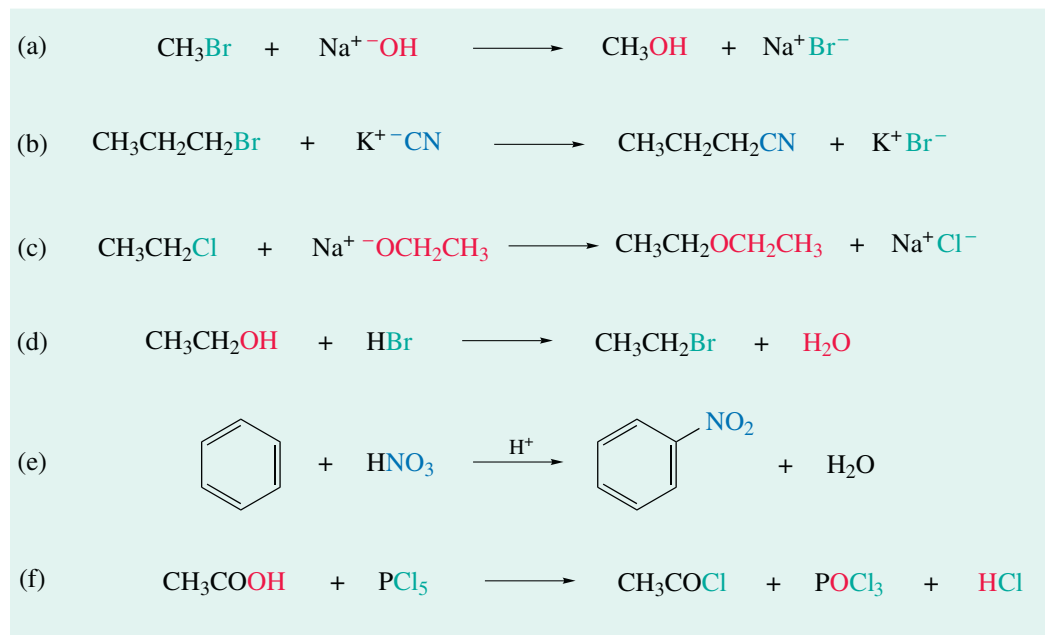


IONIC SUBSTITUTION REACTIONS

3.1 Nucleophiles, electrophiles and leaving groups

In Sections 1 and 2 we discussed a few ionic substitution reactions, and several more are listed in Table 3.1. Examples (a)–(d) are typical of the substitution reactions that we shall be discussing in this part of the book.

Table 3.1 Some typical ionic substitution reactions. Reaction (e) is shown happening in the laboratory in Figure 3.1. All organic species in (a)–(f) are available in WebLab



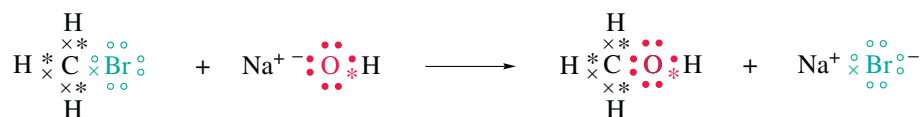
- Look at Reactions (a)–(d) in Table 3.1. What features are common to all four reactions?
- All the substrates contain a functional group (Br, Cl or OH) joined to an aliphatic carbon atom by a covalent bond. In each reaction the functional group is replaced by a group (OH, CN, OCH_2CH_3 or Br) supplied by the reagent.

This behaviour is typical of a reaction proceeding by an ionic mechanism. Let's look at Reaction (a) in greater detail, in order to see the bonding changes that are occurring.

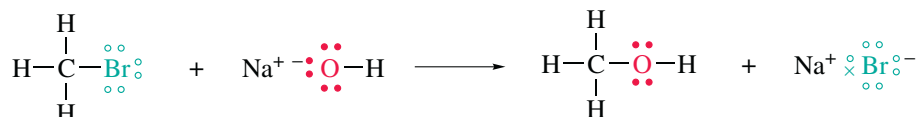
Another way of depicting this reaction is to show all the outer-shell electrons, as in the following Lewis structures (oxygen is in Group VI and bromine in Group VII of the Periodic Table)



Figure 3.1 The reaction of benzene with nitric acid: brown fumes of NO_2 are formed as a by-product.



Remember that each covalent bond (for example, C–H) comprises two shared electrons, so this reaction can be drawn as follows

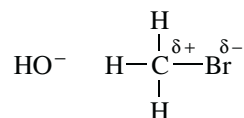


During the course of the reaction the oxygen atom of the hydroxide anion OH^- becomes covalently bonded to the carbon atom, and the bond from carbon to bromine breaks, giving a bromide anion Br^- . The sodium ion is merely a spectator as far as the bond-making and bond-breaking are concerned, which is why it is often referred to as a **spectator ion**.

For the bromide anion to be formed when the carbon–bromine bond breaks, both electrons from the bond must be donated to bromine. Similarly, in order to form a covalent bond to carbon, the oxygen atom must donate two electrons.

Bearing in mind that this reaction proceeds by an ionic mechanism (that is, the bond-making and bond-breaking involve the movement of electron pairs), you should now be able to see the electron movements needed in order to transform the reactants into the products. One of the non-bonded electron pairs on the hydroxyl oxygen atom (shown in red) can form the new bond to the carbon atom, and in order to generate the bromide anion, the C–Br bond breaks heterolytically, with both electrons (shown in green) going to the bromine atom.


We can get an indication of why this reaction occurs if we look at the polarity of the bonds in the substrate. Carbon and hydrogen have similar electronegativities so there is little charge build-up in the C–H bonds. However, there is a larger electronegativity difference between the carbon and the bromine so the bond is polarized in the sense $\text{C}^{\delta+}-\text{Br}^{\delta-}$. Thus the negatively charged hydroxide ion is attracted to the positively charged carbon bearing the bromine: (albeit slightly, see Figure 3.2 overleaf)

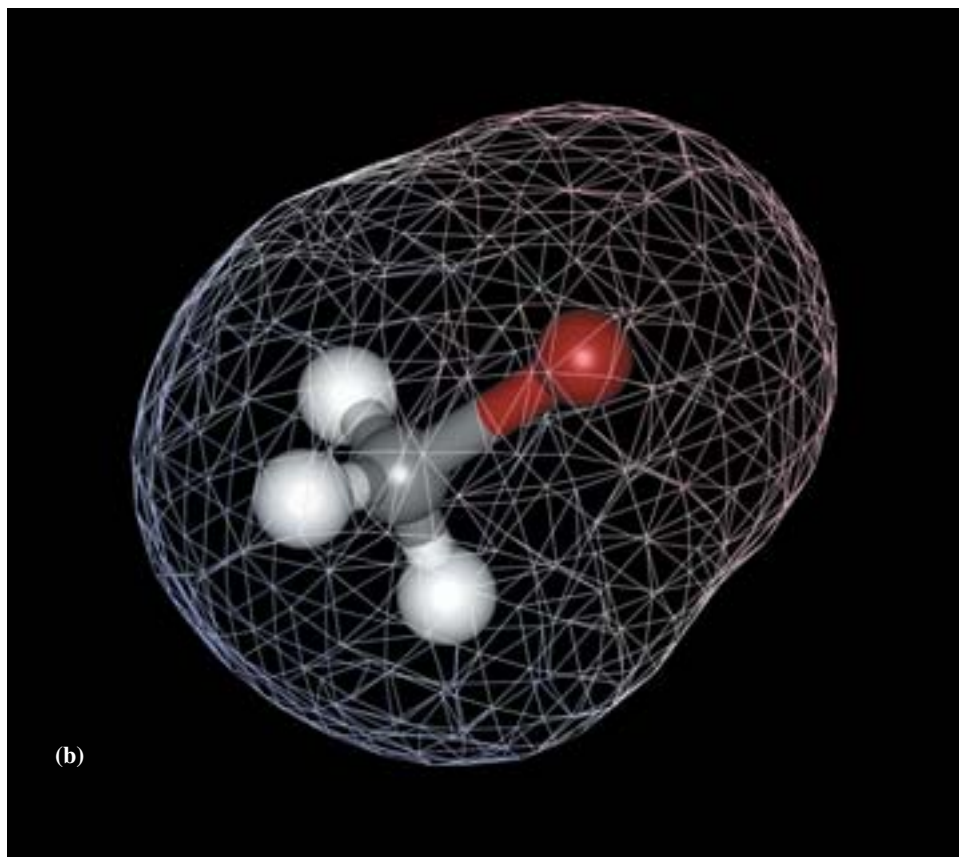
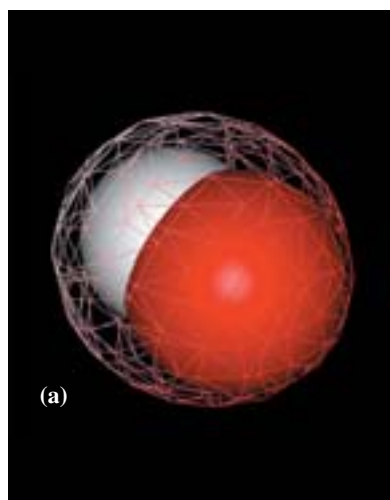


Here, then, is one rationalization of the observation that reactive sites in molecules are normally associated with functional groups. The bromine atom confers polarity on an otherwise effectively non-polar hydrocarbon framework, and ionic reagents might be expected to react at polar sites for electrostatic reasons.

The attacking group, OH^- in this example, that forms a new bond to the carbon is known as the **nucleophile**. Nucleophile means ‘lover of nuclei’, and nucleophiles try to form a covalent bond to another atom. To do this a nucleophile must possess at least one non-bonded pair of electrons, which ultimately forms a new covalent bond. As we have seen, the nucleophile is attracted to the positive charge on the

Figure 3.2

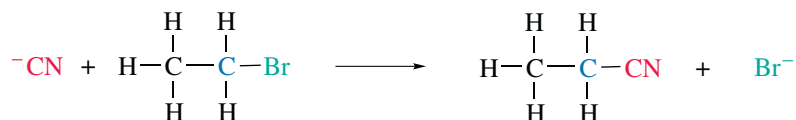
The charge density distribution in (a) the hydroxide ion and (b) bromomethane. The red areas of the surface indicate regions of high electron density, and the blue areas indicate low electron density. 



electrophilic atom. The term **electrophile** means ‘lover of electrons’ and most electrophilic atoms are positively charged or positively polarized, just as most nucleophiles are negatively charged or negatively polarized. The group that is lost, bromine in this example, is known as the **leaving group**.

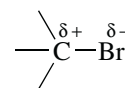
To help you keep track of what is what, in the next few sections we shall draw nucleophiles in red, electrophilic centres in blue and leaving groups in green.

- Which is the nucleophile, and which is the electrophilic atom, in the following transformation? Which is the leaving group?



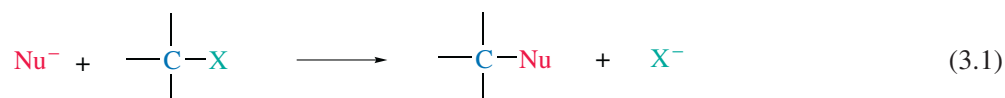
- Cyanide (${}^{-}\text{CN}$) is the nucleophile, and the carbon atom attached to bromine is the electrophilic atom. The bromine (Br) is the leaving group.

As expected in an ionic process, the position of the functional group determines the site of reaction. In this case the bromine atom renders the adjacent carbon atom electrophilic, since the carbon–bromine bond is polarized in the sense



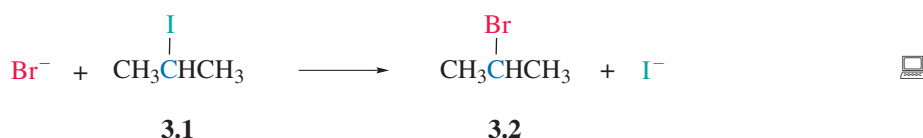
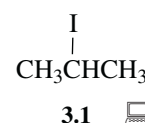
polarization of
carbon–bromine bond

We can generalize this type of substitution for any nucleophile and substrate. To simplify things we have ignored the cation for the time being, as it doesn't participate in the reaction. The general equation for this type of substitution at a saturated carbon atom can be written as follows, ignoring the spectator ions



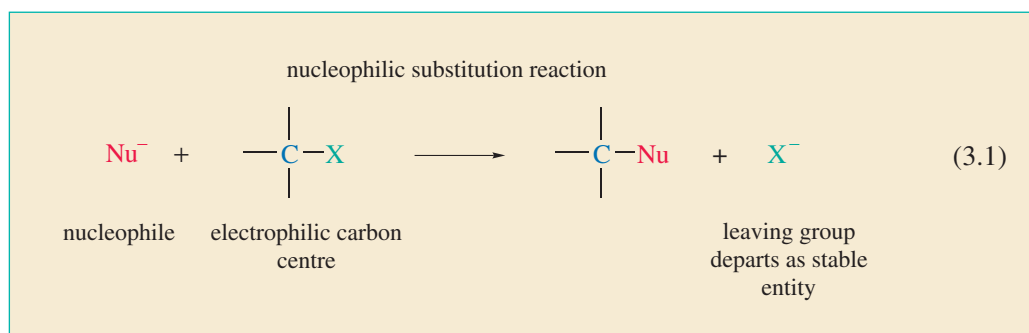
In this general form of the reaction, the nucleophile* Nu^- donates a pair of electrons to the electrophilic carbon to form a new bond and the leaving group, X, takes both electrons in the C–X bond with it when it leaves, thus forming a negatively charged anion, X^- .

- Predict the substitution product when the nucleophile Br^- reacts with 2-iodopropane (Structure 3.1) which contains the iodine leaving group.
- The product is 2-bromopropane (Structure 3.2).



This type of reaction is known as a **nucleophilic substitution reaction**, often abbreviated to **S_N reaction**. As we shall see in the next section, it is the nature of the leaving group X that is primarily responsible for the success or failure of most S_N reactions. The leaving group X serves two roles in an S_N reaction. It must form a polarized covalent bond to carbon in the substrate in order to provide the electrophilic site, but, more importantly, it must become a stable entity when it departs with a pair of electrons. For both these reasons, hydrogen atoms are not substituted in S_N reactions. To act as a leaving group, a hydrogen atom must gain a second electron, thus forming a hydride anion (H^-). However, the hydride anion is a very high-energy species. In the next section, we shall discuss the types of nucleophile and leaving group that can be employed in S_N reactions.

Let's first summarize the main features of the reaction in Equation 3.1:



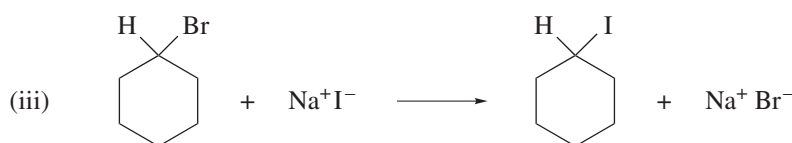
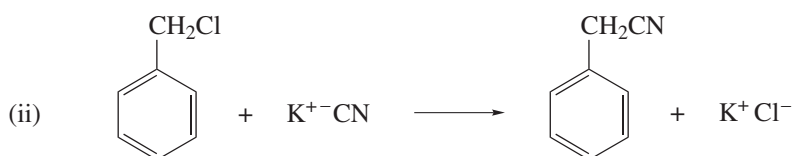
* In this book, we follow the convention of using the symbol Nu^- to represent a charged nucleophile, and Nu : to represent an uncharged nucleophile (uncharged nucleophiles are discussed in Section 3.2.1).

COMPUTER ACTIVITY 3.1 Curly arrows

At some point in the near future you should study *Curly arrows* in the CD-ROM that accompanies this book. This activity reviews the material covered so far in this book and introduces you to curly arrows, a powerful method for keeping track of electrons in bond-making and bond-breaking processes. Curly arrows are used extensively, so it is important that you have a clear understanding of their meaning. If you cannot study the CD-ROM immediately, don't worry, you can read on since the text in the next few sections does not rely on the new concepts taught on the CD-ROM.

QUESTION 3.1

Identify the nucleophile, electrophilic carbon atom, spectator ion and leaving group in each of the following S_N reactions.



Each of the organic reactants and products in (i) to (iii) above is available in WebLab ViewerLite on the CD-ROM associated with this book.

3.2 The scope of the S_N reaction

So far, you have seen that the requirements for an S_N reaction are (i) a nucleophile and (ii) a substrate containing a suitable leaving group. The S_N reaction is extremely versatile, and a large number of combinations of nucleophile and leaving group can be employed. Let's discuss first the range of nucleophiles and leaving groups, and then the practicalities of designing and carrying out a nucleophilic substitution reaction.

3.2.1 Nucleophiles

Nucleophiles were introduced in Section 3.1 and can be formally defined as follows:

All nucleophiles have at least one non-bonded pair of electrons, which ultimately form a new covalent bond.

A list of nucleophiles commonly employed in S_N reactions is given in Table 3.2, together with examples of typical reactions involving these nucleophiles. Look at this list, and check that all the nucleophiles shown are encompassed by the above definition.