Learning Guide for Chapter 9 - Alkyl Halides I

- I. Introduction to alkyl halides types of organic halides, where alkyl halides are found, preparation, spectroscopy, reactivity, nomenclature
- II. Substitution reactions of alkyl halides Introduction Mechanisms Which substitution reaction? Strong vs Weak Nucleophiles Products Stereochemistry Rate Laws Rearrangements Solvents Exclusion of aryl halides, vinyl halides, and acid chlorides Summary of Substitution Reactions
 III. Synthesis Using Substitution Reactions

I. Introduction to alkyl halides

Types of organic halides

What is the purpose of categorizing organic halides into different groups?

so that we can predict how they will react

Label the following compounds as alkyl halides, aryl halides, and acid halides.



This chapter will focus on: alkyl halides

Compounds with more than one halide can be classified by how close together the halides are. Which of these is a geminal dihalide, and which is a vicinal dihalide?



Not all compounds that contain a benzene ring are aryl halides. Classify the following. What category do they all belong to?



Organic halides may also contain a C=C. Classify the following. What category do they all belong to?



Some aromatic halides and some unsaturated halides react like are alkyl halides, and some do not. The important factor is the hybridization of the C the halogen is attached to.

sp³ carbon alkyl halide benzyl, allyl, other aromatic

sp² carbon NOT an alkyl halide aryl, vinyl

Label the following as methyl, 1°, 2°, 3°, allyl, and benzyl.



Where organic halides are found

Are organic halides common in nature? no

Why is iodine necessary in the human diet? to make thyroid hormone

Where do we get it? iodized salt What happens if you don't? goiter



How are alkyl halides used in industrial, commercial, and medical applications?



Preparation of alkyl halides

How can alkyl halides be synthesized from alkanes? halogenation

What difficulty does this reaction have?

forms multiple products; can be separated by fractional distillation, not practical in the lab

What kind of intermediate is formed in this reaction? radical

$$: \underbrace{CI} - \underbrace{CI}: \xrightarrow{hv} : \underbrace{CI} \cdot \xrightarrow{H} \xrightarrow{H} H - \underbrace{C} \cdot + H - \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: H - \underbrace{C} \cdot + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \xrightarrow{:} H - \underbrace{C} - \underbrace{CI}: + \cdot \underbrace{CI}: \underbrace{CI} - \underbrace{CI} - \underbrace{CI} - \underbrace{CI} + \underbrace{CI} - \underbrace{CI} - \underbrace{CI} - \underbrace{CI} + \underbrace{CI} - \underbrace{CI} - \underbrace{CI} + \underbrace{CI} - \underbrace{CI} + \underbrace{CI} - \underbrace{CI} + \underbrace{CI}$$

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What would the products of the following reaction be?



Why are the following reactions successful at forming only one major product?



Spectroscopy of alkyl halides

What IR bands does this alkyl halide spectrum have?



Is IR a good way to identify alkyl halides? nope - they look like alkanes

How can you locate the H's on a C with a halogen attached? chemical shift: 3-4 ppm Assign the H's on the following spectrum.



Reactivity of alkyl halides

Give the order of electronegativity of halogens atoms: F > Cl > Br > I

Give the order of size of the halogen atoms: I > Br > Cl > F

Give the order of bond strength of C-X:

C-F > C-Cl > C-Br > C-I

not reactive reactive

Show the polarity of the carbon-halogen bond:

 $\begin{array}{c}
\delta + \delta - \\
\vdots \\
\vdots \\
\end{array}$

Show how an alkyl halide can react in each of the following ways:



What do all of these reactions have in common? break C-X bond, have X- product

Nomenclature of alkyl halides

What are the two ways to name alkyl halides?

IUPAC (systematic names) - using the normal rules common names - only works for simple alkyl halides How do you construct a common name?

name of alkyl substituent + name of halide

Give the common names for the following compounds.



Why can't you write a common name for the following compound?



Review the steps for naming a compound using IUPAC rules.

1) choose the main chain or ring 1st priority - longest 2nd priority - most subst

- 2) number the chain or ring 1st priority first subst, then 2nd, etc 2nd priority alphabet
- 3) name and order substituents
- 4) add stereochemistry, if needed

Give names for the following compounds.



2-bromoethylcyclohexane

2-chloro-3-ethyl-4-methylhexane

II. Substitution reactions of alkyl halides

Introduction

What are the two types of reactions that alkyl halides can do?

substitution and elimination

Which of the reactions represented below is a substitution reaction? Which is an elimination reaction? Why?



Substitution - the ethoxy group takes the place of the chloride



Elimination - the bromide and a hydrogen are removed from the alkyl halide, (one ends up on the base, the other alone) leaving behind a C=C

Which of these will we study in this chapter? In the next?

Ch 9 - substitution Ch 10 - elimination

Mechanisms

What is a mechanism?

shows the movement of electrons in each step of the reaction

How many ways can a substitution occur? What are the mechanisms called?

2 ways - $S_N 1$ and $S_N 2$ E Nu $S_N 2:$ $\overbrace{}$ $\overbrace{}$ $\overbrace{}$ $\overbrace{}$ $\overbrace{}$ $\underset{Na^+}{::::} \xrightarrow{}$ $\overbrace{}$ $\overbrace{$ $\overbrace{}$ $\overbrace{$ $\underset{}$ $\overbrace{}$ $\overbrace{}$ $\overbrace{$ \newline $\overbrace{}$ $\overbrace{$ \newline \newline \newline \newline $\underset{}$ $\overbrace{$ \newline \newline \newline $\underset{}$ $\underset{}$ $\underset{}$ $\underset{}$ $\overbrace{$ $\underset{}$ $\underset{}$

What type of Lewis acid/base reaction is this? displacement

How could this mechanism be described? attack-push off

Where is the nucleophile, and where is the electrophile?

Why is the alkyl halide a good electrophile? the C is partially + the Cl can come off

Why is the alkoxide a good nucleophile? O is -, becomes neutral



What type of reaction is this? dissociation, association, acid/base

How could this mechanism be described? fall off, attack, deprotonate

Where are the nucleophile, electrophile, acid, and base?

Why can alkyl halides dissociate?

bond is polar Cl can come off

Why is the carbocation a good electrophile? incomplete octet, needs a bond

How are the $S_N 1$ and $S_N 2$ reactions the same?

both involve reaction with a Nu same net result - substitution

Which are the two electrophiles used in the examples? Which do you think is more reactive? Why?



What are the two nucleophiles used in the examples? Which do you think is stronger, and why?



How do the strength of the nucleophile and electrophile fit together?

S_N2: strong Nu, weak E

S_N1: weak Nu, strong E

Scenario A: strong Nu added to alkyl halide

Nu attacks! S_N2

Scenario B: weak Nu added to alkyl halide

Nu can't attack, sits around waiting until alkyl halide dissociates, then attacks carbocation - $S_{\rm N} {\rm 1}$

What determines whether an $S_N 1$ or and $S_N 2$ reaction will occur?

the strength of the nucleophile

Following the pattern of the reactions given previously, draw the mechanisms for the following reactions:

$$S_{N}^{2}$$

$$S_{N}^{2}$$

$$S_{N}^{2}$$

$$S_{N}^{2}$$

$$S_{N}^{2}$$

$$H^{O}_{H}$$

$$(weak Nu)$$

Nucleophiles in Substitution Reactions

The following are nucleophiles commonly used in substitution reactions, listed in order of nucleophilicity:



What is the cut off point between nucleophiles that follow $S_N 2$ vs. $S_N 1$ mechanisms? Why is are alcohols weak nucleophiles while alkoxides are strong nucleophiles?

charge: alkoxides - negative charge alcohols - neutral

Why won't tert-butoxide and tert-butyl alcohol work as nucleophiles?

steric hindrance - tert-butyl is too big to attack C

Why are alkyne anions the best nucleophiles?

C is the least EN

Which of the halides is the best nucleophile? Why are they all poor nucleophiles?

I- biggest

Products

Give the products of the following reactions. Then note what nucleophile produced what product. Which mechanism will each follow?



halides - alkyl halides

Stereochemistry

Can a substitution reaction involve a carbon that is a stereocenter? yes

Can a substitution reaction create a new stereocenter? no

What happens to a stereocenter involved in an S_N^2 reaction? inverted



MODELS

How does this happen?

in order to push halide off, Nu must come from behind



tetrahedral

trigonal bipyramid

tetrahedral

What happens to a stereocenter involved in an S_N1 reaction? racemized



How does this happen?

when the C+ is formed, the Nu can attack from either side



The actual ratio isn't 1 to 1 - it's more like 2 to 3. Why?

the departing Cl partly blocks one side

Rate laws

Consider the following $S_N 2$ reaction.



Draw the energy diagram for this reaction.

Which reagents are involved in the rate limiting step?

alkyl halide and nucleophile

Draw the structure of the transition state.

What would happen if you

doubled the concentration of the alkyl halide? rate would double

doubled the concentration of the nucleophile? rate would double

What is the order of the alkyl halide? the nucleophile? 1st order in both

Write the write law: rate = k[RX][Nu]

What does $S_N 2$ stand for? Substitution Nucleophilic 2nd order

What happens to the rate of $S_N 2$ reactions as the substitution increases?

MODELS	methyl CH ₃ Cl			
steric hindrance	none	a little	some	a lot
activation energy				
rate of reaction	fast	fast	slower	no reaction



Consider the following $S_N 1$ reaction.



Draw the energy diagram for this reaction.

Which is the rate limiting step?

fall off - creating a C+

Draw the structure of the transition state for this step.

Which reagents are involved in the rate limiting step? only the alkyl halide

What would happen if you

doubled the concentration of the alkyl halide? rate would double

doubled the concentration of the nucleophile or base? nothing!

What order is the alkyl halide? the nucleophile or base? alkyl halide 1st order

Write the write law: rate = k[RX]

What does S_N1 stand for? Substitution Nucleophilic 1st order

What happens to the rate of $S_N 1$ reactions as the substitution increases?

MODELS	methyl CH ₃ Cl			
carbocation stability	none	a little	some	a lot
activation energy				
rate of reaction	no reaction	no reaction	slower	fast



-ci:

Nu 0th order

How does the identity of the halogen atom affect the rate of substitution reactions?

two possible explanations:

* longer bonds break more easily RI fastest

which is more important?

more EN, more stable afterwards RF fastest

 $CH_3I > CH_3Br > CH_3Cl >> CH_3F$ too slow

Will this be true for both S_N^2 and S_N^1 reactions?

yes - C-X breaks in rate-limiting step

Rearrangements

In which substitution reaction do carbocations form? $S_{N}1$

whenever a carbocation is formed, draw it out and look for rearrangements!

Why do carbocations undergo rearrangements?

in order to become more stable

Which carbocations are mostly likely to rearrange?

2° - want to become 3°

What are the two ways in which a carbocation can rearrange?

hydride shift, alkyl shift

Which carbocation will give the product? both!

Give the substitution products in the following reaction.



Solvents

Why is a solvent useful when running a reaction?

dissolve the reagents	(you don't have to write the solvent, but you
can affect the reaction rate	usually have to use one!)

What are the important issues when considering solvents for substitution and elimination reactions?

1) polarity van der Waals - non polar dipole forces - moderate to highly polar hydrogen bonding - highly polar

2) hydrogen bonding yes - protic no - aprotic

What kind of solvent do $S_N 2$ reactions require?

high polarity solvent - to dissolve charged reagents

aprotic solvent - hydrogen bonding slows down the reaction surrounds Nu/base, makes it hard to react

What kind of solvent do $S_N 1$ reactions require?

polarity isn't important - reagents are not charged, dissolve easily

protic solvent - stabilizes the C+, increases reaction rate

What solvents are in the following categories?

nonpolar hexane, toluene no good - won't dissolve charged reagents can't stabilize C+

moderately polar ethyl acetate, dichloromethane, diethyl ether not very good

highly polar, aprotic acetone, N,N-dimethylformamide, acetonitrile

 CH_3 -C≡N: good for S_N^2 , E2

highly polar, protic

alcohols, water good for $S_N 1$, E1 - usually = Nu/base

Exclusion of aryl halides, vinyl halides, and acid chlorides

Why can't aryl halides undergo substitution reactions?

	no rxn - pi bonds block Nu from attacking		
	no rxn - C+ is too unstable		
	vinyl halides, acid chlorides have similar reasons		
Summary of Substitution Read	etions		
S _N 2 reactions:	S _N 1 reactions:		
result: halide replaced by Nu	result: halide replaced by Nu (usually minus its H)		
mechanism: 1 step	mechanism: 3 steps		
attack-push off	fall off attack deprotonate		
reagent: strong nucleophile	reagent: weak nucleophile (also a base at the end, use as solvent)		
stereochemistry: inversion	stereochemistry: racemization		
rate law: rate = k[RX][Nu]	rate law: rate = k[RX]		
alkyl halides: methyl $> 1^\circ > 2^\circ$	$^{\circ} >> 3^{\circ}$ alkyl halides: $3^{\circ} > 2^{\circ} >> 1^{\circ} >$ methyl		
RI > RBr > RC	Cl >> RF $RI > RBr > RCl >> RF$		
rearrengements? no	rearrengements? yes		
solvent: polar, aprotic	solvent: polar, protic (usually Nu)		

III. Synthesis Using Substution Reactions

What is synthesis?

figuring out how to make a compound

each reaction you learn will be a tool in your toolbox to make a specific change

substitution - alkyl halide to other functional groups

What steps should you go through?

- 1) look at the compound to decide what nucleophiles you could use
- 2) decide what alkyl halides you could use
- 3) decide if the reaction will be favorable

Consider the following target molecules:

	nucleophile	alkyl halide	rxn	favorable?
N:	_{Na} + ⁻ :c≡n: NaCN strong	1°	S _N 2	yes
N:	NaCN strong	<u></u>	S _N 2	no - slow
→_=N:	NaCN strong	\rightarrow $\ddot{c}i:$ 3°	S _N 2	no too bulky
N :	NaCN strong	Br : aryl	S _N 2	no aryl halides don't do S _N 2

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