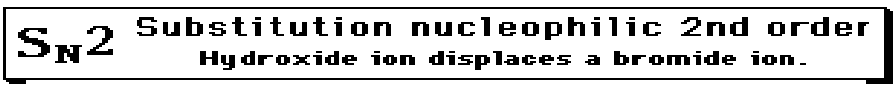
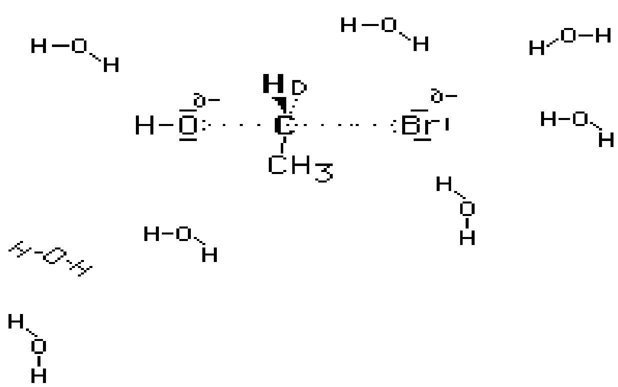
Dr. Peter Wipf

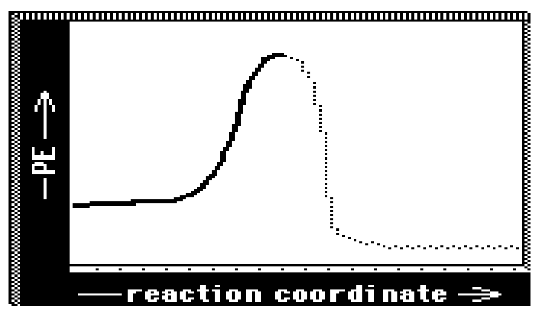
Chemistry 0310 - Organic Chemistry 1

Chapter 6. S_N2 Reactions

Nucleophilic substitution reactions occur when nucleophiles (electron-rich species) displace leaving groups on electrophiles (electron-poor species). The net result is the substitution of one group for another bonded to a carbon atom. Nucleophilicity is increased by a negative charge and an increase in the polarizability. The greater the size and the lower the electronegativity of an atom, the greater its polarizability. Leaving groups are stable species that can be detached with their bonding electrons from a molecule during reaction. Most good leaving groups are the conjugate bases of strong acids. Sulfonates (mesylates, tosylates, triflates, etc.) are popular leaving groups since they can be readily obtained from alcohols. Solvents also influence nucleophilicity.



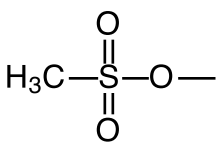
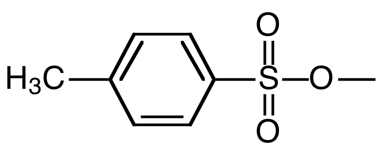
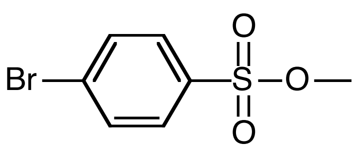
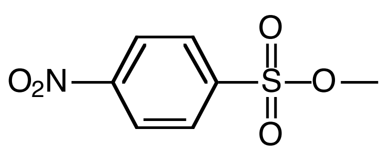
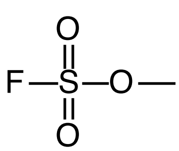
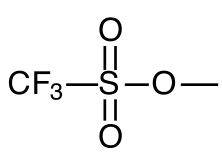
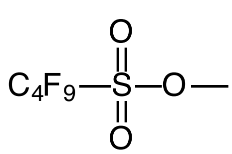




S_N2 reactions are second-order reactions whose rates depend o the concentration of both the alkyl halide and the nucleophile. The transition state of the one-step S_N2 process involves a trigonal bipyramidal carbon and results in an overall inversion of configuration. The order of reactivity of alkyl halides and alkyl sulfonates in S_N2 reactions is CH_3>1°>2°>3°.

The activation energy, $\Delta G^{\ddagger}$, determines the rate of a reaction: $k = k_o \exp(-\Delta G^{\ddagger}/RT)$. The overall change in free energy, ΔG, determines the position of the thermodynamic equilibrium. A positive sign of ΔG is characteristic for an endergonic reaction, a negative ΔG is found for an exergonic process. The rate of a reaction can be measured and provides information about its mechanism. The reaction order is the sum of the exponents in the rate equation.

Relative Leaving Group Abilities:

Leaving Group	Common Name	k_{rel}
AcO	acetate	1×10^{-10}
Cl	chloride	0.0001
Br	bromide	0.001
I	iodide	0.01
	mesylate	1.00
	tosylate	0.70
	brosylate	2.62
	nosylate	13
	fluorosulfate	29,000
	triflate	56,000
	nonaflate	120,000