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- 4 Diastereoselektivität
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- 7 Reaktiv. Subst.
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- 22 Simmons-Smith-Rkt, Carbenbildung mit Rh-Komplex
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- 24 Quenching der Hydroborierung
- 25 α -Effekt Hydroborierung, Ox-Stufen Bor
- 26 Sharpless (SAE)
- 27 Sharpless und Payne Umlegung
- 28 Pummerer Umlegung
- 29 Dihydroxylierung mit OsO₄
- 30 Asymmetrische Dihydroxylierung
- 31 Übergangszustand, AD-Merkhilfe
- 32 Allylstrain Modell
- 33 Schutzgruppen
- 34 Mechanismus mit Schutzgruppen
- 35 Cyclopropanierung
- 36 Liganden
- 37 Hydrierung von DB, Schrock-Kat.
- 38 Hydrierung, Monsanto-Prozess
- 39 Asymmetrische Hydroborierung
- 40 Unkatalys. asymm. Hydroborierung
- 41 Aldolreaktion
- 42 Stereoisomerie
- 43 Stereo, Heathcock-Exp., Zimmermann-Traxler ÜÜ
- 44 Ireland-Modell
- 45 mit HMPA, Auxiliäre
- 46 Evans-Aldol, Curtin-Hammett
- 47 Curtin-Hammett, Zimmermann-Traxler
- 48 Immernoch Evans
- 49 Curtin-Hammett, Evans Auxiliär
- 50 Abspaltung Evans

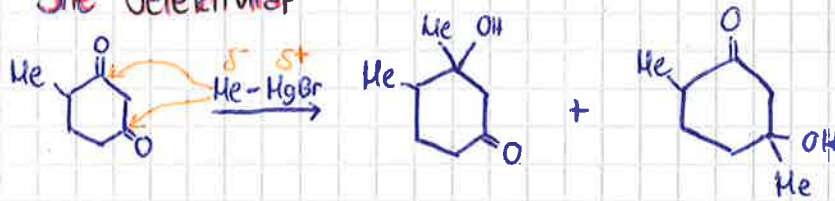
- 51 Henney, Mannich
- 52 Claisen Esterkondensation, Enolatbildung
- 53 Robinson - Amelierung, Baylis-Hillmann
- 54 Mukojama Aldol
- 55 Reformatsky Aldol, Enolatverbindungen
- 56 Enolatverbindungen
- 57 Reaktionen von Enolaten mit div. Elektrophilen + Asymm. Variante mit Evans
- 58 α -Oxidation
- 59 Nucl. Add. am Carbonyl, Cram-Modell
- 60 Cram-Chelzt-Modell
- 61 Grignard, Felkin-Ahn
- 62 Alkylierung / Crotylierung
- 63 Diastereosele., Schlosser Base
- 64 Diastereosele. & Enantiosele. über Pinacol
- 65 Brown- und Roush-Crotylierung
- 66 Roush
- 67 Transition-State-Modell
- 68 Doppelte Stereodifferenzierung
- 69 Nonlineare chirale Induktion: DAIB
- 70 DAIB Mechanismus
- 71 Myers Auxilier, RAMP/SAMP Methode
- 72 1,4 Induktion
- 73 RAMP/SAMP, Oxidationsstufen/Verbindungen
- 74 Kondensationsrkt. von Carbonylen
- 75 Michael-Reaktion
- 76 Gilman-Cupret
- 77 Lipshutz, Normant, Knochel
- 78 Stetter-Rkt
- 79 Sakurai-Rkt
- 80 Peterson-Olefinierung
- 81 Wittig-Rkt
- 82 Wittig
- 83 Wittig-Horner
- 84 HWE
- 85 Arbusov, Julia-Olefinierung
- 86 Varianten der Julia-Olefinierung
- 87 Chugaev-Eliminierung, Grieco-Protokoll
- 88 Grieco Mech., Burgess-Reagenz
- 89 Mech. Burgess
- 90 Martin-Sulfuren
- 91 Bamford-Stevens, Shepiro
- 92 (Shepiro) Olefinierung mit Ti
- 93 Alkine
- 94 Wittig-enzolig Corey-Fuchs
- 95 Gilbert-Seiffert, Ohira-Bestmann, Pericyc. Rkt.
- 96 Pericycl. Rkt.
- 97 Elektrozykl. Rkt
- 98 Orbitale dazu
- 99 disrotatorisch, conrotatorisch
- 100 Endiandrinic acid

- 101 Diels-Alder
- 102 Stereochemie Dienophil
- 103 Stereochemie Dien, Endo-Exo-Regel
- 104 Ortho/para-Regel
- 105 Endo/Exo
- 106 Reppe-Prozess, 2+2 Cyclo
- 107 2+2 Cyclo Keten + Olefin
- 108 Arndt-Eistert, Isocyanate
- 109 3+2 Cyclo, Ozonolyse
- 110 1,3 Dipole
- 111 Sigmatropische Umlagerungen, Cope, Claisen
- 112 Claisen
- 113 Claisen
- 114 α, β -Umlag, Meisenheimer, Evans, Stevens
- 115 1,3-H-Shift, 1,5-H-Shift
- 116 1,7-H-Shift
- 117 Reduktion eines Esters
- 118 Reduktion, Reagenzien
- 119 Birch-Reduktion
- 120 Oxidationen, Chrom RgZ
- 121 Hyperval. Iod-Verb., Swern, Allyl. Oxidation
- 122 Glycolspaltung

→ Kontrolle - Selektivität

→ **Konstitutionsselektivität** (Beschaffenheit-Verknüpfungsweise)

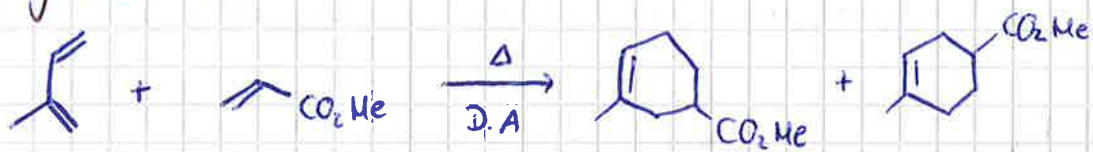
a) **Site-Selektivität**



2 gleiche Substituenten, aber nur eines davon wird angegriffen.
Eines wird bevorzugt gebildet

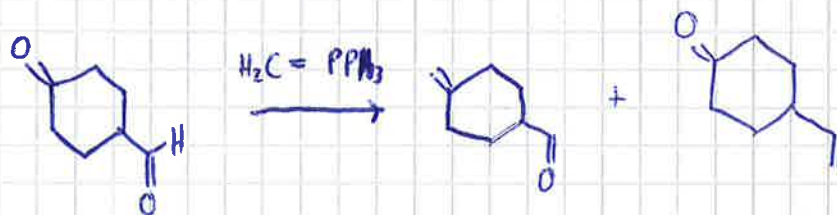
→ 1 Konstitutionsisomer bevorzugt gebildet aus Startmaterial mit 2 identen Funktionellen Gruppen

b) **Regioselektivität**



Bevorzugte Bildung eines Konstitutionsisomers bzgl. 1er funkt. Gruppe (para & meta zu Methylgruppe)

c) **Chemosелеktivität**



Bevorzugte Bildung von einem Konstitutionsisomer bezüglich 2 unterschiedlicher funktioneller Gruppen

Stereoselektivität

- bei gegebenem Konstitutionsisomer beschreibt es die räumliche Anordnung der Atome zueinander (steht es über oder unter dem Ring?)

- Konfiguration

Enantiomere → Absolutkonfiguration

a) Enantioselektivität

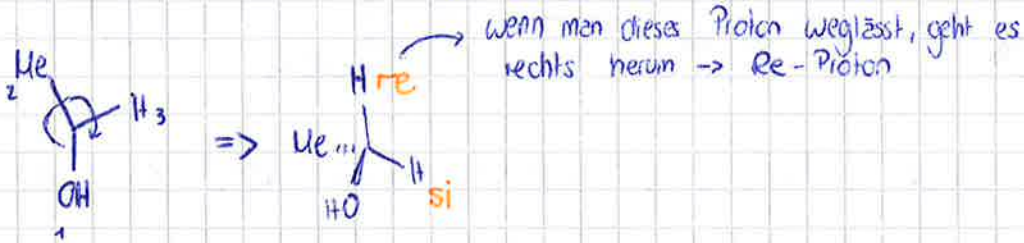


chiral nur mit 4 versch. Substituenten

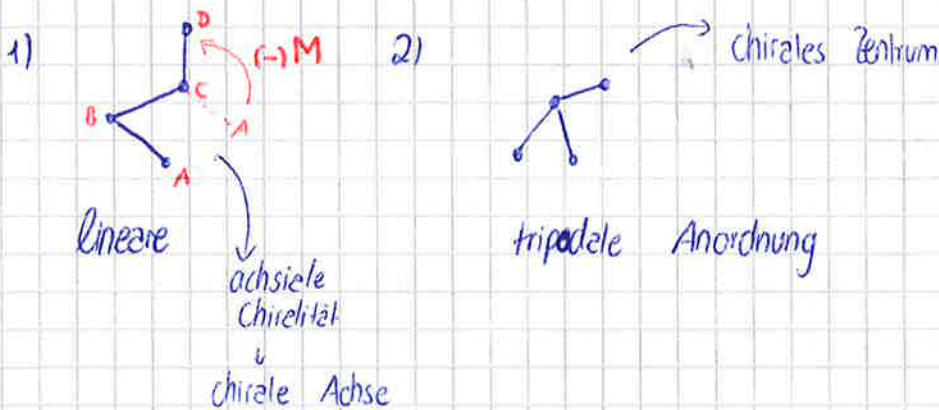
Proton muss ausgetauscht werden

prostereogenes Zentrum

Re/Si-Formalismus → sagt welches Proton abgespaltet wird



4 Punkte → 2 verschiedene Arten



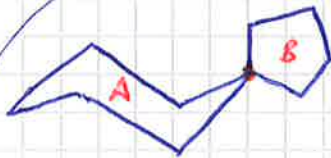
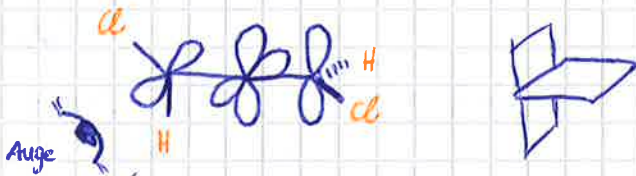
A: höchste Priorität → zu sich her drehen → wie dreht sich dann die Helix?



M & P: Nomenklatur, wie rum sich die Helix dreht

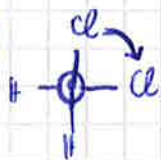
Axiale Chiralität

1. Bsp: Allene

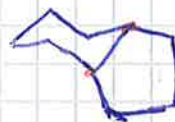


Spiro-Verbindung → Bicyclus

nur über ein C-Atom verbunden

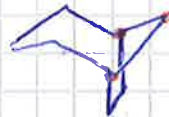


(+) - P



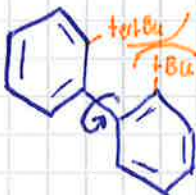
annulierte Verbind.
teilen sich 2 C-Atome

3 oder mehr C-Atome → überbrückte Verb.



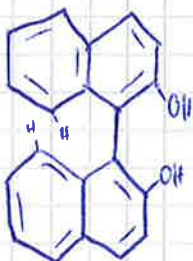
2. Bsp

Bi-Aryl



dreht 90° Grad → entweder rechts rum oder links rum

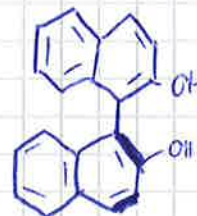
Binol (Bi-Naphthal)



in einer Ebene:

co-planare Anordnung

weicht aus, dreht sich →



→ unmöglich
↳ sterische Hinderung

Diastereoselektivität

Diastereomerie (Molekül $n > 1$
 $n = \text{Stereozentrum}$)

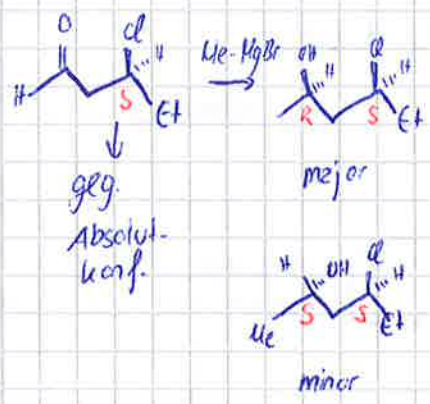
2^n Stereoisomere
 n -Stereozentren



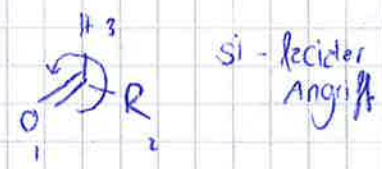
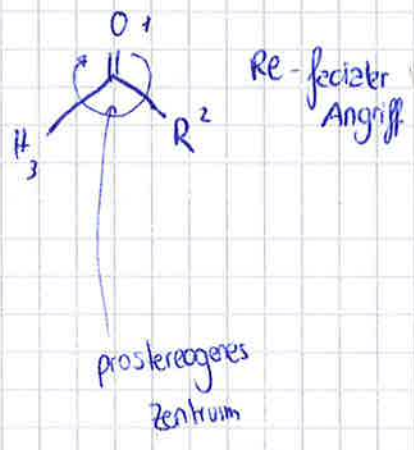
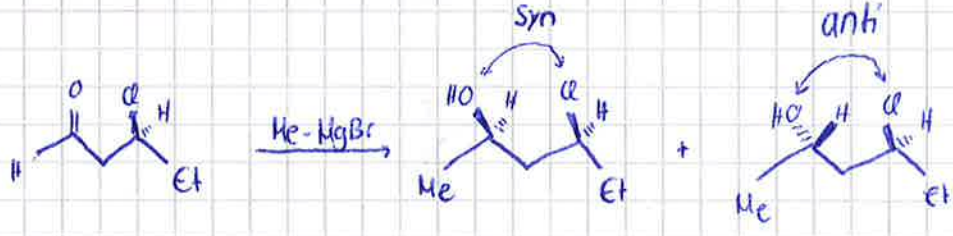
Diastereomer: ein Stereozentrum
 so lassen und eins
 ändern: z.B. RR
 oder SS

Enantiomer: beide Stereozentren
 ändern: SR

induzierte Diastereoselekt.
 \hookrightarrow ein Stereozentrum
 bestimmt über das zweite



20.10.15



u

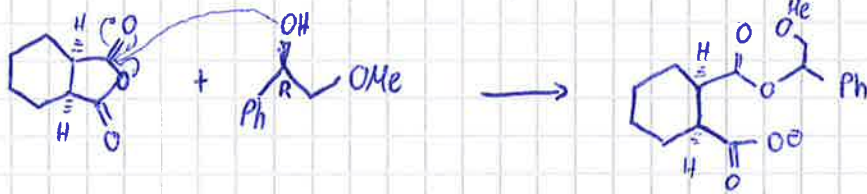
Izumi - Tai - Nomenklatur



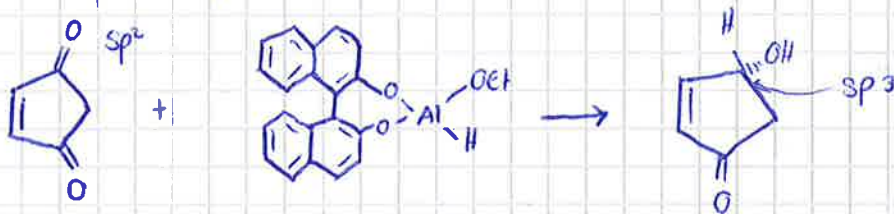
1. enantiodifferentiating reactions

a) enantiotopos diff.

Säureanhydrid + Alkohol → Carboxylat



b) enantioface diff.

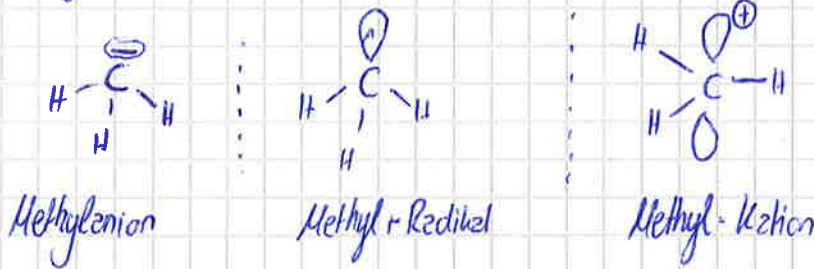


Chemie - Reaktionen

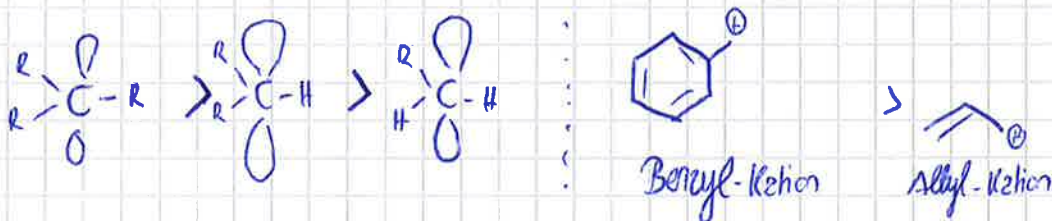
Substitution

Radikale:

→ ungepaartes Elektron



Stabilität vom Carbeniumion



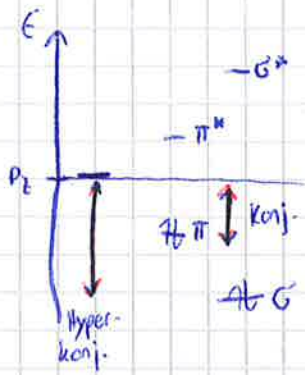
Alkyl-Kation: → Hyperkonjugation

Ph - σ³ (sp³)

Alkyl / Benzyl → Konjugation

Ph + π

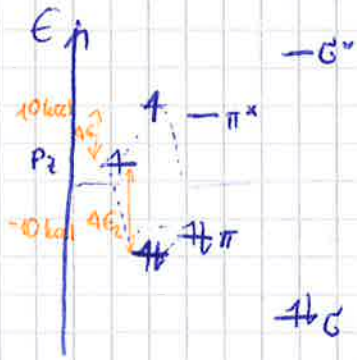
Carbeniumion bzw Carbokation



energy gap bei Konjugation kleiner
planar

Radikal

50% Anteil des MO-Schemas

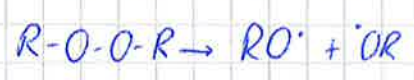
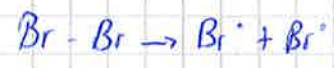


planar / tetraedisch

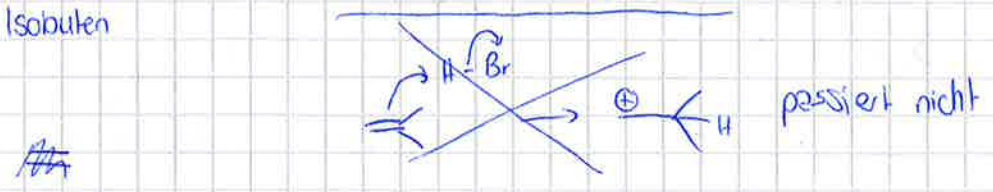
↳ R = F; Cl; Br; O; N

Erzeugung von Radikalen

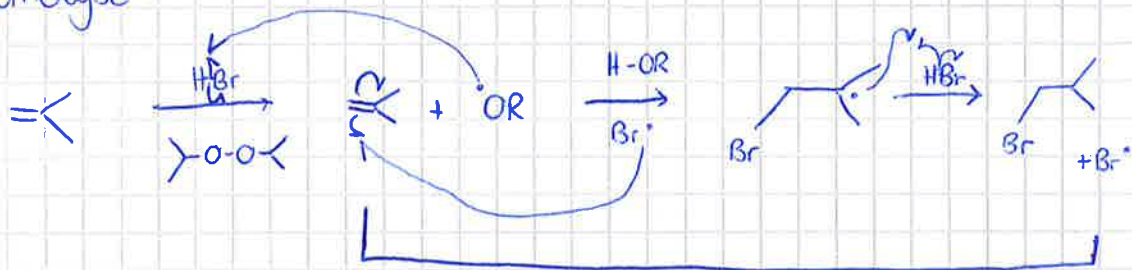
Umkehrung
Absolut-
konfig.
durch
Schwingung
durch Ebene



Heterolytische H-Br Addition an Doppelbind.



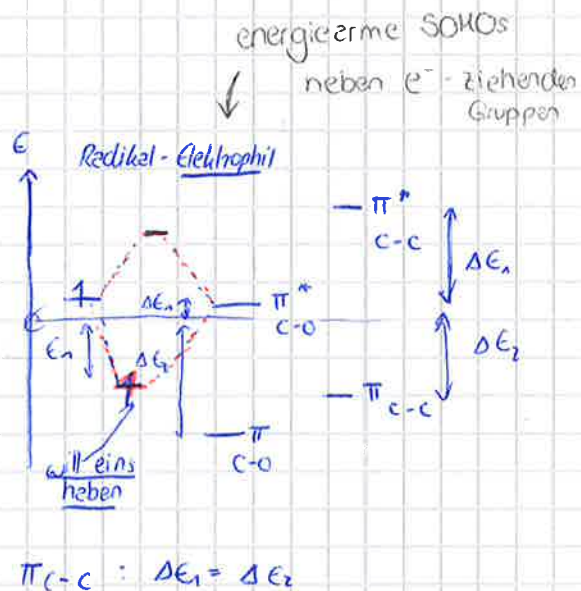
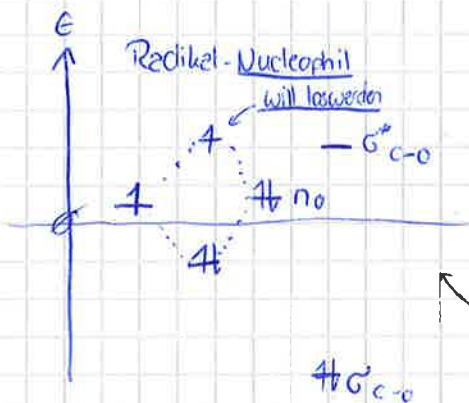
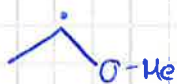
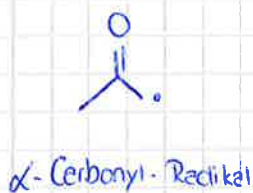
Homolyse:



Radikalkettenreaktion

Achtung: Halbpfeile!

Radikale mit funktionellen Gruppen



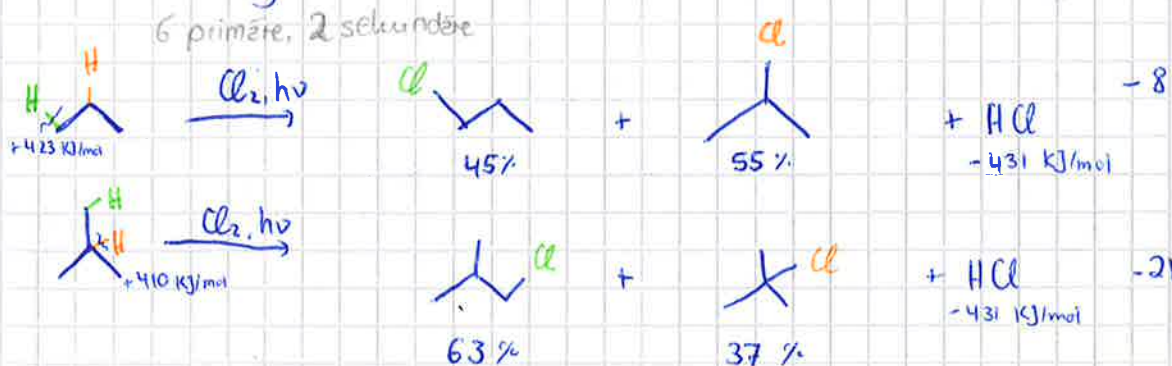
$\pi_{C-C} : \Delta E_1 = \Delta E_2$

energiereiche SOMOs neben e-schiebenden Gruppen

Radikalkettenreaktion

26.10.15

- 1) Initiation
- 2) Propagation
- 3) Terminierung

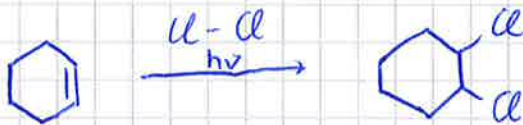
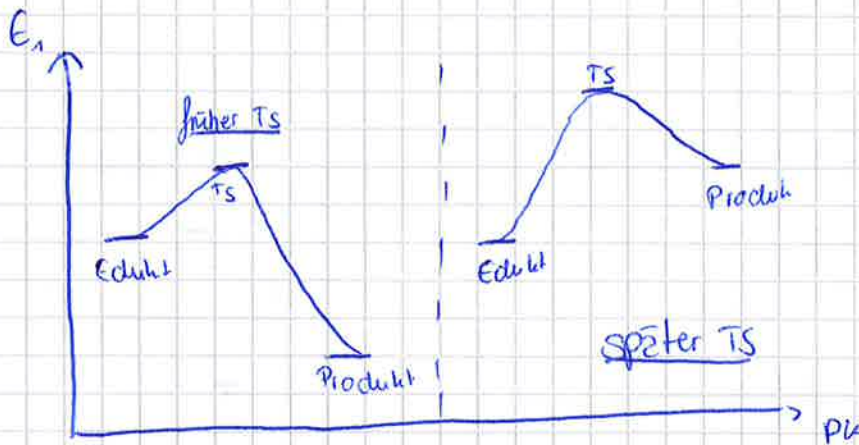


Statt $Cl_2 \rightarrow Br_2$ $H-Br -366 \text{ kJ/mol}$

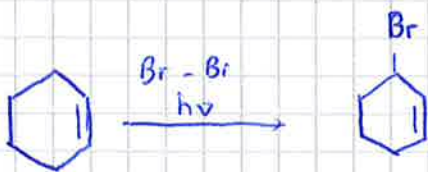
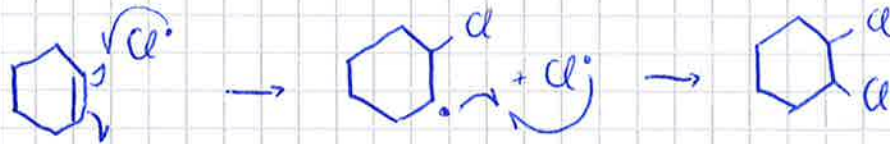
Hammond Postulat:

exergone Reaktion $\hat{=}$ früher Übergangszustand (TS) $\hat{=}$ TS ist strukturell dem Edukt ähnlich

endergone Reaktion $\hat{=}$ später Übergangszustand (TS) $\hat{=}$ TS ist strukturell dem Produkt ähnlich

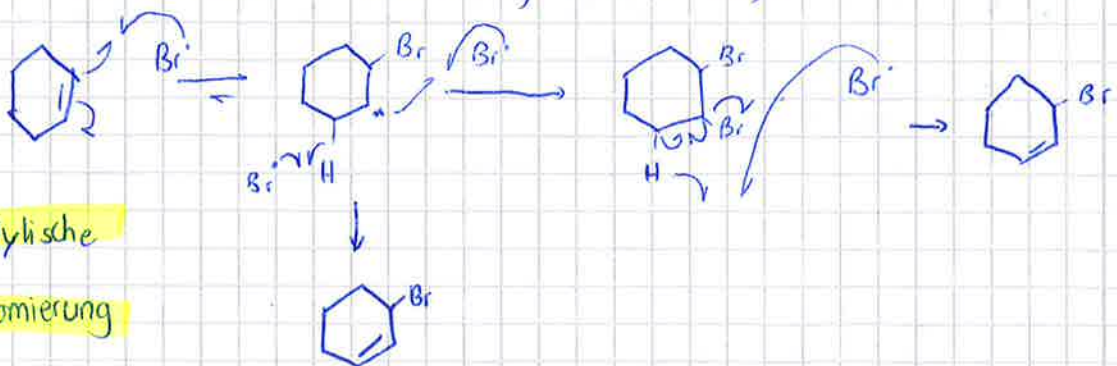


Mechanismus:



C-Cl-Bindung zu stabil um wieder gebrochen zu werden

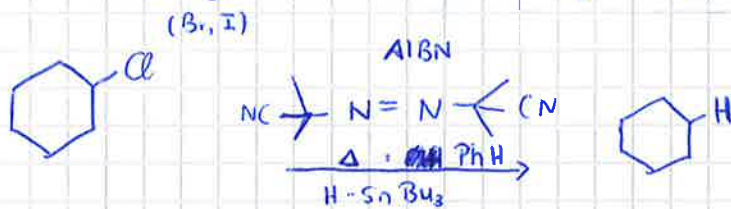
Mech: d. Bromierung v. Doppelbindung (vs. Chlorierung)



Allylische Bromierung

Barton McCombie Dehalogenierung

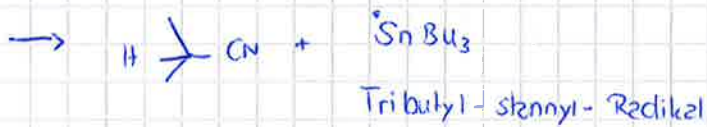
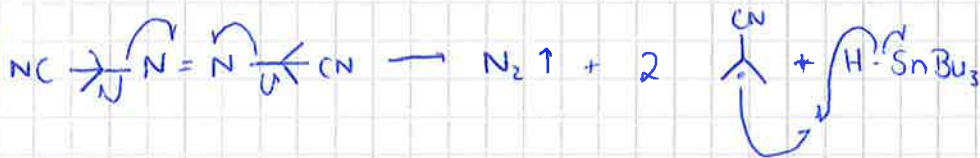
→ Umkehrung radikalischer Halogenierung v. Kohlenwasserstoffen



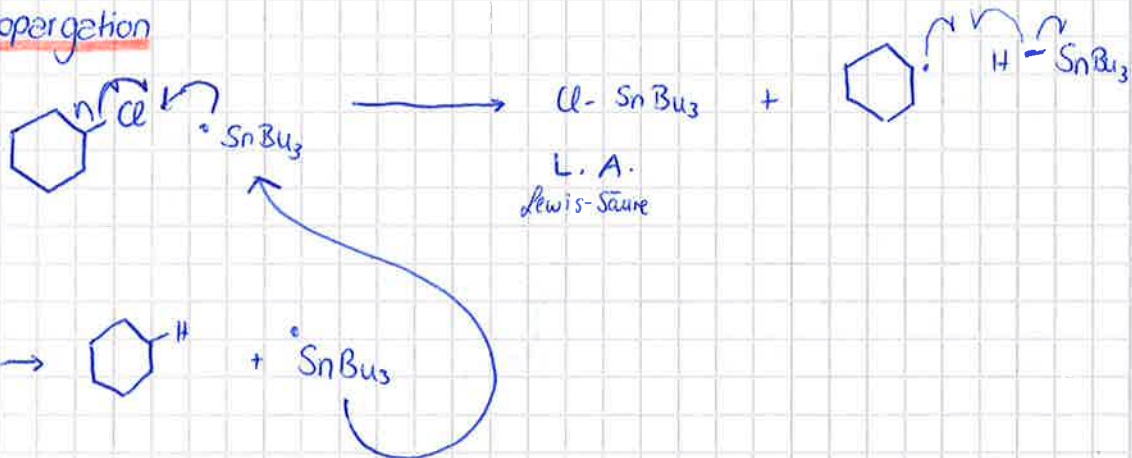
AIBN: Azobisisobutyronitril

Tributylstannen = H-SnBu₃

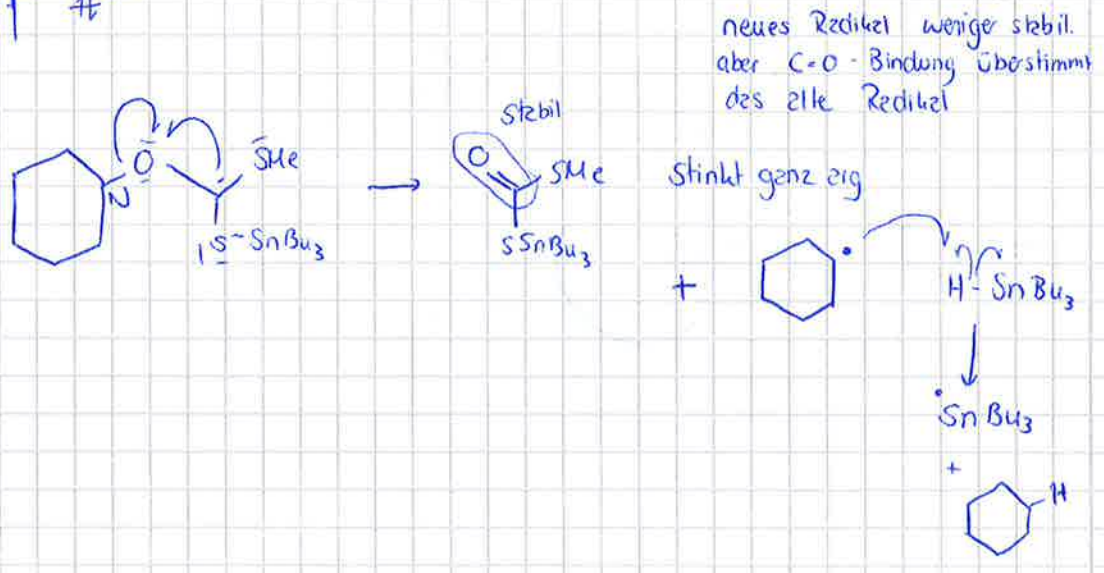
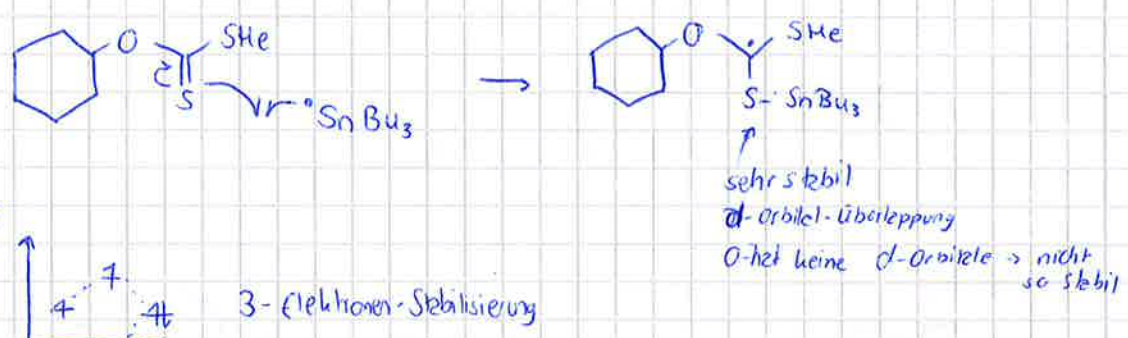
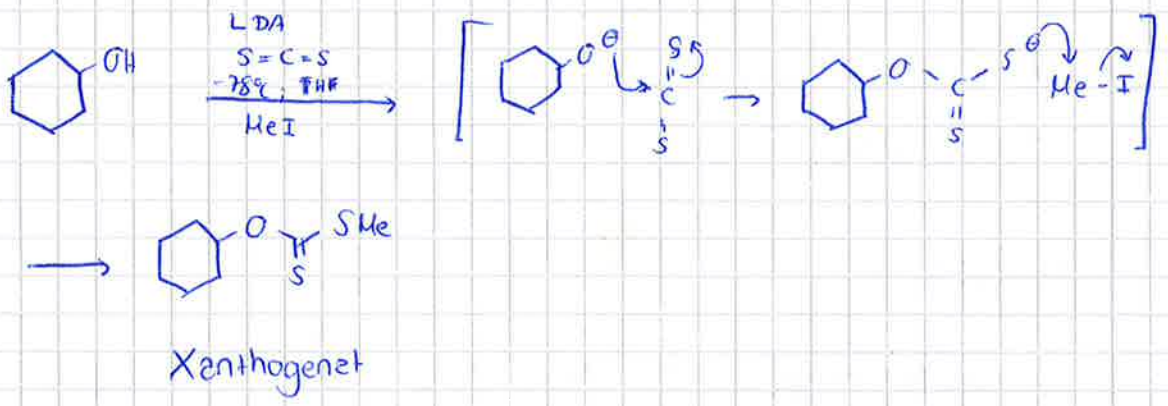
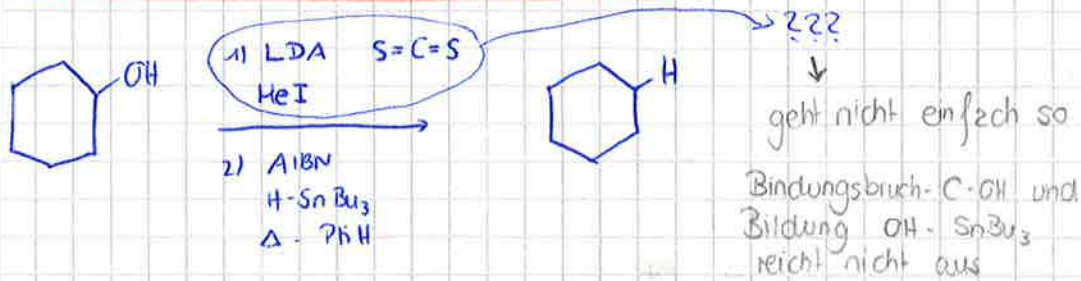
Initiation



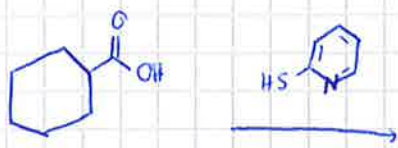
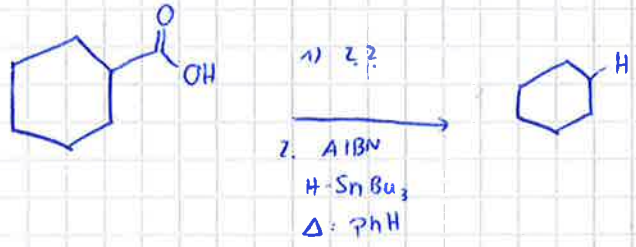
Propagation



Barton - McCombie - Deoxygenierung

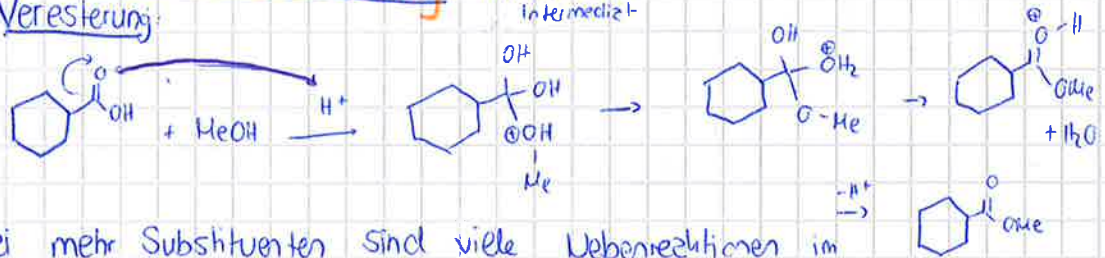


Barton- McCombie- Decarboxylierung



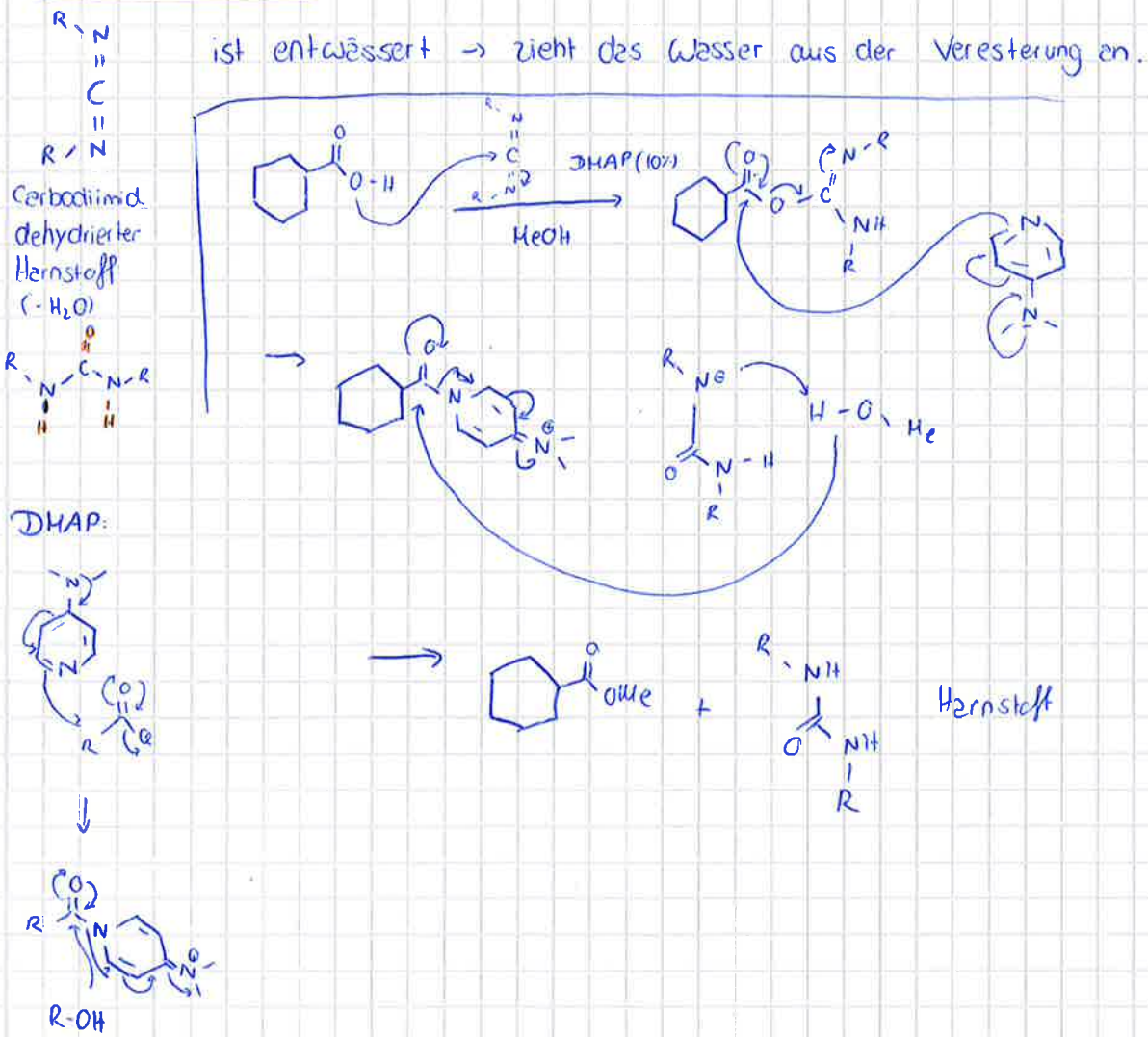
Exkurs: Veresterung

Veresterung:



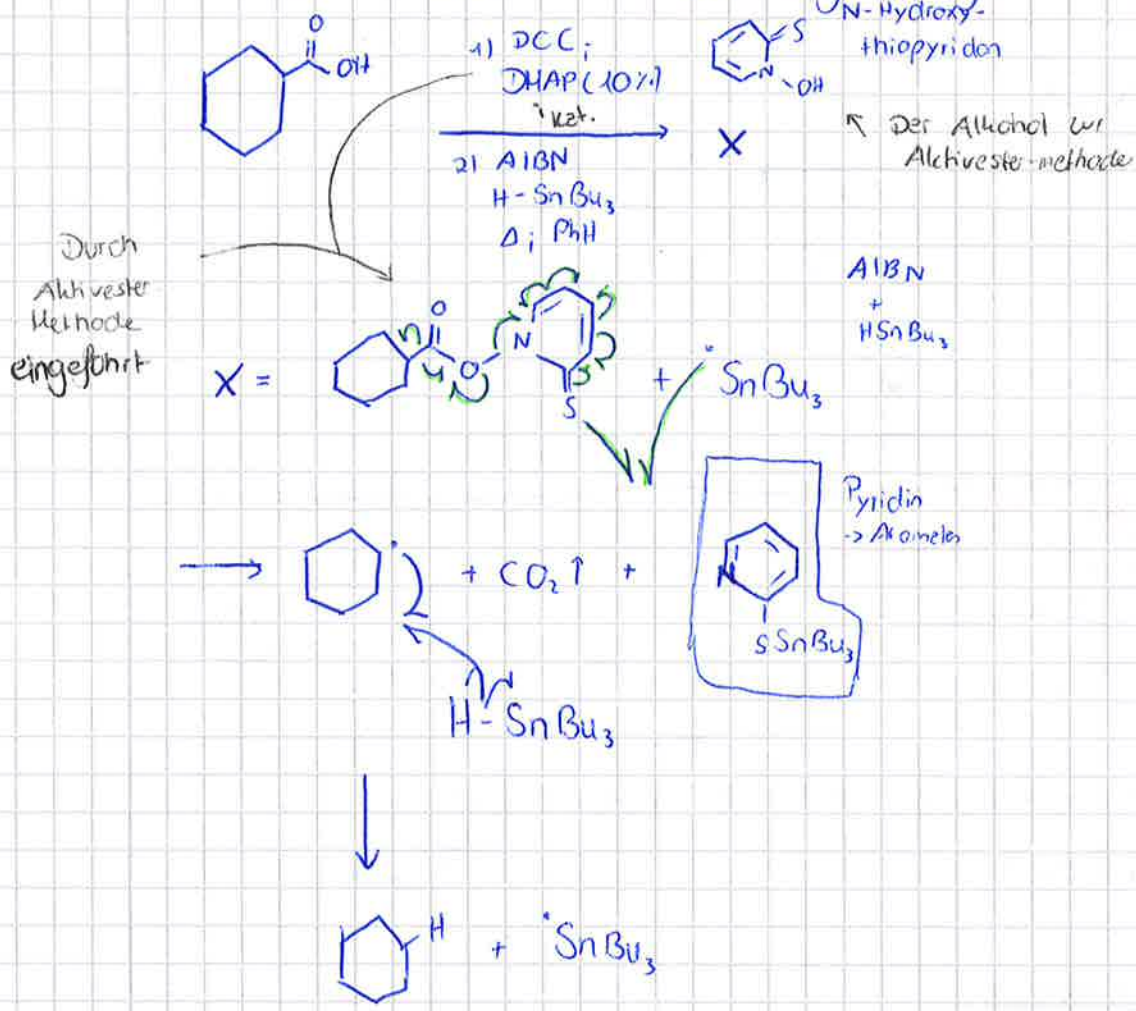
bei mehr Substituenten sind viele Nebenreaktionen im Säuren möglich
 \hookrightarrow unbrauchbar

Aktivester methode:



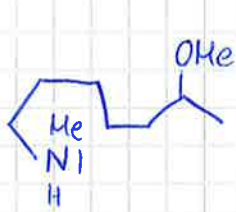
27.10.15

Barton-McCombie - Decarboxylierung

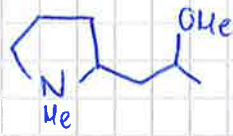


Hoffmann-Löffler-Freytag

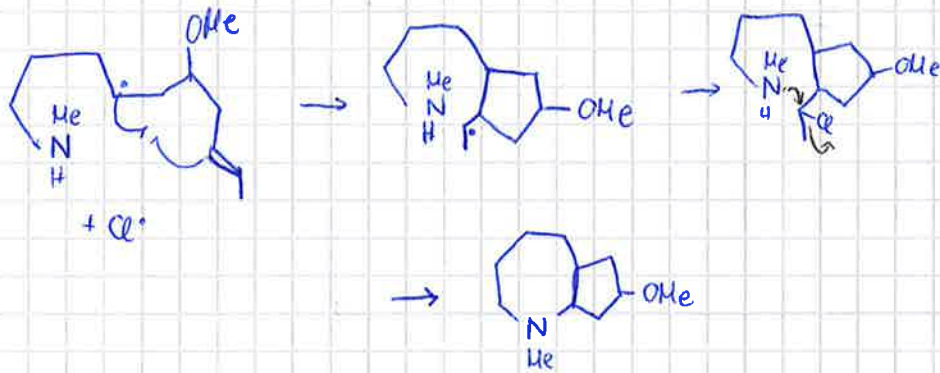
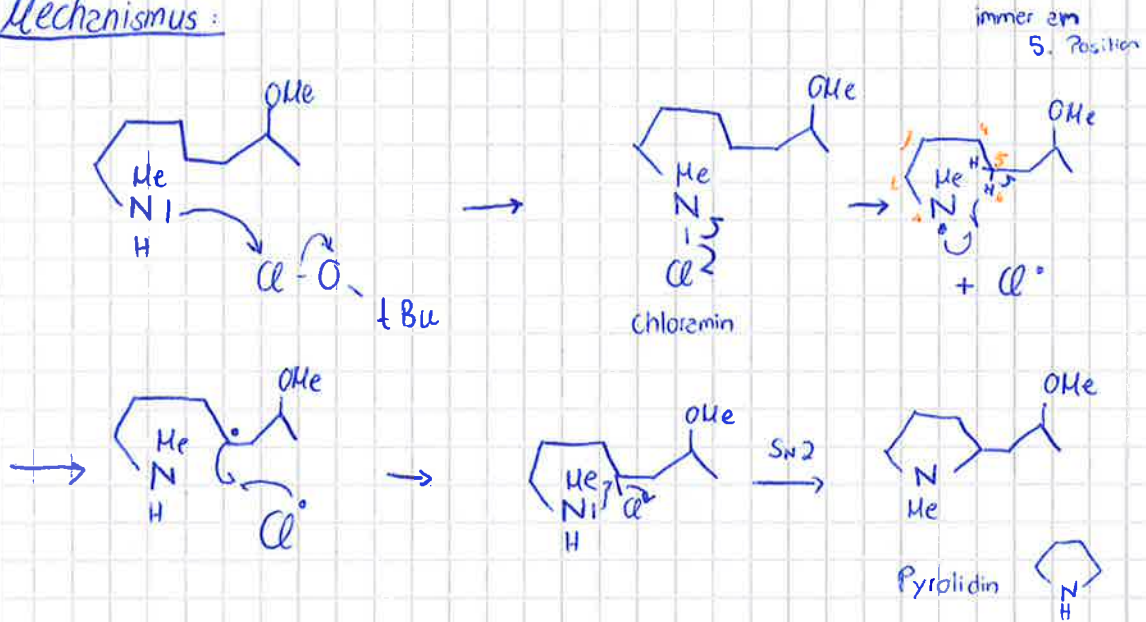
27.10.



1) $t\text{-BuO-Cl}$
 $-40^\circ\text{C} \rightarrow$
 $0^\circ\text{C}; \text{DCH}_2$
tert-Butyl-
Hypochlorit



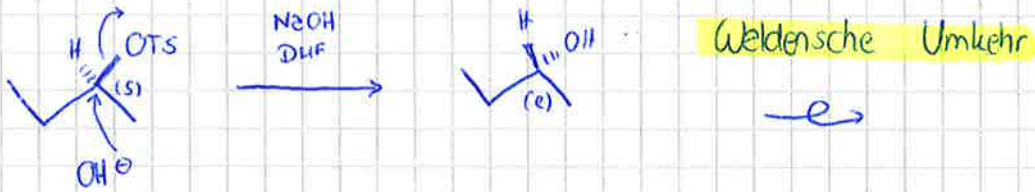
Mechanismus:



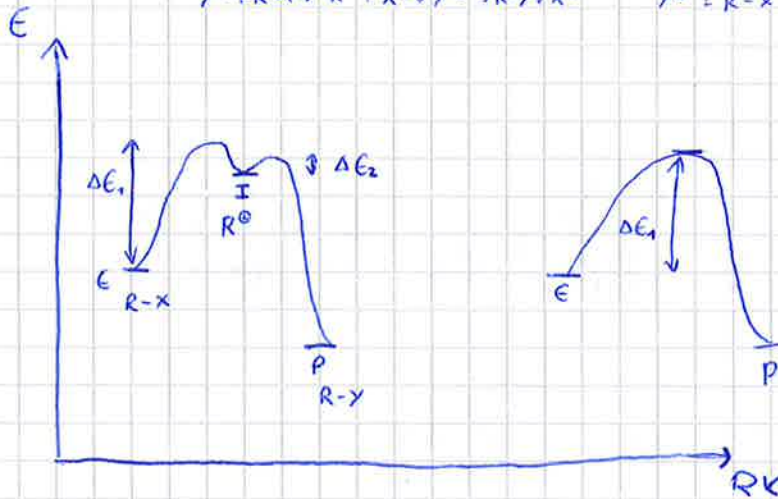
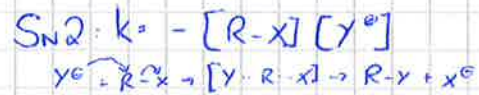
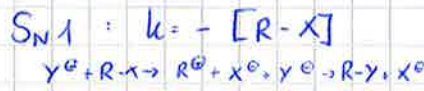
2. Teil beinhaltet eine nukleophile Substitution

Nucleophile Substitution am gesättigten C-Atom (sp^3)

- 1) Struktur des Substrats
 - 2) Beschaffenheit d. Abgangsgruppe
 - 3) " d. Nucleophile
- } Zusammenspiel folgt d. Mechanismus:
a) S_N1 b) S_N2



(sp^3)



S_N1

⋮

S_N2

Substrat

tertiäre

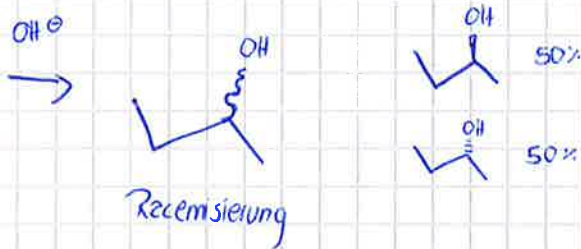
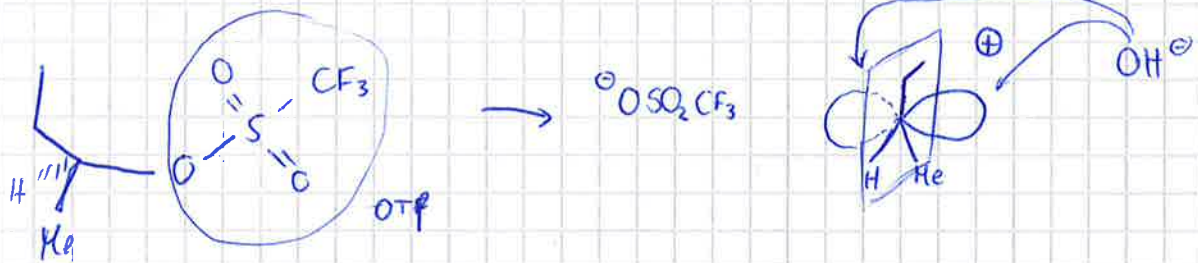
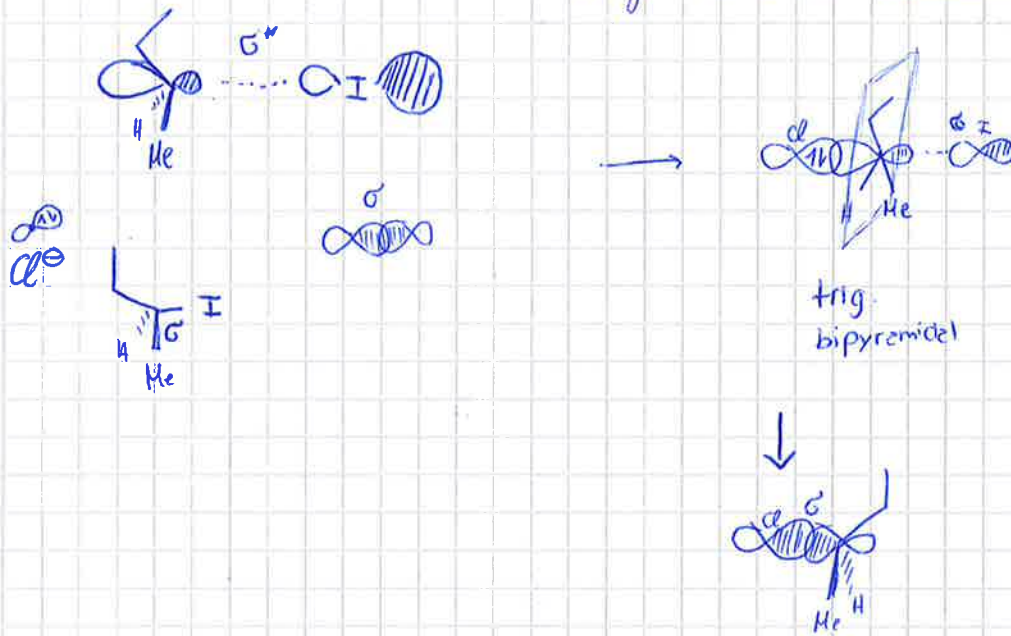
sekundäre

Me-X ; primäre

- Stabilität d. Carbeniumion
- Sterische Hinderung

- Carb. ion nicht stabil
- "keine" sterische Hinderung
- Abschlussh. am stereogenen C-Atom umgedreht

es geht immer um HOMO & LUMO

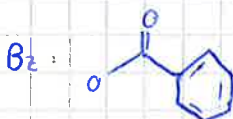
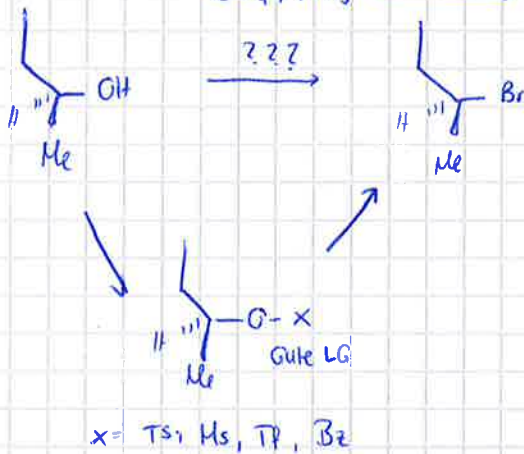


hartes/weiches Nucleophil:

wie polarisierbar ist es?

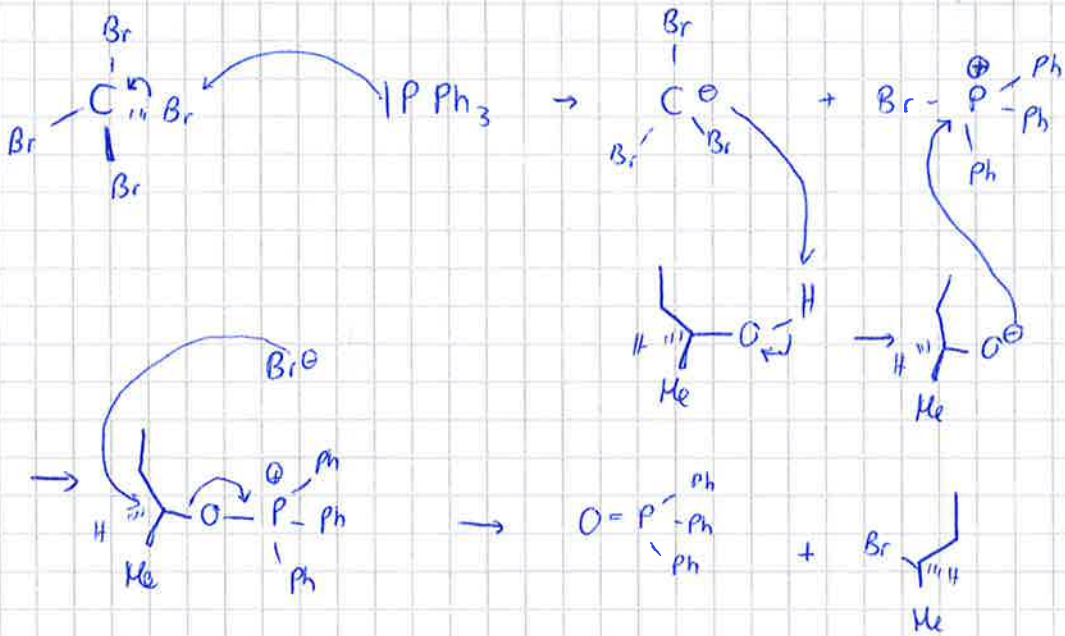
weiches bei S_N2 besser

CBr_4 i PPh_3 → Appel-Reaktion



Appel-Reaktion

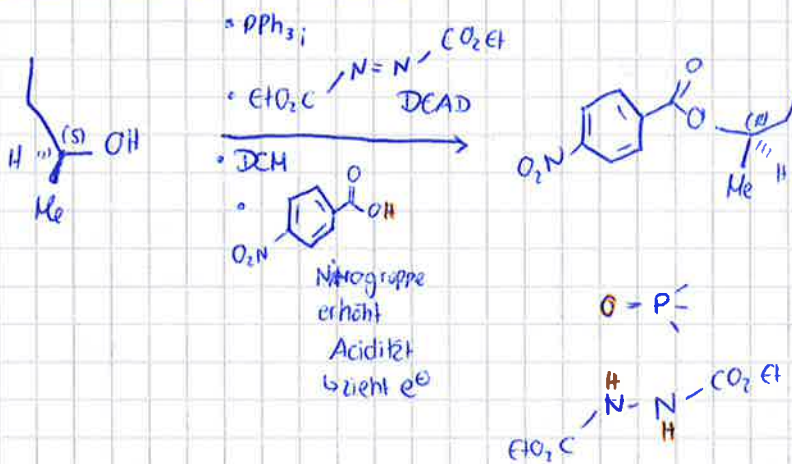
Alkohol Bromierung



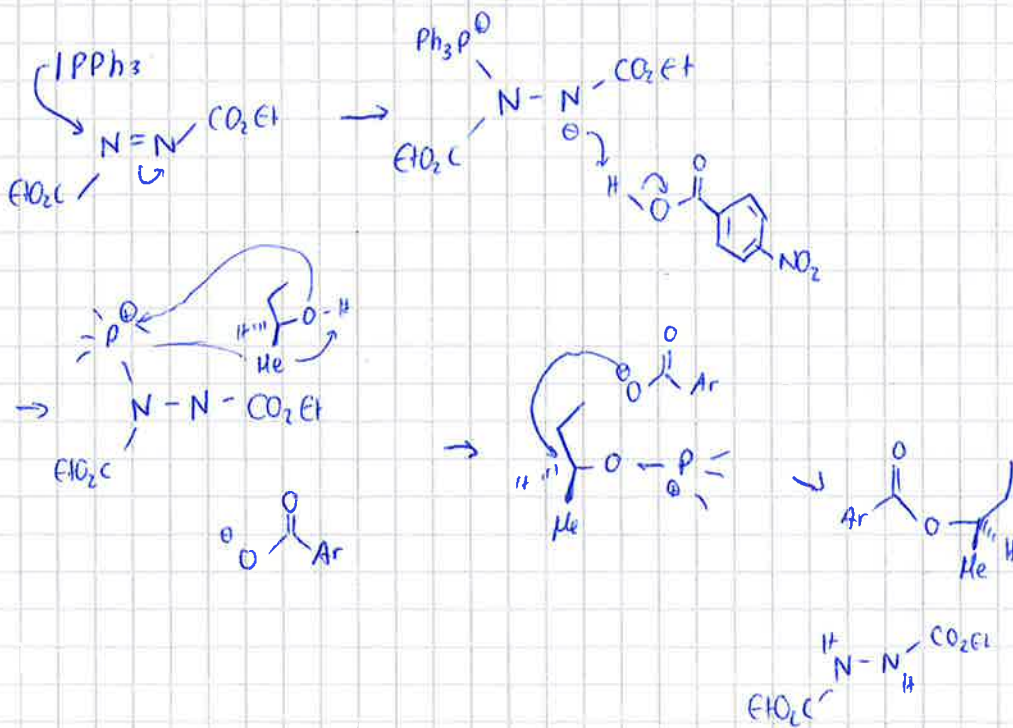
Alkohol mit Säure zu Ester

Mitsunobu-Reaktion

DEAD: Diethylazodicarboxylat



Mechanismus



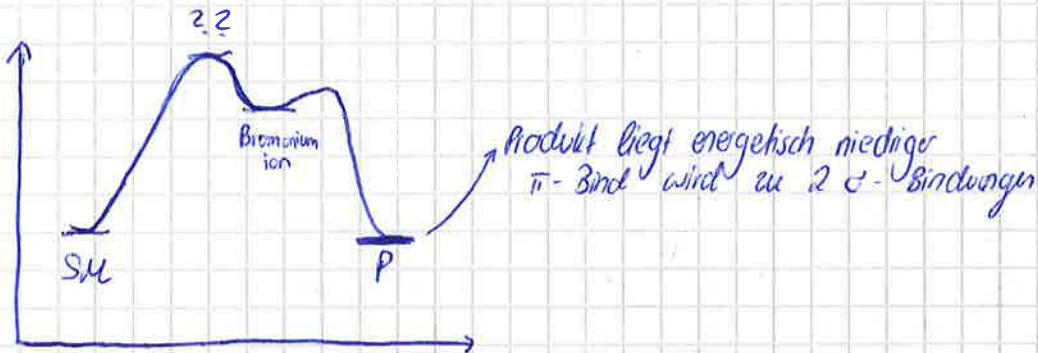
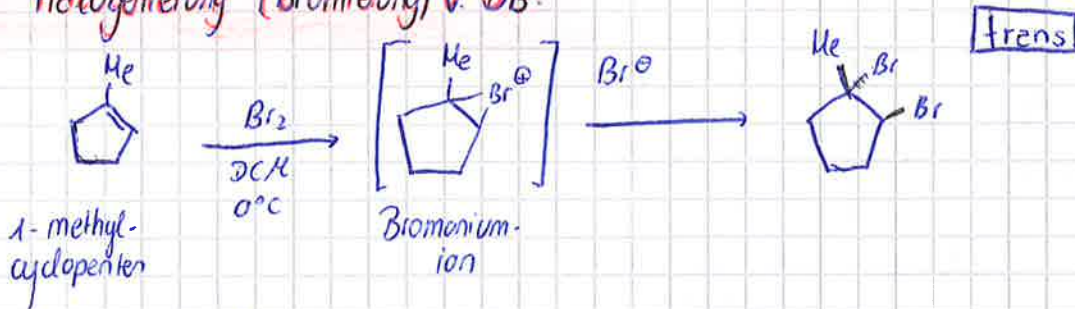
Elektrophile Addition an Doppelbindung

2.11.15

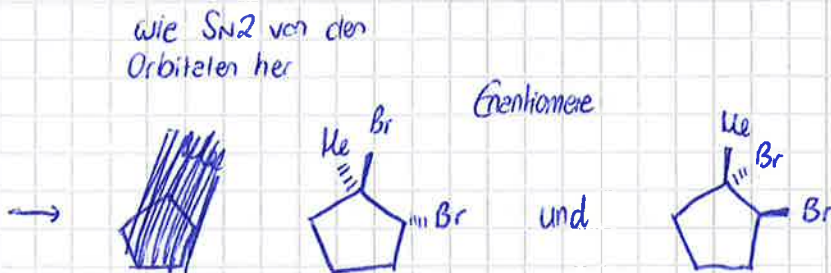
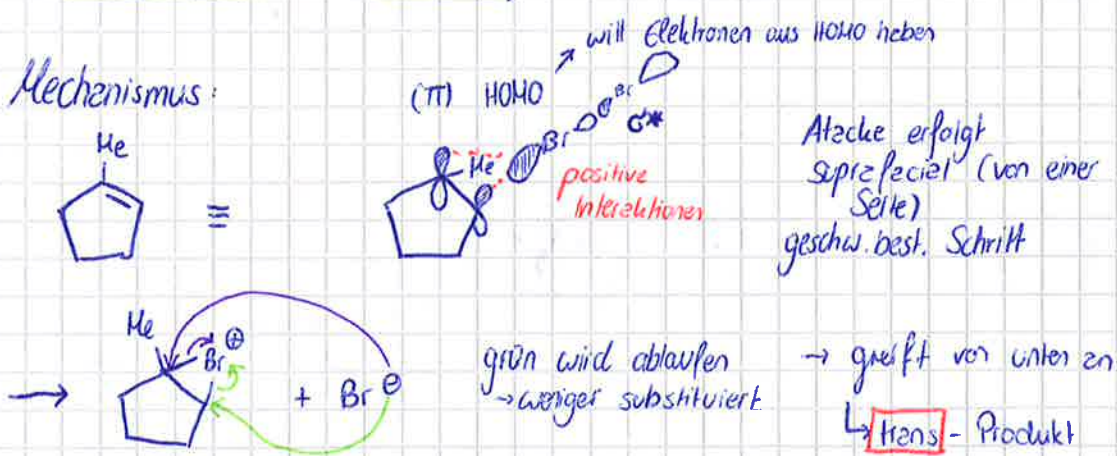
- 1) Regioselekt.
- 2) Chemo-selekt.
- 3) Stereo-selekt.

Markownikow-Regel \rightarrow Regiochemie

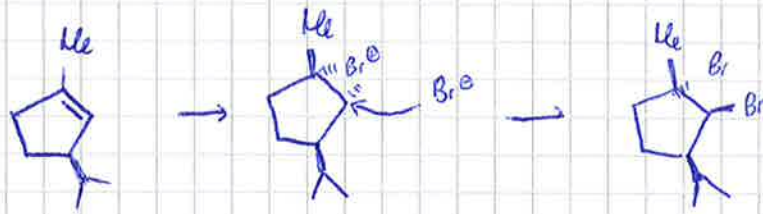
Halogenierung (Bromierung) v. DB:



Mechanismus:

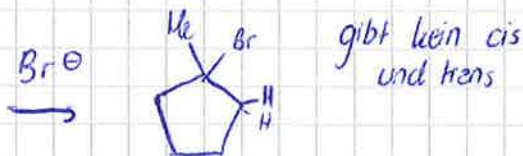
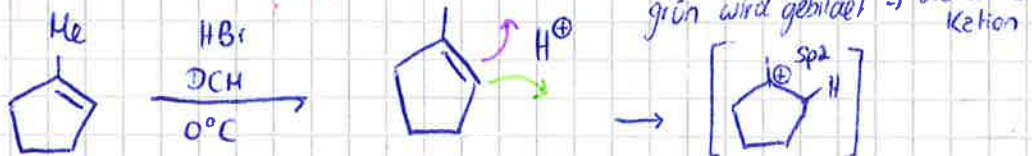


Substratkontrolle d. Stereocenters im SM (Startmaterial)



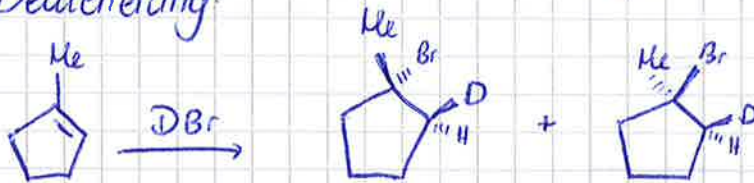
diesmal ohne
Erenhomer wegen
Isopropyl-Gr.

Hydrobromierung (Hydrohalogenierung)

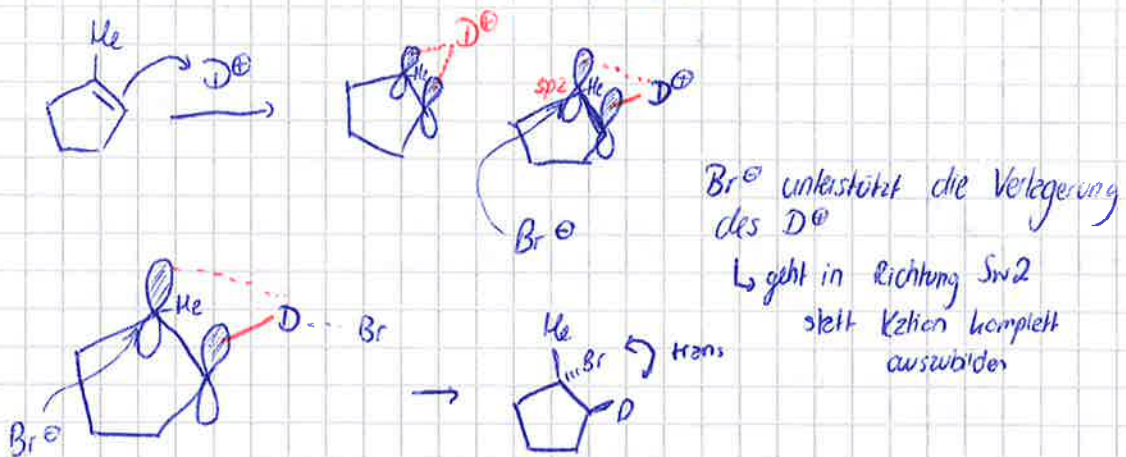


Deuterierung:

Diastereomere



sp^2 -Zentrum kann von beiden Seiten angegriffen werden

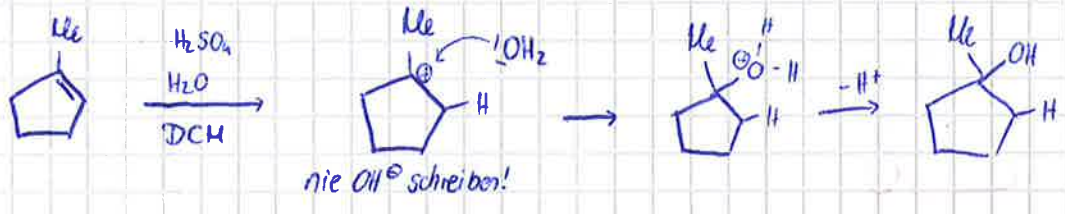


Hydrohal. : cis: tert/allyl/benzyl Kation (sehr stabiles Kation)

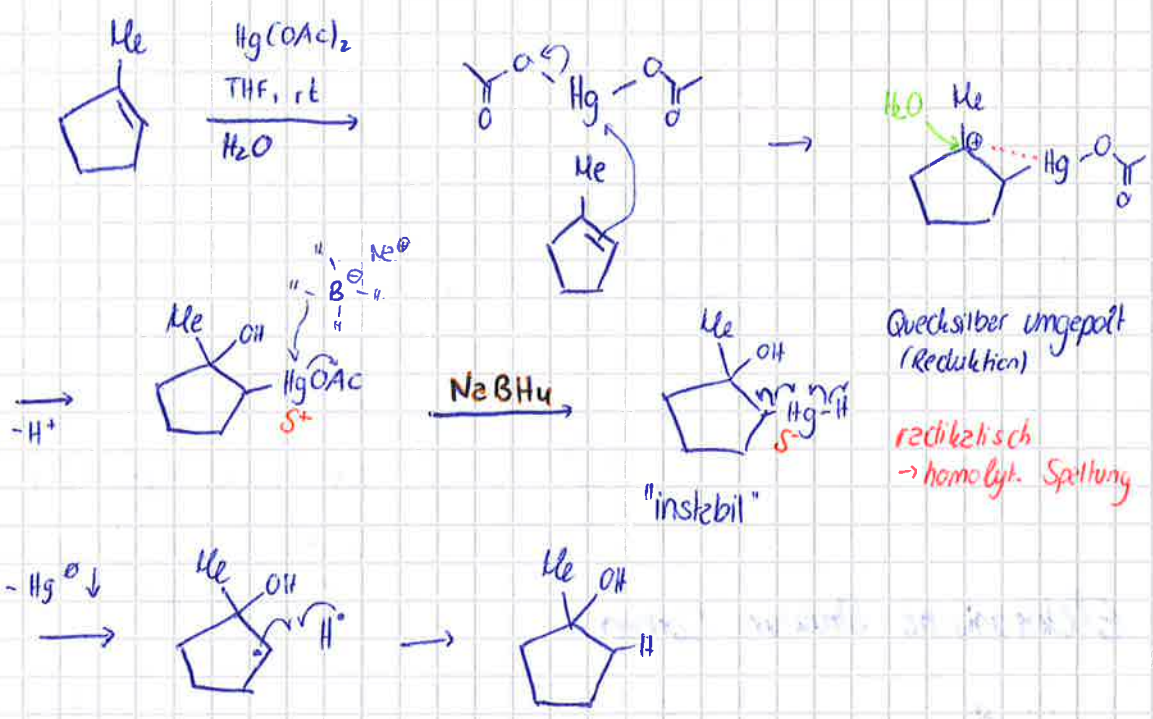
trans → sek/prim (weniger stabiles Kation)

Oxymercuration

(Äquivalent d. H_2O -Addition zu DB nach Markownikow)



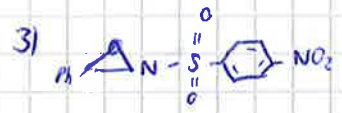
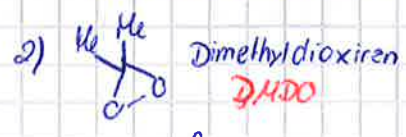
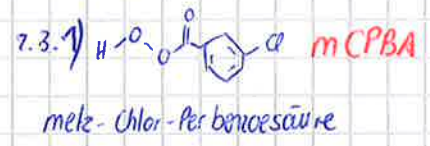
Oxymercuration (keine Säure notwendig) **milde Bedingungen**



Epoxidierung



Reagenzien: alle Persäuren

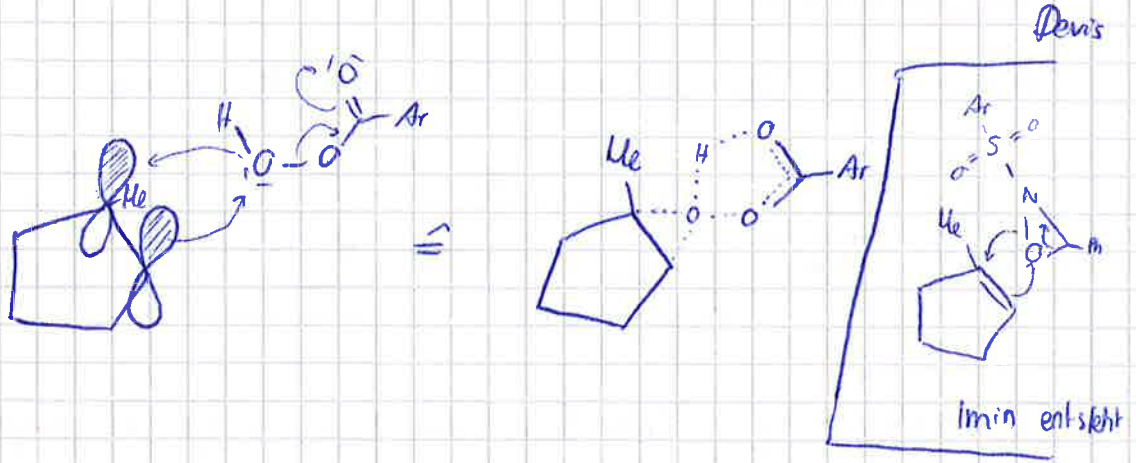


(wird aus Imid gemacht)

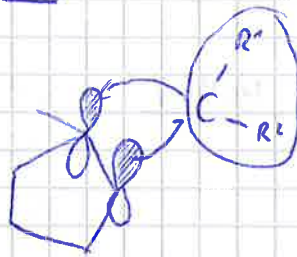
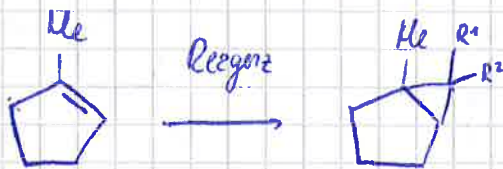
Mech.: nächste Seite



Mechanismus



Cyclopropanierung



Reaktive Zwischenstufe

Carben

Capto-destive Eigenschaften
nimmt gleichzeitig e^- auf
und gibt e^- ab

03.11.15

Elektronische Struktur Carben

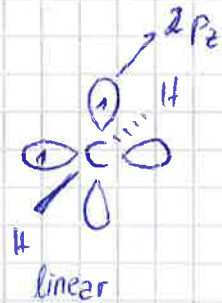


Methylen



6e⁻

gewinkelt

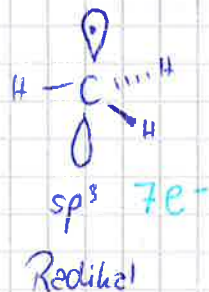
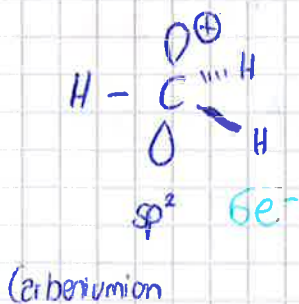


nur dann linear

energiel

10

Reaktive Intermediate



- I- Effekt Substituenten



Elektronenpaar wird besser in sp^2 stabilisiert als in p_z wenn es 2 e^- -ziehende Subst. gibt

Warum?

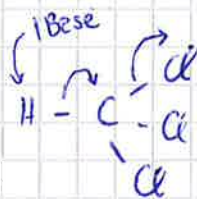
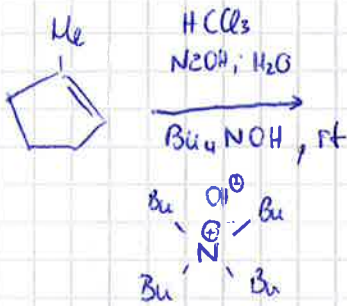
Singulett

Wellenfunktionen. Elektronendichte näher am Kern in sp^2 (wegen s), deswegen besser stabilisiert

singulett geschickter als Triplet, da die e^- des Kohlenstoffs, denen des Chlors sonst zu nahe kommen

Surrogate f. Carbene "Carbenoide"

Vorstufen zur α -Eliminierung



α -Eliminierung am selben C-Atom ein e^- -Paar derw und eins weg \rightarrow Carben entsteht

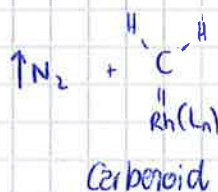
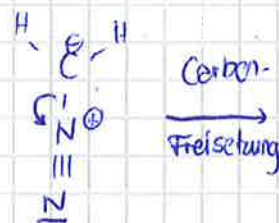


~~fehlt noch~~

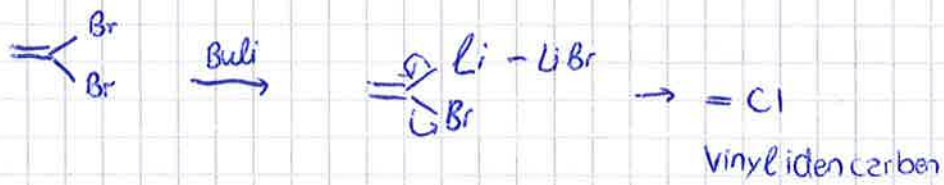
Diazo-Verb. \rightarrow Carbenbildung



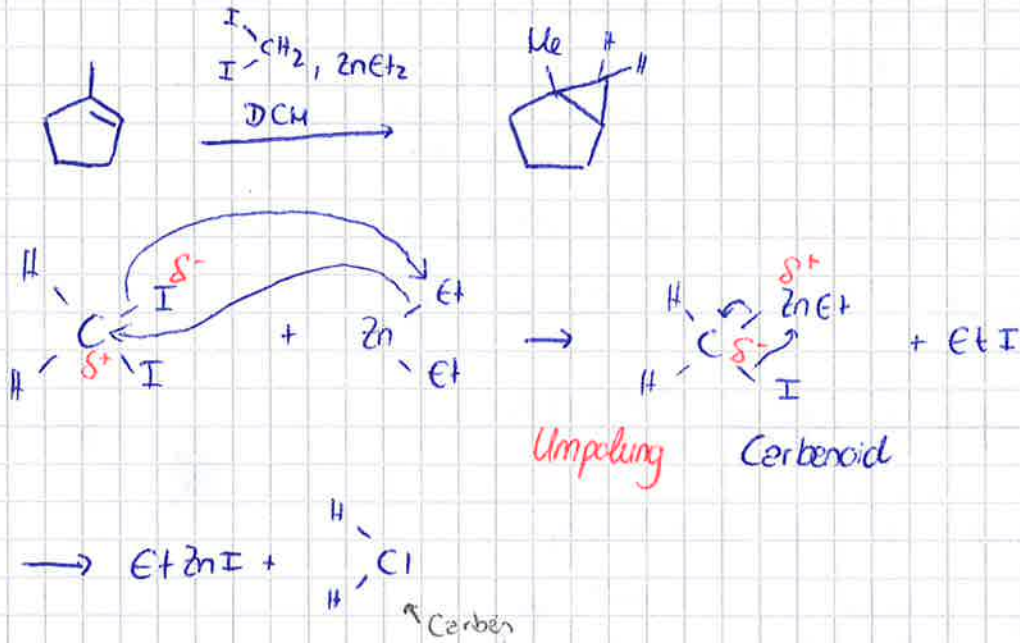
Diazo-methan reagieren mit Cu und Rh



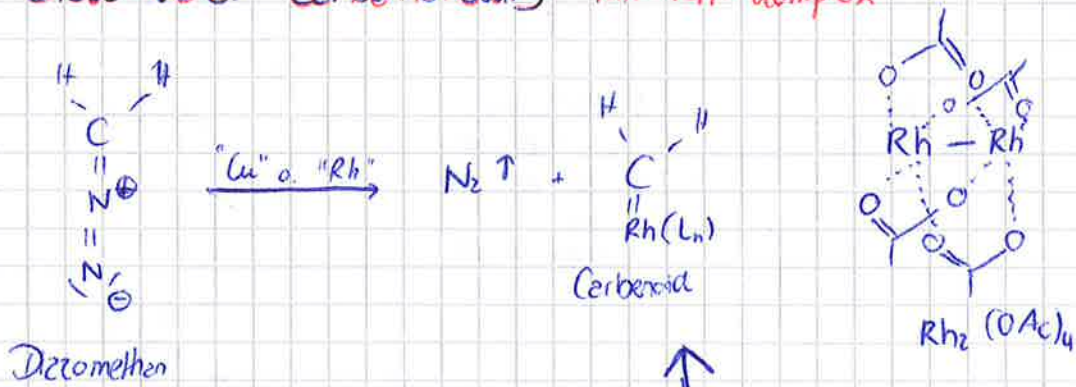
Fortsetzung auf nächster Seite



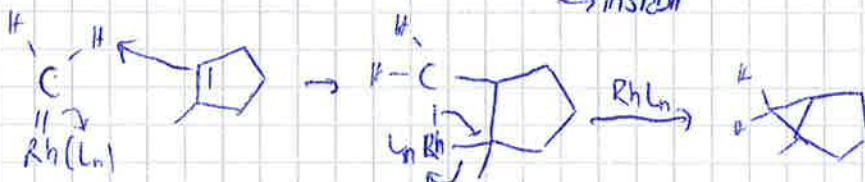
Simmons-Smith-Reaktion:



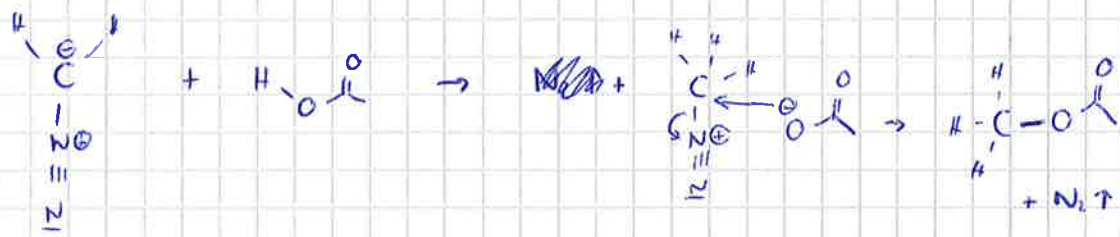
Diazo-Verb. Carbenbildung mit Rh-Komplex



Ladungstrennung
 können sich nicht
 mehr gegenseitig
 stabilisieren
 \rightarrow instabil

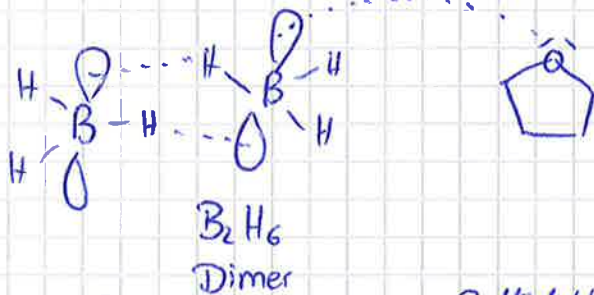
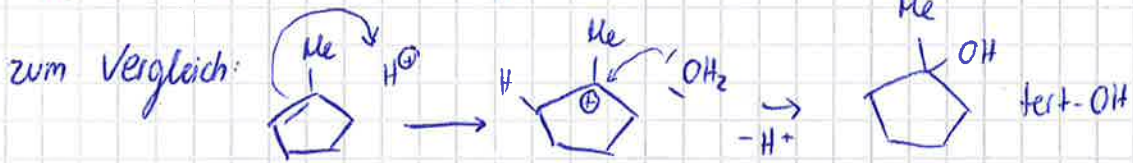


Diäzomethan kann ganz unterschiedliche Produkte ergeben, je nach Reagenz.

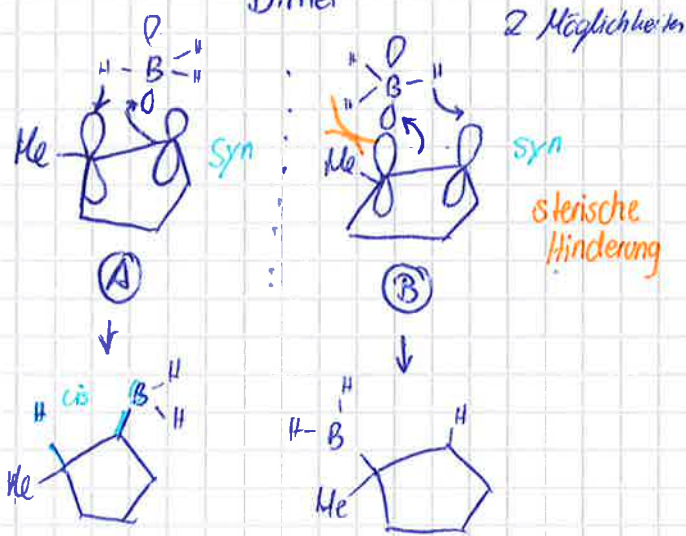


Hydroborierung

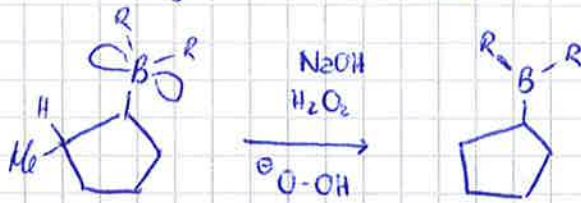
(anti-Markownikow)



THF nimmt man gern wegen den freien e^- kann Dimer aufbrechen

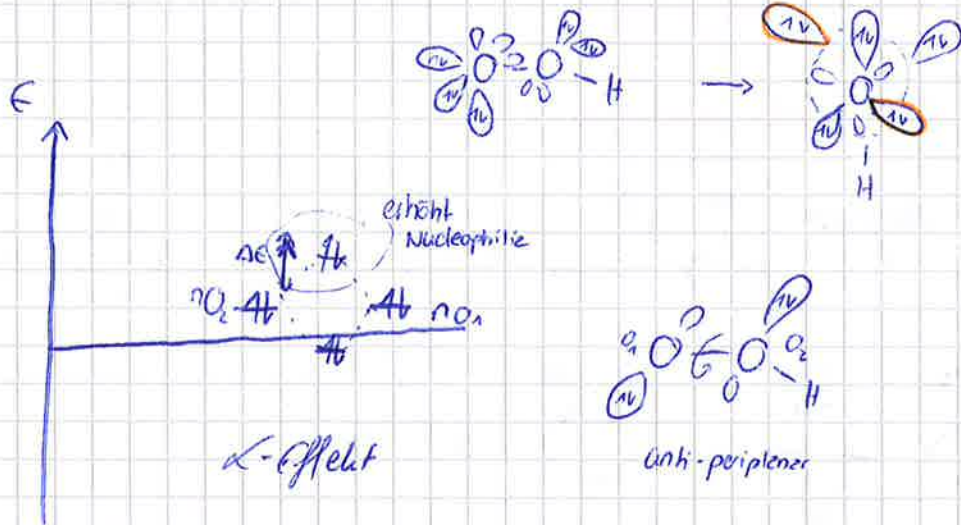


Quenching (Aufarbeitung)



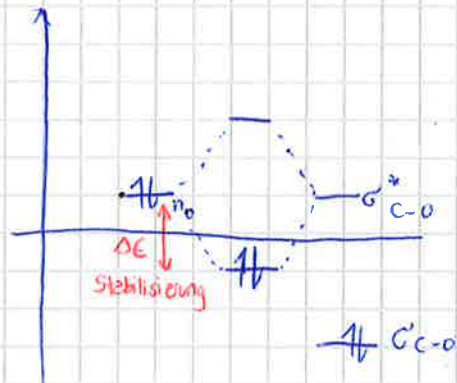
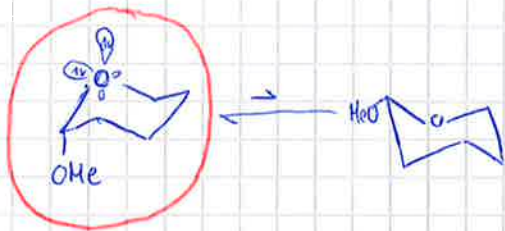
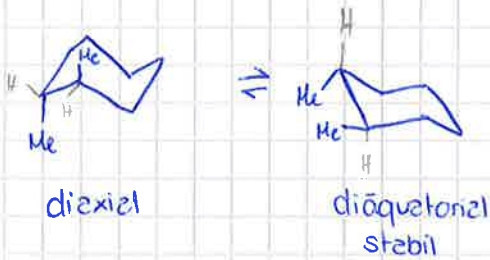
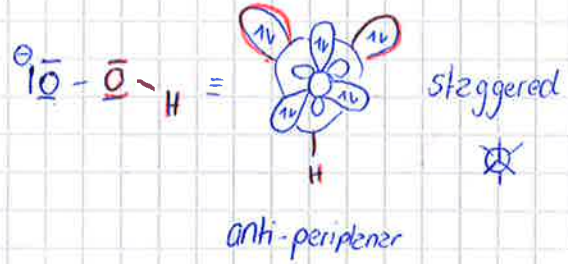
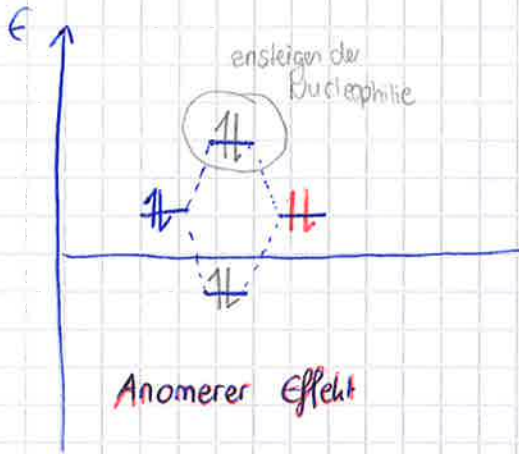
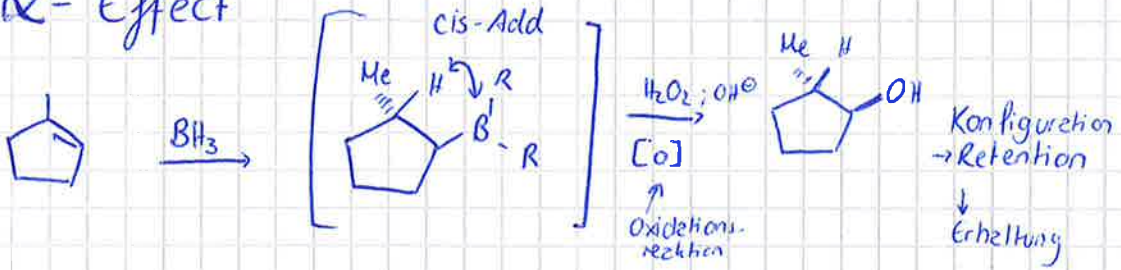
OH^- vs OOH^-

Nucleophilen!! wegen α -Effect

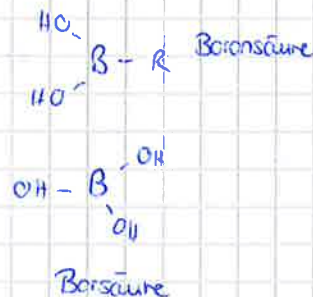
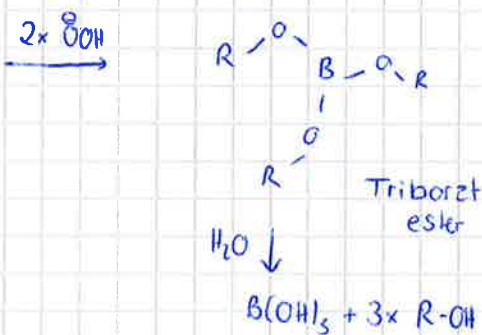


hier
sehen
sich
offen

α -Effect



Mechanismus (2. Teilschritt)



B. Sharpless 1980s Asymmetric epoxidation (katalytisch) (SAE)

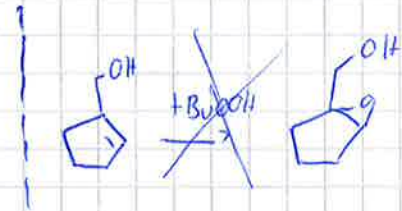
Bisher



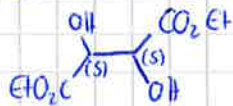
1) Allylkohol



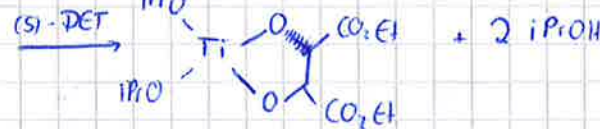
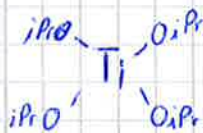
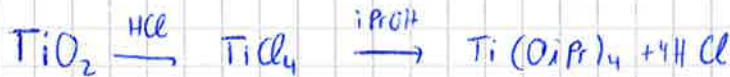
5-10% $Ti(OiPr)_4$
 10-20% DET (s)
 1 eq + BuOOH
 4 ÅHs DCM
 -78°C (-20°C)



DET:



(S,S)-Tartret

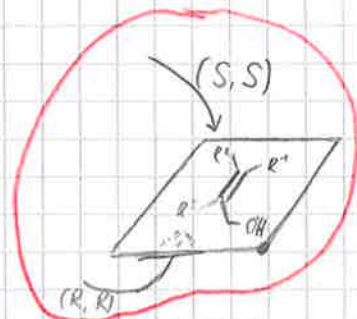
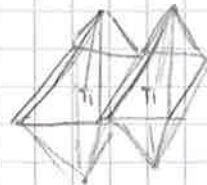
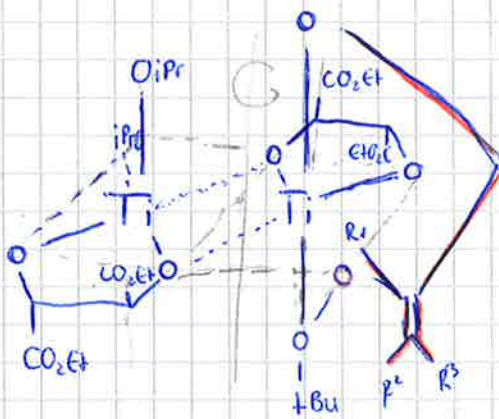


1 x Ti
 4 x iPrOH

 5 Komp

1 x Ti
 2 x iPrOH
 1 x DET

 4 Komp

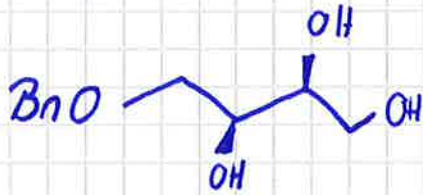
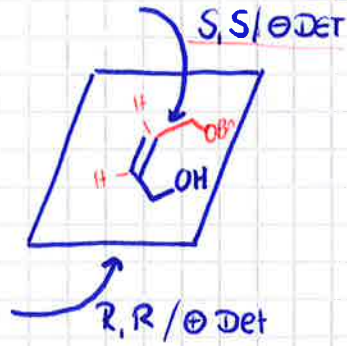


bei uns:

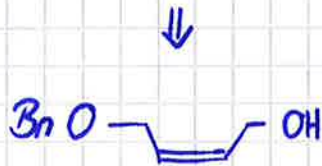


OC

16.11.15

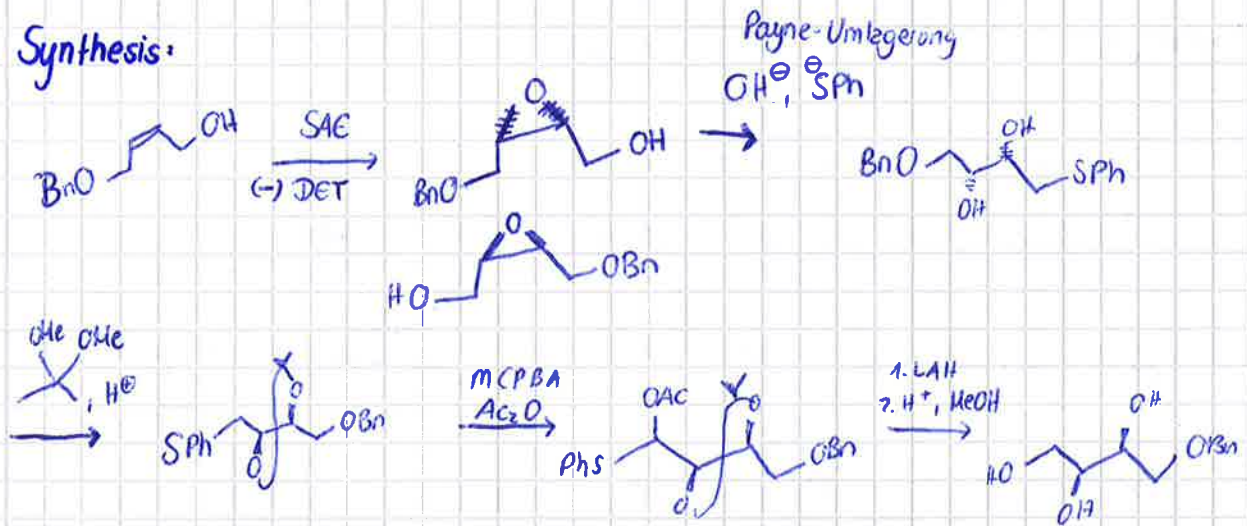


threitol
"syn" → man braucht Z- Allylalkohol

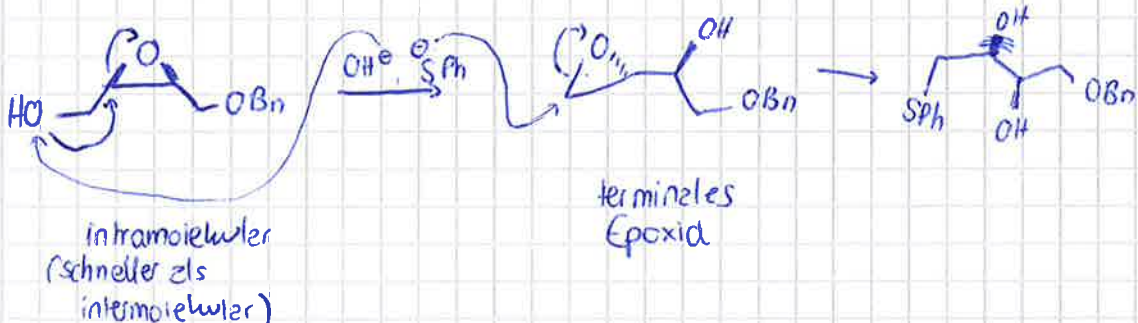


BnO = O...

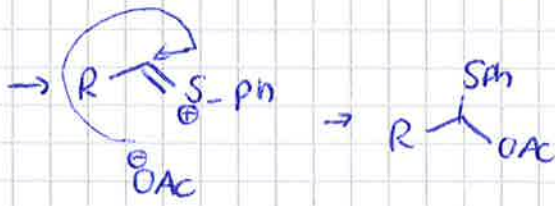
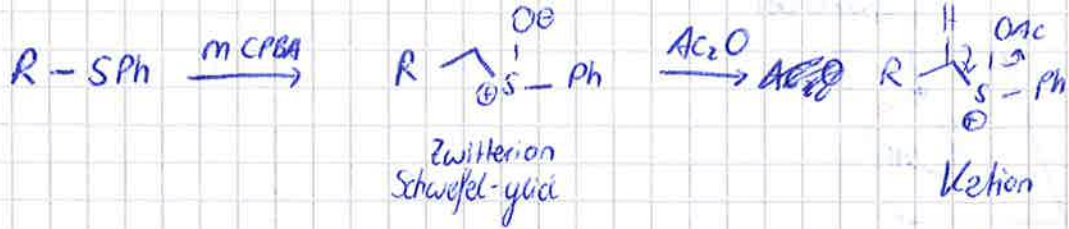
Synthesis:



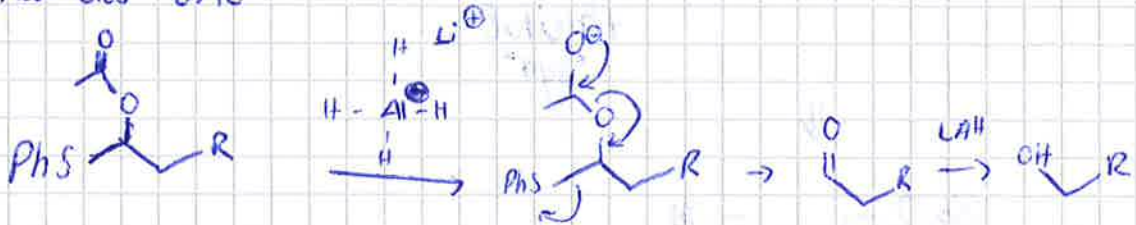
Payne-Umlagerung:



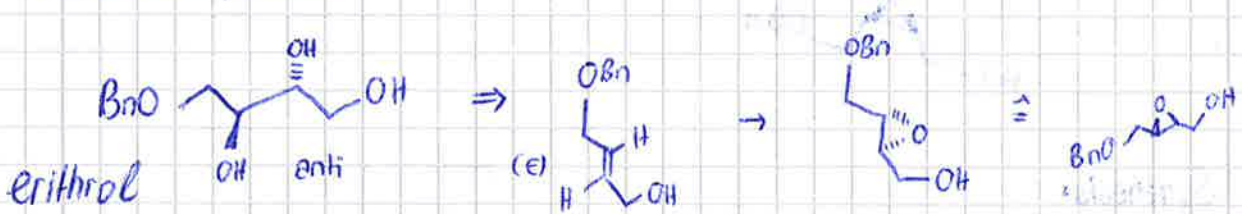
Pummerer-Umlegung



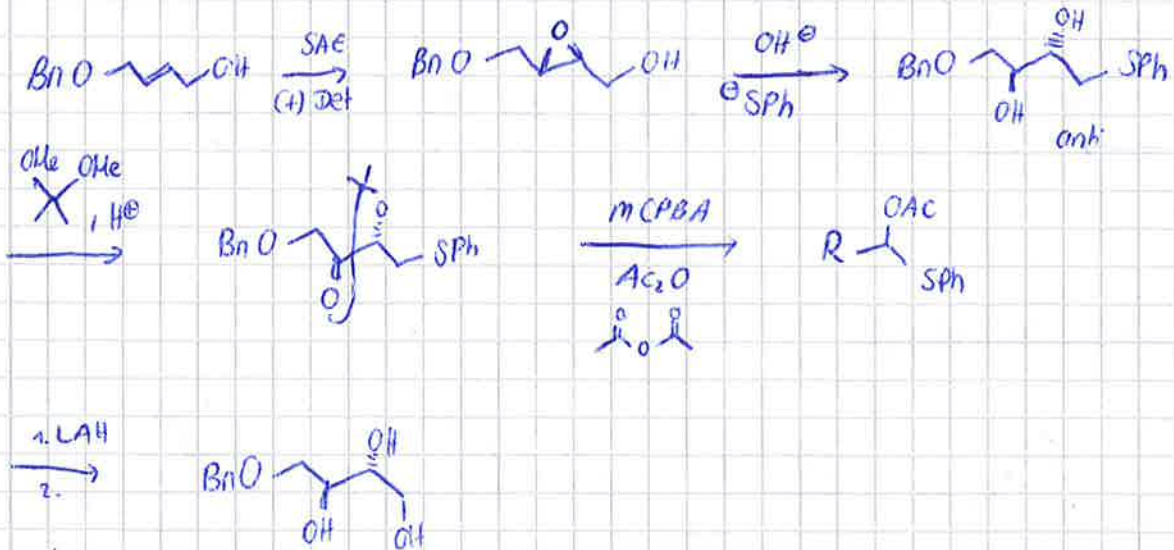
Red. des OAc



2. Beispiel

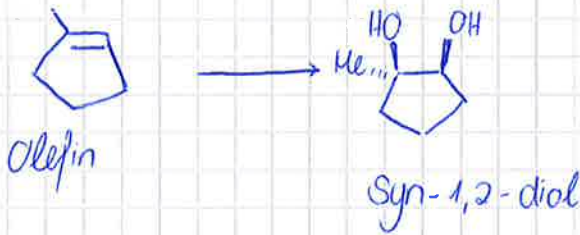


Payne-Umlegung kann nur die Stereochemie von C_3 ändern.
 C_2 muss schon richtig sein. \rightarrow deswegen R,R (+) DET



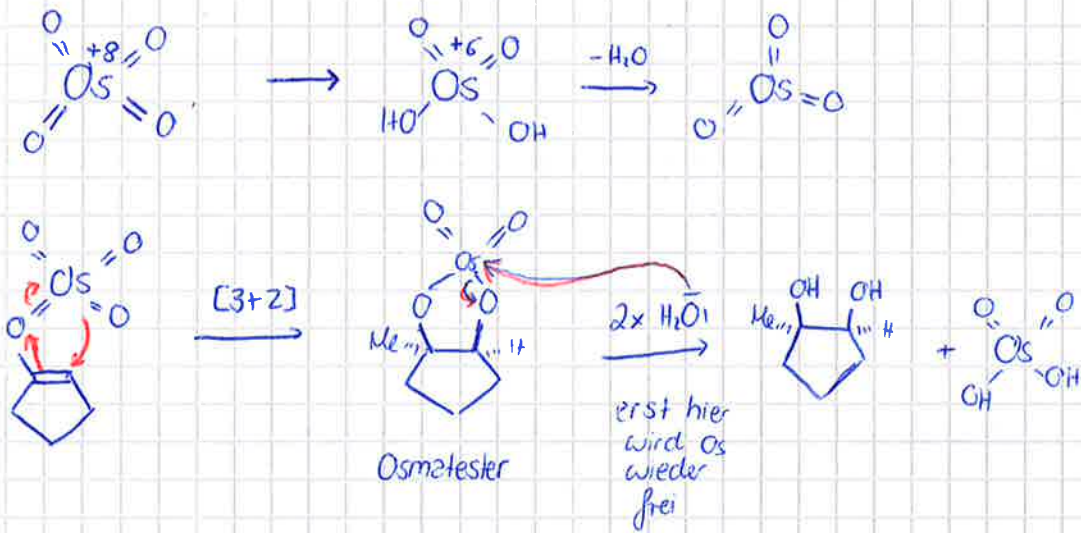
Dihydroxylierung

- Syn- Addition an Doppelbindungen



Reagenzien: OsO_4 (cat.)
 NMO (stöch)
 Aceton/ H_2O

Mechanismus

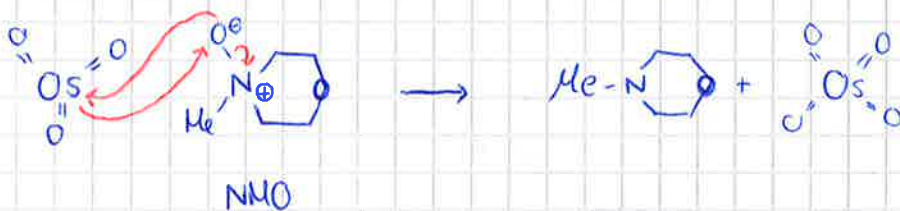


OsO_4

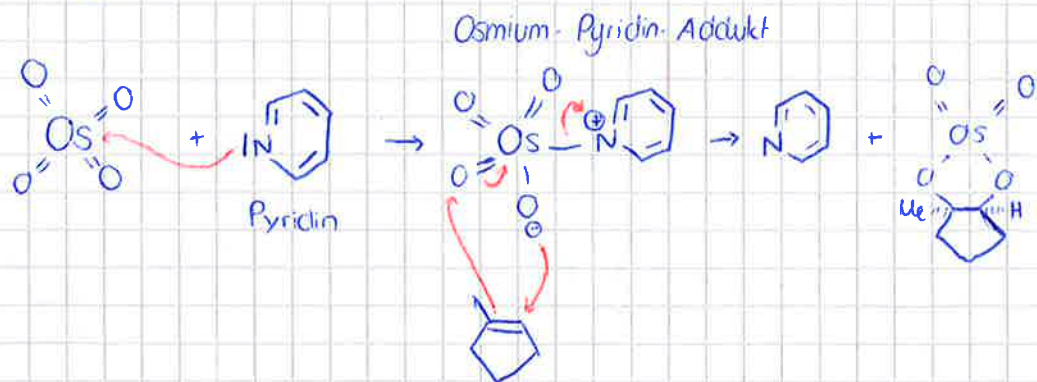
- teuer: 1g = 235€ \rightarrow stöch. no go
- sehr giftig T^+
- flüchtig bei RT $\rightarrow \text{K}_2\text{OsO}_2(\text{OH})_4 + \text{K}_3\text{Fe}(\text{CN})_6 \xrightarrow{\text{in situ}} \text{OsO}_4$

Reoxidation

NMO: N-methylmorpholin-N-oxid



Katalysatoren:

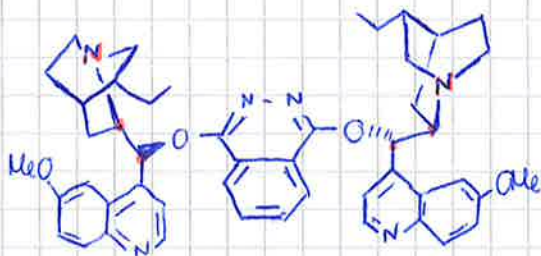


- tert. Amin beschleunigt 3+2
- Ligandenbeschleunigung
- ↳ Ansatzpunkt für asymmetrische Katalyse

Asymmetrische Dihydroxylierung (AD)

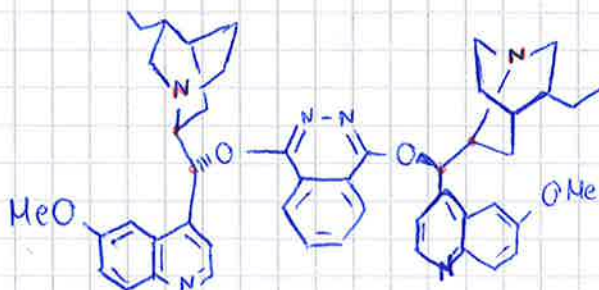
- Chiralität durch enantiomere Liganden
- Reagenzmischung kann fertig bestellt werden

AD-Mix β ($K_2OsO_2(OH)_4$, $K_3Fe(CN)_6$, K_2CO_3 , $(DHQD)_2$ PHAL)



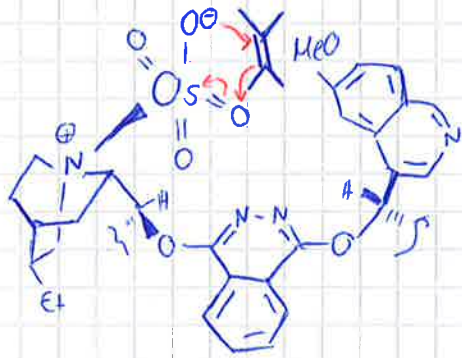
$(DHQD)_2$ PHAL = Dihydrochinidin - Phthalazin

AD-Mix α (....., $(DHQ)_2$ PHAL)



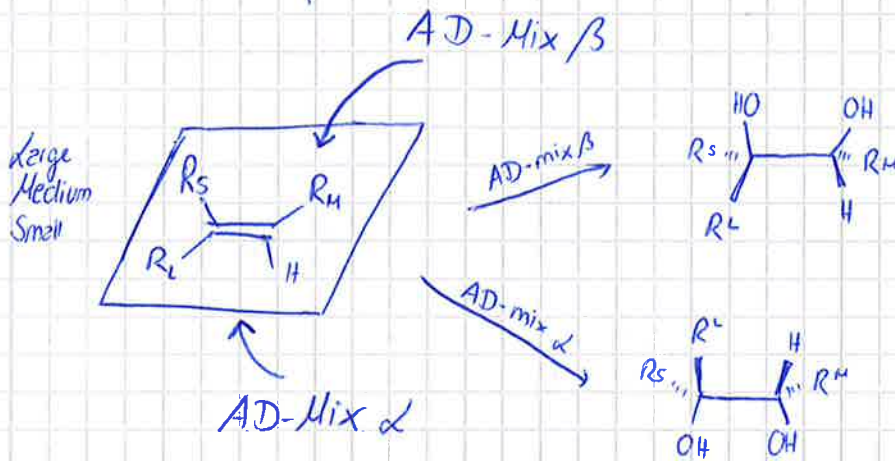
$(DHQ)_2$ PHAL = Dihydrochinin - Phthalazin

Übergangszustand

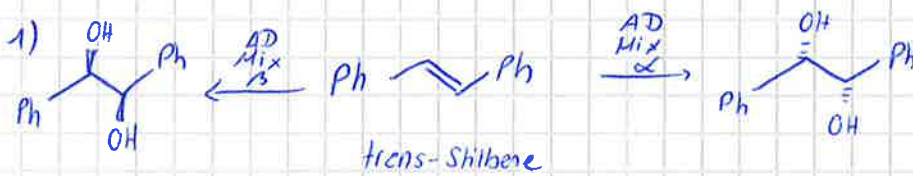


U-förmige Bindungsstelle

AD-Merkhilfe



Beispiele



20.11.15 → Vorhandene optische Aktivität im Substrat:

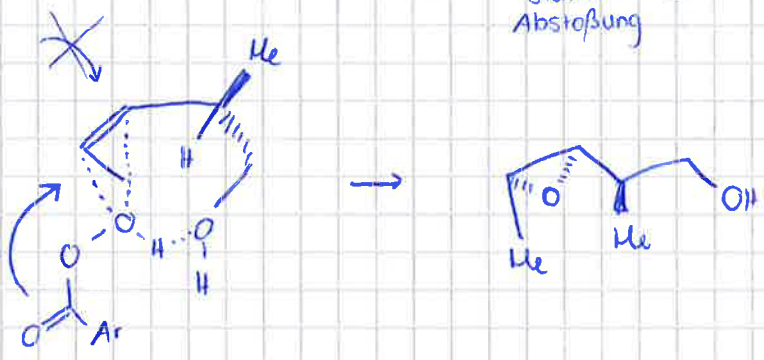
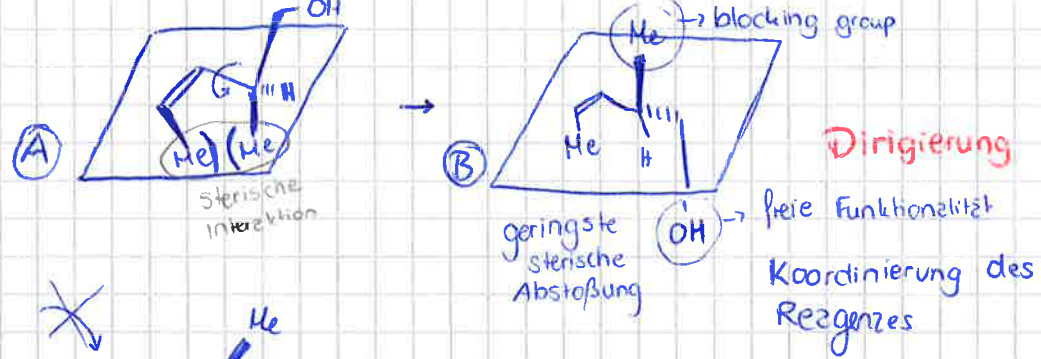
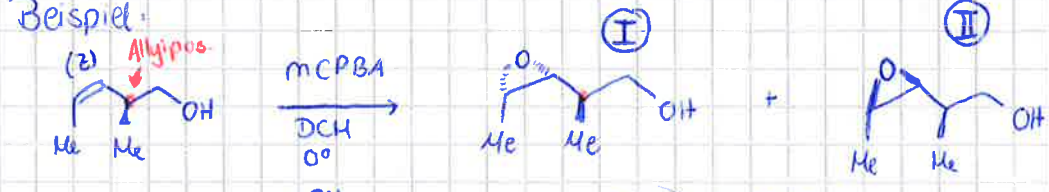
→ Diastereocontrolled reaction

↳ diastereoface → immer bei el. Add an DB

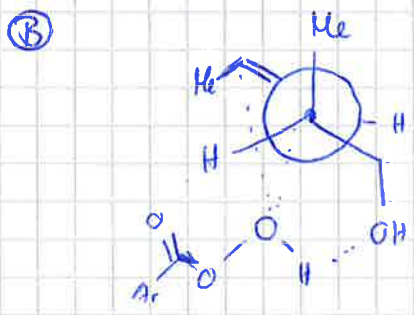
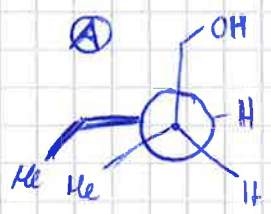
Bisher: (SAE; SAD) → enantioface controlled reactions

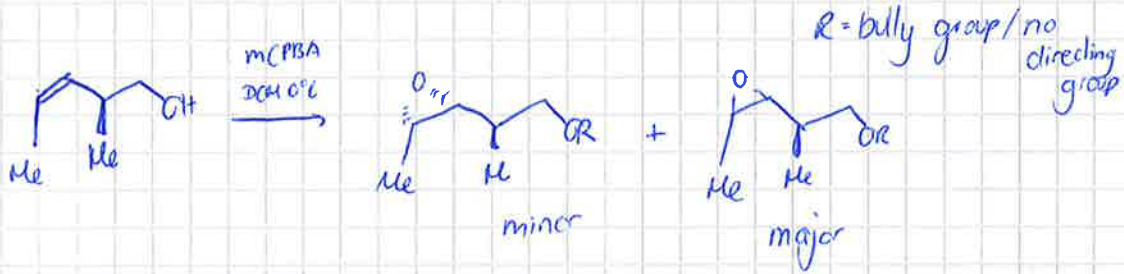
→ 1,3 Allylstrain Modell ≙ diastereoface Kontrolle bei Add an DB

Beispiel:



1,3 Allylstrain in Newman



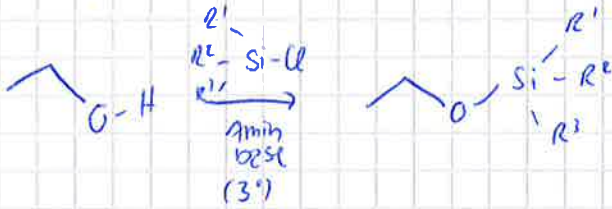


$R = \text{bulky / non-directing (Schutzgruppe)}$

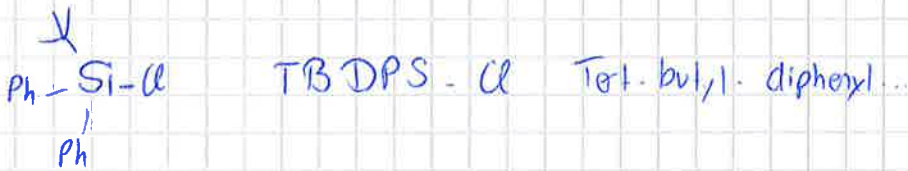
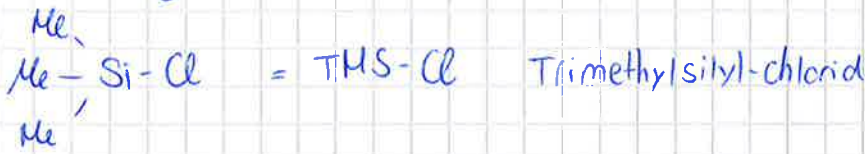
$R = t\text{Bu}$; Silylether

schwer zu spalten

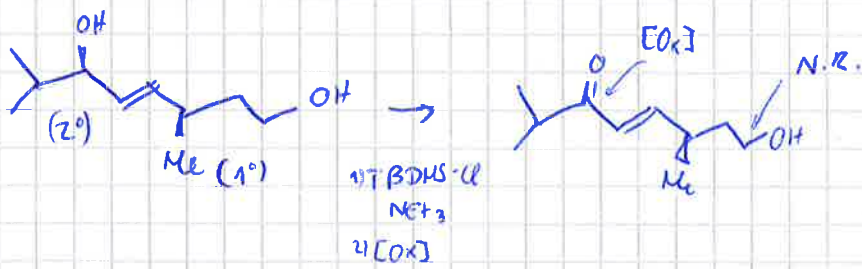
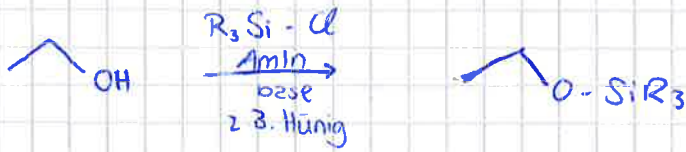
leicht zu spalten



Schutzgruppen



Mechanismus



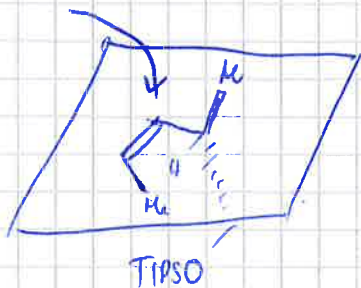
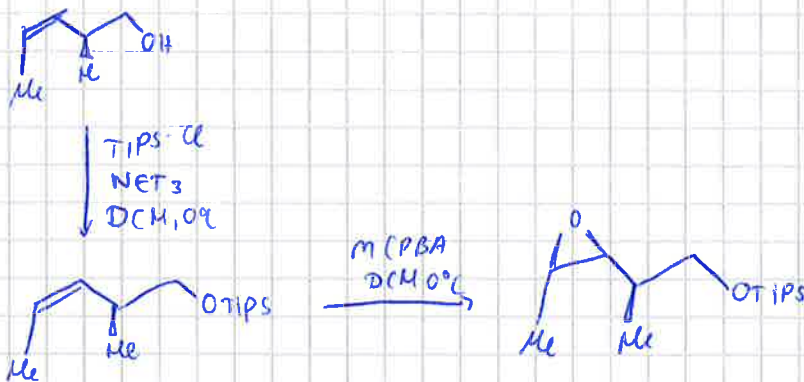
Entschützung



TMS; TES; TBDMS ; TBDFS; TIPS
TBS

→
 Zunahme d. Stabilität

TMS leicht einzuführen / leicht abzuspalten / kleinster (sterisch)
 TIPS am schlechtesten einzuführen / schlecht abzuspaltbar

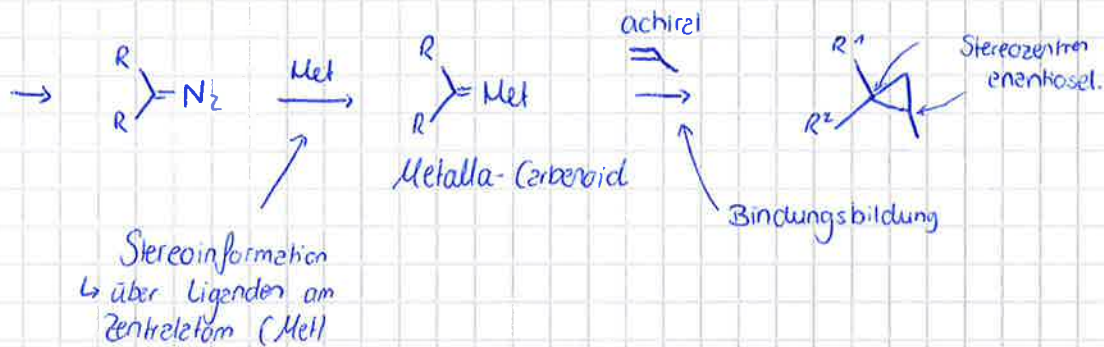


OC 23.11.15

Cyclopropanierung (katalytisch, enantioselektiv)

→ enantioface differentiating reaction (katalytisch)

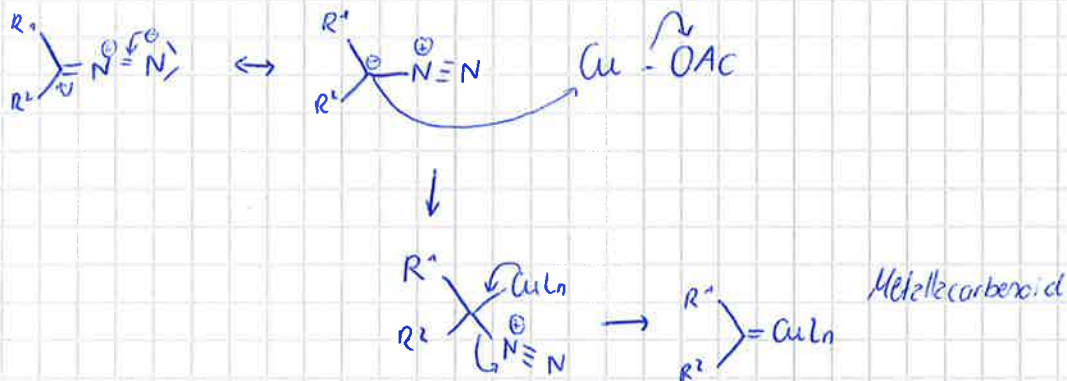
Bisher: $\begin{matrix} R \\ | \\ R-C \\ | \\ R \end{matrix} Cl$ Carben (e^- -sextett, reaktives Intermediat)



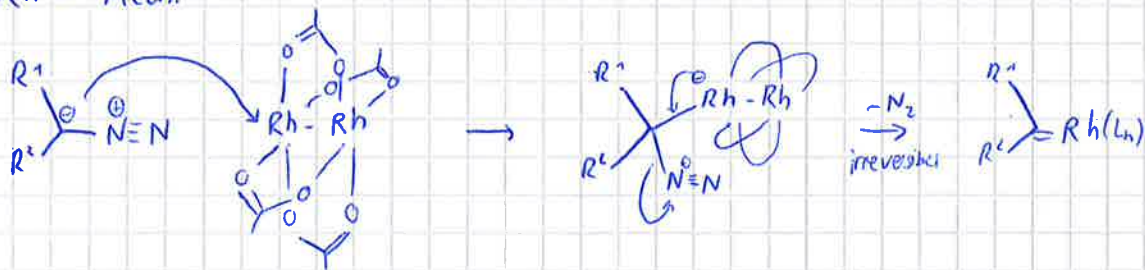
• Cu^I -katalysiert: Ligand (Semicorrin)

• Rh^I -katalysiert: Ligand (Pyroglutamat)

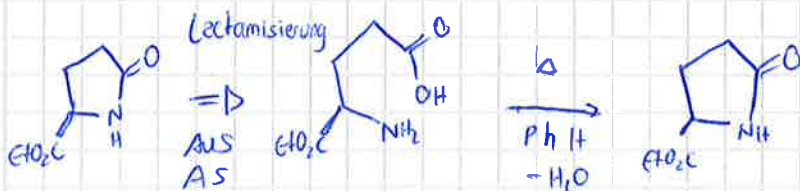
Mechanismus



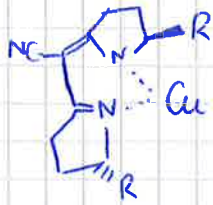
Rh^I -Mech.



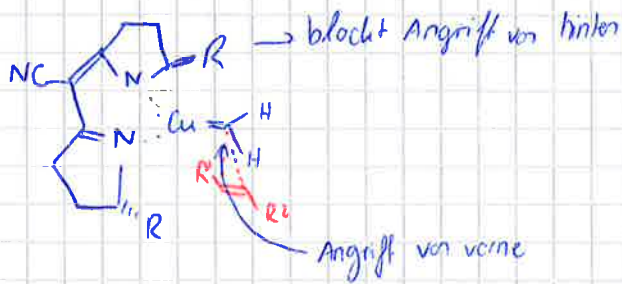
Pyroglutamat



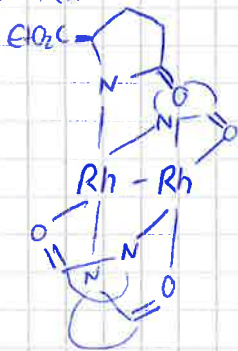
Semicarbin ligand Cu^{I}



Chirales Metalle-carbenoid (Cu^{I})

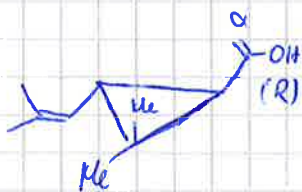


Bei Rh^{I}

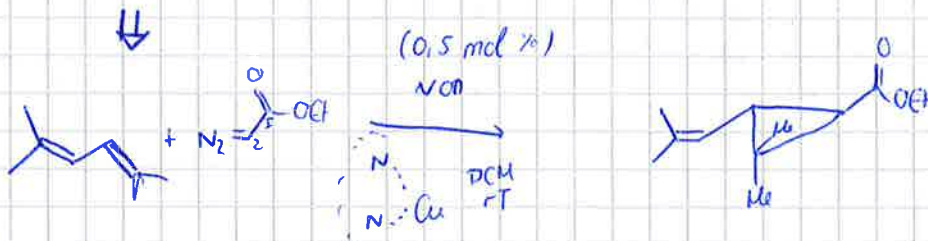


Chrysanthemic acid (Pyrethroids)

Insektizide
(im Auto)



R = variabel \rightarrow Pyrethroide

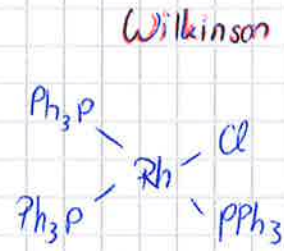
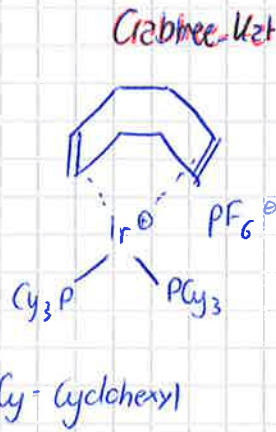
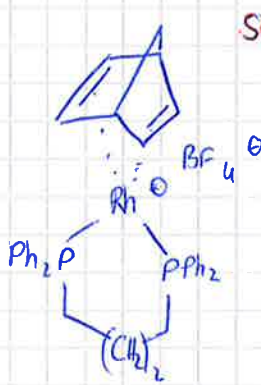


\downarrow NaOH
THF
 H_2O

Chrysanthemic acid

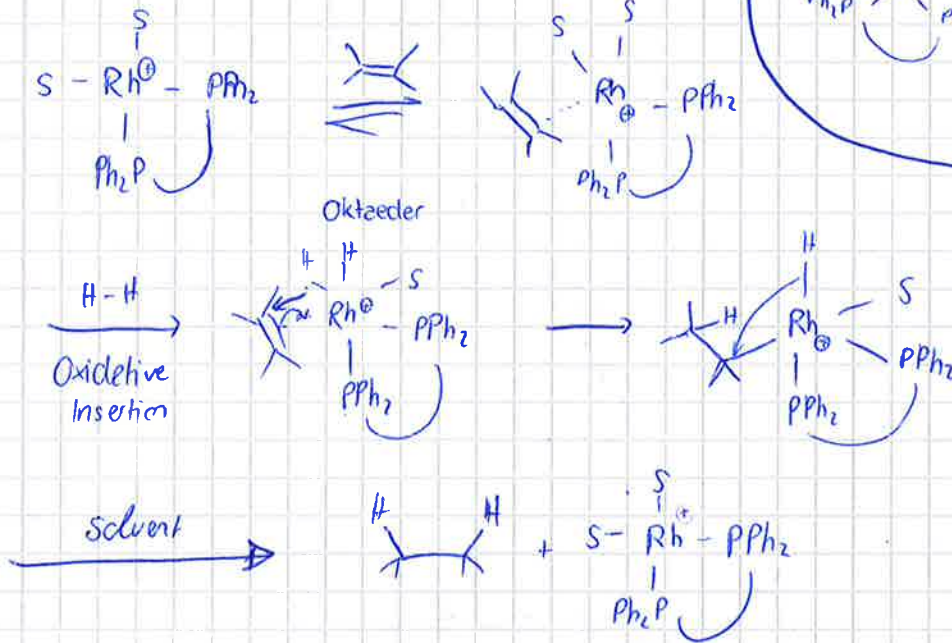
Hydrierung v. DB

- inherent Metall-katalysiert
- Transfer v. 1 Molekül H_2 auf DB

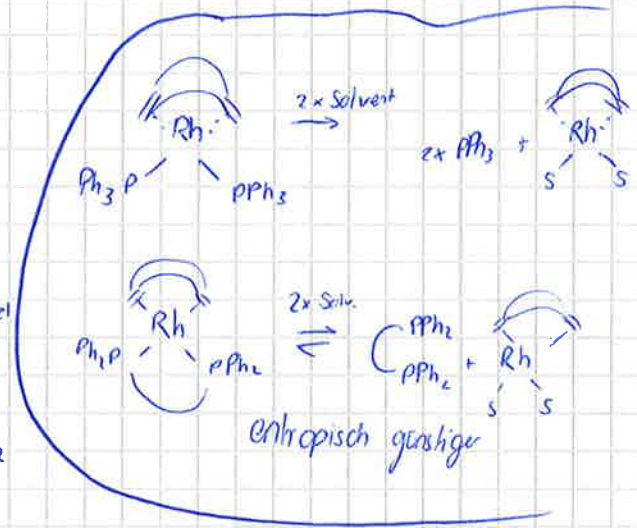


Mechanismus

Schrock:

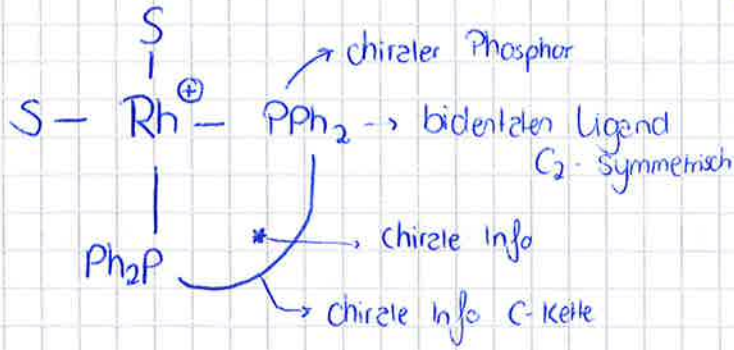


trigonal bipyramidal

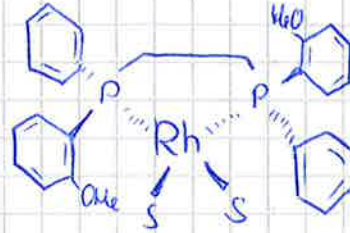
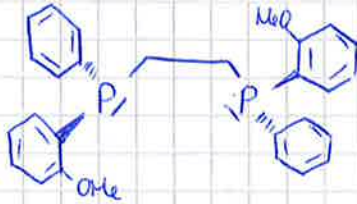


24. 11.15

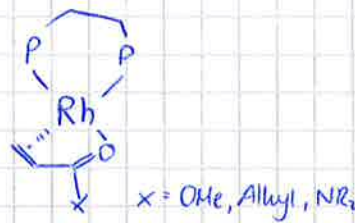
Monsanto-Prozess



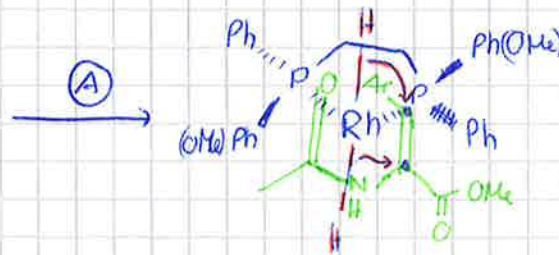
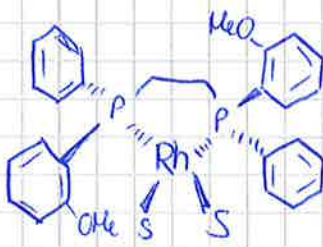
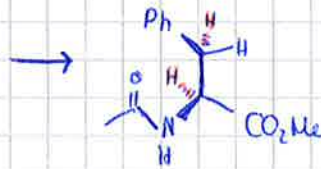
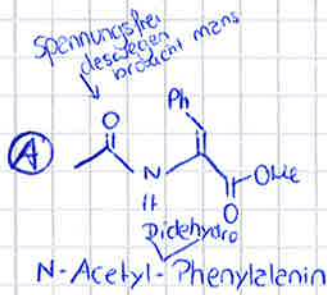
DIPAMP



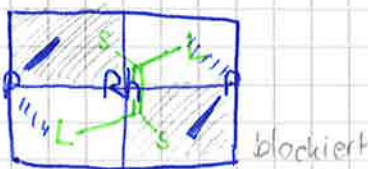
noch auf Karteikarten schreiben!
 done ✓



nicht isolierte DB
 2-fache Koord. } erhöht die ee-Werte

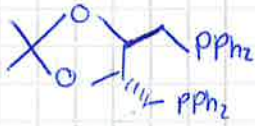


- Quadrantenmodell

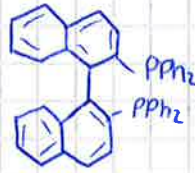


e-DB gehen besser als z-DB

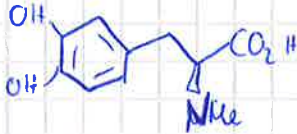
DIOP ex Tartracid
Weinsäure



BINAP
meist verwendet



L-DOPA
für Parkinson



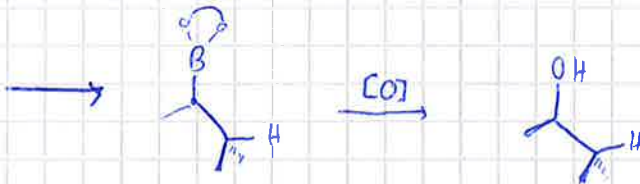
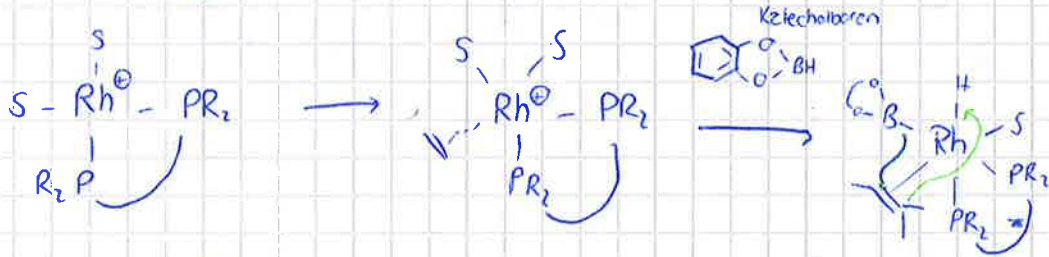
↑ das auch noch

1,2-Dihydrobenzol ≙ Kelecho

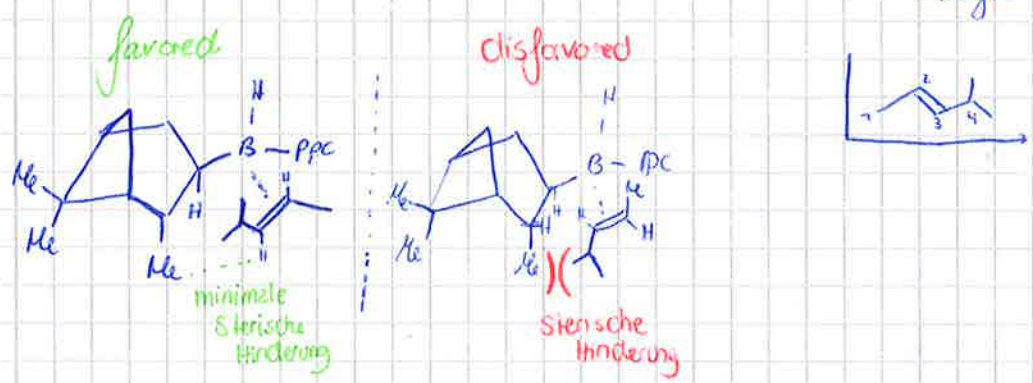
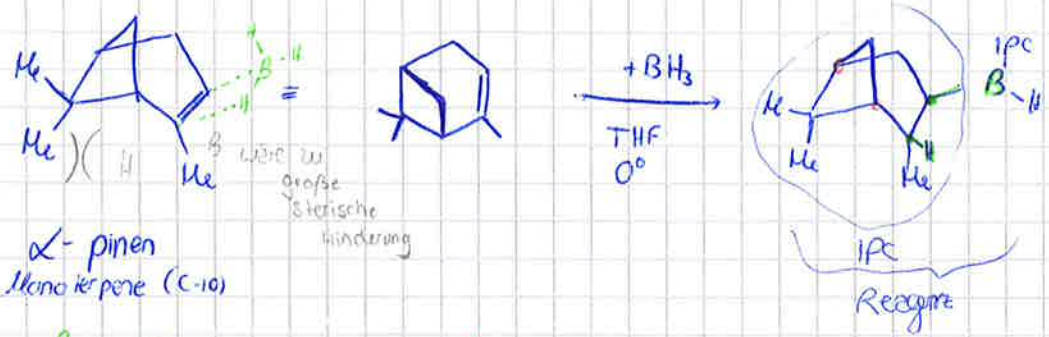
Asymmetrische Hydroborierung

→ Unkatalysiert ($\text{IPd}_2\text{B-H}$)

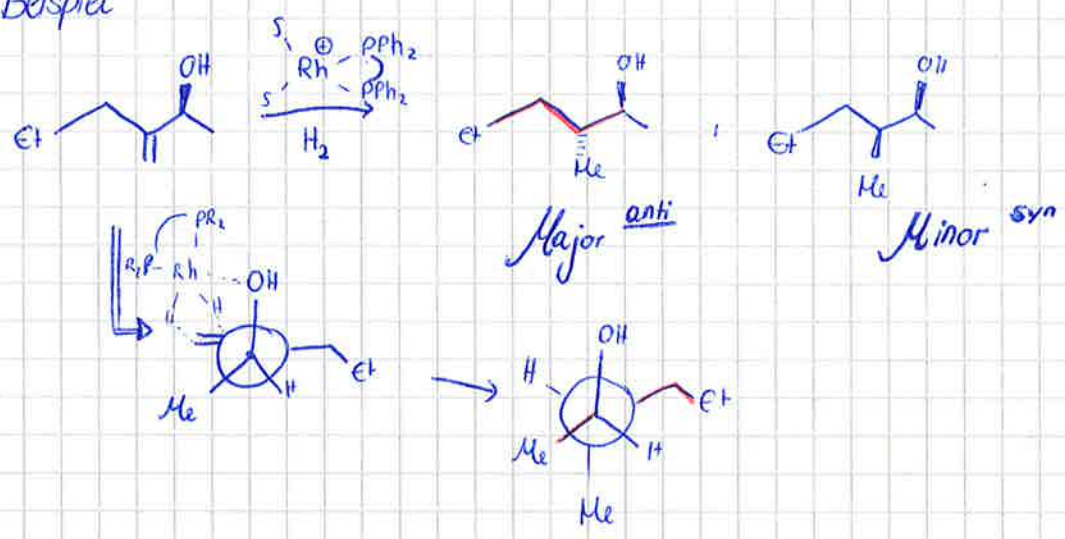
→ Rh-katalysierte Hydroborierung ($\text{H}_2 \rightarrow \text{R}_2\text{-B-H}$)



Unkatalysierte asymmetrische Hydroborierung (stoch. Reagenz)



Beispiel



Nächstes Thema

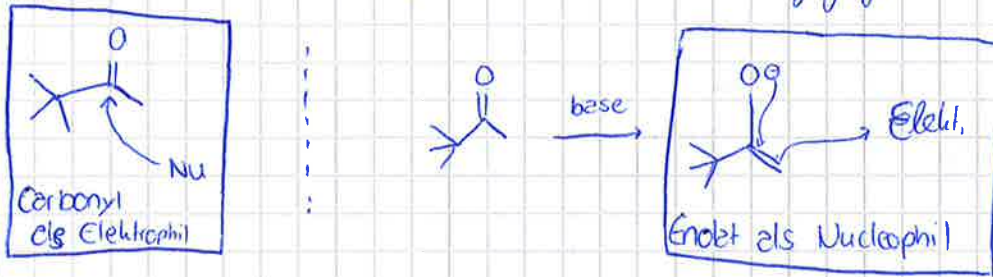
Addition an $C=X$ stärker polarisiert \rightarrow man kann mehr Reagenzien addieren

$X = O; N$

nucle. Addition

- Aldolreaktion

Carbonyl kann sowohl nuc. als auch elekt. angegriffen werden



Aldolreaktion

Reaktion eines Carbonyls mit sich selbst

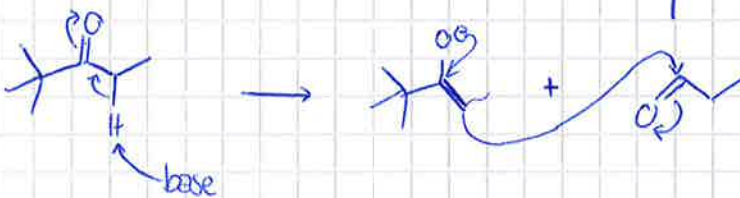
→ E/Nu = Carbonyl / Enolat

bipolarer Charakter

Vorgebe

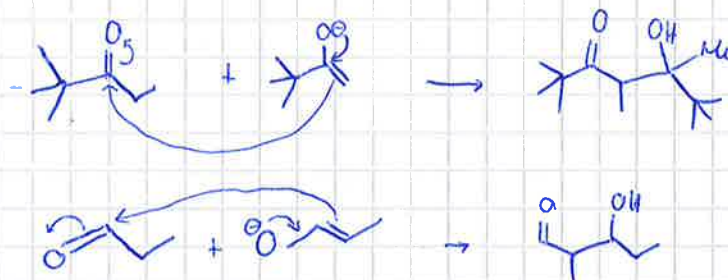


Mechanismus



Konstitutionsisomere

1) Problem d. Selbstreaktion



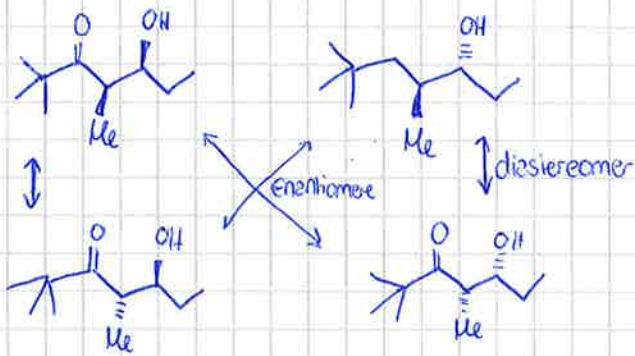
2) Problem der Kreuzreaktion



→ 4 Konstitutionsisomere
 2x Selbstreaktionsprodukt
 1x ungewünschte Kreuzreaktion

Stereoisomerie

Bsp: Aus den 4 Konstitutionsisomeren 4 Stereoisomere
d. gewünschten Produkts



diastereoface Kontrolle: syn / anti

enantioface Kontrolle: syn/syn und anti/anti

1) Problemlösung: Konstitutionsisomere in der Aldolreaktion

- nur Keton (CC(C)C(=O)CC) deprotonieren

↳ Keton + Base vorlegen → löst nicht Selbstreaktionsproblem !!!

- Vermeiden d. Selbstreaktion

Wie wird Keton + Base vorgelegt?

Base wird vorgelegt (im Überschuss)

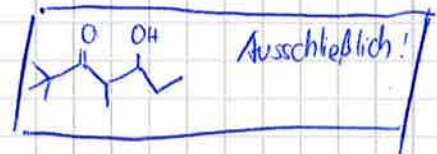
→ Keton wird zugegeben

→ Base muss quantitativ deprotonieren



; dann erst Aldehyd

⇒

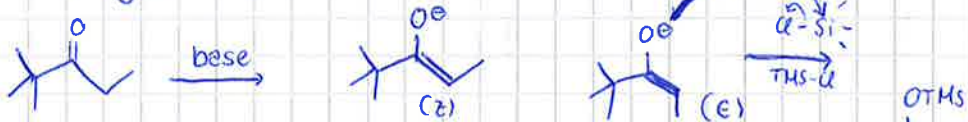


Immernoch 4 Stereoisomere

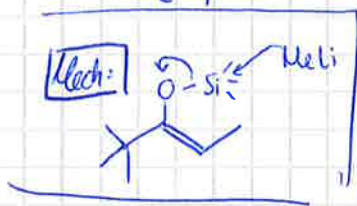
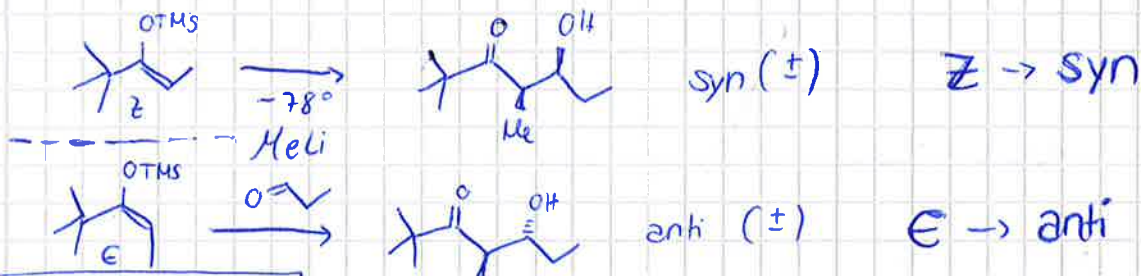
2.) Problem d. Stereoisomere (4)

→ Diastereoface Kontrolle reduzieren 4 → 2 Stereoisomere syn/oder/anti

↳ Endetgeometrie



kinet. Bedingungen (tiefe Temp)



⇒ Heathcock-Experiment

(Z)-Endet → syn (E)-Endet → anti

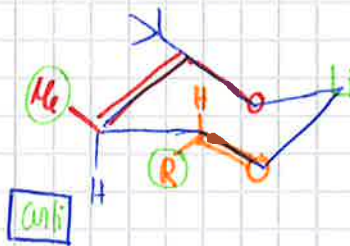
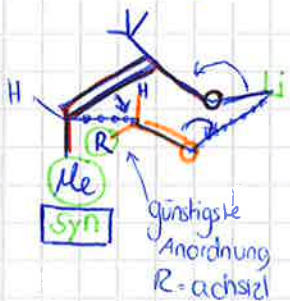
⇒ Endetgeometrie ist verantwortlich f. Diastereoface Kontrolle d.

Aldolreaktion

Erklärung liefert: **Zimmermann-Trexler Transition state**

Z-Endet

E-Endet



Diese Seite fehlt
ab hier bis

7.12.15

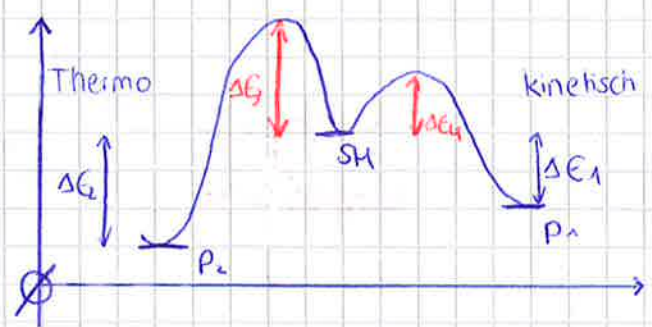
→ Selektivität bei der Darstellung d. Enolats

→ Ireland-Modell

→ Enolatbildungsprozess

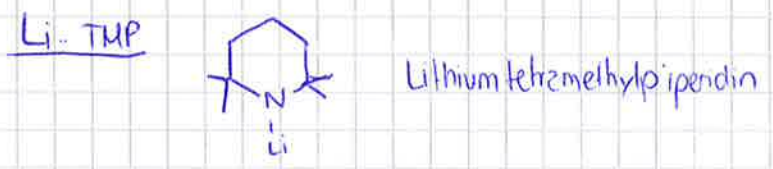
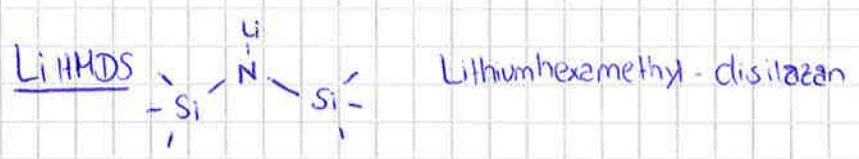
Wahl d. Base: stark genug um Rückreaktion zu verhindern

Kinetische Bedingungen

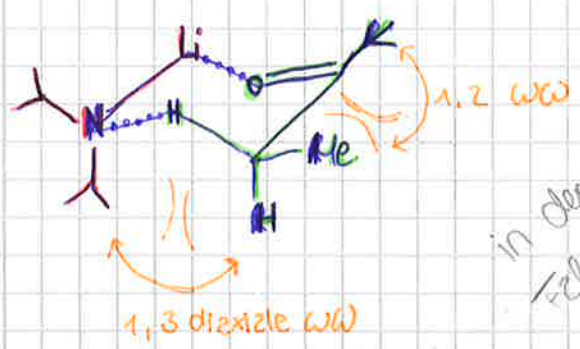


$\Delta E_2 > \Delta E_1$

- tiefe Temperatur
- starke Base



Ireland-Modell: (LDA, THF, -78°C)



in dem Falle
1,2 w/w
Schlimmer
weit intramolekular

Ketone → Z-Enolate
Ester → E-Enolate
Amide → Z-Enolate

HMPA (giftig)

sehr krebserregend
Lewis-Base



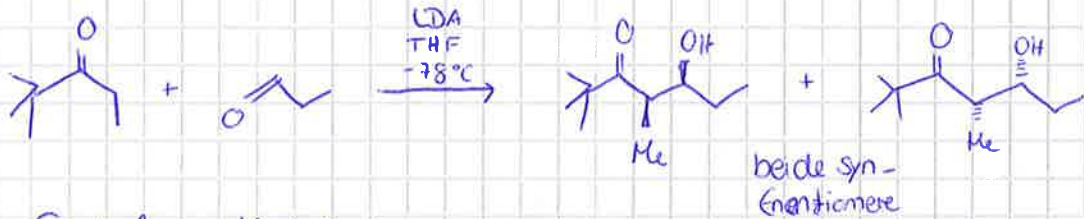
Hexamethylphosphor-triazid

bildet sehr gut Li-Komplexe

Mit HMPA

↳ komplexiert Li
→ 6-Ring aufgeweitet

Ketone → E-Enolat
Ester → Z-Enolat
Amid → E-Enolat



→ Enantiofaciale Kontrolle

Auxiliar → kovalent an Substrat

Nachteil gegenüber Katalysator:

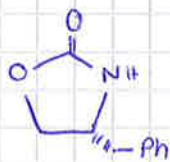
Auxiliar nach Reaktion abspalten

Auxiliar:

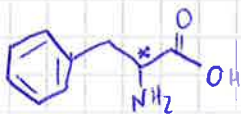
- schnell
- billig
- einfach
- opt. Aktivität vorhanden
- ↳ Bausteine aus Natur
- ↳ "ex-chiral-pool"

Aldolreaktion

• Evans-Auxiliar



ex-Phenylethylamin



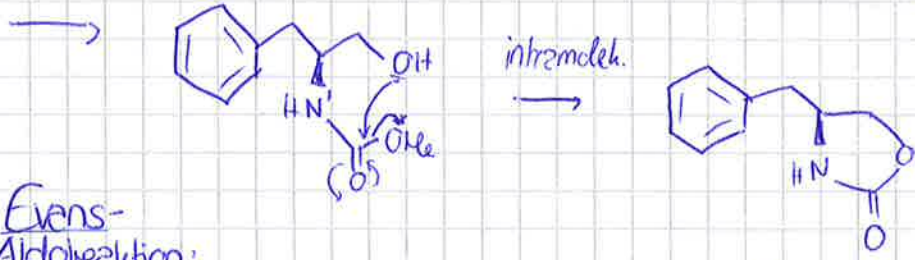
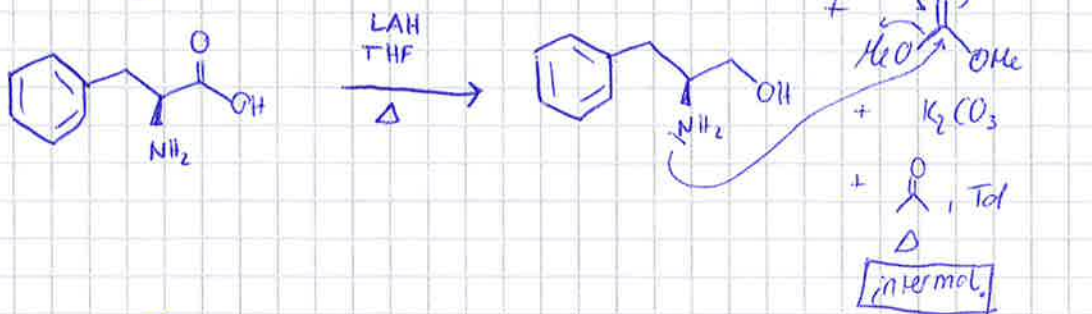
• Oppolzer-Auxiliar



ex-Camphor

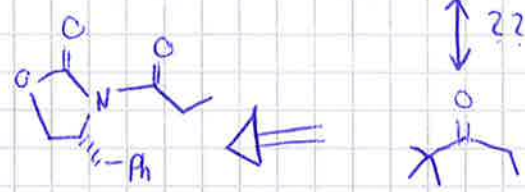


Herstellung d. Evans-Auxiliars:



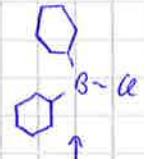
Evans-Aldolreaktion:

Bedingungen modifiziert zur klass. Aldol:
 → Base



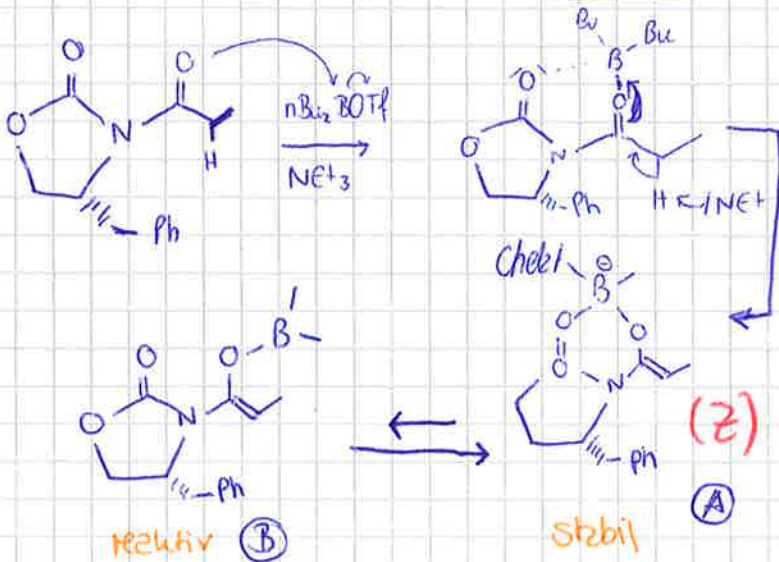
Curtin-Hammett

Bedingungen: NEt_3 ; $i\text{Pr}_2\text{NET}$ } beides schwache Basen
 (Base) \nearrow \nwarrow häufig

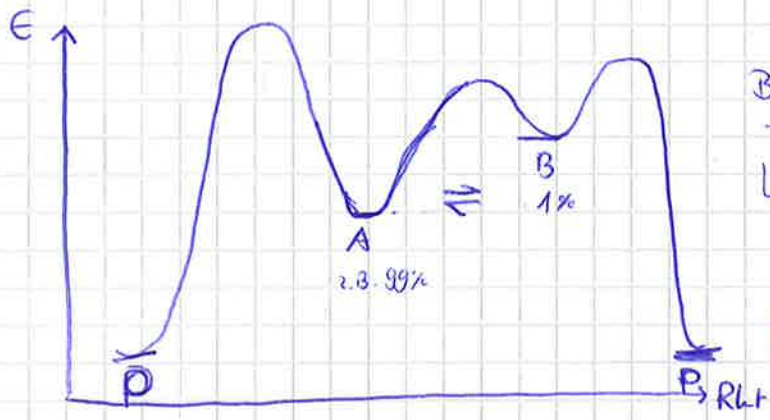


Lewis-Acid $n\text{Bu}_2\text{BOTf}$; $\text{Sn}(\text{OTf})_2$; TiCl_4 ; SnCl_4 ; SnCl_2 ; $(\text{t}^-\text{Bu})_2\text{Be}$

Warum Kombi: LA/Base



Problem für Zimmerman (6-Glied. Zyl.)
 Bei kann kein Aldehyd mehr koordinieren
 → hat schon 4 Bind. Partner



B kann abreagen
 → B wird nachgeliefert
 ↳ man schaufelt langsam von A über B zum Produkt

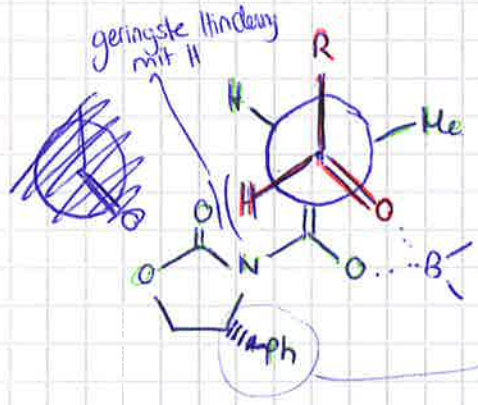
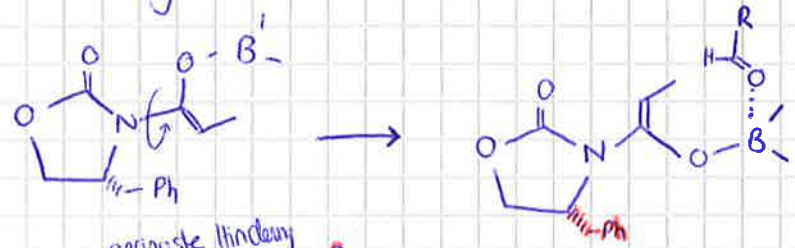
→ Curtin-Hammett-Prinzip
 → Wichtig

Reaktiv-Konformation

≠

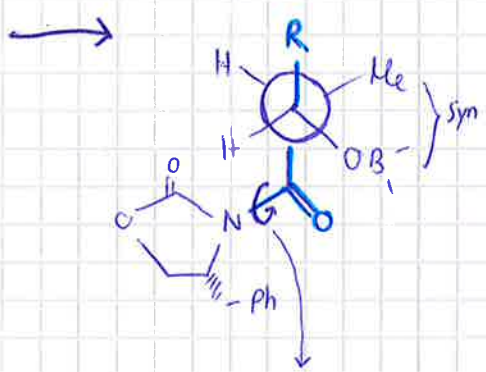
→ vorgelagertes Gleichgewicht

Thermodyn. Minimum

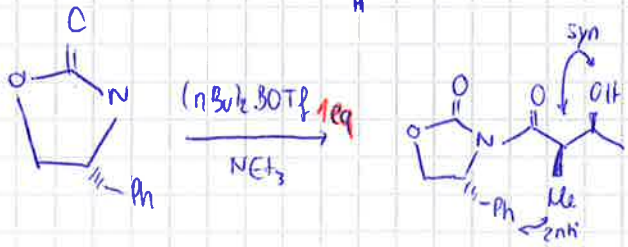
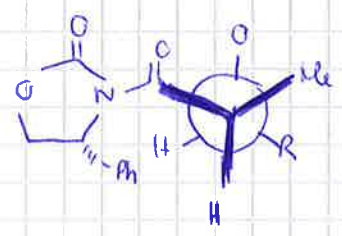
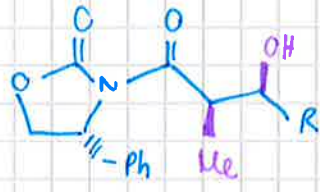


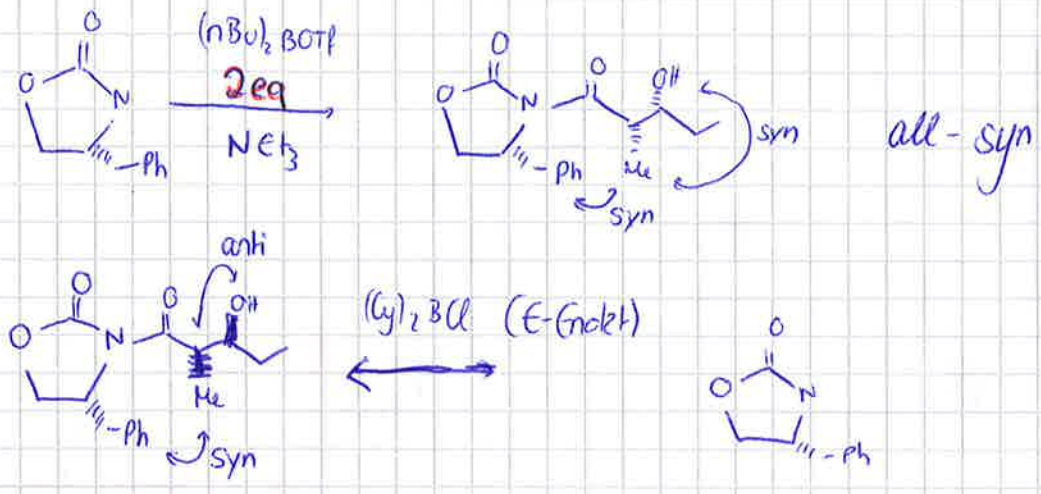
Zimmermann Trexler

Angriff von vorne
 Hinterseite abgeschirmt

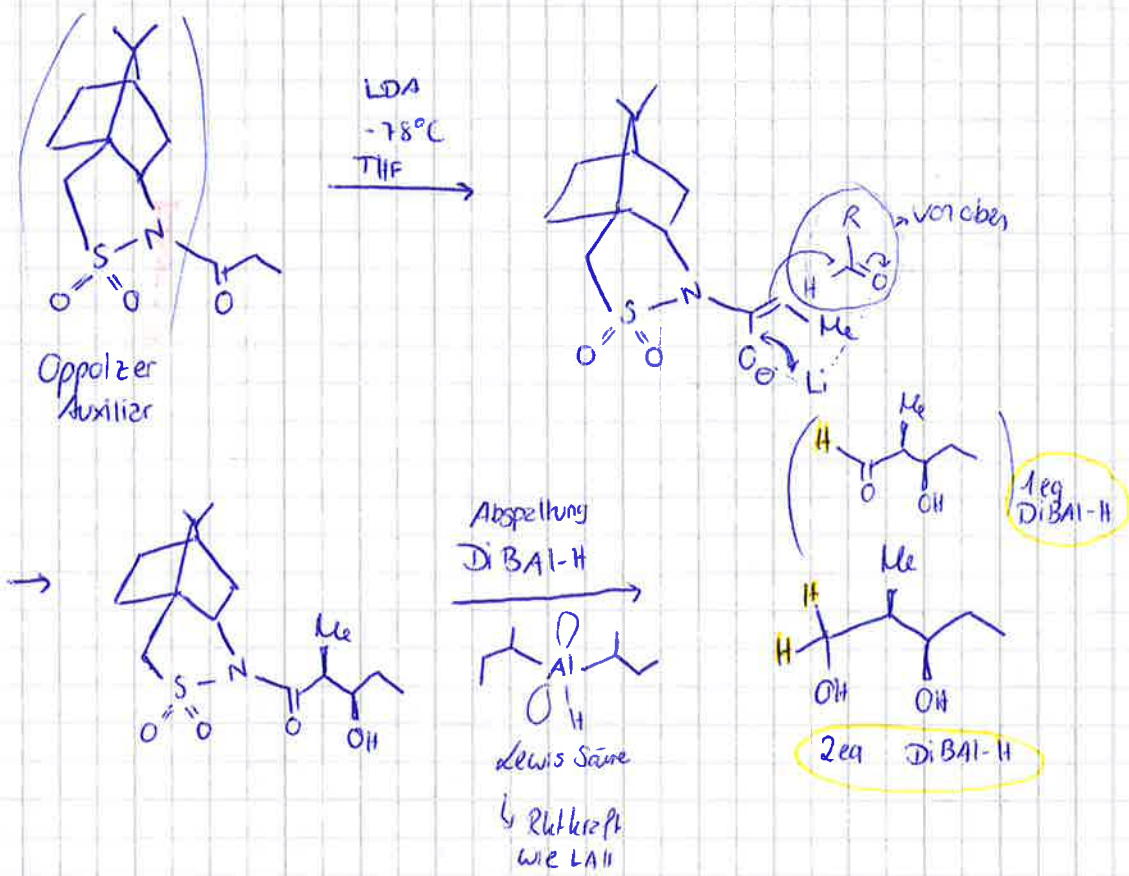


längste Kette

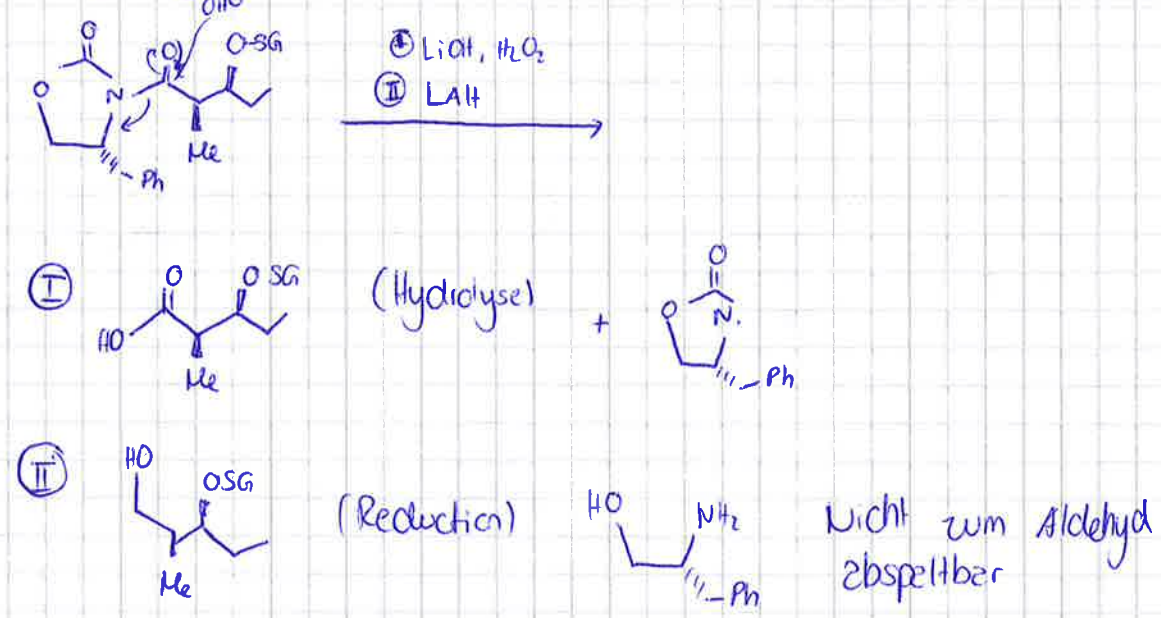




anti-anti ist das einzige was mit dem
 Auxiliar nicht möglich ist!



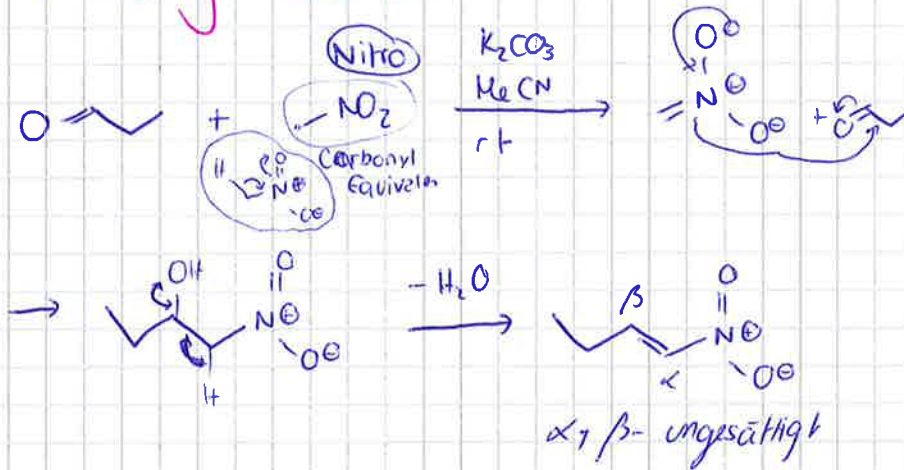
Abspaltung von Evans



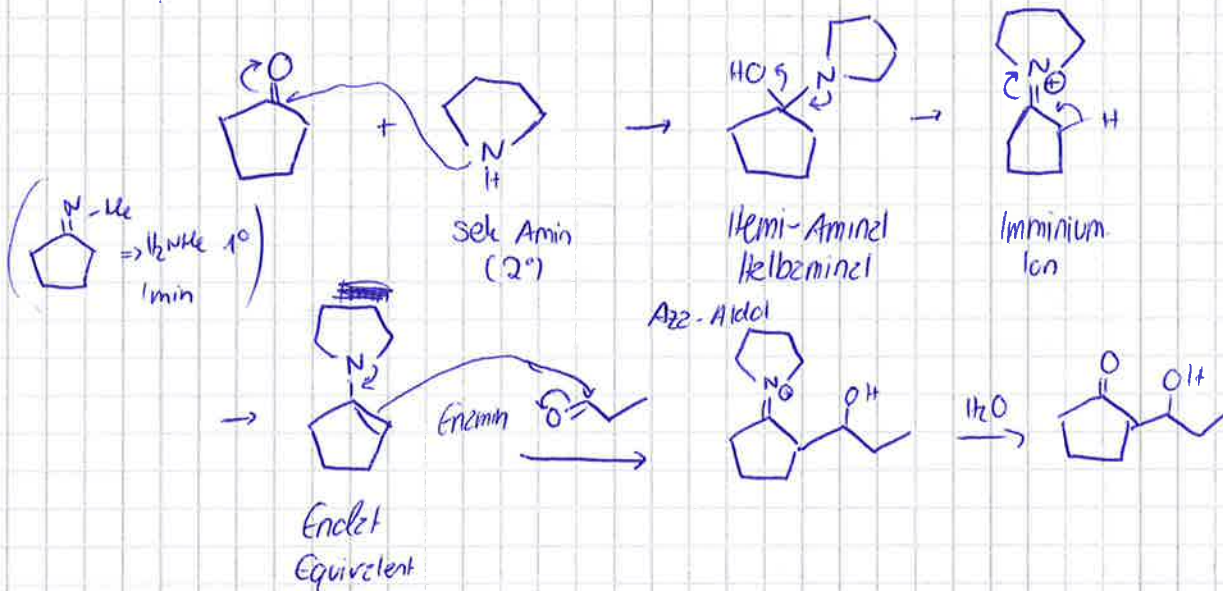
bis hier

Aldol-type Reactions:

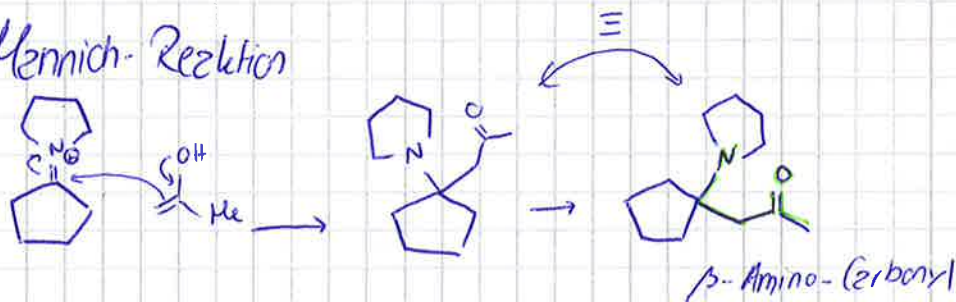
1. Henry Reaction



2. Mannich Reaction

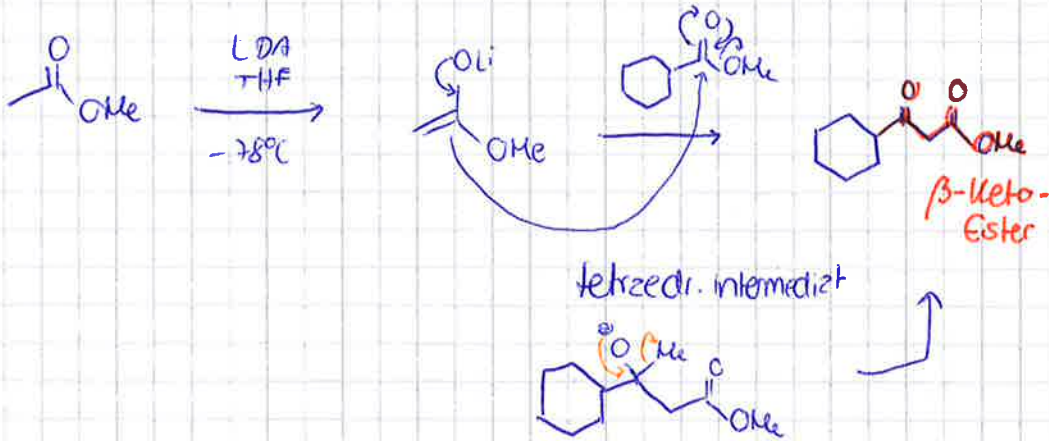


Mannich-Reaktion

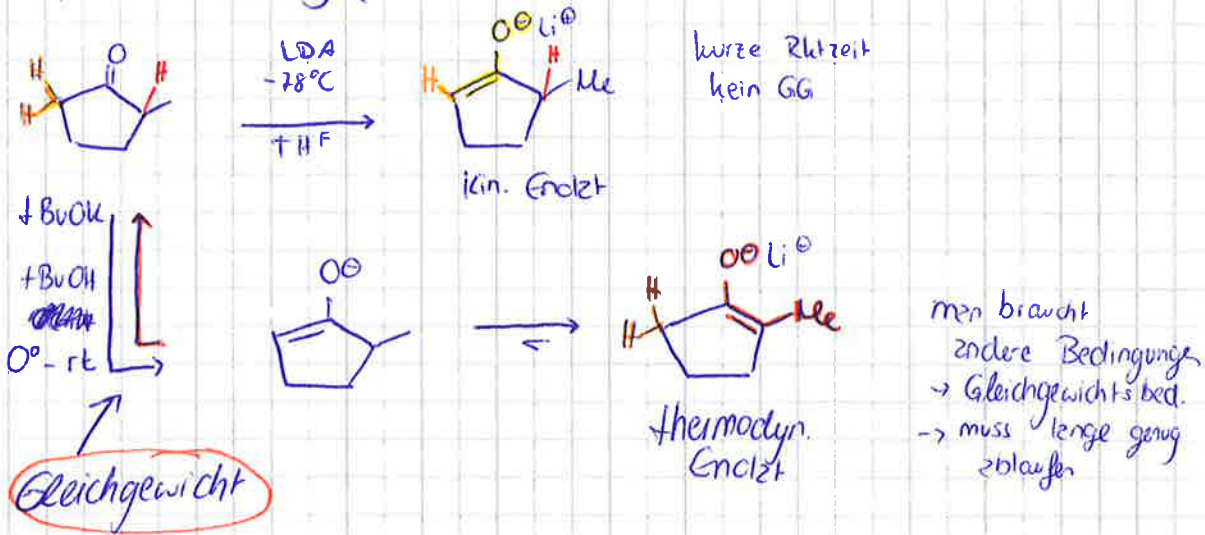




3. Claisen Esterkondensation



Enolatbildung



Thermodyn. Enolat kann auch über Enamin unter aprotischen Bedingungen generiert werden



kinetisches Enolat

- kurze Rktzeit
- tiefe Temp.
- aprot. Bedingungen
- starke Base (keine Reprotonierung)

thermodyn. Enolat

- lange Rktzeit
- Raumtemp.
- protische Beding.
- Base nicht stark

aprotisch \rightarrow Enamin-Imin GG

Enolatbildung

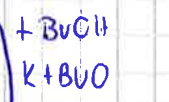
über 3 Positionen delokalisiert

acidität höher wegen Nähe zu H



kinetisches Enolat (Enon) Deprot. in α -Position

Enone \equiv α - β -ungesättigte Keten / Aldehyd / Carboxylderivat



rt



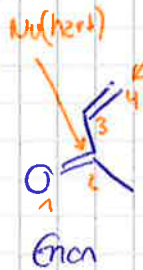
thermodyn Enolat (Enon) Deprot. in δ -Position

über 5 Positionen delokalisiert

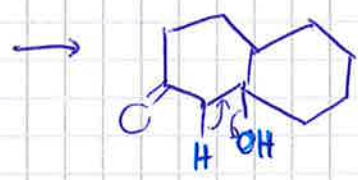
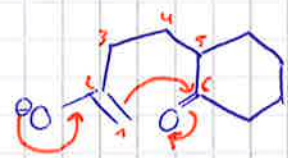
Ladungsverteilung über 5 Atome ist günstiger als über 3 Atome

4. Robinson-Annelation (Annelierung)

ich deprotoniere des Keten



1,4 Addition

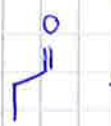


-H₂O

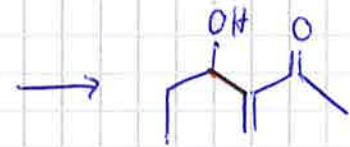
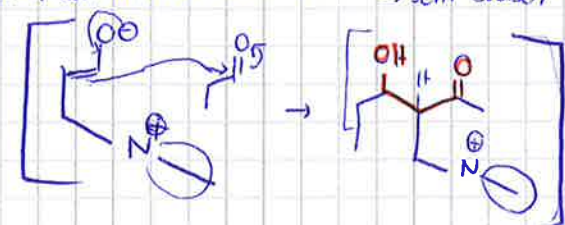


5. Baylis-Hillmann

DABCO = Diäza bicycloocten

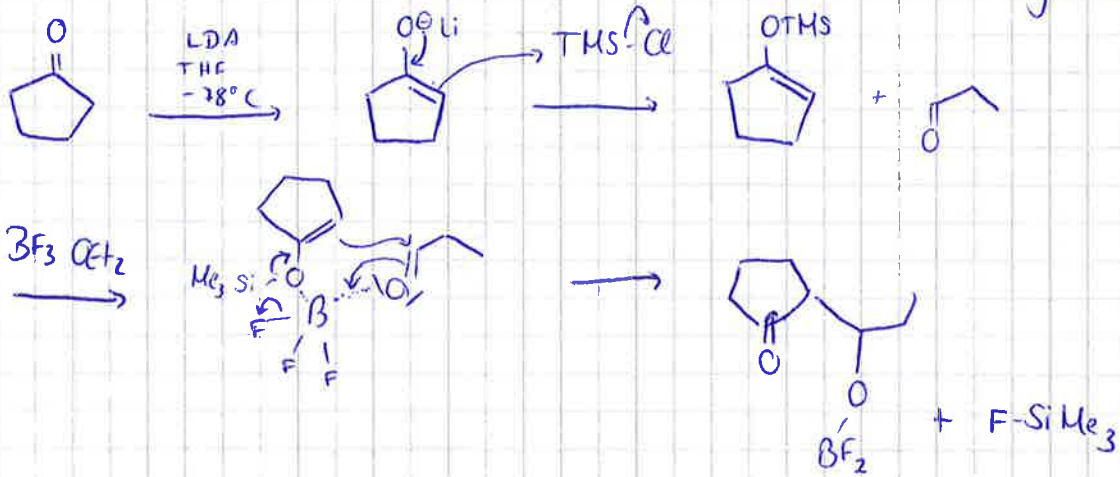


Käfig-Struktur
gerichtet \rightarrow kann nicht nach innen \rightarrow ganz kleines Dipolmoment \rightarrow sehr basisch



6. Mukojama Aldolreaktion

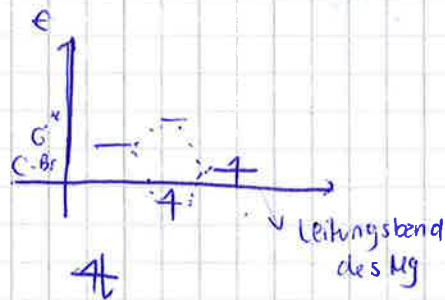
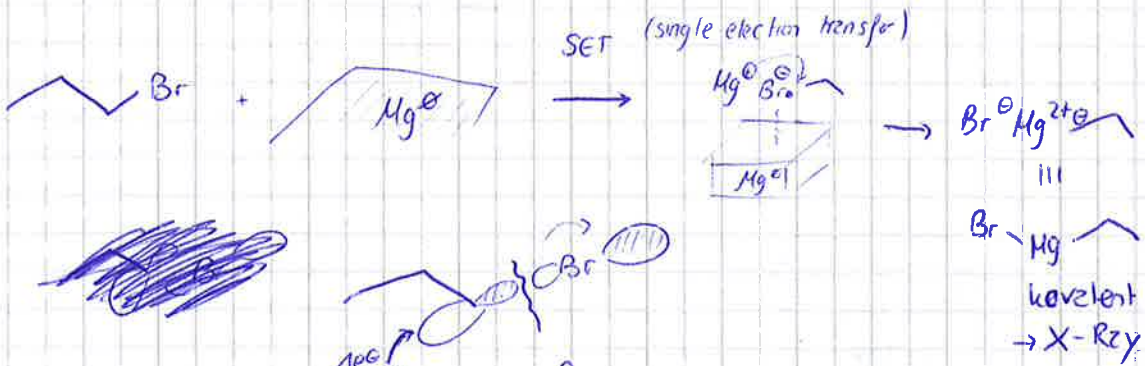
Ketone: Z-Einkete wenn
offen ketig
E-Einkete wenn
cyclisch



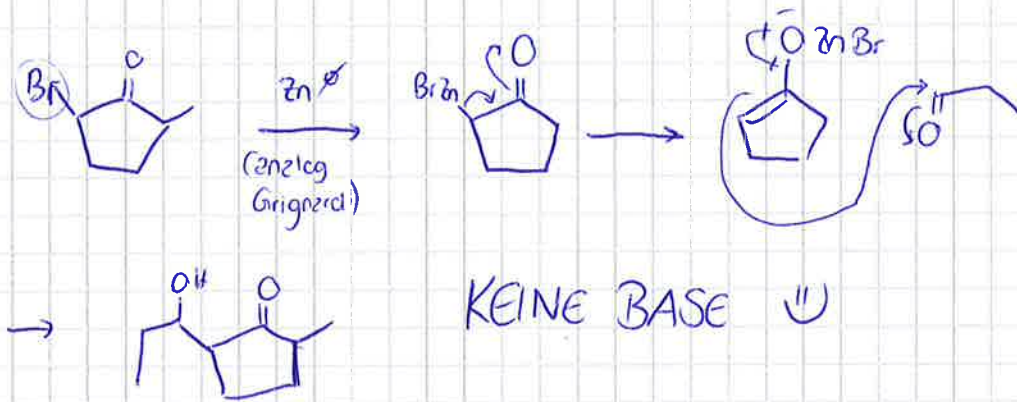
Exkurs! Organometall- Reagenzien

C-Atom zentriertes Nucleophil → C-Nucleophil

Halogen-organischen Verbindung = Startmaterial



7. Reformatsky - Aldol: (14.12)



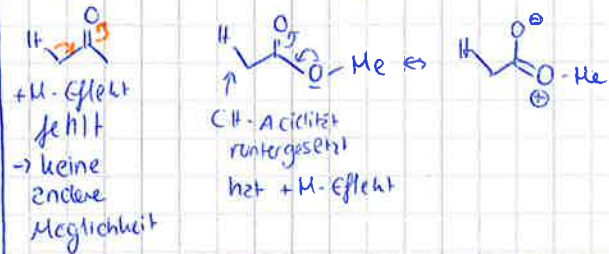
man kann natürlich auch alle 7 Reaktionen
asymmetrisch machen. ☺

15.12.15

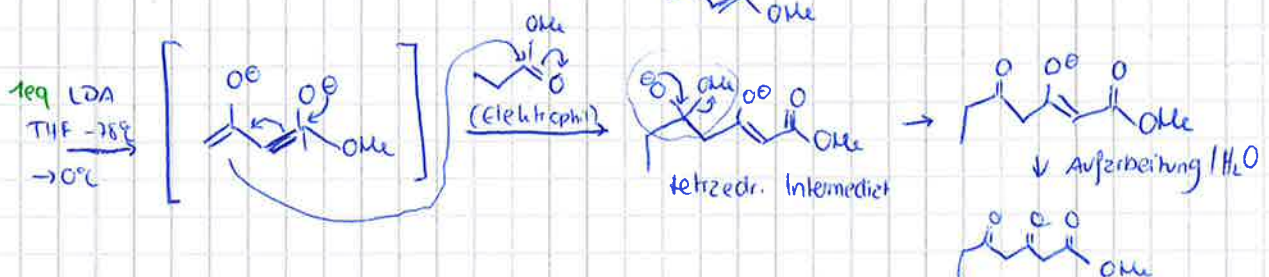
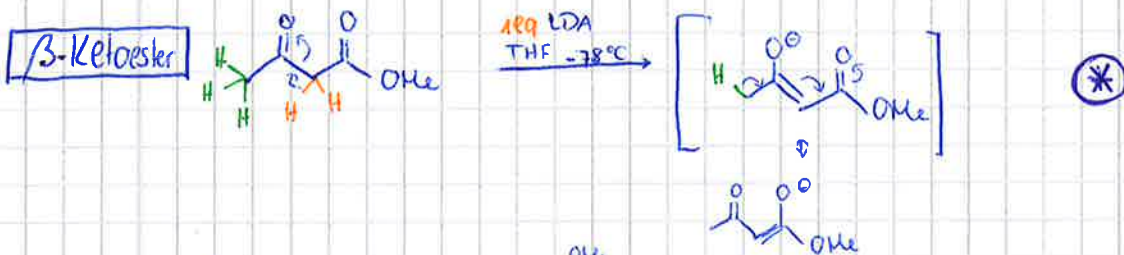
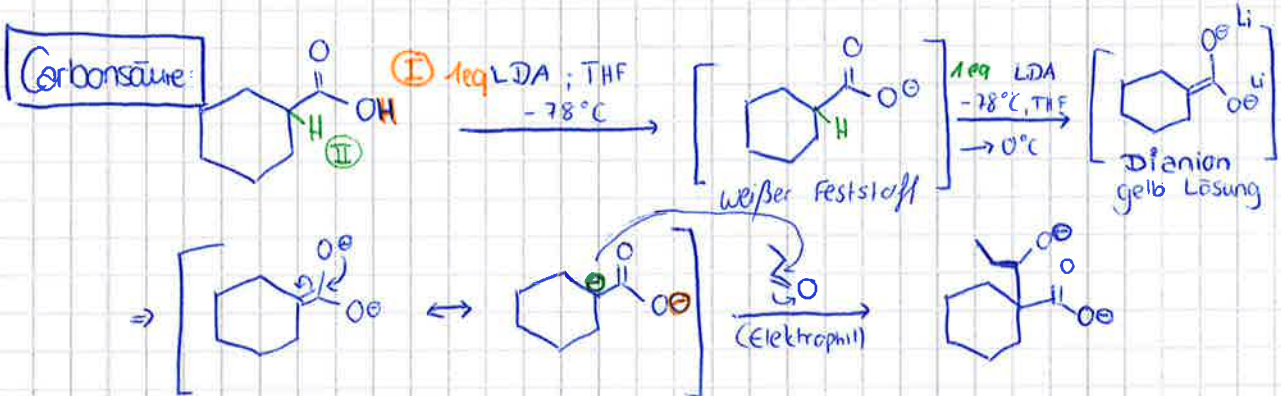
Enolat - Verbindungen aus

- Carbonsäuren
- 1°, 2°-Amide (im Gegensatz zu 3°)
- β -Ketoester

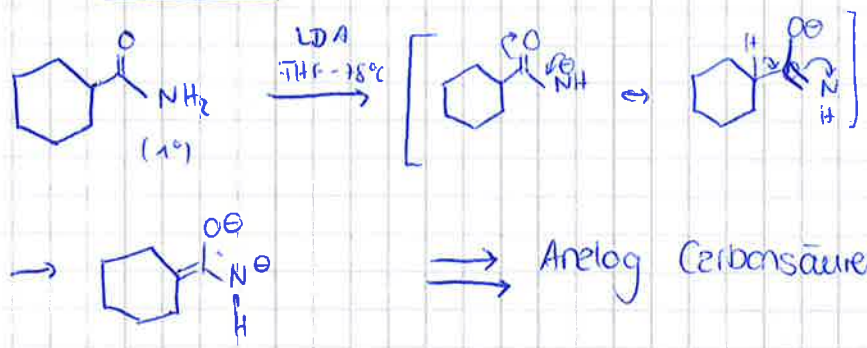
Keton, Ester \rightarrow Enolisierbarkeit



Dienion $\hat{=}$ „Enolat“



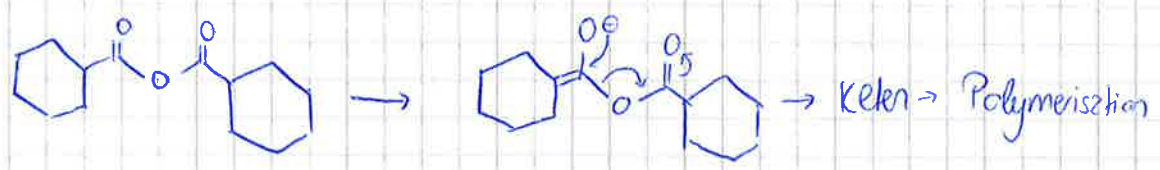
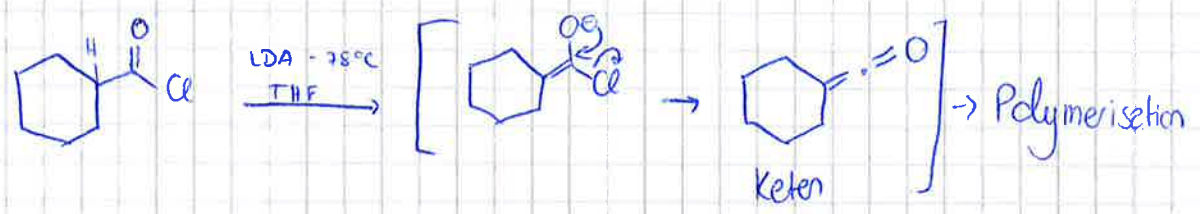
Amide (1° & 2°)



2° \rightarrow H = alkyl

**Carbonsäure-chloride
-anhydride**

keine Enolate!!



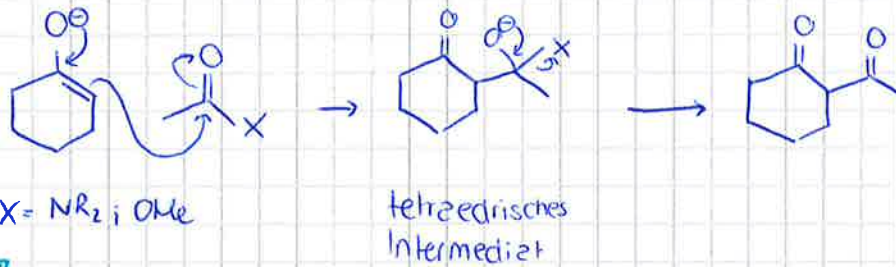
Auch für Ester \rightarrow ab 0°C



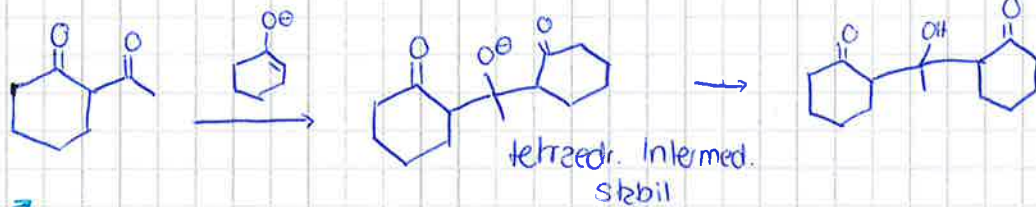
Reaktionen von Enolaten (nucl.) mit div. Elektrophile

15.12.15

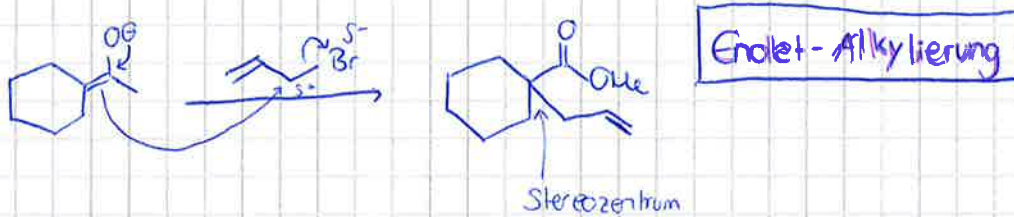
→ bisher als E^+ : Aldehyde; Ketone (Aldol); Carbonsäurederivate



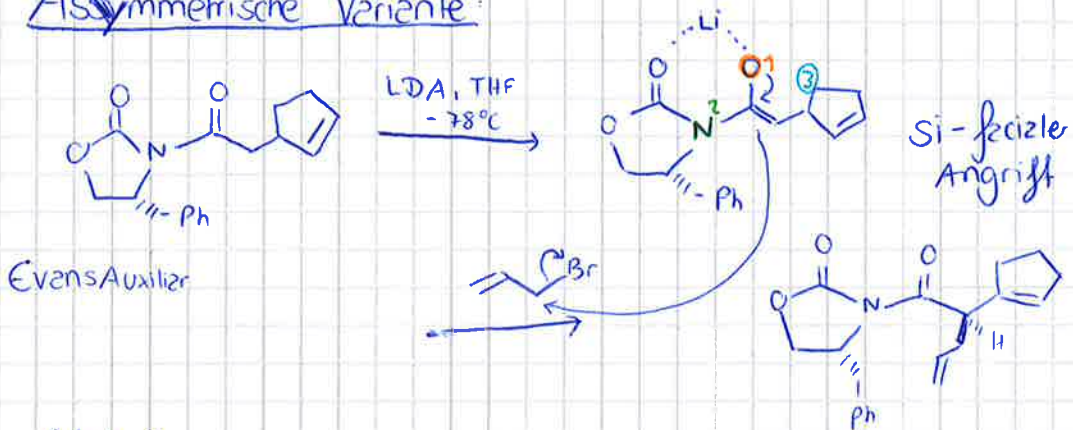
Nucleophile Substitution am sp^2 -C=O-Kohlenstoff



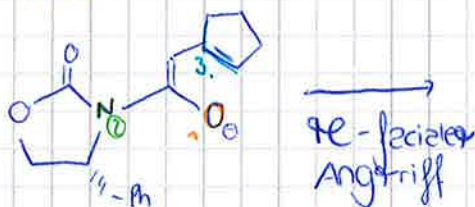
Nucleophile Addition (tetraedr. Intermed. kann nichts eliminieren → keine Substitution)



Asymmetrische Variante:



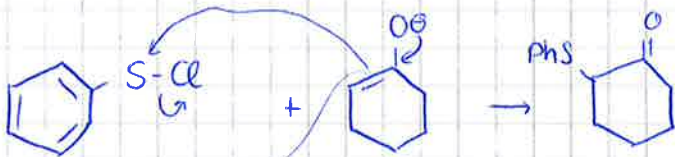
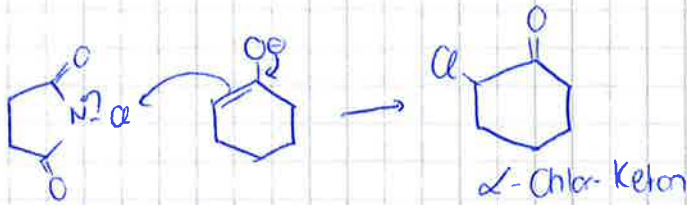
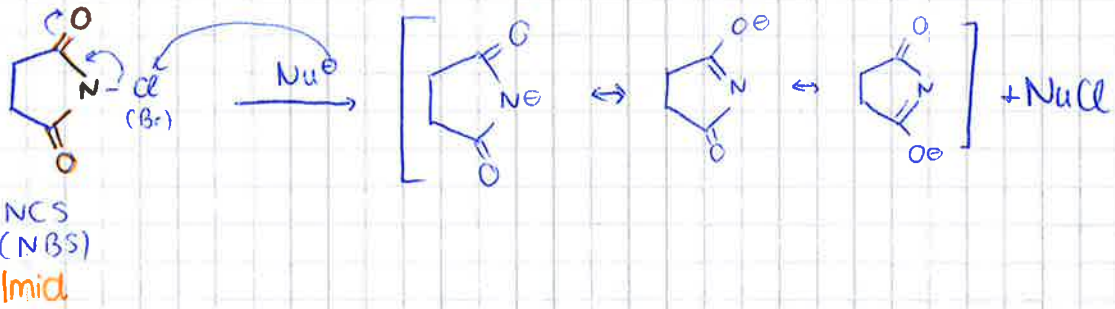
Aldol:



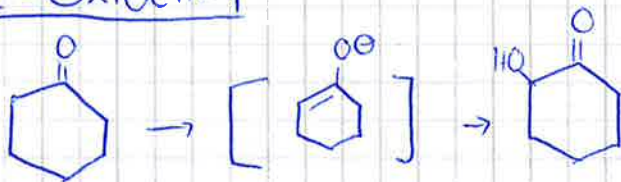
bisher für Eolet immer C-Elektrophile verwendet:

C-Elektrophil: Aldehyd, Keton; Carbonsäurederivate, Alkylhalogenide

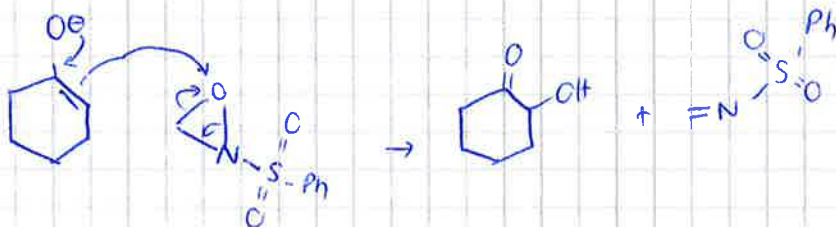
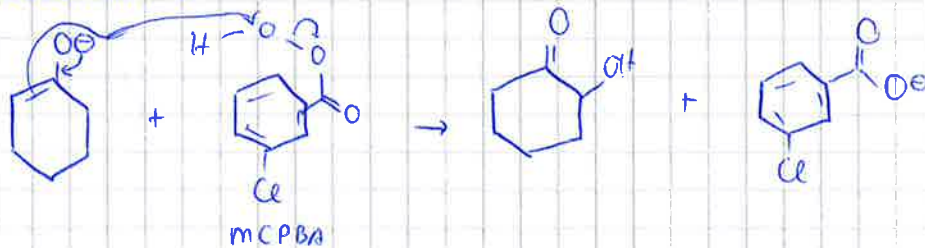
Heteroatom - Elektrophil:



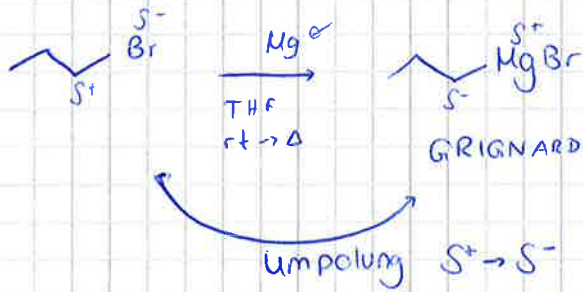
α -Oxidation



Mechanismus:



Nucleophile Addition am Carbonyl



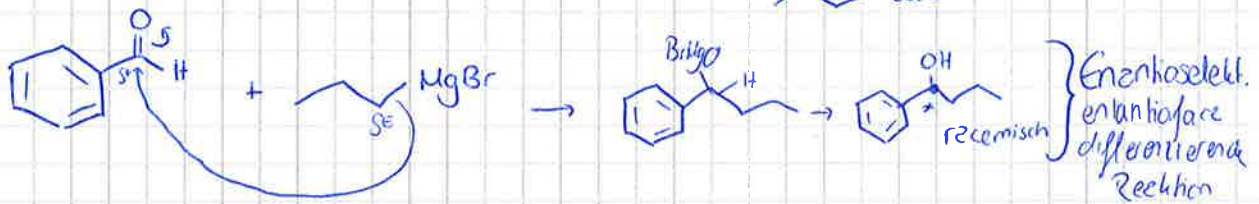
Organolithium



Organozink

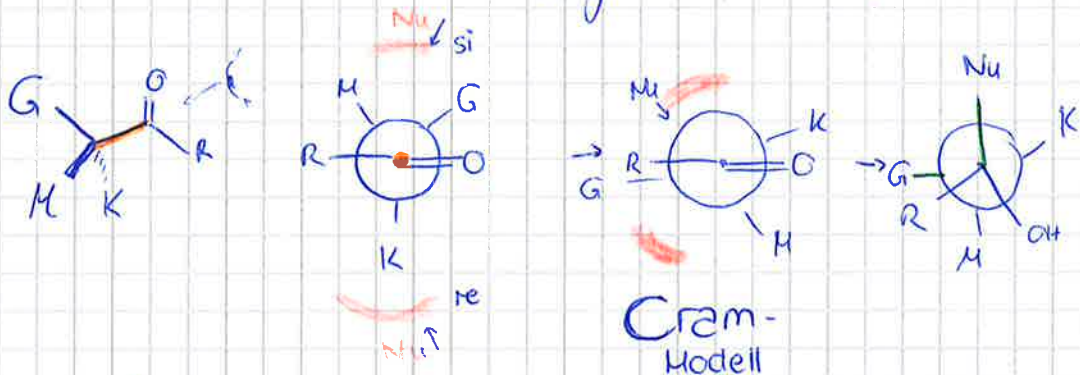
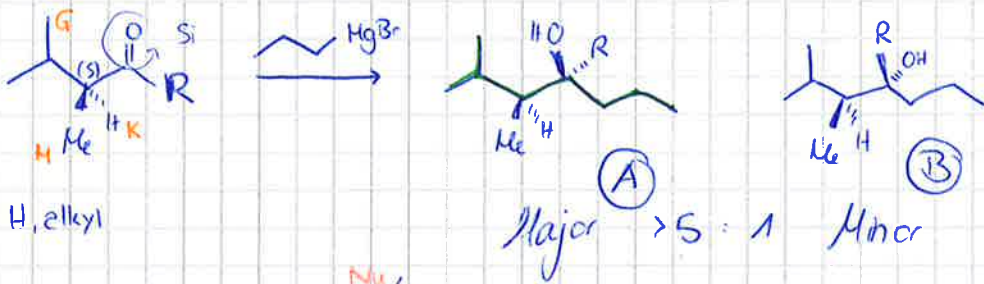


Organocuprate



Stereozentrum in α -Position v. Carbonyl
 Diastereoface differenzierende Reaktion

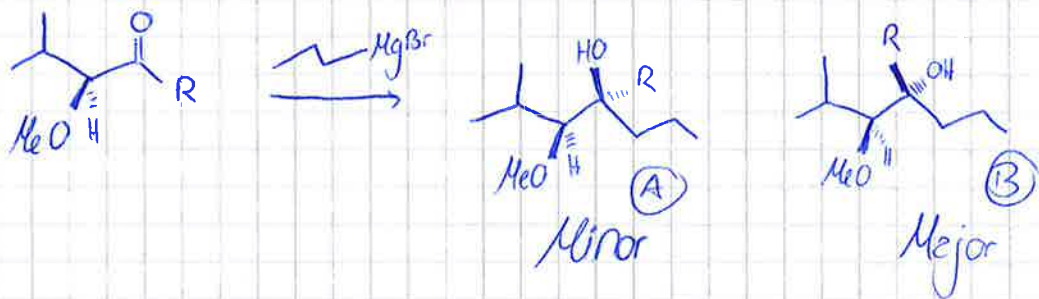
Groß
Mittel
Klein



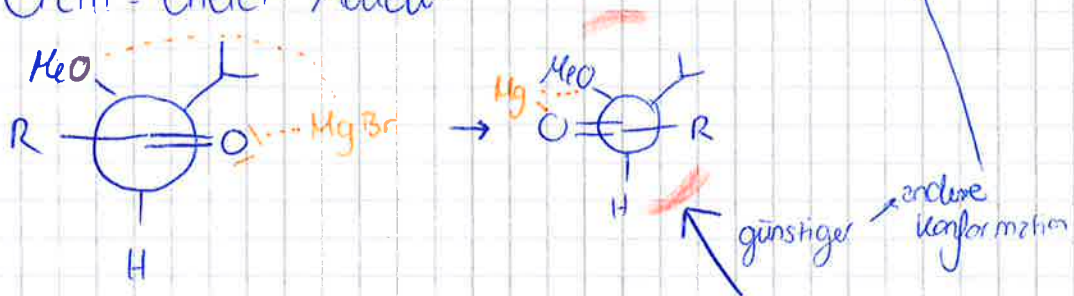
für Ketone mit
 • G; M; K basierend auf
 Raumfüllung

Nicht für: α -Heteroatom
 subst. Ketone

↓
 Dafür: Cram-Chelet



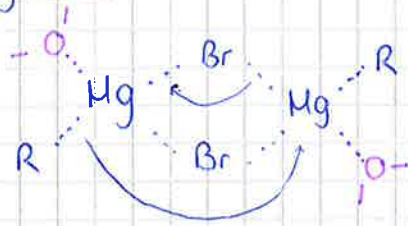
Cram - Chelet - Modell:



OC: 18.12.15

- Cram-Modell
- Cram-Chelat: \rightarrow Komplexierung Metall mit Carbonyl + α -Substrat = (O, N, Hal, S)

R-Mg-Br



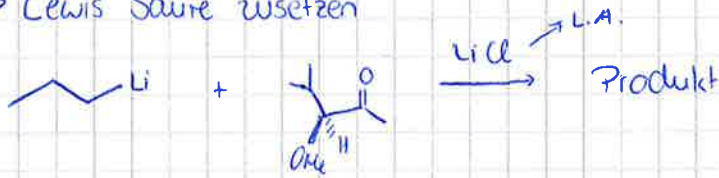
Schlenk-Gleichgewicht



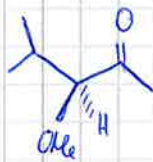
\hookrightarrow Chelatbildner im Cram-Chelat-Modell

Nach C, C. nucl. Add.

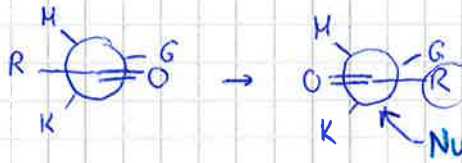
\rightarrow Lewis Säure zusetzen



Lewis Säure unterstützt die Reaktivität.



nach **Cram** (sterisch)



\uparrow sperrig

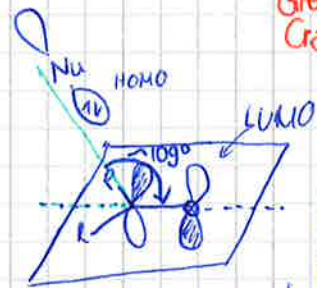
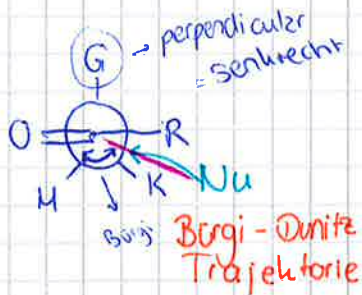
R = bulky:
 \rightarrow experimentell: Selektivität wird höher

sterische Interakt. größer

Widerspruch

Grenze des Cram-Modell

Felkin-Anh:

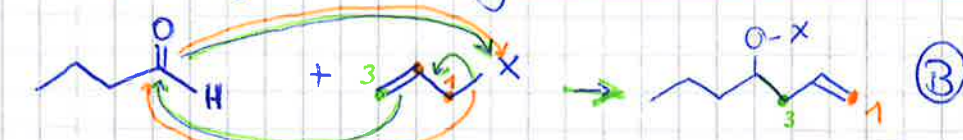


größten Overlap bei ca. 109°
 \hookrightarrow wenn blockiert KEIN ANGRIF

\uparrow
Bürgi-Dunitz!

Bürgi-Dunitz-Winkel:
ist 107° oder 103° ?

Allylierung/ Crotylierung v. Carbonylverb. (Nuc. Add)



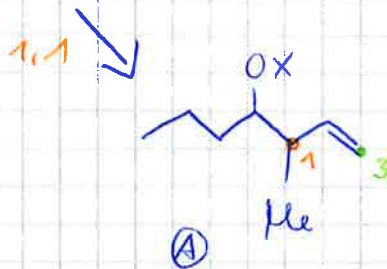
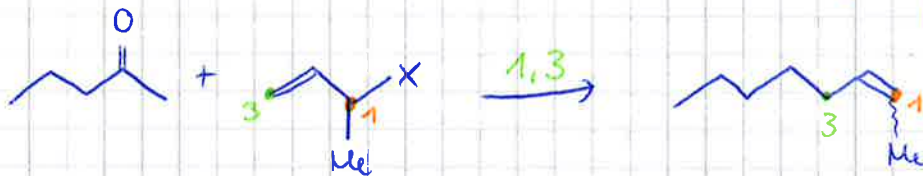
X- Borj (Ti, Sn, Cr, Ir, etc.) = Met

(1,1)



(1,3)

A ≡ B
→ weil System
Symmetrisch



A ≠ B

→ weil Allylspezies
nicht symm.



Problem

- 1,1 vs 1,3 Angriff
- Double bond geometry not defined?



Crotyl-Rest

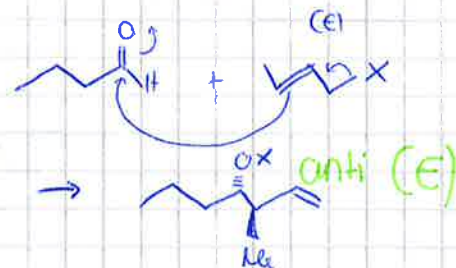


(Z)-Crotyl-Rest

X = B



(E)-Crotyl-Rest



abhängig vom
Metall

(Z) → Syn
(E) → anti



Diastereoselektivität d. Crotylierung:

Wie kommt zu Stereo: (Organoborene)

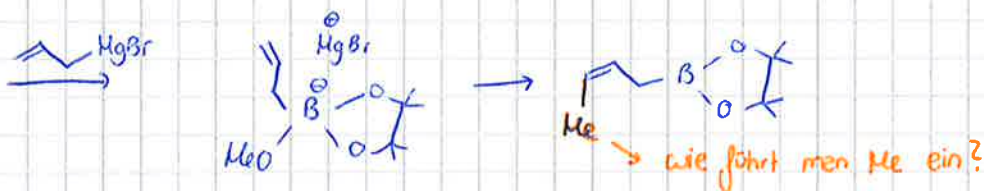
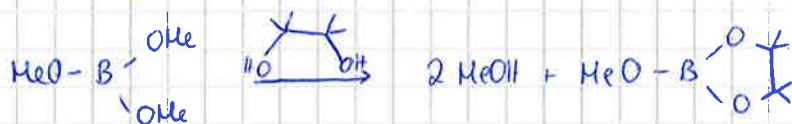
(Z)-Crotyl → syn

(E)-Crotyl → anti

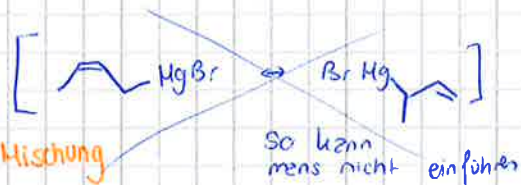
(Wir sollen auch die Pinakolreaktion kennen)



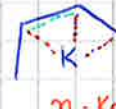
Herstellung d. Pinakolborans



Einführung über Schlosser Base Superbasische Mischung

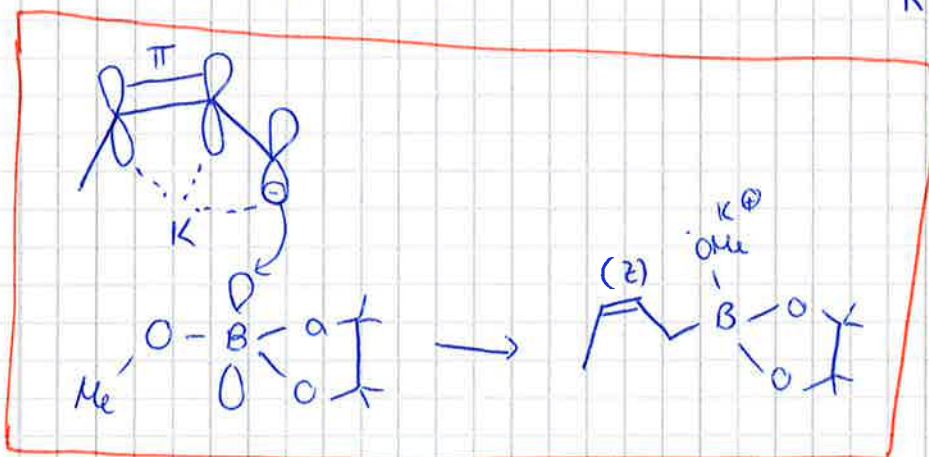
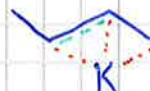
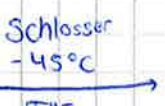


(KOBu + BuLi)

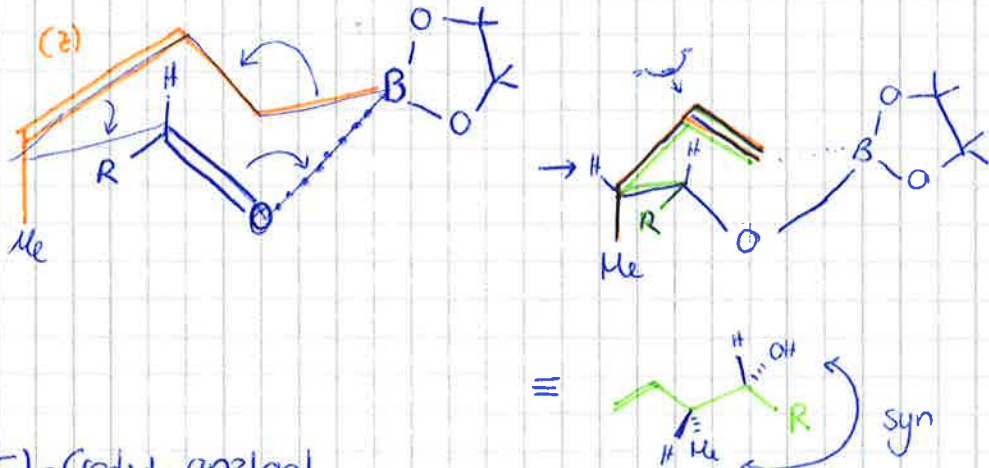
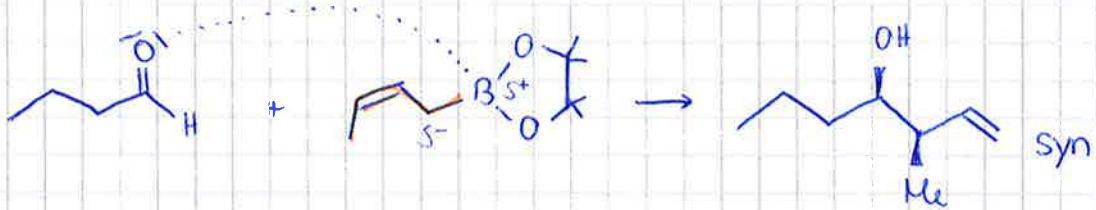


DB bleibt teils erhalten

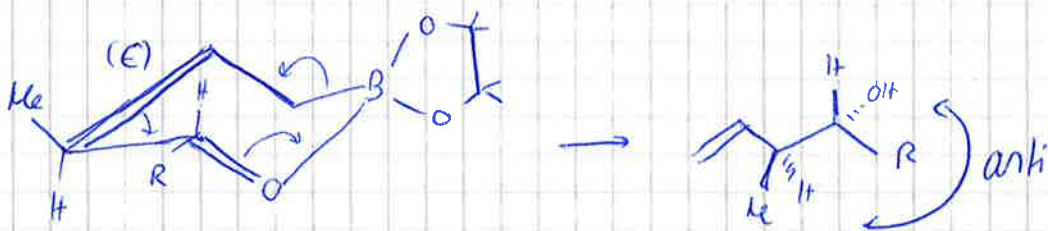
η-Komplex



Diastereoselektivität

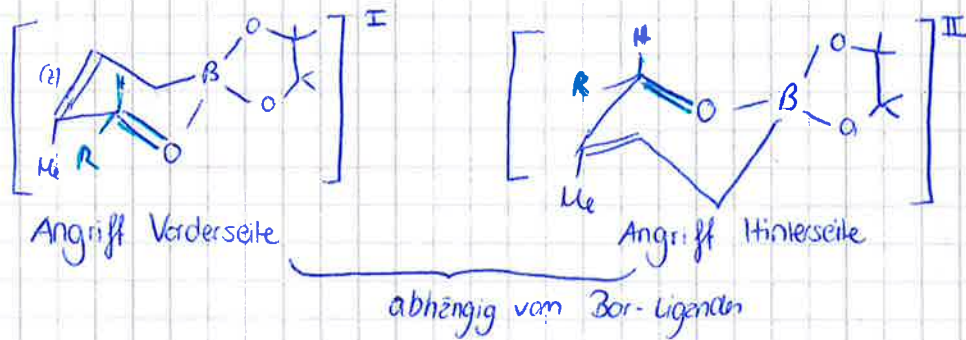


(E)-Crotyl-analog!



Enantioselektivität über **Dinekol** (Bor-Liganden) oder andere Liganden

Für (Z)-Crotyl als Bsp



Bor-Liganden:

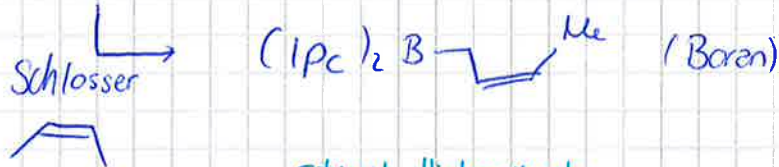
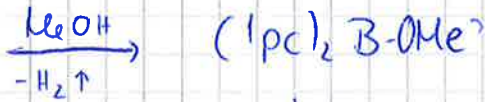
- Brown-Crotylierung
- Roush-Crotylierung

Brown:

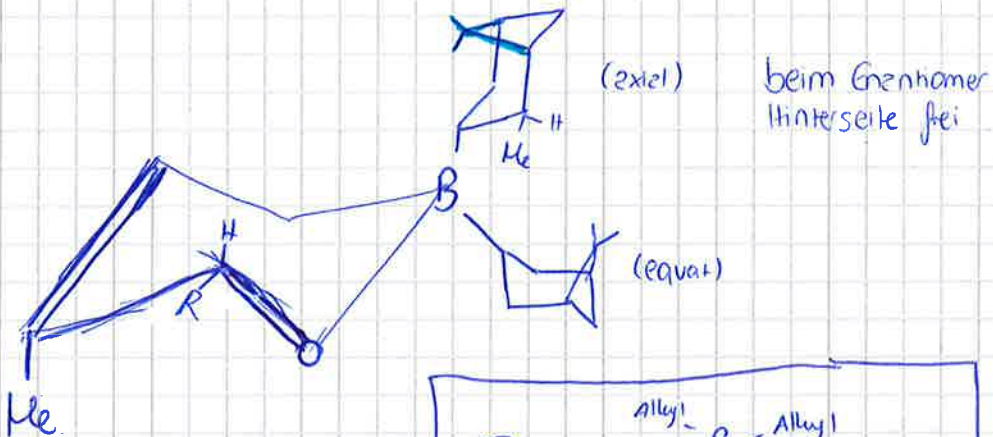


- α -pinene
- commercial
- billig
- Beide Antipozien vorhanden

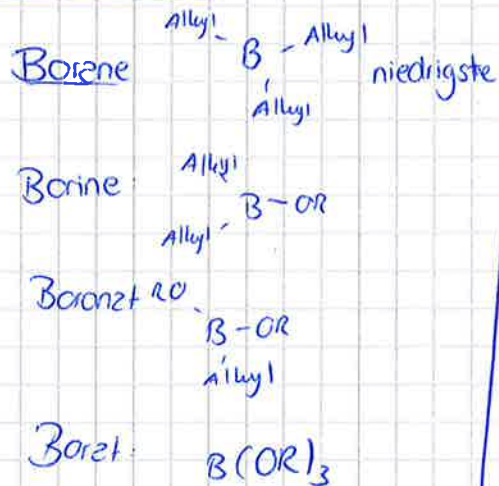
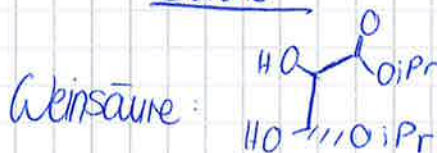
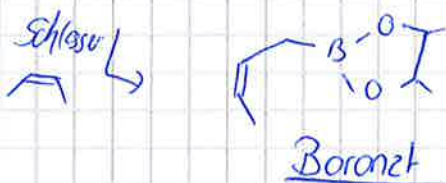
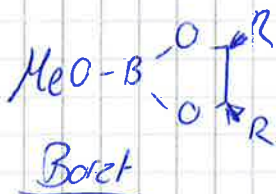
bleibt egal wie hoch
 Überschuss α -pinene
 → sterische Hinderung



Schirmt Hinterseite ab



Roush-Crotylierung

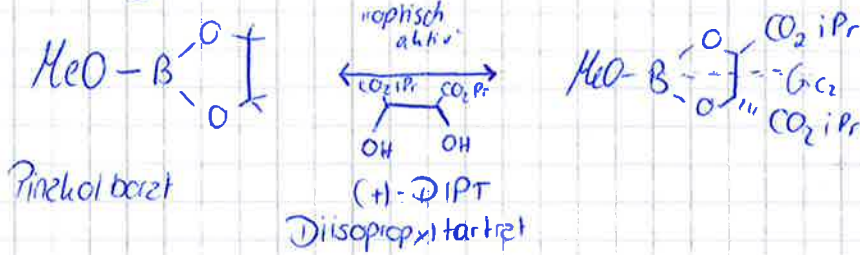


Tertet-isopropyl

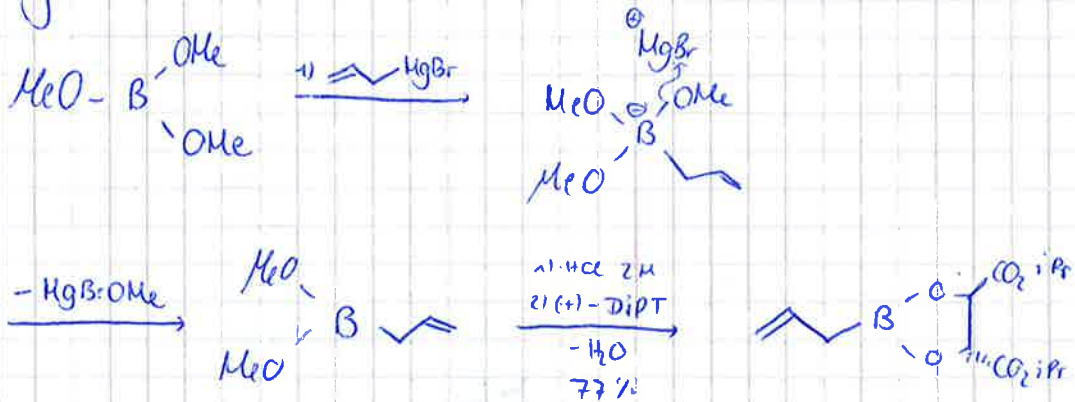
OC 21.12.15

Roush-Allylierung / Crotylierung

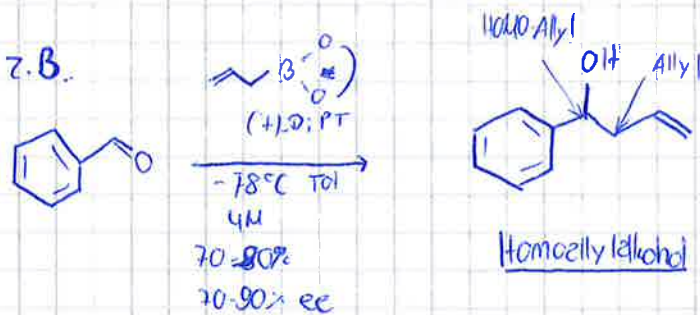
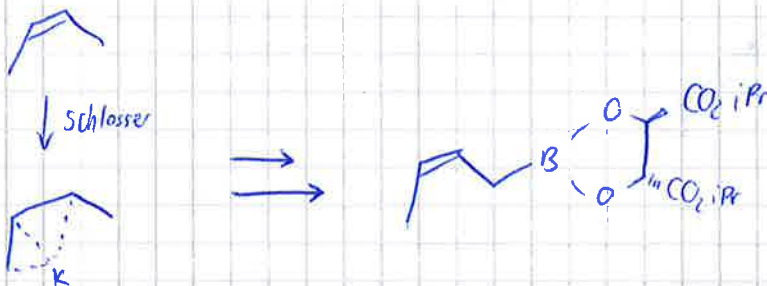
Darstellung



Synthese

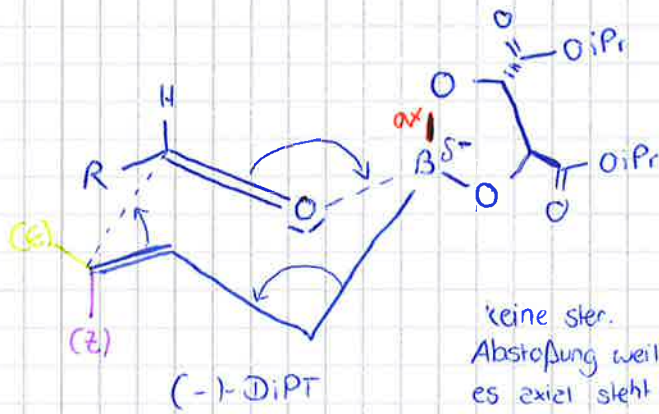


Crotylierung analog!



Allylierung: Selektivitäten gut - moderat
 Crotylierung: - " - sehr gut - exzellent

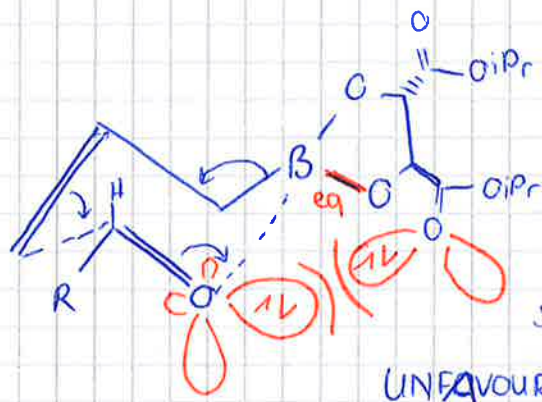
Transition-State-Modell



B-O Bindung
günstiger als
B-C Bindung
⇒ Triebkraft!

keine ster.
Abstoßung weil
es axial steht

FAVORED

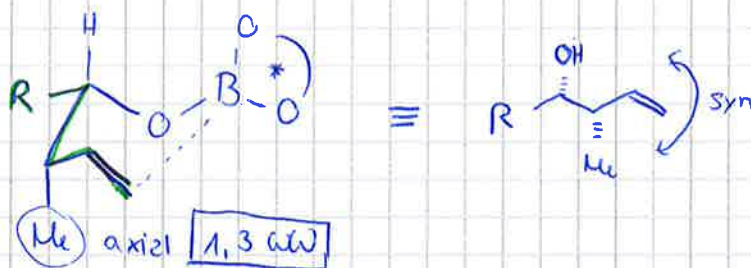


sterische Hinderung
(der freien e⁻-Peele)

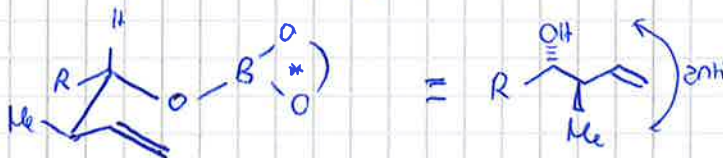
UNFAVORED

- Enantioselektivität → sekundärer MO-WW
- Crotylierung
(E) → anti
(Z) → syn

(Z)-Crotylboronat Produkt

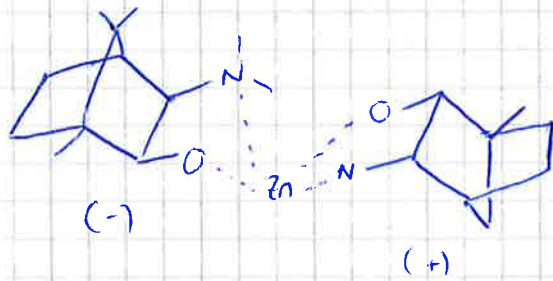
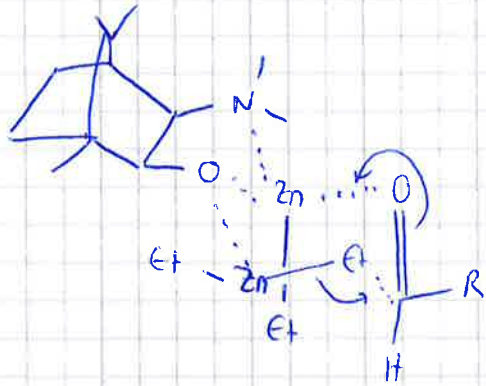


(E)-Crotylboronat Produkt



Reaktionsgeschw. v. E → größer (weil (Z) durch 1,3 WW gehindert ist)

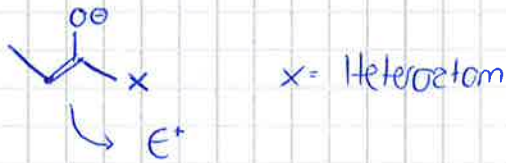
① DAIB - Mech:



OC 22.12.15

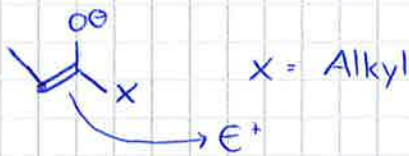
Ⓘ Myer's Auxiliar

↳ Alkylierung v. Enolaten auf der Carbonsäure Oxidationsstufe

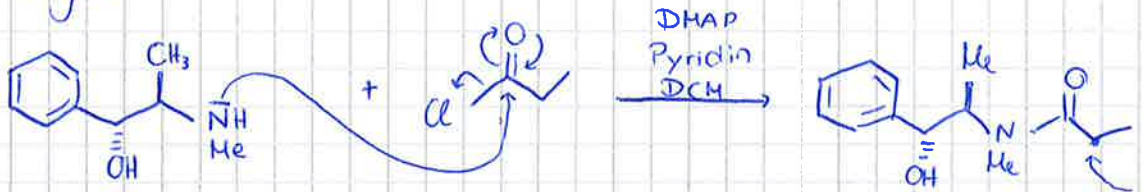


Ⓙ RAMP/SAMP Methode Ⓓ. Enders

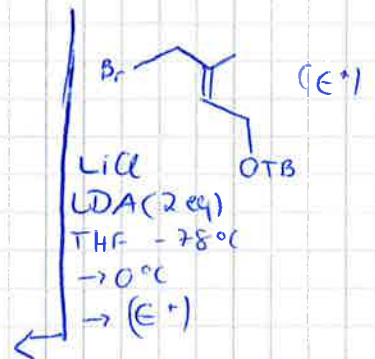
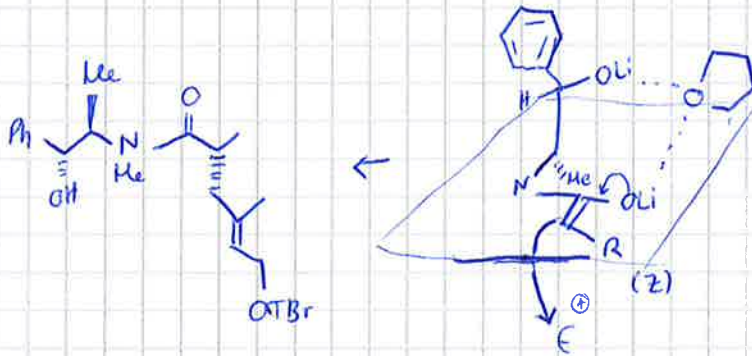
↳ Alkylierung v. Enolat auf der Carbonyl-Ox. Stufe



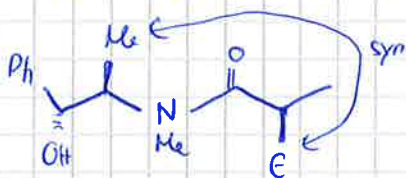
I. Myers



(R,R)-(-)-Pseudoephedrine



1,4-Induktion - syn



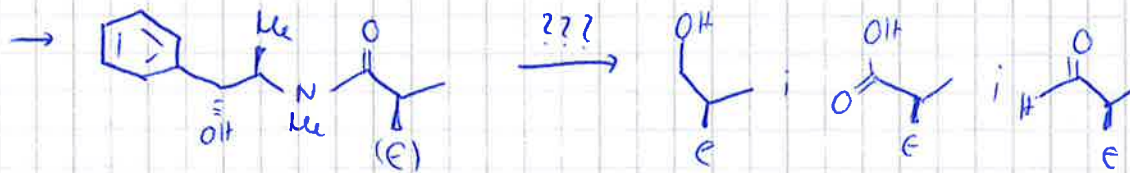
Syn \Rightarrow Alkylierung mit Halogeniden

1, 4 - Induktion

Halogenide \rightarrow syn

Epoxide \rightarrow anti

\hookrightarrow Komplexierung



Was wir eig wollen

\rightarrow wie kommen wir dahin? Myers ansatz

Möglichkeiten

- I. Zur Carbonsäure
 - II. Zum Alkohol
- } direkt

ad I. Bedingungen

- KOH, EtOH, Δ
- LiOH, H_2O_2 , $0^\circ C$, THF
- H_2SO_4 , Alkoholisches LM, H_2O , Δ

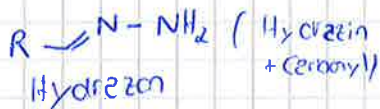
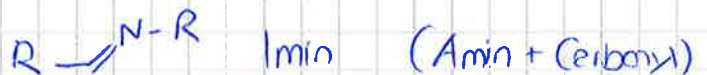
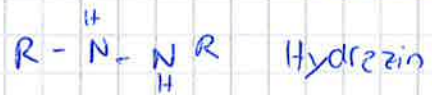
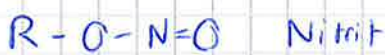
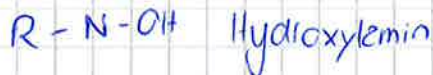
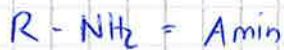
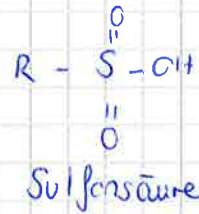
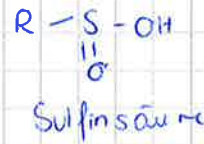
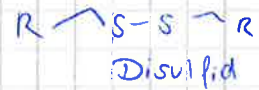
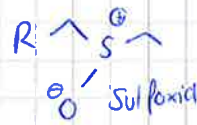
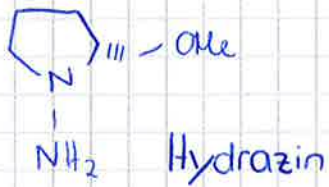
ad II Bedingungen

- LAH, THF, $0^\circ C$
- LDA ; NH_3-BH_3
 \downarrow
 $LiNH_2 (BH_3)$ $0^\circ C$
- DIBAL-H : 2 eq
- AlH_3 , BF_3

II RAUP/ SAMP

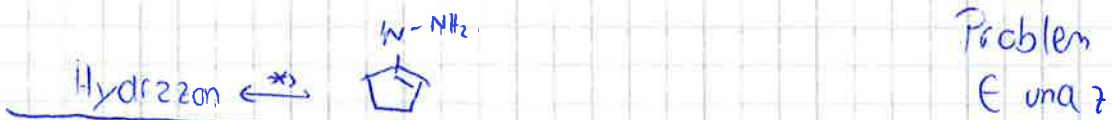
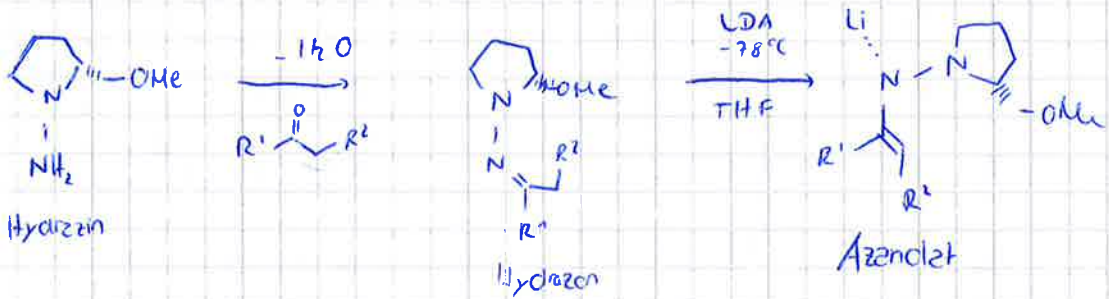
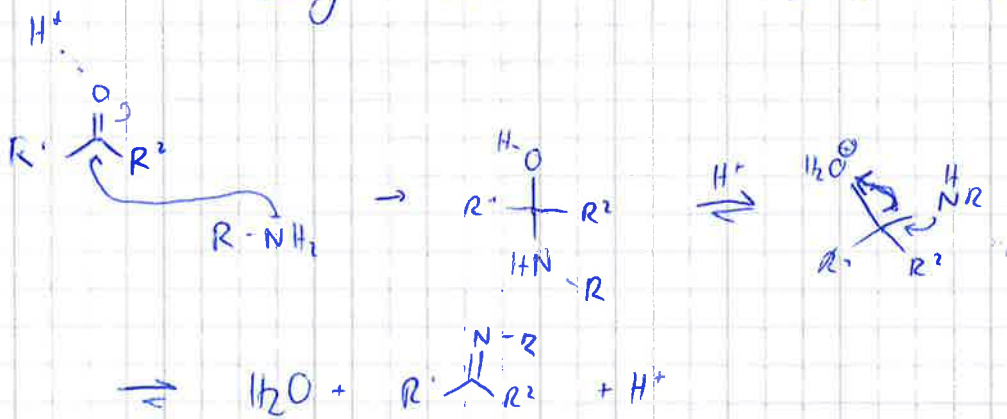
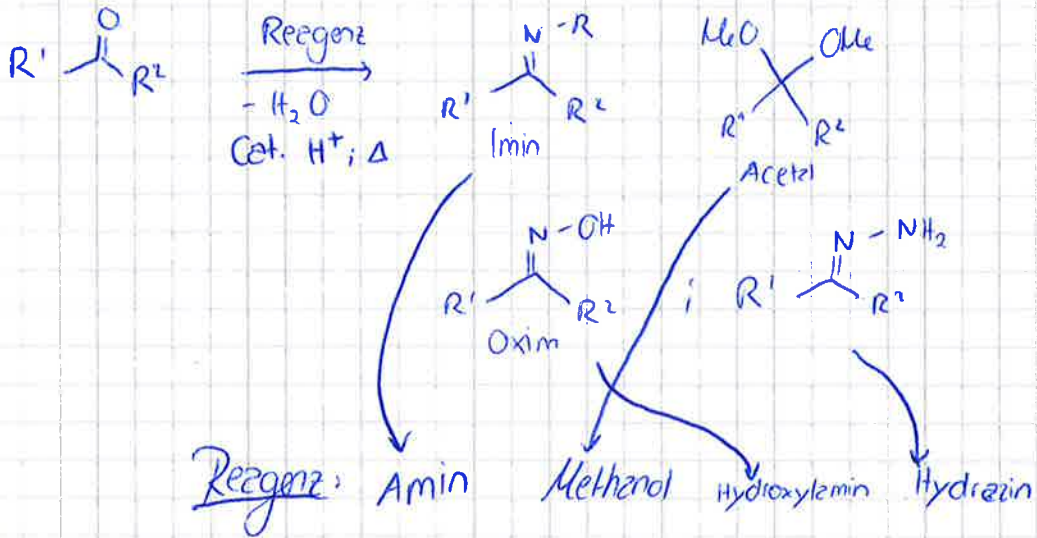
Enantiomere

(R)-AMP: N-Aminomethoxymethylpyrrolidine

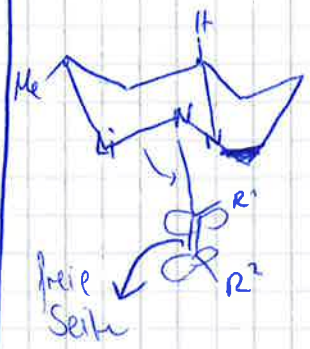
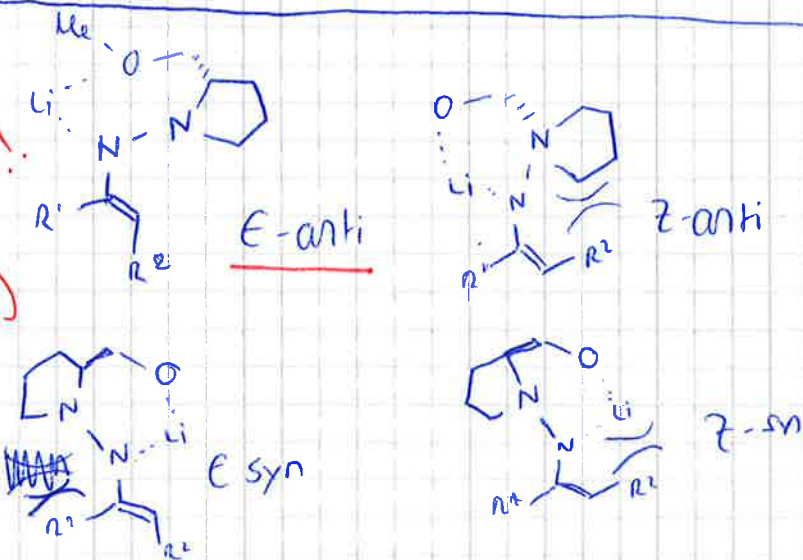


Uelavsur

Kondensationsreaktion v. Carbonylen:

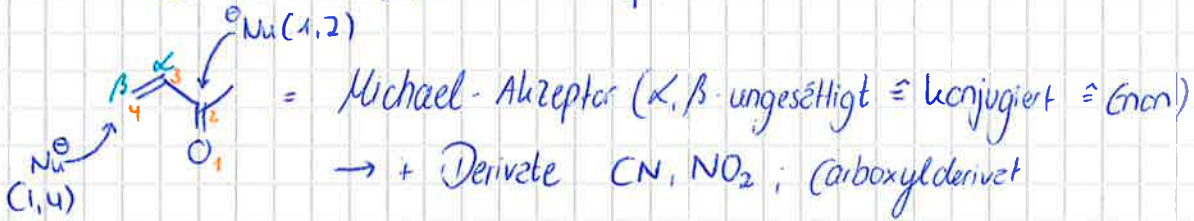


74 **R₁ und R₂ gleich!!**
Bedingung
Symmetrie



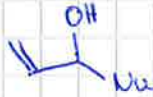
1,4-Addition an Carbonyle (Michael-Reaktion)

→ Substrat → Michael-Akzeptor



Gesamter Elektronenreichtum über 4 Atome verteilt

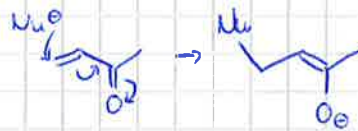
1,2-Add



1,4-Add



Mech:



Selektivität zw. 1,2 / 1,4 Add erlangen (Kontrolle)

→ Beschaffenheit d. Nu

→ weiches Nu → 1,4-Add. (R-Cu; R-Zn; R-SnR₃; R-SiR₃)

→ hartes Nu → 1,2-Add. (R-Li; R-HgBr; R-Na; R-K)

↑ leicht polarisierbar

Organo-metalle

↓ schwerer polarisierbar

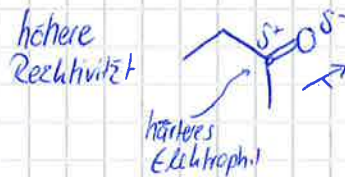
Organocuprate



→ S_N2-Reaktion (S_N2'-Rkt)

→ Epoxidöffnung

→ 1,4-Addition



hart ↔ hart
 weich ↔ weich
 molekular
 Overlap
 besser
 kommen sich
 energetisch
 näher

Einzelne Cuprate

- Gilman-Cuprat
- Lipshutz-Cuprat
- Normant-Cuprat
- Knochel-Cuprat

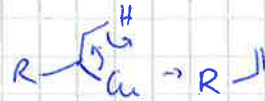
1) Gilman-Cupret



- thermolabil (-78 °C)

- sehr reaktiv

- Me-Cu; 1°(R) $R-CH_2-Cu$ 2° & 3° mechen Eliminierungen



Nachteil von R_2CuLi :

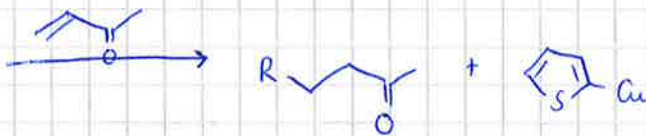
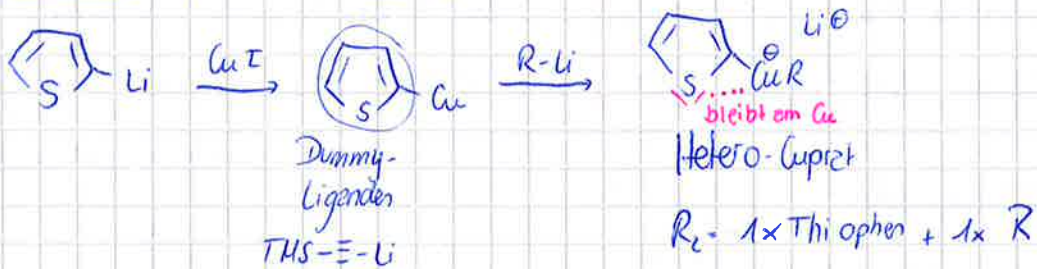


man kann nur 50% des Cuprets verwenden

Lösung: Hetero-Cupret

R_2CuLi = Homo-Cupret $R_2 = 2 \times$ gleicher Rest

Hetero Cupret (Gilman)



thermisch-stabiler (bis -30 °C)

- Epoxidöffnung

2) Lipshutz-Cuprat

Komplexbildung

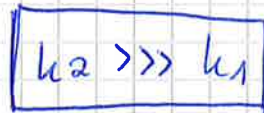
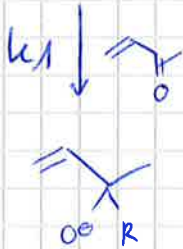
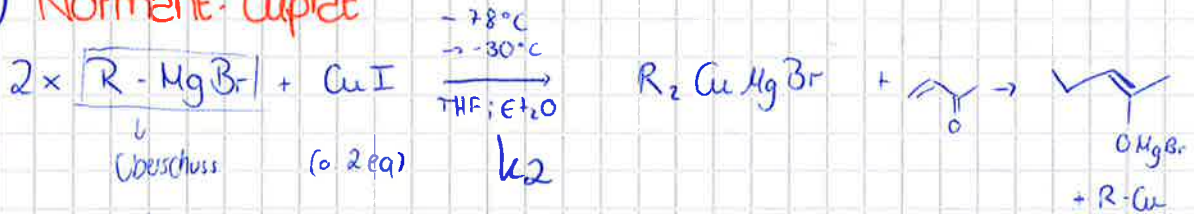


- thermisch stabiler als Gilman
- von Reaktivität mit Gilman vergleichbar
- 2° & 3° → keine Eliminierung !!
- Epoxidöffnung

ein Teil geht wieder verloren. Nicht die Möglichkeit eines Hetero-Cuprats



3) Normant-Cuprat



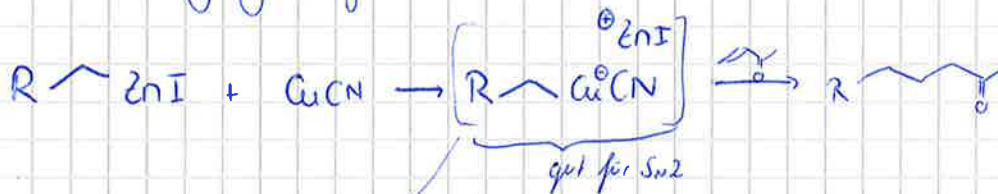
entscheidendes Kriterium für katalytische Mengen Kupfer!

ähnlich wie Lipshutz

- Epoxidöffnung

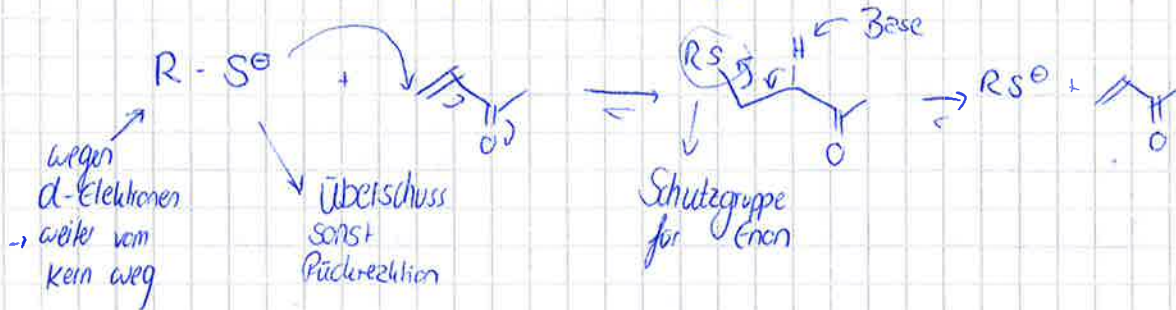
4) Knochel-Cuprat

am besten geeignet für S_N2

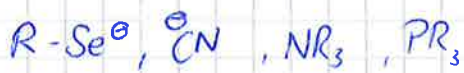


1 org Rest zu 100% übertragen

Weiche Nucleophile (nicht organometall):



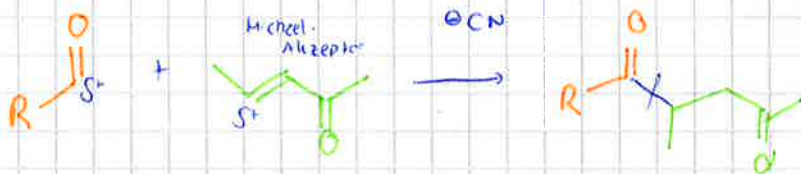
Über Konzentration kann man die Rkt steuern



Bsp für 1,4-Add:

- Robinson-Annelierung
- Mannich-Rkt
- Stetter-Rkt
- Sakurai-Rkt

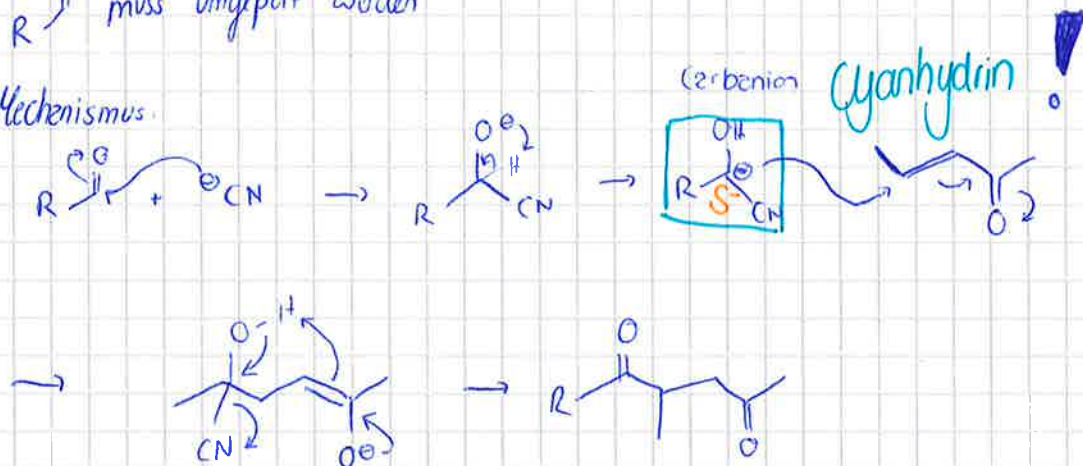
Stetter-Reaktion (Umpolung)



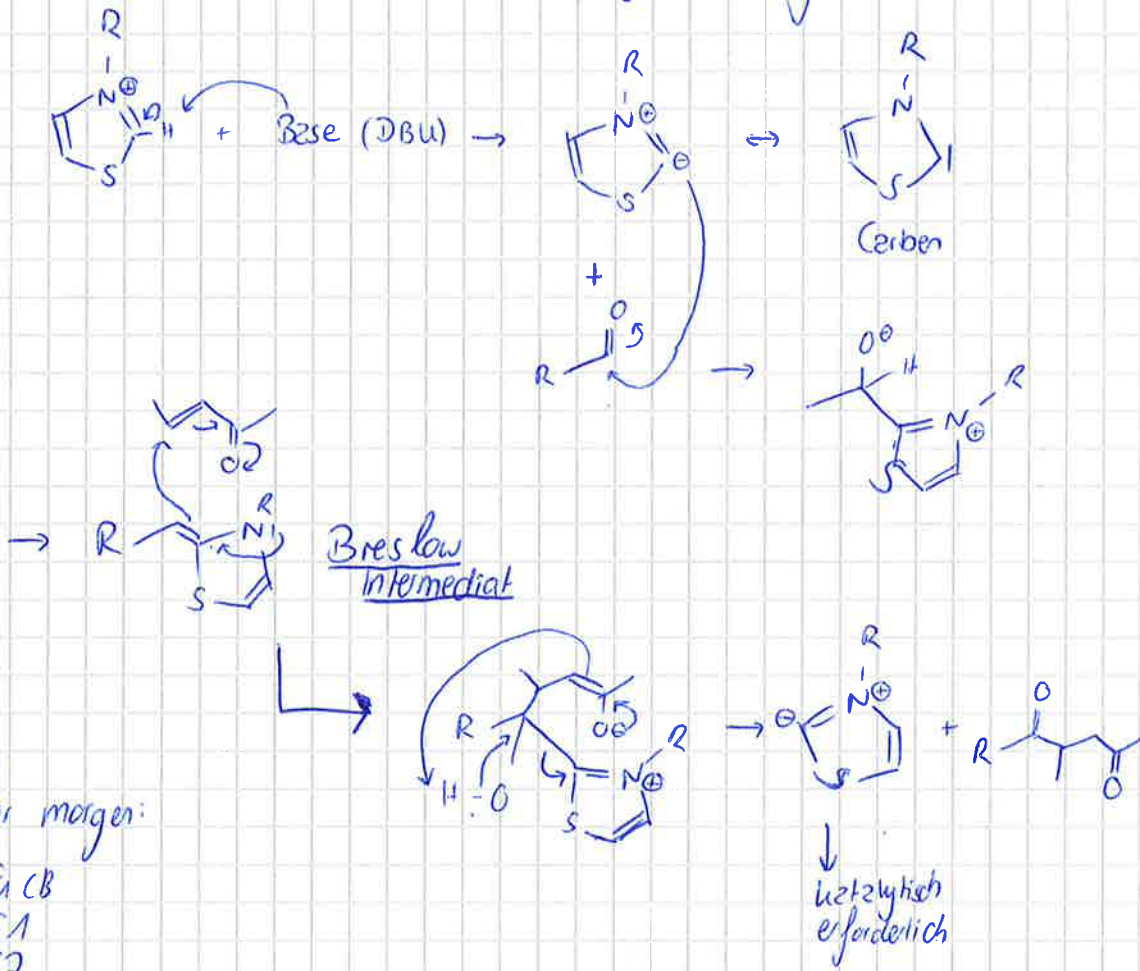
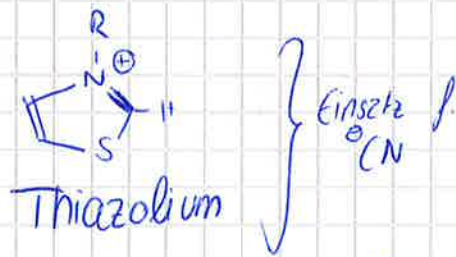
Wie kann S^+ & S^+ reagieren?

$R-C(=O)-S^+$ muss umgepolt werden

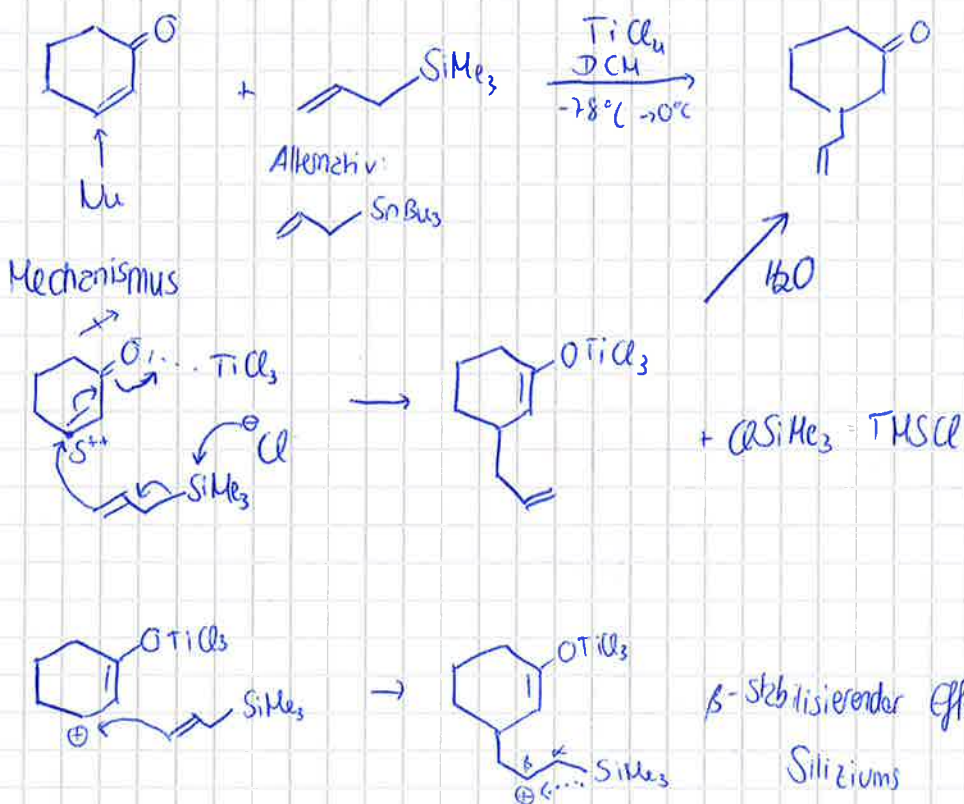
Mechanismus:



Stetter-Reaktion mit:



Sakurai-Reaktion

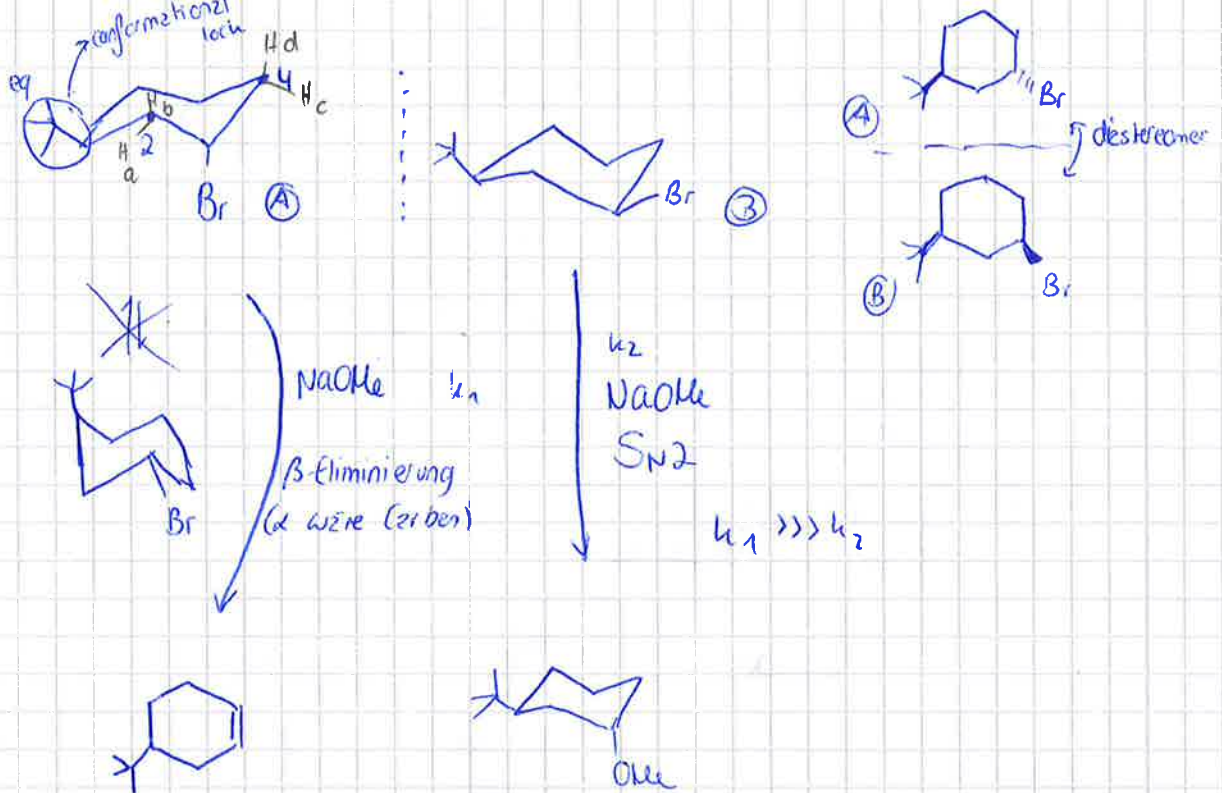


12.1.16

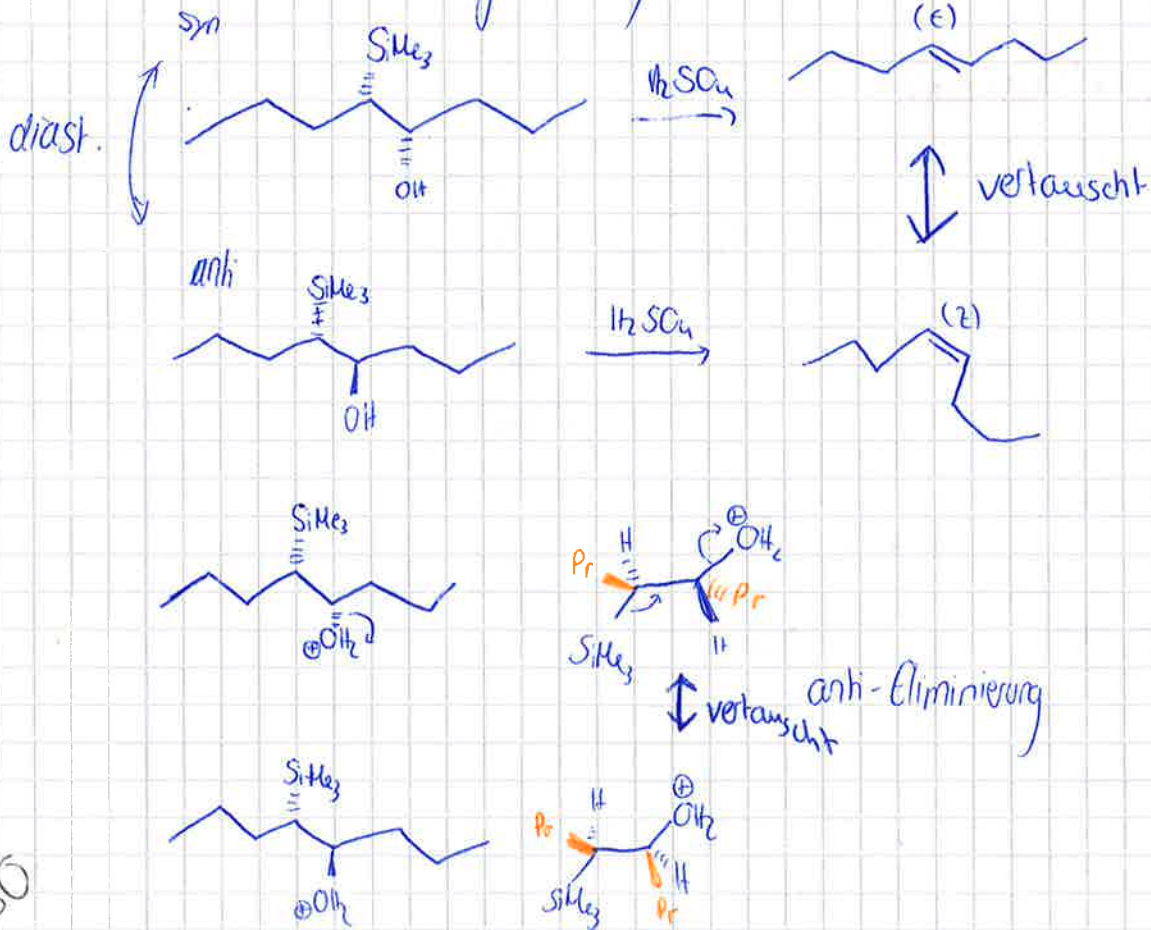
Eliminierungen / Olefinierungen

→ Ausbildung einer Mehrfachbindung

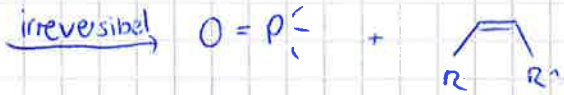
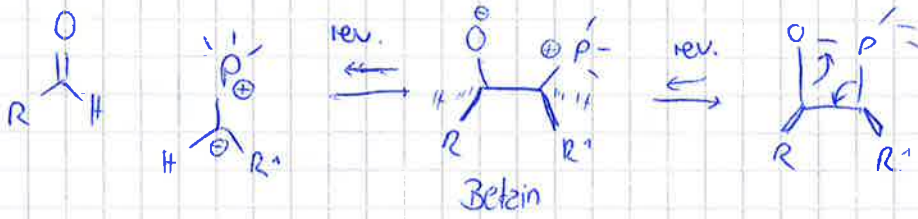
E2 immer
anti-Position
der zu
eliminierenden
Elemente
→ damit π -
Bindung entsteht



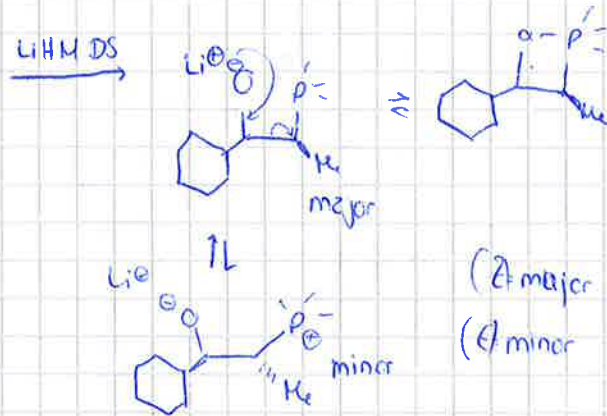
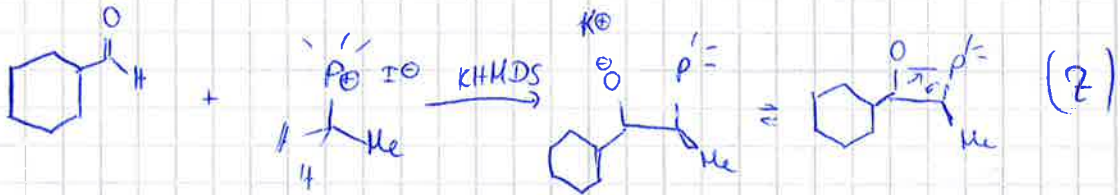
Peterson-Olefinierung



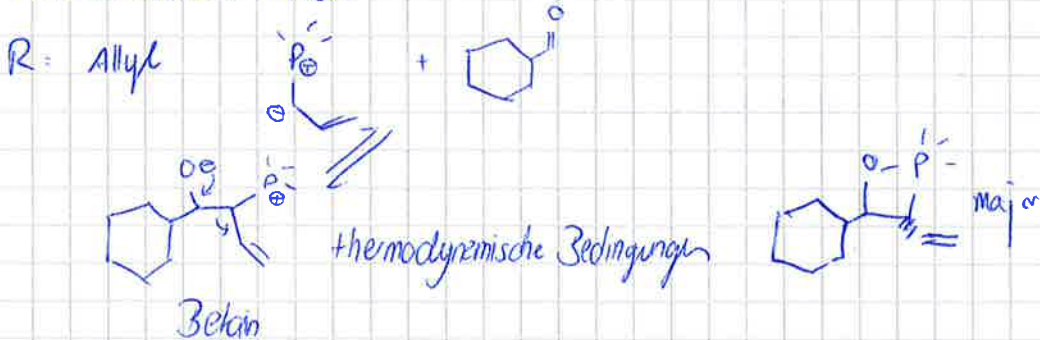
Ausbildung des Oxaphosphetans



Reversibilität: - Bedingungen (Gegenion)
 - R¹-Beschaffenheit



Stabilisiertes Ylid:



Nicht-stabilisiert: (Z)

Stabilisiert: (E)

Li, K, Na: salzfreies Wittig (Z)

Lithium-salz-induziert → (E)

↓ Schlosser-Verzichte + KOtBu

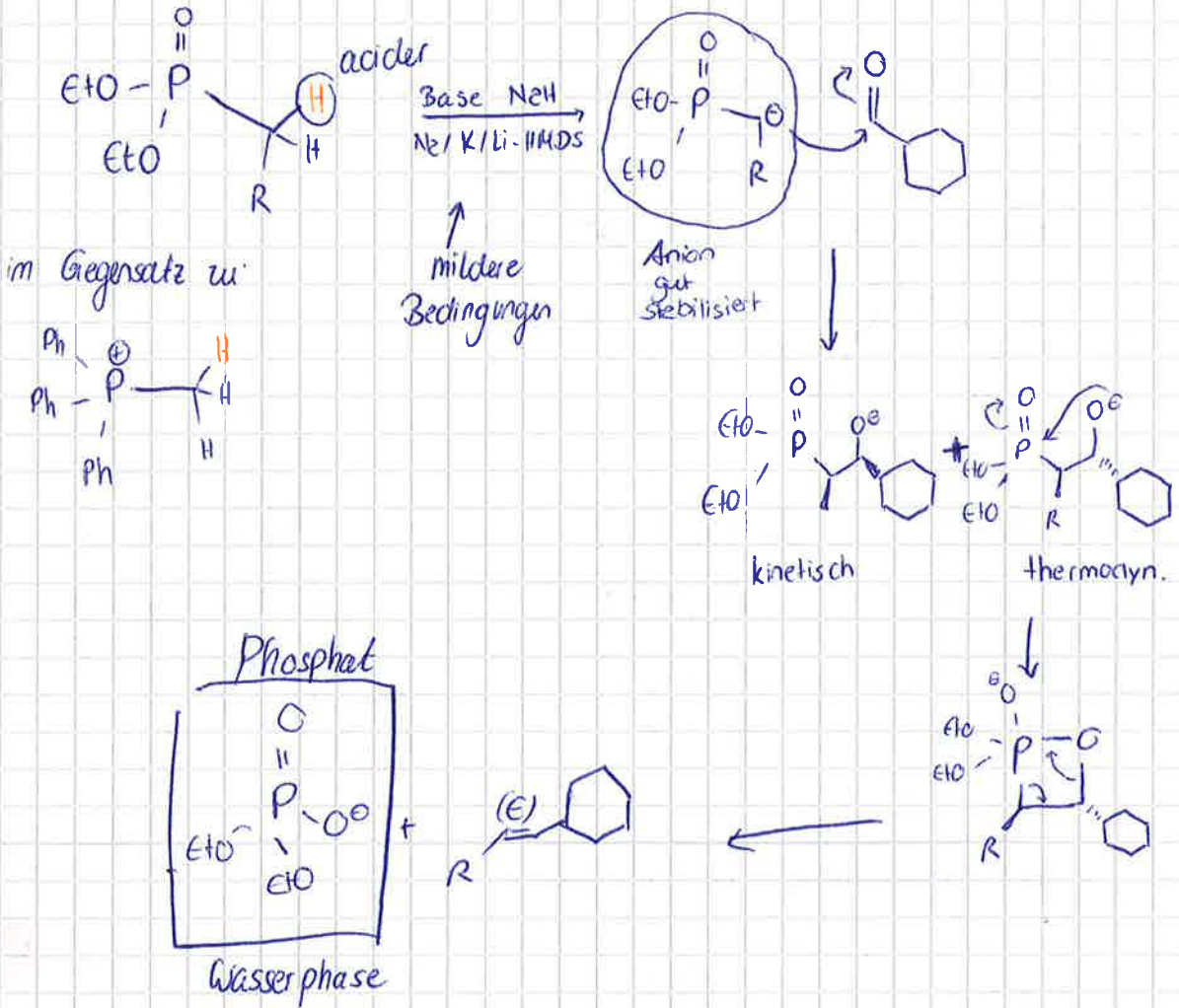
Varianten der Wittig-Reaktion

- Wittig-Horner
- Horner-Wadsworth-Emmons (HWE)!

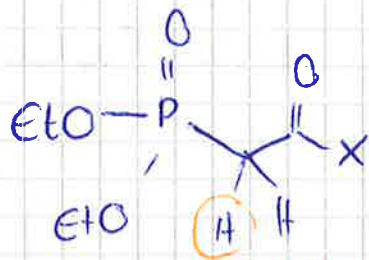
Wittig: Phosphin → Phosphinoxid

W-Horner: Phosphonit → Phosphat

Wittig-Horner: statt Phosphine → Phosphonate



Horner-Wadsworth-Emmons

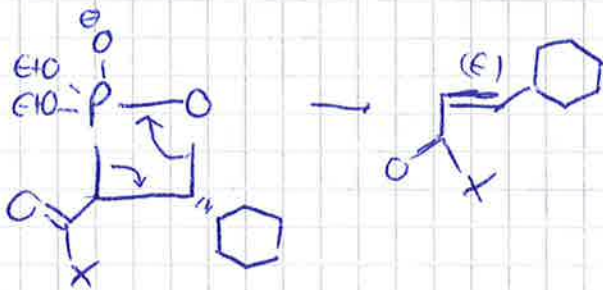


(Analog 1,3-Dicarbonyl)
 X = Alkyl, OR, NR₂...

acidischer als bei Wittig Horner
 (2 e⁻ ziehende Subst.)

β-Ketophosphonat

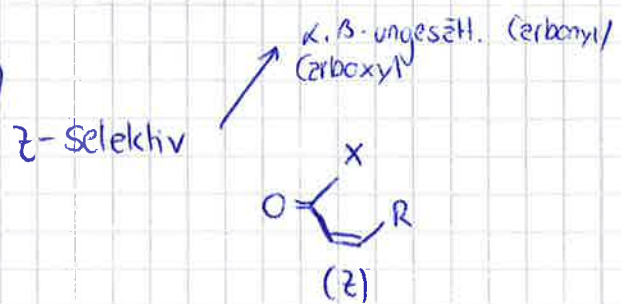
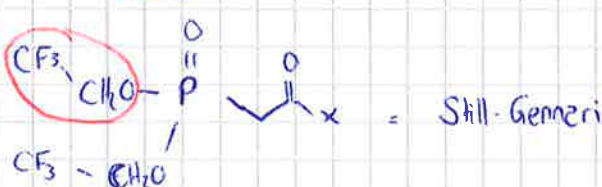
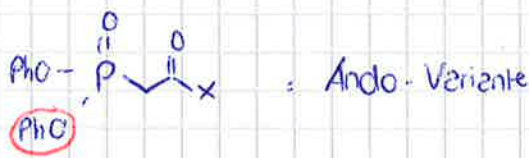
Intermediat d. Reaktion (Mechanismus analog W-H)



Wittig	Wittig-Horner	HWE
Phosphin	Phosphonat	β-Ketophosphonat
PR ₃	<chem>CCOP(=O)R</chem>	<chem>CCOP(=O)C(=O)X</chem>
R = Alkyl, Phenyl		
<p>pk (abnehmend) → acider</p>		
(Z)	(E)	(E) α,β-ungesätt. Carbonyl/Carboxyl

HWE immer E-selektiv

↳ Z-selektiv bekommen:

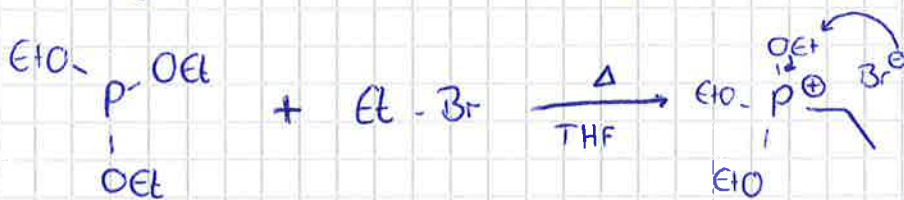


84

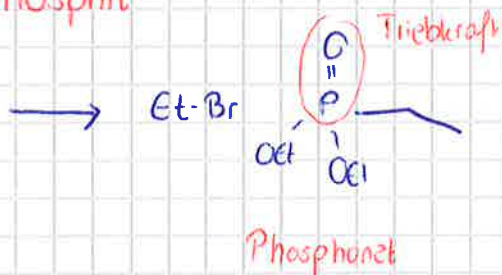
Wie macht man so einen β -Ketophosphonat?

Arbuzov-Rkt.

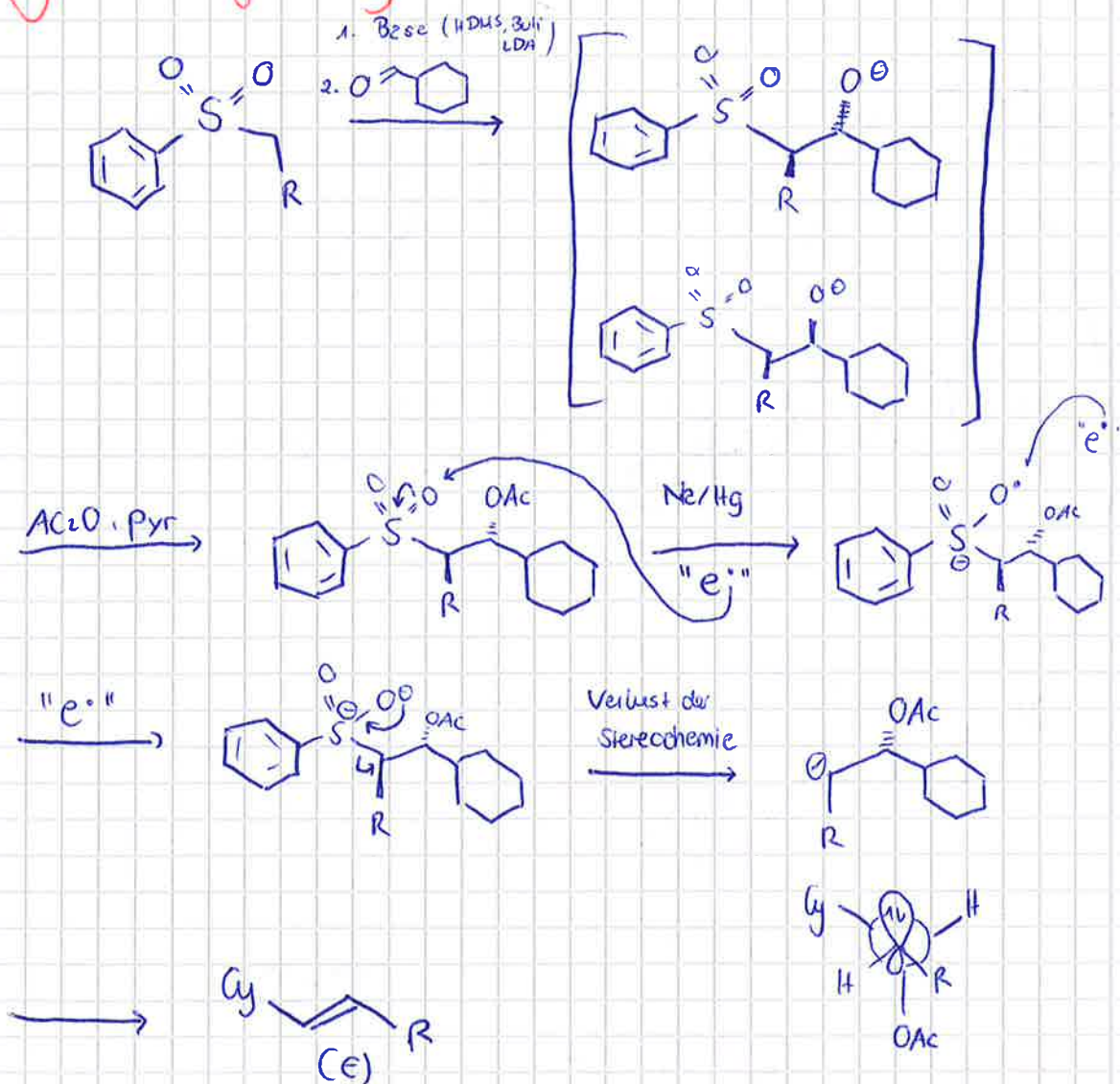
Analog Phosphoniumsalz Bildung bei Wittig (Alkylierung)



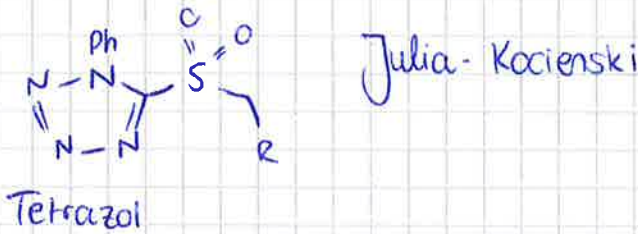
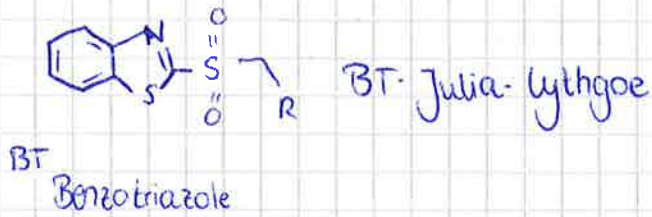
Phosphit



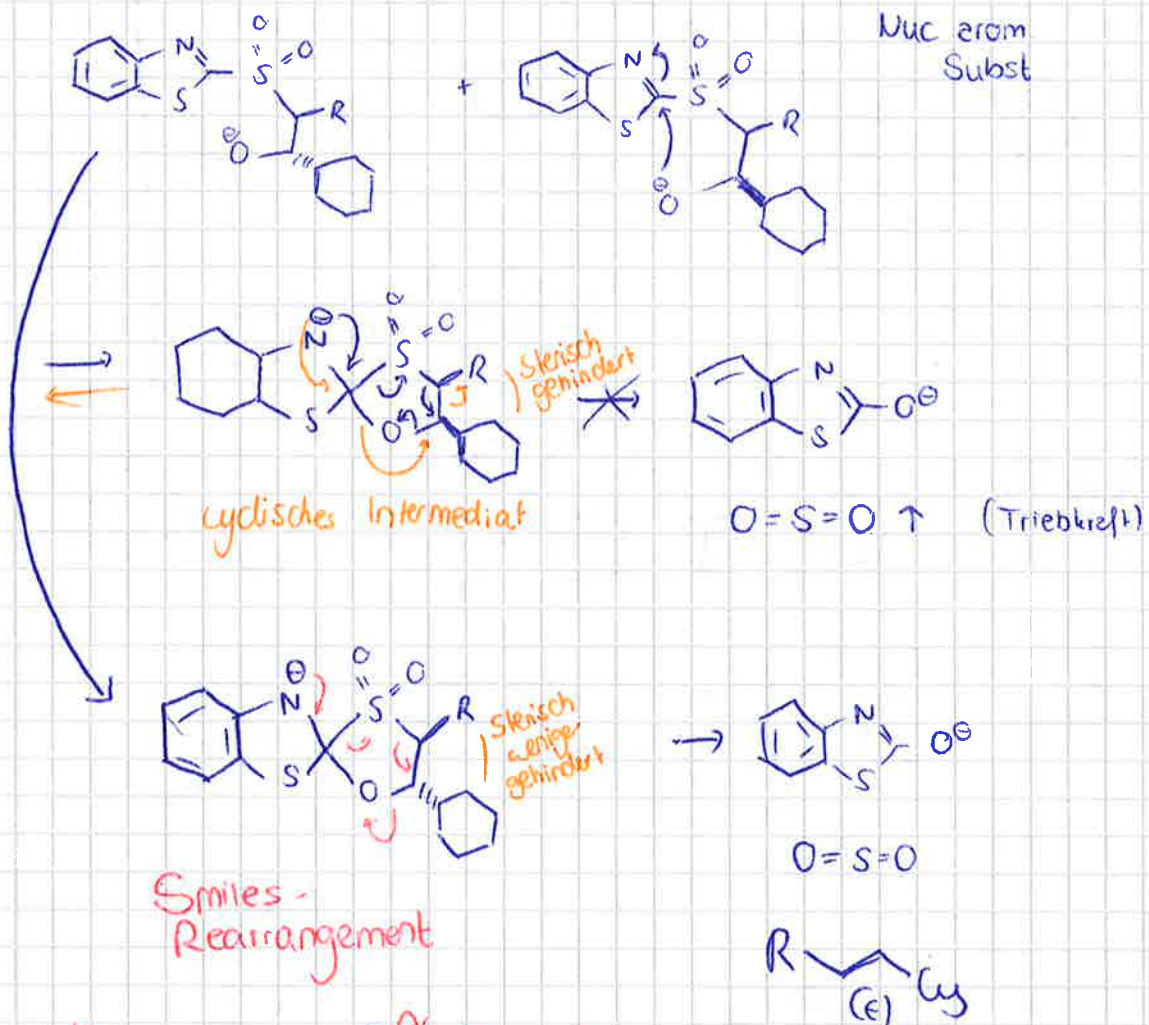
Julia-Olefinierung (E-DB)



Varianten:



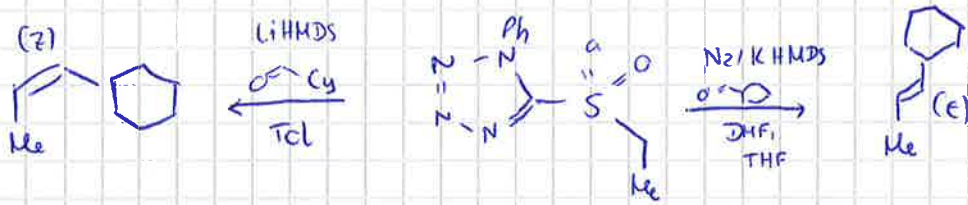
Julia-Olefinierung BT / Tetrazole



Smiles-Rearrangement

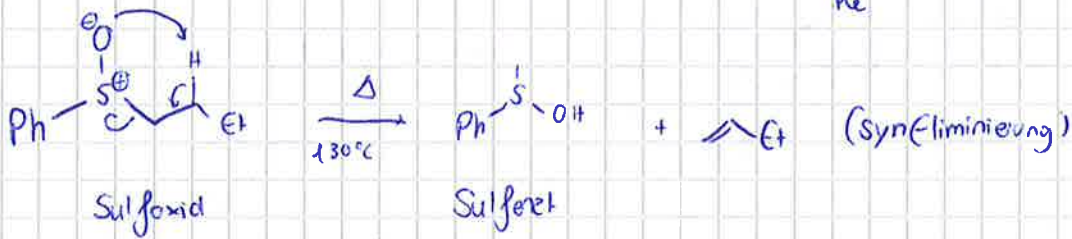
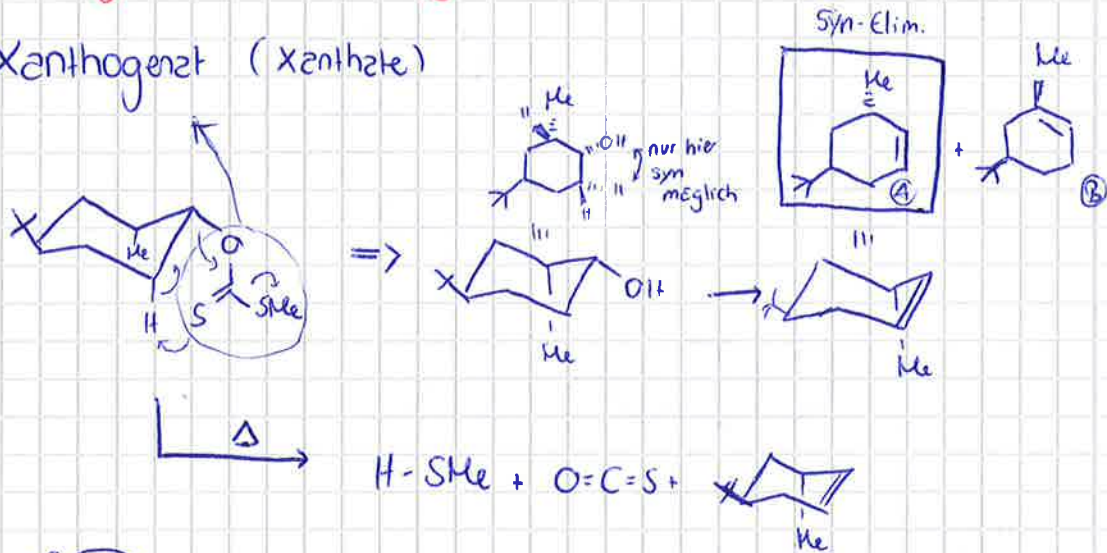


Kocienski - Variante



Chugaev-Eliminierung (syn-Eliminierung)

Xanthogenat (Xanthate)

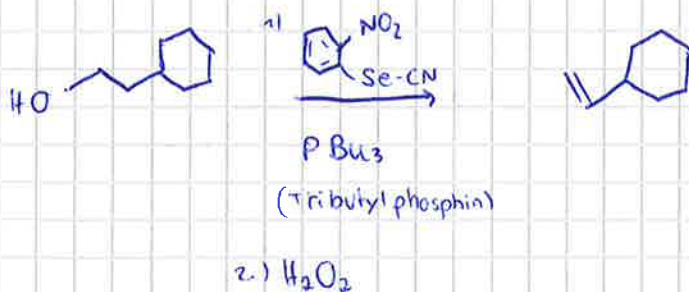


→ tiefere Eliminierungstemperaturen: Selen (Se)

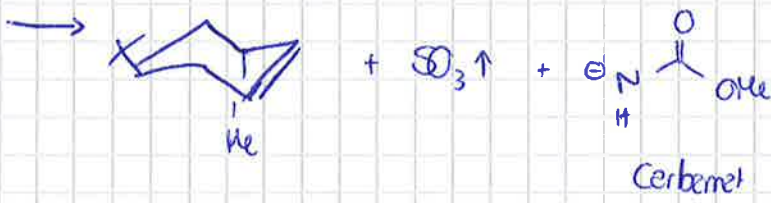
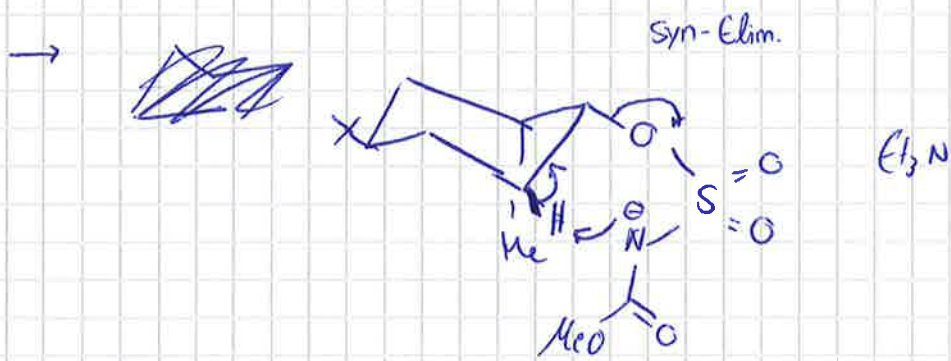
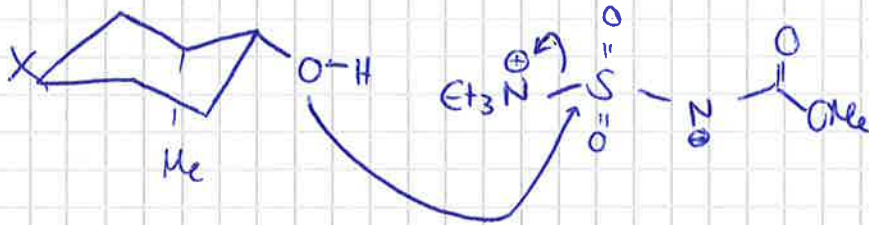
Grieco-Protokoll:

↳ selektiv (prim. Alkohole)

↳ (vogeschaltete Su2-Rekt)

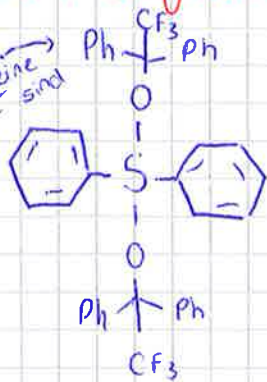


Mechanismus:



Martin-Sulfuran

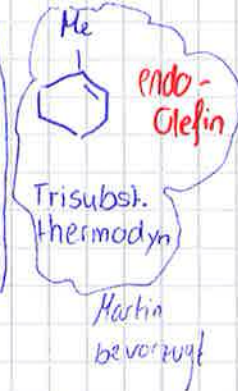
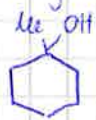
Reagenz
nur stabil
weil hier keine
β-ständige e⁻ sind



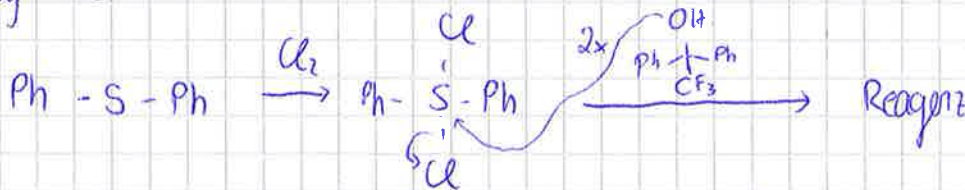
im Vergleich:

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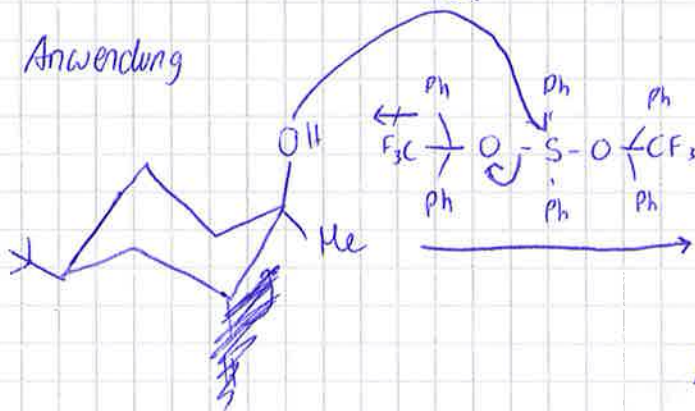
Burgess



Synthese:



Anwendung

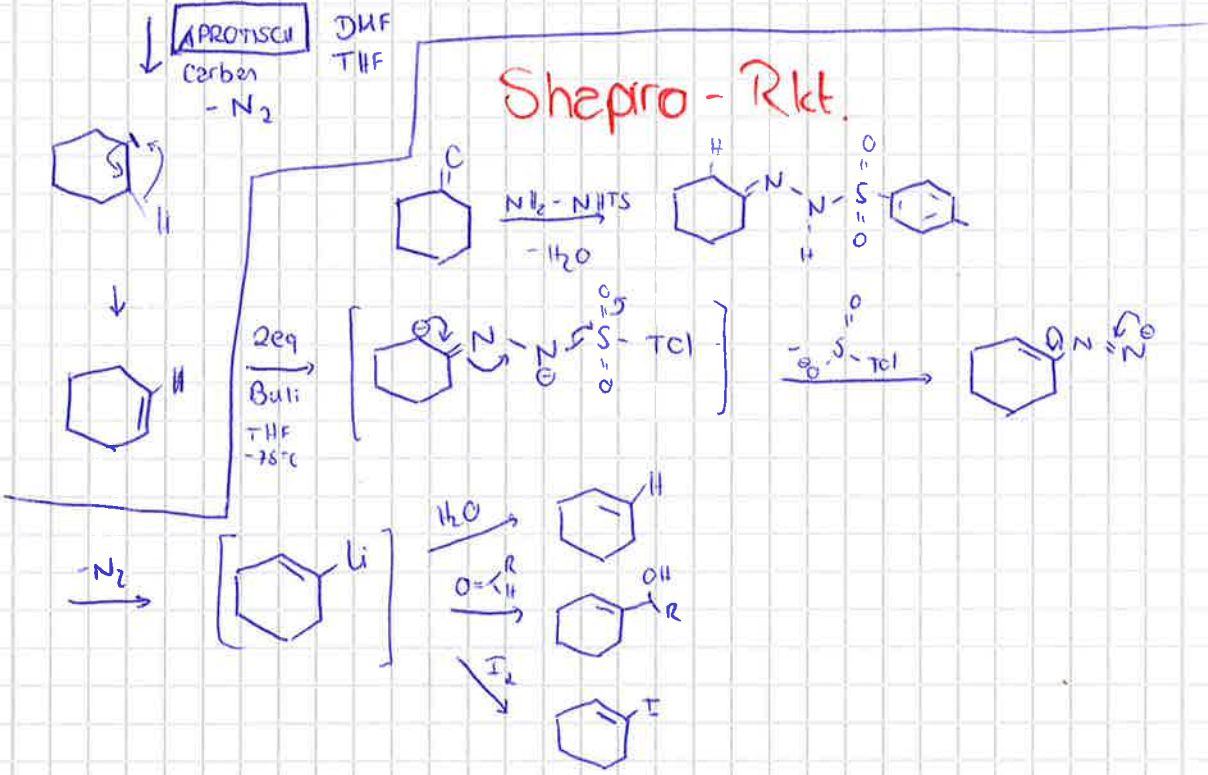
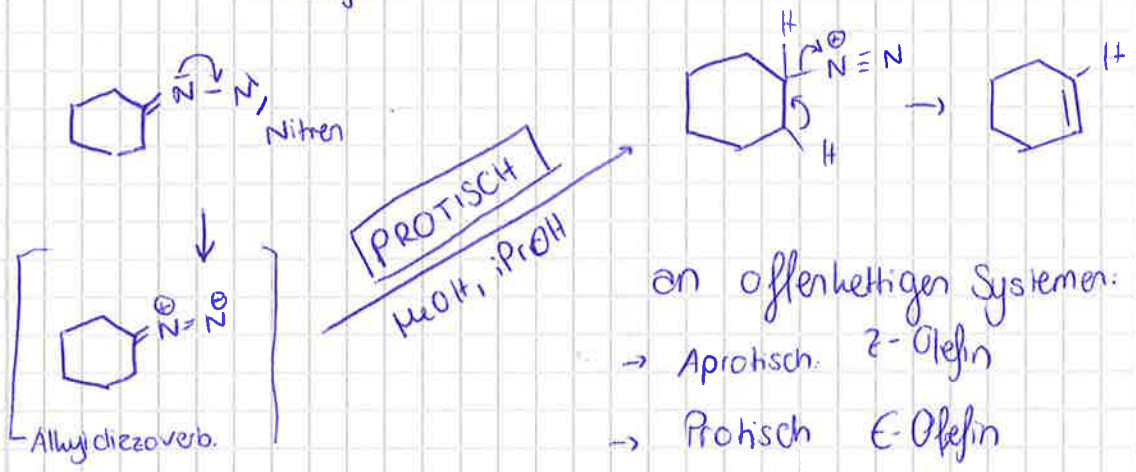
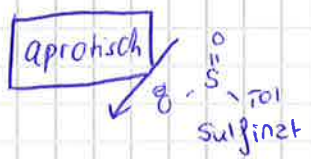
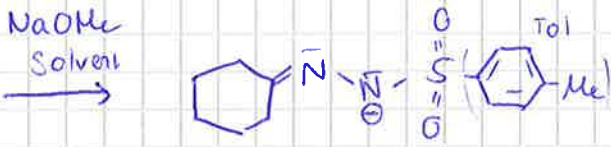
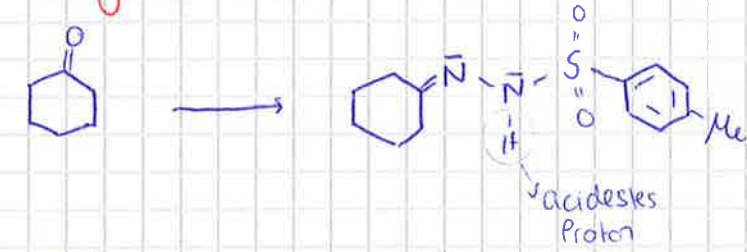


F₃C ist sehr e⁻-ziehend
→ O kann leichter abgespaltet werden

β-Eliminierung
anti-Eliminierung

25.1.16

Bamford-Stevens Rkt.

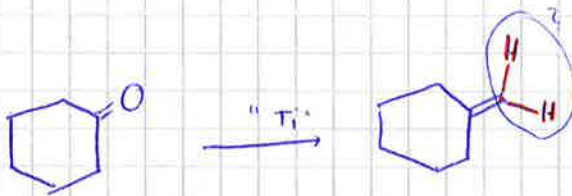
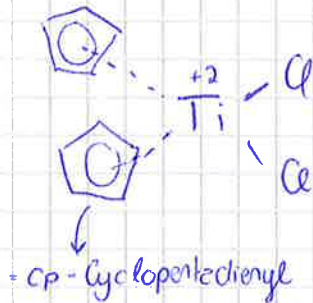


Olefinierung v. Carbonyl-Verb. über Ti

Ti⁰; Ti⁺² niedervalent → Olefinierung

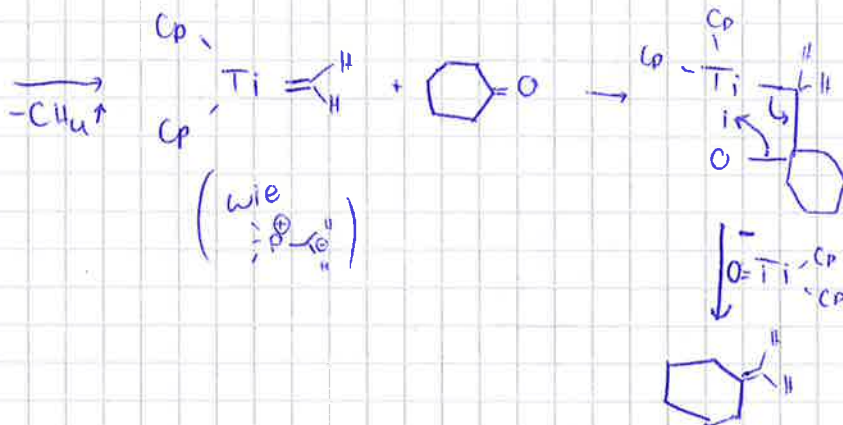
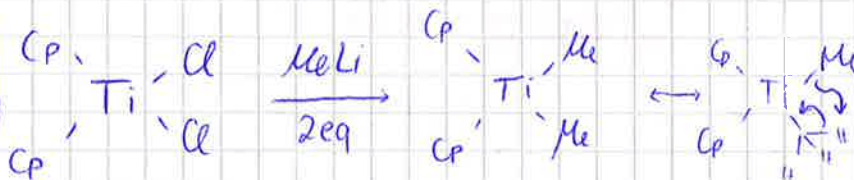
Ti^{IV} höher valent

Ti^{III} radikal Reaktionen



→ Einführung der "CH₂" Gruppe am Ti-Komplex

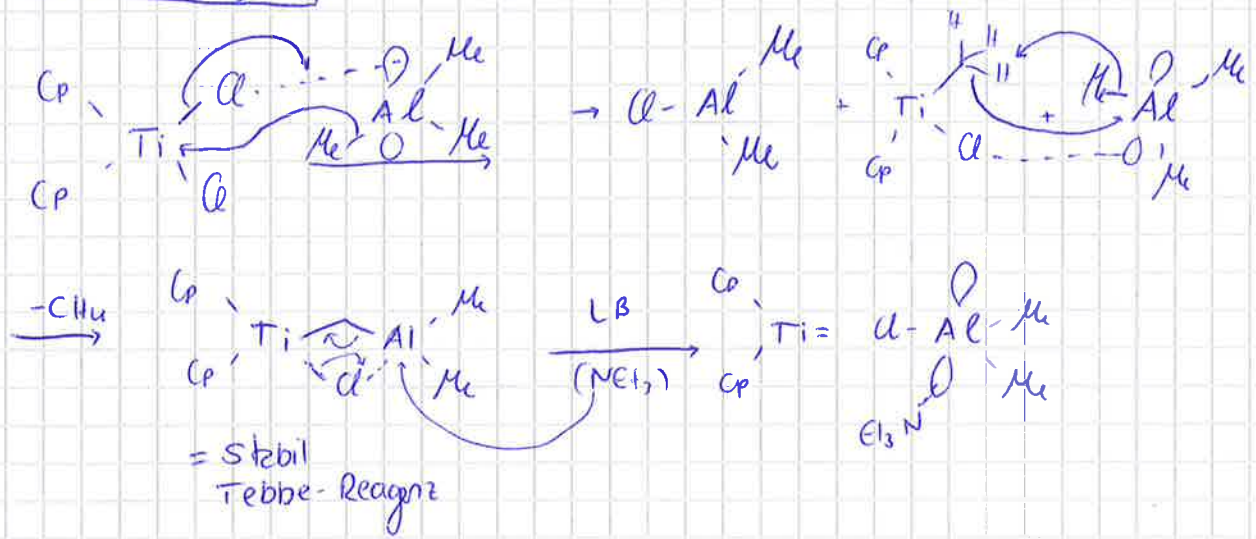
Petasis-Reagenz



Metalle-cyclo-
butanring

"analog Oxephosphoran"

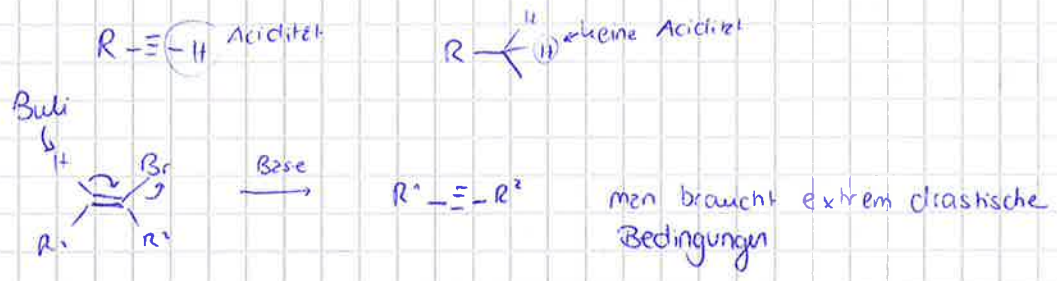
Tebbe-Reagenz



Dreifachbindungen / Alkine

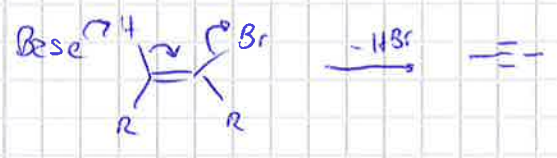


← s-Charakter nimmt zu
Acidität nimmt zu

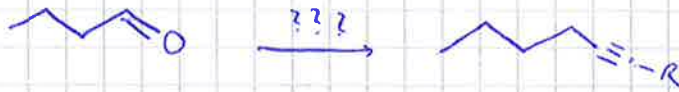


Darstellung von Alkinen

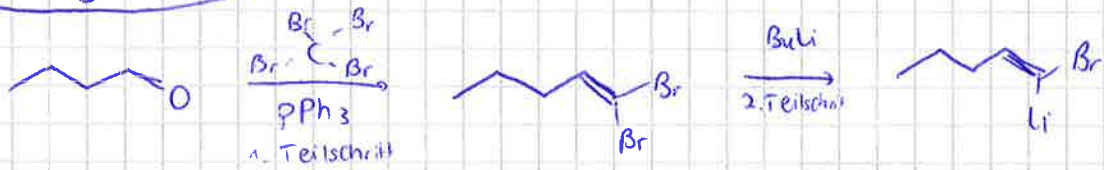
1) β-Eliminierungen v. Alkenen → geht, aber unpraktisch



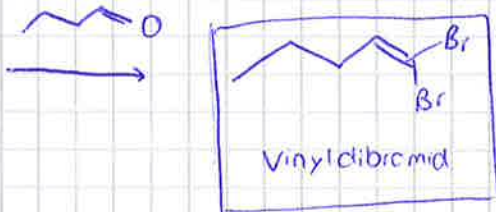
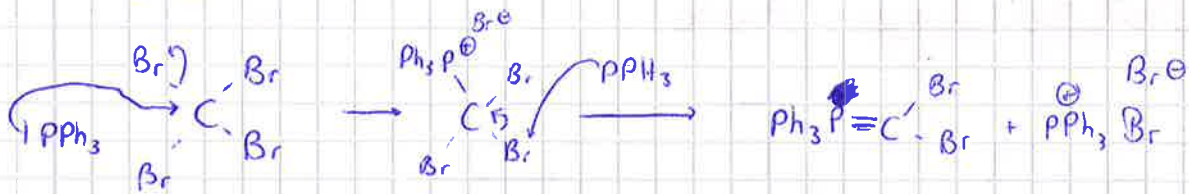
2) Wittig-analoge Reaktion



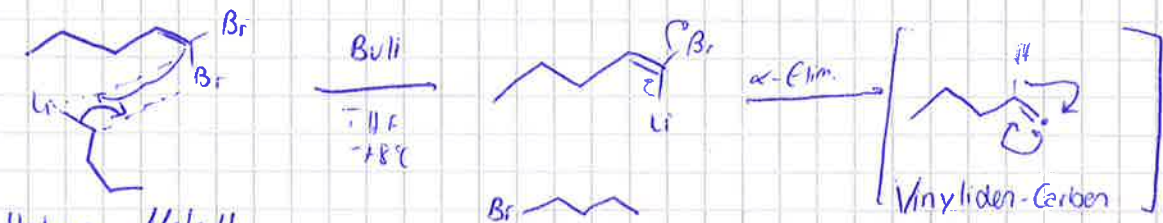
Corey-Fuchs



1. Teilschritt



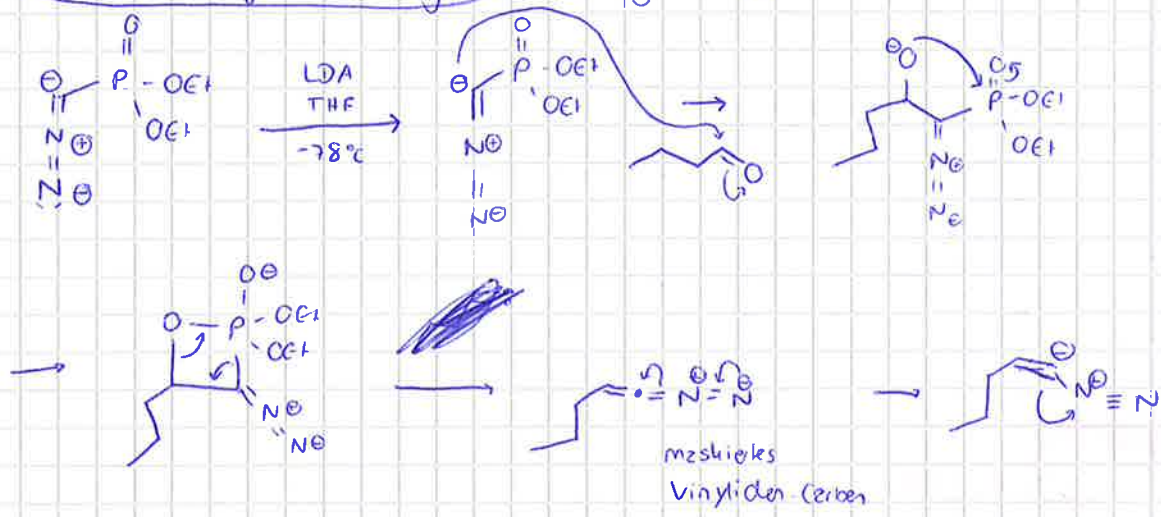
2. Teilschritt



Halogen-Metall-austausch

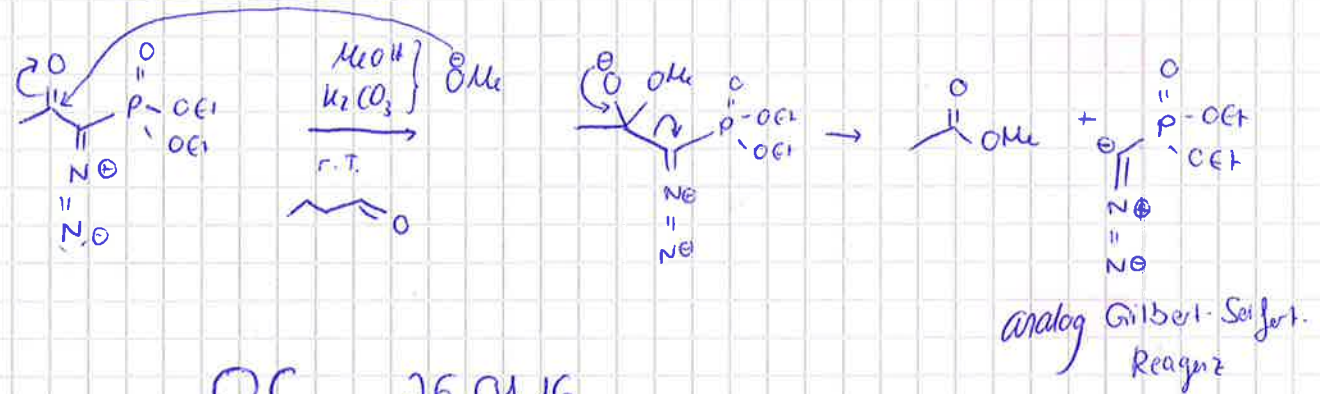


Gilbert-Seiffert-Reagenz (analog Wittig-Horner)



→ anschließend analog zu Corey-Fuchs

Ohira-Bestmann Rgz (analog HWE)



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Perizyklische Reaktionen

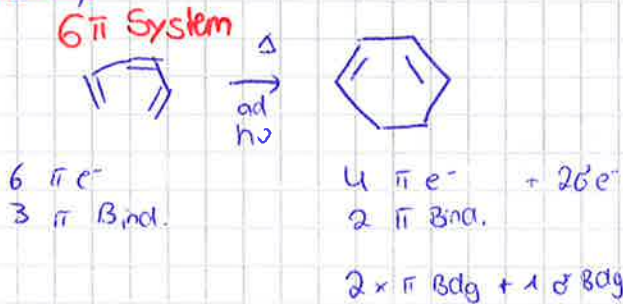
- Konzentrierte Umlagerung v. Elektronen über einen zyklischen Übergangszustand
- thermisch oder photochemisch induziert
- Rearrangement d. Elektronen unterliegt der Erhaltung der Orbitalsymmetrie d. betreffenden MO.
- Gesetzmäßigkeiten, die daraus folgen:
 - ⇒ Woodward Hofmann Regeln

Klassen: Triebkraft (Molekularorbitaländerung) → unterschiedlich

Unterscheidung in:

- 1) Elektrozykl. Rkt.
- 2) Sigmatrope Umlagerungen
- 3) Cycloadditionen (c. A.)
- 4) Chlletrope R. (spez. c. 1)
- 5) Group transfer R.

ad 1)



Triebkraft
 $1 \pi \text{-Bdg} \rightarrow 1 \sigma \text{-Bdg}$

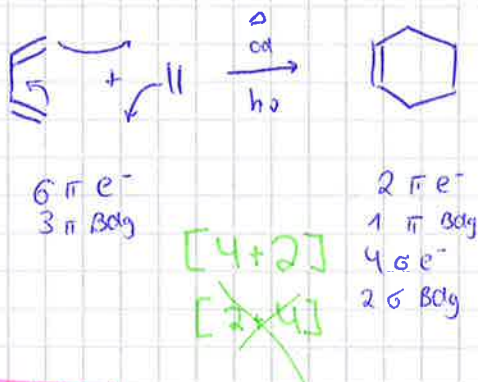
ad 2)



Entartete Reaktion
 $\Delta G = 0$

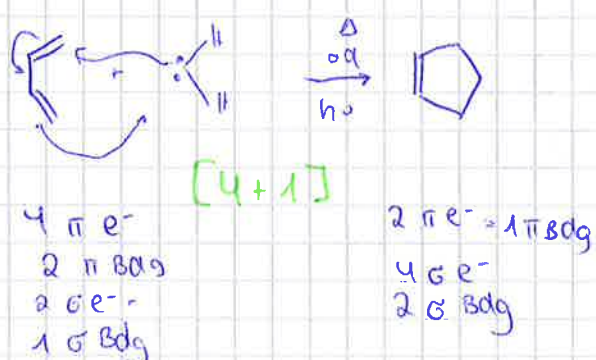
[2,3] statt [3,2] ← Allg für Berechnung
 kleinste zuerst

ad 3)



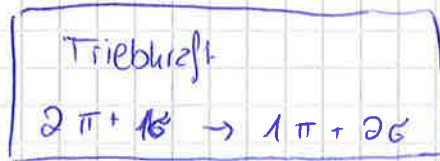
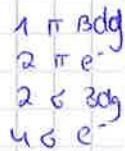
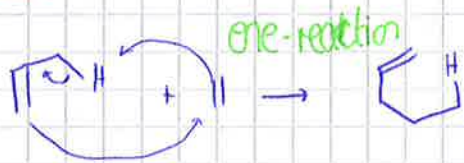
Triebkraft
 $3 \pi \text{-Bdg} \rightarrow 1 \pi \text{ Bdg} + 2 \sigma \text{ Bdg}$

ad 4)



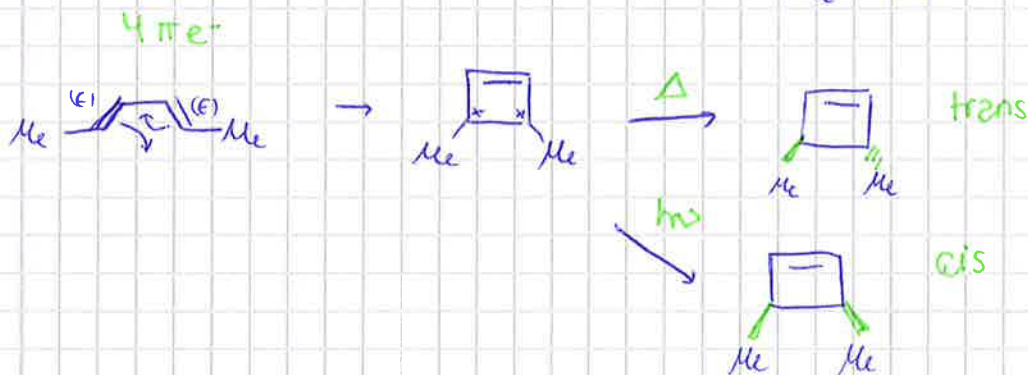
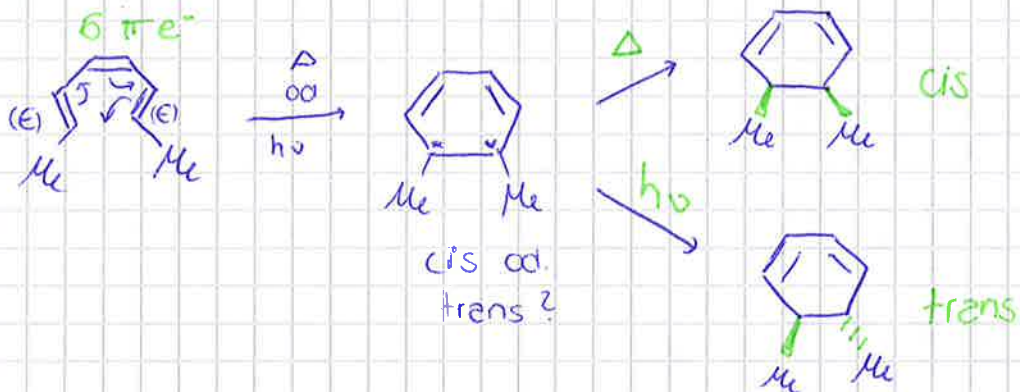
Triebkraft
 $2 \pi \text{ Bdg} + 1 \sigma \text{ Bdg} \rightarrow 2 \sigma \text{ Bdg} + 1 \pi \text{ Bdg}$

ad 5)



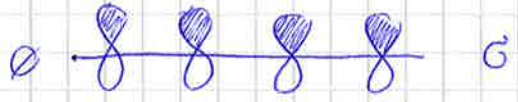
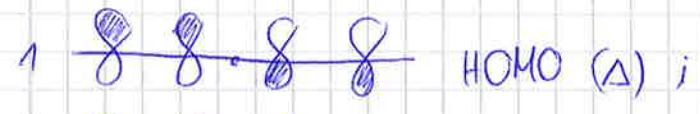
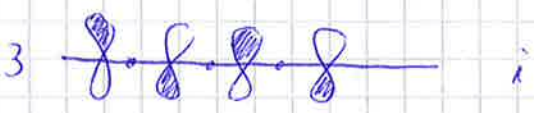
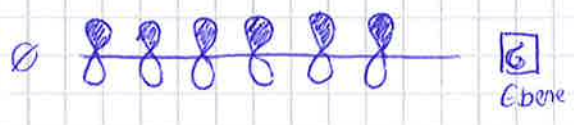
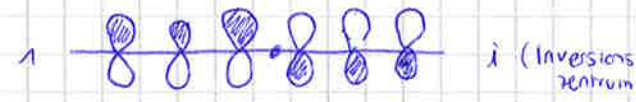
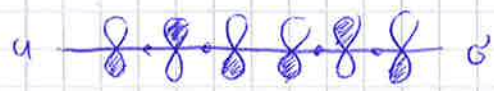
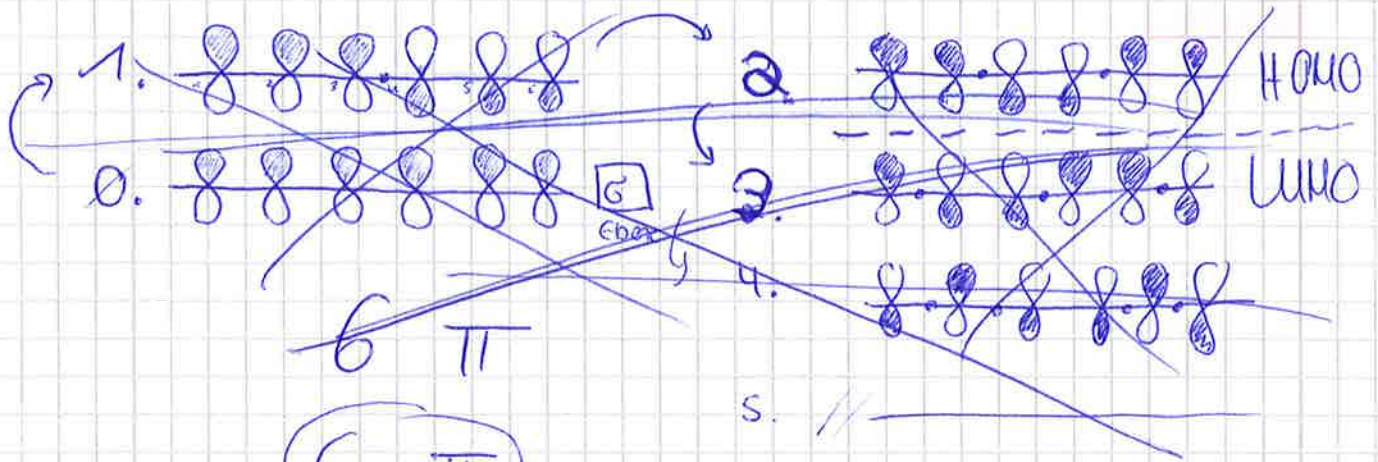
Perizyklische Reaktionen: STEREOSPEZIFISCH
und nicht stereoselektiv

Elektrozyklische Rkt:



Korrelation:

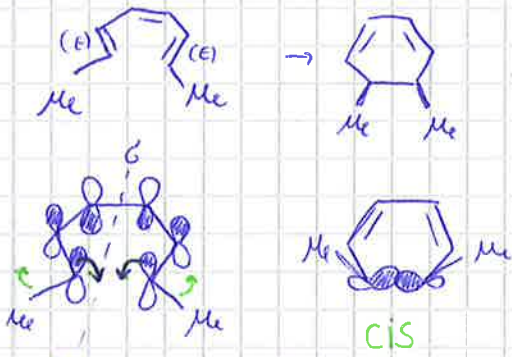
- 1) \rightarrow Doppelbindungsgeometrie im Su \rightarrow transferiert in Stereozentren im P.
- 2) Anzahl d. π e⁻ im Substrat \rightarrow korreliert
mit relativer Stereochemie bei gegebenen Bed (Δ , $h\nu$) im P.



Thermisch: Δ

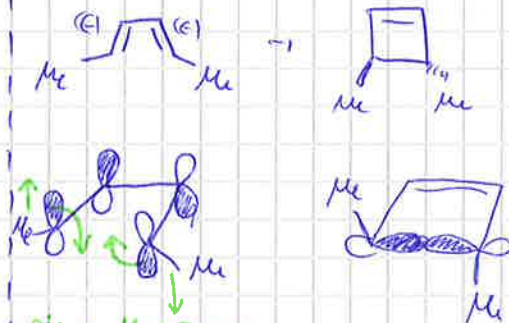
6π

4π



Methylgruppen werden nach oben gedreht

cis



eine Me-Gruppe dreht nach oben, eine nach unten

trans

disrotatorisch

$4n+2$

conrotatorisch

$4n$

$4\pi \rightarrow$	$4n$	$[n=1,2,3]$	Δ	hv
$4\pi \rightarrow$	$4n$	Δ	conrot	disrot
$6\pi \rightarrow$	$4n+2$		disrot	conrot
$8\pi \rightarrow$	$4n$		conrot	disrot
$10\pi \rightarrow$	$4n+2$		disrot	conrot
$12\pi \rightarrow$	$4n$		conrot	disrot

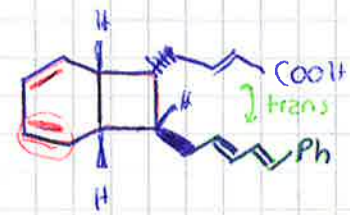
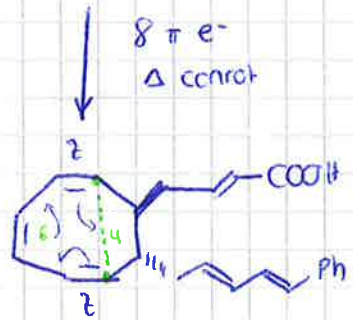
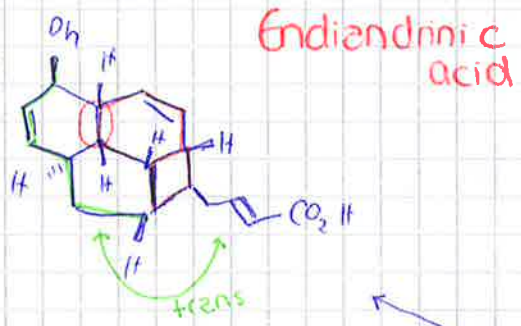
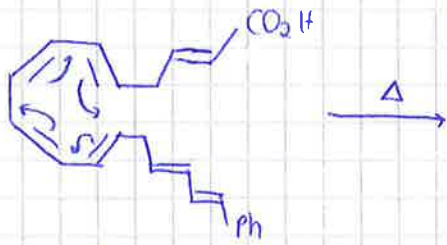
$4n \Delta$ conrot \rightarrow (E,E) trans / (E,Z) cis

$4n$ hv disrot \rightarrow (E,E) cis / (E,Z) trans

$4n+2 \Delta$ disrot \rightarrow (E,E) cis / (E,Z) trans

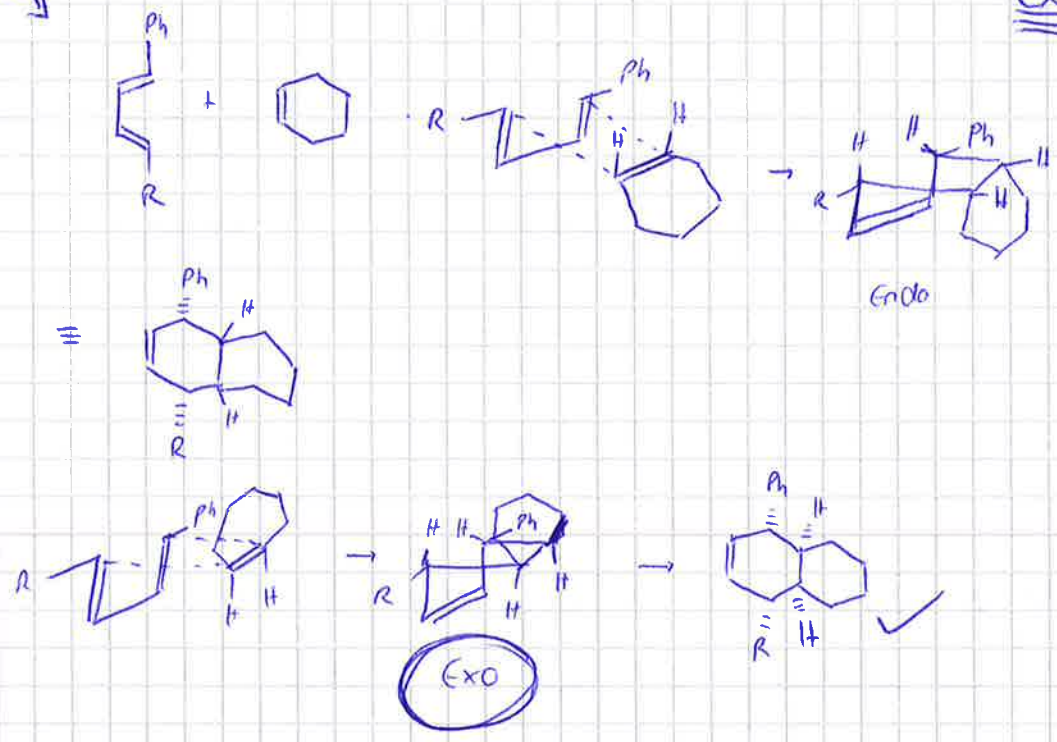
$4n+2$ hv conrot \rightarrow (E,E) trans / (E,Z) cis

Beispiel



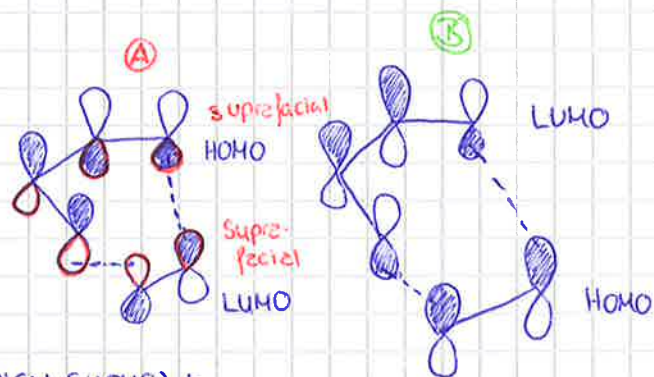
Produkt
über
[4+2]-Cycloadd.
Diels Alder
exo

(fortgesetzt
am 2.2.)



Cycloadditionen

[4+2]: Diels-Alder-Reaktion



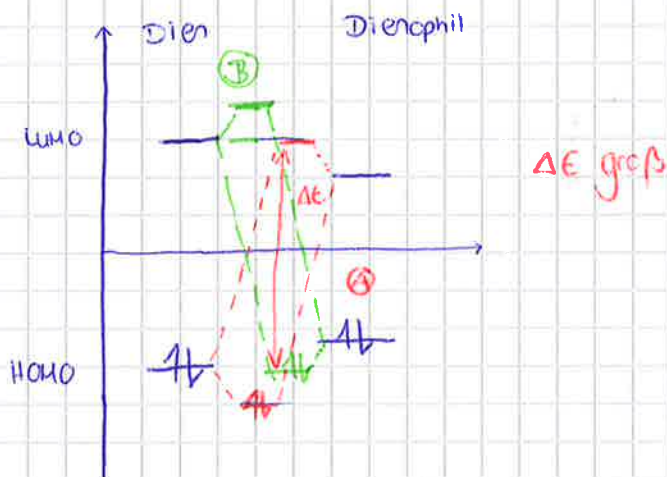
DIEN (HOMO) +
Dienophil (LUMO)

Dien (LUMO) +
Dienophil (HOMO)

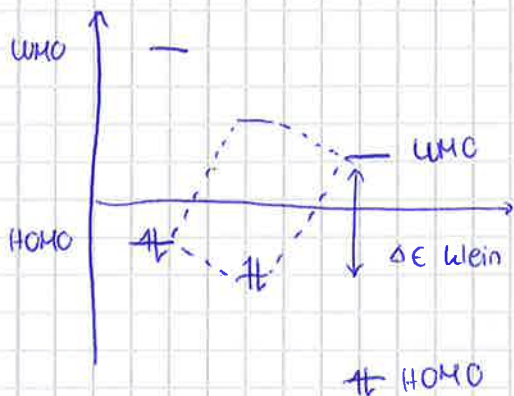
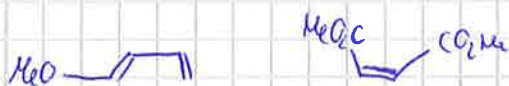
$6 \pi \text{ el.} \Rightarrow 4n+2$

→ Suprafacial (von einer Seite)

HOMO-Wechselwirkung

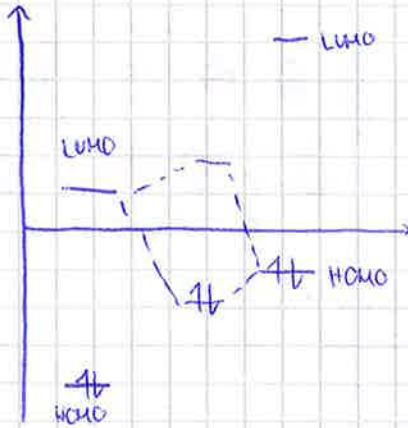
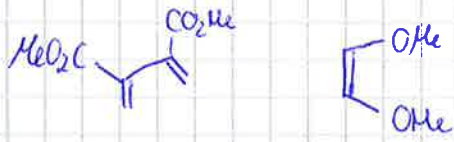


Dien → e⁻ reich / Dienophil e⁻ arm



Normal - Electron Demand D. A

Dien e⁻arm / Dienophil e⁻reich



inverse electron demand
D. A

Dien

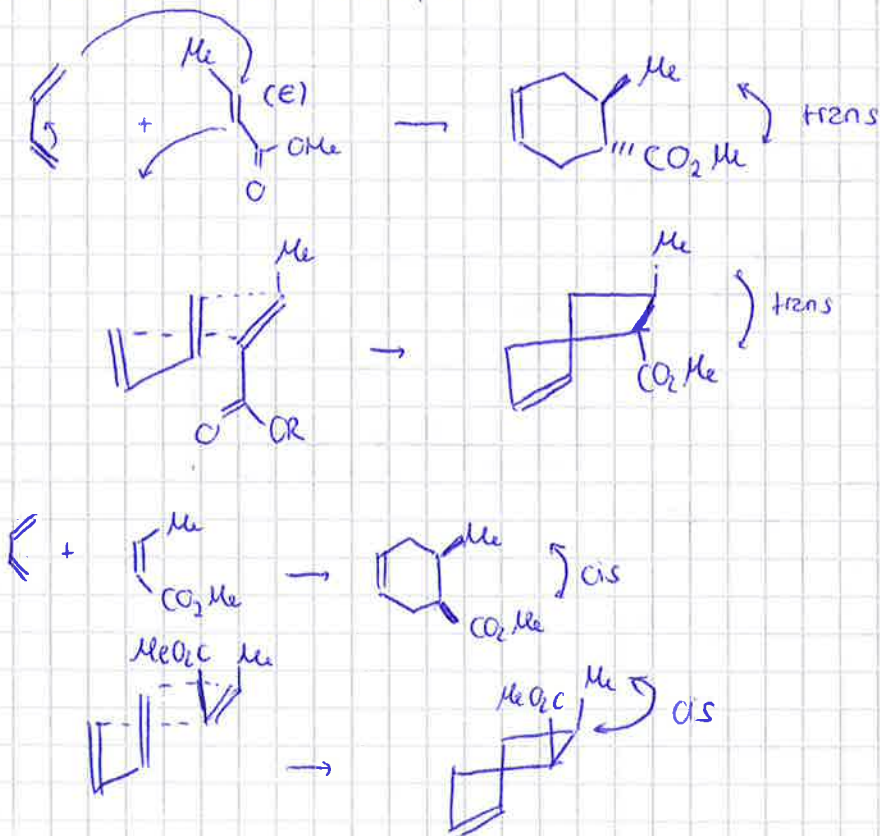
Dienophil

Stereozentren

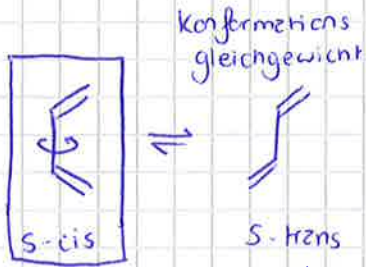


Potenziell → 4-Stereozentren

Stereochemie d. Dienophils

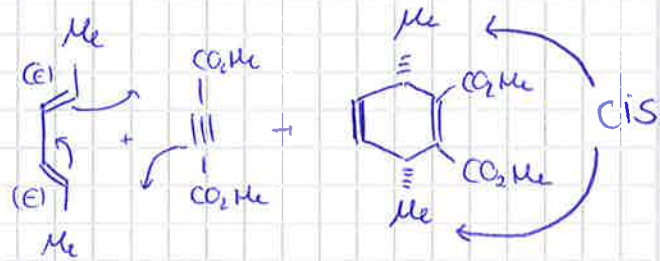


Stereochemie d. Diens



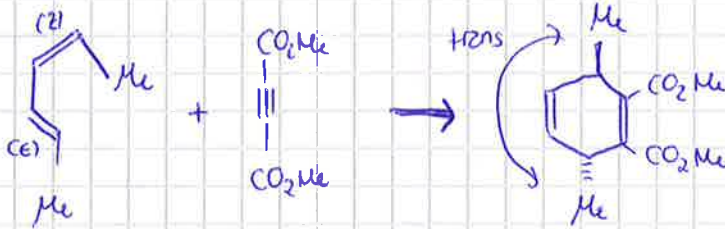
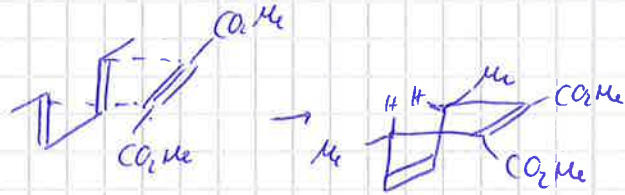
Diels-Alder

stabilere

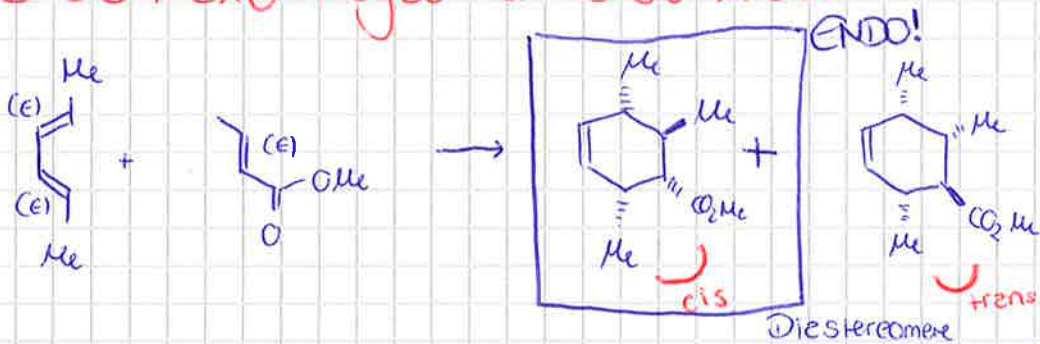


Curtin-Hammett!!

Reaktionskonformation nicht Grundkonformation



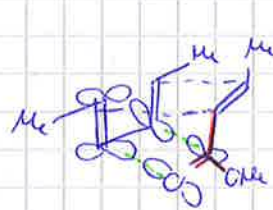
Endo / Exo-Regel d. Diels Alder:



Wichtig:

Sekundär-MO-WW

↳ Stabilisieren den \bar{u}



Endo
Estergruppe schaut IN Ringebene



Exo
Estergruppe schaut AUS Ringebene

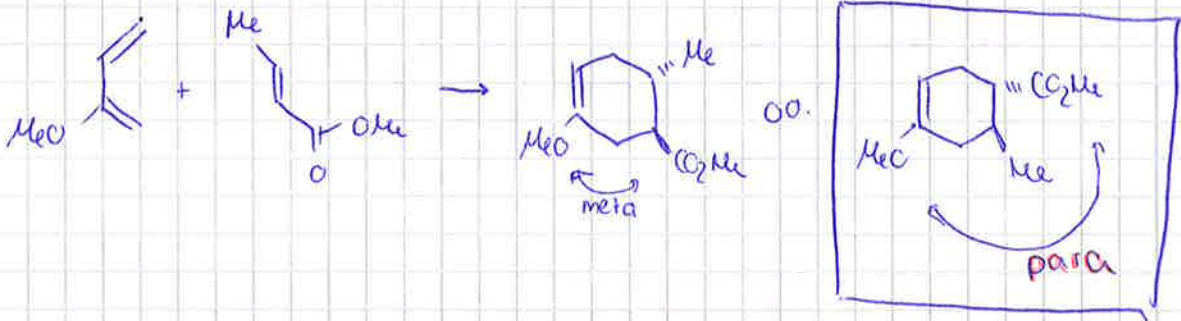
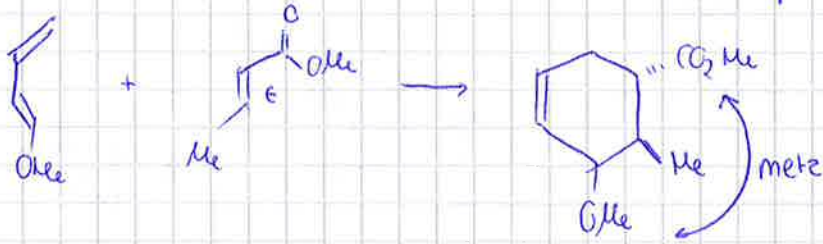
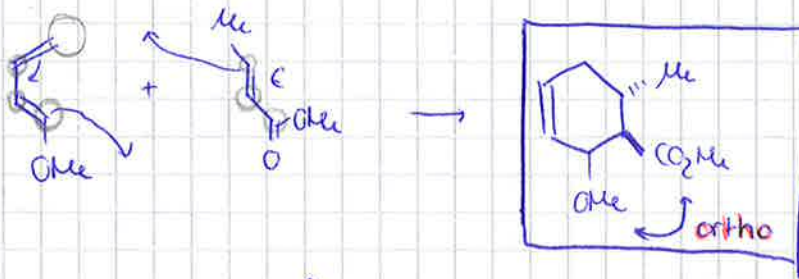
keine sek. MO-WW

Das kommt definitiv in der Klausur!

Diels-Alder ganz wichtig!

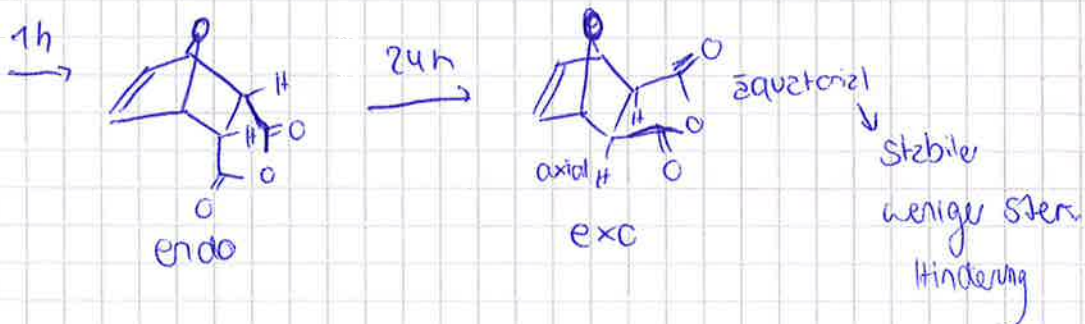
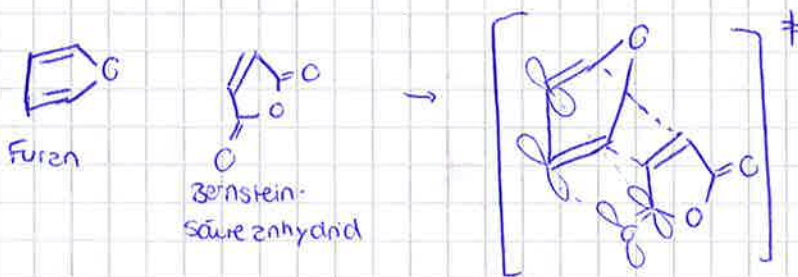
Wie sitzt der Ester? Regiochemie

Ortho/para
Regel
(Regiochemie)

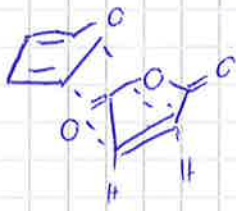


Endo ist kinetisches Produkt
nur Δ ist stabilisierter

Kinetisches vs. thermodyn. Produkt



Reaktion geht zurück

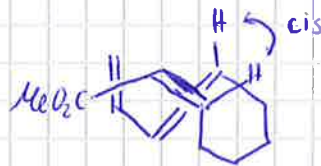
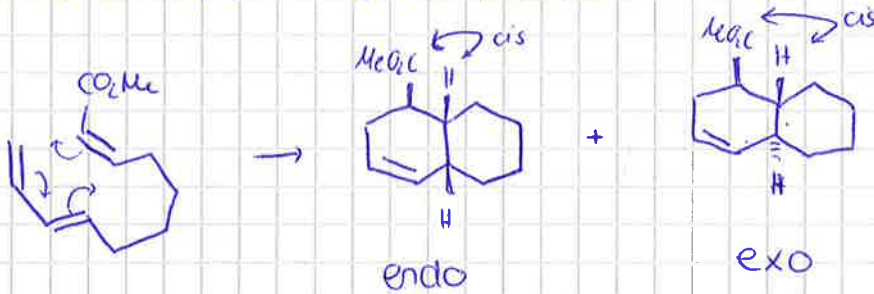


→ exo-Produkt

weniger sterische Hinderung
weniger Rückreaktion

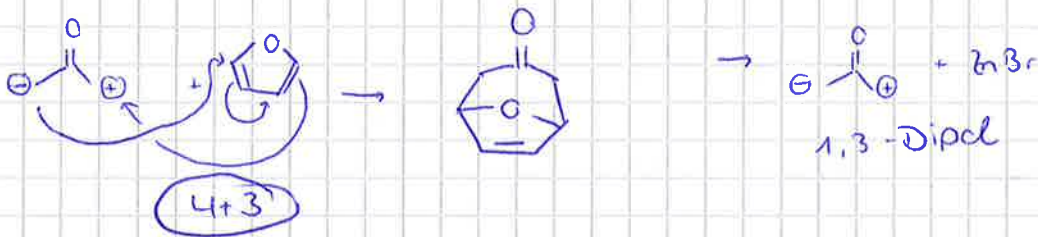
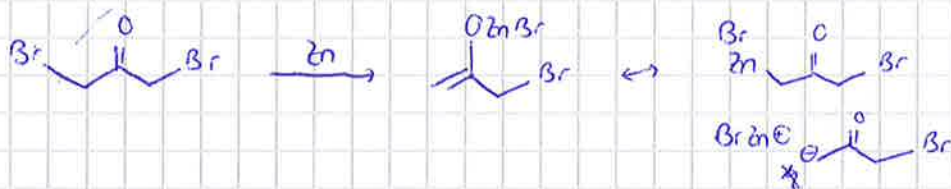
Intermolekular → ENDO

Intramolekular → ENDO / EXO

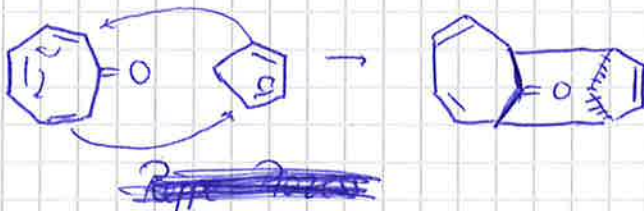


Beispiele für andere Anwendungen

[4+3]



[6+4]



Rupe- Prozess:

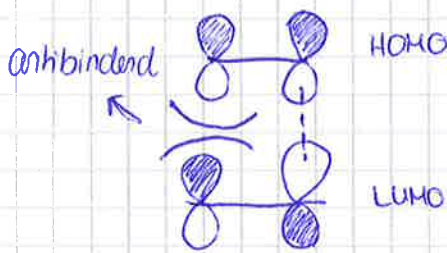


geht so nicht!
keine MO-Überlappung

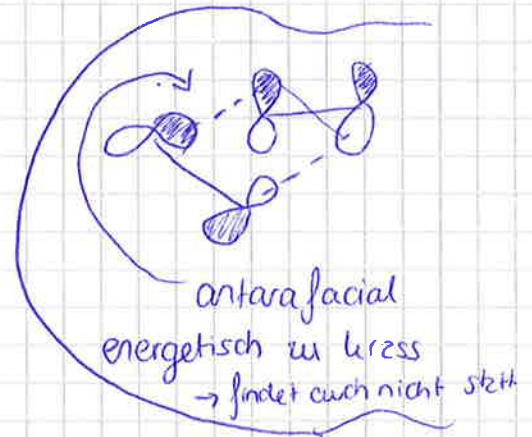
Geht mit $Ni^{0/2+}$ 1,5-Cyclooctadien

[4+4]

[2+2] Cycloaddition

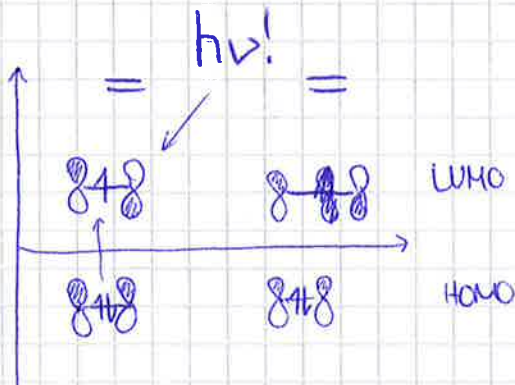


thermisch geht das nicht



$4n \rightarrow 4\pi e^- \rightarrow$ thermisch so nicht erlaubt

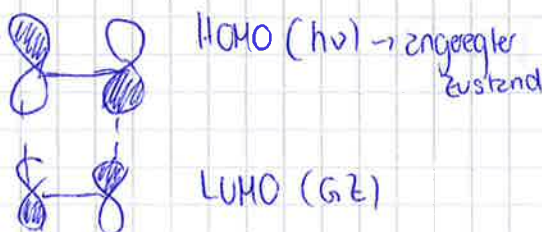
aber: photochemisch



durch Bestrahlung wird das eine LUMO des neuen HOMO.

Denn kann neues HOMO mit LUMO reagieren

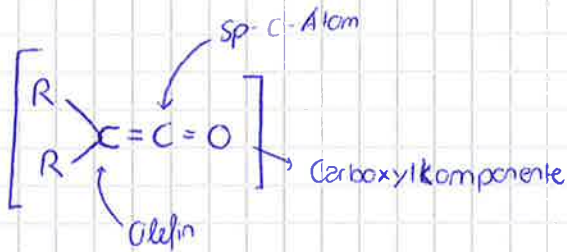
Sieht denn so aus



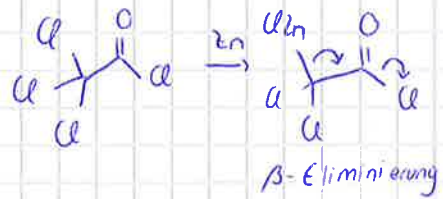
4n System
photochem.
suprafacial
 \rightarrow erlaubt

OC 22.16 [2+2] Keten + Olefin

Keten

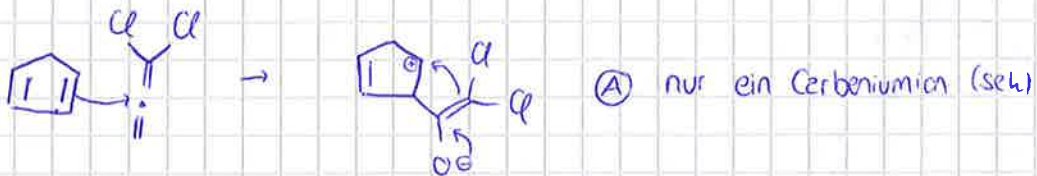
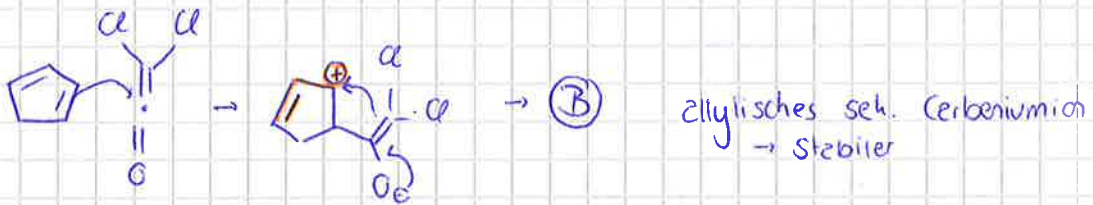
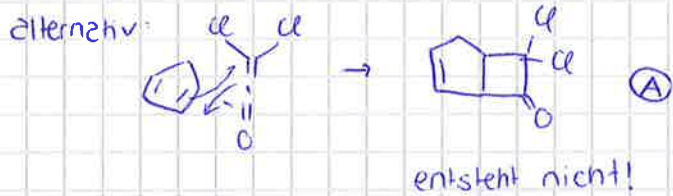
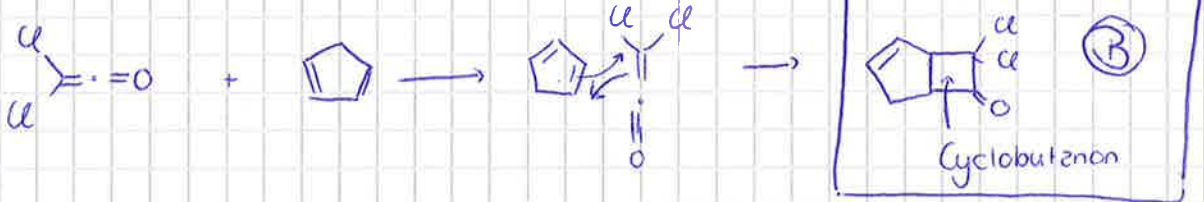


Herstellung Keten:

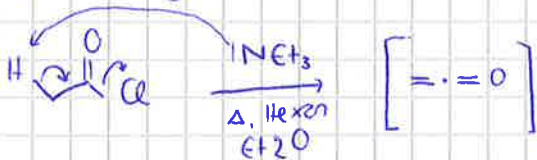


Reaktives Intermediat

Reaktion

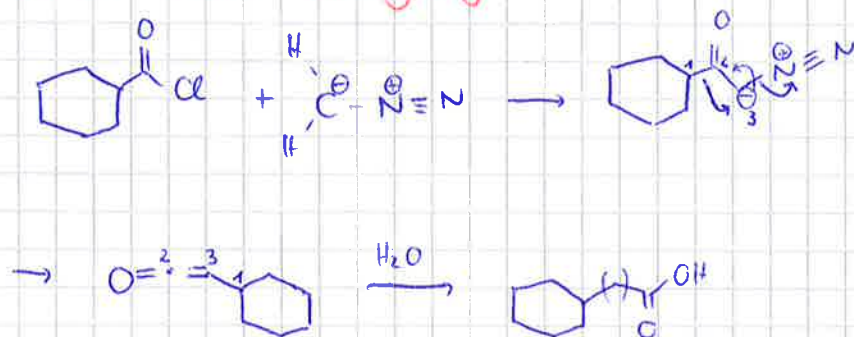


Herstellung von Keten:



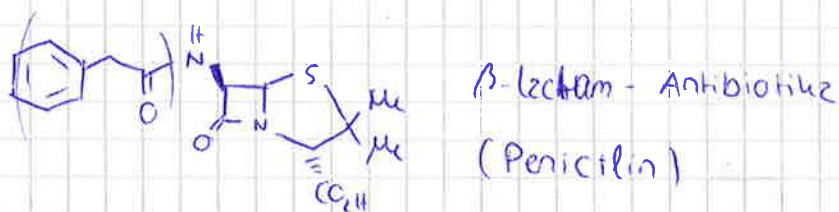
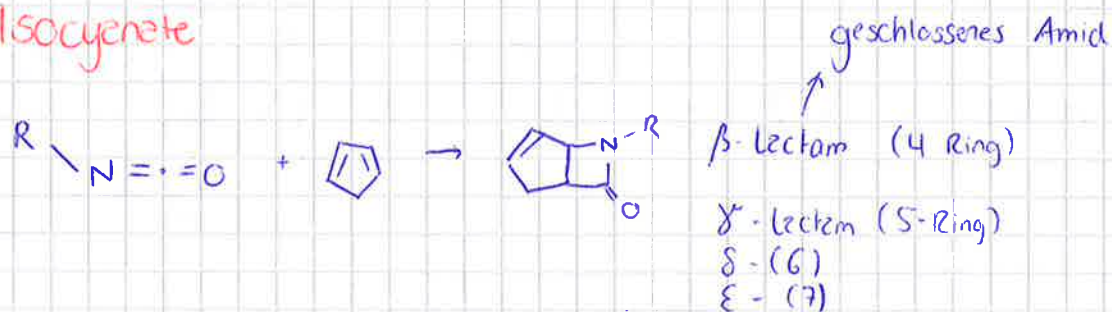
Auch Darstellung

Arndt-Eistert-Umlagerung

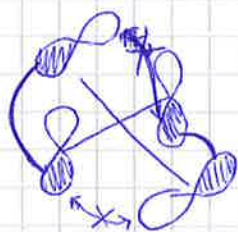


Arndt-Eistert verlängert um eine CH_2 -Gruppe

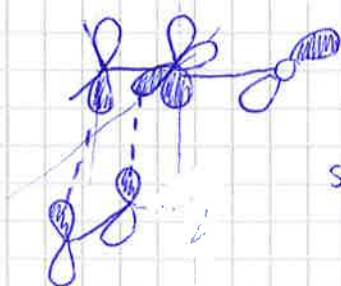
Isocyanate



Bsp für eine wichtige Synthese von β -Lactamen



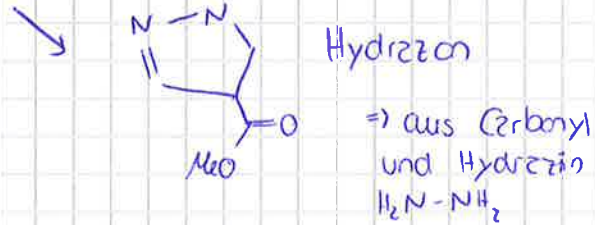
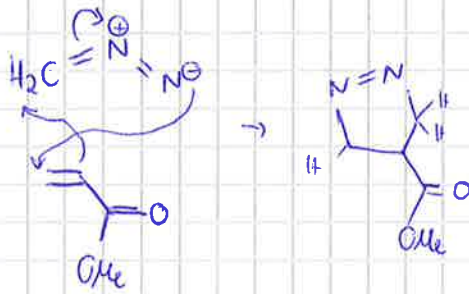
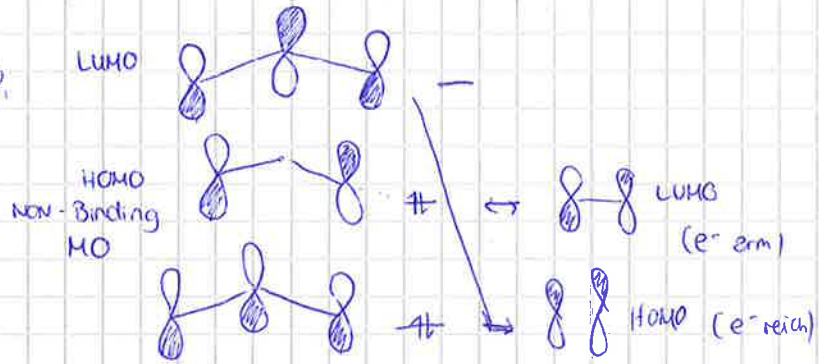
2x anbindend \rightarrow keine Treibkraft
 2x bindend
 (Reaktion eines Ketens?)



LUMO suprafacial
 HOMO suprafacial

dazum
 thermisch
 erlaubt

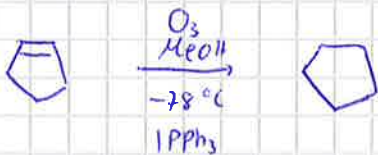
[3+2]- Cycloaddition (1,3-dipolare Cycloaddition)



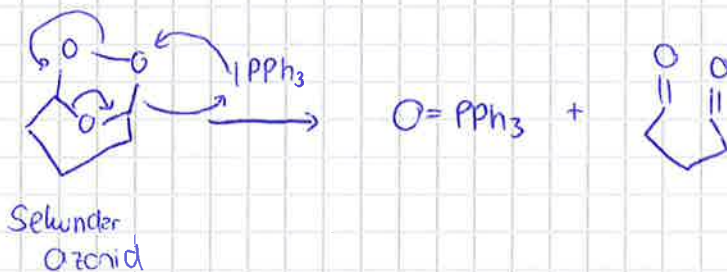
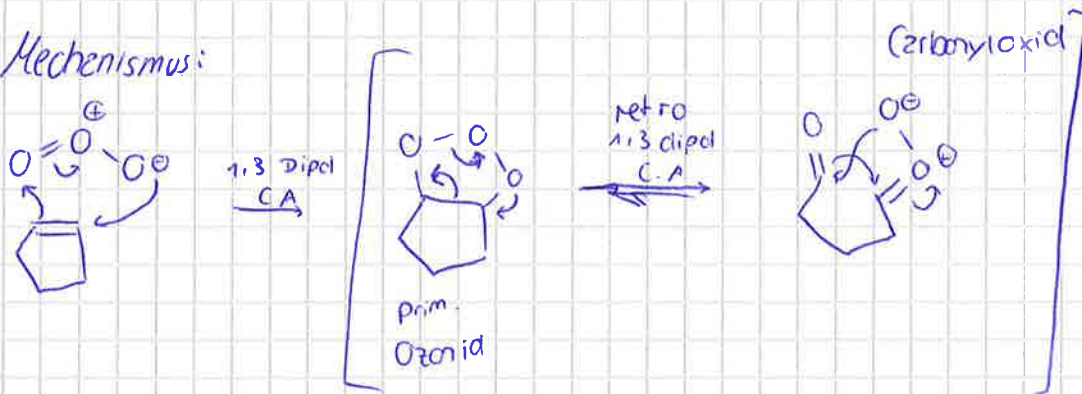
andere 1,3-Dipole

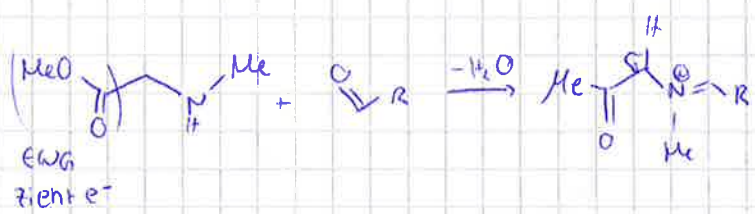
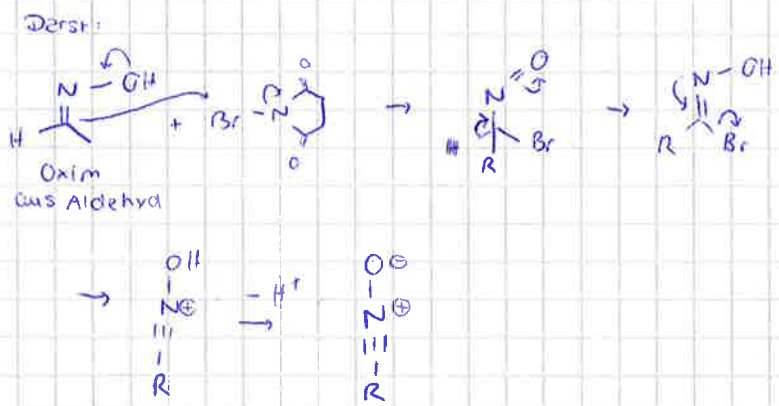
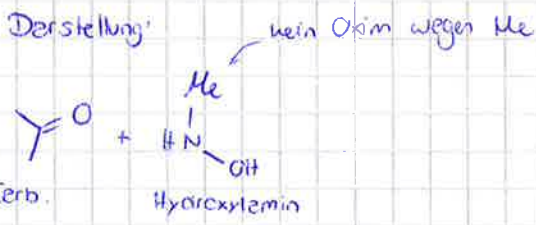
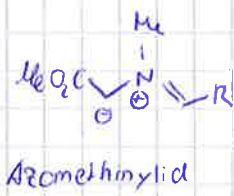


Ozonolyse



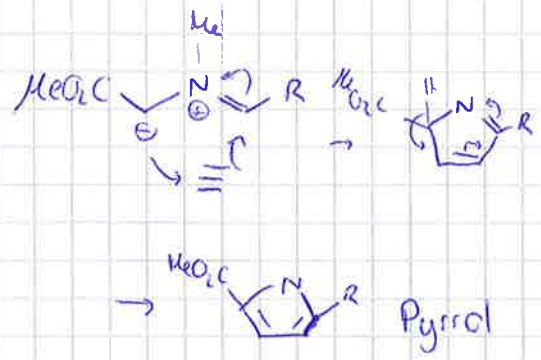
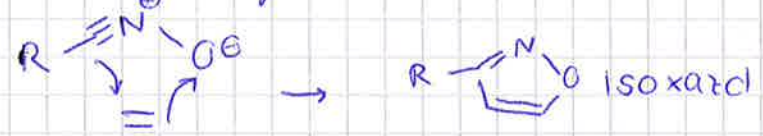
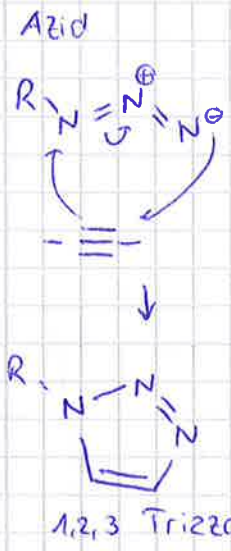
Mechanismus:





Beispiele für 1,3 Dipol c. A

Click-Chemie
(Cu-Kat.)

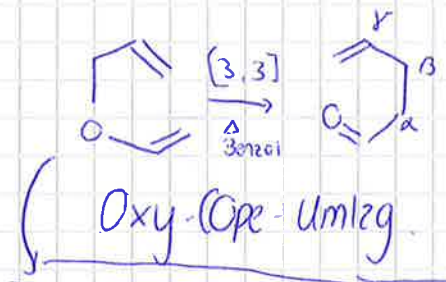


Sigmatrope Umlagerungen



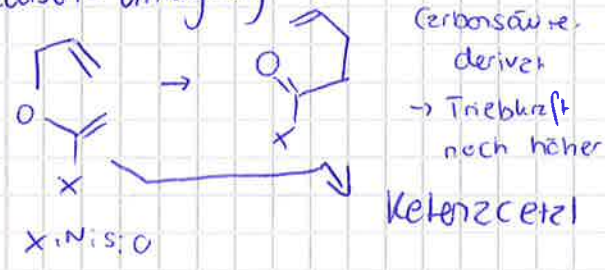
Enterteile Rkt. Cope-Umlagerung

Triebkraft



Herstellung:

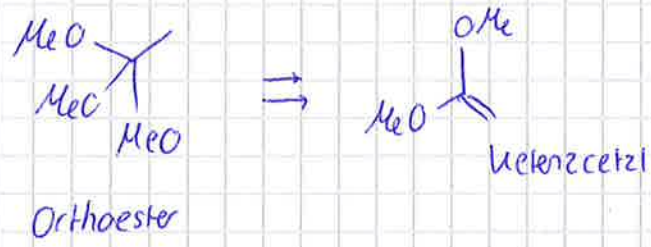
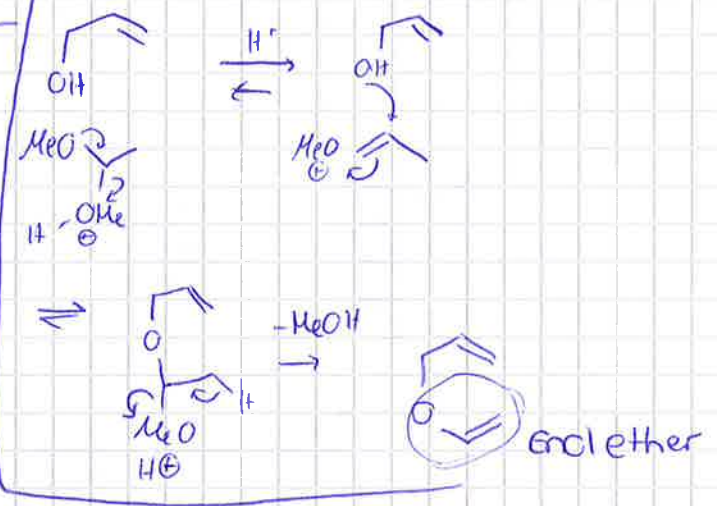
Claisen-Umlagerung



X = NMe₂ Eschenmoser-Claisen (Amid)

X = OMe Johnson-Claisen (Ester)

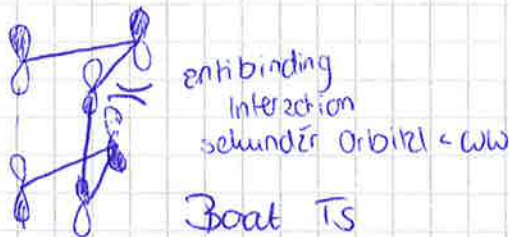
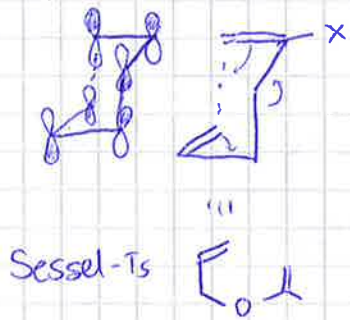
X = OTMS/OH Ireland-Claisen (Carbonsäure)



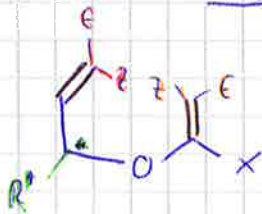
Üben!!!

OC 8.2.16

(Claisen-Umlegung (ursprüngl. Form))



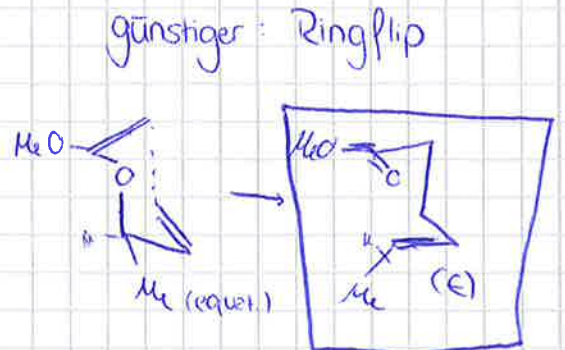
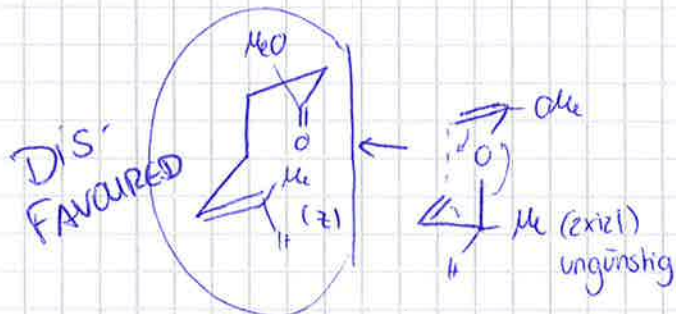
Rolle bei Ausbildung des Produkts:



- 1) Doppelbindungsgeometrie
- 2) Enolet (Ketenzettel)-Geometrie
- 3) Vorhandenes Stereozentrum am Allylalkohol

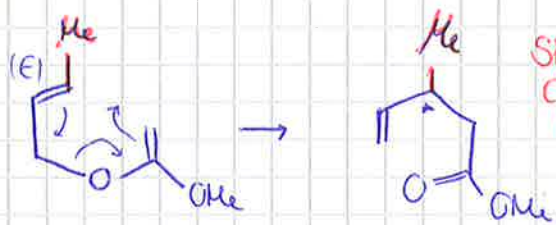
ad 3) Allyl-OH-Stereozentrum

E oder Z?



Großer Rest äquat. → günstiger → E-Geometrie

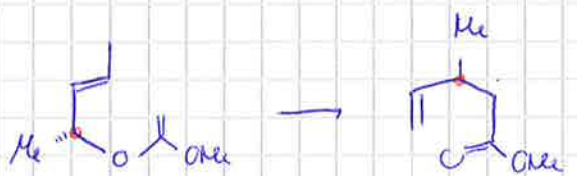
ad 1.)



Stereozentrum
C-Chiralität ohne
Heteroatom

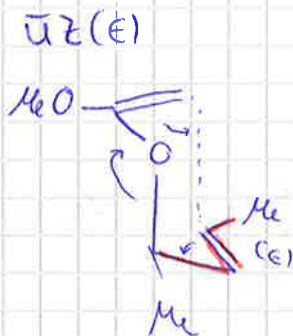
keine chirale Info Racemat

→ Mit Chiralität (Allyl-OH)

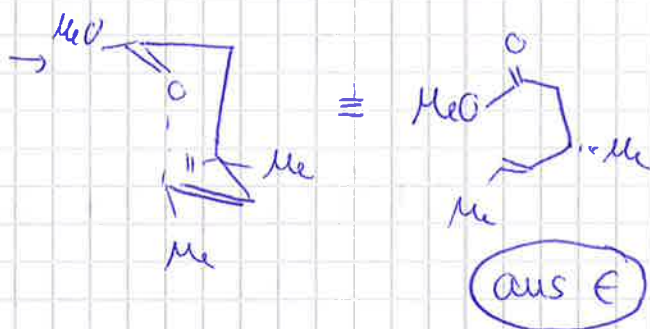
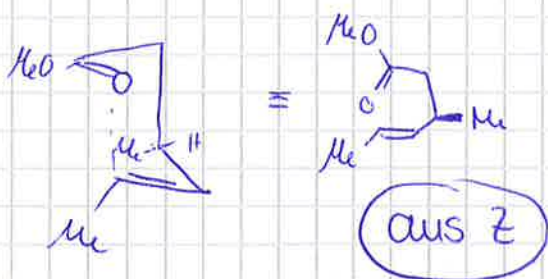


C-O-Chiralität C-C-Chiralität

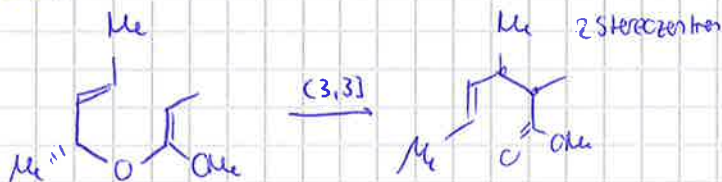
Chiralitätstransfer



aus (Z) - DB:

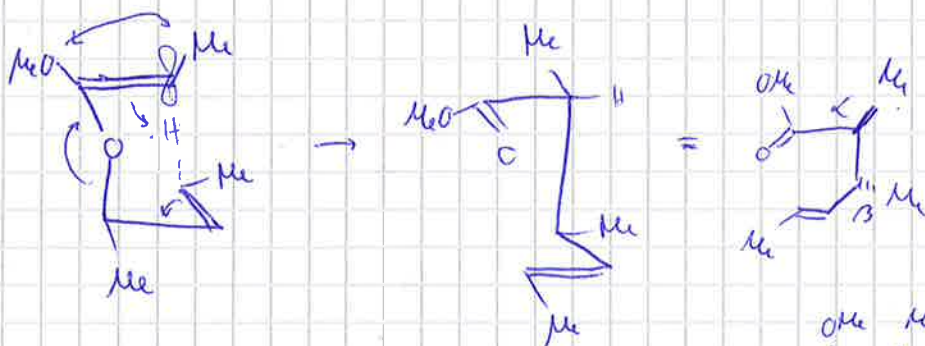


ad 2)



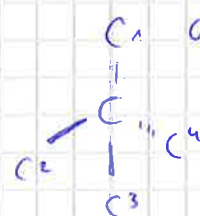
β -Stereoz. → DB Geometrie
bei gegebenem
Allyl-OH-Stereoz.

α -Stereoz. → Enoliz-Geometrie
— " — " —



Maximal mögliche 2- quaternäre Stereozentren

quat. Stereoz.



kein Heteroatom
4. verschied. C-
Reste

quat. Stereoz.

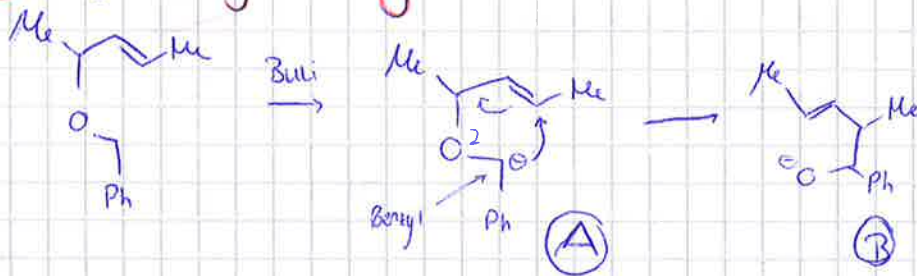
[2.3]. Sigmatropic Rearrangement



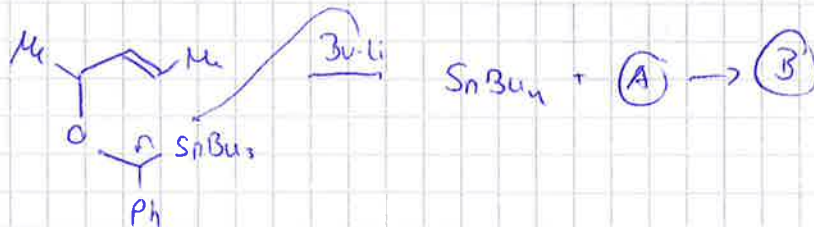
X^\ominus stabiler als $Y^\ominus \rightarrow$ Triebkraft

Stereochemie nächste Seite

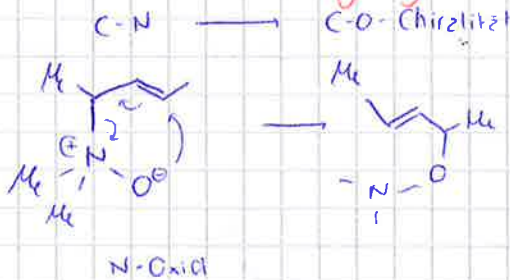
[2.3]-Wittig-Rearrangement



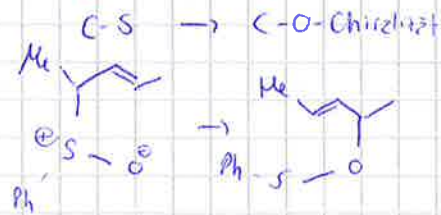
[2,3]-Wittig-Still Umlagerung (Anion wird dirigiert)



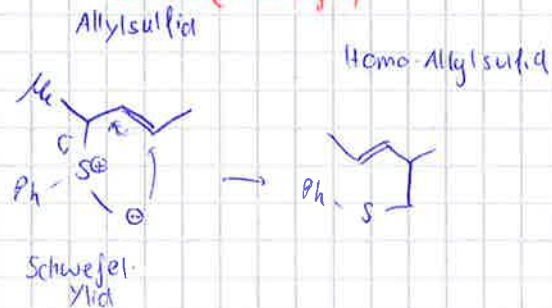
Meisenheimer Umlagerung



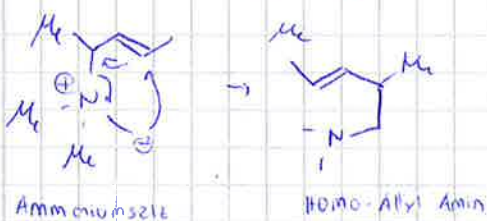
Evans-Mislow



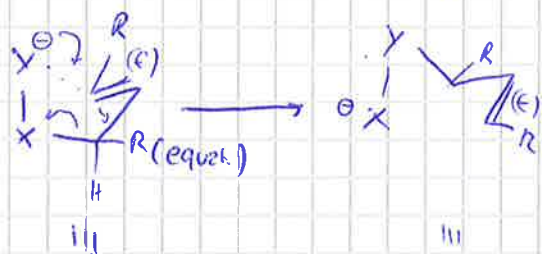
Stevens (Schwefel)



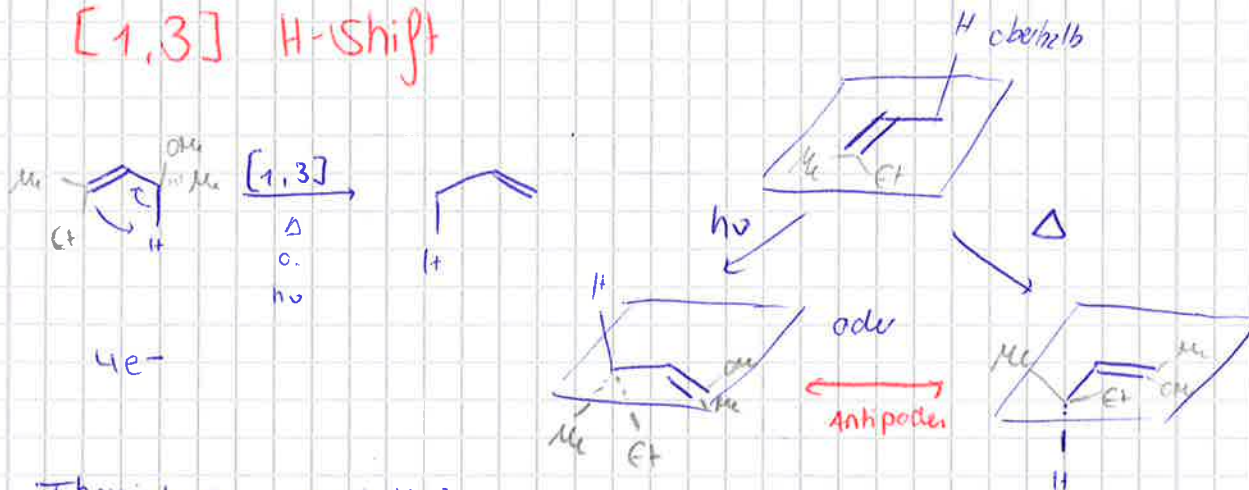
Stevens-Umlagerung



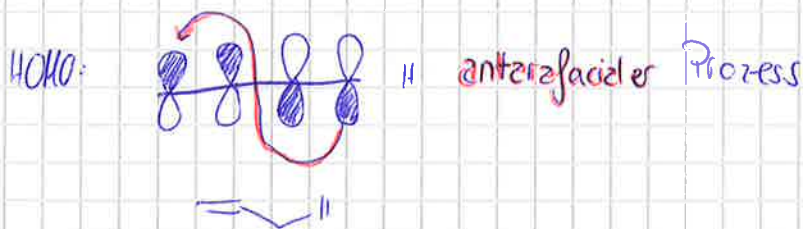
Stereochemie 2,3-Sigmatrope Umlagerung



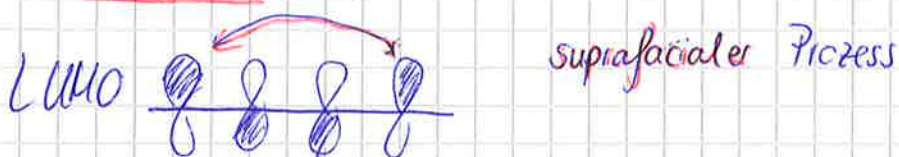
[1,3] H-Shift



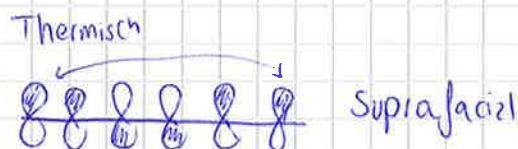
Thermisch [1,3] H-Shift $4e^-$



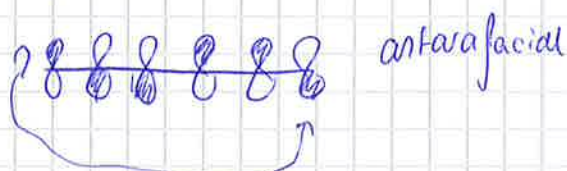
Photochemisch [1,3]



[1,5] H-Shift



photochem.



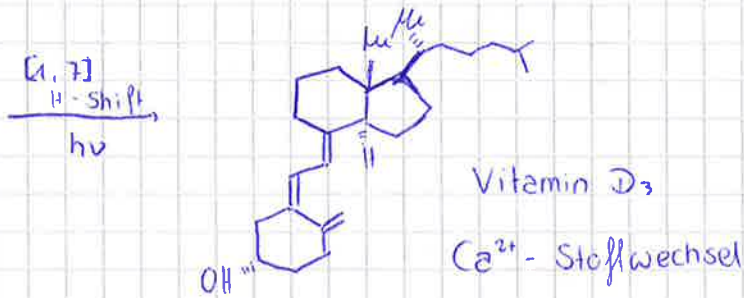
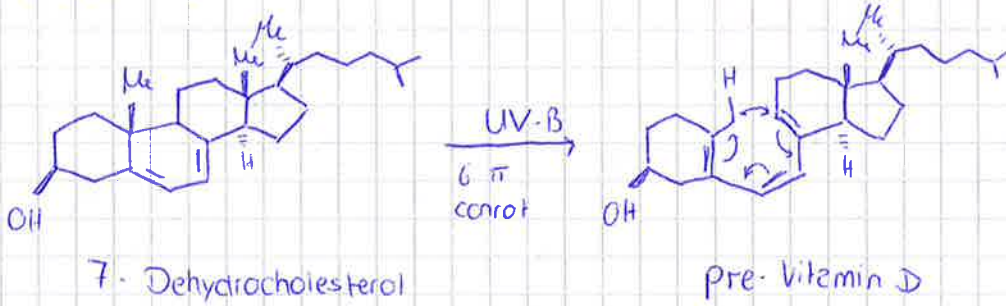
OC 92.16

[1,7] H-shift



$8e^- - 4n \rightarrow$ antarafacial thermisch
suprafacial photochemisch

Vitamin D



Oxidationen & Reduktionen

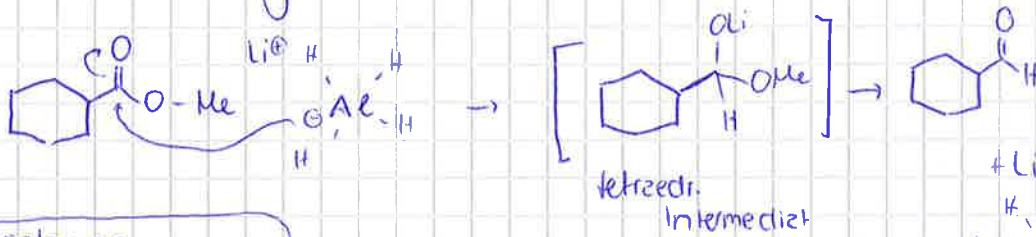
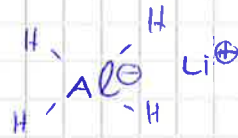


leicht zu reduzieren

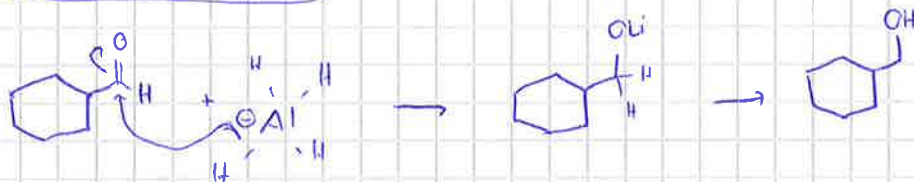
schwer

Reduktion eines Esters

a) hydridisches Reagenz

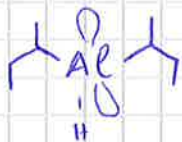


Fortsetzung
Reduktion Aldehyd

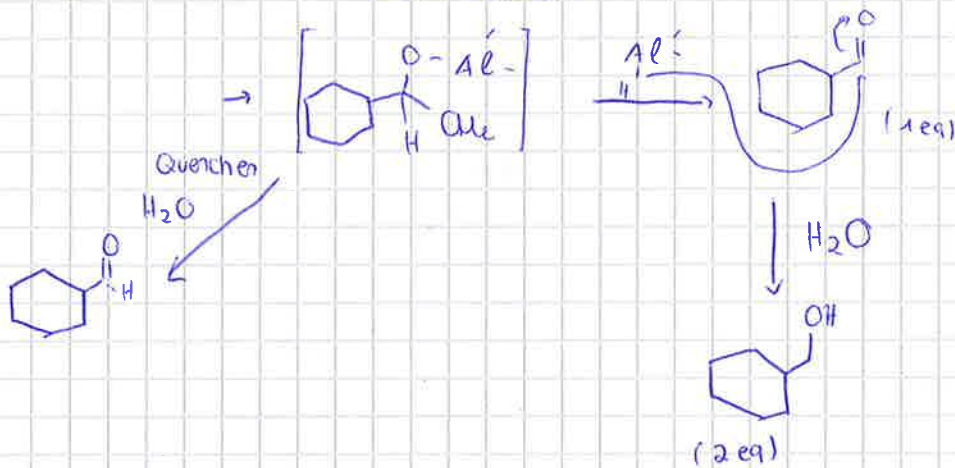


b) nicht-hydridisches Reagenz

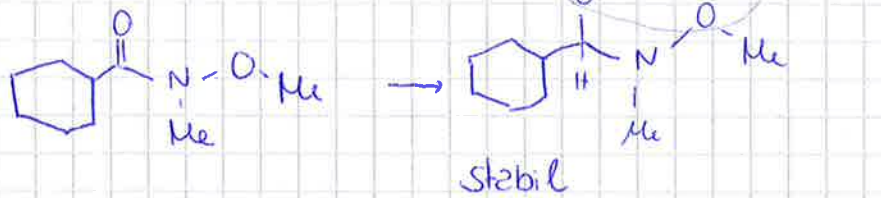
DIBAL-H $\hat{=}$ Di-isobutyl-aluminium-hydrid



Mech: $\begin{array}{c} \text{O} \\ \parallel \\ \text{Cyclohexyl}-\text{C}-\text{O}^- \end{array} \cdots \text{Al}^-$ löst sich erst negativ auf wenn es ins O koordiniert



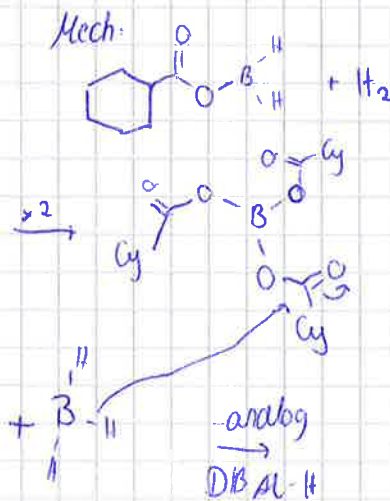
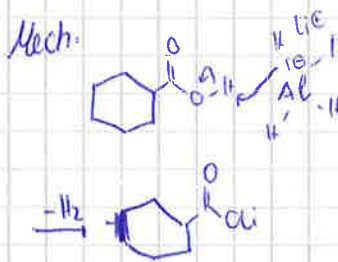
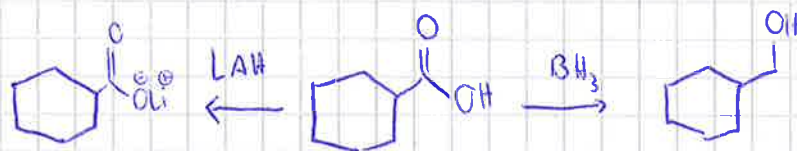
Weinreb-Amid



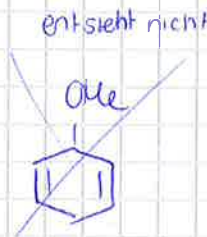
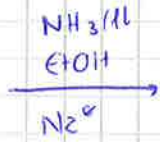
Bleibt so, bis man es mit Wasser quentscht.

Nochmal Reduktionen

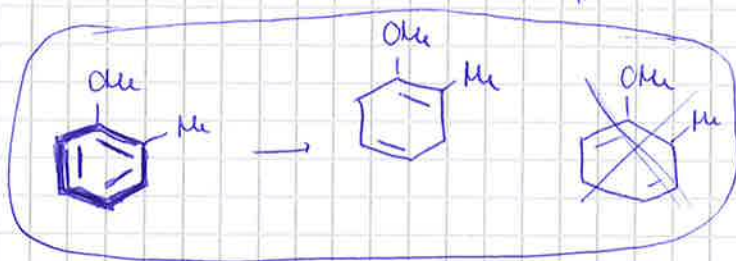
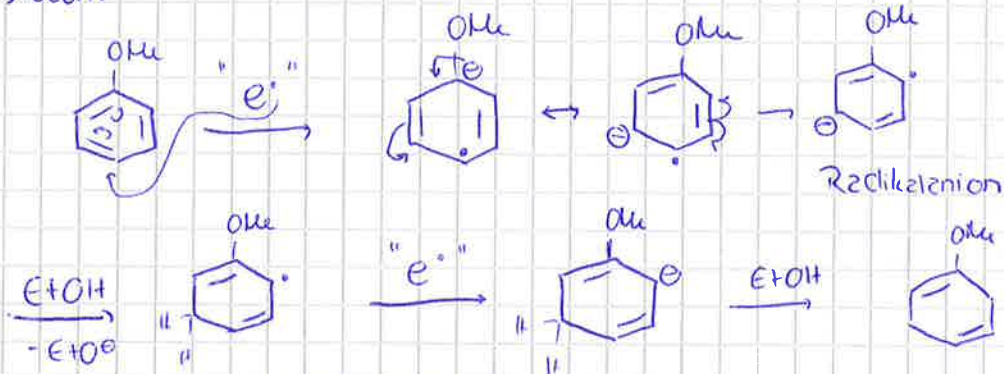
	leicht					schwer
	$\text{R}-\text{C}(=\text{O})-\text{H}$	$\text{R}-\text{C}(=\text{O})-\text{H}$	$\text{R}-\text{C}(=\text{O})-\text{R}$	$\text{R}-\text{C}(=\text{O})-\text{OMe}$	$\text{R}-\text{C}(=\text{O})-\text{NMe}_2$	$\text{R}-\text{C}(=\text{O})-\text{OH}$
① NaCOAc, Bll	✓					
② N_2CNBH_3	✓					
③ NaBH_4	✓	✓	✓			
④ LiBH_4	✓	✓	✓	✓		
⑤ DIBAL-H	✓	✓	✓	✓	Alk. $\text{R}^{\wedge}\text{O}$	✓ $\text{R}^{\wedge}\text{OH}$
⑥ LAH	✓	✓	✓	✓	Alk	✓ $\text{R}^{\wedge}\text{NH}_2$
⑦ Red. Al	✓	✓	✓	✓	Alk	✓ $\text{R}^{\wedge}\text{NH}_2$
⑧ BH_3	✓	✓	✓	✓		✓



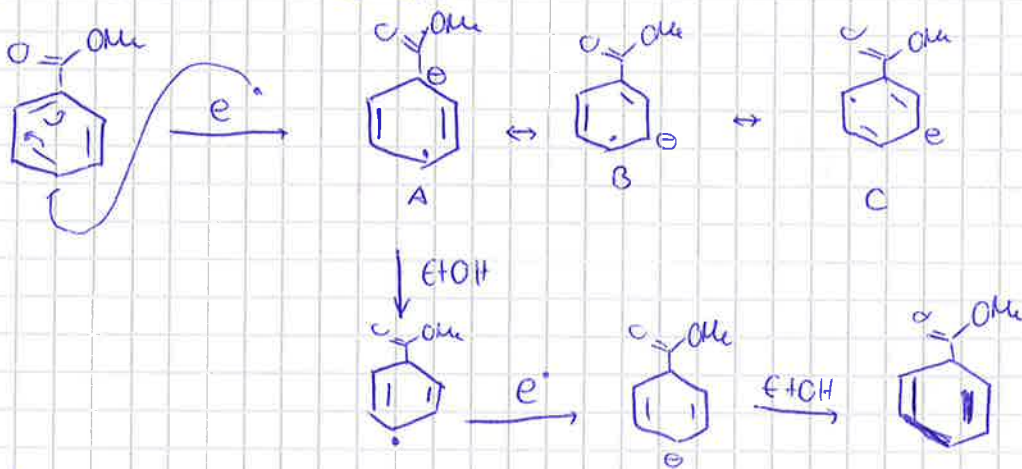
Birch-Reduktion



Mech.:



Birch e⁻armer Aromat



Σ

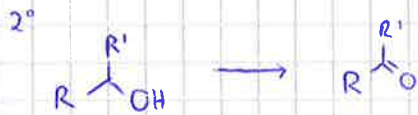
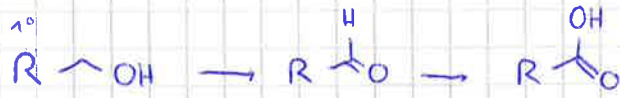
- 1) Birch 2x e⁻-Transfer
- 2) el-reich Subst sitzt an DB



- 3) el-arm Subst sitzt NICHT an DB



Oxidationen

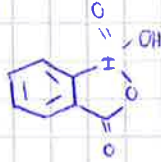


1) CrO_3

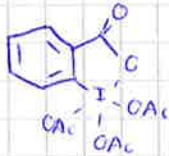
2) PCC: Pyridinium Chlorochromat

} Chrom Reagenzien

3) IBX

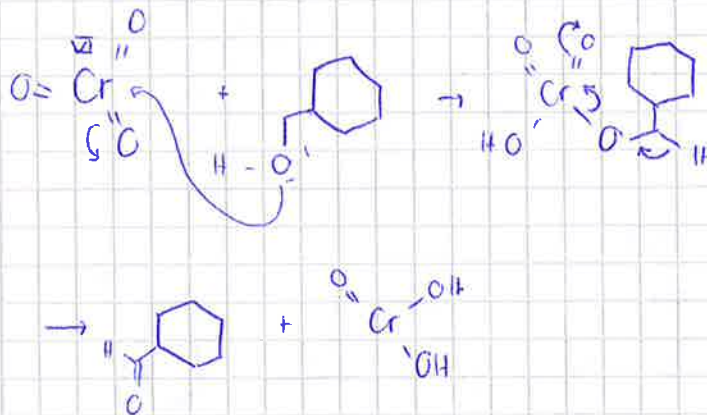


4) DMP: Dess Martin Periodinane

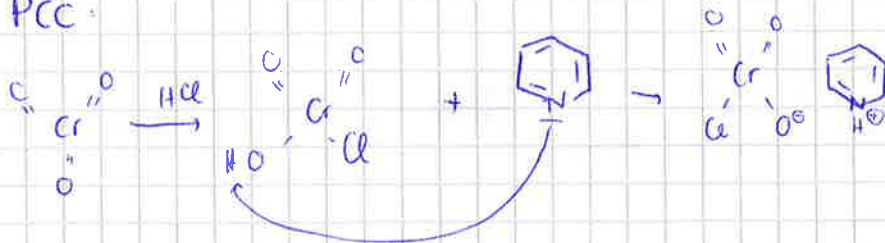


} Hypervalente Iod-Verbg

Mechanismus: $\text{CrO}_3 \rightarrow \text{Alkohol} \rightarrow \text{Carbonyl}$

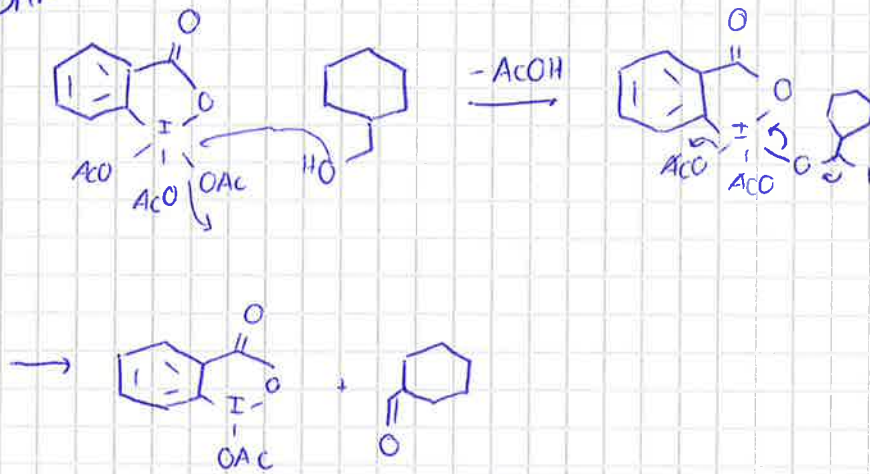


PCC:

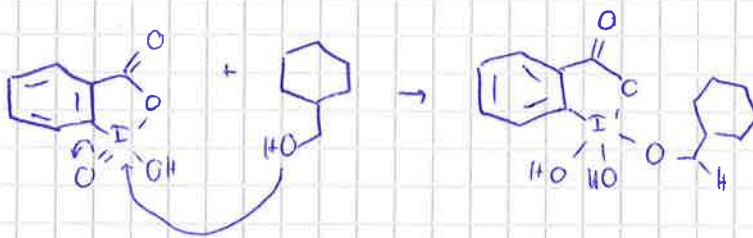


Hypervalente Iod-Verbindung:

DMP

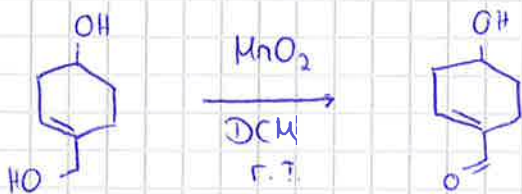


IBX

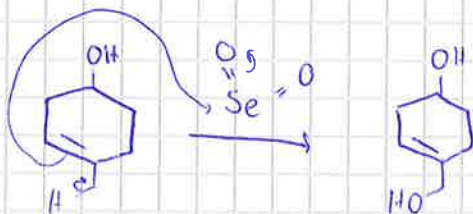


Schwern-Oxidation ist Voraussetzung

Allylische Oxidation

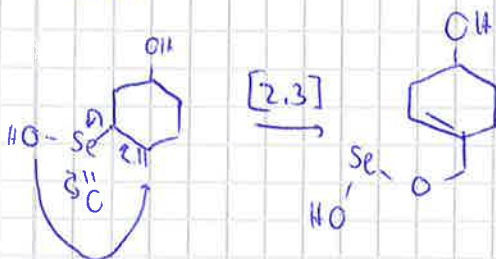


Oxidation einer bereits vorhandenen C-O-Bdg



Oxidation einer C-H-Bdg

Mech:



Glycolspaltung

