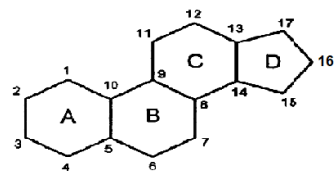


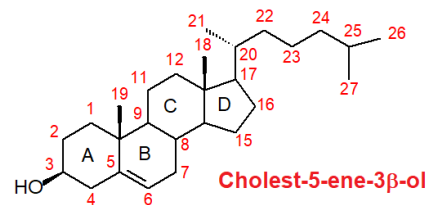
UNIT 4: Drugs acting on Endocrine system

1. Nomenclature, Stereochemistry and metabolism of steroids
2. **Sex hormones:** Testosterone, Nandralone, Progestones, Oestriol, Oestradiol, Oestrone, Diethyl stilbestrol.
3. **Drugs for erectile dysfunction:** Sildenafil, Tadalafil.
4. **Oral contraceptives:** Mifepristone, Norgestrel, Levonorgestrol
5. **Corticosteroids:** Cortisone, Hydrocortisone, Prednisolone, Betamethasone, Dexamethasone
6. **Thyroid and antithyroid drugs:** L-Thyroxine, L-Thyronine, Propylthiouracil, Methimazole.

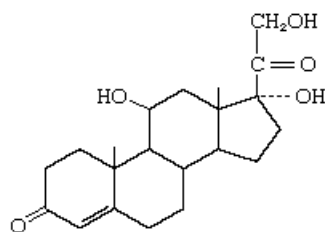
Important Steroids



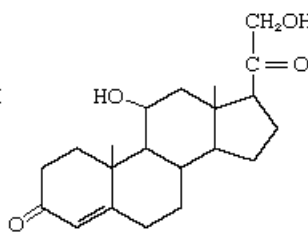
Steroidal Skeleton



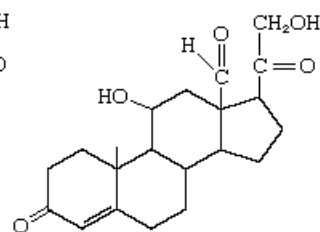
Cholesterol Ring



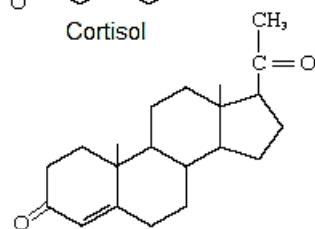
Cortisol



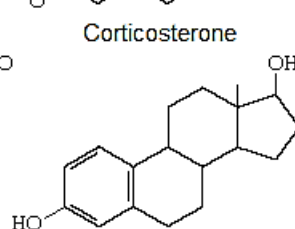
Corticosterone



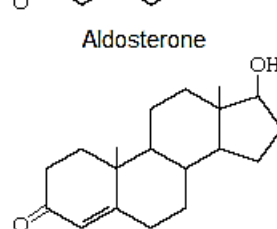
Aldosterone



Progesterone



Beta-estradiol



Testosterone

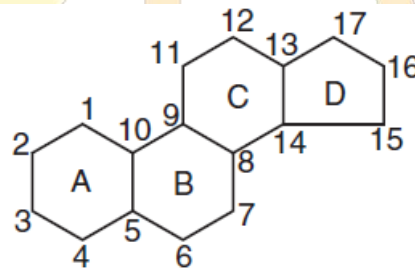
Chapter 11. Steroidal Hormone

Steroids are the most important class of biological active molecules, which show variety of biological actions. The major therapeutic classes of steroids are the following:

- ✓ **Anti-inflammatory agents:** Cortisone
- ✓ **Sex hormones:** Estrogen, progesterone, and testosterone
- ✓ **Oral contraceptives:** Norethisterone
- ✓ **Cardiac steroids:** Digitoxigenin
- ✓ **Diuretics:** Spironolactone
- ✓ **Antibiotics:** Fusidic acid
- ✓ **Vitamin D precursor:** Ergosterol

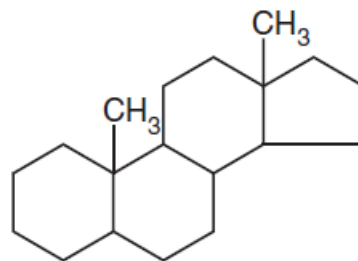
11.1. STRUCTURE AND NOMENCLATURE

Steroidal Ring (made up of 17 carbon atoms) consists of 4 fused rings: 3 cyclohexyl rings (A, B, C) which also called as perhydro phenanthrene ring and 1 cyclopentyl ring (D).

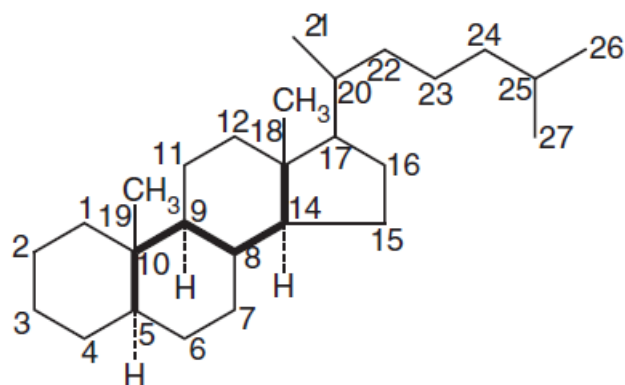


Cyclopentanoperhydrophenanthrene

Steroidal Backbone



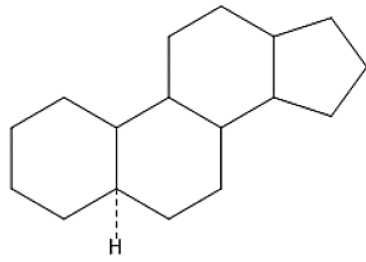
Cholestane Backbone (5 α - Cholestane)



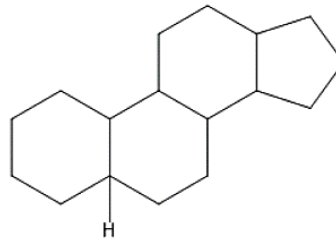
Numbering system for a steroid with reference to **5 α - Cholestane**

- ✓ **heavy dark line** indicates the ring juncture or backbone carbons are shown in the structure of 5 α -cholestane.
- ✓ **α indicates** dash/doted attachment, groups below the plane (α -configuration) and **β indicates** solid attachment, groups above the plane of the nucleus (β -configuration) and if the configuration of substituent is unknown, its bond to the nucleus is drawn as a wavy line.
- ✓ The configuration of the H at C-5 is always indicated in the name.
- ✓ Circles were sometimes used to indicate α -hydrogens and dark dots to indicate β -hydrogens.
- ✓ Compounds with 5 α -cholestane belong to allo-series, while compounds derived from 5 β -cholestane belong to the normal series.
- ✓ If the double bond is not between sequentially numbered carbons, in such cases, both carbons are indicated in the same.
- ✓ When a methyl group is missing from the side chain, this is indicated by the prefix 'nor' with the number of carbon atom, which has disappeared.

A. Gonane Ring (C17)

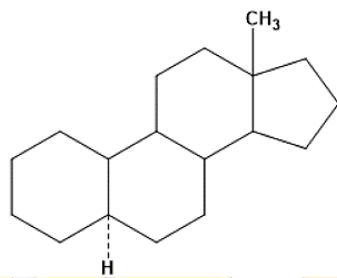


5 α Gonane

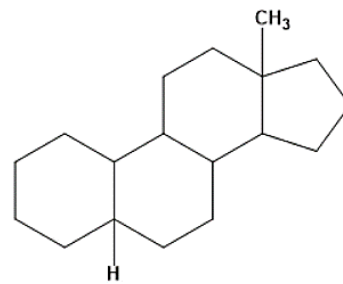


5 β Gonane

B. Estrane (Oestrane) (C18)

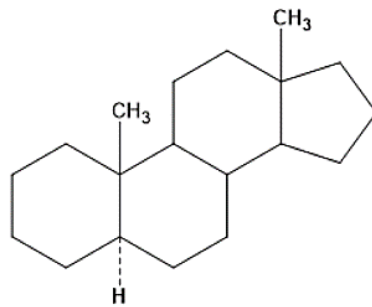


5 α Estrane

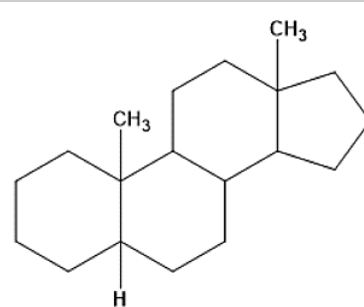


5 β Estrane

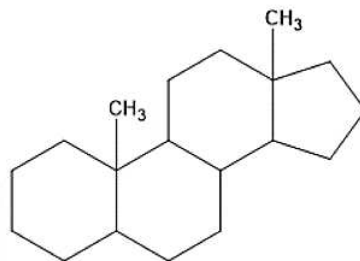
C. Androstane (C19)



5 α Androstane

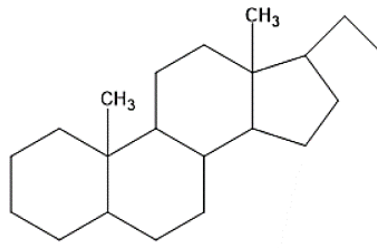


5 β Androstane



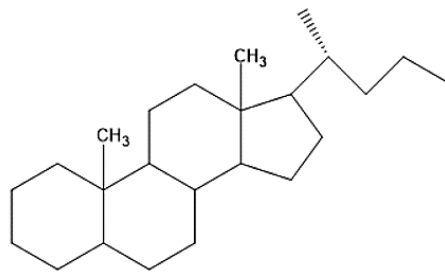
5 α Androstane or 5 β Androstane

D. Pregnane (C21)

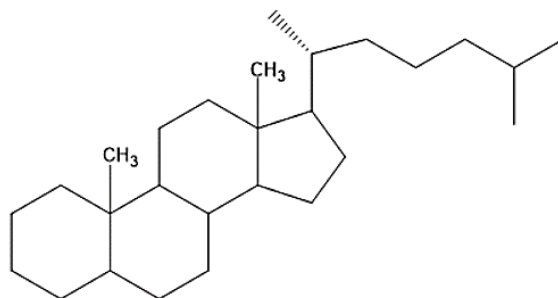


5 (α or β) Pregnane

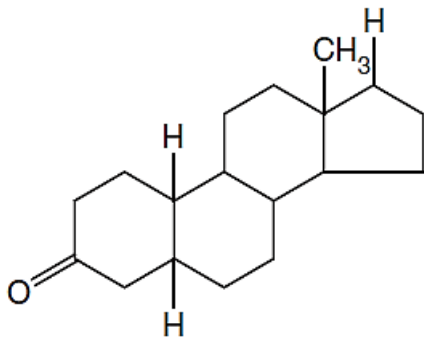
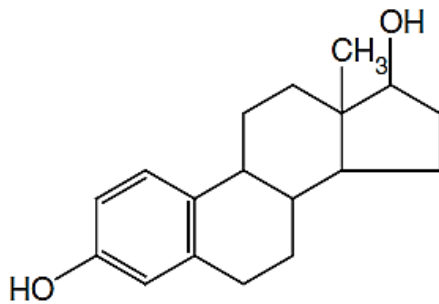
E. Cholane (C24)



F. Cholestane (C27)



Concepts
Phary

Examples:**5 β , 19-nor androst-3-one****17 β estradiol**

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



The symbol Δ is often used to designate a C = C bond in a steroid. If C = C is in between carbons 5 and 4, the compound is referred to as a Δ 4 steroid, and if the C = C bond is between positions 5 and 10, the compound is designated as Δ 5(10) steroid

Pharmacology Concepts
By Rajesh Choudhary

11.2. BIOSYNTHESIS AND METABOLISM

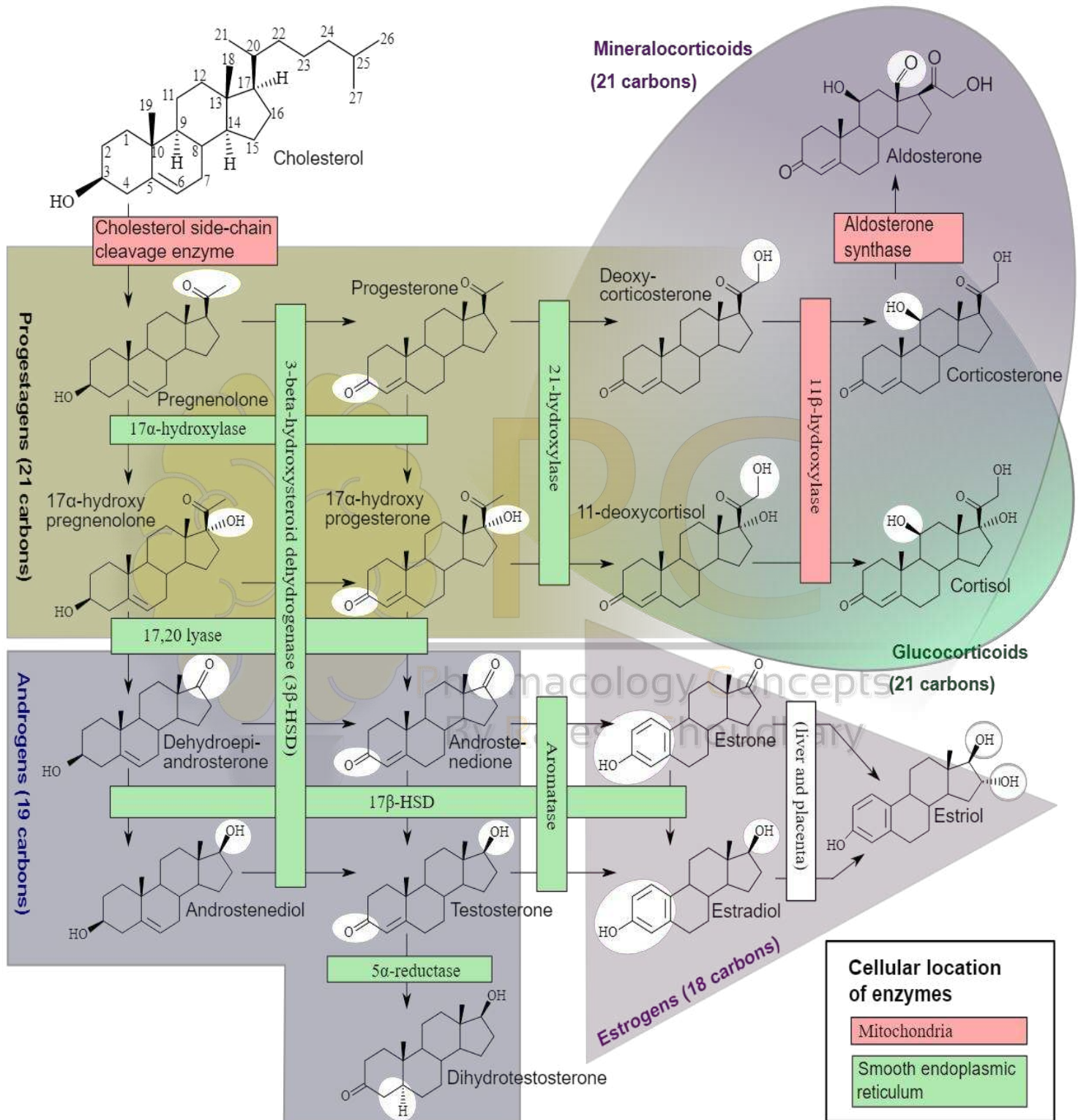


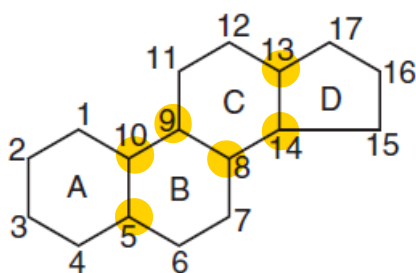
Figure: Synthesis and Metabolism of Hormone

Source: https://en.wikipedia.org/wiki/Inborn_errors_of_steroid_metabolism#/media/File:Steroidogenesis.svg

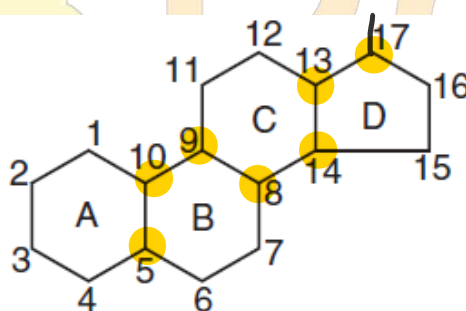
11.3. STEREOCHEMISTRY OF STEROIDS

The 3-dimensional structure of steroids are not planer in shape and they show various types of stereoisomers. Consider the following to understand the stereochemistry:

Optical Isomerism:



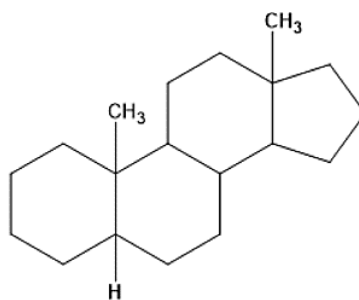
- ✓ Six asymmetric (chiral centre) carbon atom: 5, 8, 9, 10, 13, and 14
- ✓ Possible optical isomer = $2^n = 2^6 = 64$ (gonane, oestrane and Androstane)



- ✓ Seven asymmetric (chiral centre) carbon atom: 5, 8, 9, 10, 13, 14, & 17
- ✓ Possible optical isomer = $2^n = 2^7 = 128$ (pregnane, cholane, and cholestane)

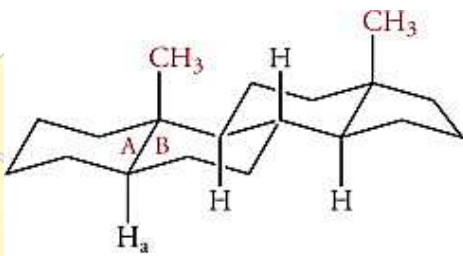
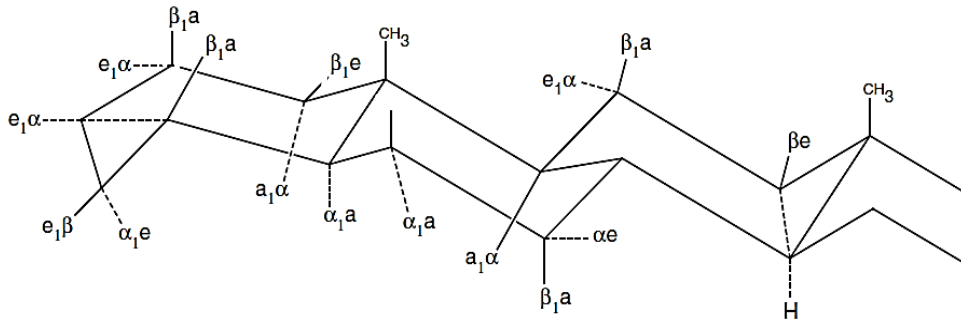
Geometrical Isomerism and Confirmations

- ✓ **Cis and Trans form**
- ✓ **Chair and Boat form**

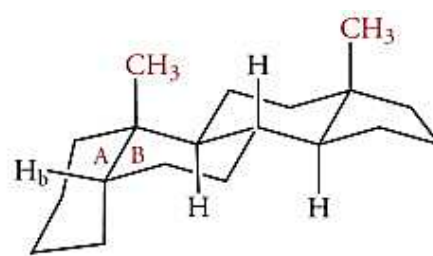


5- β Androstane

The absolute stereochemistry of the molecule and any substituent is shown with solid (β) and dashed (α) bonds; a (axial) bond is perpendicular to the plane of the molecule while equatorial bond (e) is horizontal to the plane of the molecule

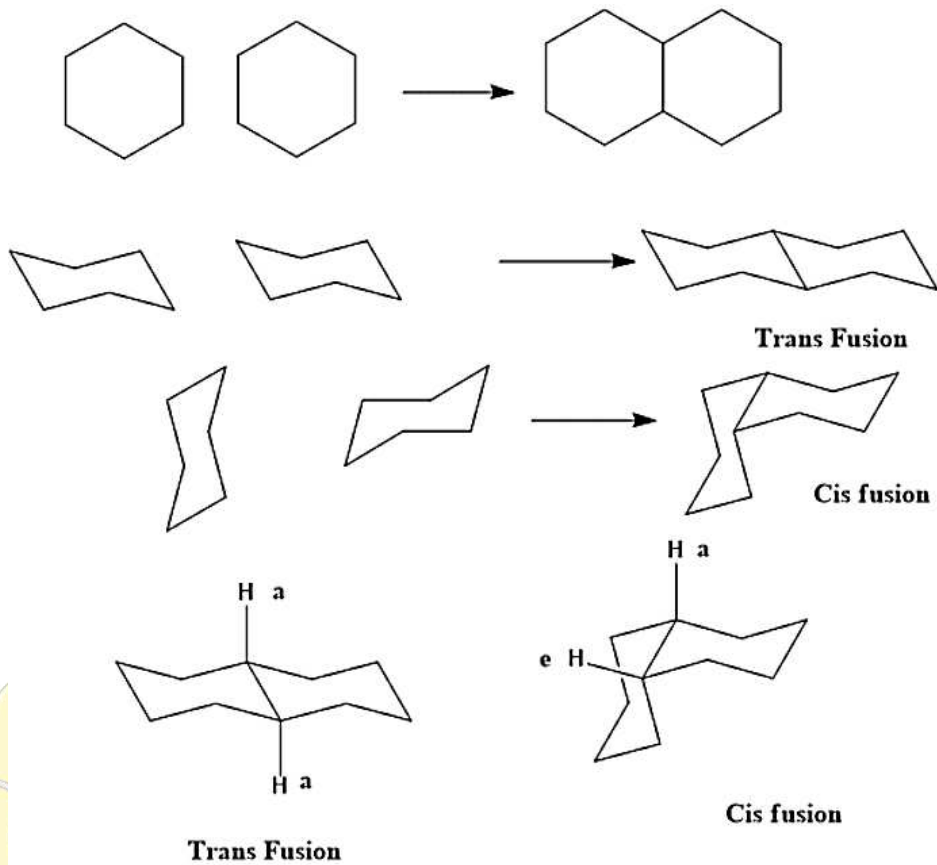


Trans (A/B) ring Junction



Cis (A/B) ring Junction

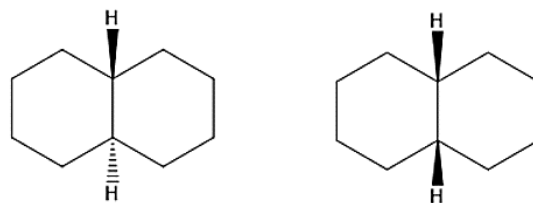
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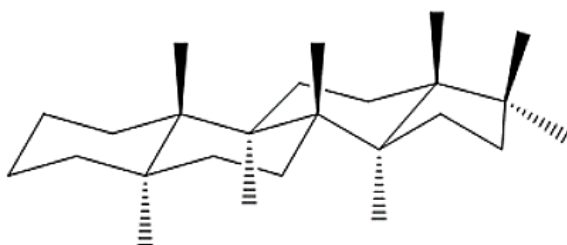
*Here Cis and trans depend on the axial and equatorial bond attachments

Cis: one axial and one equatorial

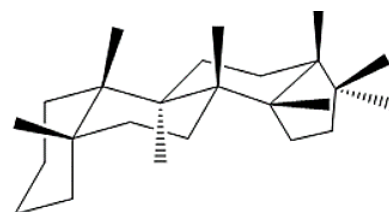
Trans: both axial



Examples:



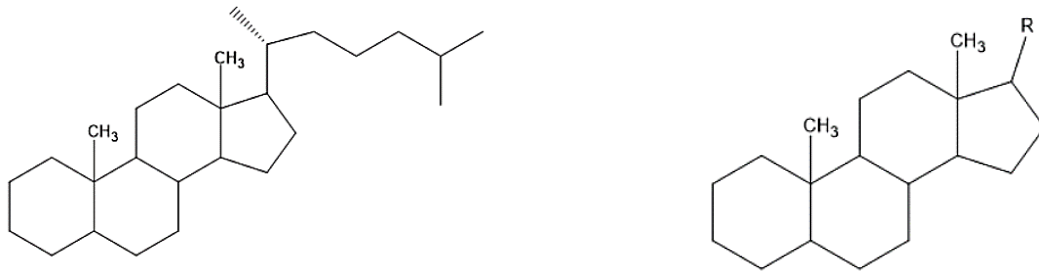
Trans(A/B)-Trans(B/C)-Trans (C/D)



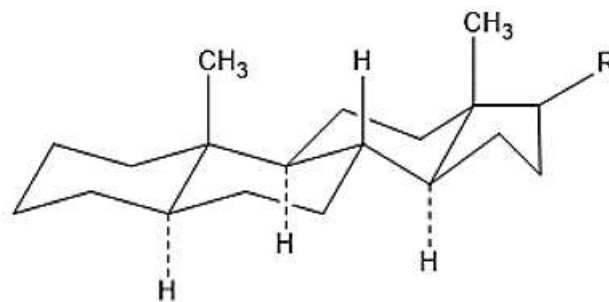
Cis(A/B)-Trans(B/C)-Cis(C/D)

- ✓ Cholestane, androstane, and pregnane can exist in two conformations, that is, chair form and boat form.
- ✓ Most of the naturally occurring saturated steroids belongs to cholestane series or coprostane series.

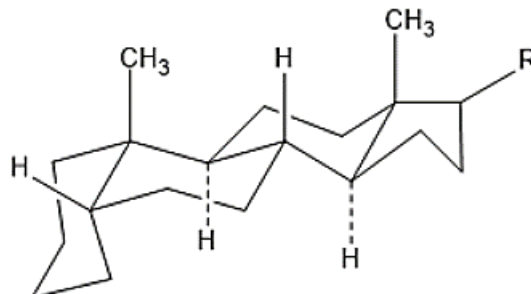
Cholestane ring



Chair confirmation is more stable than boat confirmation due to less angle strain, and hence, all cyclohexane rings in the steroid nucleus exist in the chair confirmation.



5 α Cholestane
Trans(A/B)-Trans(B/C)-Trans (C/D)



5 β Cholestane or Coprostane
Cis(A/B)-Trans(B/C)-Trans (C/D)
