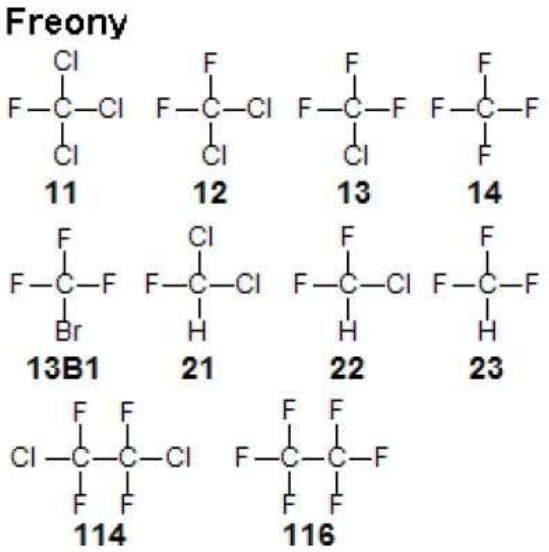
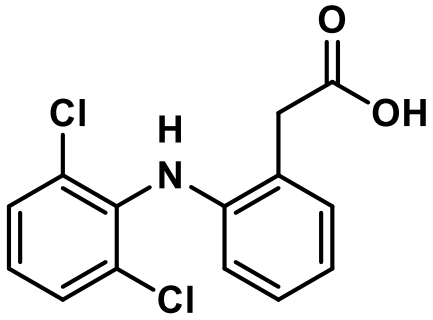
Halogenderiváty



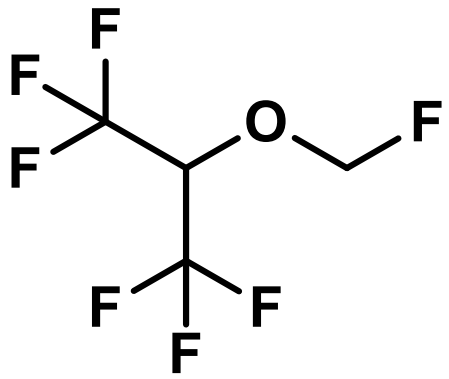
Arnika.org

Alphega.cz

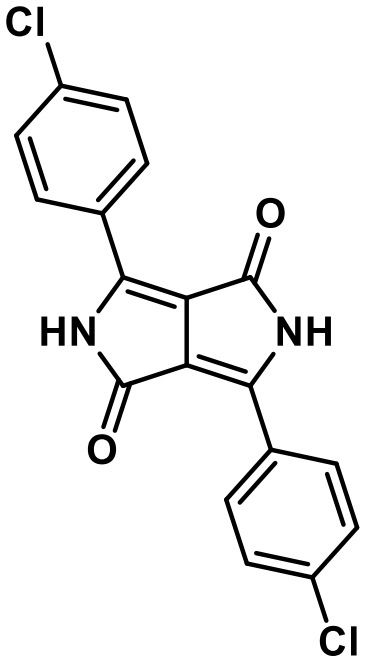


diclofenac

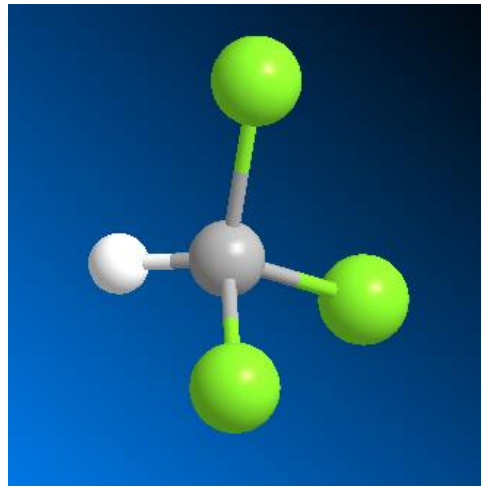
https://www.pearsondental.com/

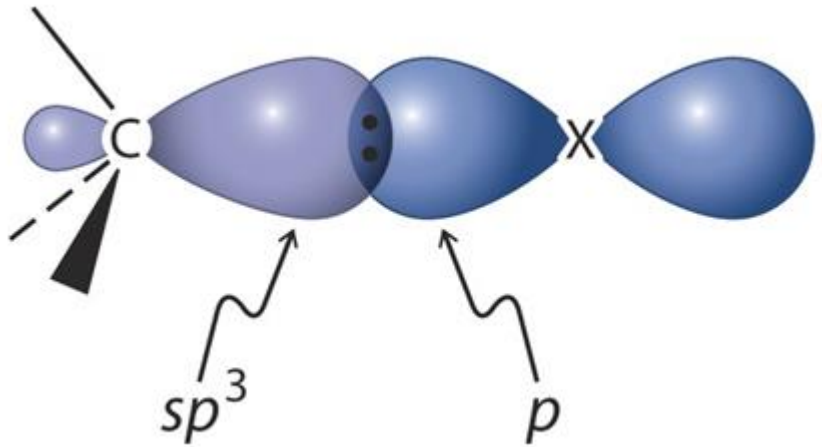


sevofluran



Diketopyrrolopyrrole (DPP) pigments

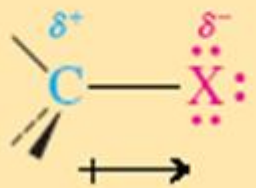




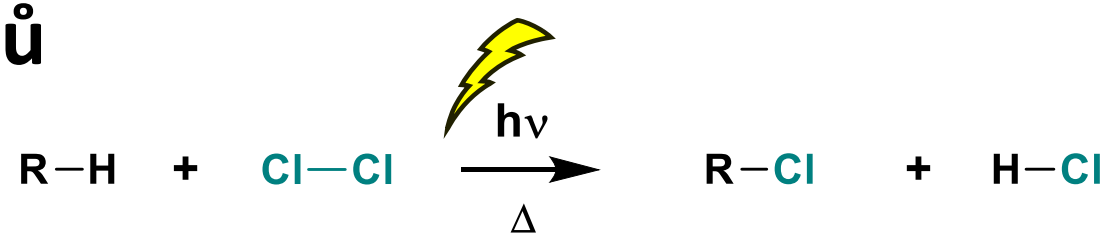
C–X Bond Lengths and Bond Strengths in CH_3X

Halomethane	Bond length (Å)	Bond strength (kcal mol^{-1})
CH_3F	1.385	110
CH_3Cl	1.784	85
CH_3Br	1.929	70
CH_3I	2.139	57

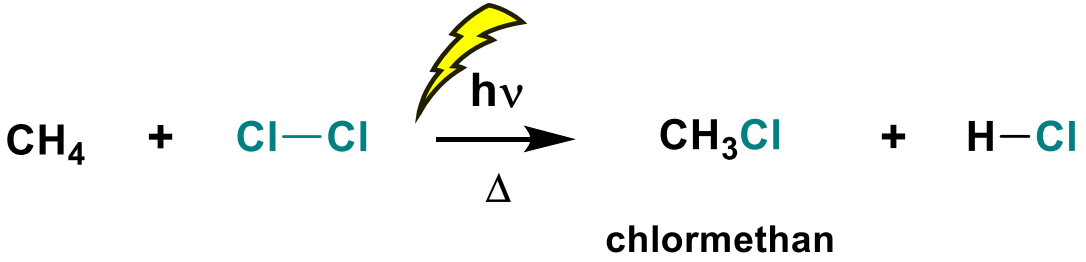
The Polar Character of the C–X Bond

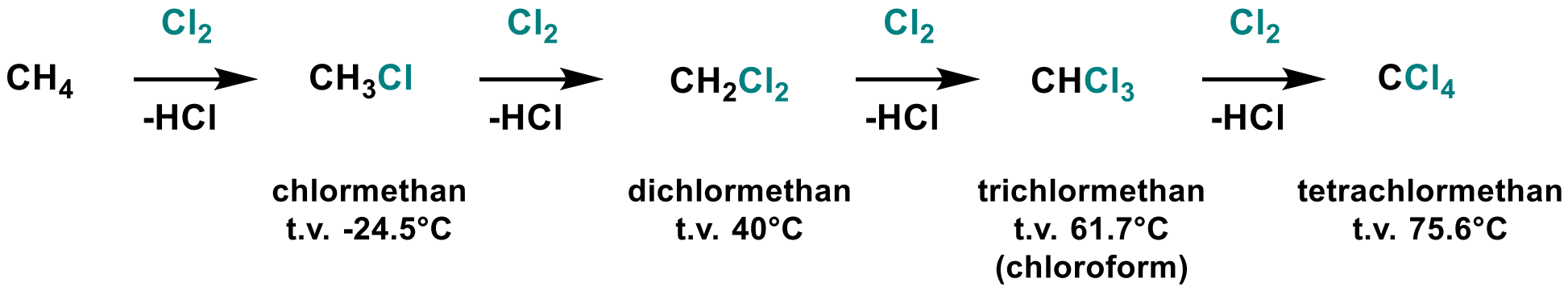


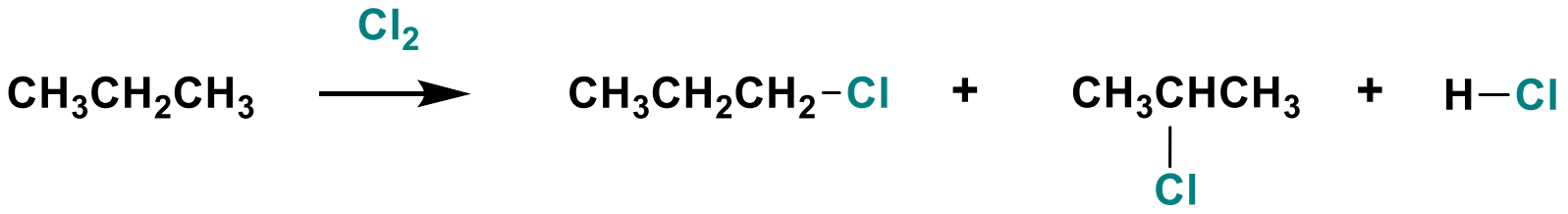
Příprava halogenderivátů

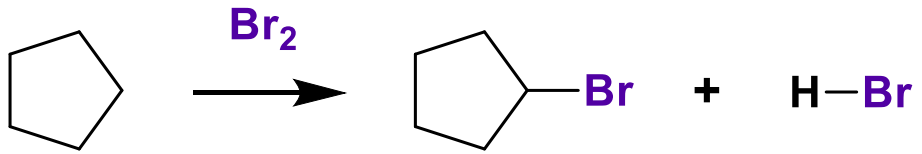


Halogenace alkanů

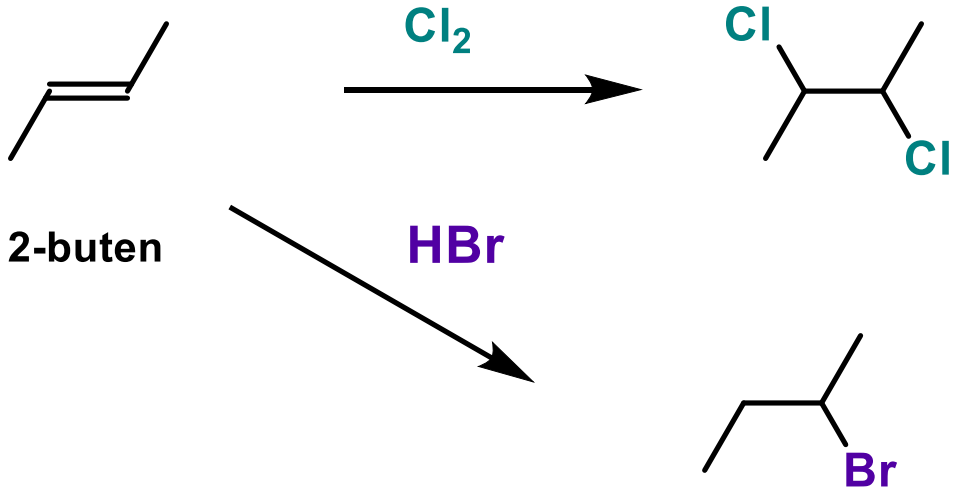






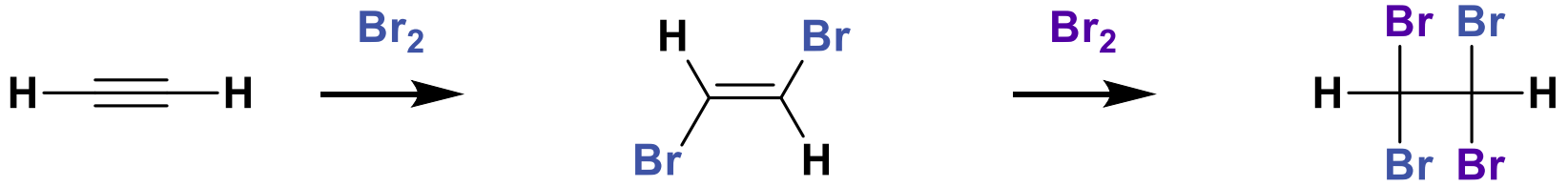


Adice na alkeny

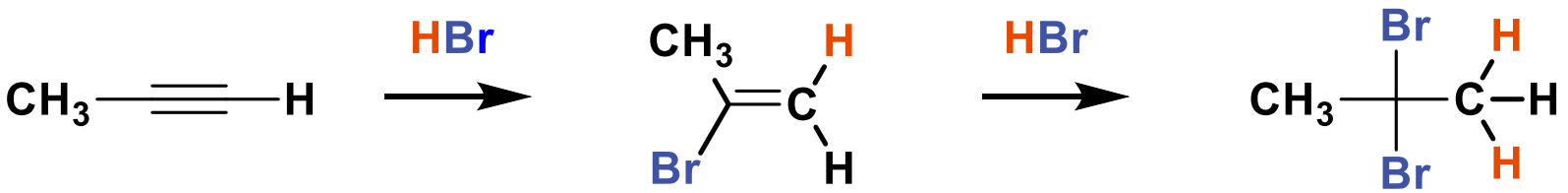


2-buten

Adice na alkyny

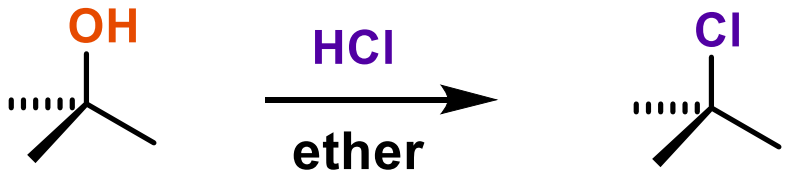


***trans*-1,2-dibromethen** **1,1,2,2-tetrabromethan**

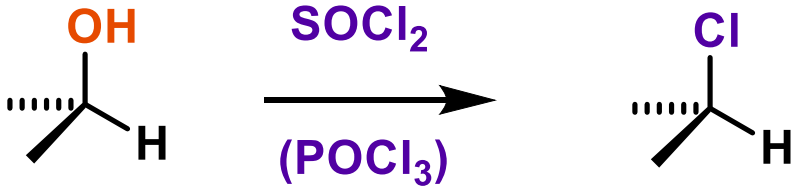


propyn **2-brompropen** **2,2-dibrompropan**

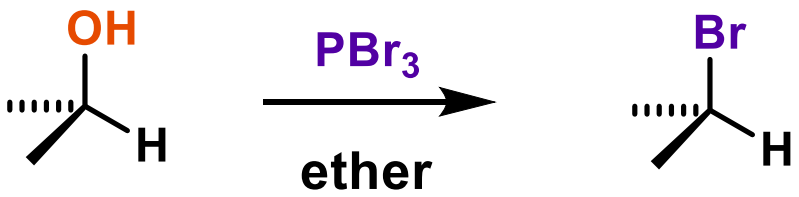
Příprava halogenderivátů z alkoholů



terciární > sekundární > primární

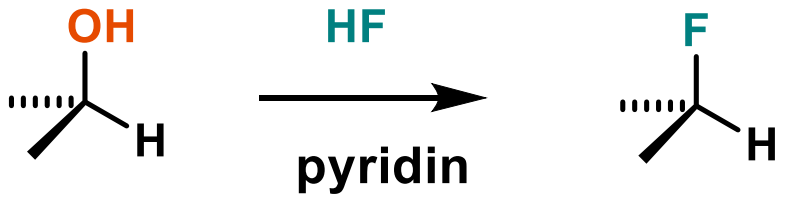


sekundární, primární

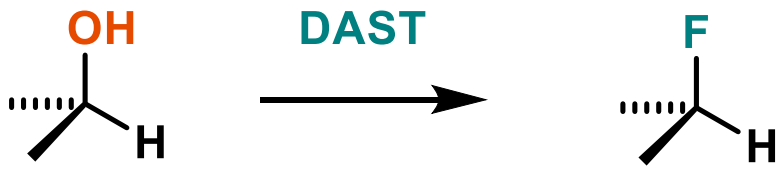


sekundární, primární

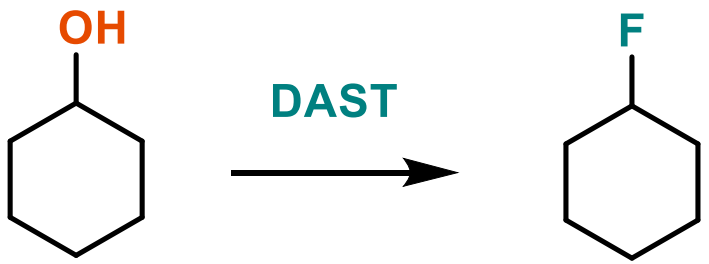
Příprava fluorderivátů z alkoholů

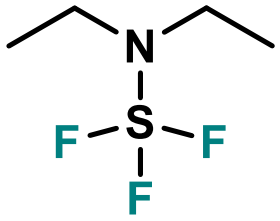


sekundární, primární



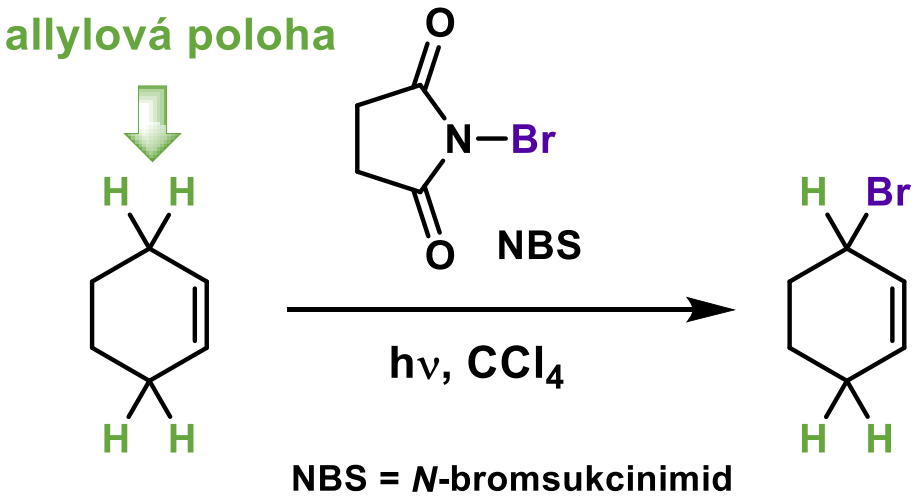
sekundární, primární



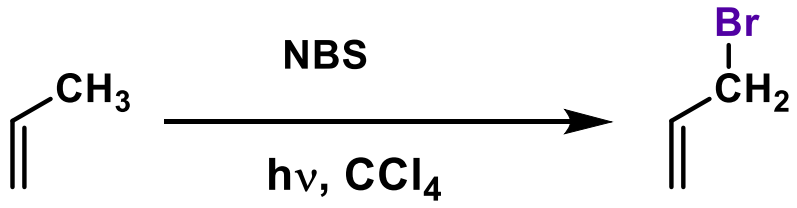


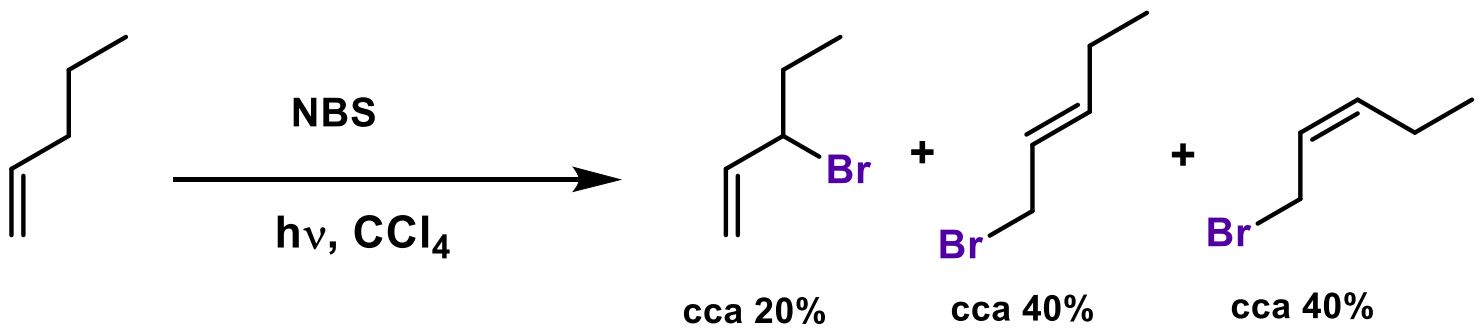
DAST = diethylaminosulfur trifluoride

Bromace v allylové poloze

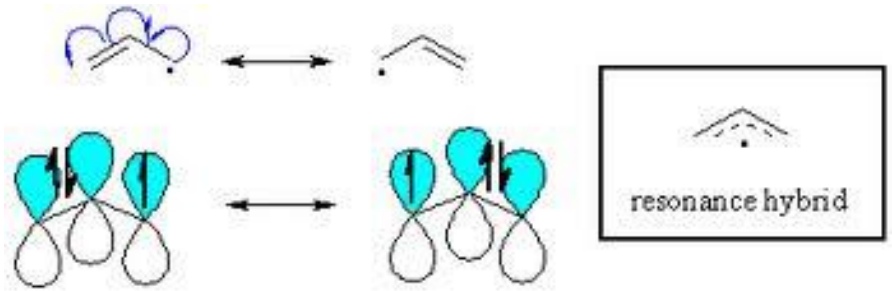


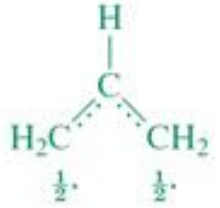
NBS = *N*-bromsukcinimid





Allylové substituce - struktury allylových radikálů, aniontů a kationtů

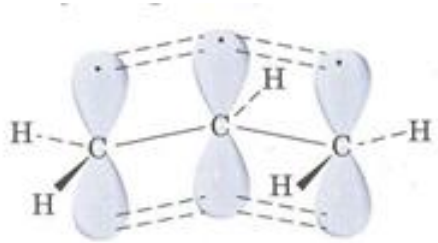


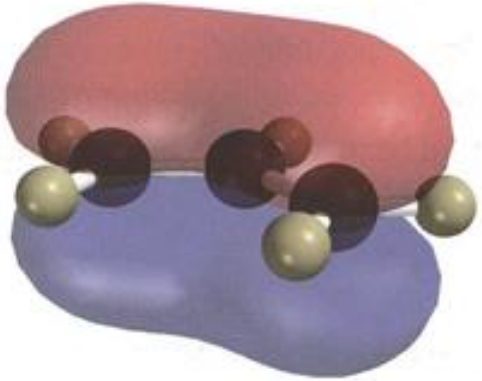


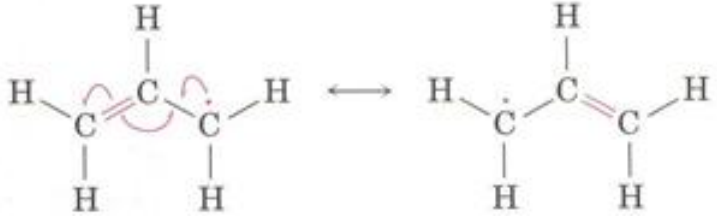
Cation

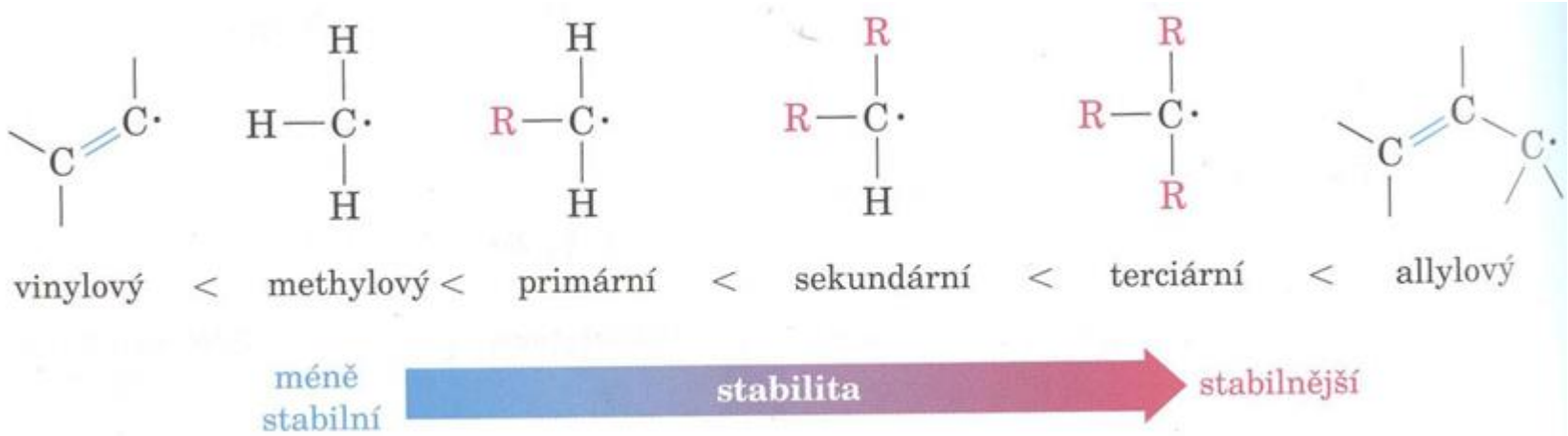
Radical

Anion



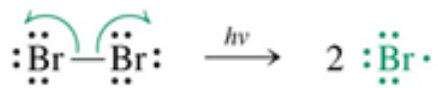


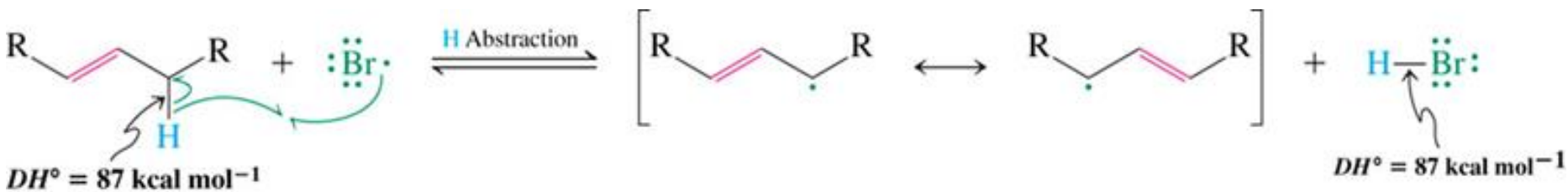




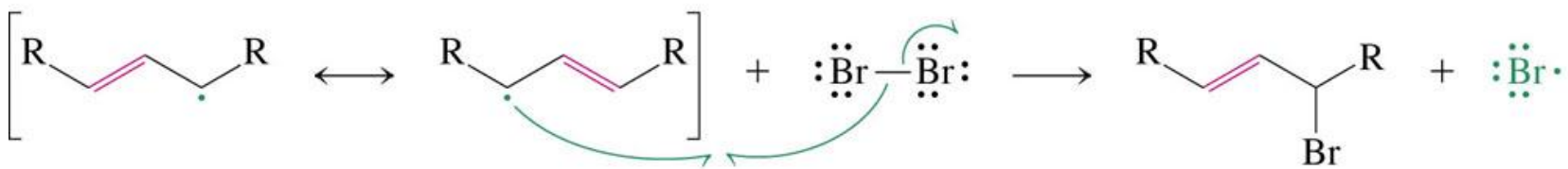
Mechanism of Allylic Bromination

Initiation step

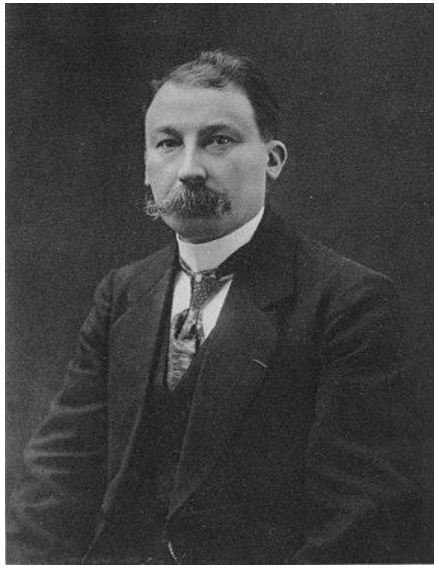




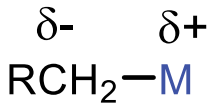
Allylic Radical

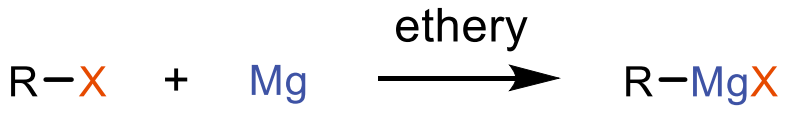


Reakce alkylhalogenidů s kovy



Victor Grignard 1871
(wiki)



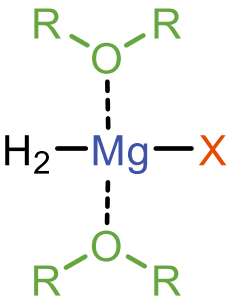


R = alkyl, aryl, alkenyl
X = Cl, Br, I

diethylether tetrahydrofuran

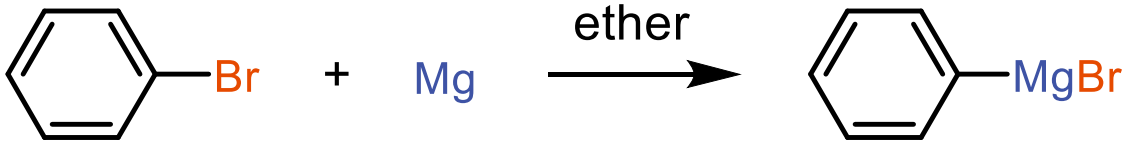
Lewisova zásada

Lewisova kyselina

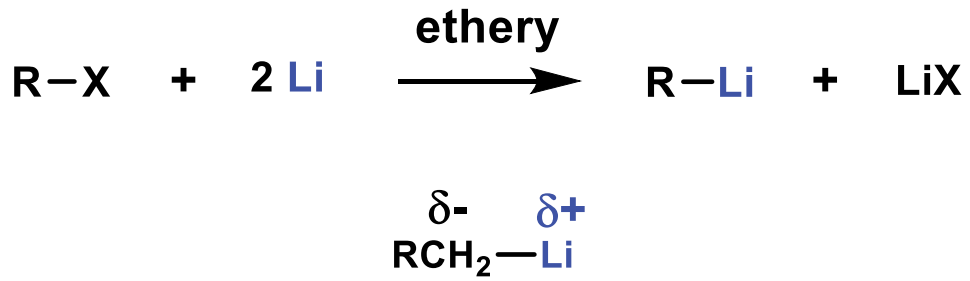


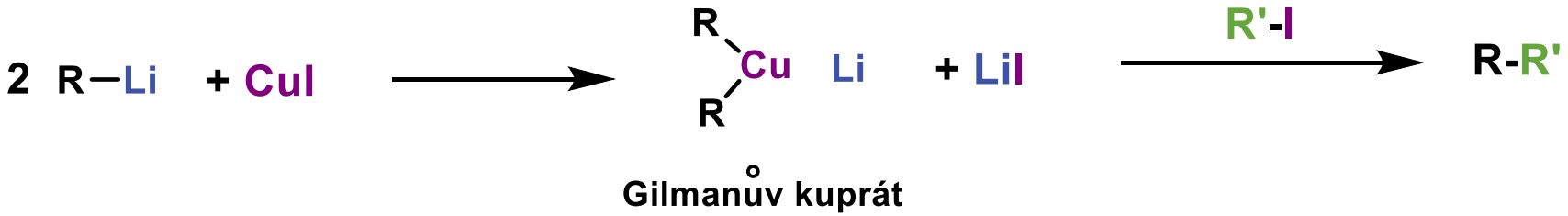
Grignardova činidla

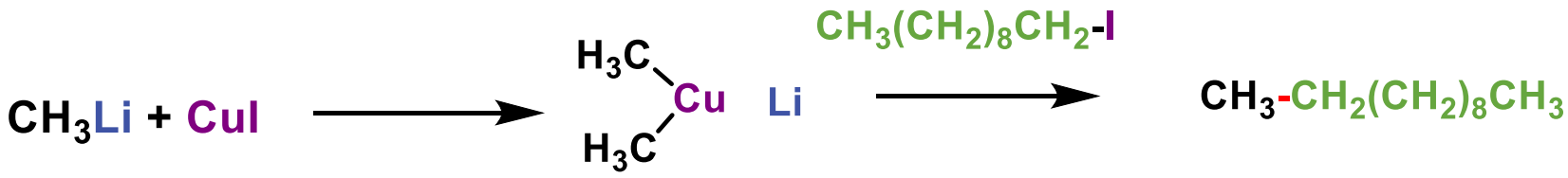
methylmagnesiumjodid

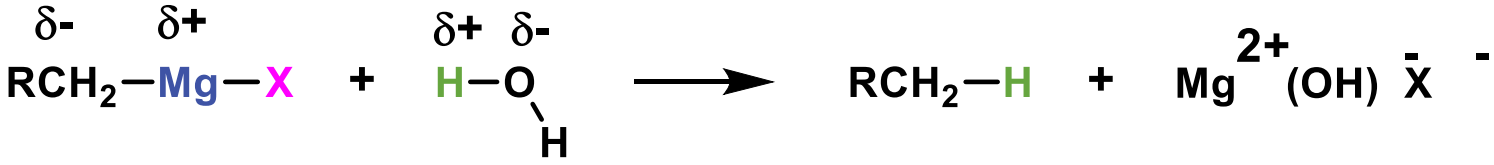


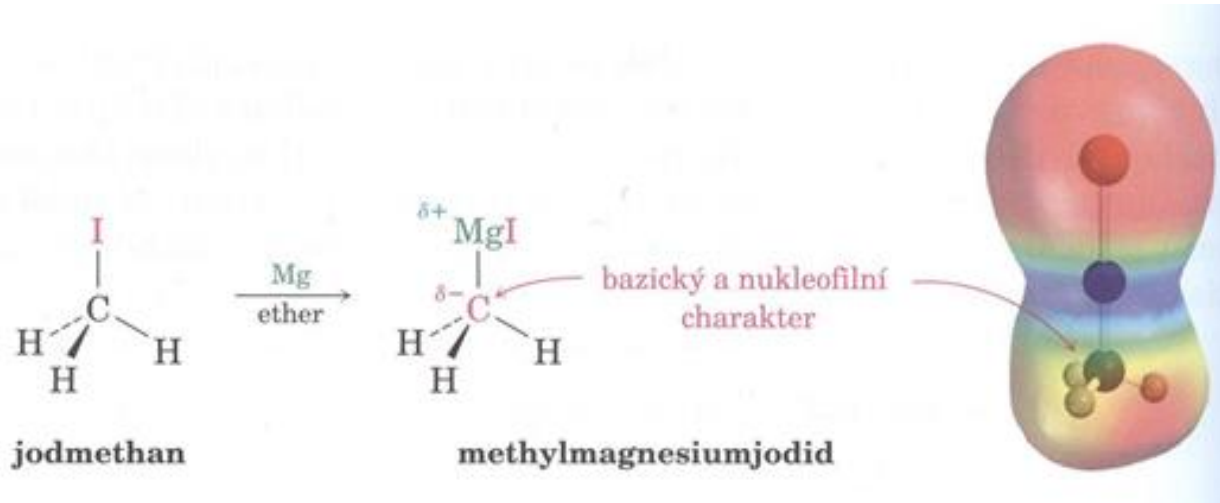
fenylmagnesiumbromid


ethery
R—X + 2 Li
R—Li + LiX
δ- δ+
RCH2—Li


2 R—Li + CuI
R
Cu
R
Li
+ LiI
R'-I
R-R'
Gilmanův kuprát


CH3Li + CuI
H3C
Cu
H3C
Li
CH3(CH2)8CH2-I
CH3-CH2(CH2)8CH3

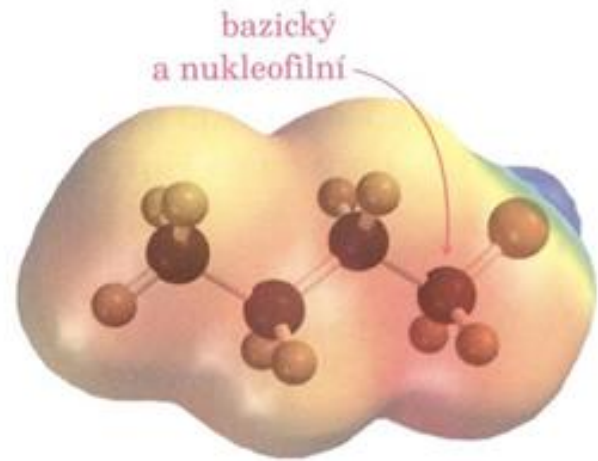

δ- δ+
RCH2—Mg—X
+
δ+ δ-
H—O
H
RCH2—H
+
Mg 2+
(OH)
X -



jodmethan **methylmagnesiumjodid**

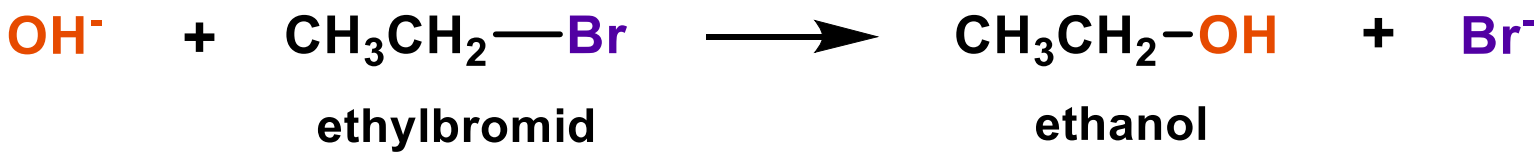
$$CH_3CH_2CH_2CH_2Br \xrightarrow[\text{pentan}]{2\ Li} CH_3CH_2CH_2CH_2Li + LiBr$$

1-brombutan **butyllithium**



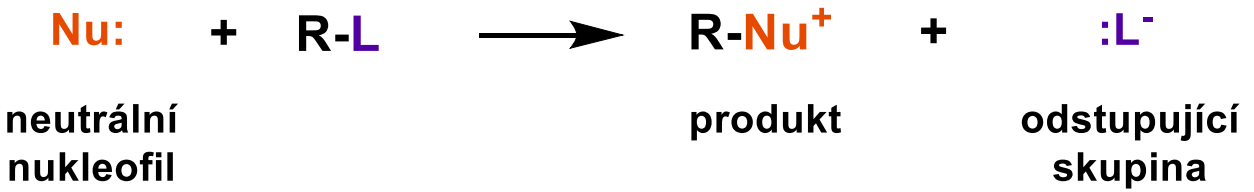
Nukleofilní substituce

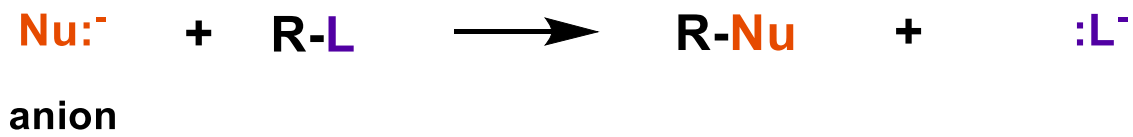
Charakteristických reakcí alkylhalogenidů jsou nukleofilní substituční reakce.



Definice nukleofilu:

nukleofil je <u>částice</u> (činidlo), které <u>poskytuje elektronový pár</u> na tvorbu nové vazby.





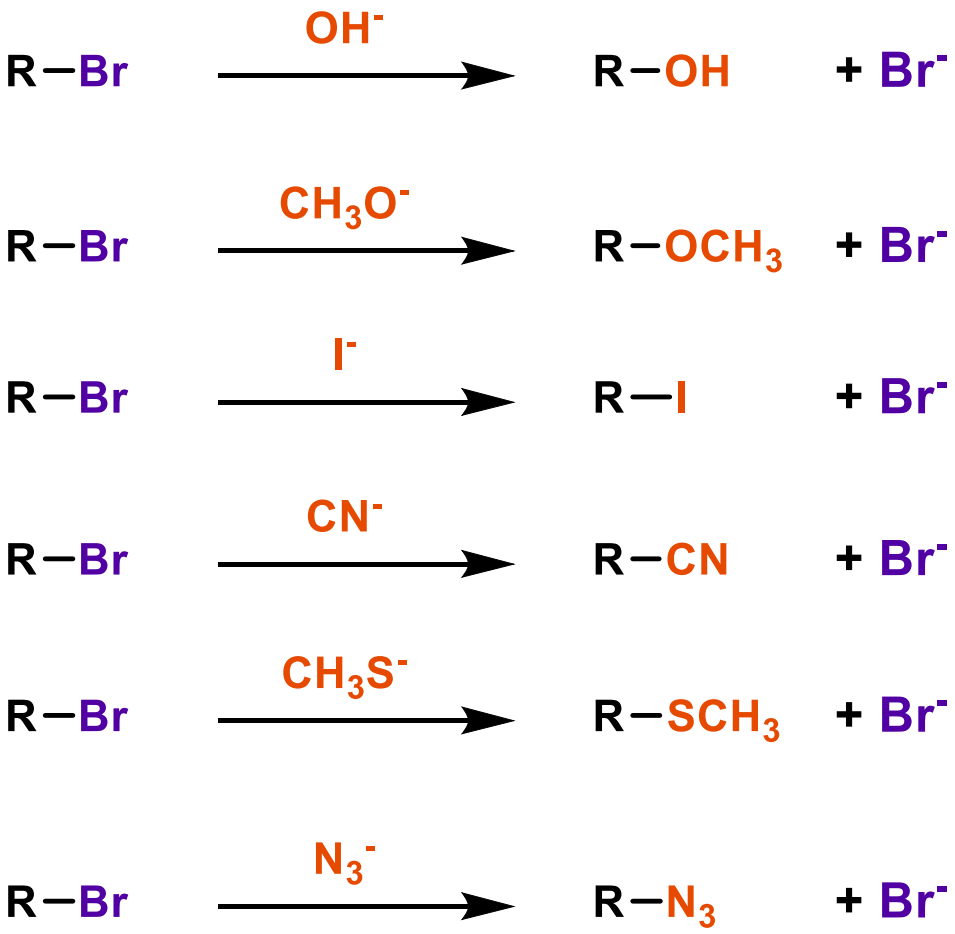
Principiálně výše uvedené vratné (reversibilní), neboť odstupující skupina je také nukleofilem nesoucí nesdílený elektronový pár. Nicméně existuje řada způsobů a jak *posunout rovnováhu žádaným směrem*:

a) Nu: je silnějším nukleofilem než odstupujícíc skupina $:L^-$,

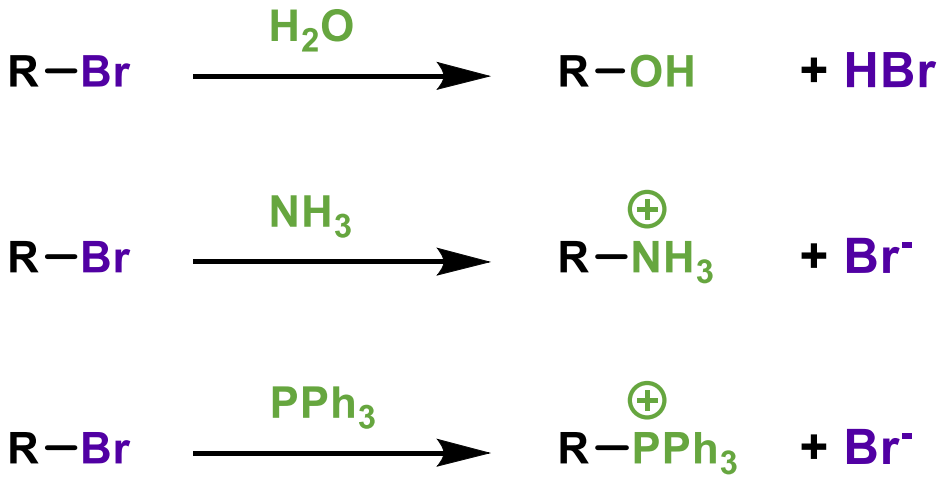
b) dále je možné posunout rovnováhu použitím nadbytku jednoho činidla, nebo

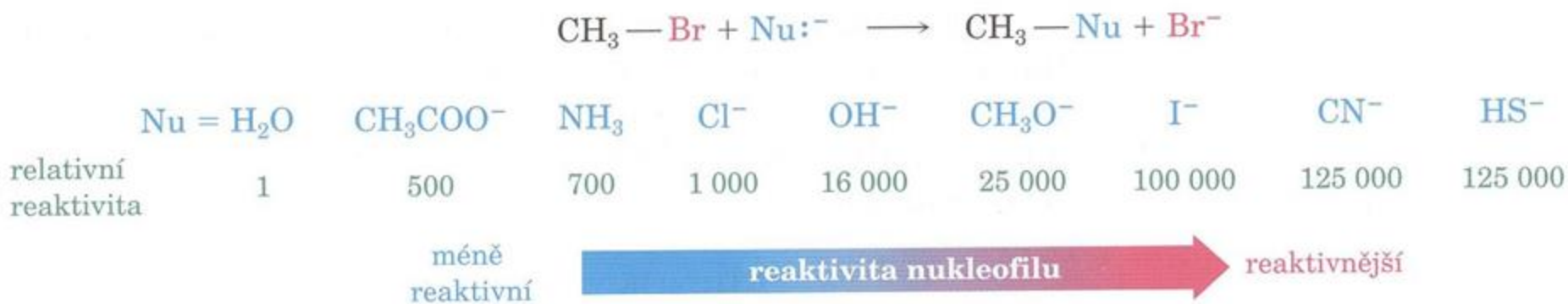
c) odstraňovat jeden z produktů z reakční směsi.

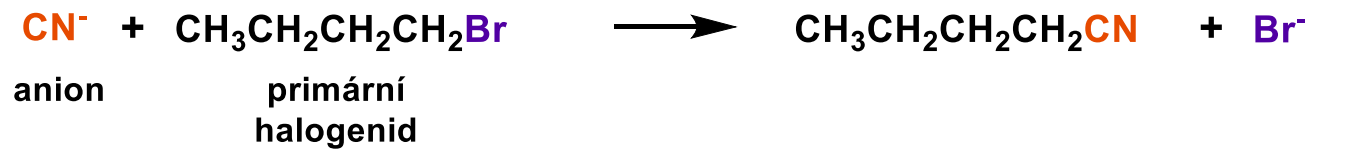
Aniontový nukleofil

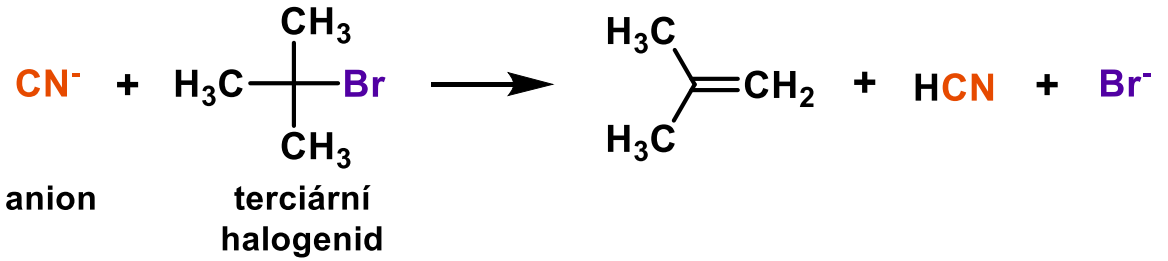


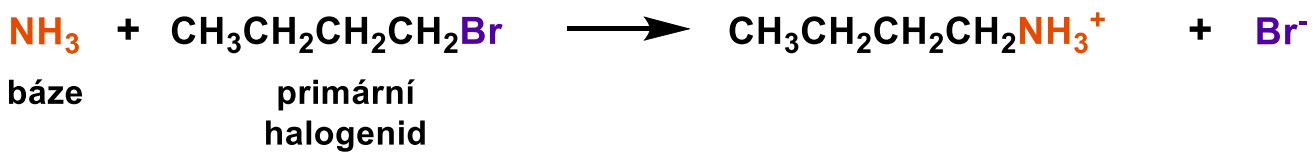
Neutrální nukleofil

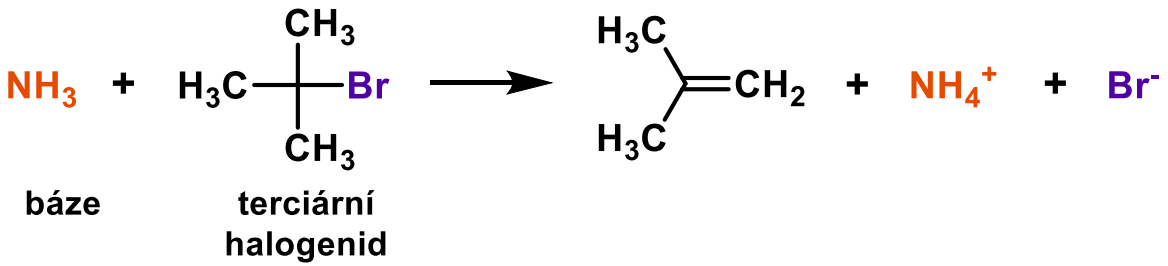


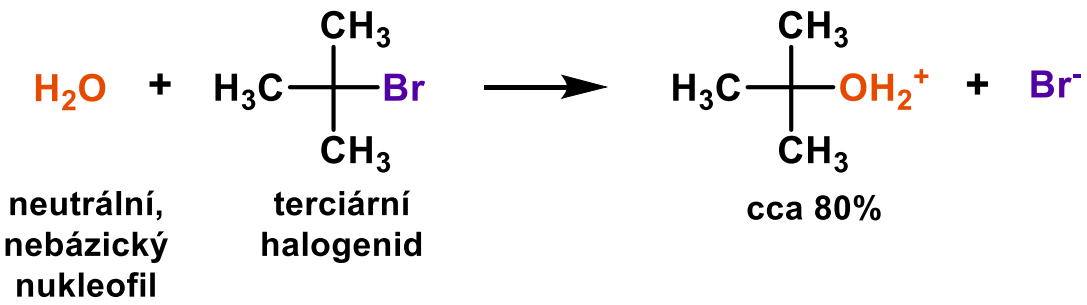

CH3—Br + Nu:⁻ ⟶ CH3—Nu + Br⁻
Nu = H2O
CH3COO⁻
NH3
Cl⁻
OH⁻
CH3O⁻
I⁻
CN⁻
HS⁻
relativní reaktivita
1
500
700
1 000
16 000
25 000
100 000
125 000
125 000
méně reaktivní
reaktivita nukleofilu
reaktivnější


CN- + CH3CH2CH2CH2Br → CH3CH2CH2CH2CN + Br-
anion
primární halogenid


CN- + H3C CH3 Br CH3 → H3C CH2 H3C + HCN + Br-
anion
terciární halogenid

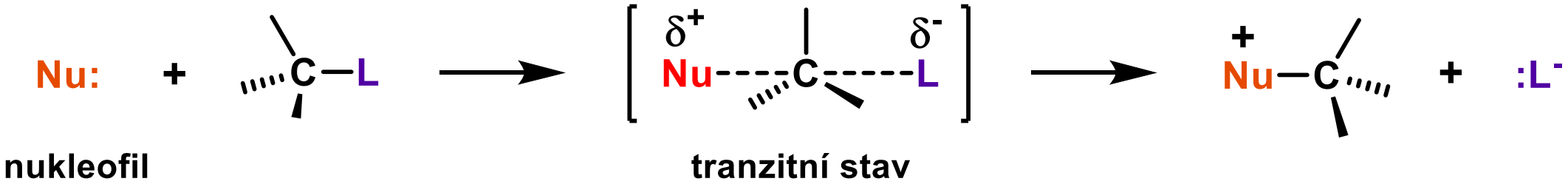

NH3 + CH3CH2CH2CH2Br → CH3CH2CH2CH2NH3+ + Br-
báze
primární halogenid


NH3 + H3C CH3 Br CH3 → H3C CH2 H3C + NH4+ + Br-
báze
terciární halogenid


H2O + H3C CH3 Br CH3 → H3C CH3 OH2+ CH3 + Br-
neutrální, nebázický nukleofil
terciární halogenid
cca 80%

Mechanismus nukleofilní substituce

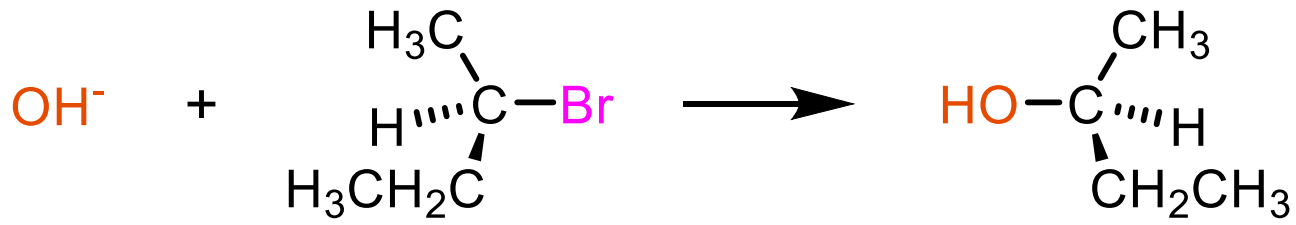
S_N2 mechanismus



S_N2 mechanismus má několik charakteristických průvodních jevů:

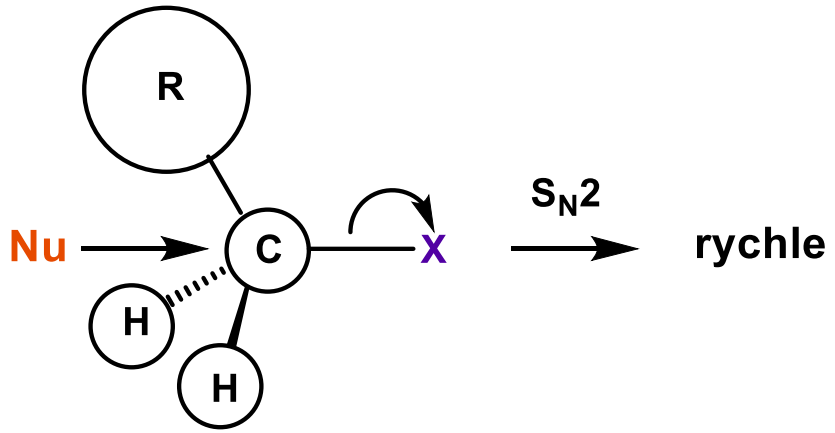
1. **Jelikož se reakce účastní nukleofil a substrát závisí reakční rychlost na koncentraci obou reaktantů.**

S_N2 substituce probíhá s inverzí konfigurace.



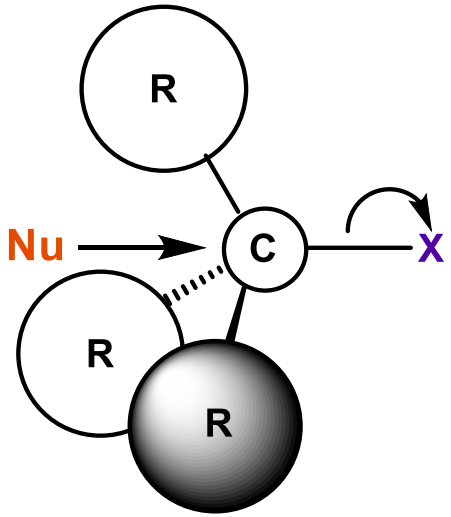
(*R*)-2-brombutan (*S*)-2-butanol

Nukleofilní substituce probíhá nejrychleji pokud je alkylová skupina substrátu methyl nebo primární alkyl a nejpomaleji v případě terciárních alkylů.



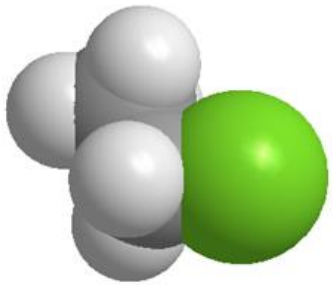
S_N2 → rychle

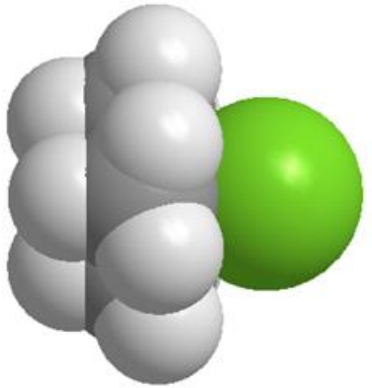
primární alkylhalogenid (odvrácená strana není bráněná)

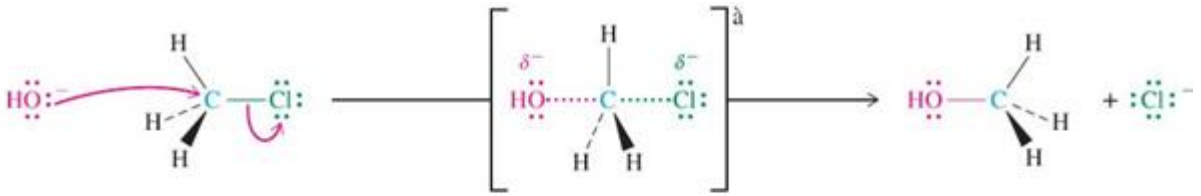


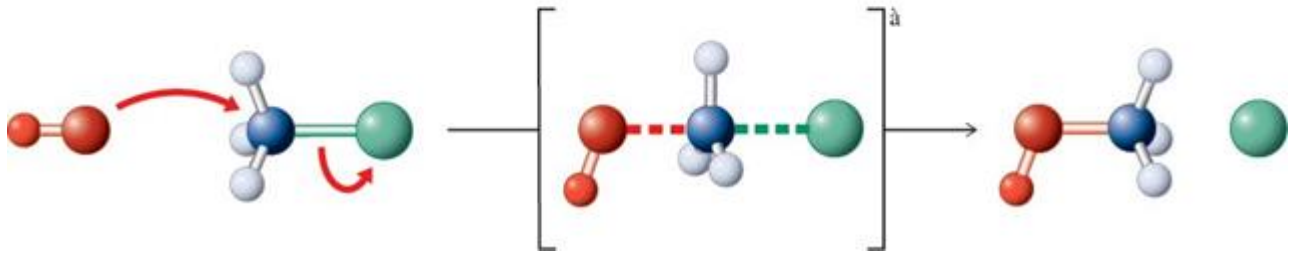
S_N2 → pomalu

terciární alkylhalogenid (odvrácená strana je bráněná)

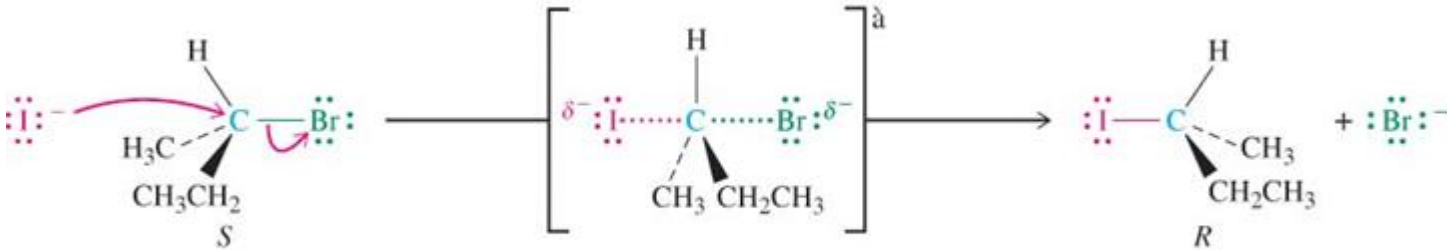








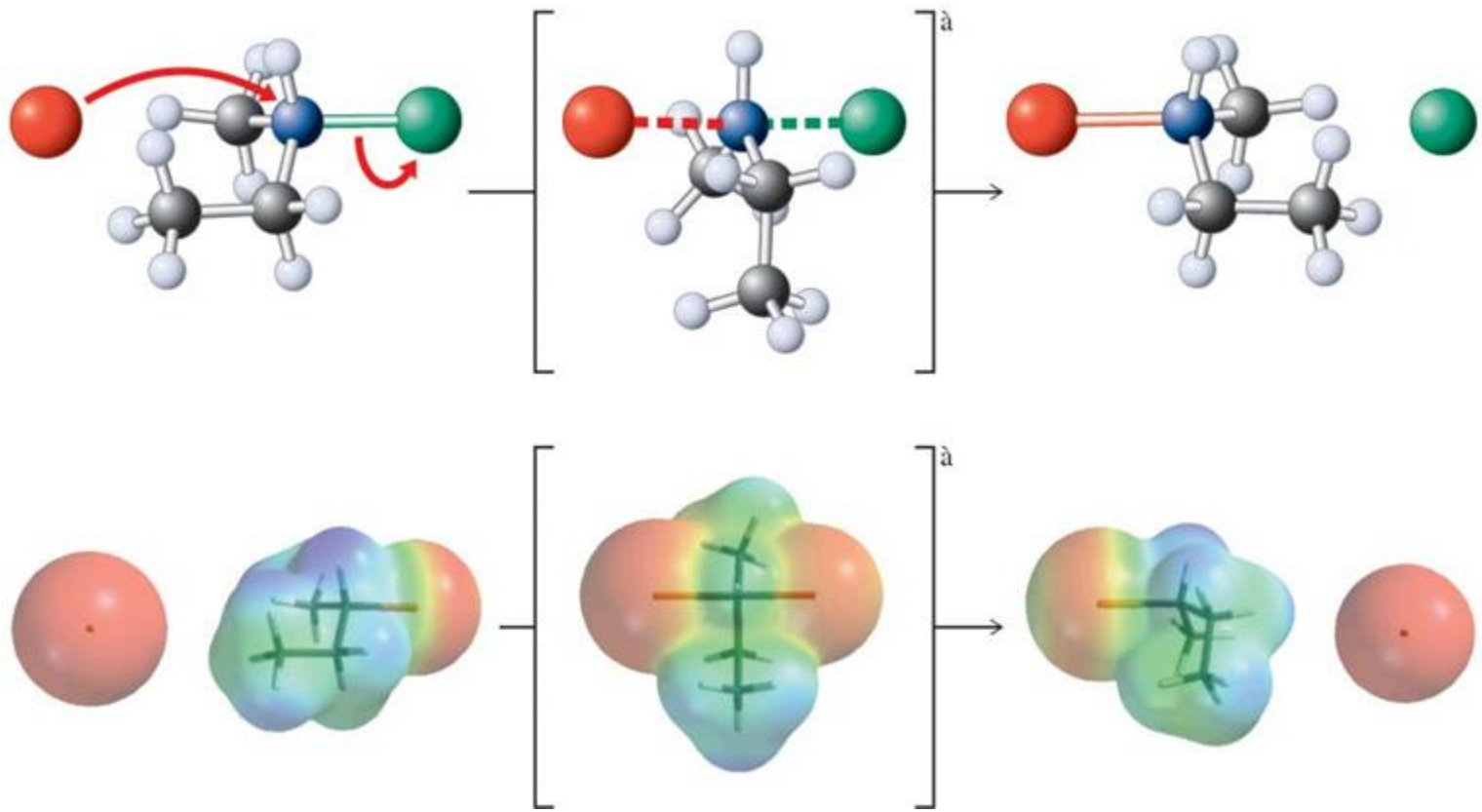
Stereochemistry of the Backside Displacement Mechanism for S_N2 Reactions

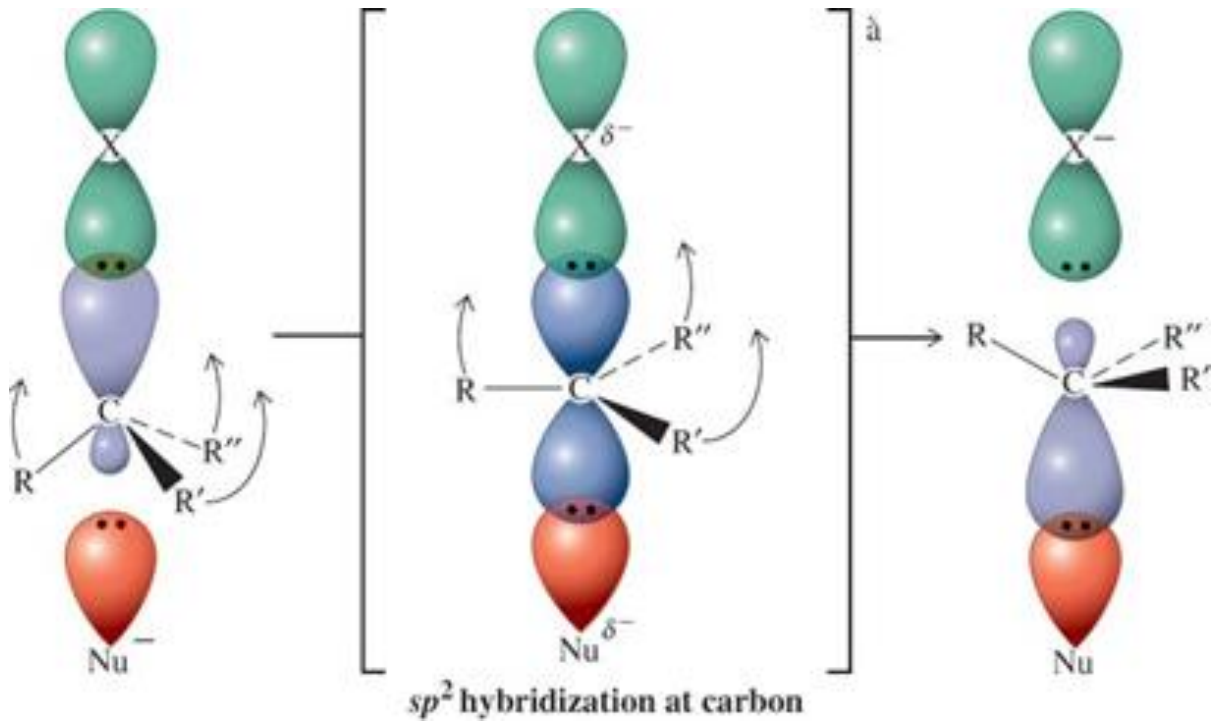


(Chiral and optically active)

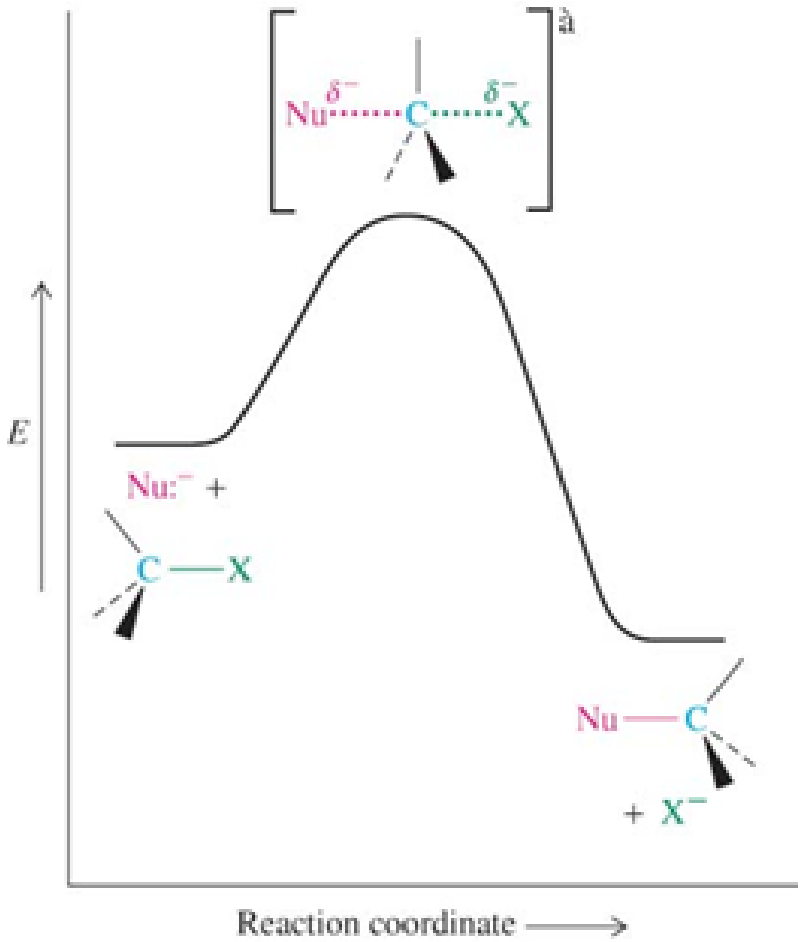
Backside displacement

(Chiral and optically active; configuration inverted)

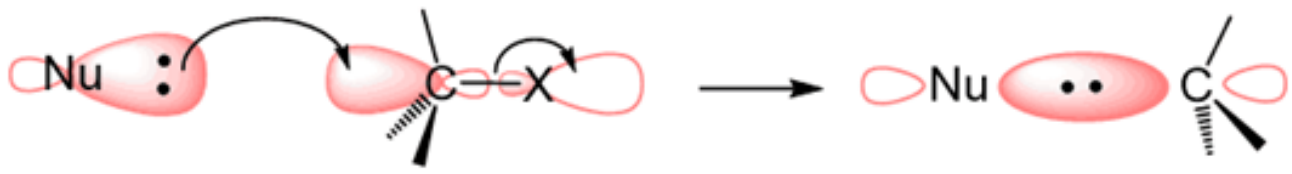

à
à



sp^2 hybridization at carbon



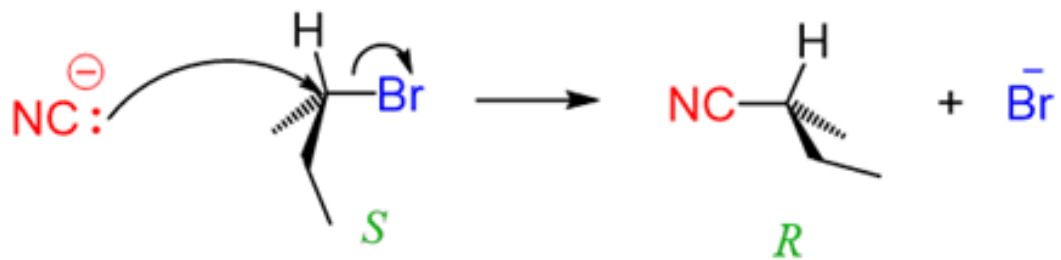
The HOMO-LUMO interaction in the S_N2 mechanism



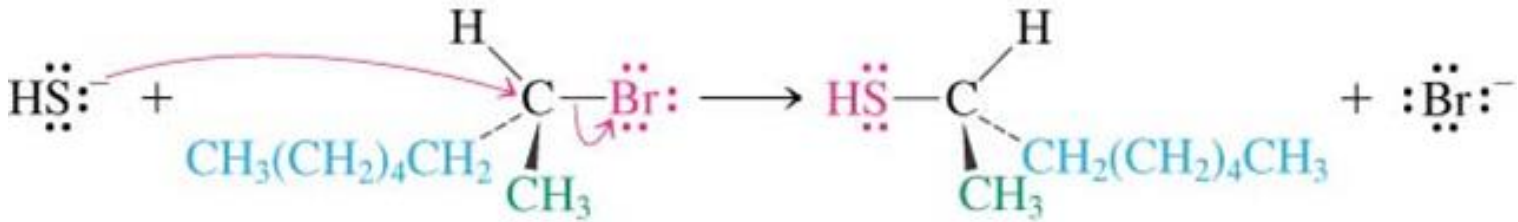
HOMO of nucleophile

LUMO of electrophile - σ* antibonding

new σ bond



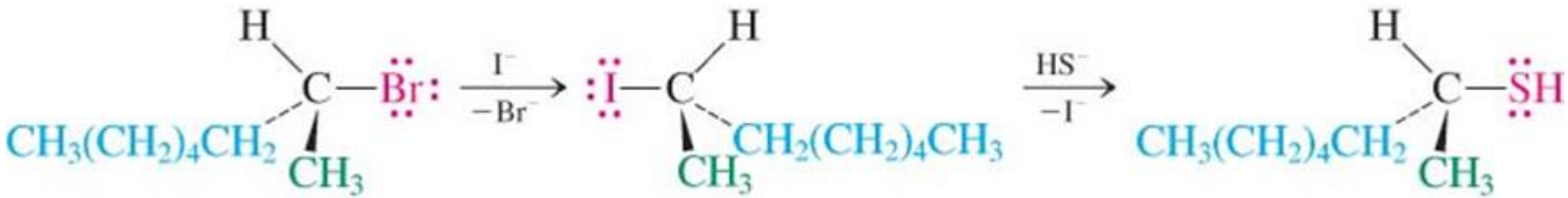
Inversion of Configuration of an Optically Pure Compound by S_N2 Reaction



(*R*)-2-Bromooctane
([α] = −34.6)

(*S*)-2-Octanethiol
([α] = +36.4)

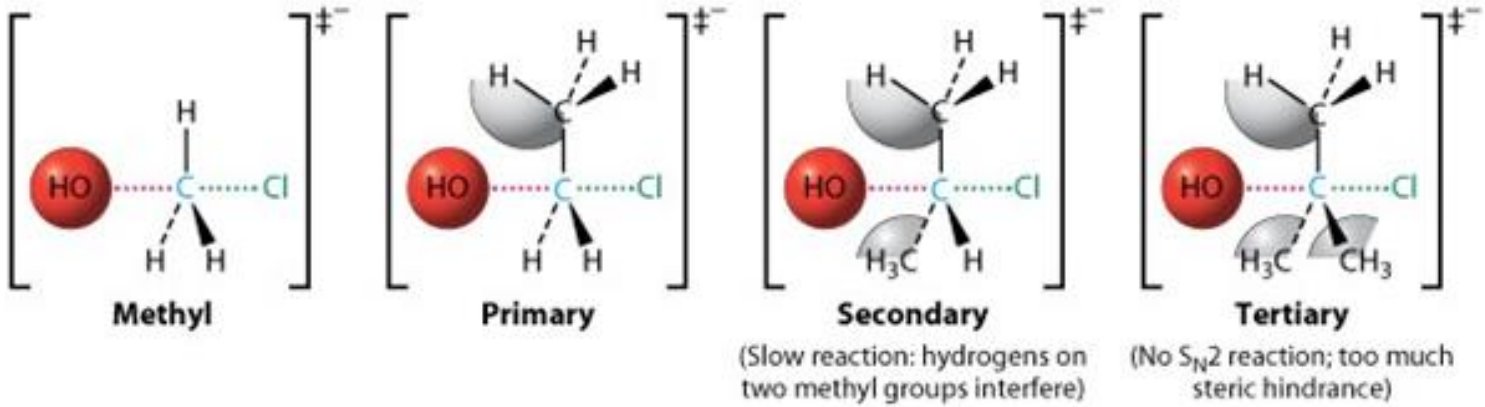
Using Double Inversion to Give Net Retention of Configuration



(*R*)-2-Bromooctane
([α] = −34.6)

(*S*)-2-Iodooctane
([α] = +46.3)

(*R*)-2-Octanethiol
([α] = −36.4)



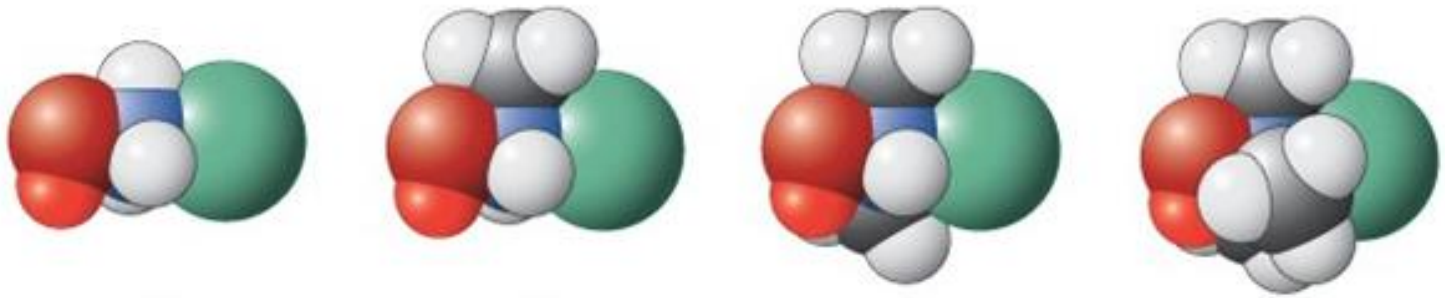
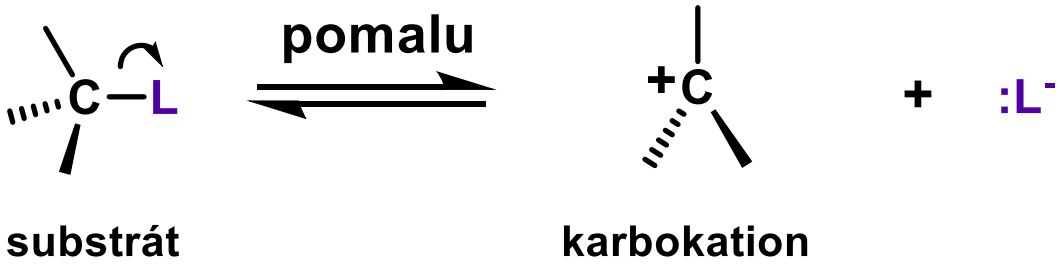


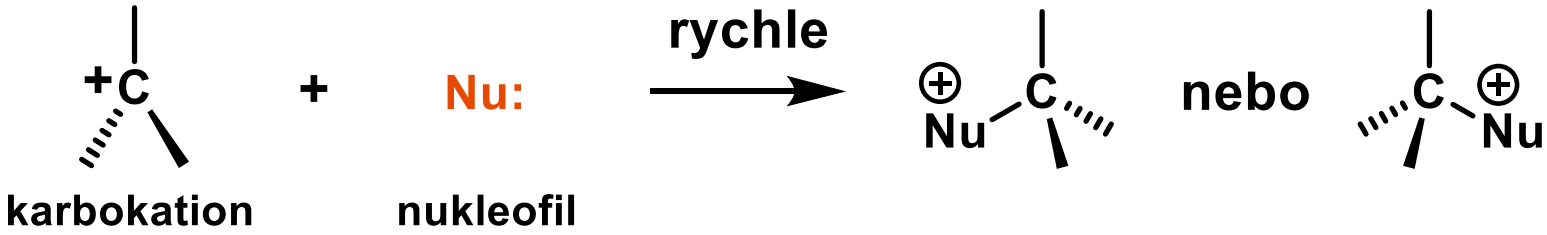
TABLE 6-8

Relative Rates of S_N2 Reaction of Branched Bromoalkanes with Iodide

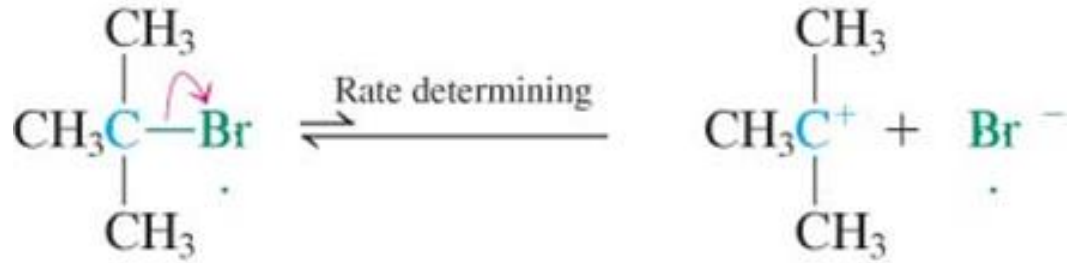
Bromoalkane	Rate
CH_3Br	145
CH_3CH_2Br	1
CH_3CHBr (CH3 branch)	0.0078
CH_3CBr (two CH3 branches)	Negligible

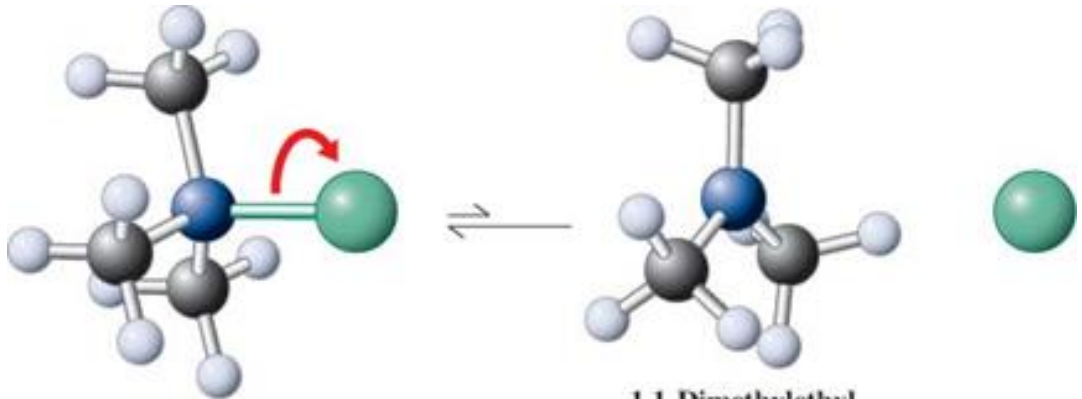
S_N1 mechanismus



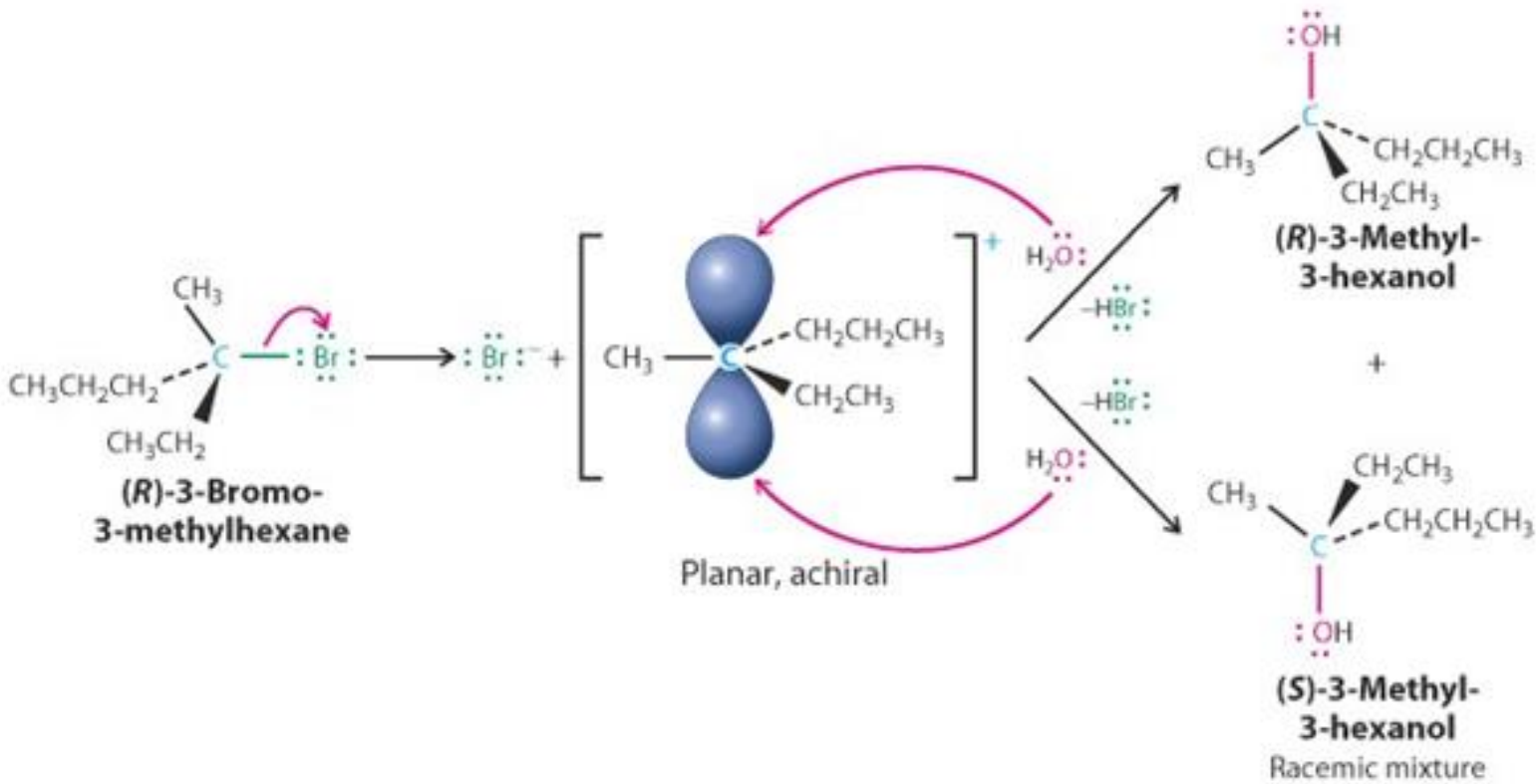


Dissociation of Halide to Form a Carbocation





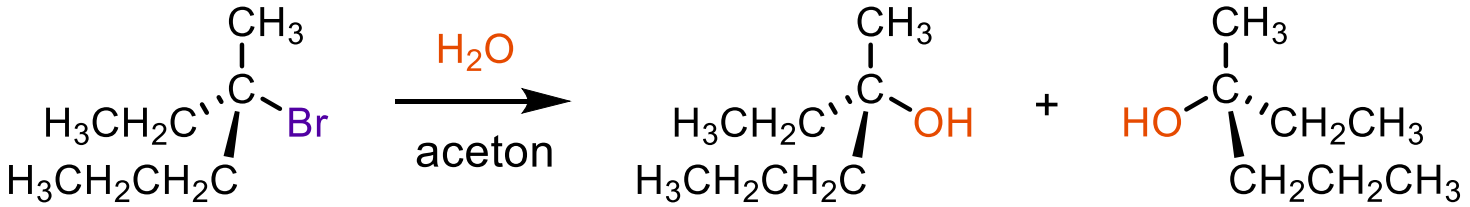
1,1-Dimethylethyl cation
(*tert*-Butyl cation)

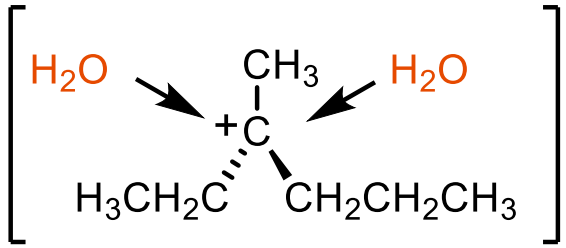

(R)-3-Bromo-
3-methylhexane
Planar, achiral
(R)-3-Methyl-
3-hexanol
+
(S)-3-Methyl-
3-hexanol
Racemic mixture

Stejně jako S_N2 mechanismus má i S_N1 mechanismus několik charakteristických průvodních jevů:

1. **Rychlost reakce nezávisí na koncentraci nukleofilu.**

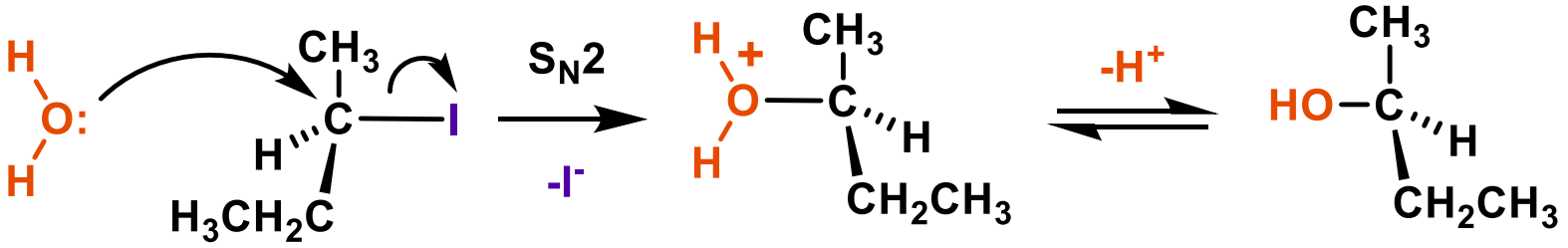
2. **Jestliže na atomu uhlíku nesoucí odstupující skupinu je centrum chirality, S_N1 substituce probíhá se ztrátou optické aktivity, tj. racemizací.**



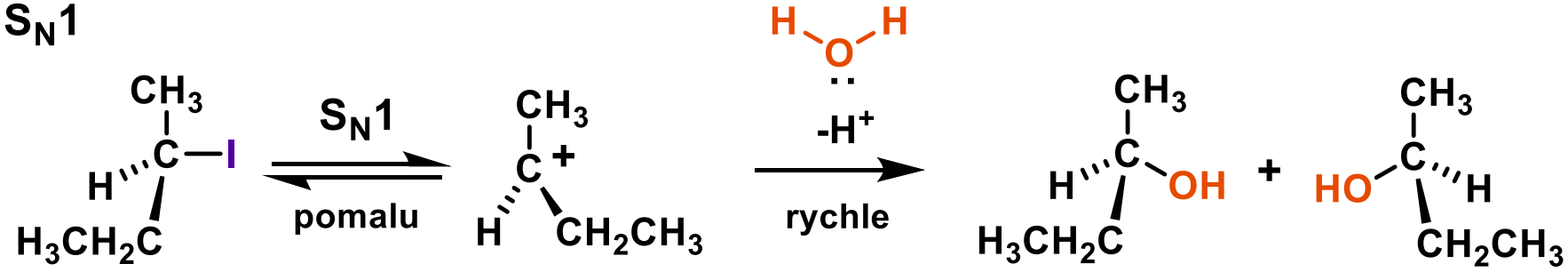


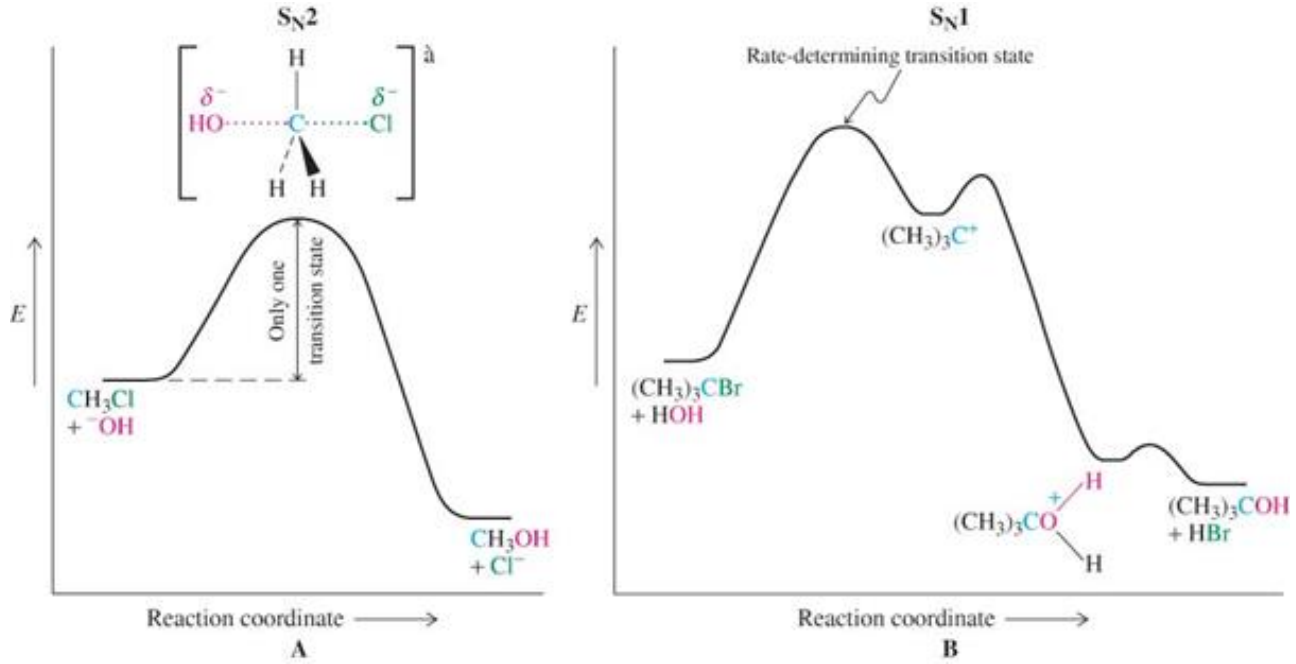
3. **Reakce je nejrychlejší v případě, že alkylová skupina substrátu je terciární a nejpomalejší, když je primární.**

S_N2

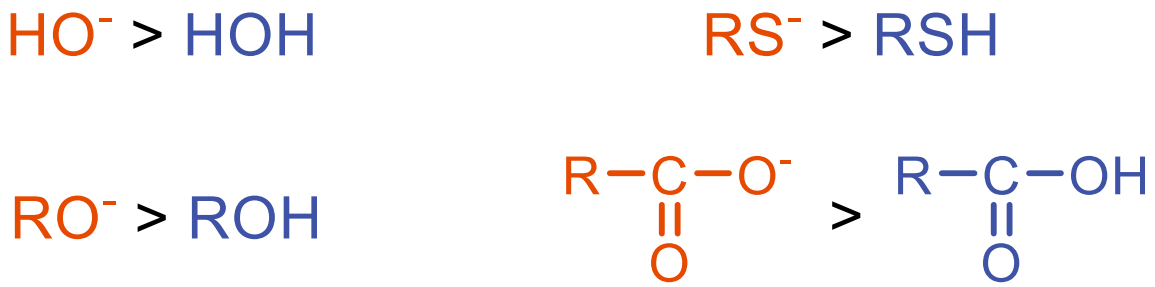

H
O:
H
CH3
C
I
H
H3CH2C
SN2
-I-
H
+
O
H
CH3
C
H
CH2CH3
-H+
CH3
HO
C
H
CH2CH3

S_N1


CH3
C
I
H
H3CH2C
SN1
pomalu
CH3
C
+
H
CH2CH3
H
O
H
-H+
rychle
CH3
C
OH
H
H3CH2C
+
CH3
C
HO
H
CH2CH3


SN2
δ−
HO
H
C
δ−
Cl
H H
à
E
Only one transition state
CH3Cl
+ −OH
CH3OH
+ Cl−
Reaction coordinate
A
SN1
Rate-determining transition state
(CH3)3C+
E
(CH3)3CBr
+ HOH
(CH3)3CO
H
H
(CH3)3COH
+ HBr
Reaction coordinate
B

1. Záporně nabité ionty jsou více nukleofilní, neboli lepší donory elektronů než odpovídající neutrální molekuly.



2. Nukleofilita prvků stoupá s klesajícím místem ve skupině periodické tabulky.

3. Nukleofilita prvků ve stejné řadě periodické tabulky klesá se stoupající elektronegativitou (tj. drží pevněji svoje elektrony)

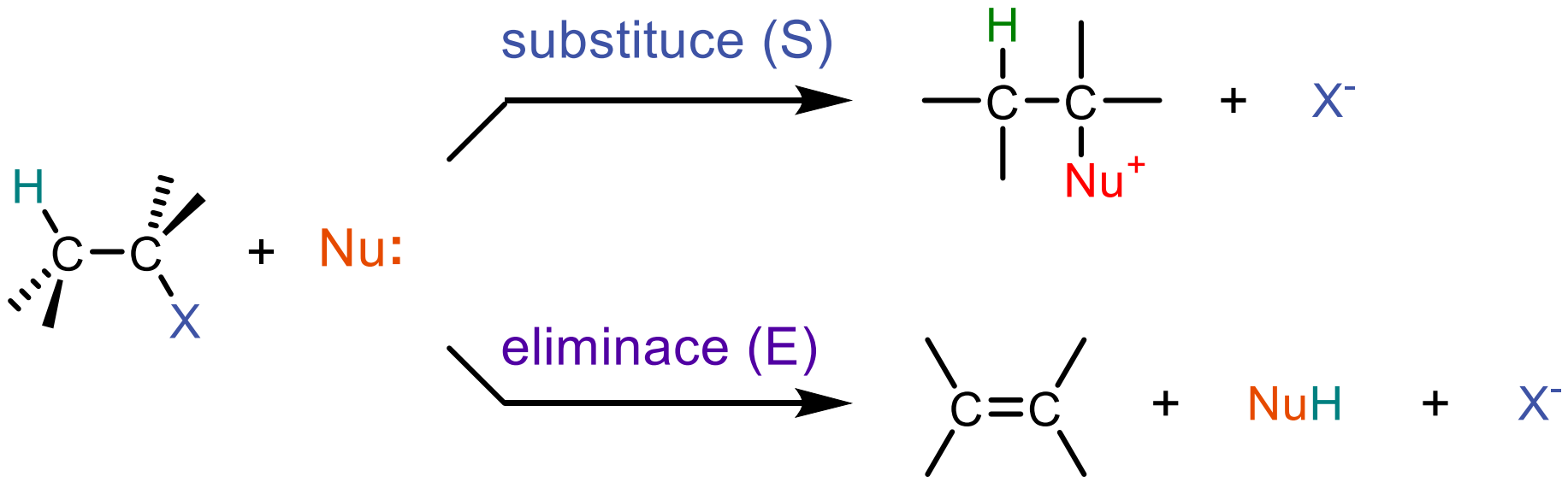
Srovnání S_N1 a S_N2 mechanismus

	S_N2 substituce	S_N1 substituce
Struktura halogenidu		
primární	běžná	vzácná*
sekundární	občas	občas
terciární	vzácná	běžná
Stereochemie	inverze	racemizace
Nukleofil	reakční rychlost závisí na koncentraci nukleofilu, mechanismus je upřednostňován pokud je nukleofil anion	reakční rychlost nezávisí na koncentraci nukleofilu, mechanismus je pravděpodobnější s neutrálními nukleofily
Rozpouštědlo	reakční rychlost je málo ovlivněná polaritou rozpouštědla (protická zpomalují)	Vzhledem k tomu, že meziprodukty jsou ionty, reakční rychlost závisí na polaritě rozpouštědla (polární protická urychlují)

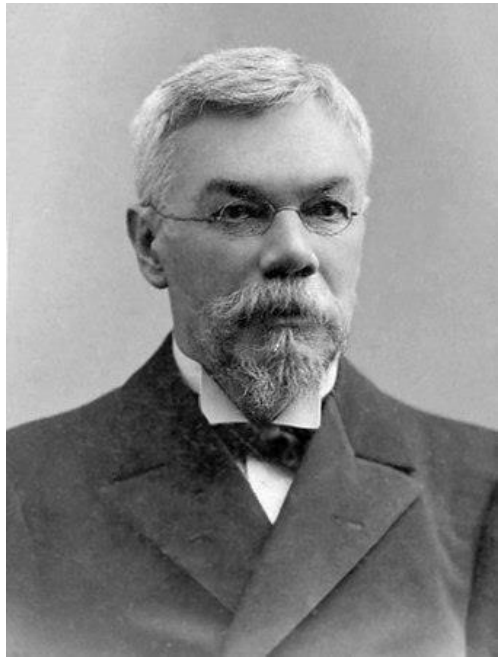
* allylové a benzylové substráty tvoří výjimku

Eliminační reakce. E2 a E1 mechanismus

Pokud molekula alkylhalogenidu, ve které je v těsném sousedství C-X skupiny (X = halogen) atom uhlíku nesoucí atom vodíku (C-H skupina), při reakci s nukleofilem mohou nastat dvě vzájemně si konkurující reakce: substituce a eliminace

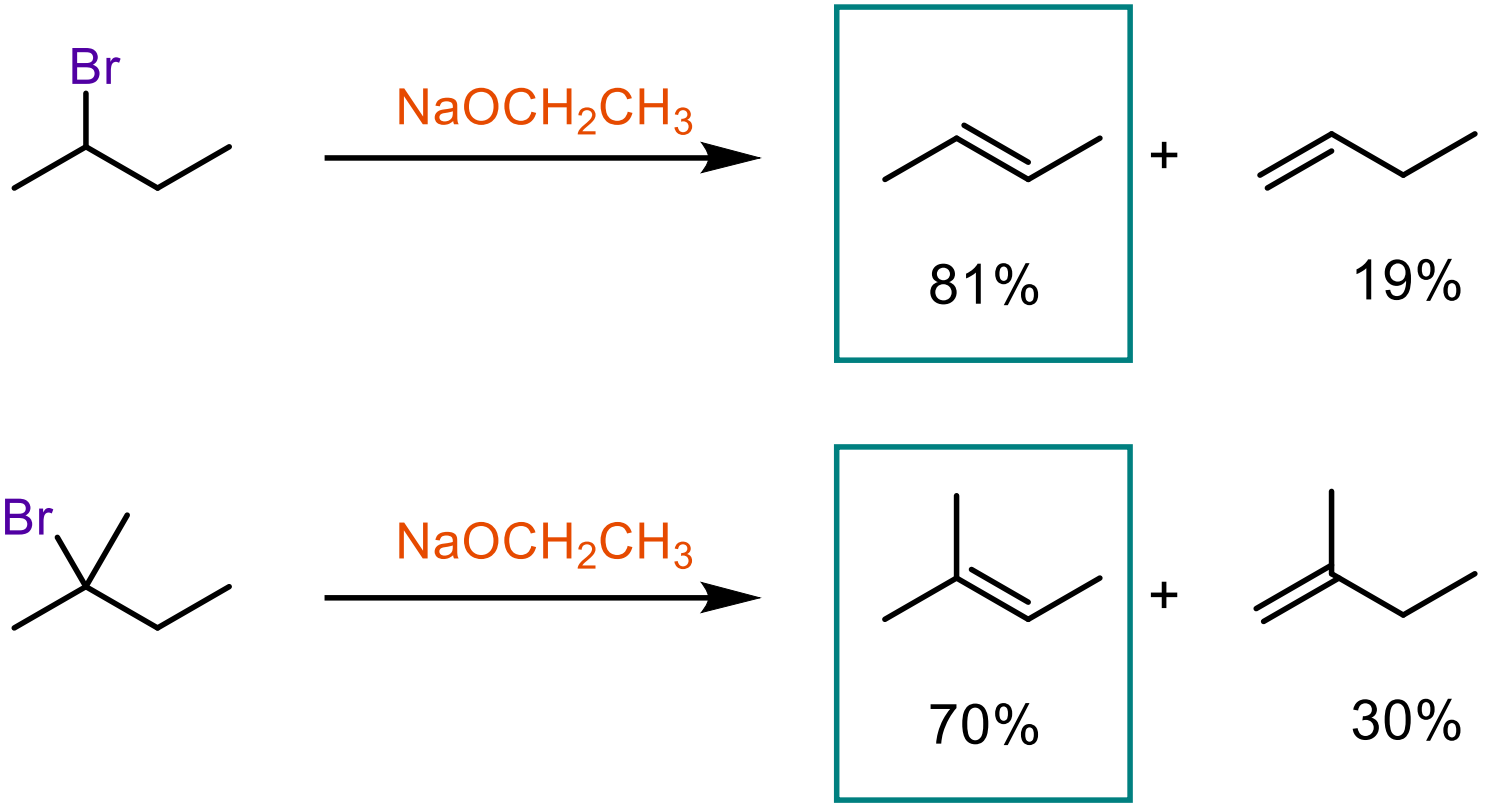


Zajcevovo pravidlo



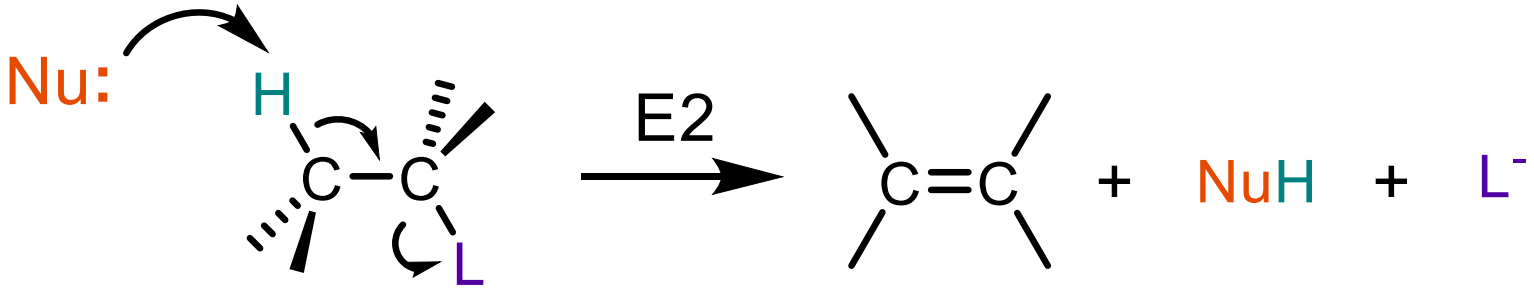
Alexandr Michajlovič Zajcev
1841
(wiki)

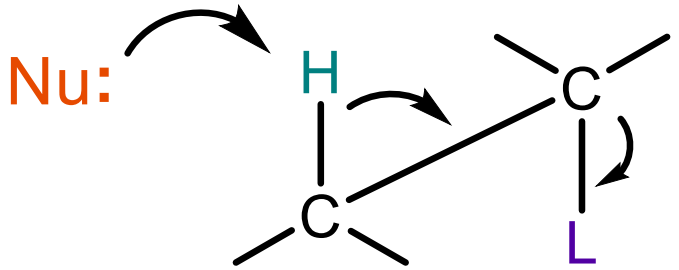
„při eliminaci jako produkt převládá **více substituovaný alken**“



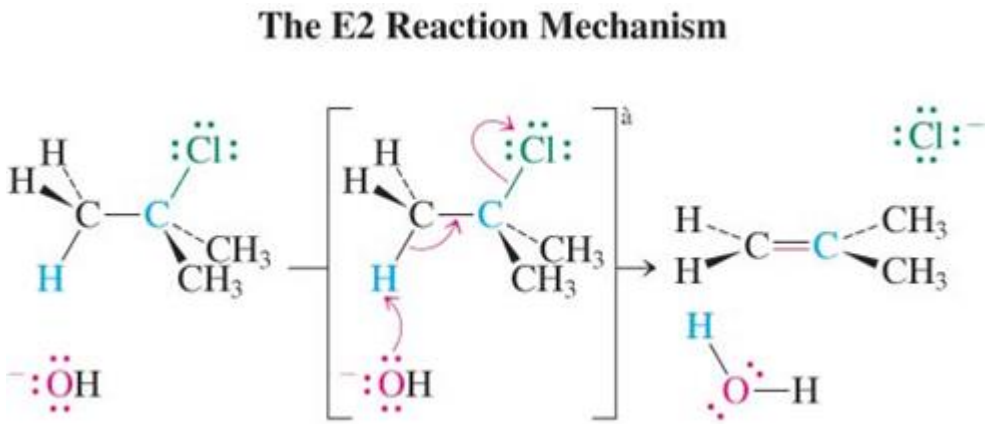
E2 mechanismus.

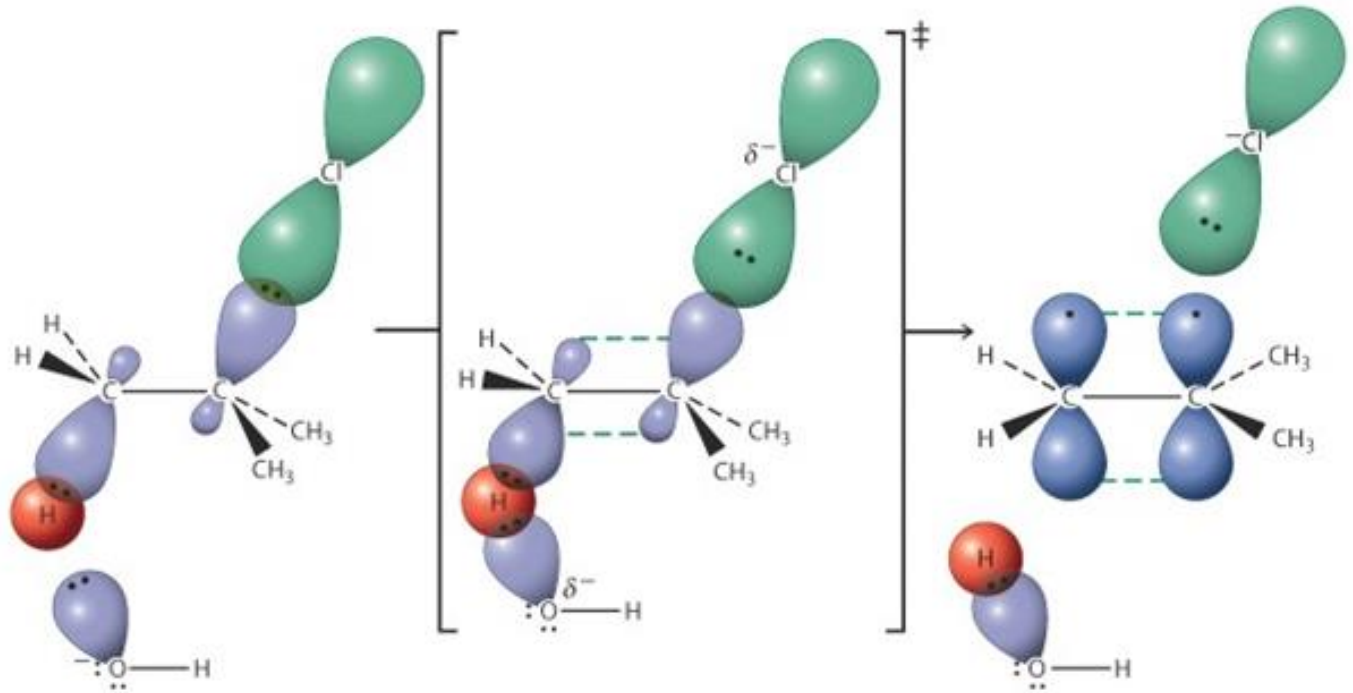
Stejně jako v případě S_N2 substituce se u E2 eliminace jedná o jednokrokový proces.

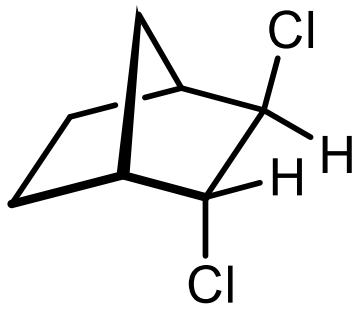




E2 reakce probíhá v jednom kroku.

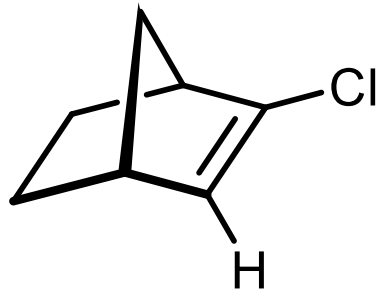


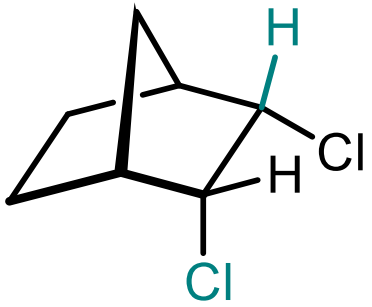




$NaOCH_3$

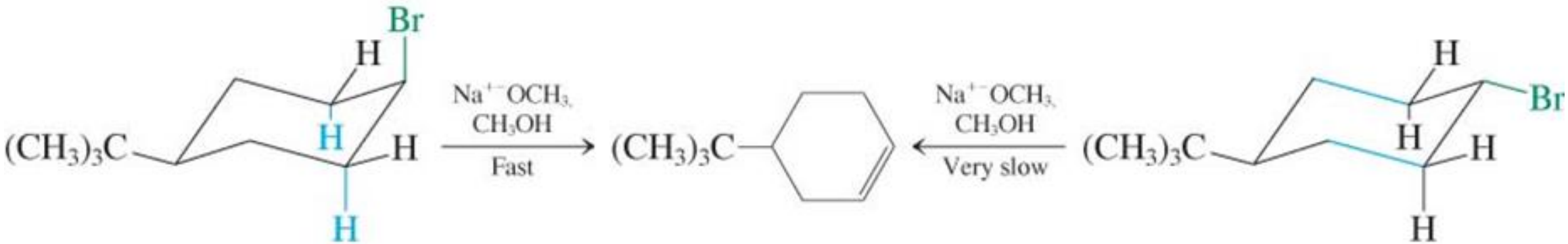
E2 pomalu



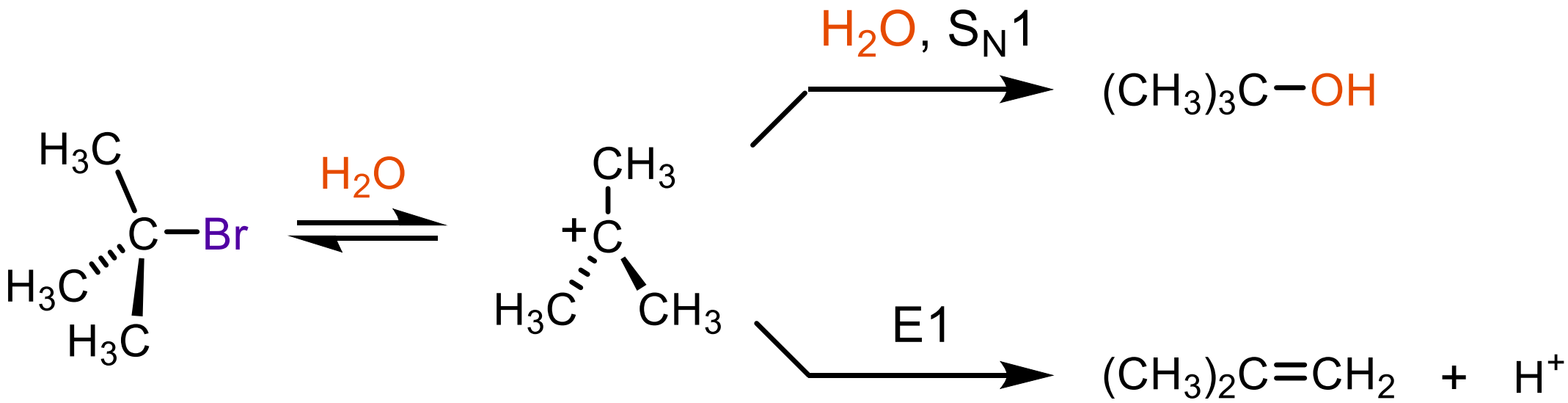


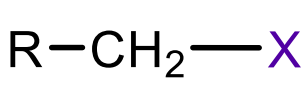
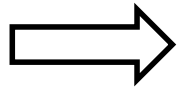
$NaOCH_3$

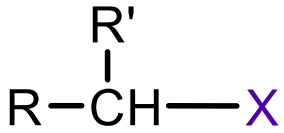
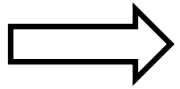
E2 rychle


Br
H
H
H
H
(CH3)3C
Na+ −OCH3
CH3OH
Fast
(CH3)3C
Na+ −OCH3
CH3OH
Very slow
(CH3)3C
H
Br
H
H
H

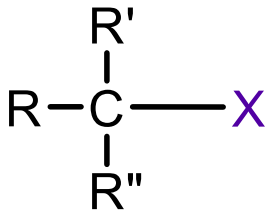
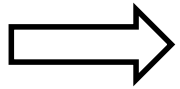
E1 mechanismus



primární   S_N2

sekundární   S_N2 s nebazickými nukleofily

E2 se silnými bázemi

terciární   obvykle **E2**

S_N1 nebo **E1** s nebazickými nukleofily