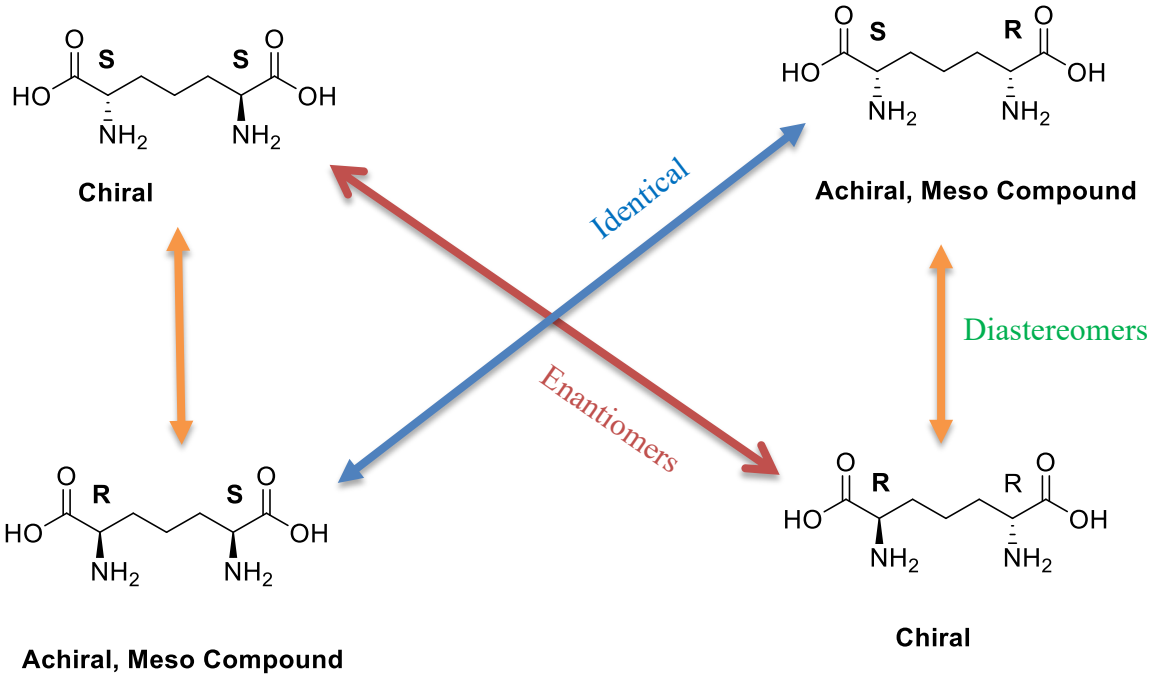
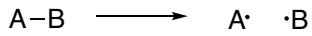
Review of concepts:



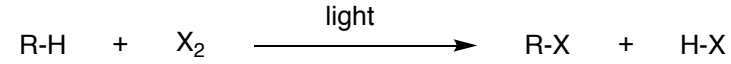
Substitution Reactions

Remember: Radical Substitution

1) **Homolytic bond breaking**



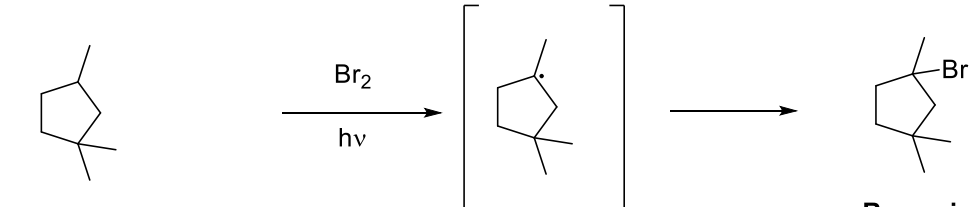
Example:



Proceeds by a radical mechanism

Alkane X=F, Cl, Br Not I

Alkyl Halide



1,1,3-trimethylcyclopentane

Racemic

Note: Although radicals are sp^3 hybridized, rapid inversion around the central C results in a loss of stereochemistry. Hence, the resulting product would be a racemic mixture.

2) Heterolytic Bond Breaking (Ionic Substitution)

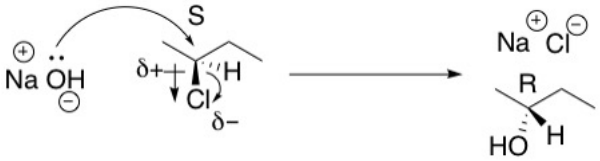
Nucleophile is a substance that seeks positive charge

Types of Nucleophilic Substitution (S_N)

S_N1 - rate depends on 1 concentration

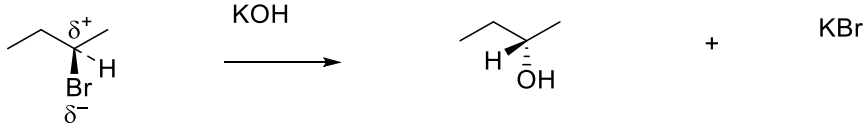
S_N2 - The rate is dependent on the concentration of the nucleophile and the nucleophile (2 concentrations)

Sn2 Mechanism



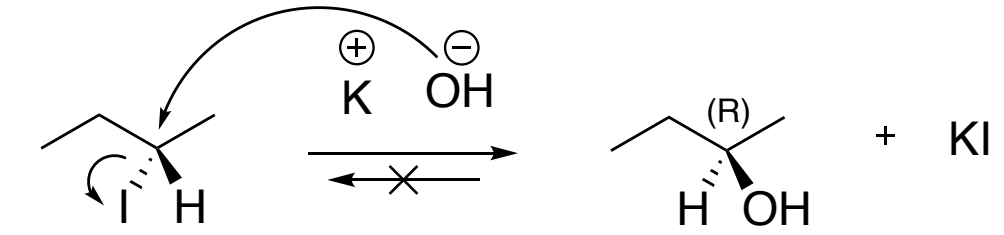
Reverse reaction will not occur.
OH^- is a terrible leaving group
- **Rate**: Depends on concentration

- Inversion of configuration (**Walden inversion)**
- **Concerted**: The bonds of the starting material break at the same time as the product bonds form.
- **Stereospecific**: stereochemistry of the starting material determines the stereochemistry of the product.
- Works for $CH_3–X$, $R–CH_2X$, R_1R_2CHX.

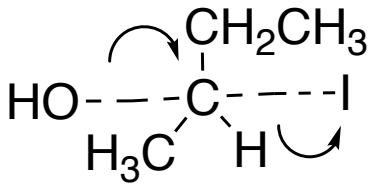


Another example of mechanism of S_N2 reaction

As such, the reaction below is not reversible:

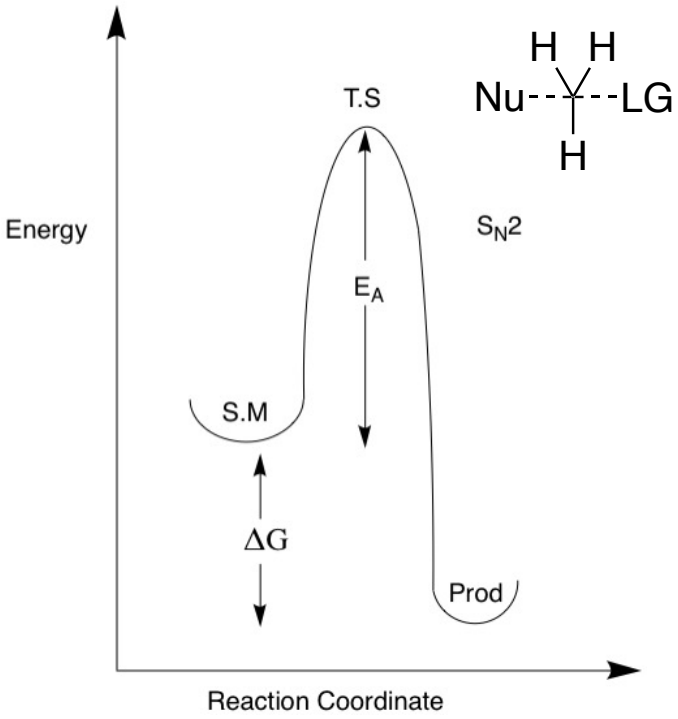


(S)-2-iodobutane inverison of stereochemistry



S_N2 always inverts stereochemistry
Favored conditions are with less steric bulk, primary best and secondary okay

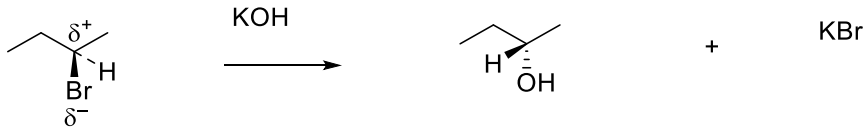
Energy Diagram of S_N2 Reaction



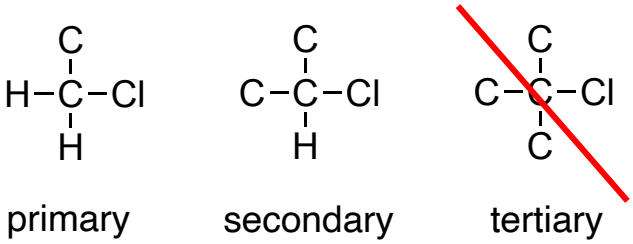
There is no intermediate in the S_N2 reaction, as it is concerted

Good Leaving Groups	Bad Leaving Groups
RSO_3^- > I^- > Br^- > Cl^- >> F^- (due to solvation)	H^-, R^- (alkyl), $^-NR_2$, ^-OR, ^-OH, F^-

HOH, HOR are okay leaving groups, but need to protonate with acid before it can leave



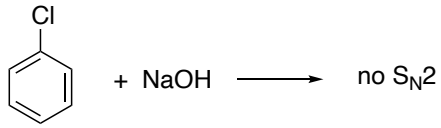
Leaving groups must be connected to a primary or secondary carbon (carbon that has at least one hydrogen, preferably 2)



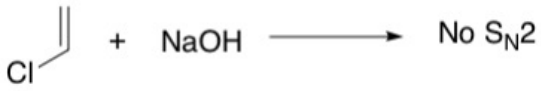
More examples of reactions that do not proceed via S_N2

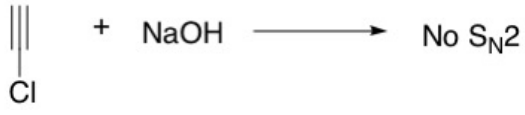
Example:

1)



2)

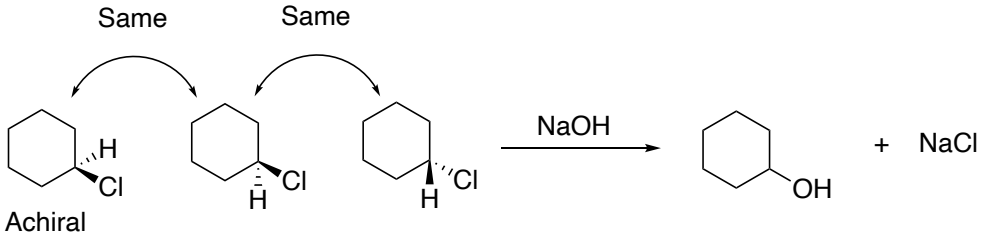




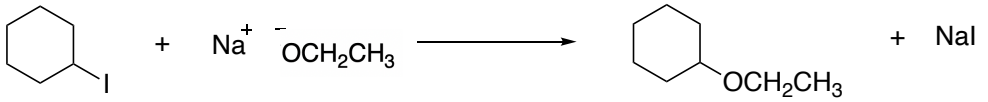
3)

Note: Methoxide (CH_3O^-) and hydroxide (^-OH) are bad leaving groups

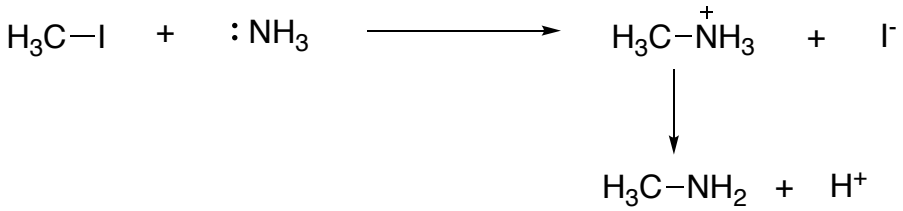
4)



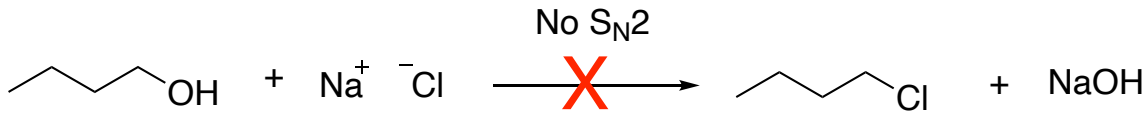
5)



6) Neutral leaving group containing lone pair

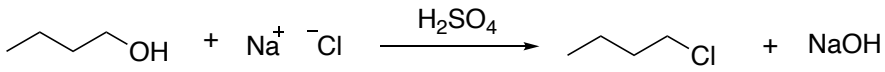


7)

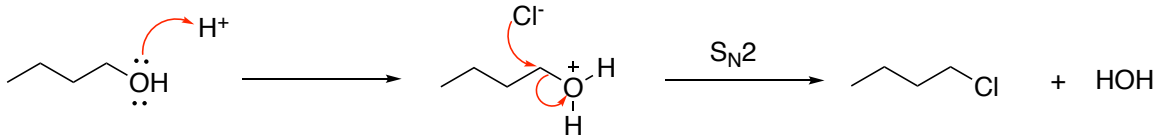


Note: OH is never a leaving group but if you add a strong acid or the reaction happen in a strongly acidic condition (see next example), the reaction will occur

8)

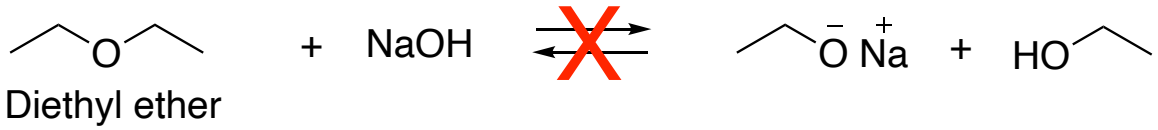


Mechanism:



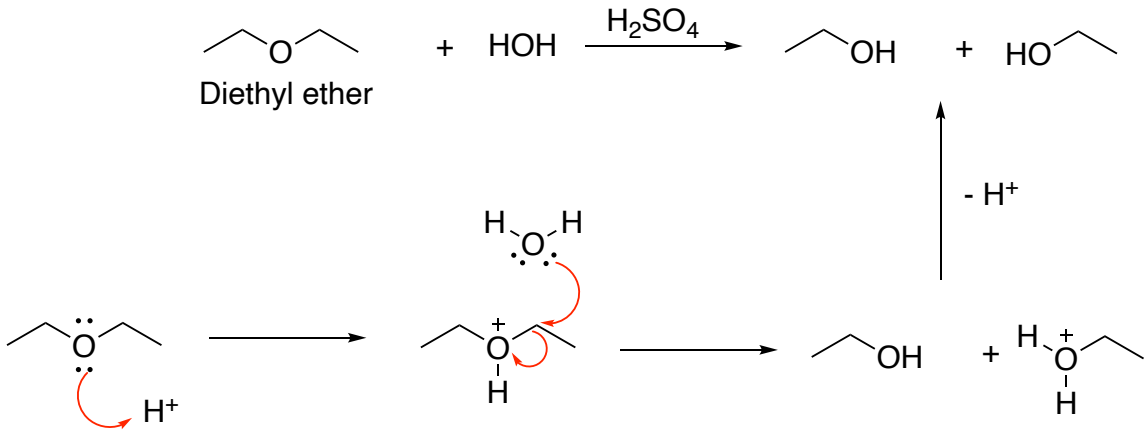
Note: The leaving group in this reaction is now HOH

9)

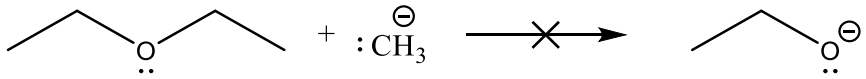


Note: Alkoxide ($^{-}$OR) or hydroxide ($^{-}$OH) are bad leaving group therefore no Sn2 reaction will occur on either direction. However, if the reaction happens in strongly acidic condition the reaction will occur. (see mechanism below)

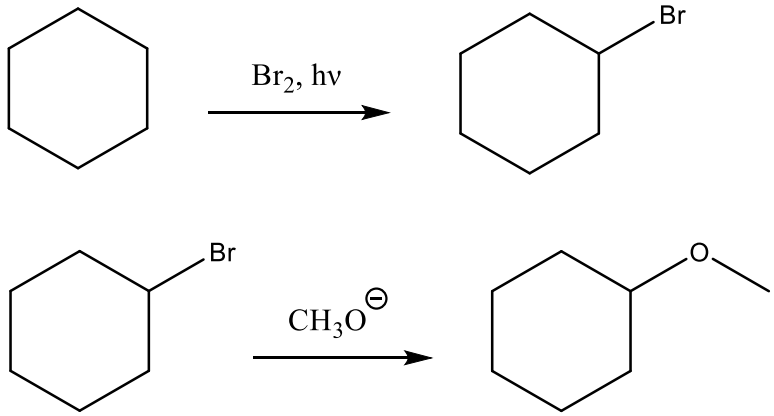
10)



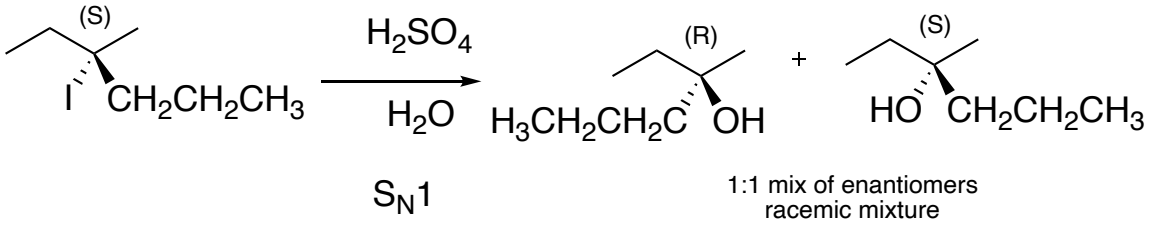
11)



12)



S_N1 Reaction:



Characteristics of S_N1 reactions:

- Stepwise
- Carbocation intermediates
- Rate dependent on concentration of substrate only
- Not stereospecific
- Favoured by heat or acid
- Works for 3° and sometimes 2° but never 1°