HALOGENO - COMPOUNDS
(HALOALKANES)

Introduction $\mathbf{C^{\delta+}\!\!-\!\!-\; X^{\delta-}\!\rightarrow}$

Halogens are much more electronegative than carbon atoms, electrons are displaced towards the halogen, X, resulting in a permanent separation of charge, hence a permanent dipole.

The electron- deficient carbon atom attached to the halogen atom would therefore be expected to undergo attack by a nucleophilic reagent (nucleus-seeking), $N:^-$, such as a negatively charged ion or a neutral molecule containing an atom with an unshared pair of electrons.

$$\mathbf{-C^{\delta+}\!\rightarrow X^{\delta-} \text{ ----------------> } -\; C-N \;+\; \underset{:}{X}^-}$$
$$\mathbf{\overset{\uparrow}{\underset{:}{N}^-}}$$

On approach of a nucleophile the slightly negative halogen atom will be repelled and finally displace (expelled with the electron pair of the C – X bond) by the incoming group.
Reactions of halogenoalkanes are ***nucleophilic substitution reactions.***
Examples of nucleophiles: OH^{-1}, NH_3, CN^{-1}, OR^{-1} (all Lewis .....)

We would expect the order of reactivity to be:
- C - F > - C - Cl > - C - Br > - C - I
Because the order of electronegativity is:
F > Cl > Br > I
Therefore the carbon in – C – F would be more positive than the carbon atom in the – C – Cl bond, hence more easily attacked by a nucleophile, (because the polarity of the carbon-halogen bond decreases and this would be expected to decrease the rate of reaction.
However, the **order of reactivity is** :

- C - I > -C - Br > -C - Cl > -C – F

The reactivity of a molecule depends primarily on the **strength of the carbon – halogen bond, and the - C - I bond is much weaker than the -C - F bond** (because the iodine atom is much larger than the fluorine atom, and the electron cloud around the larger halogen becomes diffuse, hence the C -X bond strength diminishes, and at the same time the bond length increases). Bond strength is the dominant factor:

Bond type	- C - F	- C - Cl	- C - Br	- C - I	
Bond energy	485	339	289	234	($kJ \cdot mol^{-1}$)
Bond length	**0.138**	**0.177**	**0.193**	**0.214**	(nm)

decreasing polarity of C-X bond
decreasing strength of C-X bond
bond energy decreasing
increasing rate of reaction

$$\longrightarrow$$

Recall: halogens on the benzene ring deactivate the ring, (why?). The bond energy of C - Cl in benzene is 365 $kJmol^{-1}$. However the halogen is -------------- directing. Use the above data to predict the likely order of reactivity of the following: 1-chlorobutane, 1-bromobutane, 1-iodobutane, chlorobenzene.

Preparation of Halogeno -Compounds

1. Halogenoalkanes

a) **Direct Substitution in an alkane** …

Cl_2, Br_2, will substitute in presence of UV light (not I_2)

Disadvantages … a mixture of products is obtained, difficult to separate.

b) **Addition of HX or X_2 to alkenes and alkynes**

Alkenes combine readily (HI > HBr > HCl)

Note: Markownikoff's Rule: propene + HBr

c) **Action of $P_4 + X_2$ (→ PX_3, or PX_5) on an alcohol**

$$ROH + PX_5 \longrightarrow RX + POX_3 + HX$$

d) **Action of HX on alcohol**

Relation to neutralisation – reaction type, see dehydration of alcohols: the halide ion will displace H_2O from the protonated alcohol: recall mechanism !

2. Halogenoarenes

a) **Direct Substitution**

good method: benzene derivatives obtained in the presence of halogen carrier,(Fe, FeX_3, Al, $AlCl_3$) , however in the absence of UV light addition in the benzene ring results.

b) **Toluene derivative**

methyl activates the benzene ring .: ortho and para directing.

When reacting with X_2 then substitution can occur either in the side chain or in the ring, depends on conditions …

1) if boiled with X_2, sunlight, then substitution in the side chain

2) if X_2 in the presence of a catalyst Fe, $AlCl_3$, then substitution in the ring (mixture of ortho- and para- products obtained, *Why?*).

Physical Properties

Halogenoalkanes are all mainly volatile liquids, a few are gases (CH_3Cl, CH_3Br, C_2H_5Cl). They have higher boiling points than the corresponding alkanes, due to their higher molar mass (Van-der-Waals forces increase with molar mass). Also due to dipole-dipole forces. Also in a given series of alkyl (CH_3-Cl, CH_3-Br, CH_3-I) the boiling point increases with increase in molar mass of the halogen, this is not due to dipole moment, the polarity is very similar for all the haloalkanes.

They are not soluble in H_2O, but are soluble in organic solvents.

Halogenoarenes are more stable, less volatile(higher b.pt.) and immiscible in water.

haloalkane	**bp (^{O}C)**	**molar mass (g mol^{-1})**	**dipole moment (Db)**
CH_3Cl	- 24	50.5	1.87
CH_3Br	4	95	1.81
CH_3I	42	142	1.91

Chemical Reactions

Nucleophilic Substitution Reactions

In general, only strong bases will displace the halide ion from a halogenoalkane (OH^{-1}, CN^{-1}, OR^{-1} and $RCOO^{-1}$ ions are all conjugate bases of weak acids and are, therefore, themselves strong bases).

1. Hydrolysis (*splitting up my means of H_2O is slow, and is thus brought about by aqueous alkali or dilute acid*)

a) **Only halogenoalkanes** undergo hydrolysis, **halogenoarenes are not hydrolysed**)

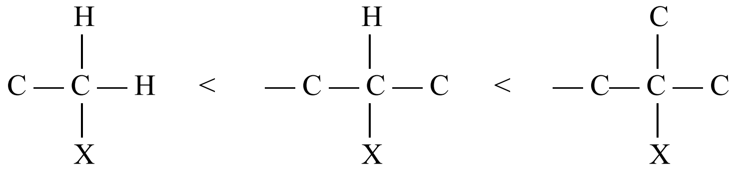
H_2O is ineffective, **.•. cold**, **dilute aqueous alkaline solution (< 60 ºC)** is used:
(NaOH, KOH) + R – X ...

$$\mathrm{R-X + H_2O \text{ ---------> } R-OH + HX}$$

b) In general, rate of nucleophilic substitution …

- C - I > - C - Br > - C - Cl > - C - F
Fastest **Slowest**

c) Position of the halogen …



$$\begin{array}{c} \mathrm{H} \\ | \\ \mathrm{C-C-H} \\ | \\ \mathrm{X} \end{array} \quad < \quad \begin{array}{c} \mathrm{H} \\ | \\ \mathrm{-C-C-C} \\ | \\ \mathrm{X} \end{array} \quad < \quad \begin{array}{c} \mathrm{C} \\ | \\ \mathrm{-C-C-C} \\ | \\ \mathrm{X} \end{array}$$

Primary Halogenoalkane Secondary Halogenoalkane Tertiary Halogenoalkane

Tertiary halogenoalkane is hydrolysed fastest.

It is also found that for a tertiary halogenoalkane the rate is only dependent on the concentration of the halogenoalkane (i.e. 1st order), whilst for a primary halogenoalkane the rate is dependent on the concentration of both halogenoalkane and the hydroxide ion (2nd order).

Explanation of Hydrolysis in terms of mechanism

Investigation of the detailed mechanism of the hydrolysis of halogenoalkanes to alcohol using experimental techniques such as kinetic studies (measurement of the reaction rates), solvent effects and change of structure of halogenoalkane, has shown that there are **TWO** extreme types of mechanisms possible for the reaction - a **one-step and a two-step: S_N2 or S_N1,** both are true and both work under different conditions.

Primary halogenoalkanes undergo **S_N2** mechanism: Rate = k $[1^0\ \text{R-X}]$
while tertiary undergo **S_N1** mechanism: Rate = k $[3^0\ \text{R-X}]$

(Secondary halogenoalkanes, 2º, undergo by both **S_N2** mechanism and **S_N1** mechanism.)

Kinetic studies show that the rate of hydrolysis of a methyl halide(.: 1º), by aqueous alkali depends on the concentration of both the halogenoalkane and the hydroxide ion, i.e ...

Rate = k [CH_3 X] [OH^{-1}] k = rate constant, (Units ?

(if [R-X] doubles, and [OH^{-1}] doubles, what is the affect on the rate of the reaction?

(A large numerical value of the rate constant indicates ......?

Details of S_N2 Mechanism

The first rate determining, .: SLOW step, of the mechanism involves the "**backside attack**", (aka: **backslide displacement**: the nucleophile approaches the C-atom from the other side opposite to the leaving group), of the OH^{-1} (a nucleophilic reagent) on the electron-deficient carbon atom of the halogenoalkane to produce a planar transition state in which the formation of the C - OH bond has begun while the C - X bond is still in the process of being broken, so that the negative charge is spread over both the oxygen and the halogen atoms. (The OH^{-1} approaches from the opposite side to prevent deflection by the negatively charged halide ion.)

The nucleophile and the halide ion are coplanar in the 5-co-ordinate transition state. .: **steric hindrance** is expected if the groups are bulky and large, i.e. the formation of this intermediate is going to be difficult for a tertiary haloalkane, leading to high E_A for the formation of the transition state.

In the next FAST stage, electrons of the C - X bond are donated to the halogen atom to give a halide ion, while the lone pair of electrons from the oxygen atom of the O - H are donated to the C – atom:

This bimolecular, one-step mechanism is described as S_N2, in which the 'S' indicated that it is a substitution reaction, the 'N' that the reaction involves the nucleophilic attack of the hydroxide ion on the halogenoalkane and the '2` that it is a bimolecular reaction, i.e. one in which two species undergo a change in the rate-determining step.

S_N2 is a "concerted reaction" i.e. it takes place in concert: attack and expulsion of leaving group is a simultaneous event ...bond breaking and bond breaking occur at the same time.

S_N2 mechanism generally, takes place in **non-polar solvents**, and it is "**stereo-specific**." This is to say that inversion of configuration takes place, in other words a transformation in which a single pure stereo isomer of starting material is converted into a single pure stereo isomer of product, D –> L or L – > D.

Details of S_N1 Mechanism

Kinetic studies show that the hydrolysis of a 3^{ry} halogenoalkane is independent of the hydroxide ion concentration and depends only on the concentration of the halogenoalkane.

$$\text{Rate} = k\,[\,3^{ry}\ \text{halogenoalkane}] \qquad \text{mol dm}^{-3}\ \text{s}^{-1}$$

This **first step is a slow**, reversible ionization in which a highly reactive carbocation is formed and a halide ion is expelled:

The carbocation has only a transient existence and rapidly reacts with the OH^{-1} (nucleophile: nucleus seeking) to form the alcohol.

Generally **polar solvents** will hydrate the bulky 3^o carbocation and stabilise them, so S_N1 will be favoured in polar solvents:

Since the slow stage of reactions involves only one molecule - the formation of the carbocation, (i.e. unimolecular), it is a substitution reaction initiated by a nucleophilic, hence S_N1.

Order of stability of carbocation is: $3^0 > 2^0 > 1^0$, hence S_N1 is facilitated for a 3^0 haloalkane, why?

Factors Affecting S_N1 and $S_N 2$ Mechanisms

	$S_N 1$	**$S_N 2$**
Electronic structure of alkyl group	Forms stable carbocation: tertiary > secondary > primary	Primary > secondary > tertiary
Size of alkyl group	Highly branched: tertiary > secondary > primary	Small branched: primary > secondary > tertiary
Type of nucleophile	Weak nucleophile	Strong nucleophile
Nature of solvent	Polar (H_2O, C_2H_5OH), low temperatures	Non-polar (benzene), high temperatures

To Explain the Ease of Hydrolysis for different Halogens

Rate of hydrolysis: $I^{-1} > Br^{-1} > Cl^{-1}$

What factors are involved in finding which mechanism takes place?

Bond Energies : which bonds need to be broken for the reaction to take place?
See Bond Energies above.

It is easier to break the - C - I bond that the - C - Cl, this is because the iodine atom is bigger .•. the electrons are further away from the nucleus. Hence activation energy is smaller for the C- I bond ($k = - A e^{-Ea/RT}$, E_a is smaller .•. k, the rate constant has a bigger value, .•. faster reaction).

R - I > R - Br > R - Cl

R - I	R - Br	R - Cl
very reactive	less reactive	least reactive
very expensive	.•. used in Lab	least expensive, used in Industry (High T, & P)

To Explain Why Reactivity on a Chain Easier Than on a Benzene Ring

Nuclear halogen on the benzene ring deactivates the ring, and the p-electrons on the halogen interact with the π-bond of the benzene ring to produce a C - X bond that is much stronger than the usual bond:

Also consider the intermediate stage in S_N 1 and S_N2: the molecules in both of the intermediates involved have undergone a flat shape, this can happen for small atoms, but in the case of benzene this can not happen (it would involve breaking the delocalisation - less stable … not feasible) …

Benzene does not undergo any nucleophilic reactions (dilute aqueous KOH, not conc. alcoholic KOH, NH_3, KCN etc.)

Early insecticides, such as DDT, contained chlorine atoms directly bonded on to a benzene ring and their resistance to substitution reactions is part of the reason why they are so persistent in the environment.

To Explain Rate of Reaction and Position of Halogen

Tertiary > Secondary > Primary

It is found that **S_N 1** takes place for tertiary halogenoalkane, whereas **S_N 2** takes place for primary halogenoalkanes.

The carbocation formed in the first step of the S_N 1 mechanism is stabilized with the introduction of successive electron-releasing alkyl groups (inductive effect), into the carbocation.

Large groups like to spread out away from each other and this can be done with **S_N1** carbocation.

Smaller groups are happy with five species on the intermediate .: S_N2.

E_A is linked to how much energy is required to make the intermediate stage, in **S_N1** difficult, because you are breaking one bond, (an energy is required) but you are not making a bond (no energy released).

The tertiary carbocation can be detected for a long time …

2. Reaction With Ammonia in Alcoholic Solution

Only halogenoalkanes react. Halogenoarenes do not react.
Ethanol is used as a solvent because the halogenoalkanes are insoluble in H_2O.

Mechanism
The mechanism is the same as for hydrolysis, primary amine is obtained as the main product if an excess of NH_3 is used. However, further substitution of 1^0 amine results …

3. Reaction With CN^{-1} in Alcoholic Solution

Only halogenoalkanes react. Halogenoarenes do not react.
KCN, (insoluble in water), is dissolved in alcohol, if it was dissolved in alkali then substitution by OH^{-1} would result.

This is a very **useful reaction as it introduces another C- atom into the chain, hence a potential method for ascending the homologous chain**. The nitrile obtained may be oxidized to an acid.

Mechanism

4. Reaction With Alkoxide ions (- C - O^{-1} -)

Recall: The alkoxide ion is obtained by reacting an alcohol with a metal ...
Example:

The alkoxide ion being a nucleophile therefore reacts with the halogenoalkane forming an ether.

Mechanism

5. Reduction of the Halogeno – compounds

Both the halogenoalkanes and the halogenoarens may be reduced by metallic reducing agents ($LiAlH_4$, Mg/Hg+H_2O) to alkanes or arenes …

Thus it can be seen that halogenoalkanes are good synthetic agents owing to ease with which the halogen can be displaced as a halide ion. Also note that in industry C-Cl compounds are used (extreme conditions employed), whereas in the lab C-Br compounds are used.

Elimination Reactions of the Halogenoalkanes

Elimination can sometimes happen instead of substitution, this is most likely with tertiary haloalkanes because:
(a) the alkyls get in the way of the incoming nucleophile,
(b) the alkyl groups in the tertiary haloalkane release electrons towards the reactive carbon making it a less reactive site.
The attacking nucleophile thus acts as a base removing a hydrogen from the edge of the molecule, because its nucleophilic pathway is blocked.
A molecule of hydrogen halide is eliminated from one molecule of R-X and an alkene is formed:

Hot concentrated alcoholic KOH or NaOH (> 100 ºC) --------> Alkenes

Only halogenoalkanes undergo this reaction.

Note : Hydrolysis via S_N 1 and S_N2 mechanism are preformed in cold dilute alkali.

Elimination reaction: when a multiple bond is formed between two neighbouring atoms and a small molecule is formed from the groups that were originally attached to these atoms.

Two possible mechanisms: **E1 and E2**

Mechanism

Elimination is more likely if a strong base is used. It if found that both substitution and elimination can take place, hence not a very good yield of products from either mechanism is obtained. The substitution and elimination reactions are similar in many respects. Elimination may occur by two main mechanisms :

i) a biomolecular, one-step mechanism (E2), Rate = k [R- X] [OH^{-1}]

ii) a unimolecular, two-step mechanism (E1), Rate = k [R - X]

E2 Mechanism

So far all of our nucleophilic reactions have involved reaction with the electrophilic carbon atoms in the molecule. Nucleophiles may also act as bases and remove a proton from the haloalkane, causing elimination of the hydrogen halide instead of substitution, the product is .: an alkene.

The bimolecular, one-step mechanism, E2, (closely resembles S_N2, undergone by 1^0), may be represented as follows:
The OH^{-1} ion acting as a base by donating an electron pair to the H-atom attached to the β – carbon atom of the halogenoalkane takes place simultaneously with the formation of the C = C bond and the expulsion of the halide ion ...

E1 Mechanism

In the unimolecular, two-step mechanism, E1, the slow ionization of the halogenoalkane to form a carbocation (this is why 3^0 halogenoalkanes undergo E1), is the rate-determining step, (similar to S_N1), followed by the loss of a proton to the hydroxide ion acting as a base …

increasing amount of branching in alkyl group

SUBSTITUTION ———————————— ELIMINATION
Primary ———————————— Tertiary

In general:

1^0 ---> high yields of substitution products, 3^0 ---> elimination exclusively

However, the elimination / substitution ratio depends on the conditions, (T, elimination has a higher E_a than the competing substitution reaction and the elimination / substitution ratio can **.•.** be increased by raising the temperature), and on the nature of the base (*stronger the base, the more important the E2 reaction …*

$CH_3COO^{-1} < OH^{-1} < OC_2H_5^{-1} < NH_2^{-1}$

increasing basic strength

S_N2 ———————————— E 2

When the ***halogen is on the side chain of the toluene, then the reaction observed are those typical of an halogenoalkane***.

Assignment

Predict the mechanism expected for the reaction of $KOH_{(aq)}$ with the following haloalkanes and write an equation to illustrate the mechanism:
(a) 1-bromobutane, (b) 2-bromo-2-methylpropane.
Describe how the rate of each of the reactions is affected when the [KOH] is doubled. Explain your reasoning. If hot, concentrated, alcoholic KOH is used instead of $KOH_{(aq)}$, predict the mechanism and the expected products. Outline a means of distinguishing between each of the haloalkanes and the products obtained from the reactions of cold aqueous $KOH_{(aq)}$ and from the reaction with hot, conc. KOH