FURAN

The least aromatic 5-membered ring

Reaction with electrophiles - Protonation

Major protonated form

Much less basic than ordinary ethers

Conc. $\text{H}_2\text{SO}_4$
Lewis acids (i.e. $\text{AlCl}_3$)
Decomp.
**Reaction with electrophiles - Nitration**

Cannot use conc. HNO₃ / H₂SO₄

**Halogenation**

**See 15.14.1.2**
**Reaction with electrophiles - Acylation**

\[
\text{R} \quad \overset{\text{R'COCl or (R'CO)₂O, } \text{BF₃} \cdot \text{Et₂O}}{\longrightarrow} \quad \overset{\text{DMF, POCl₃, "Vilsmeier"}}{\longrightarrow} \quad \text{Furfural}
\]

Also very readily available by other routes

**Alkylation**

Generally not practical (polyalkylation, polymerisation)

**Condensation with Aldehydes and Ketones**

\[
\overset{\text{RCHO, } \text{H}^+}{\longrightarrow} \quad \overset{\text{Further react.}}{\longrightarrow} \quad \overset{\text{stable}}{\text{From chloral}} \quad \text{C.f.}
\]

\[
\overset{\text{H}^+, \text{RCHO, } \text{R=H, alkyl}}{\longrightarrow} \quad \overset{\pm \text{H}^+}{\longrightarrow} \quad \overset{- \text{H₂O}}{\longrightarrow} \quad \overset{\ldots}{\text{Polymer}}
\]
**Reaction with electrophiles - Condensation with imines / iminium ions**

Unsubst furan: iminium ion must be preformed

**Reaction with oxidating agents**

Some ex. on furans activated with -NO₂ group
Metallation and further react.
**Pd-cat couplings**

\[
\begin{align*}
\text{Li} & \quad \rightarrow \quad \text{Met} \quad \text{Ar-X (or related)} \quad \text{cat Pd} \quad \rightarrow \quad \text{Ar} \quad \rightarrow \quad \text{Br} \\
& \text{cat Pd} \\
\text{EWG} & \quad \text{Heck} \quad + \quad \text{Pd(0)} \\
\text{Cu(II)} & \quad \text{+ Pd(0)}
\end{align*}
\]

**Heteroaryl-Heck**

*like an alkene in Heck*

\[
\begin{align*}
\text{Ar-X} & \quad \text{cat. Pd} \quad \rightarrow \quad \text{Ar} \\
\text{EWG} & \quad \text{Ar-Pd-X} \quad \text{Heck} \quad \rightarrow \quad \text{Ar} \quad \text{H-Pd-X}
\end{align*}
\]
**Cycloadditions**

Furanes as diene - one of the first DA examples
Furan reacts with many dienophiles (alkenes, alkynes, allenes)

\[ \text{X} + \text{O} \rightarrow \text{exo isolated (termodyn favoured)} \]
\[ \text{X=S: 100 oC, 15kbar; 42\%} \]

With \(^1\text{O}_2\)

\[ \text{O} \rightarrow \text{O} \rightarrow \text{H} \]

Furan as dienophile (only intramolec. ex)

\[ \text{X: EWG} \]

Photochemical cycloaddition

\[ \text{R}_1 \text{R} \rightarrow [2+2] \rightarrow \text{acid} \rightarrow \text{acetal} \]
**Furyl-CH$_2$-X**

**Oxyfurans**

*Butenolides (natural prod.)*

- **R=Me: β-angelica lactone**
  - Most stable

- not detectable

**Aminofurans**

- **Aminoform**
- **Unstable**

**Major**

**tetronic acid**

**ascorbic acid**

**Isol. marine sponges cytotoxic**

Luffarin W  
Luffarin B
Synthesis of Furans

Carbonyl condensations

**Strategy a - pyrroles**

**Paal Knorr**

\[ \text{Pyroles} \]

\[ \begin{align*}
O = \text{R} &\rightarrow \text{R'} \\
: \text{NH}_2 \text{R''} \\
\text{R''} &= \text{H, alkyl, aryl}
\end{align*} \]

**Strategy a\(^1\) Paal Knorr (1,4-dikacarbonyl)**

\[ \begin{align*}
\text{TsOH} &\rightarrow \text{R}_4 \text{R}_3 \\
\text{K}_2 \text{Cr}_2 \text{O}_7, \text{acid} &\rightarrow \text{H}^+ \\
\text{HO} &\rightarrow \text{HO} \text{O} \\
\text{HO} &\rightarrow \text{HO} \text{O} \text{O} \\
\text{HO} &\rightarrow \text{HO} \text{O} \text{OH} \\
\text{Br} &\rightarrow \text{Br} \text{Br} \\
\text{Br} &\rightarrow \text{Br} \text{Br} \text{Br} \\
\text{Br} &\rightarrow \text{Br} \text{Br} \text{Br} \\
\text{Br} &\rightarrow \text{Br} \text{Br} \text{Br}
\end{align*} \]

see 15.14.1.2
**Strategy b**

**Aldehyde**

ClO\_2R → HO\_2R → HO\_2R → CO\_2R → CO\_2R → H\_2O → CO\_2R

**Ketone**

ClO\_2R → HO\_2R → "Paal Knorr" → "Paal Knorr" → CO\_2R

**Wittig**

R\_2O → \(\Theta\) Ph\_3 → R\_2O \(\Theta\) Ph\_3 → "Wittig" → R\_2O \(\Theta\) Et → - EtOH → R\_2O
Pd-cat. Cyclisations etc.

\[ \text{Pd(II), H}_2\text{O} \rightarrow \text{Pd(II)} \rightarrow \text{PdX} \rightarrow \text{I} \rightarrow \text{H}_2\text{O} \]

\[ \text{heat} \rightarrow \text{Pd(II), \text{H}_2\text{O}} \rightarrow \text{Pd(II)} \rightarrow \text{PdX} \rightarrow \text{I} \rightarrow \text{H}_2\text{O} \]

Also known termal cycl.
Cycloadditions

\[
\begin{align*}
\text{Ph}_3\text{N} \xrightarrow{R \equiv \equiv R'} & \text{O} \xrightarrow{\text{PhCN}} \text{Ph} \xrightarrow{R(R')} \text{O} \xrightarrow{- \text{PhCN}} \text{R} \xrightarrow{R'} R / R' \text{ i.e. } -\text{SnBu}_3, -\text{SiMe}_3, \text{alkyls etc.}
\end{align*}
\]

c.f.

\[
\begin{align*}
\text{Ph}_3\text{S} \xrightarrow{R \equiv \equiv R'} & \text{S} \xrightarrow{- \text{PhCN}} \text{S} \xrightarrow{R(R')} \text{R}
\end{align*}
\]