



Prepared by Sarah Q. Foster for Organic Chemistry, NS 313,  
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## Steroid Stereochemistry and Cardiac Glycosides

### Steroids

\* Lipids are classified into 2 major groups

□ fats and waxes (can be hydrolyzed)

□ steroids (cannot be hydrolyzed)

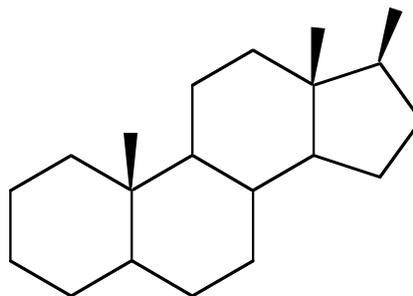
### Basic Structure of Steroids

#### \* Tetracyclic Ring System

-4 rings designated A, B, C, D

(3 hexane rings fused and 1 pentane ring)

-A, B, C rings are in the chair conformation  
but rigidity of the fusion prevents ring flipping



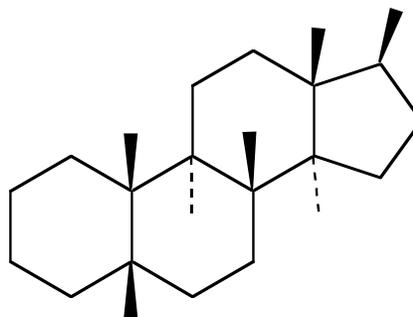
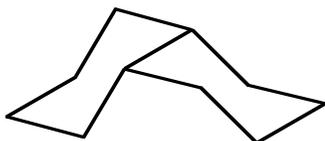
### Stereochemistry of Steroids

#### \*Cis or Trans Ring Fusion

-2 cyclohexane rings can be joined in either cis or trans conformation

Cis- Decalin (“**descalin**” = 2 fused cyclohexane rings)

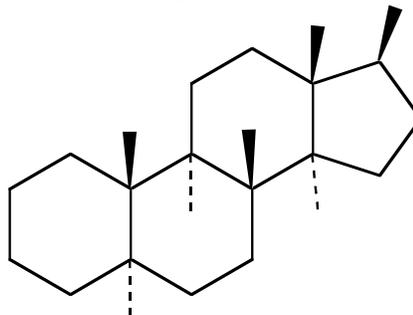
-both **angular** groups (groups at ring junction position) are on the same side of the ring (the □ or “up” side of the ring)



Trans- Decalin

-angular groups are on opposite sides of the ring

-one group on the □ side of the ring and the other on the □ side

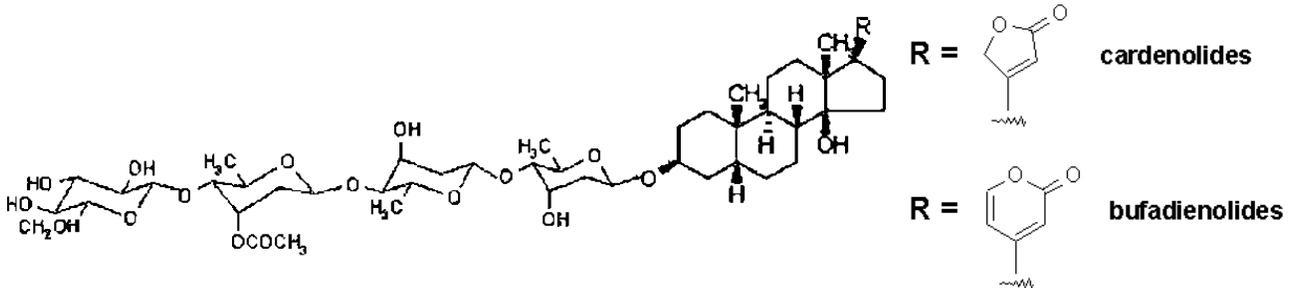


-steroids may have either cis or trans fused A/B rings (trans is more common)

- other ring fusion, B/C and C/D, are usually trans (except for special molecules like cardiac glycosides!)

## Cardiac Glycosides

- naturally occurring group of drugs- depending on dosage may have beneficial or toxic effects
- found in 11 plant families- plants use compounds for defense against herbivores
- 2 major structural features- a glycoside portion (sugar) and an aglycone-steroid portion



- digitalis found in foxglove used in US pharmacies for treatment of heart conditions
- cardiac glycosides increase force of heart muscle contraction by increasing the availability of intracellular  $\text{Ca}^{++}$  ions
- cardiac glycosides inhibit an enzyme that provides necessary energy for the  $\text{K}^+-\text{Na}^+$  exchange to occur in the  $\text{Na}^+-\text{K}^+-\text{ATPase}$  pump
- toxic amounts of cardiac glycosides decrease electric conductivity through the heart causing irregular heart activity

## Important Structural Element of Cardiac Glycosides

- steroid portion of cardiac glycoside molecule has cis fused A/B and C/D rings (B/C is trans fused)
- fused ring system forms a "U" shape
- the activity of the steroid is dependent on that specific conformation
- hydroxyl groups affect the distribution and affect duration of action

