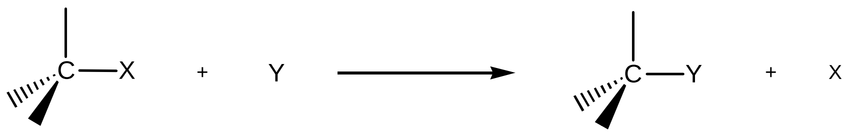
1. Gruppe: Nucleophile Substitution

1. Substitutionstypen:



Klassifizierung der Substitution je nach Natur von Y:

- Y kann ein Nukleophil sein: (ersetzt das Nukleophil X => Lewis - Base):

Bsp.: $PhS^{\ominus}$: $Na^{\oplus}$, H_3N: , $Bu^{\delta\ominus}MgBr^{\delta\oplus}$

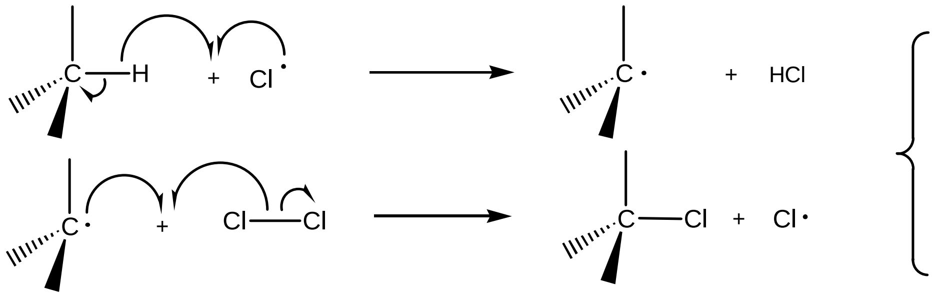
⟹ **Nukleophile Substitution**

- Y kann ein Elektrophil sein: (ersetzt das Elektrophil X => Lewis- oder Brönsted - Säure)

Bsp.: Br^+, H^+, Met^+, (Hg^{2+}, Zn^{2+}, ...)

⟹ **Elektrophile Substitution**

- Y kann ein Radikal sein: (ungepaartes Elektron)



Radikal-ketten-reaktion

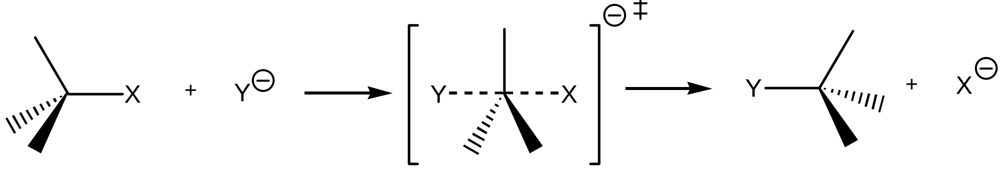
⟹ **Radikalische Substitution**

2. Nukleophile aliphatische Substitution

2.1 Klassifizierung

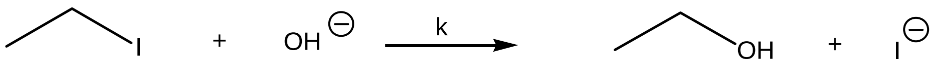
2.1.1 Kinetisches Kriterium

A:



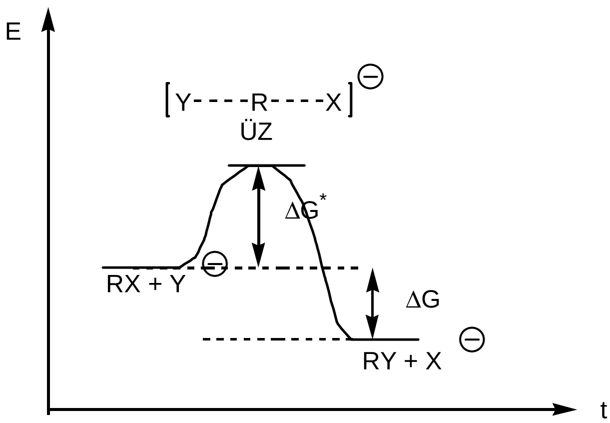
⟹ assoziativer Mechanismus

Bsp.:

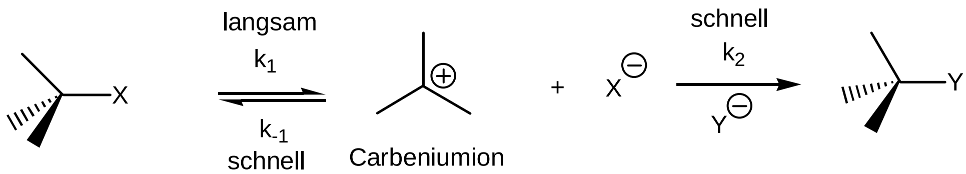


$-d[Et\text{-}I]/dt = k[Et\text{-}I][OH^-]$ Geschwindigkeit hängt von [Et-I] und [OH⁻] ab!

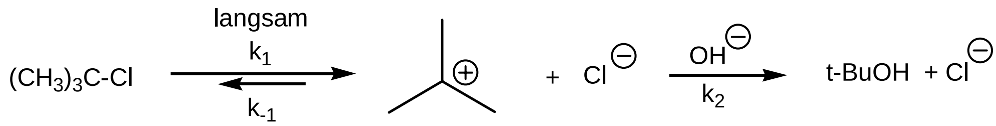
S_N2 Substitution: Kinetik 2. Ordnung



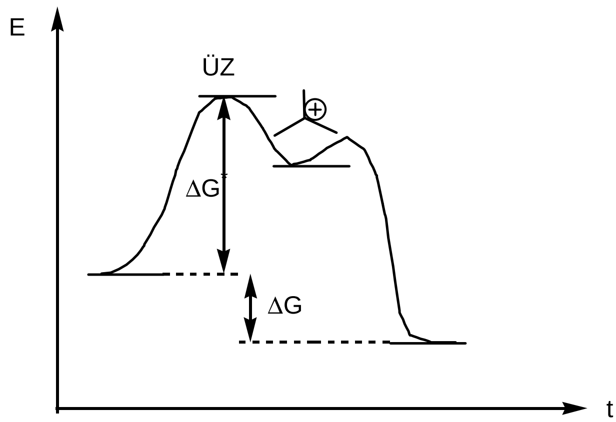
B:



Bsp.:

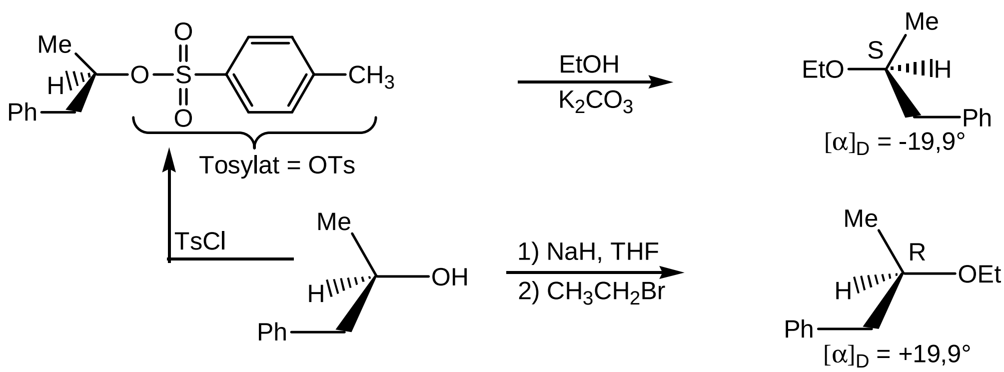


$-d[t\text{-}BuCl]/dt = k_1\,[t\text{-}BuCl]$

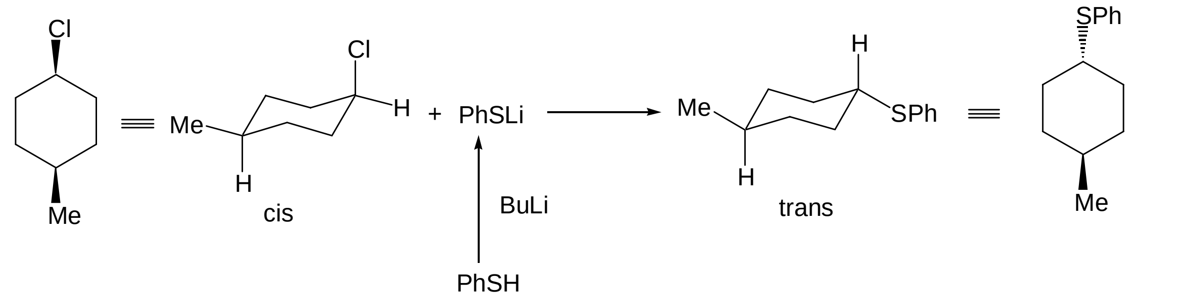


2.1.2 Stereochemisches Kriterium

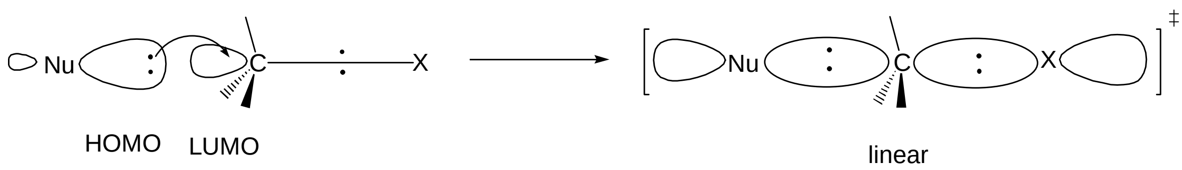
S_N2 - Reaktion:



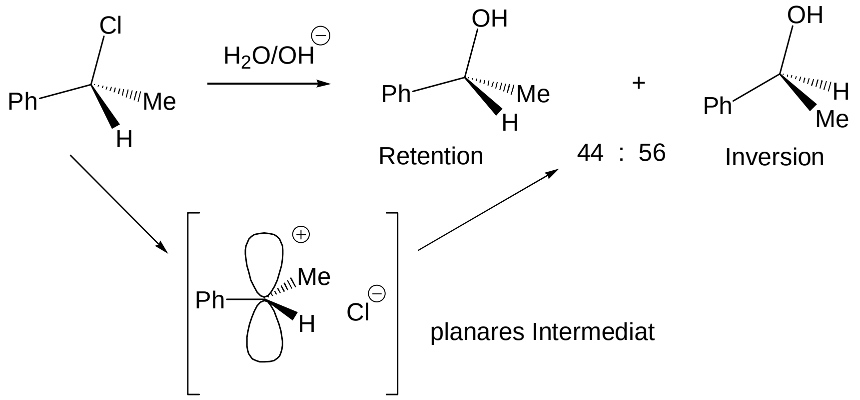
1. Gruppe: Nucleophile Substitution



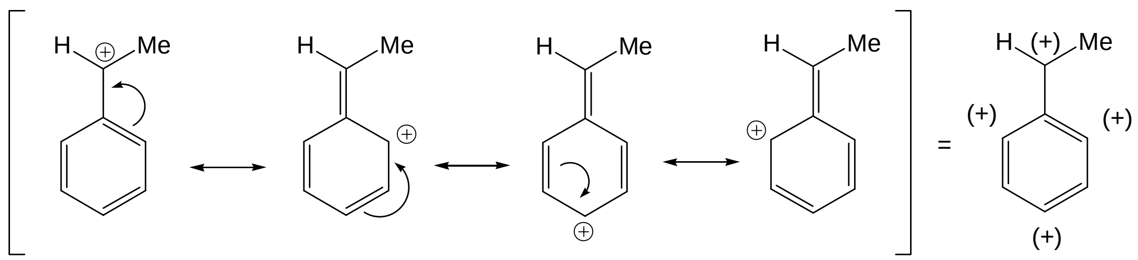
HOMO - LUMO - Betrachtung:



S_N1 - Reaktion:

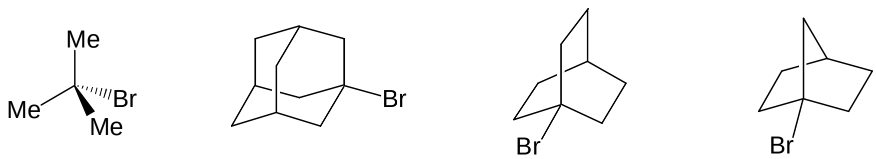


Bsp.:



S_N1 - Mechanismus verlangt ein stabiles Carbeniumion

Geometrie des Carbeniumions ist auch wichtig:



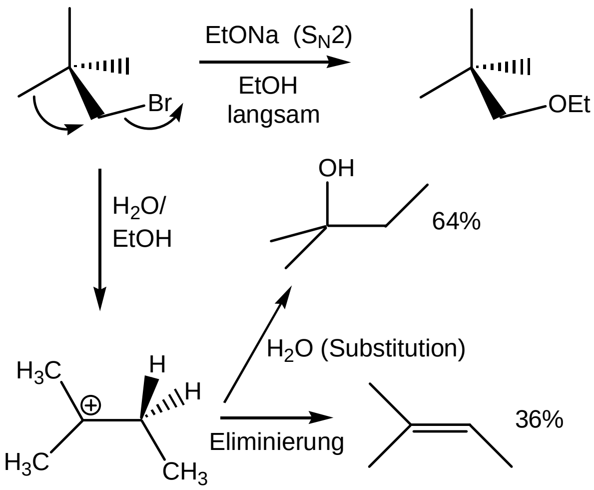
$k_{rel.}$ 1 10^{-3} 10^{-6} 10^{-12}

Solvolyse in Dioxan / Wasser = 70 : 30 bei 100°C

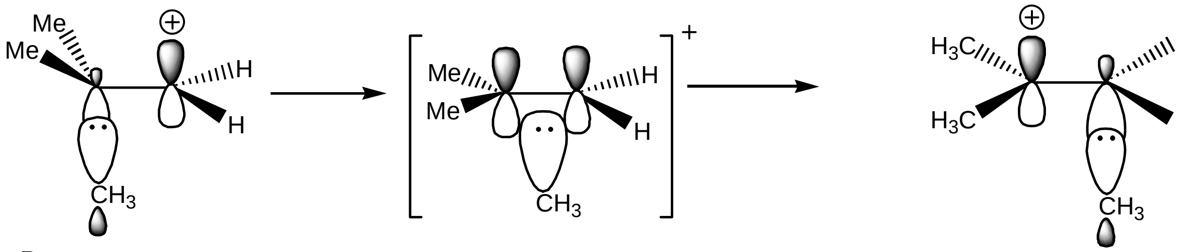
Ein Carbeniumion ist planar, daher erschweren sterische Hinderungen zur Planarität S_N1-Reaktionen

2.1.3 Carbenium - Umlagerungen

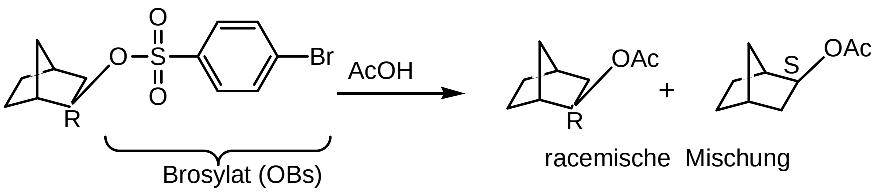
Bei S_N1 - Reaktionen werden oft Gerüstumlagerungen beobachtet



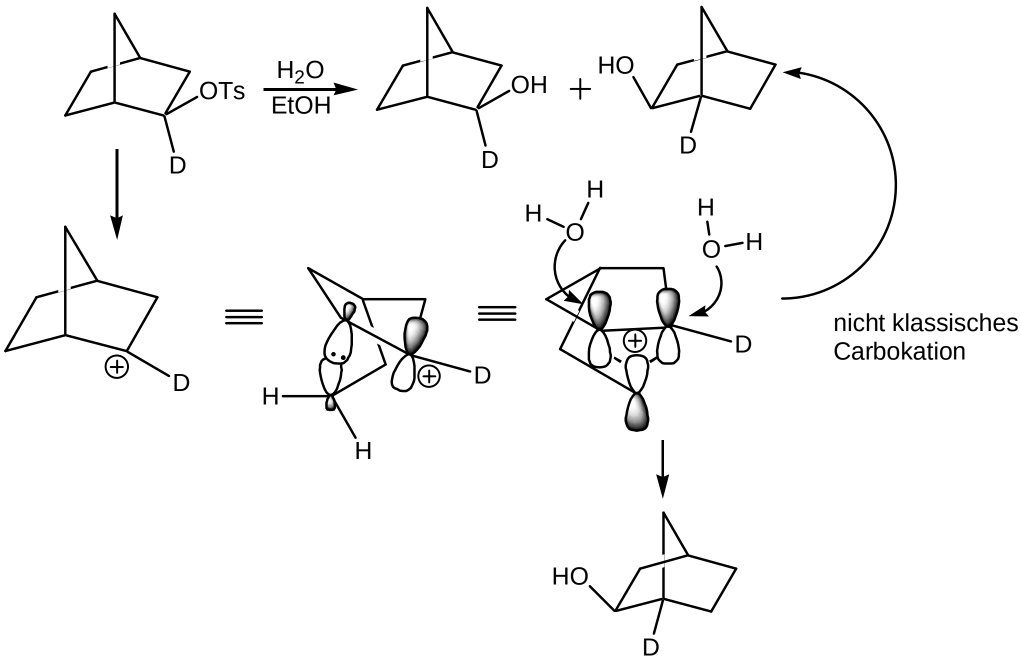
Orbitalbetrachtung (Hyperkonjugation):



Bsp.:



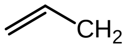
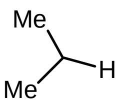
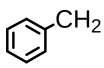
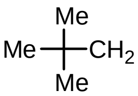
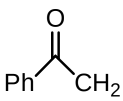
Bsp.:

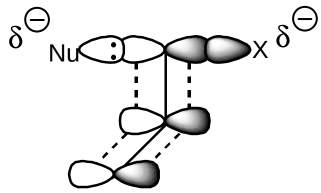


2.2 Die S_N2 - Reaktion

2.2.1 Die Struktur des Substrats

$$R\text{-}Br + I^{\ominus} \xrightarrow{\text{Aceton}} R\text{-}I + Br^{\ominus}$$

R	k_{rel}	R	k_{rel}
CH_3	30		40
Et	1		
$CH_3CH_2CH_2$	0.4		
	0.025		120
	0.00001		15000



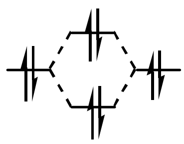
S_N2 : Me > prim > sek >> tert- ~ Neopentyl, aber Allyl, Benzyl, π-Substituenten reagieren schnell

2.2.2 Das Nukleophile Agens

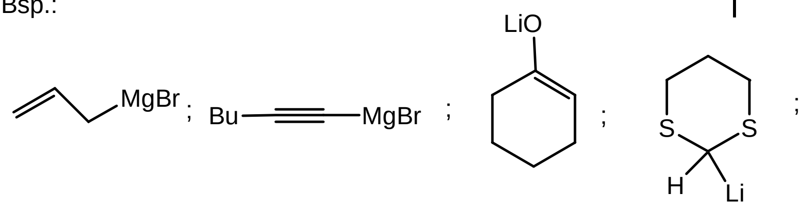
$I^{\ominus} > Br^{\ominus} > Cl^{\ominus} > F^{\ominus}$; $R_3P > R_3N$; $RSe^{\ominus} > RS^{\ominus} > RO^{\ominus}$

Nukleophilie und Basizität laufen parallel am selben Zentralatom

Nukleophilie:	$MeO^{\ominus}$	>	$PhO^{\ominus}$	>	$CH_3CO_2^{\ominus}$	>	MeOH
pk_a:	15.7		9.9		4.75		-1.7

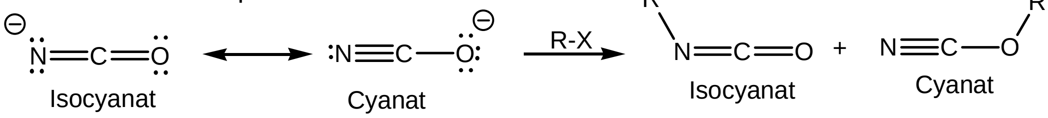
α-Effekte:
$NH_2\text{-}NH_2$, $HO\text{-}NH_2$, >> NH_3
$HO\text{-}OH > H_2O$
Vgl. 

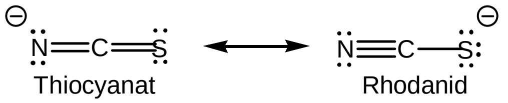
"Carbanionen" sind gute Nukleophile
Bsp.:

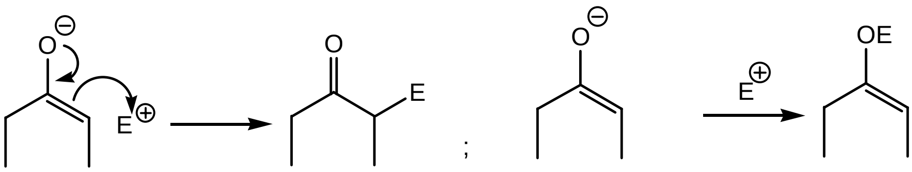


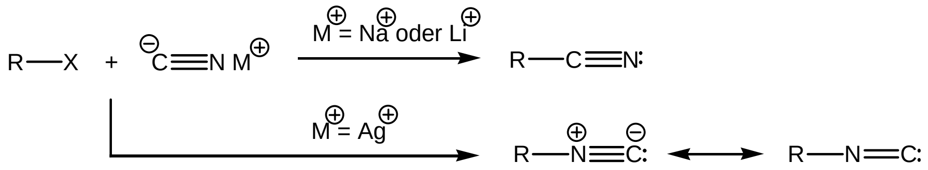
Bu_2CuLi

Ambidente Nucleophile:









•+

Pearson's Hard-Soft Prinzip (HSAB) - einfaches Modell:

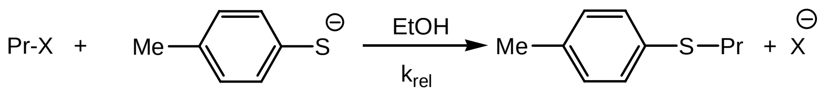
Harte Säuren:	H^+, Li^+, BF_3, CO_2, SO_3
Grenzfälle:	R_3C^+, BR_3, Zn^{2+}, SO_2, Cu^{2+}
Weiche Säuren:	RS^+, $:CH_2$, Pd^{2+}, Hg^{2+}, I^+, I_2
Harte Basen:	F^-, Cl^-, RO^-, ROH, R_2O, NH_3, N_2H_4, RNH_2, SO_4^{2-}, CO_3^{2-}, RCO_2^-, NO_3^-
Grenzfälle:	Br^-, SO_3^{2-}, NO_2^-, Ph-NH_2, Py, N_3^-

Weiche Basen: H^-, I^-, RS^-, RSH, R_2S, R_2Se, SCN^-, R_3P, CH_2=CH_2, CN^-, CO, R_3C^-

Harte Basen reagieren bevorzugt mit harten Säuren

Weiche Basen reagieren bevorzugt mit weichen Säuren

2.2.3 Die austretende Gruppe:

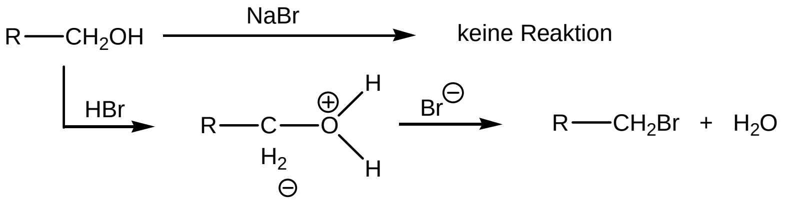


X	k_{rel}
I	1
Br	0.29
Cl	0.0007
OTs	0.12

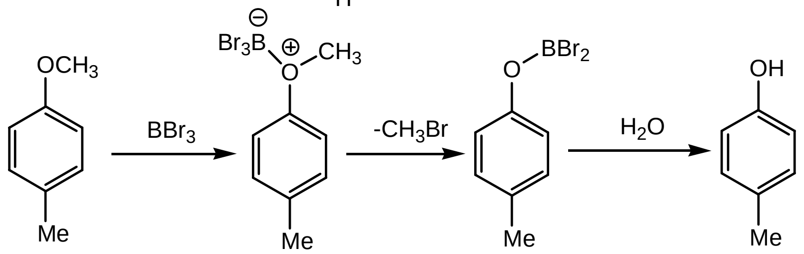
Schlechte Abgangsgruppen: OH^-, NR_2^-, OR^-, N_3^- (meistens starke Basen)

gute Abgangsgruppen: I^-, Br^-, Cl^-, SR_2, NR_3, RSO_3^-, $CF_3SO_3^-$, $C_4F_9SO_3^-$

Bsp.:



Bsp.:



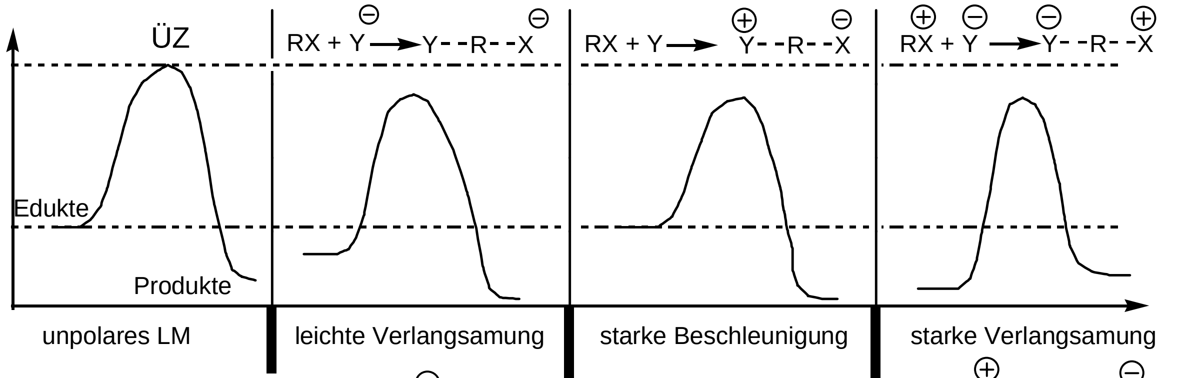
2.2.4 Solvenseffekte:

$MeI + X^{\ominus}Li^{\oplus} \xrightarrow{-Li^{\oplus}} MeX + I^{\ominus}$

X	k_{rel}: MeOH	k_{rel}: $HC(=O)NMe_2$
Cl	1	10^6
Br	20	$6 \cdot 10^5$

$BuBr + N_3^{\ominus} \longrightarrow BuN_3 + Br^{\ominus}$

Solvenz	k_{rel}
MeOH	1
DMSO	1300
DMF	2800
MeCN	5000
HMPT	200000



leichte Verlangsamung: $CH_3Br + I^{\ominus} \longrightarrow$

k_{rel} (H_2O/EtOH)= 2
k_{rel} (H_2O)= 1

starke Beschleunigung: $EtI + NEt_3 \longrightarrow$

k_{rel}(Hexan)= 1
k_{rel}(PhCN)= 2000

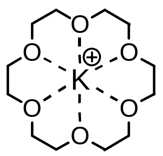
starke Verlangsamung: $CH_3\text{-}S^{\oplus}Me_2 + OH^{\ominus} \longrightarrow$

k_{rel}(EtOH)= 22000
k_{rel}(H_2O)= 1

Reaktionen in der Gasphase: $F^{\ominus} > Cl^{\ominus} > Br^{\ominus}$; $OH^{\ominus} > RO^{\ominus} > RS^{\ominus}$

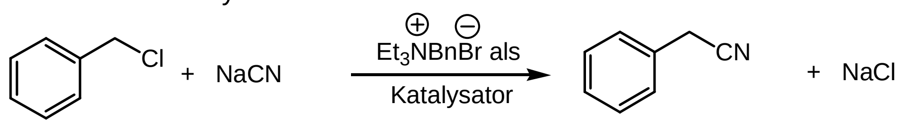
Reaktivität in aprotischen LM ist die gleiche wie in der Gasphase: $F^{\ominus} > Cl^{\ominus} > Br^{\ominus} > I^{\ominus}$

Kronenether:



[18]-Krone-6
ideal für die Komplexierung von $K^{\oplus}$
$KMnO_4$ kann mit [18]-Krone-6 in Benzol gelöst werden

Phasentransfer - Katalyse:

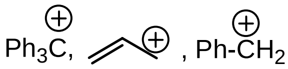


$BnCl + R_4N^{\oplus}CN^{\ominus} \longrightarrow$ schnelle Reaktion

2.3 Die S_N1 - Reaktion:

2.3.1 Die Struktur des Substrates:

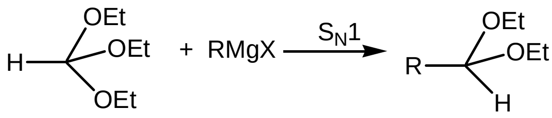
Findet nur mit stabilisierten Carbeniumionen statt:



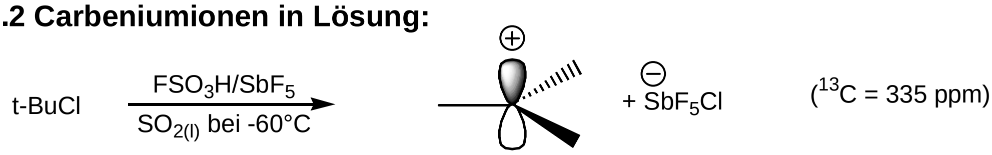
Polare LM beschleunigen S_N1 - Reaktionen:

$$t\text{-}BuBr + H_2O \underset{}{\overset{k_{rel}}{\rightleftharpoons}} t\text{-}BuOH + HBr$$

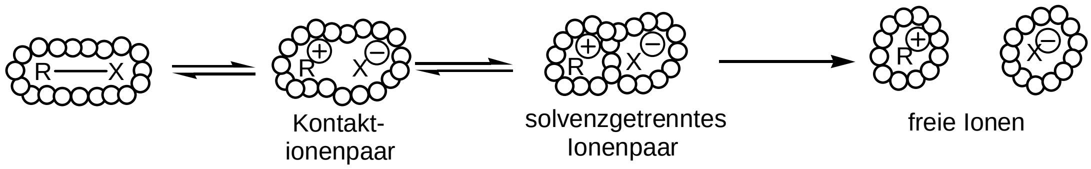
k_{rel}: Aceton/H_2O	90:10 =	1
k_{rel}:	H_2O	= 400000



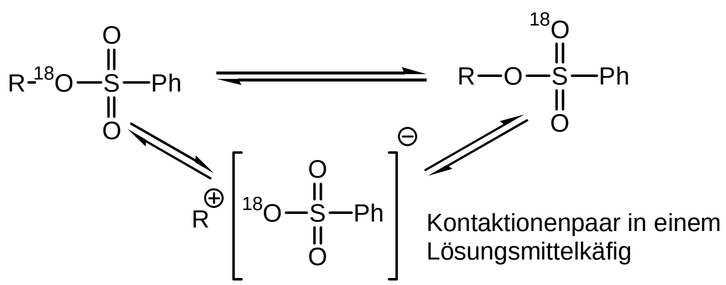
2.3.2 Carbeniumionen in Lösung:



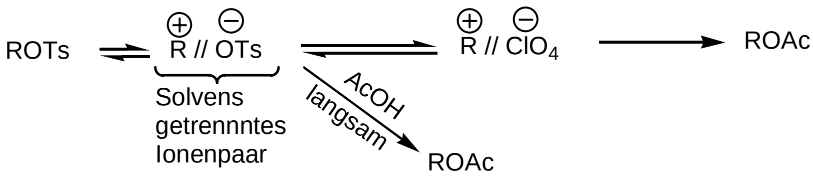
Ionisierung erfolgt über diskrete Zwischenstufen



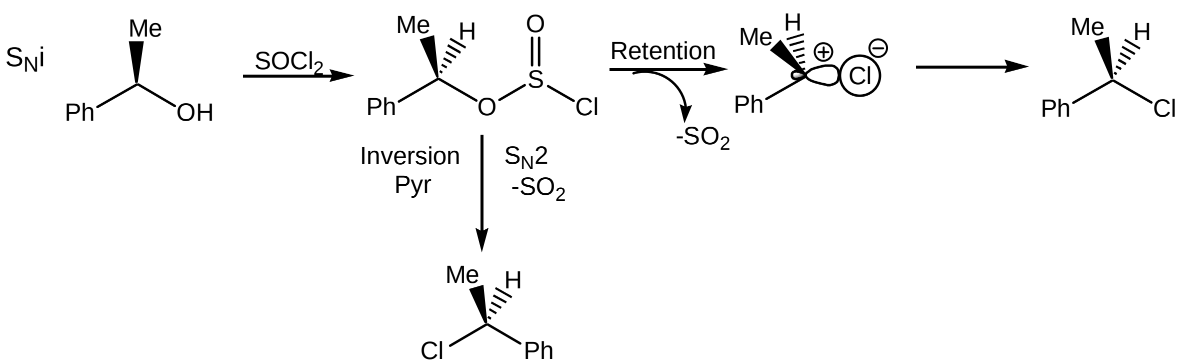
1) Isomerisierung ist rascher als Substitution:



2) Spezieller Salzeffekt: => der Zusatz kleiner Mengen $LiClO_4$ beschleunigt die Solvolyse

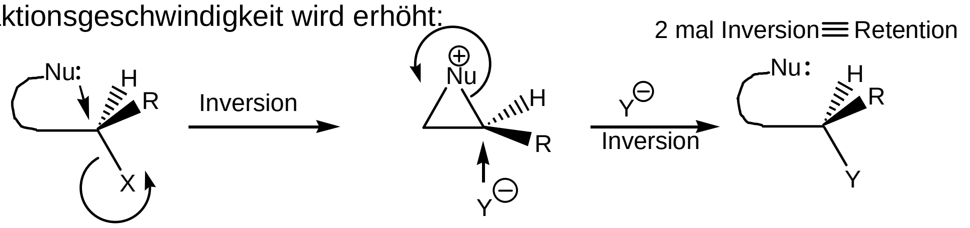


2.4 Intramolekulare S_N - Reaktion => Nachbargruppen - Effekte:

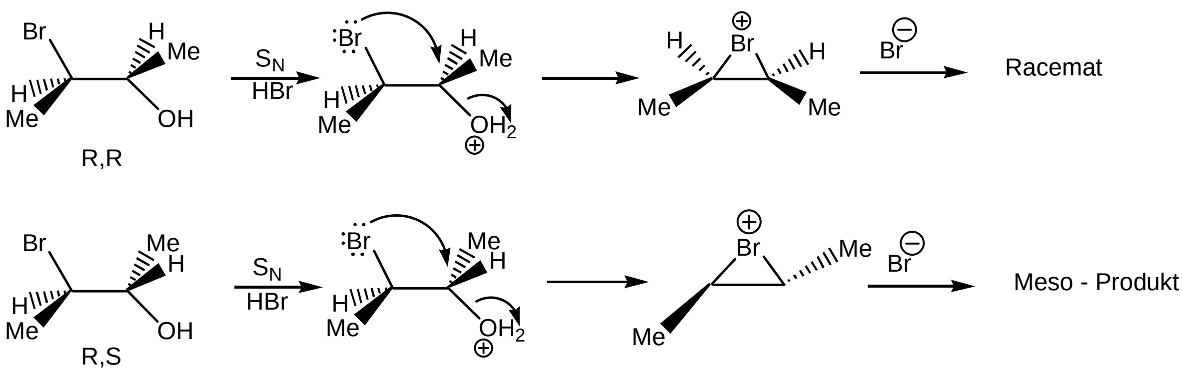


Nachbargruppeneffekte:

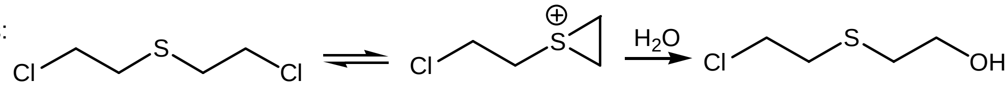
1) Reaktionsgeschwindigkeit wird erhöht:



Bsp.:

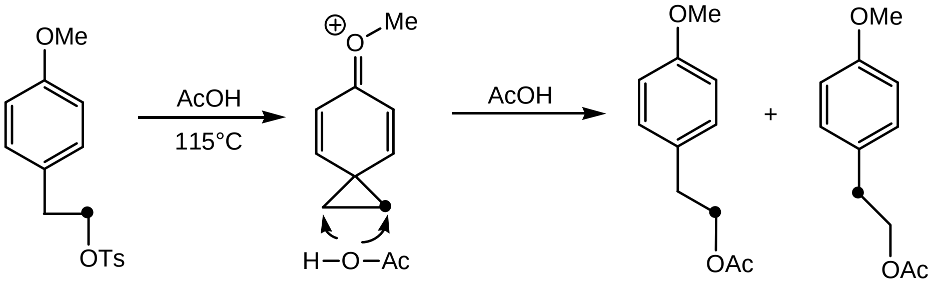


Giftgas:

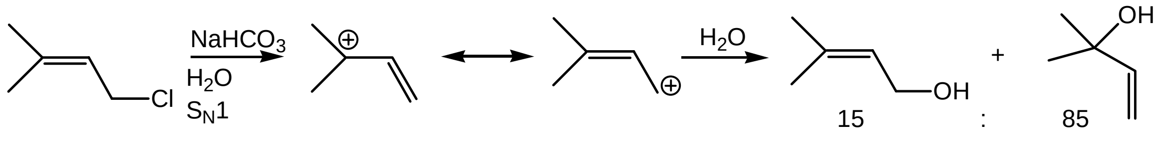


Alkylierungsreagenz (alkyliert die Lungen!)

Bsp.:



Allylische Substitution:



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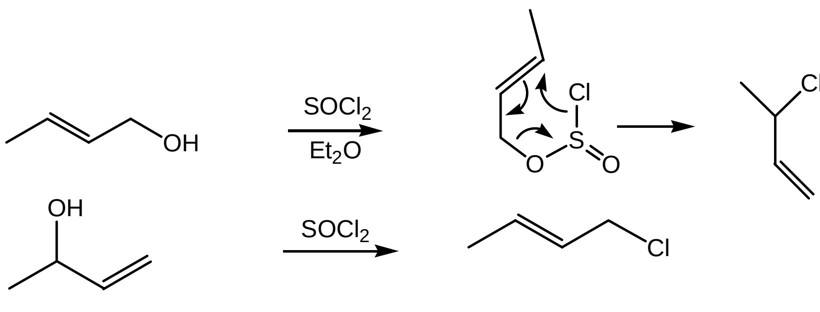
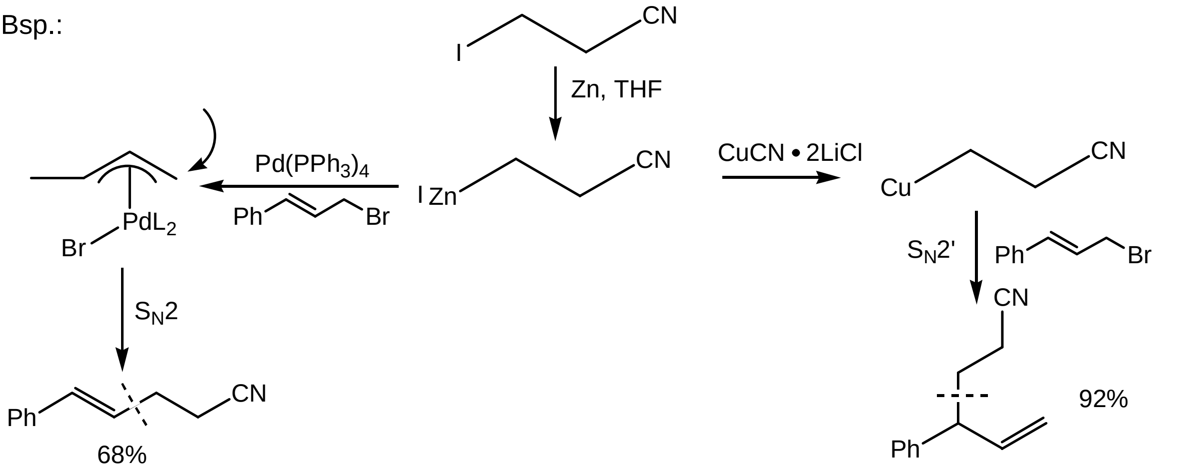


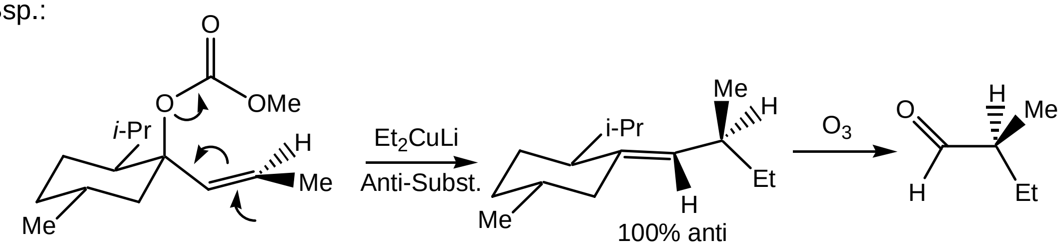
1. Gruppe: Nucleophile Substitution

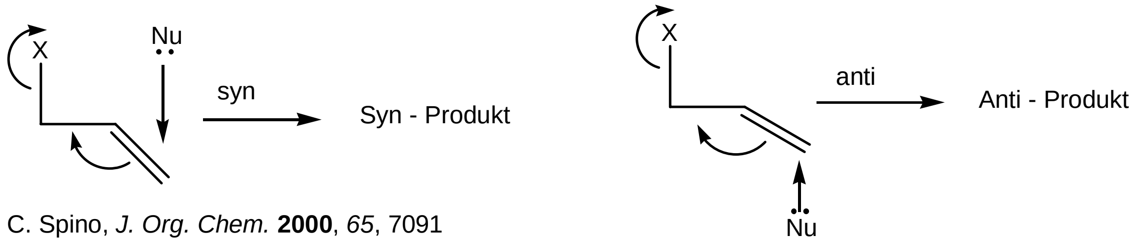
Bsp.:



Stereochemie der S_N2' - Substitution: Anti-Substitution

Bsp.:

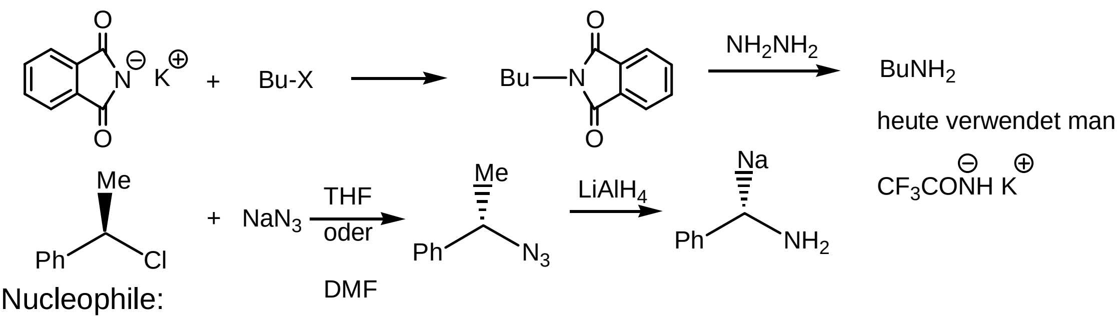




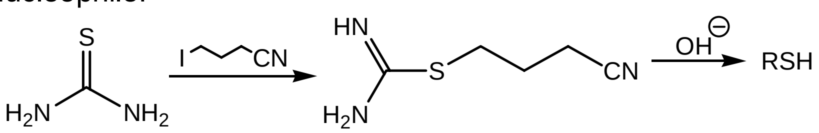
C. Spino, *J. Org. Chem.* **2000**, *65*, 7091

Weitere präparative Anwendungen:

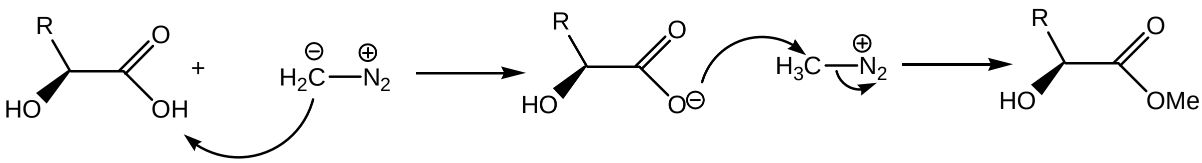
-N-Nucleophile: Gabriel - Synthese



-S-Nucleophile:

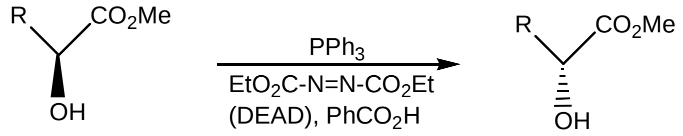


-O-Nucleophile: Methylester-Synthese

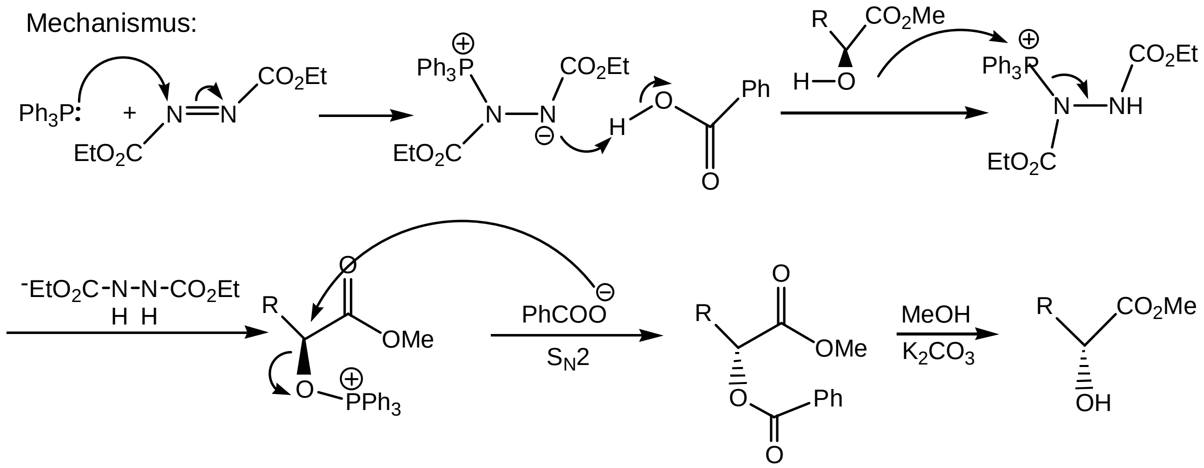


1. Gruppe: Nucleophile Substitution

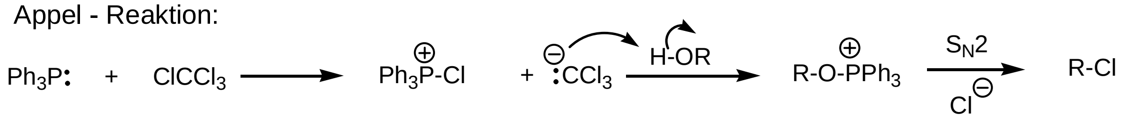
Die Mitsunobu - Inversion:



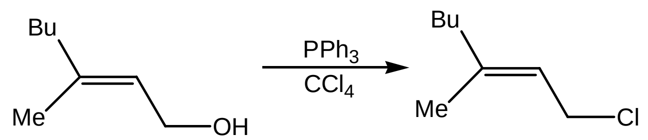
Mechanismus:



Appel - Reaktion:



Bsp.:



keine 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:
siehe OC I

Start: $X\text{-}X \xrightarrow[\text{oder } \Delta]{h\nu} 2\,X^\bullet$

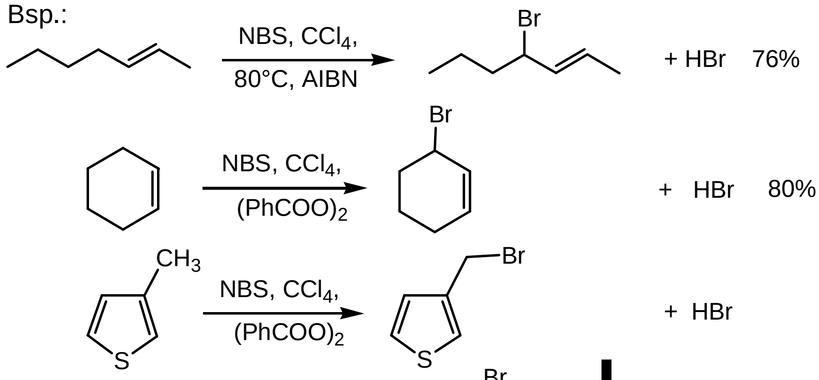
$X^\bullet + H\text{-}CH_3 \longrightarrow HX + {}^\bullet CH_3$

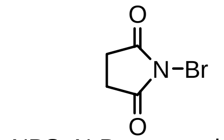
$CH_3^\bullet + X_2 \longrightarrow CH_3\text{-}X + X^\bullet$

=> Fluorierung ist explosiv
=> Chlorierung ist technisch wichtig
=> Im Labor wird bromiert
=> Keine Reaktion mit I_2

1. Gruppe: Nucleophile Substitution

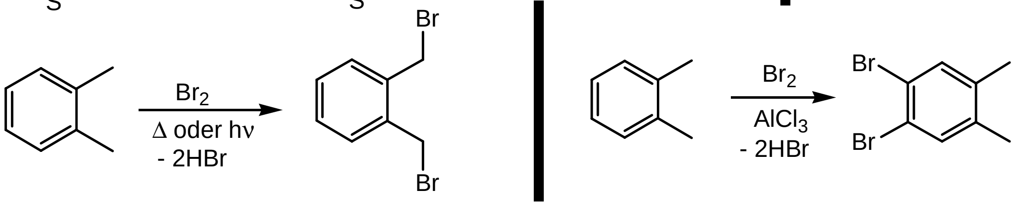
Bsp.:



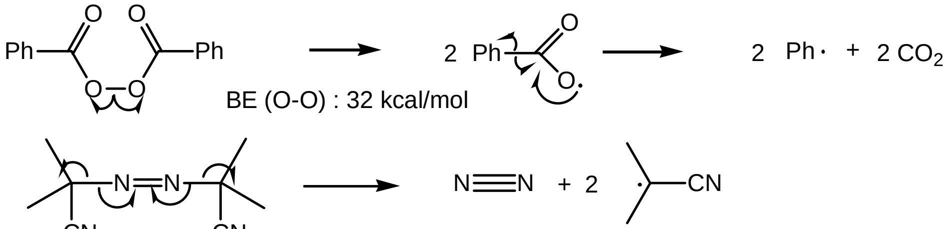


NBS: N-Brom-succinimid

AIBN: 2,2'-Azobisisobutyronitril

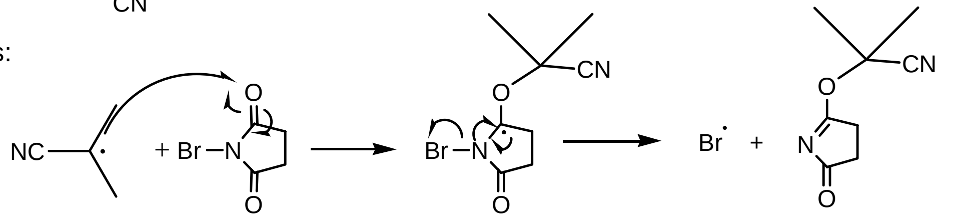


Zerfallsmechanismus der Radikalstarter:

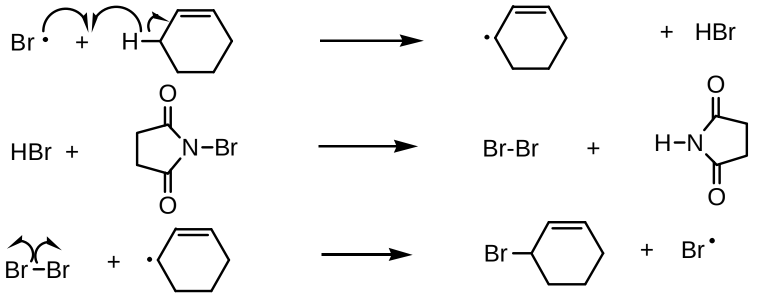


Mechanismus:

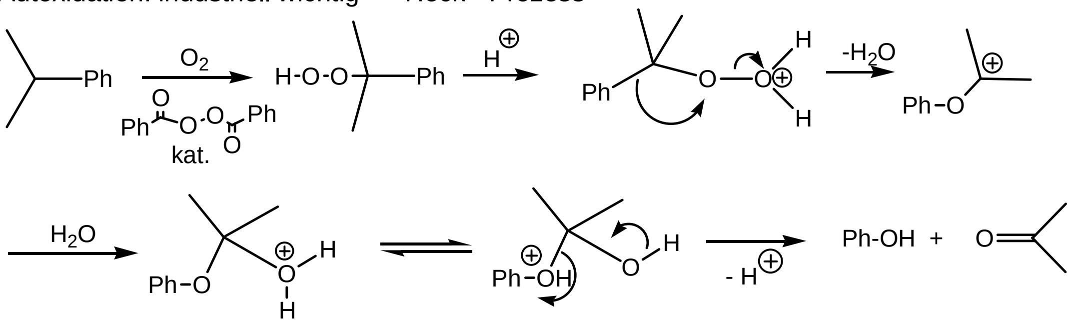
Kettenstart:



Propagationsschritte:

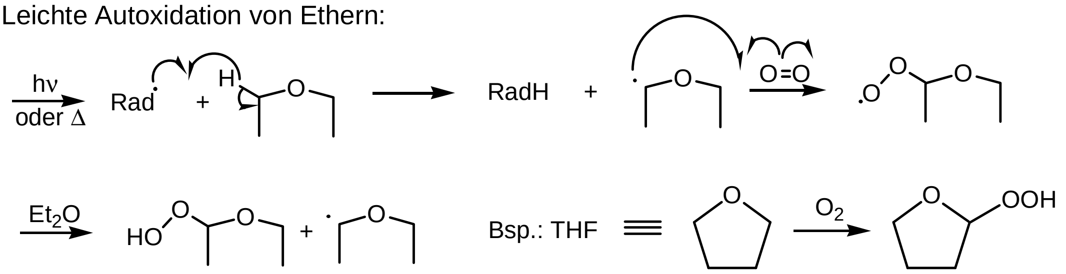


Autoxidation: industriell wichtig => Hock - Prozess

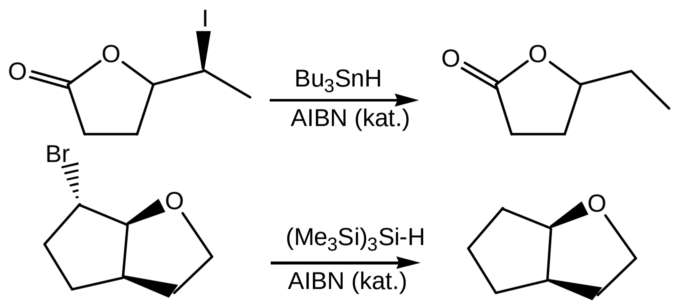


1. Gruppe: Nucleophile Substitution

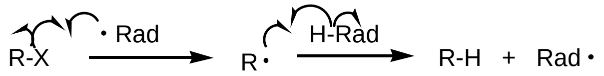
Leichte Autoxidation von Ethern:



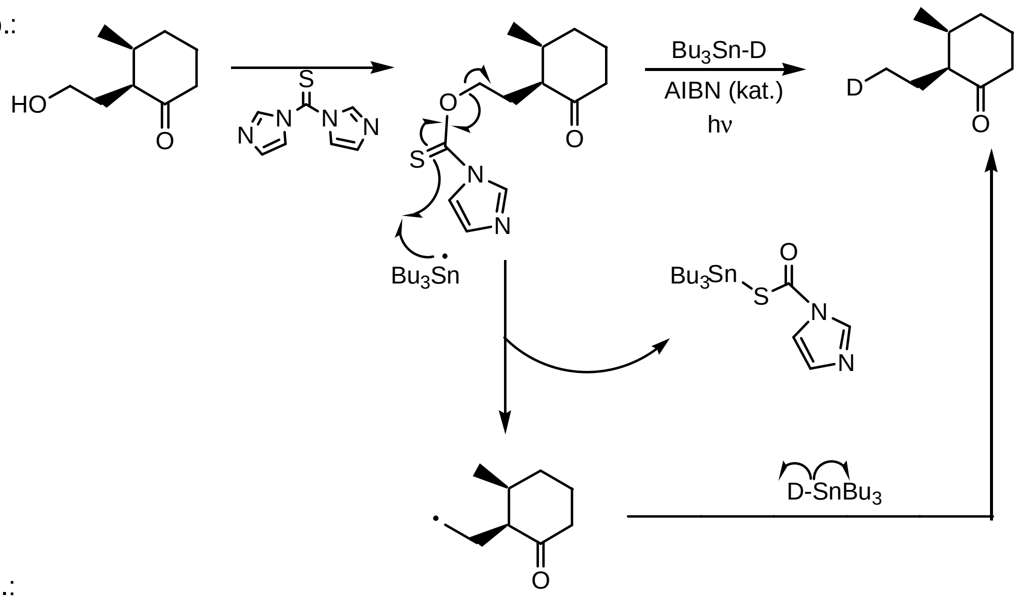
Moderne radikalische Substitutionsreaktionen:



Mechanismus:



Bsp.:



Bsp.: