

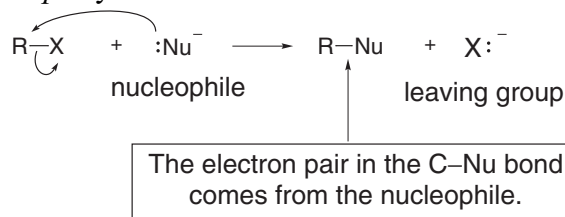
## Chapter 7: Alkyl Halides and Nucleophilic Substitution

## ◆ General facts about alkyl halides

- Alkyl halides contain a halogen atom X bonded to an  $sp^3$  hybridized carbon (7.1).
- Alkyl halides are named as halo alkanes, with the halogen as a substituent (7.2).
- Alkyl halides have a polar C–X bond, so they exhibit dipole-dipole interactions but are incapable of intermolecular hydrogen bonding (7.3).
- The polar C–X bond containing an electrophilic carbon makes alkyl halides reactive towards nucleophiles and bases (7.5).

## ◆ The central theme (7.6)

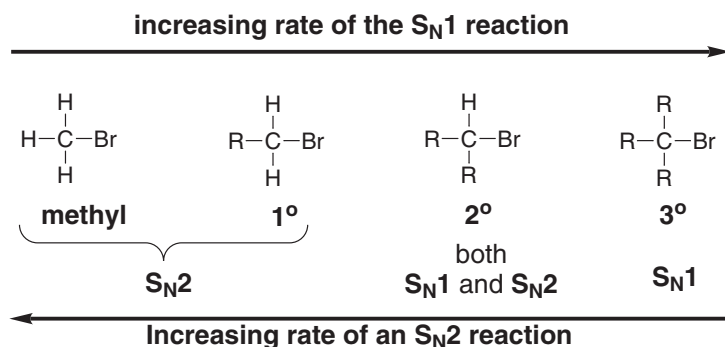
- Nucleophilic substitution is one of the two main reactions of alkyl halides. A nucleophile replaces a leaving group on an  $sp^3$  hybridized carbon.



- One  $\sigma$  bond is broken and one  $\sigma$  bond is formed.
- There are two possible mechanisms:  $S_N1$  and  $S_N2$ .

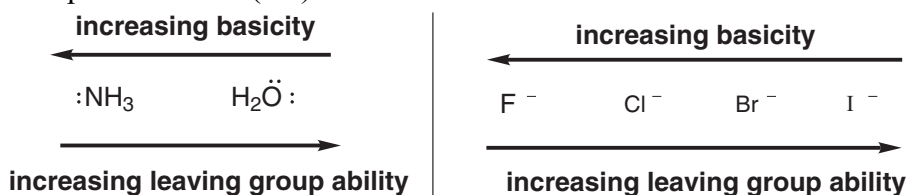
◆  $S_N1$  and  $S_N2$  mechanisms compared

	$S_N2$ mechanism	$S_N1$ mechanism
[1] Mechanism	• One step (7.11B)	• Two steps (7.13B)
[2] Alkyl halide	• Order of reactivity: $\text{CH}_3\text{X} > \text{RCH}_2\text{X} > \text{R}_2\text{CHX} > \text{R}_3\text{CX}$ (7.11D)	• Order of reactivity: $\text{R}_3\text{CX} > \text{R}_2\text{CHX} > \text{RCH}_2\text{X} > \text{CH}_3\text{X}$ (7.13D)
[3] Rate equation	• rate = $k[\text{RX}][\text{:Nu}^-]$ • second order kinetics (7.11A)	• rate = $k[\text{RX}]$ • first order kinetics (7.13A)
[4] Stereochemistry	• backside attack of the nucleophile (7.11C) • inversion of configuration at a stereogenic center	• trigonal planar carbocation intermediate (7.13C) • racemization at a stereogenic center
[5] Nucleophile	• favored by stronger nucleophiles (7.17B)	• favored by weaker nucleophiles (7.17B)
[6] Leaving group	• better leaving group $\rightarrow$ faster reaction (7.17C)	• better leaving group $\rightarrow$ faster reaction (7.17C)
[7] Solvent	• favored by polar aprotic solvents (7.17D)	• favored by polar protic solvents (7.17D)

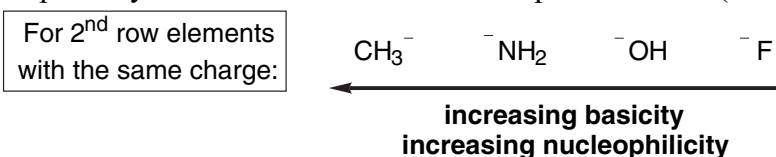


### ◆ Important trends

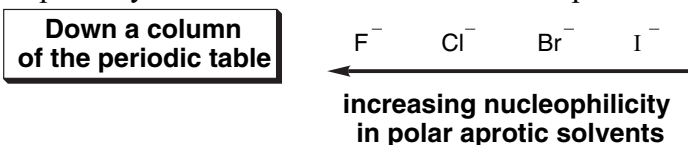
- The best leaving group is the weakest base. Leaving group ability increases across a row and down a column of the periodic table (7.7).



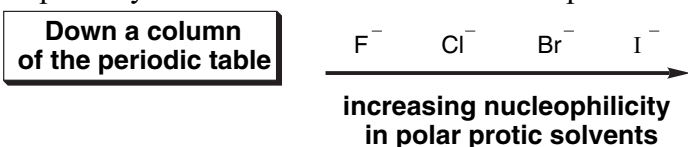
- Nucleophilicity decreases across a row of the periodic table (7.8A).



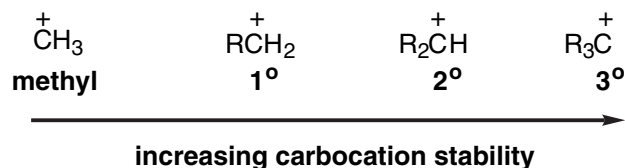
- Nucleophilicity decreases down a column of the periodic table in polar aprotic solvents (7.8C).



- Nucleophilicity increases down a column of the periodic table in polar protic solvents (7.8C).



- The stability of a carbocation increases as the number of R groups bonded to the positively charged carbon increases (7.14).



## ◆ Important principles

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Principle	Example
<ul style="list-style-type: none"><li>• Electron donating groups (such as R groups) stabilize a positive charge (7.14A).</li><li>• Steric hindrance decreases nucleophilicity but not basicity (7.8B).</li><li>• Hammond postulate: In an endothermic reaction, the more stable product is formed faster. In an exothermic reaction, this fact is not necessarily true (7.15).</li><li>• Planar, <math>sp^2</math> hybridized atoms react with reagents from both sides of the plane (7.13C).</li></ul>	<ul style="list-style-type: none"><li>• <math>3^\circ</math> Carbocations (<math>R_3C^+</math>) are more stable than <math>2^\circ</math> carbocations (<math>R_2CH^+</math>), which are more stable than <math>1^\circ</math> carbocations (<math>RCH_2^+</math>).</li><li>• <math>(CH_3)_3CO^-</math> is a stronger base but a weaker nucleophile than <math>CH_3CH_2O^-</math>.</li><li>• <math>S_N1</math> reactions are faster when more stable (more substituted) carbocations are formed, because the rate-determining step is endothermic.</li><li>• A trigonal planar carbocation reacts with nucleophiles from both sides of the plane.</li></ul>