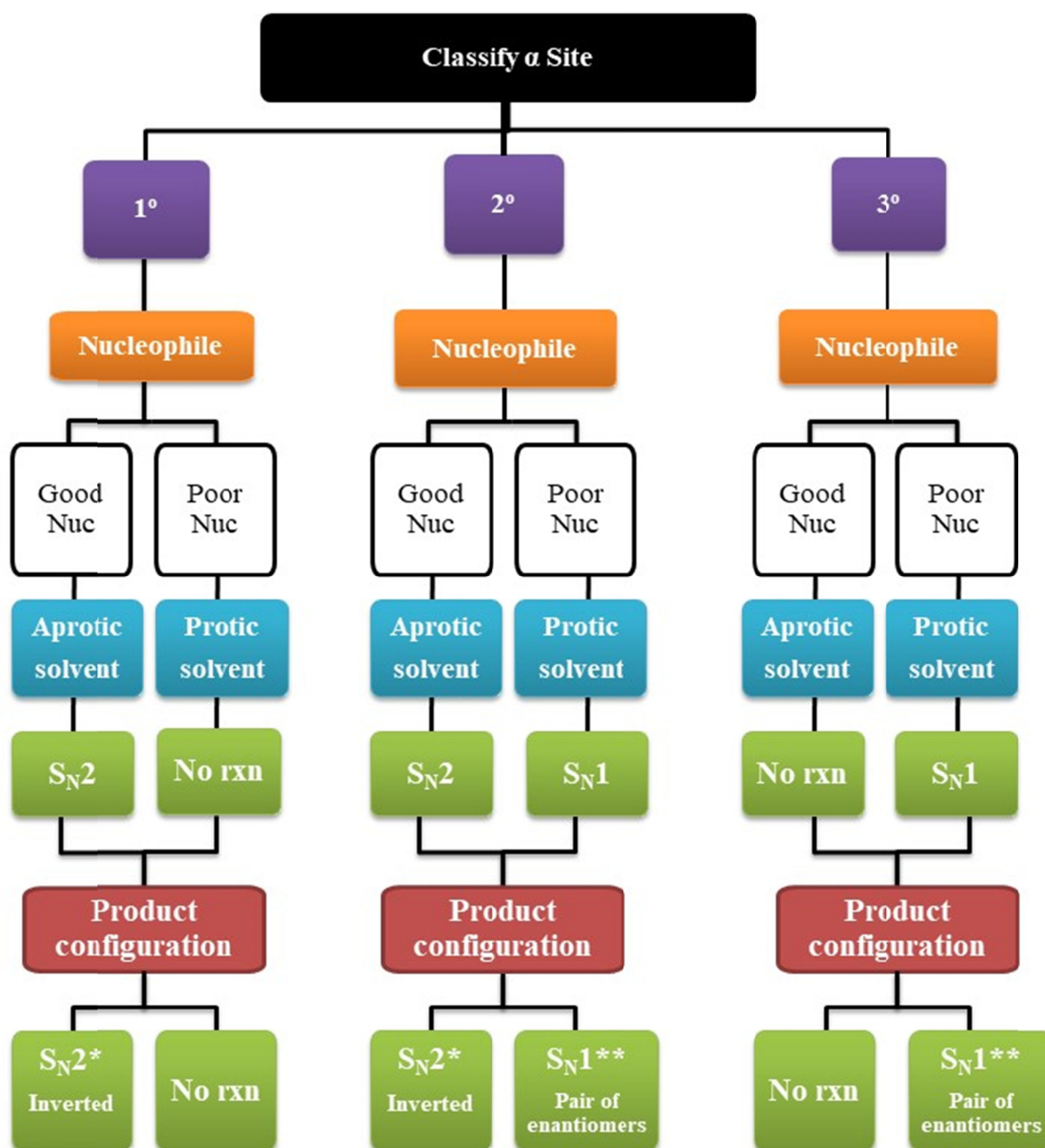


Supplementary Materials for “From Strawberry Fields to the Chemistry Classroom”

The purpose of the case study is to provide students with an engaging, group-discussion oriented resource for learning the substitution reactions of alkyl halides. The case study encourages students to mature their understanding of alkyl halides, reagents, the curved-arrow formalism, and to tone their verbal explanations. Participants had access to several handouts throughout the workshops to facilitate peer-to-peer dialogue. The handouts include:

- A flowchart that summarizes the factors that influence the substitution reactions of alkyl halides based on the classification of the α -site
- A mechanism template with examples of each type of reaction (S_N1 and S_N2)
- A chart depicting structures of strong and weak nucleophiles
- A chart depicting structures of protic and aprotic solvents

Flow chart depicting possible reaction pathways for substitution reactions of alkyl halides



* S_N2 : When the reaction occurs at a chiral center of a pure sample of a single enantiomer, a single enantiomer product with inversion of the chiral configuration is formed.

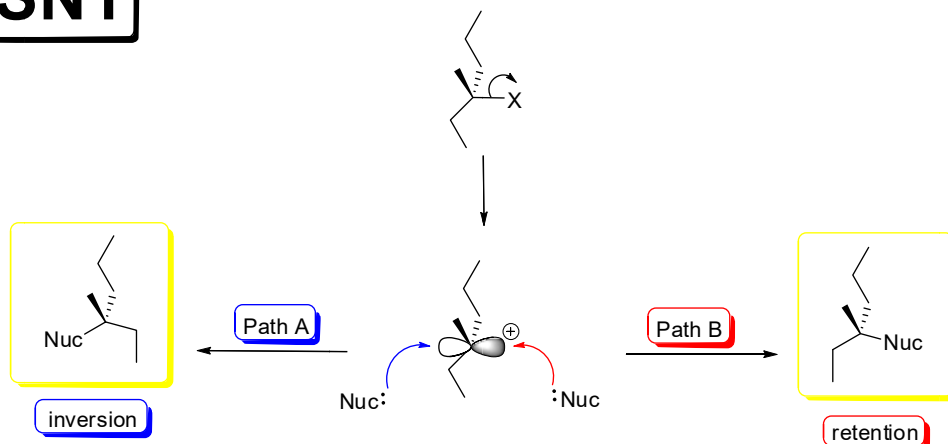
** If the leaving group in an S_N1 reaction is attached to a chiral center, a pair of enantiomers will be formed as products.

MECHANISM TEMPLATES (S_N1 and S_N2)

Nuc = Nucleophile

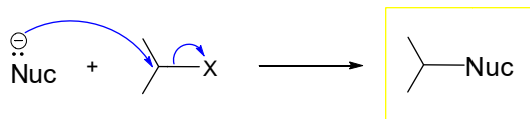
X = Leaving Group

SN1

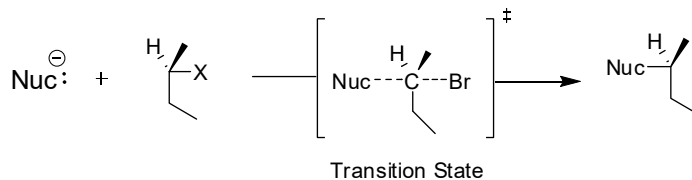


First, the carbon-halogen (C-X) bond breaks, forming a CARBOCATION intermediate. In the next step, the WEAK nucleophile attacks the carbocation to form the product. The nucleophile can approach the carbocation from either side of the plane and as a result a pair of enantiomers will be formed as products.

SN2



In ONE step the STRONG nucleophile attacks the alpha carbon - kicking off the leaving group, and forming the product.



The nucleophile attacks the carbon from the opposite side of the leaving group (back-side attack). The alkyl halide and the nucleophile come together in the transition state of the one-step reaction. When the starting material has a chiral center, a single enantiomer product with inversion of the chiral configuration is formed.

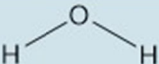
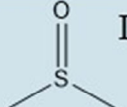
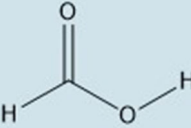
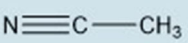
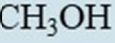
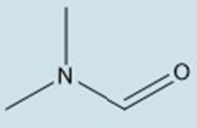
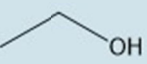
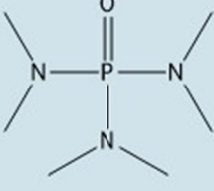


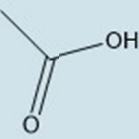
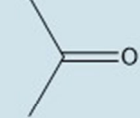
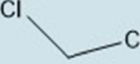

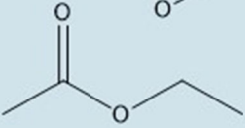
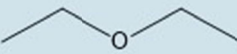
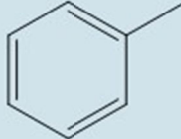
Generalized mechanisms of S_N1 and S_N2 reactions of alkyl halides.

Structures of good and weak nucleophiles

Strong/Weak Nucleophiles

STRONG (Negatively charged)	WEAK (Neutral)
$\text{CH}_3\ddot{\text{O}}:^{\ominus}$	$\text{CH}_3\ddot{\text{O}}\text{H}$
$:\text{C}\equiv\text{N}^{\ominus}$	$\text{H}-\ddot{\text{O}}-\text{H}$
$:\ddot{\text{O}}\text{H}^{\ominus}$	$\text{H}-\ddot{\text{S}}-\text{H}$
	$\text{CH}_3\text{CH}_2\ddot{\text{O}}\text{H}$
$\text{CH}_3\text{CH}_2\ddot{\text{O}}:^{\ominus}$	$\text{CH}_3\text{CH}_2\ddot{\text{N}}\text{H}_2$
$\text{>}\ddot{\text{N}}:^{\ominus}$	

Protic/Aprotic Solvents

PROTIC (Have N-H or O-H bonds)	APROTIC (No N-H or O-H bonds)
 <chem>H2O</chem>	 <chem>CS(=O)C</chem> Dimethyl Sulfoxide (DMSO)
 <chem>OC=O</chem> Formic Acid	 <chem>CC#N</chem> Acetonitrile
 <chem>CO</chem> Methanol	 <chem>CN(C)C=O</chem> Dimethyl Formamide (DMF)
 <chem>CCO</chem> Ethanol	 <chem>CN(C)P(=O)(N(C)C)N(C)C</chem> Hexamethylphosphoric Acid Triamide
 <chem>CC(C)(C)O</chem> <i>tert</i> -Butanol	 <chem>CCCCCC</chem> Hexane
 <chem>CC(=O)O</chem> Acetic Acid	 <chem>CC(=O)C</chem> Acetone
	 <chem>ClCCl</chem> Dichloromethane
	 <chem>C1CCOC1</chem> Tetrahydrofuran (THF)
	 <chem>CC(=O)OCC</chem> Ethyl Acetate (EtOAc)
	 <chem>CCOCC</chem> Diethyl Ether Et ₂ O
	 <chem>Cc1ccccc1</chem> Toluene