Structure / Reactivity Relationships

- **Basic Premise of Organic Chemistry - The nature of the chemical reaction an organic molecule undergoes is dependent upon the functional groups present in the molecule.**
- **Corollary - Structural features in the molecule at sites that are not directly involved in a particular chemical transformation can affect both the kinetics and the equilibrium of the chemical reaction.**

Structure / Reactivity Relationships

Organic chemists generally classify the manner in which substituents modify chemical reactivity into three categories:

- ★ **Inductive and Field effects (Polar effects)**
- ★ **Resonance effects (Conjugative effects)**
- ★ **Steric effects**

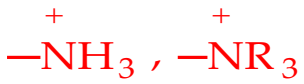
STRUCTURE / REACTIVITY RELATIONSHIPS

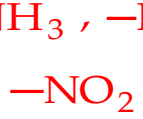
Polar Effects

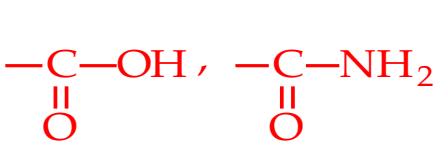
Acid	pK_a	Acid	pK_a	Acid	pK_a
CH_3COOH	4.80	CH_3COOH	4.80	CH_3COOH	4.80
$(CH_3)_3\overset{+}{N}CH_2COOH$	1.83	FCH_2COOH	2.66	$HOCH_2COOH$	3.83
$H_3\overset{+}{N}(CH_2)_4COOH$	4.27	$ClCH_2COOH$	2.86	$NCCH_2COOH$	2.43
$^{-}O_2CCH_2COOH$	5.69	$Cl_2CHCOOH$	1.30	$HOOCCH_2COOH$	2.83
$^{-}O_2C(CH_2)_4COOH$	5.41	Cl_3CCOOH	0.65	CH_3CH_2COOH	4.88
		$Cl(CH_2)_2COOH$	4.00	$(CH_3)_3CCOOH$	5.05
				$HCOOH$	3.77

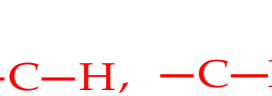
Summary of Common Substituents grouped according to their Inductive effect

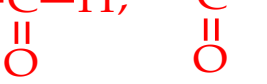
-I (electron withdrawing)

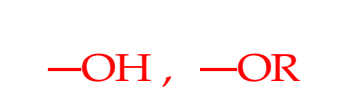


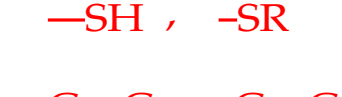


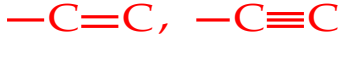




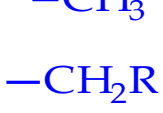


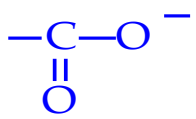






+I (electron donating)



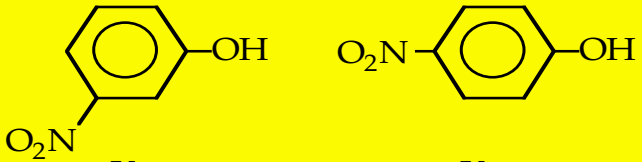


Examples of Resonance Effects

Case I:

$K_a = 6.3 \times 10^{-5}$ $K_a = 2.9 \times 10^{-5}$

Case II:



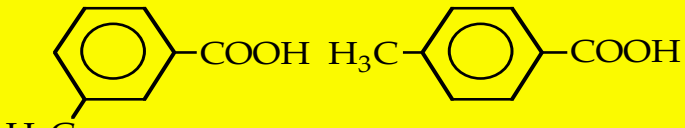
$K_{a\,meta} < K_{a\,para}$

Case III: K_b for $C_6H_5CH_2NH_2 >> K_b$ for $C_6H_5NH_2$

Case IV: K_a for $R-\underset{\underset{O}{\|}}{C}-OH > K_a$ for $R-OH$

K_b for $R-\underset{\underset{O}{\|}}{C}-NH_2 < K_b$ for $R-NH_2$

Case V:

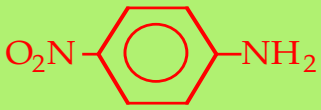
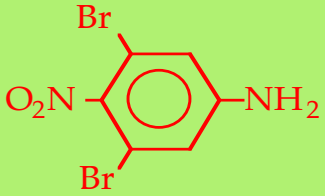


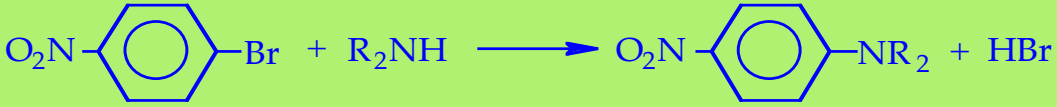
$K_{a\,meta} > K_{a\,para}$

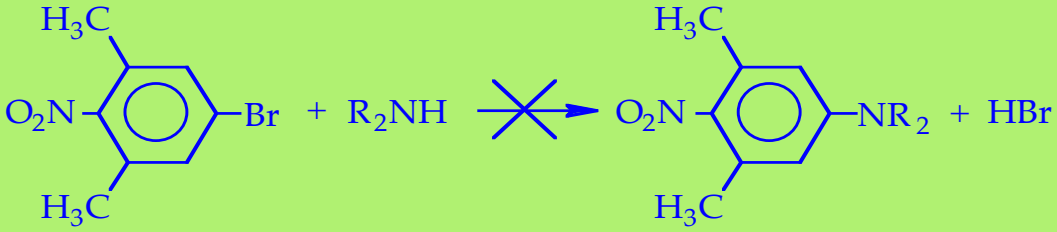
Summary of Common Substituents grouped according to Resonance and Inductive effects

-R, -I	+R, -I	+R, +I
$-NO_2$	$-F$, $-Cl$, $-Br$, $-I$	$-CH_3$
$-C\equiv N$	$-OH$, $-OR$	$-CH_2R$
$-\overset{\overset{O}{\|}}{C}-OH$, $-\overset{\overset{O}{\|}}{C}-NH_2$	$-SH$, $-SR$	$-CHR_2$
$-\overset{\overset{O}{\|}}{C}-OR$, $-\overset{\overset{O}{\|}}{C}-X$	$-NH_2$, $-NHR$, $-NR_2$	$-CR_3$
$-\overset{\overset{O}{\|}}{C}-H$, $-\overset{\overset{O}{\|}}{C}-R$	$-O-\overset{\overset{O}{\|}}{C}-R$, $-NH-\overset{\overset{O}{\|}}{C}-R$	$-O^-$, $-S^-$
$-CF_3$		

Examples of Steric Inhibition of Resonance

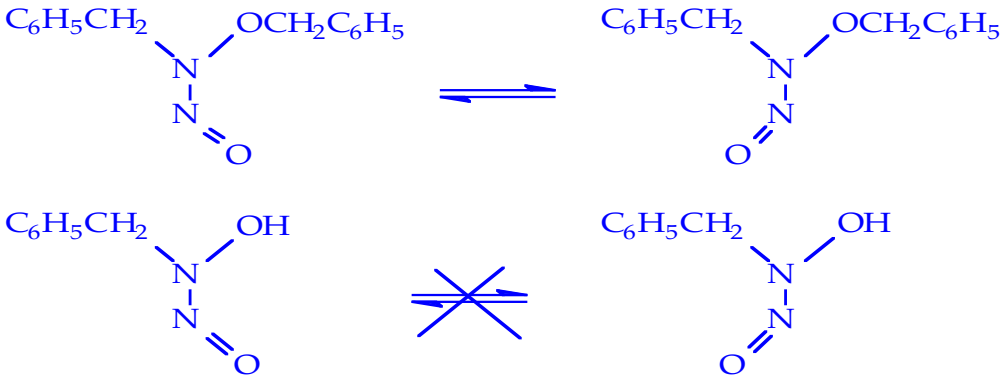
Case I:  is less basic than  despite the presence of more electron withdrawing (base weakening) groups in the latter compound.

Case II: 

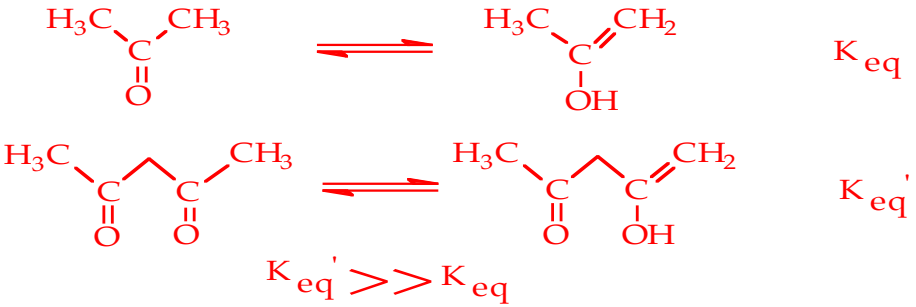


SPECIAL SUBSTITUENT EFFECT - HYDROGEN BONDING

Case I:



Case II:



Case III:

Maleic acid has an unusually large first acid ionization constant and an unusually small second acid ionization constant relative to fumaric acid.