Consider Acidity and Basicity   Recall carboxylic acids and amines (base).
        Jones: p 237-8; 149, 291, 822-826, 1086-1090, 958-963, 878-882
General terms:
        Lewis acid: capable of accepting an electron pair to form a covalent bond.
                        prototype example: **BF_3** empty orbital in valence shell

        Lewis base: capable of donating an electron pair to form a covalent bond.
                        prototype example: **$:NH_3$** low energy non-bonding electrons

In simplest case, non-bonding electron pair on Lewis base engages in overlap with empty atomic orbital
        on Lewis acid to form a "coordinate covalent bond".

Bronsted acid: capable of delivering a proton (special acid)
        e.g., **HCl**

Bronsted base: capable of accepting a proton
        e.g., **NaOH** and **NH_3**

In general: **How does the structure of a molecule affect its acidity/basicity?**

Define: equilibrium acidity:

$$H\text{-}A \rightleftharpoons H^+ + A^- \qquad\qquad K_{eq} = K_a = \frac{[H^+][A^-]}{[HA]}$$

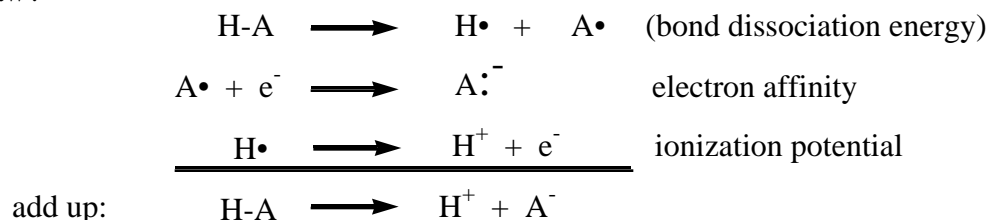If the free energy (G) of the products is equal to the free energy of the reactants, $K_{eq} = 1$
        If the products have a larger - G, more stable, and $K_{eq} > 1$
        If the reactants have a larger - G, reactants are more stable and $K_{eq} < 1$

Usually express acidity in terms of pK_a, negative log of K_a.

What are the factors which influence the pK_a?

Remember Hess's law?

$$H\text{-}A \longrightarrow H\bullet + A\bullet \quad \text{(bond dissociation energy)}$$
$$A\bullet + e^- \longrightarrow A\overset{\bullet\,-}{:} \qquad \text{electron affinity}$$
$$\underline{H\bullet \longrightarrow H^+ + e^- \qquad \text{ionization potential}}$$
$$\text{add up:} \quad H\text{-}A \longrightarrow H^+ + A^-$$

more electronegative: **higher** electron affinity (more easily form A⁻; less easily add H⁺ to A⁻)
stronger H-A bond: **higher** BDE and less easy to ionize
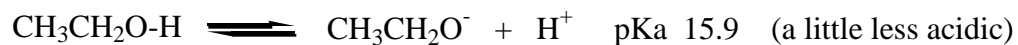
Compare acidity (ease of ionization):

	H-F	H-OH	H-NH$_2$	H-CH$_3$
pKa	3.2	15.7	ca 35	>55
EN	4.0	3.4	3.0	2.5

Electronegativity has a big effect
(bond energies are similar, except the H-F bond is unusually strong)
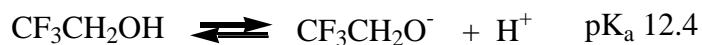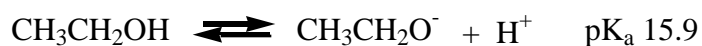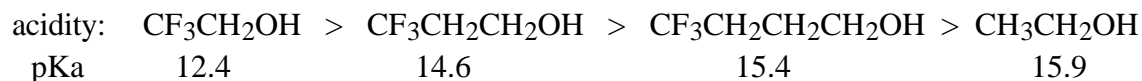
Bond dissociation energies can dominate:

	H-F	H-Cl	H-Br	H-I
BDE	135	103	88	71
EN	4.0	3.2	3.0	2.7
pKa	3.2	-7	-9	-9.5

H-OH $\rightleftharpoons$ H$^+$ + HO$^-$ pKa 15.7

CH$_3$CH$_2$O-H $\rightleftharpoons$ CH$_3$CH$_2$O$^-$ + H$^+$ pKa 15.9   (a little less acidic)

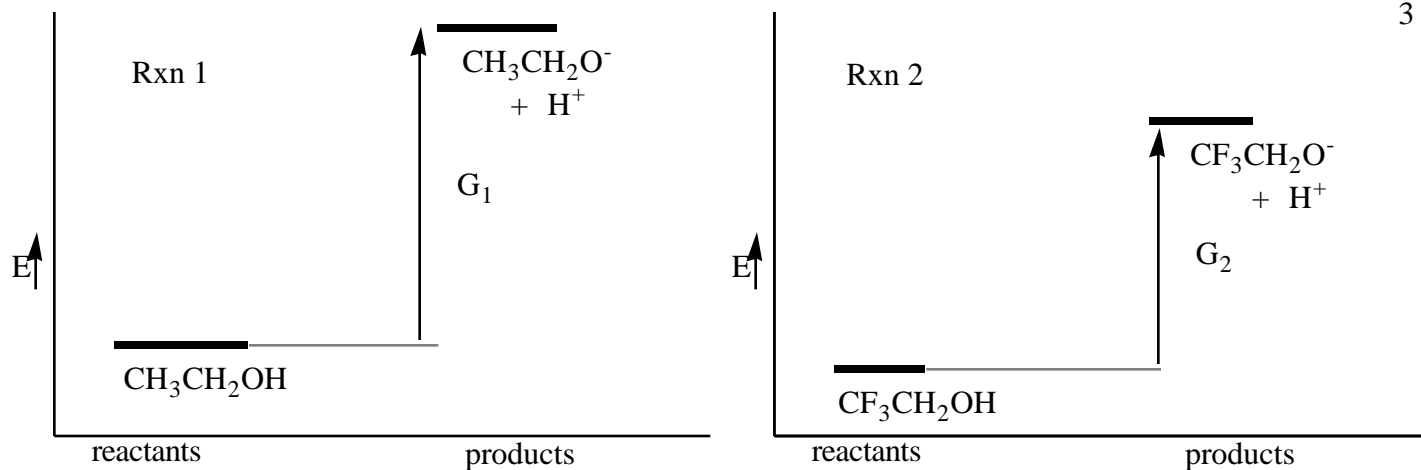CH$_3$CH$_2$O-H $\rightleftharpoons$ CH$_3$CH$_2$O$^-$ + H$^+$ pKa 15.9   (a little less acidic)

ethoxide anion, the conjugate base of ethyl alcohol

Therefore: If mix NaOH with CH$_3$CH$_2$OH,
get approx. equal amounts of NaOH, NaOCH$_2$CH$_3$, H$_2$O, CH$_3$CH$_2$OH

Consider:

acidity: CF$_3$CH$_2$OH > CF$_3$CH$_2$CH$_2$OH > CF$_3$CH$_2$CH$_2$CH$_2$OH > CH$_3$CH$_2$OH
pKa   12.4   14.6   15.4   15.9

CH$_3$CH$_2$OH $\rightleftharpoons$ CH$_3$CH$_2$O$^-$ + H$^+$ pK$_a$ 15.9

CF$_3$CH$_2$OH $\rightleftharpoons$ CF$_3$CH$_2$O$^-$ + H$^+$ pK$_a$ 12.4

Rxn 1

$CH_3CH_2O^-$
+ H^+

G_1

E

CH_3CH_2OH

reactants   products

Rxn 2

$CF_3CH_2O^-$
+ H^+

G_2

E

CF_3CH_2OH

reactants   products

$G_1 >$ G_2 Therefore, $pK_a(1)$ is $> pK_a(2)$

ethyl alcohol is a weaker acid compared to 2,2,2-trifluoroethyl alcohol

$G = 2.3RT\ [pK_a(1) - pK_a(2)]$ $=$ $(2.3)\ (2.0\ cal\ mol^{-1}\ K^{-1})\ (300^oK)\ (15.9-12.4)\ =$

ca 5000 cal/mol or 5 kcal/mol

$R = 8.31\ J\ mol^{-1}\ K^{-1}$ or $2.0\ cal\ mol^{-1}\ K^{-1}$ Assume room temperature, 300^oK

Now: **Why?**   What is responsible for the 5 kcal/mol lower energy difference?
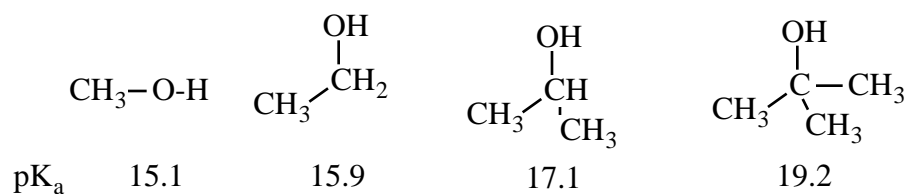
Approximation: the concentration of charge in the anion is a dominant factor in determining whether proton
loss is more-or-less favorable.

Analyze factors which influence the product after de-protonation: inductive effects
electronegativity

Focus on the ALKOXIDE ANION.   (other differences are parallel--
breaking O-H bond in both cases, no serious structural change, etc)

CF_3CH_2OH is more acidic than CH_3CH_2OH due to the inductive effect of the F substituent:

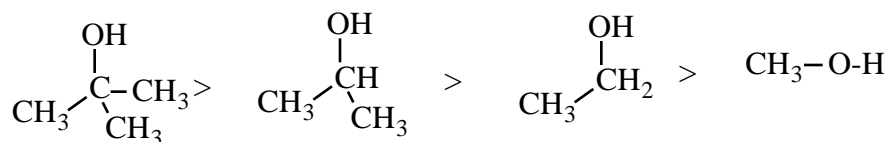Very electronegative F draws electrons from adjacent carbon, transmitted to second carbon, and then to O^-

$$CH_3\text{-O-H} \qquad \underset{CH_3}{\overset{\overset{\displaystyle OH}{|}}{CH_2}} \qquad \underset{CH_3 \quad CH_3}{\overset{\overset{\displaystyle OH}{|}}{CH}} \qquad \underset{CH_3 \quad CH_3}{\overset{\overset{\displaystyle OH}{|}}{C\text{-}CH_3}}$$

pK$_a$ 15.1   15.9   17.1   19.2

More methyl groups around carbon bearing the alkoxide anion,
less stable product,
less favorable ionization,
less acidic,
higher pK$_a$

Consider the extremes:

methyl alcohol

tertiary butanol, tert-butanol, t-butyl alcohol, 2-hydroxy-2-methylpropane, 2-methyl-2-propanol

Solvent is critical factor. Remove solvent? Gas phase acidities: Order is exactly reversed:

$$\underset{CH_3 \quad CH_3}{\overset{\overset{\displaystyle OH}{|}}{C\text{-}CH_3}} > \underset{CH_3 \quad CH_3}{\overset{\overset{\displaystyle OH}{|}}{CH}} > \underset{CH_3}{\overset{\overset{\displaystyle OH}{|}}{CH_2}} > CH_3\text{-O-H}$$

Stabilizing factors in the gas phase: polarizibility

   larger atoms are more polarizible (carbon vs hydrogen)

NOTE: Assume reactions are generally taking place in a solvent, not gas phase.

Water is a "polar, protic" solvent   High dielectric constant (78), Strong H-bonding

Dimethyl sulfoxide is a "polar, aprotic" solvent.   High dielectric constant (47)   NO H-bond donation

      HO⁻ not as well solvated
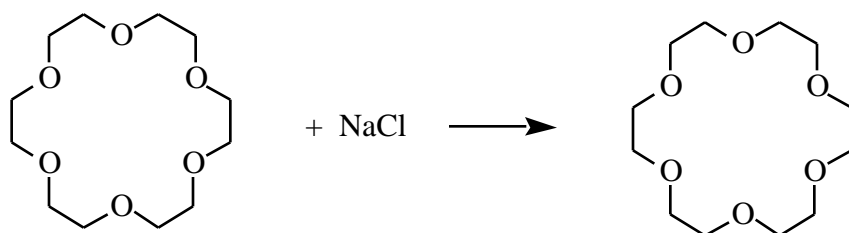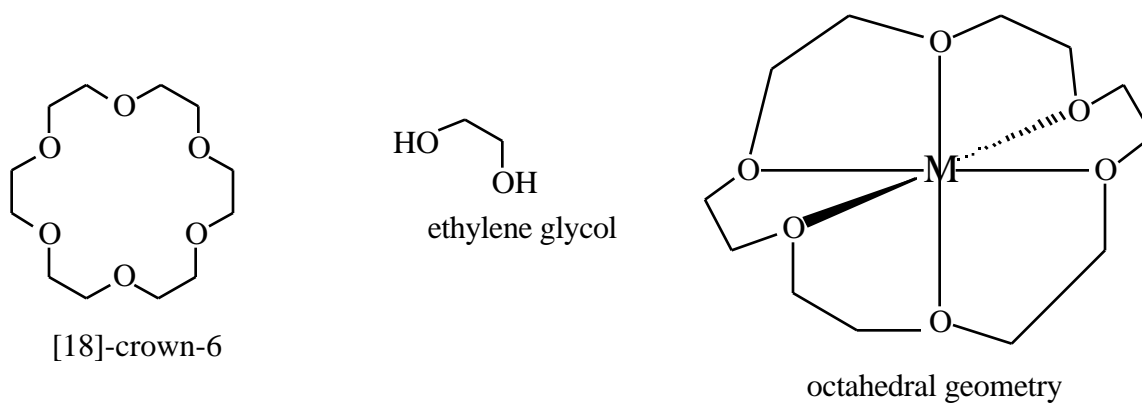
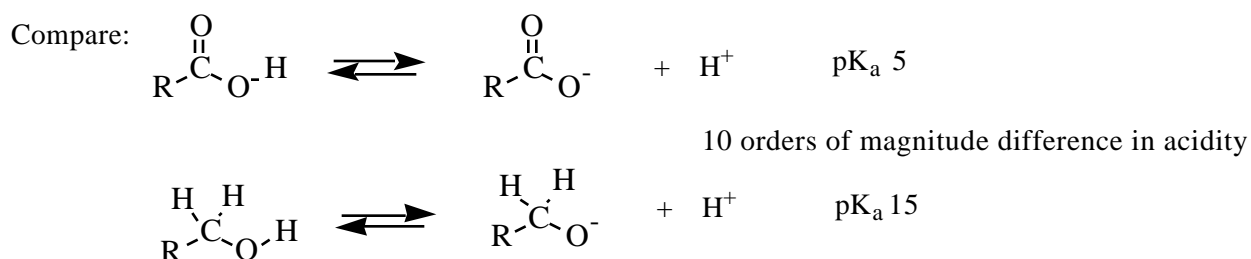NaOH is a much stronger base in DMSO compared to water

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Diethyl ether is a relatively non-polar (dielectric constant = 4.3), aprotic solvent. But it has non-bonding electrons available, it can be an electron donor:

Lewis acid/Lewis base opportunity with **cations:**

CROWN ETHERS   (Nobel prize 1992)

[18]-crown-6

ethylene glycol

octahedral geometry

+ NaCl ⟶

NEW PARAMETER: **DELOCALIZATION**

Compare:

+ H⁺   pK$_a$ 5

10 orders of magnitude difference in acidity

+ H⁺   pK$_a$ 15

The electron on the oxygen anion can be delocalized onto the other oxygen:

Good question: where are the electrons?   Answer: spread over both oxygens equally, not at the C. Difficult to write conventional bonds to express this feature. The actual molecule is **neither** of the two "localized" structures, but the "average" of the two.

Note the arrangement of p orbitals available to the carboxylate anion:

Acidity of Carboxylic Acids; Delocalization in the Anion:

Two equivalent (in energy) resonance structures, both with all bonding possibilities filled. The extra electron pair is distributed over two O atoms, much better than when localized on one O. Strong resonance stabilization, strong delocalization. Therefore a carboxylic acid is 10^{10} more acidic than a simple alcohol; the product oxygen anion is much more stabilized and therefore forms much more easily.

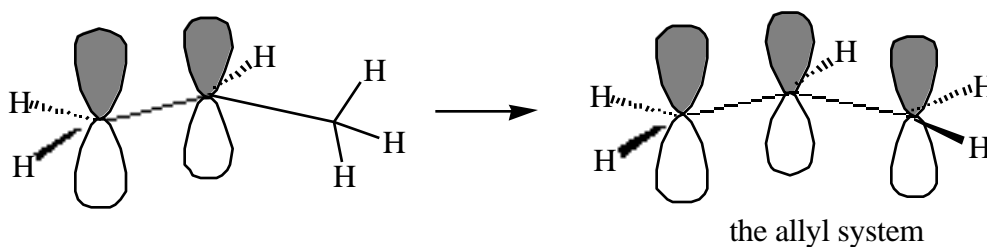**Acidity of Propene, Delocalization in the Anion:**

The dominant effect is the delocalization of charge.
        Steric, Inductive, Resonance effects help to rationalize structure/acidity

Resonance picture:

Molecular Orbital analysis for allyl systems:
        Consider the anion from propene:

the allyl system

MO picture: mix three p type atomic orbitals by linear combination   three MOs

Jones, p 531.

antibonding

non-bonding

bonding

E

p