Chapter

23 Steroids

1. INTRODUCTION

The **steroids** constitute a group of structurally related compounds that are widely distributed both in the plant and the animal kingdom. The basic nucleus of these physiologically potent and biochemically dynamic medicinal compounds do possess a more or less similar stereochemical relationship. The **steroids**, in genreal, have been found to contain either the partly or completely **hydrogenated 17H-cyclopenta-phenanthrene** nucleus.

The **steroids** include a broad-spectrum of important compounds which exhibit remarkable pharmacodynamic properties, namely : **adrenal cortical hormones**, **sex hormones**, **cardiac glycosides**, **antirachitic vitamins (Vitamin D)**, **toad poisons**, **saponins**, **bile acids** and **some alkaloids**.

Broadly speaking both **steroid** hormones and related structural analogues constitute and designate one of the most abundantly employed categories of pharmacologically active and potent agents. These **'medicinal compounds'** are invariably used as first in importance in the control and management of birth control, inflammatory conditions, **hormone-replacement therapy (HRT)**, and above all in the treatment of neoplastic diseases (cancer). Interestingly, the plethora of these agents are exclusively based on a specific common structural nucleus usually termed as the'**steroid backbone'.** However, the different **steroidal variants** essentially attribute to the specific and unique molecular targets.

2. STEROID NOMENCLATURE, NUMBERING, DOUBLE BONDS AND STEREOCHEMISTRY

The general formula for the basic structure of the above cited compounds may be represented as follows :

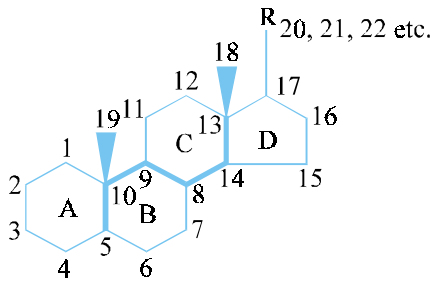


Fig. 2.3. General Steroid Formula.

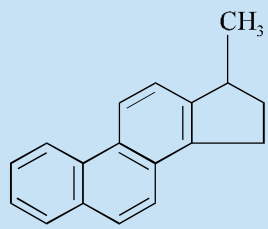
The rings are conventionally lettered and numbered as indicated above. However, in actual conformation the basic structure of **steroid** is not planar. It has also been observed that in the naturally occurring **steroidal compounds** the substitutions in the rings usually occur at C-3, C-7 and C-11 positions.

According to the standard convention the direction of projection from the plane of the ring system of substituting groups located at centres of asymmetry is usally designated by the Greek letters α and β.

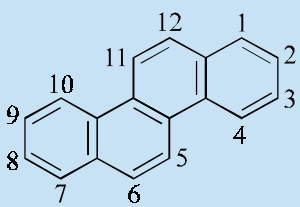
The α-substituting group is viewed as projecting beneath the ring plane and is conventionally represented by a broken line (dotted line).

The **β-substituting groups** is viewed as projecting above the ring plane and is normally represented by a solid line.

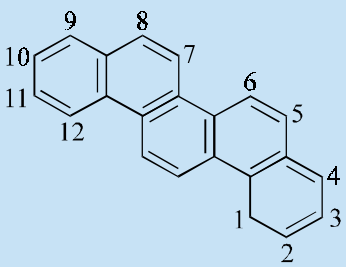
It has been observed that all the steroids on dehydrogenation with selenium at 360°C usually yield **Diel's hydrocarbon**, *i.e.*, **3′-methyl-1:2-cyclopentanophenanthrene**, whereas at 420°C, the **steroids** give mainly **chrysene** and a small amount of **picene**.



Diel's hydrocarbon



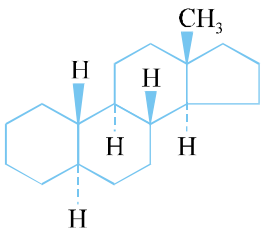
Chrysene
Or
1 : 2-Benzphenanthrene



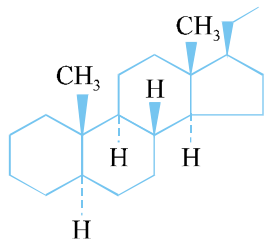
Picene
Or
1 : 2 : 7 : 8-Dibenzphen-anthrene

A few typical examples of **'steroidal drugs'** together with their **nomenclature** and **numbering** are illustrated below :

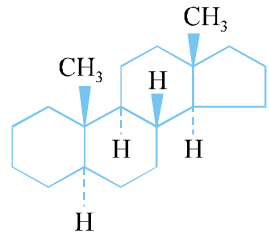
(*a*) **Common and Systematic Nomenclature :**



5α-Estrane

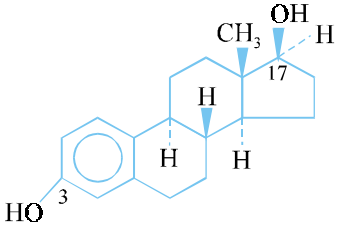


5α-Pregnane

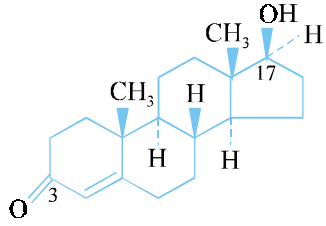


5α-Androstane

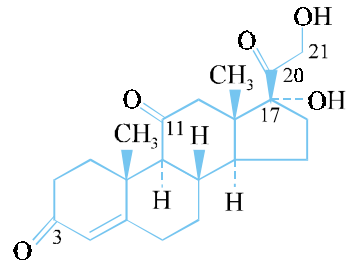
(*b*) **Nomenclature and Numbering :**



17β-Estradiol
[Estra-1, 3, 5(10)-triene-
3, 17β-diol]

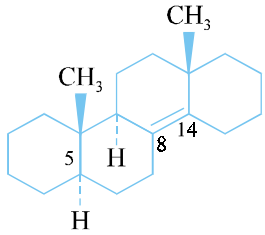


Testosterone
[17β-Hydroxyandrost-
4-en-3-one]

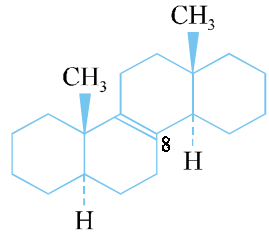


Cortisone
[17, 21-Dihydroxypregn-4-ene
– 3, 11, 20-trione]

(*c*) **Nomenclature and Double Bonds :**

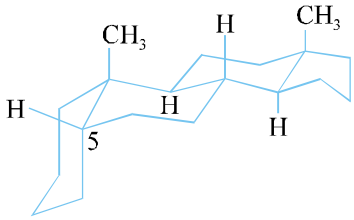


5α-Androst-8(14)-ene
or
5α-$\Delta^{8(14)}$-Androstene

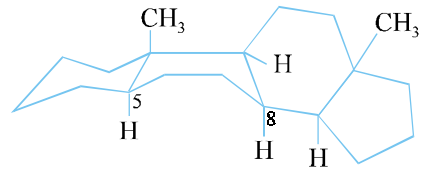


5α-Androst-8-ene
or
5α-Δ^{8}-Androstene

(*d*) **Nomenclature and Stereochemistry :**



5β-Androstane



5α, 8α-Androstane

Salient Features. The salient features with respect to the ***nomenclature*** **(IUPAC)** and **stereochemistry** are as enumerated below :

(1) Stereochemistry of the H-atom at C-5 is invariably incorporated in the 'name' itself,

(2) Stereochemistry of other H-atoms is **not** usually indicated unless and until it essentially happens to differ from **5 α-cholestane,** and

(3) Altering the stereochemistry at any of the **'ring-juncture'** with a heavy-dark line (see 'general steroid formula's Fig. 23.1) changes immensely the prevailing '**shape of the steroid'**, as may be observed in the above cited examples of **5β-androstane** and **5α, 8α-androstane**.

2.1. Diel's Hydrocarbon

It is a solid substance having a melting point 126-127°C and a molecular formula $C_{18}H_{16}$. Based on the results of oxidation reactions, X-rays crystal analysis coupled with absorption spectrum measurements it was revealed that the hydrocarbon in question could be **3′-methyl-1:2-cyclopentanophenanthrene**. The next essential step was to establish the structure of this compound by synthesis, *e.g.*, that of Harper *et al* (1934) who used the **Bogert-Cook method** commencing from :

(*i*) 2-(1-naphthyl)-ethyl-magnesium bromide

(*ii*) 2:5-dimethylcyclopentanone

2-(1-Naphthyl)-ethyl-magnesium bromide and 2:5-dimethyl-cyclopentanone react to give a condensed product which on oxidation with phosphorus pentoxide at 140°C and subsequent distillation under reduced pressure yields an intermediate. This undergoes cyclization first and later on when distilled with selenium gives the **Diel's hydrocarbon**.