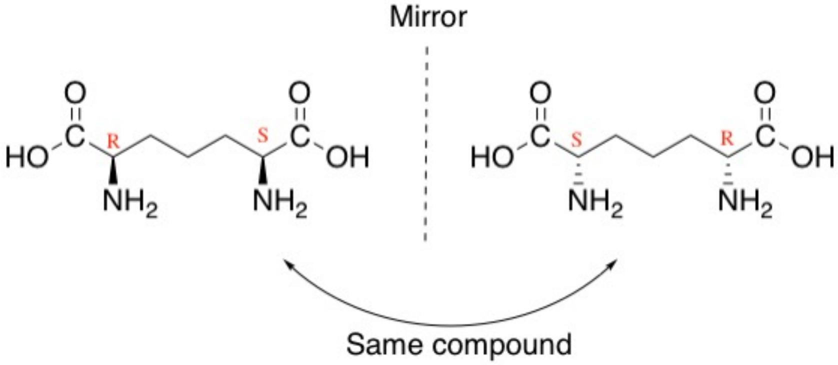
RECALL:

Identification of Chiral and Achiral (not chiral) compounds

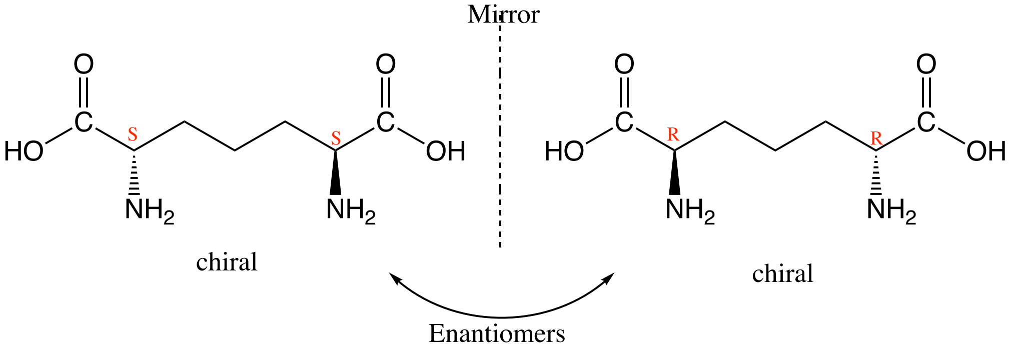
Example: Diaminopimelic acid



- The above molecule is achiral even though there are stereogenic center (s), because there is symmetry within the molecule
- These kinds of molecules are called **meso compounds,** which are compounds that contain stereocenters yet because of their symmetry, have mirror images that can be superimposed.

- All achiral molecules, including meso compounds do not rotate polarized light (i.e. $[\alpha]_D = 0$)

- Diaminopimelic acid - a component of bacterial cell wall and biosynthetic precursor to the amino acid known as lysine
- this R,S diaminopimelic acid (above) is a diastereomer of the enantiomers (S,S or R,R diaminopimelic acid) below:

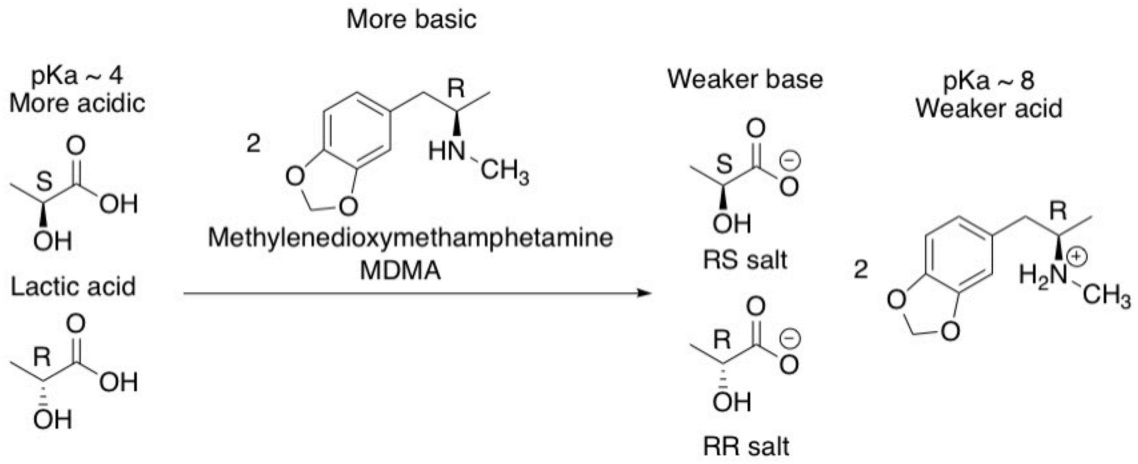


A racemic mixture (racemate) of two enantiomers in a 1:1 ratio also has an $[\alpha]_D = 0$

Resolution of Enantiomers

Definition: separation of two enantiomers

- Requires a chiral reagent



The starting material lactic acids are enantiomers of each other.
By reacting enantiomers to make a salt with an enantiomer of MDMA (another chiral molecule), one can obtain salts which are now diastereomers of each other (RS and RR). The resulting diastereomers have different melting points, boiling points, solubilities, and can be separated by crystallization.

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Substitution Reactions

<u>Remember:</u> Radical Substitution

$$\text{R-H} \quad + \quad X_2 \xrightarrow{\text{light}} \text{R-X} \quad + \quad \text{H-X}$$

Proceeds by a radical mechanism

Alkane

X=F, Cl, Br
Not I

Alkyl Halide

<u>Ionic Substitution:</u>

$$\overset{\oplus}{M} \quad \overset{\ominus}{\text{Nu:}} \quad + \quad \text{R-X} \longrightarrow \text{Nu-R} \quad + \quad \overset{\ominus}{:X} \quad \overset{\oplus}{M}$$

Nucleophile
(Seeks positive charge)

Alkyl Halide

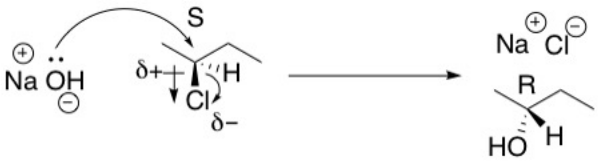
Nucleophile is a subtsnace that seeks positive charge

Types of Nucleophilic Substitution (S_N)

S_N1 - rate depends on 1 concentration

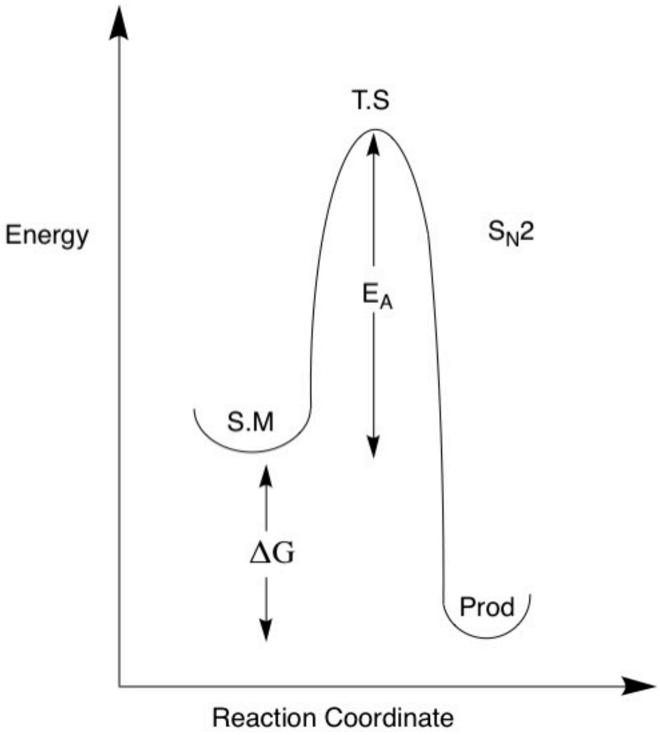
S_N2 - The rate is dependent on the concentration of the nucleophile and the nucleophile (2 concentrations)

Sn2 Mechanism



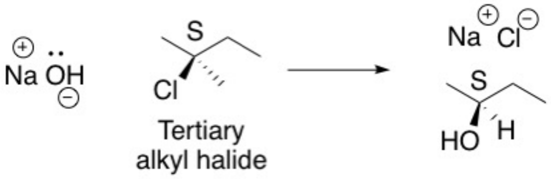
Reverse reaction will not occur.
- Inversion of configuration.
- **Concerted**: The bonds of the starting material break at the same time that the product bonds form.
- **Stereospecific**: stereochemistry of the starting material determines the stereochemistry of the product.

Energy Diagram of S_N2 Reaction



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

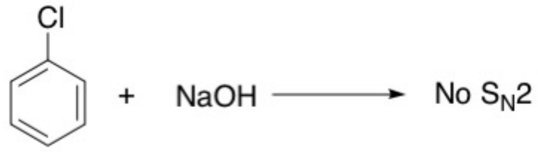
S_N1

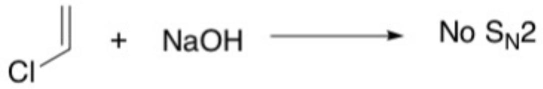


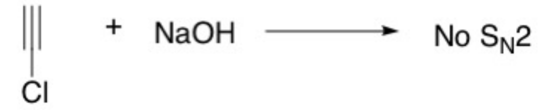
Reaction goes by an S_N1 mechanism as the nucleophile is not able to attack at the electrophilic center due to the presence of bulky groups in tertiary (3º) alkyl halides

S_N2 requires 1º or 2º alkyl halides

S_N2 will **not** occur on carbon sites that have multiple bonds.







SUMMARY

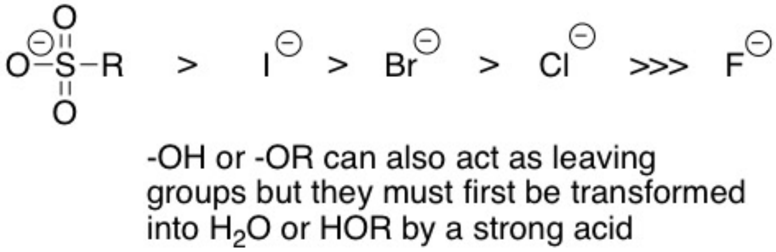
- S_N2 is stereospecific – proceeds with inversion of configuration (known as Walden inversion)
- Rate depends on two concentrations (bimolecular)
- Best if 1º halide, OK if 2º, Never on 3º, or C=C.

Never leaving groups: (negative charge not stabilized):

$F^{\ominus}$ $\overset{\ominus}{O}H$ $^{\ominus}OR$ $^{\ominus}NR_2$ $R:^{\ominus}$

Fluorine, though electronegative, is a bad leaving groups as it is small and poorly solvated.

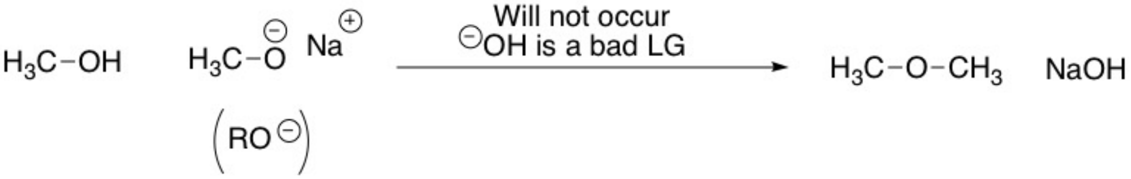
Good leaving groups



-OH or -OR can also act as leaving groups but they must first be transformed into H_2O or HOR by a strong acid

OH and OR can ONLY leave as water (HOH) or alcohol (HOR) never as anions

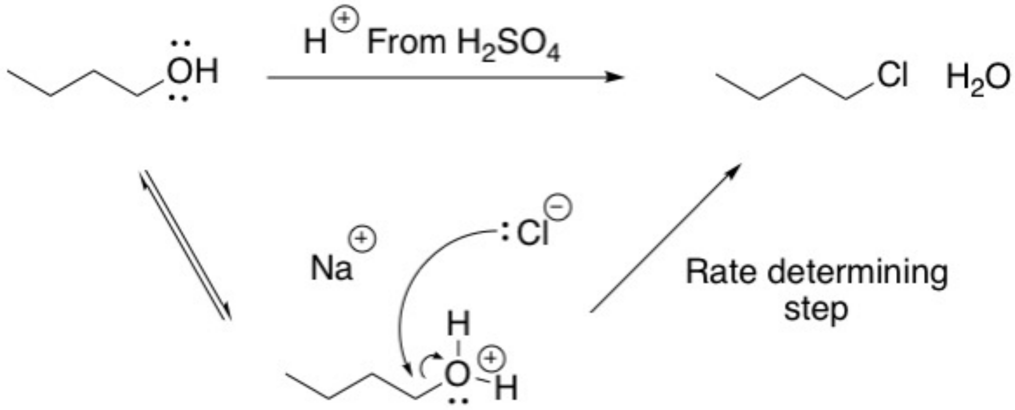
Example 1 (will not proceed to products)



- The reverse reaction will also not occur as $^{(-)}$OR is also a bad leaving group (LG).

Example 2 (will give products by S_N2 due to prior protonatgioon with HOH as leaving group)

Alcohols require an acid catalyst to transform them into a good leaving group (H_2O)



Examples 3 & 4 (S_N2 Reactions)

Top one has achiral starting material and gives achiral product

Bottom one has single diastereomer (trans-1-chloro-4-methylcyclohexane starting material is not chiral due to plane of symmetry within molecule). S_N2 Reaction gives inversion of configuration to produce single cis diastereomer (cis-4-methylcylohexan-1-ol ; you need not know how to name this yet)