Androstanes

Androsterone was first isolated by Adolf Butenandt in 1931 from the extraction of 15,000 liters of urine. Approximately 15 milligrams of material was isolated and characterized as the below structure. The structure has two methyl groups at the 10 and 13 positions, a ketone functionality at the 17 position and an alpha (α) hydroxyl group at the 3 position. This type of structure is characteristic of an androstane skeleton, which has two beta (β) methyl groups at the 10 and 13 positions. Another example of this type of skeleton is testosterone. Testosterone differs from androsterone by a double bond between positions 4 and 5, a ketone at position 3 and an alcohol at position 17. Male steroidal hormones have the androstane skeleton.



Androsterone 3α -hydroxyandrostan-17-one

Testosterone 17β-hydroxyandrost-4-en-3-one

Estranes

Estradiol was first isolated in 1929 from the extraction of 4 tons of hog ovaries. Approximately 12 milligrams of material was isolated and characterized as the below structure. The structure consists of an aromatized A ring, alcohol functionalities at positions 3 and 17 and a methyl group at position 13. This is characteristic of an estrane skeleton, which has a beta (β) methyl group at the 13 position. Female steroidal hormones have the estrane skeleton. Another example of this type of skeleton is estrone, in which the alcohol at position 17 is oxidized to a ketone.







Estradiol Estra-1,3,5-trien-3,17β-diol Estrane skeleton

Estrone

Pregnanes

Progesterone is a hormone whose levels are elevated during pregnancy in females. Its structure has the pregnane skeleton, which has two methyl groups at positions 10 and 13 and a two carbon chain at position 17. Progesterone differs from testosterone by having the side chain of two carbons at position 17.



Cortisone is a hormone of the adrenal glands that is used medically to relieve inflammation. Cortisone is a highly oxidized steroid, containing a variety of functional groups including ketones, double bonds and alcohols.



Cholestanes

Cholesterol is a major steroid found in membranes of animals, and is a precursor to a variety of other steroid structures. Cholesterol has an alcohol at the 3 position and double bond between the 4 and 5 positions and a functionalized side chain as shown below.





Cholestane skeleton

Cholesterol

Preparation of Ketones and Aldehydes from Alkenes

Ozonolysis





Examples:

Zn

O₃



1-methylcyclopentene

5-oxohexanal



Preparation of Ketones and Aldehydes from Alkynes

Addition of water to acetylenes (Markovnikov)



Mechanism:



The keto form (e.g. acetone above) is generally more stable than the enol form Note that for phenol, the enol form is much preferred to the keto form:



Addition of water to acetylenes (via boranes – overall anti-Markovnikov)



propyne

propanal

Preparation of Ketones and Aldehydes from Alcohols

Oxidation of Alcohols



[H] = reduction; addition of electrons

There are many reagents that can be used for this reaction. Only three are given in this course:

- Pyridinium chlorochromate (PCC)
 forms ketones and aldehydes
- 2) Chromic acid (Jones reagent) H₂CrO₄
 forms ketones only; aldehydes are further oxidized to carboxylic acids
- Swern oxidation oxalyl chloride, dimethyl sulfoxide (DMSO), triethylamine
 forms ketones and aldehydes

1. PCC



PCC needs an H to work (i.e., 1° or 2° alcohol but not 3° alcohols).

Examples:



(no H) *tert*-butyl alcohol 2-methyl-2-propanol



2. H₂CrO₄, same as chromic acid, Jones reagent

This reagent is orange, and as it reacts it becomes green. It turns secondary alcohols into ketones, and primary alcohols into carboxylic acids. Primary alcohols first form aldehydes, but the reagent quickly reacts with the aldehyde to from the carboxylic acid. Tertiary alcohols are inert.

Secondary Alcohol:

$$\begin{array}{ccc} & & & O \\ H_2 CrO_4 & & \parallel \\ R - CHOH - & & R - C - R' \\ & & \\ R' & & \\ \end{array}$$

Primary Alcohol:

$$\operatorname{RCH}_{2}\operatorname{OH} \xrightarrow{\operatorname{H}_{2}\operatorname{CrO}_{4}} \begin{bmatrix} O \\ B \\ - C \\ - H \end{bmatrix} \xrightarrow{\operatorname{H}_{2}\operatorname{CrO}_{4}} \begin{bmatrix} O \\ B \\ - C \\ - H \end{bmatrix}$$



The Swern Oxidation is fairly mild and <u>will oxidize primary alcohols to aldehydes</u> and secondary alcohols to ketones.



If benzyl alcohol were treated with Jones reagent, the result would be benzoic acid.



Preparation of Aldehydes from Acid Halides

