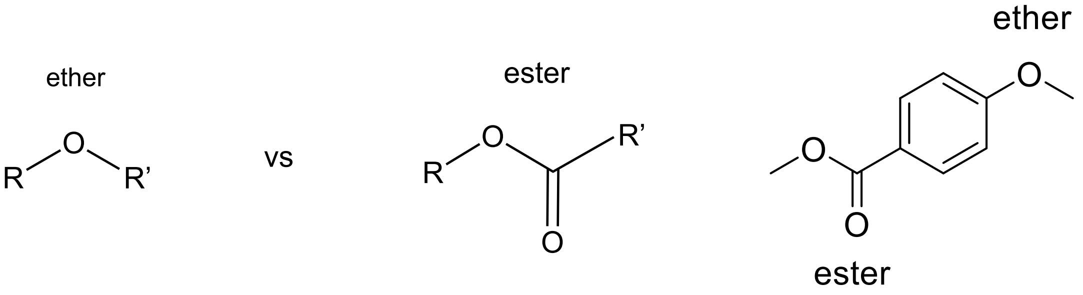
## Ethers

- Unreactive to base
- Not miscible with $H_2O$

**Recall:**

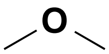
Ethers are unreactive except in strongly acidic conditions (e.g. $H_2SO_4$) to undergo SN or E
The difference between ester and ethers



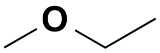
**Nomenclature:**

- In the absence of other functional groups, name the two alkyl groups attached to the O and add the word "ether"
- Low priority than alcohol
- Common name group add 'ether'

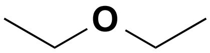
**Examples:**



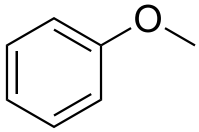
**dimethyl ether**



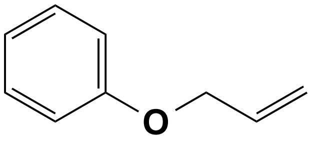
**methyl ethyl ether**



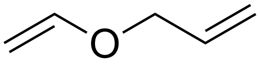
**diethyl ether**
**ethyl ether**
**ether**



methyl phenyl ether

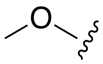


**phenyl allyl ether**

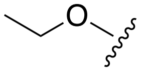


allyl vinyl ether

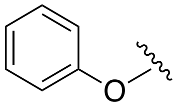
In the presence of other functional groups, name ethers as a group, drop "yl" and add "oxy" as seen below:



methoxy



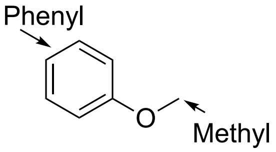
ethoxy



phenoxy

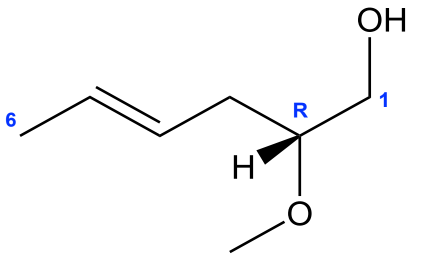
## Naming Examples

### Example 1:

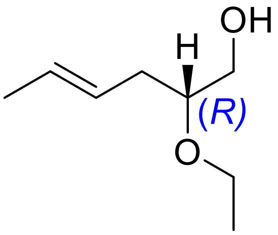


Methyl phenyl ether

### Example 2:

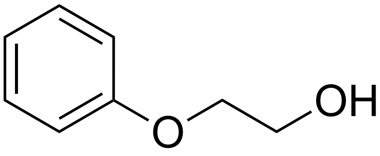


*(E)*-*R*-2-methoxyhex-4-en-1-ol



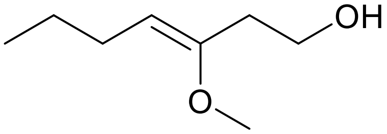
*(E)*-*R*-*2*-ethoxyhex-4-en-1-ol

**Example 3:**



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

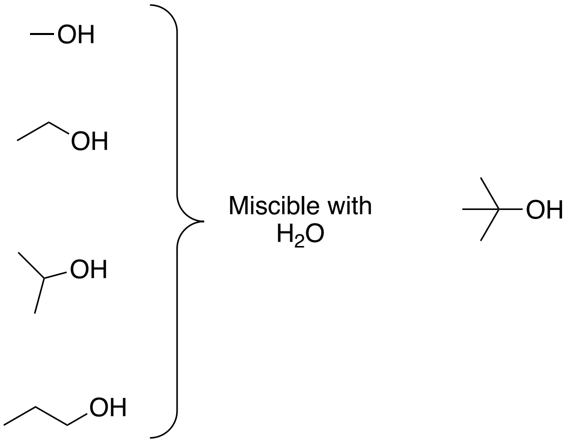
**Example 4:**



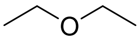
**(Z)-3-methoxyhept-3-en-1-ol**

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

**Alcohols**
**Miscibility of Alcohols with Water**



***in contrast to tert-butanol above (miscible in water) n-butanol is soluble in $H_2O$ but not miscible**



Diethyl ether – not miscible with water (density < 1.0 g/cm$^3$)

**Physical Properties of Alcohols**

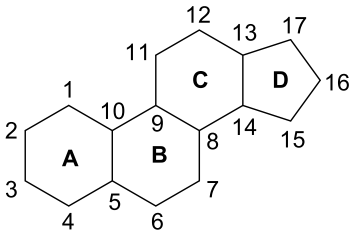
- The hydroxyl group is a very polar group. This allows small alcohols (methanol, ethanol, propanols) to be miscible with water (if the number of $C < 4$) as they are good hydrogen bond donors *and* acceptors.
- Soluble in $H_2O$, as the #C increases, the solubility decreases.
- Alcohol densities are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

## Steroids

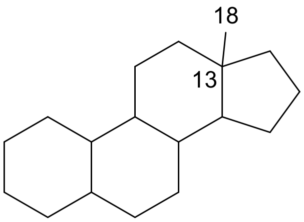


**Steroid Skeleton**

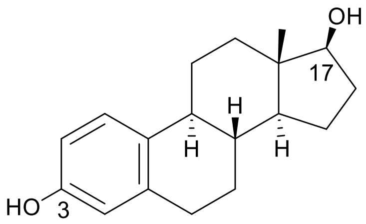
**Groups above:** β (beta)

**Groups below:** α (alpha)

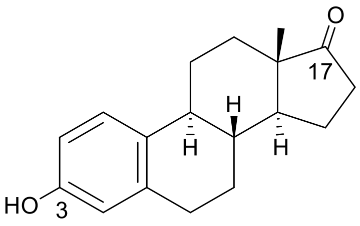
**Types of Steroids**



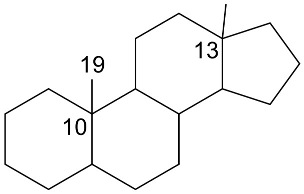
**Estrane**
Characterized by a methyl group in C13



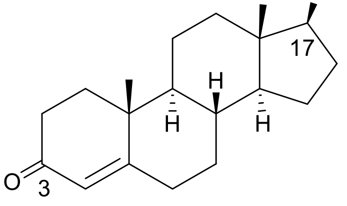
**Estradiol**



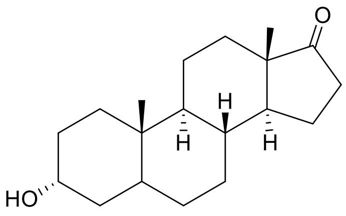
**Estrone**



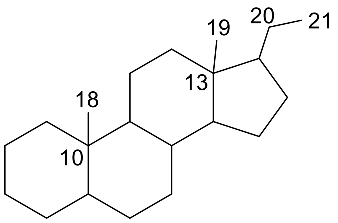
**Androstane**
Characterized by the presence of -$CH_3$ groups in C10 and C13



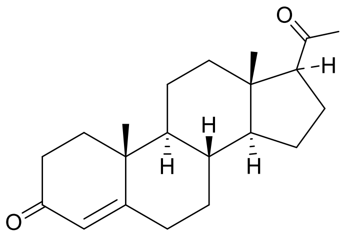
**Testosterone**



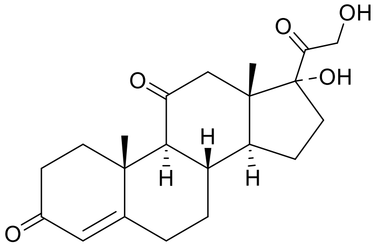
**Androsterone**



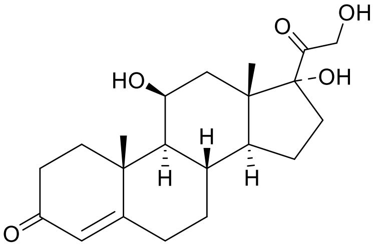
**Pregnane**
- Characterized by two -$CH_3$ groups in C10 and C13, and a substituent in C17.
- Not biologically active



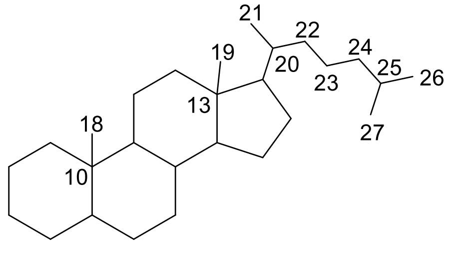
**Progesterone**
Pregnancy Hormone



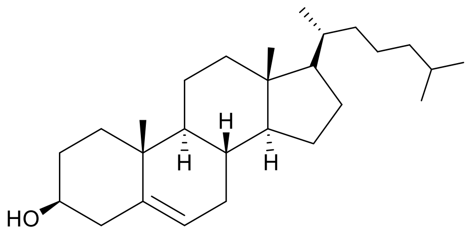
**Cortisone**
(Adrenocorticoid)
Characterized by a carbonyl at C11 and pregnane skeleton



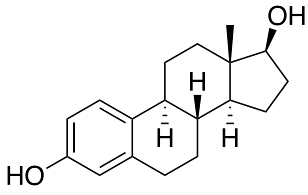
**Cortisol**
Stress Hormone



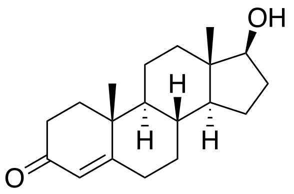
**Cholestane**



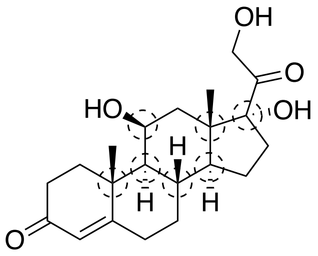
**Cholesterol**



Estradiol
-Female sex hormone

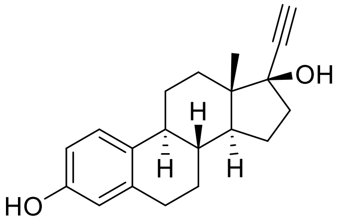


Testosterone
-Male sex hormone



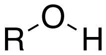
Cortisol
-Stress hormone

◌ Stereogenic centers



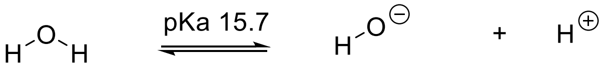
Ethinylestradiol a birth control drug

**Alcohol**



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
The pKa of hydrogen > 16
Base can remove $H^+$

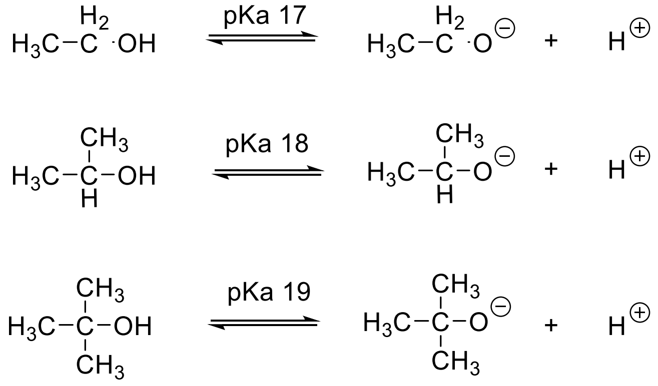
**R-O-R (Ether)**
O-R bond is hard to break
Never with base
Always acid $H_2SO_4$ for $S_N$ and E reactions
**Acidity of R–OH**



$$\mathrm{Ka} = \frac{[H^+][OH^-]}{[\mathrm{H2O}]} = 10^{-15.7} \rightarrow \mathrm{pKa} = -\log\mathrm{Ka} = 15.7$$

$$H_3C{-}OH \xrightleftharpoons{\text{pKa 16}} H_3C{-}O^{\ominus} \quad + \quad H^{\oplus}$$

$$\mathrm{Ka} = \frac{[\mathrm{H}^+][CH3O^-]}{[\mathrm{CH3OH}]} = 10^{-16} \rightarrow \mathrm{pKa} = -\mathrm{logKa} = 16$$

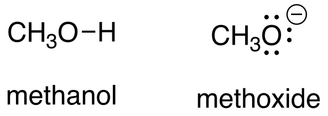


$$H_3C-\overset{H_2}{C}-OH \underset{}{\overset{\text{pKa 17}}{\rightleftharpoons}} H_3C-\overset{H_2}{C}-O^{\ominus} + H^{\oplus}$$

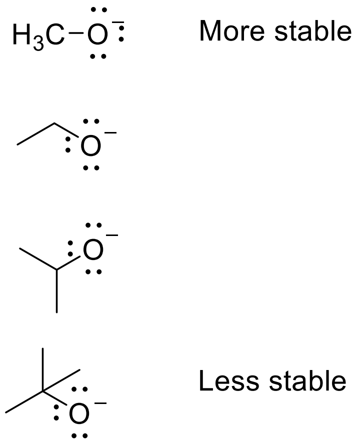
$$H_3C-\underset{H}{\overset{CH_3}{C}}-OH \overset{\text{pKa 18}}{\rightleftharpoons} H_3C-\underset{H}{\overset{CH_3}{C}}-O^{\ominus} + H^{\oplus}$$

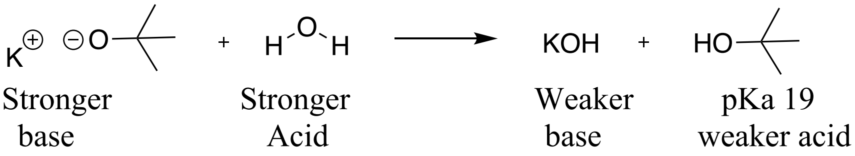
$$H_3C-\underset{CH_3}{\overset{CH_3}{C}}-OH \overset{\text{pKa 19}}{\rightleftharpoons} H_3C-\underset{CH_3}{\overset{CH_3}{C}}-O^{\ominus} + H^{\oplus}$$

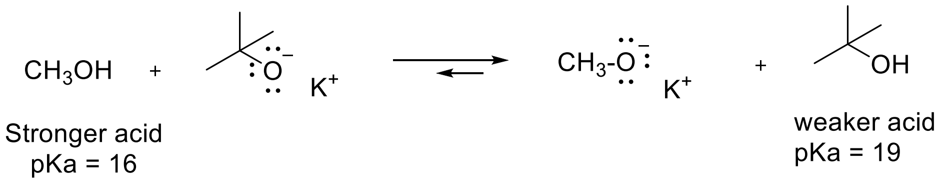
- pKa depends on conjugated base stability
- Harder to make a t-butoxide than methoxide. The alkyl group donates electron density to the C–O bond and destabilizes the negative charge (less favorable).



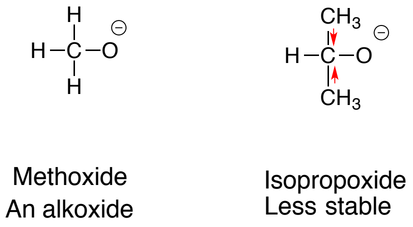
### Stability of anions







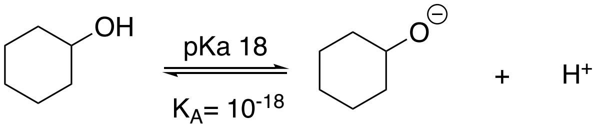
**Methoxide vs. Isopropoxide:**

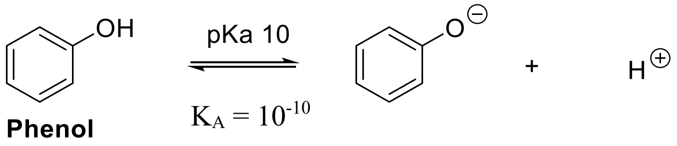


Alkyl groups donate electrons through single bonds, destabilizing the negative charge (Inductive Effect), therefore, isopropoxide is less stable than methoxide

- Inductive effect – donation or withdrawal through single bonds

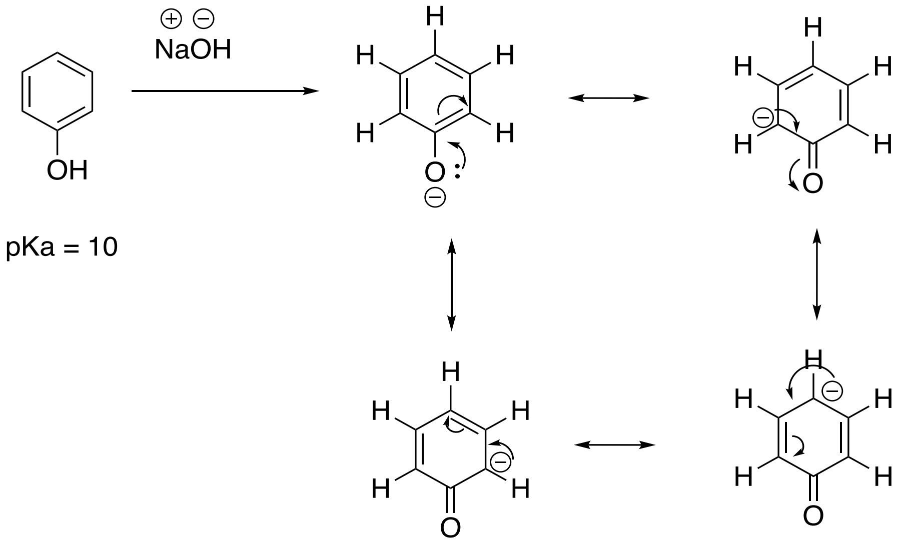
## Conjugated/Aromatic R–OH





- 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