Synthesis of Furan and Thiophene

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Lecture 5
The Paal-Knorr Thiophene Synthesis allows the generation of thiophenes by condensation of a 1,4-dicarbonyl compound in the presence of an excess of a source of sulfur such as phosphorous pentasulfide or Lawesson's reagent.
Mechanism of the Paal-Knorr Thiophene Synthesis

Reagents such as phosphorus pentasulfide or Lawesson's reagent act as sulfurizing agents as well as dehydrating agents.
2-Fiesselmann Thiophene Synthesis

Condensation reaction of ester of thioglycolic acid with α, β- acetylenic esters, which upon treatment with base result in the formation of 3- hydroxyl- 2,5- thiophene dicarboxylic acid ester then by acid and heating converted to 3- hydroxyl- 2- thiophene
3-Gewald Aminothiophene Synthesis

It consists of the base-catalyzed condensation of a ketone having an a CH2 group with a β-ketonitrile and cyclisation with elemental sulfur.
4-The Hinsberg Synthesis

Two consecutive aldol condensations between a 1, 2-dicarbonyl compound and diethyl thiodiacetates gives thiophene.
i) Thiophene can be synthesized on industrial scale by the high temperature reaction between n-butane and Sulfur.

\[ \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3 \xrightarrow{560 \, ^\circ\text{C}} \text{S} \]

ii) Thiophene can be synthesized by passing a mixture of acetylene and hydrogen sulfide through a tube containing alumina at 400°C. This method is commercially used.

\[ \text{HC}≡\text{CH} + \text{H}_2\text{S} \xrightarrow{} \text{S} \]
Paal-Knorr furan Synthesis

The Paal-Knorr furan Synthesis allows the generation of furan by condensation of a 1,4-dicarbonyl compound in the presence of an acid and dehydrating agent such as phosphorus pentaoxide.
Unsubstituted furan can be synthesized from pentose by acid and heat

\[ \text{Pentose} \xrightarrow{ZnO / 400 \, ^\circ\text{C}} \rightarrow \text{Furan} \]

\[ \text{H}_2\text{SO}_4 / \text{Heat} \quad \xrightarrow{-3\text{H}_2\text{O}} \rightarrow \text{Furan} \]
Feist benary furan synthesis

Substituted furan can obtain from the reaction of beta keto ester and alpha halo keton in the presence of pyridine.