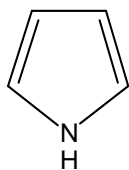
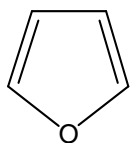
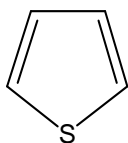


5. Spezielle 5-Ring Heterocyclen**5.1 Pyrrol, Furan, Thiophen**

pKa: -3,8



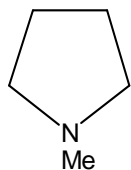
-



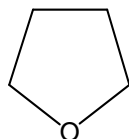
-

Eigenschaften:
elektronreiche Aromaten
Pyrrol hat auch Diencharakter

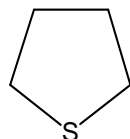
Vorkommen:
Steinkohleteer, Knochenöl
Hämoglobin, Chlorophyll



pKa: 10,4

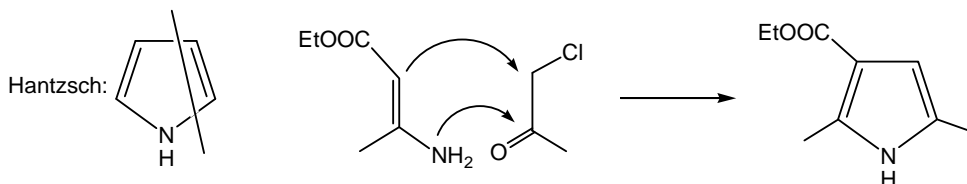
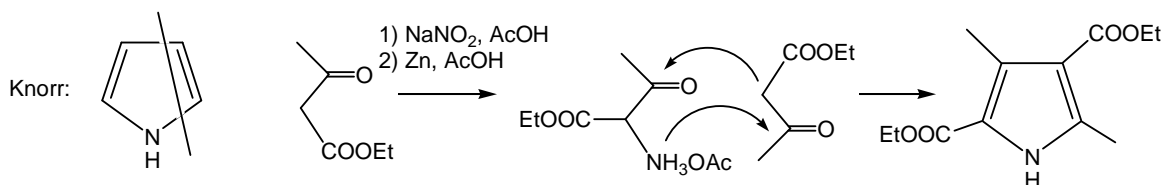
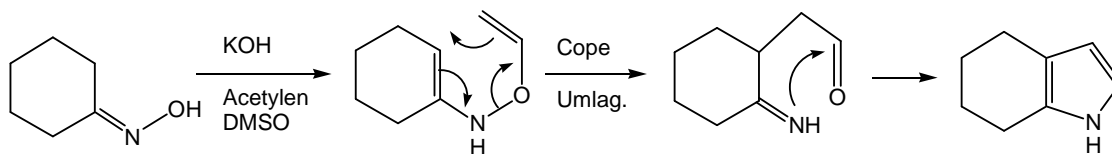
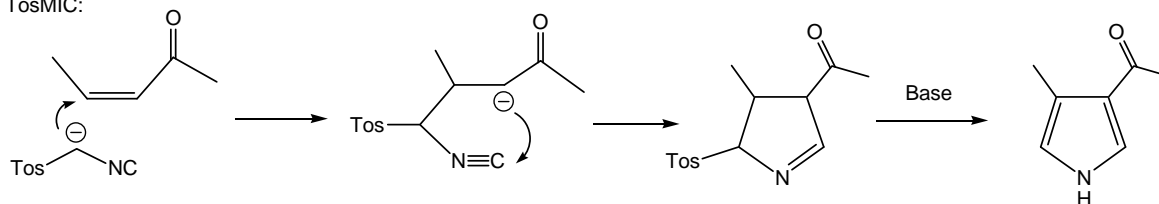


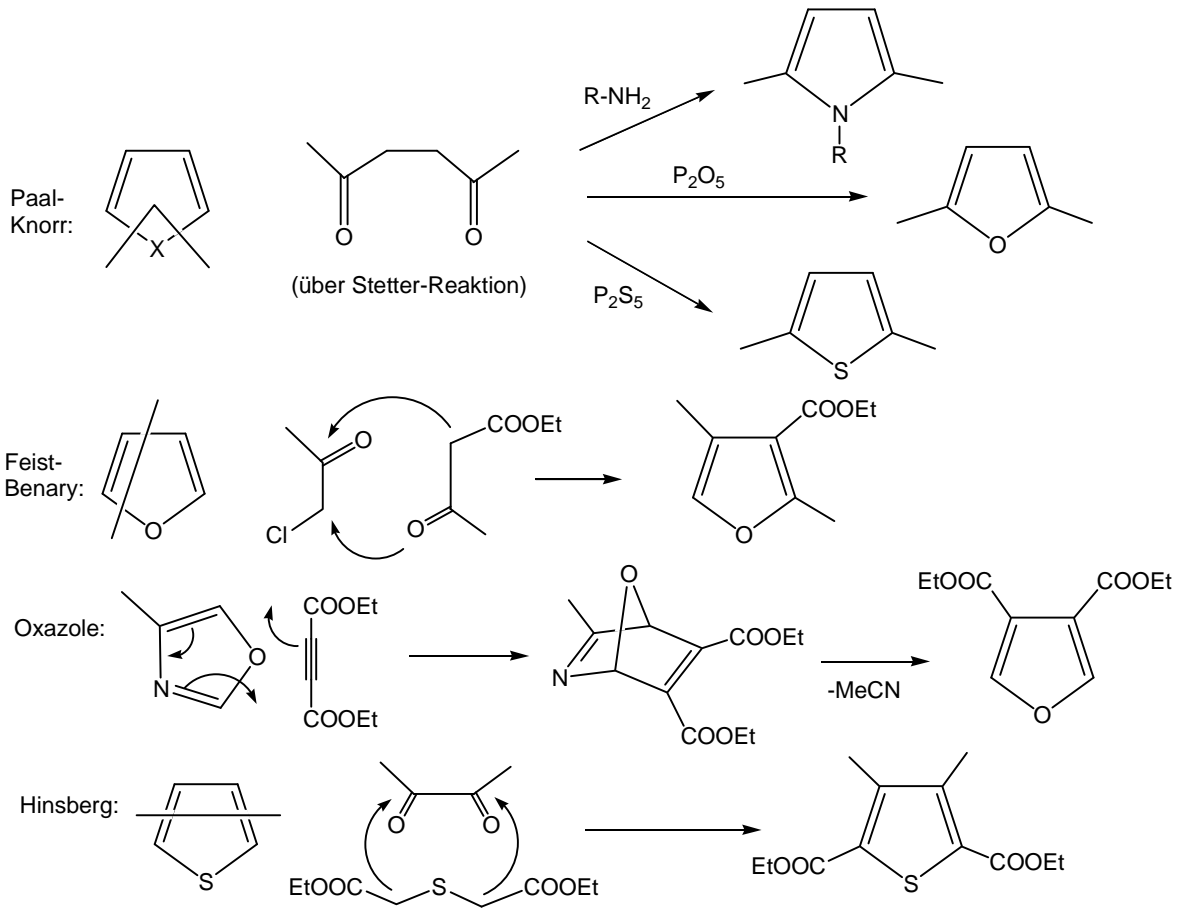
-2,1



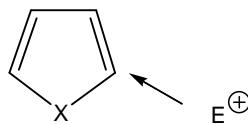
-4,5

gesättigte Vertreter
Pyrrolidin, THF, Tetrahydrothiophen
haben basische Eigenschaften

Synthesen:**Oxim + Acetylen:****TosMIC:**

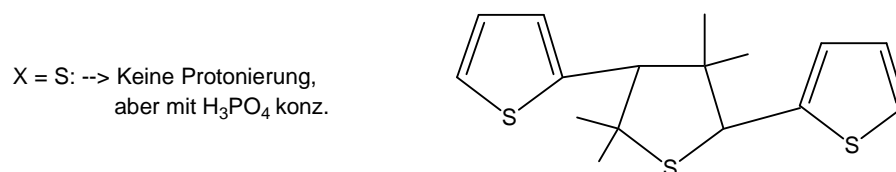
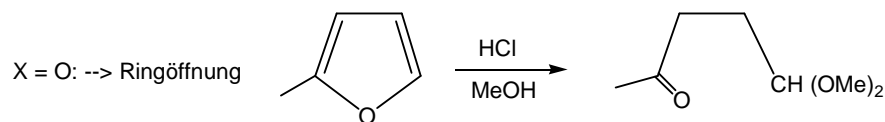
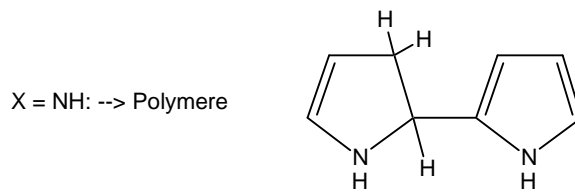
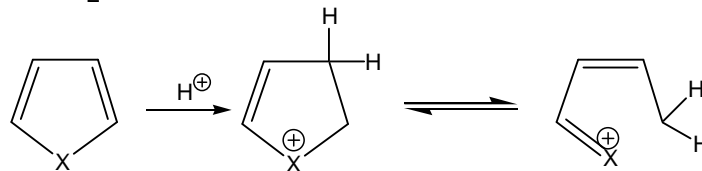


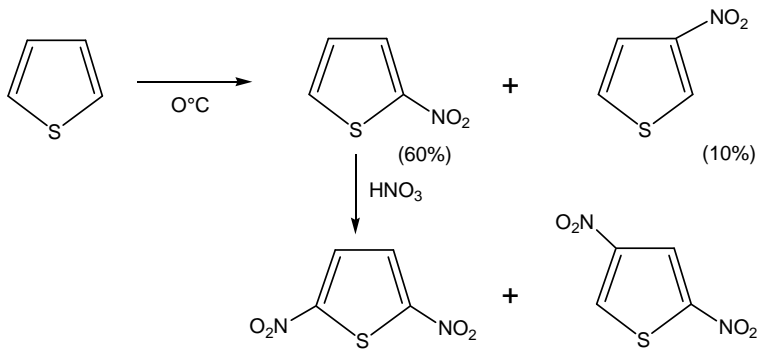
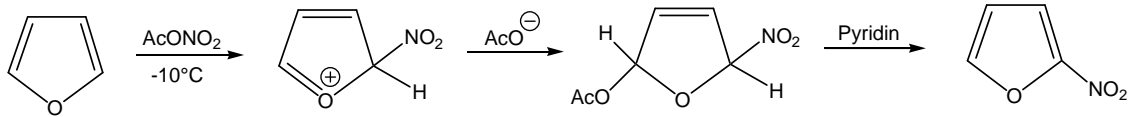
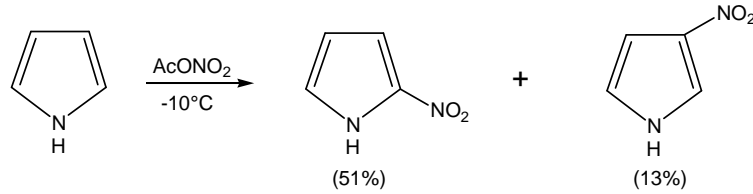
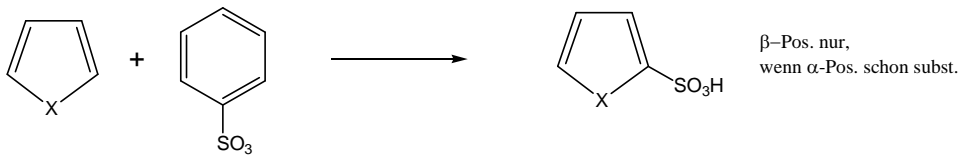
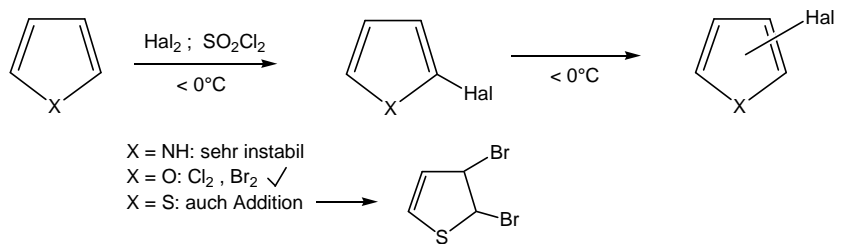
Reaktionen:



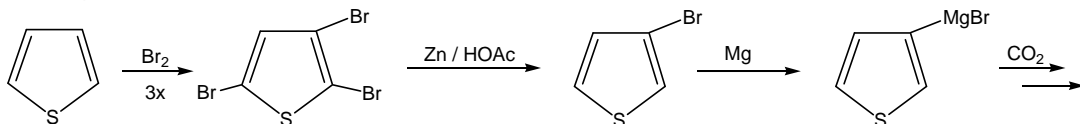
bei Pyrrol oft auch 3-Substitution
 bei Thiophen / Furan nur 2-Substitution
 bei Furan oft auch Ringöffnung / Addition / Eliminierung

Protonierung (H⁺)

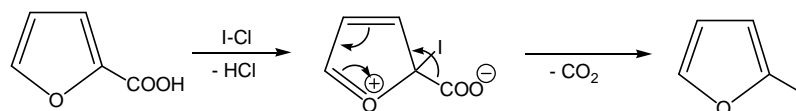


Nitrierung: (NO_2^+)Sulfonierung: milde Bedingungen notwendig!Halogenierung: milde Bedingungen

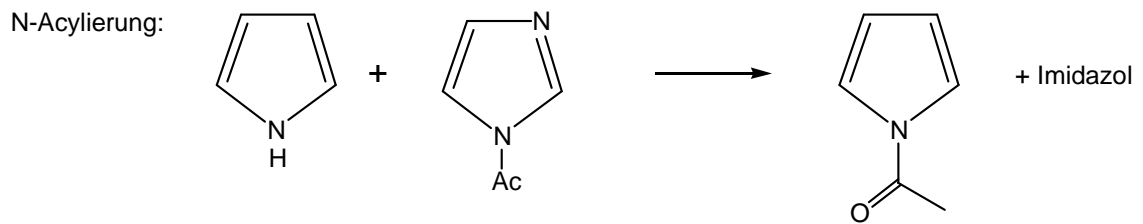
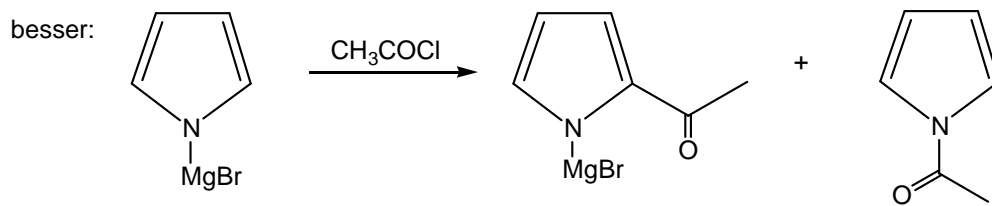
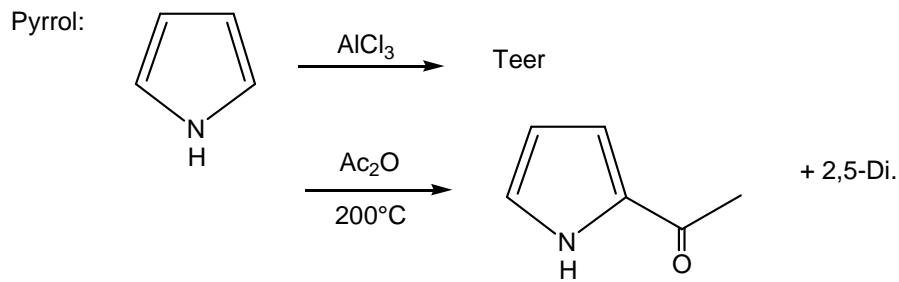
sonst bei Thiophen:



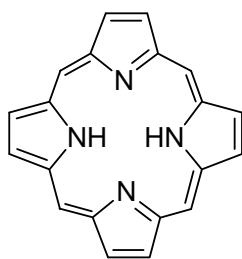
speziell: 2 - Iodfuran:



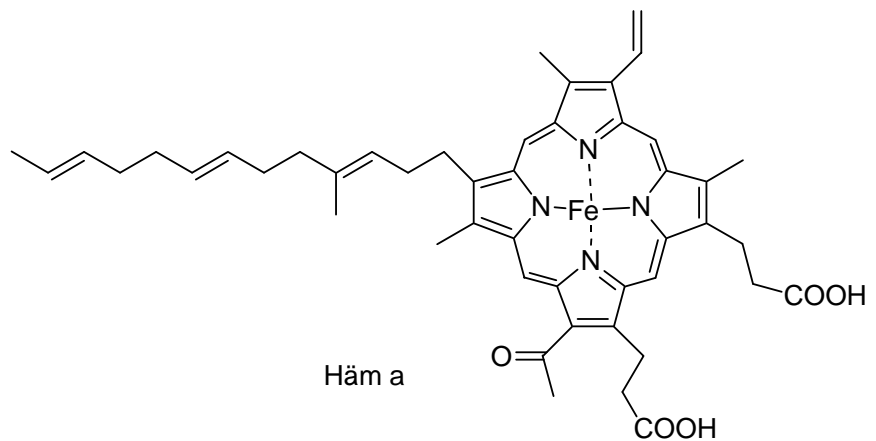
Acylierung: sehr unterschiedlich für NH, O, S
(F.-C.-Acyl.)



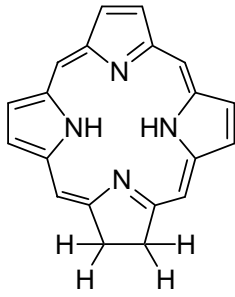
NATURSTOFFE (insb. Porphyrine):



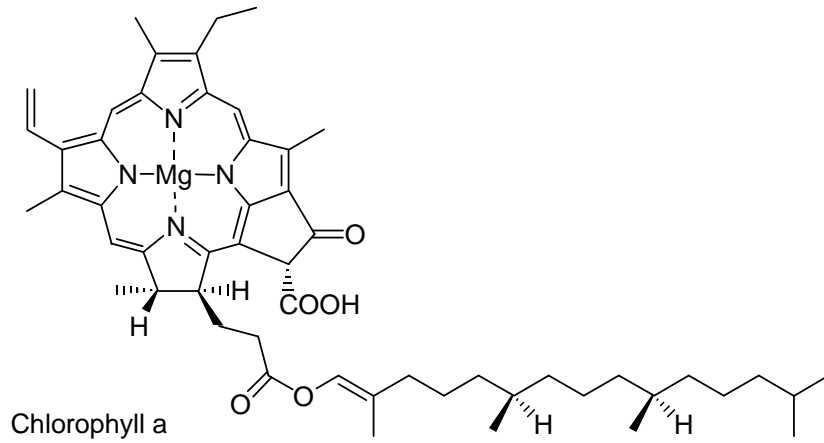
Porphyrin



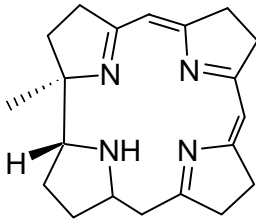
Häm a



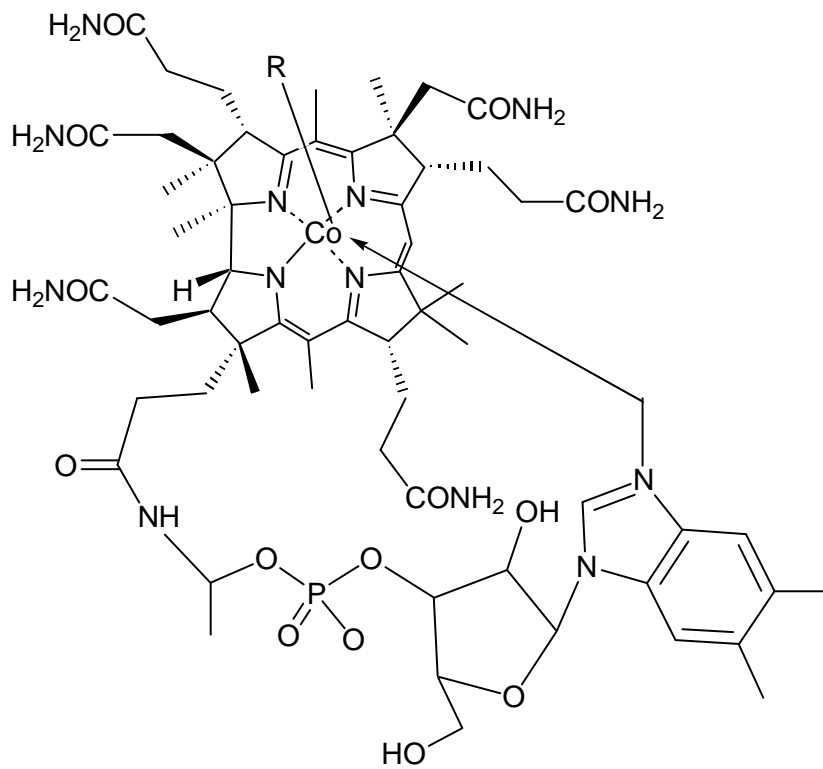
Chlorin



Chlorophyll a

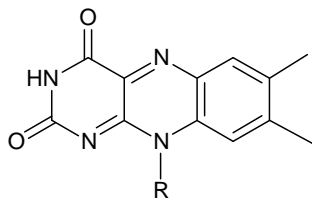


Corrin

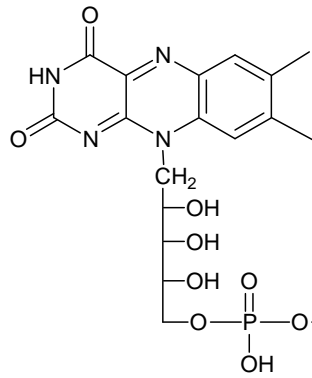
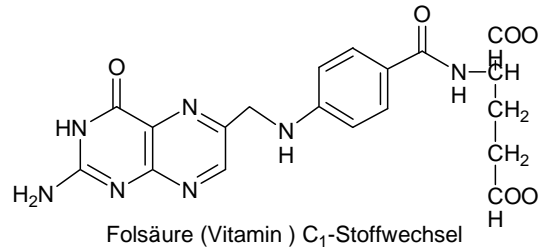


Vitamin B12

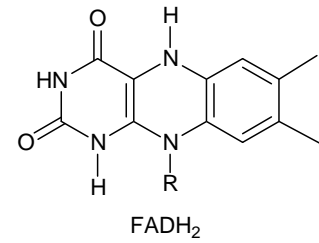
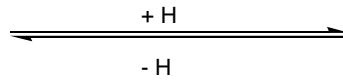
PTERIDINE



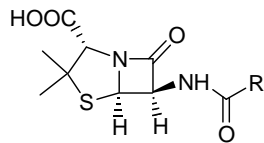
R = H Isoalloxazin (Flavin)
 R = CH₂ Riboflavin (Vitamin B2)



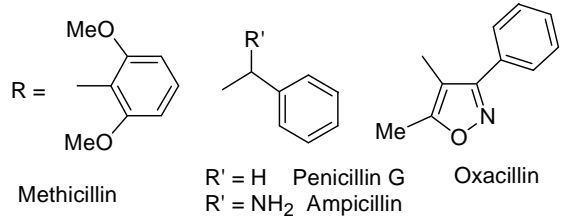
Flavin-adenin-dinucleotid (FAD)
 Cofaktor bei Oxidoreduktasen



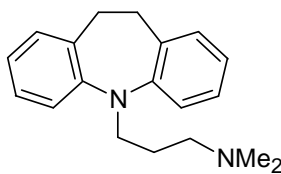
AZETIDINE



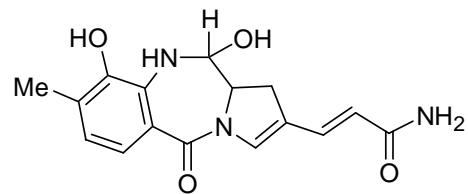
Penicilline (Fleming 1928)



AZEPINE

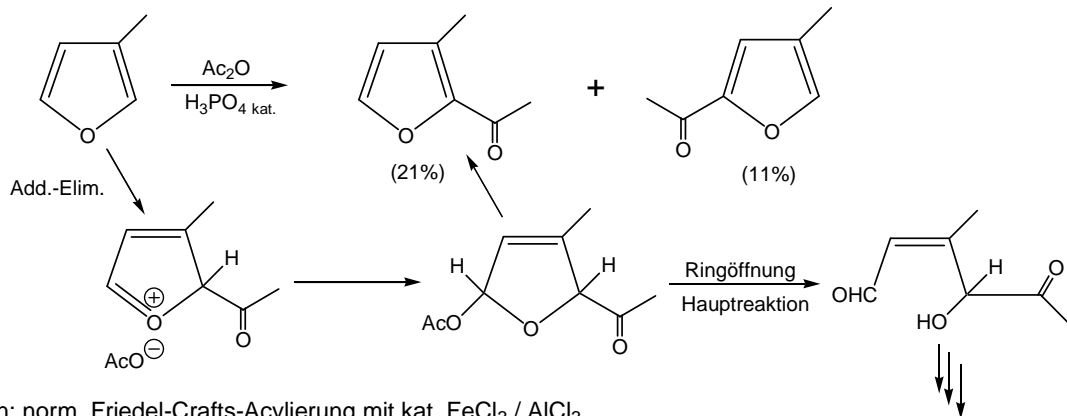


Imipramin
 (stimmungsaufhellend)

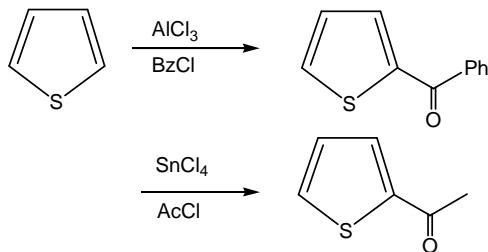


Anthramycin (Streptomyces refuineus)
 Antibiotikum (anticarcinogen)

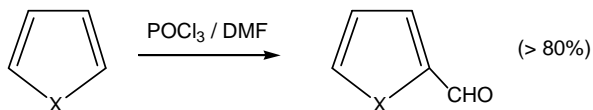
Furan: wenig reaktiv (kat. H^+ notwendig)



Thiophen: norm. Friedel-Crafts-Acylierung mit kat. $FeCl_3 / AlCl_3$

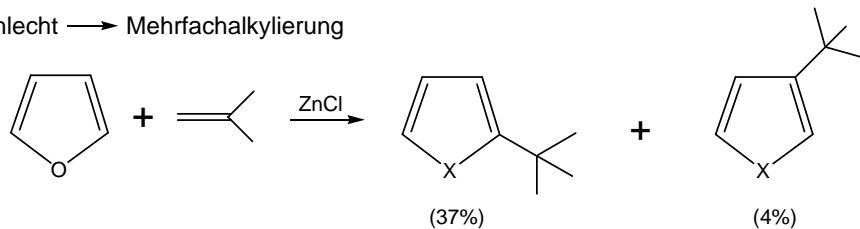


Formylierung: Vilsmeier normal mit NH, O, S

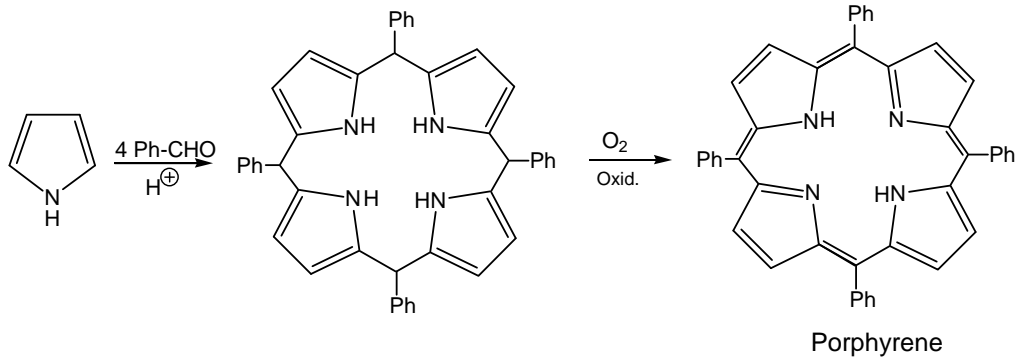
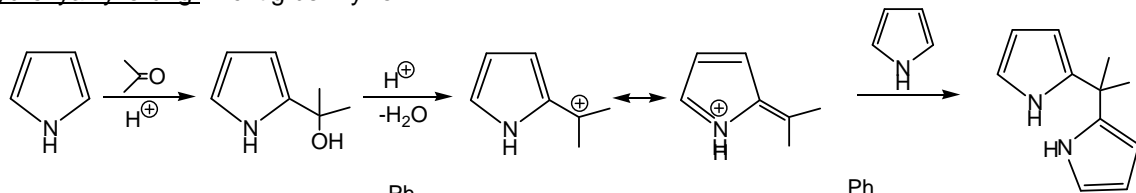


Alkylierung: schlecht \rightarrow Mehrfachalkylierung

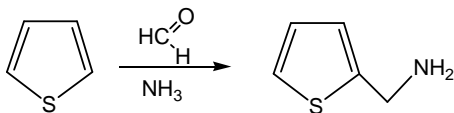
aber:



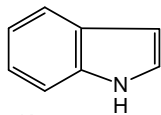
Hydroxyalkylierung: wichtig bei Pyrrol



Mannich-Reaktion: gut bei Thiophen



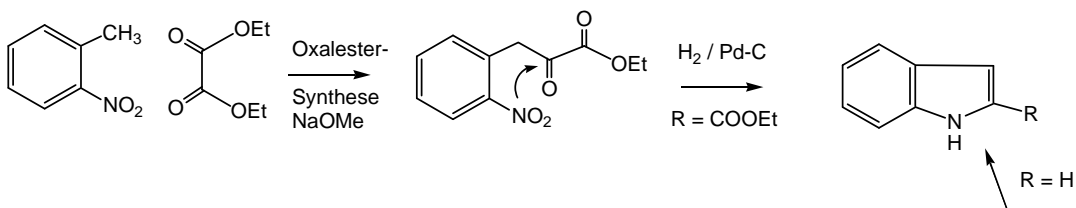
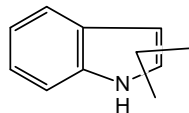
5.2 INDOLE



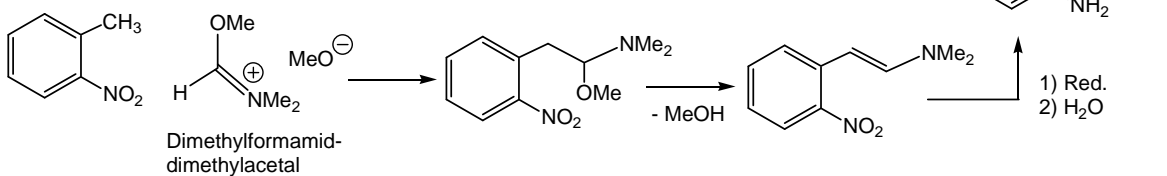
pKa = -3,5
Schmp: 232°C

Vorkommen: Steinkohleteer
viele Naturstoffe (Alkaloide)
Aminosäure Tryptophan
Geruch: blumig in verd. Lsg.
fäkalienartig in konz. Lsg.

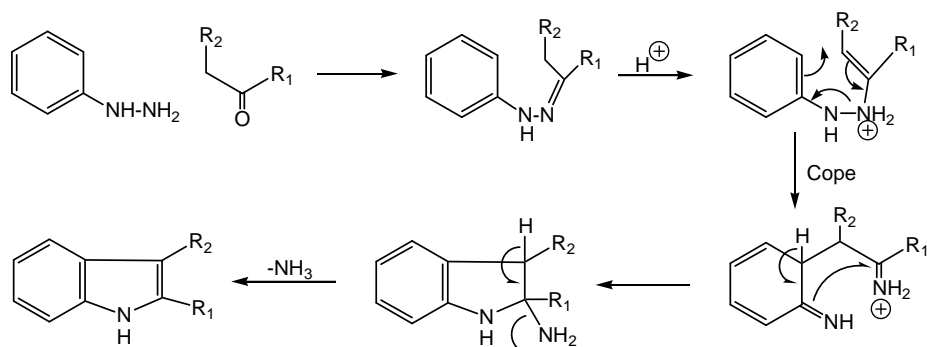
Reissert-Synthese



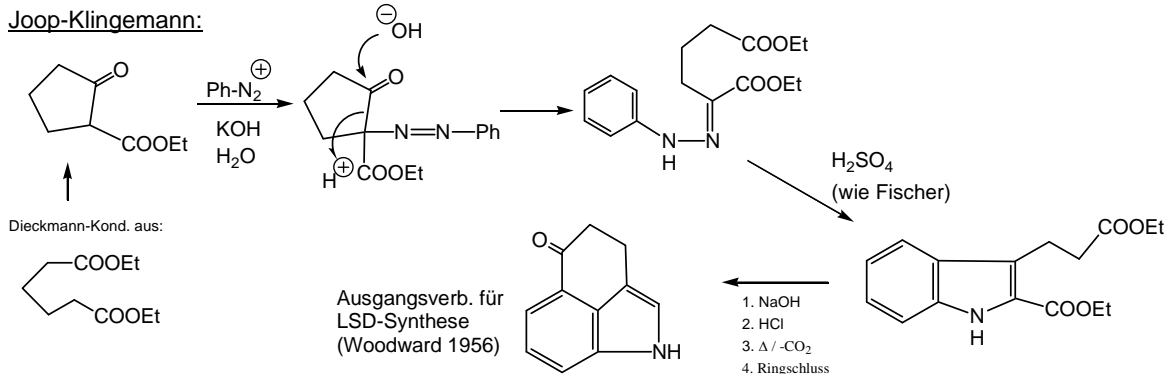
Batcho-Leimgruber-Synthese (ähnlich Reissert)



Fischer-Indol-Synthese:

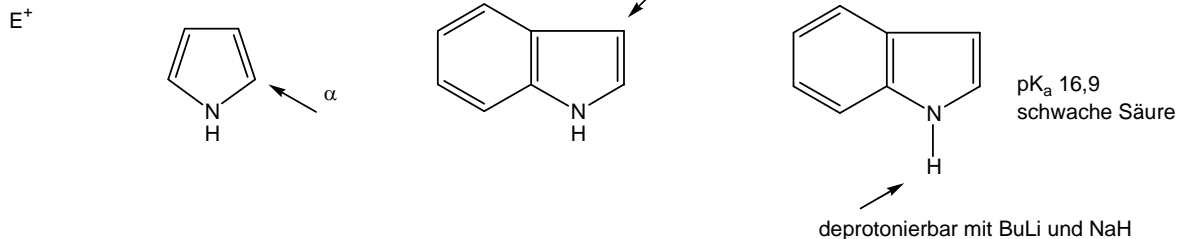


Joop-Klingemann:

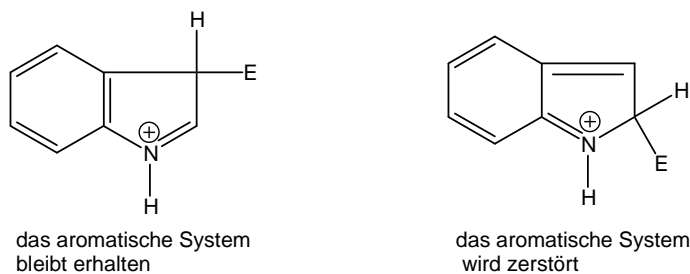


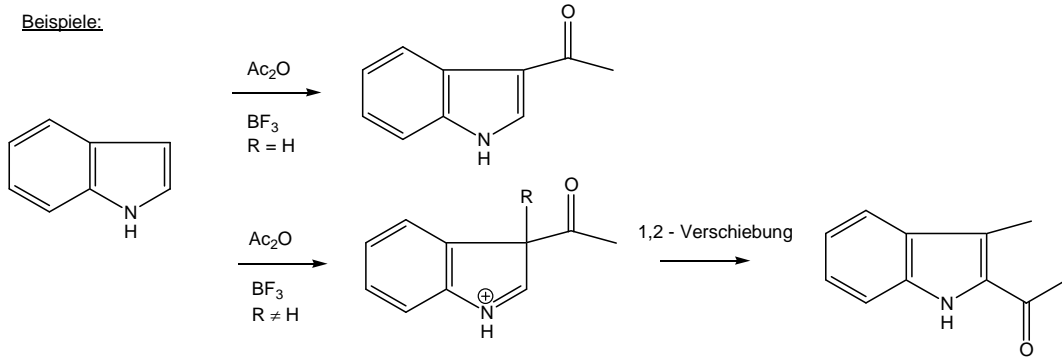
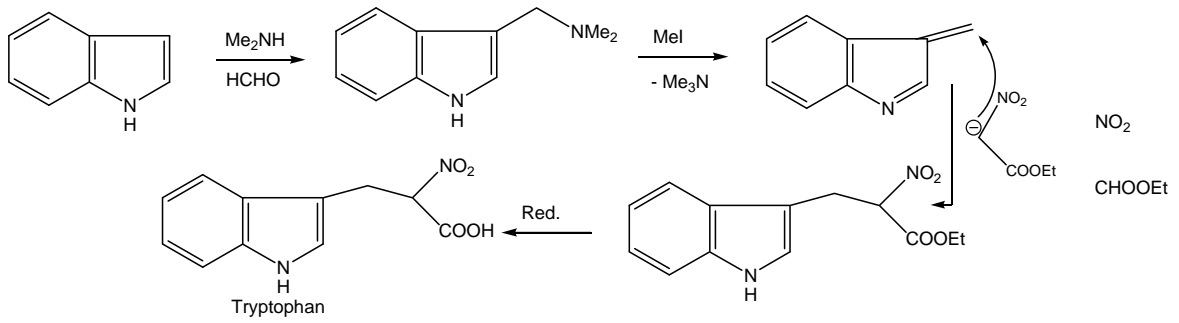
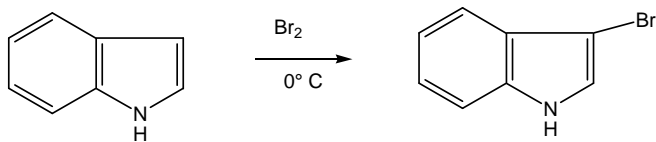
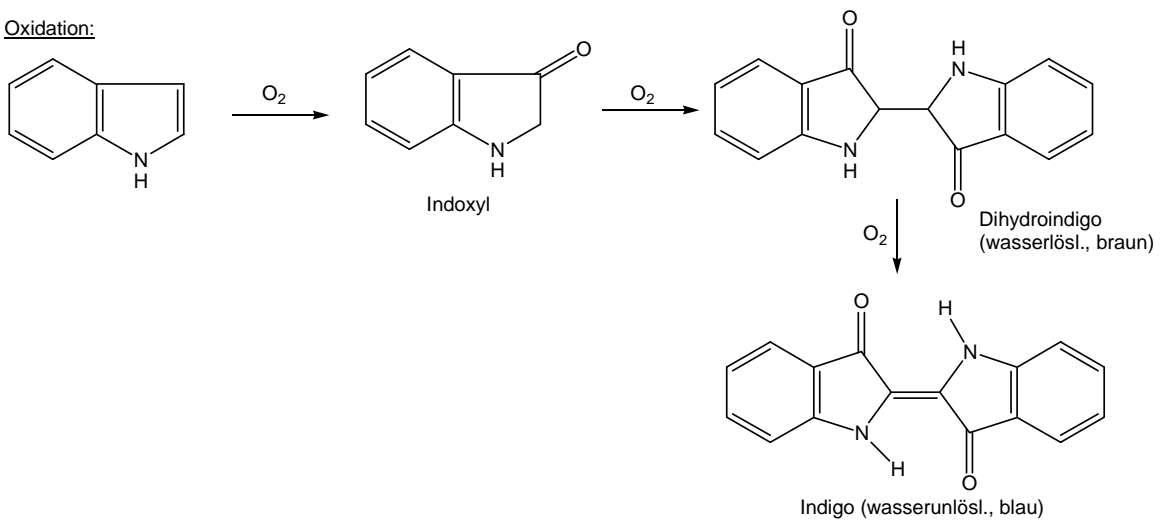
Reaktionen: Vergleichbar mit Pyrrol aber weniger reaktiv.

Unterschied:



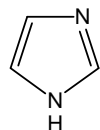
β -Angriff wegen:



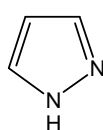
Beispiele:weitere Reaktion:MannichHalogenierung:Oxidation:

5.3 Fünf-Ringe mit zwei und mehr Heteroatomen

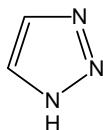
zusätzliche Stickstoffatome mit freien Elektronenpaaren in der Ringebene erhöhen die Basizität (pyridinartig). Aufgrund der stark negativen Ladung wird der elektrophile Angriff schwieriger.



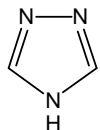
Imidazol
pK_a 14,5
-30°C



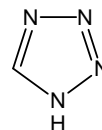
Pyrazol
pK_a 13,5



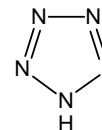
1,2,3-Triazol
pK_a 9,4



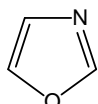
1,2,4-Triazol
-



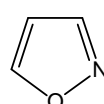
Tetrazol



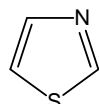
Pentazol
explosiv bei



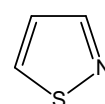
Oxazol
pK_a 13,2



Isoxazol



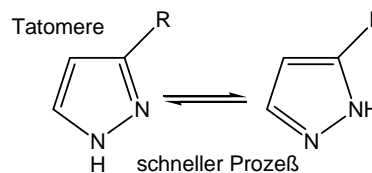
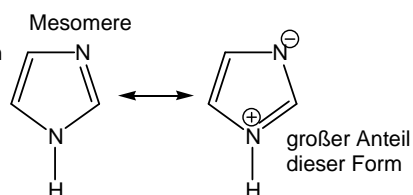
Thiazol



Isothiazol

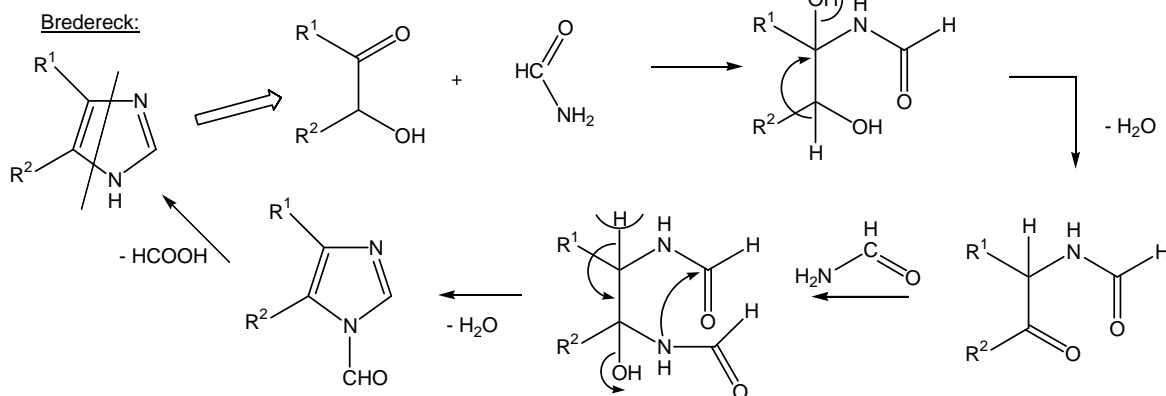
Chemische Eigenschaften:

meist sehr stabil gegen Säuren
schlechte Reaktivität mit E⁺

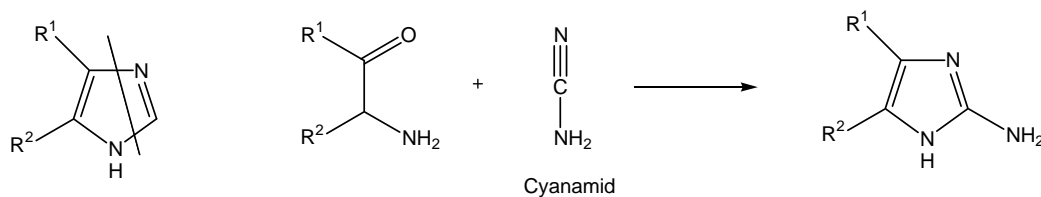


Synthesen: (auch 1,3-dipolar, siehe dort 3.3)

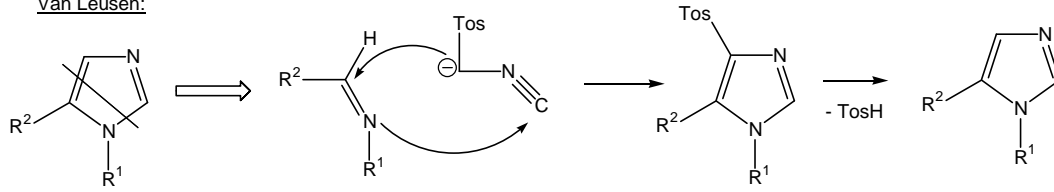
Bredereck:



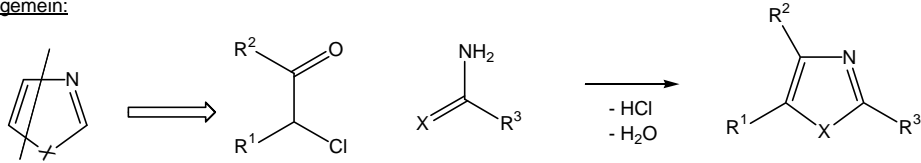
Markwald:



Van Leusen:



Allgemein:



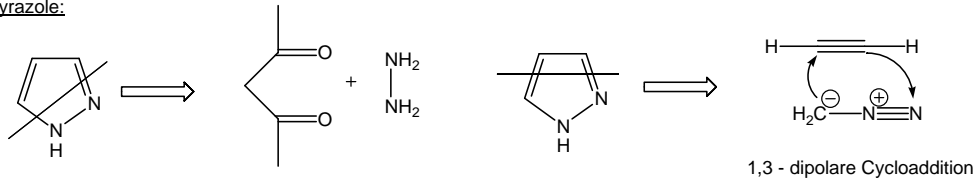
X = O Robinson-Gabriel-Synthese

X = NH Amidine
 O Säureamide
 S Thioamide

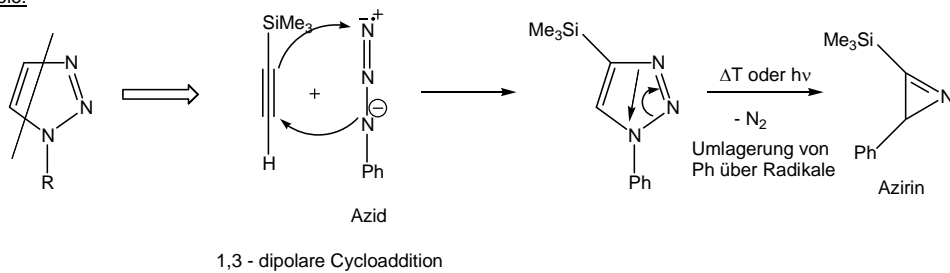
R = Alkyl, Phenyl, NH₂, OH, SH

X = S Hantzsch-Synthese

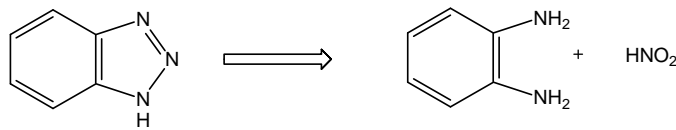
Pyrazole:



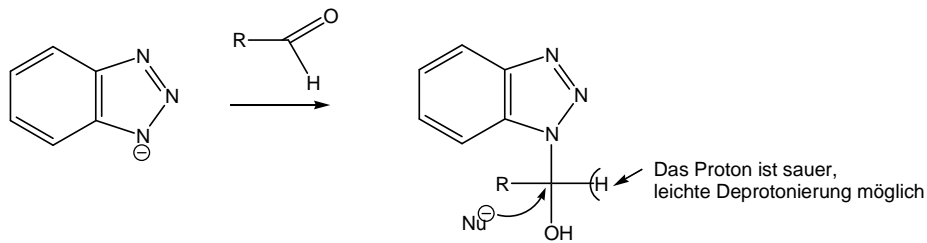
Triazole:



Benzotriazol: Katritzky (wichtig!)

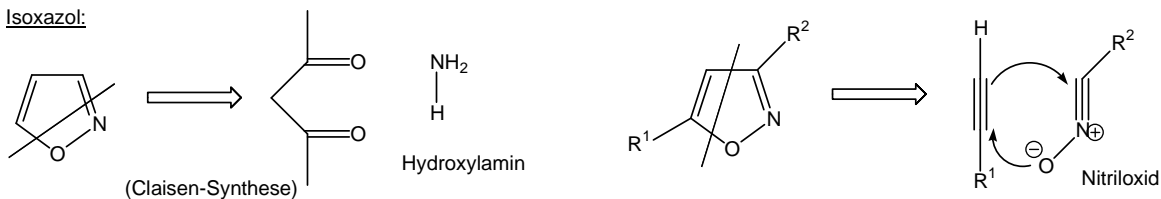


pK_a < 0 daher leichte Deprotonierung



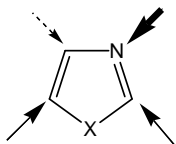
Benzotriazol ist eine sehr gute Austrittsgruppe, wie auch CN⁻ oder PhSO₂⁻
 Anwendung bei S_N

Isoxazol:

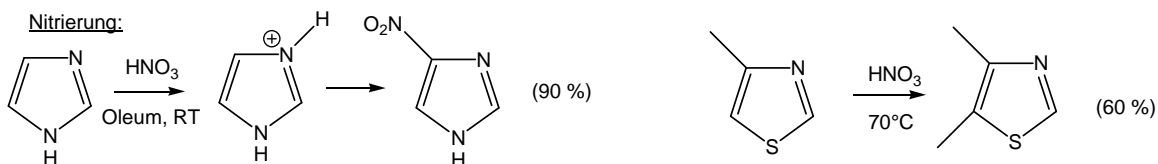


Reaktionen:

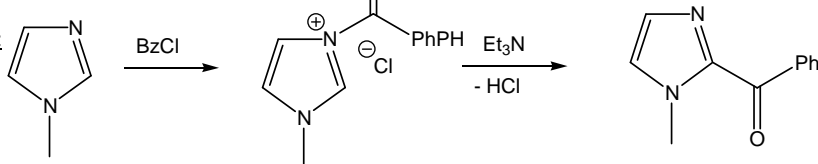
Stark deaktiviert für E⁺



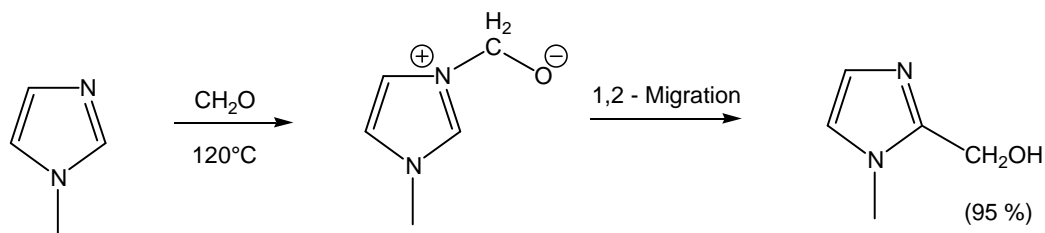
Nitrierung:



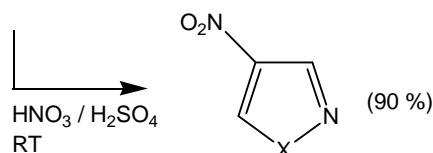
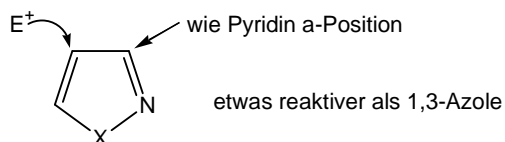
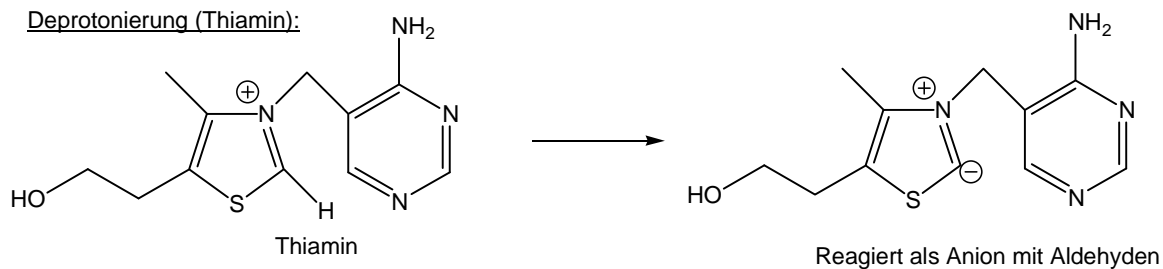
Acylierung:

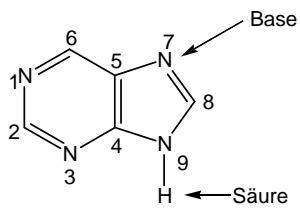


Hydroxymethylierung:



Deprotonierung (Thiamin):

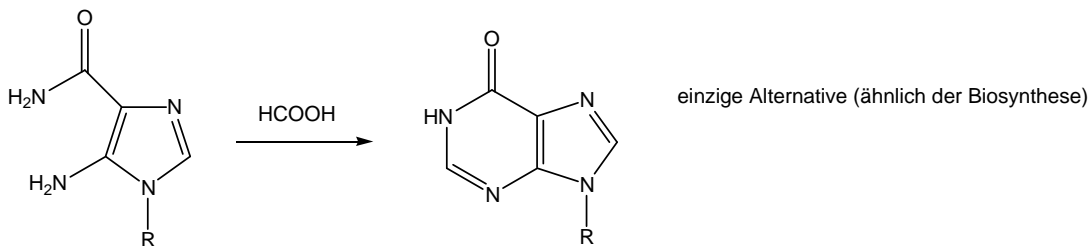
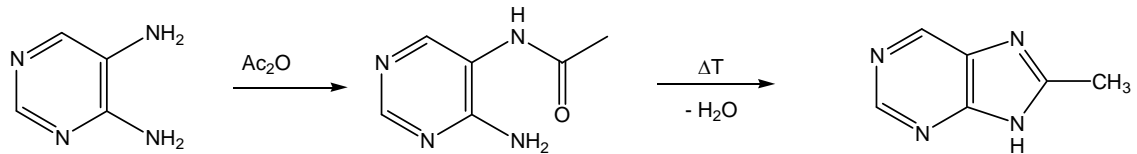


5.4 Purine

Smp.: 216 °C

pK_a 2,30
8,96

Vorkommen: Viele Naturstoffe (die Stammverbindung kommt nicht in der Natur vor), z.B. DNA (Adenosin, Guanosin), Harnsäure

Synthese: Traube-Purin-Synthese (1910)Harnsäure (Traube):