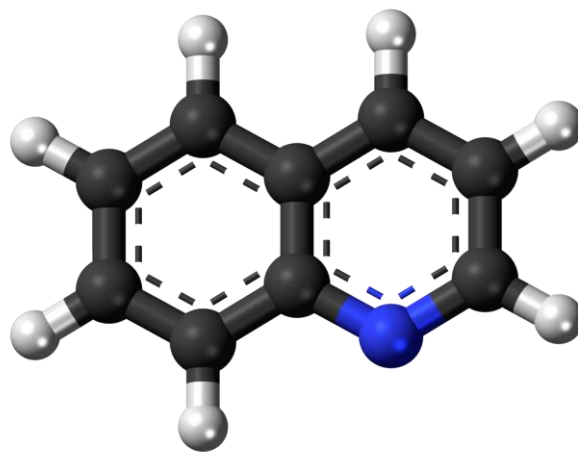


Reaction of Pyridine Part 2



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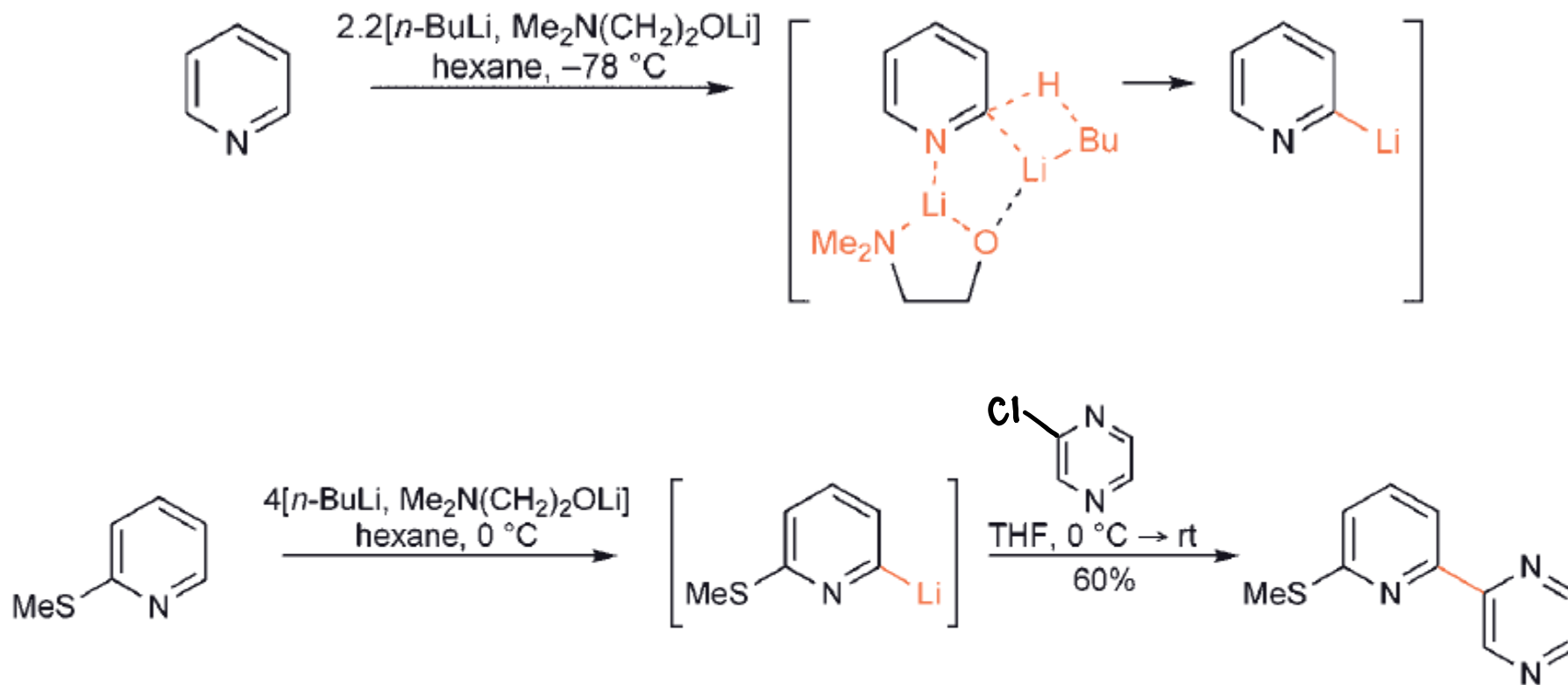
Recommended Textbook:

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

3) Metallation and Reactions of C-Metallated-Pyridines

3.1) Direct Ring C–H Metallation

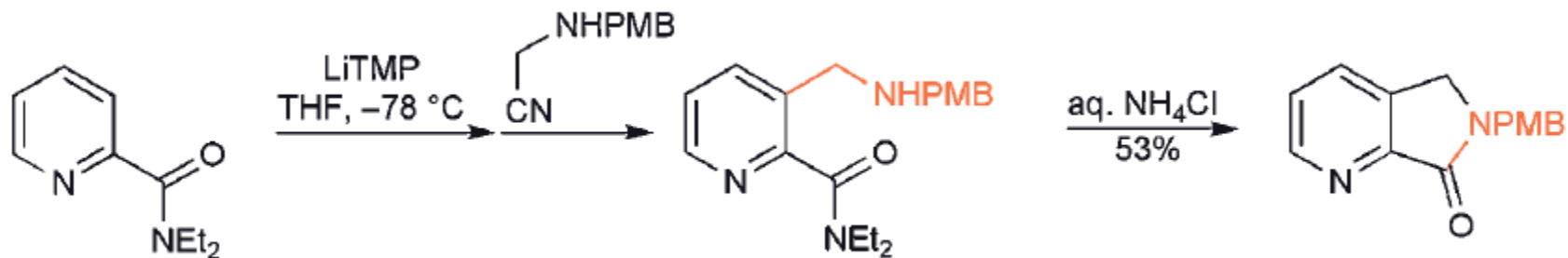
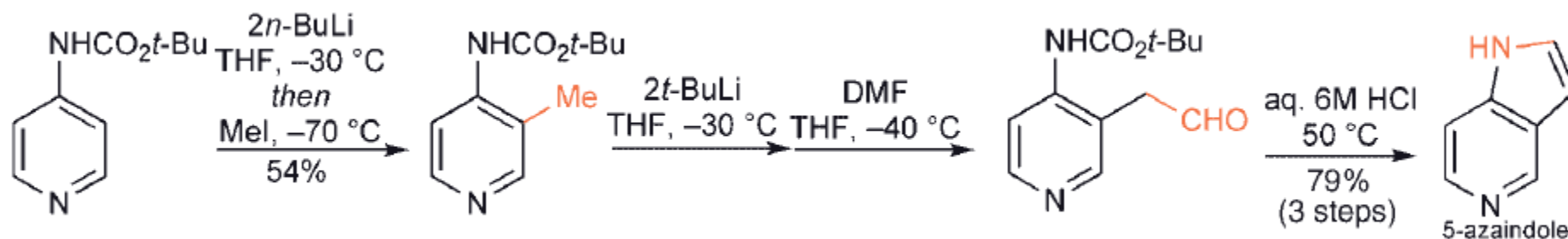
- Regioselective metallation at an α -position of a pyridine can be achieved with the mixed base produced from two mole equivalents of *n*-butyllithium with one of dimethylaminoethanol



3) Metallation and Reactions of C-Metallated-Pyridines

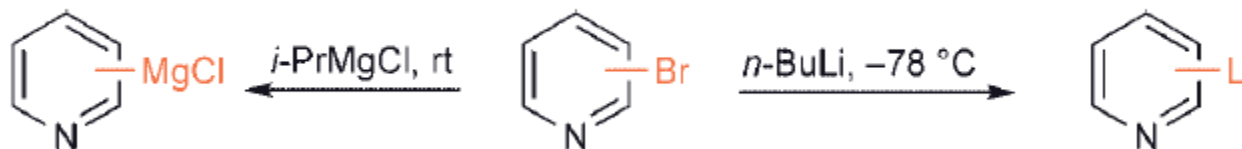
3.1) Direct Ring C–H Metallation

- Direct lithiation can be assisted by an *ortho*-directing groups

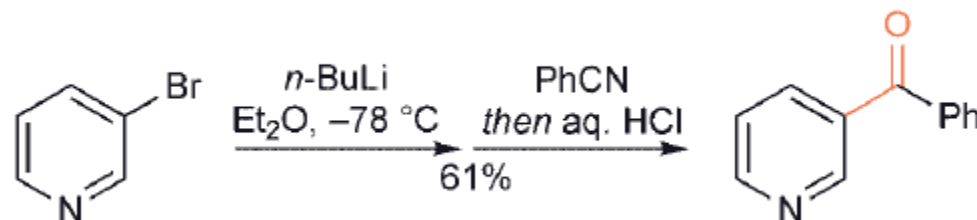


3) Metallation and Reactions of C-Metallated-Pyridines

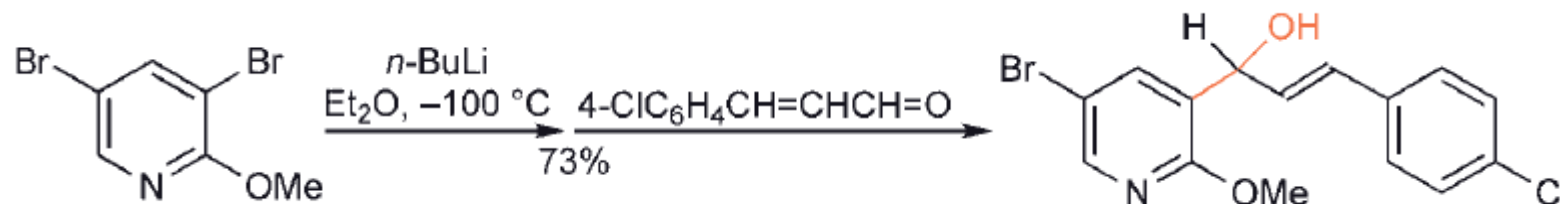
3.2) Metal-Halogen Exchange



- Lithium derivatives are easily prepared and behave as typical organometallic nucleophiles

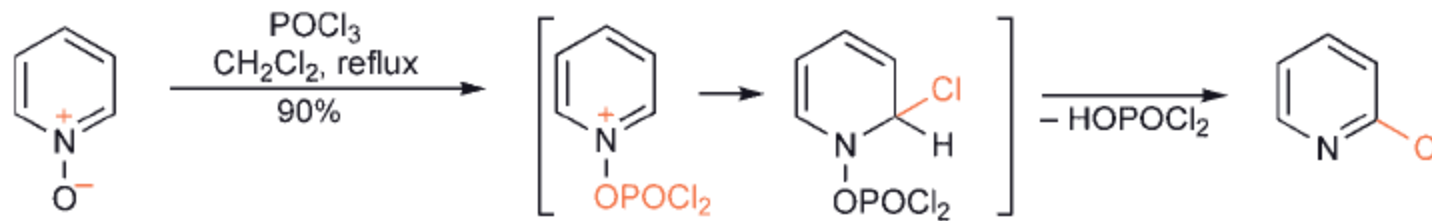


- The presence of a directing substituent can lead to regioselective metallation

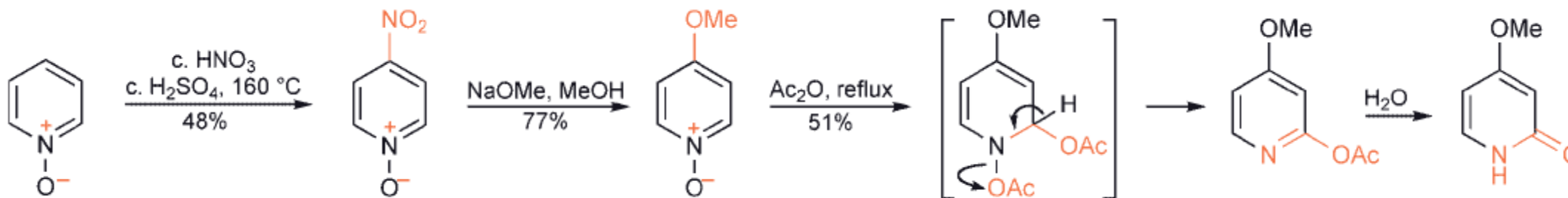


Pyridine-*N*-oxide

- A range of synthetically useful rearrangements convert pyridine *N*-oxides into variously substituted pyridines

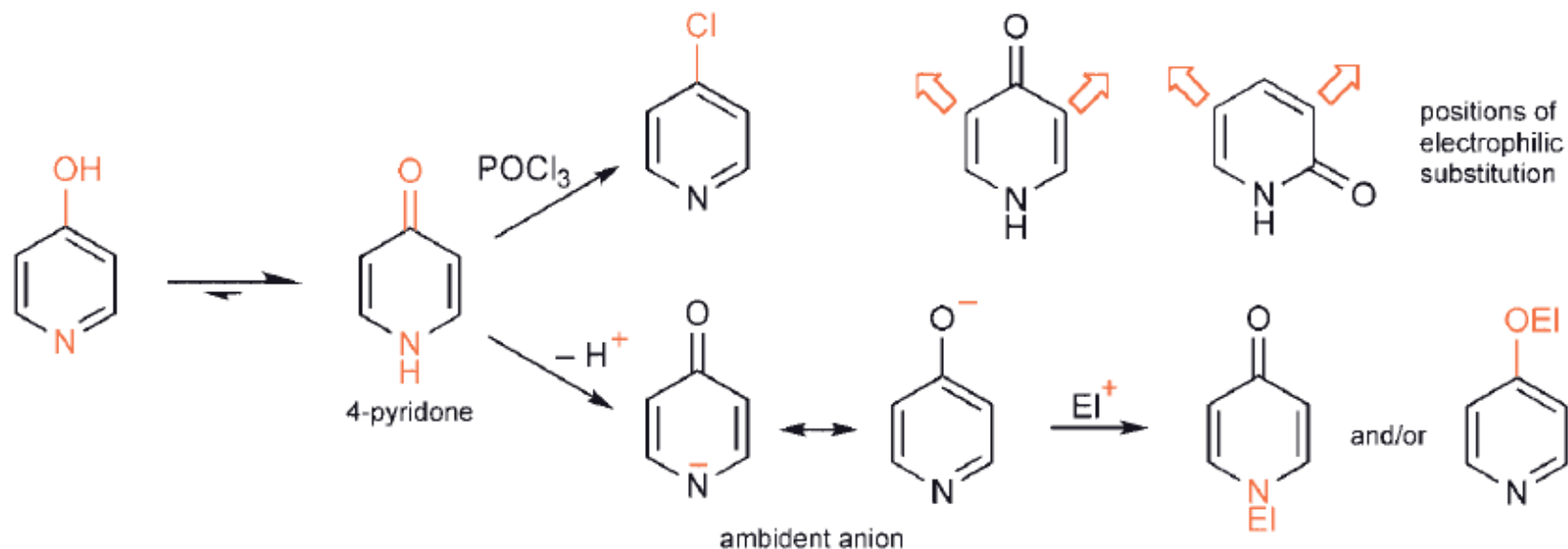


- The following sequence illustrates several aspects of *N*-oxide chemistry, including easy nucleophilic substitution (of nitro) at a γ -position



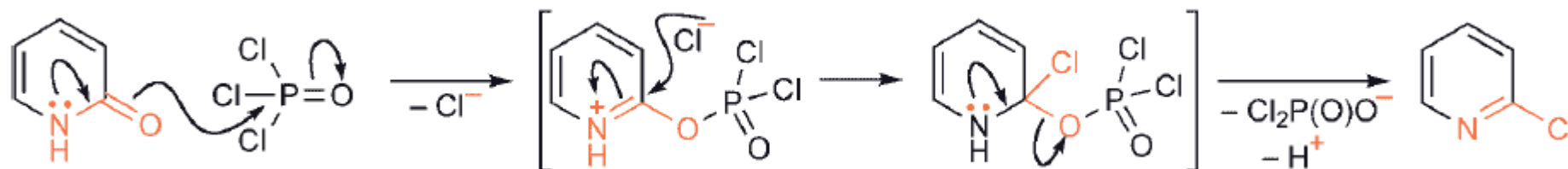
Pyridone

- Pyridones carrying oxygen at an α - or γ -position exist as **tautomers**
- There is considerable parallelism between their reactions and those of **phenols**: electrophilic substitution at *ortho* and *para* positions to the oxygen



Typical reactions of pyridones, illustrated for 4-pyridone

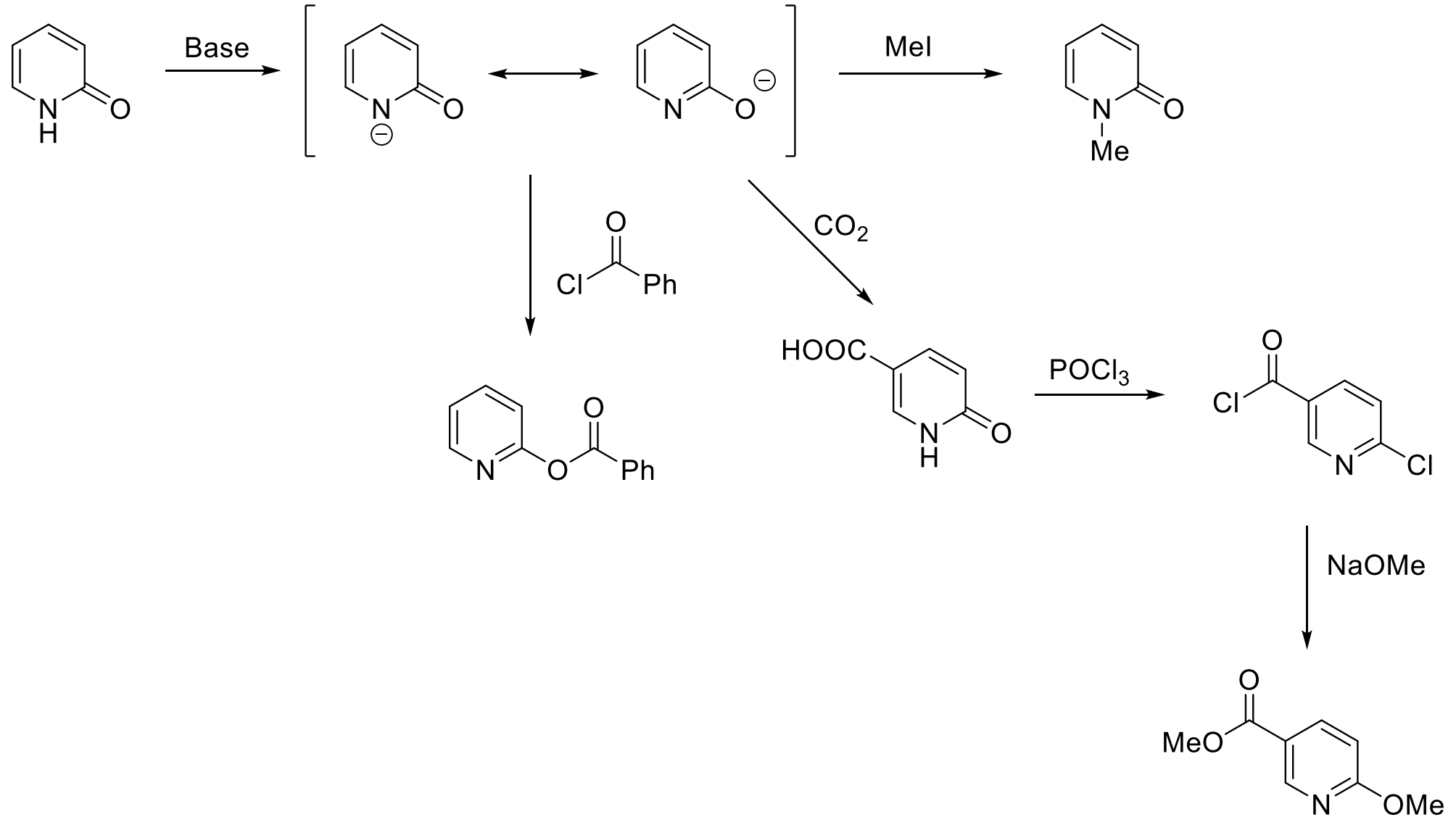
Mechanism (amide-like fashion)



Pyridone

Example

6



Alkyl-Pyridines

- The main feature of the reactivity of alkyl-pyridines is **deprotonation** of the alkyl group at the carbon adjacent to the ring



Resonance stabilisation of 'enamine' anions formed by deprotonating the methyl groups of 4- and 2-picolines

- The '**enamine**' anions produced by deprotonating α - and γ -alkyl-pyridines can participate in a wide range of reactions

Alkyl-Pyridines

Examples

