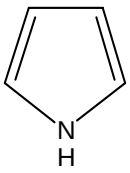
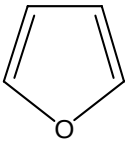
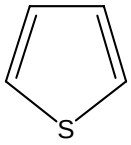
5. Spezielle 5-Ring Heterocyclen

5.1 Pyrrol, Furan, Thiophen



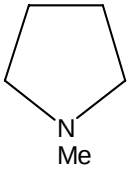


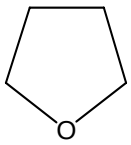


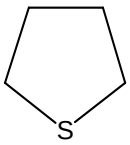
pKa: -3,8 - -

Eigenschaften:
elektronenreiche Aromaten
Pyrrol hat auch Diencharakter

Vorkommen:
Steinkohleteer, Knochenöl
Hämoglobin, Chlorophyll





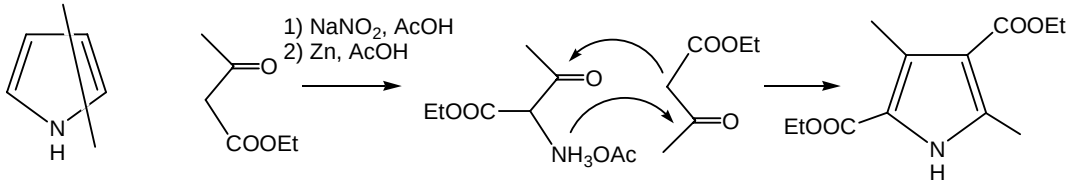


pKa: 10,4 -2,1 -4,5

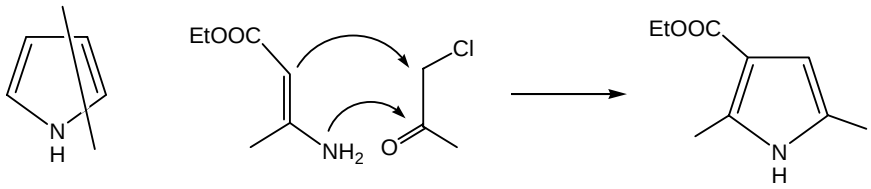
gesättigte Vertreter
Pyrrolidin, THF, Tetrahydrothiophen
haben basische Eigenschaften

Synthesen:

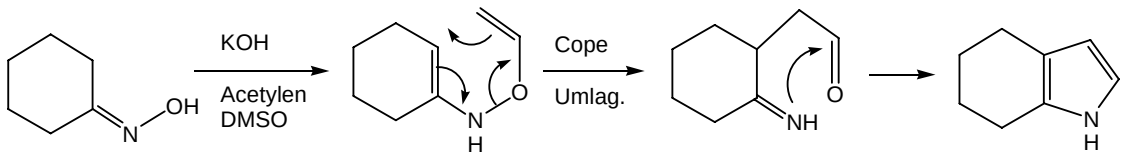
Knorr:



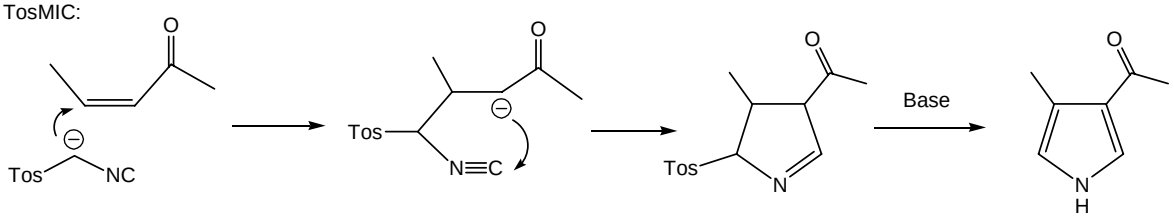
Hantzsch:

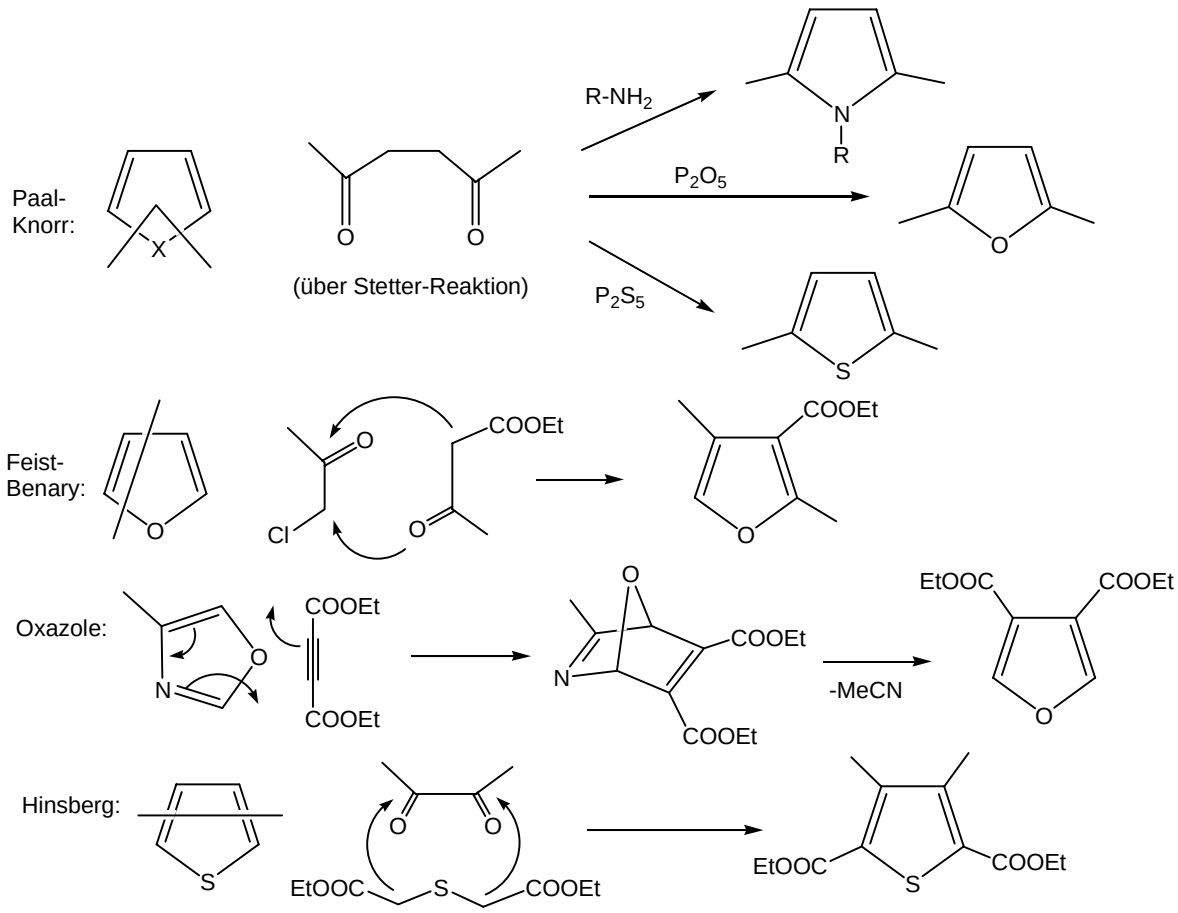


Oxim + Acetylen:

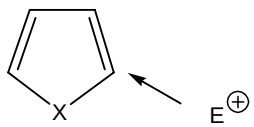


TosMIC:



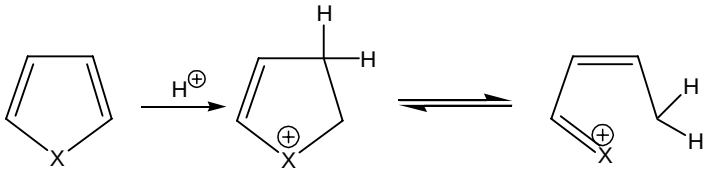


Reaktionen:

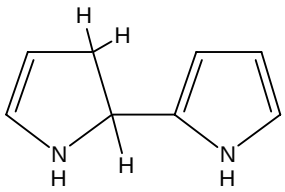


bei Pyrrol oft auch 3-Substitution
bei Thiophen / Furan nur 2-Substitution
bei Furan oft auch Ringöffnung / Addition / Eliminierung

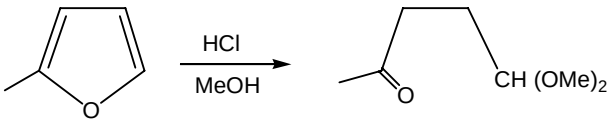
Protonierung ($H^{\oplus}$)



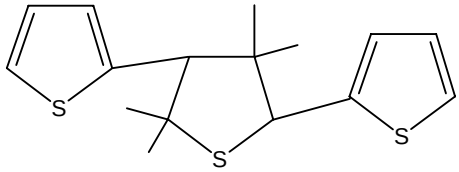
X = NH: --> Polymere



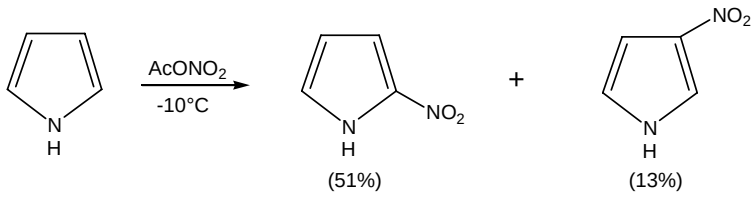
X = O: --> Ringöffnung

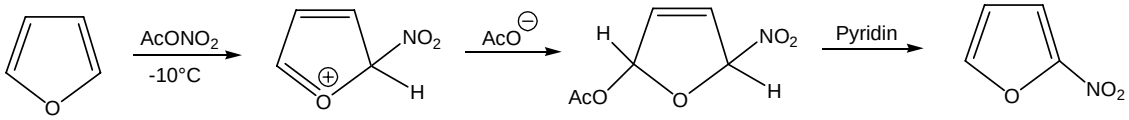


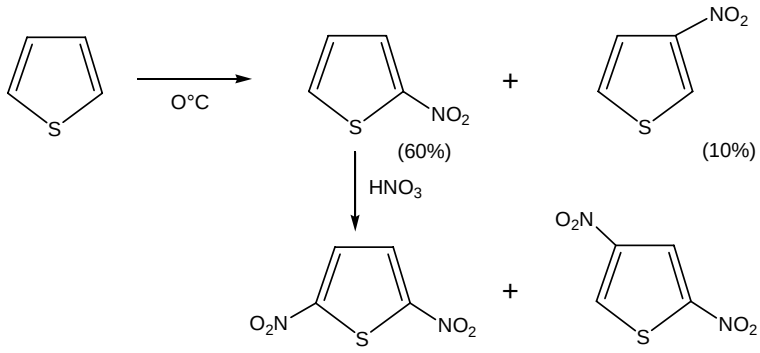
X = S: --> Keine Protonierung,
aber mit H_3PO_4 konz.



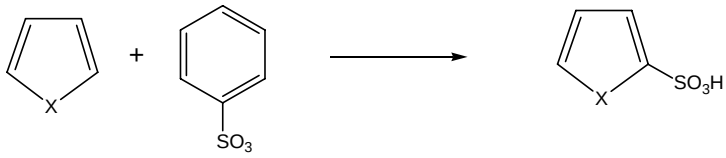
Nitrierung: (NO_2^+)





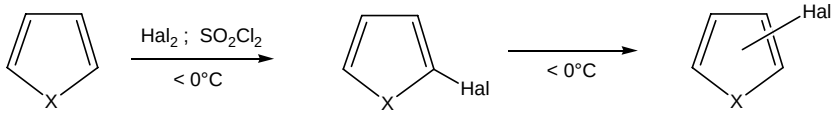


Sulfonierung: milde Bedingungen notwendig!

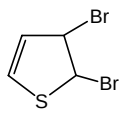


β–Pos. nur,
wenn α-Pos. schon subst.

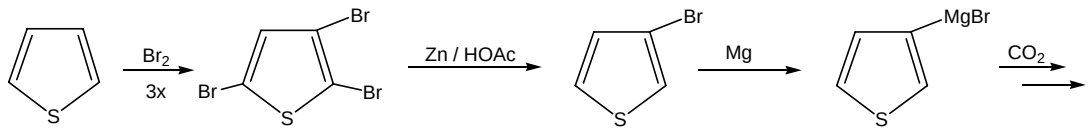
Halogenierung: milde Bedingungen



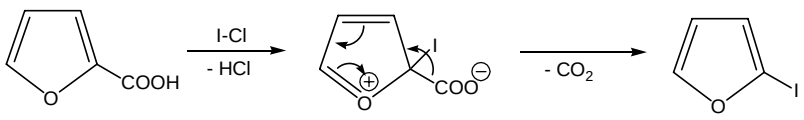
X = NH: sehr instabil
X = O: Cl_2 , Br_2 ✓
X = S: auch Addition



sonst bei Thiophen:



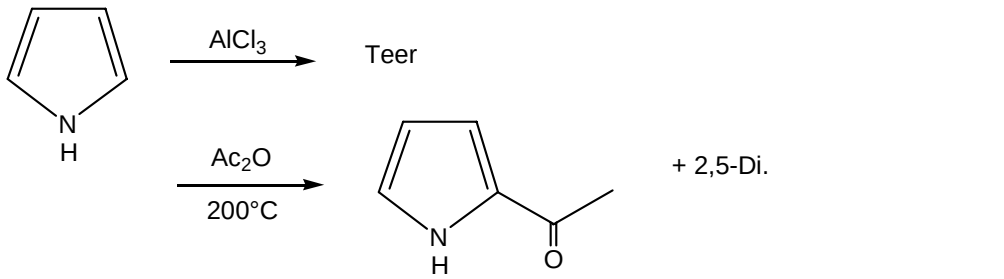
speziell: 2 - Iodfuran:



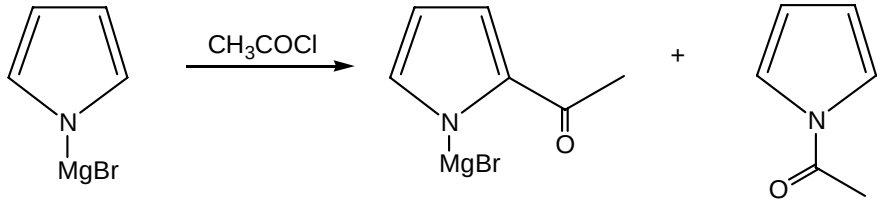
Acylierung: sehr unterschiedlich für NH, O, S

(F.-C.-Acyl.)

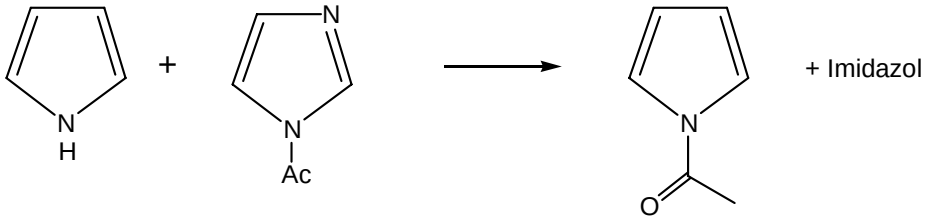
Pyrrol:



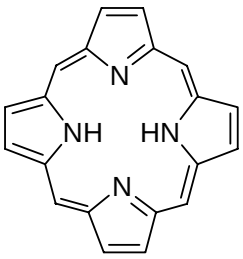
besser:



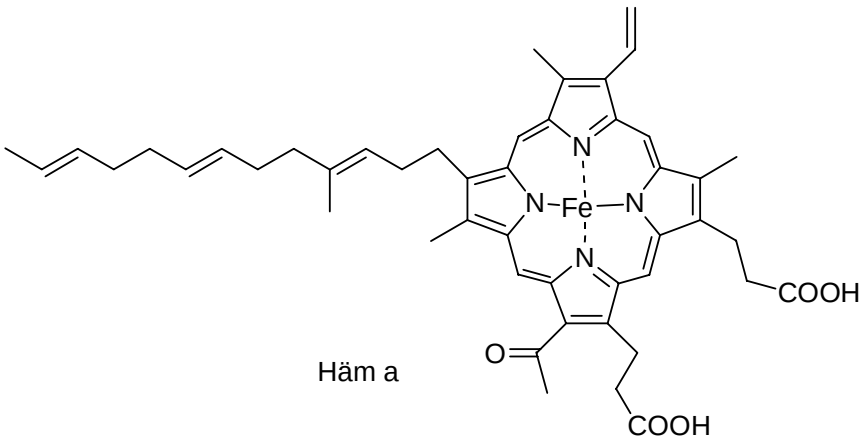
N-Acylierung:



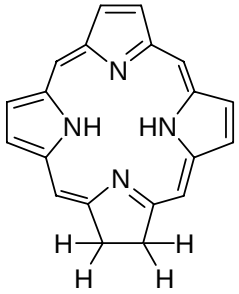
NATURSTOFFE (insb. Porphyrine):



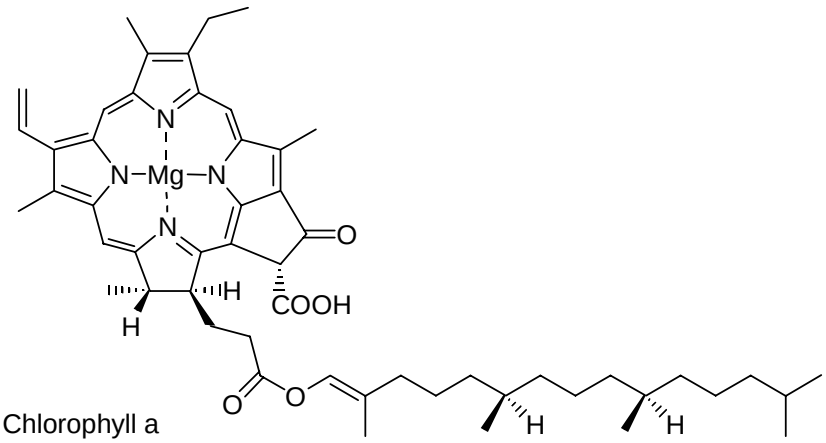
Porphyrin



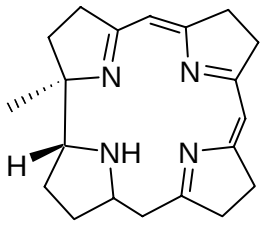
Häm a



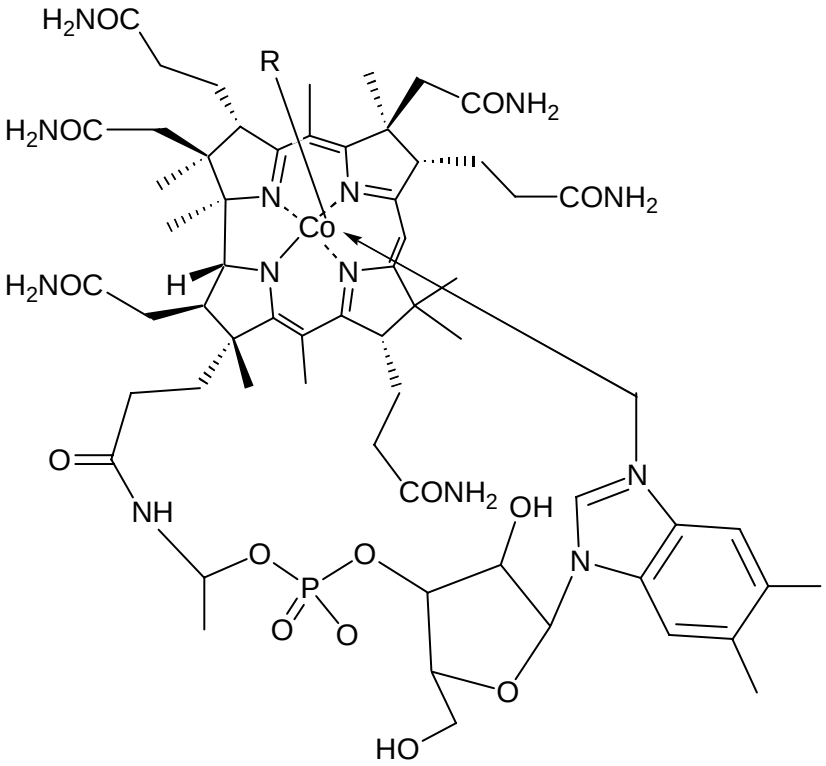
Chlorin



Chlorophyll a

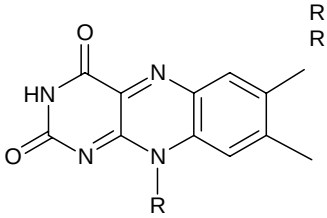


Corrin



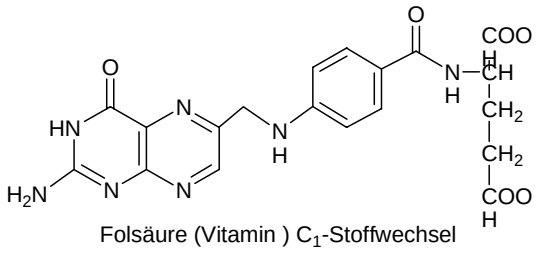
Vitamin B12

PTERIDINE

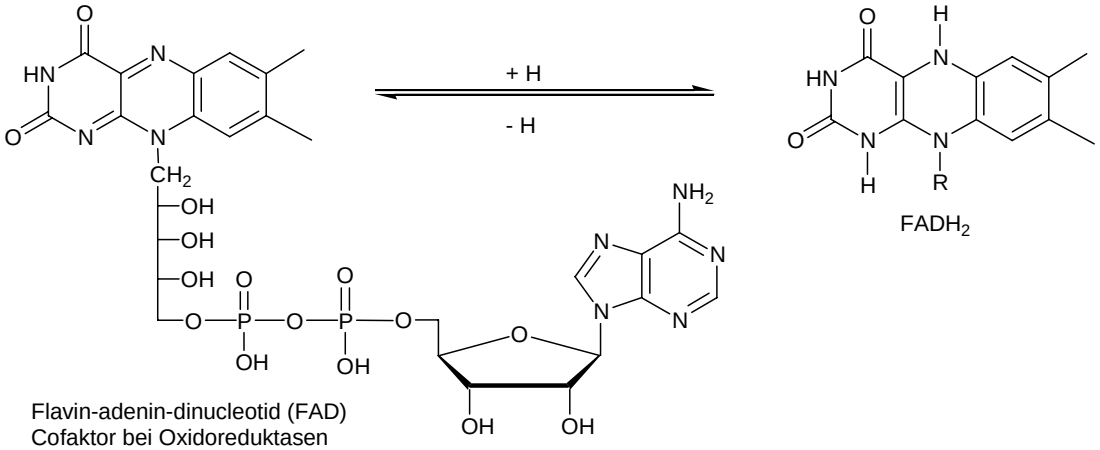


R = H Isoalloxazin (Flavin)
R = CH_2–(CHOH)$_3$–CH_2–OH

Riboflavin
(Vitamin B2)

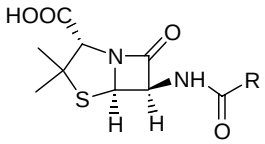


Folsäure (Vitamin) C_1-Stoffwechsel

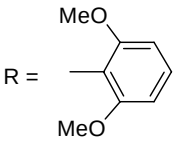


Flavin-adenin-dinucleotid (FAD)
Cofaktor bei Oxidoreduktasen

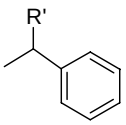
AZETIDINE



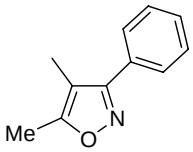
Penicilline (Fleming 1928)



Methicillin

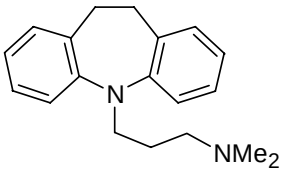


R' = H Penicillin G
R' = NH_2 Ampicillin

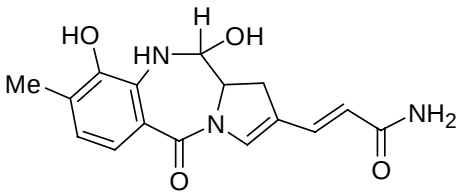


Oxacillin

AZEPINE

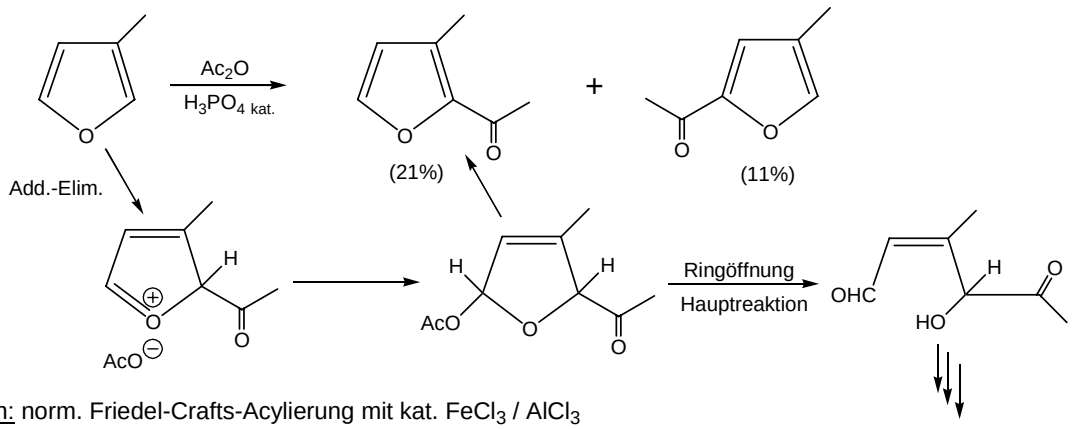


Imipramin
(stimmungsaufhellend)

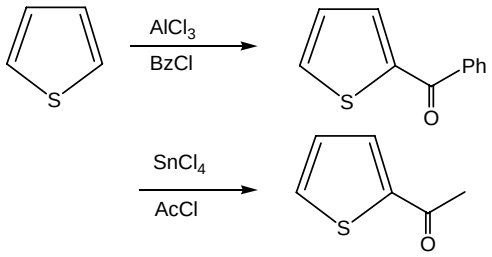


Anthramycin (Streptomyces refuineus)
Antibiotikum (anticarcinogen)

Furan: wenig reaktiv (kat. $H^{\oplus}$ notwendig)



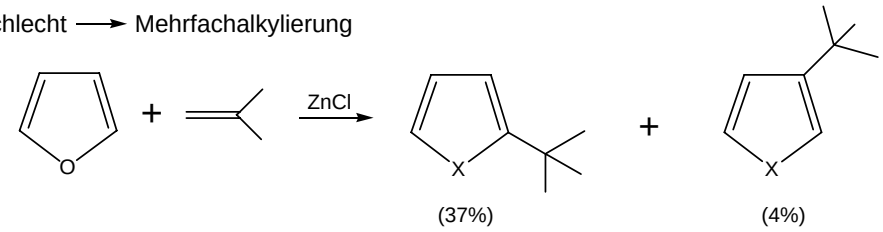
Thiophen: norm. Friedel-Crafts-Acylierung mit kat. $FeCl_3$ / $AlCl_3$



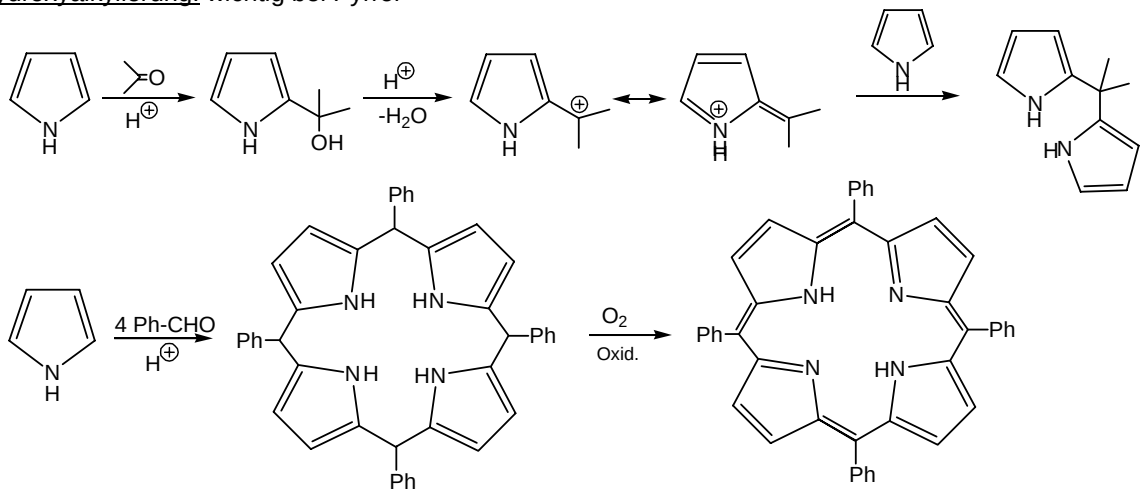
Formylierung: Vilsmeyer normal mit NH, O, S

Alkylierung: schlecht ⟶ Mehrfachalkylierung

aber:

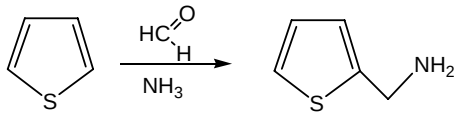


Hydroxyalkylierung: wichtig bei Pyrrol

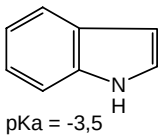


Porphyrene

Mannich-Reaktion: gut bei Thiophen



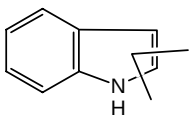
5.2 INDOLE

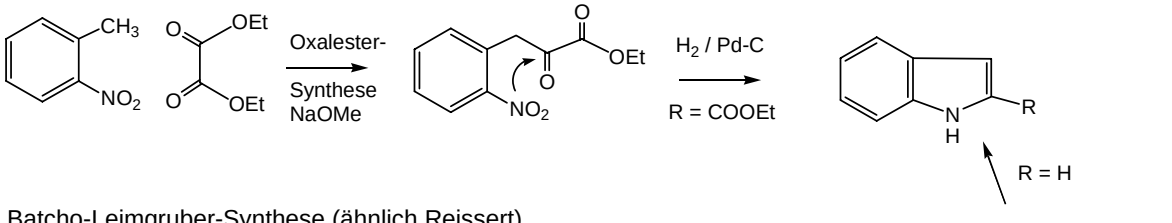


pKa = -3,5
Schmp: 232°C

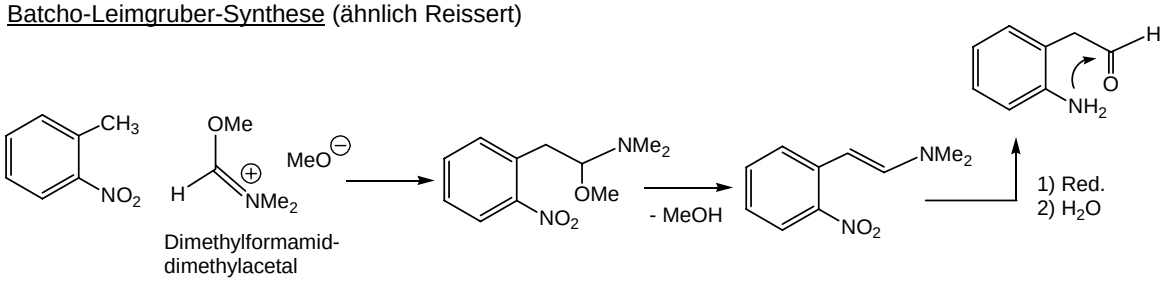
Vorkommen: Steinkohleteer
viele Narturstoffe (Alkaloide)
Aminosäure Tryptophan
Geruch: blumig in verd. Lsg.
fäkalienartig in konz. Lsg.

Reissert-Synthese



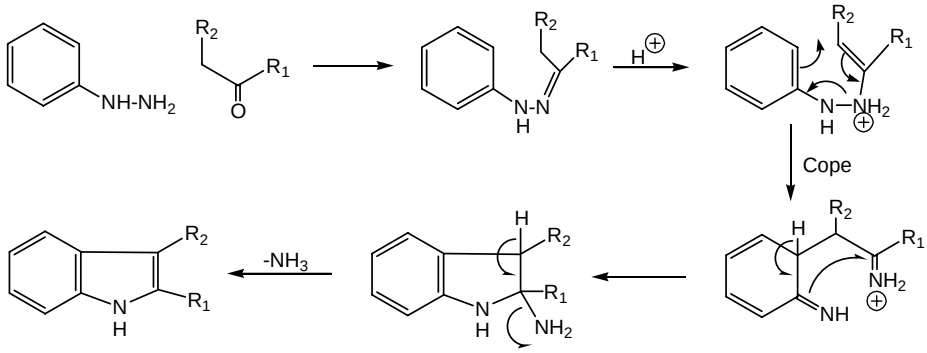


Batcho-Leimgruber-Synthese (ähnlich Reissert)

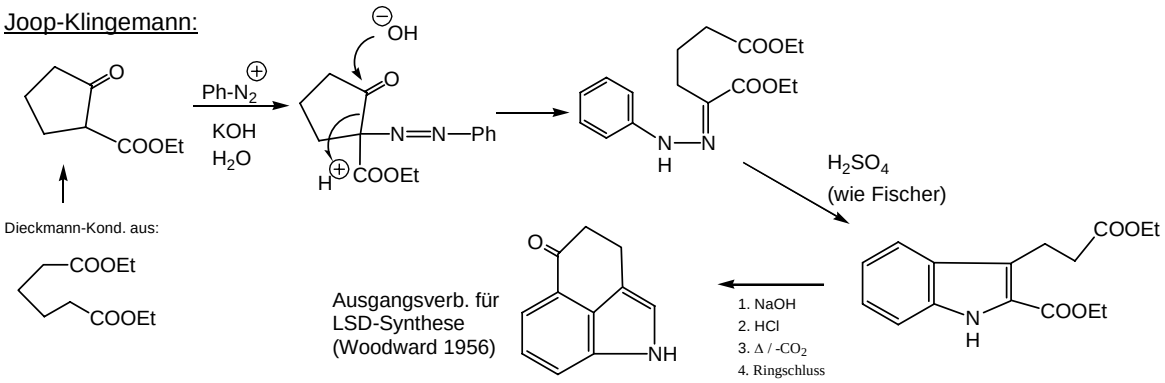


Dimethylformamid-
dimethylacetal

Fischer-Indol-Synthese:

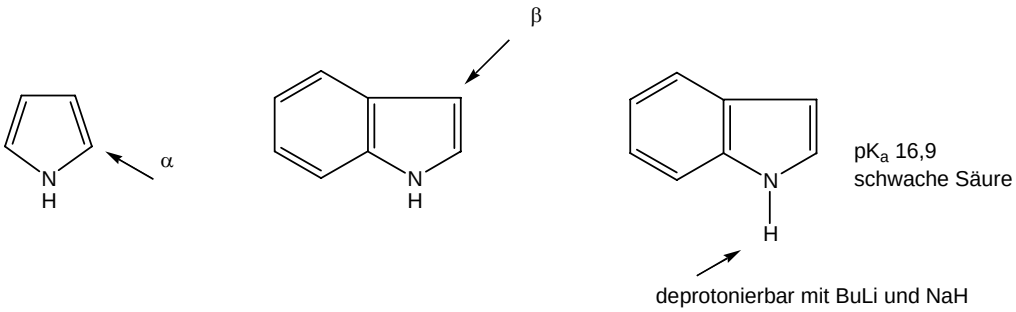


Joop-Klingemann:

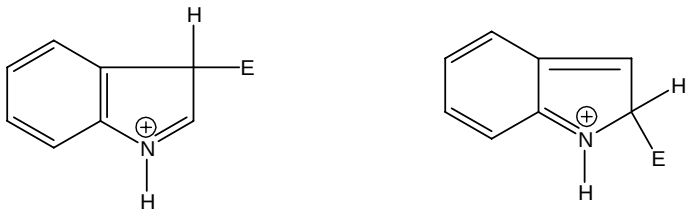


Reaktionen: Vergleichbar mit Pyrrol aber weinger reaktiv.

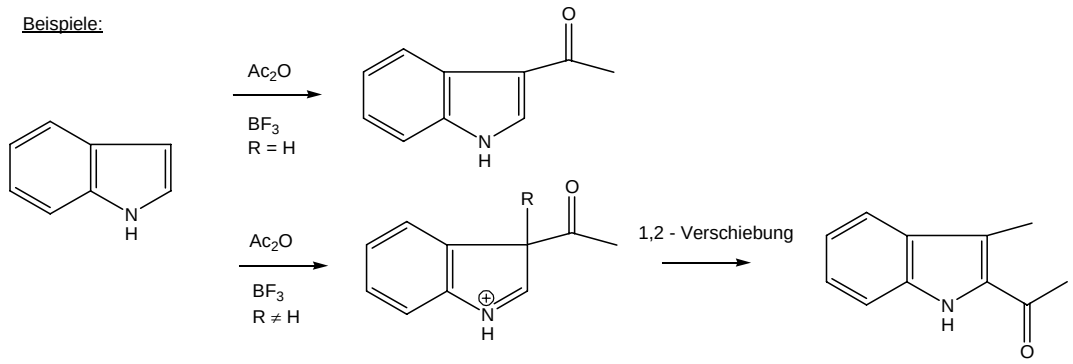
Unterschied:
E^+



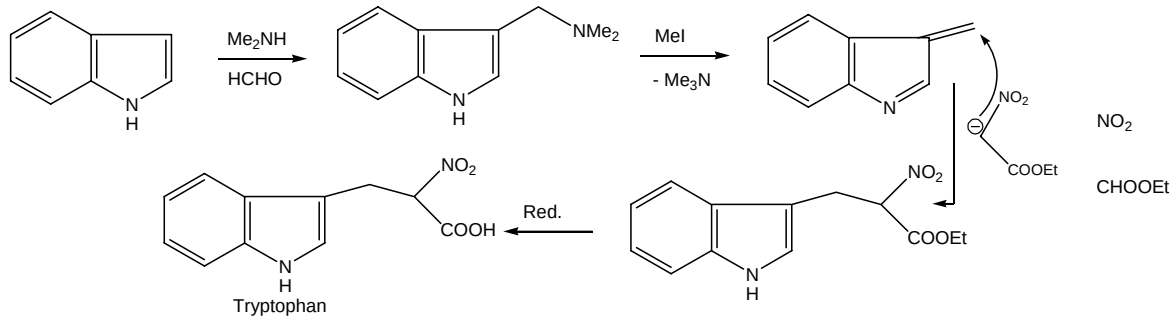
β-Angriff wegen:



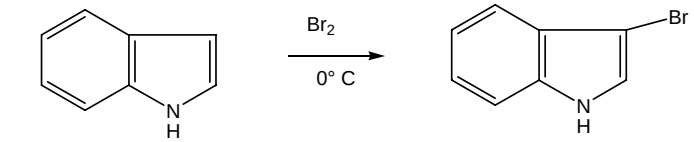
Beispiele:



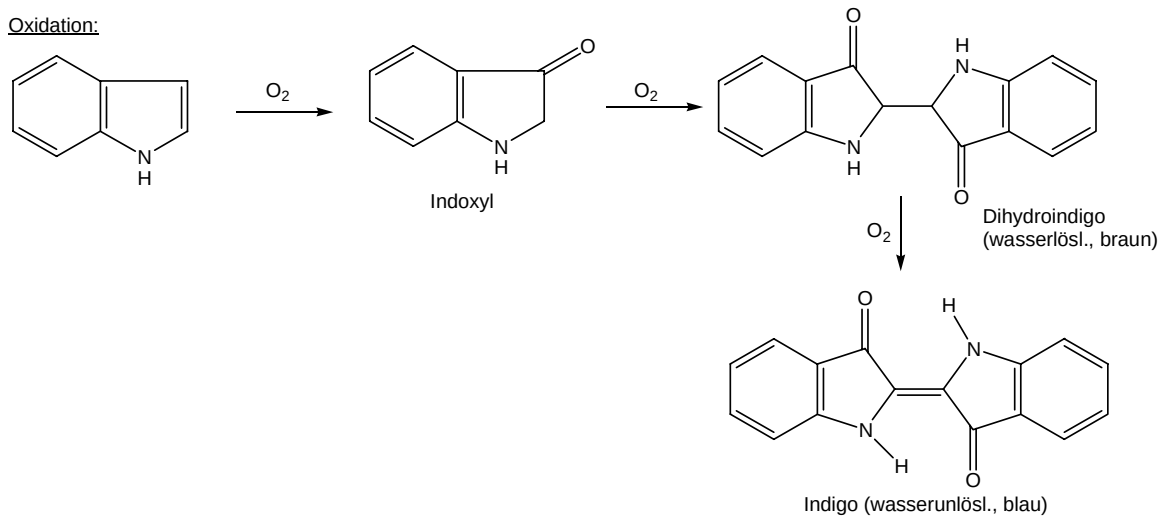
weitere Reaktion:
Mannich



Halogenierung:

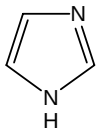


Oxidation:

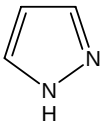


5.3 Fünf-Ringe mit zwei und mehr Hetroatomen

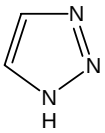
zusätzliche Srtickstoffatome mit freien Elektronenpaaren in der Ringebene erhöhen die Basizität (pyridinartig). Aufgrund der stark negativen Ladung wird der elektrophile Angriff schwieriger.



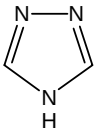
Imidazol
pk_a 14,5



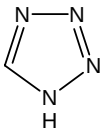
Pyrazol
pk_a 13,5



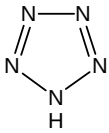
1,2,3-Triazol
pk_a 9,4



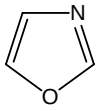
1,2,4-Triazol
-



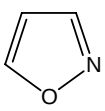
Tetrazol



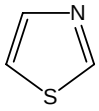
Pentazol
explosiv bei -30°C



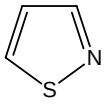
Oxazol
pk_a 13,2



Isoxazol



Thiazol



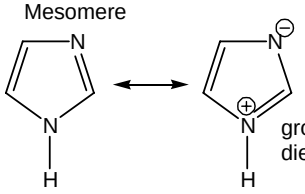
Isothiazol

Chemische Eigenschaften:

meist sehr stabil gegen Säuren

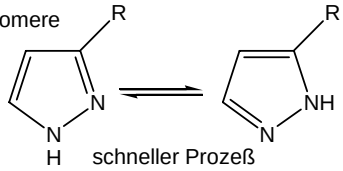
schlechte Reaktivität mit E^+

Mesomere



großer Anteil dieser Form

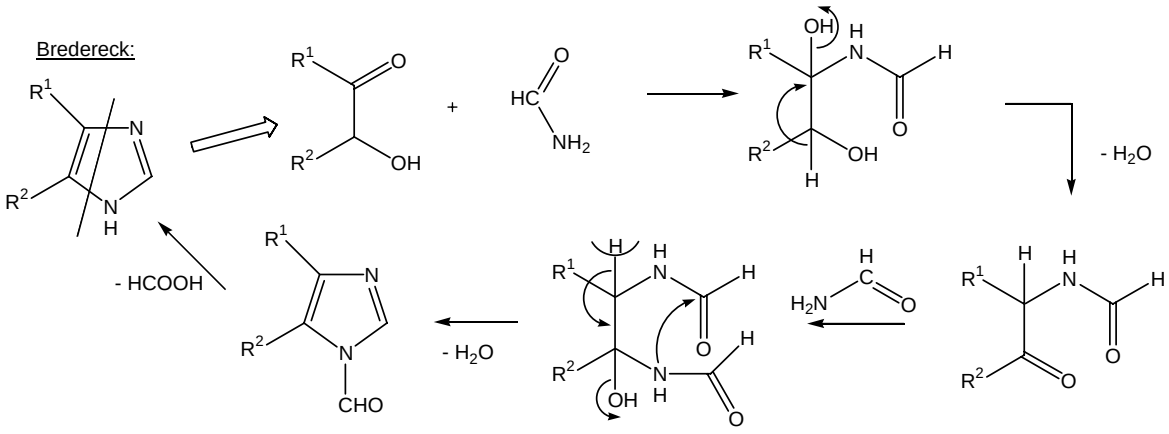
Tatomere



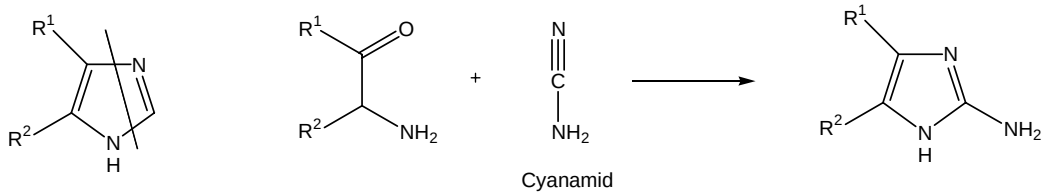
schneller Prozeß

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

Bredereck:

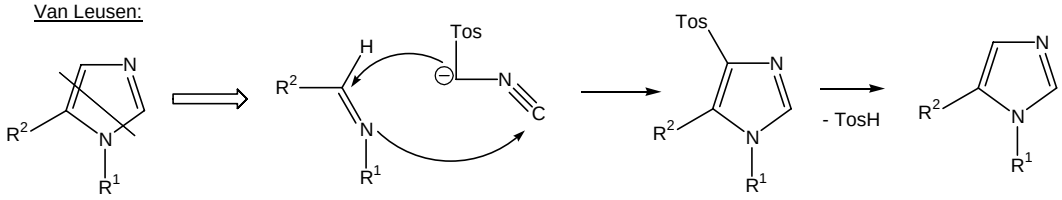


Markwald:

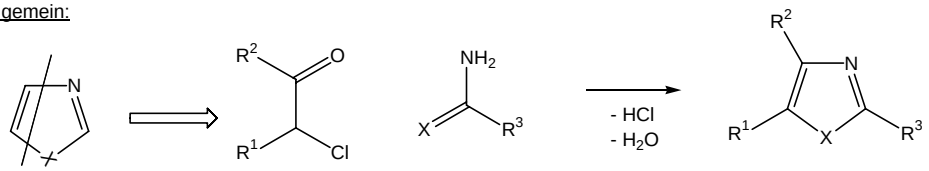


Cyanamid

Van Leusen:



Allgemein:



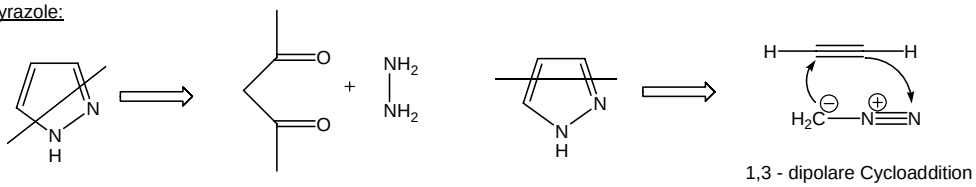
X = O Robinson-Gabriel-Synthese

X = S Hantzsche-Synthese

X = NH Amidine
O Säureamide
S Thioamide

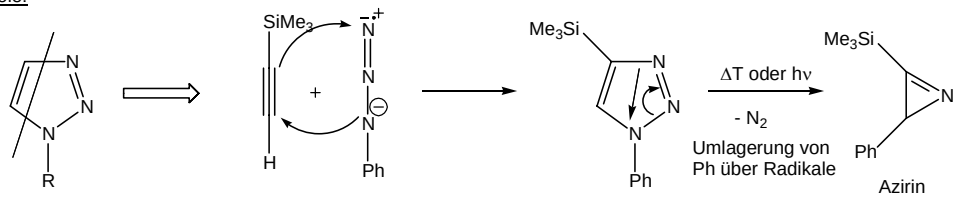
R = Alkyl, Phenyl, NH_2, OH, SH

Pyrazole:



1,3 - dipolare Cycloaddition

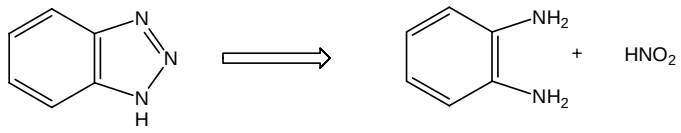
Triazole:



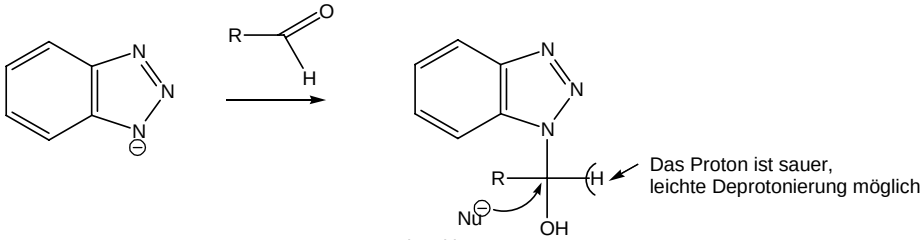
Azid

1,3 - dipolare Cycloaddition

Benzotriazol: Katritzky (wichtig!)

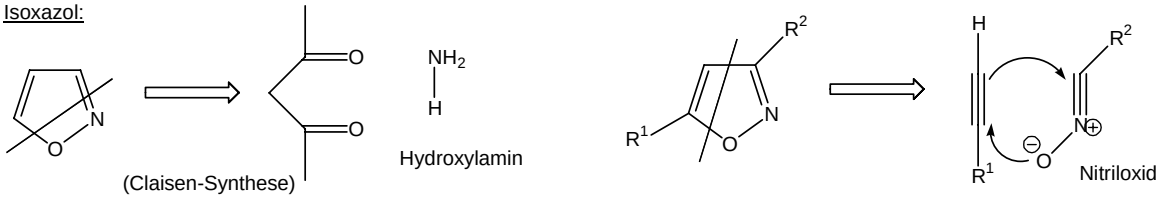


pK_a < 0 daher leichte Deprotonierung



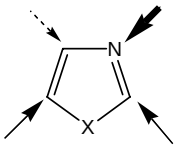
Benzotriazol ist
eine sehr gute Austrittsgruppe,
wie auch CN^- oder $PhSO_2^-$
Anwendung bei S_N

Isoxazol:

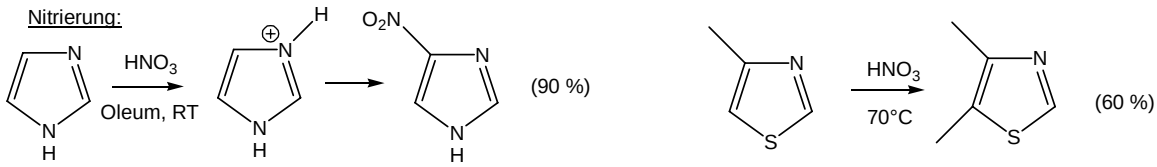


Reaktionen:

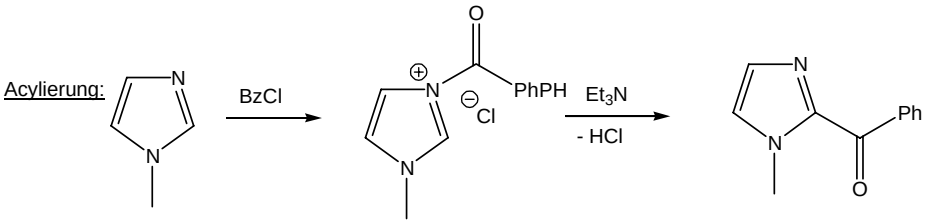
Stark desaktiviert für E^+



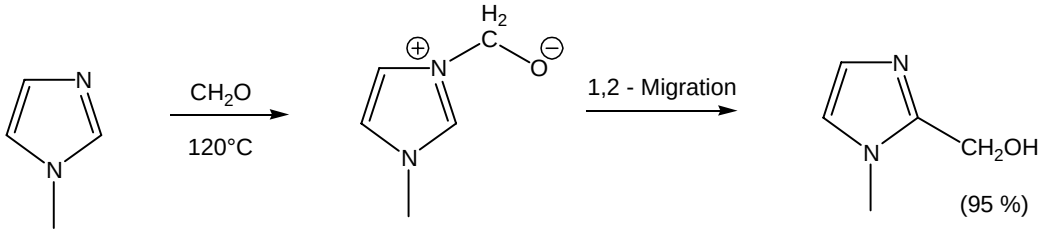
Nitrierung:



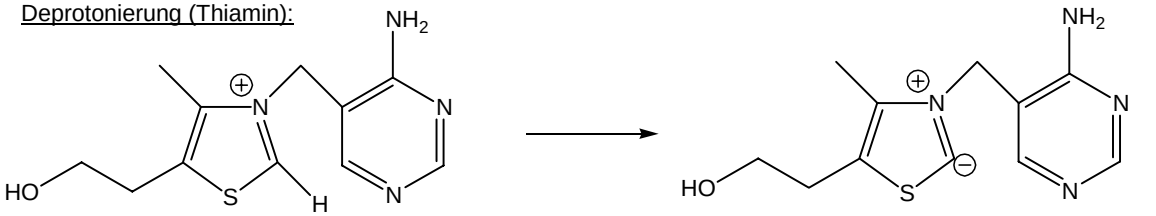
Acylierung:



Hydroxymethylierung:

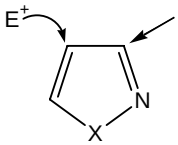


Deprotonierung (Thiamin):



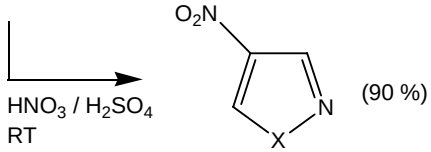
Thiamin

Reagiert als Anion mit Aldehyden

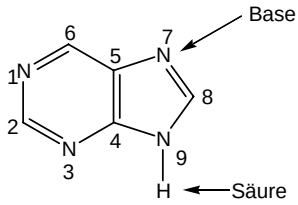


wie Pyridin a-Position

etwas reaktiver als 1,3-Azole



5.4 Purine

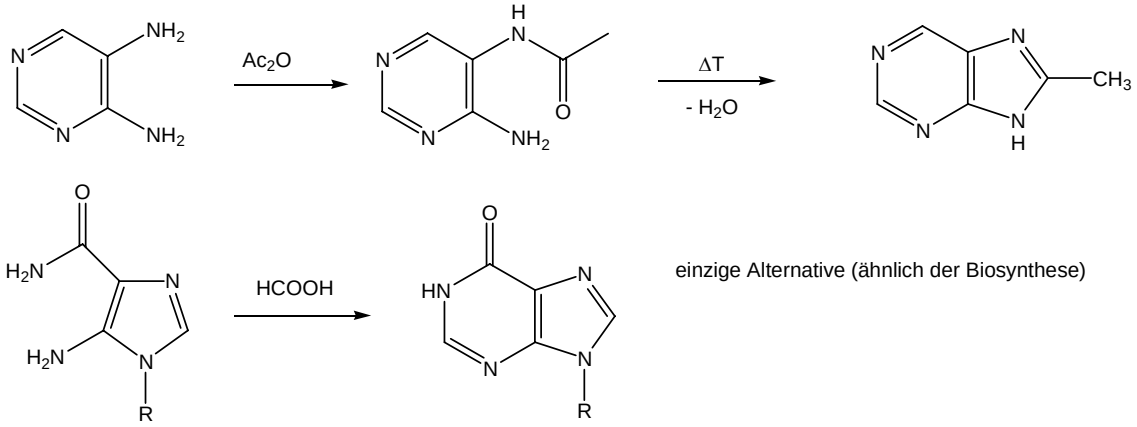


Smp.: 216 °C

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)



einzige Alternative (ähnlich der Biosynthese)

Harnsäure (Traube):