Synthetic Routes for Some Common Monocyclic Five-Membered π-Excessive Hetero ataromatic Compounds

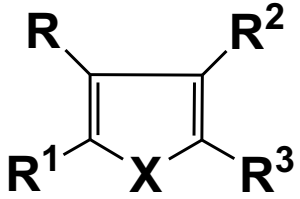
By

Assist. Prof. Oqba Nafia

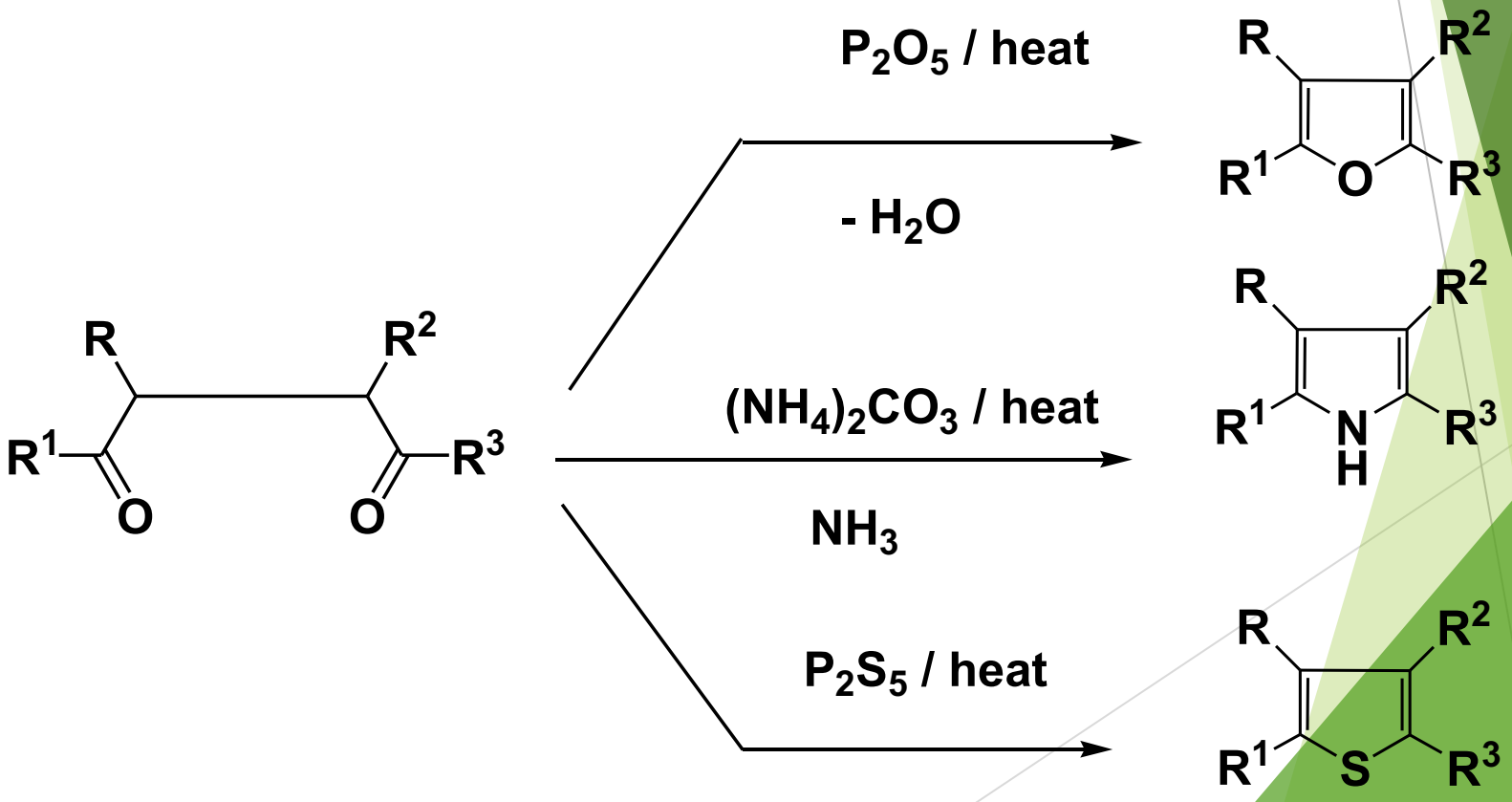
Ph.D. of Organic Chemistry "Synthesis of Hetero Cyclic"

College of Pharmacy-2020

Synthetic Routes to Five membered rings

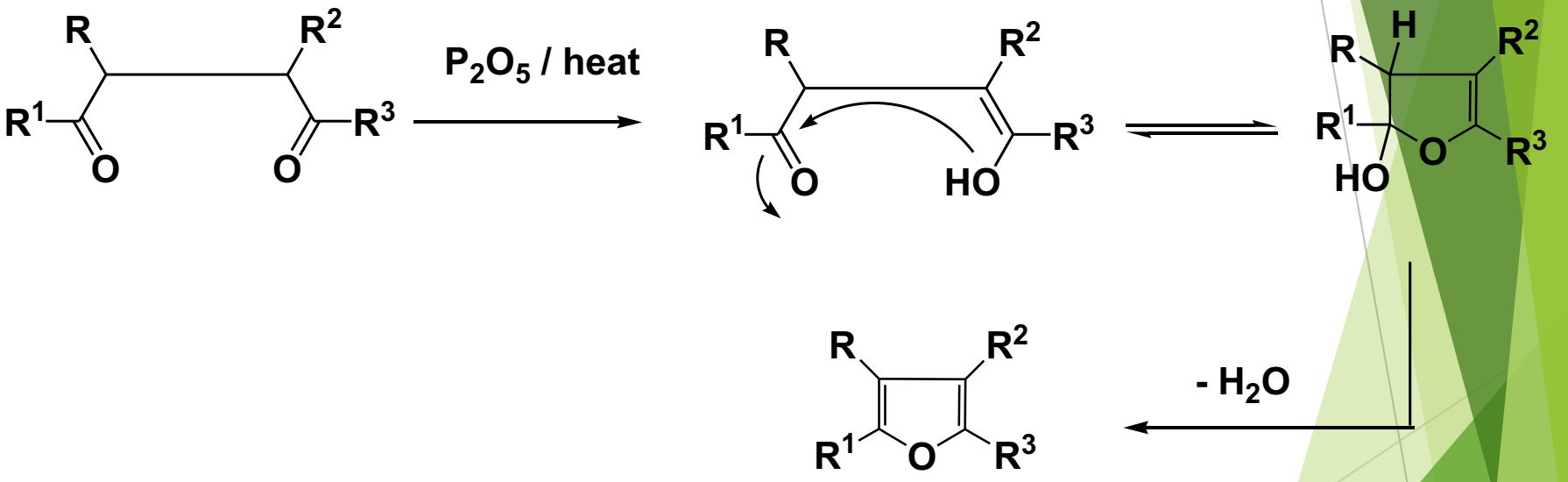


General method (Paal Synthesis)

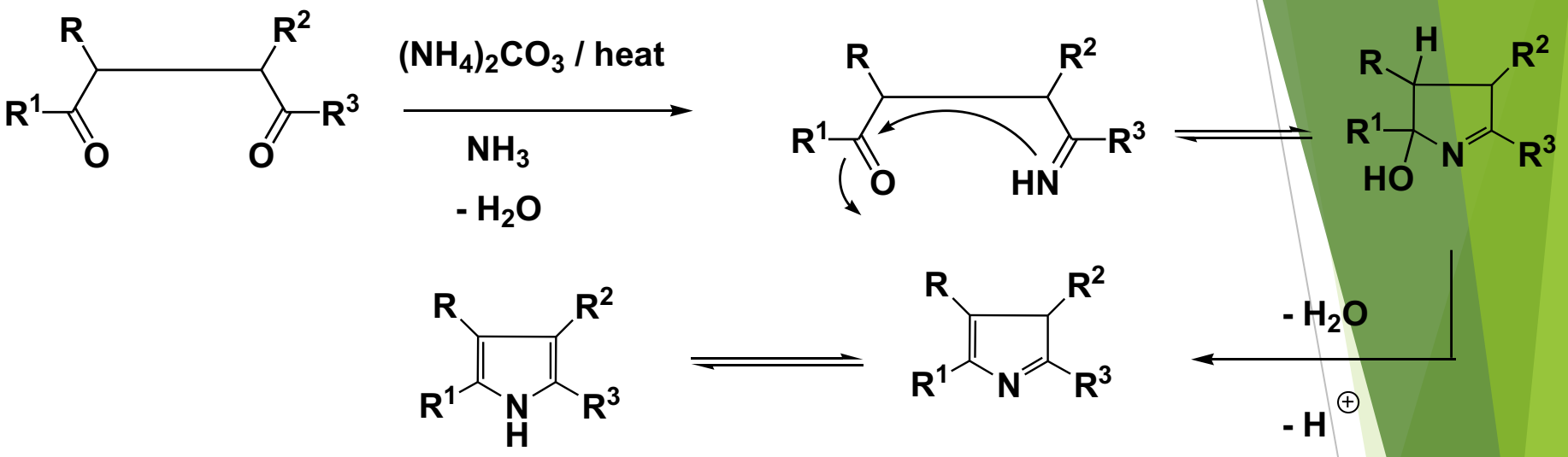


Mechanisms

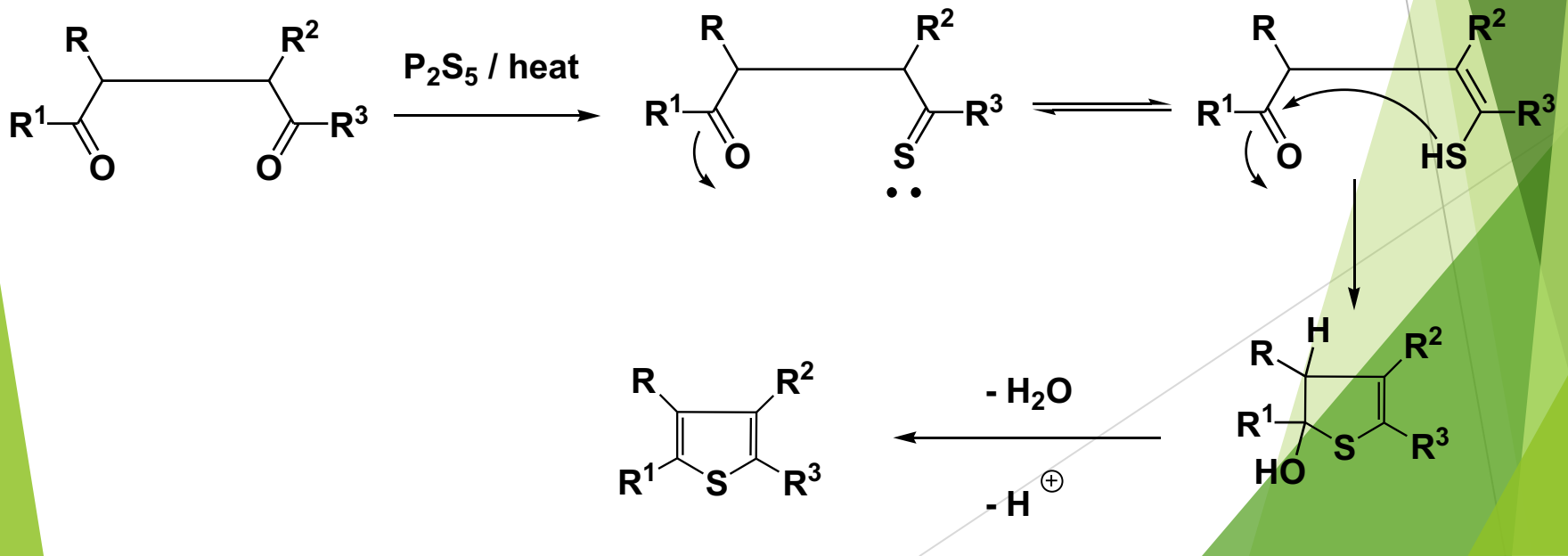
Formation of Furan



Formation of Pyrrole



Formation of Thiophene

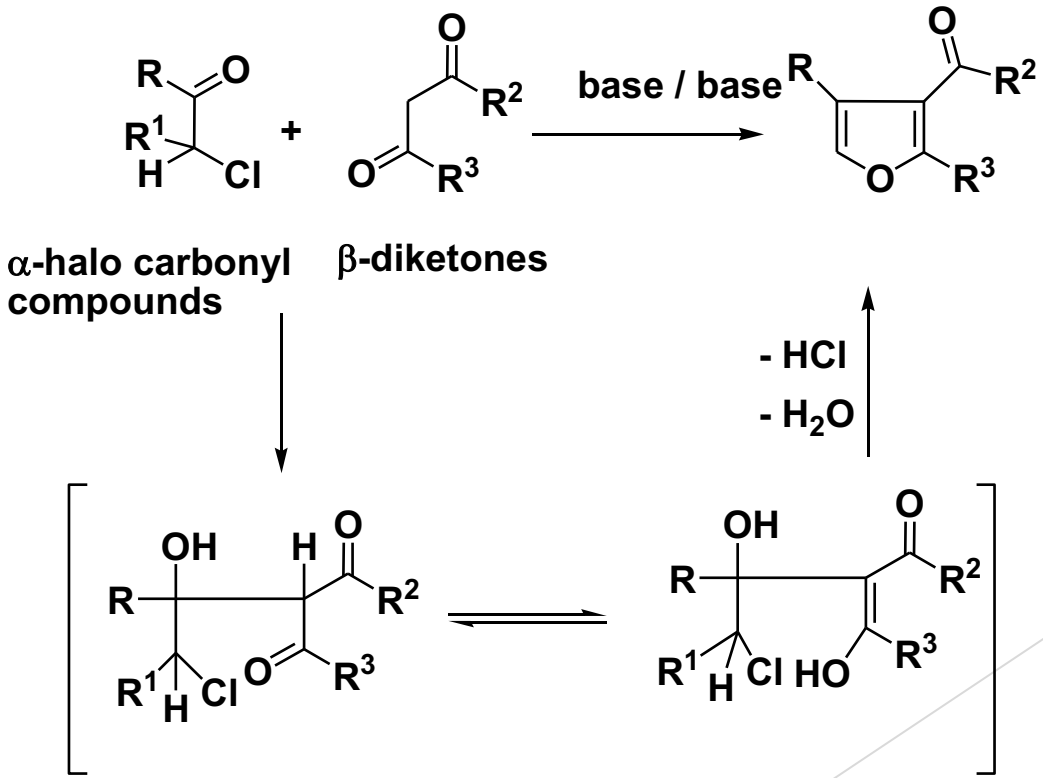


Synthesis of Furans

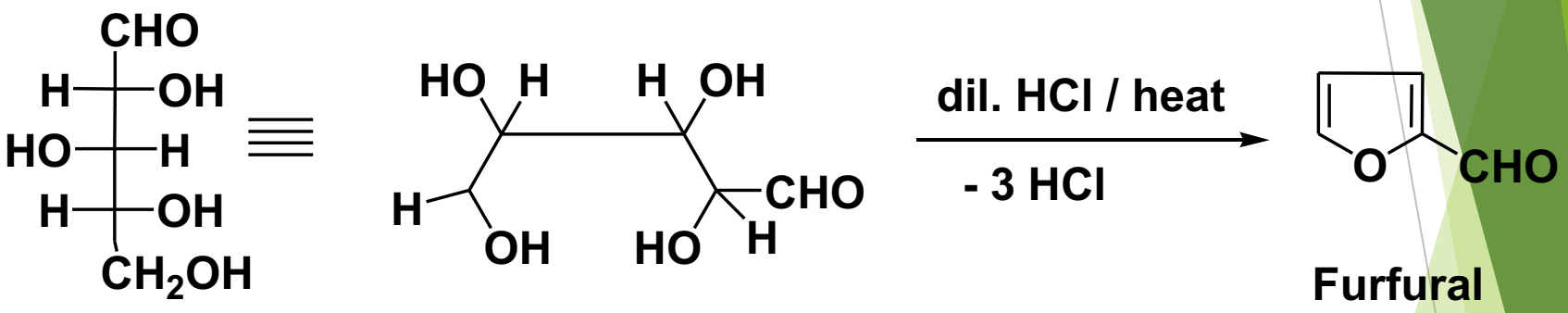
I- Paal Synthesis (as before)

(II) From α-halocarbonyl compounds (Fiest – Binary Synthesis)

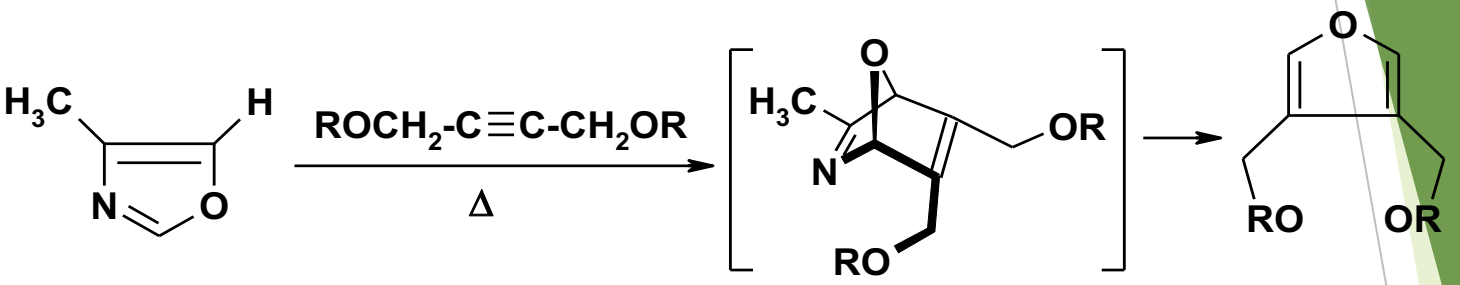
This synthesis involves an aldol condensation with the carbonyl group of the halogeno-component, followed by the formation of the oxygen ring by intramolecular displacement of halide, and finally loss of water.

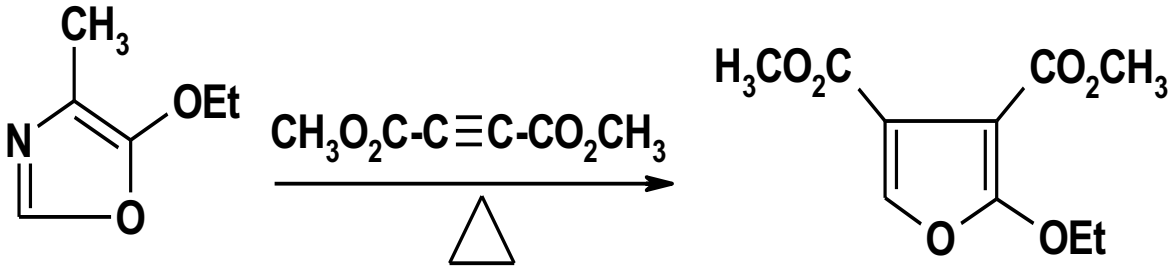


3- From Pentose



Cycloaddition reactions have also been applied to synthesis of furans.



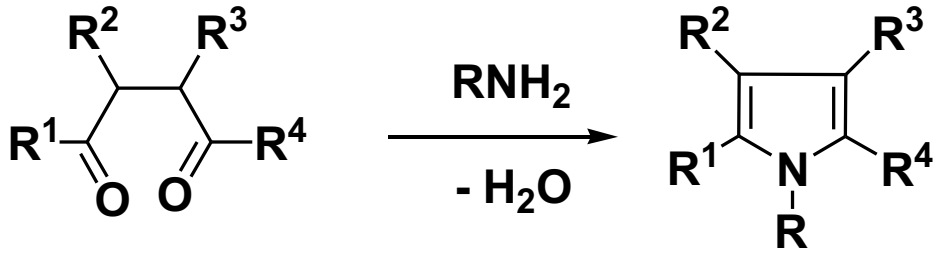


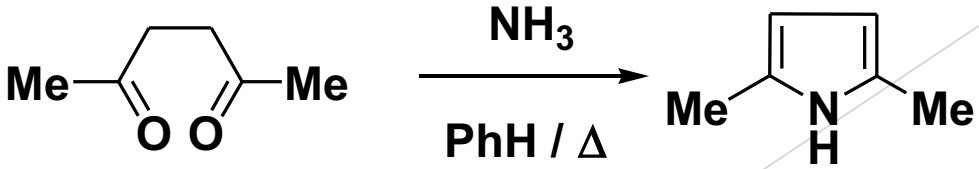
PYRROLE

There are three generally important approaches to pyrrole derivatives.

These can be summarized as shown.

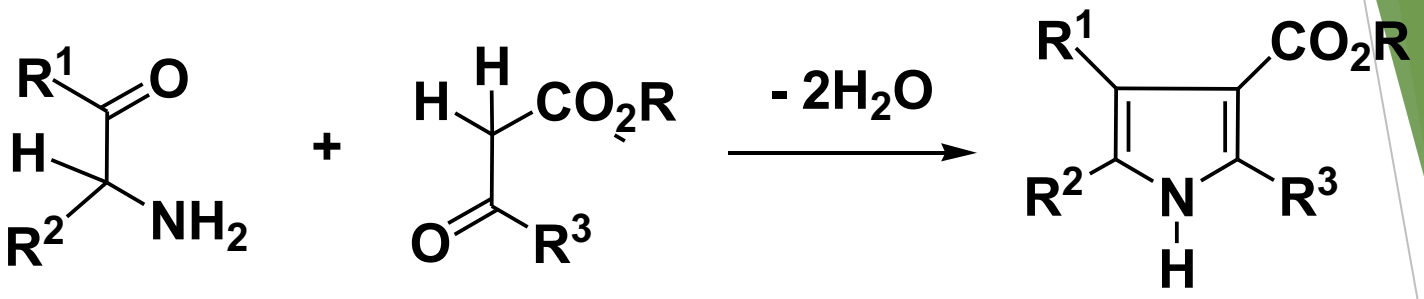
1- **Paal method** (1,4-Dicarbonyl compounds react with ammonia or primary amines to give pyrroles).



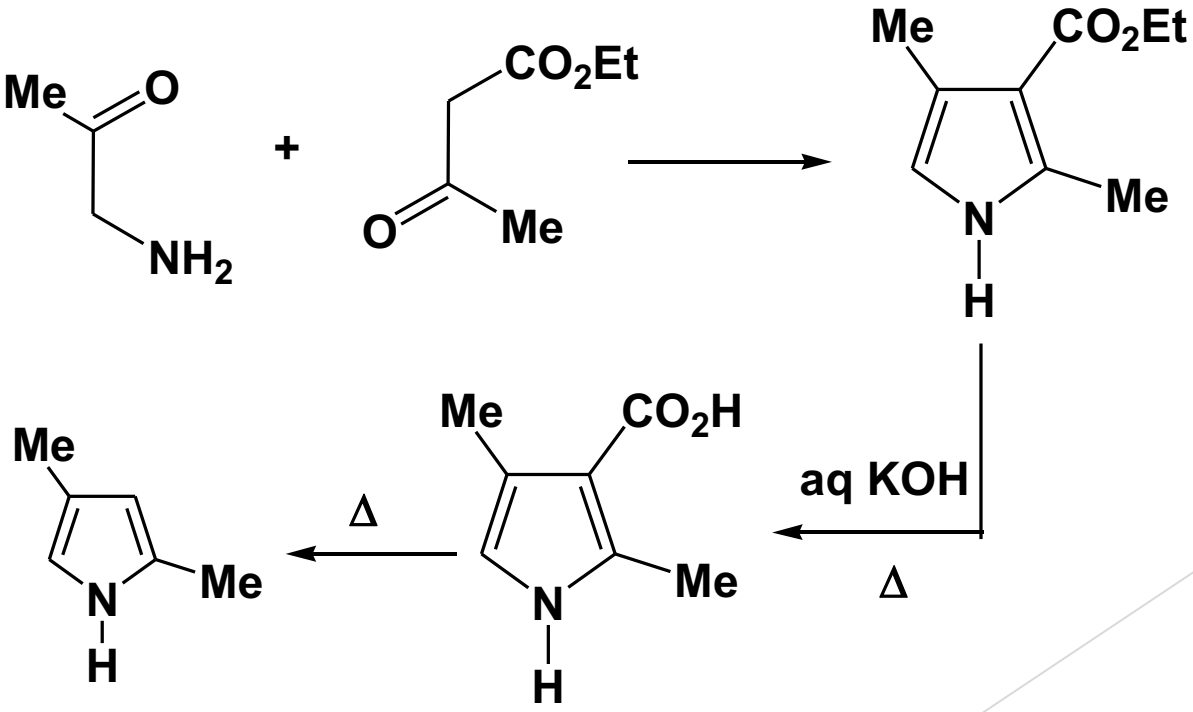


acetylacetone

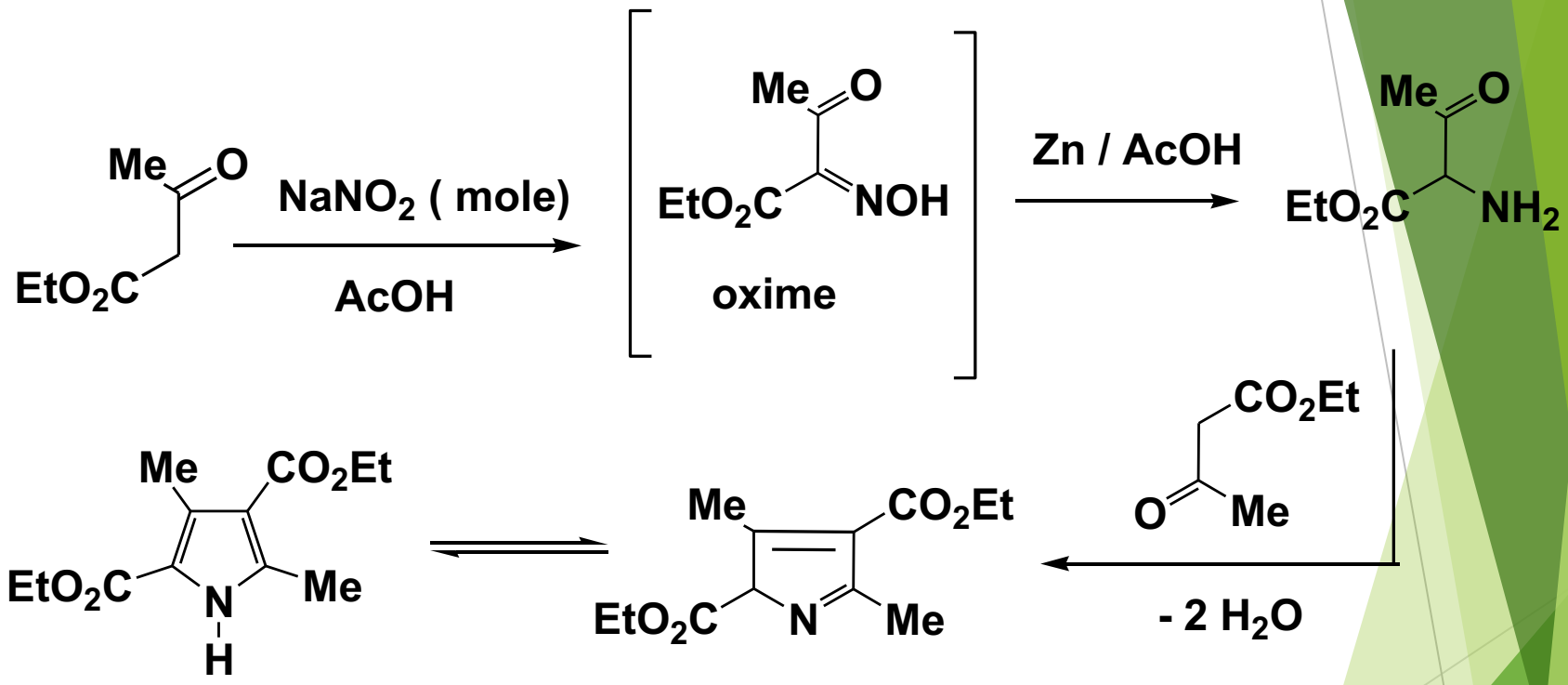
2- *Knorr Synthesis* (*From* α-Aminoketones and β-diketones)



Example 1

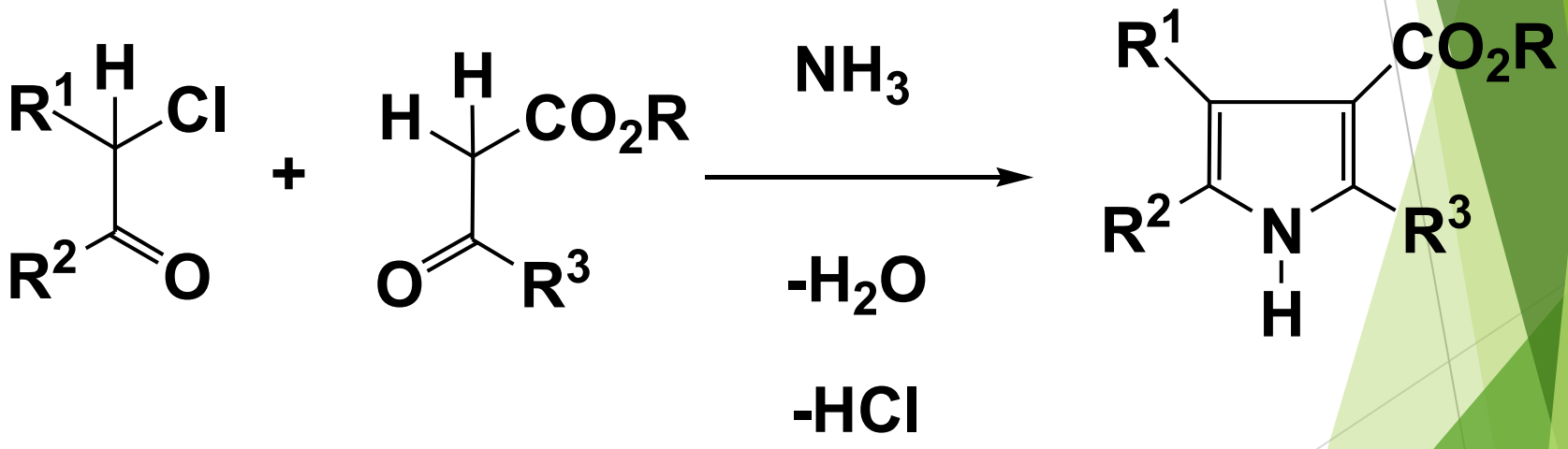


Synthesis of pyrrole-2,4-dicarboxylic esters

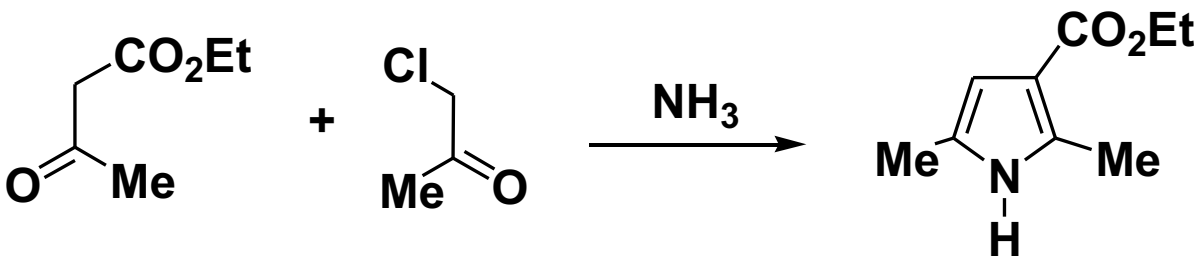


iii) *Hantzsch Synthesis*

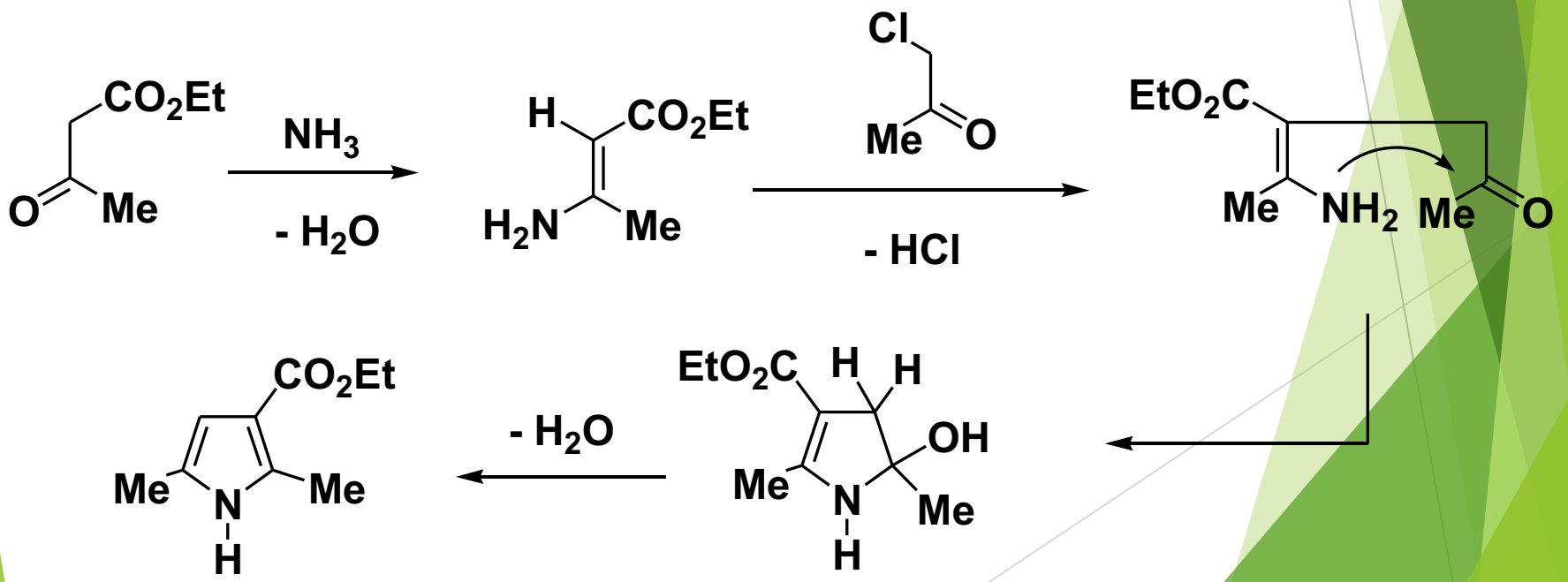
It the reaction of α-haloketones, β-ketoester and ammonia.



Example



Mechanism

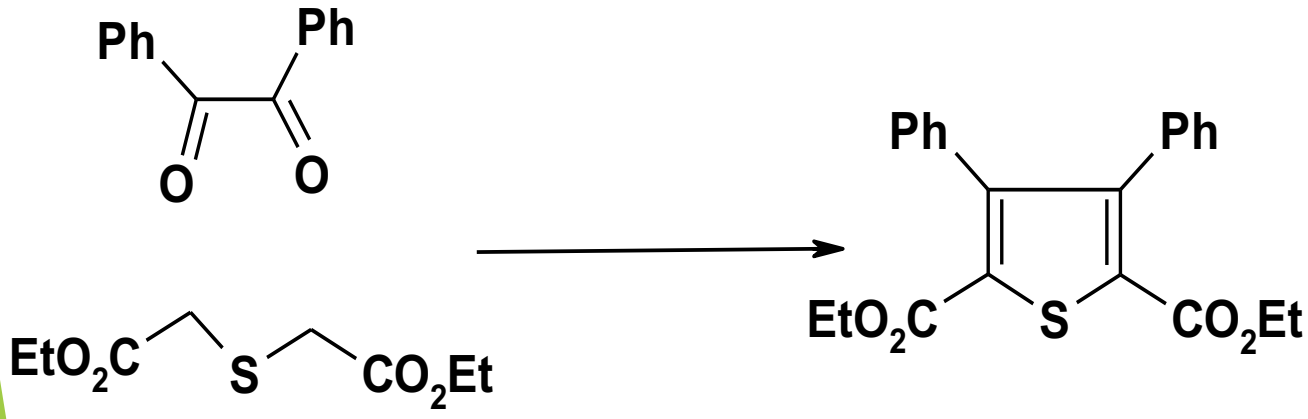


Synthesis Thiophene

1- Paal Synthesis (As before)

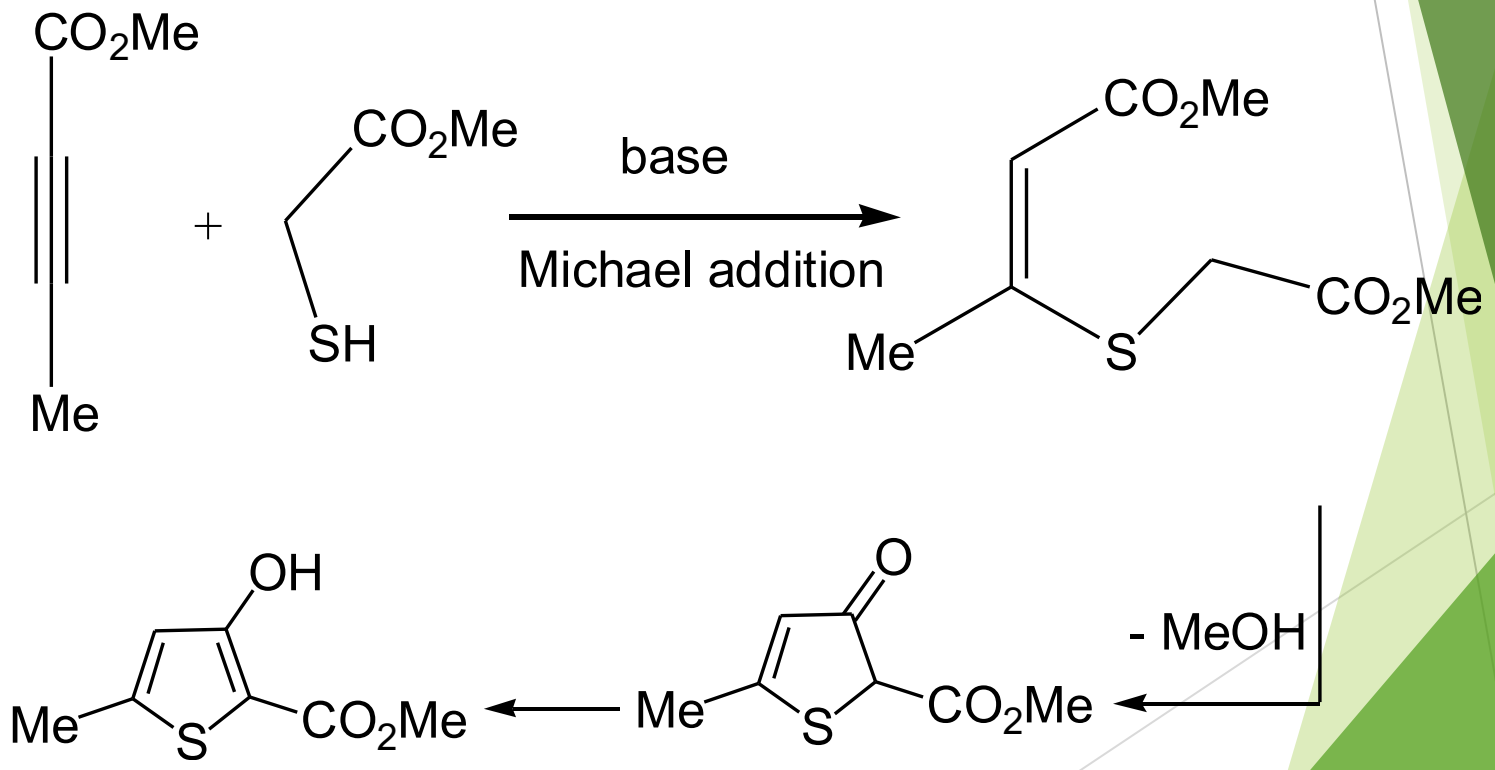
2- Hinsberg Synthesis

It is the reaction of α-diketones and diethyl thioacetate



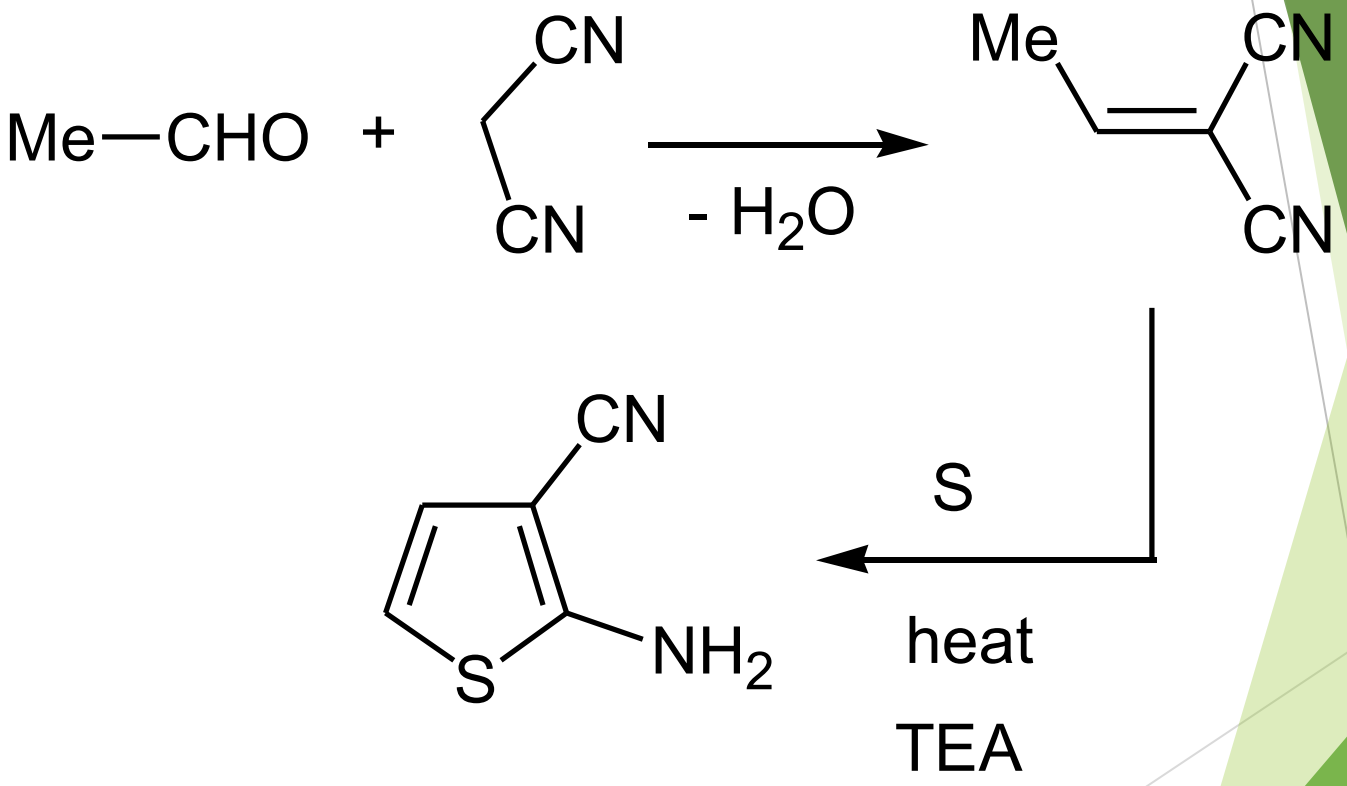
3- Fiesselmann synthesis

It is the reaction of methyl thioglycolate with unsaturated compounds like acetylenic molecules, followed by a base-catalyzed (*Dieckmann*-type cyclization) to generate substituted thiophenes

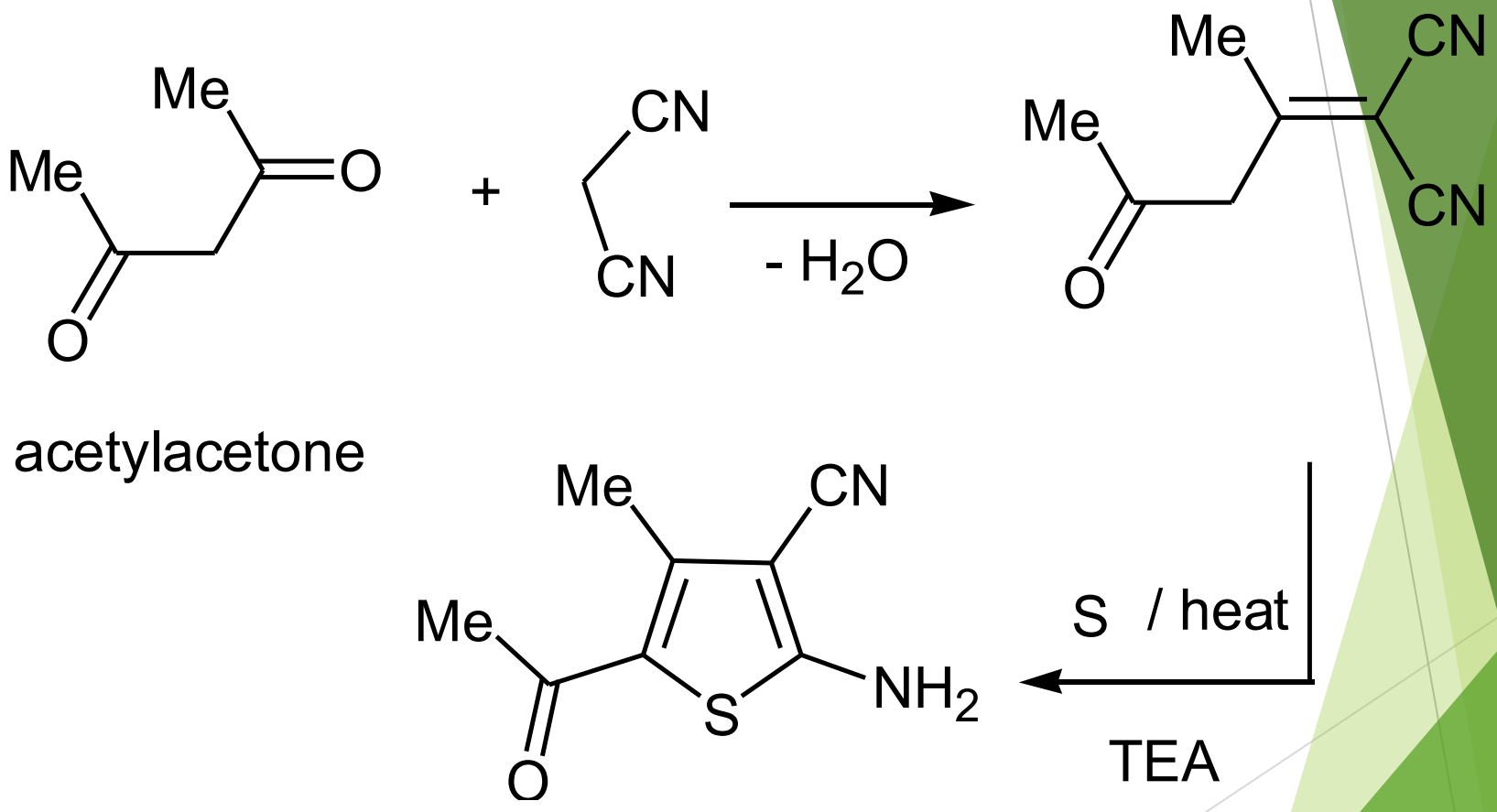


3- Gewald synthesis

Example 1



Example 2


Me
Me
O
O
+
CN
CN
- H_2O
Me
CN
Me
CN
O
acetylacetone
Me
CN
Me
S
NH_2
O
S / heat
TEA