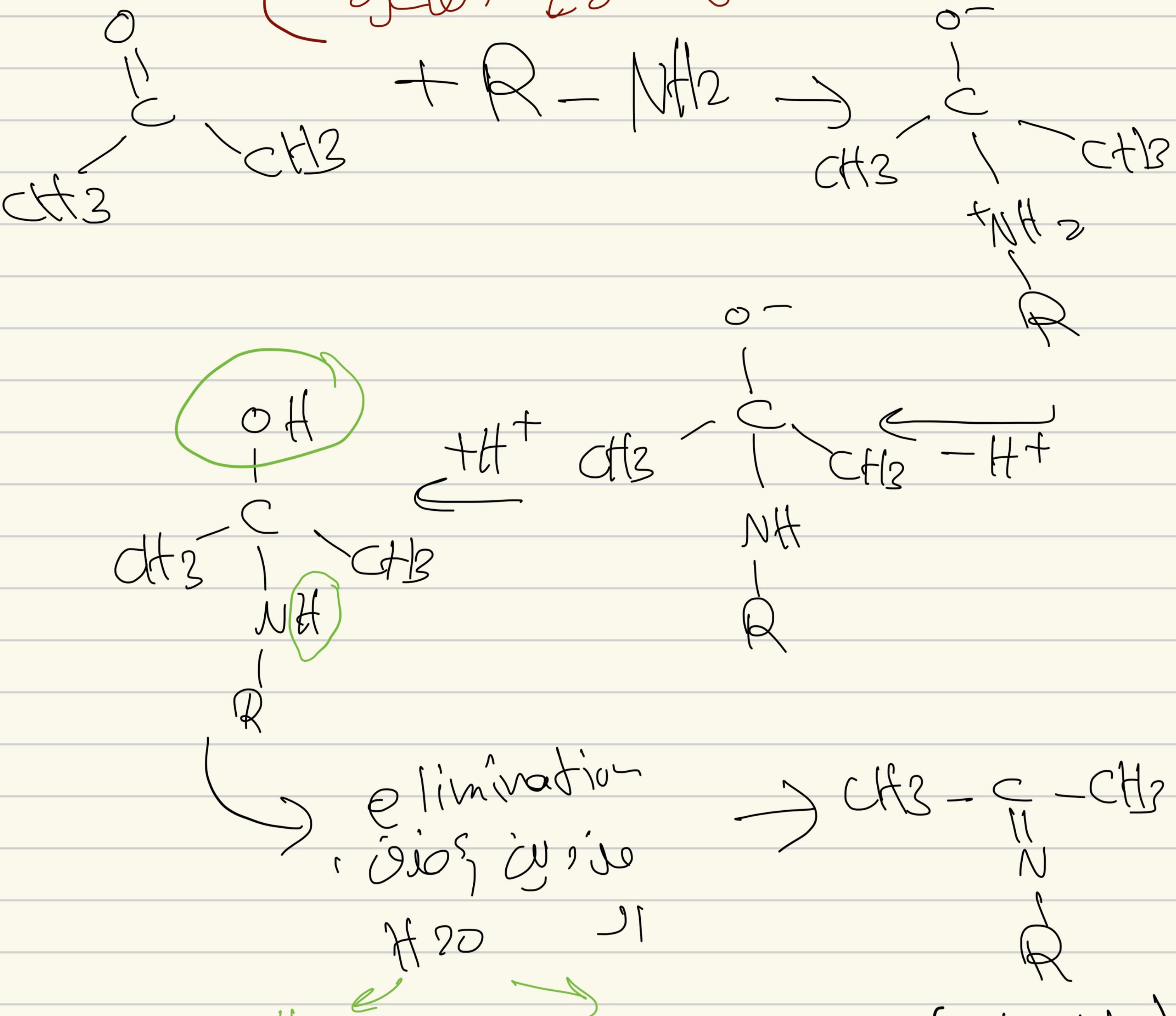
② في حال ال heteroatom ما عندها

H .... تذهب إلى الكربونات الملاصقة بالكربونة

تبعة الكربونيل وبنشيل منهم H .



مثال لتوضيح الفكرة :)



OH من كربونة الكربونيل ✓

H

أولويات

① من الـ heteroatom

② إذا الـ heteroatom ما عندها H بنوخذ من الكربونات المرتبطة مع كربونة الكربونيل

عشان أعمله فتح دوره ⇐ في طريقة نحوله أخرى ⇐ هل رح ينتج عندي مركب له

فيه الرابطة ثنائية بين c=c

أو رابطة ثنائية بين c = hetero atom

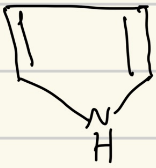
⇐ بنطلع على الـ electrophile يلي ضفته وبشوف كم H معه

إذا 2 ⇐ رح يطلع مركب c = hetero atom

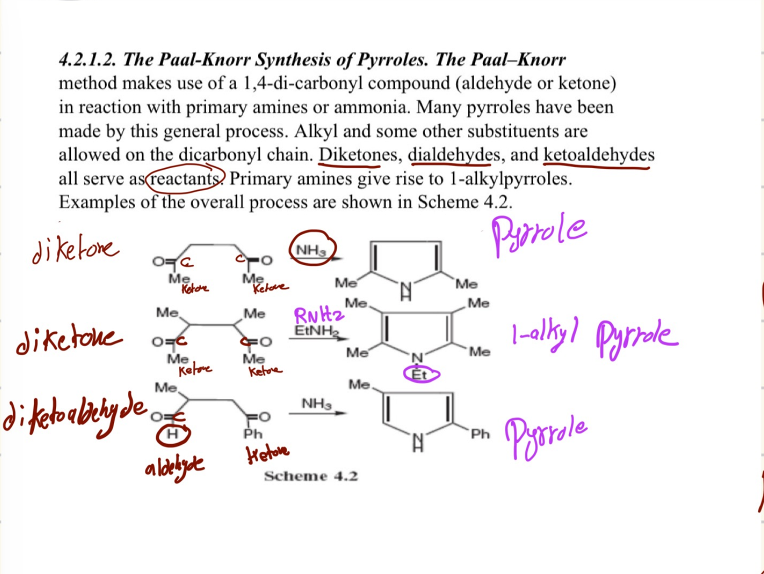
لـ إذا 1 ← رح يطلع مركب c = c

②

Synthesis of Pyrroles:



Pyrrole 2slio

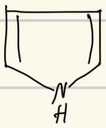


4.2.1.2. The Paal-Knorr Synthesis of Pyrroles. The Paal–Knorr method makes use of a 1,4-di-carbonyl compound (aldehyde or ketone) in reaction with primary amines or ammonia. Many pyrroles have been made by this general process. Alkyl and some other substituents are allowed on the dicarbonyl chain. Diketones, dialdehydes, and ketoaldehydes all serve as reactants. Primary amines give rise to 1-alkylpyrroles. Examples of the overall process are shown in Scheme 4.2.

Scheme 4.2

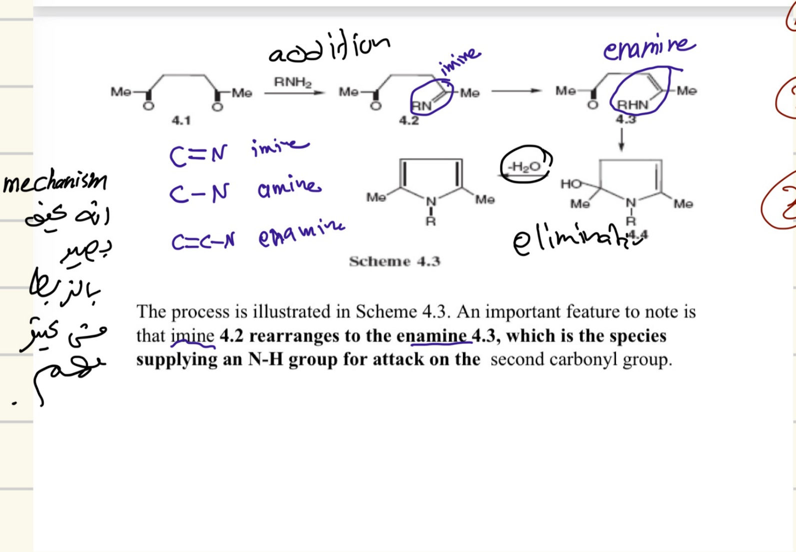
Pall – knorr ⇐ اسم طريقة التصنيع

1,4-dicarbonyl + NH3 → Pyrrole



① diketone
or
② dialdehyde
or
③ diketoaldehyde
(Reactants)

أو



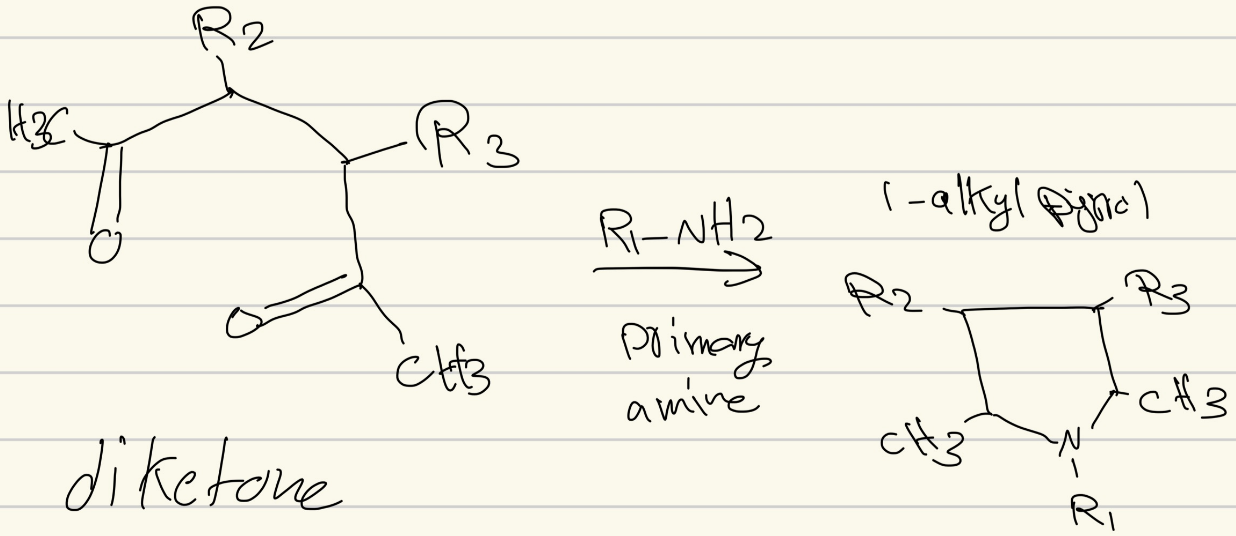
Scheme 4.3

The process is illustrated in Scheme 4.3. An important feature to note is that imine **4.2 rearranges to the enamine 4.3, which is the species supplying an N-H group for attack on the** second carbonyl group.

mechanism
انه كيف
يصير
بالزبط
شي كثير
مهم
.

1,4-dicarbonyl + RNH2 → 1-alkyl Pyrrole
"primary"
"amine"

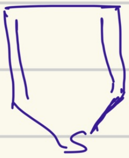
example

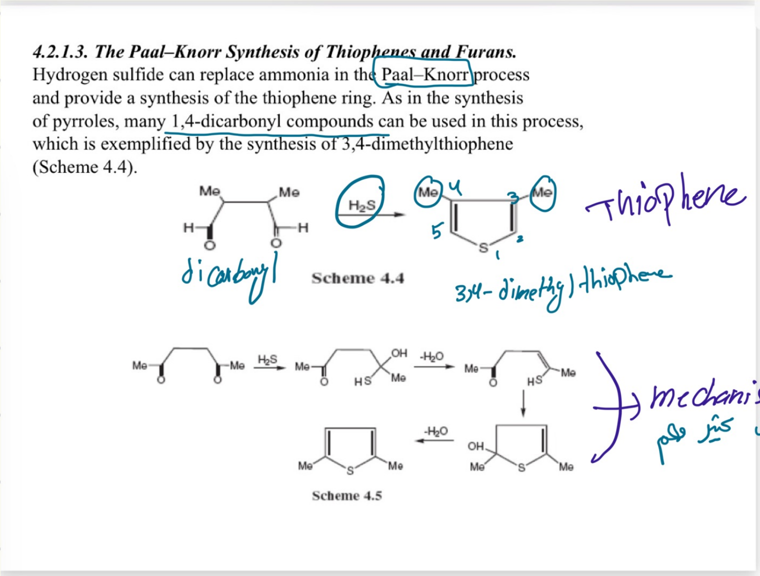


Done.

②

تصنيع ال Thiophene :





4.2.1.3. *The Paal–Knorr Synthesis of Thiophenes and Furans.*

Hydrogen sulfide can replace ammonia in the Paal–Knorr process and provide a synthesis of the thiophene ring. As in the synthesis of pyrroles, many 1,4-dicarbonyl compounds can be used in this process, which is exemplified by the synthesis of 3,4-dimethylthiophene (Scheme 4.4).

dicarbonyl

Scheme 4.4

Thiophene

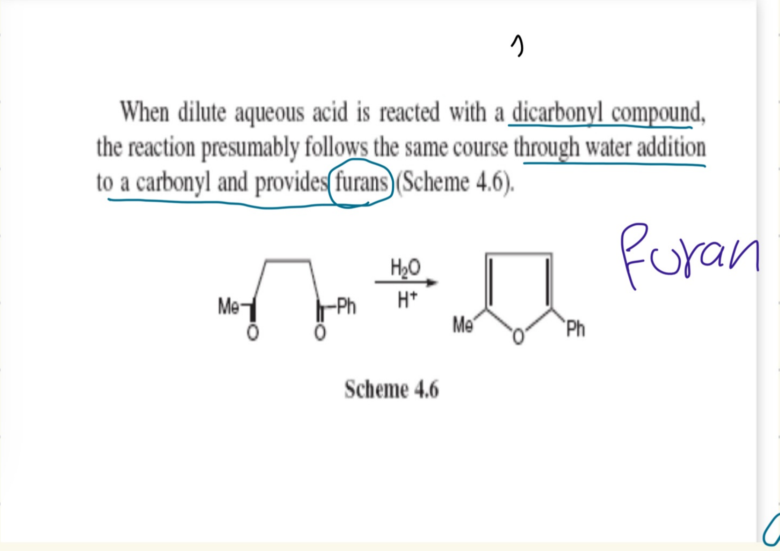
3,4- dimethyl thiophene

Scheme 4.5

mechanism
مش كثير مهم

طريقة التصنيع ← Paal-Knorr

di carbonyl + H_2S → thiophene

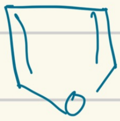


When dilute aqueous acid is reacted with a dicarbonyl compound, the reaction presumably follows the same course through water addition to a carbonyl and provides furans (Scheme 4.6).

Scheme 4.6

Furan

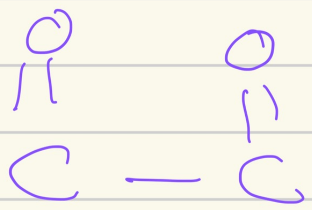
تصنيع ال Furan :



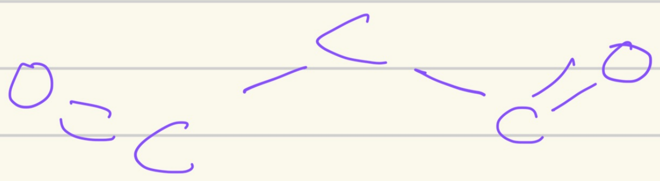
طريقة التصنيع ← Paal-Knorr

di-carbonyl + H_2O → Furan
H^+ acid catalyst
لـ بساعد
على حدوث
التفاعل.

α-dicarbonyl ⇒

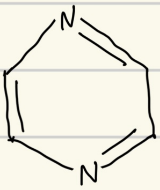


β-dicarbonyl ⇒

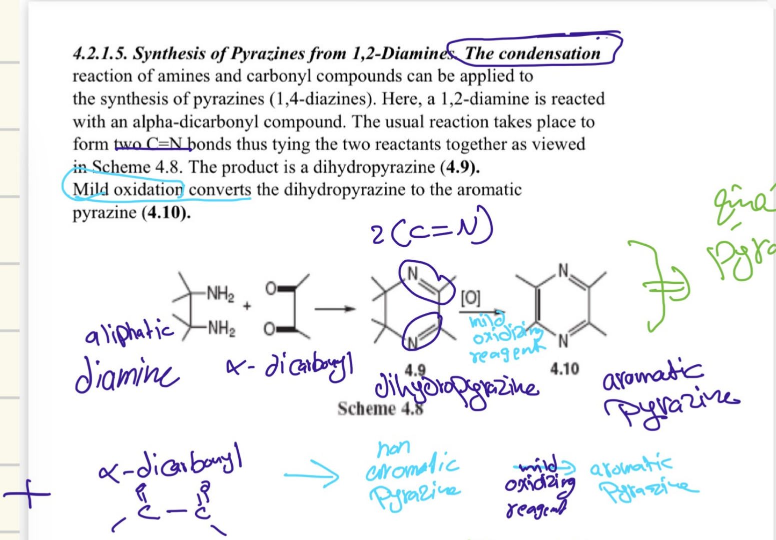


5

تحضير ال Pyrazines :



Pyrazine



4.2.1.5. Synthesis of Pyrazines from 1,2-Diamines. The condensation reaction of amines and carbonyl compounds can be applied to the synthesis of pyrazines (1,4-diazines). Here, a 1,2-diamine is reacted with an alpha-dicarbonyl compound. The usual reaction takes place to form two C=N bonds thus tying the two reactants together as viewed in Scheme 4.8. The product is a dihydropyrazine (**4.9**). Mild oxidation converts the dihydropyrazine to the aromatic pyrazine (**4.10**).

Scheme 4.8

تحضير pyrazine

condensation rxn ⇐ اسم التفاعل

diamine + α-dicarbonyl → non aromatic Pyrazine → mild oxidizing reagent → aromatic Pyrazine

كربونيل جنب بعض يلي عليهم كربونيل

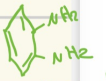
1,2-diamine + α-dicarbonyl → مركب أولي dihydropyrazine

mild oxidizing reagent [O]

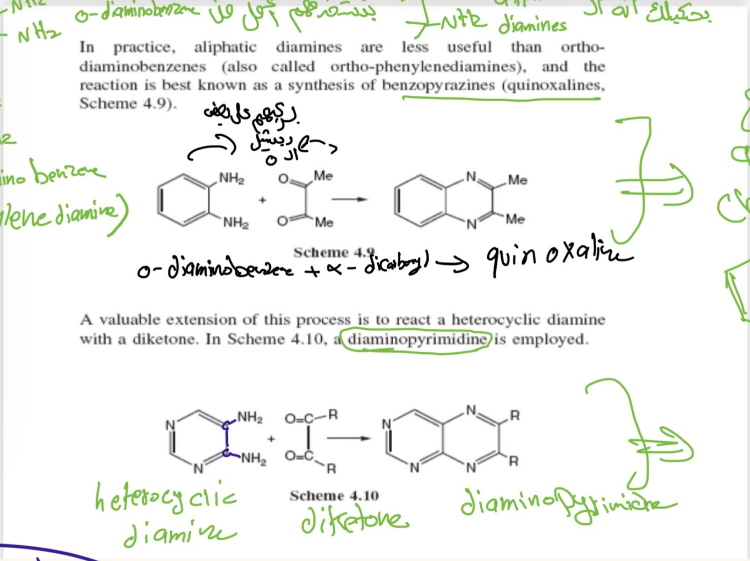
مركب نهائي aromatic Pyrazine

بحكيلك انو ال aliphatic diamines بنستخدمهم أقل من o-diaminobenzene

aliphatic diamine



o-diamino benzene (o-phenylene diamine)

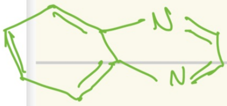


In practice, aliphatic diamines are less useful than ortho-diaminobenzenes (also called ortho-phenylenediamines), and the reaction is best known as a synthesis of benzopyrazines (quinoxalines, Scheme 4.9).

Scheme 4.9

o-diaminobenzene + α-dicarbonyl → quinoxaline

تحضير quinoxline (benzopyrazine)

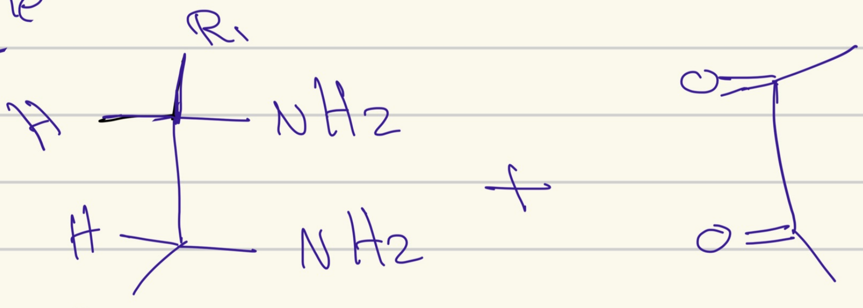


A valuable extension of this process is to react a heterocyclic diamine with a diketone. In Scheme 4.10, a diaminopyrimidine is employed.

Scheme 4.10

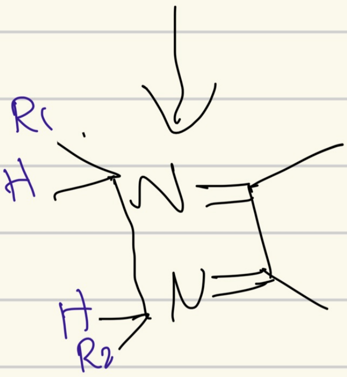
تحضير diaminopyrimidine

example



diamine α-dicarbonyl

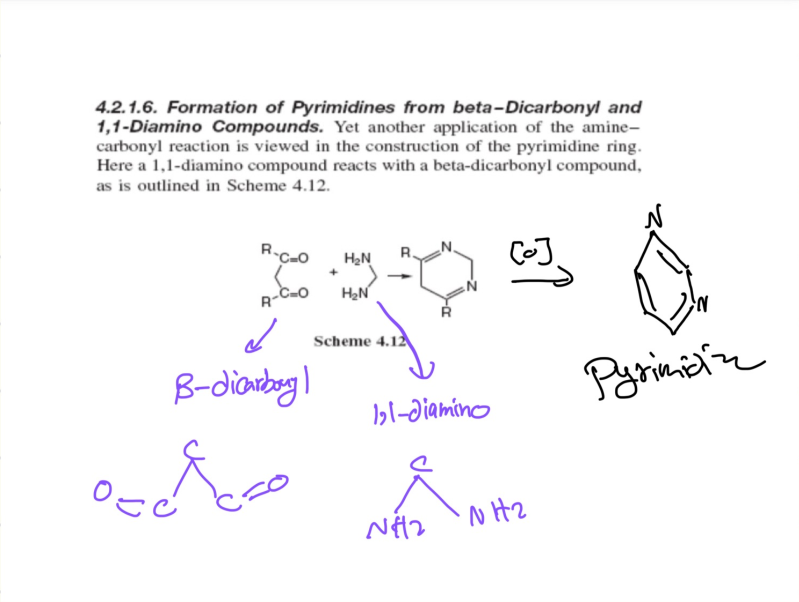
Condunsation rxn



oxidation → بنشيل 2H ⇒ والناتج نهائي

6

تحضير ال Pyrimidine :



4.2.1.6. *Formation of Pyrimidines from beta–Dicarbonyl and 1,1-Diamino Compounds.* Yet another application of the amine–carbonyl reaction is viewed in the construction of the pyrimidine ring. Here a 1,1-diamino compound reacts with a beta-dicarbonyl compound, as is outlined in Scheme 4.12.

Scheme 4.12

condunsation ⇐ اسم الطريقة