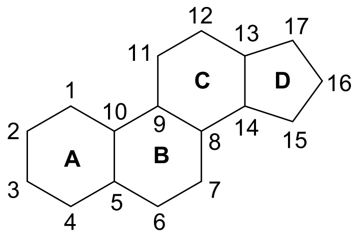
RECALL:

Steroids

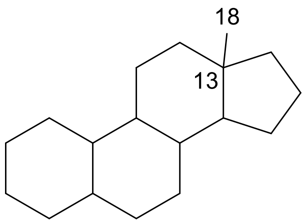


Steroid Skeleton

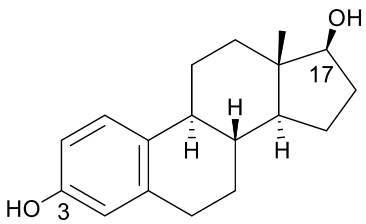
Groups above: β (beta)

Groups below: α (alpha)

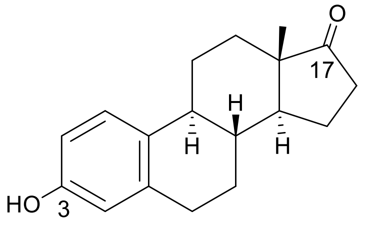
Types of Steroids



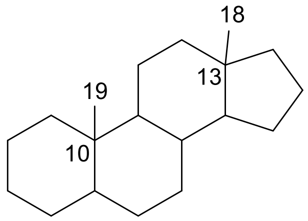
Estrane
Characterized by a methyl group in C13



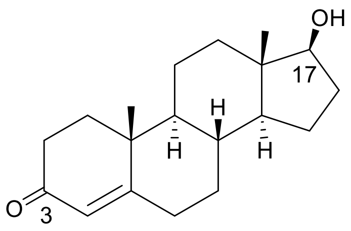
Estradiol



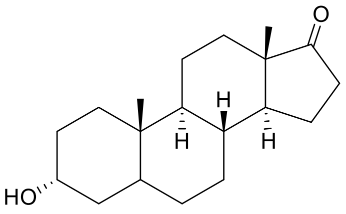
Estrone



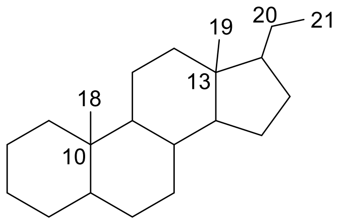
Androstane
Characterized by the presence of $-CH_3$ groups in C10 and C13



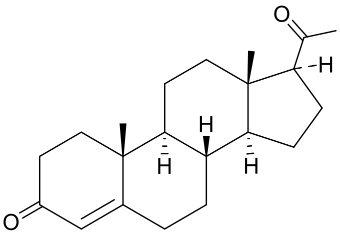
Testosterone



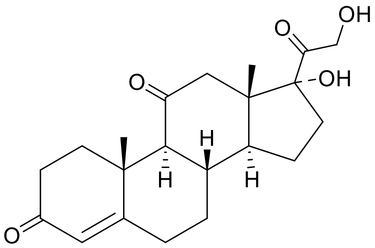
Androsterone



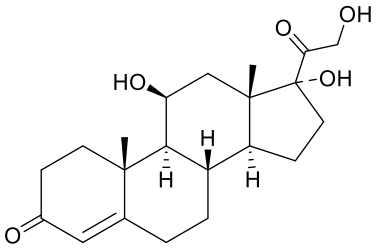
Pregnane
- Characterized by two -CH_3 groups in C10 and C13, and a substituent in C17.
- Not biologically active



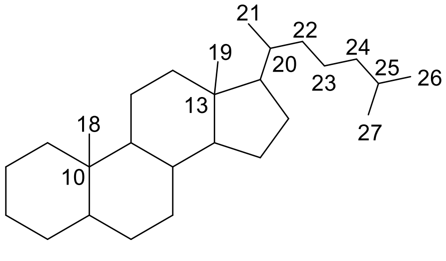
Progesterone
Pregnancy Hormone



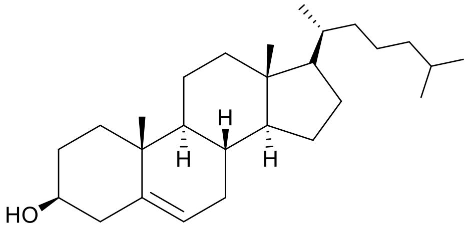
Cortisone
(Adrenocorticoid)
Characterized by a carbonyl at C11 and pregnane skeleton



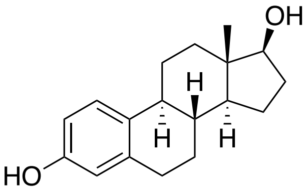
Cortisol
Stress Hormone



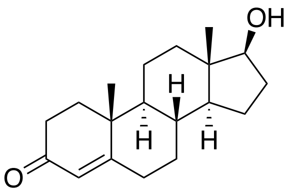
Cholestane



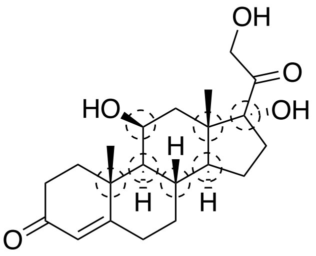
Cholesterol



Estradiol
-Female sex hormone



Testosterone
-Male sex hormone



Cortisol
-Stress hormone

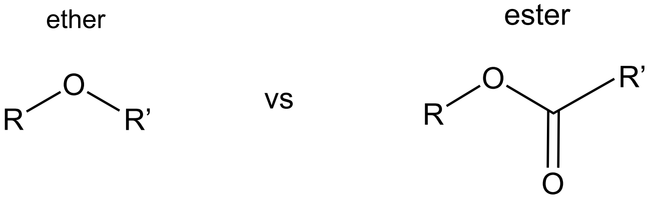
◌ Stereogenic centers

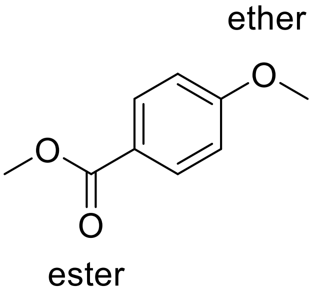
Ethers

- Unreactive to base
- Not miscible with H_2O

Recall:

Ethers are unreactive except in strongly acidic conditions (e.g. H_2SO_4) to undergo SN or E
The difference between ester and ethers

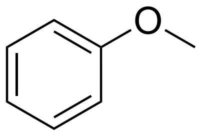




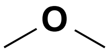
Nomenclature:

- In the absence of other functional groups, name the two alkyl groups attached to the O and add the word “ether”

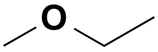
Examples:



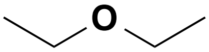
methyl phenyl ether



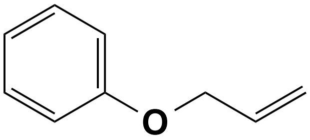
dimethyl ether



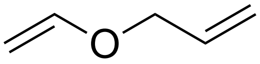
methyl ethyl ether



diethyl ether
ethyl ether
ether

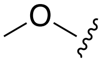


phenyl allyl ether

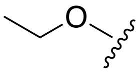


allyl vinyl ether

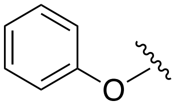
In the presence of other functional groups, name ethers as a group, drop "yl" and add "oxy" as seen below:



methoxy



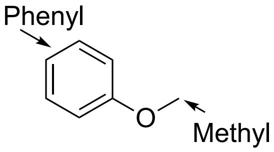
ethoxy



phenoxy

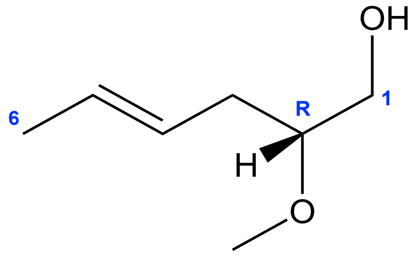
Naming Examples

Example 1:



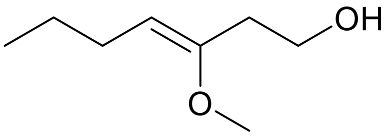
Methyl phenyl ether

Example 2:



(E)-*R*-2-methoxyhex-4-en-1-ol

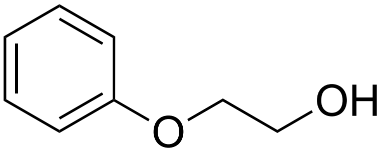
Example 3:



(Z)-3-methoxyhept-3-en-1-ol

- Alcohol (-OH) takes priority over other functional groups
- Number the longest C chain so as to give the OH group the lowest number possible

Example 4:



2-phenoxyethan-1-ol
or
2-phenoxy-1-ethanol

Alcohols

Physical Properties of Alcohols

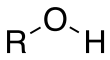
- The hydroxyl group is a very polar group. This allows small alcohols (methanol, ethanol, propanols) to be miscible with water (if the number of C < 4) as they are good hydrogen bond donors *and* acceptors.
- Soluble in H_2O, as the #C increases, the solubility decreases.
- Alcohol densities are usually $\rho < 1.0$ g/cm^3.

- They have high boiling and melting points, again due to their hydrogen bonding capabilities.

Look at the following comparisons:

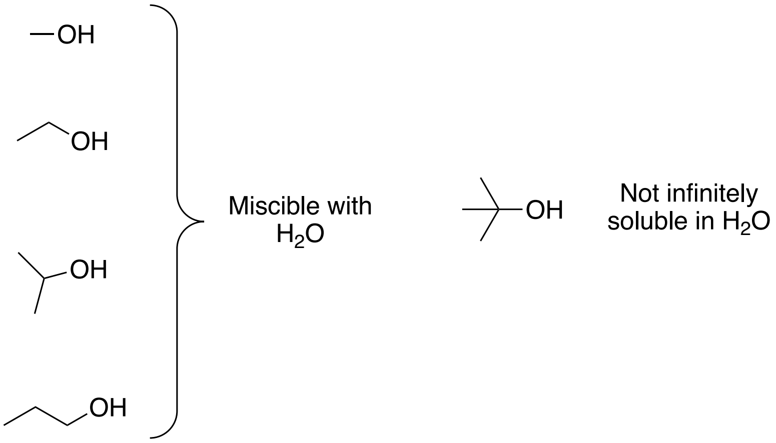
Name	Methanol	Ethane	Ethanol
Formula	CH_3OH	CH_3CH_3	CH_3CH_2OH
Molecular Weight (g/mol)	32	30	46
Boiling Point (° C)	65	-89	78.5
State (at room temp)	liquid	gas	liquid

Ethane has almost the same molecular weight as methanol. However, the boiling point is much lower than methanol. Methanol molecules like to stick together via H-bonding while ethane molecules interact with each other via hydrophobic interactions.



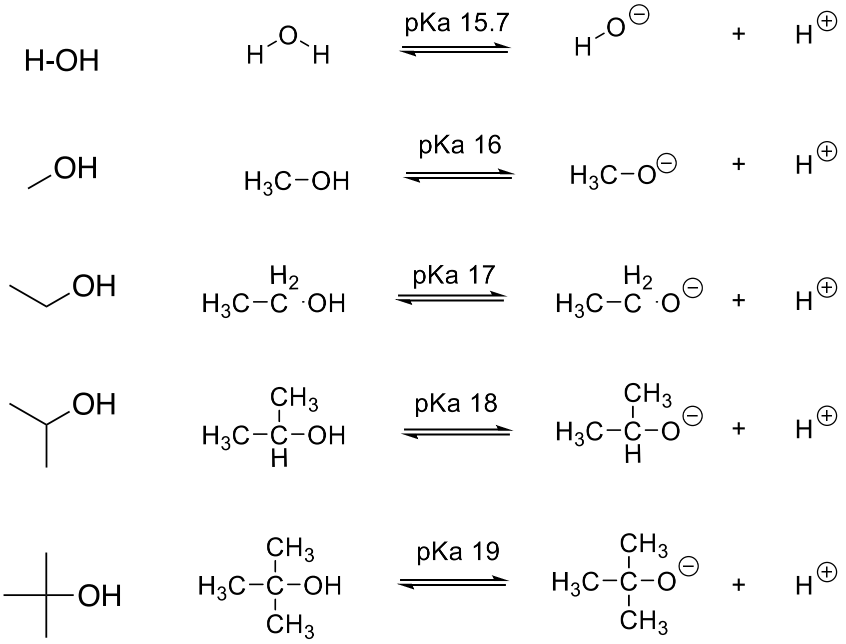
O-H bond - easy to break
R-O bond - hard to break; always needs a strong acid to break and can proceed either S_N-1 / S_N-2, or E1 / E2

Miscibility of Alcohols with Water

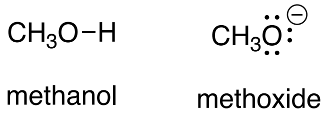


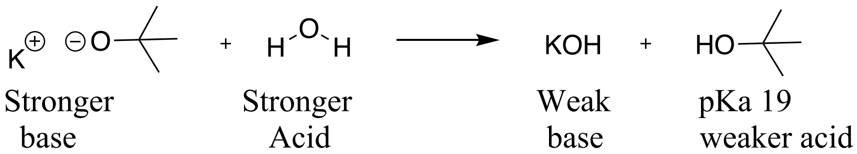
*butanol is soluble in H_2O but not miscible

Acidity of R–OH

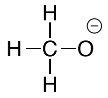


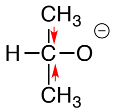
- pKa depends on conjugated base stability
- Harder to make a t-butoxide than methoxide. The alkyl group donates electron density to the C–O bond and destabilizes the negative charge (less favorable).





Methoxide vs. Isopropoxide:


Methoxide
An alkoxide

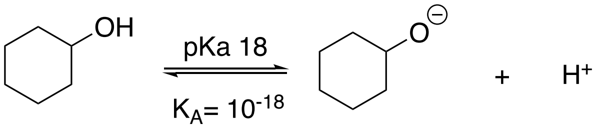


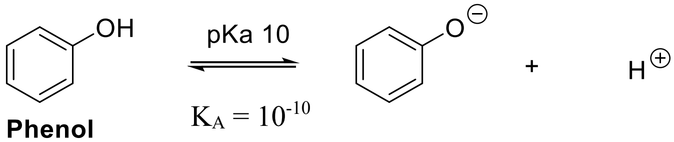
Isopropoxide
Less stable

Alkyl groups donate electrons through single bonds, destabilizing the negative charge (Inductive Effect), therefore, isopropoxide is less stable than methoxide

- Inductive effect – donation or withdrawal through single bonds

Conjugated/Aromatic R–OH

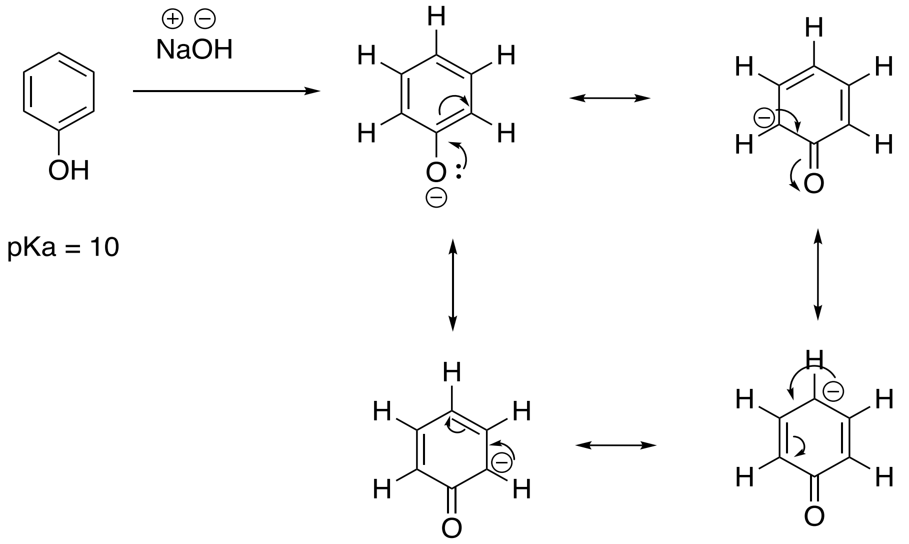




Phenol

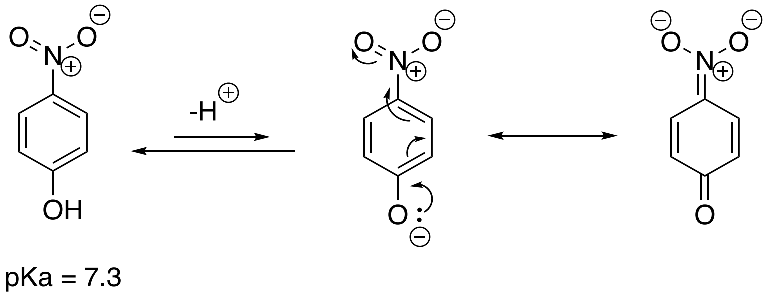
- More acidic than H_2O
- Resonance (resonance effect) takes electron density away from the O atom, resulting in stabilization of the negative charge.
- Resonance effect is strong through π system

Example 1: Phenol



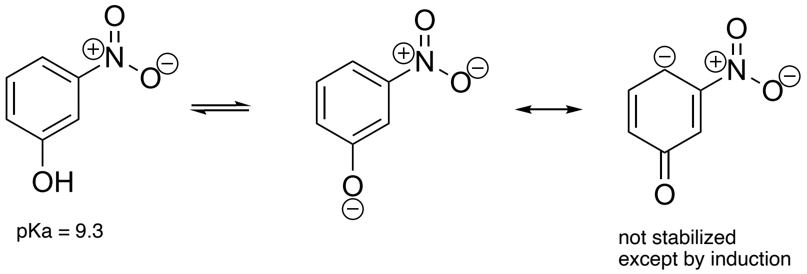
The alkoxide of phenol is a conjugated anion and is therefore much more acidic

Example 2: *p*-Nitrophenol



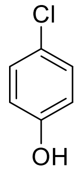
p-Nitrophenol is more acidic than phenol because on top of the resonance forms that phenol contains, *p*-nitrophenol also contains the above extra resonance form, making the proton on the alcohol even more acidic.

Example 3: *m*-Nitrophenol

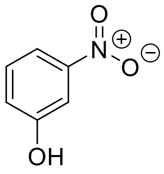


Less acidic than *p*-nitrophenol because there is less stabilization of the negative charge. The negative charge is not conjugated with the nitro group double bond.

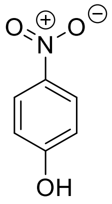
More examples:



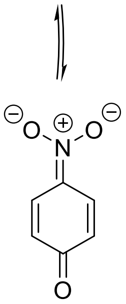
pKa 9.3
Cl is electron withdrawing so helps stabilize negative charge

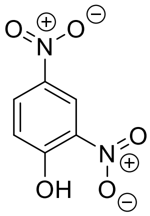


pKa 9.3

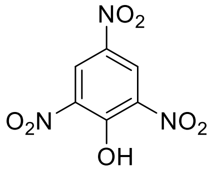


pKa 7





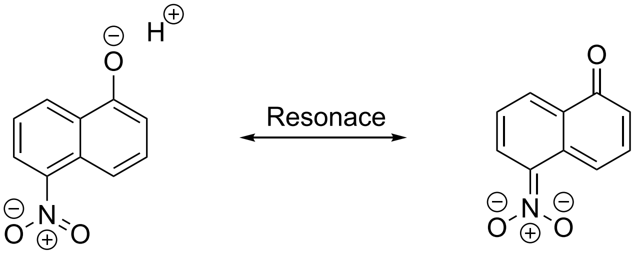
pKa 4.5



pKa 0.5

- As you get more resonance possibilities, the negative charge is more spread out across the molecules, and is more stabilized, resulting in lower pKa (more acidic).

Resonance Practice:

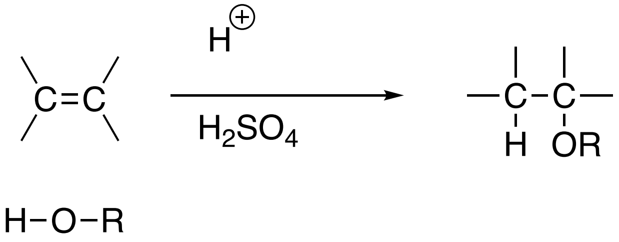


Can you push the arrows to obtain both products?

Addition Reactions:

Hemiacetal and Acetal Formation

Recall addition reaction across a double bond (i.e., ether formation)



Similarly, addition reactions can be done on carbonyls (Ketones and Aldehydes) in the presence of an acid catalyst: