HALOGEN DERIVATIVES

S_N2

$$R-X \; + \; \overline{Nu}^{\ominus} \longrightarrow R-Nu \; + \; X^{\ominus}$$

$$v = k \, . \, [\,RX] \, . \, [Nu^{\ominus}\,] = -\frac{d[RX]}{dt} = +\frac{d[RNu]}{dt}$$

bimolecular reaction - substitution $S_N 2$

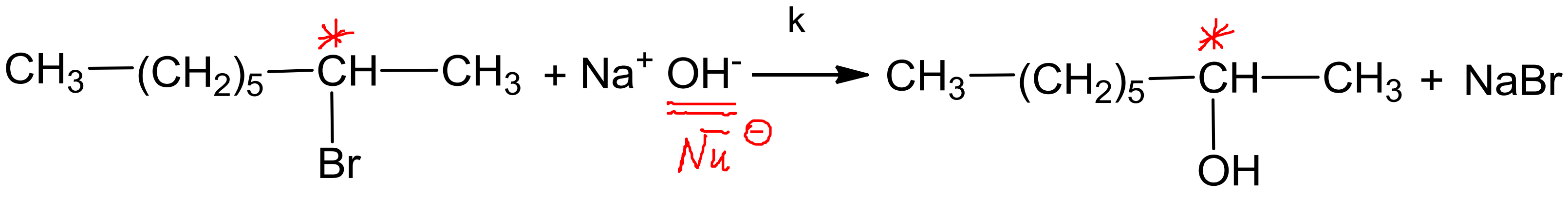
reaction is charakteristic for non-branched halogenderivatives

$$CH_3-CH_2-CH_2-Cl \; + \; CH_3-\overline{\underline{O}}|^{\ominus} \; Na^{\oplus} \longrightarrow CH_3CH_2CH_2-OCH_3 \; + \; NaCl$$

$$v = k \cdot [R-Cl] \cdot [CH_3O^{\ominus}]$$

HALOGEN DERIVATIVES

S_N2

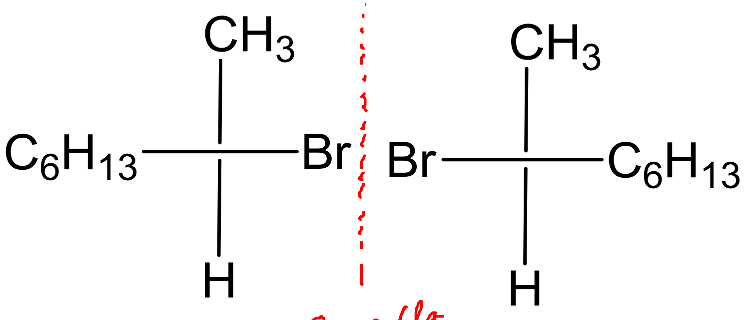


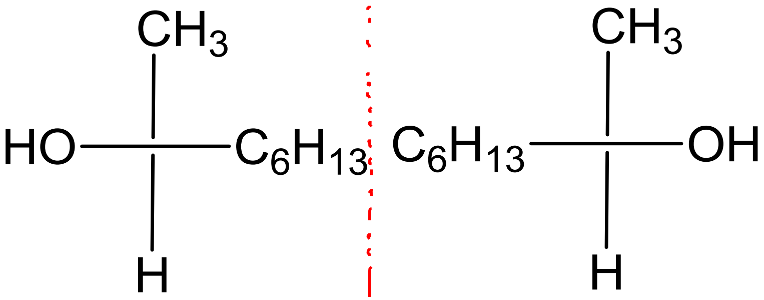
$$CH_3-(CH_2)_5-\underset{\displaystyle Br}{\overset{*}{C}H}-CH_3 + Na^+ \underset{\overline{Nu}^{\ominus}}{\underline{OH^-}} \xrightarrow{k} CH_3-(CH_2)_5-\underset{\displaystyle OH}{\overset{*}{C}H}-CH_3 + NaBr$$

2-bromoctane

octan-2-ol

$$\underline{v = k \cdot [R\text{-}Br] \cdot [HO^{\ominus}]}$$





$[\alpha]^{22}_{D} = -36^{o}$ $[\alpha]^{22}_{D} = +36^{o}$ $[\alpha]^{22}_{D} = +10{,}3^{o}$ $[\alpha]^{22}_{D} = -10{,}3^{o}$

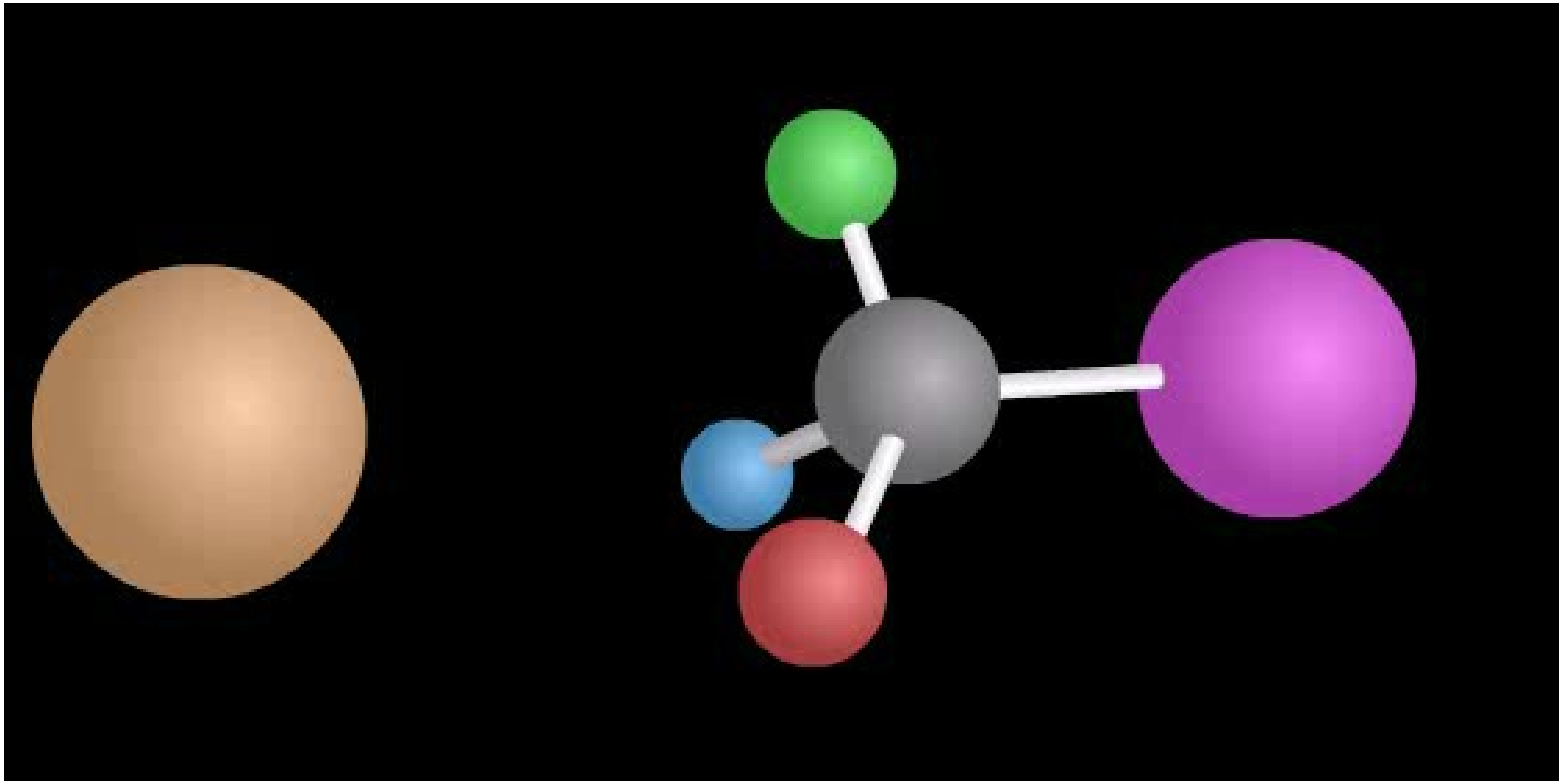
(*R*)-(-)- 2-bromoctane (*S*)-(+)- (*S*)-(+)-octan-2-ol (*R*)-(-)-

enantiomery

||(R)-2-bromoktan ⟶ (S)-oktan-2-ol

(S)- Waldenův zvrat ⟶ (R)- oktan-2-ol

Nucleophilic substitution S_N2



HALOGEN DERIVATIVES

S_N1

$$R-X + \overline{Nu}^{\ominus} \longrightarrow R-Nu + X^{\ominus}$$

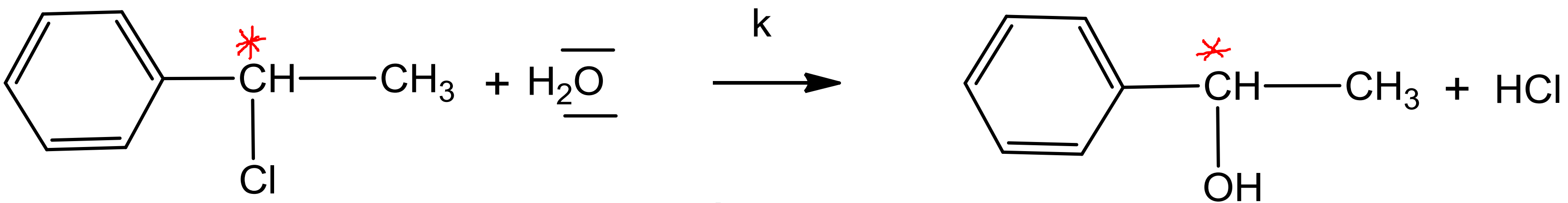
$$v = k \,.\, [\,RX\,] = -\frac{d[RX]}{dt} = +\frac{d[RNu]}{dt}$$

monomolecular reaction - substitittution S_N1

reaction is characteristic for branched halogen derivatives

HALOGEN DERIVATIVES

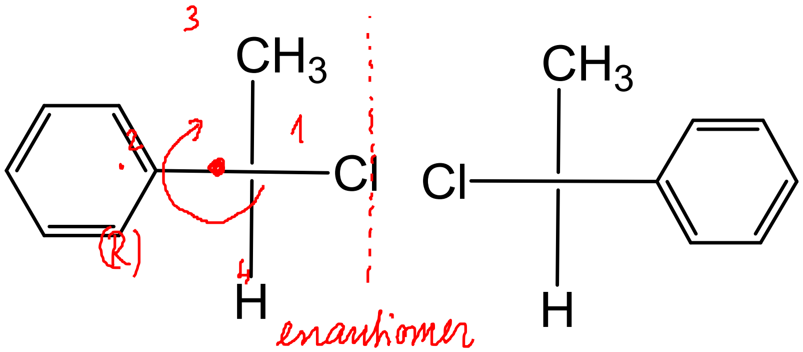
S_N1

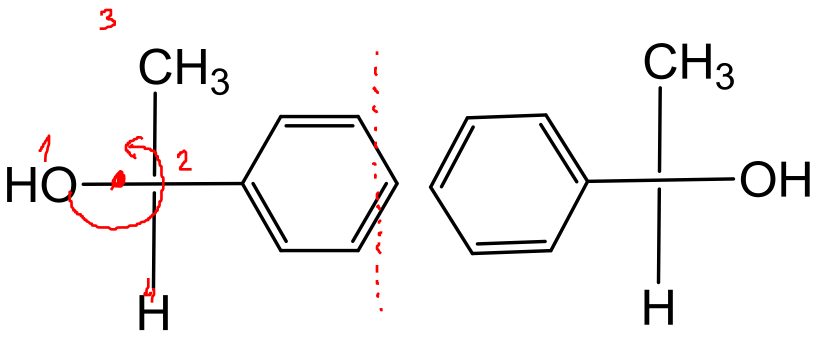


1-chloro-1-phenylethane

$v = k \cdot [R\text{-}Cl]$

1-phenylethanol





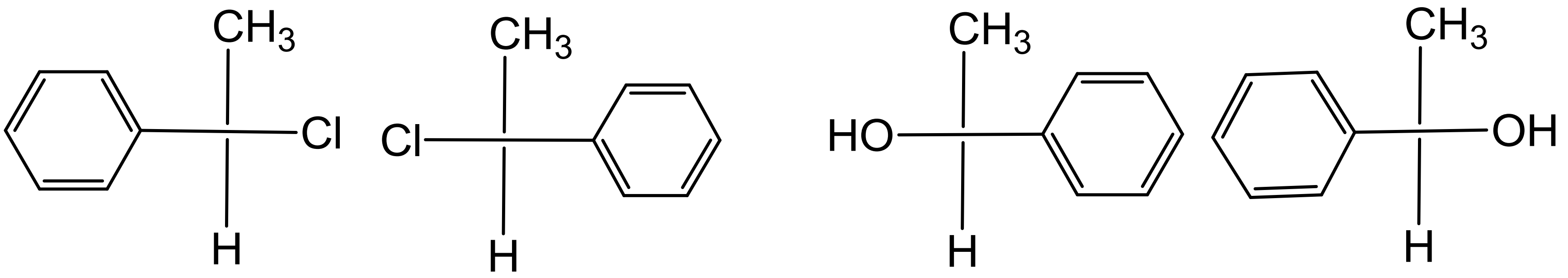
$[\alpha]^{22}_{D} = -50{,}6^{o}$ $[\alpha]^{22}_{D} = +50{,}6^{o}$ $[\alpha]^{22}_{D} = -42{,}3^{o}$ $[\alpha]^{22}_{D} = +42{,}3^{o}$

(*R*)-(-)- 1-chloro-1-phenyl ethane (*S*)-(+)-

(*S*)-(+)-1-phenylethanol (*R*)-(-)-

HALOGEN DERIVATIVES

S_N1



$[\alpha]_D^{22} = -50,6^o$ $[\alpha]_D^{22} = +50,6^o$ $[\alpha]_D^{22} = -42,3^o$ $[\alpha]_D^{22} = +42,3^o$

(*R*)-(-)- 1-chloro-1-phenyl ethane (*S*)-(+)-

(*S*)-(+)-1-phenylethanol (*R*)-(-)-

REACTION

(*R*)-(-)- 1-chloro-1-phenylethane + H_2O $\longrightarrow$ 1-phenylethanol racemická směs

$[\alpha]_D = -50,6^o$

$[\alpha]_D = +0,8^o$

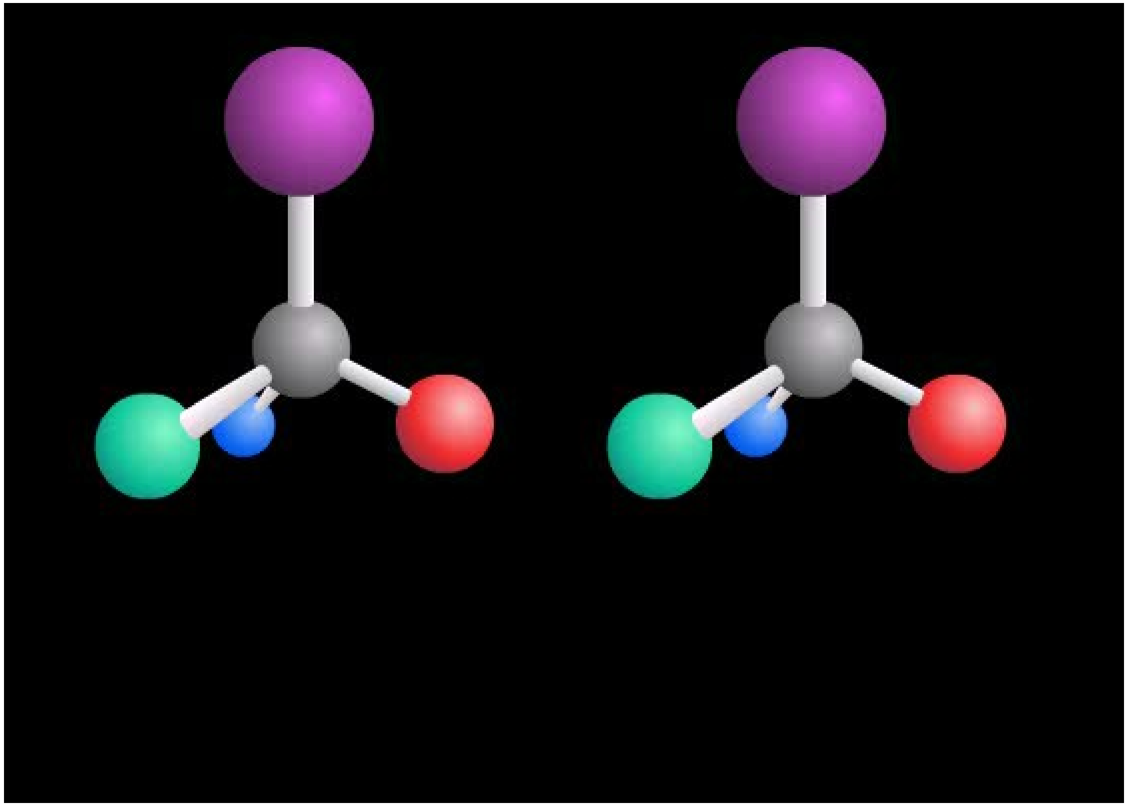
50% + 50% enantiomerů

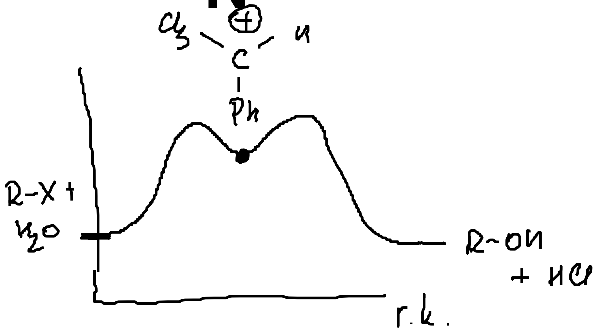
both enantiomers

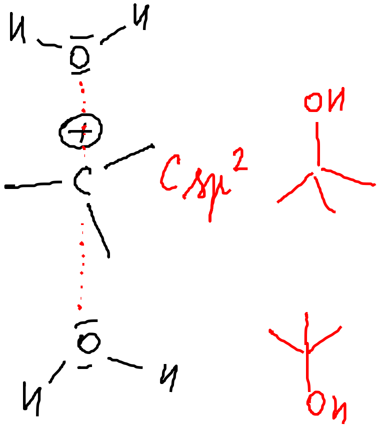
49% (S)-1-fenylethanolu
51% (R)-1-fenylethanolu

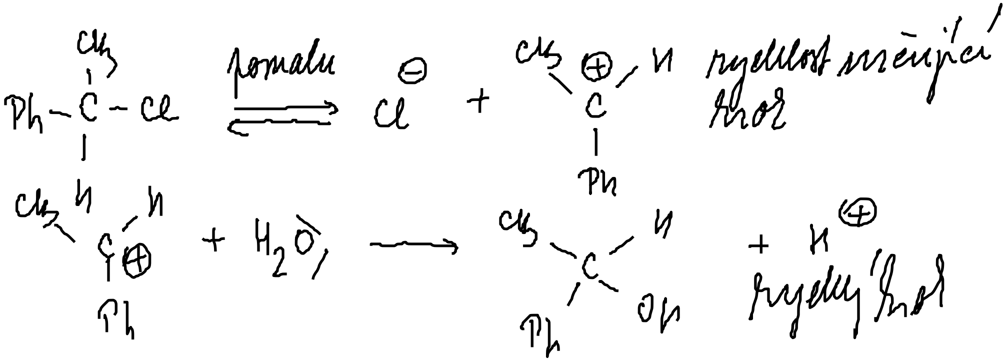
$$\text{optical purity} = \frac{+0,8}{+42,3} \cdot 100\ \% \doteq \underline{\underline{2\%}}$$

Nucleophilic substitution S_N1







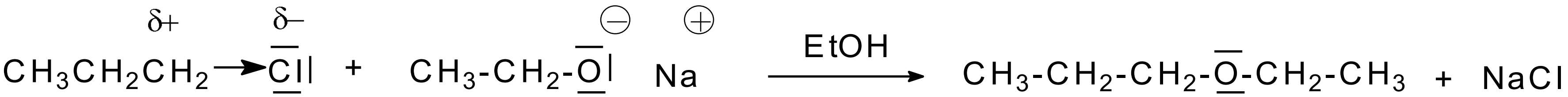


pomalu

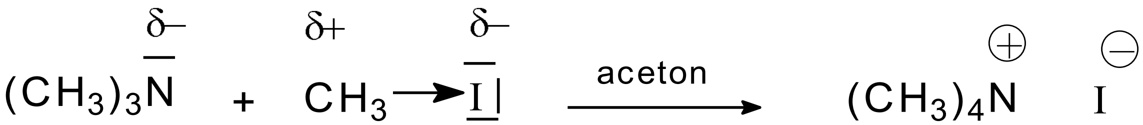
rychlost určující krok

rychlý krok

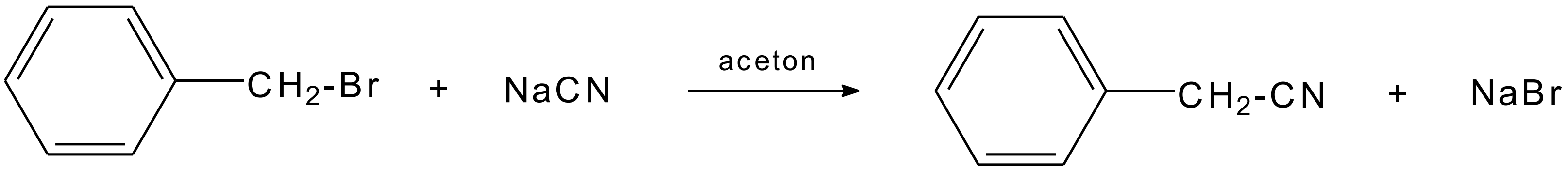
Substitution reactions examples

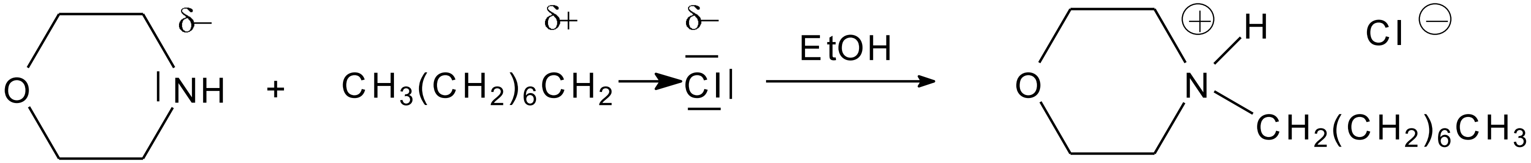


$$\overset{\delta+}{CH_3CH_2CH_2}\rightarrow\overset{\delta-}{\overline{\underline{Cl}}|} + CH_3\text{-}CH_2\text{-}\overline{\underline{O}}|^{\ominus}\ Na^{\oplus} \xrightarrow{EtOH} CH_3\text{-}CH_2\text{-}CH_2\text{-}\overline{\underline{O}}\text{-}CH_2\text{-}CH_3 + NaCl$$

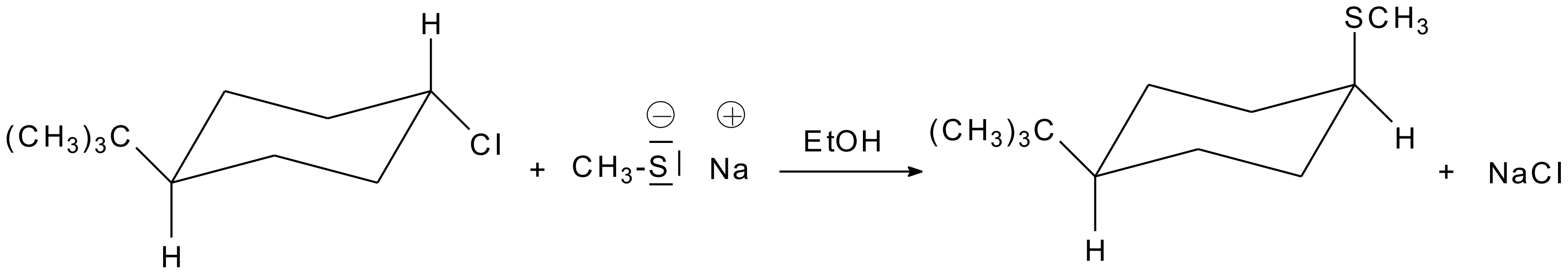


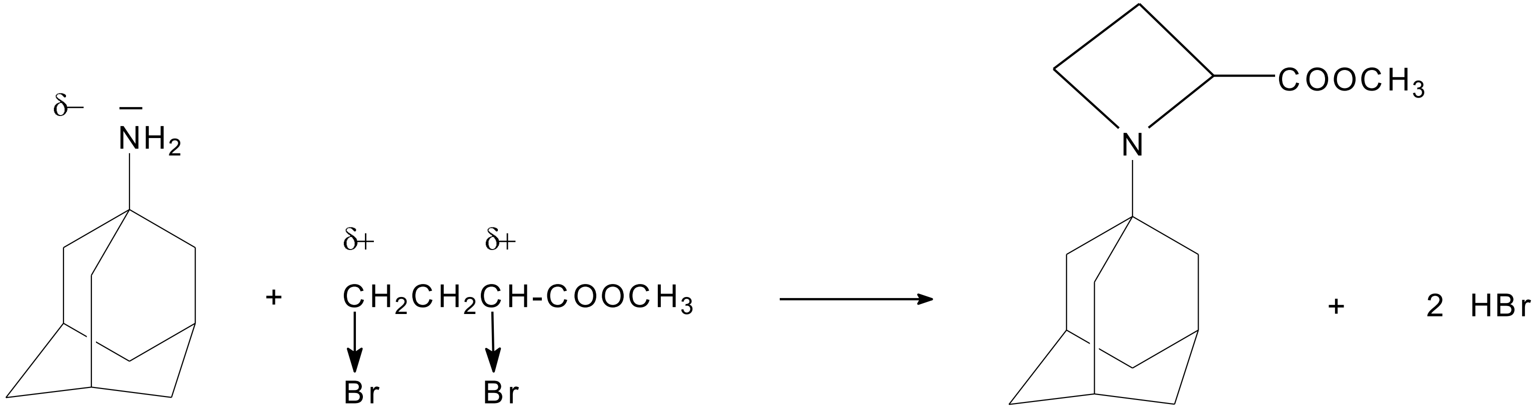
$$(CH_3)_3\overset{\delta-}{\overline{N}} + \overset{\delta+}{CH_3}\rightarrow\overset{\delta-}{\overline{\underline{I}}|} \xrightarrow{aceton} (CH_3)_4\overset{\oplus}{N}\ \overset{\ominus}{I}$$



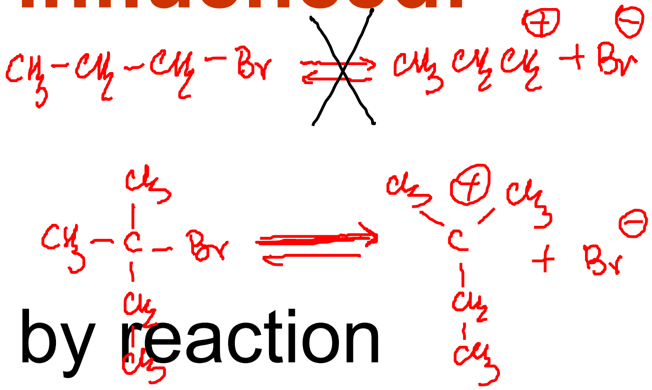


Nucleophilic substitution examples





- **The course of the reaction is influenced:**



structure: non-branched ---- S_N2

branched --- S_N1

during S_N2 different derivatives differ by reaction rate:

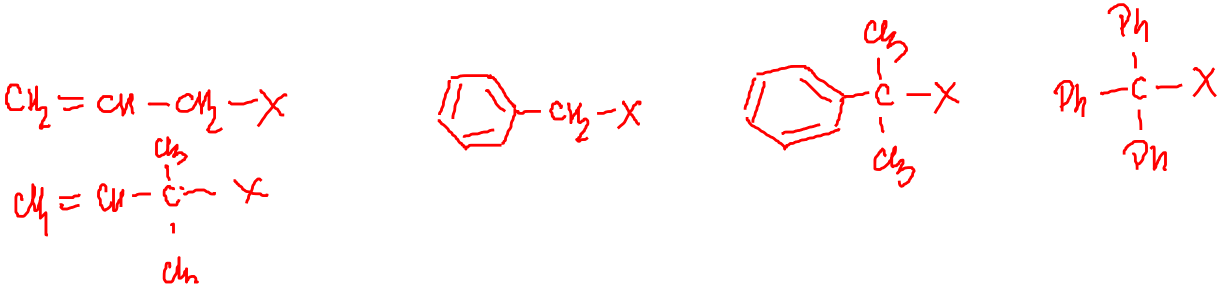
methyl>prim. halogenid>sek. hal.>terc. hal

30 1 0,02 rel. rate

the reason is sterical hindrance

during S_N1 electronic influence is plaing main role

they are limited to terciary derivatives, allyl and benzyl derivatives



The course of the reaction is influenced:

- **influence of strenght and concentration**

influence only at S_N2 (at S_N1 in rate equation the concentration is not included)

-nucleophility in the periodic table is growing from left to right and from top down

O F
S Cl
Br
I

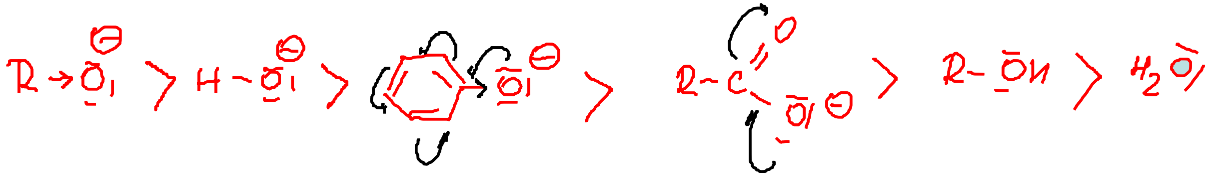
$RO^{\ominus} < RS^{\ominus}$

$Br^{\ominus} < J^{\ominus}$

-charged atom(ion) is more nucleophilic than its conjugated acid (neutral molecule)

$CH_3-O^{\ominus} > CH_3-OH$ $HO^{\ominus} > H_2O$

-nucleophility is paralel with basicity



Course of the reaction is influenced:

- solevent

types of solvents:

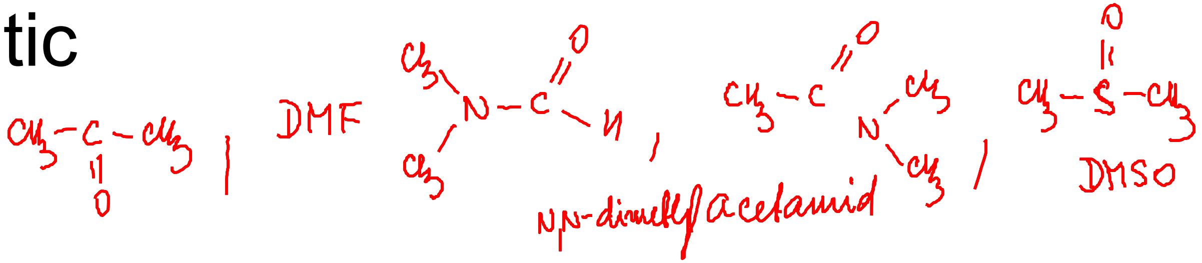
nonpolar

hexan, heptan, petrolether, benzen, toluen, xylen

polar protic

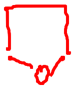
H_2O, CH_3OH, CH_3CH_2-OH, $R-SH$

aprotic



$CH_3-C(=O)-CH_3$, DMF $(CH_3)_2N-C(=O)-H$, $CH_3-C(=O)-N(CH_3)_2$, $CH_3-S(=O)-CH_3$

$CH_3-C\equiv N$

($CH_3-CH_2-O-CH_2CH_3$)  THF)

Course of the reaction is influenced :

- nucleophility is changing with polarity of solvent

-in polar solvent the bigger atom is more nucleophilic

(polarisibility is higher – softer reagent; small atom is solvated by hydrogen bridges and this way its reactivity is decreased)

R-SH > ROH

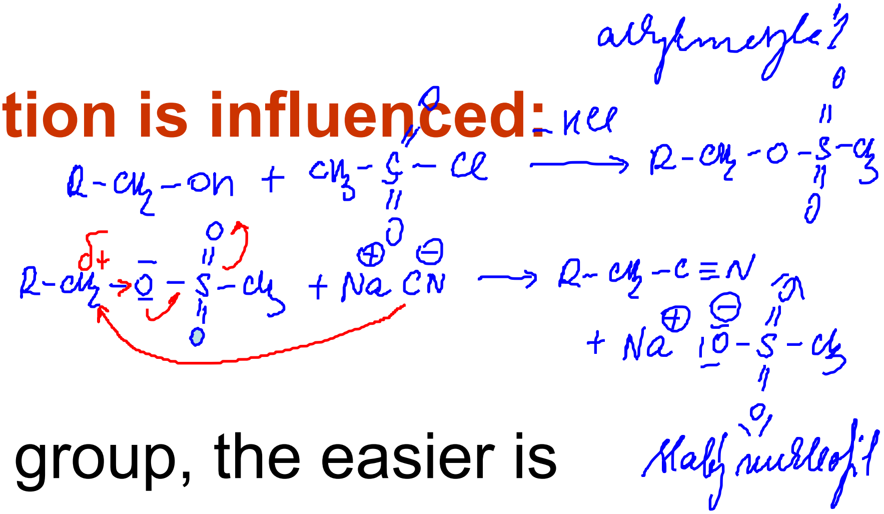
$J^- > Br^- > Cl^- > F^-$

- in aprotic solvent is the dependence just opposite

- $F^- > Cl^- > Br^- > I^-$

The course of the reaction is influenced:

- by leaving group



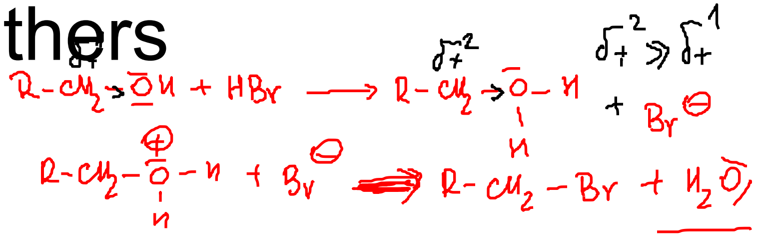
- the more stabil is the leaving group, the easier is substitution

$I^- > Br^- > Cl^- > F^-$

- in acidic medium we can support the substitution i.e. alcohols or ethers

$R-CH_2-\overline{O}H + Nu^{\ominus} \rightleftarrows R-CH_2-Nu + |\overline{O}H^{\ominus}$

velmi silný nukleofil



- very important group of leaving species are groups with sulfur (tosylates, mesylates, nosylates, brosylates etc.)