Elements of Organic Chem. CHM 201 - Dr. Stanley

Ch 7 - Substitution Reactions of Alkyl Halides

Sections 7.1 - 7.6, Suggested Problems: 1-5, Quick Quiz (skip 4, 5, 7, 16, 19, 20), 9-35 (odd)

Substitution Reactions

Ex. $H-\ddot{O}:^{\ominus}$ $CH_3-\ddot{Cl}:$ $\longrightarrow$ $H-O-CH_3$ $+ :\ddot{Cl}:^{\ominus}$

Nucleophile (Nu:) "nucleus-loving"
- → e⁻ rich (lone pair or π bond), can have ⊖ charge
- → seeks e⁻ deficient species (δ^+ or ⊕)

Electrophile (E^+) "electron-loving"
- → e⁻ poor (δ^+ or ⊕)
- → seeks e⁻ rich species

Leaving Group (LG)
- → group leaves + takes 2e⁻ with it
- → stable groups (weak bases) make good LG's (e.g. $Cl^{\ominus}$, $Br^{\ominus}$, $I^{\ominus}$)

General Reaction: $R-LG + Nu: \longrightarrow R-Nu + LG:$

Possible mechanisms?

* Simultaneous (concerted)
* Stepwise (LG leaves 1st)

SN2 Substitution Nucleophilic Bimolecular

Ex. $CH_3\ddot{O}:^{\ominus}$ + CH_3CH_2-I $\longrightarrow$

Mechanism: one step

SN2 Kinetics

Rate = $k[CH_3O^{\ominus}][CH_3CH_2I]$

→ rate dependent on both Nu: + E+

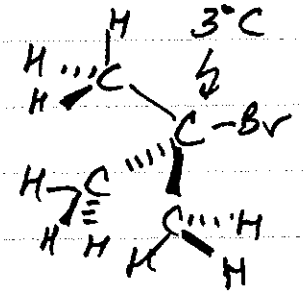
→ bimolecular rxn

Sterics affect rate of SN2

kinetics experiment: $R\text{-}Br + :\overset{\ominus}{C}N \longrightarrow R\text{-}CN + Br^{\ominus}$

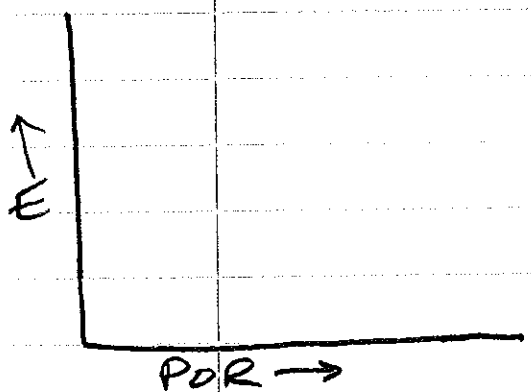
R Group	Abbrev	C Type	Relative Rate
CH_3-			
CH_3CH_2-			
$CH_3CH(CH_3)$-			
$(CH_3)_3C$-			

Consider tButyl bromide

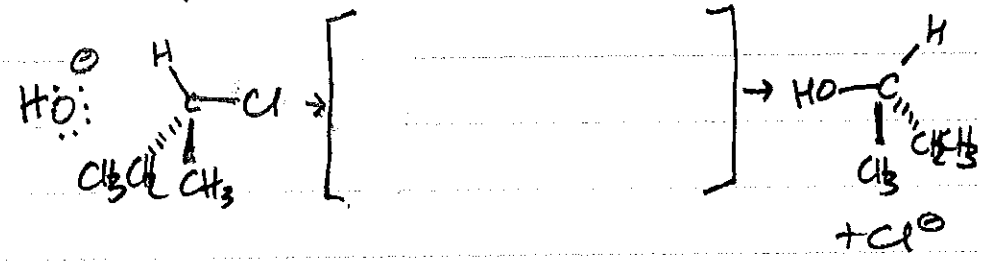


Rate of S_N2 (by type of RX):

SN2 E vs. POR Diagram



Transition state:



Backside Attack

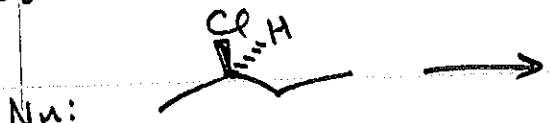
↓

Inversion of Stereochem.

(like a flipped umbrella)

*If LG is too sterically hindered (3°)

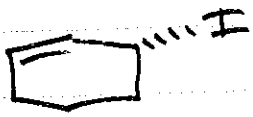
Nu: must approach from behind for backside attack.



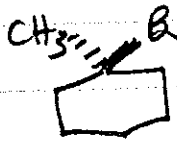
S_N2 Summary

→ 1-step mechanism
→ Backside attack!
→ inversion of stereochemistry
→ requires 1) unhindered LG
2) good Nu: (⊖charge or $:NH_3$)
→ Rate (Rx) methyl > 1° > 2° >> 3°
(based on sterics)

Predict major product (S_N2)



$NaOH \longrightarrow$

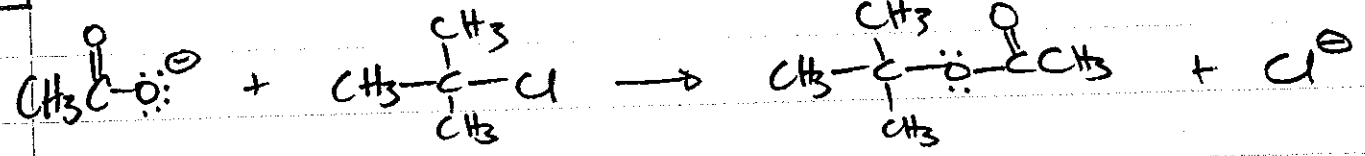


$+ NaCN \longrightarrow$

$+ NaOCH_3 \longrightarrow$

$NH_3 + CH_3-Br \longrightarrow$

S_N1 Substitution Nucleophilic Unimolecular

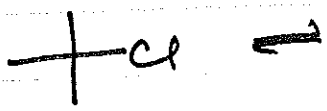


could this be an S_N2?

Still substitution - new mech

S_N1 Mechanism (2 key steps, but usually 3 steps) 7-4

① Loss of LG



② Addition of Nu:

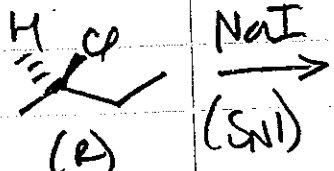
S_N1 Kinetics Rate = $k[tBuCl]$

→ rate-determining step involves E^+ only
→ rate is independent of $[Nu^-]$
→ A more stable carbocation will be formed faster

Rate of S_N1 :
(by Rx type)

Stereochemistry of S_N1

S_N1 results in racemization (loss of stereochemistry) because of the achiral carbocation intermediate



S_N1 Summary

- stepwise mechanism via carbocation
- more stable carbocation, _____ reaction benzyl/allyl/3° > 2° >> 1° >> C
- racemization occurs
- requires no strong Nu (usually reaction w/solvent: H_2O or ROH)

California State Polytechnic University, Pomona

Elements of Organic Chemistry, CHM 201, Dr. Laurie S. Starkey

Chapter 7 Summary: Substitution Reactions of Alkyl Halides (Brown & Poon textbook) (7.1 – 7.6)

I. Substitution Reactions (R-LG → R-Nu)
   a. Electrophiles (E^+)
      i. Contain + or δ^+ sites (e.g., alkyl halides, carbocations)
   b. Nucleophiles (Nu:)
      i. Contain a source of electrons (e.g., lone pair or pi bond)
      ii. More stable → less reactive, weaker Nu:
      iii. More electron-rich → better Nu:
      iv. Less electronegative → better Nu:
      v. Larger atom → more polarizable, better Nu:
   c. Leaving Groups
      i. Stable species (weak bases) make good leaving group (e.g., Cl^-, Br^-, I^-)
      ii. A good LG makes a favorable substitution reaction ($\Delta G < 0$)

II. S_N2 mechanism (one step)
   a. Back-side attack with inversion of stereochemistry
   b. Steric hindrance slows the S_N2 reaction
   c. Requires good Nu: (X^-, R_3N, CN^-, N_3^-, RS^-, RO^-)

III. S_N1 mechanism
   a. Two key steps, via carbocation
   b. More stable carbocation, faster S_N1 reaction
   c. Racemization occurs, due to achiral intermediate

IV. S_N2 vs., S_N1
   a. If an S_N2 <u>can</u> happen, it <u>will</u> happen!

Suggested Textbook Problems: in-chapter problems 1-5, Quick Quiz (SKIP 4, 5, 7, 16, 19, 20) and end-of-chapter problems 9-35 (odd only) and 43abef.

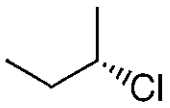
Summary of Chapter 7 Substitution Reactions

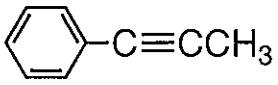
Alkyl Group (RX)	S_N1 (Carbocation!)	S_N2 (Back-Side Attack!)
3° (tertiary)	common	rare (N/R)
2° (secondary)	sometimes	sometimes
1° (primary)	rare (N/R)	common
CH_3 (methyl)	never (N/R)	common
allyl or benzyl	common	common (if not 3°)

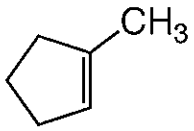
Dr. Laurie S. Starkey, Elements of Organic Chemistry, CHM 201, Cal Poly Pomona

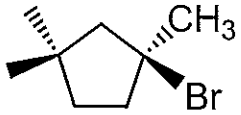
Exam II Predict the Product(s): Alkene/Alkyne Reactions and S_N2 vs S_N1 Reactions

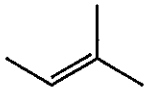
In the box provided, indicate the mechanism involved in each of the following reactions ("Add" for addition, S_N1 or S_N2; if no reaction is expected, write NR) and then predict the major product(s) expected. Remember to indicate stereochemistry, when appropriate.

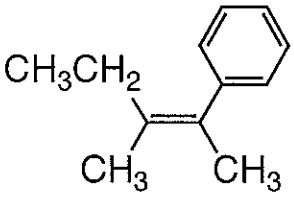
a)  $\xrightarrow{NH_3}$

b)  $\xrightarrow[\text{Lindlar's}]{H_2\text{ (excess)}}$

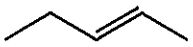
c)  $\xrightarrow[H_2SO_4]{H_2O}$

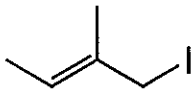
d)  $\xrightarrow{H_2O}$

e)  $\xrightarrow{HCl}$

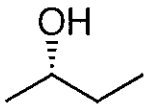
f)  $\xrightarrow[Pd]{H_2\text{ (excess)}}$

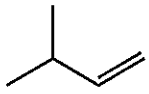
g) CH_3I $\xrightarrow{H_2O}$

h)  $\xrightarrow{HBr}$

i)  $\xrightarrow{CH_3OH}$

hint: two products

j)  $\xrightarrow{NaCN}$

k)  $\xrightarrow[\text{hint: rearrangement}]{H_2O,\ H_2SO_4}$