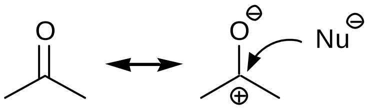
6. Gruppe: Carbonylverbindungen

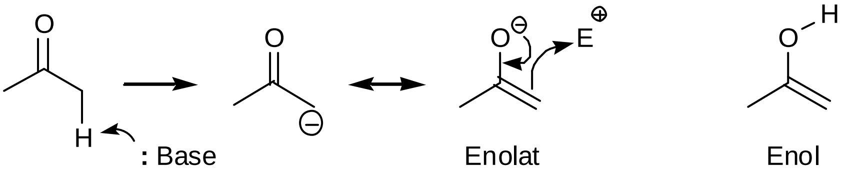
1) Darstellung von Aldehyden und Ketonen

1.1. Reaktivität der Carbonylgruppe:

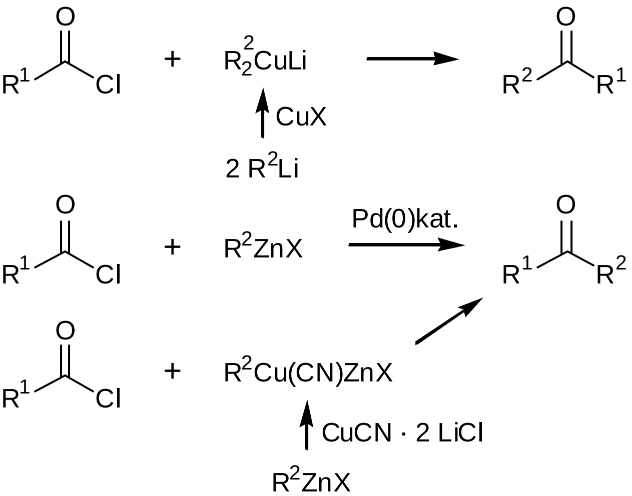


C=C : 146 kcal/mol

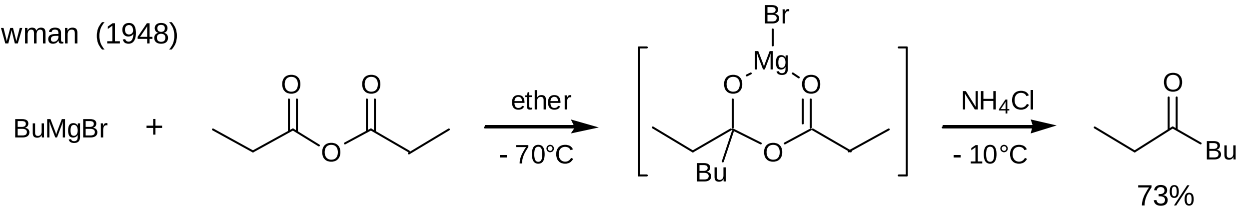
C=O : 175 kcal/mol



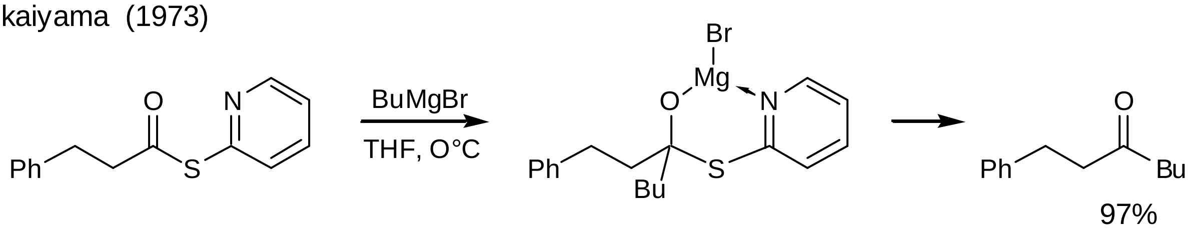
1.2. Metallorganische Synthese

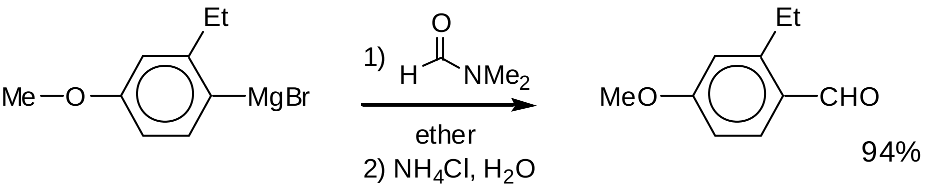


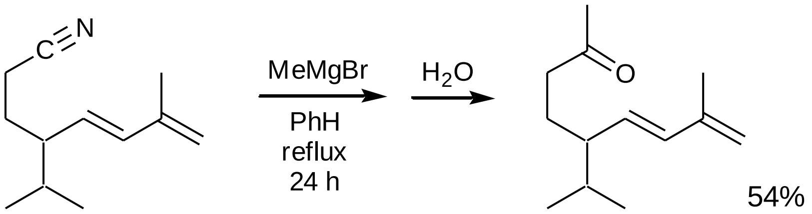
Newman (1948)

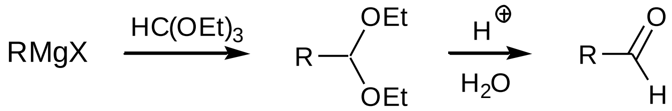


Mukaiyama (1973)



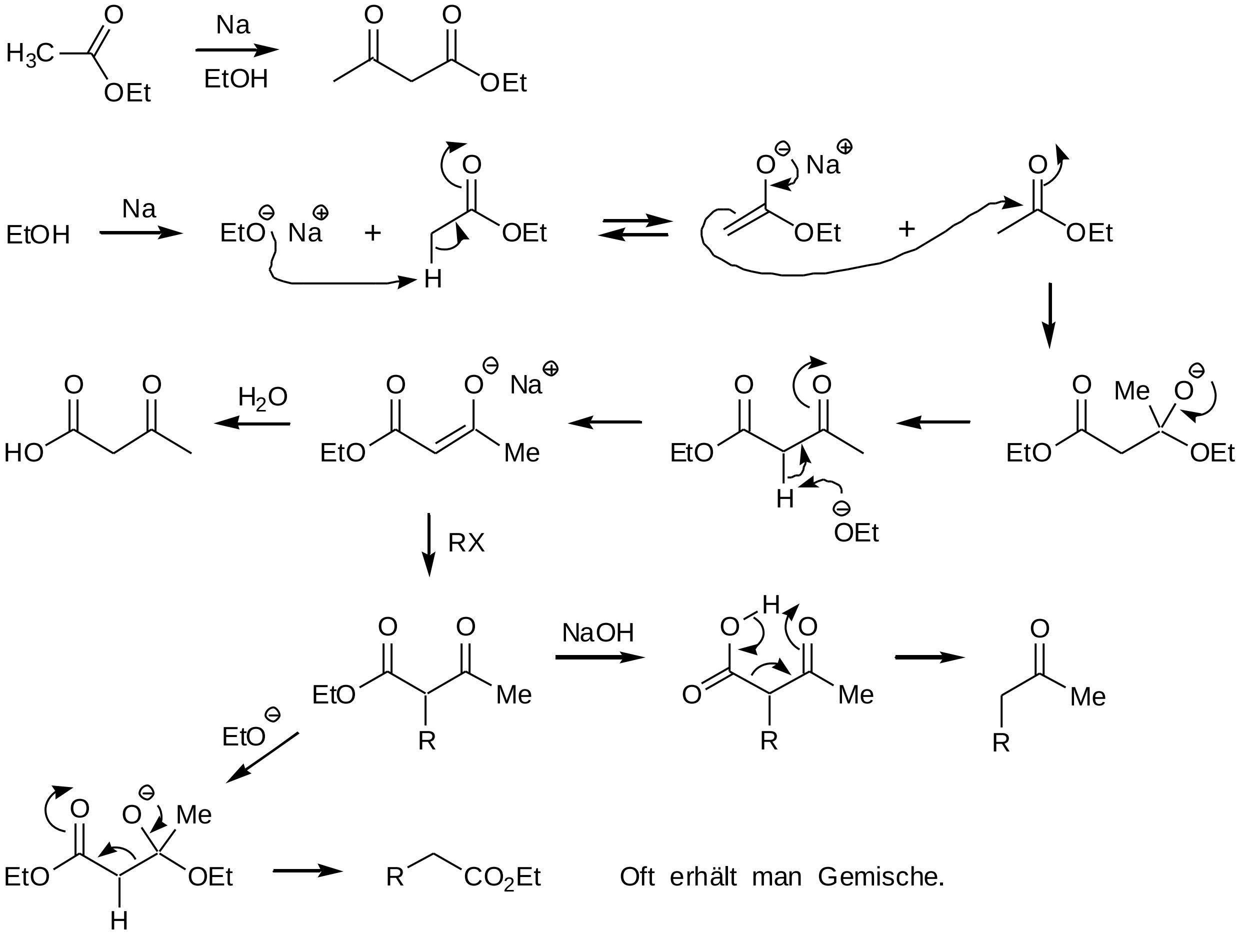






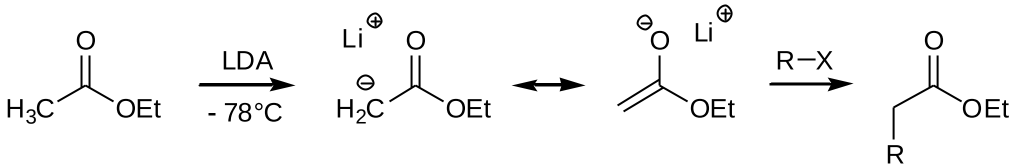
1.3. Enolat-Chemie

Claisen-Kondensation



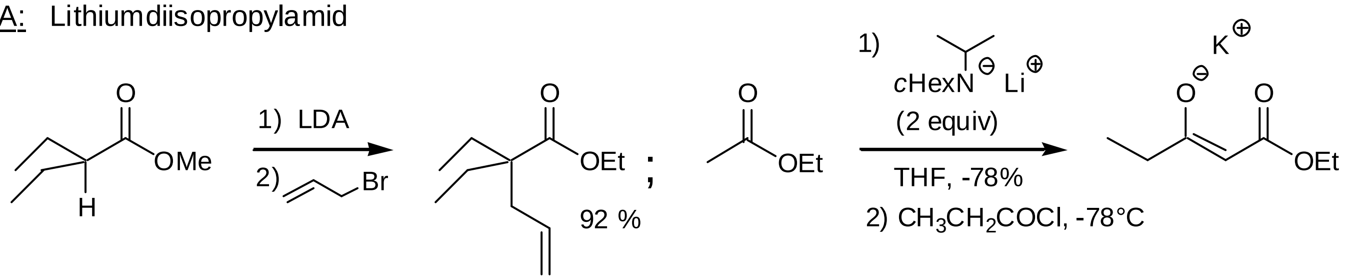
Oft erhält man Gemische.

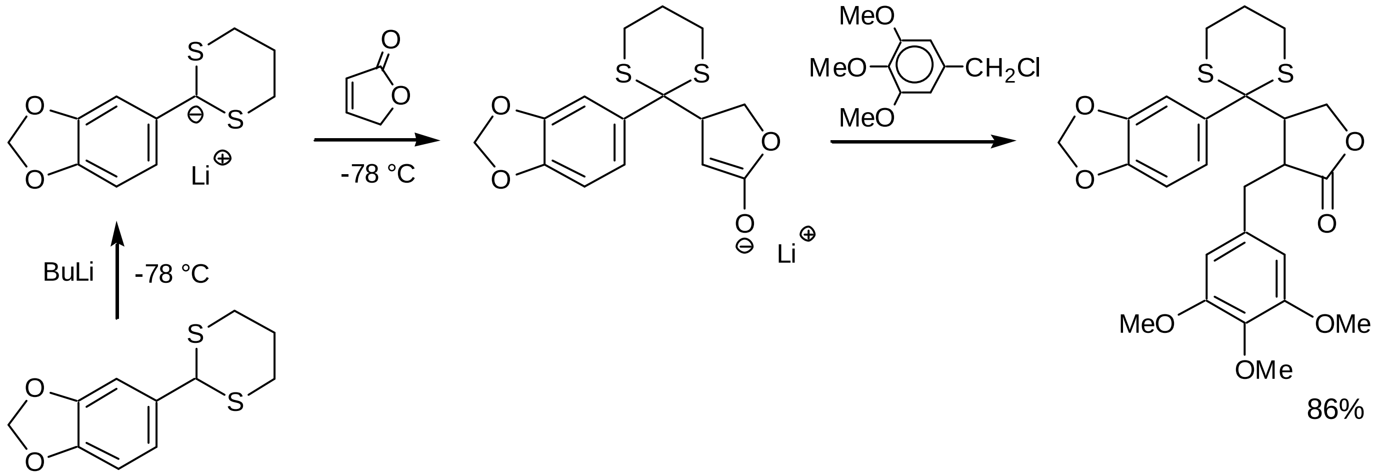
<u>Moderne Methode:</u> Stöchiometische Bildung des Lithium-Enolats



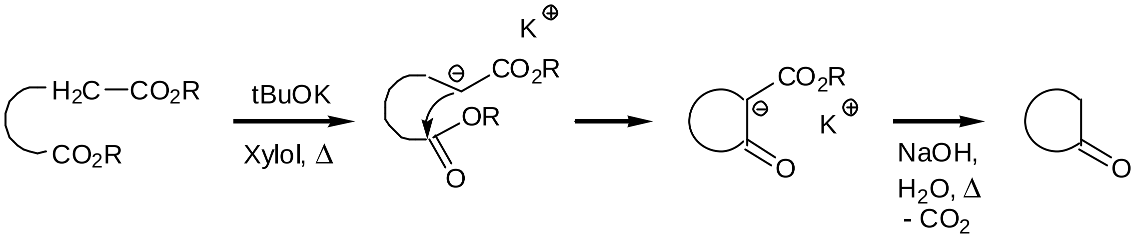
6. Gruppe: Carbonylverbindungen

LDA: Lithiumdiisopropylamid

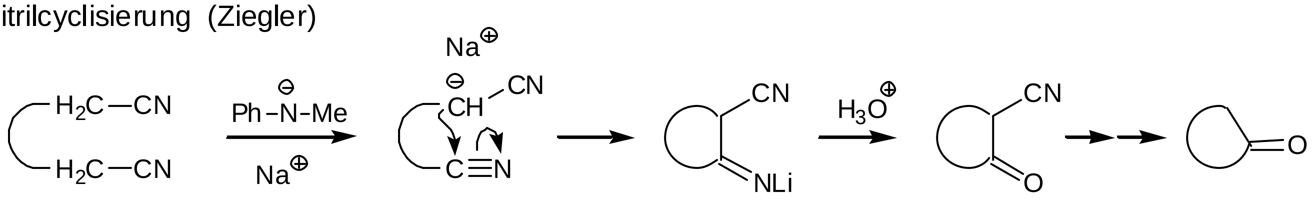




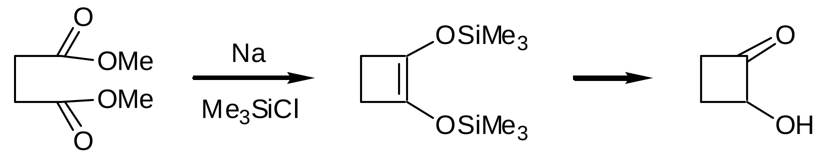
Intramoleculare Dieckmann-Kondensation



Dinitrilcyclisierung (Ziegler)

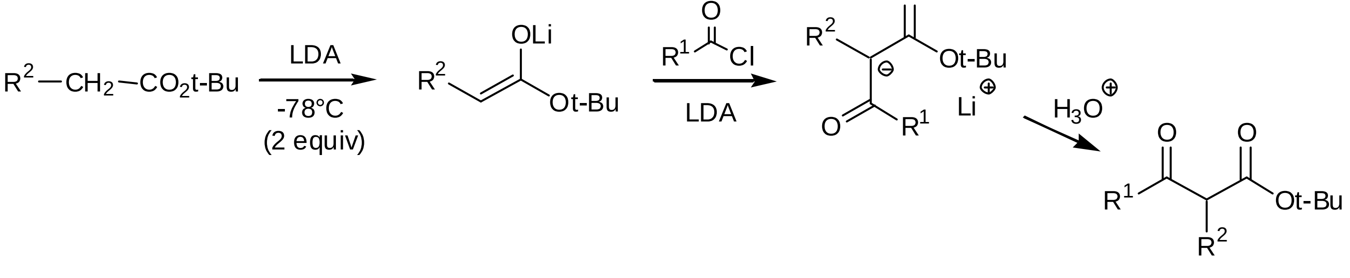


Acyloinkondensation



Ausbeute: 9- bzw. 10-Ringe: 30-42%; größere Ringe: > 90%

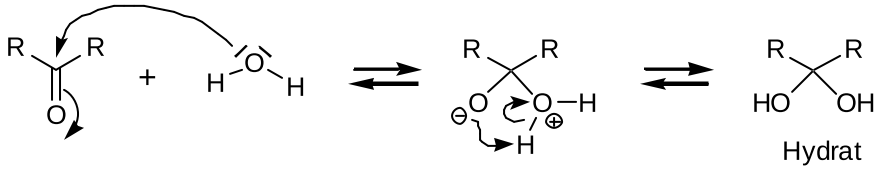
gekreuzte Esterkondensation

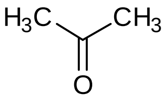


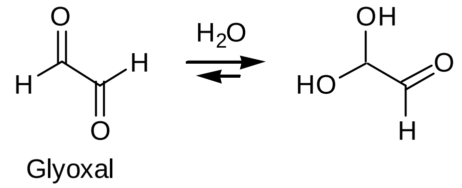
2) Reaktionen der Carbonylverbindungen

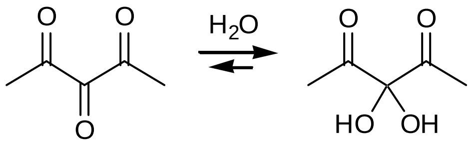
2.1. Addition nucleophiler Verbindungen

2.1.1. Addition von Wasser

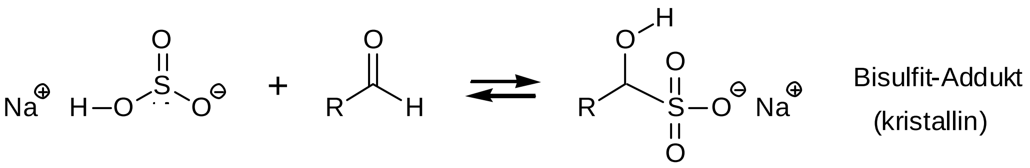


Verbindung	% Hydrat in H_2O
$H_2C{=}O$	> 98
CH_3CHO	64
CCl_3CHO	100
	0.1

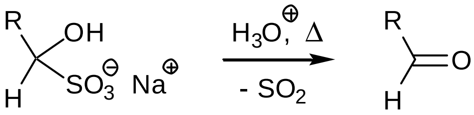




2.1.2. Addition von $NaHSO_3$ (Hydrogensulfit)

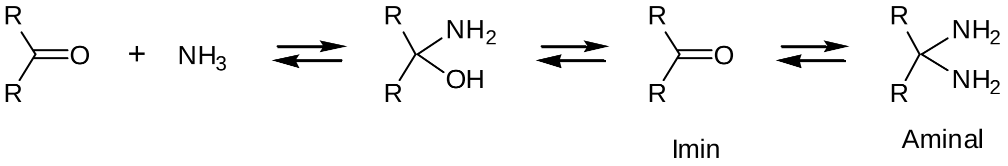


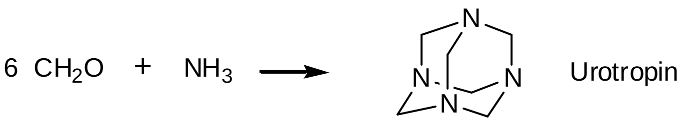
Spaltung des Adduktes durch $H_3O^{\oplus}$

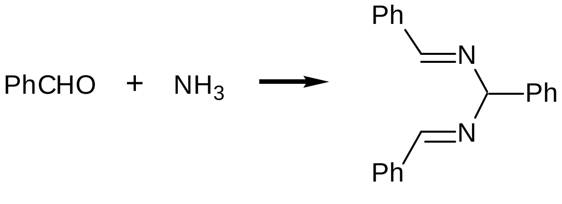


2.1.3. Addition von Aminen

$\underline{NH_3}$

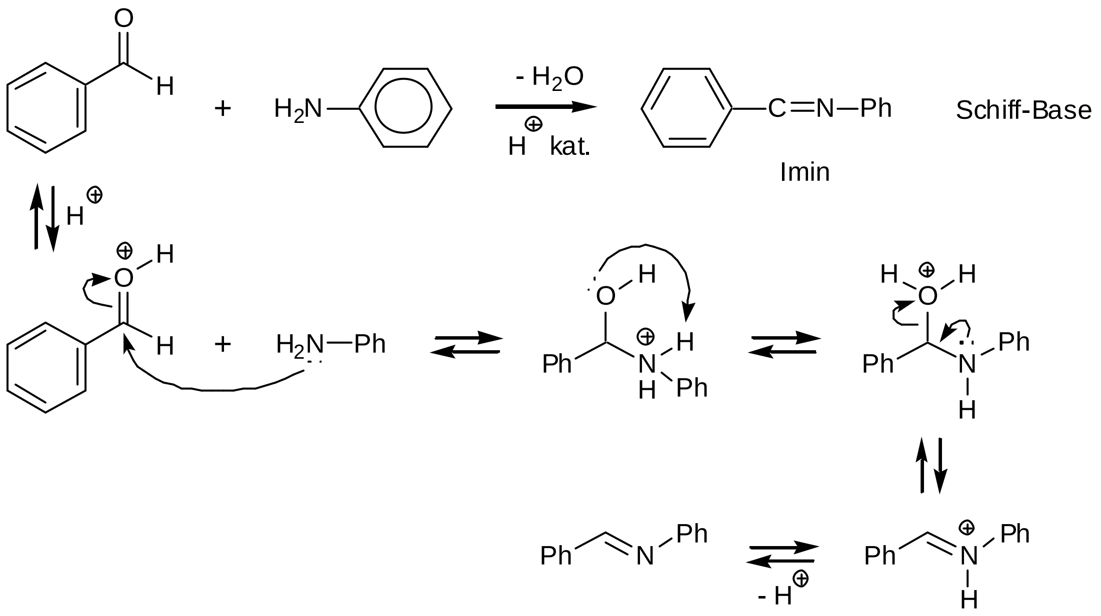




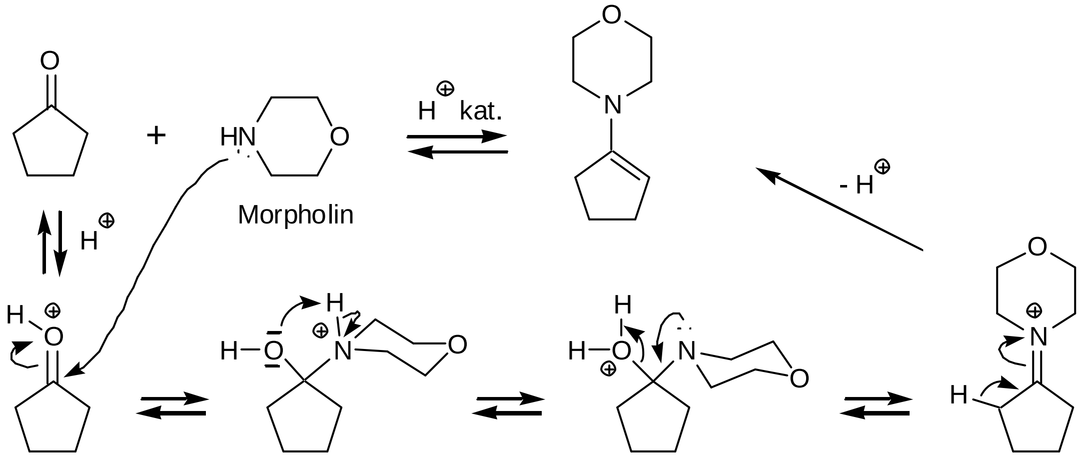


6. Gruppe: Carbonylverbindungen

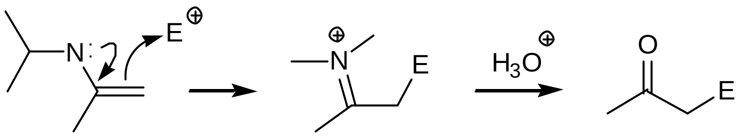
Primäre Amine

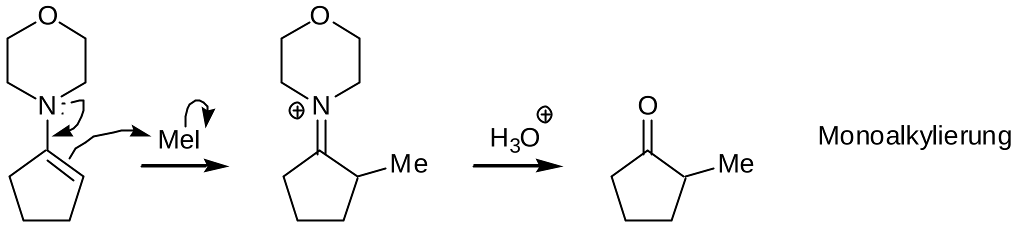


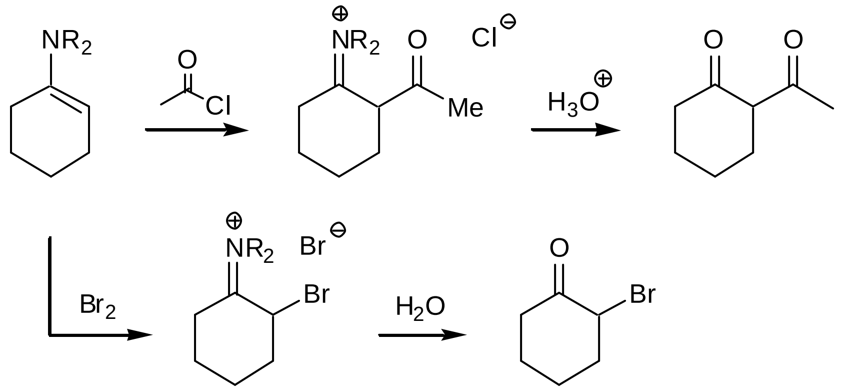
Sekundäre Amine



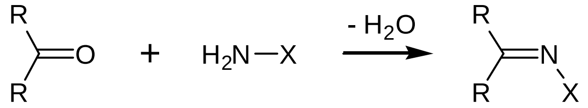
Reaktivität von Enaminen







Hydroxylamin- und Hydrazin-Addition



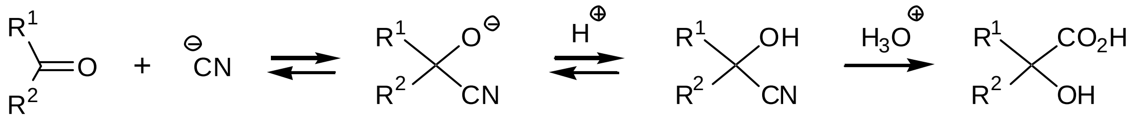
X = OH : Oxim

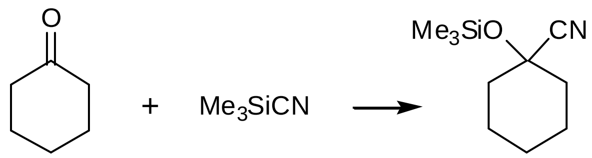
X = NHR^1 : Hydrazon

X = NH-CONH$_2$: Semicarbazon

2.1.4. Addition von HCN

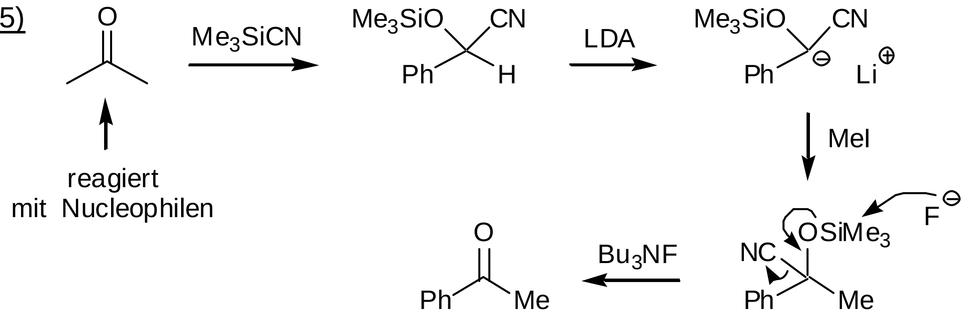
$$HCN + Base \longrightarrow {}^{\ominus}CN + \overset{\oplus}{B}H$$



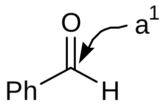


Umpolung der Reaktivität

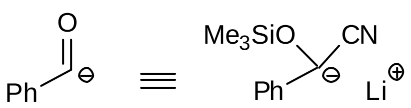
Hünig (1975)



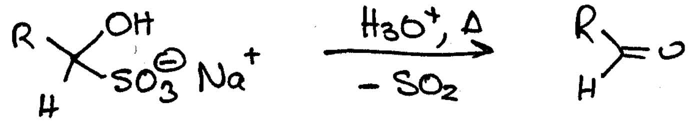
Normale Reaktivität :



Umpolung :

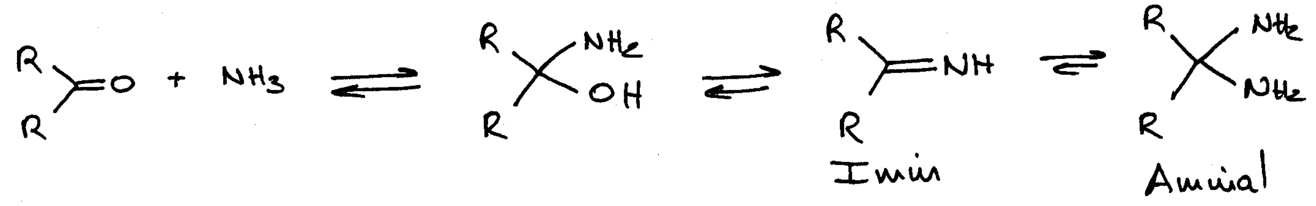


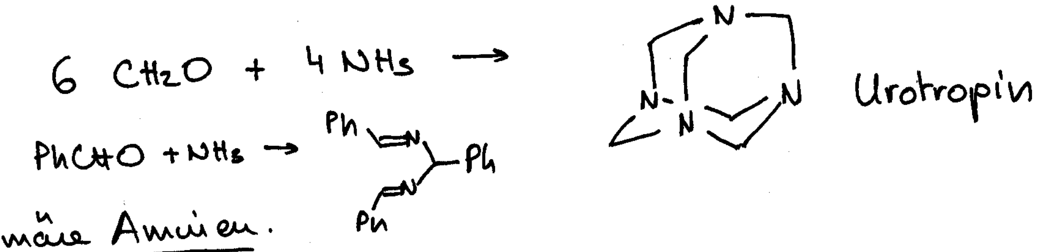
Spaltung der Addukt mit H_3O^+



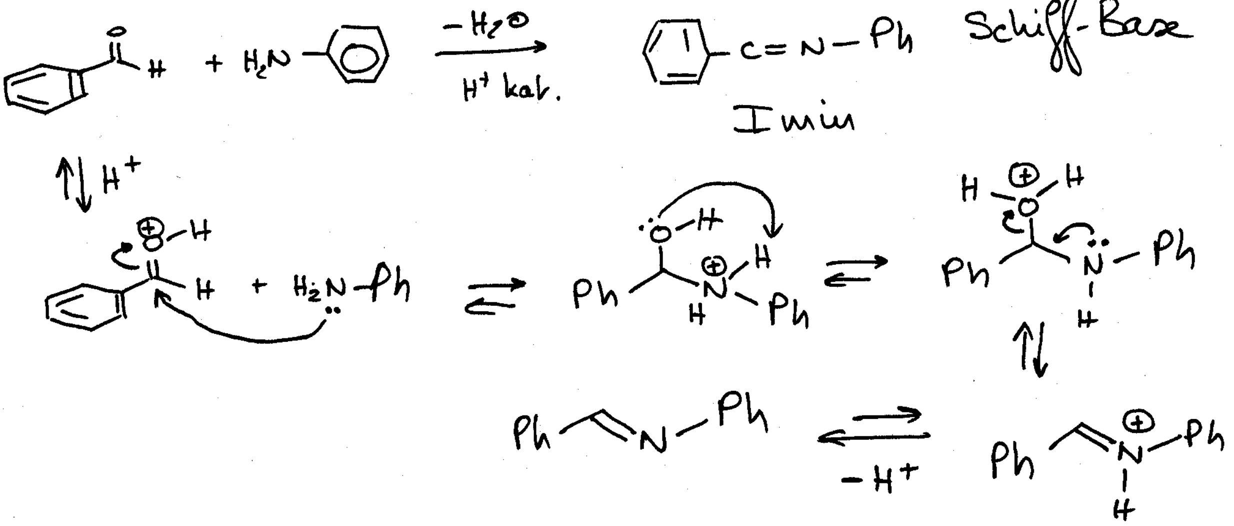
2.1.3. Addition von Aminen

NH_3

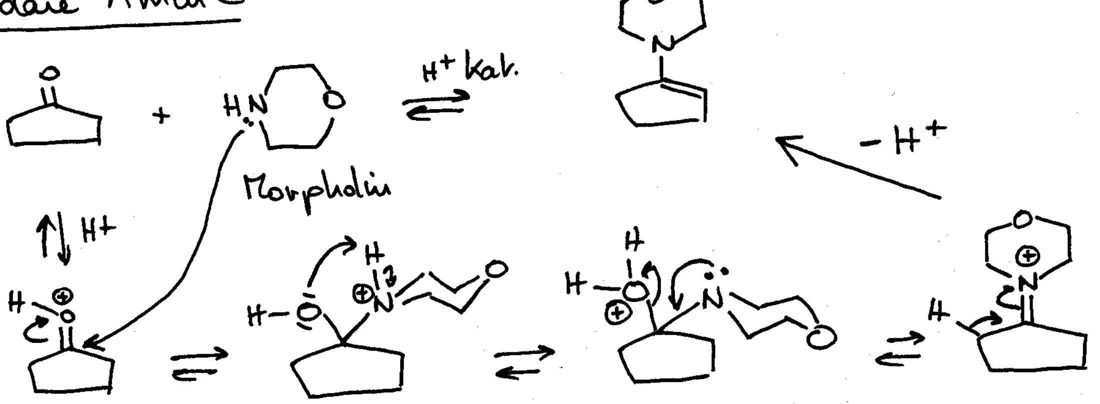




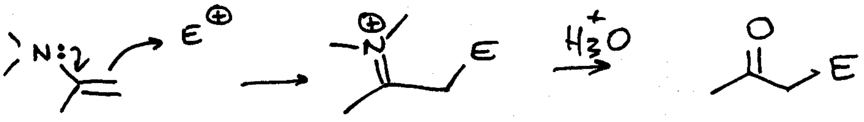
Primäre Aminen.

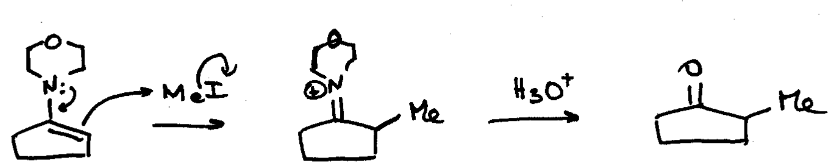


Sekundäre Amine

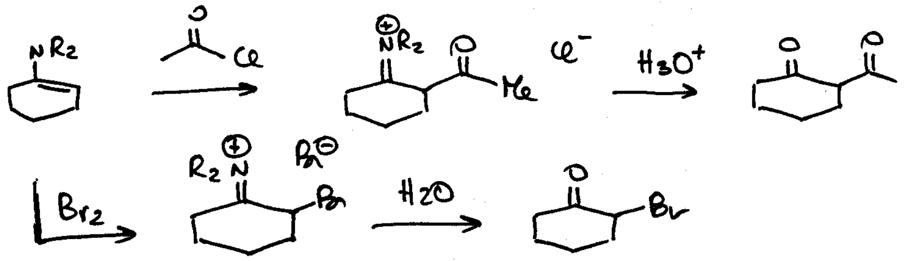


Reaktivität von Enamine



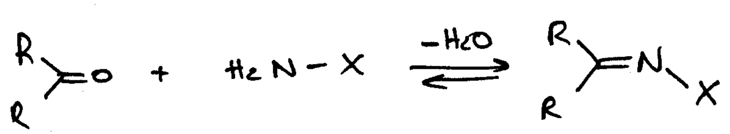


Monoalkylierung



Monoacetylierung

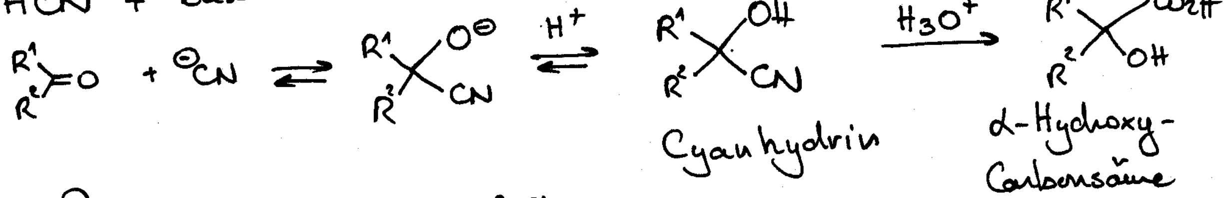
Hydroxylamin und Hydrazin Addition

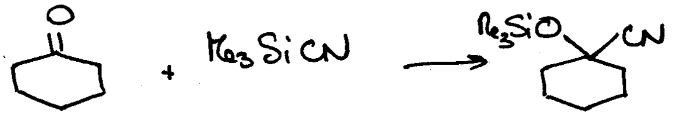


X	
OH	Oxim
NHR'	Hydrazon
$NH-\overset{O}{\overset{\|}{C}}-NH_2$	Semicarbazon

2.1.4. Addition von HCN

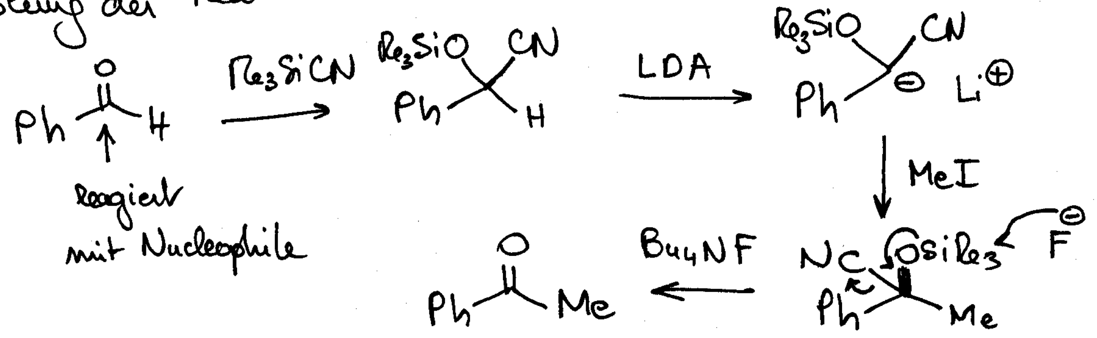
$HCN + Base \longrightarrow {}^{\ominus}CN + \overset{\oplus}{B}H$



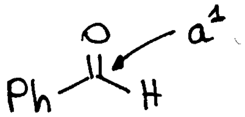


Umpolung der Reaktivität

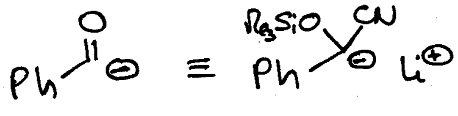
Hünig (1975)



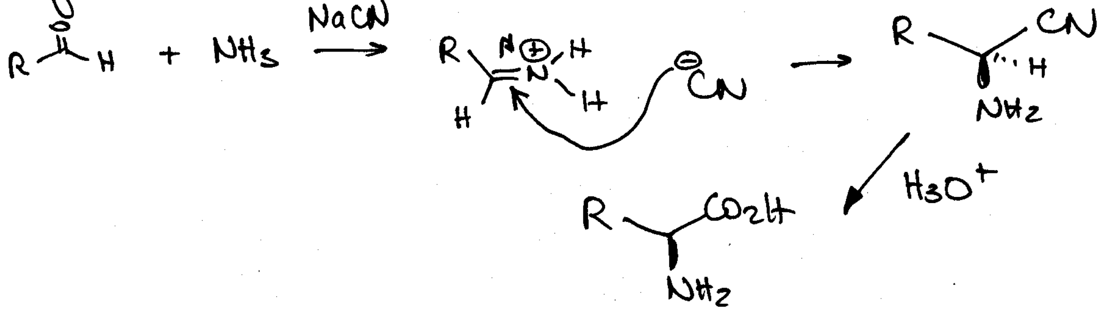
Normale Reaktivität :



Umpolung :

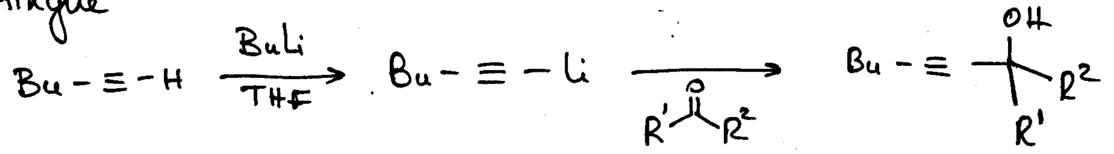


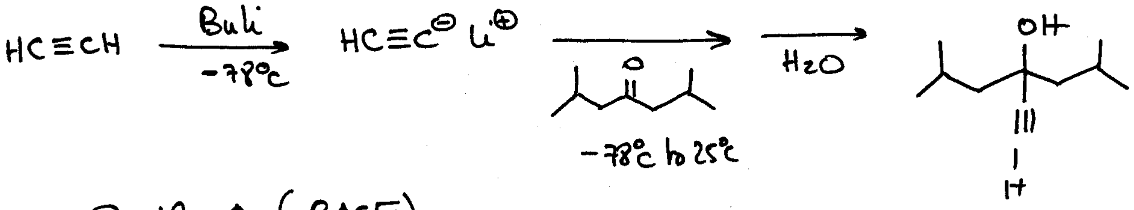
Strecker-Synthese von α-Aminosäuren



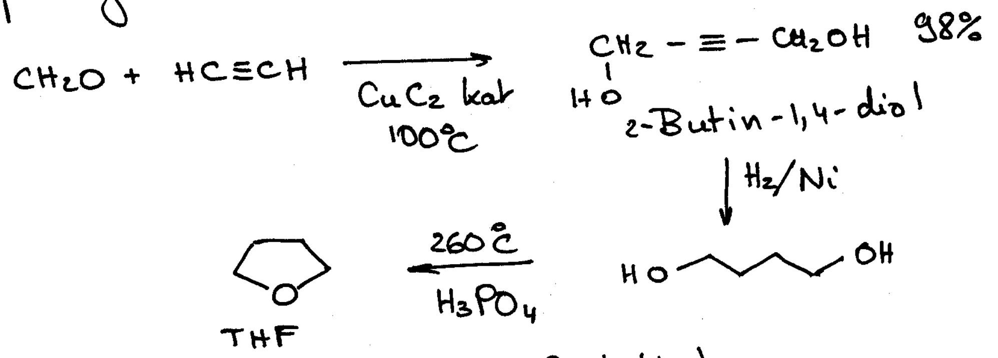
2.1.5. Addition von metallorganische Reagenzien

Alkyne

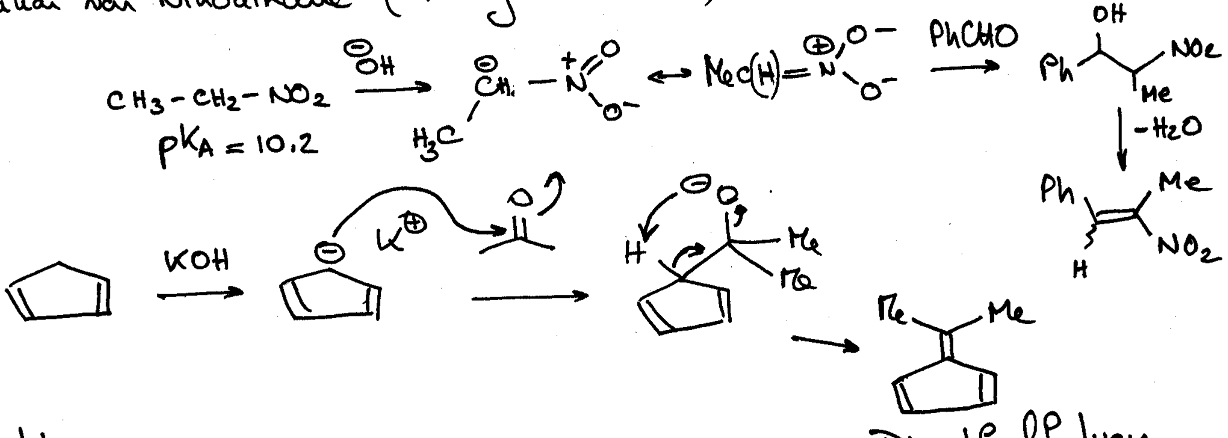




Reppe-Synthese (BASF)

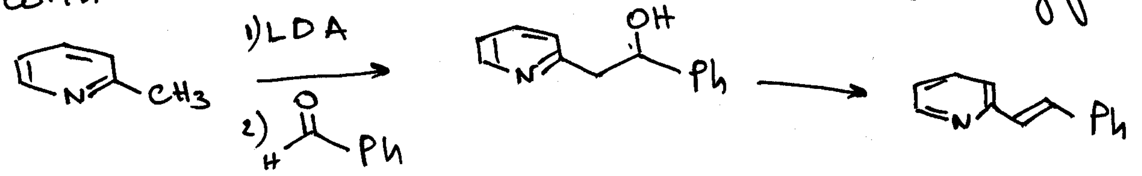


Addition von Nitroalkane (Henry-Reaktion)

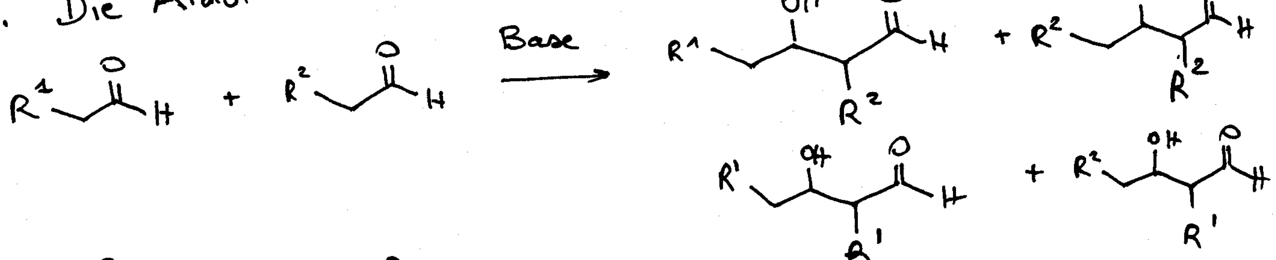


Dimethylfulven

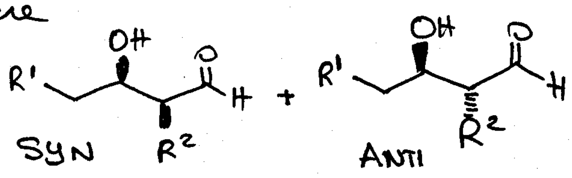
Picolin

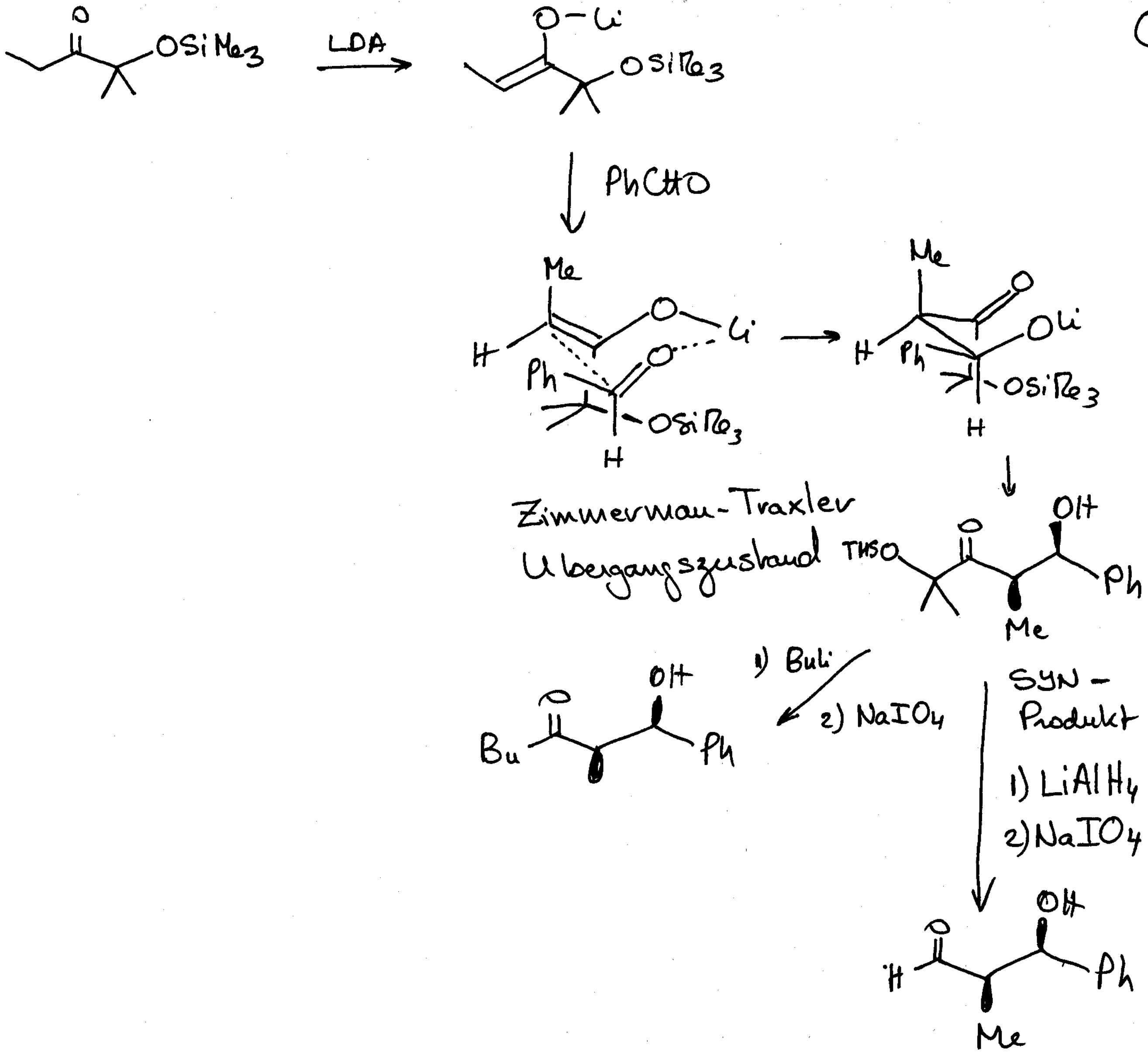


2.2. Die Aldol-Reaktion

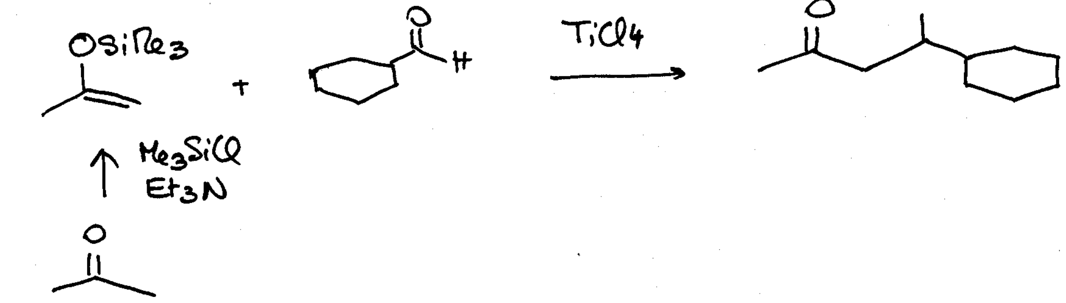


Gemische von Regioisomere und Stereoisomere

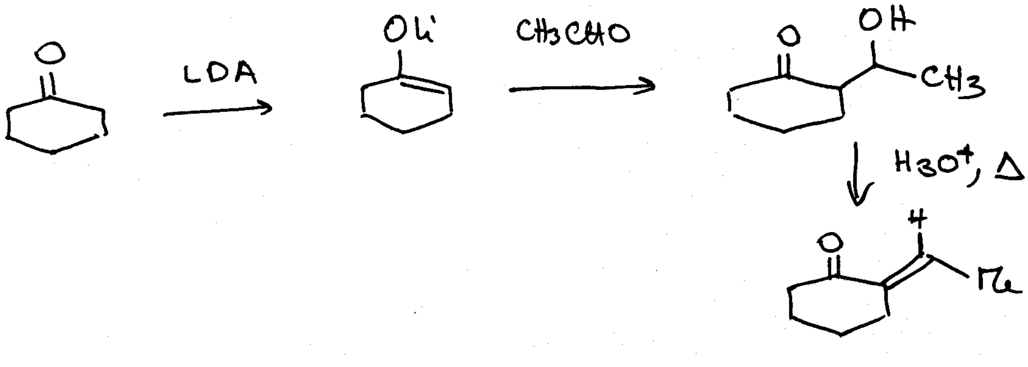




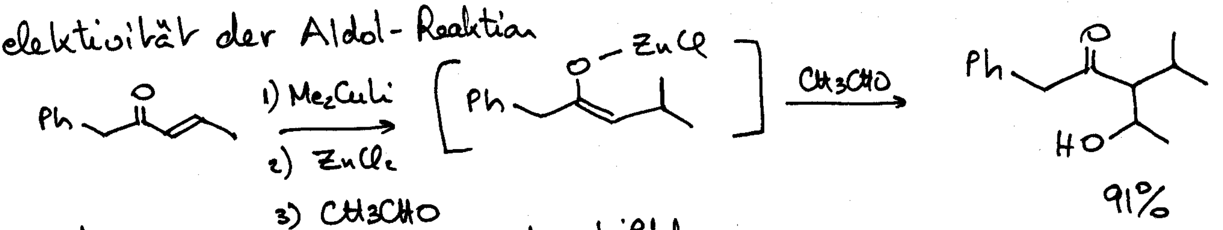
Mukaiyama - Methode



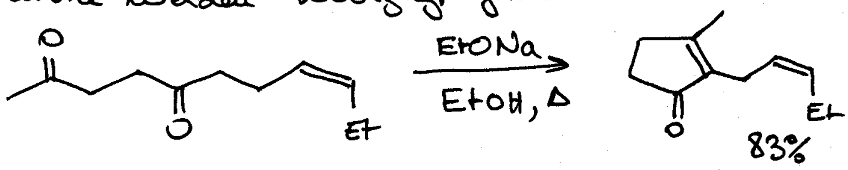
Aldol - Kondensation

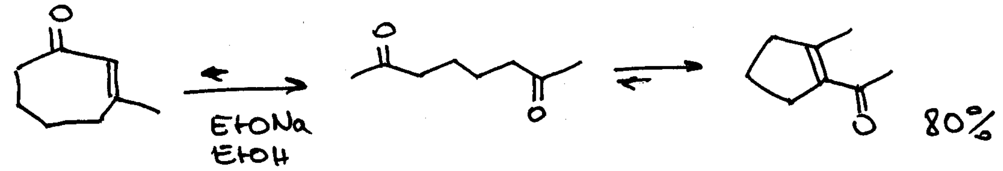


Selektivität der Aldol-Reaktion

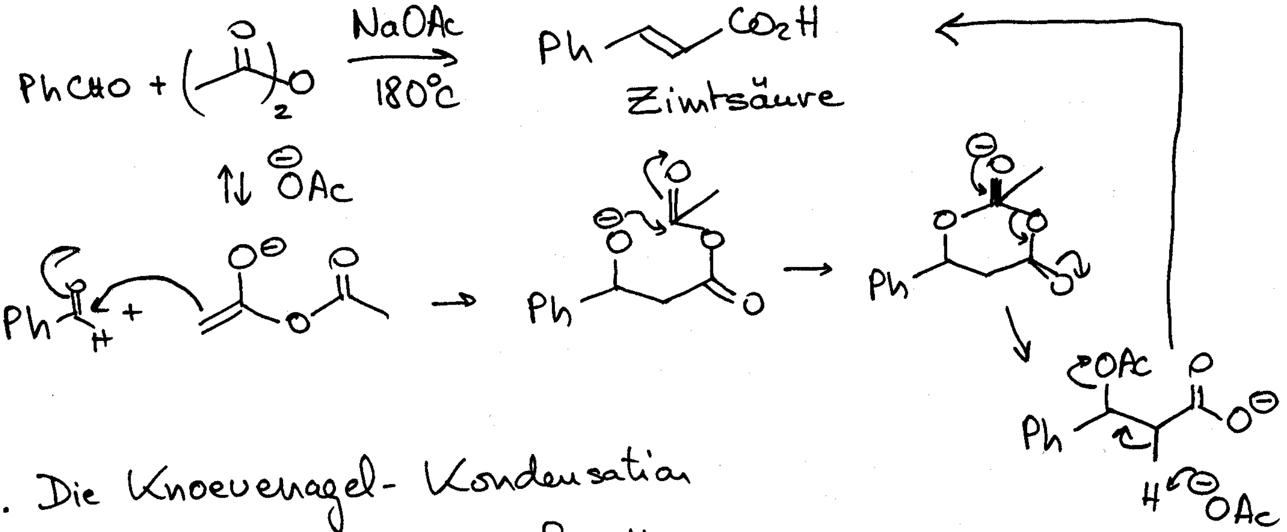


Cyclopentanone werden bevorzugt gebildet

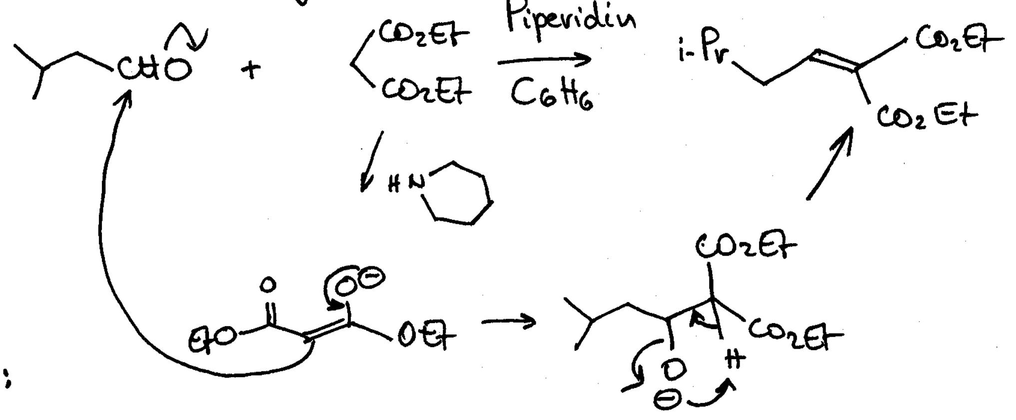




2.3. Die Perkin-Reaktion

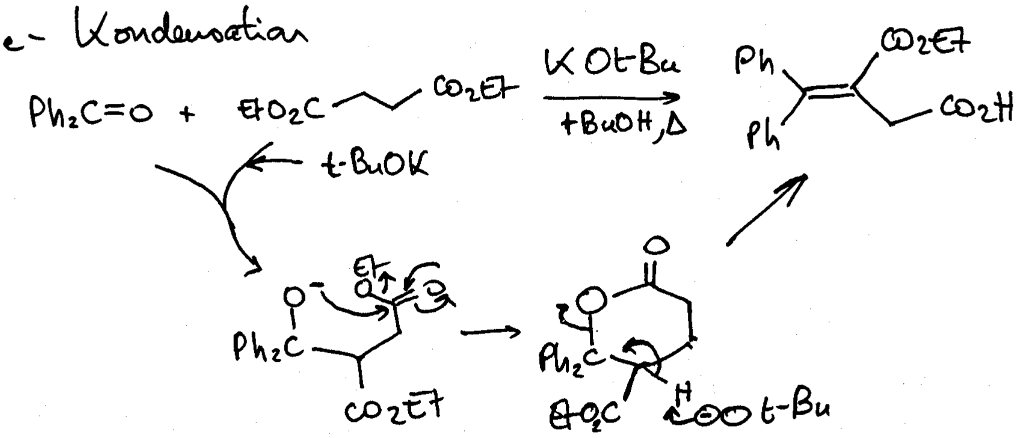


2.4. Die Knoevenagel-Kondensation

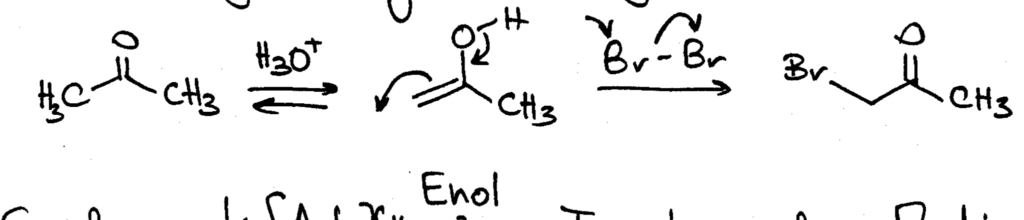


Analog:

die Stobbe-Kondensation

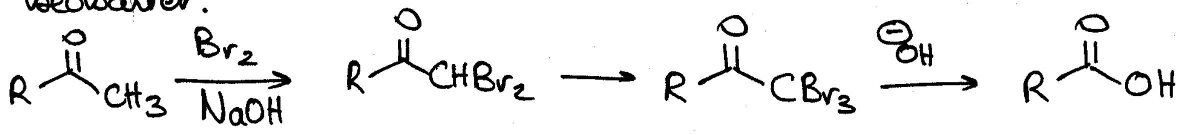


2.5. α-Halogenierung von Aldehyden und Ketonen



Monohalogenierung

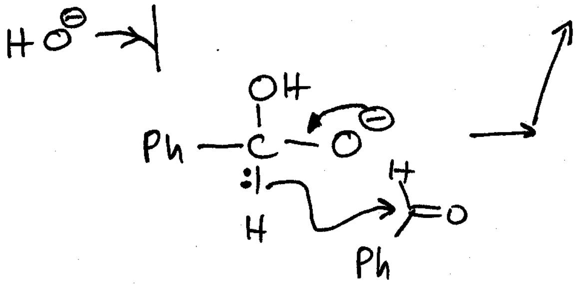
Geschw. = $k\,[\text{Aceton}][H_3O^+]$. Im basischen Medium wird eine Polybromierung beobachtet.



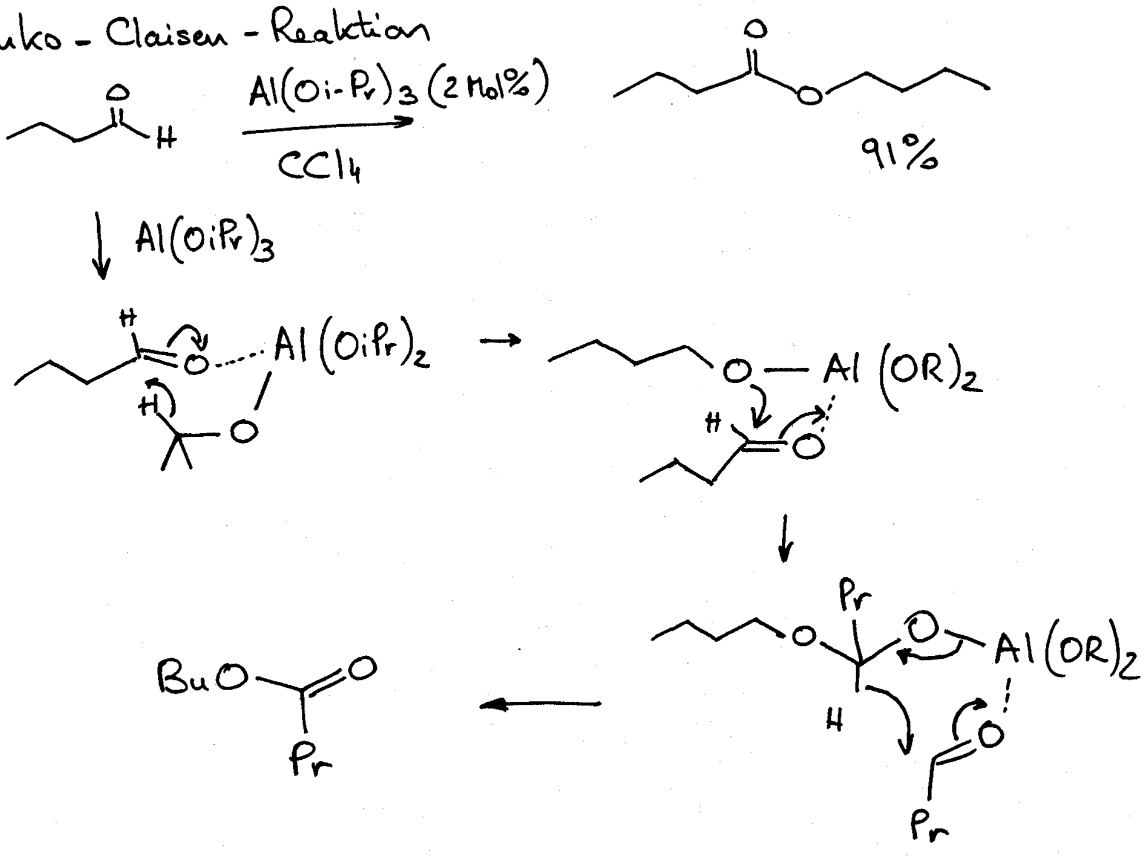
Haloform-Reaktion

2.6. Cannizarro-Reaktion

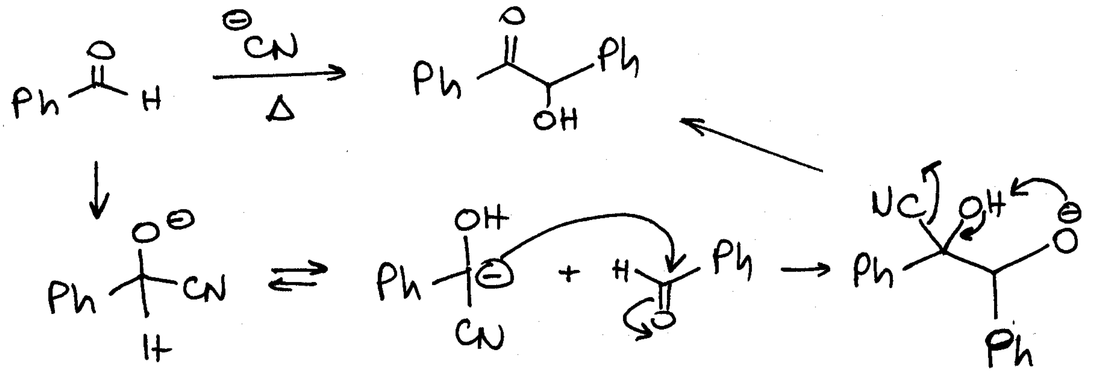
$$PhCHO \xrightarrow{OH^-} PhCH_2OH + PhCOO^{\ominus}$$



Tischenko-Claisen-Reaktion

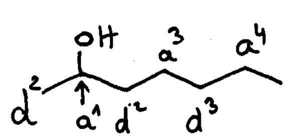


The Benzoin-Kondensation

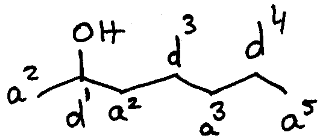


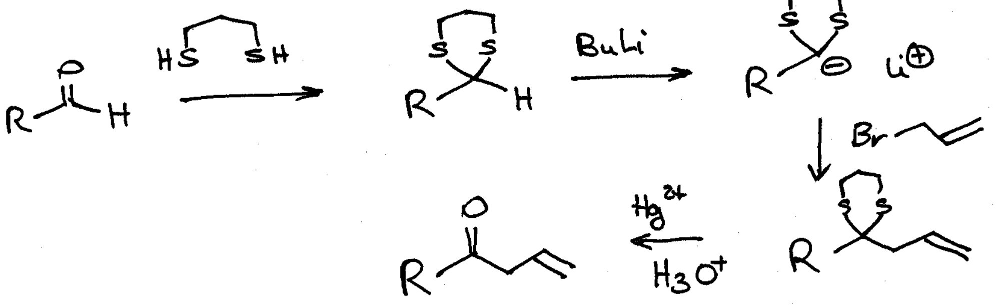
Umpolung der Reaktivität

Normale Reaktivität

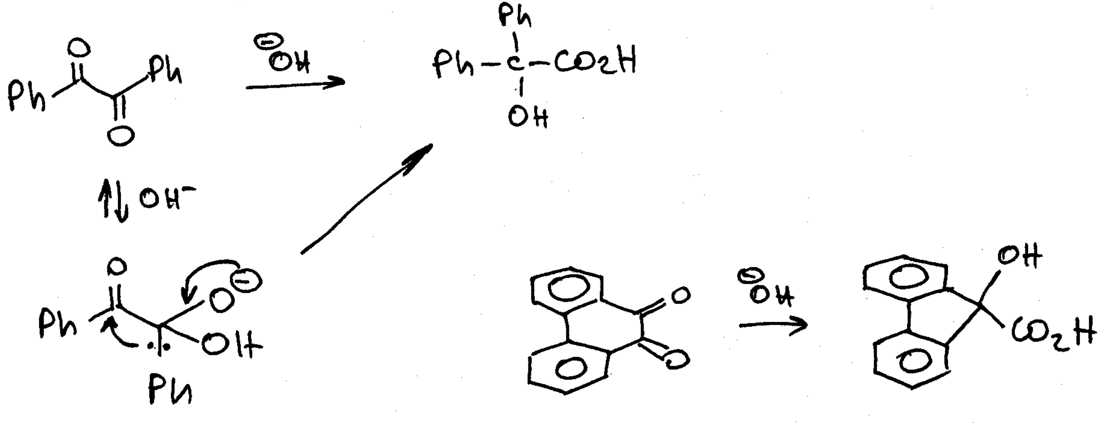


Umpolung : der Reaktivität





2.7. Die Benzilsäure-Umlagerung



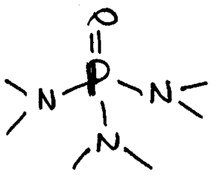
2.8. Reaktionen mit metallorganische Verbindungen

2.8.1. Einführung

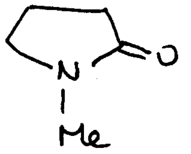
$\overset{-\delta}{R}-\overset{+\delta}{Met}$ Reaktivit. $RLi > RMgX > RZnX > R-Sn\lessgtr$

je elektropositiver das Metal desto reaktiver ist die entsprechende metallorganische Species. Die Reaktivität steigt auch nach erhöhten p Charakter: $C_{sp} < C_{sp^2} < C_{sp^3}(\text{prim}) < C_{sp^3}(\text{sek}) < C_{sp^3}(\text{tert})$

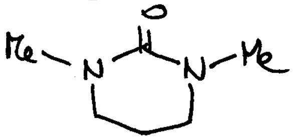
Metallorganische Verbindungen sind meistens reaktiver in THF als in Ether und reaktiver in Ether als in Hexan. Die Verwendung eines polaren LM wie HMPT oder NMP beschleunigt viele metallorganische Reaktionen. **D**MPU ist auch gut geeignet.



HMPT



NMP

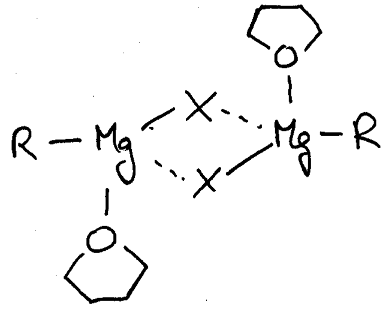


DMPU

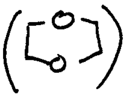
2.8.2. Reaktionen von Grignard-Verbindungen

$$R-X \xrightarrow[\text{Ether oder THF}]{Mg} R-MgX \rightleftarrows R_2Mg + MgX_2$$

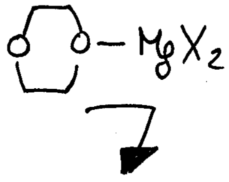
Struktur in Lösung



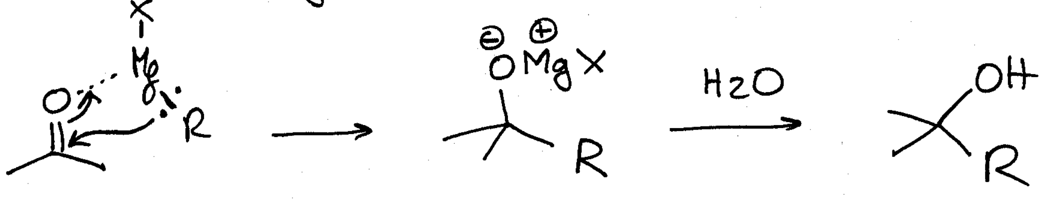
in Dioxan (



) ist MgX_2 unlöslich



Reaktion mit Carbonyl-Verbindungen



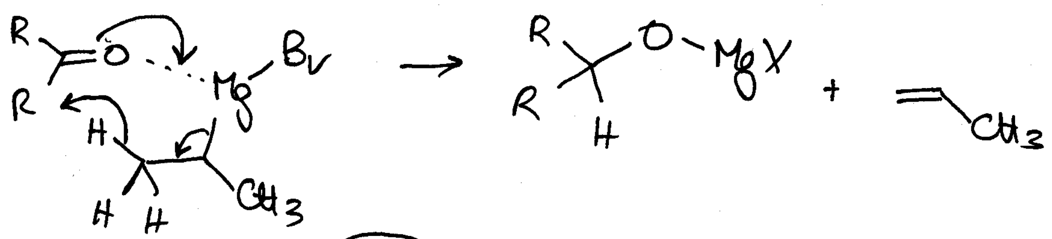
Aldehyde → sek. Alkohole

Ketone → tert. Alkohole

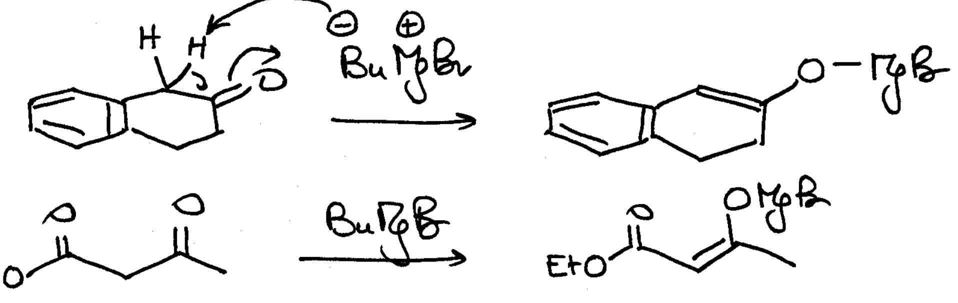
CH_2O → primäre Alkohole

Nebenreaktionen

Reduktion:



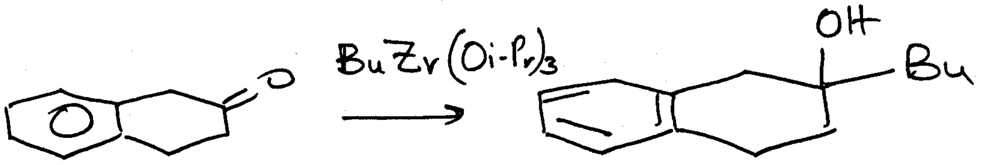
Enolisierung

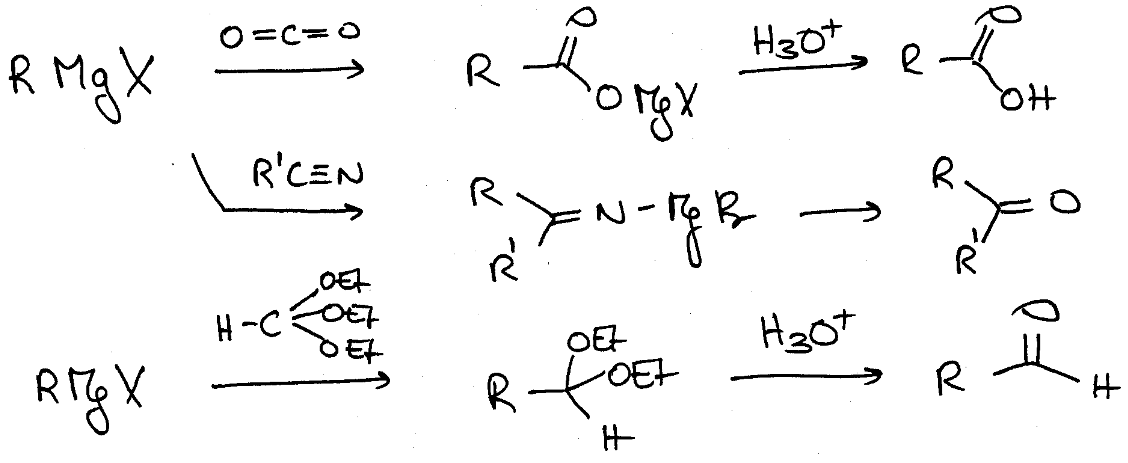


Lösung des Problems : Ummetallierung

Imamoto $\mathrm{BuMgBr} \xrightarrow{\mathrm{CeCl_3}} \mathrm{BuCeCl_2}$

Reetz-Seebach $\mathrm{BuMgBr} \xrightarrow[\mathrm{ClTi(Oi\text{-}Pr)_3}]{} \mathrm{BuTi(Oi\text{-}Pr)_3}$





Substitution - Reaktionen

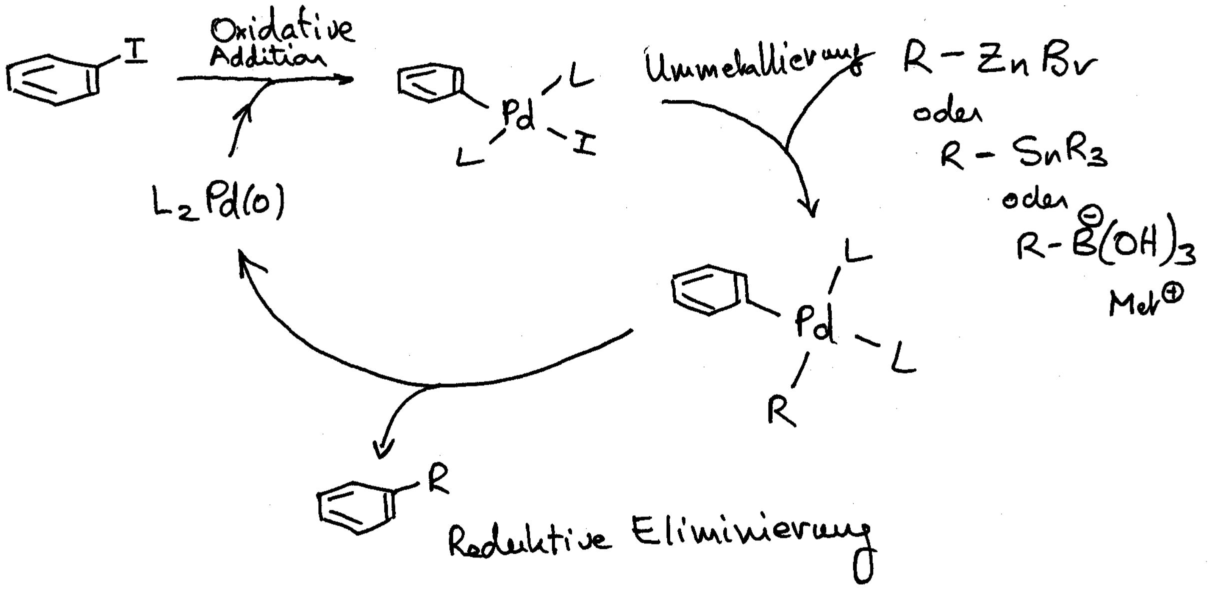
$\mathrm{RMgX} \xrightarrow{\mathrm{CuI}} \mathrm{RCu} \xrightarrow{\mathrm{ICH_2R^1}} \mathrm{R{-}CH_2R'}$

$\mathrm{RMgX} \xrightarrow{\mathrm{ZnBr_2}} \mathrm{RZnBr} \xrightarrow[\mathrm{Pd(0)\ Kat.}]{\mathrm{Ph{-}I}} \mathrm{R{-}Ph}$

$\mathrm{RMgX} \xrightarrow[\mathrm{2)\ H_2O}]{\mathrm{1)\ B(OMe)_3}} \mathrm{RB(OH)_2} \xrightarrow[\mathrm{Cs_2CO_3,\ \Delta}]{\mathrm{PhI,\ Pd(0)Kat}} \mathrm{R{-}Ph}$

luft stabil

Substitution an Csp²-Zentren.



2.8.3. Reaktionen und Synthesen von Lithium-Verbindungen

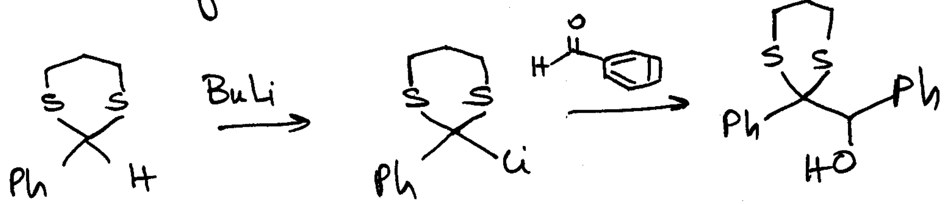
Herstellung Methode 1 $BuCl + 2Li \xrightarrow[-LiCl]{} BuLi$

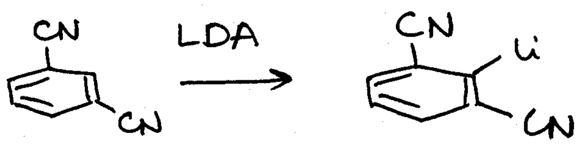
BuLi ist reaktiver als BuMgBr

z.B.: $BuLi + CH_2{=}CH_2 \longrightarrow Bu\!\left(CH_2-CH_2\right)_n CH_2-\overset{\ominus}{C}H_2\ Li^{\oplus}$

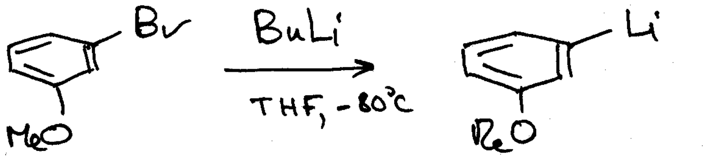
Polyethylen

Herstellungsmethode 2: Metallierung

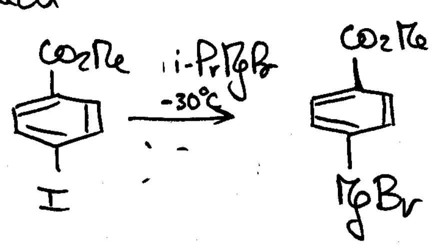


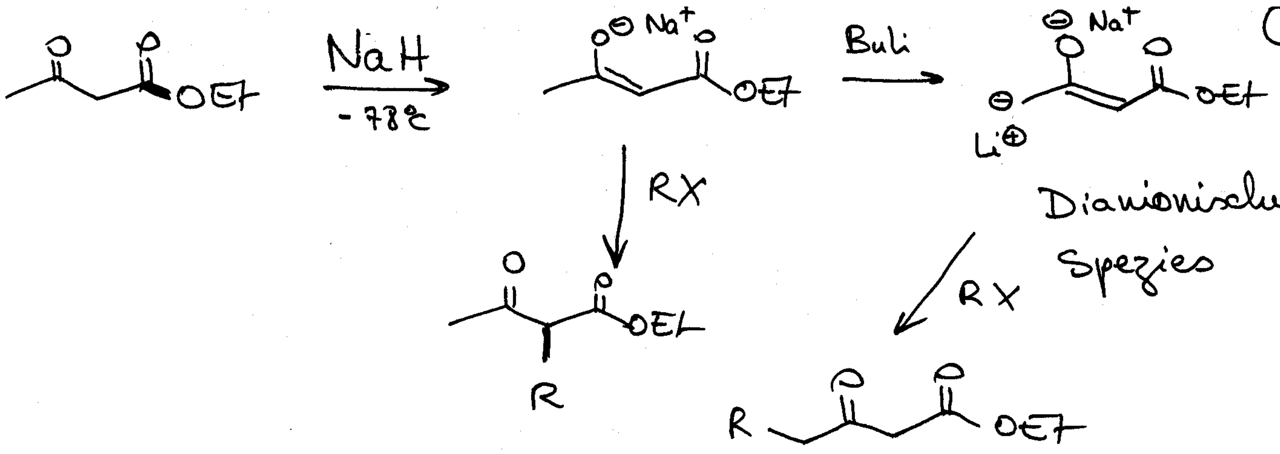


Herstellungsmethode 3: Halogen-Lithium-Austausch

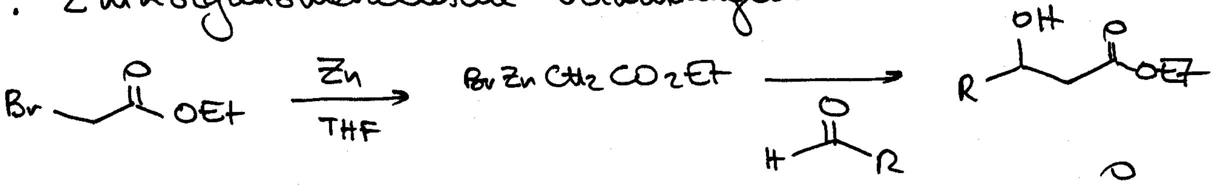


Vgl.

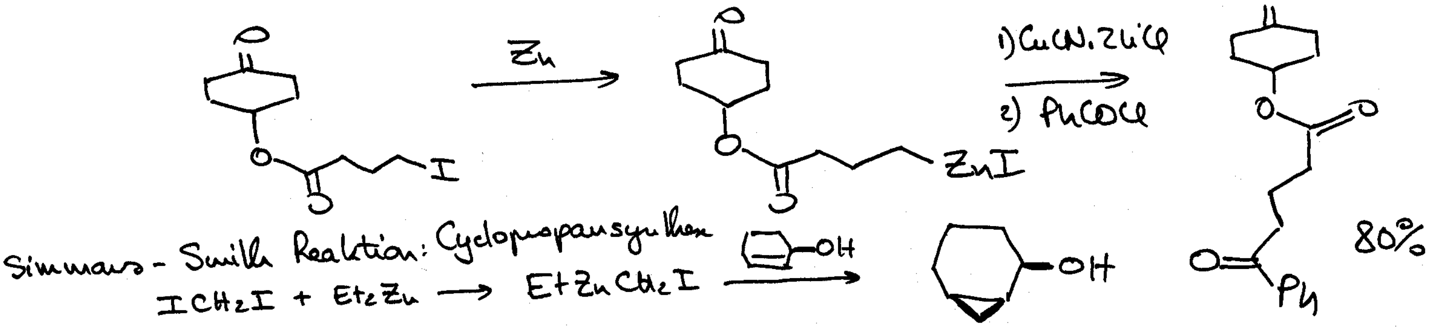




2.8.4. Zinkorganometallische Verbindungen

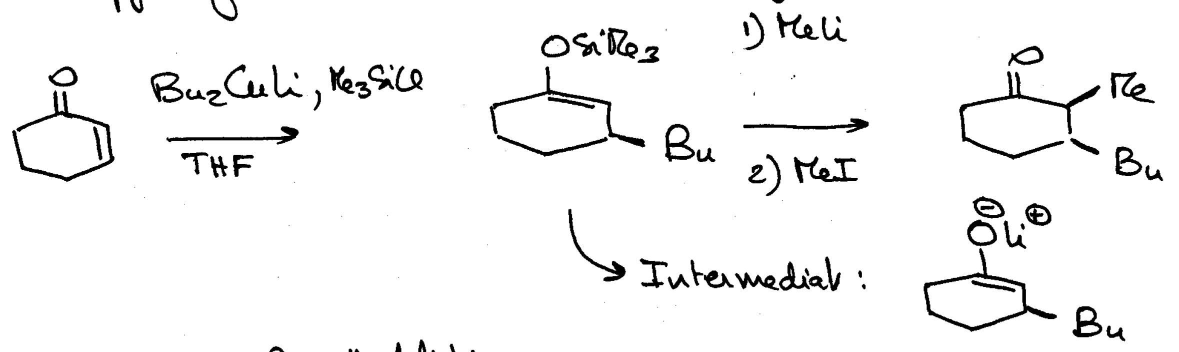


Simmons-Smith Reaktion: Cyclopropansynthese

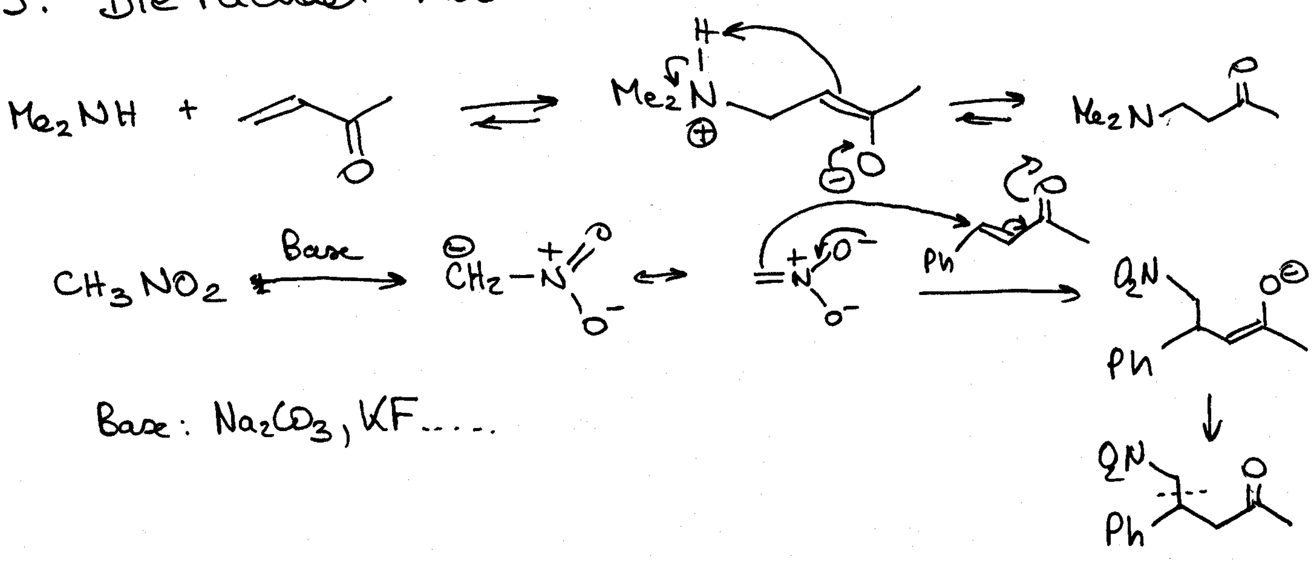


$ICH_2I + Et_2Zn \longrightarrow EtZnCH_2I$

2.8.5. Kupferorganometallische Verbindungen

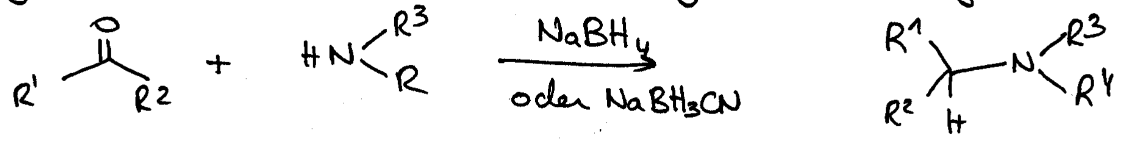


2.9. Die Michael-Addition

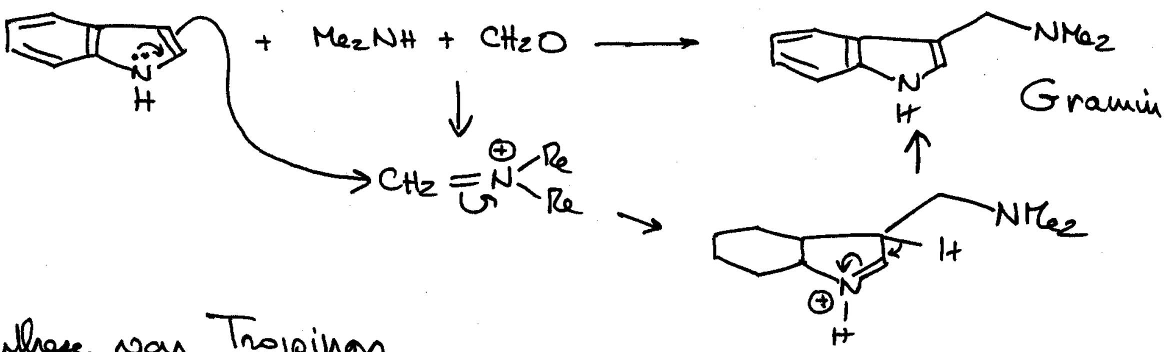


Base: Na_2CO_3, KF....

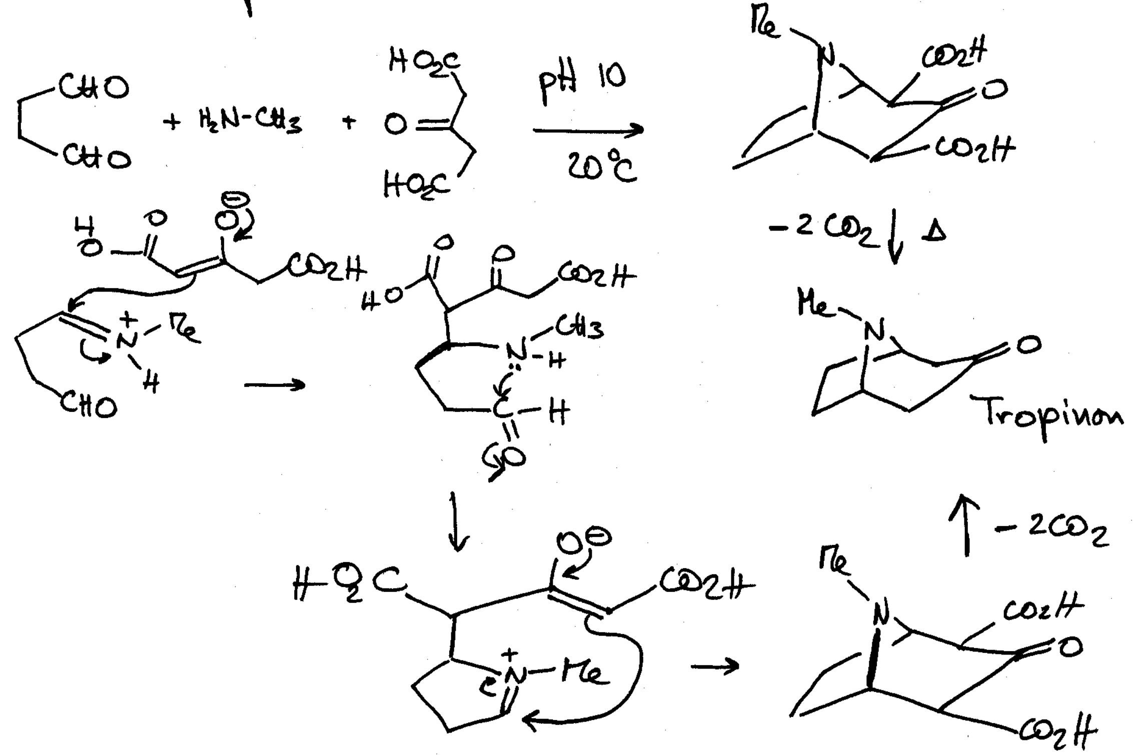
Vgl. mit der Reduktive Aminierung von Carbonyl-Verbindungen



Synthese von Gramin

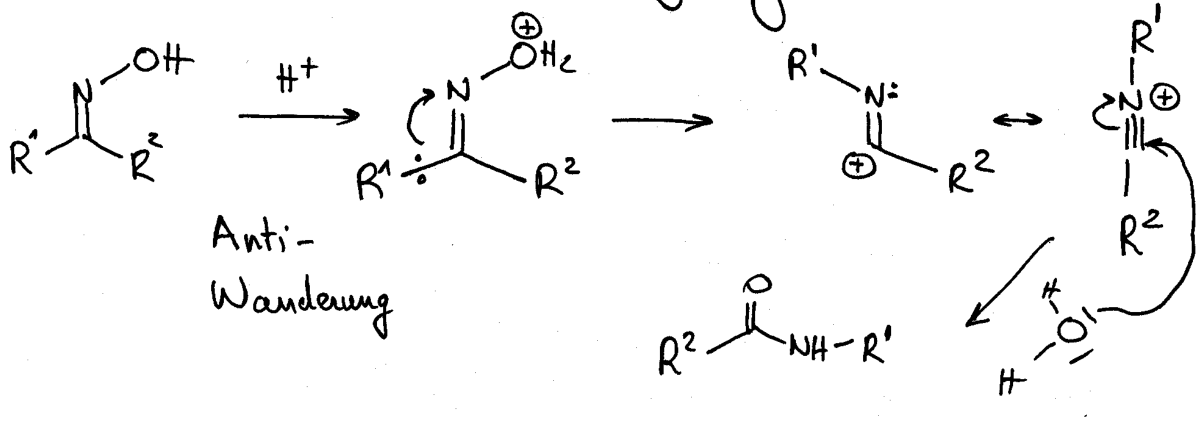


Synthese von Tropinon

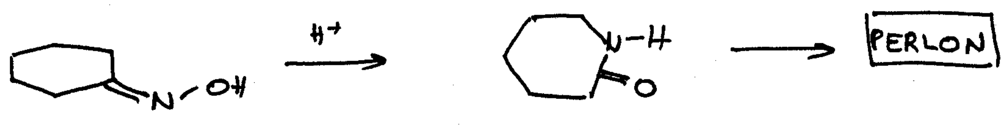


3. Umlagerungsreaktionen

3.1. Die Beckmann-Umlagerung

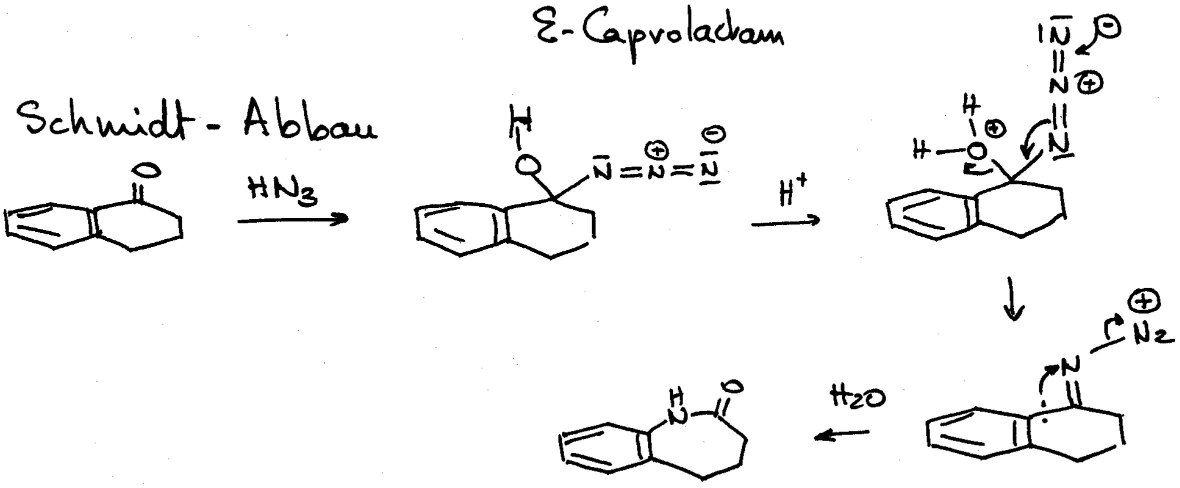


von Cyclohexanon zu Perlon



ε-Caprolactam

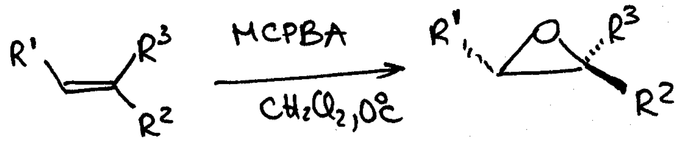
3.2. Schmidt-Abbau



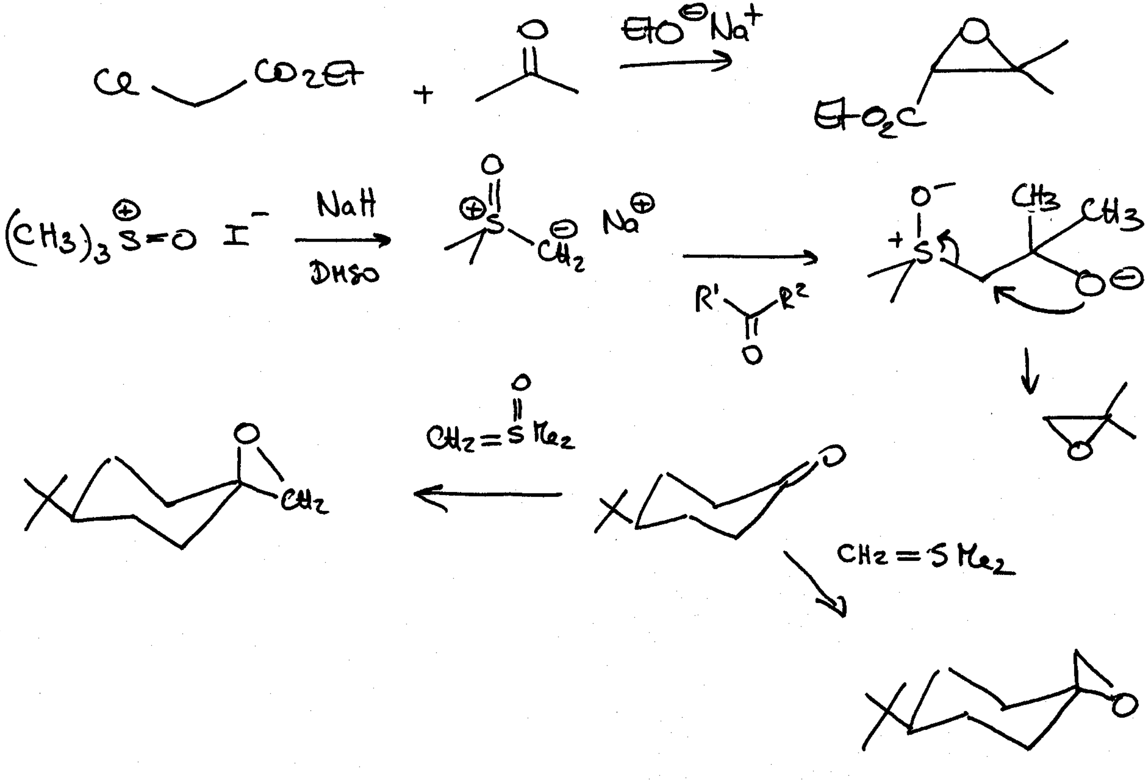
4. Synthese ausgewählter Heterocyclen

4.1. Oxirane

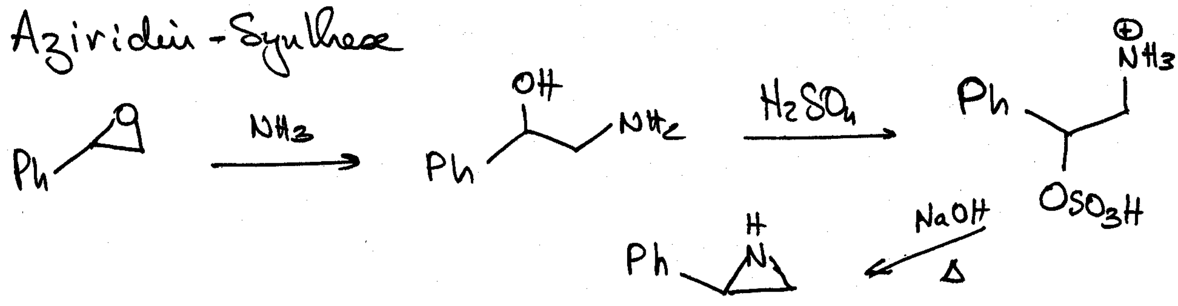
a)



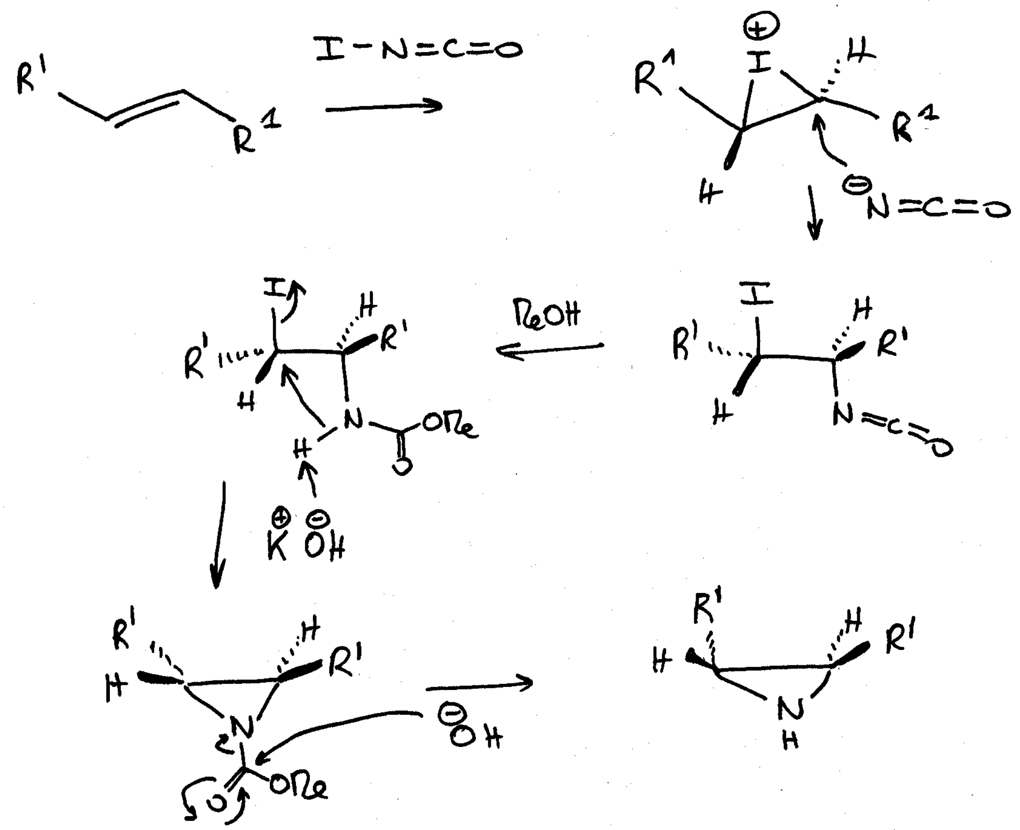
b) Darzens-Glycidester-Synthese



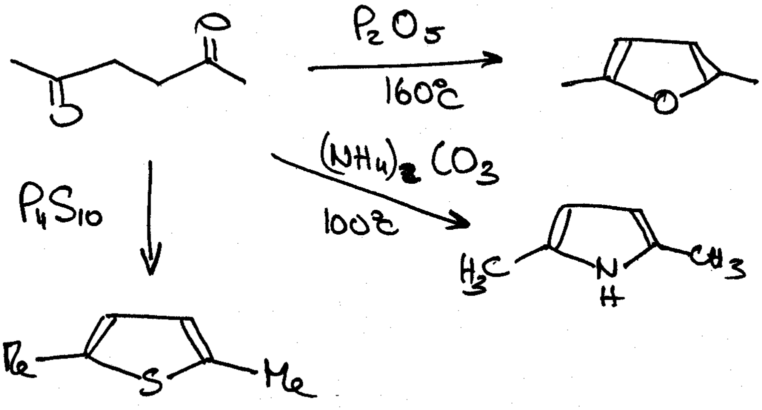
4.2 Aziridin-Synthese



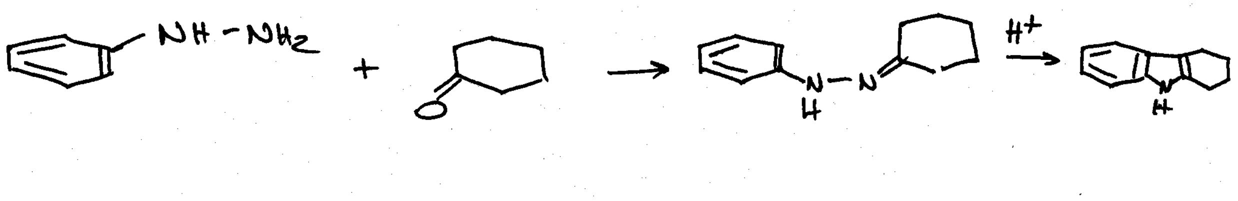
Mildere Methode

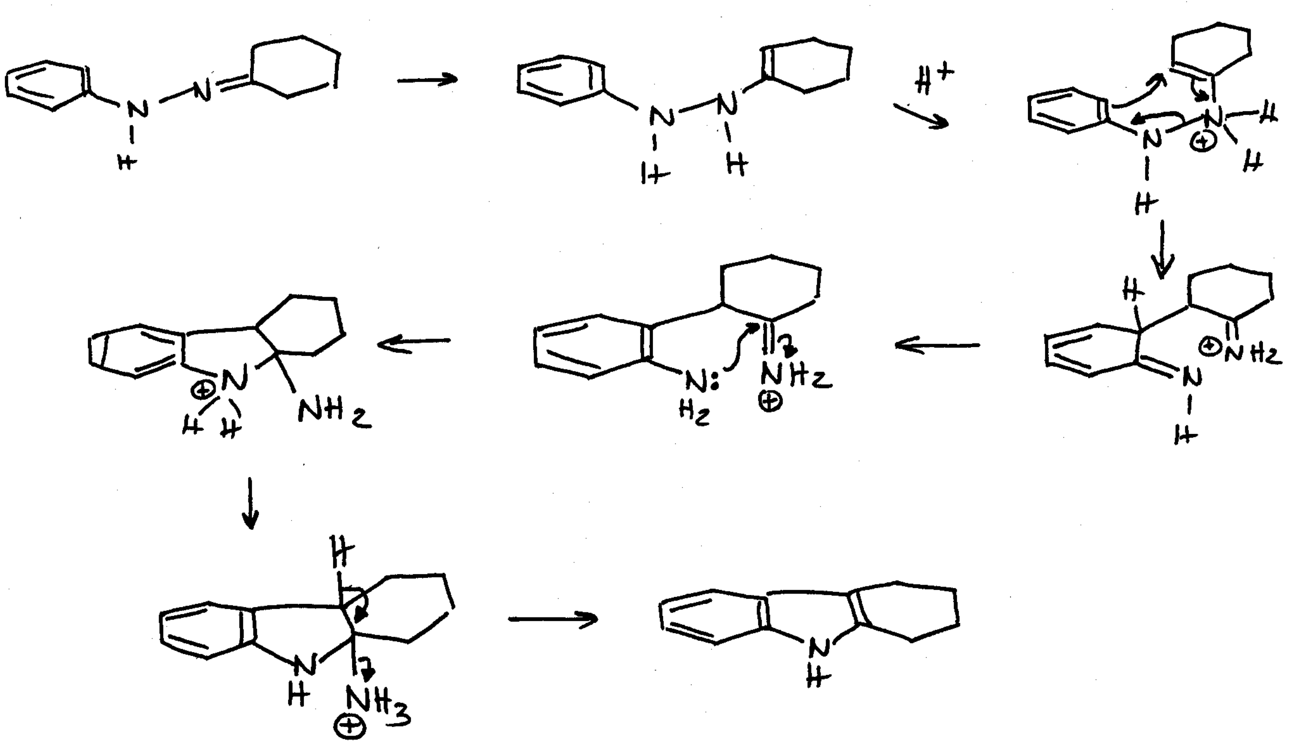


4.3 Furane, Pyrrole und Thiophene



4.4. Fischer-Indolsynthese





4.5. Hantzsch - Pyridinsynthese