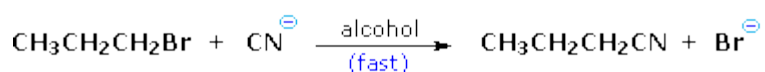


The Variables of Organic Reactions

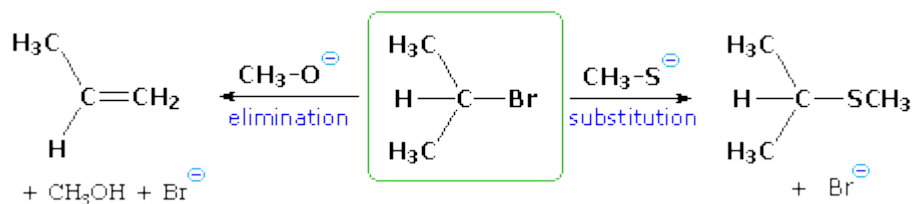
In an effort to understand how and why reactions of functional groups take place in the way they do, chemists try to discover just how different molecules and ions interact with each other as they come together. To this end, **it is important to consider the various properties and characteristics of a reaction that may be observed and/or measured as the reaction proceeds**. The most common and useful of these are listed below:

1. Reactants and Reagents

A. Reactant Structure: Variations in the structure of the reactant may have a marked influence on the course of a reaction, even though the functional group is unchanged. Thus, reaction of 1-bromopropane with sodium cyanide proceeds smoothly to yield butanenitrile, whereas 1-bromo-2,2-dimethylpropane fails to give any product and is recovered unchanged. In contrast, both alkyl bromides form Grignard reagents (RMgBr) on reaction with magnesium.



B. Reagent Characteristics: Apparently minor changes in a reagent may lead to a significant change in the course of a reaction. For example, 2-bromopropane gives a substitution reaction with sodium methylthiolate but undergoes predominant elimination on treatment with sodium methoxide.



2. Product Selectivity

A. Regioselectivity: It is often the case that addition and elimination reactions may, in principle, proceed to more than one product. Thus 1-butene might add HBr to give either 1-bromobutane or 2-bromobutane, depending on which carbon of the double bond receives the hydrogen and which the bromine. If one possible product out of two or more is formed preferentially, the reaction is said to be regioselective.



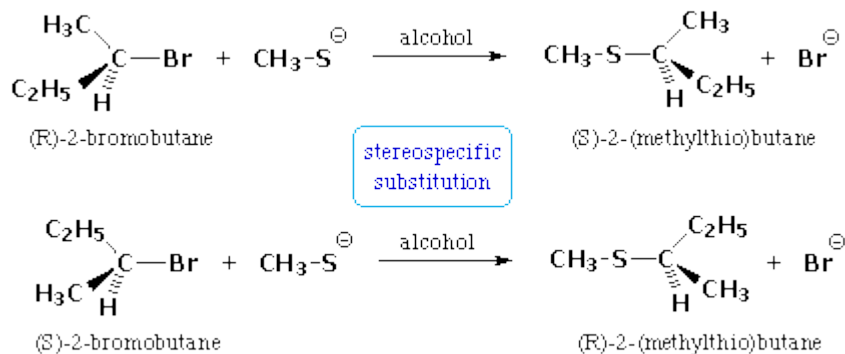
Simple substitution reactions are not normally considered regioselective, since by definition only one constitutional product is possible. However, rearrangements are known to occur during some reactions.

B. Stereoselectivity: If the reaction products are such that stereoisomers may be formed, a reaction that yields one stereoisomer preferentially is said to be stereoselective. In the addition of bromine to cyclohexene, for example, *cis* and *trans*-1,2-dibromocyclohexane are both possible products of the addition. Since the *trans*-isomer is the only isolated product, this reaction is stereoselective.



C. Stereospecificity: This term is applied to cases in which stereoisomeric reactants behave differently in a given reaction. Examples include:

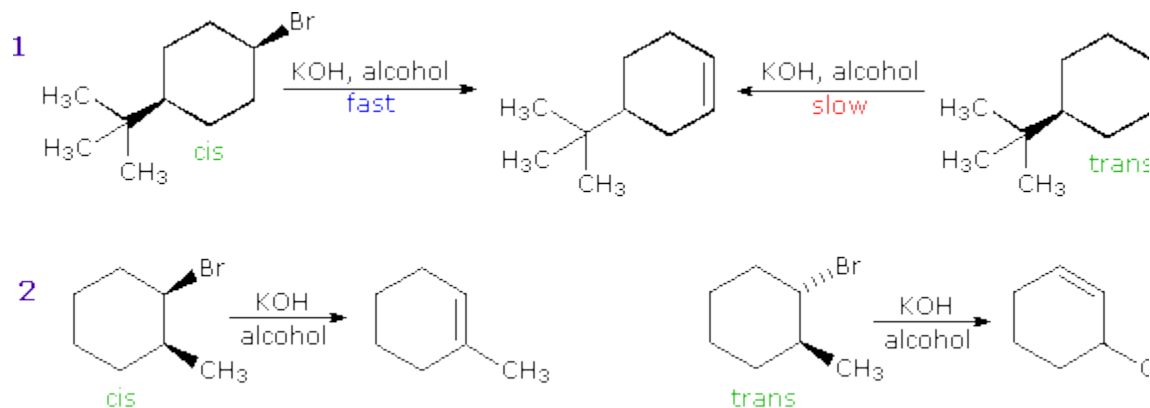
(i) Formation of different stereoisomeric products, as in the reaction of enantiomeric 2-bromobutane isomers with sodium methylthiolate, shown in the following diagram.



Here, the (R)-reactant gives the configurationally inverted (S)-product, and (S)-reactant produces (R)-product. The (R) and (S) notations for configuration are described in a [later section](#) of this text.

(ii) Different rates of reaction, as in the base-induced elimination of *cis* & *trans*-4-tert-butylcyclohexyl bromide (equation 1 below).

(iii) Different reaction paths leading to different products, as in the base-induced elimination of *cis* & *trans*-2-methylcyclohexyl bromide (equation 2 below).



The mechanisms of these substitution and elimination reactions are discussed in the alkyl halide section of this text.

3. Reaction Characteristics

A. Reaction Rates: Some reactions proceed very rapidly, and some so slowly that they are not normally observed. Among the variables that influence reaction rates are temperature (reactions are usually faster at a higher temperature), solvent, and reactant / reagent concentrations. Useful information about reaction mechanisms may be obtained by studying the manner in which the rate of a reaction changes as the concentrations of the reactant and reagents are varied. This field of study is called **kinetics**.

B. Intermediates: Many reactions proceed in a stepwise fashion. This can be convincingly demonstrated if an intermediate species can be isolated and shown to proceed to the same products under the reaction conditions. Some intermediates are stable compounds in their own right; however, some are so reactive that isolation is not possible. Nevertheless, evidence for their existence may be obtained by other means, including spectroscopic observation or inference from kinetic results.

4. Factors that Influence Reactions

It is helpful to identify some general features of a reaction that have a significant influence on its facility. Some of the most important of these are:

A. Energetics: The potential energy of a reacting system changes as the reaction progresses. The overall change may be **exothermic** (energy is released) or **endothermic** (energy must be added), and there is usually an **activation energy** requirement as well. Tables of Standard Bond Energies are widely used by chemists for estimating the energy change in a proposed reaction. As a rule, compounds constructed of strong covalent bonds are more stable than compounds incorporating one or more relatively weak bonds.

B. Electronic Effects: The distribution of electrons at sites of reaction (functional groups) is a particularly important factor. Electron deficient species or groups, which may or may not be positively charged, are attracted to electron rich species or groups, which may or may not be negatively charged. We refer to these species as **electrophiles & nucleophiles** respectively. In

general, *opposites attract and like repel*.

The charge distribution in a molecule is usually discussed with respect to two interacting effects: An **inductive effect**, which is a function of the electronegativity differences that exist between atoms (and groups); and a **resonance effect**, in which electrons move in a discontinuous fashion between parts of a molecule.

C. Steric Effects: Atoms occupy space. When they are crowded together, van der Waals repulsions produce an unfavorable **steric hindrance**. Steric hindrance may influence conformational equilibria, as well as destabilizing transition states of reactions.

D. Stereoelectronic Effects: In many reactions atomic or molecular orbitals interact in a manner that has an optimal configurational or geometrical alignment. Departure from this alignment inhibits the reaction.

E. Solvent Effects: Most reactions are conducted in solution, not in a gaseous state. The solvent selected for a given reaction may exert a strong influence on its course. Remember, solvents are chemicals, and most undergo chemical reaction under the right conditions.

Source : <http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/react1.htm#rx2>