

Vorlesung zum Grundpraktikum Organische Chemie

1. Gruppe: Aliphatische Substitution

1. Substitutionstypen
2. Nucleophile aliphatische Substitution
 - 2.1. Klassifizierung
 - 2.1.1. Kinetisches Kriterium
 - 2.1.2. Stereochemisches Kriterium
 - 2.1.3. Carbenium-Umlagerung
 - 2.2. Die S_N2 -Reaktion
 - 2.2.1. Die Struktur des Substrats
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 - 2.2.4. Lösungsmittelleffekte
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 - 2.4. Intramolekulare S_N -Reaktionen; Nachbargruppen-Effekte
 - 2.5. Substitutionen an Allyl-Derivaten
 - 2.6. Präparative Aspekte
3. Radikalische aliphatische Substitutionen
 - 3.1. Radikalische Halogenisierungen
 - 3.2. Weitere Radikal-Substitutionen

Empfohlene Literatur:

1. Clayden, Greeves, Warren and Wothers: Organic Chemistry, Oxford Press 2001, ISBN 0 19 850346 6.
2. Carey, Sundberg: Organische Chemie, VCH 1995, ISBN 3-527-29217-9
3. R. Brückner: Reaktionsmechanismen, Spektrum der Wissenschaft 1996, ISBN 3-86025-363-8
4. S. Warren: Chemistry of the Carbonyl Group. A Programmed Approach to Organic Reaction Mechanisms, John Wiley 2000, ISBN 0471 92104 1
5. M. B. Smith, J. March: March's Advanced Organic Chemistry, VCH 2001, ISBN 0471-58589-0

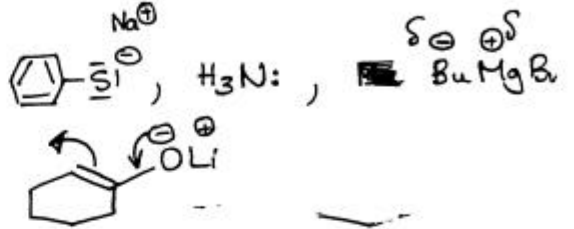
1. Substitutionstypen

①



Klassifizierung der Substitution je nach Natur von Y

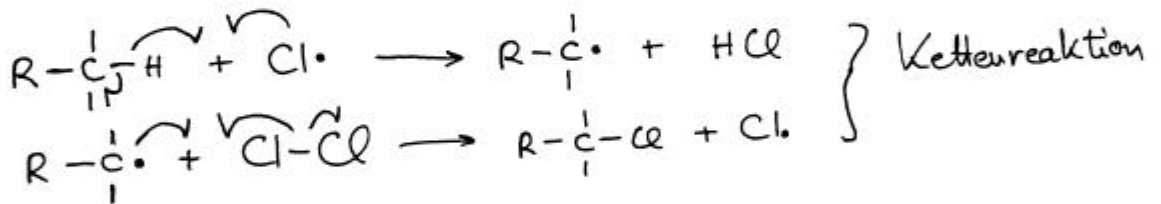
- Y kann ein Nukleophil sein: (Lewis-Base) (Ersatz des Nukleophil X)
 - $\text{C}_6\text{H}_5\text{Si}^{\ominus}\text{Na}^{\oplus}$, $\text{H}_3\text{N}:$, BuMgBr (Lewis-Base)
 - \Rightarrow Nukleophile Substitution



- Y kann ein Elektrophil sein: (Lewis oder Brønstedt-Säure) (Ersatz des Elektrophil X)
 - Br^{\oplus} , H^{\oplus} , Met^{\oplus} (Hg^{2+} , Zn^{2+} , ...)

\Rightarrow Elektrophile Substitution

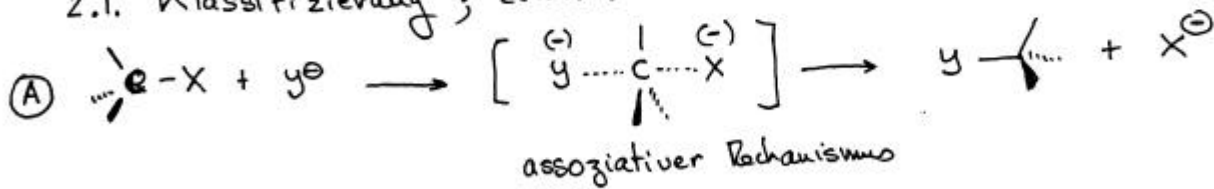
- Y kann ein Radikal sein: (ungepaartes e^-)



\Rightarrow Radikalische Substitution

2. Nukleophile aliphatische Substitution

2.1. Klassifizierung; 2.1.1. Kinetisches Kuberium



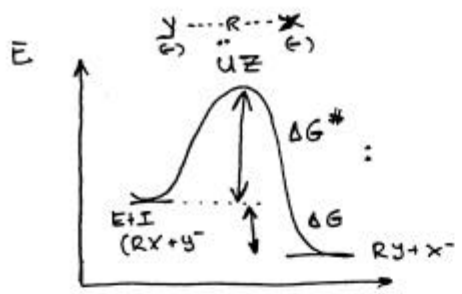
$$-\frac{d[\text{EtI}]}{dt} = k[\text{EtI}][\text{OH}^{\ominus}] \quad \text{Geschwindigkeit hängt ab von EtI und OH}^{\ominus}$$

Substitution

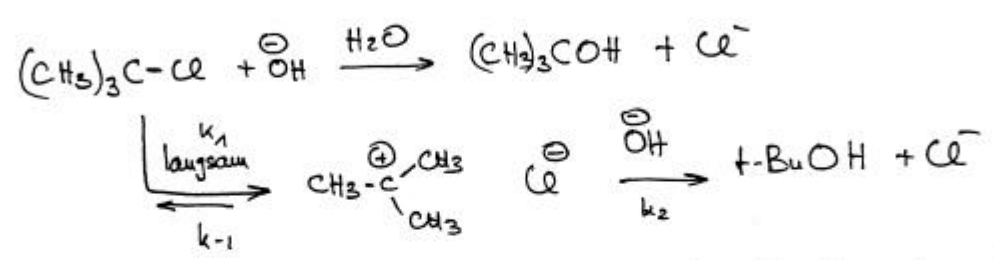
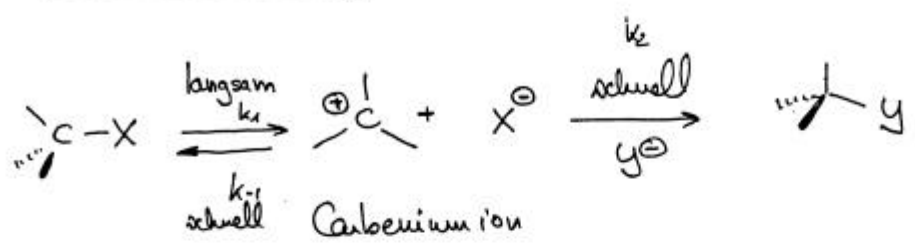
$\text{S}_{\text{N}}2$

Nukleophil

Kinetik 2. Ordnung

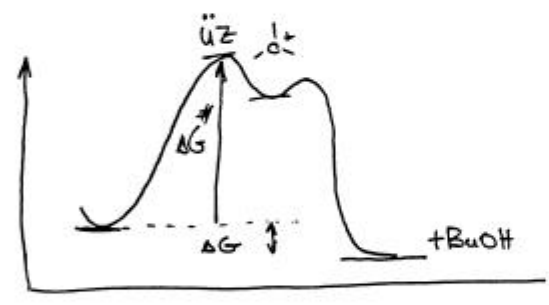


B

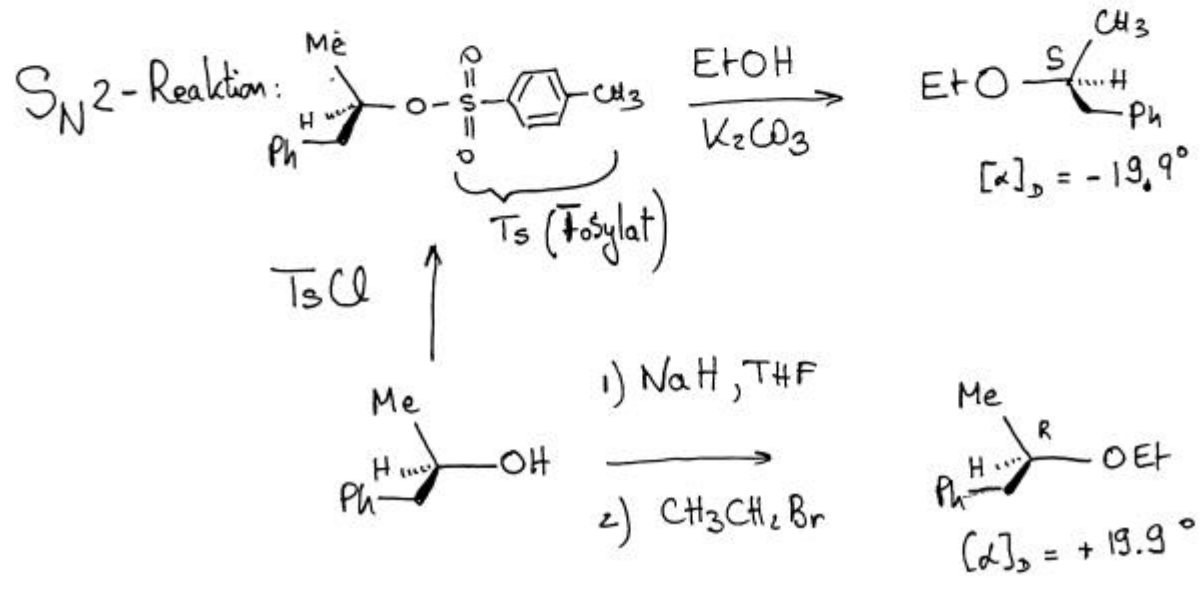


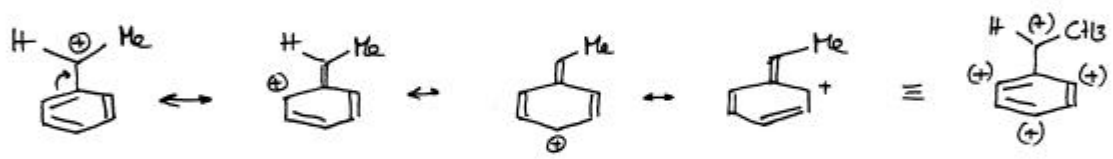
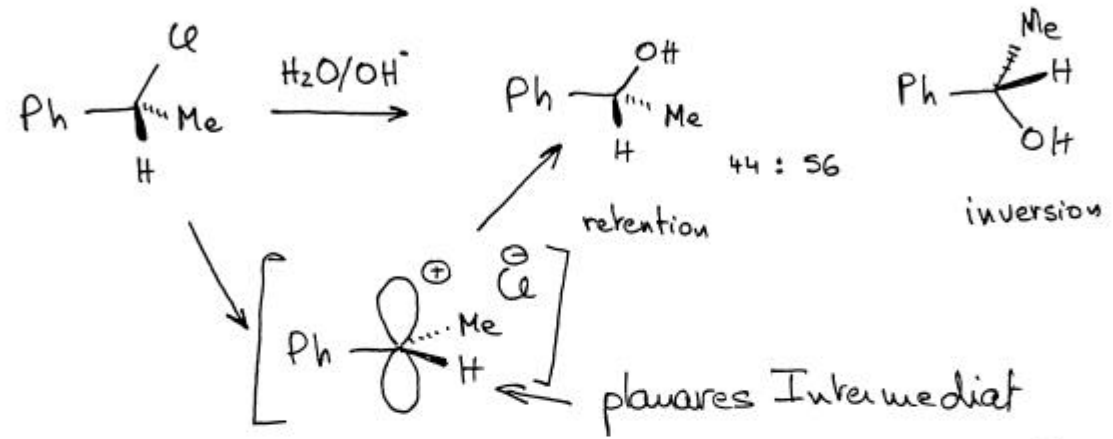
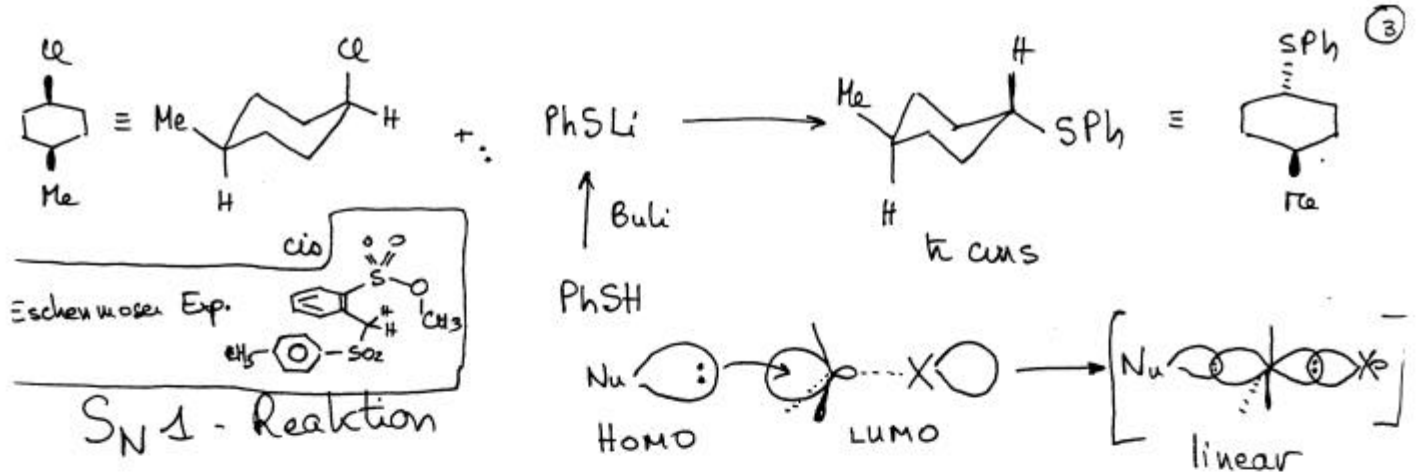
$$-\frac{d[\text{t-BuCl}]}{dt} = k_2 [\text{t-BuCl}]$$

genaue Kinetik gibt: $k_2 \cdot \frac{k_2}{k_{-1} + k_2}$
 aber $k_2 \gg k_{-1}$



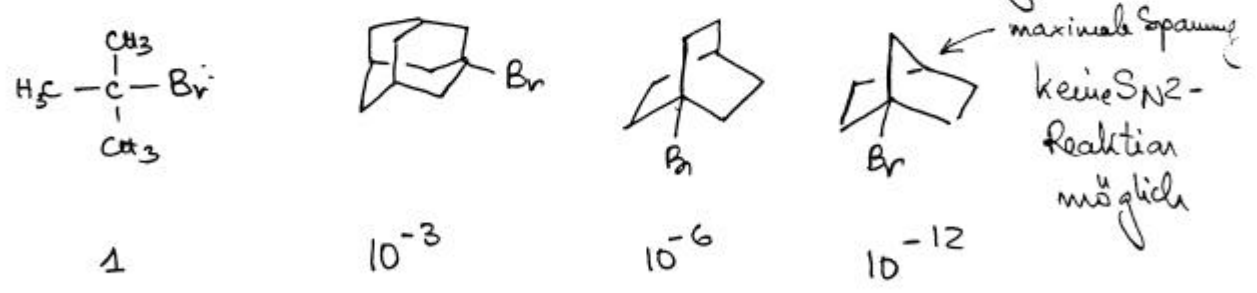
2.1.2. Stereochemisches Kriterium





S_N1 -Mechanismus \equiv stabiles Carbeniumion

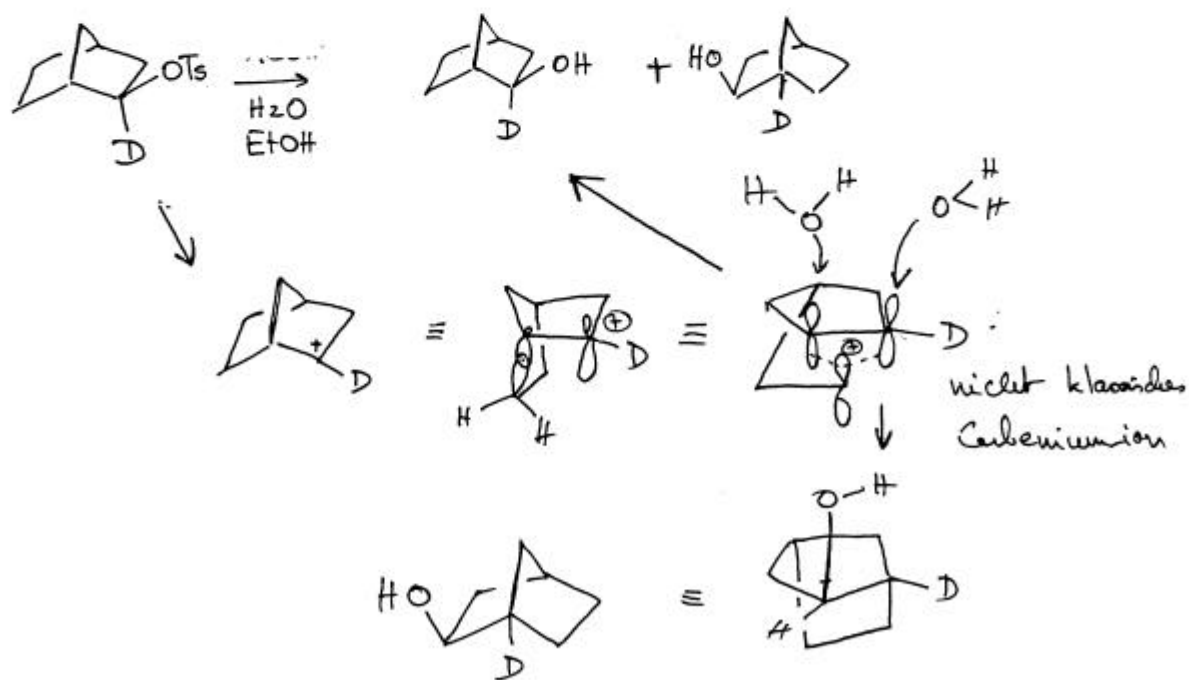
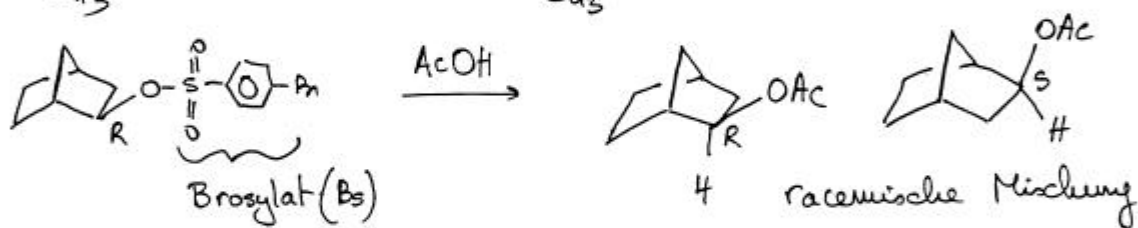
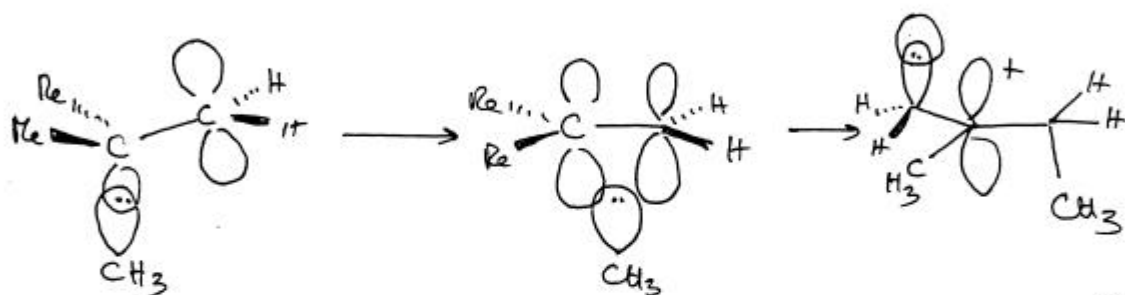
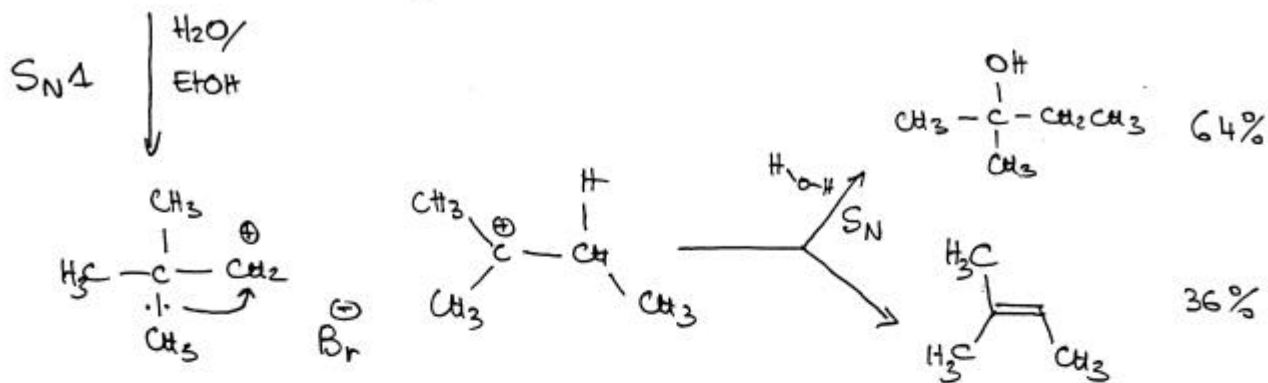
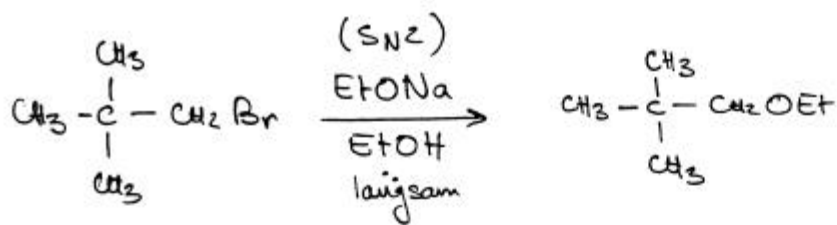
Geometrie des Carbeniumion ist auch wichtig:



Solvolys in Dioxan: $H_2O = 70:30$ bei $100^\circ C$

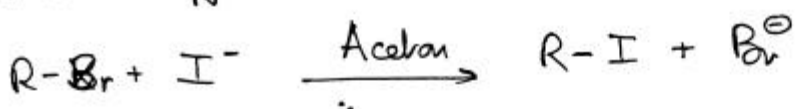
2.1.3. Carbenium-Umlagerungen


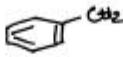
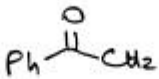
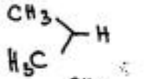
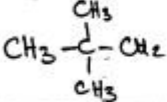
Bei S_N2 -Reaktionen Umlagerungen durch Nachbar^{gruppen}effekt
 Bei S_N1 -Reaktionen oft Gerüstumlagerungen

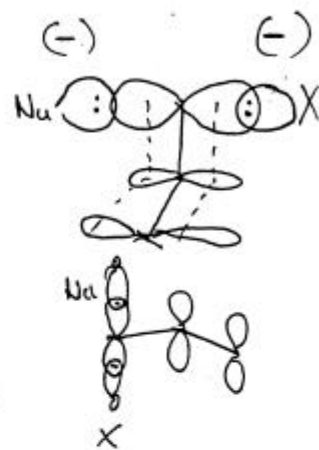


2.2. Die S_N2 - Reaktion 2.2.1. Die Struktur des Substrats.

(5)



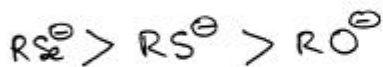
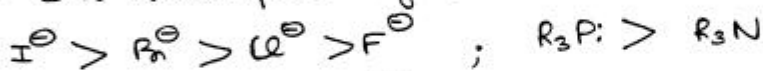
R	k _{rel}	R	k _{rel}
CH ₃	30		40
Et	1		120
CH ₃ CH ₂ CH ₂	0.4		15000
	0.025		
	0.00001 (10 ⁻⁵)		



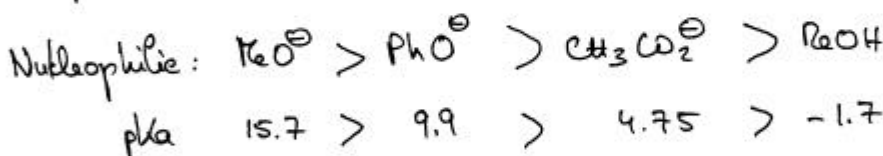
S_N2 : Me > prim > sek >> tert- ~ Neopentyl


Allyl, benzyl, π-substituenten

2.2.2. Das Nukleophile Agens

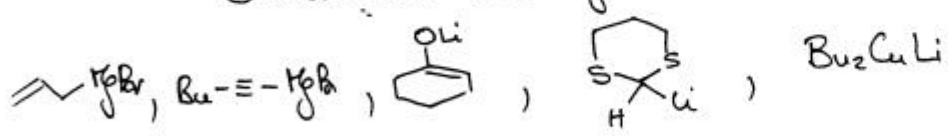


Nukleophilie und Basizität laufen parallel am selben Zentralatom

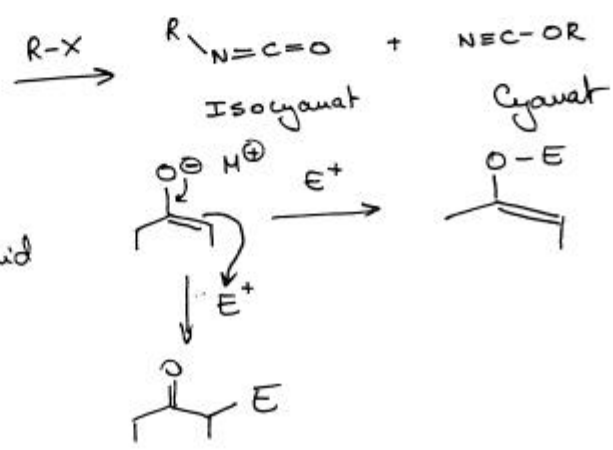
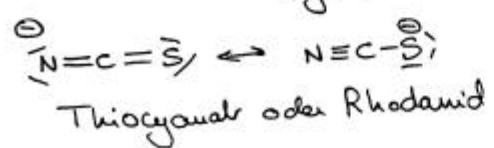
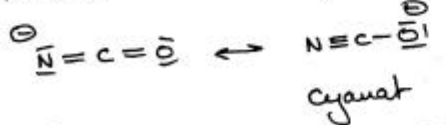


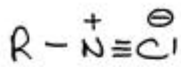
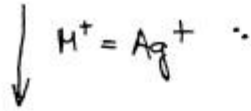
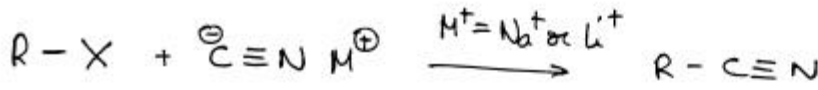
α-Effekte
 NH₂-NH₂, HO-NH₂ >> NH₂
 HO-OH > OH₂ 

"Carbanionen" sind gute Nukleophile



Ambidente Nukleophile





Prinzip der harten und weichen Säuren und Basen (Pearson) HSAB

Klopman Gleichung $\Delta E = \underbrace{-\frac{q_s q_t}{\epsilon R_{st}}}_{\text{elektrostatic Teil}} + \underbrace{2 \sum_{\text{occupied orbitals of S}} \sum_{\text{unoccupied orbitals of molecule T}} \frac{(c_s^m c_t^m \Delta \beta_{st})^2}{E_m^* - E_n}}_{\text{covalenter Teil}}$

Harte Säuren: $H^+, Li^+, BF_3, CO_2, SO_3$

Grenzfälle: $R_3C^+, BR_3, Zn^{2+}, SO_2, Cu^{2+}$

Weiche Säuren: $R-S^{\oplus}, :CH_2, Pd^{2+}, Hg^{2+}, I^+, I_2$

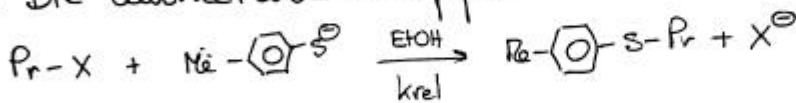
Harte Basen: $F^-, Cl^-, RO^-, ROH, R_2O, NH_3, N_2H_4, RNH_2, SO_4^{2-}, CO_3^{2-}, RCO_2^-, NO_3^-$

Grenzfälle: $Br^-, SO_3^{2-}, NO_2^-, Pt-NH_2, Py, N_3^-$

Weiche Basen: $H^-, I^-, RS^-, RSH, R_2S, R_2S, SCN^-, R_3P, CH_2=CH_2, \ominus CN, CO, R_2C^{\ominus}$

Hart reagiert bevorzugt mit hart
Weich " " " weich

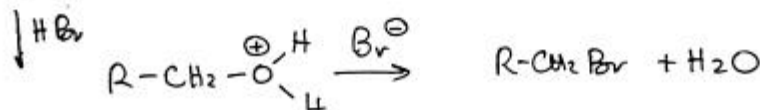
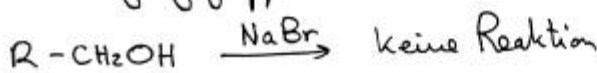
2.2.3. Die austretende Gruppe

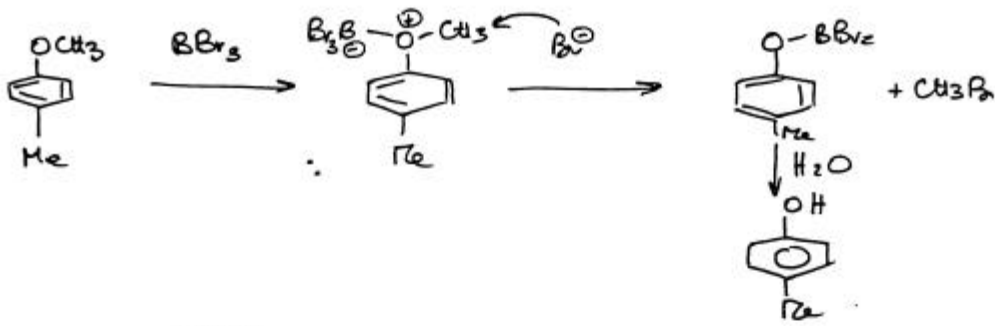


X	krel
I	1
Br	0.29
O	0.0007
OTs	0.12

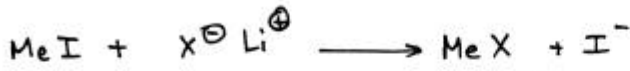
schlechte Abgangsgruppe $\ominus OH, \ominus NR_2, \ominus OR, \ominus N_3$ (meistens starke Basen)

gute Abgangsgruppe: $I^{\ominus}, Br^{\ominus}, Cl^{\ominus}, SR_2, NR_3, RSO_3^{\ominus}, CF_3SO_3^{\ominus}, C_4F_9SO_2^{\ominus}$
Nonafat

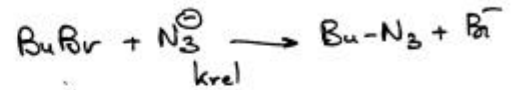




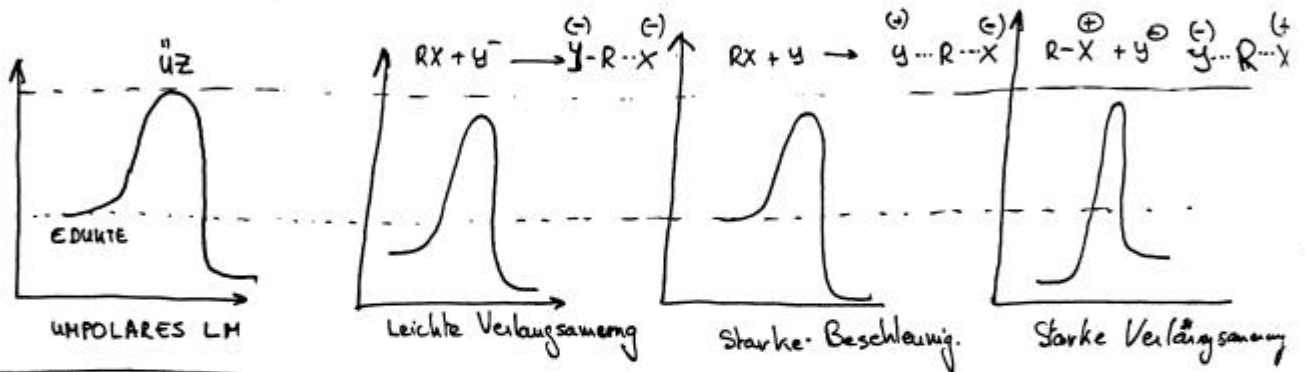
2.2.4. Solvenseffekte



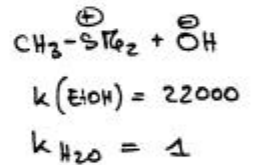
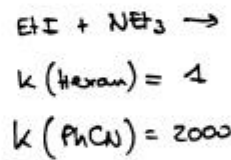
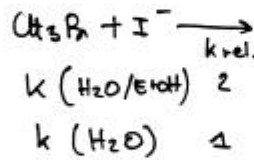
X	MeOH	H ₂ O
Cl ⁻	1	10 ⁶
Br ⁻	20	6 · 10 ⁵



Solvent	k _{rel}
EtOH	1
DMSO	1300
DMF	2800
PhCN	5000
HMPT	200 000



Dipolmoment μ (Debye)
H ₂ O 1.84
EtOH 1.66
CH ₃ CN 3.44
DMSO 3.9
DMF 3.86
HMPT 5.54

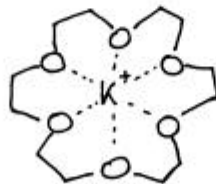


Reaktivität in der Gasphase $\text{F}^- > \text{Cl}^- > \text{Br}^-$ $\text{OH}^- > \text{RO}^- > \text{RS}^-$

Reaktivität in aprotischen LM gleichwie in der Gasphase



Kronenether

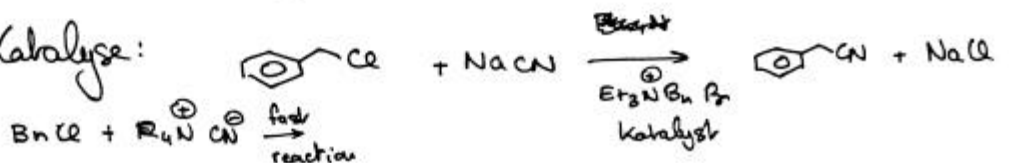


[18]-Krone-6

ideal für die Komplexierung von K^+

KMnO_4 kann in Benzol mit [18]-Krone-6 gelöst werden.

Phasentransfer-Katalyse:



2.3. Die S_N1 Reaktion

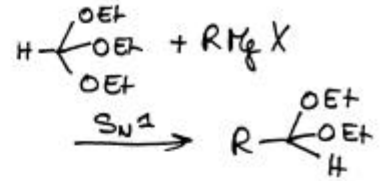
2.3.1. Die Struktur des Substrats

Findet nur statt mit stabilisierte Carbeniumionen Ph_3C^+ , $\text{CH}_2=\text{CH}_2^+$, $\text{Ph}-\text{C}^+$ (8)

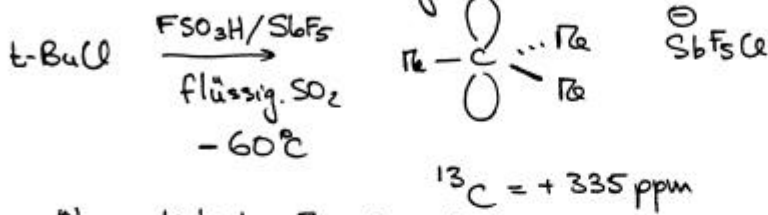
Polare LM beschleunigen S_N1-Reaktionen



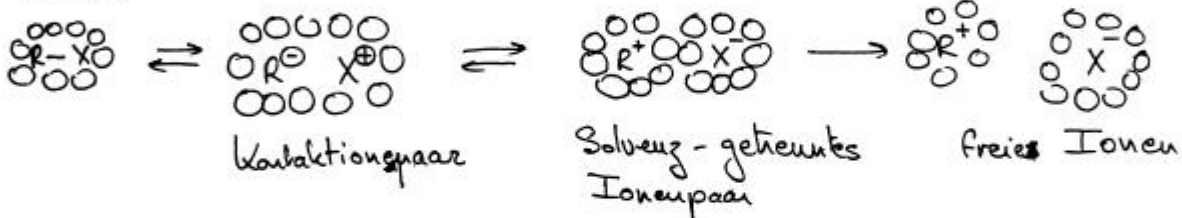
Acetan/H₂O 90:10 1
H₂O 400000



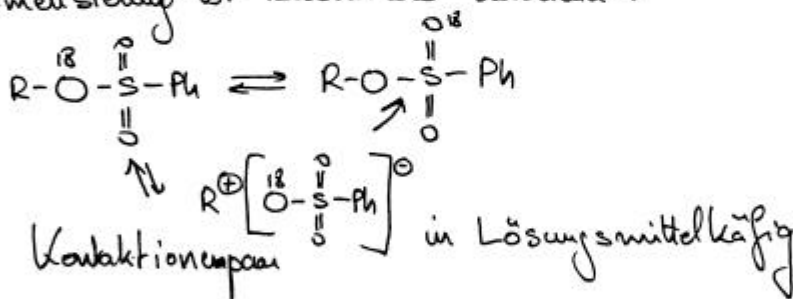
2.3. Carbeniumionen in Lösung



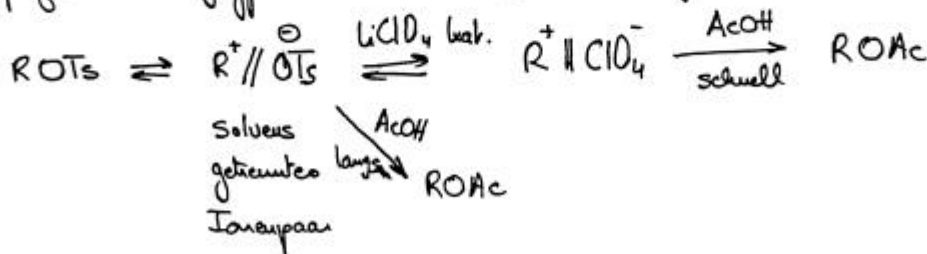
Ionisierung über diskrete Zwischenstufen
Winstein



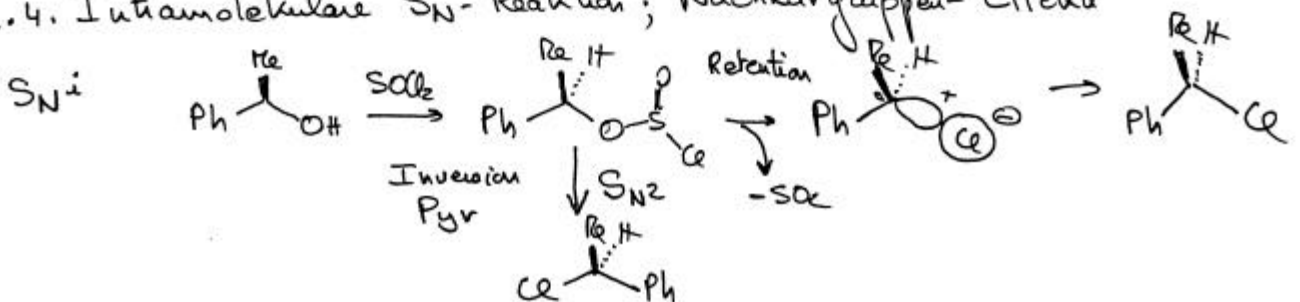
1) Isomerisierung ist rascher als Substitution



2) Spezieller Salzeffekt: der Zusatz kleiner Mengen LiClO₄ beschleunigt die Solvolyse



2.4. Intramolekulare S_N-Reaktion; Nachbargruppen-Effekte

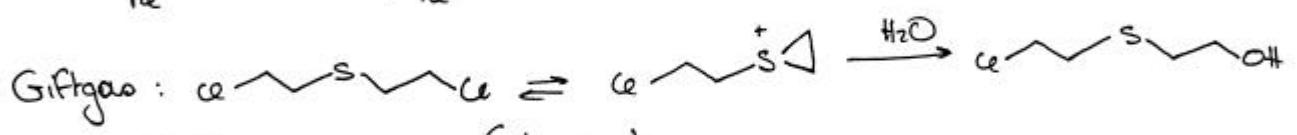
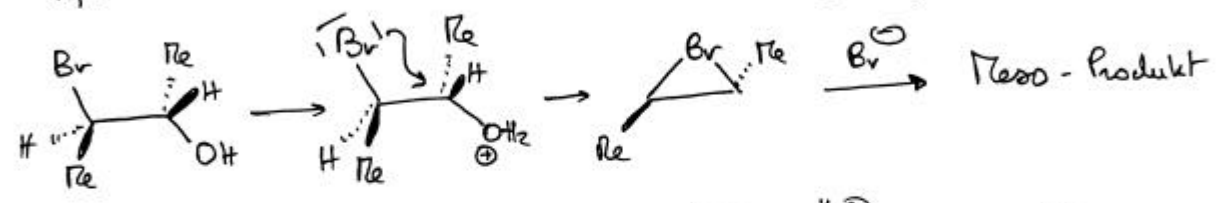
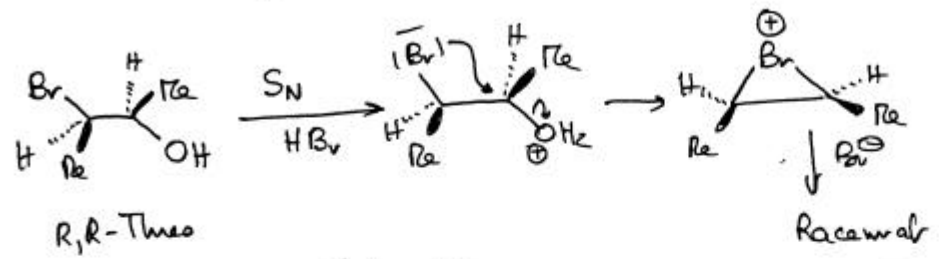


Nachbargruppeneffekte

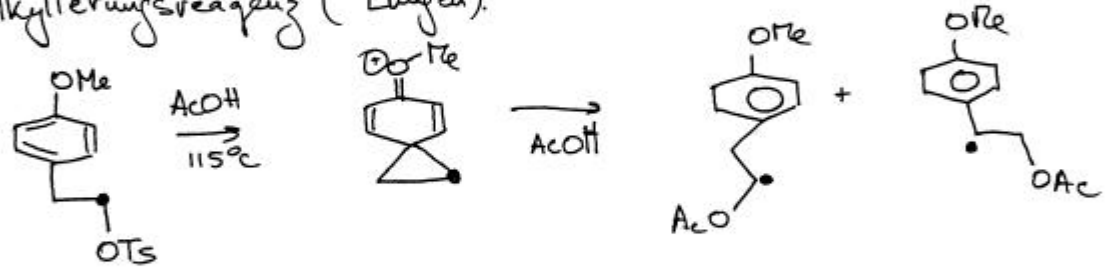
1) Reaktionsgeschwindigkeit erhöht



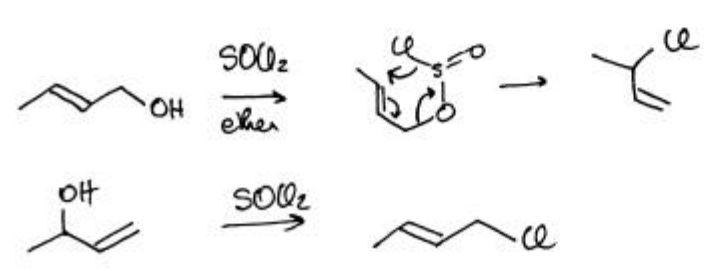
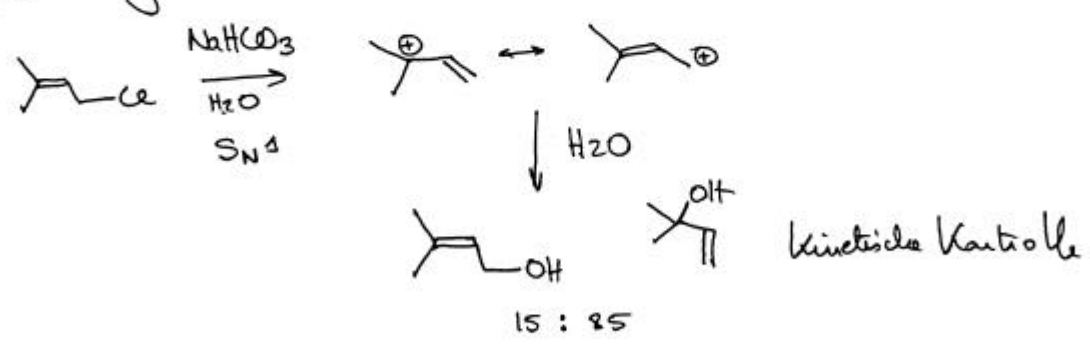
2x Inv. \equiv Retention

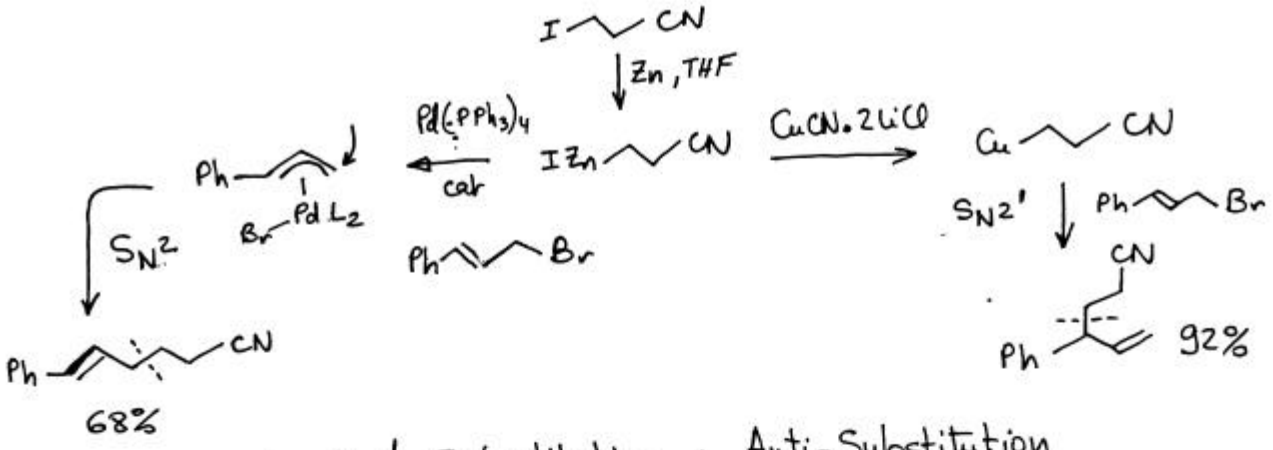


Alkylierungsreagenz (Lungen)

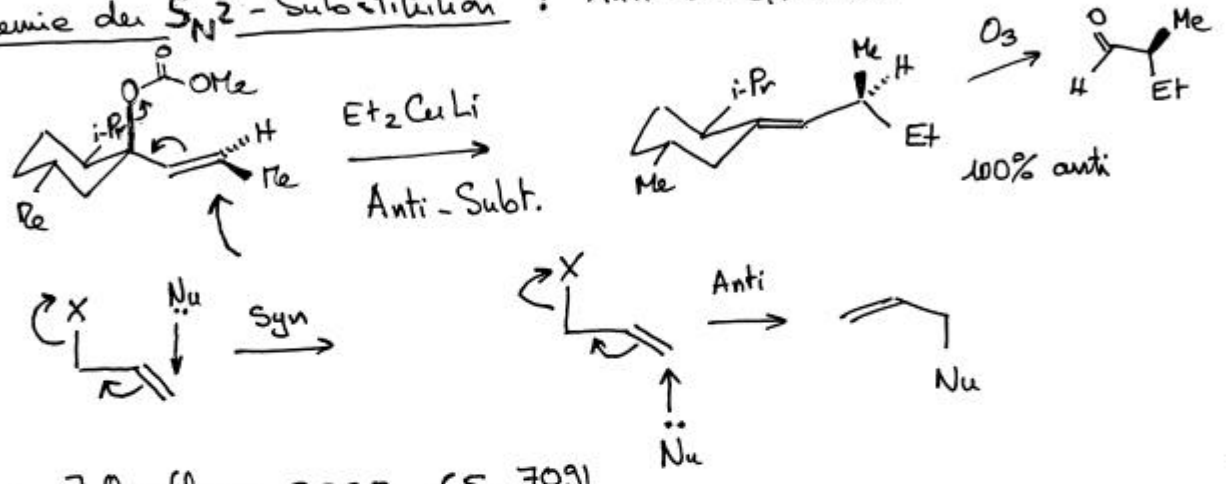


2.5. Allylische Substitution





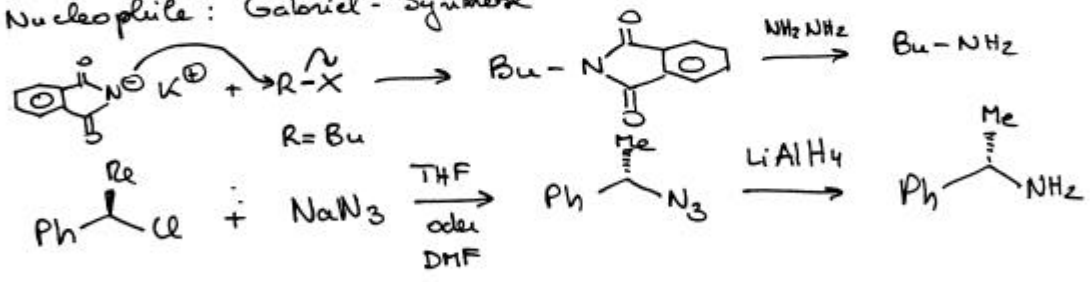
Stereochemie der S_N2' -Substitution : Anti-Substitution



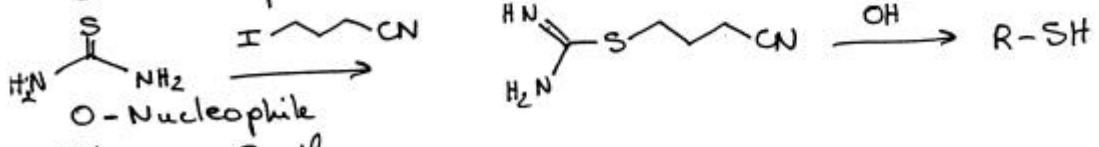
C. Spino, J. Org. Chem. 2000, 65, 7091

Weitere präparative Anwendungen

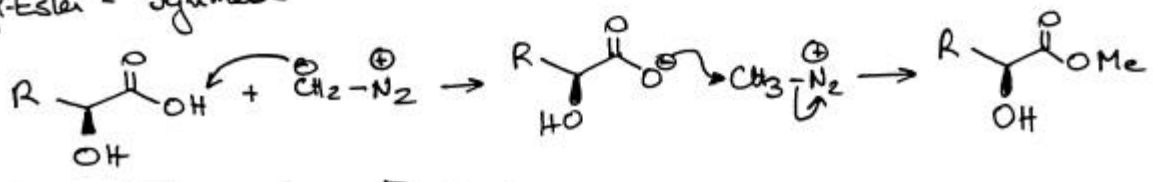
- N-Nucleophile: Gabriel-Synthese



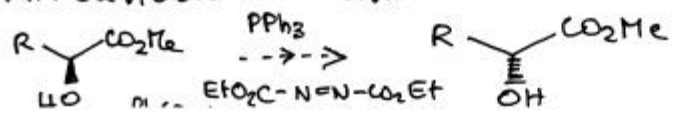
-S-Nucleophile

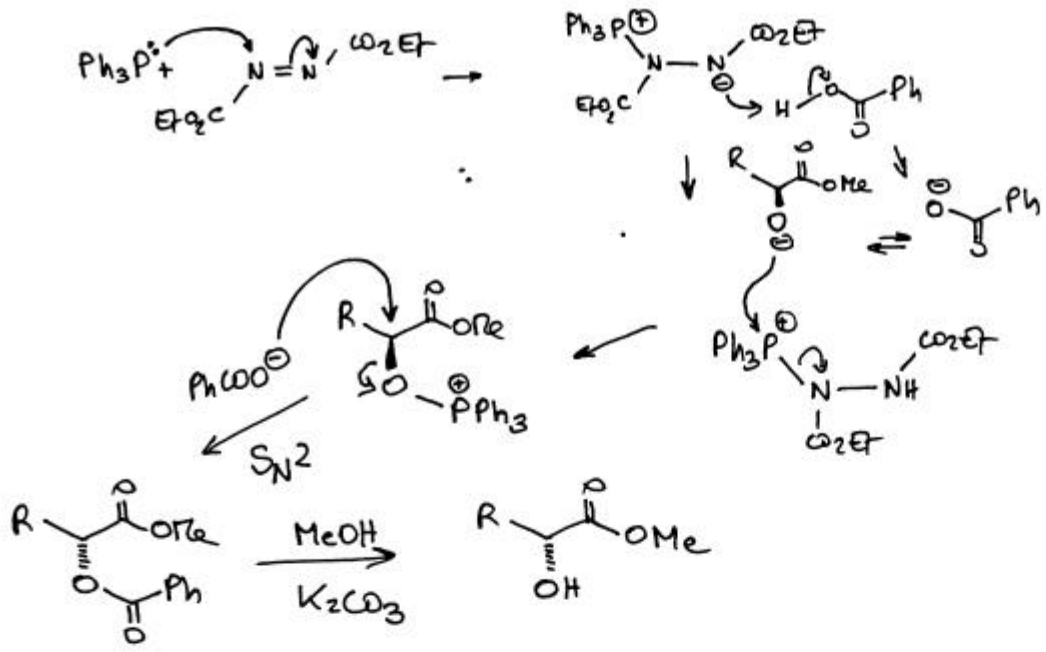


Methyl-Ester-Synthese

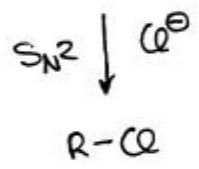
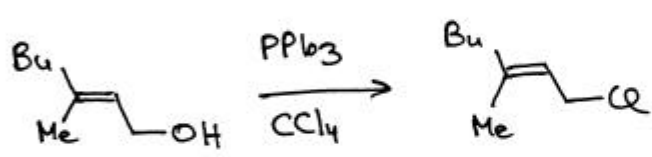
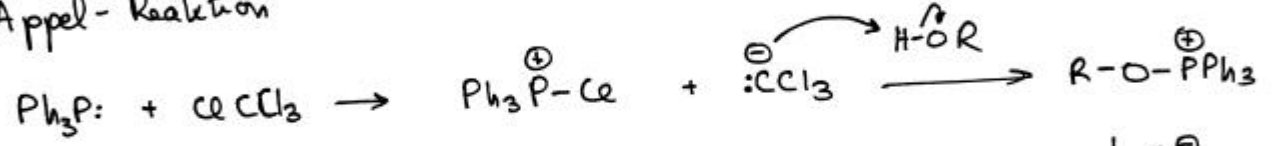


Die Mitsunobu-Inversion





Appel-Reaktion



kein Isomerisierung der Doppelbindung!

3. Radikalische aliphatische Substitutionen

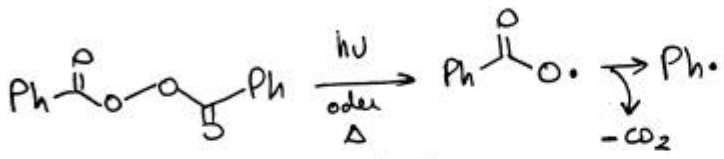
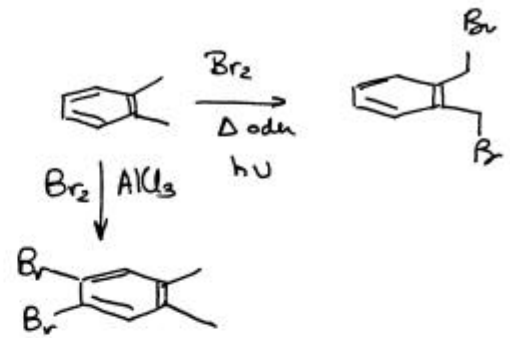
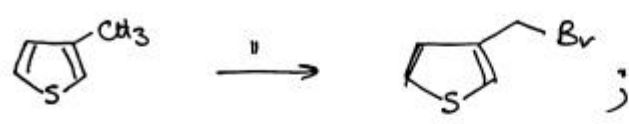
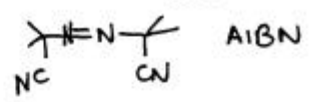
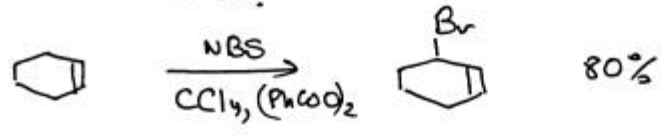
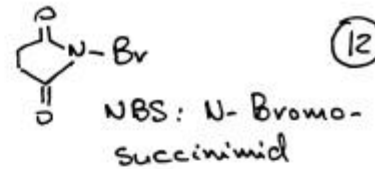
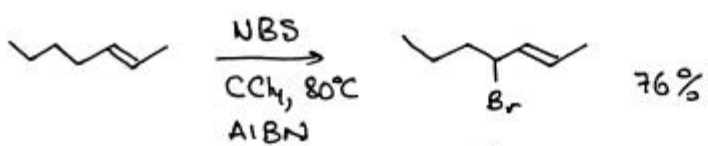
3.1. Radikalische Halogenierungen

Radikalische Reaktionen sind abhängig von der Thermodynamik

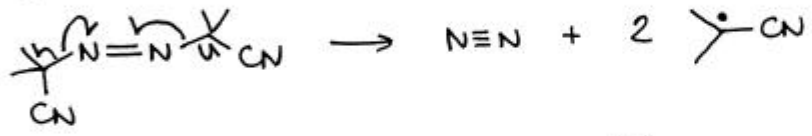
Eine Kettenreaktion ist nur möglich für exotherme Reaktionen.

Strahl: $X-X \xrightarrow{h\nu \text{ oder } \Delta} 2 X^\cdot$	F	Cl	Br	I
$X^\cdot + H-CH_3 \rightarrow HX + \cdot CH_3$	+37	+58	+46	+36.5
$CH_3^\cdot + X_2 \rightarrow CH_3-X + X^\cdot$	-32	+1	+17	+33
	-72	-26	-24	-20
	-104	-25	-7	+13
	explosiv	<	<	ungünstig

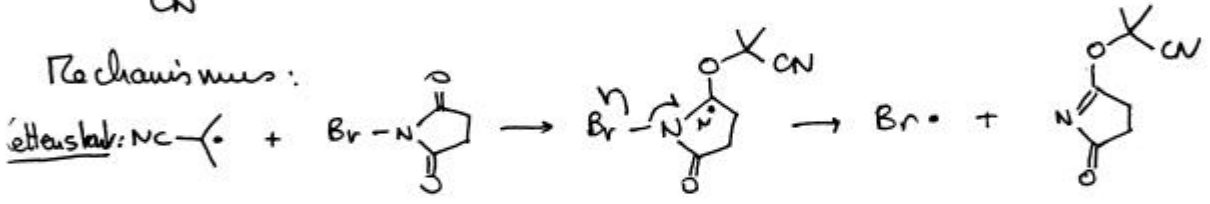
Chlorierung: technisch wichtig
Im Labor: brominierung



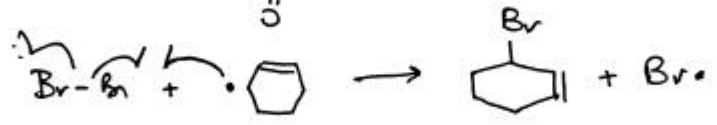
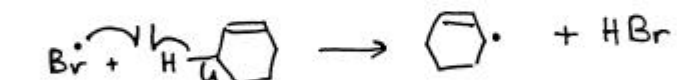
O-O : 32 kcal/mol



Mechanismus:



Propagationschritte



Auoxidation
Industriell wichtig

