UNIT 13 ORGANIC PHOTOCHEMISTRY

Structure

13.1 INTRODUCTION

In the previous block you have studied free radical reactions. We mentioned that free radicals can be generated by homolytic cleavage of a bond. These can also be formed by thermal methods or by photolysis. We also learnt that the thermal methods require considerable energy in the form of heat. Unlike thermal methods, in photolysis the energy is provided by light absorbed by the molecules. In this unit we shall consider the chemistry of such reactions, i.e., organic photochemistry.

Photochemistry deals with the effect of light in causing or modifying chemical changes. Organic photochemistry applies photochemical methods to organic chemistry and *vice-versa*. It is an interdisciplinary topic. The chemical reactions of organic molecules caused by light absorption are quite fascinating and have a wide applicability.

Photochemical reactions have been in progress in nature almost from the time the earth was formed and might have even led to the origin of life on earth. It is generally accepted that combination of ammonia, carbon dioxide and water in presence of sunlight produces amino acids which in turn are transformed to proteins - the building blocks of both animals and plants.

$$NH_3 + CO_2 + H_2O \xrightarrow{h\nu} \text{amino acids} \longrightarrow \text{proteins}$$

Another photoreaction, photosynthesis, is primarily responsible for sustenance of life. In this process, light energy is stored as chemical energy by the plants. In a simple way, photosynthesis can be represented as :

$$H_2O + CO_2 \xrightarrow[\text{Chlorophyll}]{h\nu} \text{carbohydrates} + O_2$$

According to Planck, $E = h\nu$, where E is the energy of radiation, h is the Planck's constant and ν is the frequency of rediation. Light energy is thus represented by $h\nu$

Formation of vitamins D_2 and D_3 and the reaction involved in the chemistry of vision are amongst many reactions which take place in the presence of light.

We shall begin the study of photochemistry by examining its elementary aspects.

Following photochemical reactions will be discussed in this unit :

- photochemical decomposition,
- hydrogen abstraction,
- reduction,
- *cis-trans* isomerisation,
- photosensitisation, and
- cycloaddition.

Finally there will be a discussion of some of the important applications of photochemical reactions.

Objectives

After studying this unit, you should be able to :

- explain the nature of electronic excitation of molecules by absorption of light,
- differentiate between photochemical and thermal reactions,
- describe photochemical reactions such as decomposition, hydrogen abstraction, reduction and *cis-trans* isomerisation,
- explain the role of sensitisers in photoreactions, and
- outline the special features of photochemical reactions.

13.2 SOME ELEMENTARY ASPECTS OF PHOTOCHEMISTRY

Most photochemical reactions can be considered to occur in three stages :

1) Absorption of electromagnetic radiation to produce electronically excited states;
2) Primary photochemical reactions involving excited electronic states; and
3) Secondary or dark reactions whereby the products of the primary photochemical reactions are converted to stable products.

However, light absorbed by a molecule will not necessarily produce a chemical change. The absorbed energy can be lost by different processes.

In this section we will first briefly review the interaction of electromagnetic radiations with organic molecules. Then we will discuss electronic transitions and the fate of the excited molecules.

As said above, for a photochemical reaction to begin, light (electromagnetic radiation) must be absorbed by the molecule and hence, the molecule must possess an absorption band corresponding to the wavelength or wave number or frequency of incident light. Therefore, the subject of spectroscopy is closely related to photochemistry. In Units 7 and 8 of the course 'Atoms and Molecules' and Unit 4 of the course 'Organic Chemistry', we discussed how radiation from various regions of the electromagnetic spectrum interacts with organic molecules. Before discussing the chemical changes that result from the absorption of light, let us review briefly the interaction of electromagnetic radiation with organic molecules.

When a molecule absorbs electromagnetic radiation, it is raised from its ground state of minimum energy to an excited state of higher energy. This process is referred to as excitation. Excitation in the rotational, vibrational or electronic energy levels of molecules results from absorption in microwave, infrared, visible and ultraviolet region of the electromagnetic spectrum. The changes brought about in organic molecules by electromagnetic radiations are summarised in Table 13.1. A change in the rotational levels

of a molecule requires absorption of low energy only and it corresponds to microwave region. The change in the vibrational levels of a molecule requires 10-100 times more energy and this corresponds to the infrared region of the electromagnetic spectrum. The electronic energy levels requires promotion of an electron from one molecular orbital to another of higher energy, and this is even more energy-demanding than vibrational excitation. In fact, more than ten times of the energy required for vibrational excitation is required for electronic energy level transitions. For an electronic energy level transition, there must be absorption in the ultraviolet and visible regions of the electromagnetic spectrum.

Table 13.1 : The effects of various kinds of radiation on molecules

		Type	Effect on absorbing molecule
Increasing energy	↑	Ultraviolet and visible	Electronic excitation
		Infrared	Vibrational excitation
		Microwaves and radio waves	Rotational

It is the electronic excitation that is of prime importance in organic photochemistry, although it is inevitably accompanied by some increase in vibrational and rotational energies. We shall, therefore, concentrate on the effects of visible and ultraviolet light on organic molecules.

Absorption by a molecule, of radiation in the ultraviolet (200-400 nm) or visible (400-800 nm) regions of the electromagnetic spectrum can result in an excited state. The energy absorbed is comparable in magnitude with the bond dissociation energy associated with organic molecules. For example, if absorption occurs at λ 250 nm, the energy associated with this transition can be calculated by the following equation,

$$E = h\nu = h\,\frac{c}{\lambda}$$

where h is the Planck's constant (6.626×10^{-34} J s) and
c is the velocity of light (2.998×10^{8} m s^{-1}).

$$E = \frac{6.626 \times 10^{-34}\,(\text{J s}) \times 2.998 \times 10^{8}\,(\text{m s}^{-1})}{250 \times 10^{-9}\,(\text{m})}$$

$$= 7.94 \times 10^{-19}\ \text{J}.$$

We can compare the energy associated with this wavelength with the bond energies, once we get this energy in molar quantities as we do for bond energy. For this, we have to multiply the value obtained above, by Avogadro number (6.022×10^{23}).

$E = 6.022 \times 10^{23} \times 7.94 \times 10^{-19}\ \text{J mol}^{-1}$

$= 47.85 \times 10^{4}\ \text{J mol}^{-1}$ or

$= 478.5\ \text{kJ mol}^{-1}$.

This is greater than the bond dissociation energy of a carbon-carbon σ-bond (347 kJ mol^{-1}). It is not surprising, therefore, that C–C bond breakage and subsequent chemical reaction can be induced by excitation with ultraviolet light.

Now consider briefly the electronic transitions in organic molecule.

13.2.1 Electronic Transitions

According to molecular orbital theory (which we discussed in Unit 5 of 'Atoms and Molecules') the interactions of atomic orbitals leads to the formation of bonding and antibonding molecular orbitals. Depending on the nature of the overlapping atomic orbitals, bonding molecular orbitals may be of σ type, with the electron density being concentrated along the internuclear axis. They may also be of the π type where the electron density is concentrated on either side of the internuclear axis. Electron density probability

contours for electrons occupying σ and π (bonding), σ* and π* (antibonding) orbitals are shown in Fig. 13.1 (a). The relative energies of these orbitals and that of nonbonding orbital *n*, are given in Fig. 13.1 (b).

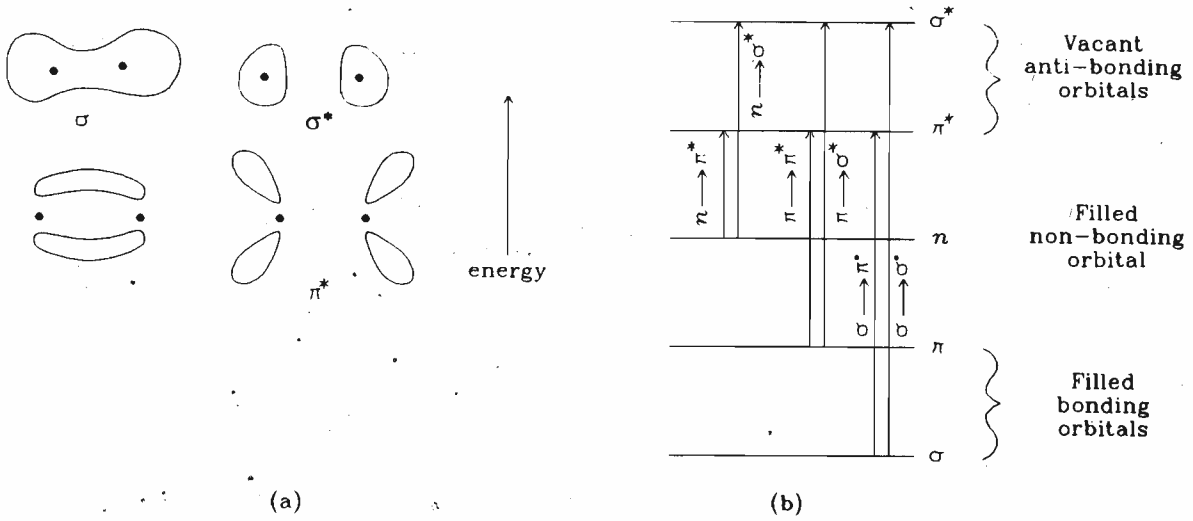

Fig. 13.1 : Shapes and relative energies of molecular orbitals
a) Bonding and antibonding orbitals,
b) Relative energies of orbitals and possible transitions between them

When excitation takes place, and electron from one of the filled orbitals (σ, π or *n*) gets excited to one of the vacant antibonding orbitals (σ* or π*). Since various excitations are possible, there are various absorptions, corresponding to these transitions :

$\sigma \rightarrow \sigma^*$, $\sigma \rightarrow \pi^*$, $\pi \rightarrow \sigma^*$, $\pi \rightarrow \pi^*$, $n \rightarrow \sigma^*$, $n \rightarrow \pi^*$

As expected, the electrons require a high energy for excitation to σ* level. The order of decreasing energy for the absorption is as follows :

$\sigma \rightarrow \sigma^* > \sigma \rightarrow \pi^* > \pi \rightarrow \sigma^* > \pi \rightarrow \pi^* \sim n \rightarrow \sigma^* > n \rightarrow \pi^*$

Of all the possible transitions, the last three account for absorption in the region, 200-800 nm, while others demand much higher energy. The last three transitions are also responsible for the bulk of organic photochemical reactions.

In the previous courses we also mentioned that the wavelength of absorption for any particular transition is dependent on the structure of a molecule. For example the $\pi \rightarrow \pi^*$ transition in ethene occurs at 171 nm, while in butadiene it is observed at 213 nm. As conjugation is increased, the energy required for $\pi \rightarrow \pi^*$ excitation decreases and the transition occurs at longer wavelength. The $n \rightarrow \pi^*$ excitation of saturated carbonyl Compounds such as propanone (acetone) occur at 279 nm.

So far we have not discussed the electronic arrangement in molecular orbital during electronic transition. We have noted previously (Atoms and Molecules course) that in the ground state of many molecules, electrons are generally paired and their spins (represented as $+\frac{1}{2}$ or $-\frac{1}{2}$) cancel each other. If spins of the electrons of a molecule cancel regardless of whether the electrons are all paired in orbitals the molecule is said to be in the **singlet state**. If all the electrons are paired in their ground state orbitals, the molecule is said to be in the **ground singlet state**, (S_0).

When a molecule absorbs a photon of ultra violet or visible light, an electron is promoted from a ground state orbital to an excited state orbital. If the spin state of the electron that absorbs the energy does not change, that is, the molecule is still in the singlet state, the molecule is said to be in the **excited singlet state**, S_1. A molecule may be in higher excited state, i.e., S_2, S_3, ..., depending on the energy of the excited state. When a molecule goes from higher to lower excited state, the electron immediately drops to the lowest energy excited singlet state (S_1) by a process called **internal conversion**. The energy lost during internal conversion is transformed into heat and molecular motion.

The excited state also can have unpaired electrons. That is, spin state of electrons of the molecule do not cancel because the spin state of one electron in the molecule has changed.

The nomenclature *S* and *T* follows from the multiplicity (*M*) observed in atomic absorption and emission spectra. *M* is equal to $2S + 1$, where *S* is the total spin of the system. Thus, with a spin paired system, $S = 0$ and $M = 1$ (singlet), and for a spin-parallel system $S = 1$ and $M = 3$ (triplet).

States with unpaired electrons are called triplet state (T,). and normally are more stable than the corresponding singlet states. The electronic configuration for ground singlet (S_0), excited singlet (S_1) and triplet (T_1) states of the π electrons of ethene are shown in Fig. 13.2.

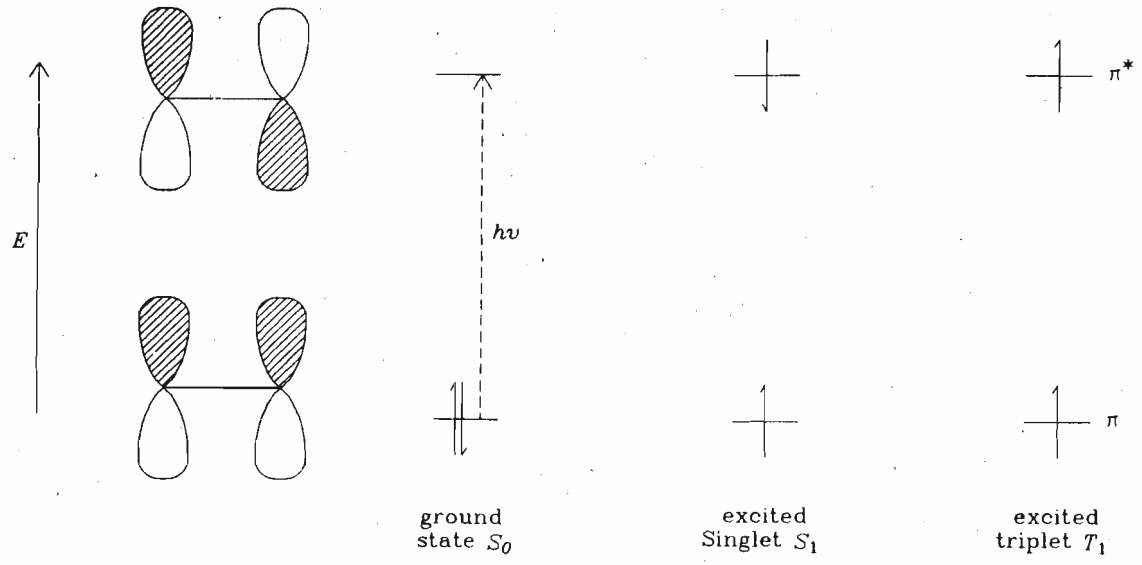

Fig. 13.2 : $\pi \rightarrow \pi^*$ excitation of ethene.

The $n - \pi^*$ excitation of a carbonyl group is depicted in Fig. 13.3, and again singlet and triplet excited states are possible. As said above, the $n - \pi^*$ excitation is energetically more favoured than the $\pi - \pi^*$ transition.

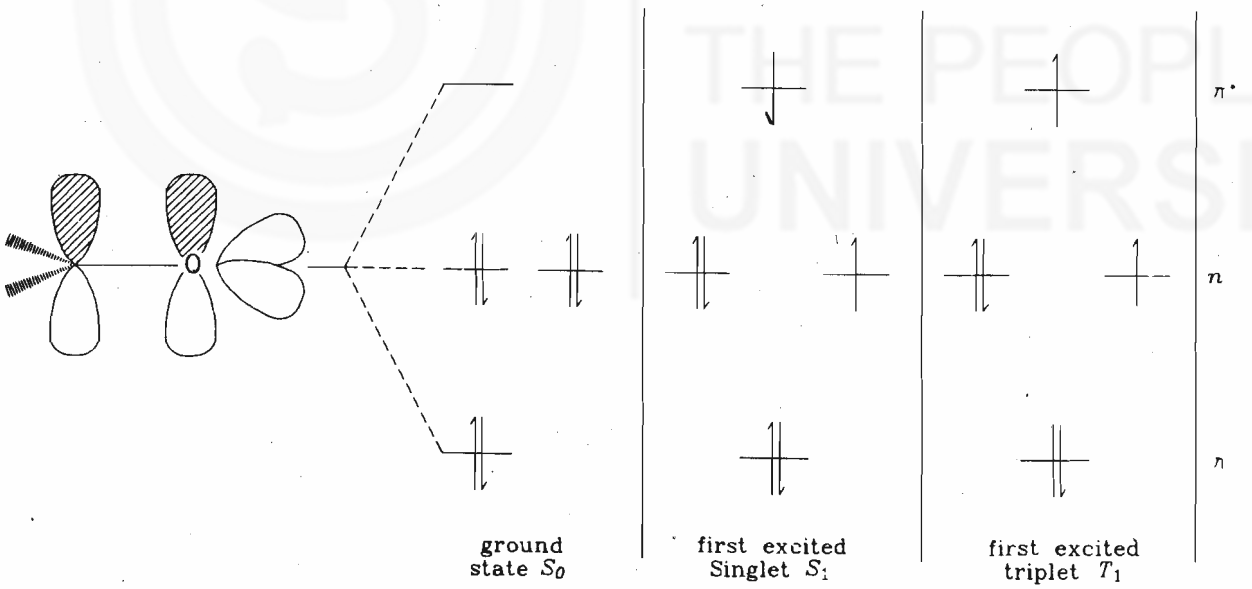

Fig. 13.3 : $n - \pi^*$ excitation in carbonyl compound.

Electronic transitions occur (10^{-15} s), more rapidly than a molecular vibration (10^{-13} s), and consequently at the instant of excitation, only electrons are reorganised, the heavier nuclei retain their ground state geometry. The statement of this condition is referred to as the **Franck-Condon** principle. It states that the relative nuclear positions are unaltered in electronic excitation, these correspond to the vertical transitions shown on the potential energy diagram in Fig. 13.4. After the excitation, however, geometrical changes can occur very rapidly.

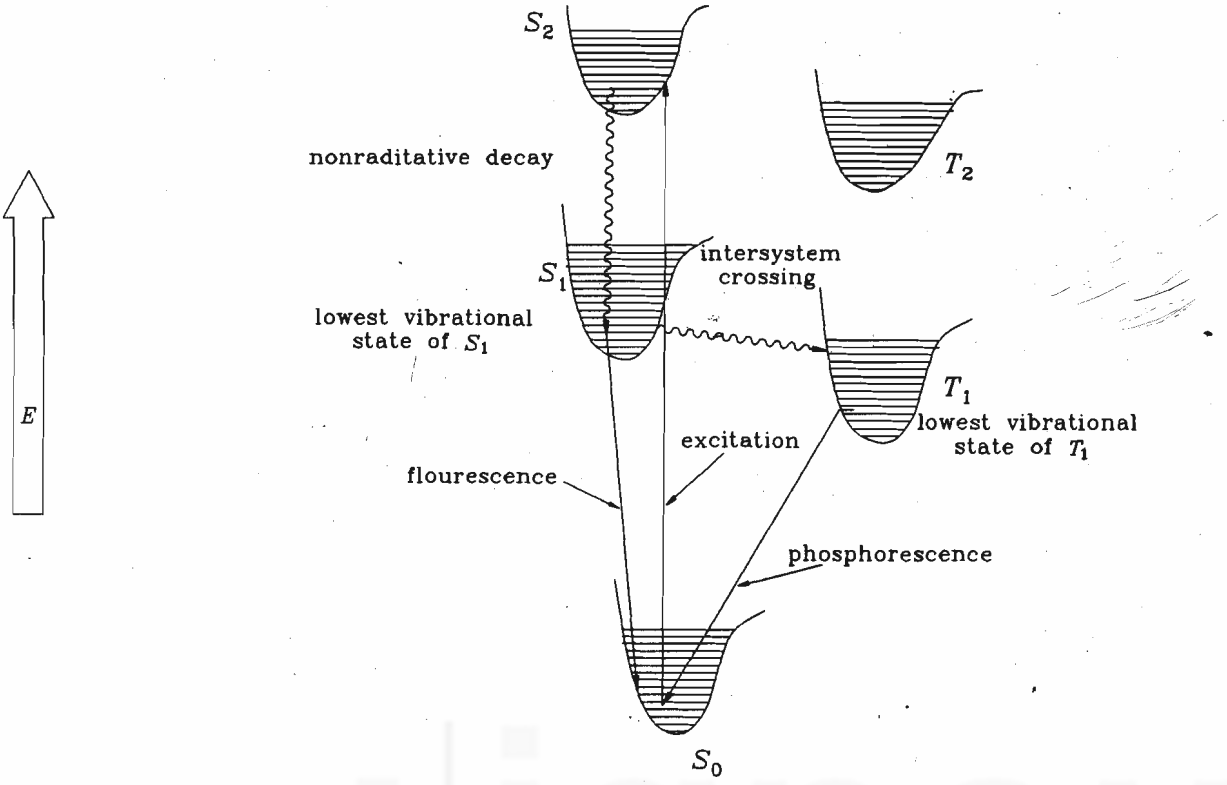

Fig. 13.4 : Energy level diagram and summary of photochemical process. Nonradiative process are shown as wavylines.

The equilibrium internuclear distance of the excited state will be greater than that of the ground state, as a consequence of excitation from a bonding molecular orbital to an antibonding molecular orbital. A molecule in the ground state will exist in one of its lowest vibrational levels, represented by the horizontal lines in Fig. 13.4. Excitation, obeying the Franck-Condon principle, will afford the first excited singlet of the molecule that is higher in vibrational energy. The excess vibrational energy of the excited state will be rapidly lost by molecular collisions and dissipated as heat. Electronic transitions can occur from any vibrational level of the ground state to any vibrational level of the excited state. Thus, the energy required to affect an electronic transition will vary within a limited range and give rise to a broad absorption band as observed in ultraviolet and visible spectra (see spectrum of propanone in Fig. 13.5).

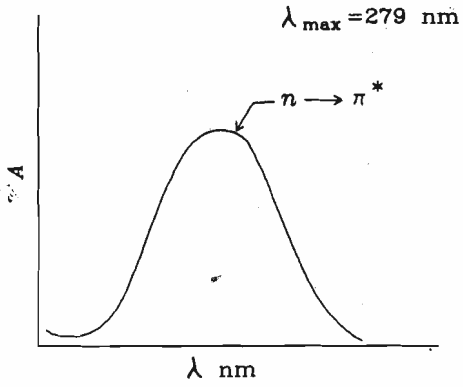

Fig. 13.5 : Spectrum of propanone (acetone)

As you know, the intensity of an absorption band follows Beer-Lambert law, which can be expressed mathematically as,

$$\log_{10} \frac{I_0}{I} = A = \varepsilon c l$$

where I_0 and I are the intensities of the incident and transmitted radiation respectively, A is defined as the absorbance, c, the concentration (mol dm^{-3}), l is the path length (1 cm) and ε

is defined as the molar extinction coefficient (m^2 mol^{-1}) and is a measure of a transition probability. For a singlet $\pi - \pi^*$ excitation, normally ε has value in the range 10^2-10^4 m^2 mol^{-1}, indicating a high probability of excitation, while for a singlet $n \rightarrow \pi^*$ process, ε is usually in the range 1-5 m^2 mol^{-1}. For singlet to triplet excitation processes the extinction coefficients are very small and less than unity, indicating the low probability of these transitions.

Application of quantum mechanical theory to electronic excitation process has led to a set of **selection rules** by which transition can be classified as allowed, or forbidden. They are :

1) All excitation processes involving conservation of spin (or multiplicity) are allowed, e.g., $S_0 \rightarrow S_1$, $S_1 \rightarrow S_0$, while those involving a change in spin are spin forbidden, e.g., $S_0 \rightarrow T_1$.

2) Excitation processes between states with the same symmetry are allowed, e.g., $\pi \rightarrow \pi^*$ singlet excitation of ethene, while transitions between states of different symmetry are symmetry forbidden, e.g., $n \rightarrow \pi^*$

Although $S_0 \rightarrow T_1$ and $n \rightarrow \pi^*$ excitations are forbidden processes, they are, in fact, often observed owing to a breakdown in the selection rules.

Now the question is what is the fate of the electronically excited molecule? Once formed, the excited singlet and triplet states will either undergo chemical reaction (photochemical reaction) or lose their excitation energy by either a **radiative** or a **non-radiative process** In the next section, we will take up the details of the fate of the excited molecules.

13.2.2 Fate of the Excited Molecules

Most molecules are singlets in the ground state (all electron spins paired), and the first excited state on light absorption is usually a singlet state, S_1. As we have seen, promotions from S_0 to triplet are 'forbidden'. S_1 excited state has a very short life time (10^{-8} to 10^{-7} sec). The excess energy possessed in the singlet state can be dissipated by one or more of the following ways:

1) S_1 can return to ground state (S_0) by emission of light or a photon. This process is called **fluorescence.** Flourescent light has longer wavelength than the light required for the original excitation.

2) Deactivation to a higher vibrational level of the ground state by a non-radiative process. This is an internal conversion. The excited vibrational level again gives energy to its environment until it achieves an equilibrium distribution with the lowest vibrational level. The net result of all of these changes is the conversion of the original light energy into heat.

3) S_1 can undergo intersystem crossing to a triplet excited state by a non-radiative process.

4) S_1 can undergo chemical transformation such as decomposition, isomerisation or chemical reaction with surrounding molecules leading to a new product (non-radiative). This process forms the basis of organic photochemistry, which will be described in a later section.

5) S_1 can transfer its excess electronic energy to other molecules and become converted to S_0. This process is called singlet energy transfer **(photosensitisation)** and is symbolised as $S_1 + S'_0$ (acceptor) $\rightarrow S_0 + S'_1$ (acceptor). This kind of energy transfer is also a very important aspect of photochemistry.

A molecule in the triplet excited state has a longer life time (10^{-2} to 10^{-1} sec). It behaves as a radical and participates in bimolecular reactions, e.g., photosensitisation, which will be described later.

The energy loss from a triplet state can take place by one or more of the following ways :

1) T_1 can return to ground state (S_0) by emission of light or a photon. This process is called **phosphorescence.** As in the case of fluorescence, the wavelength of the phosphorescent light is longer than that of the initially exciting light. Phosphorescence is a low probability event because of the change in electron spin required. It is generally observed only at low temperatures for which thermal events

have been slowed down. For bezene at 73 K, the absorption of light at 254 nm leads to fluorescence centered at 290 nm and phosphorescence at 340 nm.

2) T_1 can undergo internal conversion to a higher vibrational level of the ground state (non-radiative).

3) T_1 can undergo intersystem crossing to a singlet state, S_0 (non-radiative). The net result in this case is again the conversion of light energy to heat.

4) In this process T_1 can convert to T_1 of an isomeric molecule or it can intersystem cross to S_0 of an isomer. Either process result in photochemical isomerisation. Alternatively, T_1 can react on collision with another molecule to initiate a photochemical reaction.

5) T_1 can transfer its electronic spin to another molecule and become converted to S_0. This process is called triplet energy transfer (photosensitisation) and is symbolised as,

$$T_1 + S'_0 \text{ (acceptor)} \rightarrow S_0 + T'_1 \text{ (acceptor)}$$

This transformation is also a very important aspect of photochemistry.

The above paths of excited singlet and triplet states are further illustrated by two schematic representations. One is shown in Fig. 13.4 and other is shown in Fig 13.6, which is also called Jablonski diagram.

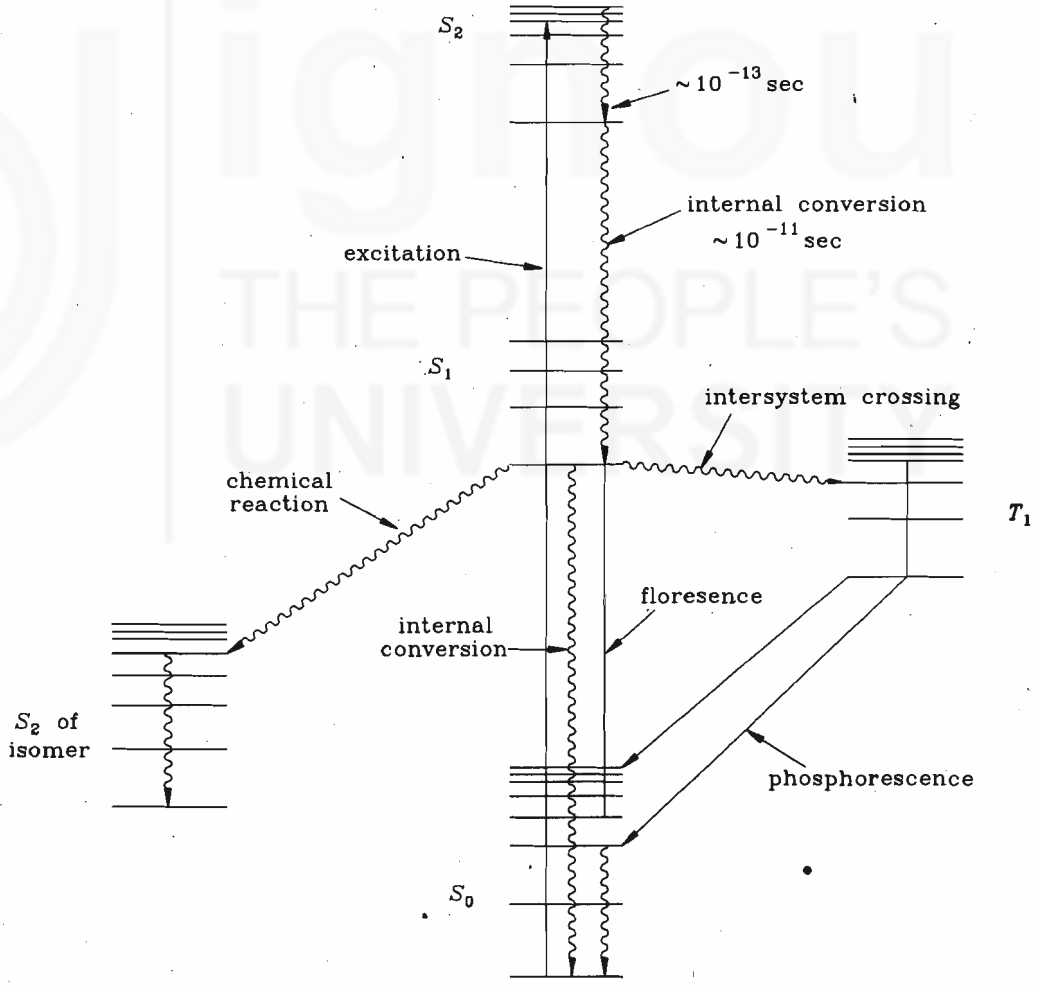

Fig. 13.6 : A Jablonski diagram showing excitation and deactivation routes.

Excited states can also be quenched. Quenching is essentially the same physical process as sensitisation, but the word "quenched" is applied when a photoexcited state of the reactant is deactivated by transferring its energy to another molecule in solution. This substance is called a quencher.

We are further summarising these physical processes undergone by excited molecule in Table 13.2.

Table 13.2 : Physical processes undergone by excited molecules

$S_0 + h\nu \rightarrow S_1$	Excitation
$S_1 \rightsquigarrow S_1$ + heat	Vibrational relaxation
$S_1 \rightarrow S_0 + h\nu$	Fluorescence
$S_1 \rightsquigarrow S_0$ + heat	Internal conversion
$S_1 \rightsquigarrow T_1$	Intersystem crossing
$T_1 \rightsquigarrow T_1$ + heat	Vibrational relaxation
$T_1 \rightarrow S_0 + h\nu$	Phosphorescence
$T_1 \rightsquigarrow S_0$ + heat	Intersystem crossing
$S_1 + S'_0 \rightarrow S_0 + S'_1$	Singlet-singlet transfer (photosensitisation)
$T_1 + S'_0 \rightarrow S_0 + T'_1$	Triplet-triplet transfer (photosensitisation)

13.2.3 Difference Between Photochemical and Thermal Reactions

Now in this background you can understand the difference between the thermal and photochemical reactions. Thermal reactions occur through higher vibrational levels of the ground state, whereas, photochemical reactions take place through electronic excited states (singlet or triplet). Thermal reactions involve lesser energy (63-209 kJ mol^{-1}) as compared to photochemical reactions (209-627 kJ mol^{-1}). Light-induced reactions are thus comparatively high energy processes.

Many organic compounds get blackened at elevated temperature. Thermal reactions very often lead to tar-like products. In photochemical reactions, the light energy is absorbed by the reactants at room temperature or even below room temperature, the reaction vessel may be immersed in a cooling bath. Quite often, specially at high concentration of the reactants, photoreactions lead to polymeric products. In such cases low concentration of reactants are used in practice.

We have already illustrated, the complementary relationship between thermal and photochemical reactions by considering pericyclic reaction in Unit 12. There we have used the frontier orbital method for analysing the mechanism of both thermal and photo induced reactions. We have also discussed how a forbidden thermal reaction is symmetrically allowed in photo induced conditions.

Having learned the special features of photochemical reactions we will take up some examples of carbonyl compounds and alkenes to familiarise ourselves with the common reaction types.

Before going on to study common photochemical reactions, try the following SAQs.

SAQ 1

The UV spectrum of propanone (acetone) shows two absorption maxima at 190 (ε =1100) and 279 (ε = 15) nm, which is due to $n \rightarrow \pi^*$ transition. Explain.

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SAQ 2

Calculate energy in kJ mol^{-1} associated with electromagnetic radiation of wavelength 500 nm.

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13.3 PHOTOCHEMICAL REACTIONS

We have said that the energy of visible and ultraviolet light is of the same order of magnitude as that of covalent bond. Therefore, when a molecule absorbs a photon of light, it may cleave into two parts. This process is known as **photolysis.** (Cleavage is caused by light). We have already discussed the photolysis of Cl_2 into $2Cl^{\bullet}$ as the initiation step in free radical halogenation. Let us discuss few more reactions.

13.3.1 Photolysis of Propanone (Acetone)

The term photolysis is used when light absorption of molecules leads to cleavage of bonds. A typical example is the photochemical decomposition of propanone (acetone). Absorption of light by propanone results in the formation of an excited state which has sufficient energy to undergo cleavage of a C—C bond (the weakest bond in molecule). The nature of products is dependent on temperature. At high temperature carbon monoxide and ethane are formed. The reaction path is shown as :

$$CH_3COCH_3 \xrightarrow[(i)]{h\nu} [CH_3COCH_3]^* \xrightarrow[(ii)]{} \dot{C}H_3 + CH_3\dot{C}{=}O$$

$$CH_3\dot{C}{=}O \longrightarrow \dot{C}H_3 + CO$$

$$2\dot{C}H_3 \longrightarrow C_2H_6$$

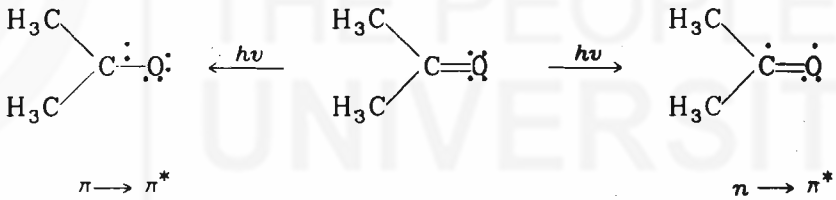
Propanone vapour undergoes a photo dissociation reaction with 313 nm light with quantum yield (ϕ) somewhat by the unity.

The efficiency of photochemical process is defined by the product quantum yield, ϕ where

$$\phi = \frac{\text{The number of molecules reacting per unit volume per unit in time}}{\text{number of photons ed per unit volume unit time}}$$

In most photochemical reactions the quantum yield for any particular product will range from zero to unity.

Absorption of light by propanone gives rise to it as excited state ($n \rightarrow \pi^*$ transition). It could be either a singlet or a triplet. It has been shown that the above reaction occurs more efficiently through the triplet state. The carbon-carbon bond (generally the one α to the C = O group), being weaker as compared to carbon-oxygen double bond, is broken in the first two steps. Dimerisation of methyl radicals gives ethane in the last step. Among these steps, the first step reaction is a primary photochemical reaction. The other steps are dark reactions. The excited state has been shown above by putting the molecular formula in a bracket with an asterisk. It is not possible to draw an explicit structure of the excited state using conventional bonds because the excited electron is not present in a bonding orbital. Sometimes the excited states are represented as :



At room temperature, photolysis of propanone gives 2, 3-butanedione (biacetyl), ethanal (acetaldehyde), methane and 2, 5 hexanedione. The reaction path is shown as :

$$CH_3COCH_3 \xrightarrow{h\nu} [CH_3COCH_3]^* \longrightarrow CH_3\dot{C}{=}O + \dot{C}H_3$$

$$2CH_3\dot{C}{=}O \longrightarrow CH_3\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}CH_3$$

2,3–butanedione
(biacetyl)

$$CH_3\dot{C}=O + CH_3COCH_3 \longrightarrow CH_3\overset{H}{\overset{|}{C}}{=}O + \dot{C}H_2COCH_3$$

ethanal

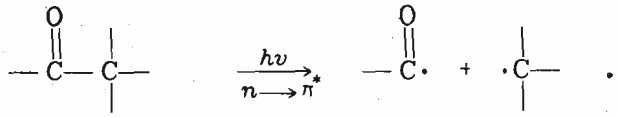
$$\dot{C}H_3 + CH_3COCH_3 \longrightarrow CH_4 + \dot{C}H_2COCH_3$$

methane

$$2\dot{C}H_2COCH_3 \longrightarrow CH_3COCH_2CH_2COCH_3$$

2,5 –hexanedione

In unsymmetrical ketones (having different alkyl groups) preferential cleavage gives the more stable alkyl radical. Photochemical reactions of ketones, and also of aldehydes, by fission of carbon-carbon bond and elimination of carbon monoxide, are termed as the **Norrish type I** processes after the eminent photochemist, R.G.W. Norrish who received the 1961 Nobel Prize in Chemistry for his work on photochemical reactions.



SAQ 3

Write a mechanism for formation of cyclobutane from the photolysis of cyclopentanone.

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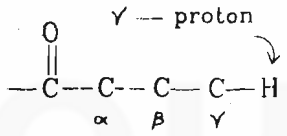
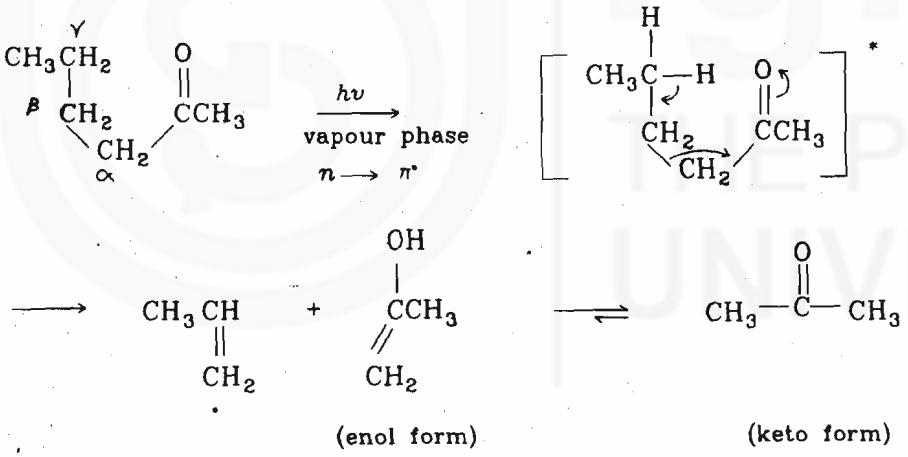
13.3.2 Photolysis of 2-Hexanone

In ketones, where one of the alkyl groups has three or more carbon atoms and the γ-carbon is attached to one or more hydrogen atoms, the photochemical course of decomposition is different from that described above. In these cases, the excited state of ketone undergoes an intramolecular hydrogen transfer (from γ-carbon to oxygen of the carbonyl group) accompanied by the fission of α – β carbon-carbon bond in the alkyl group. The products are an alkene and a simpler ketone (through its enol form). This process is commonly known as **Norrish type II** reaction. An illustrative example is the photolysis of 2-hexanone to propene and propanone shown below:

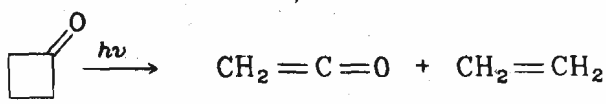


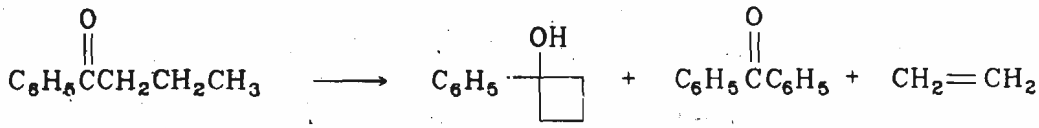


The hydrogen attached to γ-carbon atom (which gets transferred later), oxygen and four carbon atoms constitute a six-membered transition state. Such a transition state is considered much favourable for bond making and breaking to occur. Elimination of carbon monoxide (Norrish type I process) could also take place, but to a lesser extent. Propanone, the product of photocleavage of 2-hexanone can undergo Norrish type I reaction (described in 13.3.1). Thus, photolysis of 2-hexanone gives a complex mixture of products consisting of propene, propanone, ethane and carbon monoxide.

SAQ 4

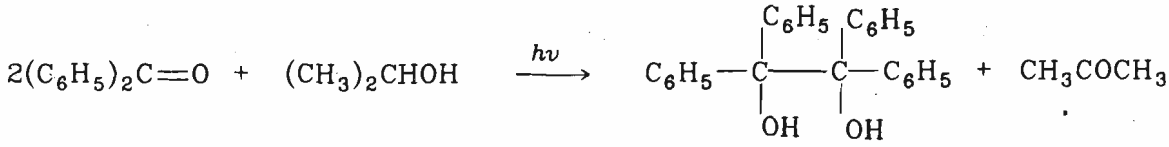
Give the mechanistic paths in the following reactions.

a) 

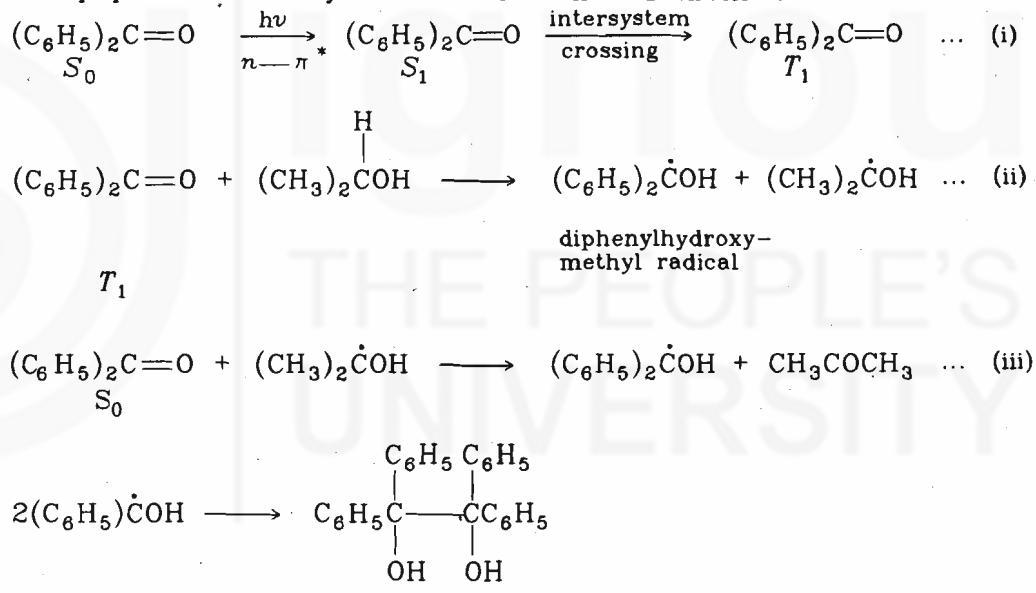
b) 

13.3.3 Photoreductive Dimerisation of Diphenylmethanone (Benzophenone)

You have learned earlier that reduction of diphenylmethanone (benzophenone) by zinc and ethanoic acid (acetic acid) gives benzopinacol. This reaction also occurs when a solution of diphenylmethanone in an alcoholic solvent (preferably 2-propanol) is exposed to sunlight. It is known as the photoreductive dimerisation and has been studied in great detail.

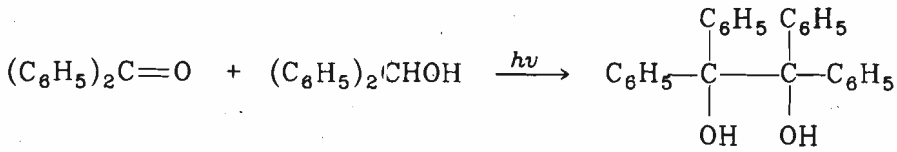


It has been observed that the quantum yield for benzopinacol is unity. This means that each molecule of excited diphenylmethanone gives rise to one molecule of benzopinacol. Further, no fluorescence of diphenylmethanone is observed. Hence, a triplet excited state may be involved in the above reaction. Since a $n \rightarrow \pi^*$ triplet has more radical character than a $\pi \rightarrow \pi^*$ triplet, it is generally believed that a $n \rightarrow \pi^*$ triplet excited state abstracts a hydrogen atom from 2-propanol more efficiently. The mechanistic details are shown below :

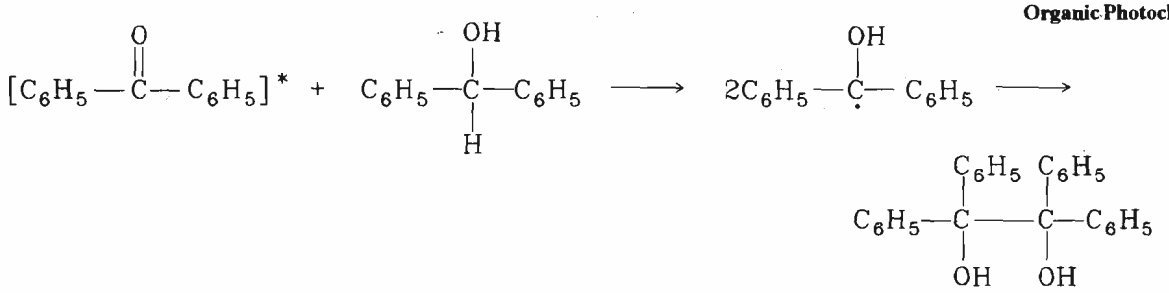


Diphenylhydroxymethyl (benzhydrol) radicals [$(C_6H_5)_2\dot{C}OH$] are formed by abstraction of hydrogen from 2-propanol by a triplet excited diphenylmethanone (step ii) and also by abstraction of a hydrogen from 2-hydroxy-2-propyl radical by diphenylmethanone in ground state (step iii). The 2-hydroxy-2-propyl radical has a very short life-time. It transfers its hydroxylic hydrogen too rapidly (step iii) and gets converted to propanone rather than undergoing dimerisation to pinacol [$(CH_3)_2COHCOH(CH_3)_2$]. This step (iii) is energetically favourable because of the greater possibility for delocalisation of the odd electron in diphenylhydroxymethyl radical than the 2-hydroxy-2-propyl radical.

Diphenylmethanone also gives benzopinacol on irradiation in a low concentration of diphenylmethanol (benzhydrol).



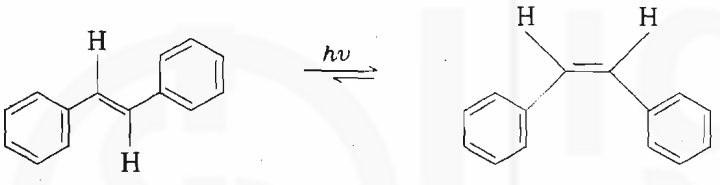
The mechanism is similar to that for isopropyl alcohol as the reducing agent :



This reaction supports the view that the excited state of diphenylmethanone has a relatively longer life-time and hence a triplet state (and not a singlet state) is involved in this reaction. Calculations have shown that the singlet excited state of diphenylmethanone undergoes intersystem crossing to triplet state very rapidly.

13.3.4 Photoisomerisation of *Cis*- and *Trans*-1, 2-diphenylethene (Stilbene)

Geometrical isomerisation is a typical photoreaction of many olefinic compounds. The photochemical *cis-trans* isomerisation of 1, 2-diphenylethenes (stilbenes) has been studied in great detail. Irradiation of a solution of *trans*- 1, 2-diphenylethene in hexane with UV light results in the formation of the *cis*-isomer. After sometime the *cis-trans* ratio becomes constant and does not change as the irradiation is continued. This condition is called a photostationary state (the rates of formation and disappearance of each of the transient molecular entities formed are equal) and is also reached on irradiation of the *cis*-isomer. It has been observed that the equilibrium favours the formation of the *cis*-isomer.

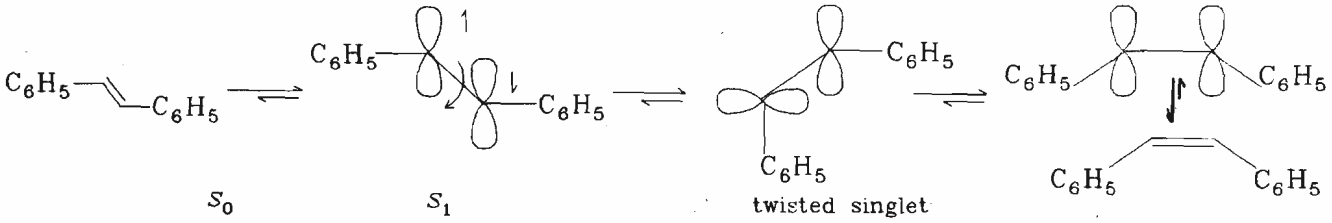


trans –1,2– diphenylethene
λ_{max} (ϵ) = 295mm (16300)

cis – 1,2 – diphenylethene
276mm (2280)

The *trans* isomer is more stable as *cis*-1, 2-diphenylethene is distorted from planarity due to the non-bonded interaction between the *ortho* hydrogens in the benzene rings. Thermal equilibrium would favour the conversion of *cis*-1, 2-diphenylethene to its *trans* isomer.

Although both isomers absorb light, the *trans* isomer, having a higher extinction coefficient and absorbing at a longer wavelength, gets excited much more rapidly to the singlet state than *cis*-1, 2-diphenylethene. Rotation about carbon-carbon bond relieves the unfavourable interaction between the singly filled orbitals of carbon atoms and gives rise to the "twisted" or "non-planar" singlet state. These steps are shown as :

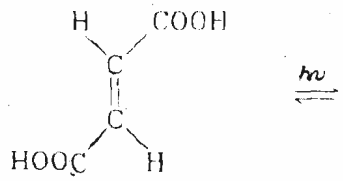


S_0 S_1 twisted singlet

Thus, photoequilibrium favours the formation of the *cis*-isomer. It is different from the thermal equilibrium described above. The singlet excited states of *cis*- and *trans*-1, 2-diphenylethene arise from a $\pi \rightarrow \pi^*$ transition, since in the absence of any heteroatom the non-bonding orbitals do not contain any electron. In alkenes and dienes, the triplet state has a much higher energy as compared to the singlet state which makes the intersystem crossing (S_1 to T_1 state) quite inefficient. Thus, many photoreactions of alkenes and dienes on direct irradiation (in the absence of a photo sensitiser) occur through their excited singlet states. The above isomerisation also occurs in presence of photosensitisers. The results are described in next subsection.

SAQ 5

Complete the following reaction.



13.3.5 Photosensitisation

The photochemical *cis-trans* isomerisation of alkenes can also occur in a sensitised reaction, but its path is different from the unsensitised one.

Before going in detail of photosensitisation reactions, let us define the term sensitisation. Excitation of a ground state molecule by another excited molecule by energy transfer is termed as sensitisation, and the deactivation of the excited molecule is termed as quenching. Both sensitisation and quenching play an important role in organic photochemistry. We have already mentioned photosensitisation i.e., singlet energy transfer and triplet energy transfer in subsection 13.2.2.

$S_1 + S'_0$ (acceptor) $\rightarrow S_0 + S'_1$ (acceptor)

$T_1 + S'_0$ (acceptor) $\rightarrow S_0 + T'_1$ (acceptor)

The process of photosensitisation allows the attainment of an excited state otherwise difficult to attain. For example, in alkenes it is difficult to get a significant triplet state population by $S_1 \rightarrow T_1$ intersystem crossing. The triplet state, however, can be obtained by the transfer of excitation energy from a different molecule in the triplet state. For this purpose we use sensitiser, usually a ketone such as diphenylmethanone (benzophenone) or 1-(2-naphthyl) ethanone. The sensitiser is raised by an $n \rightarrow \pi^*$ transition from the singlet ground state (S_0) to an excited state (S_1) by absorption of light. Intersystem crossing then occurs rapidly to give the triplet state (T_1) of the sensitiser.

$$\underset{(S_0)}{\text{Sens}} \rightarrow \underset{(S_1)}{[\text{Sens}]^*} \xrightarrow[\text{Crossing}]{\text{intersystem}} \underset{(T_1)}{[\text{Sens}]^*}$$

In next step excitation of alkene takes place by energy transfer from the triplet state of the sensitiser. During this process the net electron spin is conserved, which means that the alkene will be excited to the triplet state :

$$\begin{array}{ccccccc} [\text{sens}]^* & + & \text{alkene} & \longrightarrow & \text{sens} & + & [\text{alkene}]^* \\ \uparrow\downarrow & & \uparrow\downarrow & & \uparrow\downarrow & & \uparrow\downarrow \\ T_1 & & S'_0\ (\text{acceptor}) & & S_0 & & T'_1\ (\text{acceptor}) \end{array}$$

Intersystem crossing in ketones is quite efficient, the S_1 state gives the triplet state of benzophenone.

Let us consider now a specific example which further illustrates the use of sensitisation in photochemistry.

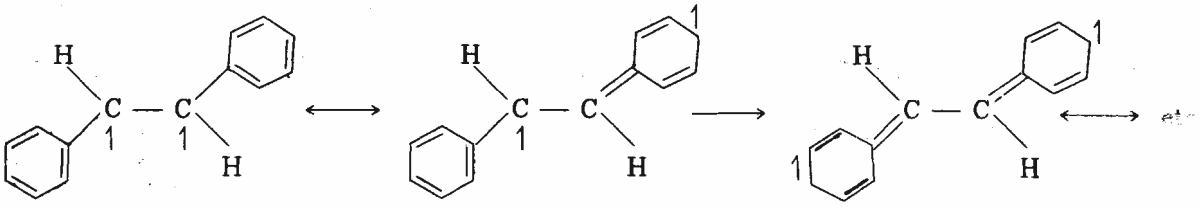
In the presence of a sensitiser, the triplet excited state of *trans*-1, 2-diphenylethene takes part in photochemical reaction. The sensitiser such as diphenylmethanone, as shown above, absorbs light and by an $n \rightarrow \pi^*$ transition is excited to its singlet state (S_1) from its ground state (S_0).

$$\underset{(S_0)}{(C_6H_5)_2CO} \xrightarrow[n \rightarrow \pi^*]{h\nu} \underset{(S_1)}{[(C_6H_5)_2CO]^*} \xrightarrow[\text{crossing}]{\text{Intersystem}} \underset{(T_1)}{[(C_6H_5)_2CO]^*}$$

The excitation energy is transferred from diphenylmethanone in triplet state to *trans*-1, 2-diphenylethene molecule in its ground state by collisional process to give triplet state of *trans*-1, 2-diphenylethene whereby diphenylmethanone is deactivated to its ground state.

$$[(C_6H_5)_2CO]^* + (C_6H_5)_2\,C_2H_2 \longrightarrow (C_6H_5)_2\,CO + [C_6H_5)_2\,C_2H_2]^*$$
$$T_1 \qquad S'_0 \text{ (acceptor)} \qquad\qquad S_0 \qquad T'_1 \text{ (acceptor)}$$

The triplet diphenylmethanone acts as a donor and *trans*-1, 2-diphenylethene in its ground state acts as an acceptor of the excitation energy. In this process the total spins are conserved, i.e., a triplet and a singlet give rise to a new triplet and a new singlet species. The triplet state of 1, 2-diphenylethene is stabilised by resonance :



trans-1, 2-diphenylethene

It is noticeable that the two ethenic carbones in the triplet 1, 2-diphenylethene do not possess much double-bond character and hence lesser energy would be required to effect a rotation about the central C—C bond. This would lead to a rapid interconversion between the triplets of *cis*-and *trans*-1, 2-diphenylethene.

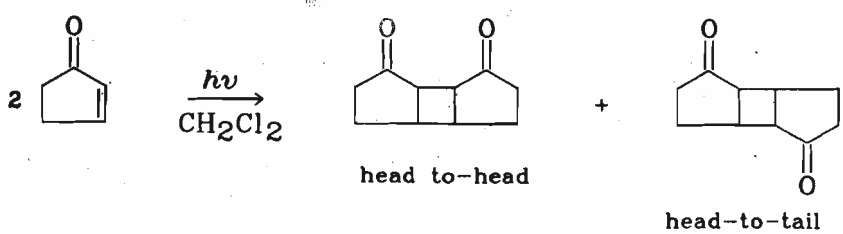
The triplet states of *cis*- and *trans*-1, 2-diphenylethene would form ground state 1, 2-diphenylethenes by either phosphorescence or by internal conversion. Thus, irradiation of either *cis*- or *trans*-1, 2-diphenylethene with light would give a mixture of both isomers. The above explanation of the *cis-trans* isomerisation in the presence of a sensitiser is a simple one (perhaps is oversimplifies one). There are other ways of understanding the above process, e.g., involving a phantom triplet which can be formed directly from the ground state (a forbidden transition).

In photosensitisation, the excitation energy of the sensitiser triplet must be higher than those of the triplets of the *cis* and *trans* isomers for efficient energy transfer. The triplet energy of diphenylmethanone, *cis* and *trans*-1, 2-diphenylethenes are 288.42, 238.26 and 204.82 kJ mol^{-1}, respectively. This tells us that diphenylmethanone is an efficient sensitiser in the photoconversion of *cis*- and *trans*-1, 2-diphenylethenes.

A common ($\pi \rightarrow \pi$) triplet state is assumed to be the intermediate in each one of cis and *trans* stilbenes. The triplet state is referred to as the perpendicular triplet state and is termed as phantom triplet state.

13.3.6 Cycloaddition

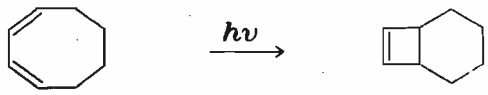
Photochemical cycloaddition of olefines to give four-membered rings is a synthetically useful process. One familiar example is the dimerisation of cyclopentenone on irradiation with light in dichloromethane solution to give a mixture of "head to head" and "head to tail" dimers. These dimers may be formed via an excimer (excited dimer) derived from the ($\pi \rightarrow \pi^*$) cyclopentenone and a molecule of ground state cyclopentene.



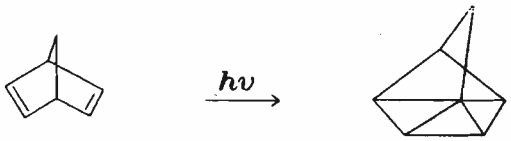
head to-head

head-to-tail

The photocycloaddition could also proceed in an intramolecular fashion. For example,

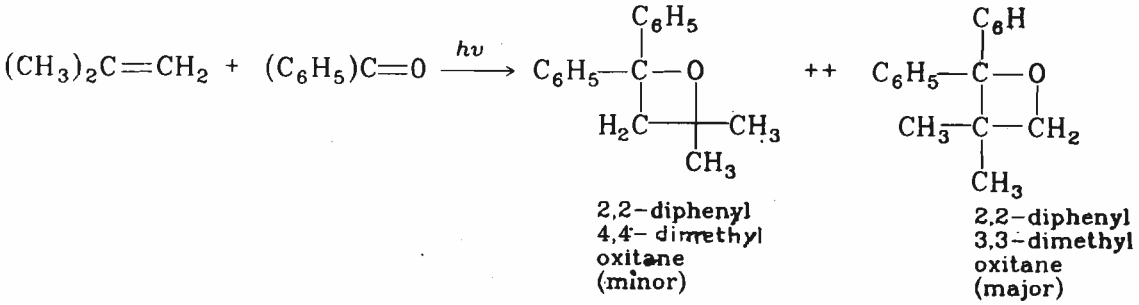


1.3 – cycloctadiene bicyclo[4.2.0] oct-7 ene



norbornadiene quadricyclene

Heterocycles are formed when one of the multiple bonds includes a heteroatom, e.g.,

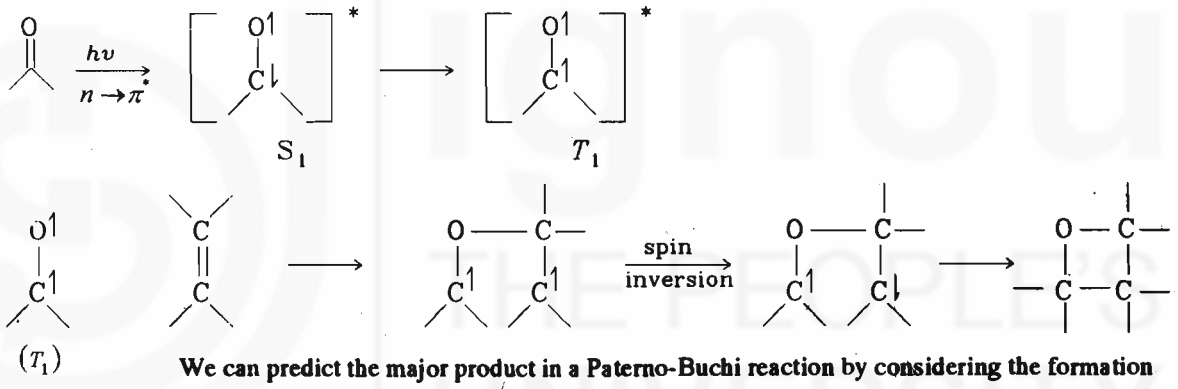


2,2-diphenyl 4,4- dimethyl oxitane (minor)

2,2-diphenyl 3,3-dimethyl oxitane (major)

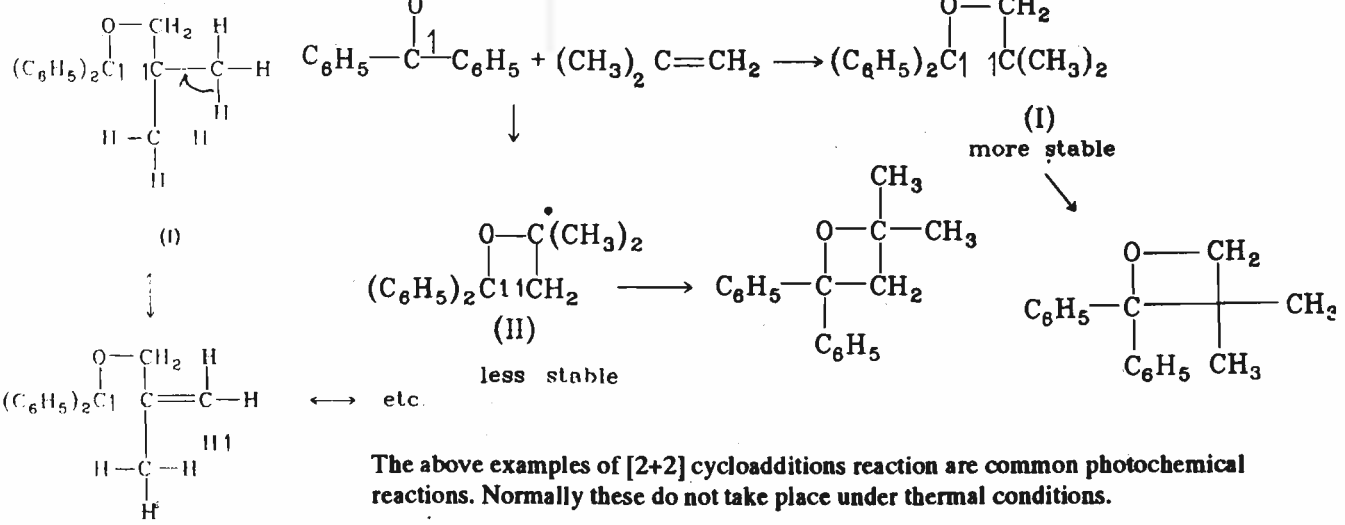
This photoaddition of an alkene and a ketone is known as **Paterno-Buchi reaction.**

In this reaction, the ground state alkene (S_0) reacts with an excited state (usually T_1) of the carbonyl compound by way of a diradical intermediate.



We can predict the major product in a Paterno-Buchi reaction by considering the formation of biradical during the course of reaction.

(I) is more stable than (II) due to additional hyperconjugation structures indicated below :



The above examples of [2+2] cycloadditions reaction are common photochemical reactions. Normally these do not take place under thermal conditions.

SAQ 6

Give the mechanistic paths in the following reactions

(a) $CH_2=CH-CH=CH_2 \xrightarrow[(C_6H_5)_2CO]{h\nu}$

(b) $CH_2=CH-CH=CH_2 \xrightarrow[\text{pentane}]{h\nu \ (250nm)}$

13.4 APPLICATIONS OF PHOTOCHEMICAL REACTIONS

Photochemical reactions have a great impact on biology and technology, both good and bad. Photosynthesis in plants, vision in all animals, and the formation of vitamin D (the antirachitic vitamin) are due to photochemical reactions. The destructive effects of ultraviolet radiation on all forms of life are due to the changes brought about in the DNA of cells by photochemical reactions. The harmful effects of over-exposure to sunlight and the resulting incidence of skin cancer are well established.

The technical applications of photochemistry are manifold. The dye industry is based on the fact that many organic compounds absorb particular wavelengths of visible light. Dye chemistry has helped establish the relationship between chemical structure and colour, which also is important in colour printing and colour photography. We cover some of these important applications of photochemistry briefly in this section.

Photosynthesis is a complex process in which carbon dioxide is reduced to give simple sugars and sugar derivatives. This is catalysed by the green pigment chlorophyll and various enzymes. Many other cellular constituents are also involved. Sunlight is absorbed and acts as the source of energy :

$$nCO_2 + nH_2O \xrightarrow[\text{chlorophyll}]{h\nu} (CH_2O)_n + O_2$$

Absorption of sunlight is usually shown to proceed in two stages in which activation of chlorophyll by sunlight appears to provide the energy needed. In the first, water is oxidised to oxygen and $NADP^+$ (nicotinamide adenine dinucleotide phosphate) is reduced to NADPH :

$$NADP^+ + H_2O \xrightarrow[\text{chlorophyll}]{h\nu} NADPH + 1/2O_2 + H^+$$

In the second step, ADP (adenosine diphosphate) is converted to ATP (adenosine triphosphate) in the photosynthetic phosphorylation :

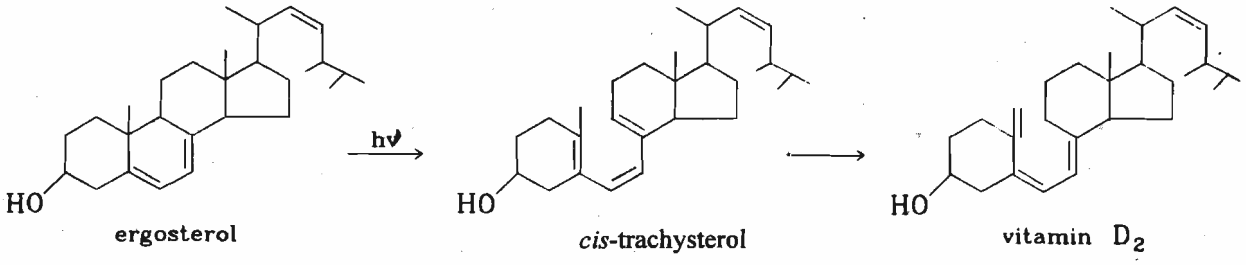
$$ADP + H_3PO_4 \xrightarrow[\text{chlorophyll}]{h\nu} ATP + H_2O$$

It is believed that NADPH and ATP store in them the light energy and provide it to convert carbon dioxide to sugars.

The photochemical *cis-trans* isomerisation occurs in the chemistry of vision. *Cis*-retinal combines with opsin (a protein) in the dark to give rhodopsin (a light sensitive compound). This compound is present in rods of the retina in the eye. It absorbs light at 500 nm and breaks down to opsin and *trans*-retinal. The isomerisation of *cis*-to *trans*-retinal is accompanied by configurational change which excites the nerve cell. The *trans*-isomer is converted to *cis*-retinal by an enzyme and the cycle is repeated.

Another application of photochemistry is in the formation of vitamin D_2. Irradiation of the steroid ergosterol with light leads to *cis*-tachysterol (pre vitamin D_2) by a ring opening

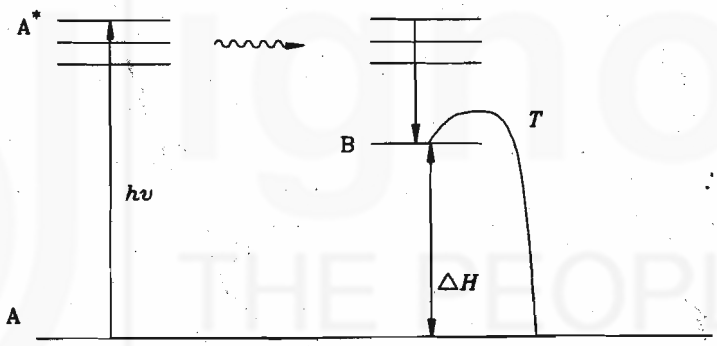
process. The latter thermally isomerises to vitamin D_2 (calciferol).



ergosterol *cis*-trachysterol vitamin D_2

Similarly, Vitamin D_3 is formed from 7-dehydro cholesterol. Milk and other food are irradiated with light to increase the vitamin D content.

Various attempts are being made for conservation of solar energy. One of these makes use of photocylisation reaction. An example of this has been given earlier in 13.3.6 in the photoconversion of norbornadiene to quadricyclene. Different norbornadiene derivatives and analogues have been tried to achieve the storage of solar energy. In general, a molecule A absorbs sunlight and through its electronically excited state is converted to another molecule B. The ground state energy of B is greater than of A. The difference of energy (ΔH) is stored in B. This is released when B is converted to A via a transition state (T).



13.5 SUMMARY

In this unit we have discussed organic photochemistry. We are summarising what we have studied so far :

- The electronic excitation of molecules to initiate chemical reactions occurs by absorption of visible or ultraviolet light. The energy input results in promotion of a bonding or nonbonding electron into an antibonding orbital. Quantum mechanics predicts which electronic transitions are favourable.
- In the ground state of most molecules all electrons are paired and they are said to be in ground singlet state, S_0. Excited state can result in one of the two possible electron arrangements : the arrangement with the electron spins paired is termed the singlet state, S_1, and that with the electron spins parallel is termed the triplet state, T_1.
- The excited molecule may undergo a chemical reaction or return to the ground state by one of the following means : it may fluoresce, it may undergo vibrational relaxation to a lower singlet state, or all the way to the ground singlet state (S_0); or it may undergo intersystem crossing to produce a longer-lived triplet state ($S_1 \rightarrow T_1$) which may, in turn, phosphoresce, or it may undergo a chemical reaction, or act as a photosensitiser in transferring its energy to a second molecule.
- The excited molecules return to ground state configuration by various radiative and nonradiative relaxation processes. When these involve bond making or breaking,

photoreactions occur. Many light-induced chemical reactions resemble free radical processes.

- Carbonyl compounds are mostly excited through a $n \rightarrow \pi^*$ transition, though a $\pi \rightarrow \pi^*$ transition occurs sometimes, preferably in enones (i.e., olefines containing carbonyl groups). The excited molecule mainly undergoes decomposition, intra- and inter-molecular hydrogen abstraction and cycloaddition. In many reactions, carbonyl compounds act as efficient photosensitisers.
- In alkene, $\pi \rightarrow \pi^*$ transition generally leads to isomerisation, inter- and intra-molecular cycloaddition and ring opening reactions. The unsensitised reactions generally proceed through the singlet excited states of olefines.
- Table 13.2 represents an overview of molecular photochemistry which we have encountered in this unit.

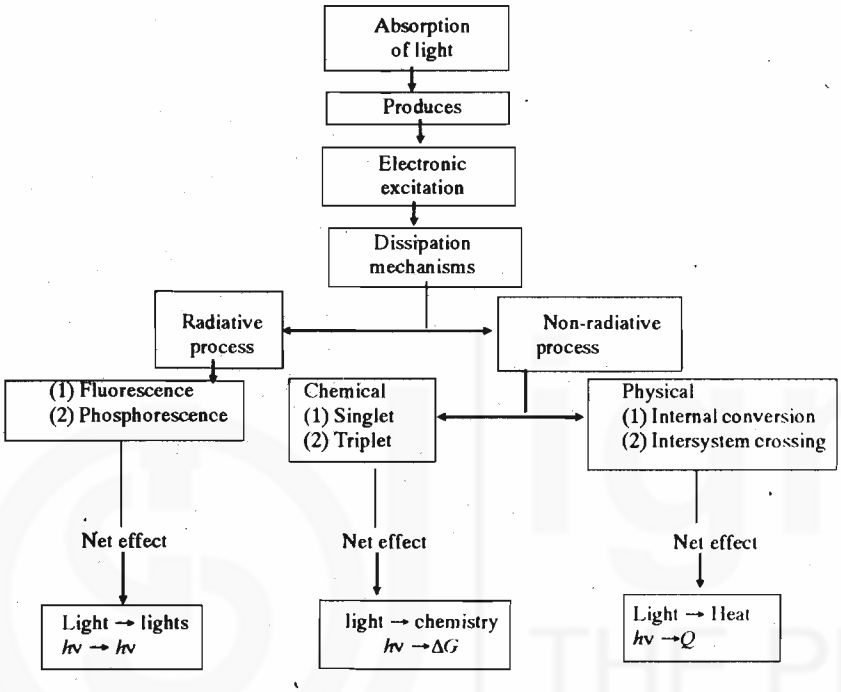


Fig. 13.2 : Important processes involved in a molecular photochemistry

13.6 TERMINAL QUESTIONS

1) Give two differences between photochemical and thermal reaction

2) Define following terms

   a) Fluorescence
   b) Phosphorescence
   c) Photosensitisation
   d) Internal conversion
   e) Intersystem crossing

3) Write mechanism for following type of reaction

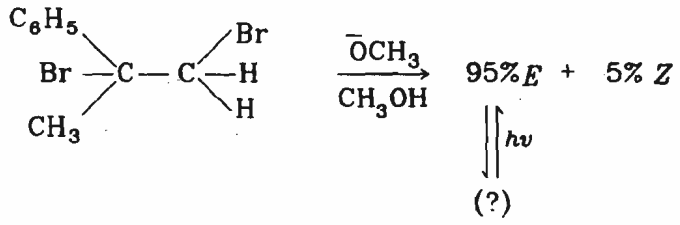
   a) Norrish type I
   b) Norrish type II
   c) Paterno-Buchi reaction

4) Complete the following photochemical reactions

a) $(CH_3)_3C-\overset{\overset{O}{\|}}{C}-C(CH_3)_3 \xrightarrow{h\nu}$

b) $CH_3-\overset{\overset{O}{\|}}{C}-CH_3 \xrightarrow{h\nu}$

c) $C_6H_5-\overset{\overset{O}{\|}}{C}-C_6H_5 + CH_3\overset{\overset{OH}{|}}{C}HCH_3 \xrightarrow{h\nu}$

d) 

13.7 ANSWERS

Self Assessment Questions

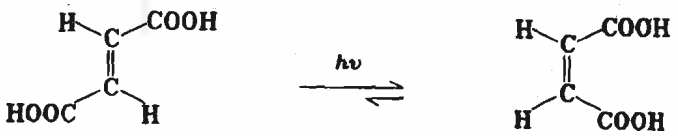
1) Absorption maxima at 279 nm (ε = 15) is due to $n \rightarrow \pi^*$ transition. For further explanation see subsection 13.2.1.

2) 239.25 kJ mol^{-1}

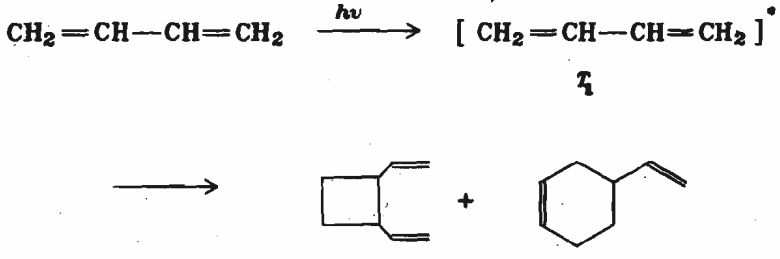
3) Norrish type I (See subsection 13.3.1)

4) (a) and (b) Norrish type II (See subsection 13.3.2)

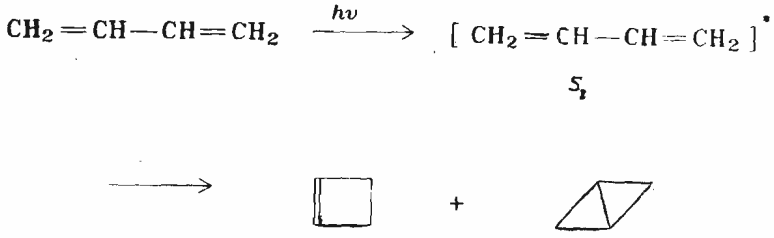
5) This is an example of *cis-trans* isamerisation:



6) a) This is an example of photodimerisation sensitised



b) This is an example of intramolecular cycloaddition.



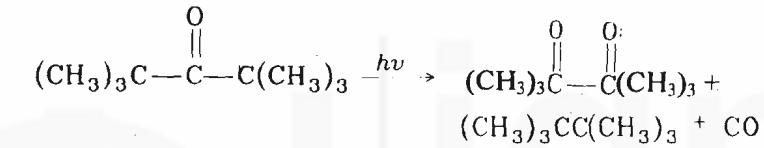
Terminal Questions

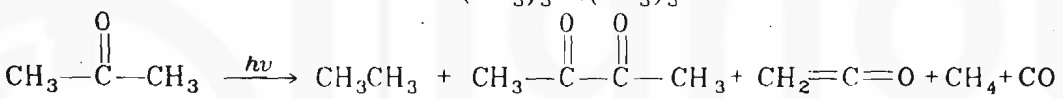
1) See subsection 13.2.3

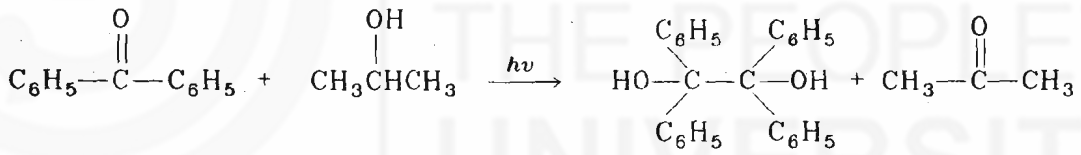
2) See subsection 13.2.2

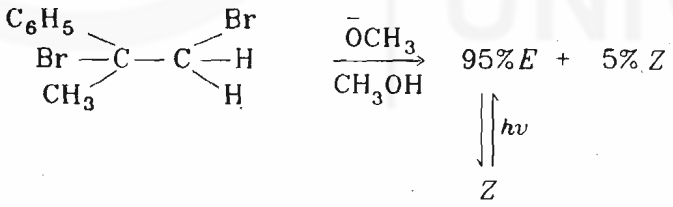
3) a) See subsection 13.3.1
   b) See subsection 13.3.2
   c) See subsection 13.3.6

4)

a) 

b) 

c) 

d) 

UNIT 14 STRATEGY OF ORGANIC SYNTHESIS

Structure

14.1 INTRODUCTION

So far in this course we have studied different types of chemical reactions and their mechanism. Most of the organic transformations you have studied so far were single step transformations. In this unit you will see how complex organic molecules can be synthesised through a series of chemical transformations. This is what organic synthesis essentially implies.

Organic synthesis is the preparation of a desired compound from readily available materials. Sometimes this involves one or two steps only, but usually several steps may be needed to reach the desired goal. Organic synthesis is a test of a chemists ability to conduct and control organic reactions.

Why do we go in for multi-step syntheses of organic compounds? There are many reasons. Often synthesis is utilised as a final proof of molecular structure of natural products isolated from plant and animal sources. Identity (undepressed mixed melting point for solids and IR spectrum) between the samples obtained from nature and independent synthesis confirms the structure which is deduced by chemical, physical and analytical methods. Synthesis provides requisite amount of compounds useful to us as drugs, insecticides, pesticides, insect attractants, dyes etc. which are not available in sufficient quantities from nature. It also leads to unknown compounds which might be useful. It helps us to test predictions about the behaviour of compounds and also to create new ones.

In this unit you will learn how a synthetic problem can be tackled with the knowledge of chemical reactions you have learned so far.

Objectives

After studying this unit, you should be able to :

- describe criteria such as yield, cost and time which decide the suitability of the starting materials and route of a synthesis,

- identify the synthons and relate them to the reagent(s) used in the reaction,
- describe reactions of skeleton building and functional changes,
- distinguish between chemoselectivity, regioselectivity and stereoselectivity and explain when each type of selectivity needs to be considered,
- identify the use of activating, deactivating and protecting groups in an organic synthesis,
- plan simple organic syntheses keeping the above in mind, and
- explain the uses of acetoacetic ester, malonic ester and Grignard reagents in organic synthesis,

14.2 PLANNING A SYNTHESIS

Before we study the processes that are used to develop a synthetic plan or strategy for making a compound, let us understand the criteria which govern the choice of the most suitable starting material and the most suitable synthetic route out of the many leading to any given target molecule. For example, the following different sets of reactions lead to propanone :

i) $CH_3CHO + CH_3MgI \xrightarrow[(2)\,H^+/H_2O]{(1)(C_2H_5)_2O} CH_3\underset{\displaystyle OH}{\underset{|}{C}}HCH_3 \xrightarrow[H_2SO_4]{CrO_3} CH_3COCH_3$

ii) $H_2C{=}C(CH_3)_2 \xrightarrow[(2)\ H_2O/H_2O_2]{(1)\ O_3} CH_3COCH_3 + HCO_2H$

iii) $CH_3CN + CH_3MgI \xrightarrow{(C_2H_5)_2O} CH_3\underset{\displaystyle NMgI}{\underset{\|}{C}}CH_3 \xrightarrow{H^+/H_2O} CH_3COCH_3 + Mg(NH_2)I$

iv) $2CH_3CO_2C_2H_5 \xrightarrow[C_2H_5OH]{NaOC_2H_5} CH_3COCH_2CO_2C_2H_5 \xrightarrow[2)\ H^+/H_2O]{1)\ OH^-/H_2O} CH_3COCH_3$

We have to select one method out of the above which is the best. How can we select the most suitable method out of the available choices to synthesise a particular compound? Three main considerations have to be kept in mind while choosing from the available alternatives. These are : 1) overall yield, 2) cost of the materials and 3) length of the time required for synthesis.

1) **Overall yield :** The overall yield of a product is the yield over several steps used in its synthesis. Thus each step should have high yield. Percentage yield, which is a way of expressing the efficiency of a reaction can be calculated from the actual and theoretical yield :

$$\% \text{ yield} = \frac{\text{actual yield in g}}{\text{theoretical yield in g}} \times 100$$

A ten-step synthesis averaging 80% yield per step will give an overall yield of only 10.7%.

Theoretical yield in g can be calculated by multiplying the theoretical yield in mole of the product by its gram molecular weight.

No competitive reaction should take place in any step as this will lower the yield of the desired product and also introduce the problem of separation in the case more than one product is formed.

2) **Cost of materials :** The choice should be such in which the cheapest and the most readily available starting materials are used. For this, one should have a fairly good working knowledge of what types of starting materials are commercially available and what is the cost of the chemicals. A good rule of thumb is that most monofunctional aliphatic compounds containing five or fewer carbons are readily available. Similarly, many aromatic compounds are available, these include benzene derivatives with one or two functional group substituents. Reactions requiring heavy equipment and tedious separations should be avoided.

3) **Time required for synthesis :** The synthesis should have fewest steps. The more the steps used in a synthesis, the longer is the time required. Those alternatives which use an unreactive starting compound or a compound which might readily undergo a side reaction, or a product which is not feasible must be avoided. Beside these criteria, safety is also to be considered. The following examples illustrate these features.

Example 1

Preparation of *n*-propylphenyl ether

Path 1 $CH_3CH_2CH_2Br$ + Na^+O^-–C$_6$H$_5$ ⟶ $CH_3CH_2CH_2$–O–C$_6$H$_5$

1-bromopropane sodium phenoxide

Path 2 C$_6$H$_5$–Br + $Na^+O^-CH_2CH_2CH_3$ ⟶ C$_6$H$_5$–O$CH_2CH_2CH_3$

bromobenzene sodium *n*-propoxide

Path 2 is not feasible as bromobenzene is not reactive towards nucleophilic substitutions.

Example 2

Preparation of ethyl *tert*-butyl ether

In path 2 the *tert*-butyl bromide will undergo mainly elimination while bromoethane in

Path 1 CH_3CH_2Br + $(CH_3)_3CO^-Na^+$ ⟶ CH_3CH_2–O–C(CH_3)$_2$–CH_3

bromoethane sodium *tert* -butoxide

Path 2 $(CH_3)_3CBr$ + $CH_3CH_2O^-Na^+$ ⟶ CH_3–C(CH_3)$_2$–O–CH_2CH_3

tert -butyl bromide dium ethoxide

path 1 will undergo mainly substitution. The disadvantage of a slow reaction of *tert*-butyl alcohol and sodium as compared to ethanol and sodium is compensated by getting the desired product.

Example 3

Preparation of 1-propanol form propene

Path 1 $CH_3CH{=}CH_2 \xrightarrow[H_2SO_4]{H_2O} CH_3CH_2CH_2OH$

Path 2 $CH_3CH{=}CH_2 + HBr \xrightarrow[\text{peroxide}]{\text{Oxygen or}} CH_3{-}CH_2{-}CH_2{-}Br \xrightarrow{OH^-/H_2O} CH_3CH_2CH_2OH$

Path 1 is not feasible as 2-propanol will be formed (Markownikoff addition). In path 2 two steps are required but it leads to the desired product.

Example 4

Preparation of 2-propanol

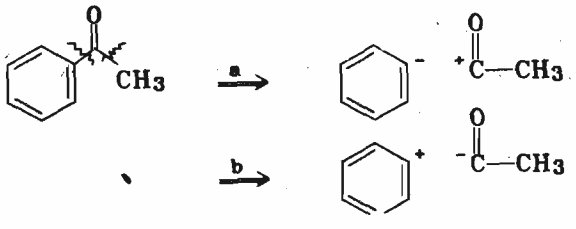
Path 1 $CH_3CH{=}CH_2 \xrightarrow[H_2SO_4]{H_2O} CH_3CHOHCH_3$

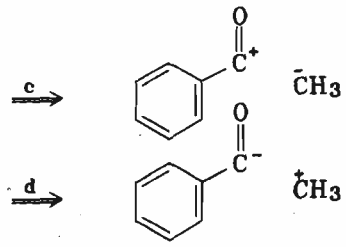
Path 2 $CH_3CH{=}CH_2 + HBr \longrightarrow CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH_3 \xrightarrow{OH^-/H_2O} CH_3CH(OH)CH_3$

One step method in path 1 is preferred as it would give a high yield of the product.

Moreover, in path 1 the cost of sulphuric acid is less than that of hydrobromic acid and sodium hydroxide required in path 2.

With this background, let us see how we can plan a synthesis. We start planning from the molecule that we want ultimately to make, the **target molecule**, and then work backwards to the structures of **available starting materials**. This process is called **retrosynthesis** or disconnecting approach. We generally use a double-line arrow (⇒)to indicate a reaction written backwards. The actual reaction is reverse. To further illustrate this point, let us see how we plan a synthesis of phenylethanone (acetophenone). This molecule can be disconnected in the following ways :





In this example + and - fragments actually represent electrophiles and nucleophiles, respectively. These fragments are called synthons. In planning an organic synthesis, our next step is to identify which organic substrates/reagent are related to these fragments, i.e., synthons. For example, here $C_6H_5^-$ can be easily related to an organometallic compound of benzene and $CH_3^+C{=}O$ to an appropriate carboxylic acid or its derivative CH_3COY. Similarly, fragments of synthetic routes b, c and d can be related to appropriate nucleophilic and electrophilic entities. These organic molecules which we use to achieve the target molecule are called **precursors**. In Table 14.1, we are summarising some possible synthons and corresponding commonly used reagents. For complex organic molecules, after each disconnection, the organic precursors may not be readily available. Therefore, they are further disconnected, until suitable starting materials are identified. These steps must be made in light of the consideration such as availability of synthetic methods to carry out the desired transformation in the forward synthetic direction overall yield, cost of materials and time. The graphic representation of such an analysis is called a **synthetic tree.**

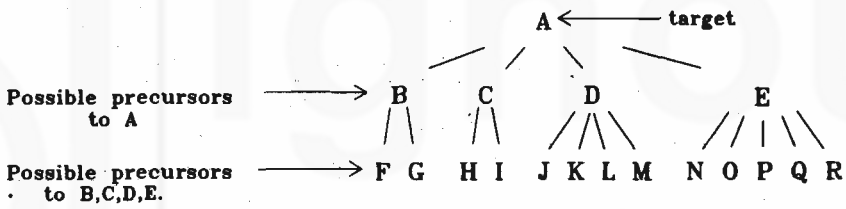
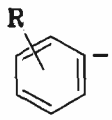
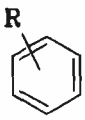
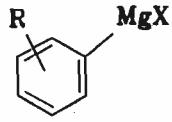
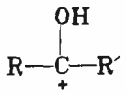
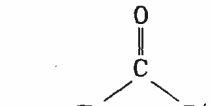
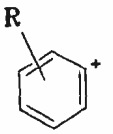
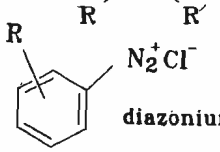


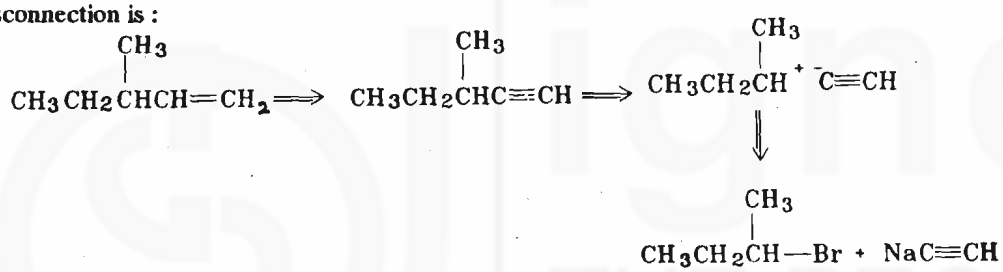
Table 14.1 : Synthons and corresponding reagents.

Synthon	Reagent	Comments
NUCLEOPHILIC		
RO^-	ROH, alcohols	also $Na^+ {}^-OR$ or $K^+ {}^-OR$
RR'N-	RR'NH, amines	
R^-	RMgX, Grignard reagents RLi, organolithium reagent	also R_2Cd or R_2CuLi in reaction with acid chlorides in Friedel-Crafts reactions;
	 (substituted benzene)	also 
$R-C{\equiv}C^-$	R– C≡CH, alkynes	via alkynide anion
$^-C{\equiv}N$	$M^+ {}^-CN$, inorganic cyanides	

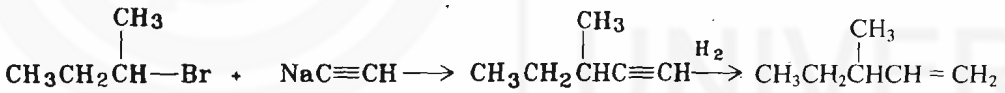
ELECTROPHILIC

R^+	RX, haloalkanes	
$R-\overset{+}{C}=O$	RCOY, acid derivatives; for example, RCOCl, acid chlorides	Also $(RCO)_2O$, acid anhydrides, and RCOOR', esters;
	RCOOH, carboxylic acid	in reaction with organolithiums
	RCN, nitriles	in reaction with Grignard reagents
$R-\overset{+}{C}H-OH$	RCHO, aldehydes	
		
	 diazonium salts	in the reaction with Cu·CN, etc.

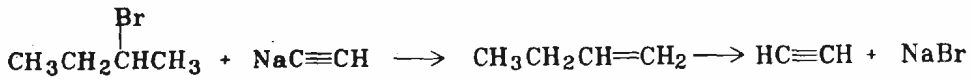
Now, consider the synthesis of 3-methyl-1-pentene. For this compound one of the possible disconnection is :



Therefore, we can synthesis 3-methyl-1-pentene using 2-bromoubtane and sodium, acetylide.

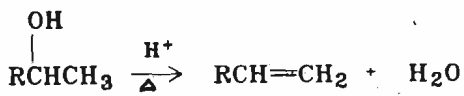


If you recall the reaction of acetylide ions with secondary alkyl halides you will find that the reaction causes elimination.



Therefore, this direct two step synthesis of 3-methyl-1-pentene is not feasible. This example illustrates an important aspect of synthesis design. After writing our possible route to the desired product, a careful review of the chemistry involved is required. In the above example, C=C group is the functional group. We should now review other methods whereby this functional group can be introduced into a molecule.

a) Dehydration of an alcohol

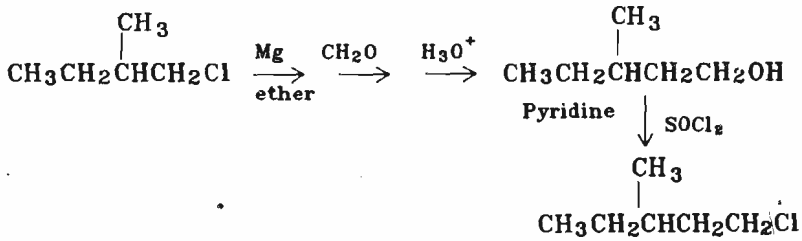


b) Elimination of HX from an alkyl halide

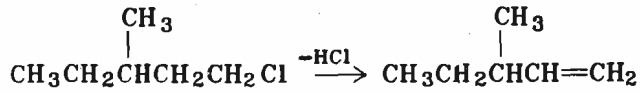
c) Wittig reaction

$$RCHO + (C_6H_5)_3P{=}CH_2 \longrightarrow RCH{=}CH_2 + (C_6H_5)_3P{=}O$$

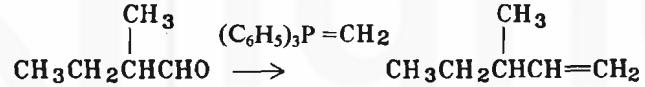
For the problem under consideration, alcohol dehydration is not suitable, since carbocation rearrangement would result in a mixture of products. Base catalysed elimination of an alkyl halide is a possibility. As you can guess, the required halide, 1-chloro-3-methyl pentane contains six carbons and is not readily available. Thus we would have to synthesise it. Of course, this is easily accomplished as follows :



The final step is to create the carbon-carbon double bond by the base-catalysed elimination reaction.



Now consider the last approach for the creation of a carbon-carbon double bond i.e., Wittig reaction. In this case, the reaction of readily available 2-methylbutanal with methylene-triphenylphosphorane would yield the target molecule in one step.



Now, we can expect that this is a more efficient synthesis of 3-methyl-1-pentene than the two routes considered heretofore, since only one step is involved and it gives a good yield. If we consider the total cost involved in synthesis we find that Wittig method is more expensive. Consequently, for the preparation of a larger quantity of 3-methyl-1-pentene, the longer route (b) is preferred. From this exercise we can also conclude that two main types of reactions are used for making a target molecule from the available starting materials (1) for skeleton building; (2) for functional changes. Now let us discuss these reactions briefly.

Skeleton building : The actual carbon skeleton in the final product is to be constructed from smaller units, i.e., synthons.

As discussedearlier a synthon is a structural unit within a molecule that can be formed and/or assembled by known or conceivable synthetic methods. A choice is made for the creation of specific carbon-carbon bonds in a given sequence indicating, the particular synthon units to be used to give the desired product. The nature of bond formation depends on the functional groups present in the organic compounds with which synthon are related. Since synthon are usually linear, carbon-carbon bond formation is required at chain-branching sites.

The main reaction types used to construct a carbon skeleton are :

i) **Electrophilic-nucleophilic reactions :** These are most common. They require basic condition and use carbanionic nucleophiles e.g., organometallics and enolate ions. The common reactions in this category are knoevenagel, Perkin, Doebner, Stobbe, Darzens, Enamine, Mannich, Michael, Wittig etc. However, Friedel-Crafts reactions, though in this category, are acid-catalysed (See Units 3, 4, and 6).

ii) **Pericyclic reactions :** These include the photochemical [2+2] [4+2] cycloadditions. Diels-Alder reaction provides a convenient route to cyclic compounds. Cope and Claisen rearrangements are not so common. Addition of

carbenes to double bonds also gives cyclic compounds (See Units 9 and 12 of this course).

iii) **Rearrangements :** These are often used for making or breaking carbon-carbon bonds in a desired direction. Arndt-Eistert, Hofmann, Curtius, Beckmann, Schmidt, Baeyer-Villiger, Wolff, Favorski Benzilic acid rearrangement etc. are commonly used (See Unit 11 of this course).

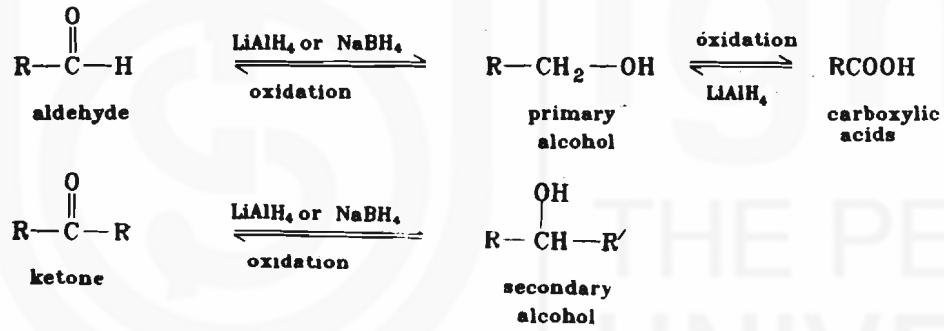
iv) **Oxidation-reduction reactions :** Examples are reductive couplings such as acyloin coupling to give pinacol and oxidative coupling of copper acetylides (See Unit 8).

We are not going into details of the above mentioned skeleton building reaction as we have already discussed these reactions in previous units. However, we will discuss skeleton building reactions of acetoacetic ester, malonic ester and Grignard reagent in section 15.5 - 15.7.

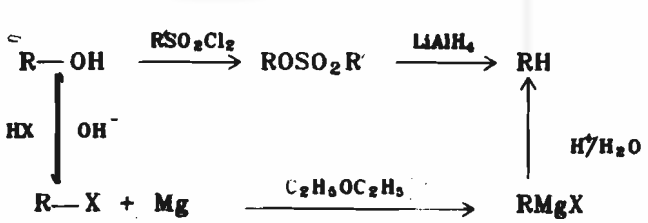
Functional changes : Interconversion of functional groups is usually necessary in various synthetic steps. Functionality resulting in one step has to be suitably changed depending upon the requirement of the next step. The final change has to be made to give the functional group of the desired product. Thus a thorough knowledge of carbon-carbon and carbon-heteroatom bond formation reactions and functional group interconversion plays a key role in syntheses.

It may be mentioned that a racemic mixture is formed when an asymmetric centre is created in a reaction from symmetric starting materials. In such cases a resolution of the racemic mixture gives optically active products.

All this requires a complete command on organic reactions. One of the representative interconversions is the reduction of carbonyl function to alcohols and the reverse reaction (oxidation). These are shown as :



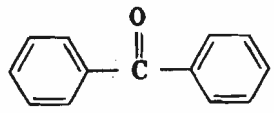
Conversion of alcohols to sulphonate esters and alkyl halides is done for subsequent substitution and Grignard reaction, respectively.



SAQ 1

Use the disconnection approach to identify reagents appropriate to the synthon of following compounds :

a) $(CH_3)_2CHCH_2CCH_2CH_2CH_3$

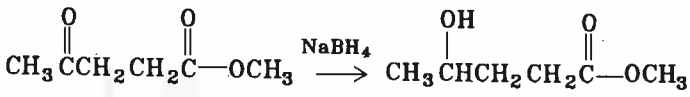
b) 

14.3 CONTROL IN SYNTHESIS

So far we have discussed how we identify readily available starting materials and the possible synthetic routes to achieve a particular target molecule. We have also discussed how we choose one synthetic route in preference to other potential routes.

Now consider a molecule which is capable of being attacked by a reagent to produce more than one product. In order to control the synthesis so that the desired product is obtained in high yield, we have to maximise the selectivity of the process. There are three types of selectivity: chemoselectivity, regioselectivity and stereoselectivity. Let us discuss them in some detail :

Chemoselectivity : Chemoselectivity can be achieved when a molecule has two similar groups, but these groups have different reactivity. In such cases, reaction can be preferentially effected at the more reactive site. For example if we want to synthesise compounds B starting from compound A, it can be achieved by using $NaBH_4$.

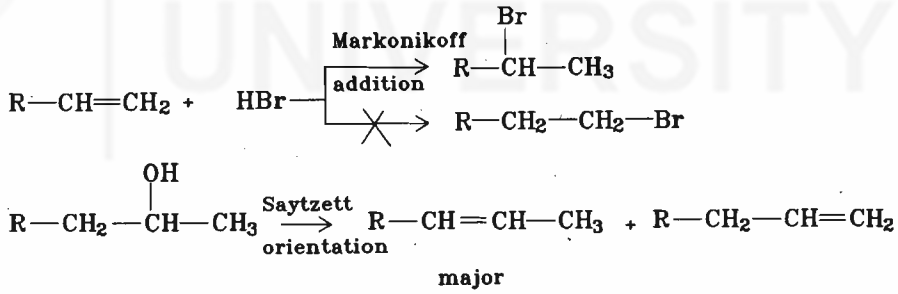


A B

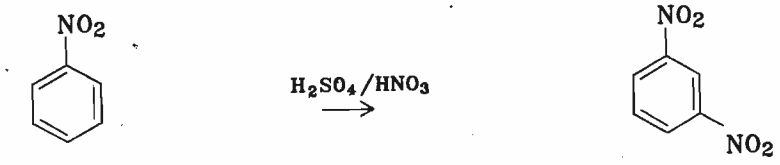
$NaBH_4$ reacts selectively and reduces the ketonic carbon group, it does not affect carbonyl group of the ester. If we use $LiAlH_4$, both the carbonyl groups are reduced and we do not get the desired compound.

Similarly, chemoselectivity can also be achieved by using reactivity difference of functional groups caused by substituents and using selective reagents for their oxidation or reduction.

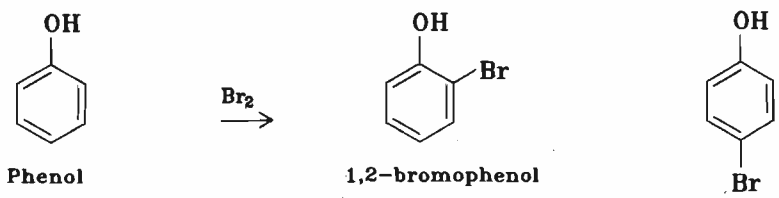
Regioselectivity : If a molecule has more than one possible reactive site, but in a reaction we get only one major product, the reaction is regioselective. You are familiar with the Markownikoff addition and Saytzeff orientations; these reactions are regioselective.



Electrophilic substitution of monosubstituted benzenes is also regioselective.

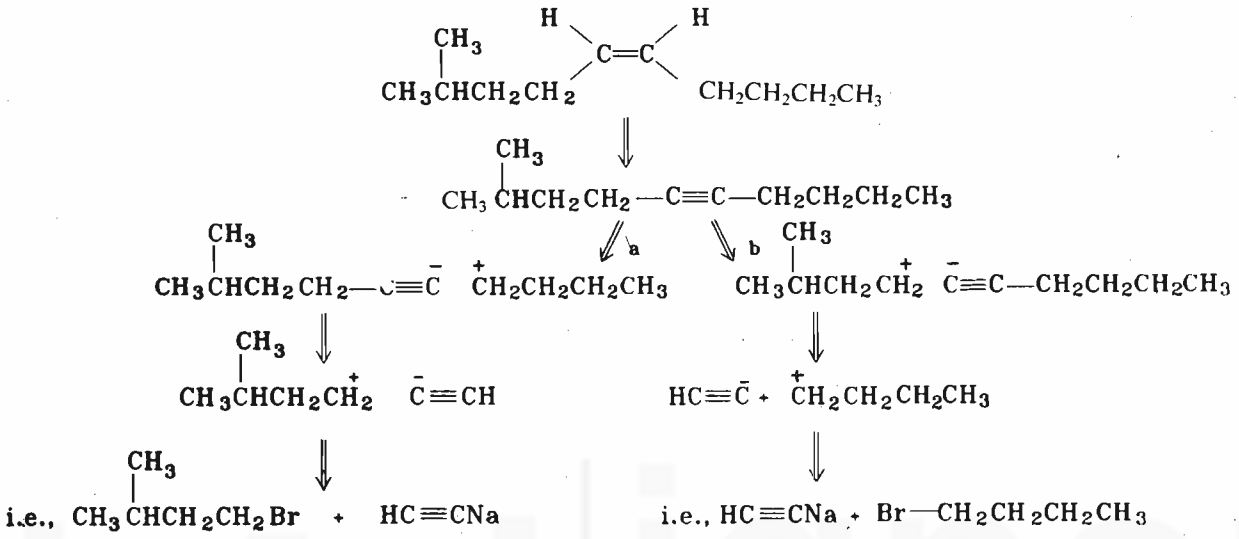


Nitrobenzene 1,3–dinitrobenzene

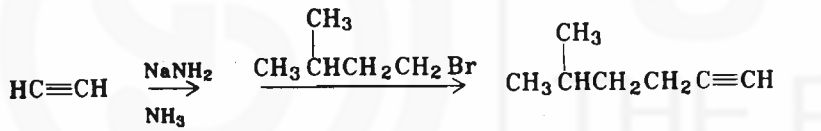


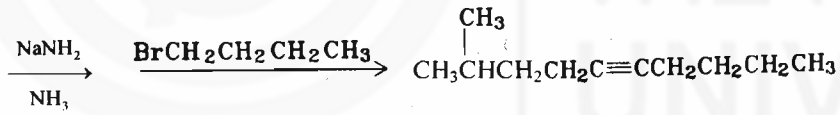
Phenol 1,2–bromophenol 1,4–bromophenol

Stereoselectivity : It is an important consideration when a reaction gives more than one stereoisomer, but only one of them is desired. For example, consider planning a synthesis of *cis*-2-methyl-5-decene. Let us look at our target molecule and consider the possibilities.

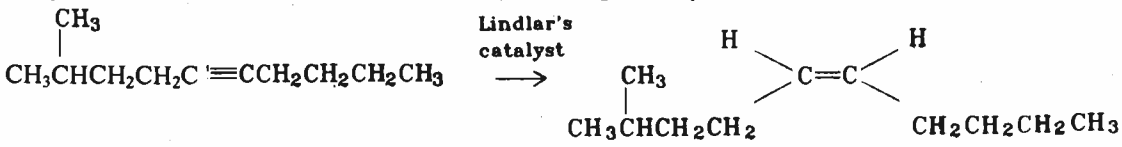


From the above it is clear that target compound can be easily made from readily available compounds like ethyne (acetylene) and suitable alkyl halides.





Now the final product can be obtained by reduction of the alkyne. But this may yield a mixture of *cis* and *trans* isomers. Therefore, we need to incorporate in our strategy a reaction that gives the *cis* isomer preferentially, i.e., introduce stereoselectivity. You may recall that the hydrogenation of an alkyne using Lindlar's catalyst is stereoselective and it gives only *cis* alkene. So we will use this method for reducing the alkynes.

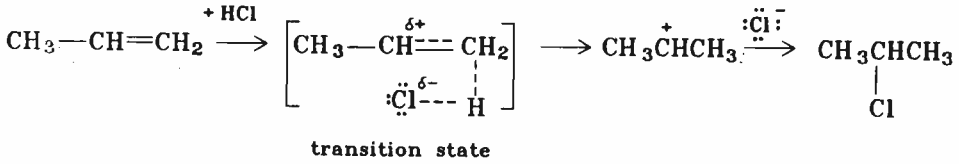


14.4 ACTIVATING, DEACTIVATING AND PROTECTING GROUPS

We can sometime achieve selectivity by using activating deactivating or protecting groups. Let us first consider effects of activating and deactivating groups.

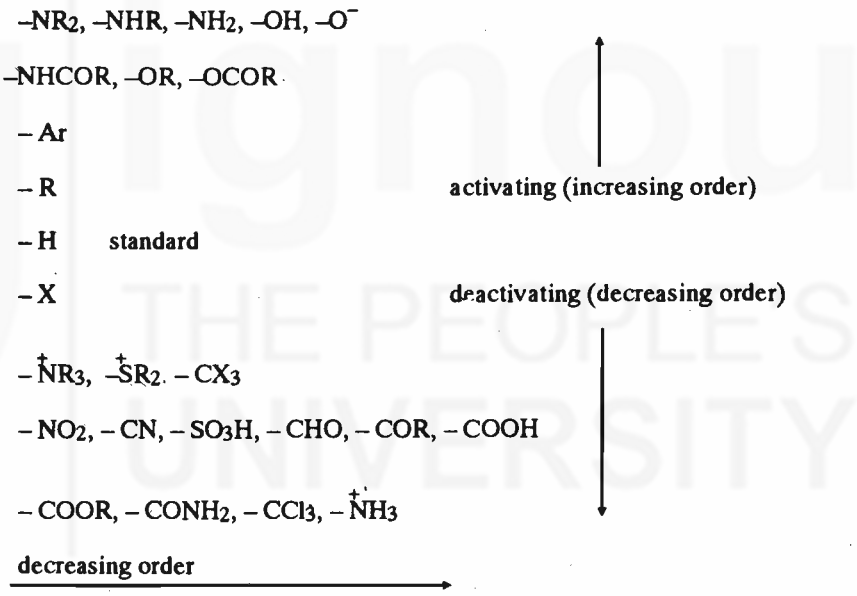
Activating and Deactivating Groups

You have learned in Unit 7 that electrophilic addition to an alkene proceeds via carbocations, in accordance with Markownikoff rule. Propene reacts with hydrogen chloride to give 2-chloropropane.



Electron-donating groups on sp^2 carbons tend to disperse the incipient positive charge in the carbocation and also in the transition state. This factor stabilises the transition state as well as the carbocation and thus accelerates their formation. So, electron-donating groups activate electrophilic addition to alkenes. On the other hand, electron-withdrawing groups tend to intensify the positive charge. The result is destabilisation of the transition state as well as of carbocations. The presence of electron-withdrawing groups, therefore, slows down the rate of addition. So you can see why vinyl chloride is less reactive in addition reactions as compared to ethene.

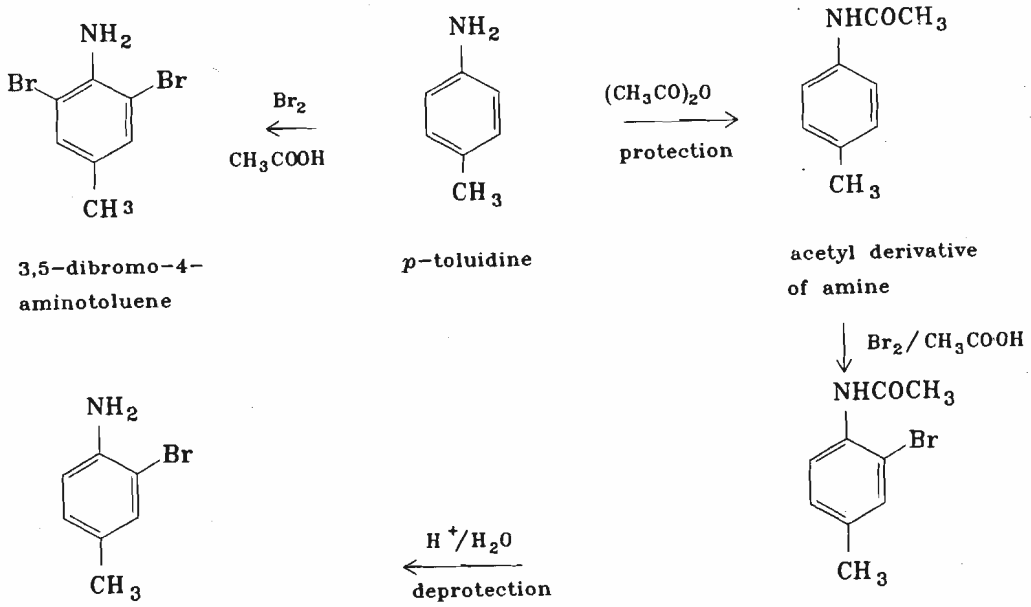
We have also learnt in Unit 4 about the activating and deactivating groups in electrophilic aromatic substitution. The presence of electron-donating groups accelerate the rate of substitution. The effect of groups which are electron-donating by resonance +R is much larger than those which operate only through inductive effect (+I). These are known as activating groups. On the other hand, electron-withdrawing groups (–I and/or - R), if present, tend to retard the rate of electrophilic aromatic substitution. These are termed as deactivating groups. Halogens are –I and +R type and have smaller deactivation effect as compared to those groups e.g., NO_2 etc. which are electron-withdrawing both by inductive and resonance effects (–I and –R). The following table lists the activating and deactivating groups in electrophilic aromatic substitutions.



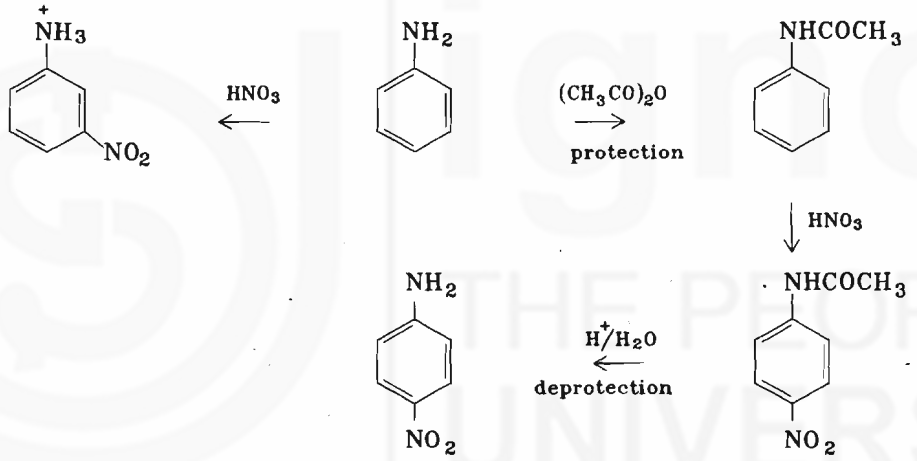
in Unit 4, we have learnt that the nucleophilic substitution of aryl halides is accelerated by the electron-withdrawing groups especially at the *ortho* or *para* position to halogen and hindered by electron-donating groups. In the above reactions, electron-withdrawing groups like $–NO_2$, –NO, –CN, $–\overset{+}{N}_2$ etc. act as activating groups.

Protecting group

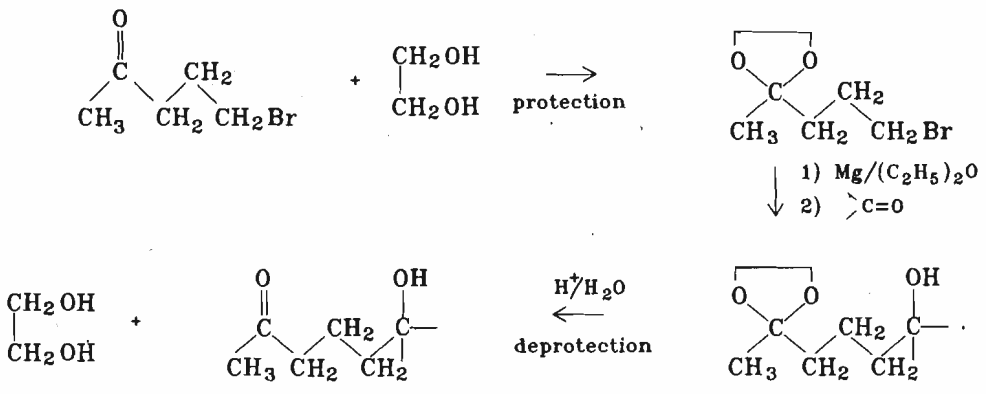
Aromatic amines are highly reactive compounds due to the activating effect of NH_2 group. They undergo electrophilic substitution quite readily. To get a desired product, the amino group is very often protected by acetylation. Substitution of the corresponding acetyl derivative is followed by the hydrolysis (deprotection) to give the desired product. This is illustrated in the following example (preparation of 3-bromo-4-aninotoluene from *p*-toluidine).



In nitration, nitric acid oxidises the ring in aromatic amines, thus reducing the yield of nitroamine. Moreover a *meta* substituted product is formed as amino group gets protonated. To avoid these complications amino group is protected before nitration. This is shown in the conversion of aniline to *p*-nitroaniline.

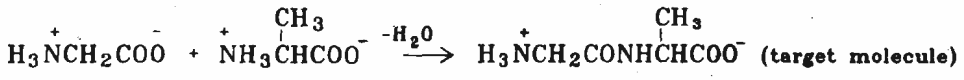


Similarly if a reaction is desired at only one site of a bifunctional molecule, the other group must be protected first. For example, if a Grignard reagent is to be prepared from a halogenated ketone, the carbonyl group must be protected. This can be done by conversion to ketal and the carbonyl group can be regenerated at a later stage. This becomes necessary so as to avoid the reaction of carbonyl group with Grignard reagent. The following sequence of reactions provide such an example:



The importance of protection and deprotection is significant in peptide syntheses. For

example, in the preparation of glycylalanine, the amide linkage can be formed by treating a mixture of glycine and alanine with some condensing agent to remove the water formed.



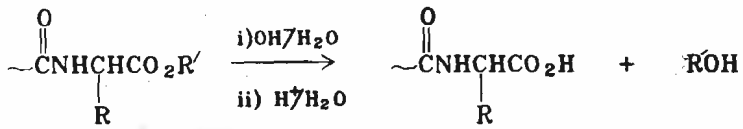
However, direct condensation of the two amino acids will give a mixture of four different dipeptides.

glycine + alanine → gly.ala + ala.gly + gly.gly + ala.ala

These dipeptides can react further to give higher peptides. Thus instead of getting the desired dipeptide (gly.ala) a complex mixture will be formed.

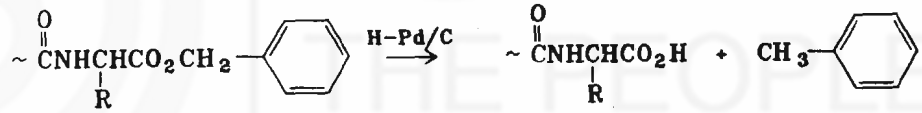
To avoid the formation of a mixture of di and higher peptides, it is desirable to protect the amino group of glycine and the carboxy group of alanine so that only the desired dipeptide (gly.ala) is formed.

Protection of carboxy groups is done by conversion into a methyl, ethyl or benzyl ester. The protecting groups can be removed by alkaline hydrolysis without affecting the amide bond of a peptide.

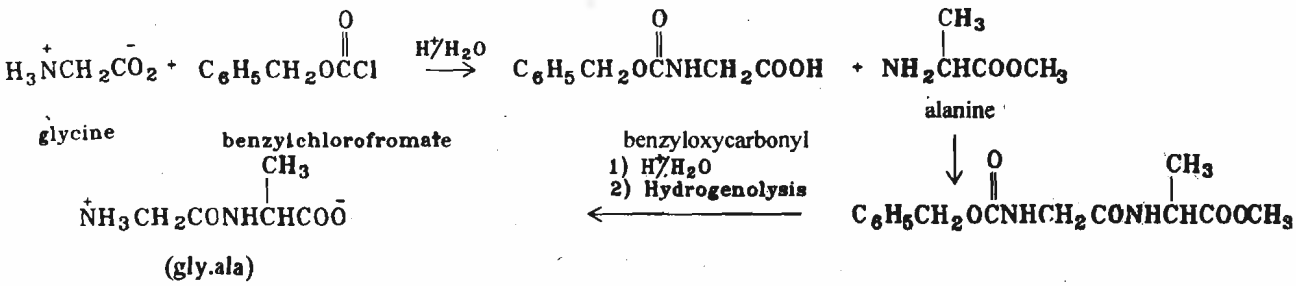


R′ = CH_3— or C_2H_5—

Benzyl esters have the advantage of being cleaved by hydrogenolysis



Amino group can be protected by treatment of the amino acid with benzylchloroformate. The benzyloxycarbonyl derivative is reacted with methyl ester of another amino acid to form the dipeptide derivative from which the dipeptide may be generated by hydrolysis followed by hydrogenolysis. The following reaction sequence explains this procedure:



Other protecting agents for amino group are *tert*-butylazidoformate or phthalic anhydride.

So far we have discussed how we plan an organic synthesis and how we achieve the selectivity of a reaction to get the desired product in high yield. We have also briefly mentioned some important reactions which are used for the syntheses of organic compounds. Now in the next section we will condiser the reaction of enolates, salt of carbonyl compounds and Grignard reagents which contain nucleophilic carbon atoms. Enolates and Grignard reagents are important reagents for building complex molecules.

Before going into detail of the reactions of compounds which give enolate ions, let us try the following SAQs.

SAQ 2

a) Plan a synthesis of aspirin.

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b) Plan a synthesis of *cis* and *trans* 1, 2-diphenylethenes (stilbene).

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SAQ 3

Plan a synthesis of metachloroethyl benzene.

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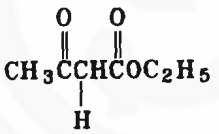
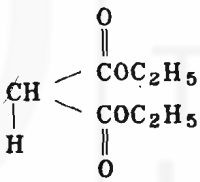
14.5 SYNTHESES USING ACETOACETIC ESTER

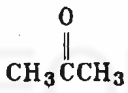
Enolate anions act as effective nucleophiles in substitution reactions. Formation of enolate ions is facilitated by the presence of two adjacent electron-withdrawing groups. Compounds which contain electron-withdrawing groups attached to a methylene group are known as active methylene compounds. Two examples of this class extensively used in synthesis are acetoacetic ester (ethyl acetoacetate and malonic ester (diethyl malonate).



pK_a = 11

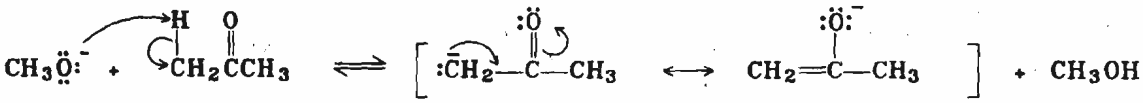


pK_a = 13



pK_a = 20

Recall from Unit 6 that α hydrogen to a carbonyl group is acidic and can be removed by a strong base. The α hydrogen is acidic primarily because of resonance stabilisation of the product enolate ion.



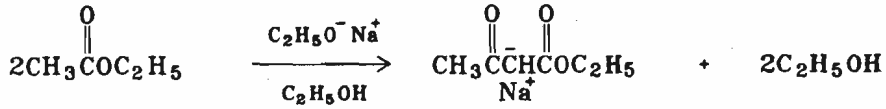
Resonance structure for the enolate ion of propanone (acetone)

Further where a hydrogen is alpha to two carbonyl groups, the negative charge on the anion can be delocalised by both the C=O groups. Such a hydrogen is more acidic than that of an alcohol.

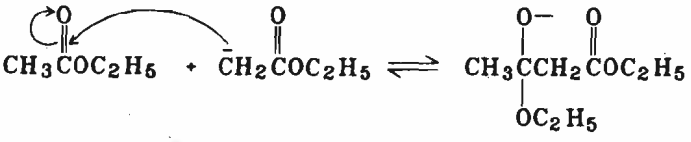
pK_a = 11 favoured pK_a = 15.8

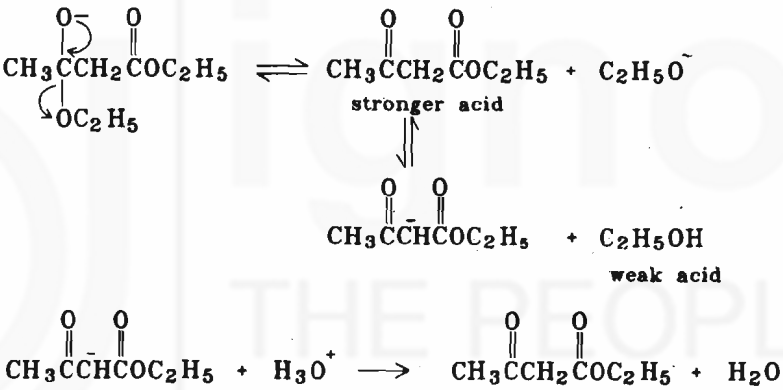
The acidic nature of α hydrogens of acetoacetic and molonic ester is responsible for their reactivity. With this background, now we will study the chemistry of acetoacetic ester.

Acetoacetic ester is prepared by self-condensation of ethyl ethanoate (ethyl acetate). This occurs when ethyl ethanoate is treated with sodium ethoxide in refluxing ethanol (Claisen condensation).

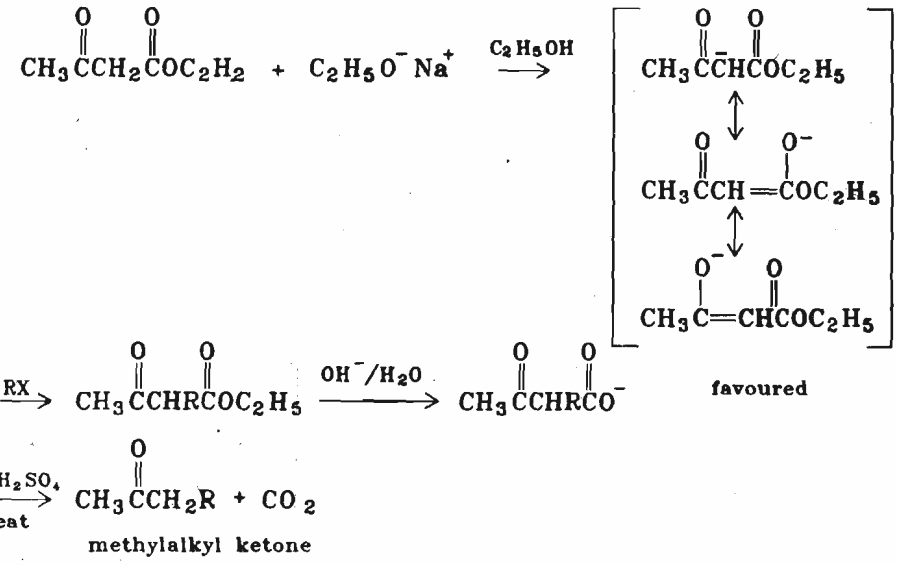


Initial hydrogen abstraction followed by nucleophilic attack, subsequent loss of ethanol and protonation result in the formation of product.

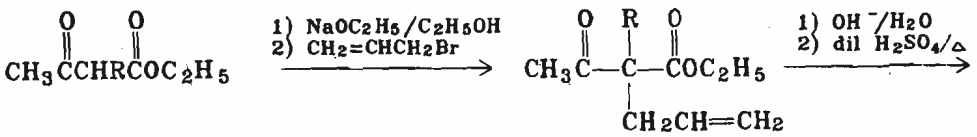


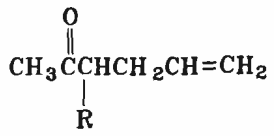


The following reactions illustrate the synthetic uses of acetoacetic ester in which three factors are important. 1) High acidity of α-hydrogens in acetoacetic ester, so treatment with a suitable base like sodium ethoxide generates the enolate ion; 2) high nucleophilic reactivity of the enolate ion in displacing halogen from alkyl halides and similar alkylating agents; and 3) extreme ease of decarboxylation of β ketoacids. The corresponding steps are shown in the conversion of acetoacetic ester into ketones.



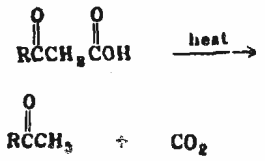
The monoalkyl acetoacetic ester may be treated with a base followed by addition of a different alkyl or allyl halide; alkaline hydrolysis (saponification) and decarboxylation (warming with dil.acids) gives a ketone that is branched at the α-carbon.



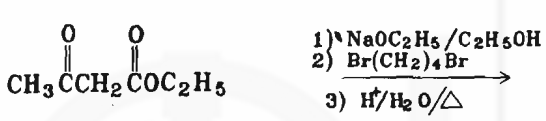


3-alkylhex-5-en-2-one

β-Keto acids and β-[illegible]id undergo decarbox[illegible] (loss of CO_2) when heated. temperature necessary depends on the individual compound.

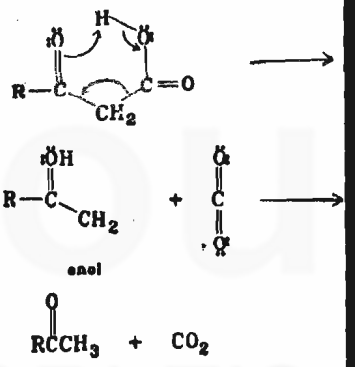


Cyclic products (3, 5, 6 and 7 carbon rings) are formed if the dialkylation is done using a dihaloalkane.



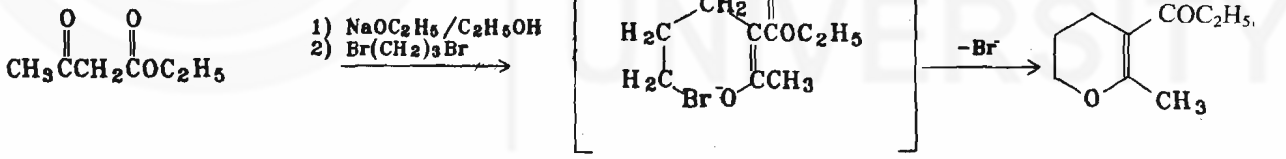
Cyclopentyl methyl ketone

Mechanism : Decarboxylation takes place through a cyclic transition state

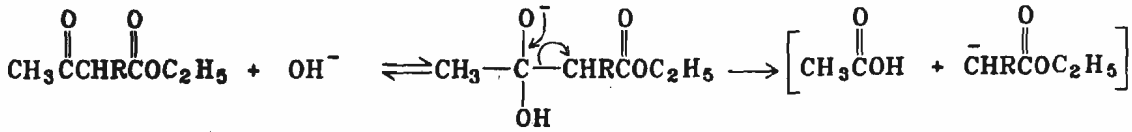


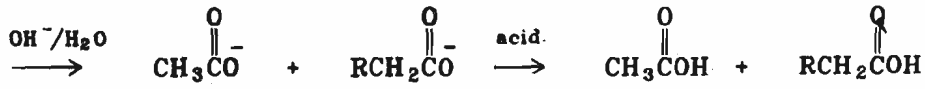
enol

An attempt to prepare a substituted four membered ring results in the formation of dihydropyran derivative.

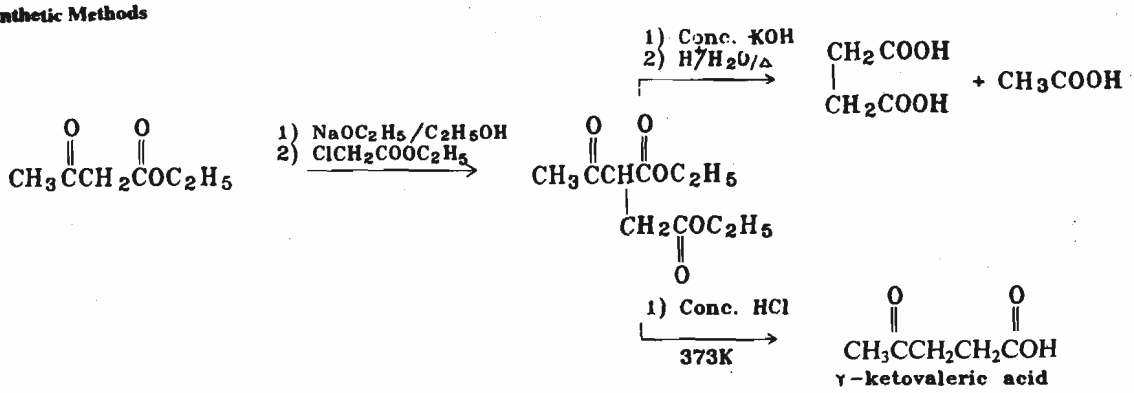


Alkylacetoacetic esters react with strong alkali by a different path to give anion of carboxylic acids. In this reaction, a reversal of Claisen condensation occurs.



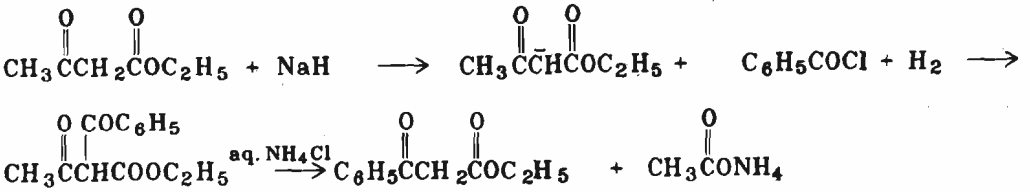


Keto acids can be prepared by treating acetoacetic ester with a base, subsequent addition of chloroester, followed by hydrolysis and decarboxylation. If concentrated alkali is used, the product is a dicarboxylic acid.

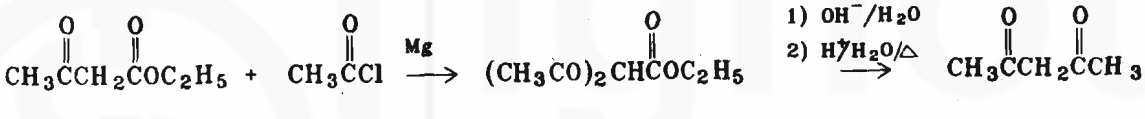


This procedure can be extended for the preparation of long chain keto acids.

Treatment of the enolate ion with either benzoyl chloride or anhydride results in acylation.

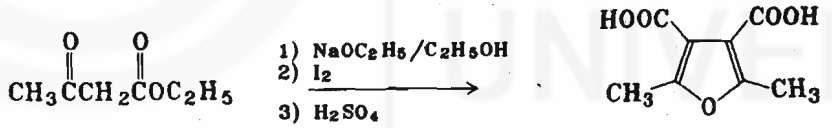


1, 3-Diketones are obtained from acetoacetic ester by treatment with acid chlorides in the presence of magesium followed by hydrolysis and decarboxylation.

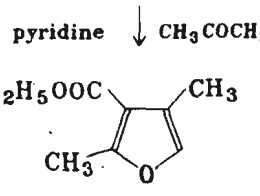


pentane 2,4-dione

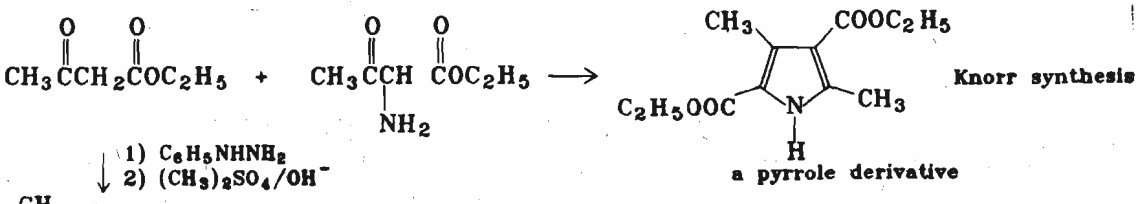
Many heterocyclic compounds can be obtained from ethylacetoacetate. Some common reactions are given below:



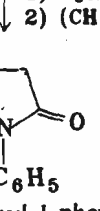
a furan derivative



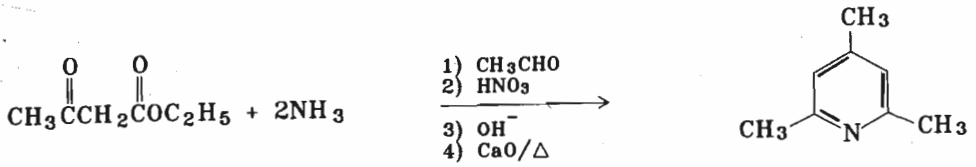
a furan derivative



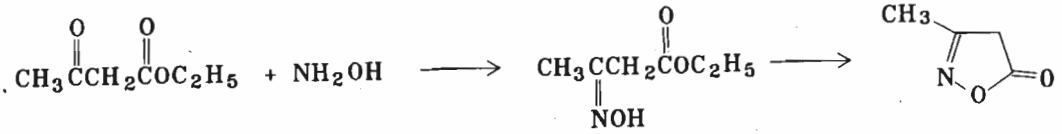
a pyrrole derivative



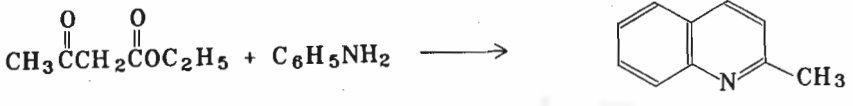
2,3-dimethyl-1-phenylpyrazol-5-one



2, 4, 6–trimethylpyridine

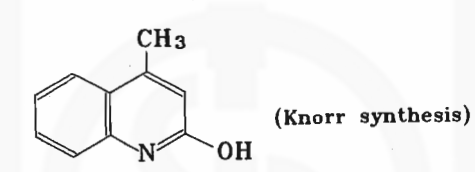


5–isoxazolone



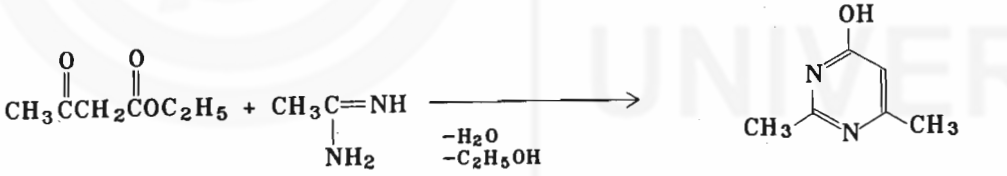
(Conrad–Limpach synthesis)

a quinoline derivative



(Knorr synthesis)

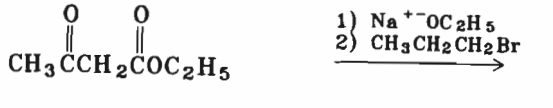
a quinoline derivative
(major product)

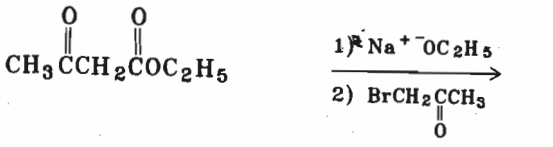


a pyrimidine derivative

SAQ 4

Predict the products of the following reactions:

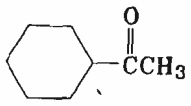
a) 

b) 

SAQ 5

Show how the following compounds could be prepared from acetoacetic ester.

(a) $(CH_3CH_2)_2CHCCH_3$ (O above the carbonyl)

(b) 

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14.6 SYNTHESES USING MALONIC ESTER

Malonic ester (diethyl malonate)is prepared by the reaction of sodium chloroethanoate with cyanide ion followed by addition of ethanol in acidic conditions.

$$\underset{\text{Cl}}{\overset{}{CH_2COO^-Na^+}} \xrightarrow{CN^-} \underset{\text{CN}}{\overset{}{CH_2COO^-Na^+}} \xrightarrow{C_2H_5OH/H^+} C_2H_5O\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}OC_2H_5$$

Malonic ester, like acetoacetic ester, when treated with base, generates the enolate ions which are very reactive. Addition of alkylating agents followed by hydrolysis and decarboxylation gives carboxylic acids. Mono or dialkyl ethanoic acids are preferably prepared by this method, as ketones are formed as side products from acetoacetic ester.

$$CH_2(CO_2C_2H_5)_2 \xrightarrow[2)\ RX]{1)\ NaOC_2H_5/C_2H_5OH} RCH(CO_2C_2H_5)_2 \xrightarrow[\Delta]{HCl} RCH_2COOH$$

$$RCH(CO_2C_2H_5)_2 \xrightarrow[2)\ R'X]{1)\ NaOC_2H_5/C_2H_5OH} RCR'(CO_2C_2H_5)_2 \xrightarrow[\Delta]{HCl} RCHR'COOH$$

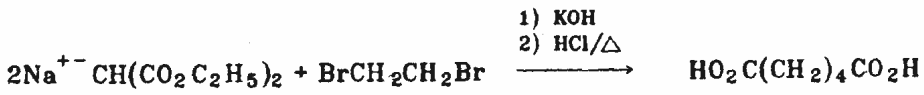
Treatment of malonic ester with either sodium metal or sodium hydride followed by reaction with an acid chloride and subsequent refluxing ethanoic acid or with *p*-toluene sulphonic acid in ethanoic acid gives ketones.

$$CH_2(CO_2C_2H_5)_2 \xrightarrow[2)\ RCOCl]{1)\ Na\ or\ NaH} RCOCH(CO_2C_2H_5)_2 \xrightarrow[\text{reflux}]{CH_3COOH} \underset{\text{alkylmethyl ketones}}{RCOCH_3}$$

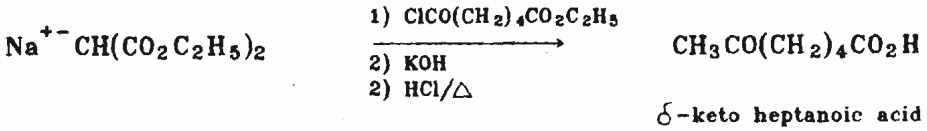
Dicarboxylic acids are obtained by treatment with a base followed by addition of α-chloro carboxylate. Alkaline hydrolysis and subsequent decarboxylation (heating in acidic medium) give the product.

$$CH_2(CO_2C_2H_5)_2 \xrightarrow[\substack{2)\ ClCH_2CO_2C_2H_5 \\ 3)\ OH^-/H_2O \\ 4)\ H^+/\Delta}]{1)\ NaOC_2H_5/C_2H_5OH} \underset{\text{CH}_2\text{COOH}}{\overset{\text{CH}_2\text{COOH}}{}}$$

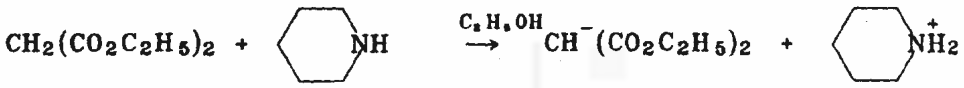
Adipic acid can be obtained by treating malonate ion with 1, 2-dibromoethane followed by hydrolysis and decarboxylation.

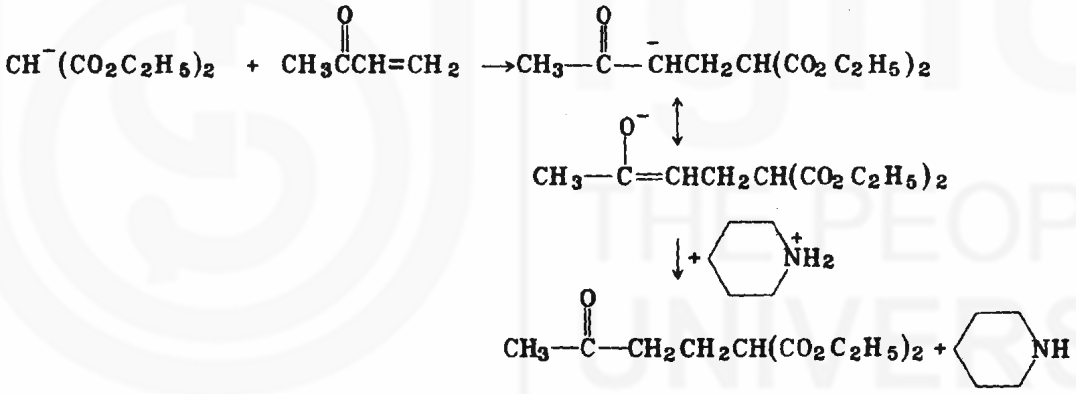


The above method has been extended to prepare keto acids.



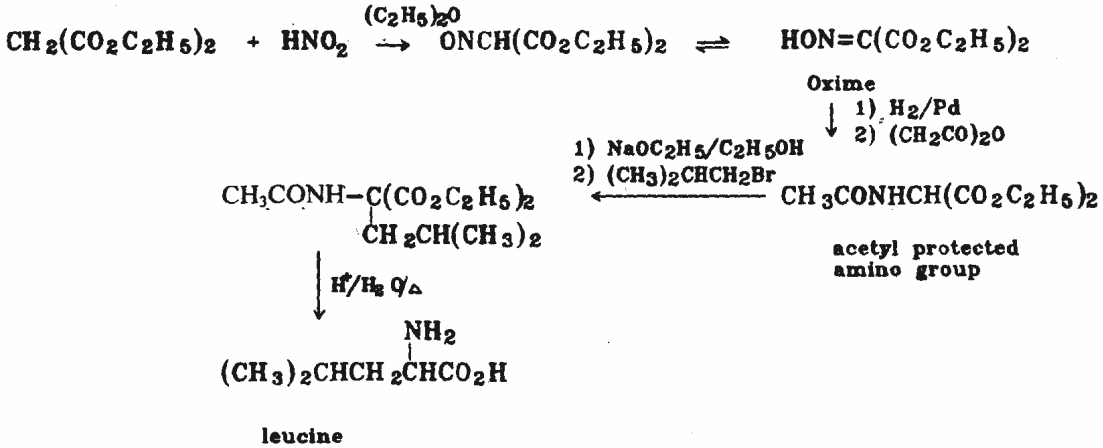
Carbanion from malonic ester also takes part in conjugate addition (Michael reaction). Bases like piperidine in catalytic amounts are often used

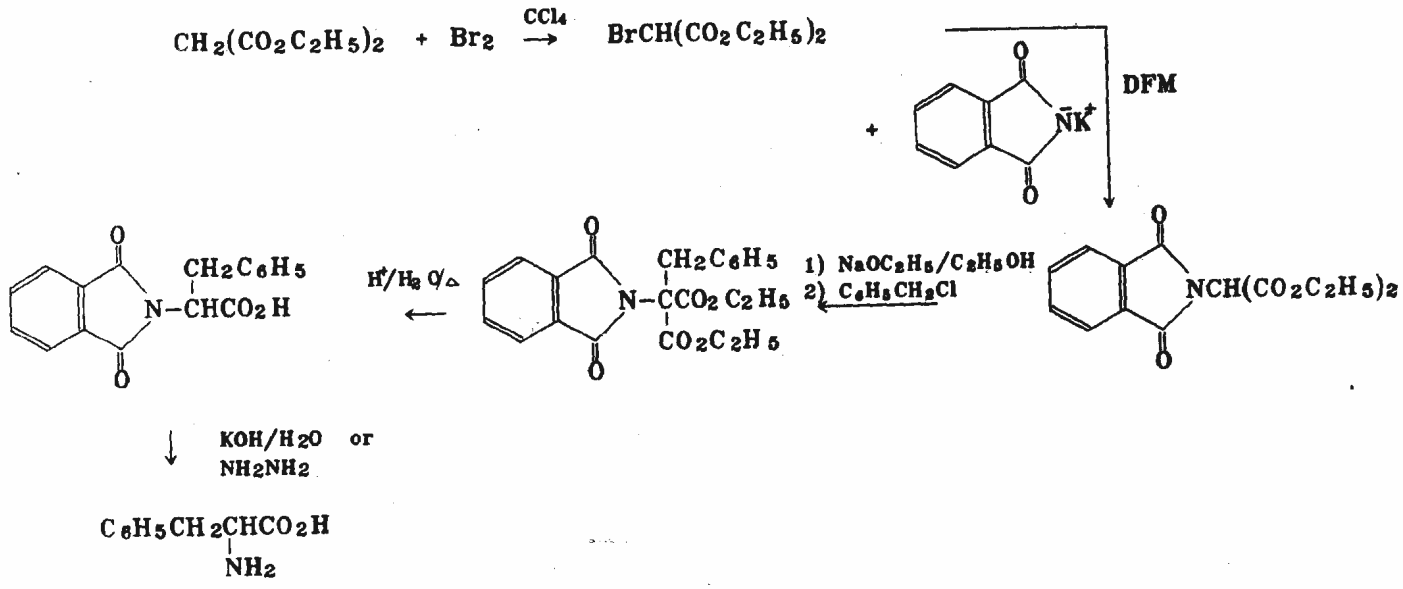




ethyl-2-carboethoxy-5-
oxo hexanoate

Malonic ester has been also used in the syntheses of amino acids as shown in the following reactions:

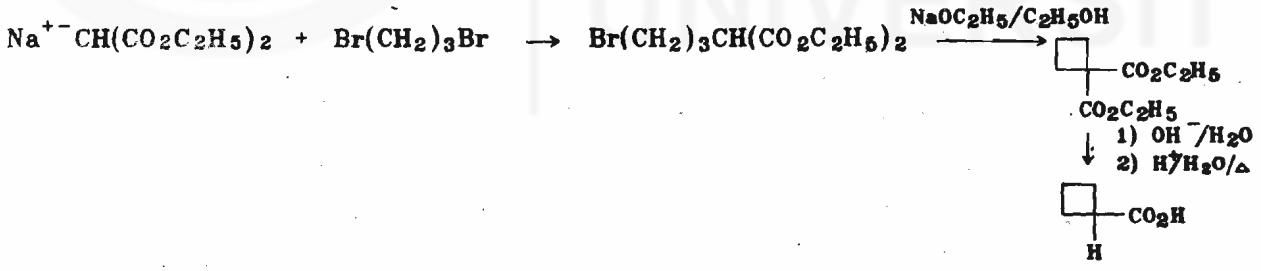




phenyl alanine

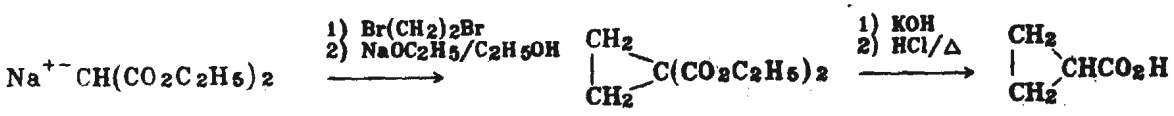
The reaction of malonic ester with benzaldehyde in presence of a secondary amine gives an α–β unsaturated compound (Knoevenagel reaction).

Alicyclic compounds have been prepared by the reaction of malonate anion with dihaloalkanes, intramolecular alkylation is favoured over the reaction with a second molecule of dihaloalkane.

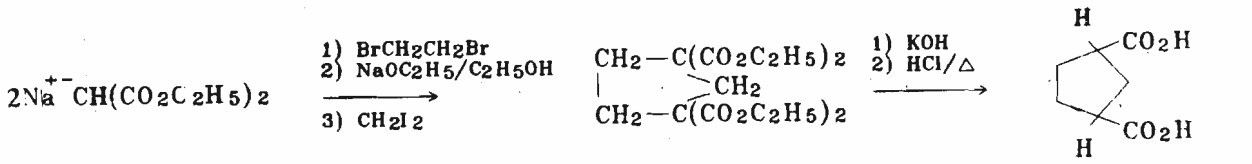


cyclobutane carboxylic acid

This way three to seven membered ring compounds can be obtained easily. The yield though is highest for cyclopentane derivatives and lowest for seven membered rings.

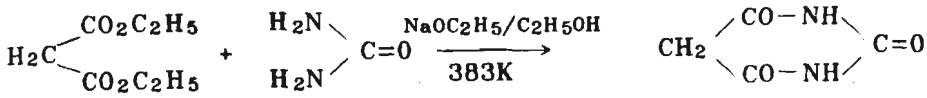


cyclopropane carboxylic acid



cyclopentane
1,3–dicarboxylic acid

Condensation of malonic ester with urea in presence of a base gives malonyl urea or barbituric acid, a parent compound of a number of sedatives known as barbiturates



SAQ 6

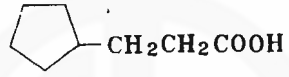
Predict the product of the following reactions :

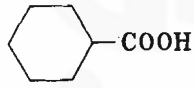
a) $CH_2(COOC_2H_5)_2$ → (1) $Na^{+-}OC_2H_5$ (2) $CH_3CH_2CH_2Br$

b) $CH_2(COOC_2H_5)_2$ → (1) $Na^{+-}OC_2H_5$ (2) CH_3CH_2I → (1) H_2O, OH^-/heat (2) H^+

SAQ 7

Show how you could synthesise the following compounds:

a) 

b) 

14.7 SYNTHESES USING GRIGNARD REAGENTS

Organomagnesium halides are commonly known as Grignard reagents. They are highly reactive. Their reactions with a variety of substrates account for their utility in organic syntheses.

Grignard reagents are freshly prepared for a reaction, for this the organohalogen compound is slowly added to a mixture of magnesium metal and ether. Dry and inert (N_2) atmosphere is necessary. Even the solvent and the reagents should be free from oxygen, water or carbon dioxide. The Grignard reagent should not have any of the following groups: carboxy, hydroxy, carbonyl, amino, nitrile, sulphonic acid. The Grignard reagent reacts readily with these groups. In general, the reagent may have halogen, aklyl, aryl, alkoxy groups. The reaction between the organohalogen compound and magnesium starts after some time and the mixture becomes cloudy. It is an exothermic reaction. The Grignard reagent isn't isolated. The substrate in dry ether is slowly added to it.

In some cases to avoid side reactions, ether is replaced by tetrahydrofuran.

$$CH_2{=}CHBr + Mg \xrightarrow{THF} CH_2{=}CHMgBr$$

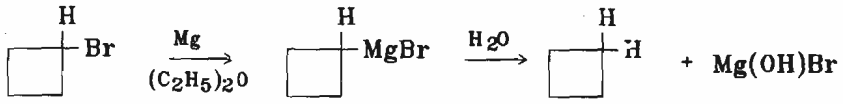
Sometimes alkyl magnesium halides are treated with acidic hydrocarbons such as acetylene to prepare the desired Grignard reagent.

$CH_3MgBr + CH_3C{\equiv}CH \rightarrow CH_4 + CH_3C{\equiv}CMgBr$

With active hydrogen compounds such as water, alcohols, acetylenes and primary and secondary amines Grignard reagents react rapidly to form hydrocarbons. One example is given by the following reaction.

$RMgX + R'OH \rightarrow RH + Mg(OR')X$

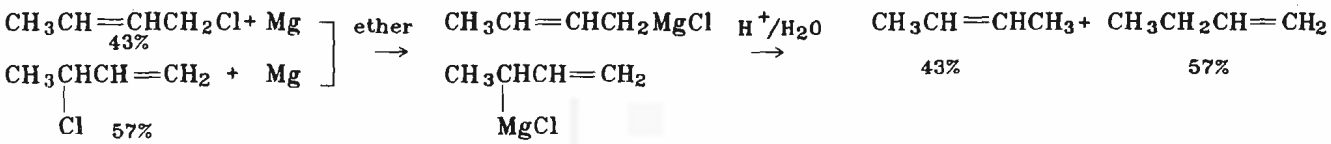
This reaction finds a useful application in replacing a halogen bound to carbon by a hydrogen.



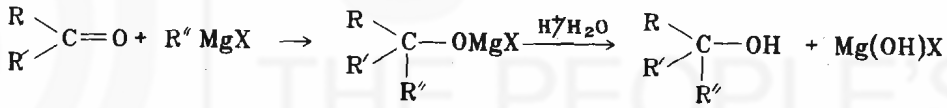
cyclobutylbromide cyclobutane

The above reaction is also used as an analytical method for determination of the number of active hydrogens in a compound (**Zerewitinoff method**).

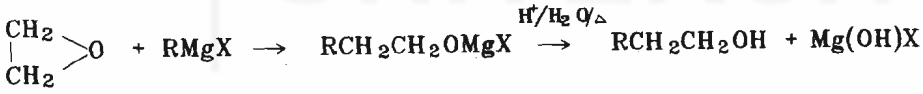
Allyl magnesium halides decomposes with dilute acids to give a mixture of hydrocarbons. When a mixture isomeric allylic halides is used to prepare Grignard reagents, the product distribution is unchanged.

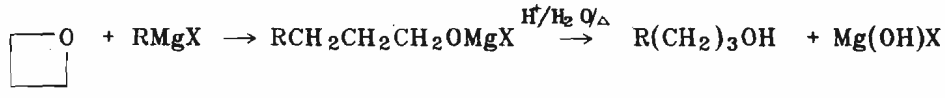


The reaction of Grignard reagents with carbonyl compounds and subsequent decomposition with dilute acid gives alcohols. The nature of alcohol depends on the starting compounds. With methanal (R, R′ = H) a primary alcohol, with other aldehydes (R = alkyl, R′ = H secondary alcohols, and with ketones (R = R′ = alkyl) tertiary alcohols are obtained.

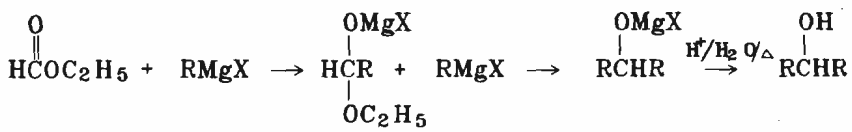


Primary alcohols are also obtained from the reaction of Grignard reagents with ethylene oxide or oxirane.

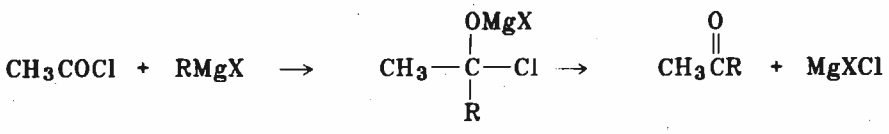




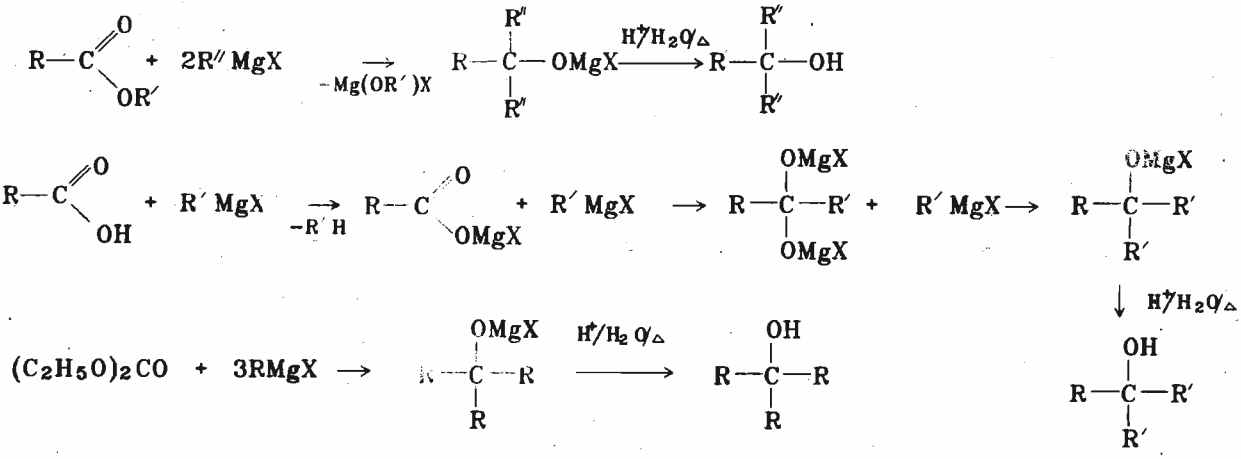
Secondary alcohols are also obtained from the reaction of Grignard reagents with ethyl mathanoate (ethyl formate).



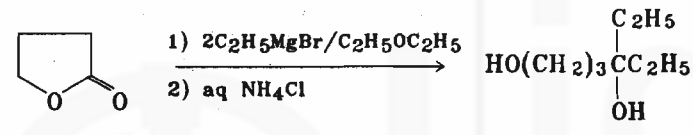
Acid chlorides react with Grignard reagents to give ketones which further react to give tertiary alcohols (as above).



Esters (except methanoates), carboxylic acids and ethyl carbonate react with Grignard reagents giving tertiary alcohols.

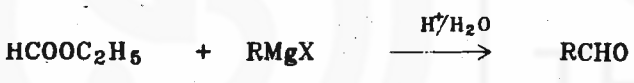


Lactones behave as open chain esters and undergo ring opening with Grignard reagents to give diols.

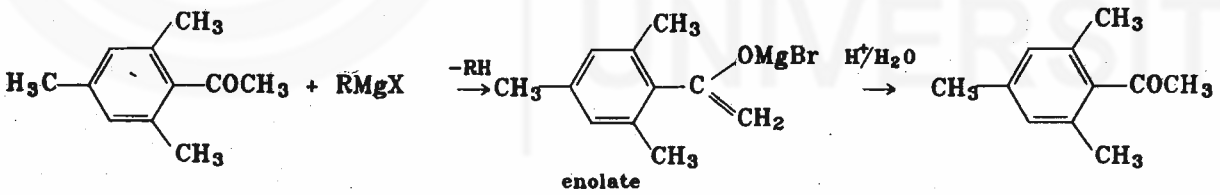


γ -butyrolactone

Alkyl methanoates react with Grignard reagents (1:1 mole) giving aldehydes.

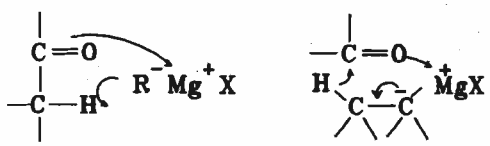


Sterically hindered ketones undergo enolisation when treated with Grignard reagents.



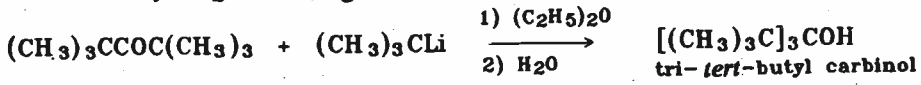
enolate

Addition of dilute acid in normal workup regenerates the starting ketones. The carbanionic carbon of Grignard reagent acts as a base to give the magnesium salt of the enolate ion. Magnesium acts a Lewis acid to coordinate with carbonyl oxygen. The carbanionic part of Grignard reagent can either attack the carbonyl carbon (a) or abstract a β-hydrogen (b) to



(a) (b)

convert the sterically hindered ketones to *tert* alcohols alkyl lithium reagents are used in preference to alkyl magnesium reagents.



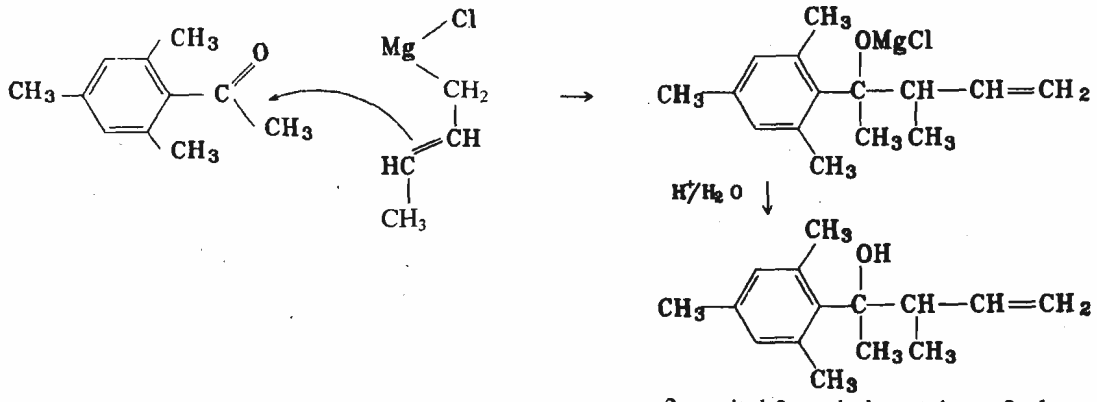
tri- *tert*-butyl carbinol

Another type of side reaction can occur if the Grignard reagent has a β-hydrogen. In this case the carbonyl function is reduced and an alkene is formed as in (b) above. For example,

$$(CH_3)_2CHCOCH(CH_3)_2 \xrightarrow[2)\ H^+/H_2O]{1)\ (CH_3)_2CHMgBr} (CH_3)_2CHCHOHCH(CH_3)_2 + CH_3CH{=}CH_2$$

diisopropy ketone

The sterically hindered ketones give addition products with allylic magnesium halides.



2-mesityl-3-methyl pent-4-ene-2-ol

Grignard reagents form addition products with oxygen. Subsequent acid hydrolysis gives primary alcohols.

$$RMgX + O_2 \rightarrow ROOMgX \xrightarrow{+RMgX} 2ROMgX \xrightarrow{H^+/H_2O} 2ROH$$

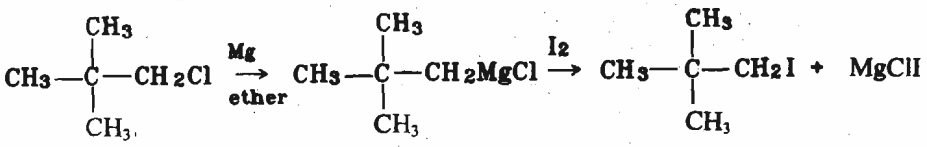
A similar reaction occurs with sulphur to give thiols. Addition of oxygen at lower temperature, followed by hydrolysis lead to alkyl hydroperoxides.

$$RMgX + O_2 \xrightarrow[203K]{} ROOMgX \xrightarrow{H^+/H_2O} ROOH$$

Alkyl magnesium chlorides react with iodine to give alkyl iodides.

$$RMgCl + I_2 \rightarrow RI + MgClI$$

This replacement can be used successfully in cases where S_N1 and S_N2 reactions are either slow or unpractical. For example,



By pouring Grignard reagent onto finely powdered dry ice and subsequent hydrolysis carboxylic acids are obtained.

$$RMgX + CO_2 \rightarrow R\overset{O}{\overset{\|}{C}}OMgX \xrightarrow{H^+/H_2O} R\overset{O}{\overset{\|}{C}}OH$$

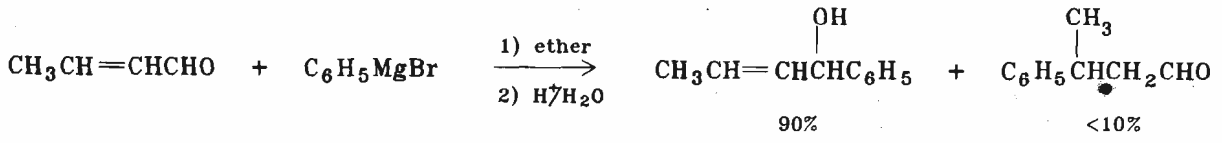
The reaction of Grignard reagents with N-dialkyl amides or nitriles give ketones.

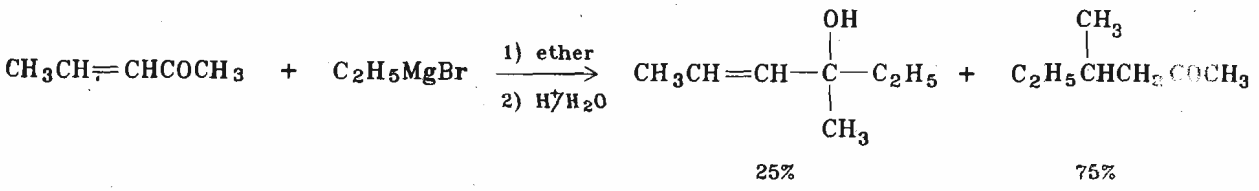
$$RCON(CH_3)_2 + R'MgX \xrightarrow{H^+/H_2O} RCOR' \xleftarrow[2)\ H_2O]{1)\ R'MgX} RCN$$

Formamides undergo similar reactions to give aldehydes.

Grignard reagents favour 1,2-addition with α, β-unsaturated aldehydes, while with the

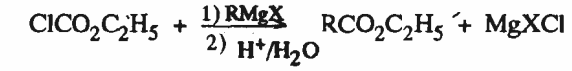
corresponding ketones give mostly, 1,4 addition products.





Coupling reaction is observed when Grignard reagent is treated with alkyl halides in presence of cobalt chloride

Esters are formed when ethyl chloroformate reacts with Grignard reagents.



SAQ 8

Name the suitable Grignard reagents and ketones to be used to prepare $CH_3(CH_2)_3C(CH_3)_2$, 2-methyl-2-hexanol

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14.8 SUMMARY

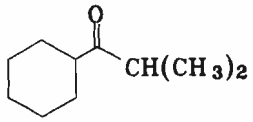
In this unit, we have discussed the strategy of organic synthesis. We are summarising below some important points :

- In a synthesis yield, cost and time are the factors which decide the suitability of the starting materials and the synthetic route.
- The retrosynthesis or disconnection approach identifies synthons and relates the synthons to the reagent used in the reaction. It also help us in identifying a variety of potential routes to the target molecule.
- Final product can be synthesised in high yield by increasing selectivity. There are three types of selectivity: chemoselectivity, regioselectivity and stereoselectivity. Selectivity can also be achieved by using suitable activating, deactivating and protecting groups.
- Reagents such as acetoacetic ester, malonic ester and Grignard reagents are the building blocks for organic synthesis.

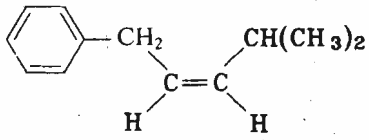
14.9 TERMINAL QUESTIONS

1) Use retrosynthetic approach to devise synthesis for following compounds, identify synthons and corresponding reagents

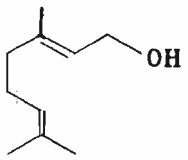
a)



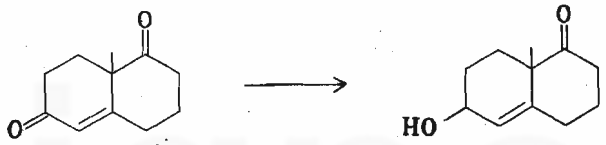
b)



2) Plan a synthesis of geraniol, a monopterpene which is isolated from rose flower. It has following structure.



3) Develop a synthesis of the following compound from the starting material indicated and other required reagents.



4) Write the steps used for the following conversions:

(a) aniline to *p*-bromoaniline

(b) aniline to *o*-bromoaniline

5) Starting with either acetoacetic ester or malonic ester how are the following compounds obtained

(a) 5-methyl-2-hexanone

(b) 3-methyl-2-hexanone

(c) 2-methyl butanoic acid

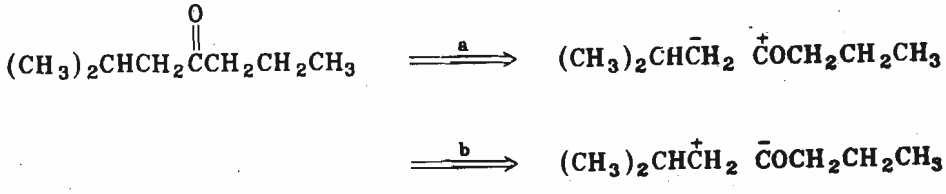
(d) glutamic acid

(e) allylethanoic acid

14.10 ANSWERS

Self Assessment Questions

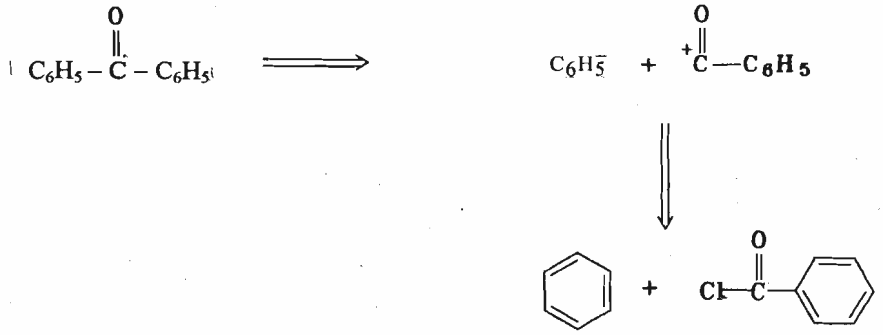
1) a) Disconnection of the — CH_2—CO bond generates two pair of synthon.



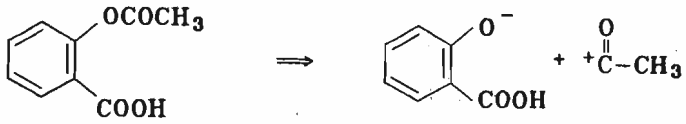
First pair of synthon, $(CH_3)_2CHCH_2^-$ and $^+COCH_2CH_2CH_3$ can be related to following suitable reagents:

$(CH_3)_2CHCH_2MgBr$ and $CH_3CH_2CH_2CN$, respectively.

b) Target molecule may be disconnected, hence, Friedel-Crafts alcylation of benzene is identified as a suitable syntheses.



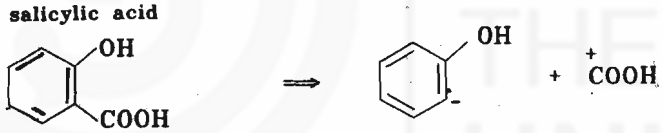
2) a) Asprin is disconnected as follows:



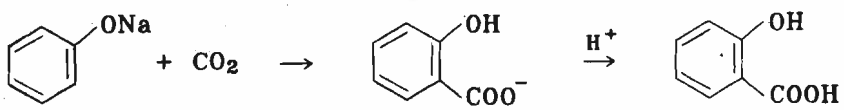
The reagents corresponding to these synthon are the salicyclic acid and ethanoic acid (acetic acid) or acetic anhydride.

But salicyclic acid is not readily available, therefore, it is further disconnected

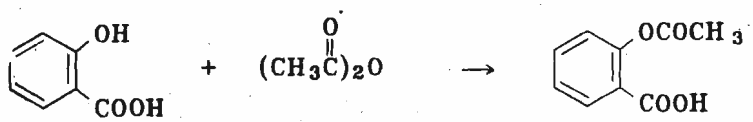
salicylic acid



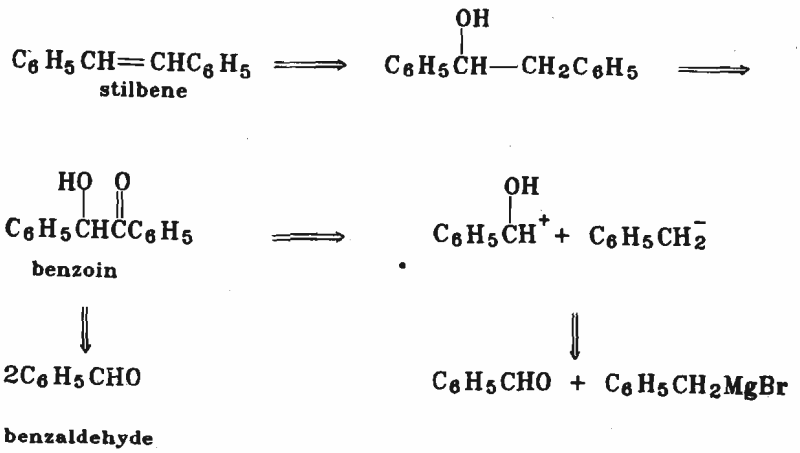
These synthon can be related to readily available reagents phenol and carbondioxide, hence, Kolbe reaction is identified as a suitable method of synthesis of



From salicyclic acid asprin can be obtained in high yield by the reaction of acetic anhydride



b) Apply the principle of retrosynthesis to identify synthetic strategies for the stilbene.

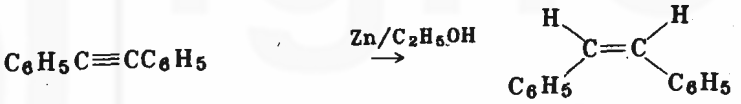


Thus, stilbene can be prepared by reducing benzoin which we obtained from benzaldehyde by benzoin condensation, or by treating benzyl magnesium bromide with benzaldehyde and dehydrating the product.

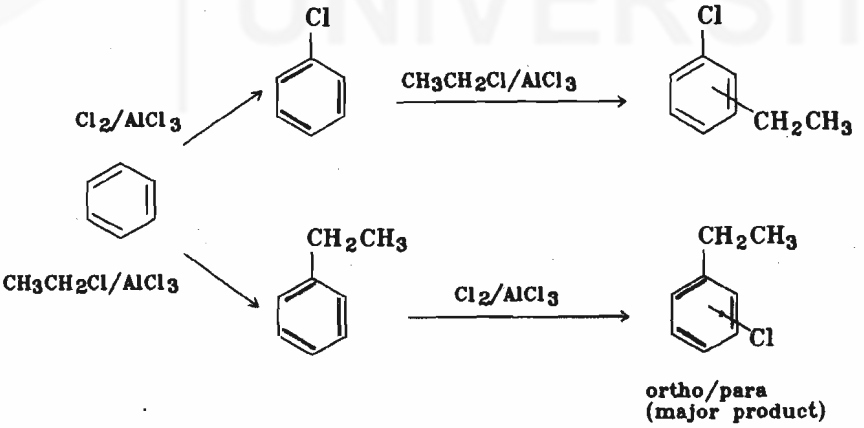
$$C_6H_5CHO \xrightarrow{KCN} C_6H_5CHOHCOC_6H_5 \xrightarrow{\text{reduction}} C_6H_5CHOHCH_2C_6H_5 \xrightarrow{-H_2O} C_6H_5CH{=}CHC_6H_5$$

$$C_6H_5CHO + C_6H_5CH_2MgBr \xrightarrow[2)\ H^+/H_2O]{1)\ \text{dry ether}} C_6H_5CHOHCH_2C_6H_5 \xrightarrow{-H_2O} C_6H_5CH{=}CHC_6H_5$$

But both the process give more stable *trans*-stilbene. Therefore, we have to select some stereospecific reaction. *Cis* stilbene may be prepared by reducing diphenylacetylene with zinc dust and ethanol

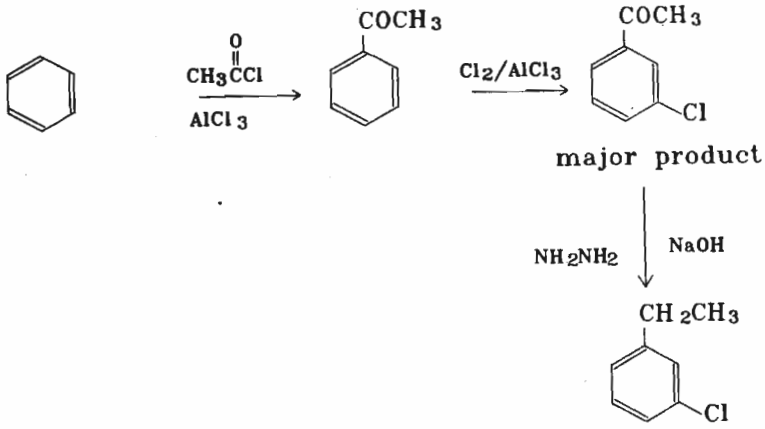


3) If we try to prepare target molecule by chlorination of ethyl benzene or alkylation of chlorobenzene, we will get *ortho* and *para* products as both methyl and chloro groups are *ortho/para* directing. The following strategies will, therefore, fail:



ortho/para
(major product)

What we have to do is first to introduce a *meta*-directing group that will direct the second substituent into correct position, and which can then be transformed to the substituent that is required.



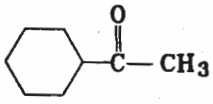
4) a) $CH_3CCH_2COC_2H_5$ → 1) $\bar{N}a\bar{O}C_2H_5$ 2) $CH_3CH_2CH_2Br$ → $CH_3CCHCOC_2H_5$ ($CH_2CH_2CH_3$) → H^+/H_2O, heat → $CH_3CCH_2CH_2CH_2CH_3$ (2-hexanone)

b) $CH_3CCH_2COC_2H_5$ → 1) $NaOC_2H_5$ 2) $BrCH_2CCH_3$ (O) → $CH_3CCHCOC_2H_5$ (CH_2CCH_3, O) → H^+/H_2O, heat → $CH_3CCH_2CH_2CCH_3$ (2,5 hexanedione)

5) a) $CH_3CCH_2COC_2H_5$ → 1) base 2) CH_3CH_2X → $CH_3CCHCOC_2H_5$ (CH_2CH_3) → 1) base 2) CH_3CH_2X → $CH_3C(C_2H_5)_2COC_2H_5$

→ H^+/H_2O, heat → $CH_3CCH(CH_2CH_3)_2$

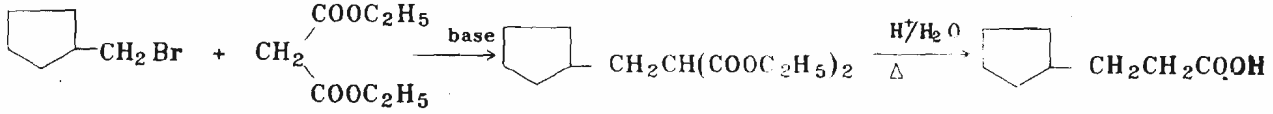
b) $CH_3CCH_2COC_2H_5$ → 1) base 2) $Br(CH_2)_5Br$ → $CH_3CCHCOC_2H_5$ ($(CH_2)_5Br$)

→ H^+/H_2O, △ → 

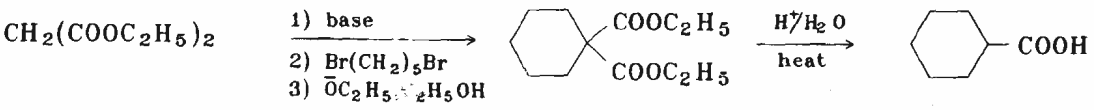
6) a) $CH_2(COOC_2H_5)_2$ → 1) $\overset{+}{N}a\overset{-}{O}C_2H_5$ 2) $CH_3CH_2CH_2Br$ → $CH_3CH_2CH_2CH(COOC_2H_5)_2$

b) $CH_2(COOC_2H_5)_2 \xrightarrow[2)\ CH_3CH_2I]{1)\ \overset{+}{N}a\bar{O}C_2H_5} CH_3CH_2CH(COOC_2H_5)_2 \xrightarrow[2)\ H^+]{1)\ OH^-/H_2O,\ \Delta} CH_3CH_2CH_2COOH$

) a)



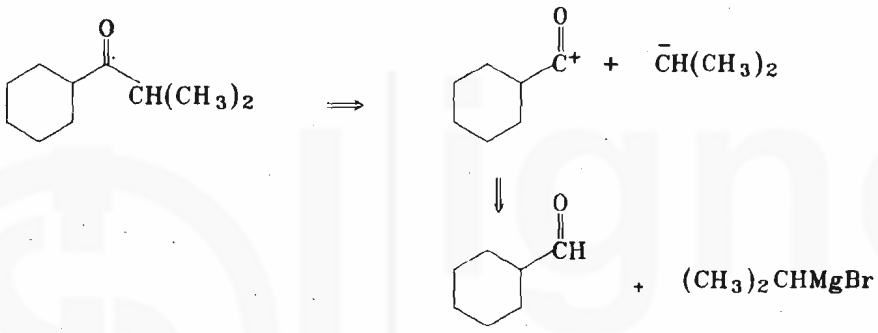
b)



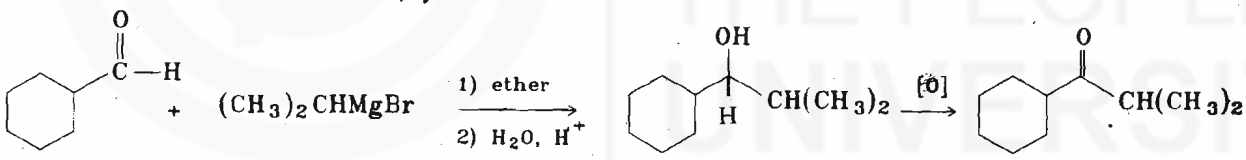
8) Butylmagnesium halide and propanone (acetone) not methyl magnesium halide and 2-hexanone (reason: propanone is readily available).

Terminal Questions

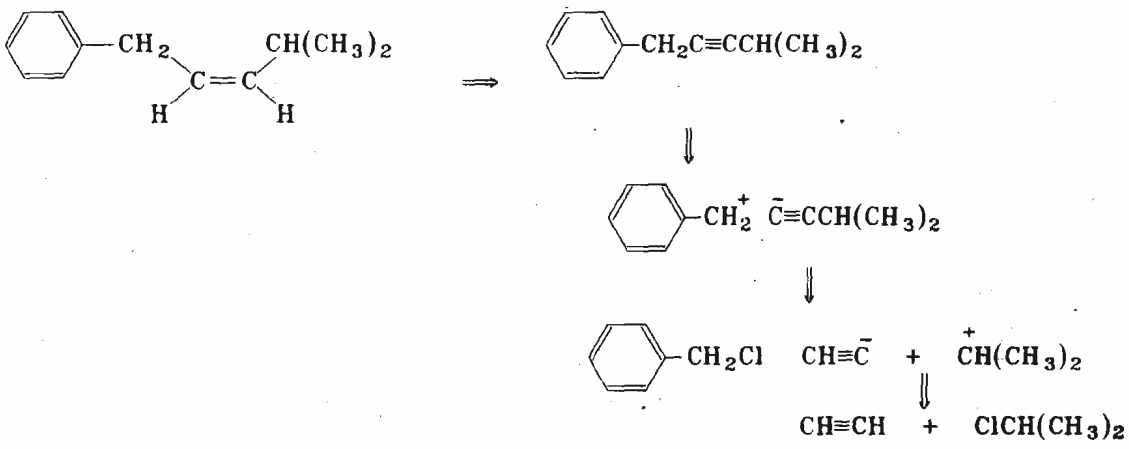
1) a)



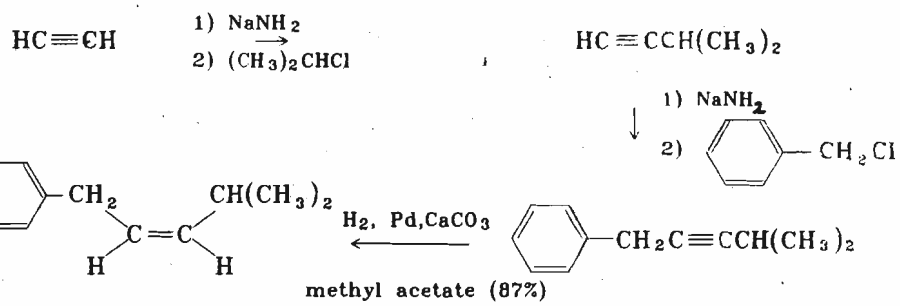
Therefore, synthesis can be written as



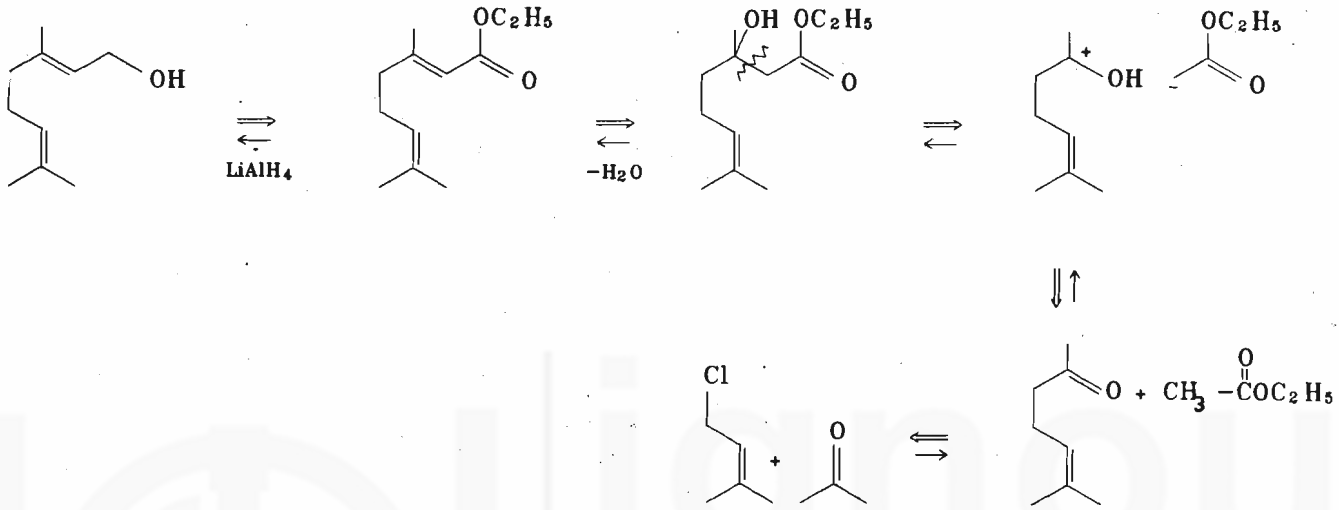
b)



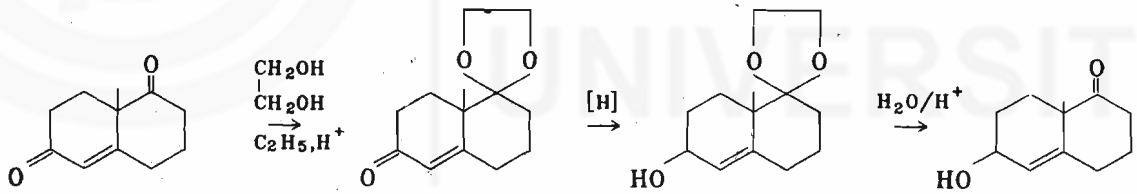
synthesis starts at acetylene and shown below



2) Suitable route to geraniol and the strategies can be summarised as



3) In the starting compound we have two ketones one is saturated and the other is unsaturated. As you know α, β-unsaturated ketones are less reactive towards nucleophile, therefore, we can protect saturated ketone with ethylene glycol without affecting α, β- unsaturated ketone. Target molecule can be prepared as follows:



4) Treatment of starting material with

a) aniline (i) acetylation (ii) bromination (iii) acid hydrolysis

b) aniline (i) sulphonation (ii) $(CH_3CO)_2O$ (iii) Br_2 (iv) $H^+/H_2O,\Delta$

5) a) Treatment of acetoacetic ester with

(i) 1) $NaOC_2H_5/C_2H_5OH$) 2) $(CH_3)_2CHCH_2Br$

(ii) OH^-/H_2O (iii) $H^+/H_2O,\Delta$

b) Treatment of acetoacetic ester with

(i) 1) $NaOC_2H_5/C_2H_5OH$ 2) $CH_3CH_2CH_2Br$

(ii) 1) $NaOC_2H_5/C_2H_5OH$ 2) CH_3Br

(iii) OH^-/H_2O (iv) $H^+/H_2O,\Delta$

c) Treatment of malonic ester with

(i) 1) $NaOC_2H_5/C_2H_5OH$ 2) $CH_3CH_2CH_2Br$

(ii) 1) $NaOC_2H_5/C_2H_5OH$ 2) CH_3Br

(iii) OH^-/H_2O (iv) $H^+/H_2O,\Delta$

Treatment of malonic ester with

d) (i) Br_2/CCl_4

(ii) potassium phthalimide/DMF

(iii) 1) $NaOC_2H_5/C_2H_5OH$ 2) chloroethylpropionate

(iv) $H^+/H_2O,\Delta$

5) Treatment of malonic ester with

(i) 1) $NaOC_2H_5/C_2H_5OH$ 2) allylchloride

(ii) $H^+/H_2O,\Delta$

UNIT 15 CASE STUDY OF SOME CHEMICALS OF DAILY USE-I

Structure

15.1 INTRODUCTION

Chemistry has been described as "an integrated study of the preparation, properties, structure and reactions of the chemical elements and their compounds and of the systems which they form". This knowledge enables chemists to design and produce chemical substance with properties to serve a wide variety of human needs. The chemical substance we daily use cover an unimaginable wide range from drugs, food, fuels to all kinds of materials. In fact, chemistry is the one science on which such a large number of industries are based.

So far, in this course, we have exposed you to the basic concepts of organic chemistry in order to help you understand how particular reactions take place. In this unit and the next one, we shall show you how this basic knowledge is used in the industrial production of organic substance of daily use. We have chosen for our discussion synthetic polymers, synthetic fibres, soaps, synthetic detergents, synthetic drugs and synthetic dyes.

Objectives

After studying this unit, you should be able to :

- differentiate between lab process and industrial process,
- classify synthetic polymers as themosetting resins, thermoplastics, fibres and elastomers based on physical properties; as addition and condensation polymers based on the type of reaction involved; and as chain growth and step growth polymers based on the nature of polymerisation,
- describe the manufacture of polyethyene, and poly (ethylene terephthalate),
- define soaps and synthetic detergents, and
- describe the manufacture of soap and synthetic detergent.

15.2 Industrial Process

You must have synthesised simple organic compound in a chemistry laboratory at some stage during your studies. This must have made you to realise that in laboratory synthesis convenience is typically the most important consideration. We use glassware in a laboratory which allows visual monitoring of the reaction, apart from it being generally unaffected by corrosive effects of the chemicals. Because the amounts of materials used are small, hazardous chemicals can be handled by using fumehoods or safety shields. And expense, although always a consideration, is not the primary factor.

In industrial production, products have to be manufactured at competitive rates, by a safe and viable process. Economy and safety, therefore, become critical factors. Following are some of the important criteria that have to be considered in the location of a chemical industry and the design of the plant :

The **batch technique** resembles the way the lab experiment is carried out. It is time consuming process and involves following steps.

1. Bring the reactants to reactor (Kettle) and loading.
2. Carry out reaction.
3. Time for analysing and safety checks.
4. Adjust temperature before transfer.
5. Transferring product from reactor to isolation vessel.
6. Cleaning.

- choice of the process and availability of raw materials,
- engineering problems associated with carrying out reactions on large scale,
- separation of the product,
- disposal of byproducts
- safety.

We will briefly discuss each of these.

Choice of the process and availability of the raw materials

Since cost is one of the major considerations in an industrial process, we need to look for cheap raw materials and the cheapest method of production. The cheapest method may or may not be the most straight forward and easy one. In addition to cost, availability of raw materials is crucial; often industries are located where raw materials are easily and cheaply available. To cut costs on raw materials, industries often prefer to work them up from a natural source rather than purchase them from the market.

Engineering problems associated with carrying out reactions on large scale

Industrial production is not exactly a scaling up of a laboratory preparation. Apart from the viability of the chemical reaction, various engineering problems have to be taken care of as follows :

- One has to see whether the laboratory conditions can be simulated on a large scale. For instance, a temperature of 1273K can be produced in a small localised area for short periods, but it would not be easy heat up a large reactor, handling a few kilograms, upto this temperature.
- Control of the reaction parameters like temperature, pressure, amounts for volumes of reactants and products in the reaction vessel is extremely important to avoid a run-away reaction.
- Problems, like turbulence in the reaction vessel, which dissipate themselves or can be managed easily under laboratory conditions, need special handling in large scale production.
- In industry, continuous reactors in which reactants are fed at one end and products drawn off at the other end are preferred to batch reactors (laboratory processes are batch processes). Fig. 15.1 (a) shows examples of typical 500 dm^3 Jacketed batch reactor equipped with agitator,Various inlets and a bottom outlet; and (c) and (d) Continuous flow reactors. Continuous reactors are more efficient, but this changes the whole perspective as far as the plant design is concerned. Design of the reactor and residence time has to be decided to give optimum yield. The product has to be separated from unreacted raw materials which are recycled to increase the yield.

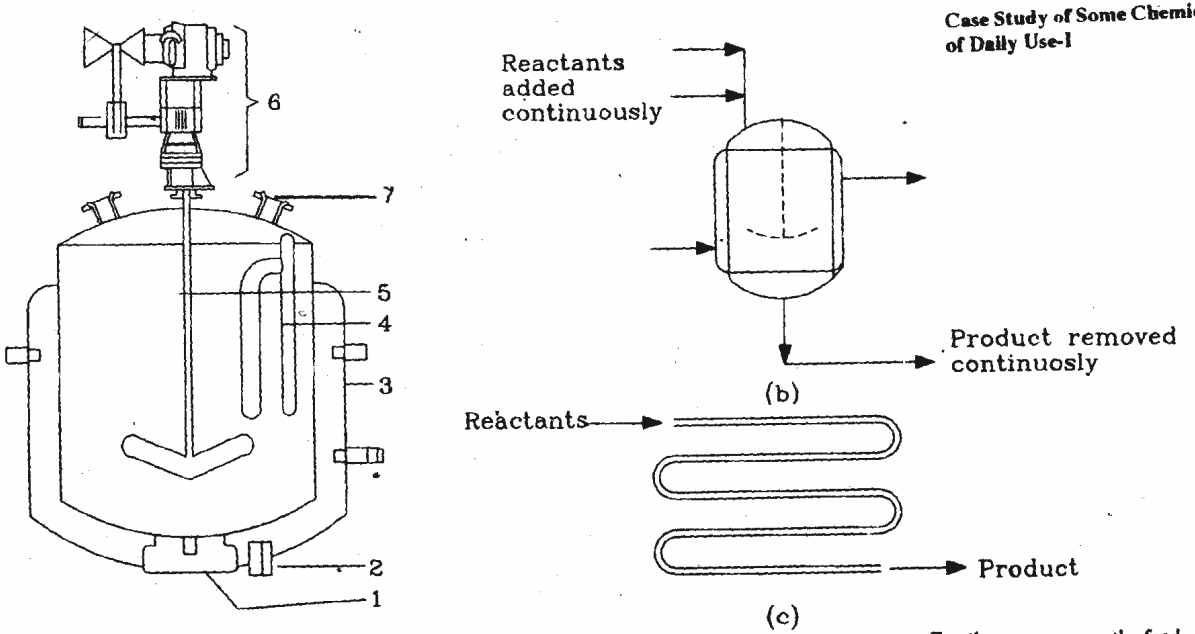


Fig 15.1 : **(a) Diagram of a typical manufacturing chemical reactor. (1) Outlet nozzle (2) Jaket drain (3) Jaket : Heating and cooling of reaction mixture can be carried out by circulating fluid in it (4) Baffle (5) Agitator (6) Drive (7) Nozzles**
(b) and (c) : Continuous flow reactors

In Continuous process the feed materials are continuously added to the reactor and the product is continuously with drawn from the vessel. This eliminates the "dead time" lost when a series of batch runs are performed. Continuous process clearly require remodification in reactor design.

Reactors, containers, connecting pipes, and accessories of an industrial plant like heat exchangers, etc are all made of metal. Glass is not suitable because of its fragile nature. Visually, this necessitates use of different kinds of gauges to monitor various reactor parameters, since monitoring cannot be done. Further corrosion becomes a major problem and one of the cost factors to be considered, both in the choice of the process and the design of the plant. One of the major areas of research in chemistry today is production of corrosion resistant materials.

Separation

Separation and purification of the product is an important factor in deciding on an industrial process.

The product must be produced in a form in which it can be easily separated from unreacted starting materials and byproducts. Laborious, time consuming separation and purification by techniques like chromatography may not be feasible on an industrial scale.

Disposal of byproducts

In laboratory preparations, byproducts are simply disposed off. Byproducts of an industrial process would pose a potential environmental hazard if disposed of indiscriminately, and therefore suitable and safe mode for their disposal has to be devised. In order to reduce costs of production, industries generally try not to waste their byproducts. These are either marketed as such or transformed into some other useful product. Example are the isolation of glycerine in saponification process for soap making or conversion of bagasse from a sugar mill into particle board.

Safety

It is worth realising that any chemical is potentially hazardous if not handled properly. Therefore, in industry, where chemicals are handled in large amounts precautions have to be stringent to the limit of becoming fool proof in order to avoid accidents.

So you can see that great care has to be taken in the development of an industrial process to ensure safe and economic operation. The development of an industrial chemical process typically involves the following steps :

i) A need for a particular product is identified.

ii) The relevant chemistry is studied on a small scale in a laboratory. Various ways of producing the desired material are evaluated in terms of costs and potential hazards.

Polymers usually contain molecules having different chain lengths.

iii) The above data are evaluated by chemists, chemical engineers, business managers, safety engineers and others to determine which of the possibilities is most feasible.

iv) A pilot plant test of the process is carried out. The scale of the pilot plant is between the laboratory and a manufacturing plant. The purpose of this test is to make sure that the reaction is efficient on a large scale, to test the reactor design, to evaluate hazards, to gather information about its environmental impact and to determine its cost.

In this unit we will discuss case studies pertaining to the manufacture of synthetic polymers, soap and detergents, to illustrate the wide range of chemical reactions and techniques used in the commercial world. Case studies related to drugs and dyes will be taken up in Unit 16.

15.3 SYNTHETIC POLYMERS

When all monomer units are identical a homopolymer formed. Copolymers consist of more than one kind of monomer unit which can be arranged from variety of ways

$$n\,A \longrightarrow A\text{-}(A)_{n-2}\text{-}A$$

homopolymer

$$n\,A + n\,B \longrightarrow A\text{-}(B\text{-}A)_{n-1}\text{-}B$$

copolymer

Polymeric materials like hides, natural resins, flax, cotton, silk, wool, shellac, wood, bitumin, etc have been employed to satisfy human needs since prehistoric days. Carbohydrates, such as starch and cellulose, proteins, nucleic acids on which all forms of life depend are all polymeric in nature. The first truly synthetic polymers were prepared by Bakeland by condensation of phenol and methanal (formaldehyde) at the turn of this century. Since then, rapid advances have taken place in this fast growing area. In this section we will describe some basic concepts about synthetic polymers. In next two sections we will discuss industrial processing of ethylene polymers and fibre forming polymers.

A polymer is a large molecule (macromolecule) built up by the repetition of small simple chemical units. The repeat unit of the polymer is usually equivalent or nearly equivalent to the starting material from which the polymer is formed. The term polymer is derived from Greek words 'poly' and 'meros' meaning many parts; the building blocks or the starting materials for polymers are known as monomers. For example, polyethylene is constructed from ethene monomers

$$n\,CH_2{=}CH_2 \longrightarrow -\left(\begin{matrix}H & H\\ | & |\\ C & -\,C\\ | & |\\ H & H\end{matrix}\right)_n-$$

where n represents a large number, usually several thousand. In contrast to small molecules, polymeric molecules can have essentially the same chemical composition but widely different molecular weights. This arises because of the fact that a different number of same repeating units may be present in the polymer. The number of repeat units in a polymer chain is called as degree of polymerisation $(\overline{DP})$ and is given by the ratio of the average molecular weight of the polymer $(\overline{M})$ to the molecular weight of the repeat unit (M_0).

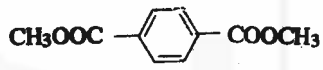
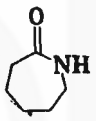
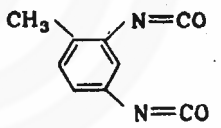
$$\overline{DP} = \frac{\overline{M}}{M_0}$$

The average molecular weights of the polymers are usually very high ($10^3 - 10^7$ or more g mol^{-1}). In still other cases, polymers with infinite molecular weights may be obtained by cross-linking reactions or network formation. Such a network polymer is stable to heat and cannot be made to flow or melt. Thus, an infusible and insoluble structure is obtained.

An optimum molecular weight is essential for attainment of unique properties of polymeric materials. Properties such as density, refractive index, and hardness of high polymers are independent of molecular weight. Melt viscosity, softening temperature, tensible and impact strengths are related to the length of polymer chain. Tensible and impact strength increase with an increase in chain length and then level off.

Polymers have been used as plastics, fibres, surface coatings (paints) and rubber. They are currently being used in almost every industry in one form or other. Table 15.1 shows some of the important polymers, their monomer and uses.

Table 15.1 : Some Important Polymers and their Uses

Polymer	Monomer		Use
	Name	Formula	
Chain growth polymer			
Polyethylene	Ethene (ethylene)	$CH_2 = CH_2$	Packaging, bottles, cable insulation, films and sheets.
Polypropylene	Propene (propylene)	$CH_2 = CHCH_3$	Automotive mouldings, rope, carpet, fibres
Poly-vinyl chloride	Chloroethene (vinyl chloride)	$CH_2 = CHCl$	Insulation, films, pipes
Polystyrene	Styrene	$CH_2 = CHC_6H_5$	Foam and molded articles
Teflon	Tetrafluoro-ethene	$CF_2 = CF_2$	Valves and gaskets, coatings
Orlon, Acrilan	Acrylonitrile	$CH_2 = CHCN$	Fibres
Polyvinyl acetate	Vinylacetate	$CH_2 = CHOCOCH_3$	Paints, adhesives
Step growth polymers			
Nylon 66	Adipic acid Hexamethylene diamine	$HOOC(CH_2)_4COOH$ $H_2N(CH_2)_6NH_2$	Fibres, clothing, tyre cord bearings
Dacron, Terylene, Mylar	Ethylene glycol Dimethyl terphthalate	$HOCH_2CH_2OH$ 	Fibres, clothing, film
Nylon 6, Perlon	Caprolactam		Fibres
Polyurethane Spandex	Poly (2-butene -1, 4-diol) Tolylene diisocyanate	$HO-(-CH_2CH=CHCH_2-)_n-OH$ 	Fire cord Foams, Fibres, Coatings
Copolymers			
Saran	Vinyl chloride Vinylidene chloride	$H_2C = CHCl$ $CH_2 = CCl_2$	Food wrappings, fibres
SBR (styrene-butadiene rubber)	Styrene (25%) Butadiene (75%)	$H_2C = CHC_6H_5$ $H_2C = CHCH = CH_2$	Tyres
Viton	Hexafluoropropene Vinylidene fluoride	$F_2C = CFCF_3$ $H_2C = CF_2$	Gaskets, rubber articles
Nitrile rubber	Acrylonitrile Butadiene	$H_2C = CHCN$ $H_2C = CH\text{-}CH = CH_2$	Latex, adhesives, gasoline hoses
Butyl rubber	Isobutylene Isoprene	$H_2C = C(CH_3)_2$ $H_2C = C(CH_3)\,CH = CH_2$	Inner tubes
ABC (initials of three monomers)	Acrylonitrile Butadiene Styrene	$H_2C = CHCN$ $H_2C = CHCH = CH_2$ $H_2C = CHC_6H_5$	Pipes, high-impact applications

15.3.1 Raw Materials for Polymer Industry

Three important sources of raw materials for polymer industry are :

a) Vegetable sources

b) Coal

c) Petroleum

Before the Second World War, vegetable sources were the most important sources of these materials. Gradually, however, the emphasis shifted from vegetable sources to coal based raw materials and later to petroleum. Early grades of polyethylene were obtained from sugar-cane via molasses, ethyl alcohol and ethene. Until the mid 1950s coal was the main raw material for European plastic industry. Coal tar, obtained on destructive distillation of coal, was an important source of aromatic chemicals such as benzene, methylbenzene, (toluene), phenol, naphthalene, etc. From these chemicals, monomers such as adipic acid, hexamethylene diamine, caprolactam, phenol, formaldehyde, styrene, etc. were produced which were used for the manufacture of polyamides, phenol-formaldehyde resins, polystyrene, etc. Calcium carbide obtained from coke and calcium oxide has been used for the production of ethyne (acetylene) which would then be converted to acrylonitrile, vinyl chloride, vinyl acetate and other vinyl monomers. However, gradually the emphasis shifted from vegetable sources and coal based materials towards petroleum. Ethene, vinyl chloride, terephthalic acid, ethene glycol, styrene, vinyl acetate, acrylonitrile, methanal (formaldehyde), ethylene oxide are nowadays produced from petroleum sources. Since the petroleum feedstock is also dwindling and is limited, therefore, attempts are being made to prepare polymers from easily renewable resources. Hence processes based on vegetable sources may be revived in the future.

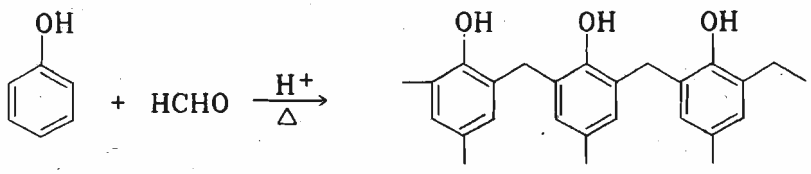
15.3.2 Classification of Polymers

We will now discuss the classification of synthetic polymers. Polymers are classified in many ways.

A. Polymer structure and physical properties

The classification of synthetic polymers according to their physical properties is a useful exercise because it allows us to make a rough correlation between structure and properties. In general, we can divide polymers into four major categories: thermosetting resins, thermoplastics, fibres and elastomers

Thermosetting resins may be liquid or made to flow under pressure to any desired form. In the presence of a catalyst, heat, or radiation they undergo an irreversible chemical reaction or curing to yield a network polymer. The curing reaction can be either an addition reaction of unsaturated groups or a condensation reaction between different functional groups. The most familiar example is Bakelite. It is a phenolic resin produced by the reaction of phenol and methanal (formaldehyde). On heating water is eliminated, many cross links are formed and the polymer sets into a stable, rock-like mass.



Thermoplastics, on the other hand, are normally solids at room temperature. They soften or melt at high temperature and become solid again on cooling. This cycle can be repeated. Thus, thermoplastics can be easily processed to different shaped articles by the application of heat and pressure. These polymers are used as plastics. Polyalkenes, poly (vinyl chloride), polystyrene etc. are some of the important thermoplastics available today. Amongst polyalkenes polyethylene and polypropylene rank as two of the most important derivatives. The consumption of polyethylene and polypropylene has increased dramatically since 1960s, due to their low costs and useful properties.

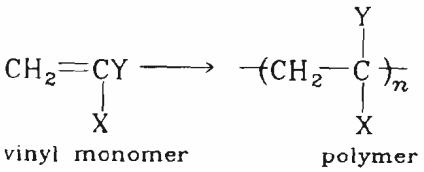
Fibres are the threads produced by extruding a molten polymer through small holes in a die or spinnert. The fibres are then cooled and drawn out. Nylon is a familiar example of this class.

Elastomers are polymers that have the ability to stretch out and spring back to their original shapes. These polymer must have cross-links. Natural rubber is one example of an elastomer.

B. Addition and Condensation Polymers

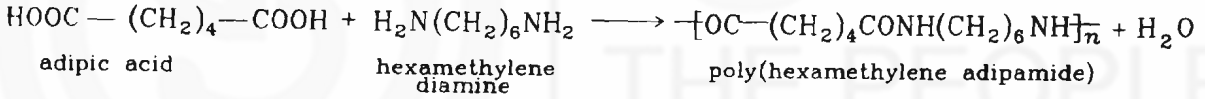
Polymers have been classified by Carothers on the basis of compositional difference between the polymer and the monomer(s) from which they are derived. In the original classification given in 1929 by Carothers, the polymers were classified into addition and condensation types.

Addition polymers are those in which repeating unit has the same composition as the monomer from which it is derived. In other words, the empirical formula of the monomer and polymer is the same. Majority of such polymers are based on vinyl monomers. The polymerisation is carried out by opening of the bond by appropriate initiating species. Several example of such polymers are commercially available. The general structure can be described as follows :

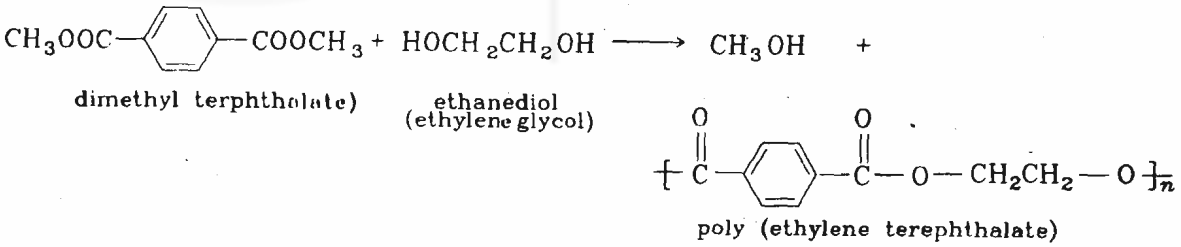


Some typical vinyl monomers and polymers derived from them are given in Table 15.1.

Condensation polymers are formed from low molecular weight polyfunctional monomers by condensation reactions. These polymerisations are accompanied by elimination of small molecules such as water, methanol, HCl, etc. In order to form the polymer backbone, more than one functional group is required per monomer molecule. For a condensation reaction, such functional groups have to be different. These different functionalities may be present in two different monomers (A-A, B-B type) or may be in the same monomer (A-B type). This is illustrated by polyamidation, and polyesterification reactions :

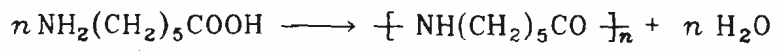


Polyamidation Reaction



polyesterification reaction

In these examples, similar type of functional groups are present in each monomer and hence two monomers of different functionalities are used. Polyamidation or esterification reaction can also be carried out by using one monomer only having different functionality.



In polycondensation reactions, the repeat unit is different from either of the monomers. Thus the empirical formula of monomers and polymers is not identical.

C. Chain Growth and Step Growth Polymerisation

However, it was soon realised that the classification of Carothers is inadequate. A polymer

can be synthesised by several different routes, some of which may be classified as addition while others as condensation. Thus polyethylene of high molecular weight could be prepared from ethene (addition polymerisation) or diazomethane (condensation polymerisation). The polymer so obtained is a tough solid melting in the range of 388-403 K.

$$n\,CH_2{=}CH_2 \longrightarrow \{CH_2{-}CH_2\}_n$$

$$n\,CH_2N_2 \longrightarrow \{CH_2\}_n + n\,N_2$$

Polyethylene could also be prepared by Wurtz reaction

$$n\,Br(CH_2)_{10}\,Br + 2n\,Na \longrightarrow \{(CH_2)_{10}\}_n + 2n\,NaBr$$

However, the polymer thus obtained is of low molecular weight and waxy solid. The chemical structure of the polymer obtained by three different routes is similar but the difference in molecular weight, which is due to different growth mechanism, is responsible for variation in physical properties. Flory, therefore, emphasised the need to classify the polymers on the basis of growth mechanism as step-growth and chain growth polymerisation. The characteristics of these growth reactions are markedly different from each other.

The chain growth reaction is initiated by some sort of active centre (either free radicals or ionic groups) and comprises of three kinetically different steps of initiation, propagation and termination reactions.

Initiation step-generation of active centre C*

$$C^* + M \xrightarrow{k_i} CM^*$$

$$\text{propagation step} - CM^* + n\,M \xrightarrow{k_p} C(M)\,n\,M^*$$

$$\text{termination step} - C(M)\,nM^* \xrightarrow{k_t} \text{polymer}$$

In these reactions, the magnitude of k_p is greater than k_t, which in turn is greater than k_i. The polymer formed by such a reaction usually has a carbon backbone with pendant substituents. Since the propagation reaction is much faster than initiation, high molecular weight polymer is formed at the initial stages of the reaction. The monomer concentration decreases steadily throughout the reaction. Long reaction time give high yield, but only a marginal effect on molecular weight is observed.

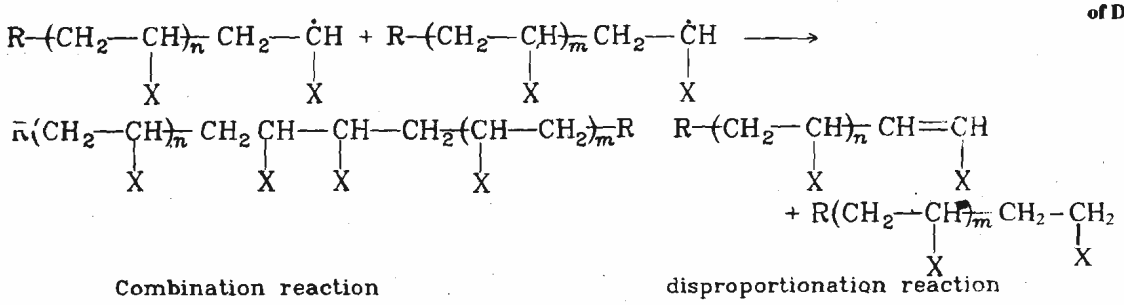
In a free radical chain growth polymerisation, the initiator fragment radical $\dot{R}$ adds to the monomer molecule, thereby generating the monomer radical, which, in turn, adds to a double bond in the propagation step.

$$In \xrightarrow{k_d} 2\dot{R}$$

$$\dot{R} + CH_2{=}\underset{\displaystyle X}{\underset{|}{CH}} \xrightarrow{k_i} R{-}CH_2{-}\underset{\displaystyle X}{\underset{|}{\dot{C}H}}$$

$$RCH_2\underset{\displaystyle X}{\underset{|}{\dot{C}H}} + n\,CH_2{=}\underset{\displaystyle X}{\underset{|}{CH}} \xrightarrow{k_p} R\{CH_2{-}\underset{\displaystyle X}{\underset{|}{CH}}\}_n + CH_2\underset{\displaystyle X}{\underset{|}{\dot{C}H}}$$

Co-reaction of two propagating radicals by combination or disproportionation results in the termination reaction.



Combination reaction disproportionation reaction

Monomers which have electron donating groups attached to one of the double bond carbon atoms have a tendency to form carbocation ions in the presence of proton donors and may be polymerised by cationic mechanism. The number of common monomers (Table 15.2) polymerised cationically is limited. Substituents which stabilise the intermediate carbocation ion also help in polymerisation.

Table 15.2 : Monomers polymerised by cationic mechanism

Monomer	Mol wt. of the polymer	Type of substituent
Ethene	low	no substituent
Propene	medium (~5000)	CH_3 (electron donating)
Isobutylene	high (~10^6)	$2CH_3$ (electron donating)
Vinyl ethers	high (~10^6)	ether (stabilises carbonium ion)
α-Methyl styrene	high (~10^6)	methyl and phenyl
Styrene	high (~10^6)	phenyl group (stabilises carbonium ion)

Monomers bearing electron withdrawing substituents increase the electrophilic character of the double bond. The electron density of the active centre generated by the attack of a suitable nucleophile (amide ion, carbanion) on such monomers is lowered by the substituent leading to its stabilisation. Such monomers are polymerised by carbanionic mechanism. Examples of chain growth polymers are given in Table 15.1.

In a step growth polymerisation, the reaction proceeds by stepwise intermolecular condensation of monomers having functionality greater than one. In constrast to chain growth, the monomers disappear early in the reaction and dimer, trimer, tetramer, etc. are formed. The polymer molecular weight increases throughout the reaction. In order to get high molecular weight polymer, long reaction times are required. Examples of step growth polymers are given in Table 15.1.

With this background now, we will take up the case study of the production of polyethylene, and poly (ethylene terephthalate) (PET).

SAQ 1

Classify following polymers as chain growth, step growth or copolymers.

a) Teflon

b) Polyvinyl acetate

c) Dacron

d) Butyl rubber

15.4 CASE STUDY OF THE PRODUCTION OF POLYETHYLENE

Polyethylene is the largest volume commodity plastic in the world. The main features of these polymers are excellent electrical insulation properties over a wide range of

frequencies, very good chemical resistance, good process-ability, toughness, flexibility and transparency (in thin films form). Crystallinity is one of the most important properties which characterises the different polyethylenes. Difference in crystallinity is responsible for difference in density and other characteristic properties of the polymers.

The polyethylene (PE) industry has been conveniently classified in the past on the basis of product density : a ultra low density PE (sp gr 0.89 - 0.915), low density polyethylene (LDPE) or high pressure polyethylene (sp gr 0.915 - 0.94) and high density polyethylene (HDPE) or low pressure polyethylene (sp gr 0.95 - 0.97). Nowadays polyethylenes are more appropriately described as branched PE and linear PE. Low density polyethylene (LDPE) contains 15-25 short chain branches per 1000 carbon atoms. It also contains many long chain branches. These branches sterically hinder crystallisation and reduce density. In high density polyethylene (HDPE) very few short chain branches are present. This results in a molecule which can pack very tightly in a folded plate form and yields a product with a high density.

LDPE was first produced by ICI (Imperial Chemical Industries) in 1939 using an oxygen or free radical initiated process. High pressure (345 MPa) and high temperatures (~673 K) are used in LDPE production. A new technology for obtaining low density PE has been developed which operates at less than 2 MPa and near 373 K. These new products, called linear low density PE (LLDPE) have definite advantages over those made by high pressure process and are revolutionising the polyethylene industry. In this technology ethylene is polymerised with an alpha olefin such as 1-butene, 1-hexene, 1-octene, or 4-methyl-1-pentene. The number of branches and the density of the product is controlled by the concentration of the α-olefin in the polyethylene backbone.

High density PE is made with an organometallic catalyst at a low pressure. At present, two classes of catalysts are used for the commercial manufacture of HDPE. These are

a) transition metal oxide based catalysts (Phillips catalyst)

b) transition metal halide/organometallic catalysts (Zieglar-Natta catalyst).

The technologies available for HDPE manufacture are solution, slurry or suspension, and gas-phase polymerisation. Slurry (suspension) polymerisation is the most widely used method for producing low molecular weight to ultra high molecular weight HDPE. The product has improved tensile and tear strengths and has applications in blow molded bottles, pipe and tubing.

In India the beginning of PE industry was made in 1959 by ICI Calcutta, using industrial alcohol as a source of ethene. Union Carbide India Ltd (UCIL), Bombay and Indian Petrochemicals Corporation Ltd (IPCL), Vadodara set up their plants of LDPE production in 1961 and 1978 respectively. HDPE production started in 1968 in India. The status of PE industries in India is given in Table 15.3. The application pattern of various types of PE is summarised in Table 15.4.

Table 15.3 : Polyethylene and PVC Industries in India

Company and Location		Product	Installed capacity MTA	Technology
IPCL, Vadodara	LDPE	80,000		Tubular
Union Carbide, Bombay	LDPE	20,000		Tubular
IEL	LDPE	12,000		Autoclave
IPCL, Nagothane (MGCC)	LDPE	80,000		Autoclave
PIL, Bombay	HDPE	50,000		Liquid Slurry process
IPCL, Nagothane	LLDPE	80,000		—

Table 15.4 : Application Pattern of Polyethylene

LDPE & LLDPE	Food packagings Non-food packagings Extrusion coatings Injection moldings Wire & Cables Rotation moldings
HDPE	Woven sacks Injection molding Blow molding Monofilament film Pipes & others

Typical Processes

Although there are many processes, the operations that are common to most of these plants are :

1) Catalyst formation and activation
2) Monomer purification
3) Reaction
4) Flashing and separation of unreacted monomer
5) Drying of monomer (and solvents, if used)
6) Monomer and solvent recovery
7) Addition and blending of additives with the polymer powder or granules
8) Melting, mixing, melt filtering, and pelletizing in an extrusion line
9) Bulk storage, blending, bulk loading and packaging.

LDPE

Two processes are employed for LDPE manufacture.

Reaction time in a reactor is known as residence time.

a) Batch process b) Continuous process

Batch Process

Because of high residence time batch process does not give reproducible results. It is difficult to control various reaction parameters in this process. Long chain branching due to transfer to polymer becomes excessive. This affects the physical properties of polymer.

Continuous Process

Continuous process allows better balance and control of polymerisation. A flow diagram of a commercial high-pressure process using oxygen or peroxides for catalysts is shown in Fig 15.2. For this process we require high-purity ethene. The first step involves the demethaniser, where a mixture of methane-ethene is removed and recycled. The feed passes to a demethaniser, where 99.8% ethene is taken overhead, and the bottoms (ethene) recycled. A free-radical yielding catalyst, such as a peroxide, is added to the high-purity ethene, compressed to operating pressure (150 MPa), and fed to the tubular reactor which is maintained at 460 K. These reactors (less than 2-3 cm diameter but upto 60 m in length) with very high linear velocities at the higher pressures give reaction times of minutes or less. The conversion per pass is low (15-30%), but the overall process is rapid and economical. The effluent from the reactor passes to a high-pressure separation in which the polymer is separated from the gas and/or liquid phases at the end of each pass and ethene monomer recycled after purification. The polyethylene is extruded, pellitised, and dried. The product is purged with nitrogen and ready storage. The process may involve multiple additions of monomer, initiator, and chain transfer agents along the tube length.

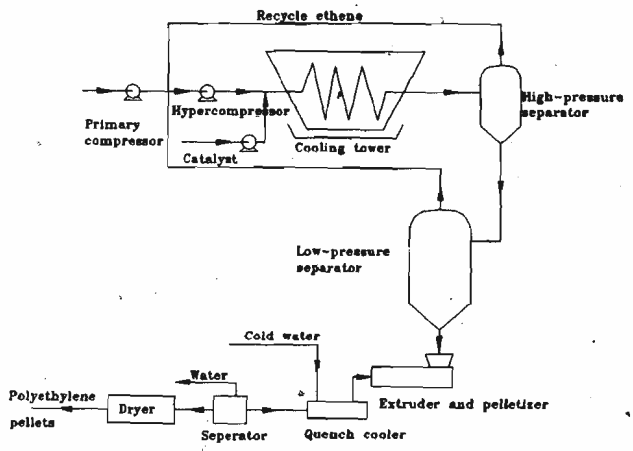


Fig 15.2 : Low-density polyethylene by high-pressure processing.

The product number average molecular weight is generally in the range of 20,000 - 50,000 depending on process conditions. The polymer is usually extended into a ribbon and chopped up or granulated.

HDPE

Phillips catalyst consists of a transition metal oxide (CrO_3, MoO_3, Ni_2O_3, or V_2O_5) physically dispersed and supported on another material referred to as the support, i.e. silica (SiO_2), alumina (Al_2O_3), charcoal, clay, etc. The support metal oxide is activated toward polymerisation by reduction (heating in the presence of CO or H_2 but in the absence of O_2 or by treatment with NaH or $LiBH_4$). The reducing agent is referred to as a promoter or activator.

Ziegler-Natta catalysts are a combination of a Group I-III organometallic compound and a Group IV-VIII transition metal compound. Some of the examples are $(C_2H_5)_3$ Al + $TiCl_4$; $(i\text{-}C_4H_9)_3$ Al + VCl_3, $(C_2H_5)_2$ Zn + Ti $(OH)_4$, etc.

A recently developed gas phase process is a dominant process for producing high-density polyethylene. The polymer separation from initiator and diluent as well as product drying steps are completely eliminated. The reactor is a fluid bed reactor (at about 20 atm. and 358-373K) in which ethene and initiator are fed in and polyethylene exists as a dense mixture polymer in the unreacted monomer. The initiator employed is a highly efficient chromium oxide supported initiator activated by aluminium alkyl.

Process Conditions

A large number of low pressure polyethylene processes have been commercialised. However, for purposes of illustration we will discuss the Phillips Particle Form process. This process produces polyethlene as a slurry in a hydrocarbon diluent. A simplified schematic of this process is shown in Fig 15.3.

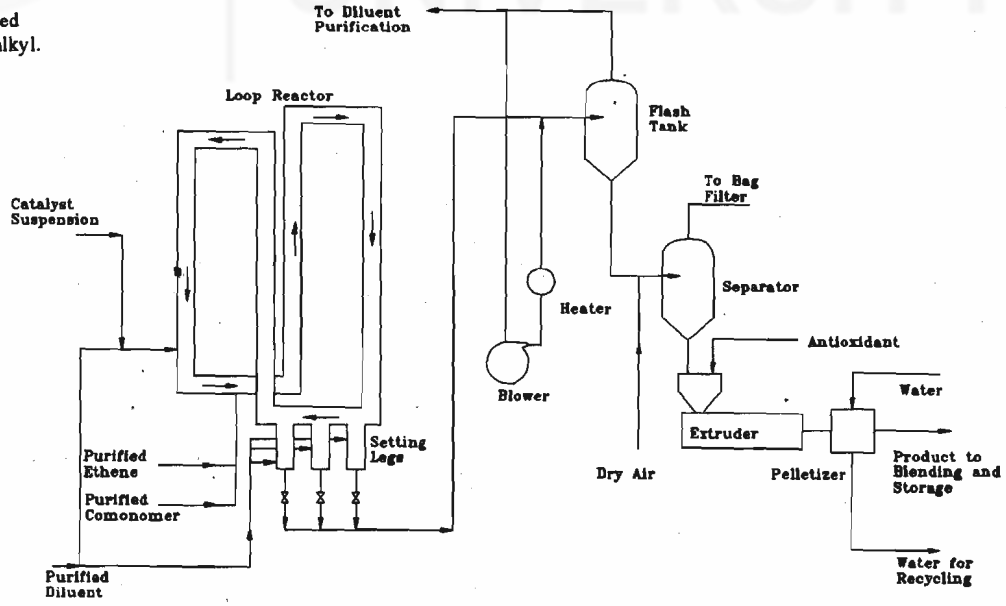


Fig. 15.3 : Phillips Partide Form Polyethylene Process.

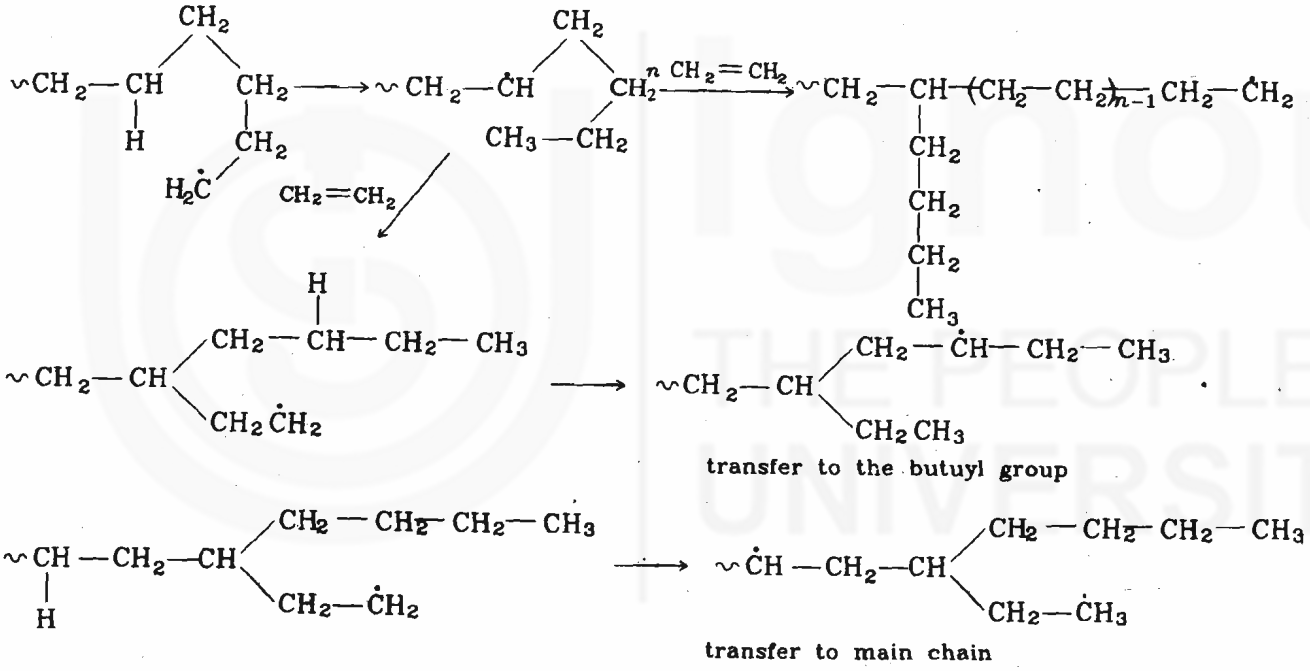
Slurry processes are more beneficial from the viewpoint of polymer separation and purification. Polymerisation is carried out in an inert atmosphere (usually nitrogen) in a hydrocarbon diluent (such as *n*-hexane or cyclohexane) at moderate temperatures (323 - 390 K) and pressures (0.5 - 2 MPa) in stirred batch reactors. The Ziegler-Natta initiator is prepared separately with the diluent and added to the reaction mixture. Polymer precipitates as it forms and the viscosity increases with conversion. The initiator is deactivated by adding water or alcohol. Thus polymer-metal bond is destroyed and initiator becomes soluble. The polymer product is filtered, residual diluent removed by treatment with steam, and final drying is achieved by blowing hot air over the powdered product. The product is mixed with appropriate additives, as desired, and packed.

The sharp termodynamic melting point of a organic compound is denoted by T_m.

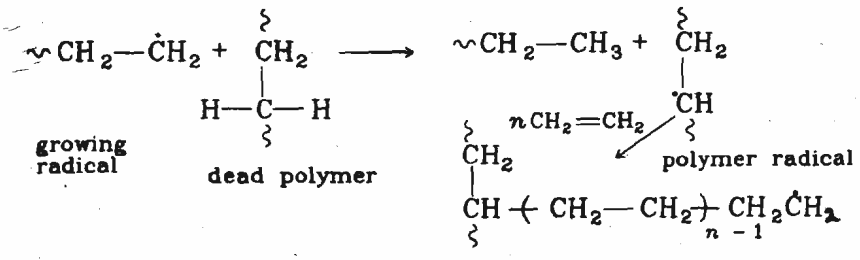
Structure and Properties of Polyethylene

Polyethylene is essentially a long chain aliphatic hydrocarbon having a C—C flexible backbone with no strong intermolecular attraction. It has a low glass transition temperature and a crystalline melting point (T_m) in the range of 381-405K. The exact value of T_m depends on the molecular structure. The strength of the polymer is due to the fact that crystallisation allows close molecular packing. The high crystallisation leads to opaque structures. If development of large crystalline structure is prevented, as in rapidly chilled films, then transparent films can be obtained.

Polyethylene prepared by high pressure technique (LDPE) has butyl or ethyl branches which arise as a result of back biting reaction.



In addition to short chain branches, long branches, which probably arise by transfer mechanism during polymerisation, are also present.



Mechanism for formation of long branch in LDPE

SAQ 2

How would you differentiate LDPE from HDPE ?

15.5 CASE STUDY OF THE PRODUCTION OF FIBRE FORMING POLYMERS

Semicrystalline polymers having high melting points, high tensile strength and capability of being spun into filaments, belong to the class of fibres. The filaments are drawn to align both polymer chains and crystalline regions, and in some cases to induce crystallinity or increase crystallinity thereby increasing the tensile strength. The chemical structure of plastic and fibres in several cases, is the same and many of the polymers can be used in crystalline form as fibres and in bulk form as plastics. Thus PE and nylon-6, 6 have been used both as plastic and fibres. In the following text preparation of an important fibre forming polymer, poly (ethylene terephthalate) (PET) is described.

Poly (ethylene terephthalate)

J.R. Whinfield and J.T. Dickson investigated synthesis and properties of aromatic polyesters and were successful in developing the well known PET fibre (Terylene, Dacron). This polymer can also be used in film form (Mylar) and as a moulding powder.

There are several routes for the synthesis of PET, here we have taken up two : transesterification process and direct esterification process.

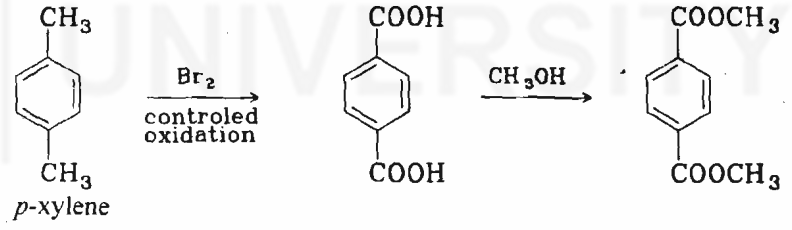
Raw Materials

Dimethyl terephthalate (DMT) and monoethylene glycol (MEG) are required for transesterification process whereas terephthalic acid (TPA) and monoethylene glycol for direct esterification process.

Preparation of raw material

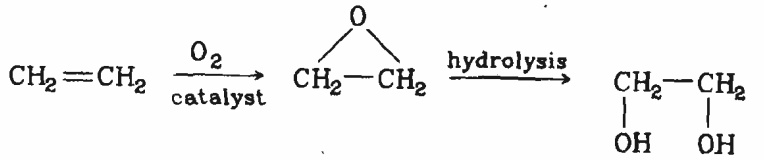
Terephthalic acid/ester

i)



p-xylene

ii)



ethylene glycol
(1,2-ethanediol)

Polymerisation Process

Polymerisation is carried out through intermediate diglycol terephthalate (DGT). This has an advantage over direct mixture of monomers subject to polycondensation, in the following way:

i) Condensation polymerisation is generally applied to a structurally uniform, chemically pure monomeric starting material.

ii) Side reaction is minimised.

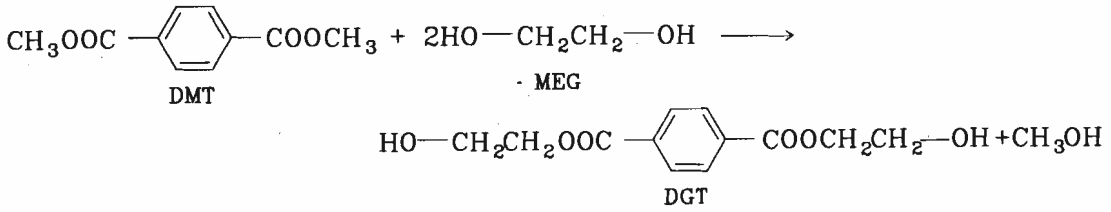
iii) Rate of reaction is fast.

iv) Good quality of polymer is obtained.

Diglycol terephthalate (DGT) can be prepared by following two methods :

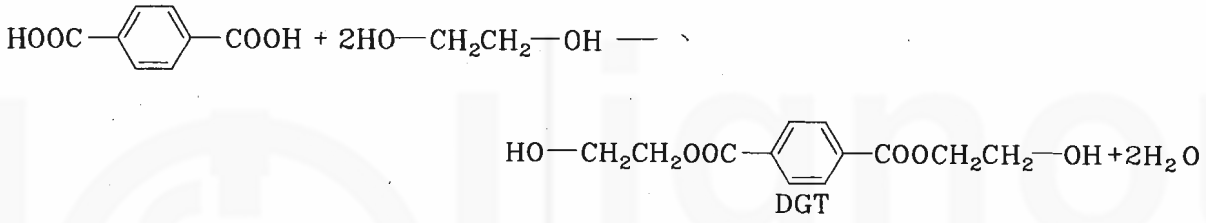
a) Transesterification

In this method DMT and MEG are taken.

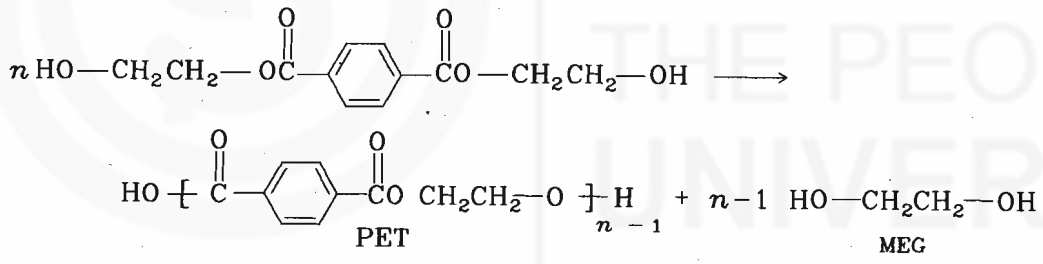


b) Direct esterification

TPA and MEG are taken for this process.



After DGT is formed, the polycondensation step is similar in both the methods. The reaction occurring in polycondensation stage is as follows :



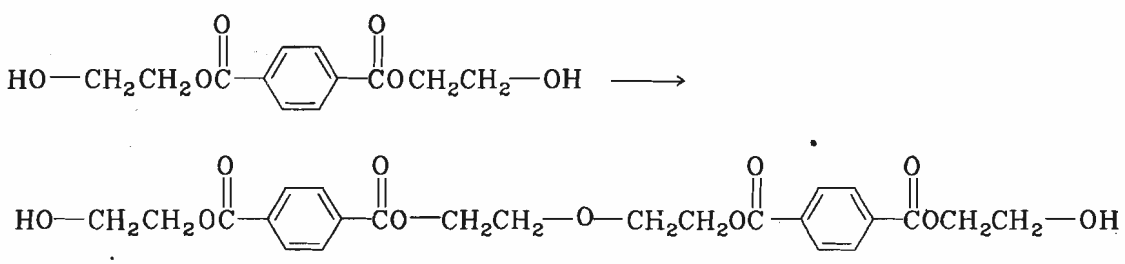
The details of preparation of DGT by transesterification and direct esterification process are given below.

Preparation of DGT by Transesterification

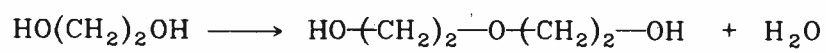
Transesterification involves DMT and MEG and is a slow process. It requires a catalyst to enhance the process. The catalyst can be a metal, a metal oxide or a metal salt. Usually metal oxide or a metal salt of a weak or volatile acid is used. Catalysts used are in the range of 0.02-2%.

Some of the side reactions occurring during this step are as follows.

a) Formation of ether linkage

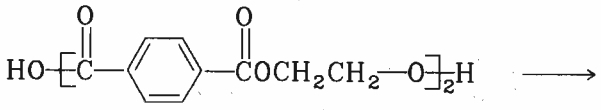


b) Formation of diethylene glycol

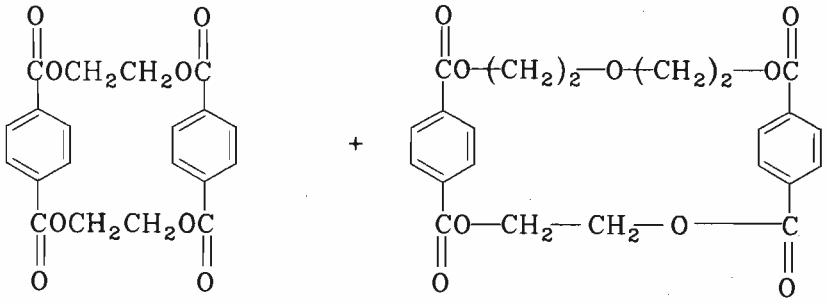


Each mole % of DEG depresses PET m.p. by 2.5K.

c) Other side products are



In industrial process reaction vessel is known as Kettle.



Process

Dissolution of DMT in MEG is an important part of the process. In one method MEG is heated at 423K and DMT is added to it. Both are mixed. An other way of doing this is that DMT is melted at 423K and MEG heated to the same temperature i.e. 423K, separately. Both are mixed together.

The melting and subsequent mixing process has got several advantages over the dissolution process. These are : i) the solution is produced more rapidly, ii) the premelting of DMT provides better stability to the melt, iii) side reactions are less and iv) residence time in Kettle is less.

Catalyst added to the dissolving Kettle is in the form of suspension (30%). Titanium dioxide is added in the proportion of 0.3 - 0.6% of DMT. A small current of nitrogen gas is passed through the Kettle to provide an inert atmosphere. Stirring is done during the process of mixing.

Transesterification is done in a separate vessel. With smaller batches, the reaction is carried out below the boiling point of MEG (470K) and without a reflux column. In this case, DMT sometimes sublimes and clogs the condensers and outlet pipes. The reaction time is longer. In the method, the reaction is done at boiling point of MEG. The reflux column returns the MEG to the reaction mixture. This method is suitable for large scale production. The sublimed DMT is continuously rinsed back by the condensing MEG to the reaction mixture. As the reaction temperature is high, shorter reaction time is necessary. Completion of the reaction is indicated by steady reducing flow of methanol.

Preparation of DGT by Direct Esterification

This method has certain advantages over the transesterification process. For example,

i) Cost of TPA is usually less than DMT.

ii) During DGT formation, by product methanol is not formed.

iii) It is a salt catalysed process.

iv) Product quality is superior to the other method.

v) Product has higher molecular weight in direct esterification process.

TPA itself accelerates the esterification. However, if necessary, stronger acids or esters of titanic acid can be used as additional catalysts.

The side reactions occurring in this case are similar to those happening in transestrification

step. However, ether formation is more in this case. The higher ether formation tendency can be suppressed by the addition of a small amount of NaOH or an organic quaternary hydroxide.

Process

Esterification can be carried out in the vessel as used in the case of transesterification step. Solubility of TPA is low in MEG. It requires a temperature of 513-533K at a pressure of 40 Pa to prepare the mixture in the proportion of TPA = MEG = 1 : 1 to 1 : 1.3.

The process proceeds smoothly and the byproduct water is allowed to distil off from the system. Hence, no reflux system attachment is necessary as required for methanol reflux in transesterification process.

Polycondensation

This stage is common to both the transesterification and direct esterification processes. If necessary, a second dose of catalyst is added here. The attainment of final molecular weight of polymer is not chemically controlled but diffusion controlled. Hence gradual reduction of pressure upto 25 Pa is made to obtain a high molecular weight polymer.

During polycondensation stage a number of degradation reactions occur, this affects the product. Thus molecular weight is lowered, yellow colour developed and carboxylic end-groups increase. Side reaction can be minimised by using thermal stabilisers such as phosphorous or phosphoric acid salts, using low pressure and short diffusion path in polycondensation stage, by addition of 0.5-2% of a diphenyl ester at an intermediate stage of polycondensation. Polymerisation time is greatly reduced by rate acceleration and hence carboxylic end groups decrease.

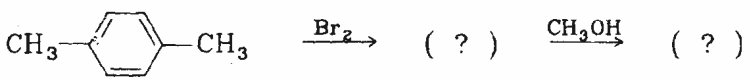
Process

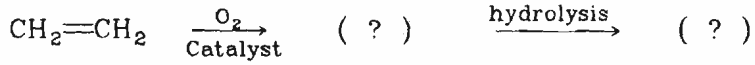
Several factors determine the polymer grade produced during polycondensation. Most important of them are the reaction temperature, vacuum, agitation, the type of vessel and the type and concentration of the catalyst used.

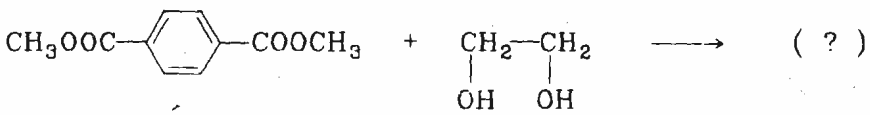
The polycondensation vessel is similar to the transestrification vessel. The melt from the esterification/transesterification process is filtered through a cylindrical mild steel gauge or ceramic material by a nitrogen pressure of 0.1-0.2 MPa to polycondensation vessel. The charging melt consists of DGT, its oligomers and glycol. The agitator is started at a speed of 40-60 rpm and vacuum (upto 0.1 MPa) applied while raising the temperature to 543K. When the required viscosity is reached the melt is forced out by means of a booster pump. The extruded filaments are cooled by passing through cold water bath. This is followed by cutting and drying.

SAQ 3

Complete following chemical equations.

a) 

b) 

c) 

15.6 SOAPS AND SYNTHETIC DETERGENTS

In this section, we shall take up the manufacture of soaps and detergents. We use these materials in our daily life as laundry products, toilet soaps, shampoos, dishwashing products and cleaning products. Soaps and detergents are also used for industrial purposes, these include cleaning compounds, hospital germicides, fabric conditioners, emulsifiers for

cosmetics, flowing and wetting agents for agricultural chemicals and rubber processing. Their recent potential use is to enhance oil recovery from oil wells. Before we go into a detailed account of the manufacture of soaps and detergents, let us consider their chemistry Soaps are the sodium or potassium salts of higher fatty acids. They are generally made by the action of a hot caustic soda (NaOH) or caustic potash (KOH) solution on tallow and fatty oils. This reaction is known as saponification and it also gives glycerine as valuable byproduct.

The word saponification means the making of soaps.

Sodium carbonate and potassium carbonate are not suitable for saponifying glycerides but they can saponify fatty acids effectively. Potassium soaps are soft and more soluble in water than sodium soaps.

If a fatty acid is available as starting material, soap can be made simply by neutralising with alkali

$C_{17}H_{35}COOH + NaOH \rightarrow C_{17}H_{35}COONa + H_2O$

$$\begin{array}{l} CH_2—OCO(CH_2)_nCH_3 \\ | \\ CH—OCO(CH_2)_nCH_3 \\ | \\ CH_2—OCO(CH_2)_nCH_3 \end{array} + 3\ NaOH \longrightarrow \begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + 3CH_3(CH_2)_nCOO^-Na$$

glyeride (oils and fats)

where n = 11 to 17

Once the saponification is complete, salt is added to help precipitate the soap, the water layer containing glycerine drawn off, and the glycerine is recovered by distillation. The soap is purified by boiling the fresh water to leach out excess caustic and glycerine. Additives such as builders, dyes, and perfumes are added. The solid soap is then melted and poured into a mold.

Let us now discuss the cleaning action of soaps. The dirt particles that cling to the textile fibres are generally covered by a layer of oil molecules, called grease. These oil molecules are nonpolar and hence repel water. Hence water cannot wash such dirt particles out of cloth by itself.

On the addition of soap, (i) grease molecules get attached to the nonpolar hydrocarbon tail of the alkyl carboxylate ion (due to London forces) and ii) its polar end is directed towards water (due to ion-dipole interaction). This results in the lowering of interfacial tension between grease and water. Because of this emulsifying action of soap, grease and hence dirt is washed out of clothes (Fig. 15.4).

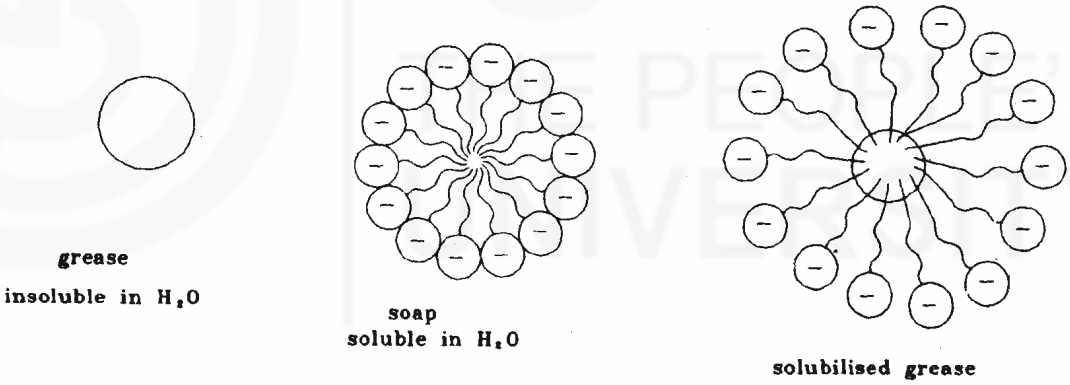


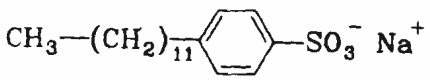
Fig. 15.4 : Soap micelles interacting with grease.

Soaps are not effective as cleansers when used in hard water. This is because the calcium and magnesium ions present in hard water form a precipitate of calcium and magnesium salts of alkyl carboxylates.

$$2RCO_2^- + Ca^{2+} \rightarrow \underset{\text{insoluble}}{(RCO_2)Ca}$$

- This results in the loss of cleansing action of soap due to decrease in fatty acids ion concentration in water,
- increase of binding of the grease to the cloth, giving it a dull colour.

To solve this problem of hard water, detergents are used in the place of soaps. Detergents are of two types — anionic and cationic. The anionic detergents are generally the sodium salts of linear alkylbenzene (LAB) sulphonic acids.



The cationic detergents are generally quaternary ammonium salts of the type,

$(CH_3)_3\ R\ N^+\ Cl^-$

where R is a long chain of alkyl groups containing between 12 and 18 carbon atoms.

As far as cleansing action is concerned, detergents like soaps act as emulsifiers between grease and water. Further in presence of hard water, detergents do not form precipitates. For example, calcium or magnesium salts of LAB sulphonates are soluble in water. Hence detergents can be used even in hard water.

Now we will see how soap is manufactured. But before that try following SAQ.

SAQ 4

Explain why soaps are not effective as cleansers when used in hard water?

.....

.....

.....

Like fats and lipids, proteins are also responsible for some of the 'dirt'. This dirt can't be removed by soaps and detergents. This problem has led to the development of detergents that also contain enzymes that catalyse the "digestion" of the proteins. Such enzyme-containing detergents are quite popular nowadays. Example is 'Arial'.

15.7 CASE STUDY OF THE PRODUCTION OF SOAPS

Raw Materials

Naturally occurring fats and oils are the principal raw materials for soap making. Properties of the resulting soap are the main criteria for selecting the starting materials. Nature of the soap is determined by the amount and composition of the component fatty acid in the starting fat or oil. In general, fatty acids with chain length less than 12 carbons are not preferred since their soaps have poor surface activity and skin irritation tendencies. The upper limit of chain length is 18, beyond which the resulting soaps are too insoluble, and again poor surface activity is observed. Unsaturation in the fatty materials must also be carefully considered, a fatty acid mixture with a high degree of unsaturation yields soaps which tend to be soft, susceptible to oxidation and have poor surface activity. Average fatty acid composition of some fats and oils is given below. It helps us in deciding which fat or oil is suitable for soap manufacture.

Table 15.5 : Average fatty acid composition of some important fats and oils

Chemical Formula		Tallow	Lard	Coconut	Palm	Castor
Saturated Acids						
Caproic	$C_6H_{12}O_2$			0.2		
Caprylic	$C_8H_{16}O_2$			8.0		
Capric	$C_{10}H_{20}O_2$			7.0		
Lauric	$C_{12}H_{24}O_2$			48.0		
Myristic	$C_{14}H_{28}O_2$	2.0	1.0	17.5	1.0	
Palmitic	$C_{16}H_{32}O_2$	30.0	26.0	8.8	42.5	
Stearic	$C_{18}H_{36}O_2$	21.0	11.0	2.0	4.0	2.0
Arachidic	$C_{20}H_{40}O_2$					
Behenic	$C_{22}H_{44}O_2$					
Lignoceric	$C_{24}H_{48}O_2$				Trace	
Unsaturated Acids						
Myristoleic	$C_{14}H_{26}O_2$					
Palmitoleic	$C_{16}H_{30}O_2$					
Oleic	$C_{18}H_{34}O_2$	45.0	58.0	6.0	43.0	8.6
Linoleic	$C_{18}H_{32}O_2$	2.0	3.5	2.5	9.5	3.5
Linolenic	$C_{18}H_{30}O_2$					
Elaedostearic	$C_{18}H_{30}O_2$					
Ricinoleic	$C_{18}H_{34}O_2$					85.9
C_{20} Unsaturated						
C_{22} Unsaturated						

Inorganic Raw Materials

Caustic soda (sodium hydroxide) and sodium chloride (salt) are the commonly used inorganic raw materials. Potassium hydroxide (caustic potash) is employed almost exclusively in making soft soaps (liquids or pastes). Potassium soaps are more water soluble than the sodium soaps. Sometimes, we use sodium silicate, sodium carbonate, and trisodium phosphate as builders to achieve special properties in the final soap.

Manufacture

Soap can be manufactured by batch manufacturing method or by continuous process. Batch process is suitable only for small factories or for special and limited production. Let us first discuss batch process.

Batch process is also known as Kettle process. In this process, soap is made in a steel Kettle, with a slightly conical bottom (see Fig. 15.5). The size of the kettle depends on the batch size. A solution of calculated amount of caustic soda, enough to combine with all the fatty acids liberated, is run into the kettle, and the melted fats or oils are then pumped in.

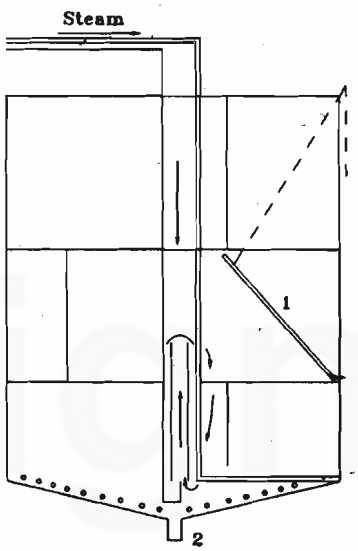


Fig. 15.5 : Kettle for soap manufacture by batch process

(1) the soap is pumped out through swing pipe

(2) run-off for lye liquors and glycerine liquors

The mixture is heated by steam which enters through a perforated coil laid on the bottom of the kettle. The kettle is kept boiling until saponification is essentially completed. This generally requires 4 hours. Salt is then added and allowed to dissolve. Boiling is continued until the soap has separated, forming the upper layer. The lower layer contains glycerine (usually about 4 per cent) and salt, and is drawn off at the bottom of the kettle. The whole of this saponification process generally takes 8 hours. Next day, this soap is again treated with some caustic soda and water and is boiled so that glycerine which is left with this soap is dissolved. The solution forming the lower layer again is run off at the bottom and combined with the first lot of glycerine in water.

On the third day, NaOH solution is again run into the kettle and boiled with the soap. Any unreacted fat or oil left untreated is saponified. Further, fatty acid which may form during reaction is also neutralised. After setting, the NaOH solution is run off and is used in new batch.

On the fourth day, the soap is boiled with water. Now, the melted soap acquires a smooth, glossy appearance. On setting, three layers are formed. The upper layer is the melted soap. The middle layer or nigre is dark in colour. It is a mixture of the soap solution and impurities. The very small lowest layer contains some alkali. The melted soap is pumped away. Nigre may remain in the tank to be worked into the next batch. The lower layer is wasted.

Sponification by kettle process can also be carried out in cold and semiboiled conditions. But this process does not permit recovery of glycerine byproduct and product is generally inferior to soap made by full boiled method.

The melted 'neat' soap produced by this method contains 30-35 per cent water. The 'neat' soap can also be manufactured by continuous process.

Continuous Soap-making

The continuous saponification technique can produce in two hours the same amount of

soap made in several days by traditional batch method. Fig. 15.6 shows a plant set-up of continuous method to produce neat soap. Many types of continuous process are available; here we discuss the **continuous fat splitting and neutralisation method.**

In this process, before saponification, fats and oils are split and distilled to yield the light-coloured fatty acid. This process is operated by mixing a zinc oxide catalyst into the blended fat feedstock which reacts counter currently with water in 20 m tall stainless-steel hydrolysing tower at a high temperature, 523K, and pressure 4 MPa. A continuous stream of crude fatty acids is withdrawn from the top and crude glycerin is taken out from the bottom.

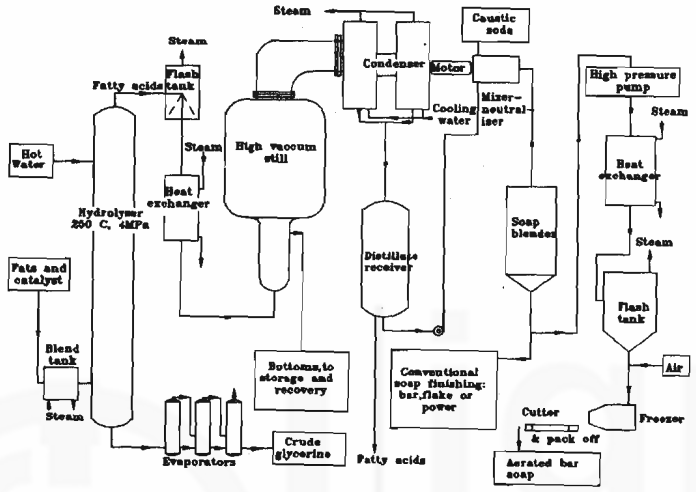


Fig. 15.6 : Continuous process for the production of fatty acids and soaps.

The fatty acids are purified by distillation under vacuum, which takes the place of washing and the separation of neat soap and nigre for the removal of bodies and other colour impurities. Although the fatty acids resulting from the above method may be used as such for saponification, usually a separation into more useful components is made. To separate fatty acids of different chain length, distillation is employed, vacuum fractionation distillation being the most widely used.

Neutralisation of fatty acids is accomplished by continuous high-speed mixing with caustic soda solution and salt to produce neat soap. Now let us specify the main advantages of soap manufactured by this process as compared with kettle process :

Fats, grease and oils are difficult or impossible to bleach satisfactorily

i) improved soap colour from a crude fat without extensive pretreatment,

ii) improved glycerine recovery,

iii) flexibility in the control, and

iv) less space, time and labour is required.

Neat soap produced by either the kettle or continuous saponification procedures contains 30-35% water, 0.002 to 0.10% NaOH, 0.3 to 0.6% NaCl. This neat soap still requires a number of steps to obtain useful end products. The simplest method of converting neat soap to a solid form suitable for forming into bars is known as framing. This consists of running the neat soap into portable frames and allowing it to solidify in the form of large cakes. Upto 7 days are required for the soap to solidify in this fashion. More rapid processing is accomplished by drying the neat soap to 10-15% water for bar soap production or 5-10% for flake production in various types of drying equipment.

Soap flakes or bars obtained from the drying step are used as feedstock for various end products, including toilet bars, laundry soaps, and spray dried laundry products. High quality toilet soap is obtained from the milled soap. The word milled refers to the fact that, during processing, the soap goes through several sets of heavy rolls, or mills, which mix

and cleaned it. Because of the milling operation the finished soap lathers better and has a generally improved performance, especially in cold water. The milling operation is also the way in which fragrant perfumes are incorporated into cold soap. After milling operation, the soap is pressed into a smooth cylinder and is extruded continuously. It is then cut into bars, stamped and wrapped. Fig. 15.7 depicts the over all steps employed to obtain the final soap products.

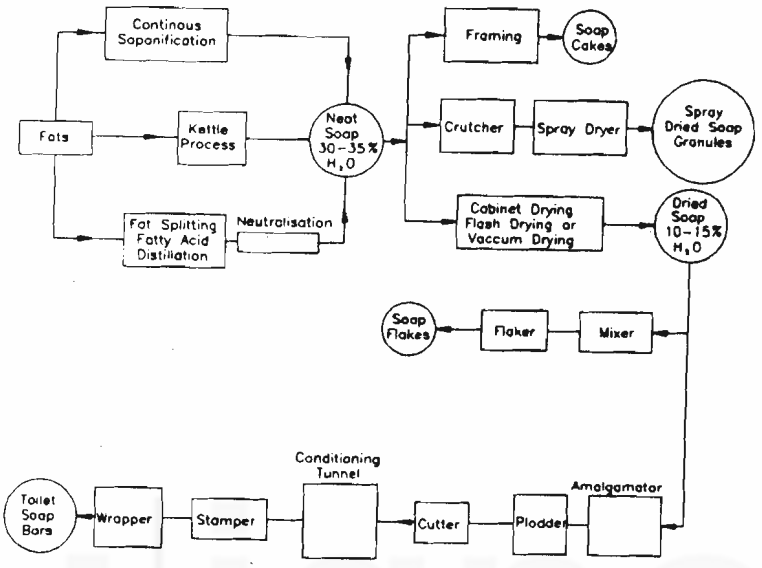


Fig. 15.7 : Soap product flowchart

15.7 CASE STUDY OF THE PRODUCTION OF SYNTHETIC DETERGENTS

Sodium alkyl sulphates and sodium salts of linear alkylbenzene (LAB) sulphonic acids are the most widely used synthetic detergents. To prepare these detergents, fatty alcohol like lauryl alcohol must be sulphated to lauryl sulphuric acid and a linear alkylbenzene sulphonated to an acid form. Then these acid forms are neutralised with a base such as sodium hydroxide. We commonly use oleum for sulphation and sulphonation. The chemical reactions involved in oleum sulphation and sulphonation are as follows :

Sulphation of fatty alcohol

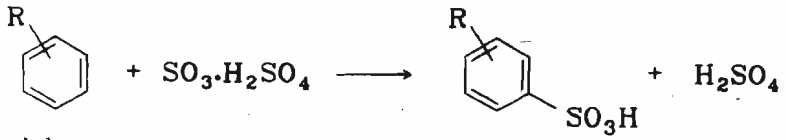
$$CH_3(CH_2)_nOH + \underset{\text{oleum}}{SO_3{\cdot}H_2SO_4} \longrightarrow CH_3(CH_2)_nOSO_3H$$

$$(n = C_{11}—C_{13})$$

Neutralisation

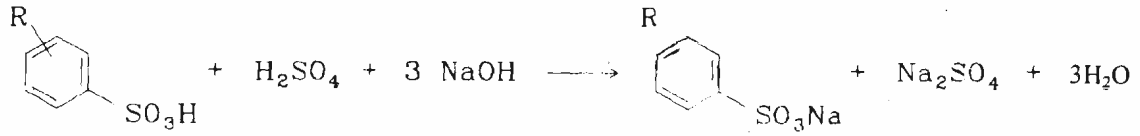
$$CH_3(CH_2)_nOSO_3H + NaOH \longrightarrow CH_3(CH_2)_nOSO_3Na + H_2O$$

Sulphonation of linear alkylbenzene



alkyl benzene — oleum — alkyl benzene sulphonic acid

Neutralisation



Manufacture

Raw Materials

Following raw materials are required in kgs for the production of granules of 1t heavy duty detergents.

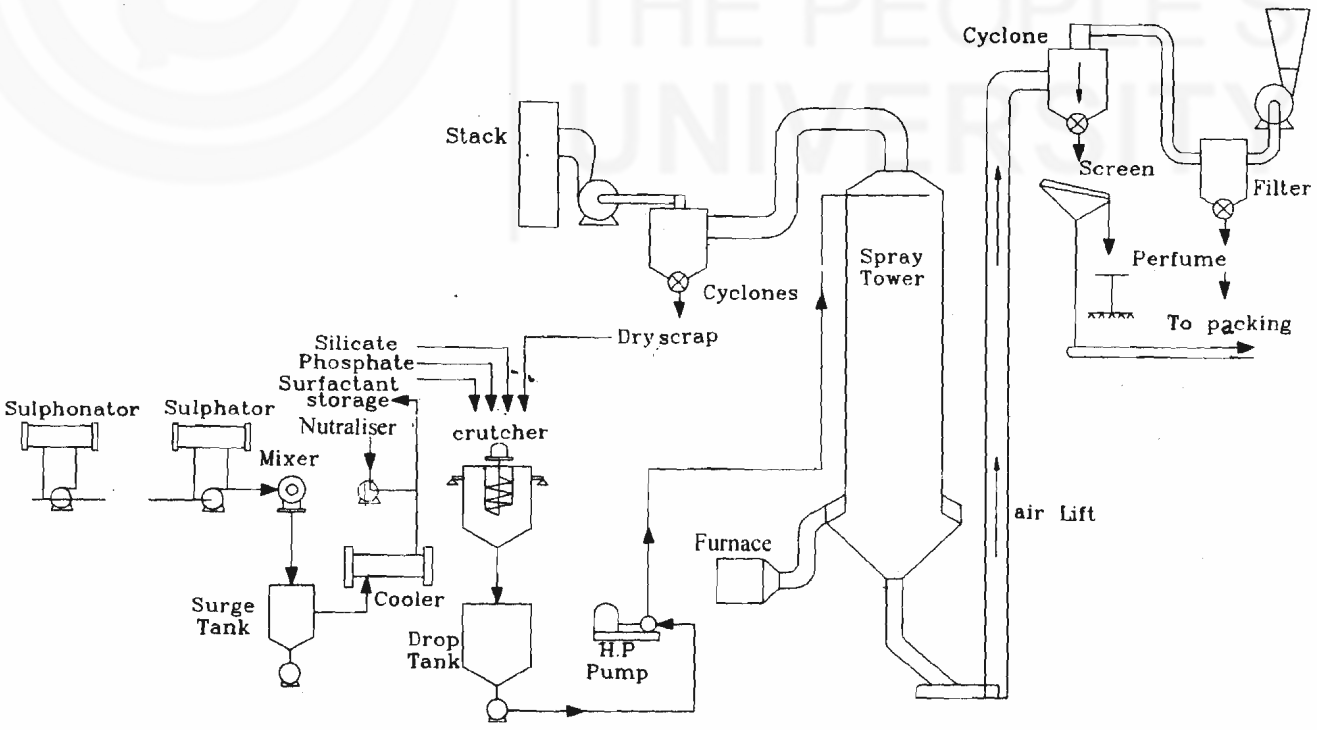
Surfactant Materials

Alkylbenzene (petrochemical)	75
Fatty alcohol (from tallow)	175
Oleum	150
NaOH solution	200
Builder Sodium tripolyphosphate	500
Sodium silicate	125
Miscellaneous additives	30

The detergents in pure forms are too concentrated for use in small amounts. For this reason they are diluted in such a way that they can be easily measured for use. To solve these problems detergents are generally mixed with materials called builders and filling agents. They make the end product easily measurable and convert the detergent into a form which can be handled easily. The builders also improve soil suspending and detergent action in the product. Examples are sodium tripoly phosphate, sodium silicate, soda ash, sodium bicarbonate etc.

Process

The manufacture of the detergent is shown in Fig 15.8. Alkyl benzene is introduced continuously into the sulphonator with the requisite amount of oleum, using the dominant bath principle shown in Fig. 15.9 to control the heat of sulphonation conversion to maintain the temperature at about 328K. Into the sulphonated mixture is fed the fatty tallow alcohol and more of oleum. All are pumped through the sulphater, also operating on the dominant bath principle, to maintain the temperature at 323K to 328K, thus manufacturing a mixture of surfactants.



The sulphonated-sulphated product is neutralised with NaOH solution under controlled

temperature to maintain fluidity of the surfactant slurry. The surfactant slurry is conducted to storage.

The surfactant slurry, sodium tripolyphosphate and most of the miscellaneous additives are introduced into the crutcher. A considerable amount of the water is removed, and the paste is thickened by the tripolyphosphate hydration reaction

$$Na_5P_3O_{11} + 6H_2O \longrightarrow Na_5P_3O_{11}\,6H_2O$$

Sodium tripolyphosphate — sodium tripolyphosphate hexahydrate

This mixture is pumped to an upper storey, where it is sprayed under high pressure into the 24 m high spray tower, counter to hot air from the furnace. Dried granules of acceptable shape and size and suitable density are formed. The dried granules are transferred to an upper storey again by an air lift which cools them from 388K and stabilises the granules. The granules are separated in a cyclone, screened, perfumed and packed.

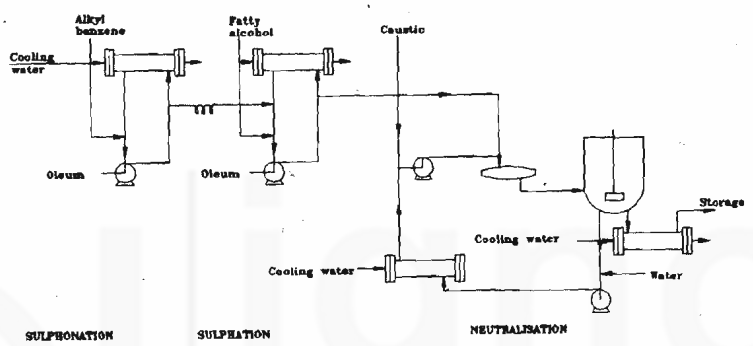
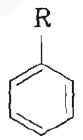


Fig. 15.9 : Continuous series sulphonation-sulphation, ending with neutralization, in the circulating heat-exchanging bath to control heat.

SAQ 5

Complete following chemical equations :

a)  + $SO_3.H_2SO_4 \longrightarrow ? \xrightarrow{NaOH} ?$

b) $CH_3(CH_2)_{11}OH + SO_3.H_2SO_4 \longrightarrow ? \xrightarrow{NaOH} ?$

c) $\begin{matrix} CH_2OCOR \\ | \\ CHOCOR \\ | \\ CH_2OCOR \end{matrix} + NaOH \longrightarrow ?$

15.9 SUMMARY

In this unit we have discussed case study of some chemicals of daily use. We are summarising what we have studied so far :

- Criteria like choice of the process, availability of raw materials, engineering problems associated with carrying out reactions on large scale and separation of the products, disposal of byproducts and supply have to be considered in the location of a chemical industry and the design of the plant.

- Polymer is simply a large molecule built up by repetitive bonding together of many smaller units (monomers). We use polymers as plastics, fibres, surface coatings (paints) and rubber.
- Polymers can be classified on the basis of structure and physical properties : themosetting resins, thermoplastics, fibers and elastomer; method of synthesis : addition and condensation polymers; and growth mechanism : step growth and chaingrowth polymers.
- Two types of polyethylene have been available — High density polyethylene (HDPE), produced by low-pressure method, is used mainly for blow-moulded containers and injection moulded articles and pipe. Low-densing polyethylene (LDPE), produced by high-pressure method, is used mainly for plastic film.
- Poly (ethylene terephthalate) (PET) can be prepared by transesterification process or direct esterification process.
- Soaps and detergents belong to general class of compounds called surfactants (from surface-active agents), which are compounds that can lower the surface tension of water and are used for cleaning purpose. One major disadvantage of soap is that they are not effective as cleansers when used in hard water. To solve this problem, synthetic detergents are used in place of soaps.
- To prepare synthetic detergents, fatty alcohol like lauryl alcohol must be sulphated to lauryl sulphuric acid and a linear alkylbenzene sulphonated to acid form. Then these acid forms are neutralised with a base such as sodium hydroxide.

15.10 TERMINAL QUESTIONS

1) Discuss the industrial process of LDPE.
2) Describe the cleaning action of soaps.
3) How would you prepare diglycol terphthalate (DGT)? Give details of the preparation of DGT by transesterification method.
4) Discuss the manufacture of soaps by batch process.

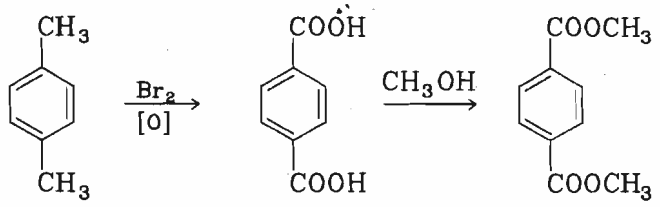
15.11 ANSWERS

Self Assessment Questions

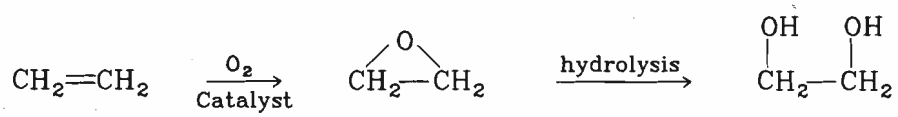
1) a) Teflon - chain growth polymer
   b) Poly (vinyl acetate) - chain growth polymer
   c) Dacron - Step growth polymer
   d) Butyl rubber - copolymer

2) Low density polyethylene has sp gr which vary from 0.915 to 0.940 and it contains many short chain and long chain branches. On the other hand high density polyethylene has sp gr which vary from 0.95 to 0.97 and has only few short chain branches.

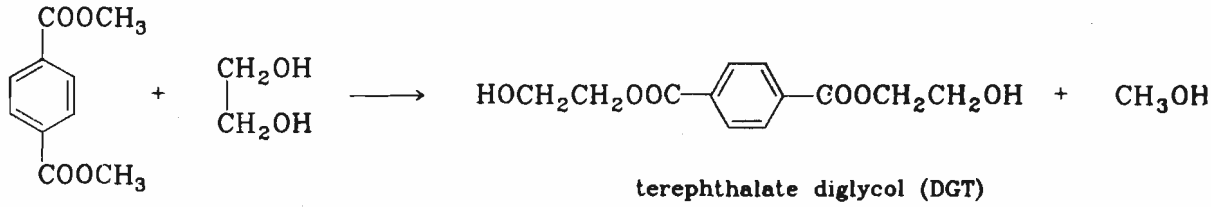
3) a)



b)



c)



terephthalate diglycol (DGT)

4) **Soaps are not effective as cleansers when used in hard water. This is because the calcium and magnesium ions present in hard water form a precipitate of calcium and magnesium salts of alkyl carboxylates.**

$$2RCO_2^- + Ca^{2+} \rightarrow (RCO_2)Ca \downarrow$$

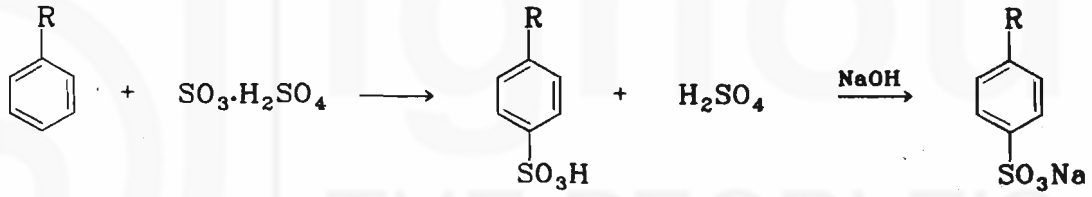
soap

This results in

- **the loss of cleansing action of soap due to decrease in fatty acids ion concentration in water,**
- **increase in binding of the grease to the cloth giving it a dull colour.**

5)

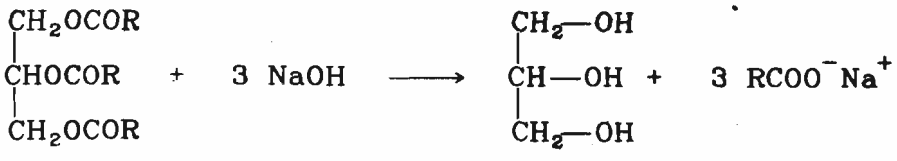
a)



b) $CH_3(CH_2)_{11}OH + SO_3.H_2SO_4 \longrightarrow CH_3(CH_2)_{11}OSO_3H$

$$\xrightarrow{NaOH} CH_3(CH_2)_{11}OSO_3^-Na^+ + H_2O$$

c)



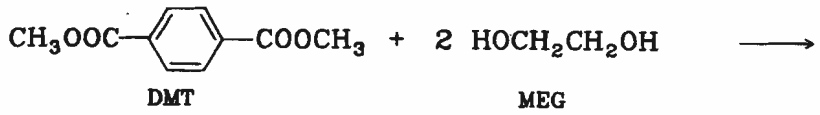
Terminal Questions

1) **See section 15.4**

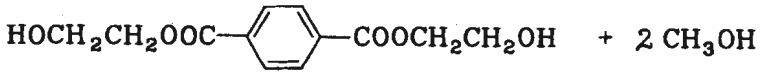
2) **On the addition of soap, (i) grease** molecules get attached tot he nonpolar **hydrocarbon tail of the soap (due to London forces) and (ii) its polar end is directed towards water (due to ion dipole interaction). This results in the lowering of the interfacial tension between grease and water. Because of this emulsifying action of soap, grease and hence dirt is washed out of clothes. To further explain it, give Fig. 15.3.**

3) **Diglycol terephthalate (DGT) can be prepared by following two methods :**

a) **Transesterification : In this method dimethyl terephthalate** (DMT) and **monoethylene glycol (MEG) are taken.**

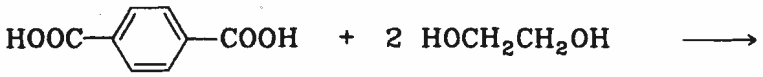


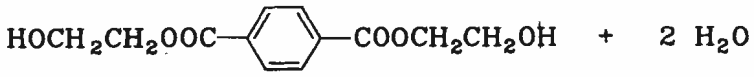
DMT MEG



DGT

b) **Direct esterification : Terephthatic acid (TPA) and monoethylene glycol are taken for this process.**





For the detail of transesterification please see section 15.5.

4) **See section 5.7.**

UNIT 16 CASE STUDY OF SOME CHEMICALS OF DAILY USE - II

Structure

16.1 INTRODUCTION

In Unit 15, we have discussed the chemistry and the manufacture of plastics, fibres, soaps and detergents. In this unit we shall deal with the chemistry and production of dyes and synthetic drugs.

First we will illustrate how the knowledge of organic chemistry, specially, photochemistry is essential for understanding the chemistry of dyes. Then we shall classify the dyes and thereafter consider the case study of the production of azo dyes. Finally, we shall take up the classification of drugs and the case study of the production of aspirin and pencillin

Objectives

After studying this unit, you should be able to :

- explain the relationship between chemical structure and colour,
- classify organic dyes according to their mode of application and chemical composition,
- discuss the manufacture of a mono azo dye,
- explain how new drugs are developed,
- classify drugs according to their action, and
- discuss the production of aspirin and pencillin

16.2 DYES

In Unit 13, we discussed how compounds can be excited electronically by electromagnetic radiation. In this section we shall use this knowledge to explain why certain substances like dyes are coloured. We shall also establish the relationship between chemical structure

and colour. But before this, let us define dyes.

Dyes are intensely coloured substances that can be used to produce a significant degree of colouration when dispersed in or reacted with, other materials. The colouration by a dye takes place through a process which at least temporarily, destroys the crystal structure of the substance. This latter point distinguishes dyes from pigments which are almost always applied in an aggregated or crystalline-insoluble form. The primary use of dyes is in textile colouration, although substantial quantities are consumed for colouring such diverse materials as leather, paper, plastics, petroleum products and food.

Previously, dyes were obtained from vegetable or animal sources. You may be well familiar with indigo dye which is also used as a brightener for washed white clothes. Indigo occurs as a glycoside in the leaf of the indigo plant. It is much used in the textile industries.

In modern times indigo dye is used to produce large quantities of blue denim.

Modern dyes are products of synthetic organic chemistry. To be of commercial interest, dyes must have high colour intensity. The colour produced by the dye must stay for a long time. Let us now see how the knowledge of photochemistry and organic chemistry help us in achieving these parameters.

16.3 COLOUR AND CONSTITUTION

As discussed in Unit 13 on photochemistry, all organic compounds can be excited electronically by ultraviolet and visible region of electromagnetic radiation. For most organic compounds these electronic transitions are in the ultraviolet region of the spectrum and these compounds are white and colourless. However, when a substance absorbs light in the visible range (about 400-780 nm), it appears to possess a particular colour. Each coloured material absorbs a particular portion of the visible light which is characteristic of the colour of the substance. The colour that a substance possesses, is due to, the light transmitted by it. For example, a compound X, undergoing an electronic transition by absorbing visible light in the region 435-480 nm absorbs blue light from the visible spectrum. The transmitted light is recognised by the eye as being yellow. It is customary to call the observed colour as the **complementary colour** or the substraction colour, in relation to the colour of the visible light absorbed. The complementary colours [column (iii)] for different portions of absorbed light in the visible region [column (ii)] are given in Table 16.1. The wavelength region corresponding to the absorbed light is given in column (i).

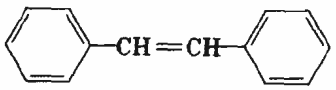
Table 16.1 : Colour and Wavelength

Wavelength of light (nm) absorbed (i)	Colour of the light absorbed (ii)	Complementry (or substration) colour seen (iii)
400-435	Violet	Green-yellow
435-480	Blue	Yellow
480-490	Green-blue	Orange
490-500	Blue-green	Red
500-560	Green	Purple (magenta)
560-580	Yellow-green	Violet
580-595	Yellow	Blue
595-605	Orange	Green-blue
605-750	Red	Blue-green

Intensely coloured materials like dyes have absorption in the visible region. For these dyes, such electronic absorptions generally give rise to $\pi \rightarrow \pi^*$ or $n \rightarrow \pi^*$ transitions. Further these compounds have an extended π–π conjugation. Thus colour in organic compound is generally a property of π-structure. If the absorption band is narrow or sharp, the colour will appear to us as bright or brilliant. A broad absorption band, or more than one band in the visible region, gives dull colours.

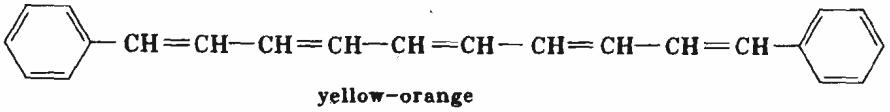
A change in absorption from the blue to the red end of the spectrum corresponds to a

decrease in the energy of the associated electronic transitions. This trend is due to increasing conjugation of multiple bonds. For instance, 1, 2-diphenylethene is colourless, whereas l, 10-diphenyl-1, 3, 5, 7, 9-decapentaene is yellow-orange.



colourless

λ_{max} 319 nm



yellow-orange

λ_{max} 424 nm

In other words, the more extended a planar system of conjugated bonds is, the smaller the energy difference between the ground and excited states. This effect is shown schematically in Fig.16.1, from which you can see that conjugation stabilises both the ground state and excited state. Thus, the gap between the states narrows with increasing conjugation, and absorption shifts to longer wavelengths.

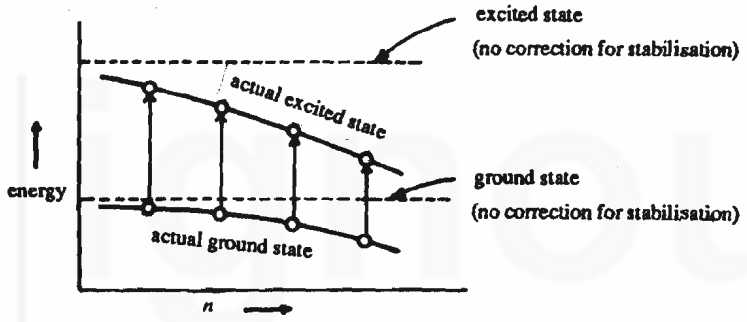
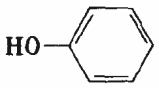


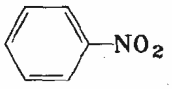
Fig. 16.1 : Schematic relationship between stabilisation ground and excited state of system with *n* conjugated double bonds.

The effect of substituents on colours associated with conjugated systems is of particular interest in the study of dyes, because most dyes have relatively short conjugated systems and would not be intensely coloured in the absence of substituent groups. To explain the effect of substituents we will discuss the spectrum of 4-nitrobenzenol (4-nitrophenol), even though the compound has no value as a dye. It is a pale yellow compound (λ_{max} 320 nm). Its close relatives are benzene, phenol and nitrobenzene.

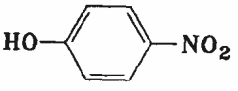
max 204 nm
ε 7,400



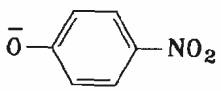
211 nm
6,200



270 nm
7,800



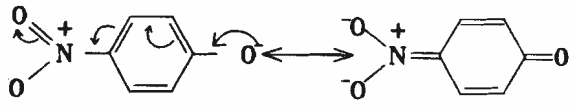
λ max 320 nm
ε 9,000



400 nm
15,000

The conjugated π system common to all four compounds is that of the benzenoid ring, which is called the absorbing **chromophore.** The hydroxyl and nitro substituents can be

seen indvidually to shift the λ_{max} of the chromophore to longer wavelengths. However, the combined effect of the two substituents is much more dramatic, especially if the OH group is converted to the corresponding anion, 4-nitrobenzenolate. Now λ_{max} is shifted into the visible region, giving a yellow colour, and because ε is large, the colour is intense. Thus, properly chosen substituents can shift the main benzenoid absorption band from the ultraviolet into the visible region of the spectrum. Such substituents are often called **auxochromes.** They act by extending the conjugation of the chromophore and are particularly effective in causing large shifts towards the visible region when one substituent is π-electron donor and the other a π-electron acceptor. Thus, with the 4-nitrobenzenolate ion, interaction between the strongly electron-donating $-O^-$ group and strongly electron-accepting $-NO_2$ group provides significant stabilisation.



Resonance stabilisation of this kind must be more important in the excited state than in the ground state if it is to narrow the energy gap between them (Fig.16.1). It is observed that substitution of an electron – attracting group (such as $-NO_2$) at one end of benzene ring and an electron–donating group (such as $-O^-$) at the other end particularly is favourable to the stabilisation of the excited state (relative to the ground state).

You can understand from the foregoing discussion that many intensely coloured organic compounds have conjugated structure and substituents. In some cases the substituents may be cationic or anionic. These substituents have electron donating or withdrawing effect with respect to the conjugated system. Such compounds provide us with many useful dyes, pigments, indicators, and food colouring. These substances are also responsible for the colouration in plants and animals.

The studies of the chemical structure of dyes helps us in understanding the methods of,

- developing new dyes,
- enhancing the intensity of colours,
- improving the colour quality (long standing)
- identifying proper substituents which could enable the fixing of the dye to the fabric.

The last aspect mentioned above relates to the role of a substituent group in enhancing the solubility, of a dye and increasing its affinity for the textile fibre.

SAQ 1

For the light absorption in the range given below, specify the colour observed :

a) 560-580 nm b) 580-595 nm

c) 480-490 nm d) 608-750 nm

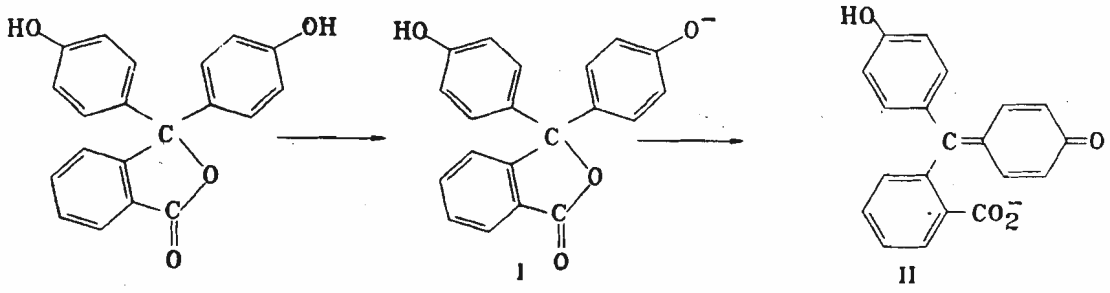
.....

.....

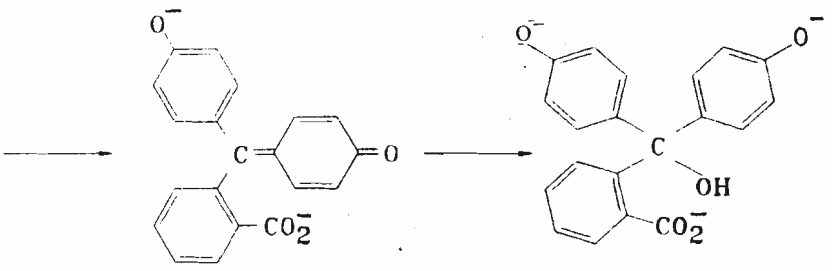
.....

SAQ 2

Phenolphthalein indicator undergoes the following changes as a neutral solution is made more and more basic



I II



III IV

Among these structures which would you expect to absorb at highest wavelength of visible light ? Explain.

.....

.....

.....

16.4 CLASSIFICATION OF DYES

Dyes may be classified in various ways, according to

- colour
- origin
- substrates to which they are applied (such as cotton, silk, wool, leather, paper, etc.)
- methods of application, and
- chemical structure.

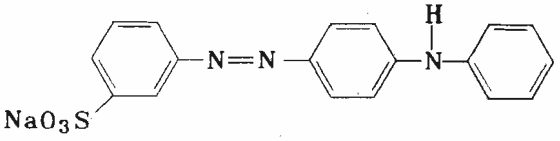
For our present purpose, the last two grouping will be quite useful.

Classification of Dyes Based on Method of Application

The dye names used in this unit are those given in the "Colour Index", publication sponsored by the Society of Dyers and Colourists (England) and American Association of Textile Chemists and Colourists.

For the convenience of the dyer, dyes are classified according to the method of application. The best classification method available is that used in the Colour Index, a publication sponsored by the Society of Dyers and Colourists (England) and the American Association of Textile Chemists and Colorists.

Acid Dyes : Acid dyes depend on the presence of one or more acidic groups for their attachment to textile fibers. These are usually sulphonic acid groups which serve to make the dye soluble in water. An example of this class is Acid yellow 36 (Metalin yellow).



Acid yellow 36 (Metalin yellow)

Acid dyes are used to dye fibers containing basic groups, such as wool, silk and polyamides. Application is usually made under acidic conditions which cause protonation of the basic group. The dyeing process may be described as follows :

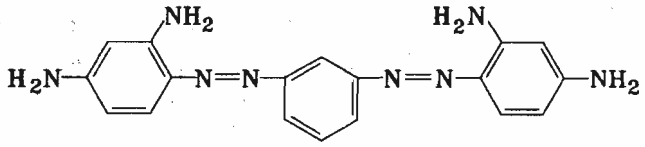
$Dye^- + H^+ + Fiber \qquad Dye^- H^+ - Fiber$

It should be noted that this process is reversible. Generally, acid dyes can be removed from fiber by washing.

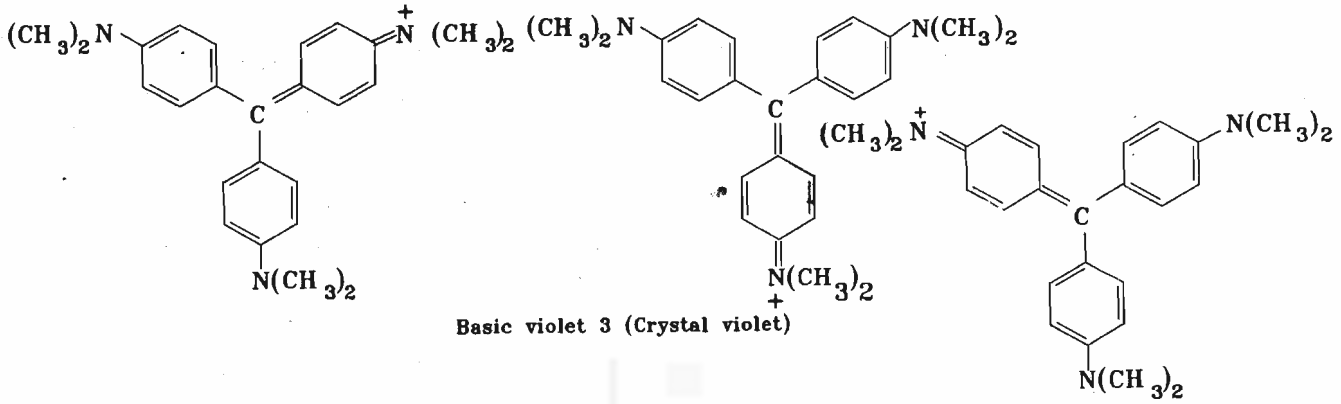
Basic or Cationic Dyes : Cationic dyes become attached to fibers by formation of salt linkage with anionic or acidic groups in the fibers. Basic dyes are those which have a basic amino group which is protonated under the acid conditions of the dye bath.

Anthraquinone Dyes : In anthraquinone dyes the chromophore is the carbonyl group,

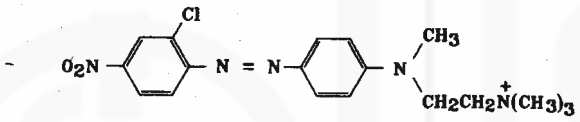
Three examples for cationic dyes are given below :



Basic Brown 1 (Bismark Brown)



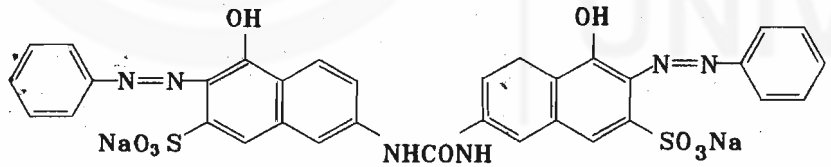
Basic violet 3 (Crystal violet)



Basic red 18

Direct Dyes : Dyes which can be applied to the fiber directly from an aqueous solution. There are a class of dyes that become strongly adsorbed on cellulose. They usually bear sulphonic acid group, but are not considered acid dyes since these groups are not used as a means of attachment to the fiber. Direct orange 26 is a typical direct dye.

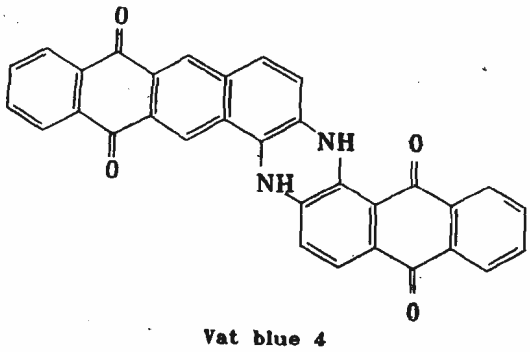
A fast dye does not decolourise over a period of time.



Direct orange 26

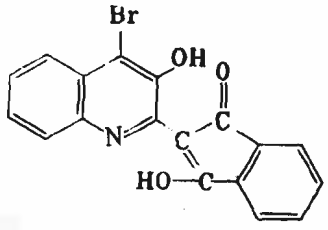
Vat Dyes are insoluble dyes. They are reduced with sodium hydrosulphide (NaHS) in a strongly alkaline medium to give a soluble form that has affinity for cellulose. This reduction operation was previously carried out in wooden vats and hence the name, vat dye. After the reduced dye has been adsorbed on the fiber, the original insoluble dye is reformed by oxidation with air or chemicals. The dyes produced in this way are very fast. In most cases, such dyes are not decolourised by action of light or by washings over a period of time. An example of a vat dye is Vat blue 4 (Indanthrone).

Mordants help in binding the dye to the fibre.



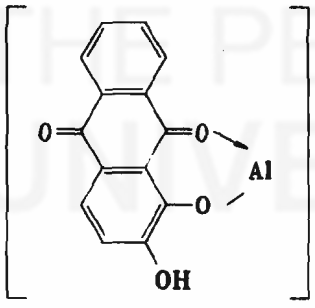
Vat blue 4

Disperse Dyes are non-ionic dyes having low water solubility and are capable of dissolving in certain synthetic fibers. Their fiber attraction is due to the formation of a solid solution, since, being uncharged, there is no driving force to form salt linkages. These dyes are primarily used for polyester fibers. Disperse yellow 64 is an example of disperse dyes.



Disperse yellow 64 (Quinophtualone)

Mordant Dyes require a pretreatment of the fiber with a mordant material which is designed to bind the dye. The mordant becomes attached to the fiber and then combines with the dye to form an insoluble complex called a 'lake'. An example of a mordant is aluminium hydroxide that has been precipitated in cotton fiber. This mordant is capable of binding such dyes as Mordant red 11 by formation of an aluminium lake.



Mordant red 11 (alizarin) mordanted with Al^{3+}

Classification of Dyes Based on Chemical Structures

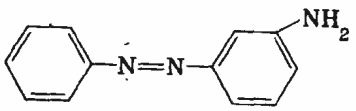
So far we discussed the classification based on the methods of application. Now let us discuss the classification based on chemical structures of the dyes.

Dyes contain functional groups which can give rise to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions. As mentioned earlier, such transitions are responsible for the colour of the dyes. Examples of such functional groups, called **chromophores**, are the azo group, the carbonyl group (in quinone) and the extended conjugated chain. Some of the principal chemical classes of dyes are given below :

Azo dyes

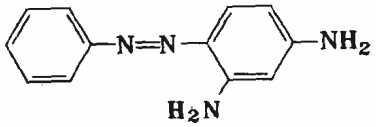
These dyes form the largest chemical class of dyestuffs. These dyes number in thousands. They consist of a diazotized amine coupled to an amine or a phenol. They have one or more azo linkages (–N = N–). Based on the number of azo groups, we can classify azo dyes as follows :

Monoazo Dyes : Monoazo dyes contain only one azo (–N = N–) linkage. Some examples of monoazo dyes are given below.



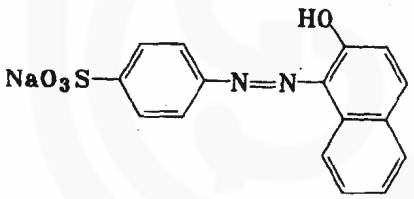
Solvent yellow 1
(Aniline yellow)

Used as a dye for oil and coat ing materials.



Basic orange 2

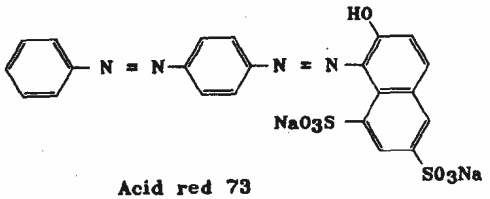
Limited use on textiles but of importance for colouring paper, leather and woodstains.



Acid orange 7

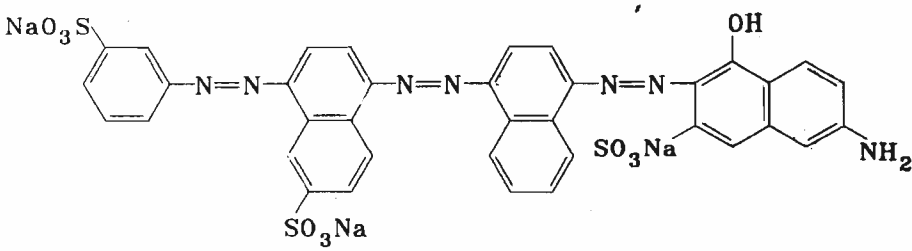
Used on textile fibers, such as, wool, silk and nylon as well as on paper and leather.

Disazo Dyes : Disazo dyes contain two azo linkages. Acid Red 73 (Brilliant Crocein M) is an example of this class. It is used to colour wool, leather and paper.



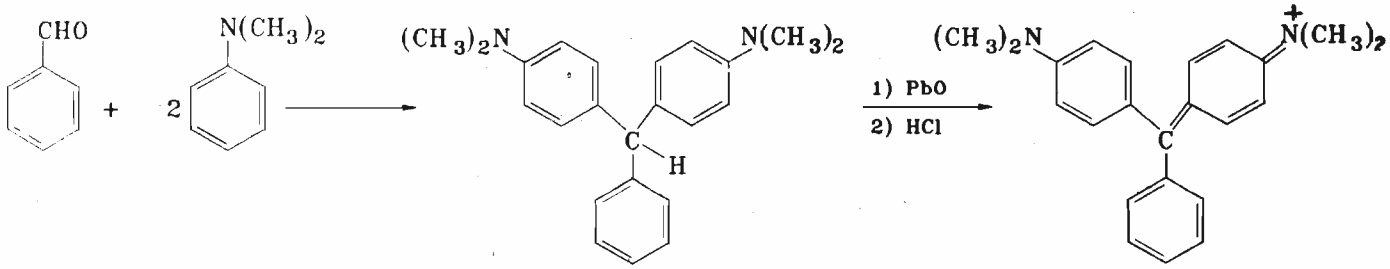
Acid red 73

Polyazo Dyes : These azo dye contain three, four or more azo linkages. Those with three (trisazo) and four (tetrakisazo) are quite common. An example of an important trisazo dye is Direct blue 110. This dye is used for colouring cellulose, wood and silk.



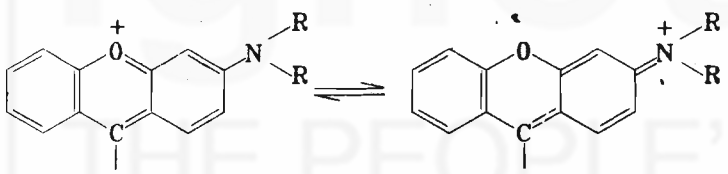
Direct blue 110

Triphenylmethane Dyes : Triphenylmethane dyes have triphenylmethyl group. They are basic dyes and are suitable for wool or silk or cotton. Basic green 4 (Malachite green) is a typical example and is prepared by condensing benzaldehyde with N, N- dimethylaniline and oxidising the intermediate leuco base.

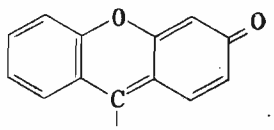


benzaldehyde N,N–dimethyl–aniline leucobase Basic green 4

Xanthene Dyes : The chromophore of the aminoxanthene dyes is the resonance stabilised structure shown below, where R = H, alkyl or aryl. The hydroxy xanthenes can be stabilised by the loss of a proton, forming an uncharged system in which the chromophore is a quinoid structure.

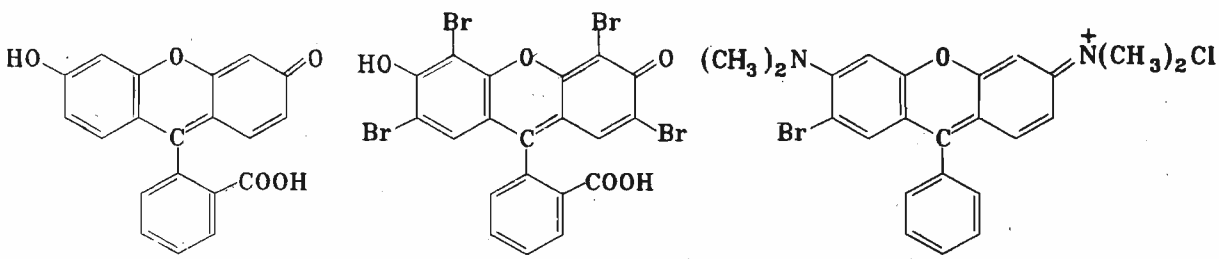


Aminoxanthene chromophore



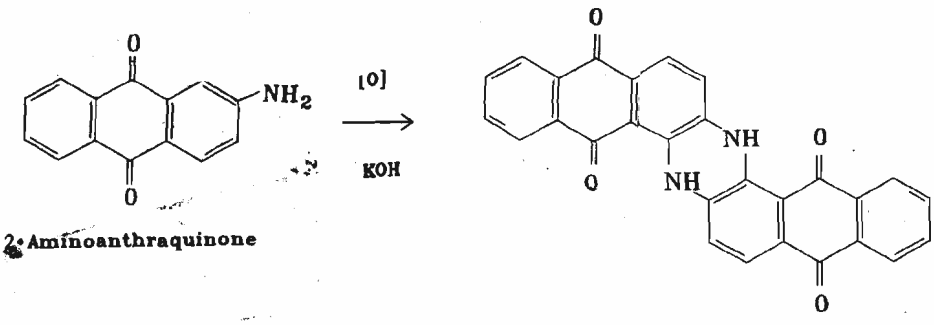
Hydroxyxanthene chromophore

Acid yellow 73 (Fluorescene), Acid red 87 (Eosin), and Basic violet 10 are examples of xanthene dyes.



Acid yellow 73 Acid red 87 Basic violet 10

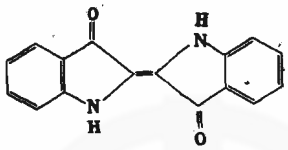
Anthraquinone Dyes : In anthraquinone dyes the chromophore is the carbonyl group, which may be present once or several times. These dyes are generally vat dyes as examplified by Mordant red 11 (alizarin). More complex examples are compounds prepared by oxidising anthraquinone derivatives under basic conditions.



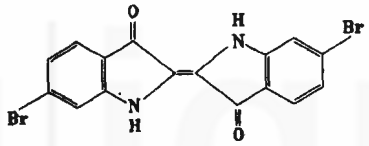
2-Aminoanthraquinone

Vat blue 4

Indigoid Dyes : Indigoid dyes are also vat dyes, as represented by indigo itself. Dibromo indigo is an example of this class. In earlier times, it was used only by rich people.

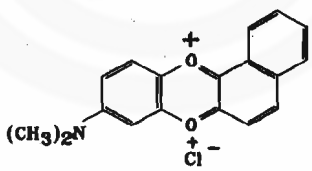


Indigo



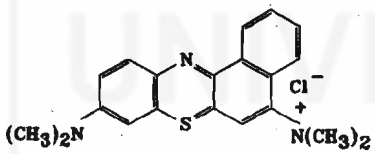
6,6'-Dibromoindigo

Azine Dyes : Azine dyes are derivatives of phenoxazine, phenothiazine or phenoazine. Some examples of azine dyes are given below :



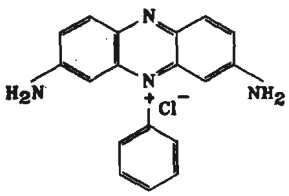
Basic blue

(a phenoxazine dye)



Basic blue 9

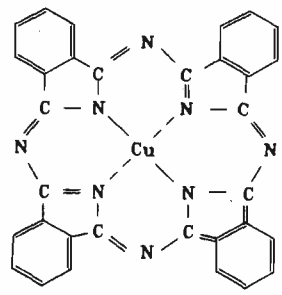
(a phenothiazine dye)



Safranine B

(a phenoazine dye)

Phthalocyanines : The phthalocyanines constitute an important class of synthetic pigments and dyes. An important member of this class is Pigment blue 15 (Copper phthalocyanine), a brilliant blue pigment that can be prepared by heating phthalonitrile with copper.



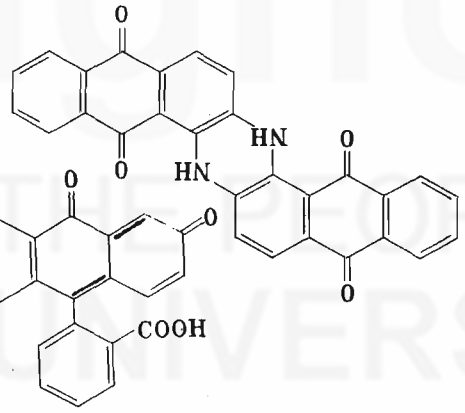
Pigment blue 15

So far we have discussed the different classes of dyes. Let us now study the production of azo dyes as a typical example. But before that try the following SAQs.

SAQ 3

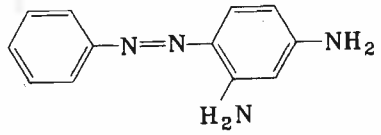
Classify following dyes on the basis of their methods of application.

a)

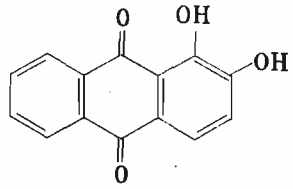


b)

c)



d)



SAQ 4

Give atleast one example of each of following

a) Azo dyes

b) Xanthene dyes

c) Anthraquinene dyes

d) Indigoid Dyes

e) Azine Dyes

16.5 CASE STUDY OF THE PRODUCTION OF AZO DYES

The apparatus required for the manufacture of a typical azo dye is indicated in Fig.16.2. We explain the manufacturing process of azo dyes considering the example of Disperse yellow 3.

Disperse dyes are used as aqueous dispersions of finely divided dyes or colloidal suspensions that form solid solutions of the dye within the fiber. They are especially useful for polyester synthetic fibers.

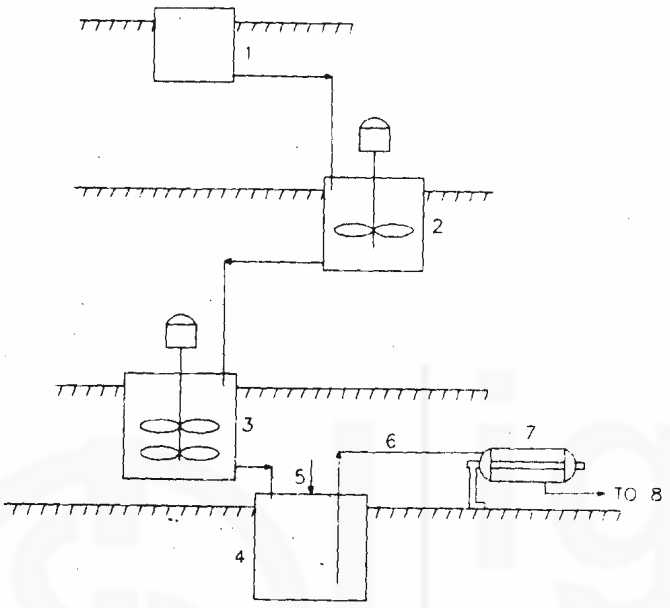
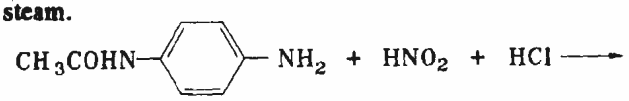
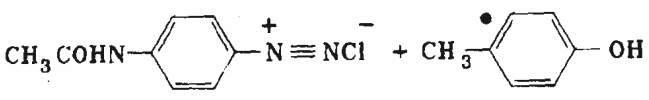


Fig. 16.2: Schematic diagram for manufacture of a monoazo dye.
1 Sodium Nitrate solution tank
2 Make-up and diazotisation tub
3 Coupling tub
4 Blow case
5 Compressed air line
6 Discharge line to press
7 Press
8 Vacuum dryer

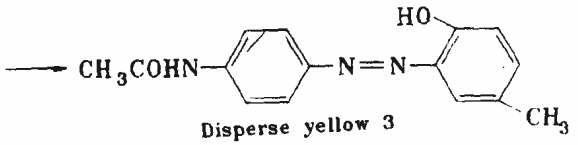
p-Aminoacetanilide is suspended in water in a wooden or brick-lined tub (Tub 2). The tub is equipped with an agitator for complete mixing of the contents. Two moles of hydrochloric acid per mole of amine are added. The contents are brought to the boiling condition by passing steam into the tub. As soon as the *p*-aminoacetanilide has dissolved, ice is added. One mole of sodium nitrite solution in Tank 1, is run slowly into Tub 2 for about two hours. In the meantime, two moles of *p*-cresol are dissolved in an excess of sodaash in water in Tub 3, and to this the content of Tub 2 are added with stirring. Enough ice is added to keep the temperature at about 278K. The dye separates in parts as the coupling proceeds. When the coupling is complete the contents of Tub 3 are warmed with steam.



***p*-aminoacetanilide**



***p*-cresol**



Disperse yellow 3

The suspension of dye is filtered. The filtered solid mass is washed and freed from most of the adhering mother liquor by blowing the compressed air through it. The moist solid is dried using an air drier. Vacuum driers may also be used. The dried dye is powdered and mixed with a suitable dispering medium in order to keep colour uniformity.

16.6 DRUGS

We can define drugs as the chemical substances used for the treatment or prevention of diseases in humans or animals. Presently, it is the responsibility of the pharmaceutical industry to provide efficient and safe drugs for the treatment of various diseases. The products of these industries are different from those of other industries as they directly affect our health.

Chemicals used as drugs should be in the purest possible form. Unlike other industrial chemicals, drugs need to be examined carefully prior to sale, specifically for their potency, toxicity, sterility and moisture content (since this may affect the stability of drugs). Let us examine each of these factors. Potency is the efficiency of a drug in treating or preventing a particular disease. Potency is determined by comparison with a standard to insure consistent clinical results. Toxicity is determined by the toxic effect of the drug on humans when taken internally. Sterility refers to the absence of microorganisms.

A numerical code system is maintained for each batch of the drugs. This facilitates the withdrawal of a particular lot of a drug after its expiry period or for any other reason.

Only few drugs such as quinine, smallpox vaccine, morphine, cocaine, aspirin, insulin, etc. were known before the beginning of the sulpha and antibiotic age. These drugs were extracted from plants and animals. A new era in drug research and manufacture dawned with the synthesis of sulphanilamide (in 1932) and penicillin (in 1940). Since then intense research efforts have led to many effective drugs.

Drugs have a major role to play in ensuring a healthy life. Diseases like malaria, tuberculosis and cholera which used to take a heavy toll of life, have been controlled to varying degrees of success. No cases of plague have been reported in India since 1967. Smallpox which was a dreadful disease, has been almost eradicated. The mortality rate has come down from 27.4 per thousand in 1951 to an estimated 10.9 per thousand in 1988 and life expectancy at birth has increased from 32 in 1946-51 to over 58.6 in 1986-91. The infant mortality rate has come down from 146 in the 50s to 94 in 1988. This has been possible only with the usage of new wonder drugs. Most drugs in common use are organic compounds.

In the next section of this unit we will highlight how the knowledge of organic chemistry can help us in designing new drugs.

16.7 DEVELOPMENT OF NEW DRUGS

Organic compounds, natural or synthetic, are the chief source of drugs. These compounds may be obtained; (i) directly from naturally occurring materials of both plant and animal origin, or (ii) from the synthetic modification of naturally occurring compounds such as morphine, atropine, steroids and cocaine. These organic compounds have been shown to possess useful medicinal properties. The above two approaches are mainly responsible for the development of many drugs. (iii) Third approach is that of pure synthesis. Synthetic methods are being increasingly used nowadays for developing new drugs.

Work to develop drugs is carried out more or less along the following lines,

1) First remedial materials from plants and animals are isolated are located. The active ingredients are isolated. After establishing the chemical structures of these natural products various structural modification are made in them and their effect as drugs are studied. This work sometimes leads to the discovery of a new drug which has less side effects and is more physiologically active. Once a new drug is discovered, attempts are made to synthesise it from readily available materials. The synthesis of such substances requires a knowledge of functional groups and synthetic techniques. So that desired drug can be produced at low cost. In Unit 14, we have already discussed how organic synthesis of a compound are carried out from readily available materials.

2) Obtaining drugs as a result of purely synthetic methods depend on both skill and luck. First an animal is given a simulation of the disease. A cure is sought by trial

and error using synthetic chemicals which we feel have some drug value. Once a useful compound is found similar to above method its derivatives are prepared and their effects are studied under similar conditions.

Research in pharmaceutical industries has led to introduction of more and more new drugs in modern time. Fig. 16.3 outlines the various steps in the development of a new drug. Such a development requires the skill and experience of an organisation of chemists, biochemists, biologists, microbiologists, doctors, pathologists, toxicologists, pharmacists and engineers working together to discover and develop a new drug.

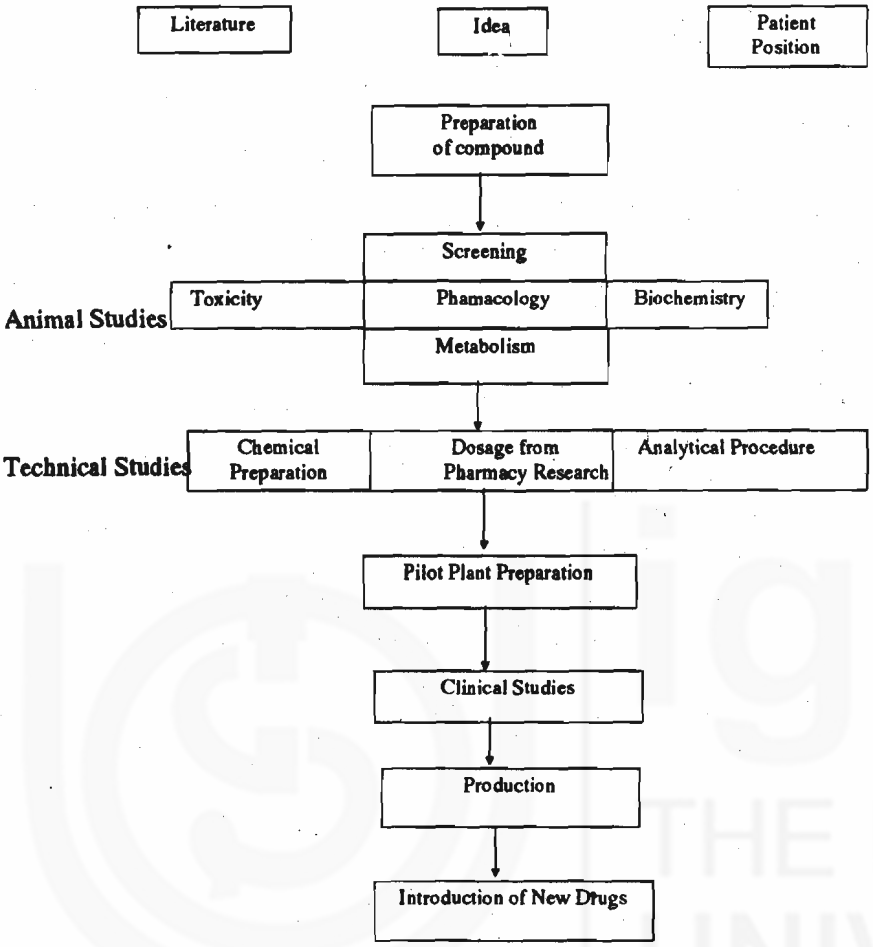


Fig. 16.3 : Representation of stages in the development of a new drug from idea to market.

16.8 CLASSIFICATION OF DRUGS

The most common classification of drugs is based upon their action. Table 16.2 lists major divisions of drugs according to their action and examples of each.

Table 16.2: Drug classification and examples

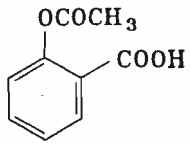
Major Drug Group	General Drug Names
Analgesics (pain reducing drugs)	Aspirin, acetaminophene, phenacetin morphen, meperidine, methadone propoxyphene
Gastro Intestinal Agent : Antacids (reduce excess stomach acid)	Compounds like sodium bicarbonate magnesium carbonate, mixture of magnesium hydroxide and aluminium hydroxide
Anti-infectious : Antibacterial agents	Sulphadiazine, sulphisoxazole, sulphamethoxazole
Antibiotics	Pencillin G, ampicillin, cephalexin erythromycin, streptomycin,

	chlotetracyclin, chloramphenicol
Antimalarials	Pamaquine, chloroquine, proguanil
Antidepressants	Doxepin, imipramine, amitriptylin
Antihistamines	Diphenhydramine, chlorphenitramine, tripelennamine
Anti-inflammatory agent : steroidal	Cortisone acetate, prednisolone, Dexamethasone
non-steroidal	Ibuprofen
Cardiovascular drugs	Digitoxin
Diuretic agents	Hydrochlorothiazide, spironolactone, triamterene, furosemide
Central nervous system stimulants	Amphetamine sulphate, methylphenidate
Central Nervous System Depressants	
Sedative and hypnotic	Phenobarbital, glutethimide, mathaqualone.
Tranquilizer	Hydralazine, methyldopa, reserpine, clonidine, Guanethidine, prazosin, metoprolol
Antianxiety agent	Meprobamate, chlordiazepoxide and Diazepam
Hormones	Thyroid stimulants, growth stimulants cartisone, birth-control pills (progeton, estrogen)
Vaccines	Antigens against disease such as polio
Nutritional factors	Vitamin supplements
Diagnostic agents	Barium sulphate for X-rays

For the drugs mentioned above, we are not going to study the mode of action. But we shall explain the use of these drugs by illustrating one or two examples.

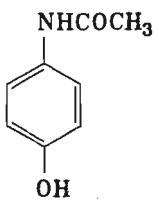
An addicting drug makes the patient use it repeatedly. The patient becomes psychologically dependent on these drugs.

Analgesics help in relieving pain without affecting the individual's consciousness. Aspirin is the best example of a simple analgesic and this gives relief from headache and muscle ache. This is not an addicting drug.

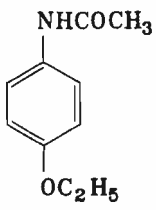


Aspirin (acetylsalicylic acid)

Other example of this type of analgesic are acetaminophen and phenacetin. These compounds are not so harmful to the stomach as aspirin.

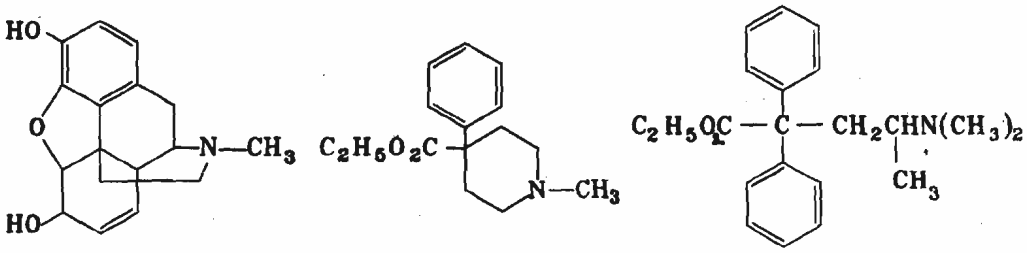


Acetaminophen



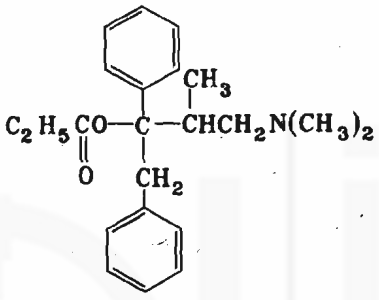
Phenacetin

Other type of analgesics are called narcotic analgesics, which are used primarily for the relief of severe pain; they are of addicting type. Examples are morphine, meperidine and methadone.



Morphine Meperidine Methadone

One of the most commonly prescribed pain reliever is propoxyphene hydrochloride (Darvon), which does not usually cause addiction.

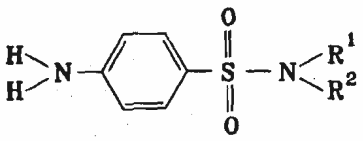


Propoxyphene

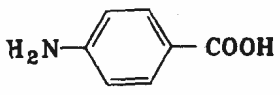
Antacids are most commonly used drugs for the stomach. The walls of the stomach secrete 0.1 *M* HCl. This prevents the growth of bacteria and creates an environment in which enzymes can break down proteins. If there is too much acid in the stomach discomfort can result. Many antacids are available to neutralise excess stomach acid. Generally, they are weak bases. Examples,

Sodium bicarbonate	Magnesium oxide or Magnesium hydroxide
Magnesium carbonate	Aluminium oxide or Aluminium hydroxide

Antibacterial agents : Sulphonamide and the related compounds, called sulpha drugs, were earlier being used to combat bacterial infection. These drugs have a structure similar to that of *p*-aminobenzoic acid.



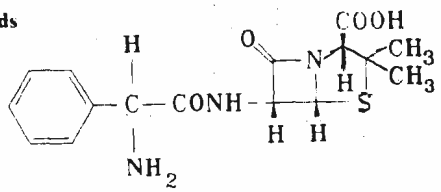
sulphanilamide ($R^1 = R^2 = H$)



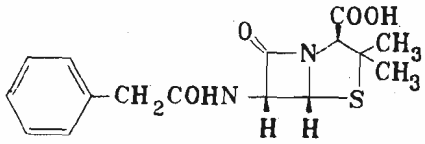
p-aminobenzoic acid

Over 5000 sulpha drugs have been synthesised and tested. They all resemble sulphonamide in structure but differ with respect to R^1 and R^2 groups.

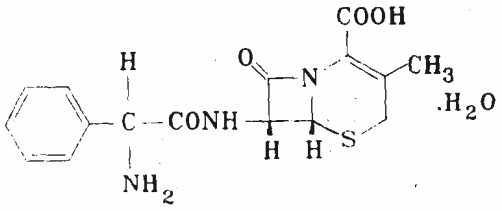
Antibiotics : The term antibiotic was introduced by Waksman in 1942. An antibiotic can be defined as a chemical substance produced by a micro-organism that can inhibit growth of, or even destroy, other micro-organism. Since the introduction of penicillin (1941), over 60 antibiotics have been developed to a stage where they are of value in treating infectious diseases. Antibiotics are generally produced by growing the appropriate organism in a specially prepared medium. The structure of some widely used antibiotics are given below :



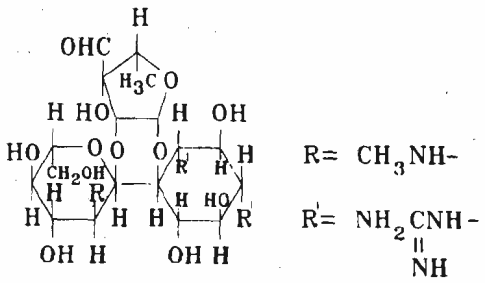
ampicillin



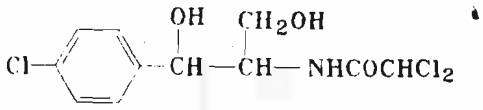
Penicillin G



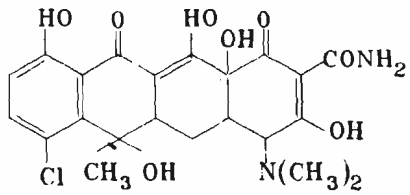
Cephalexin



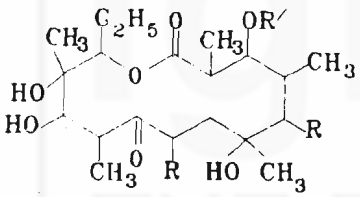
Streptomycin



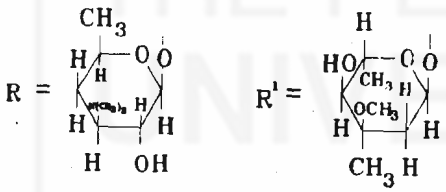
Chloramphenicol



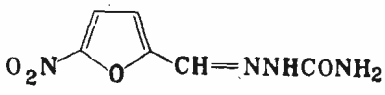
Chlortetracycline



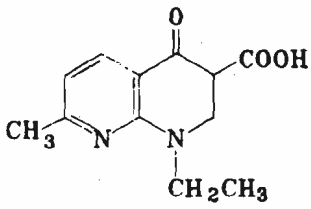
Erythromycin



By chemical modification of naturally occurring antibiotic, it is possible to obtain products with desirable properties which are not found in the natural product. Nowadays some purely synthetic antibiotics are also available. Some of these have structures that resemble those of antibiotics derived from natural source, while others bear little resemblance to their natural parallels. Two synthetic compounds which belong to the latter group have the following structures.

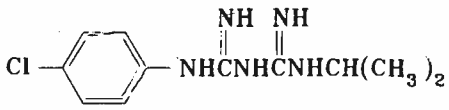


Nitrofurazone(Furacin)

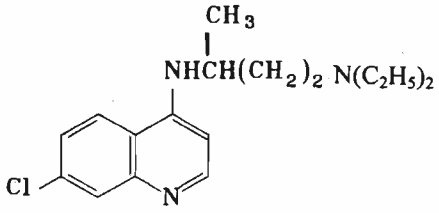


Nalidixic acid

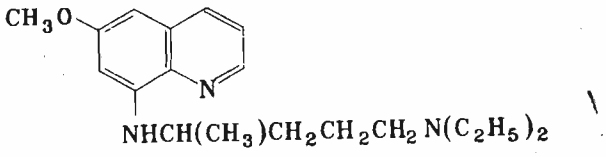
Antimalarials : Cinchona alkaloids have been in use as an antimalarial drug since 16th century. In recent past a number of synthetic drugs were tested for their antimalarial action. Some examples are given below :



Proguanil

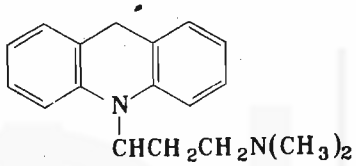


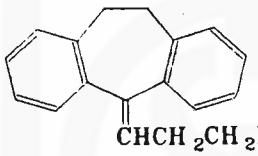
Chloroquine



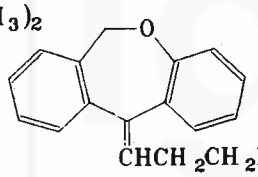
Pamaquine

Antidepressants : These drugs have been commonly used in recent years to relieve the symptoms of mental depression. The chemical structure of two antidepressants, are given below :

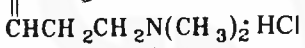




Imipramine hydrochloride (Tofranil)



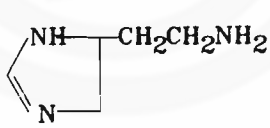
.HCl



Amitriptyline hydroch...ide (Elavil)

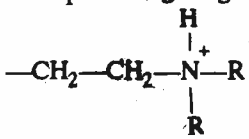
Doxepin

Anti-histamines are thought to act by preventing the action of histamine :

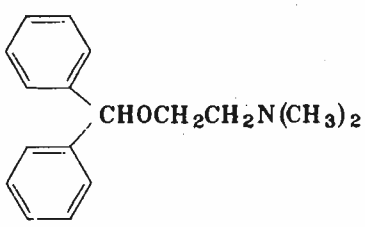


There are two types of anti-histamines H_1 and H_2 blockers. H_1- blockers are useful in the treatment of nasal allergies; particularly hay fever. They are also used to treat vomitting. H_2-blockers are used to reduce the secretion of gastric acid (antiulcer agent).

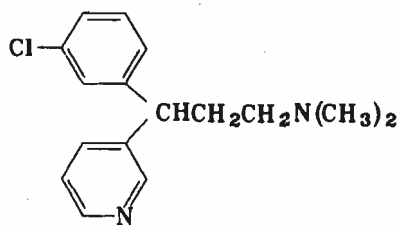
All H_1 blocking drugs have the group



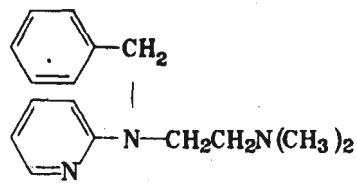
Examples,



Diphenydramine

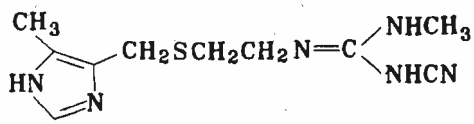


Chloropheniramine



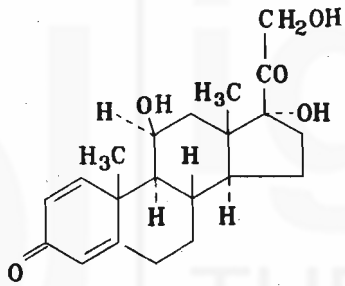
Tripelennamine

Cimetidine is an example of H_2-blockers

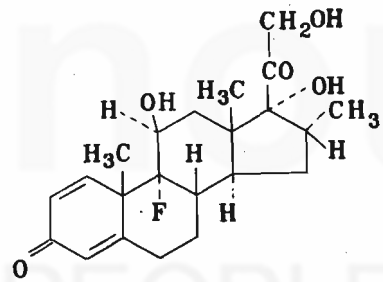


Cimetidine

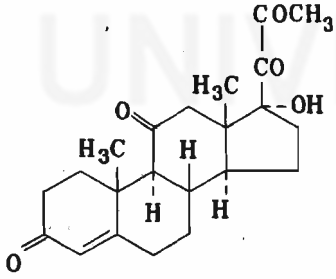
Anti-inflammatory agents : are the agents which reduce the inflammation (swelling). Cortisone is the first steroidal anti-inflammatory susbtance. Modification of the structure **led to more active compounds with specific anti-inflammatory properties. For example, Prednisolone and dexamethasone are widely used in the treatment of arthritis.**



Prednisolone

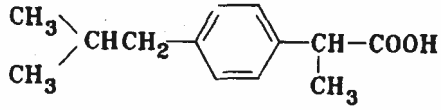


Dexamethasone



Cortisone acetate

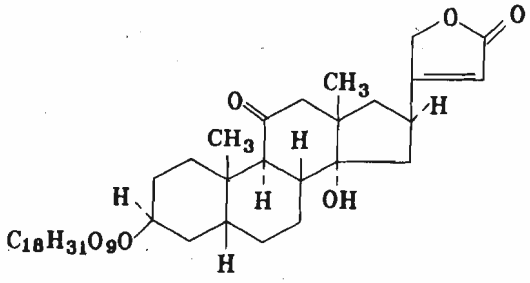
Ibuprofen is an example of nonsteroidal anti-inflammatory agents.



Ibuprofen

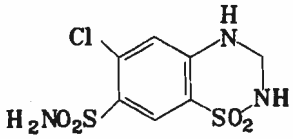
Cardiovascular drugs : Cardiovascular drugs are used for the heart and circulatory system. Fibrillation, and same other heart diseases may often be controlled by cardiac glycosides. An important and typical representative of this type is digitoxin. It is obtained

by extraction from a plant known as digitalis.

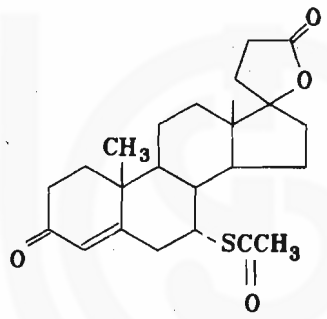


Digitoxin

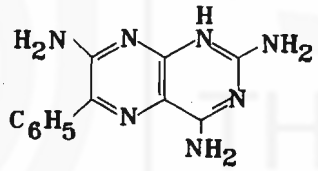
Diuretic agents : Diuretics are drugs used to increase the volume of urine excreted by the kidneys. They are used in Oedema, cardiac failure, renal disorders and liver disorders.



Hydrochlorothiazide
Thiazide

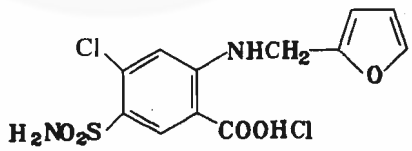


Spironolactone



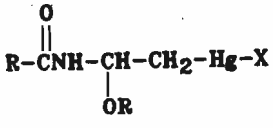
Triamterina

Potassium-sparing diuretics



Furosemide
High-ceiling diuretic

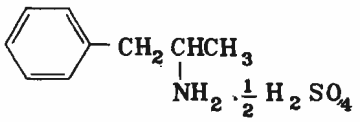
Earlier mercurial diuretics were used which have following general structure :



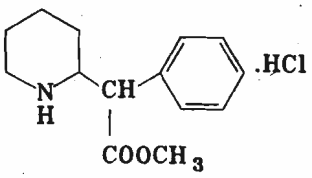
Because of the possible side effects due to mercury content, mercurial diuretics are not used now.

Central nervous system (CNS) stimulants

CNS stimulants has been restricted because of the abuse potential of such agents. amphetamine sulphate and methylphenidate are examples of this type of drug.

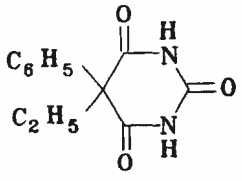


Amphetamine sulphate

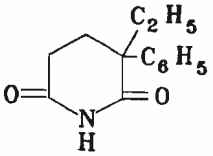


Methylphenidate

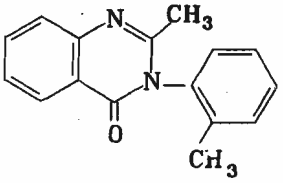
Sedatives and hypnotics : Sedative and hypnotics are used mainly to produce drowsiness. They are generally central nervous depressants. The use of these drugs has been restricted because of their abuse potential. Examples are shown below :



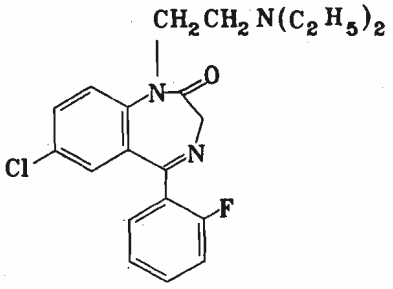
Phenobarbital



Glutethimide

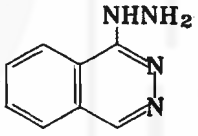


Methaqualone

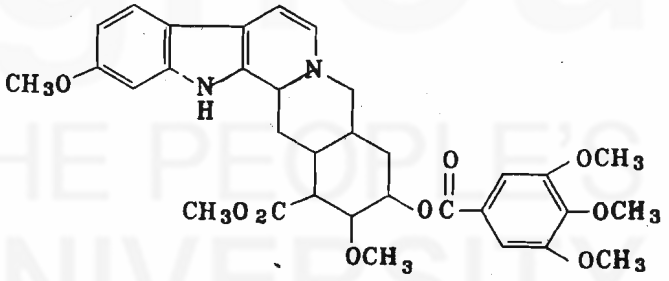


Flurazepam hydrochloride

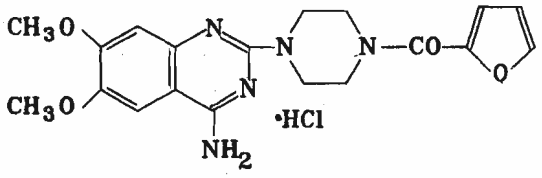
Tranquilisers : Nervous tension, alongwith the fatigue and lack of sleep troubles us all at one time or the other. Fortunately, in recent years tranquilisers have been developed that reduces hypertension. Examples of some widely used agents are shown below :



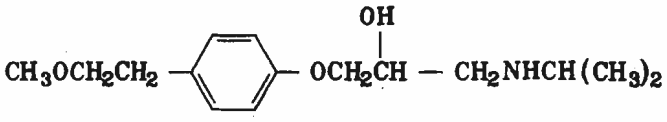
Hydralazine



Reserpine

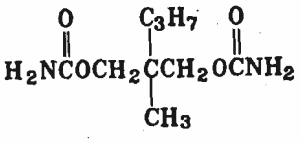


Prazosin

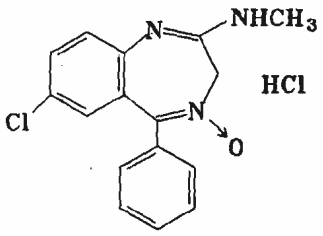


Metoprolol

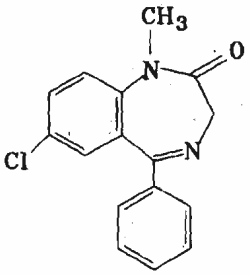
Antianxiety Agents (minor tranquilizer) are widely used for the relief of mild anxiety and tension. Example,



Meprobamate

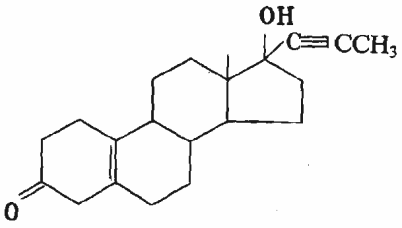


Chlordiazepoxide



Diazepan

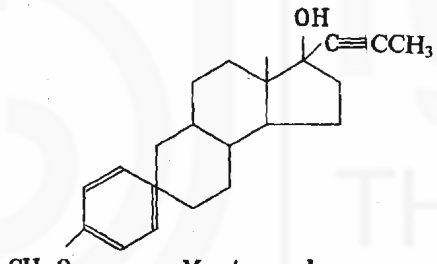
Hormones : Oral contraceptives, constitute one of the most widely used methods of birth control. These tablets contain chemically synthesised hormones – esterogen and progestin



Norethynodrel

(Progestin)

Hormones are substances that act as messengers in the body. Hormones control many processes such as growth and pregnancy.



Mestranol

(Estrogen)

Vaccines and other Immunising Agents : Vaccines help in resisting (provide immunity against) certain bacterial and viral infections. Some examples are given below :

Typhoid Vaccine

Smallpox Vaccine

Oral Polio Vaccine

Mumps Vaccine

Measles Vaccine

Influenza Vaccine

Immunisation : is a way of producing artificial resistance to an infectious disease.

SAQ 5

Match the drug in the left column with its class in the right column.

a)	Phenobarbital	i)	Antidepressants
b)	Furosemide	ii)	Analgesics
c)	Digitoxin	iii)	Antibiotics

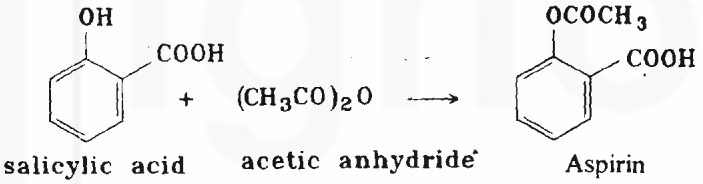
d)	Cortisone acetate	iv)	Antibacterials
e)	Doxcepin	v)	Diuretic agents
f)	Streptomycin	vi)	Sedatives and hypnotics
g)	Diazepam	vii)	Antianxiety agents
h)	Morphine	viii)	Anti-inflammatory agent
i)	sulphanilamide	ix)	Cardio Vascular drug

16.9 CASE STUDIES OF THE PRODUCTION OF ASPIRIN AND PENICILLIN

Most of the above mentioned compounds are prepared by chemical synthesis, generally by a batch process. Antibiotics are exception and are obtained by fermentation and extraction process. Industrial preparation is generally carried out in reactors, varying in size from 200 dm^3 to several thousand dm^3. Depending on the reaction, either stainless steel or glass lined steel reactors are used. To illustrate chemical manufacturing procedures used in the pharmaceutical industry, let us consider the case studies of the production of aspirin and penicillin.

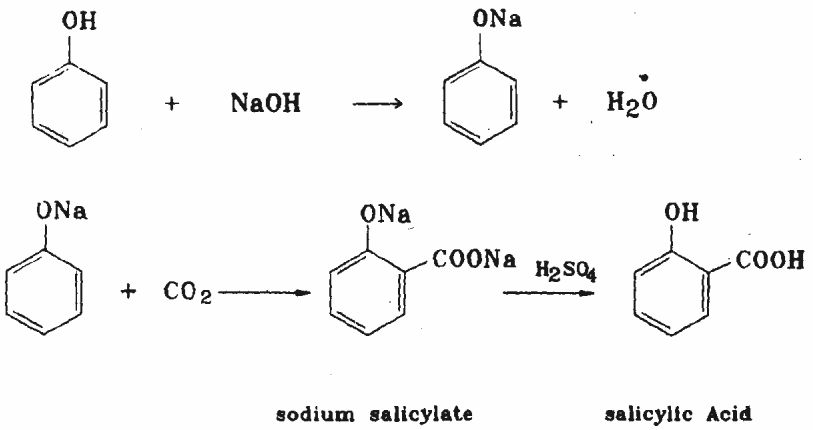
Production of Aspirin

A commercial process that gives good yields, high purity and low cost for the production of aspirin is shown in Fig 16.4.



In this process, salicylic acid powder and acetic anhydride are reacted in the medium of the mother liquor from the previous batch in a 2500 dm^3 glass-lined reactor for 2 to 3 hours. The mass is then pumped through a stainless steel filter to a crystalising kettle which may be a 2500 dm^3 glass lined reactor. The temperature is reduced to 276 K. On completing the crystallisation step, the batch is transferred to the slurry tank and fed to the centrifuge. The remaining liquid, known as mother liquor, is drawn off. The portion of this mother liquor is used alongwith the starting materials in the next batches of the production of aspirin. The mother liquor not used for the next batch is sent to the still for the acetic acid recovery. The acetic acid is separated by distillation. The aspirin crystals are dried to yield bulk aspirin.

The salicylic acid which is required for the production of aspirin is prepared by the Schmidt modification of the Kolbe reaction.



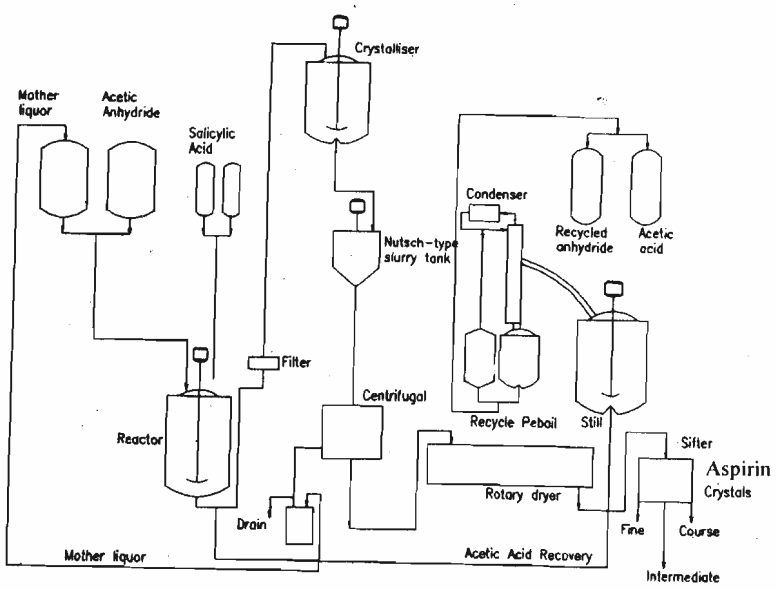


Fig. 16.4 : Flow diagram for the production of bulk aspirin.

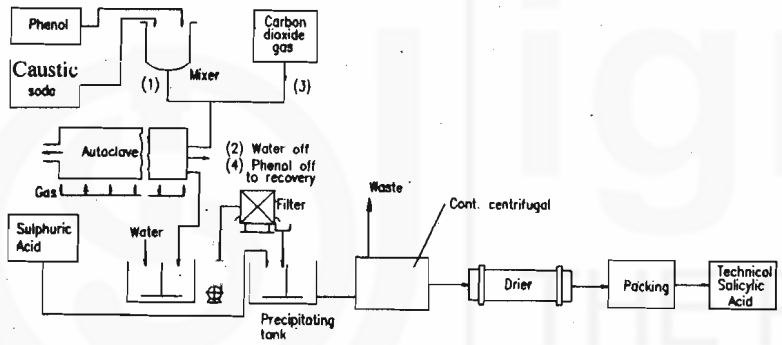
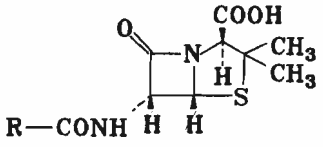


Fig. 16.5 : Flow diagram for the production of salicylic acid.

Production of Penicillin

Manufacture of penicillin is a typical example for the production of antibiotics. the mold used industrially is from the **Penicillium chrysogenum** group. A number of penicillins differing only in the composition of the R group, have been produced by the penicillin molds. Penicillin G (R = $C_6H_5 — CH_2$) is a widely used penicillin drug. The general structure of penicillin is given below :



R=$C_6H_5CH_2$ – Penicillin G (benzylpenicillin)

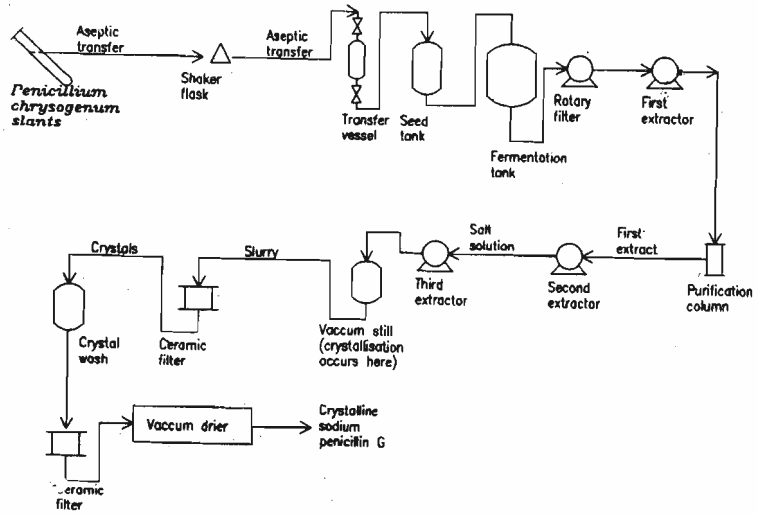


Fig. 16.6 : Flow diagram for the production of penicillin.

The steps in Fig.16.6 may be separated into the following stages :

Fermentation : Various fermentation methods are known which are used to produce penicillin on a large scale. Out of them submerged fermentation method is commonly used for the commercial production. In this process, the **Penicillium chrysogenium** is used as seed for the fermentation. It is prepared by growing a master stock culture of the mold from lyophylized spores on a nutrient agar substratums with incubation. Several dm^3 of culture medium, generally constituting 5 to 10 per cent of the charge, are prepared in a series of seed tanks to seed a large tank.

The fermentation medium is prepared from corn steep liquor, to which 2 to 4 per cent lactose is added, along with inorganic materials such as calcium carbonate, potassium phosphate, magnesium sulphate and traces of iron, copper and zinc salts. After adjusting the pH to 4.5 to 5.0 the fermentation medium is fed into the fermenter which is equipped with a vertical agitator, a means of introducing air which has been sterilised by filtration and coils for controlling temperature. Following sterilisation of the fermenter, the 'seed' (mold) is introduced through sterile pipelines by air pressure. During fermentation, the temperature is maintained at 296 to 300K. Sterile air permits growth of the aerobic mold, agitation distributes it uniformly in the batch. Fermentation is completed in 50 to 90 hours.

Separation of Penicillin : After fermentation, the batch is cooled to 278K because of the instability of penicillin at room temperature and the mycelin (cells and insoluble metabolic products) are removed by filtration on a rotatory drum filter. The filtrates contain the antibiotic which initially is separated by solvent-extraction process. In this process, filtered liquor (beer) is adjusted to a pH 2.5 with phosphoric acid, resulting in an acid form of penicillin. Continuous counter current extraction is carried out with amyl acetate, in specially designed extractors. The amylacetate portion is treated with buffered phosphate (pH 6.5 - 7.5) and sodium bicarbonate to form the sodium salt of penicillin G. This material is made sterile by filtration and is freed of water and other solvents by crystallisation, crystalline penicillin is thereby formed which, when dried, may be packed in bulk in polyethylene bags, or stainless steel containers,

16.10 SUMMARY

In this Unit we have discussed the chemistry of dyes and drugs along with case studies of the production of an azo dye, aspirin and penicillin. Here, we are summarising what we have studied so far :

- Dyes are intensely coloured substances that can be used to produce a significant degree of colouration where dispersed in or react with other materials.
- Dyes owe their colour to their ability to absorb light in the visible region of the spectrum (400 - 800 nm). Absorption is generally caused by $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ electronic transitions in the molecule. They have conjugated structures (chromophores)

and substituents (auxochromes).

- Dyes are classified according to the methods of their application into following groups: Acid dyes, Basic dyes, Direct dyes, Vat dyes, Disperse dyes and Mordant dyes. They can also be classified according to their chemical composition into following classes : Azo dyes, Triphenylmethane dyes, Xanthene dyes, Anthraquinone dyes, Indigoid dyes, Azine dyes and Phthalocyanines.
- Manufacture of Disperse yellow 3 can be carried out by coupling of diazotised aminoacetanilide with *p*-cresol.
- Drugs can be defined as the chemical substances used for the treatment or prevention of diseases in humans or animals.
- Drugs can be classified in general therapeutic groups such as Analgesics, Gastro intenstinal agents, anti-infections, Antidepressants, Antihistamines, Anti-inflammatory agents, Cardio vascular drugs, Diuretic agents, Central nervous system stimulants, Central nervous system depressants, Hormones, Vaccines Nutritional factors, etc.
- Commercially, aspirin can be prepared by acetylation of salicylic acid with acetic anhydride.
- Penicillin is produced by growing the Penicillium Chrysogenum mold in specially prepared medium.

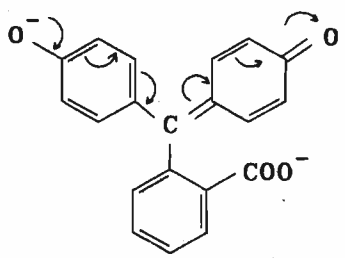
16.11 TERMINAL QUESTIONS

1) Classify dyes on the basic of their applications and give at least one example of each class.
2) Classify dyes on the basis of their chemical compositions and give one example of each class.
3) How is monoazo dye manufactured?
4) What is the difference between a narcotic analgesic and simple analgesic? Give exampics of each type.
5) Give production of penicillin G.

16.12 ANSWERS

Self Assessment Questions

1) (a) Violet; (b) Blue; (c) Orange; (d) Blue-green
2) III structure. It is more stabilised by resonance.



3) a) Vat dye b) Acid dye c) Basic dye d) Mordant dye
4) a) Basic orange 2 b) Basic violet 10 c) Vat blue 4 d) indigo e) Basic blue 6
5) (a) vi; (b) v; (c) ix; (d) viii; (e) i; (f) iii; (g) vii; (h) ii (i) iv

Terminal Questions

1) See text section 16.4.

2) See text section 16.4.

3) See text section 16.5.

4) Narcotic analgesic are all addicting (ie producing psychological, and some time physical dependence). They are usedprimarily for the relief of severe pain. Example is morphine. On the other hand non narcotic analgesic are non-addicting and are used for simple pain. Example is aspirin.

5) See text section 16.9.

FURTHER READINGS

1) *Organic Chemistry* ; sixth edition; R.T. Morrison and R.N. Boyd; Prentice-Hall of India Pvt. Ltd.

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3) *Reaction Mechamism and Reagents in Organic Chemistry*; 12th edition; Gundeep R. Chatwal; Himalay Publishing House.

5) *Molecular Reactions and photochemistry*; Charles H. Depay and Orville L. Chapman; Prentice Hall of India Private Limited.

6) *Organic Synthesis*; Ireland; Prentice Hall of India Private Limited.