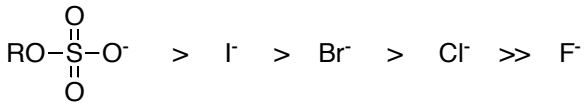
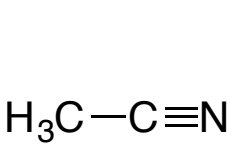
Nucleophilic Substitution Reactions

Good Leaving Groups

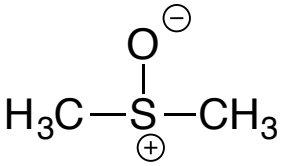


The order of halide leaving group ability is due to solvation and size.

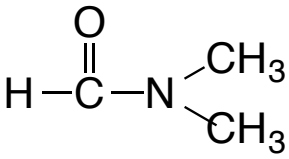
Polar aprotic solvents are good at assisting anion departure:



acetonitrile

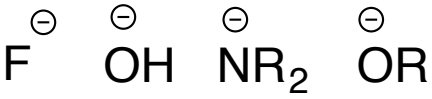


dimethyl sulfoxide
DMSO

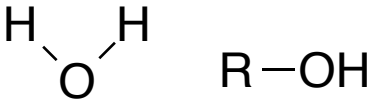


dimethyl formamide
DMF

WORST Leaving Groups

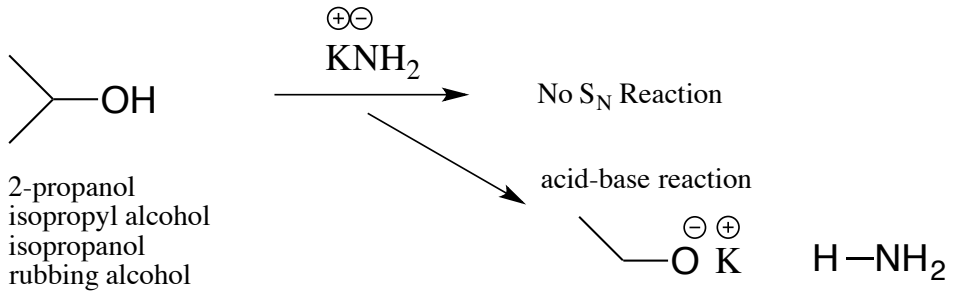


CAREFUL – Good Leaving Groups – ACID required



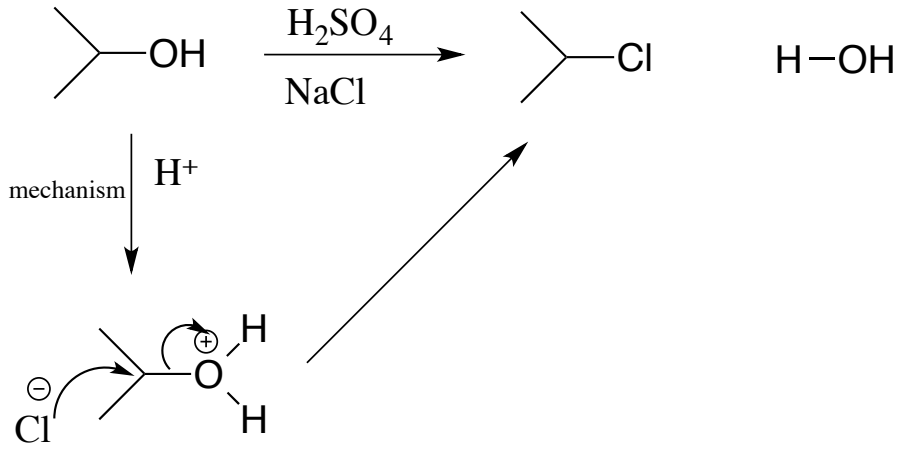
water alcohol

Example 1:

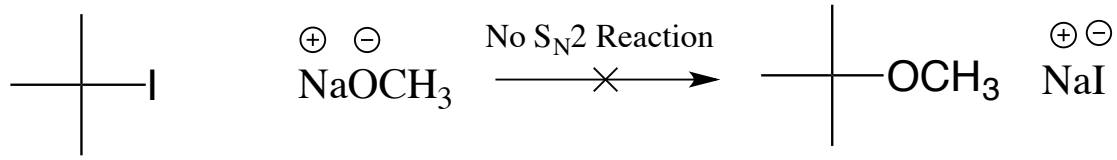


2-propanol
isopropyl alcohol
isopropanol
rubbing alcohol

BUT

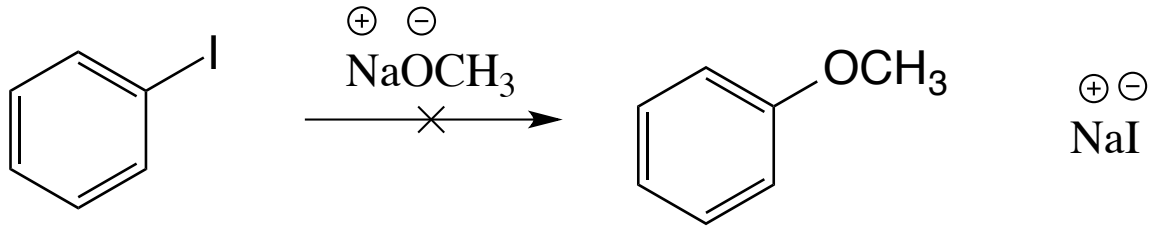


Example 2:



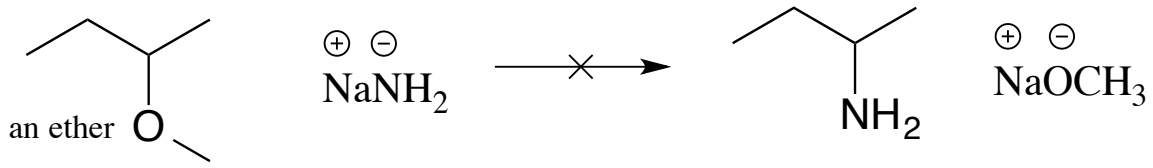
get E2 Rxn – alkene -No S_N2 reaction because the leaving group is attached to a 3° center

Example 3:



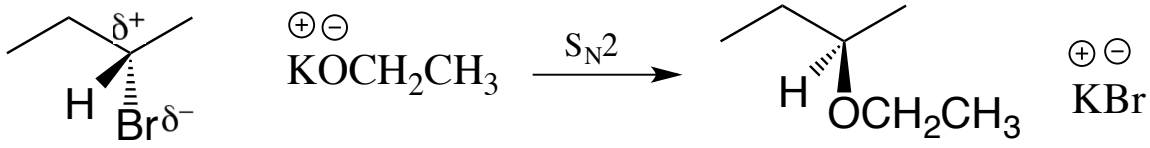
No product formed - No S_N2 reaction. C=C can't undergo Walden inversion.

Example 4:



No S_N2 reaction. Methoxide is a bad leaving group.

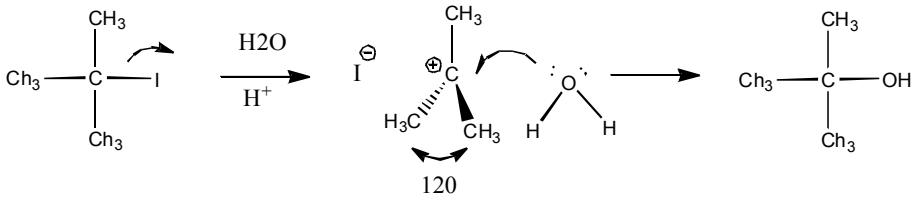
Example 5:



2° center. The more stable base (bromide) is produced. S_N2 proceeds with inversion of stereochemistry.

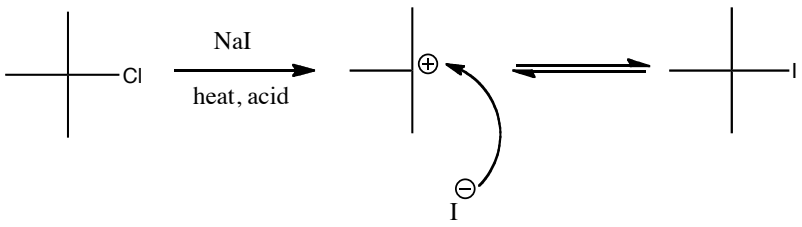
S_N1 Reactions - Substitution Nucleophilic Unimolecular

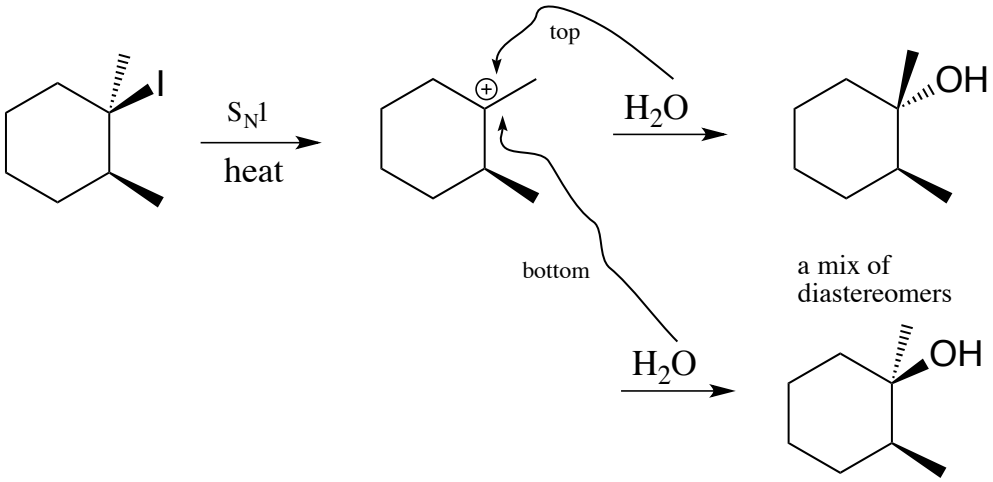
- Rate depends on 1 concentration
- Stepwise (not concerted)
- Carbocation intermediate
- Not stereospecific
- Favoured for 3° centres with leaving group. Acid favours.



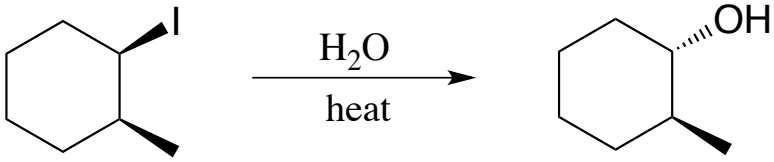
- Formation of the carbocation is slow → rate-determining step. Reaction of the carbocation with a nucleophile is fast.
- Intermediate is formed. 3 carbons attached to central carbon.
    - sp^2 hybridized, planar geometry. Loses any stereochemistry it had. Water can attack from above or below.

More examples:



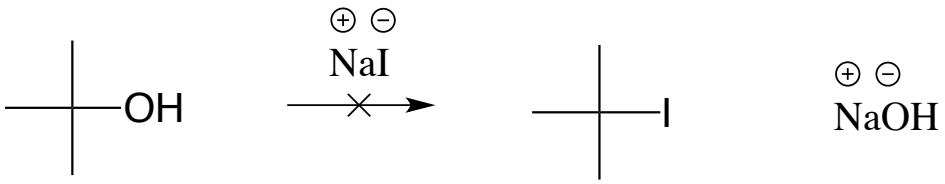


S_N1 or S_N2?



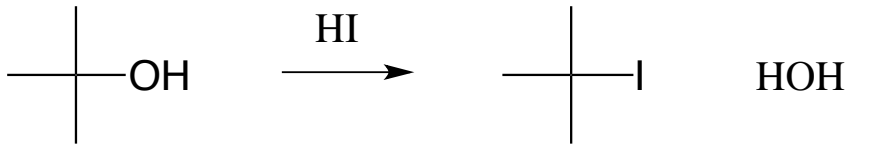
Substitution stereochemistry has inverted → S_N2

- No carbocation intermediate
- Rate depends on two concentrations



tert-butyl alcohol

No reaction. Hydroxide is a terrible leaving group.



H_2O is a good leaving group. 3° carbon → S_N1