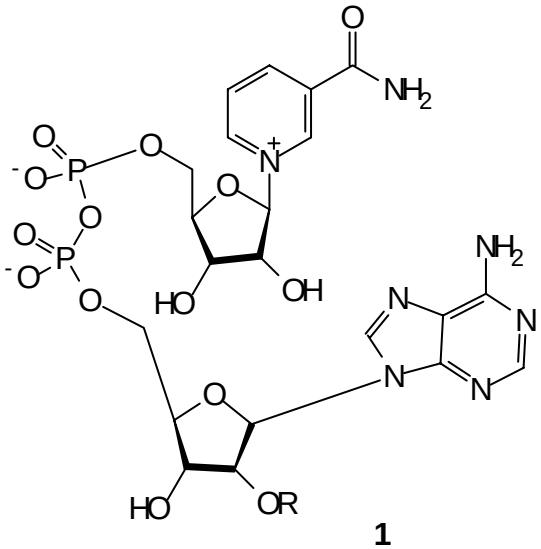
Six-Membered Ring Systems

7.1 pyridines

7.1.1 Introduction



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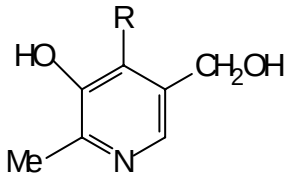

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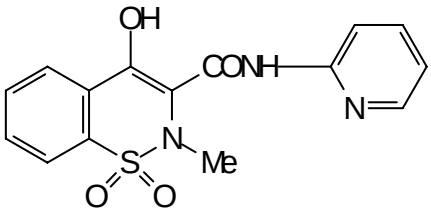

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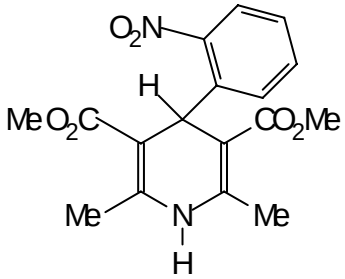

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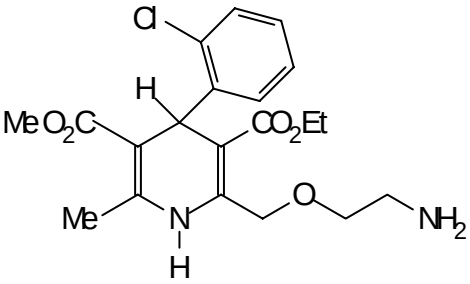

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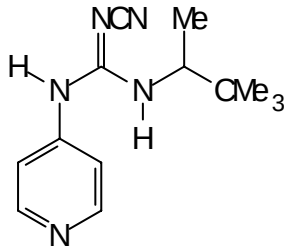

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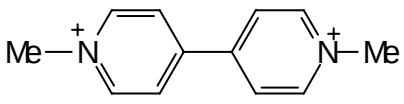

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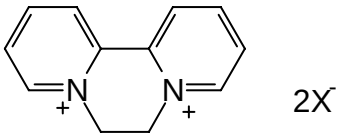

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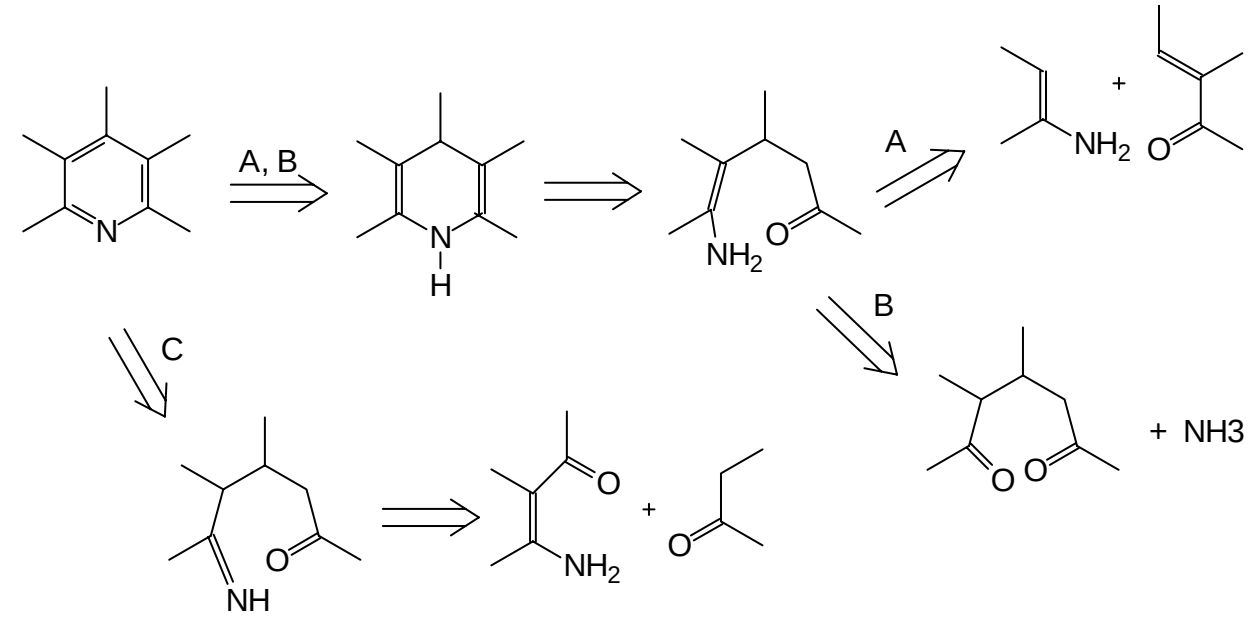
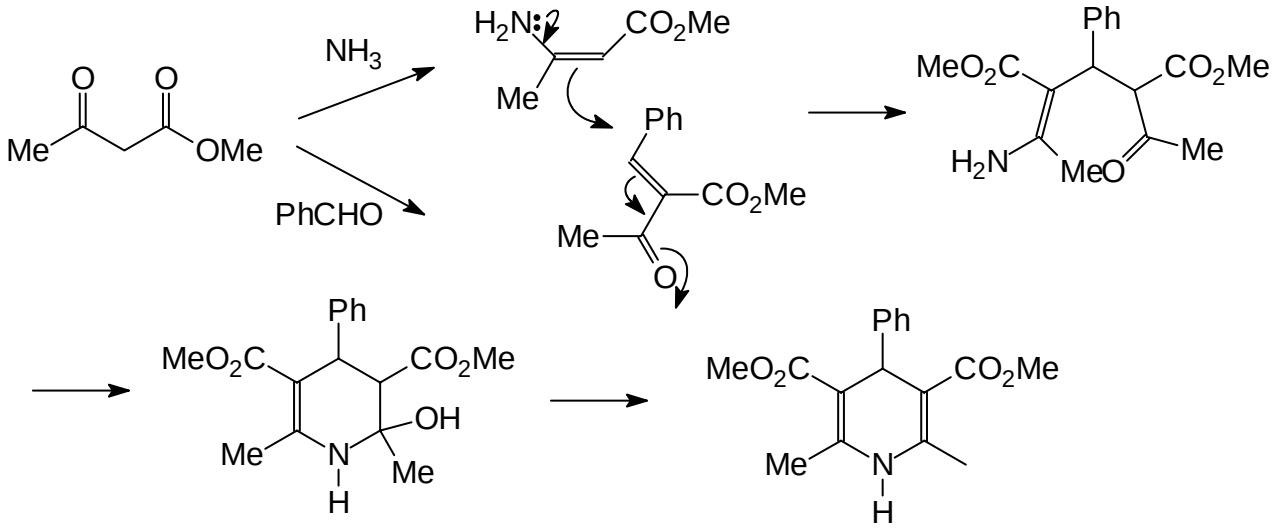
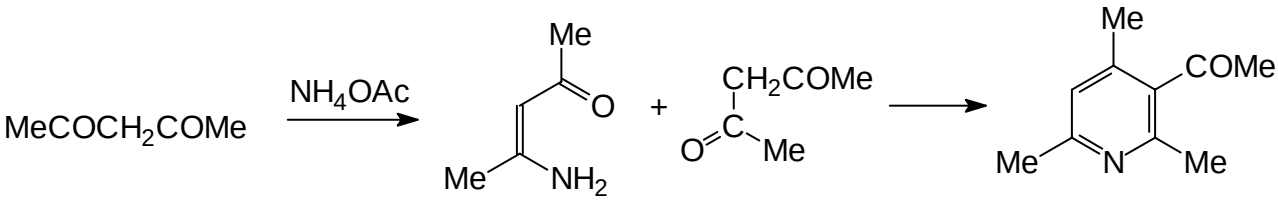
7.1.2 Ring synthesis



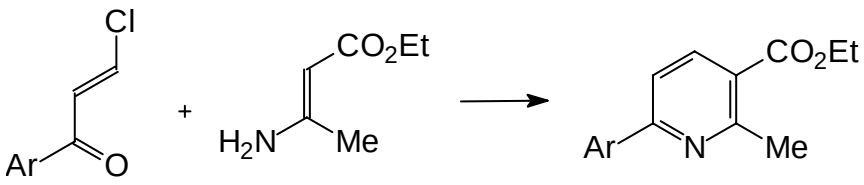
Analysis of three cyclization routes to pyridines

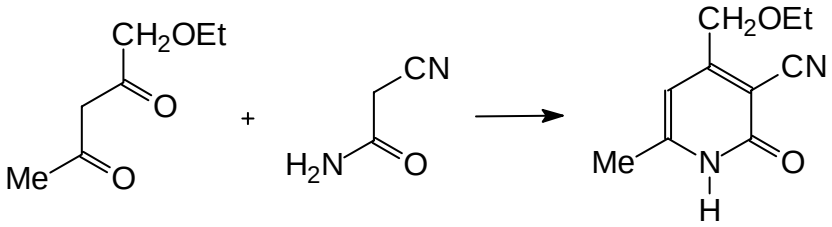


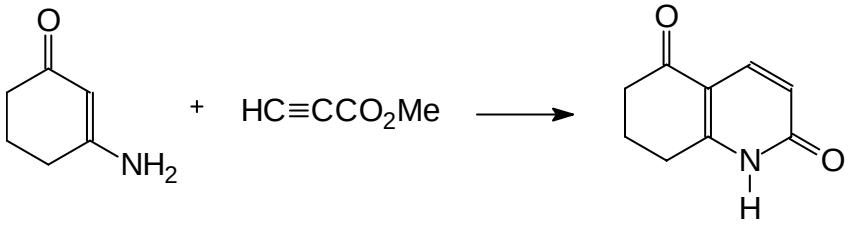
An example of the Hantzsch dihydropyridine synthesis

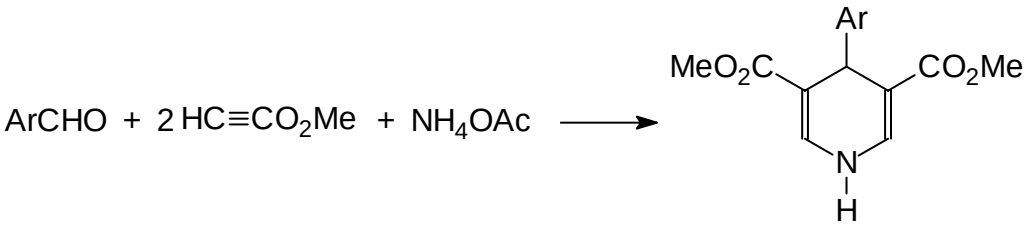


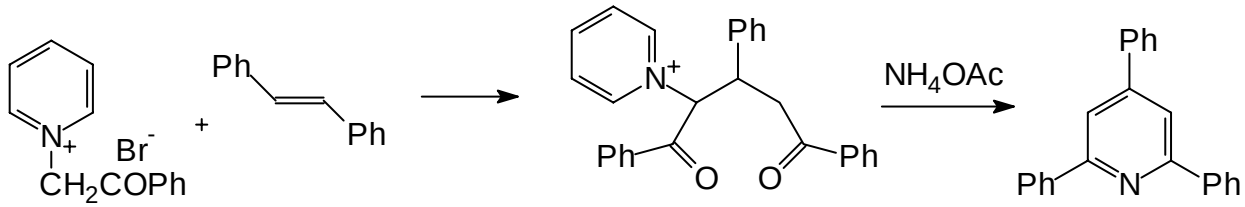
Formation of 3-acetyl-2,4,6-trimethylpyridine from pentane-2,4-dione and ammonium acetate



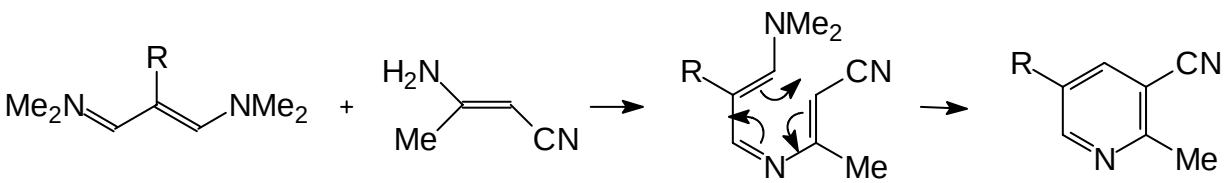


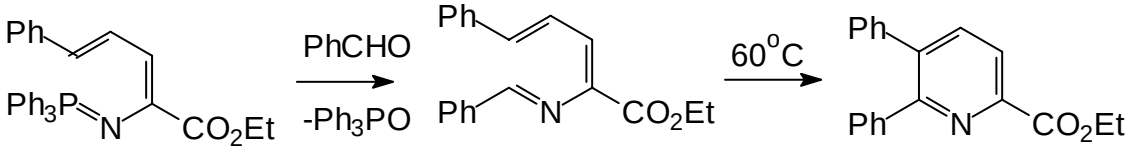


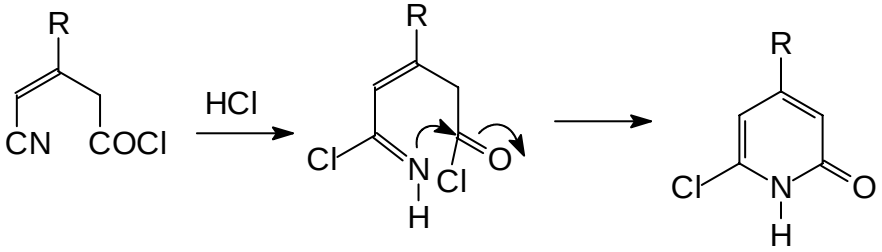




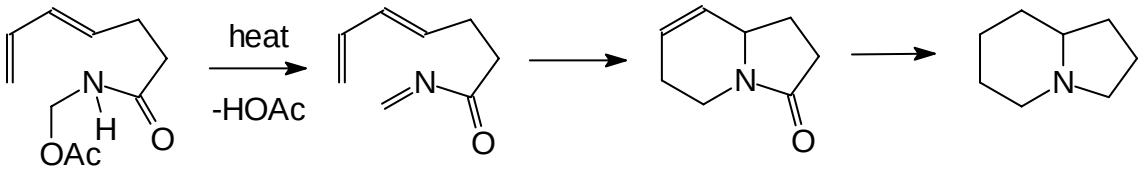
Related cyclization routes to pyridines





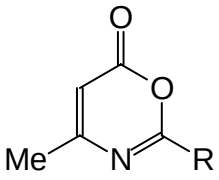
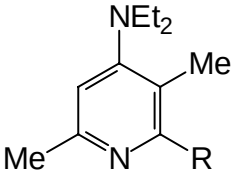
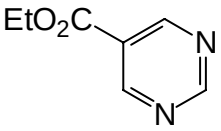
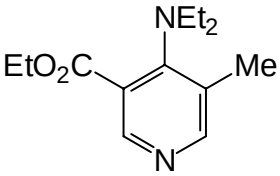
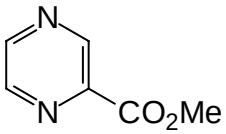
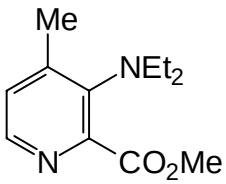
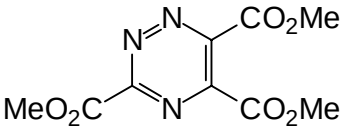
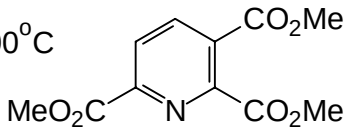


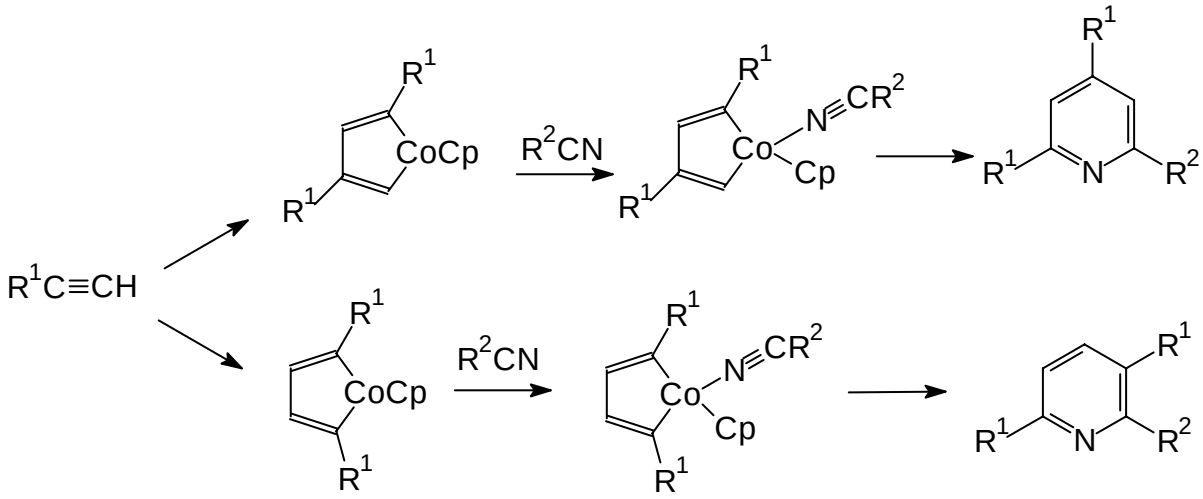
Other cyclization processes



Synthesis of δ-coniceine by intramolecular Diels-Alder addition

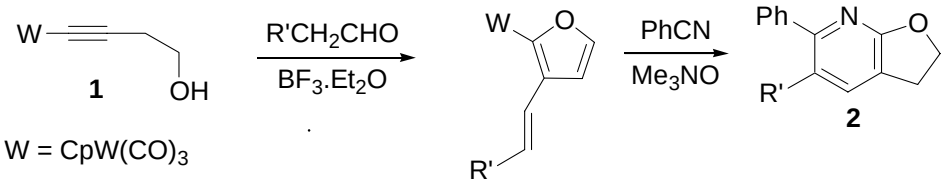
Pyridine synthesis by cycloaddition of alkenes and alkynes to heterocyclic dienes

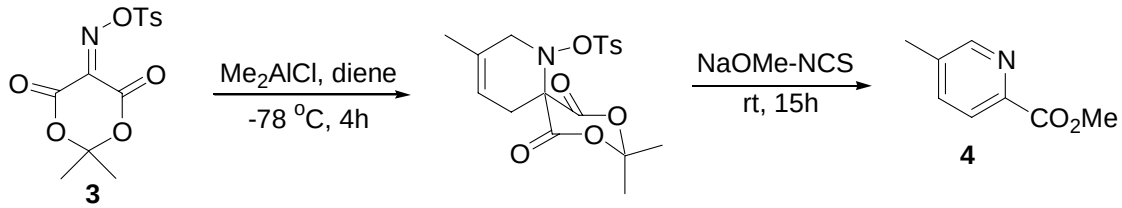
Diene	Dienophile	Conditions	Product
	$Et_2NC{\equiv}CMe$	Et_2O, 20°C	
	$Et_2NC{\equiv}CMe$	MeCN, 80°C	
	$Et_2NC{\equiv}CMe$	$CHCl_3$, 25°C	
	HC≡CHOAc	dioxane, 100°C	

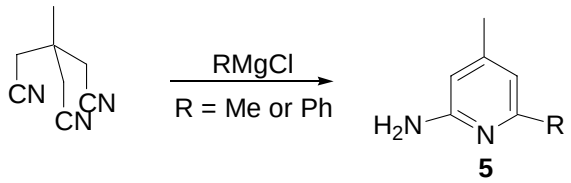


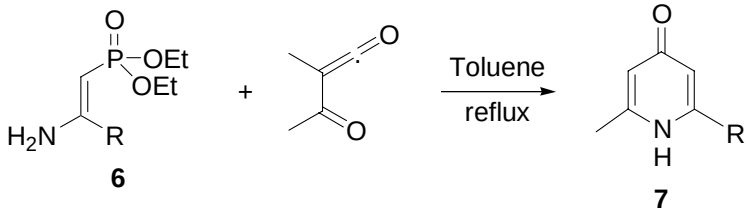
Cobalt-catalyzed formation of pyridines from alkynes and nitriles

Preparation of pyridine in 1998

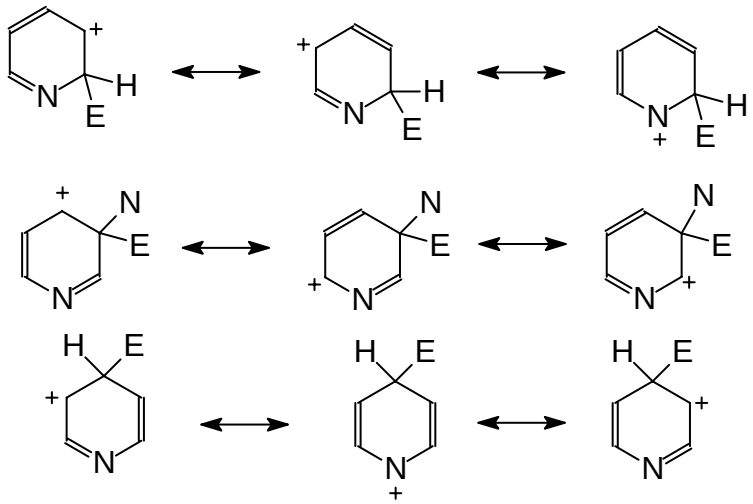




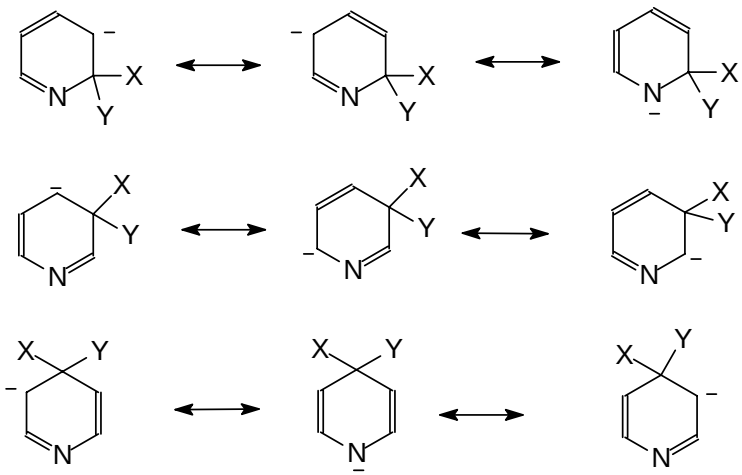




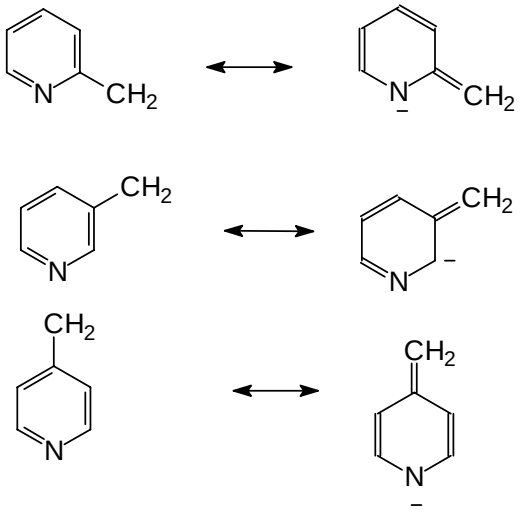
7.1.3 General features of the chemistry of pyridines



Intermediates in the electrophilic substitution of pyridine



Intermediates in the nucleophilic displacement of X^- by Y^- in X-substituted pyridines

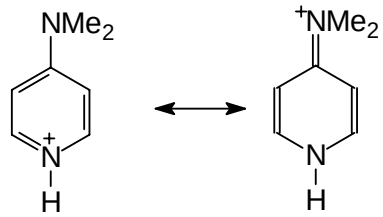


Carbanions derived from methylpyridines

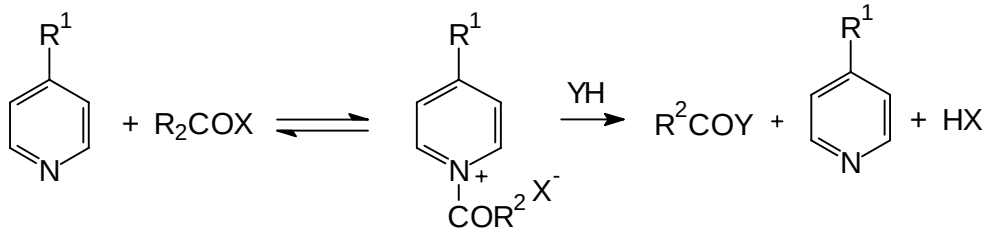
7.1.4 Basicity

pKa values (20°C, H_2O) of protonated pyridines

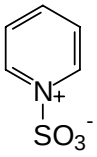
Substituent	pKa
None	5.23
2-NH_2	6.86
3-NH_2	5.98
4-NH_2	9.17
2-OMe	3.28
4-OMe	6.62
4-NO_2	1.61
2-CN	-0.26
4-CN	1.90



7.1.5 Alkylation, acylation and complexation on nitrogen



Nucleophilic catalysis of acylation



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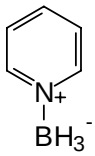

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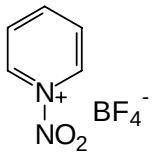

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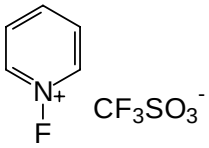

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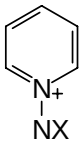

(X = COR, SO_2R)

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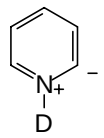
7.1.6 Electrophilic substitution at carbon



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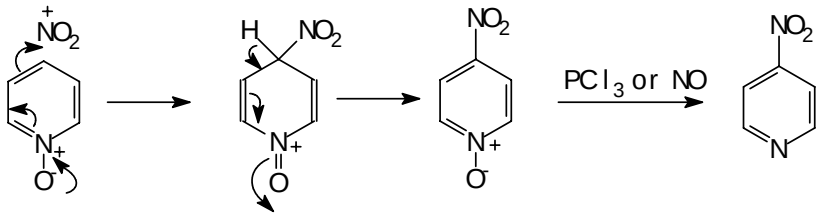
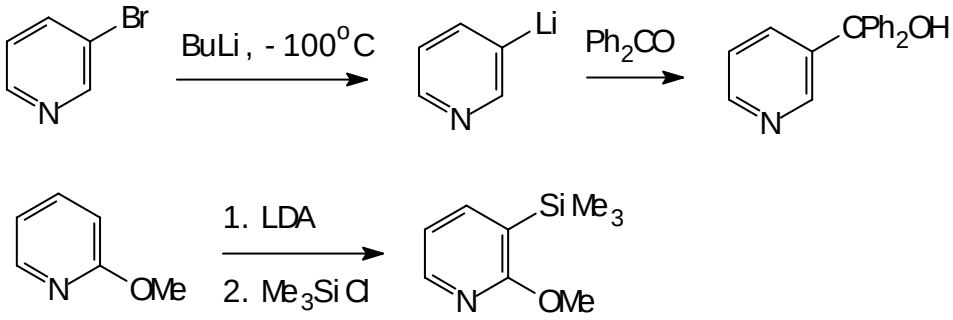
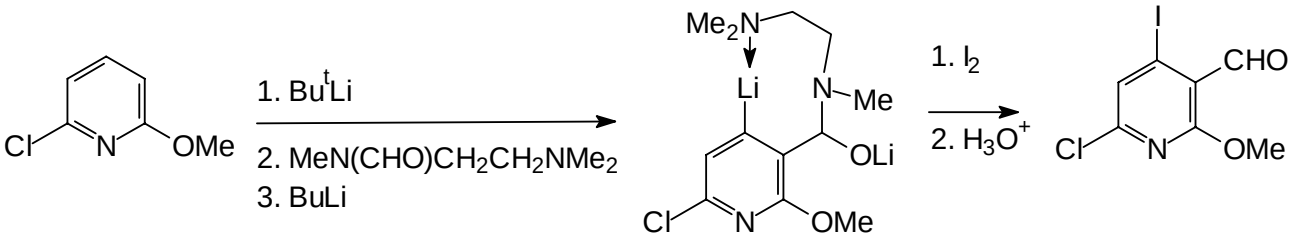


Nitration of pyridine N-oxide



Electrophilic substitution by way of lithiated intermediates.

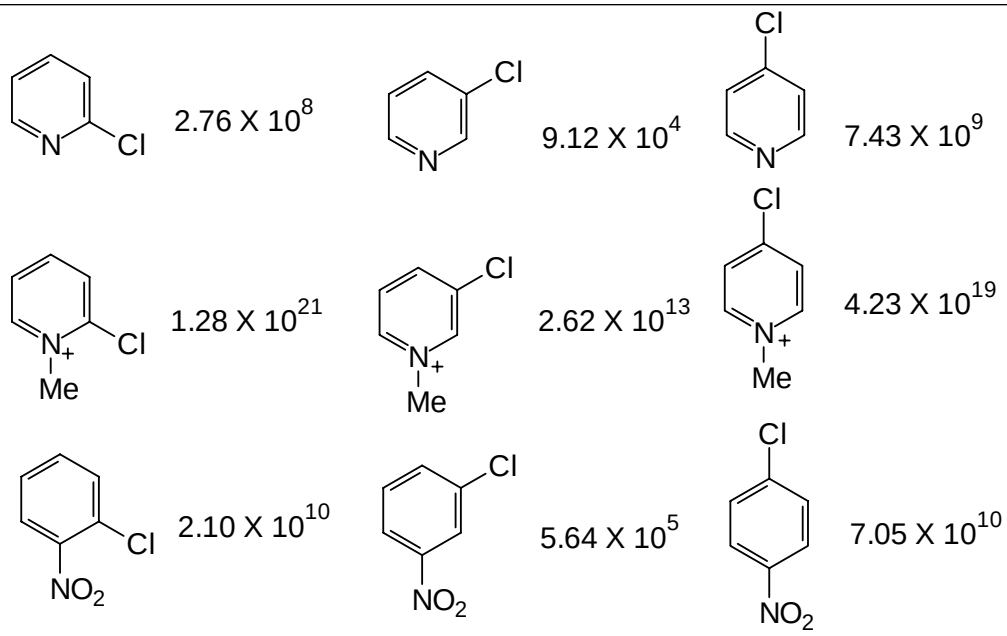


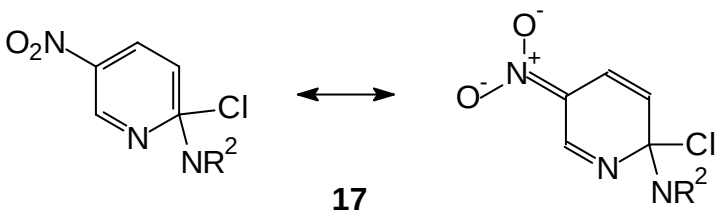
Sequential electrophilic substitution of 2-chloro-6-methoxypyridine by directed lithiation

7.1.7 Nucleophilic substitution

Rate factors for benzene and pyridine derivatives in the reaction

$$ArCl + MeO^- \rightarrow ArOMe + Cl^-$$





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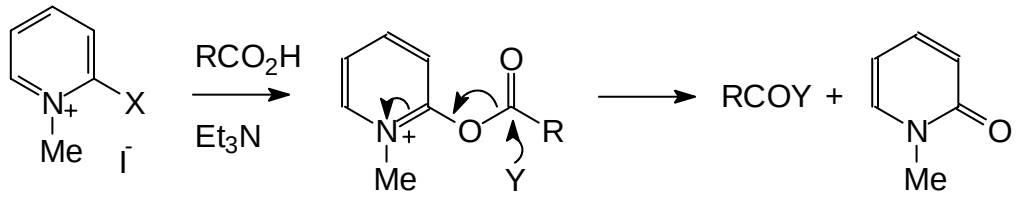
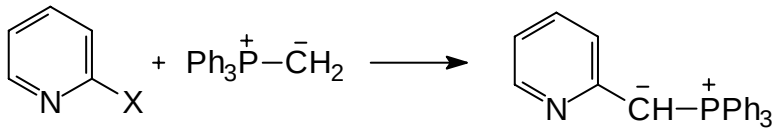
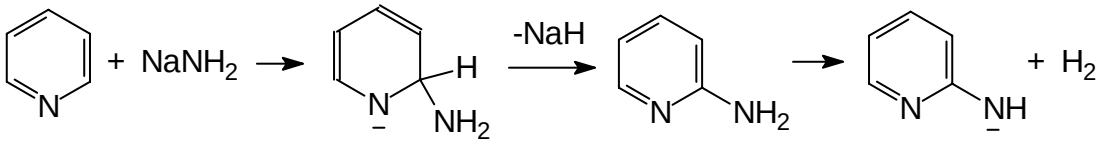


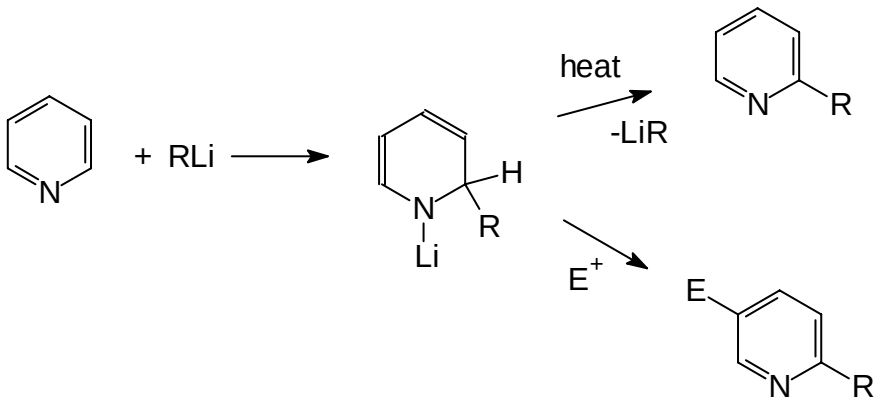
Generation and reaction of 2-acyloxypyridinium salts



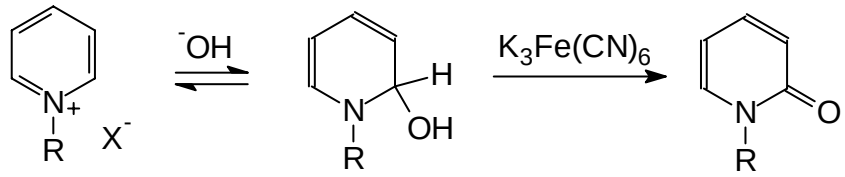
Formation of triphenylphosphonium 2-pyridylmethylide



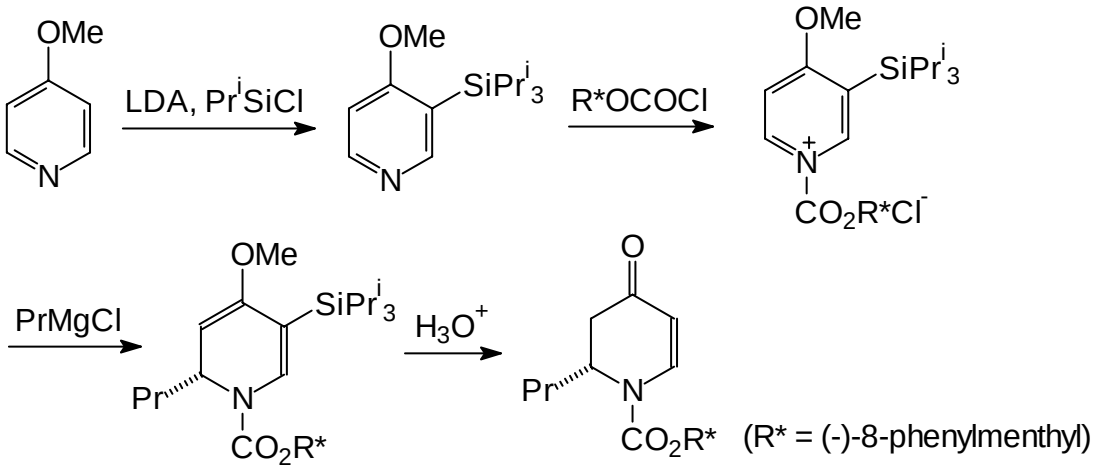
The Chichibabin reaction



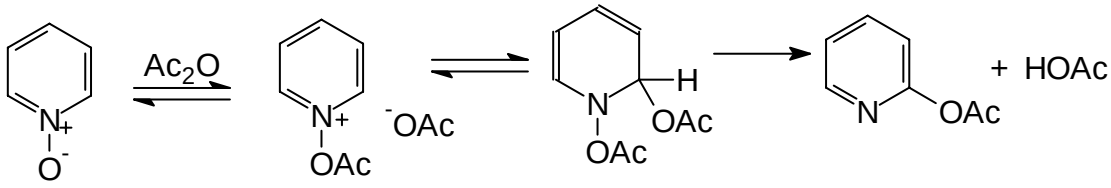
Addition of organolithium reagents to pyridine and reaction of the adducts

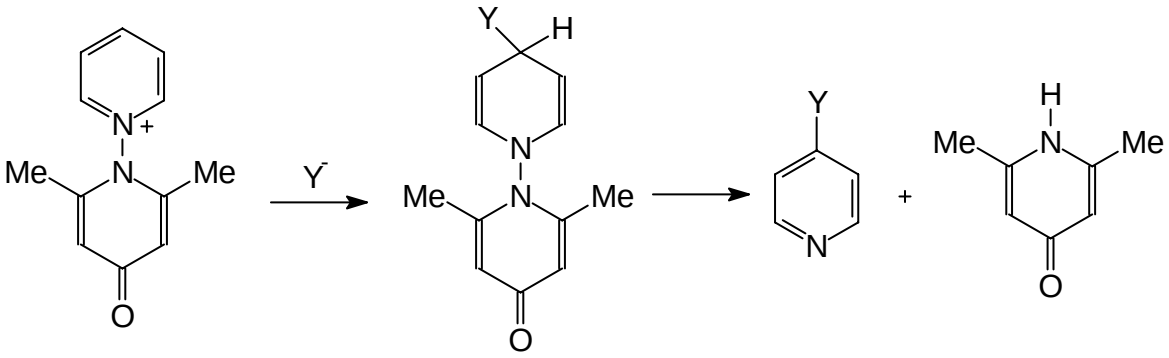


Formation and oxidation of pseudobases from N-alkylpyridinium salts

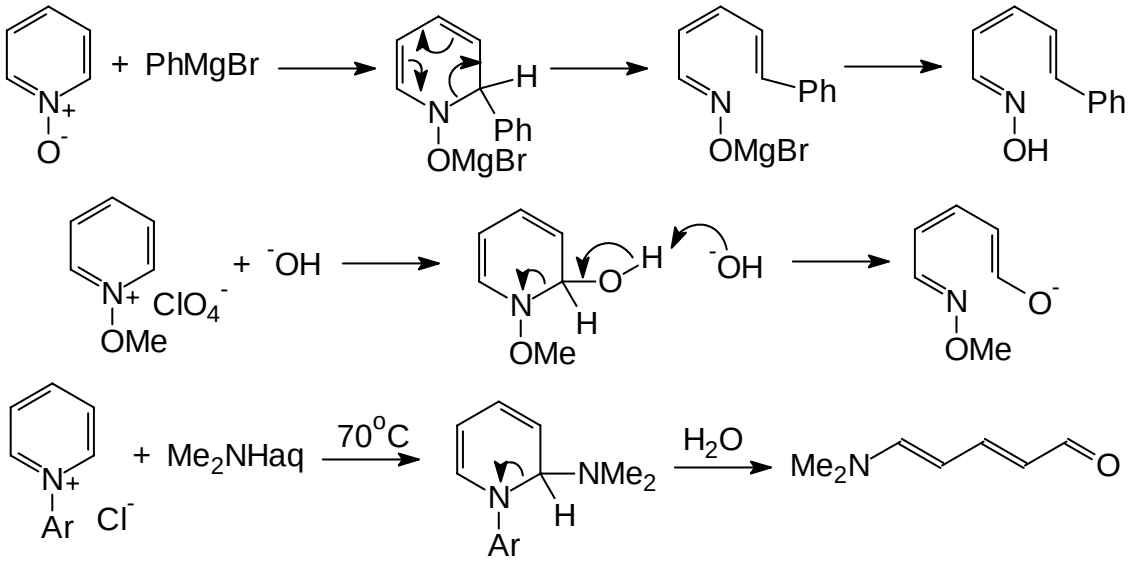


Synthesis of a chiral dihydropyridine from 4-methoxypyridine





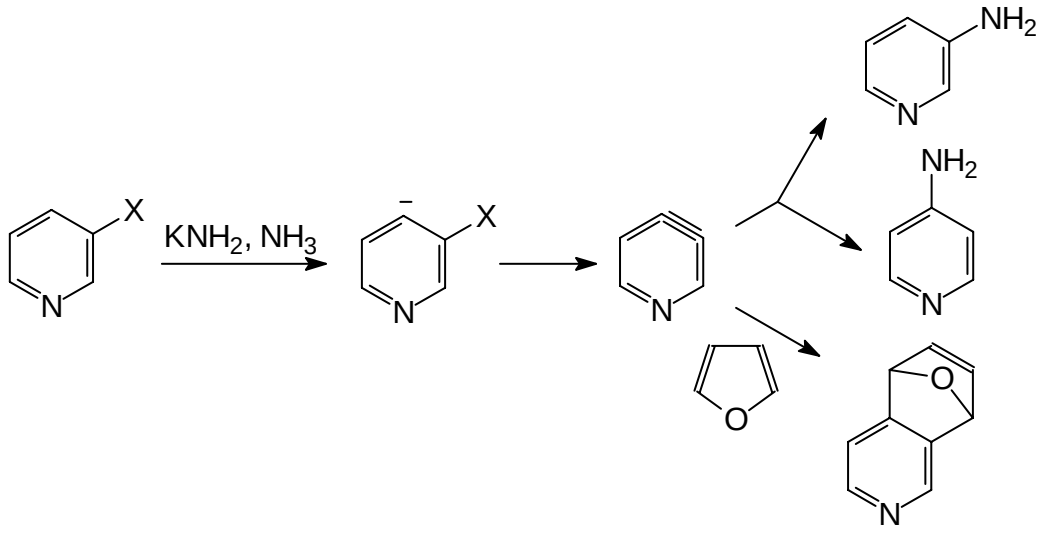
Selective nucleophilic attack on pyridinium salts.



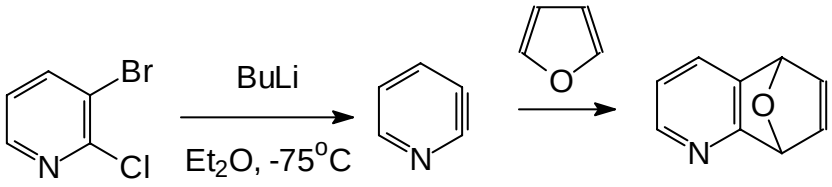
(Ar = $C_6H_3(NO_2)_2$-2,4)

Nucleophilic ring opening.

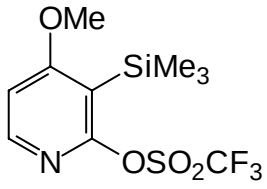
7.1.8 Didehydropyridines (pyridines)



Generation of 3,4-didehydropyridine



Generation of 2,3-didehydropyridine



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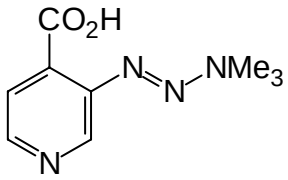

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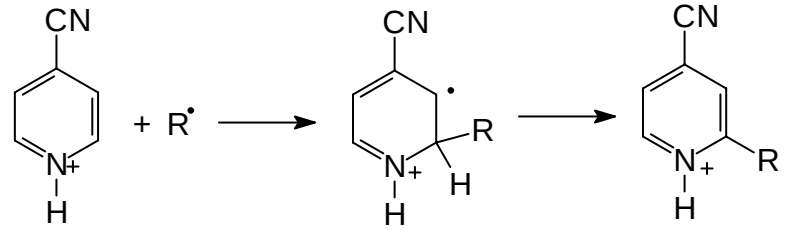
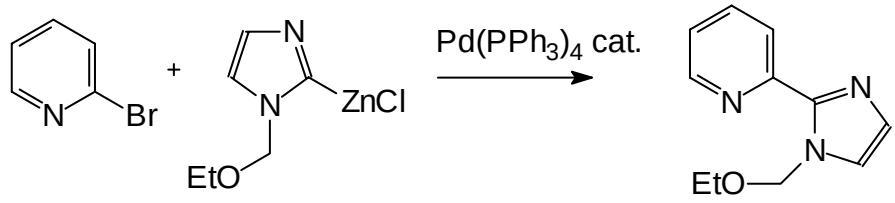
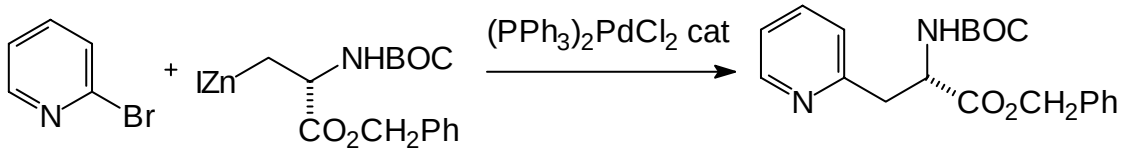
7.1.9 Radical substitution

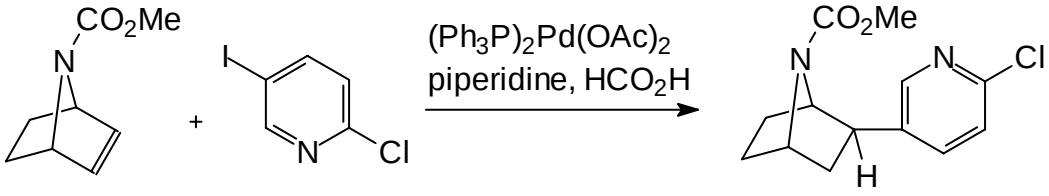


7.1.10 Palladium-catalyzed coupling reactions and Heck reactions



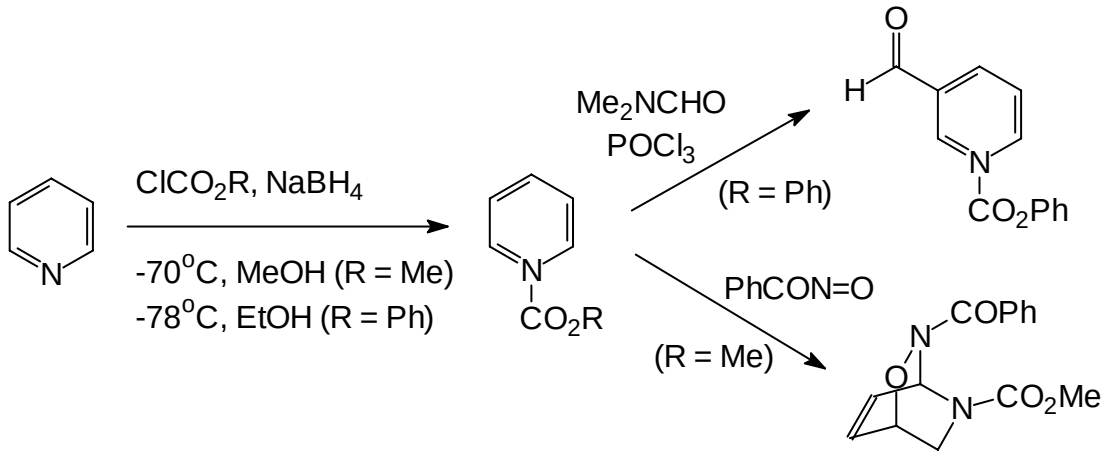


Palladium-catalysed cross-coupling reactions of 2-bromopyridine

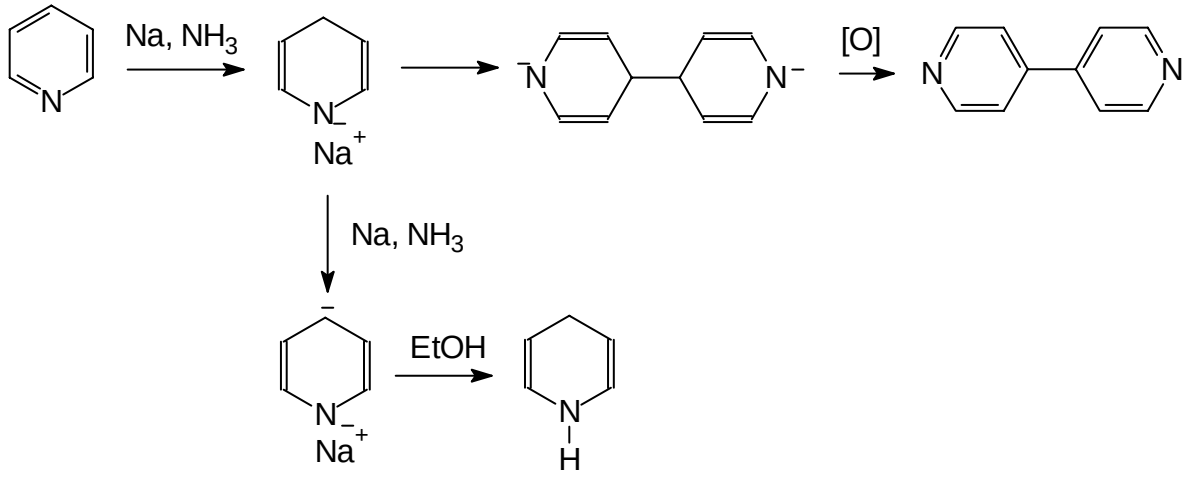


A Heck reaction of 2-chloro-5-iodopyridine.

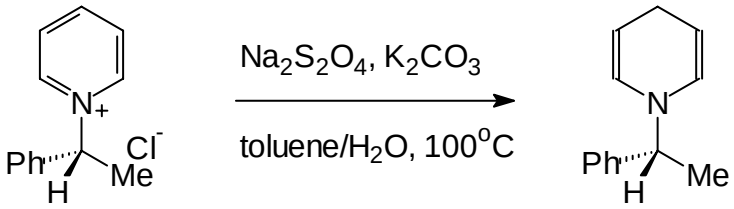
7.1.11 Reduction of pyridines and pyridinium salts: dihydropyridines



Examples of formation and reactions of 1,2-dihydropyridine-1-carboxylic esters.



Birch reduction of pyridines.



Reduction of an N-alkylpyridinium salt with sodium dithionite.