

E26 A NUCLEOPHILIC SUBSTITUTION REACTION

Preparation of 2-chloro-2-methylpropane

INTRODUCTION

The simplest organic molecules contain only the elements carbon and hydrogen. As these elements have similar electronegativities, the resultant compounds are essentially non-polar. Further, if all the carbon atoms are sp^3 hybridised (*i.e.* there are no π -bonds), the molecule will be quite unreactive.

Carbon forms strong bonds with a large number of other elements (called hetero-atoms). In the majority of cases, there is a large difference between the electronegativities of carbon and the hetero-atom, and the resultant bond is therefore polarised. This means that many organic molecules have slightly negatively charged (δ^-) and slightly positively charged (δ^+) centres. These centres are very important in a vast number of chemical reactions and have been given special names - *viz.* **nucleophile** and **electrophile**.

A **nucleophile** has an electron rich site and forms a bond by donating an electron pair to an electrophile. (From the Greek for “nucleus loving”.) Examples of nucleophiles are:

Cl^-	OH^-	$\begin{array}{c} \text{H} \\ \diagdown \\ \text{O} \cdot\delta^- \\ \diagup \\ \text{H} \end{array}$	carbon atom in $\overset{\ominus}{\text{C}}\text{H}_3\overset{\oplus}{\text{Mg}}\text{Cl}$	π -bond in $\begin{array}{c} \text{H} & & \text{H} \\ & \diagdown & / \\ & \text{C}=\text{C} \\ & / & \diagdown \\ \text{H} & & \text{H} \end{array}$
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An **electrophile** has an electron-poor site and will react with the electron pair of a nucleophile to form a bond. (From the Greek for “electron loving”.) Examples of electrophiles are:

H^+	$\overset{\oplus}{\text{C}}\text{H}_3$	carbon atom in $\overset{\delta^+}{\text{C}}\text{H}_3-\overset{\delta^-}{\text{Cl}}$	carbon atom in $\begin{array}{c} \delta^- \\ \text{O} \\ \cdot \\ \text{O}=\text{C} \delta^+ \\ \diagup \\ \text{H} \end{array}$
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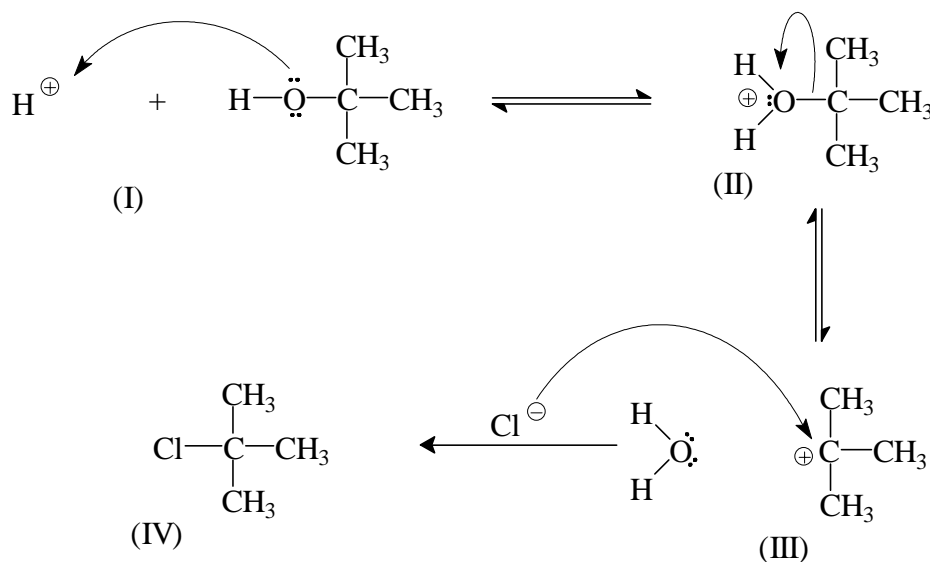
The most common reaction of the functional groups in saturated alkyl compounds is nucleophilic substitution. The nucleophile, or electron rich species, attacks the electrophilic carbon of the alkyl group to give the substituted product. A different nucleophile is generated as a by-product of the reaction.

Table E26-1 on the following page gives a number of examples of nucleophilic substitution reactions. Note the use of “curly arrows”, which indicate the movement of electrons, *i.e.* the breaking and formation of bonds. The nucleophilic and electrophilic centres in the starting materials are indicated with δ^- and δ^+ symbols respectively.

Table E26-1 Mechanism of some Nucleophilic Substitution Reactions

Substrate	Nucleophile	Products
	OH^-	$\text{CH}_3\text{CH}_2\text{-OH}$ and Br^-
	$\text{CH}_3\text{CH}_2\text{-O}^-$	$\text{CH}_3\text{-O-CH}_2\text{CH}_3$ and I^-
	NH_2^-	$\text{C}_6\text{H}_5\text{-CH}_2\text{-NH}_2$ and Cl^-
	$(\text{CH}_3)_3\text{N:}$	$(\text{CH}_3)_3\text{N}^+\text{Br}^-$

In this experiment, 2-chloro-2-methylpropane is prepared from 2-methyl-2-propanol by the action of concentrated hydrochloric acid. The mechanism of the reaction is shown below.



Not all nucleophiles react with all electrophiles. For a nucleophilic substitution reaction to occur, it is necessary that the bond to be broken does so at an appreciable rate. This is highly dependent on the nature of the **leaving group** (displaced nucleophile). Note that the actual leaving group in this reaction is H_2O , not OH^- . Also note the formation of the electron-deficient **intermediate** (III), which is called a **carbocation**.

This reaction takes place rapidly at room temperature and its ease is typical of tertiary alcohols. By contrast, secondary alcohols require more drastic conditions to undergo reaction with the same reagent, and primary alcohols more forcing conditions still (*e.g.* heating at high temperature for many hours).

The ease with which a nucleophilic substitution reaction proceeds, or indeed whether a reaction will “go” at all, is dependent on the exact mechanism of the reaction, the nature of the attacking nucleophile, the nature of the leaving group, the stability of any carbocation generated, temperature, the relative concentrations of reagents, *etc.*

In general, the most stable nucleophiles are the best leaving groups, and can be readily identified - they are the conjugate bases of strong acids.

The following species are all good leaving groups: I^\ominus , Br^\ominus , Cl^\ominus , H_2O

The following species are all poor leaving groups: OH^\ominus , CN^\ominus , F^\ominus , $(\text{CH}_3)_2\text{NH}$

The starting material and product of this reaction have markedly different physical properties, which makes it a relatively simple matter to isolate the desired product in a pure state. The alcohol is soluble in water and has the higher boiling point whilst the alkyl halide has the lower boiling point and is insoluble in water.

2-Chloro-2-methylpropane boils at 51 °C. This experiment is therefore a good indication of your manipulative skill. The compound will obviously evaporate if left in an open vessel for long.

2-Methyl-2-propanol has b.p. 83 °C and m.p. 25 °C. In cold weather it is therefore solid at room temperature.

SAFETY

Materials	Nature
2-methyl-2-propanol 2-chloro-2-methylpropane hydrochloric acid calcium chloride	

Indicate, by signing, that you have understood the information in the safety table.

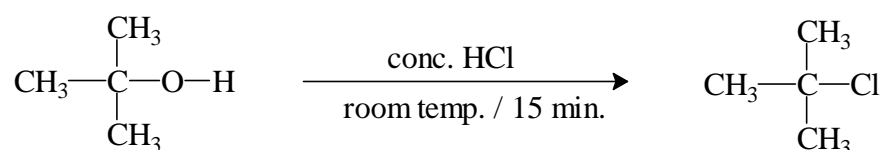
I understand the safety information	Demonstrator's Initials
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LAB-WORK

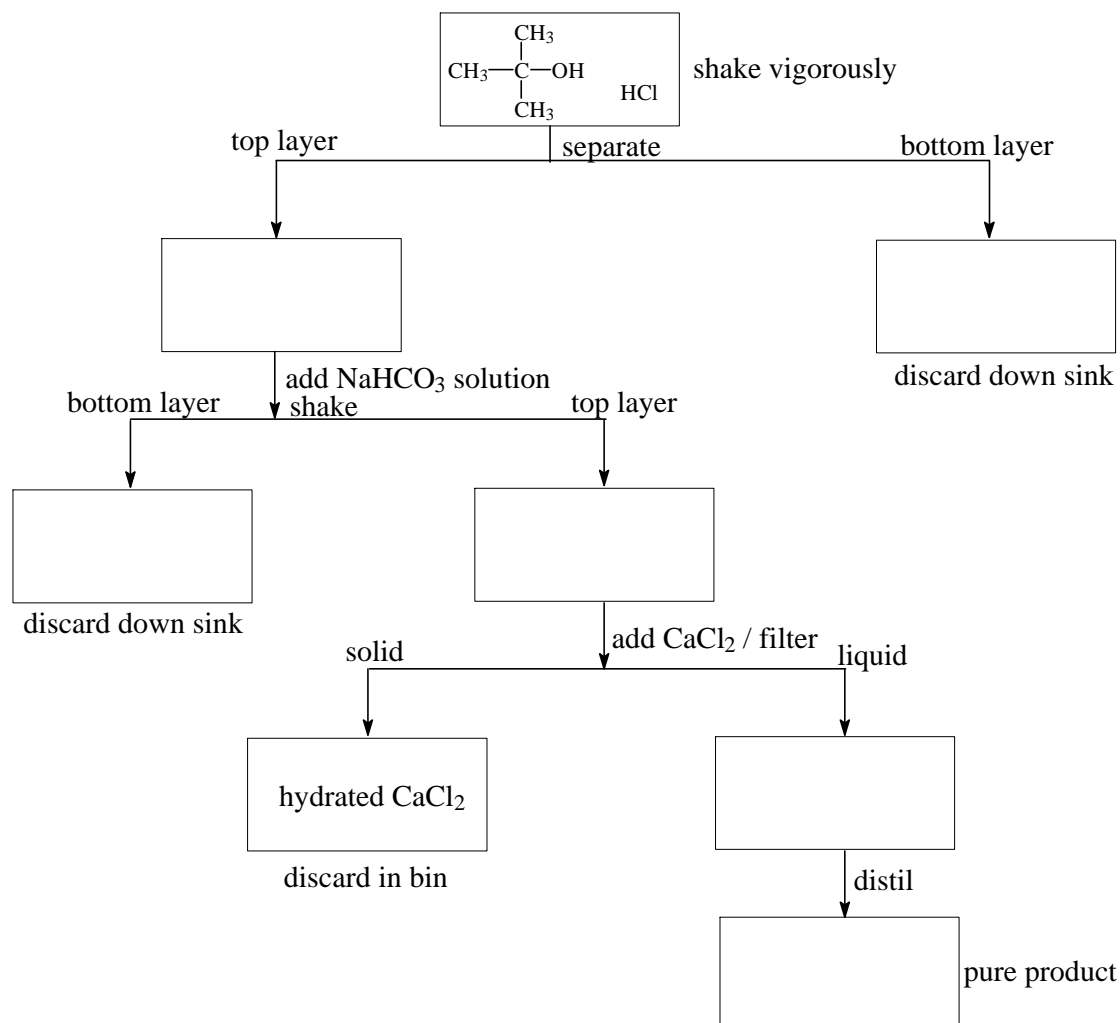
Physical properties of 2-chloro-2-methylpropane and 2-methyl-2-propanol

Test the miscibility of these two compounds with water in the following way. Set up a clean semi-micro test-tube containing 0.5 mL of water. Add 3 drops of 2-chloro-2-methylpropane, shake, and observe whether or not the liquids are miscible. If the liquids are immiscible note which is less dense. Repeat using 2-methyl-2-propanol in place of the alkyl halide. Summarise your results below.

The reaction between 2-methyl-2-propanol and hydrochloric acid can be represented as follows.



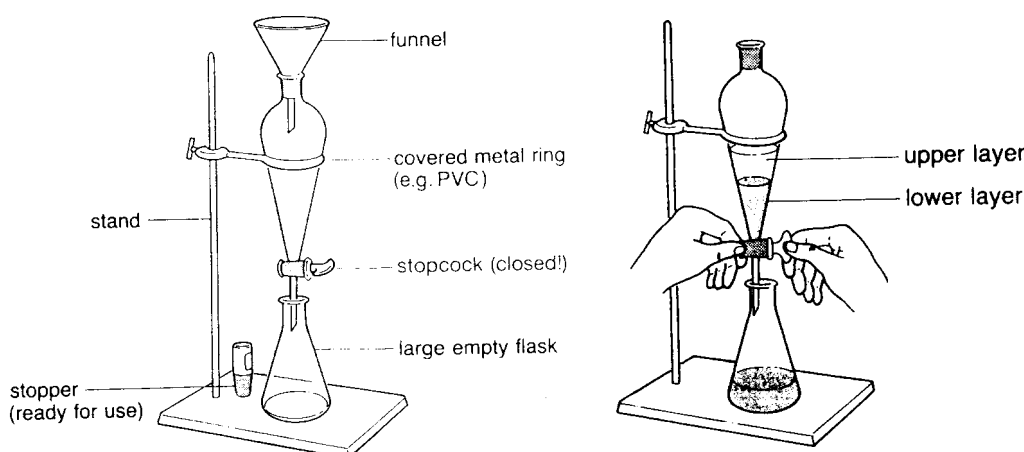
The full sequence of operations, however, is best summarised using a flow chart. Complete the following flow chart.



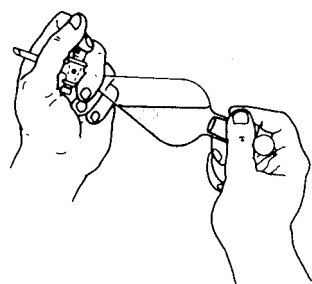
Preparation of 2-chloro-2-methylpropane

Warning: This reaction is carried out in a stoppered separatory funnel. The product is volatile and gas pressure builds up inside the funnel. It is important that you vent this built-up pressure on a regular basis. Failure to do so may result in the stopper being blown out and the contents of the funnel (10 M HCl) being sprayed all over you or your neighbour. Do not proceed until you have been fully instructed by your demonstrator in the correct use of the separatory funnel.

1) In a clean 100 mL conical flask collect 2-methyl-2-propanol (15.0 g = 19.0 mL) from the calibrated dispenser. Support a 250 mL separatory funnel on a retort stand and ring. **Ensure that the tap is closed.** Transfer the 2-methyl-2-propanol to the separatory funnel and add concentrated hydrochloric acid from a measuring cylinder (60 mL, 10 M, kept in fume hood). Swirl the funnel until the two liquids are thoroughly mixed. Stopper the funnel, invert it and immediately relieve the pressure by opening the tap. Close the tap and shake the funnel gently for **2 - 3 seconds only**. Again, relieve the pressure **immediately**. Repeat the procedure of shaking followed by the regular release of pressure for approximately 15 minutes. Allow the layers to separate. If conversion is complete, the lower acid layer should be clear.



2) **Remove the stopper**, run off the lower acid phase and shake the remaining 2-chloro-2-methylpropane with sodium hydrogencarbonate solution (5%, 10 mL) to remove traces of acid. Shake **cautiously** to begin with, and relieve pressure of evolved CO_2 by inverting the funnel and opening the tap. Remove the lower aqueous layer. Now pour the crude product out of the top of the separatory funnel into a small dry conical flask. Dry the 2-chloro-2-methylpropane over a spatula full of anhydrous calcium chloride. Calcium chloride is used as the desiccant in this experiment as in addition to absorbing water, it also absorbs alcohols (and some other classes of compounds). It therefore removes traces of the starting alcohol as well as water.

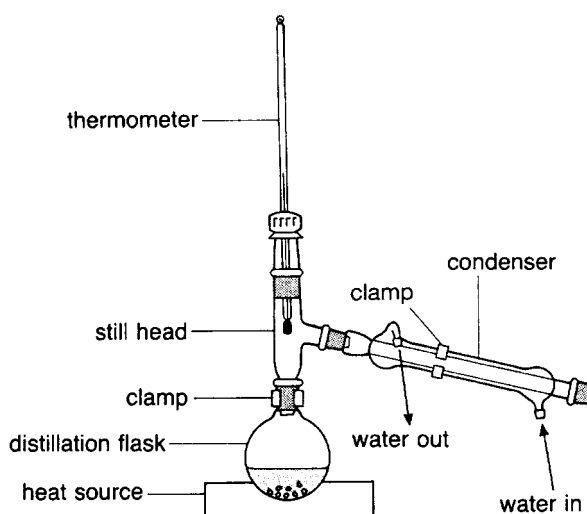


Holding a separatory funnel during shaking;

Always point the stem away from others during venting (opening the tap to reduce pressure)

Purification of 2-chloro-2-methylpropane.

Set up a distillation apparatus with a 50 mL pear-shaped distilling flask and weigh a clean and dry 100 mL conical flask. Filter the dried product through a small fluted paper into the distilling flask, add three anti-bumping granules and distil the liquid from a steam bath. Collect the fraction of b.p. 49-52 °C in the weighed sample tube cooled in an ice bath. When all the product has distilled, stopper the tube, and determine the yield and % yield (to nearest %).



Mass of product + conical flask	g
Mass of conical flask	g
Mass of product	g
% yield of product	%

Submit your product to your demonstrator for inspection.

Demonstrator's Comment	Initials

A selection of spectra of 2-methyl-2-propanol is given on page E26-7.

At what frequency does the O-H stretching vibration occur in the infrared spectrum?

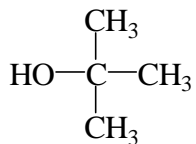
What is the chemical shift (in ppm) of the signal associated with the hydrogen of the alkyl groups in the ^1H NMR spectrum?

What do you expect the ratio of the signal areas to be in the ^1H NMR spectrum of 2-methyl-2-propanol?

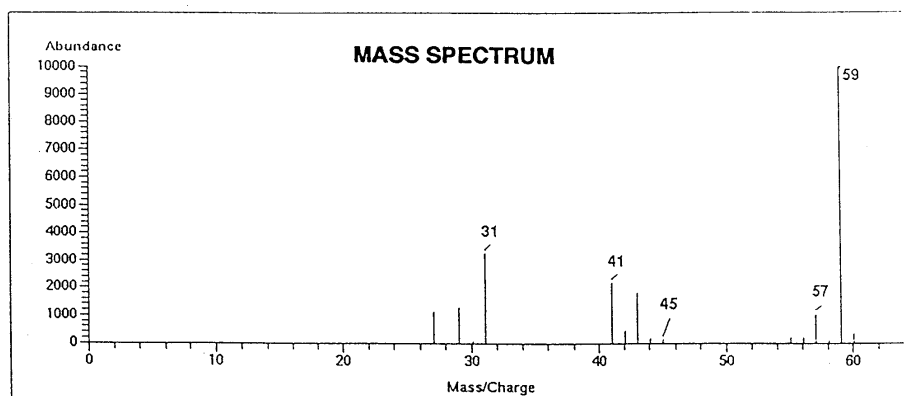
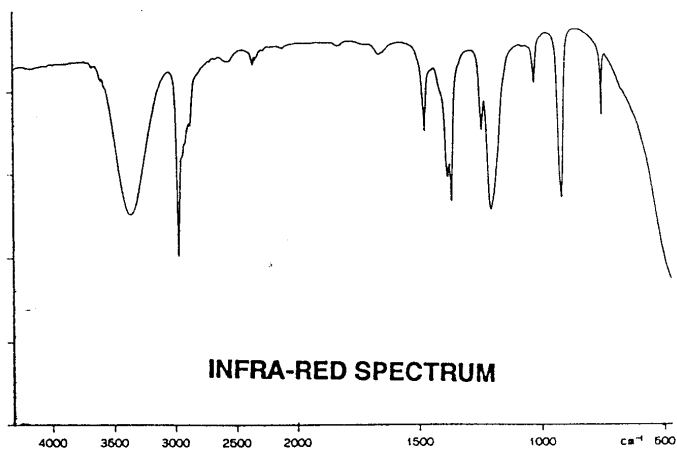
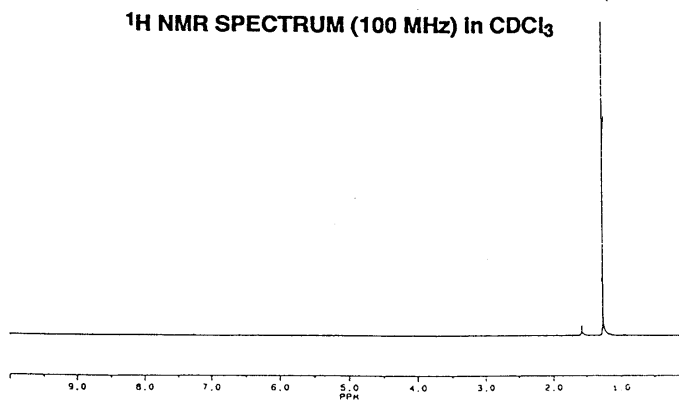
Tertiary alcohols do not give molecular ion peaks. What do you think is the molecular formula of the species that gives rise to the peak at $m/z = 59$ in the mass spectrum of 2-methyl-2-propanol?

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Spectroscopic identification of 2-methyl-2-propanol

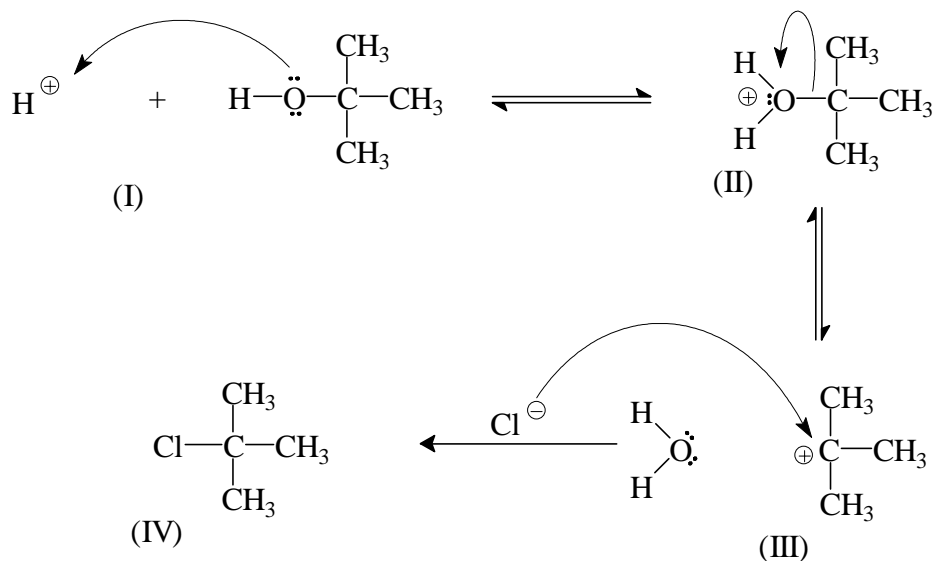


2-methyl-2-propanol

(tert-butyl alcohol)¹H NMR SPECTRUM (100 MHz) in CDCl₃

POST-WORK

Consider the mechanism of the reaction given in the Introduction and repeated below.



What general name is given to the positively charged species, (III)?

Would you expect 2-propanol, $(\text{CH}_3)_2\text{CHOH}$, to undergo the same reaction more or less readily? Give a reason for your answer.

No reaction occurs when 2-methyl-2-propanol is shaken with concentrated aqueous potassium chloride. Account in mechanistic terms for the difference in reactivity between HCl and KCl (that is, explain why H^{\oplus} is necessary in addition to Cl^{\ominus}).

Why does 2-methyl-2-propanol have a higher boiling point than 2-chloro-2-methylpropane, although its molecular weight is lower? (Hint: consider the intermolecular bonding in the two compounds.)

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