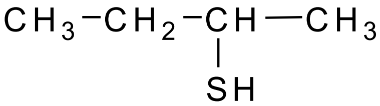
Sulfur analogs of alcohols, phenols and ethers

CH_3-CH_2-SH ethanthiol

thioles (earlier mercaptanes)



$CH_3-CH_2-CH(SH)-CH_3$ butan-2-thiol

$CH_3-CH_2-S-CH_3$ ethylmethylsulfid

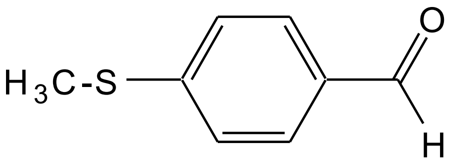
sulfides

CH_3-S-CH_3 dimethylsulfid

Prefix -- **sulfanyl**

event. **alkylsulfanyl**

$HS-CH_2-CH_2-OH$ 2-sulfanylethanol

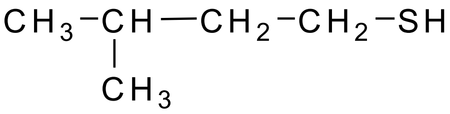


4-methylsulfanylbenzaldehyd

Sulfur analogs of alcohols, phenols and ethers

When compared with alcohols they are more volatile (the hydrogen bonds formed here are not so strong) and therefore smell also in small quantity

Ethanol	b.v. 78°C
Ethanthiol	b.v. 37°C

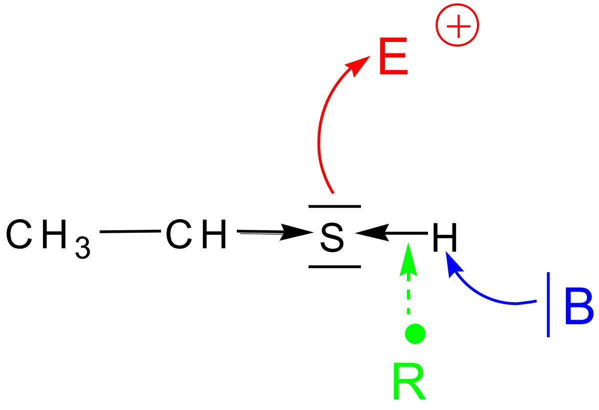


$$CH_3-\underset{\displaystyle CH_3}{\underset{|}{CH}}-CH_2-CH_2-SH$$

3-methylbutanthiol

$H_2C=CH-CH_2-SH$ diallylsulfid

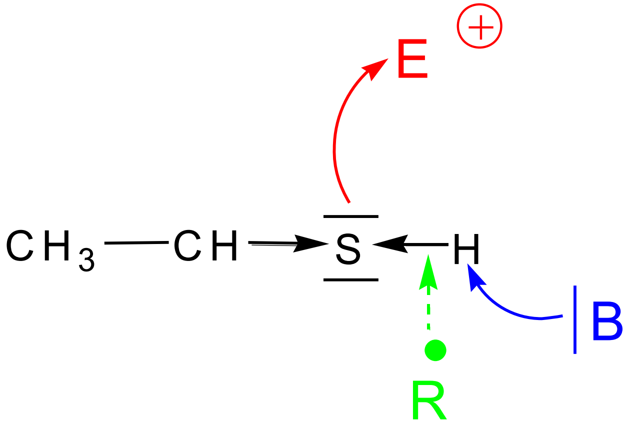
$CH_3-CH_2-CH_2-SH$ propanthiol



General reactivity:

1. Sulfur atom is nucleophilic and reacts very well with all electrophilic centra
2. Hydrogen atom at sulfur is acidic
3. The bond S-H is only little polar and therefore radical splitting is possible to expect

Sulfur analogs of alcohols, phenols and ethers

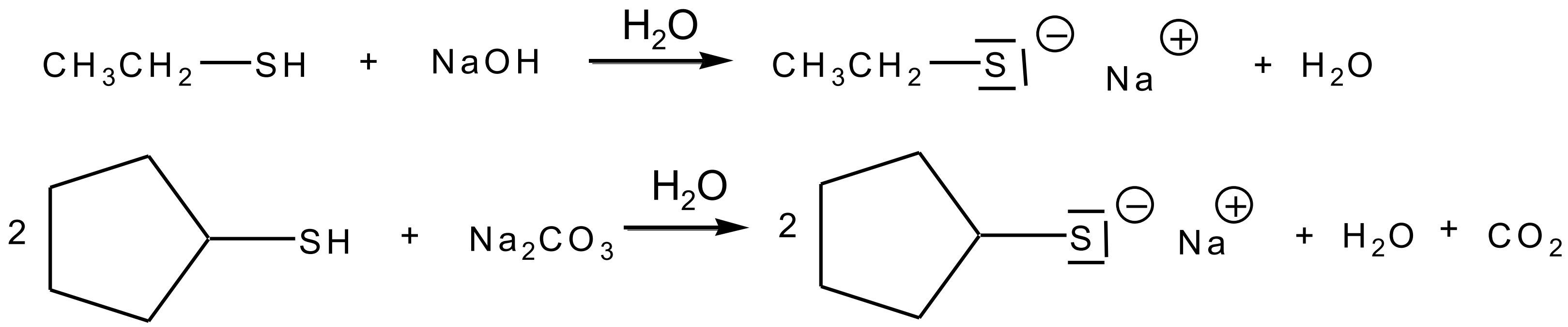


General reactivity:

1. Sulfur atom is nucleophilic and reacts very well with all electrophilic centra
2. Hydrogen atom at sulfur is acidic
3. The bond S-H is only little polar and therefore radical splitting is possible to expect

Hydrogen atom is more acidic than in alcohols and therefore can be removed even by a weak base and in water

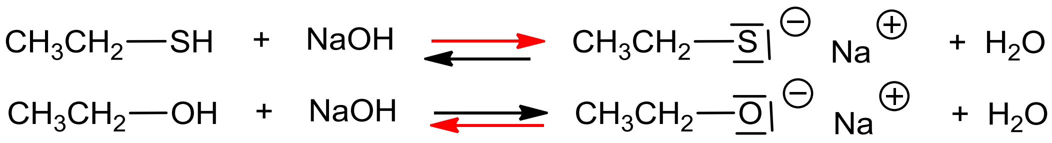
$pK_a = 10$ (thiol) compare $pK_a = 16$ (alcoholes)



$$CH_3CH_2{-}SH + NaOH \xrightarrow{H_2O} CH_3CH_2{-}S^{\ominus}\ Na^{\oplus} + H_2O$$

Sulfur analogs of alcohols, phenols and ethers

thiol is stronger acid than **alcohol**



$$CH_3CH_2{-}SH + NaOH \rightleftharpoons CH_3CH_2{-}\overline{\underline{S}}|^{\ominus}\ Na^{\oplus} + H_2O$$

$$CH_3CH_2{-}OH + NaOH \rightleftharpoons CH_3CH_2{-}\overline{\underline{O}}|^{\ominus}\ Na^{\oplus} + H_2O$$

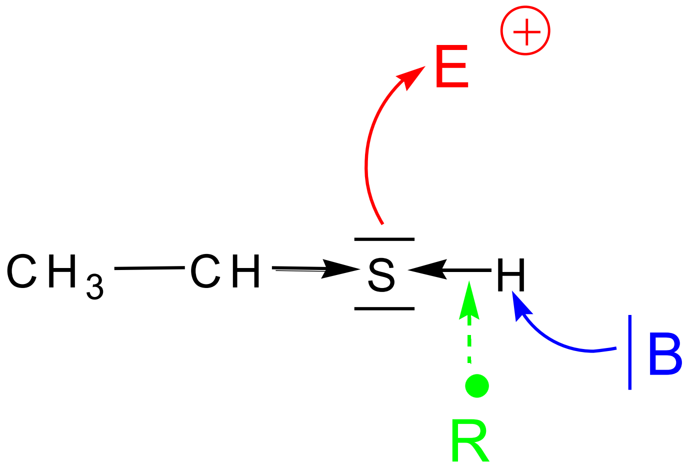
acid	base
alcohol < thiol	alcoholate > thiolate

!Be carefull! Thiolate is stronger nucleophile than alkoholate

It is caused by better polarizibility of sulfur

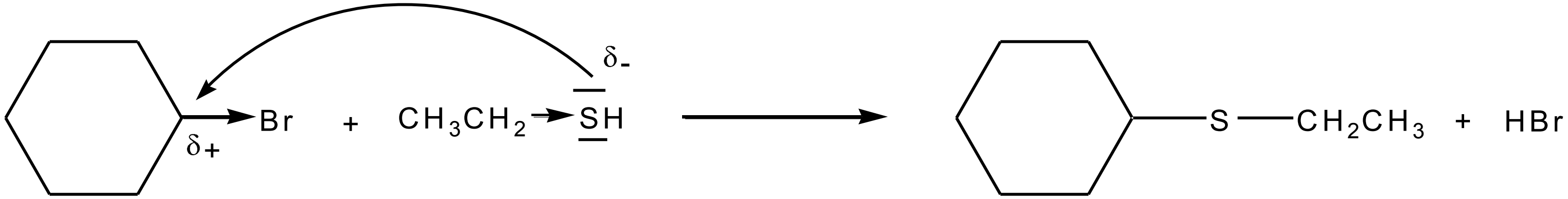
Alcoholates rather enter into elimination reactions and thiolates prefer nucleophilic substitution reactions

Sulfur analogs of alcohols, phenols and ethers

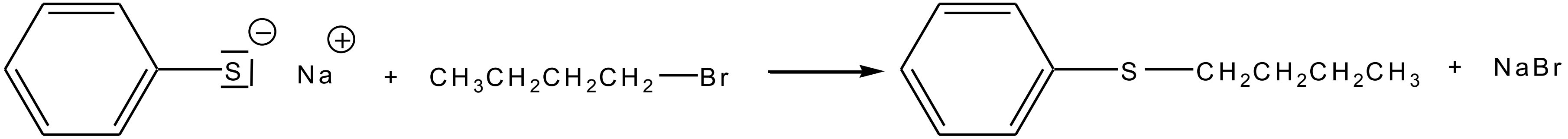


General reactivity:

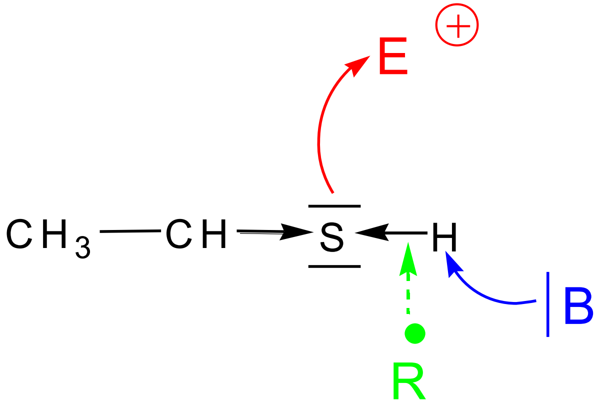
1. **Sulfur atom is nucleophilic and reacts very well with all electrophilic centra**
2. Hydrogen atom at sulfur is acidic
3. The bond S-H is only little polar and therefore radical splitting is possible to expect



$$CH_3CH_2{-}Cl \; + \; HS{-}CH_2CH_3 \longrightarrow CH_3CH_2{-}S{-}CH_2CH_3 \; + \; HCl$$



Sulfur analogs of alcohols, phenols and ethers



General reactivity:

1. Sulfur atom is nucleophilic and reacts very well with all electrophilic centra
2. Hydrogen atom at sulfur is acidic
3. The bond S-H is only little polar and therefore radical splitting is possible to expect

Bond **C – S is less polar than bond C – O** (oxygen atom is more electronegative)

the bond is difficult to split
– substitution is difficult

$$R^1\text{—SH} \xrightarrow{h\nu} R^1S\bullet + H\bullet$$

the formed radicals enter dimerization - **formation of disulfides**

$$R^1\text{—SH} \xrightarrow{O\bullet} R^1\text{—}S\bullet + H\bullet \longrightarrow R^1\text{—S—S—}R^1 + H_2$$

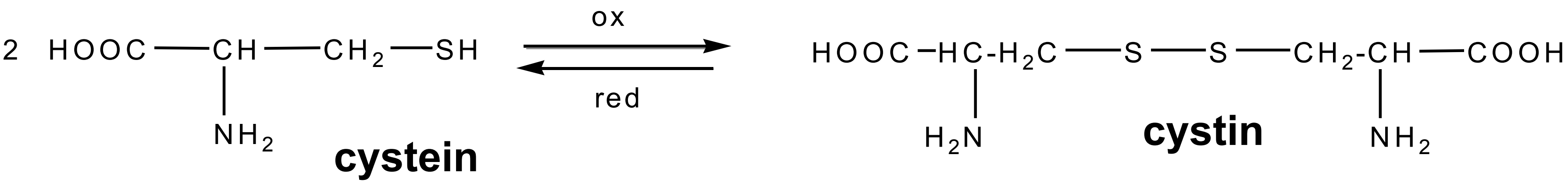
dialkyldisulfid

Sulfur analogs of alcohols, phenols and ethers

$$R-SH \underset{red}{\overset{ox}{\rightleftharpoons}} R-S-S-R$$

thiol disulfid

reversible process in a brain – responsible for process of remembering

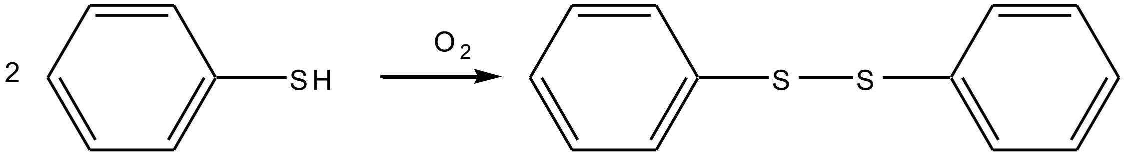


$$2\ HOOC-\underset{NH_2}{CH}-CH_2-SH \underset{red}{\overset{ox}{\rightleftharpoons}} HOOC-\underset{H_2N}{HC}-H_2C-S-S-CH_2-\underset{NH_2}{CH}-COOH$$

cystein

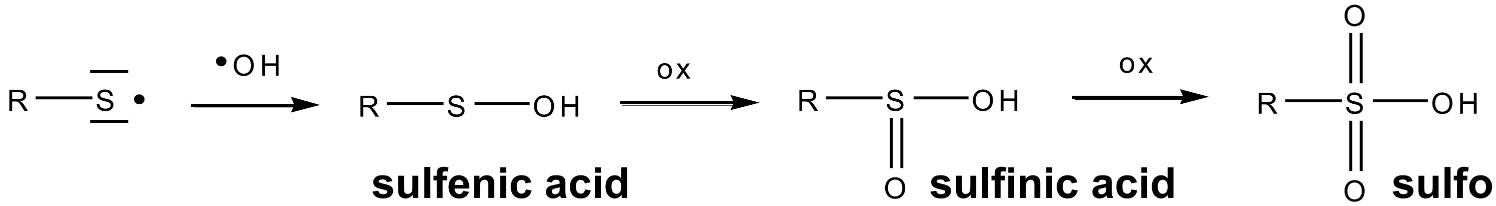
cystin

sulfur derivatives undergo easy oxidation



gentle oxidation reagents

$$2\ CH_3CH_2-S^{\ominus}\ K^{\oplus} \xrightarrow{I_2} 2\ KI + CH_3CH_2-S-S-CH_2CH_3$$

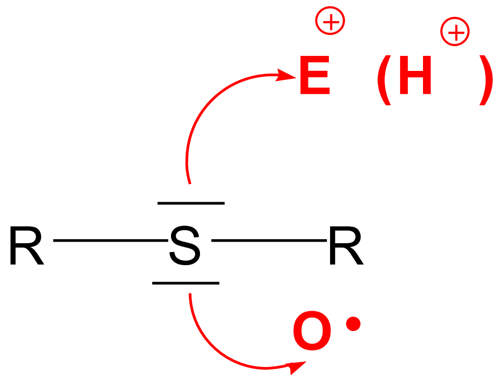


$$R-\overline{\underline{S}}\bullet \xrightarrow{\bullet OH} R-S-OH \xrightarrow{ox} R-\underset{\underset{O}{\|}}{S}-OH \xrightarrow{ox} R-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-OH$$

sulfenic acid **sulfinic acid** **sulfonic acid**

strong oxidation reagents (HNO_3, $KMnO_4$ ….)

Sulfur analogs of alcohols, phenols and ethers

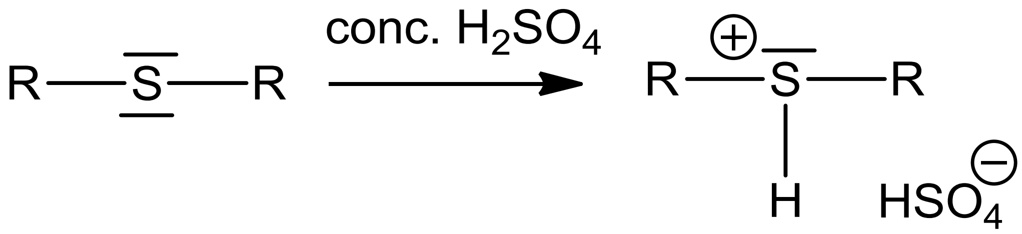


General reactivity :

1. **basic properties**
2. high nucleophility
3. sensitivity against oxidation

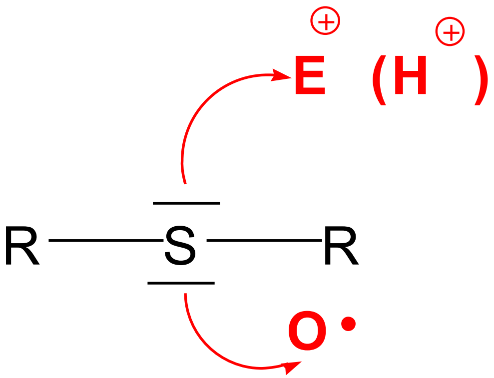
SULFIDES

in properties similar to ethers, but they have higher boiling temperatures then ethers



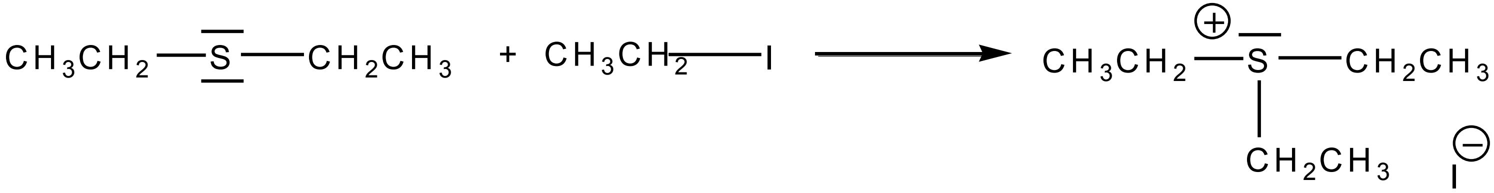
in acids they dissolve under formation of sulfonium salts, which in water split back

Sulfur analogs of alcohols, phenols and ethers

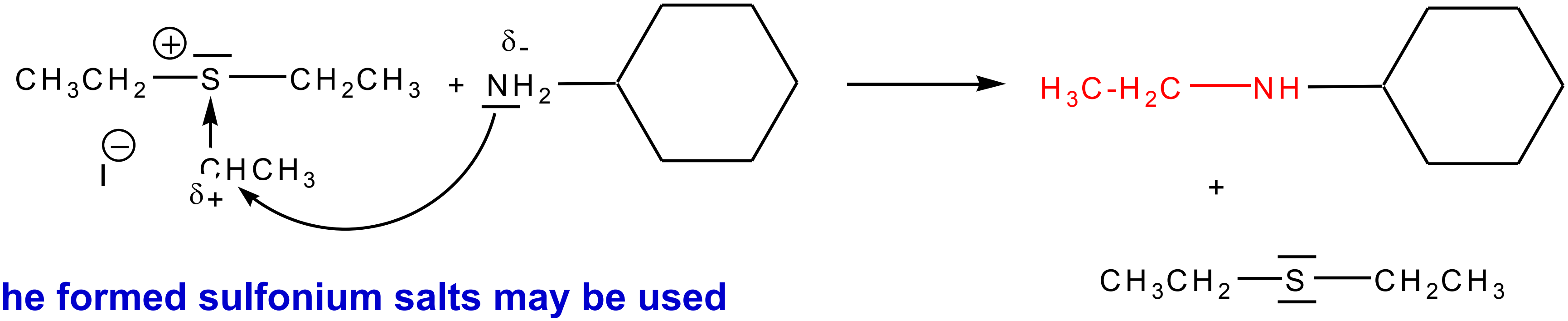


General reactivity :

1. **basic properties**
2. high nucleophility
3. sensitivity against oxidation



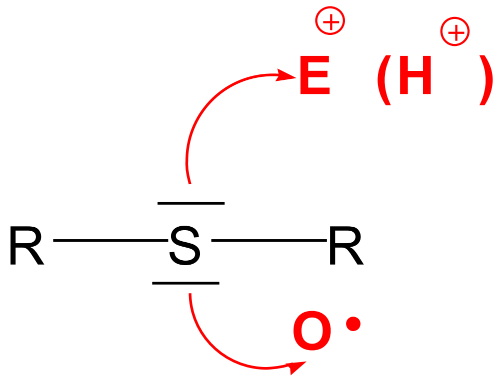
$$CH_3CH_2-\overline{\underline{S}}-CH_2CH_3 + CH_3CH_2-I \longrightarrow CH_3CH_2-\overset{\oplus}{S}(CH_2CH_3)-CH_2CH_3 \quad I^{\ominus}$$



$$CH_3CH_2-\overset{\oplus}{S}(CH_2CH_3)-CH_2CH_3\;I^{\ominus} + \overset{\delta-}{NH_2}-C_6H_{11} \longrightarrow H_3C\text{-}H_2C-NH-C_6H_{11} + CH_3CH_2-\overline{\underline{S}}-CH_2CH_3$$

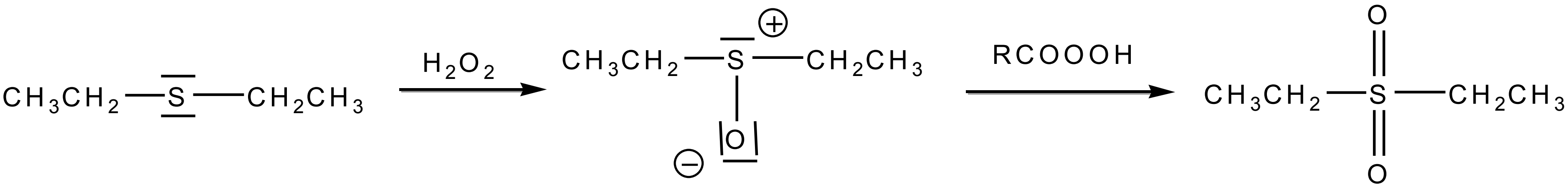
the formed sulfonium salts may be used for alkylation of nucleophiles

Sulfur analogs of alcohols, phenols and ethers



General reactivity :

1. basic properties
2. high nucleophility
3. **sensitivity against oxidation**



$$CH_3CH_2-S-CH_2CH_3 \xrightarrow{H_2O_2} CH_3CH_2-\overset{\oplus}{S}(-\overset{\ominus}{O})-CH_2CH_3 \xrightarrow{RCOOOH} CH_3CH_2-S(=O)_2-CH_2CH_3$$

sulfoxide

diethysulfoxide

sulfone

diethylsulfone

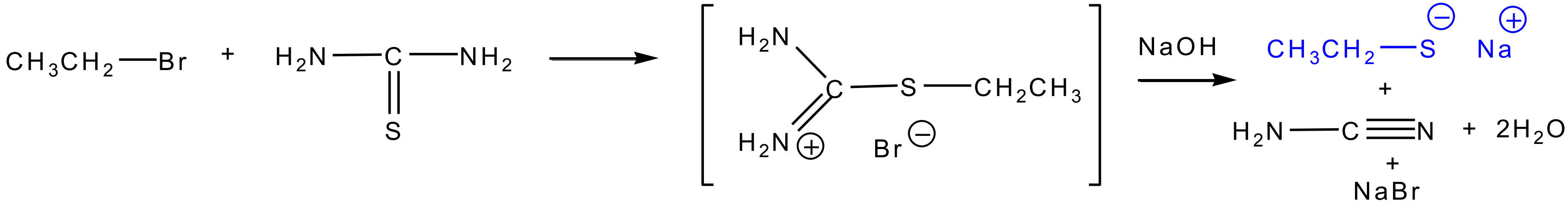
Sulfoxides are very good solvents for both organic and inorganic compompounds (salts) – application in S_N reactions, deuterated DMSO excelent solvent for NMR.

Sulfones are very well crystallizing compounds suitable for a purification of sulfur compounds.

Preparation of sulfur analogs of alcohols, phenols and ethers

Preparation of thioles

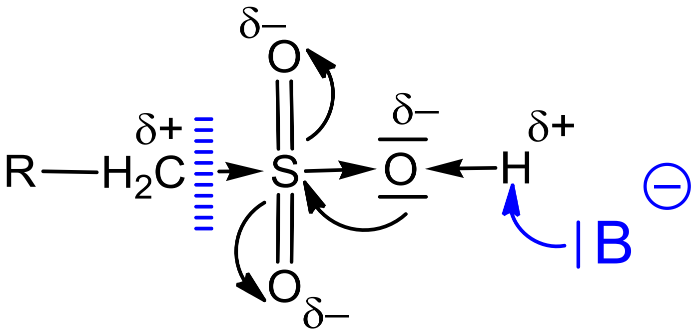
$CH_3CH_2-Br \; + \; K^+ \; HS^- \; (H_2S + KOH) \longrightarrow CH_3CH_2-SH$



Preparation of sulfides

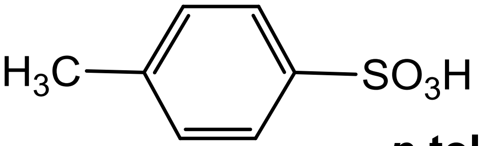
$$CH_3CH_2-SH \xrightarrow{NaOH} CH_3CH_2-\overset{\ominus}{S} \; \overset{\oplus}{Na} \xrightarrow{R-Br} CH_3CH_2-S-R \; + \; NaBr$$

Sulfonic acids and derivates



reactivity of molecule:

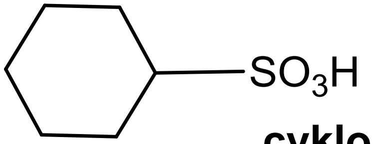
1. **proton dissociation**
2. **C – S bond is very difficult to split**
3. **nukleofilic attack at sulfur is not probable**



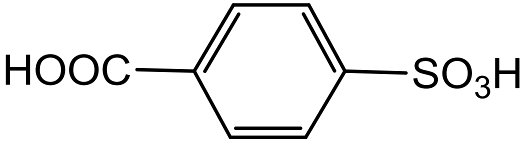
***p*-toluensulfonic acid**

CH_3-SO_3H

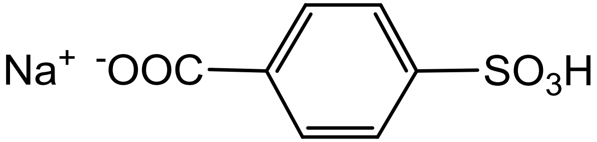
methansulfonic acid



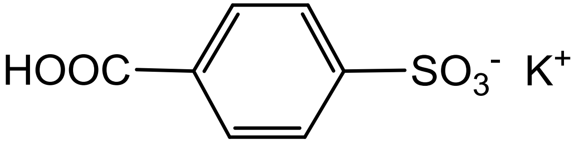
cyklohexansulfonic acid



4-sulfobenzooic acid

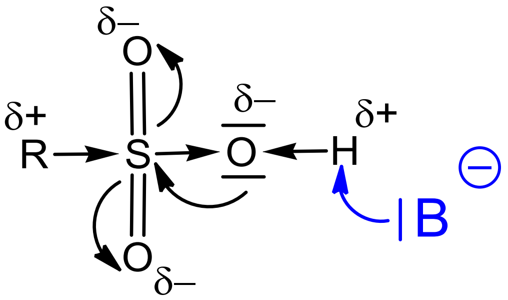


sodium 4-sulfobenzencarboxylate



potassium 4-carboxybenzensulfononate

Sulfonic acids and derivates



reactivity of molecule:

1. **proton dissociation**
2. C – S bond is very difficult to split
3. nukleofilic attack at sulfur is not probable

very strong acid is forming salts with near every base

$pK_a \approx 0,5$

sodium benzensulfonate

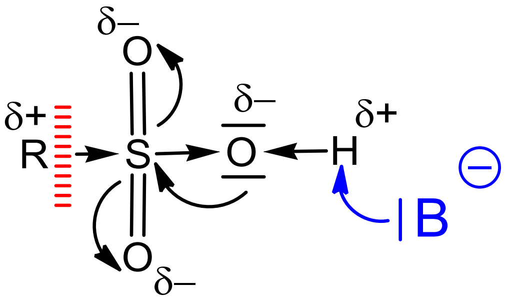
potassium *p*-toluenbenzensulfonate

potassium methansulfonate

in the contrary to carboxylic acids, Ca^{2+} a Ba^{2+} salts of sulfonic acids are soluble in water – therefore are used as detergents

the presence of sulfonic group in organic molecule increase solubility in water

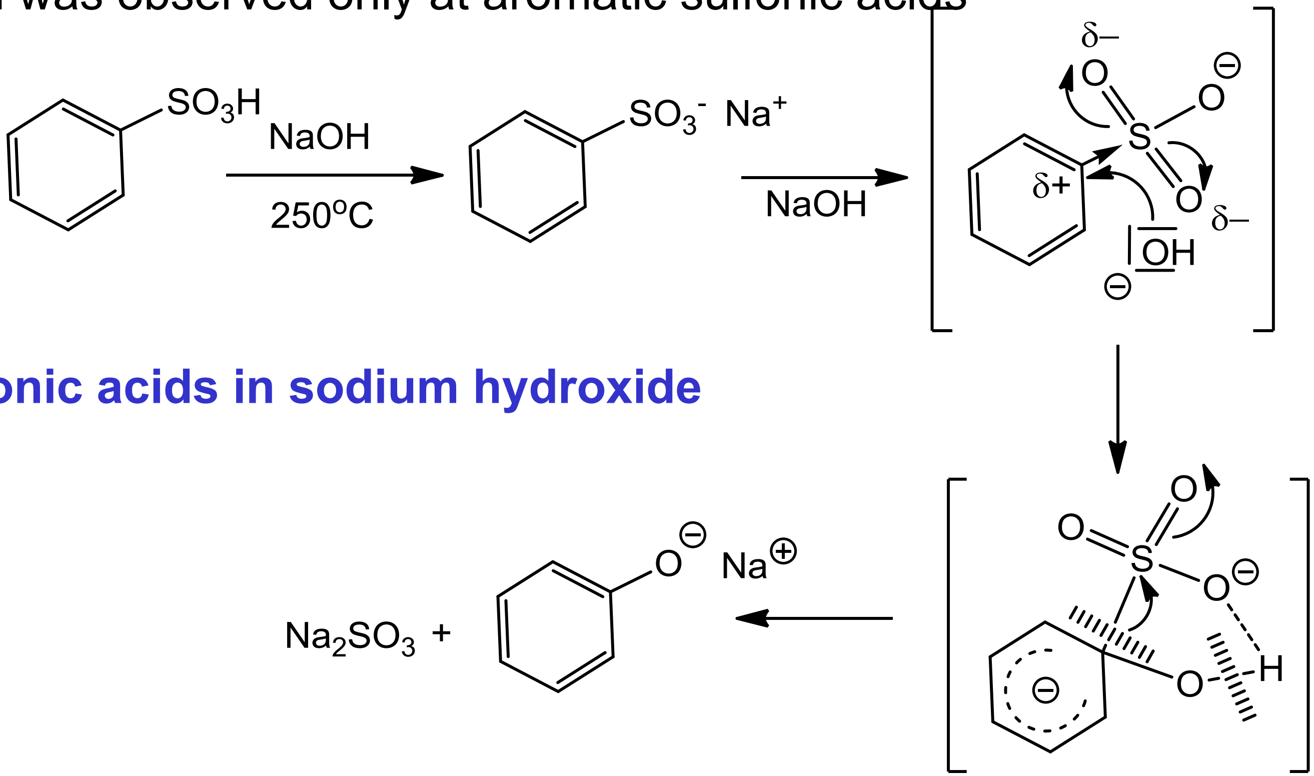
Sulfonic acids and derivates



reactivity of molecule:

1. proton dissociation
2. **C – S bond is very difficult to split**
3. nukleofilic attack at sulfur is not probable

splitting C-S bond was observed only at aromatic sulfonic acids

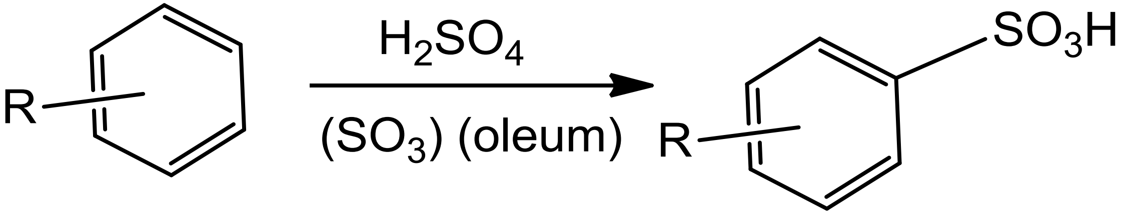


melting of sulfonic acids in sodium hydroxide

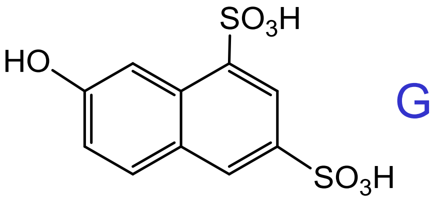
Sulfonic acids and derivates

Preparation of sulfonic acids

aromatic sulfonic acids are prepared by sulfonation of aromates - reaction S_EAr

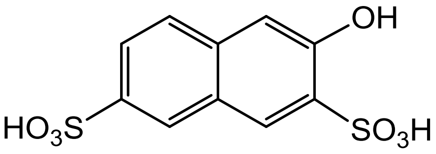


important are more sulfonated derivatives as dye components



G-acid

R -acid



Sulfonic acids and derivates

Preparation of sulfonic acids

alifatic sulfonic acids are prepared:

oxidation of thioles

$$CH_3CH_2{-}SH \xrightarrow{HNO_3} CH_3CH_2{-}SO_3H$$

sulfoxidation of alkanes (radical substitution)

$$SO_2 + O_2 \xrightarrow{h\nu}$$

$$R{-}CH_3 + SO_2 + 1/2\ O_2 \longrightarrow R{-}CH_2{-}SO_3H$$

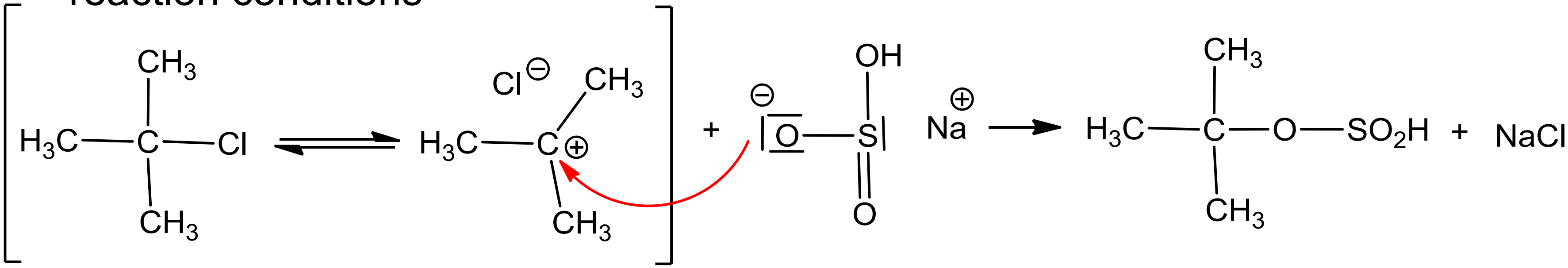
nukleofilic substitution of halogen derivatives

$$R{-}Cl + NaHSO_3 \longrightarrow R{-}SO_3H + NaCl$$

Ambidentní ionty

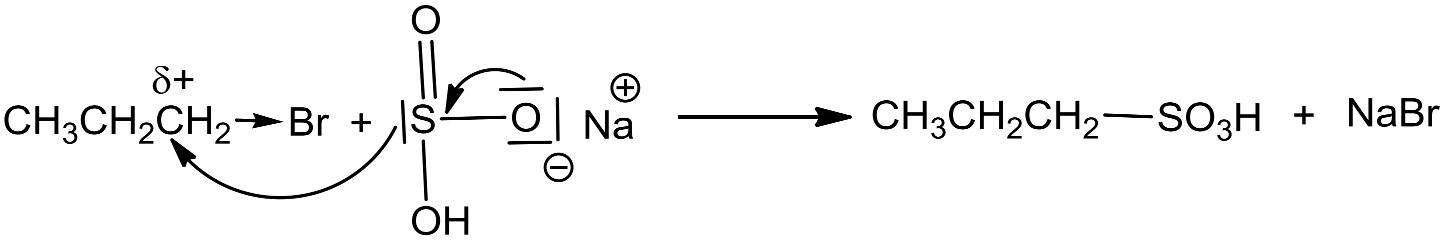
Ambidentní ionts - ionts, which are able to react at more reaction centres

results of the reaction depend upon the structure of substrate and reaction conditions



during the reaction proceeding by mechanism S_N1, the atom of ambident anion, which reacts with carbocation, is that atom carrying the charge

hard center (electrophile) reacts with hard nucleophile



during reaction proceeding by mechanism S_N2, with the reaction center reacts atom with higher polarizability – we can observe reaction of soft centers

Ambident ions

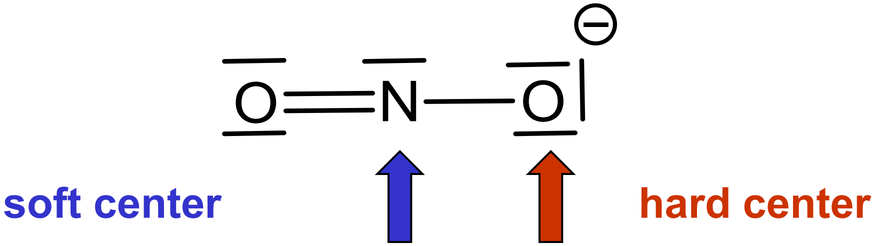
Ambident ions

Kornblum rule

During S_N1 reaction reacts at ambident iont the atom with bigger charge, during S_N2 reaction reacts the atom with better polarizability

$$CH_3CH_2{-}Br + Na^+ \; NO_2^- \longrightarrow ?$$

structure of anion



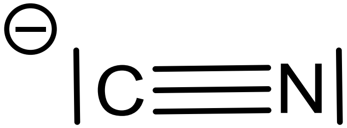
$$CH_3CH_2{-}Br + Na^+ \; NO_2^- \longrightarrow CH_3CH_2{-}NO_2 + NaBr$$

in our case nitrocompound is formed

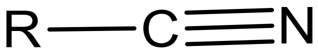
Ambident ions

Ambident ions

reaction with cyanide anion

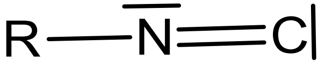


during S_N2 reacts less electronegative carbon atom



nitril is formed

during S_N1 reacts more electronegative atom

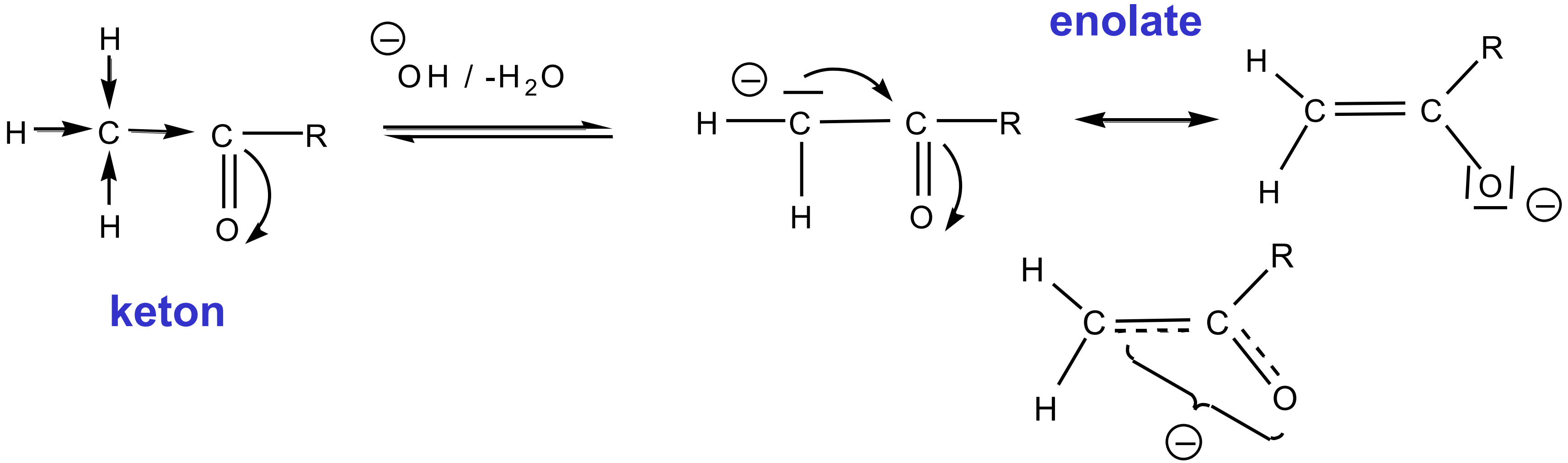


isocyanide is formed

when isocyanide is the expected compound, we can help ourselves blocking activity of carbon atom by formation of silver salt – we apply as reagent silver cyanide (AgCN)

Ambident ions

Ambident ions



The negative charge may be localized either at carbon or oxygen atom
(in reality is delocalized)

Enolate reacts as nucleophile with alkyl halogenides in dependence, which halogen is bound at alkyl

→ **here is direction in which the hardness is going down**

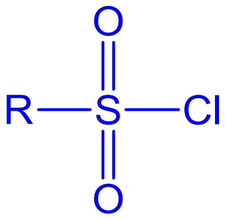
$R\text{-}CH_2\text{-}Cl > R\text{-}CH_2\text{-}Br > R\text{-}CH_2\text{-}I$

alkyl chloride reacts at oxygen atom

alkyl iodide reacts at carbon atom

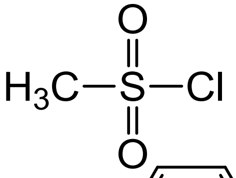
trimethylsilyl at oxygen

Sulfonic acids functional derivatives



$R-SO_2-Cl$

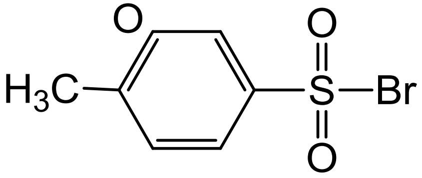
chlorides (halogenides)



H_3C-SO_2-Cl

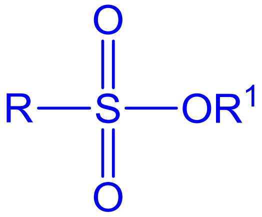
methanesulfonic acid chloride

methanesulfochlorid



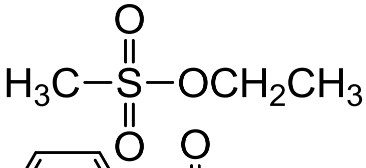
p-toluenesulfonic acid bromide

p-toluenesulfobromide



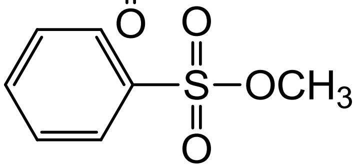
$R-SO_2-OR^1$

esters

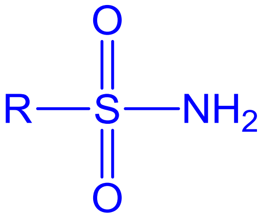


$H_3C-SO_2-OCH_2CH_3$

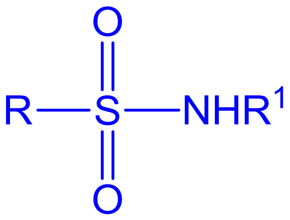
ethyl-methansulfonate



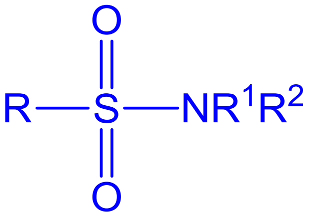
methyl-benzenesulfonate



$R-SO_2-NH_2$

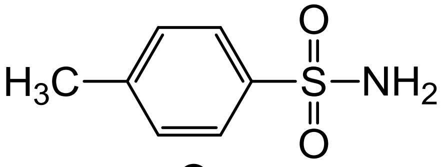


$R-SO_2-NHR^1$

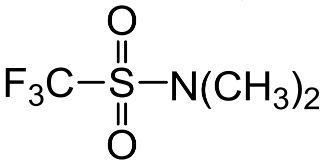


$R-SO_2-NR^1R^2$

amides (N-alkylamides, N,N-dialkylamides)



p-toluenesulfonamide

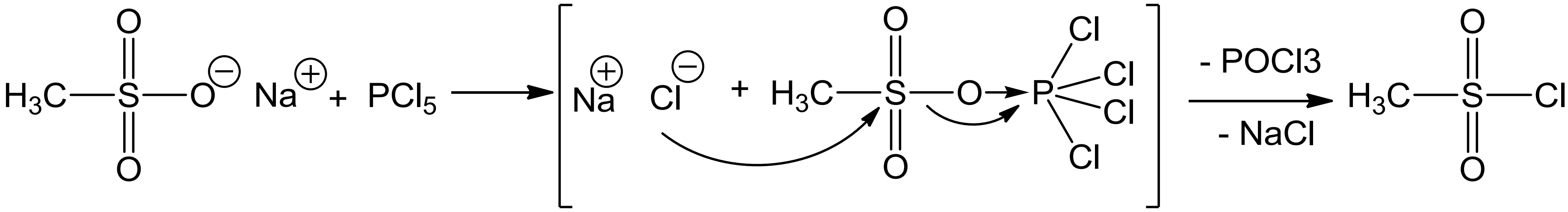


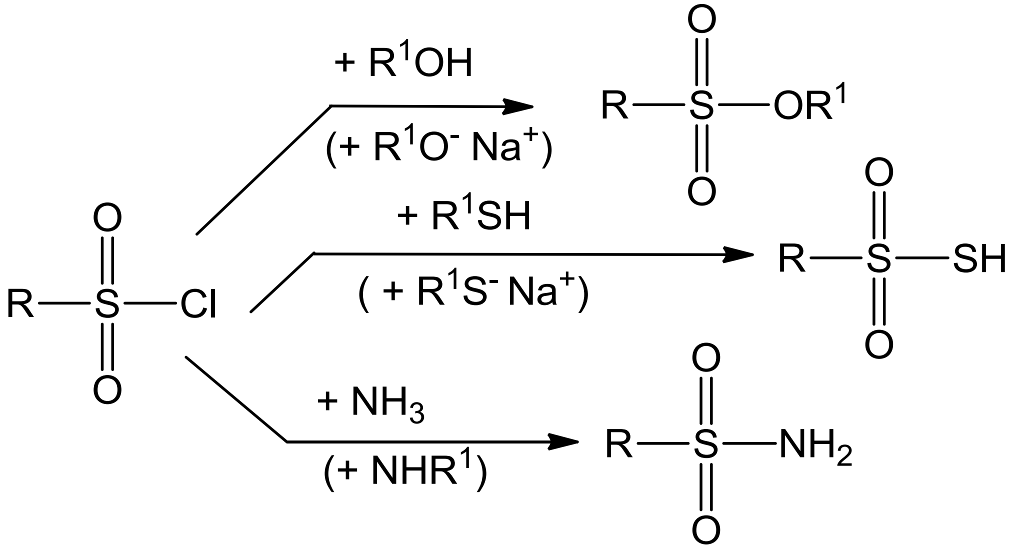
$F_3C-SO_2-N(CH_3)_2$

trifluormethanesulfonic acid *N,N*-dimethylamide

Sulfonic acids functional derivatives

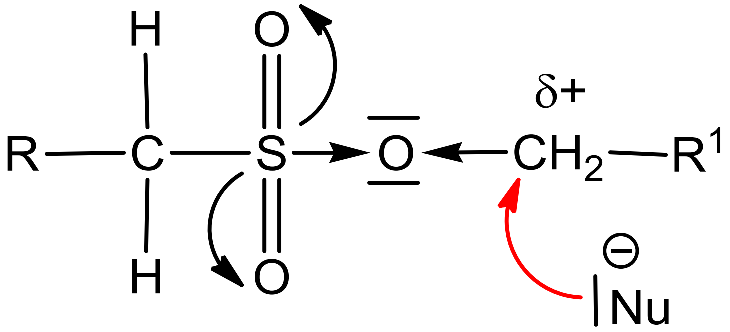
The source for preparation of all other derivatives are sulfonic acids and from them acid chlorides



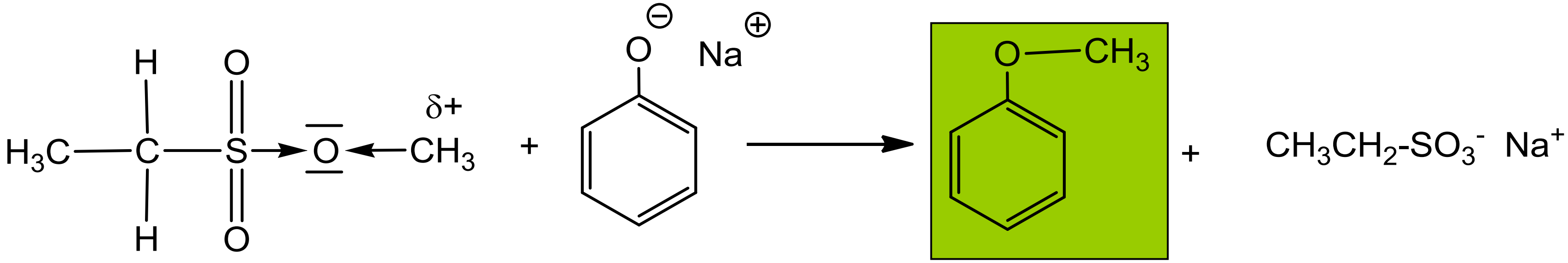


Sulfonic acids esters

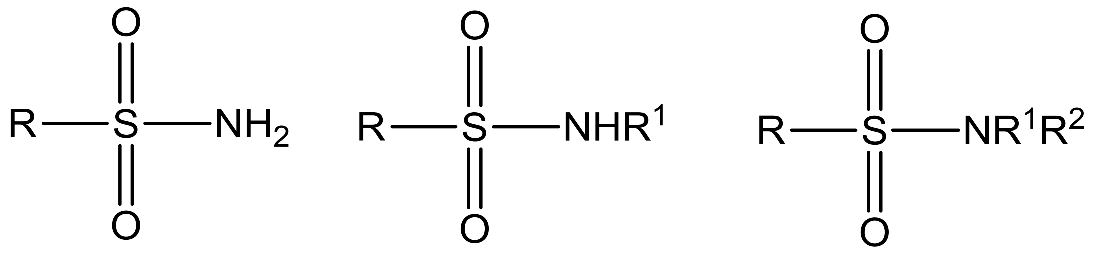
alkyl (aryl) sulfonates



attack of nucleophile leads to very easy leaving rest of sulfonic acid in the form of sulfonate salt and formation of product substitution

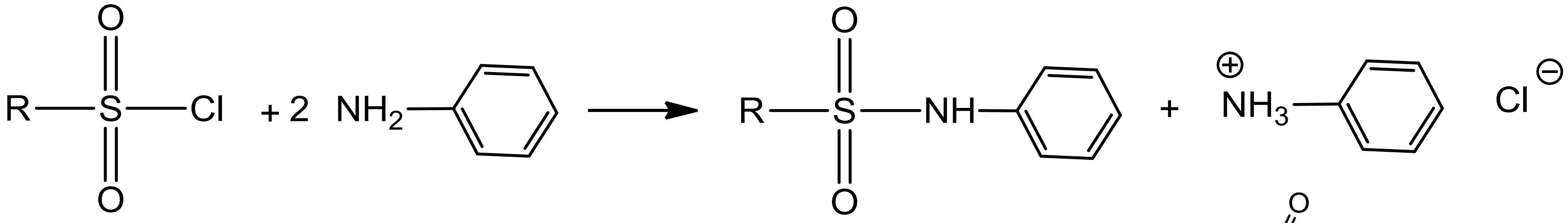


Sulfonamides

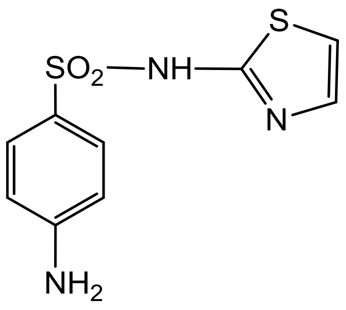


preparation by the reaction of sulfonylchlorides with amines in an excess

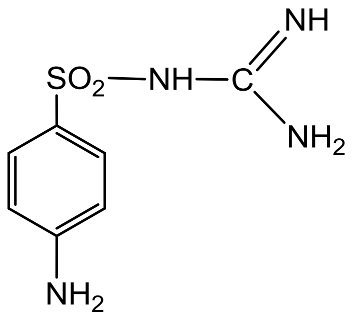
in case the amine is expensive, the second molecule maybe substituted by a tert. amin (triethylamin nebo pyridin)



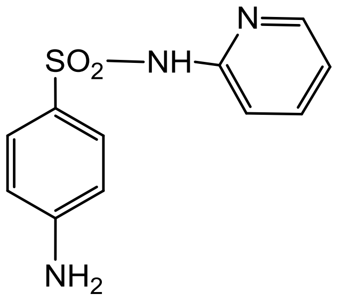
important sulfonamides



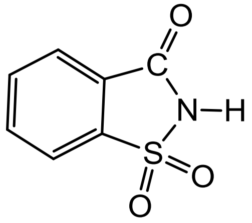
sulfothiazole



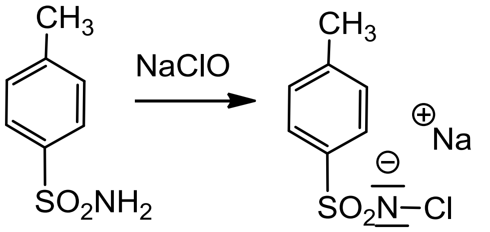
sulfaguanidine



sulfapyridine

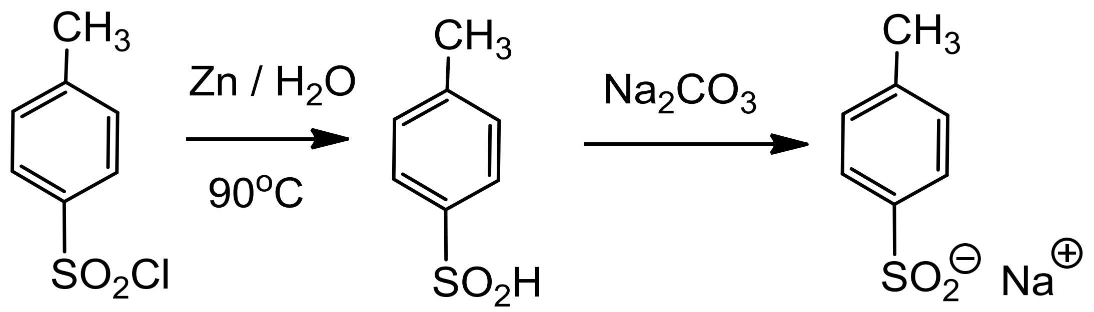


saccharin



chloramine T

Reduction of sulfonic acids

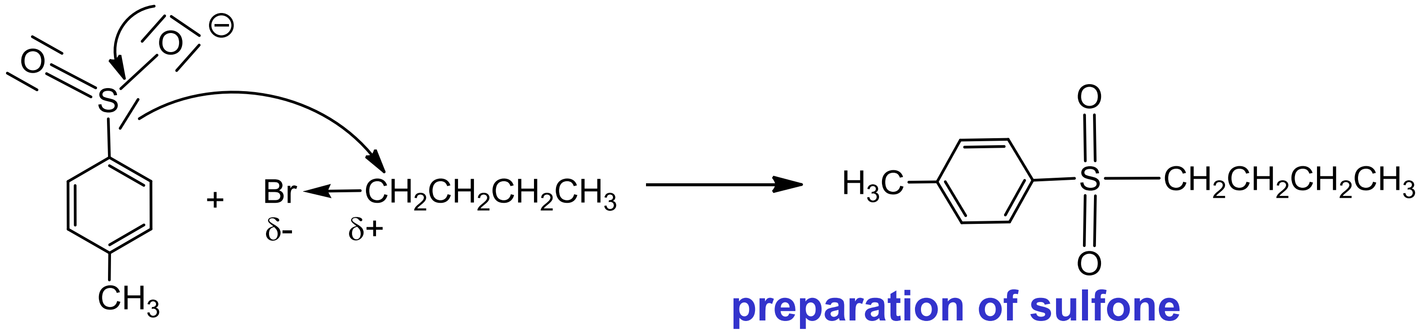


sulfinic acid

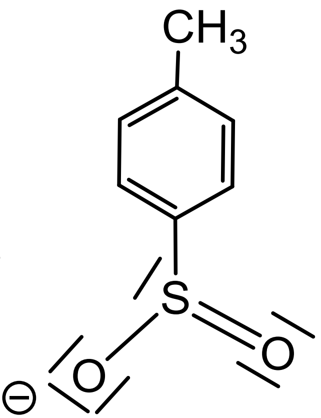
sodium sulfinate

the salts of sulfinic acids are **ambident nucleophiles**

with soft electrofiles at sulfur



preparation of sulfone



with hard electrophiles at oxygen