PYRYLIUM IONS AND PYRONES
(chapt 7-9)

Electron deficient ring:
- No react. with electrophiles
- No react. with radicals
- Reaction with nucleophiles
- (Reacts in cycloadditions)

PYRYLIUM IONS

Aromatic - Reactive
Counter ion often ClO$_4^-$

c.f.:
Com. avail. (SciFinder) ca 170 in 2007

Reactions with nucleophiles

1,2-Add. - Ring opening!

Nu: Water, alcohols, ammonia, amines, organometallics / carbanions, Wittig reagents, hydrides

1,4-add. common on flavylium
**ANRORC (add. of Nu., Ring Opening and Ring Closure)**

\[
\text{Nu} = -XH_2 (-\text{NH}_2, -\text{CH}_2R)
\]

**More stable aromatic rings**

**Good yields**

**Availability starting material**

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**Cycloadditions**

3-oxidopyryliums

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**1,3-Dipol**

**Further transformations to 7-membered rings**
Pyrones

Reactions with Electrophiles

2-Pyrone
E
\[ \text{Me}_3\text{BF}_4 \]
\[ \text{Me}_2\text{SO}_4 \]
\[ \text{ClO}_4 \]
Not stable

4-Pyrone
\[ \text{Me}_3\text{OBF}_4 \]
\[ \text{Me}_2\text{SO}_4 \]
\[ \text{ClO}_4 \]
No E-fil Ar Subst

E-fil Aromatic Substitution like products, but by other mechanisms
Reactions with Nucleophiles

**lactone**

\[
\text{Nu}^+ + \text{Nu} \rightarrow \text{Nu}^- + \text{Nu}^+ \\
\text{Nu}^- + \text{Nu} \rightarrow \text{Nu}^+ + \text{Nu}^-
\]

**NH}_3, amines, CN^-**

\[
\text{NH}_3 + \text{Nu} \rightarrow \text{NH}_3^+ + \text{Nu}^- \\
\text{NH}_3^- + \text{Nu} \rightarrow \text{NH}_3^+ + \text{Nu}^-
\]

**OH^-, RMgX**

\[
\text{OH}^- + \text{Nu} \rightarrow \text{OH}^- + \text{Nu}^+ \\
\text{OH}^- + \text{Nu}^+ \rightarrow \text{OH}^- + \text{Nu}^+
\]

**NH}_3, amines OH^-**

\[
\text{NH}_3 + \text{Nu} \rightarrow \text{NH}_3^- + \text{Nu}^+ \\
\text{NH}_3^- + \text{Nu}^+ \rightarrow \text{NH}_3^- + \text{Nu}^+
\]

**ClO}_4^-**

\[
\text{ClO}_4^- + \text{Nu} \rightarrow \text{ClO}_4^- + \text{Nu}^+ \\
\text{ClO}_4^- + \text{Nu}^+ \rightarrow \text{ClO}_4^- + \text{Nu}^+
\]
**Cycloadditions**

Diene in DA react.

[2+2] with tosyl isocyanate

Dienophile in DA react.

Benzopyrilium

No E-fil Ar subst in benzene ring (in contrast to (iso)quinolines)

Chromylium Isochromylium

Flavylium

Selectivity?

- ROH at C-4 u. mild cond
- Ammonia / amines mixt
- Soft carbanions at C-4
- NB! C-2 attack leads to ring opening
Benzopyrones

Coumarin  Isocoumarin  Chromone

React with E-files

\[
\text{Benzopyrone} \xrightarrow{\text{H}^+ / \text{E}^+} \text{Intermed. strongly acidic cond.} \xrightarrow{\text{E}} \text{Reaction Product}
\]

(also subst. in benzene ring for coumarines u. acidic cond)

React with E-files u neutral conditions

React with Nu-files

Reacts with Nu-files (ring openings)

Metallation
Synthesis - Pyrylium

Synthesis - Pyrylium

Synthesis - Pyrylium

Synthesis - Pyrylium
Synthesis - Pyrones

\[
\begin{align*}
&\text{OHHOOH} \rightarrow \text{H}_2\text{O} \\
&\text{OHOOH} + \text{OO} \rightarrow \\
&\text{OOOOHH} \rightarrow \text{H}_2\text{O} \\
\end{align*}
\]

Natural products etc.

Anthocyanines:
- Gycosides of polyhydroxyflavylium (Aglycon = anthocyanidin)
- Colored (red / violet / blue) pigments, red / blue flowers, blueberries, grapes (red wine) etc.
- Antioxidants - Polyphenols - Radical scavengers

Cyanidine / Cyanidol

\[
\begin{align*}
&\text{O-!-D-glucose} \rightarrow \\
&R=\text{OH}, R'=\text{H}: \text{cyanin} \\
&R=R'=\text{OMe}: \text{Malvin}
\end{align*}
\]
**Natural products etc.**

4-Pyrone  Chromone  Flavon

Kawapyrones:
- Isolated from Káwa
- Relaxing drug used in Polynesia

Flavonoids:
- Gycosides of polyhydroxyflavon
- Colored (yellow) pigments in plants
- Antioxidants Polyphenols - Radical scavengers

R = H: Quercetin
R = L-Rhamnose: Quercetrin
R = D-Glucose-L-Rhamnose: Rutin

Rothenone
- Insecticide
- Parasites in rivers

Psoralenes
- Isolated from various plants
- Photochemotherapy against psoriasis
- [2+2] cycloadd. with cytosin / thymin in DNA

R = R' = H: Psoralen
R = H, R' = OMe: Xantotoxin (8-MOP) - Metoksalen - Geroxalen(R)

**Natural products etc.**

2-Pyrone  Coumarin

Psoralenes
- Isolated from various plants
- Photochemotherapy against psoriasis
- [2+2] cycloadd. with cytosin / thymin in DNA
Dicoumarol
- Anticoagulant - Vit K antagonist
- Sweet clover disease

Sweet clover (Melilotus officinalis)

Warfarin - Marevan®

Aflatoxines
- From Aspergillus flavus (fungus)
- Attacks nuts etc.
- Carcinogenic