A GENERAL SUBSTITUTION REACTION

A GENERAL ELIMINATION REACTION

NUCLEOPHILES			ELECTROPHILES
Good	*Okay*	*Poor*	*Alkyl Halides, RX* (Not aryl or vinyl)
			Activated Alcohols, ROH_2, ROSCl, $ROPBr_2$, ROTos

Add these to your N&E list

LEAVING GROUP CONSIDERATIONS *(Same idea as considering the stability of a conjugate base)*	
Good leaving groups:	**Bad Leaving Groups** *(Not leaving groups)*
Bigger is better!	
Neutral or resonance-stabilized leaving groups are good.	

SOLVENTS	
Polar, aprotic	*Polar, protic*

SUBSTITUTION REACTIONS: S_N1 vs. S_N2

All of the following substitution reactions proceed as shown (there may be some elimination products as well, but we'll worry about that later). At first glance, the products of substitution reactions are the same whether they go by S_N1 or S_N2 mechanism but there are a couple factors that stand out. Use the following steps to determine whether the reaction occurred by S_N1 or S_N2 mechanism.

1. Substitution of the alkyl halide:

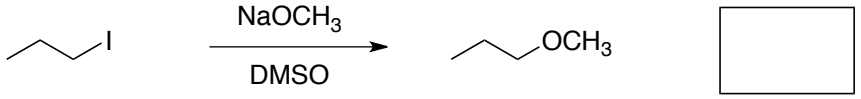
Methyl or primary alkyl halides proceed by S_N2.
Tertiary alkyl halides proceed by S_N1.
Secondary alkyl halides can go either way, depending on the solvent – go to step 2.

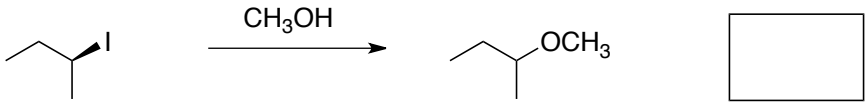
2. Solvent (skip unless secondary alkyl halide):

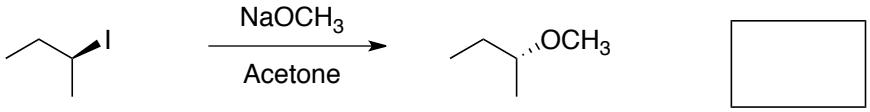
Aprotic solvents will favor S_N2.
Protic solvents will favor S_N1.

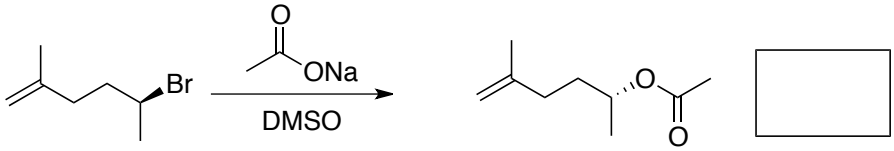
3. Stereochemistry:

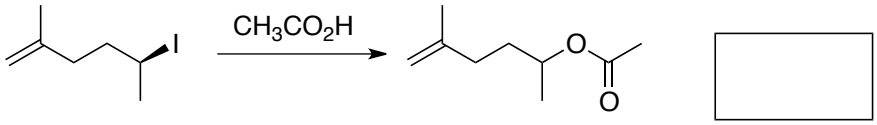
A single chiral product must have come from an S_N2 reaction.
A racemic mixture must have come from an S_N1 reaction.

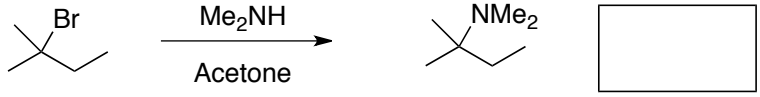
(1) 

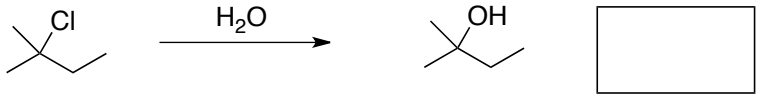
(2) 

(3) 

(4) 

(5) 

(6) 

(7) 

ELIMINATION REACTIONS: E1 vs. E2

The products of an elimination reaction, whether by E1 or E2, almost always look identical. The difference is that the E1 mechanism occurs with weak bases and the E2 mechanism occurs in the presence of strong bases. Also, there are stereochemical concerns in the E2 mechanism. Use the examples of weak and strong bases to determine the products of each reaction

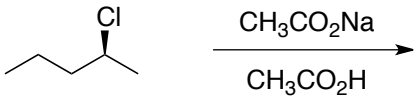
Strong bases (E2) – Alkoxides, Hydroxide

Weak bases (E1) – Water, Alcohols, Carboxylates

(1) 

(2) 

(3) 

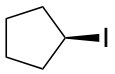
(4) 

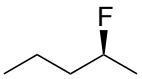
SUBSITUTION AND ELIMINATION REACTIONS:
S_N1 vs. S_N2 vs. E1 vs. E2 vs. NR

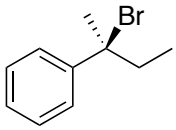
Below are reactions of alkyl halides with nucleophiles and/or bases. Some reactions will give only one product; others will give a mixture. Recall the specific conditions required for only one reaction mechanism to be favored (except for E1).

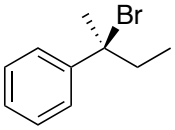
S_N1 – tertiary alkyl halide	E1 – (always a mixture with Substitution)
S_N2 – methyl alkyl halide	E2 – potassium *tert*-butoxide, KOt-Bu, $KOC(CH_3)_3$

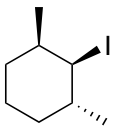
If any one of those conditions is not met (for example, a secondary alkyl halide), determine whether the reagent is a nucleophile (substitution), base (elimination), or both.
Look out for non-leaving groups!

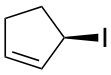
(1)  NaCl, Acetone (S_N2) →

(2)  KOt-Bu, t-BuOH →

(3)  CH_3OH →

(4)  $NaOCH_3$, CH_3OH →

(5)  KOt-Bu, t-BuOH →

(6)  HBr →

(7) CH_3I NaCl, Acetone →