ALIPHATIC NUCLEOPHILIC SUBSTITUTION REACTIONS

$$R\overset{\curvearrowright}{-}X \quad + \quad Y\!: \longrightarrow R-Y \quad + \quad X\!:$$

Types of Nucelophilic Substitution Reactions

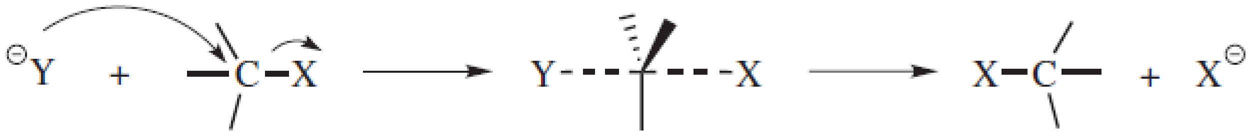
Type I $\quad R-I \quad + \quad OH^{-} \longrightarrow R-OH \quad + \quad I^{-}$

Type II $\quad R-I \quad + \quad NMe_3 \longrightarrow R-\overset{\oplus}{N}Me_3 \quad + \quad I^{-}$

Type III $\quad R-\overset{\oplus}{N}Me_3 \quad + \quad OH^{-} \longrightarrow R-OH \quad + \quad NMe_3$

Type IV $\quad R-\overset{\oplus}{N}Me_3 \quad + \quad H_2S \longrightarrow R-\overset{\oplus}{S}H_2 \quad + \quad NMe_3$

NUCLEOPHILIC SUBSTITUTION BIMOLECULAR REACTIONS (S_N2)



1. Kinetic Evidence

$$\text{Rate} = k[\text{RX}][\text{Y}]$$

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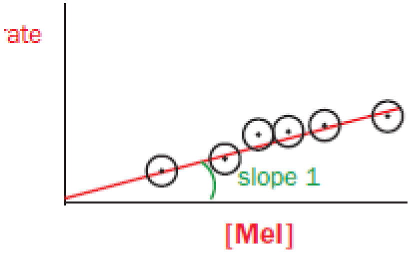
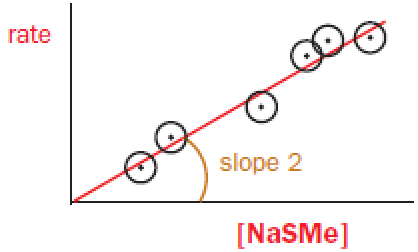
If nucleophile is in excess e.g. solvent (Pseudo-First Order Reaction)





rate = k_2[MeSNa][MeI]

If [MeSNa] is constant, the equation becomes

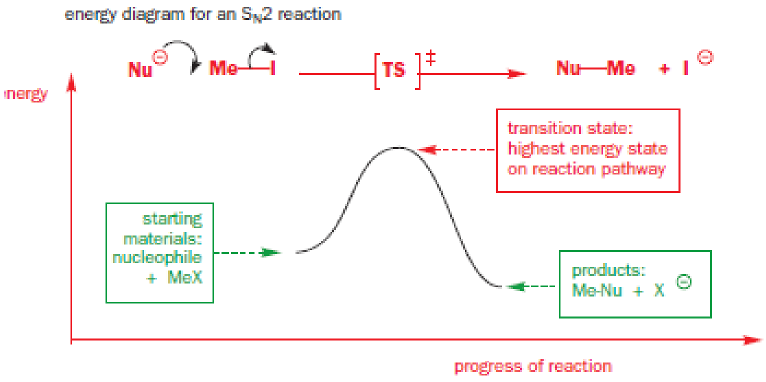
rate = k_a[MeI] where k_a = k_2[MeSNa]

If [MeI] is constant, the equation becomes

rate = k_b[MeSNa] where k_b = k_2[MeI]

If you examine the graphs you will see that the slopes are different because

slope 1 = k_a = k_2[MeSNa], but slope 2 = k_b = k_2[MeI]

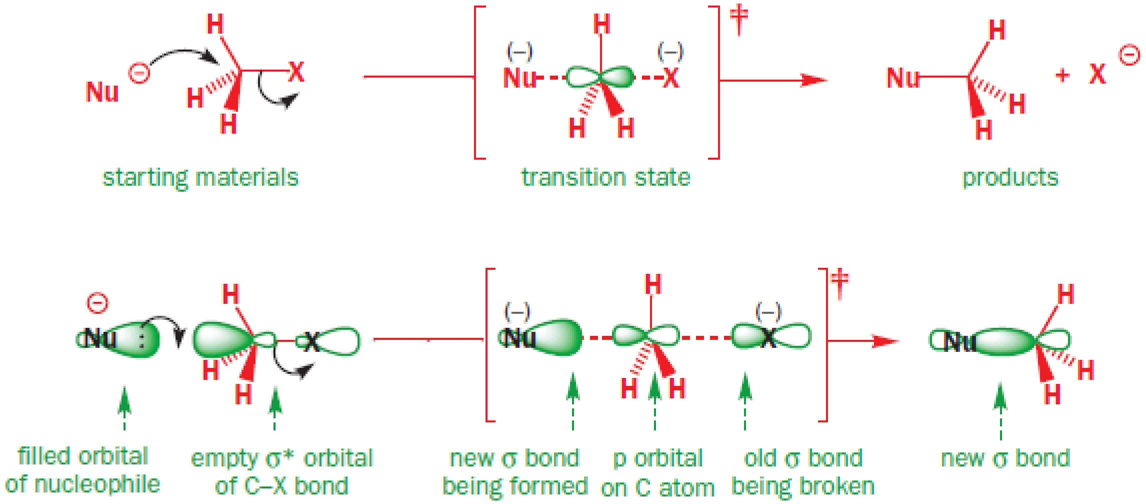


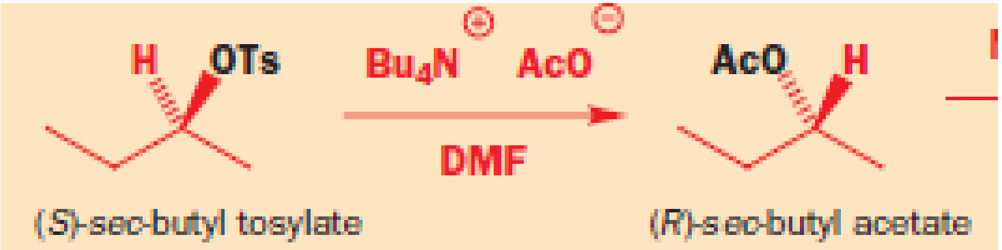
The rate of S_N2 reaction depends upon

(I) The nucelophile **(ii) The carbon skeleton (Structure of substrate)** **(iii) The leaving group**

2. Stereochemical Evidence

- *Inversion of Configuration occurs*

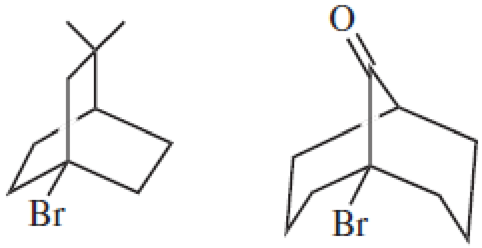




(*S*)-sec-butyl tosylate

(*R*)-sec-butyl acetate

3. S_N2 reactions cannot occur at bridgehead



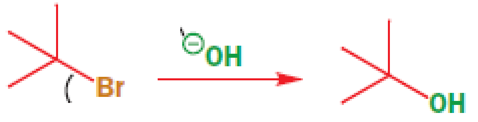
NUCLEOPHILIC SUBSTITUTION UNIMOLECULAR REACTIONS (S_N1)

Step 1 $$R{-}X \underset{}{\overset{\text{slow}}{\rightleftharpoons}} R^+ + X$$

Step 2 $$R^+ + Y \xrightarrow{\text{fast}} R{-}Y$$

1. Kinetic Evidence

$$\text{Rate} = k[\text{RX}]$$

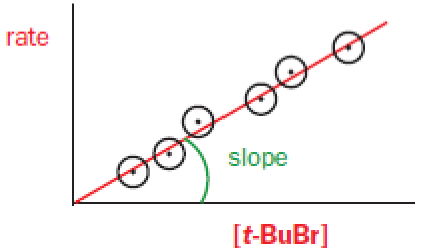


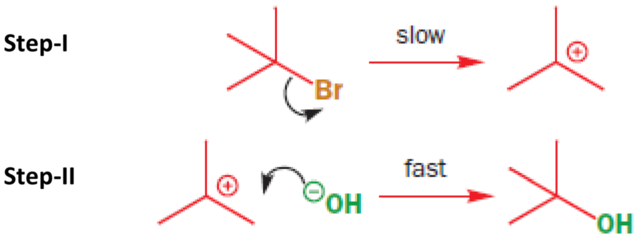
rate = k_1[*t*-BuBr]

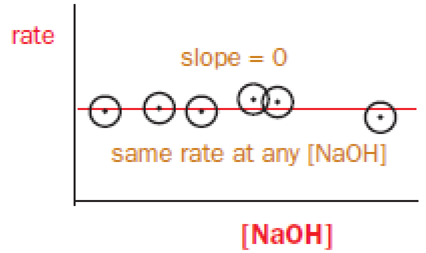
The rate of S_N1 reaction depends upon

(i) The carbon skeleton (Structure of substrate)

(ii) The leaving group







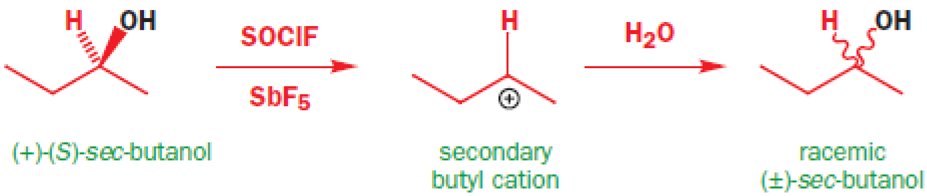
$$\text{RX} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{R}^+ + \text{X}$$

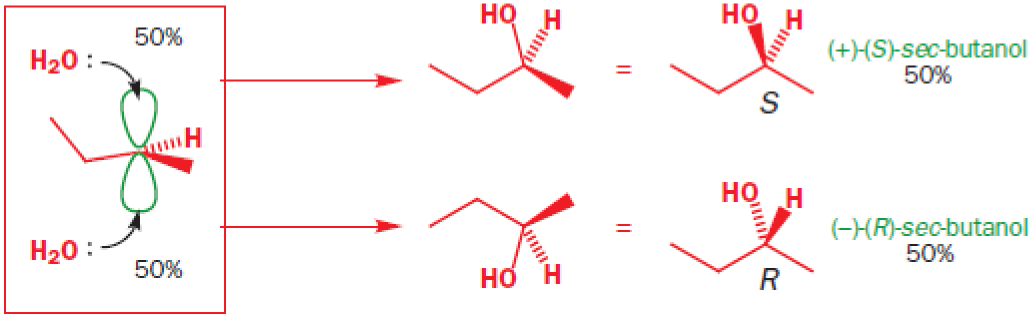
$$\text{R}^+ + \text{Y} \xrightarrow{k_2} \text{RY}$$

$$\text{Rate} = \frac{k_1 k_2 [\text{RX}][\text{Y}]}{k_{-1}[\text{X}] + k_2[\text{Y}]}$$

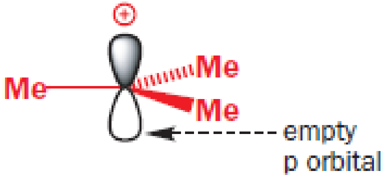
- If other than first step is the slow step then S_N1 reactions may show complex kinetics.
- The complex kinetics can be treated by Steady State Approximation for example.

2. Stereochemical Evidence





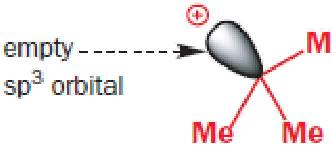
planar structure
for the *t*-butyl cation



correct

less repulsion between
bonding pairs of electrons

tetrahedral structure
for the *t*-butyl cation



incorrect

more repulsion between
bonding pairs of electrons

Ion Paris in S_N1 Mechanism

$$\mathrm{R{-}X} \rightleftharpoons \mathrm{R^+X^-} \rightleftharpoons \mathrm{R^+\|X^-} \rightleftharpoons \mathrm{R^+ + X^-}$$

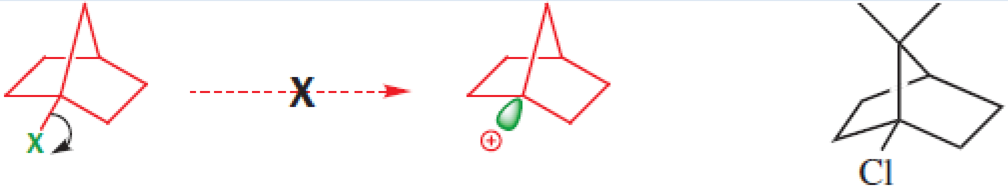
Contact ion pair

Solvent separated ion pair

Dissociated ion pair

- *Complete Racemization to Partial Racemization*

3. S_N1 reactions cannot occur at bridgehead



- *It is because carbocation is sp^2-hybridized and therefore must be planar. However, planarity cannot be achieved at bridgehead*

4. Mass Law Effect or Common Ion Effect

Step 1 $\quad R{-}X \overset{\text{slow}}{\rightleftharpoons} R^+ + \overset{-}{X}$

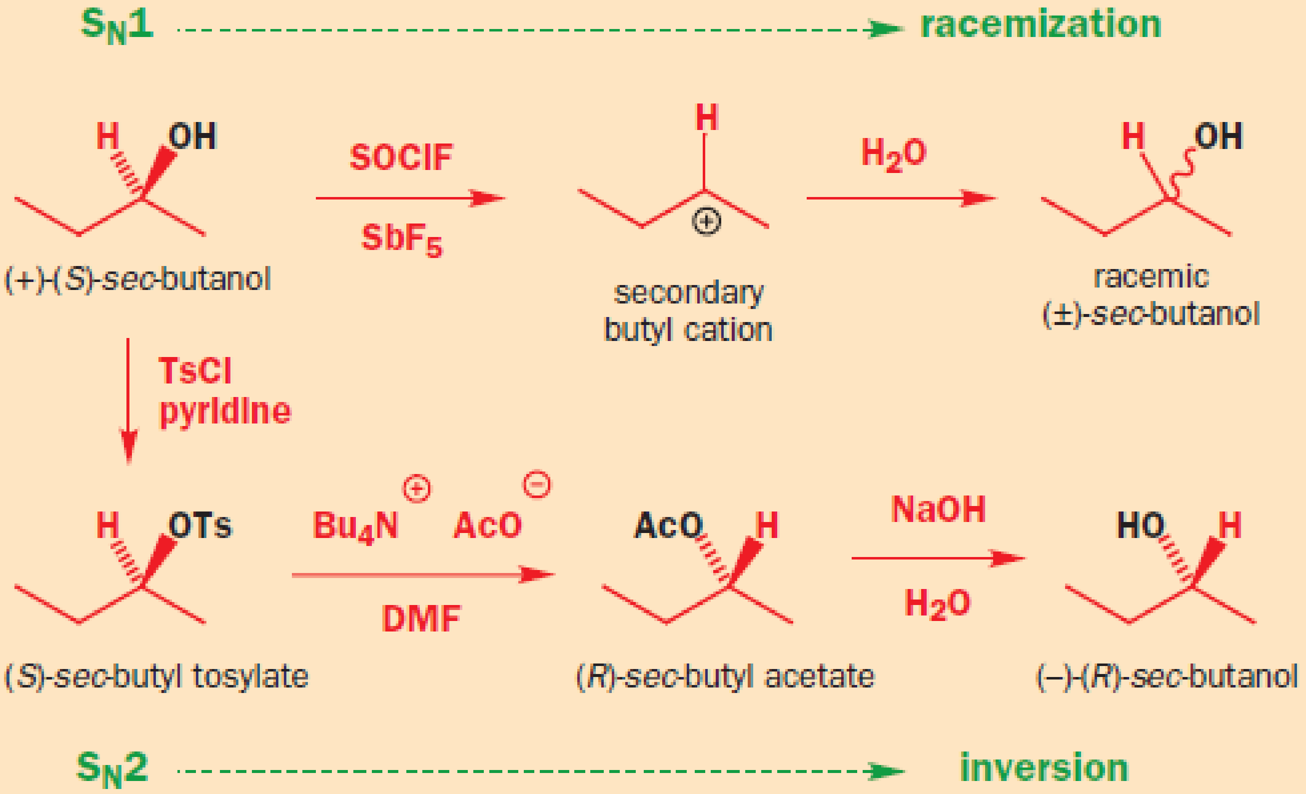
Step 2 $\quad R^+ + \overset{-}{Y} \xrightarrow{\text{fast}} R{-}Y$

- *Adding a salt having common ion, X^-, would push the first step in backward direction.*
- *Hence, the rate of S_N1 reaction will decrease.*

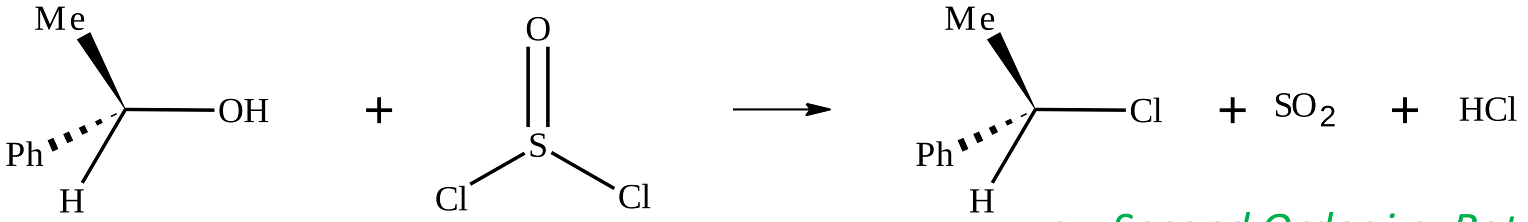
5. Salt Effect

- *Since polar ions are produced in this reaction, therefore, increase in polarity of solvent increases the rate of reaction.*
- *The ionic strength or the polarity of the medium can be increased by adding salts that don’t have common ion.*

- The S_N2 reaction goes with inversion of configuration at the carbon atom under attack but the S_N1 reaction generally goes with racemization

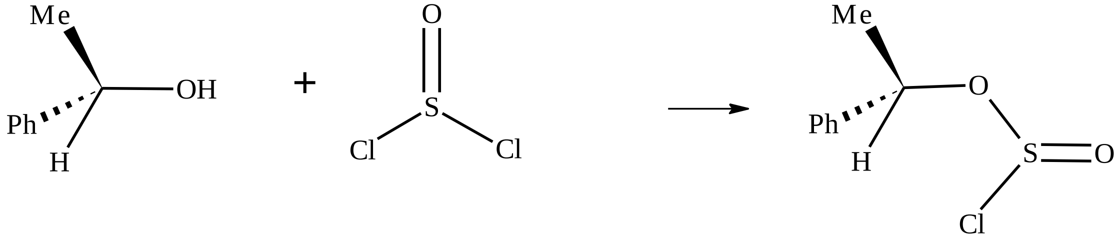


NUCLEOPHILIC SUBSTITUTION INTERNAL REACTIONS (S_Ni)

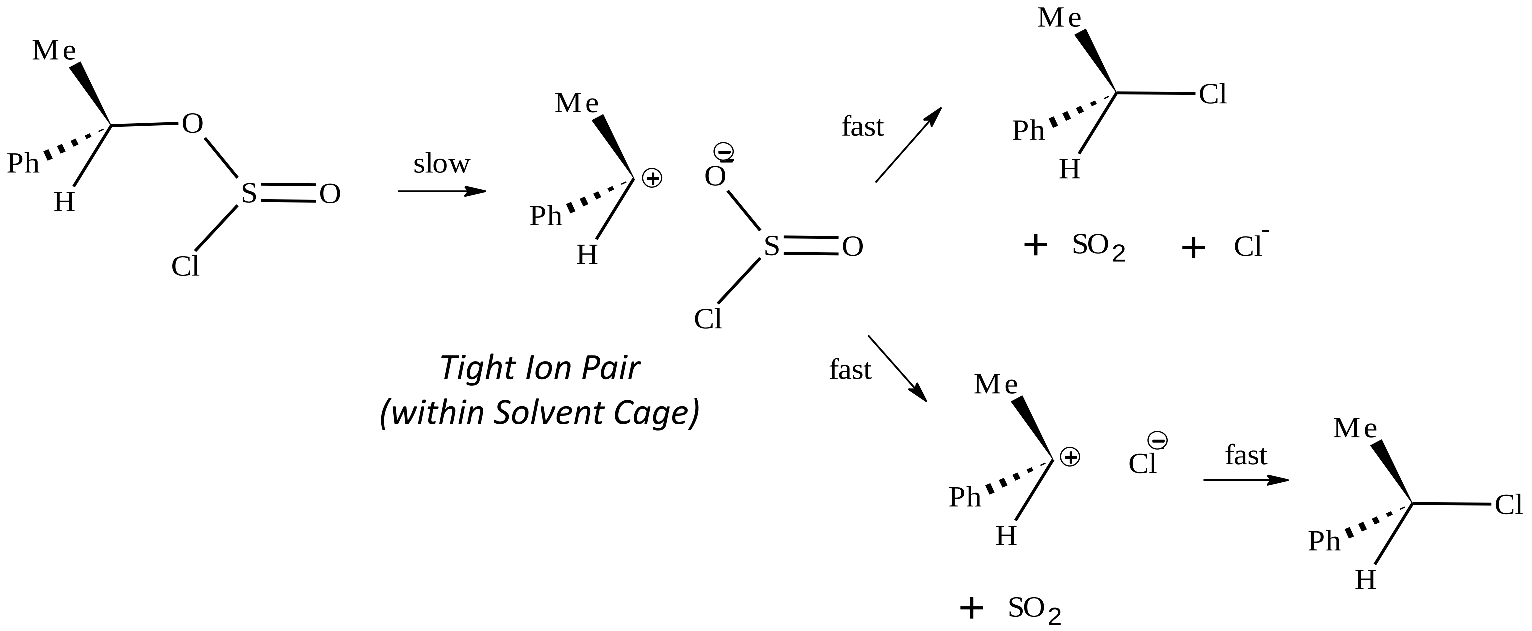


- *Second Order i.e. Rate = k(ROH)[$SOCl_2$]*
- *Retention of Configuration*

- *The Mechanism*

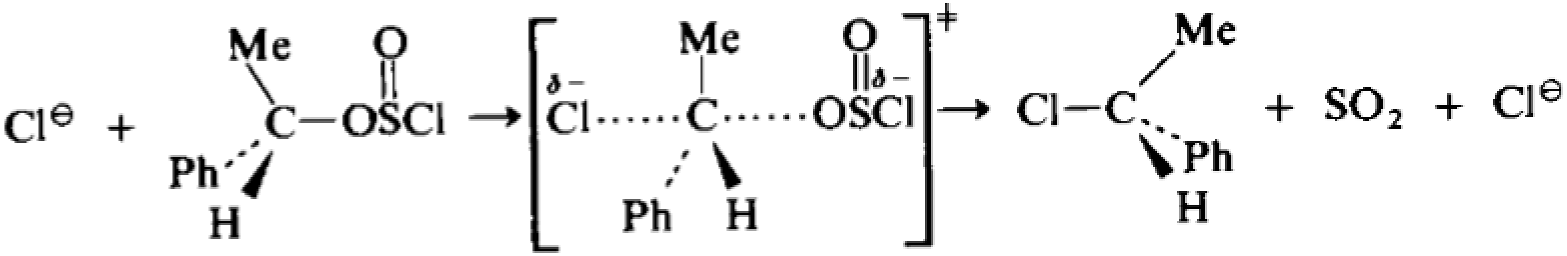


- *Reaction of ROH and $SOCl_2$ is second order*
- *Simple heating of ROSOCl is first order*



Tight Ion Pair
(within Solvent Cage)

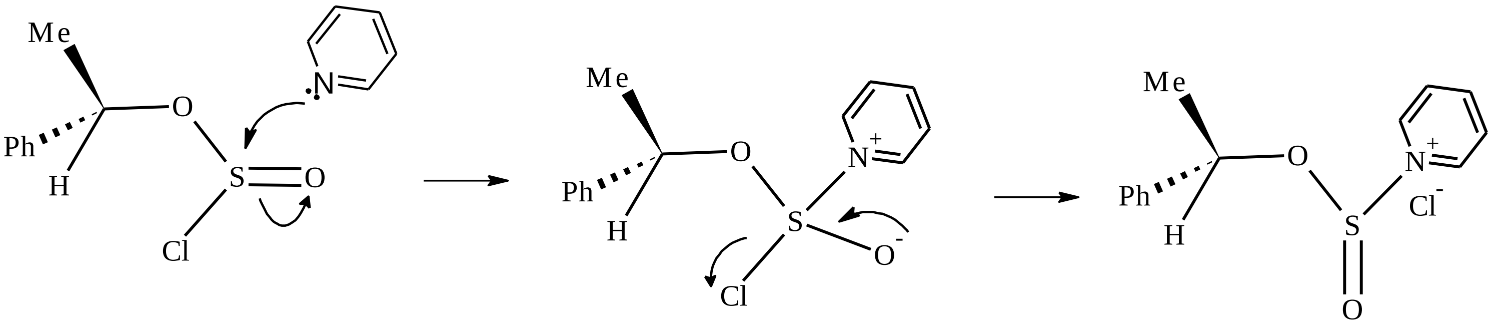
- *Adding pyridine shifts the reaction to normal S_N2 mechanism.*

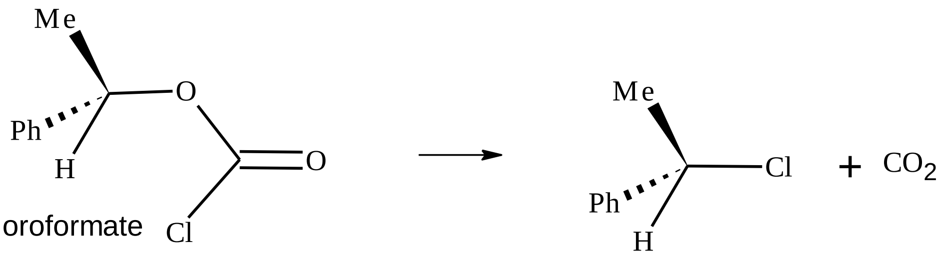


- *Second Order i.e. Rate = k(ROH)[SOCl$_2$]*
- *Inversion of Configuration*

$$ROSOCl + C_5H_5N \rightarrow ROSO\overset{+}{N}C_5H_5\overset{-}{Cl} \rightarrow ROSO\overset{+}{N}C_5H_5 + \overset{-}{Cl}$$

Free nucleophile

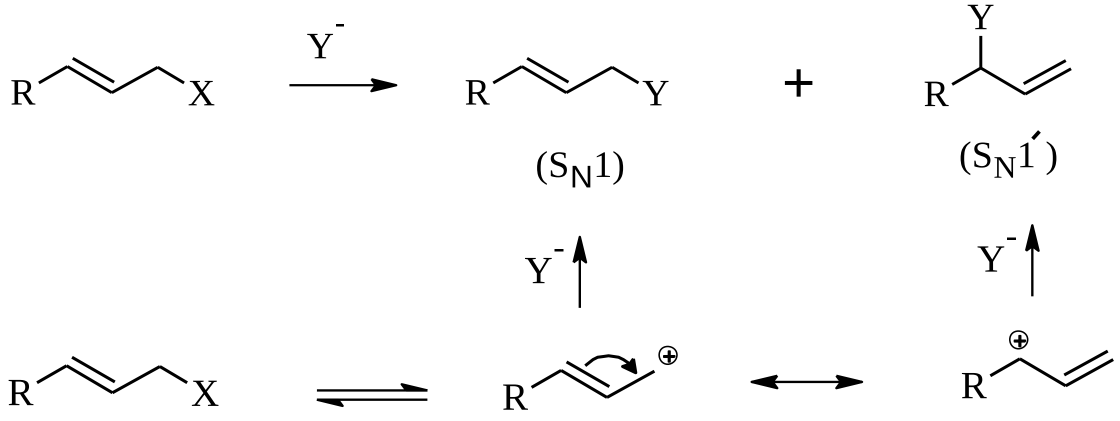




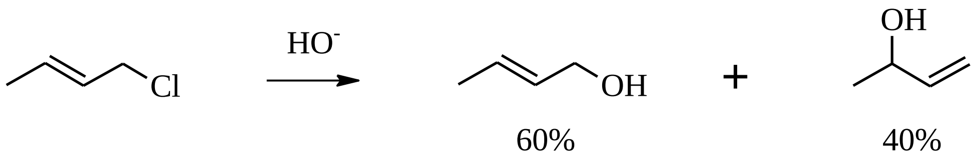
Alkyl chloroformate

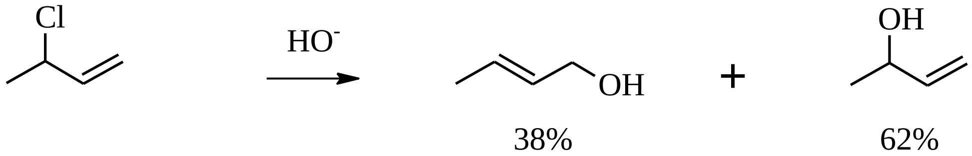
Nucleophilic Substitution at an Allylic Carbon: Allylic Rearrangements

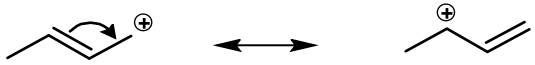
S_N1'



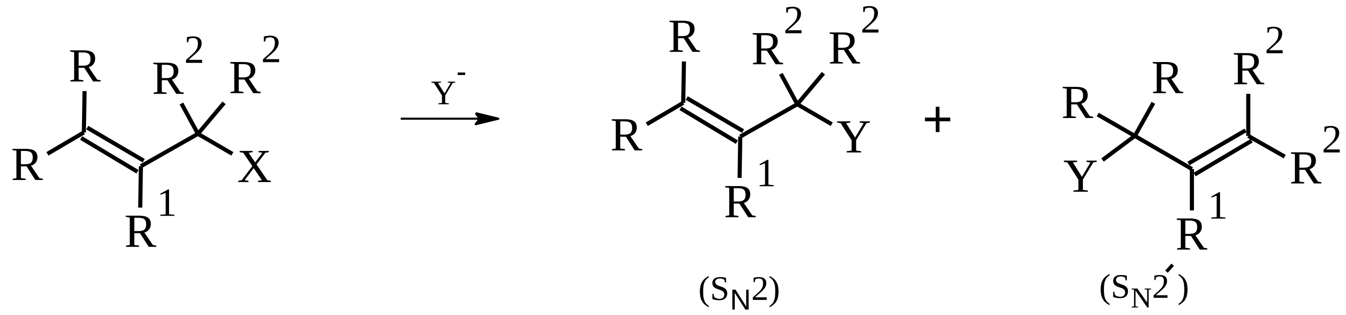
Ion Pairs in S_N1'

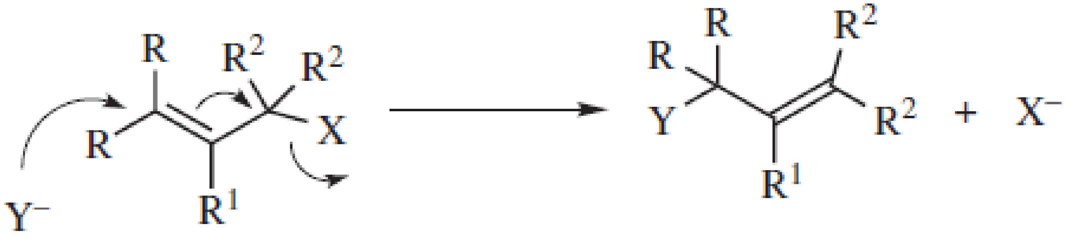




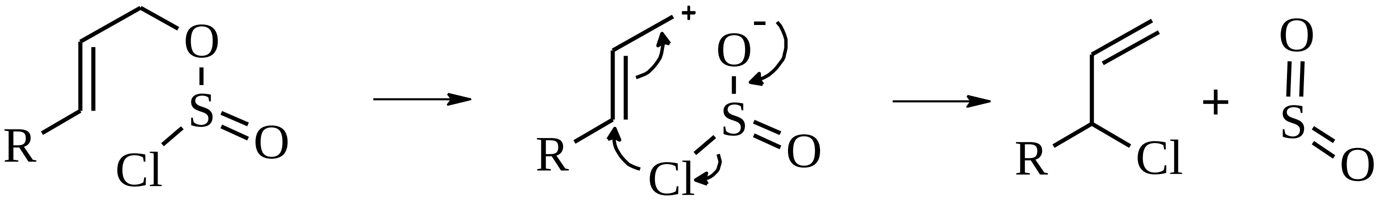


S_N2'

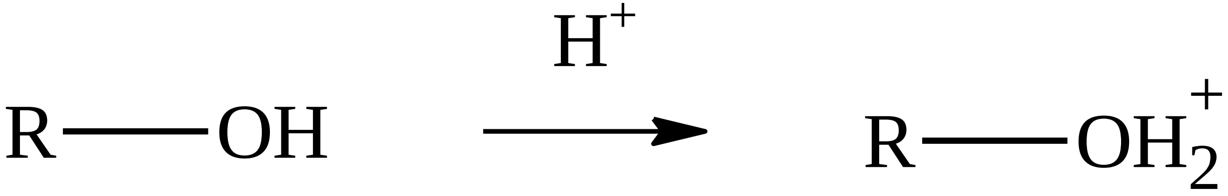




S_Ni'



S_N1cA or A1 mechanism & S_N2cA or A2 mechanism



$$R{-}OH \xrightarrow{H^+} R{-}OH_2^+$$

- The First step above incorporate the symbol cA (conjugate acid)
- The next step will decide whether it is S_N1 or S_N2 mechanism