Stereoisomeric 2,3-dihydroxybutanoic acids

Figure 7.9

Representation of (2R, 3R)-dihydroxybutanoic acid

Figure 7.10

The three stereoisomeric 2,3-butanediols shown in conformations used to generate Fischer projections

Figure 7.11

Meso-2, 3-butanediol

Figure 7.12

Stereogenic centers in cholic acid

Figure 7.13

Chapter 8 - Nucleophilic Substitution

Chapter 8

- **Definitions - nucleophile, electrophile, leaving group**
- **Functional Group Transformations using Nucleophiles**
- **Examples of Nucleophiles**
- **Properties of Leaving Groups**
- **The S_N2 reaction revisited**

Nucleophilic Substitution

<u>nucleophile</u> is a Lewis base (electron-pair donor)

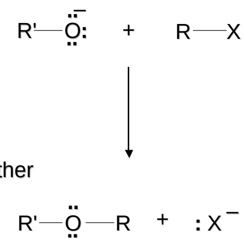
often negatively charged and used as
Na^+ or K^+ salt

substrate is usually an <u>alkyl halide</u>

Table 8.1 Examples of Nucleophilic Substitution

Alkoxide ion as the nucleophile

gives an ether



Example

$(CH_3)_2CHCH_2ONa$ + CH_3CH_2Br

↓ Isobutyl alcohol

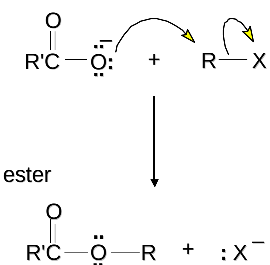
$(CH_3)_2CHCH_2OCH_2CH_3$ + NaBr

Ethyl isobutyl ether (66%)

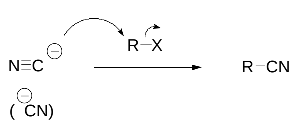
Table 8.1 Examples of Nucleophilic Substitution

Carboxylate ion as the nucleophile

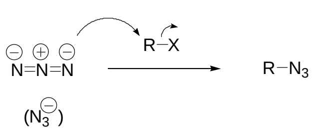
gives an ester



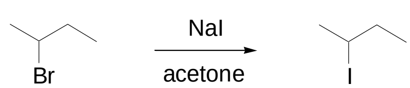
Cyanide as nucleophile



Azide as nucleophile



Halides as Nucleophiles



NaI is soluble in acetone, NaCl and NaBr are not

Halides are very good leaving groups:

I^- better than Br^- which is better than Cl^-

F^- is not used as a leaving group

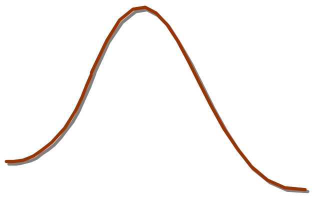
The S_N2 mechanism of Nucleophilic Substitution

Example:

$CH_3Br + HO^- \longrightarrow CH_3OH + Br^-$

rate = $k[CH_3Br][HO^-]$

inference: rate-determining step is bimolecular



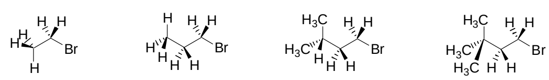
Orbital description of nucleophilic substitution by the S_N2 mechanism

Figure 8.2

Steric hindrance effects on rates of bimolecular nucleophilic substitution (S_N2) reactions

Figure 8.3

Table 8.3 - Relative rates of reaction of different primary alkyl bromides



ethyl bromide	propyl bromide	isobutyl bromide	neopentyl bromide
1.0	0.8	0.036	0.00002

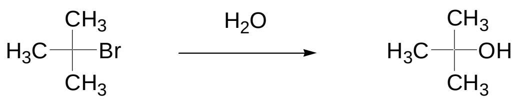
Table 8.4 - discussion of relative nucleophilicity

Solvation of a chloride by ion-dipole

Figure 8.4

Choice of solvent is important for S_N2 - polar aprotic used often

The S_N1 reaction revisited



Tertiary system - favours S_N1 - carbocation possible

Carbocation will be the electrophile

Water will be the nucleophile

Energy diagram for nucleophilic substitution by the S_N1 mechanism

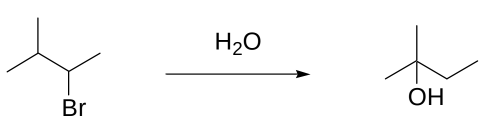
Figure 8.6

Relative rates of reaction by the S_N1 pathway

Table 8.5

Formation of a racemic product - Figure 8.7

Carbocation rearrangements also possible



Look for change in the product skeleton.

Rearrangement (in this case hydride shift) to generate a more stable carbocation.

Choice of solvent important

More polar solvents (higher dielectric constant) will help stabilize the ionic intermediates.

Substitution vs. Elimination - Figure 8.11

Sulfonate esters as leaving groups