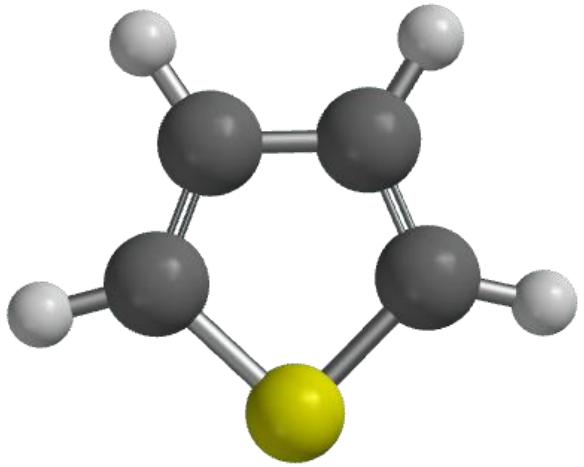
2302687 – Heterocyclic Compounds – Part I

Lecture 5-2

Ring Synthesis of Pyrrole



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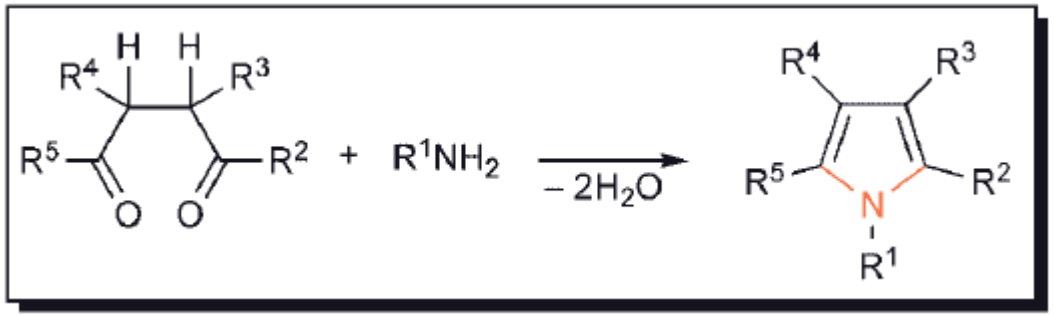
Recommended Textbook:

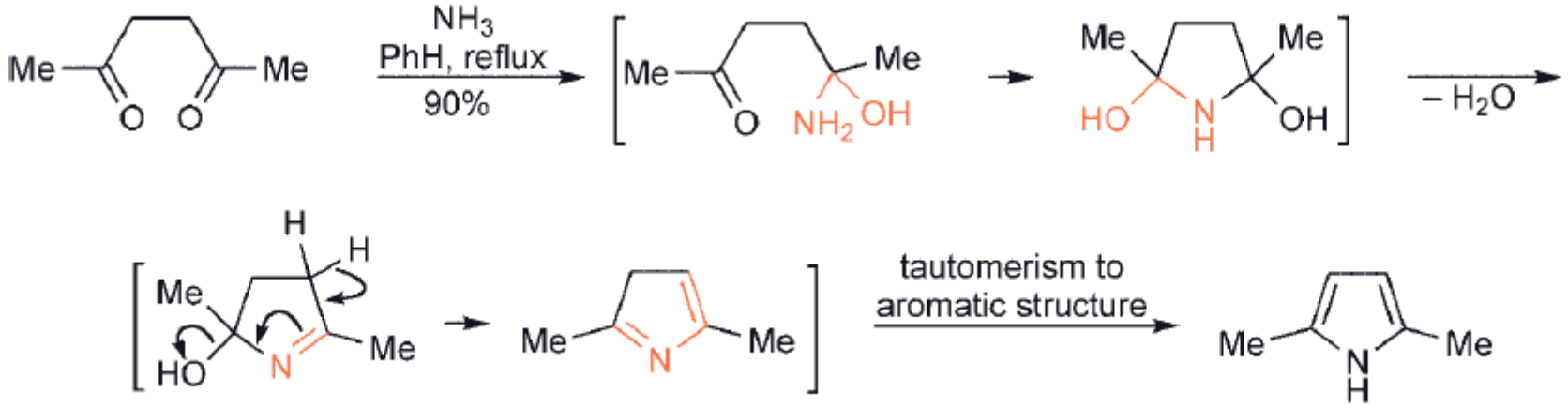
Heterocyclic Chemistry, 5th Edition, J. A. Joule, K. Mills, **2010**, Wiley

Ring Synthesis of Pyrroles

1) From 1,4-Dicarbonyl Compounds and Ammonia or Primary Amines

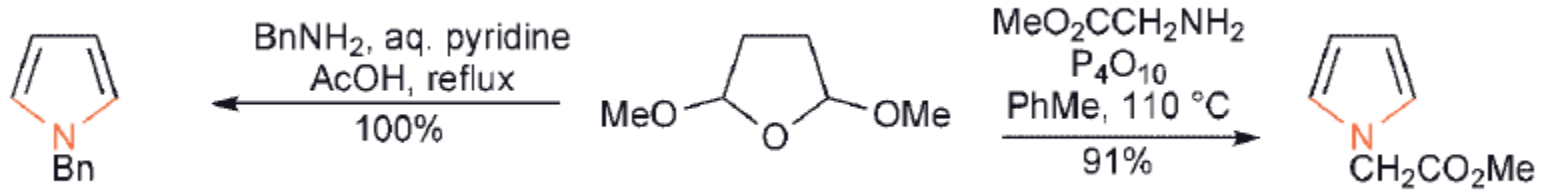


The Paal – Knorr Synthesis



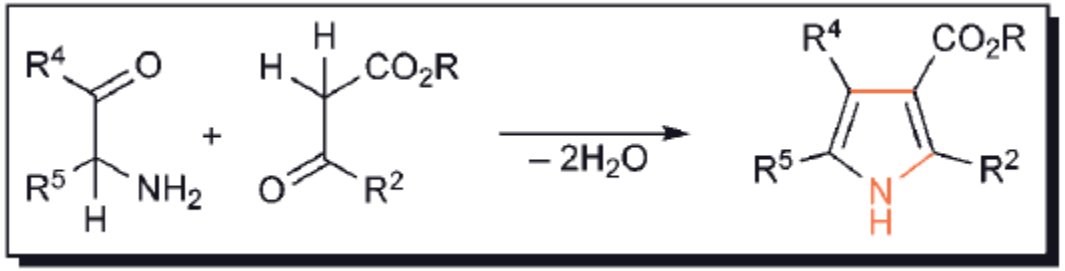
Ring Synthesis of Pyrroles

1) From 1,4-Dicarbonyl Compounds and Ammonia or Primary Amines



Ring Synthesis of Pyrroles

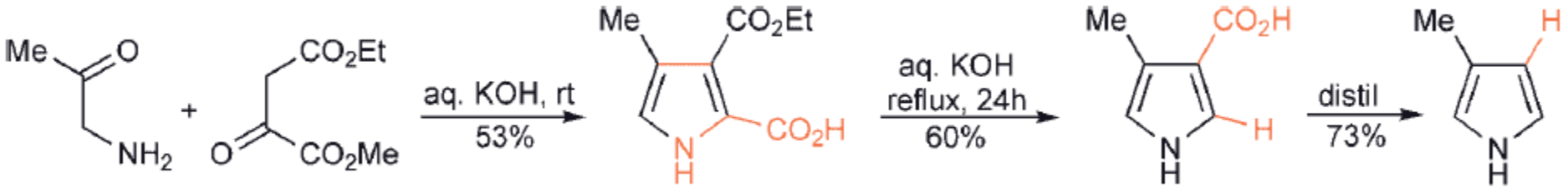
2) From *α*-Aminocarbonyl-Compounds and Activated Ketones



The Knorr Synthesis

This widely used general approach to pyrroles utilizes two components:

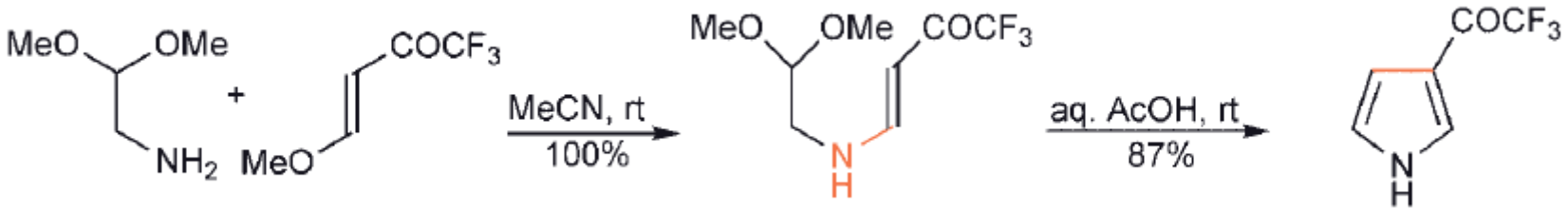
- The α-aminocarbonyl component, supplies the nitrogen and C-2 and C-3
- The 2nd component supplies the remaining two carbons and must possess a **methylene group α to a carbonyl**



Ring Synthesis of Pyrroles

2) From *α*-Aminocarbonyl-Compounds and Activated Ketones

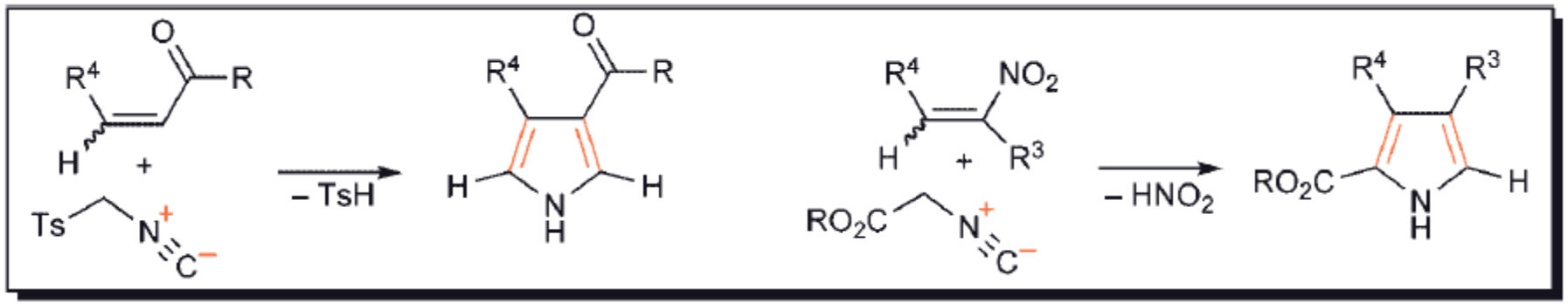
Since free α-aminocarbonyl compounds self-condense very readily, carbonyl-protected amines have been used



Ring Synthesis of Pyrroles

3) From Isocyanides

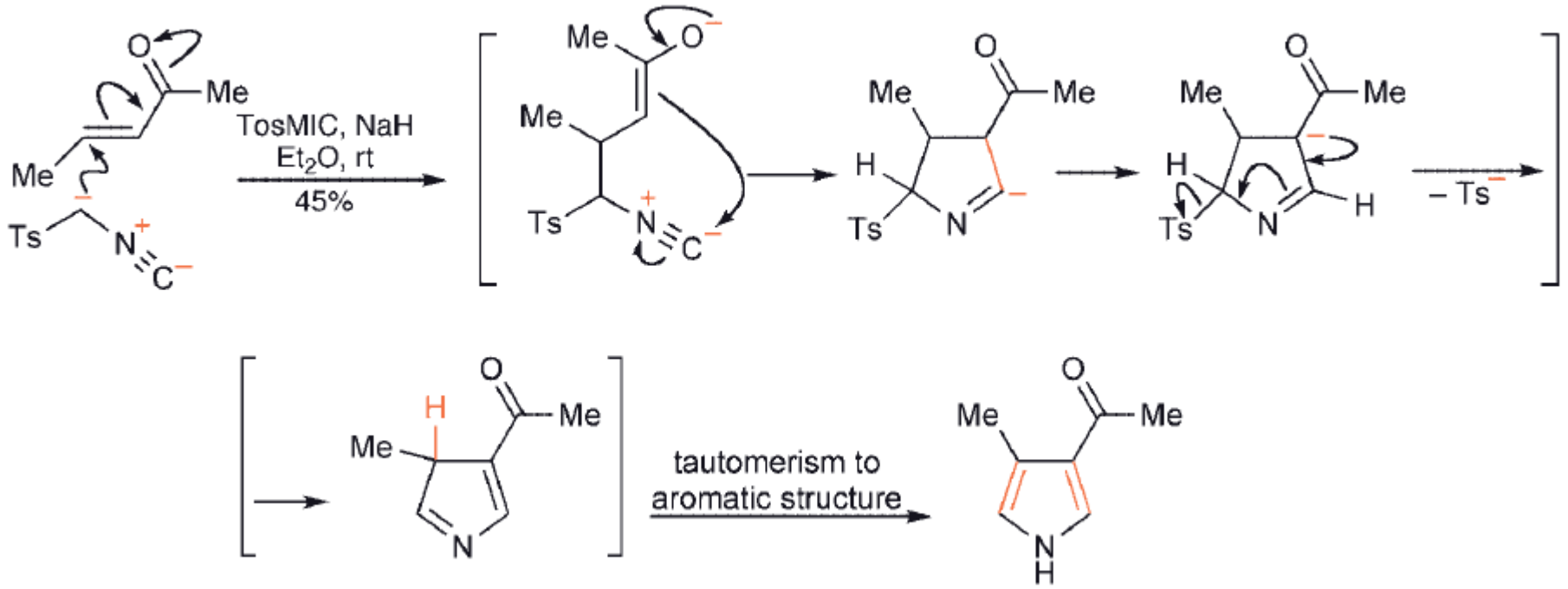
- Tosylmethyl isocyanide anion reacts with *α*,*β*-unsaturated esters, ketones or sulfones with loss of toluenesulfinate
- Isocyanoacetates react with *α*,*β*-unsaturated nitro-compounds with loss of nitrous acid



Ring Synthesis of Pyrroles

3) From Isocyanides

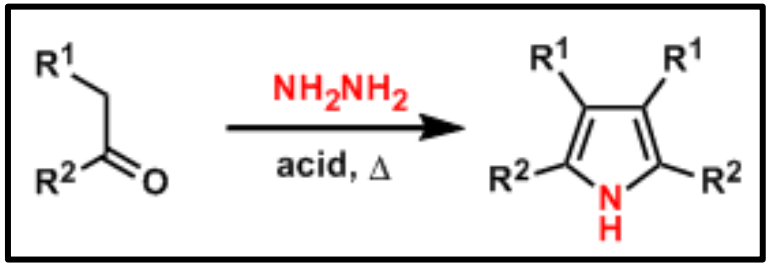
The van Leusen Synthesis



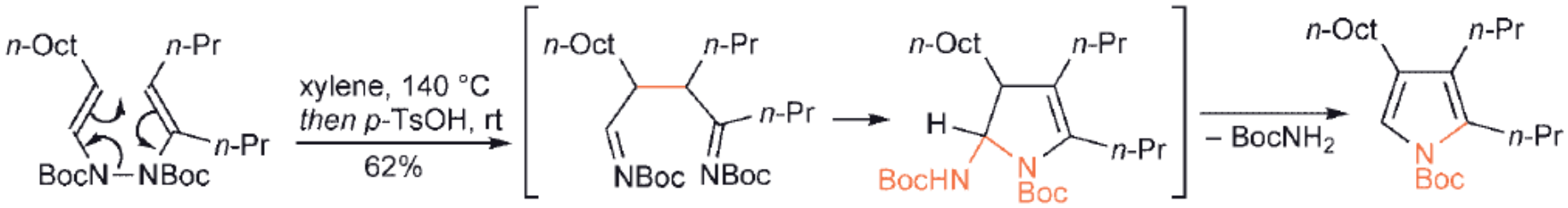
Ring Synthesis of Pyrroles

4) From Azines

The Piloty – Robinson Synthesis

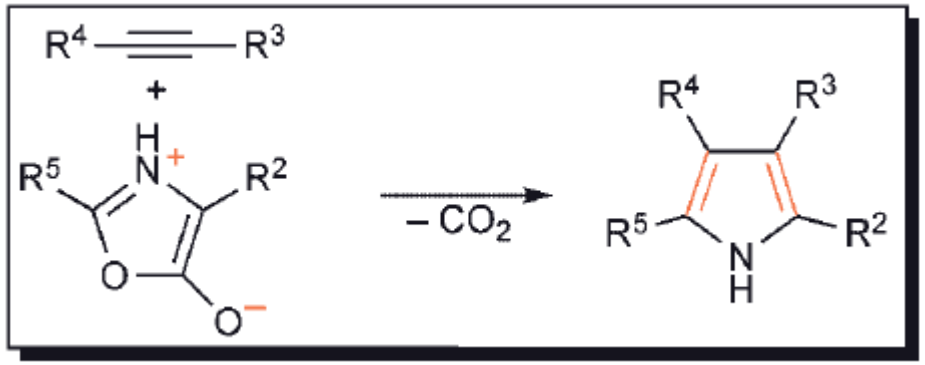


Example



Ring Synthesis of Pyrroles

5) From Alkynes and Oxido-Oxazoliums



Dipolar cycloaddition of alkynes to mesoionic oxido-oxazoliums, followed by expulsion of carbon dioxide, yields pyrroles