Quantitative Measurement of Substituent Effects on Chemical Reactivity

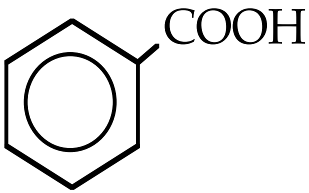
Objective: To measure quantitatively or semi-quantitatively the degree to which substituents can modify reaction equilibria and/or reaction rates based solely on their ability to either donate or withdraw electron density to or from a remote reaction site.

Polar Effects in Aromatic Systems

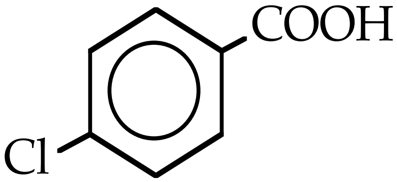
Hammett σ-constants are derived from an investigation of substituent electronic effects on the ionization constants of meta- and para-substituted benzoic acids in aqueous medium at 25°C. The more positive the σ-value is, the more electron withdrawing the substituent; the more negative the σ-value is, the more electron donating the substituent.

$$\mathrm{Log}\ \frac{K_X}{K_H} = \sigma_X$$

Example:



$K_a = 6.25\mathrm{x}10^{-5}$



$K_a = 10.0\mathrm{x}10^{-5}$

$$\mathrm{Log}\ \frac{10.0\mathrm{x}10^{-5}}{6.25\mathrm{x}10^{-5}} = 0.204 = \sigma_p \text{ for Cl}$$

HAMMETT EQUATION AND RHO VALUES

Once σ-values for a set of substituents are known, they can be used to derive information regarding the sensitivity of other reactions to substituent effects relative to the standard reaction (i.e. benzoic acid ionization).

Hammett Equation

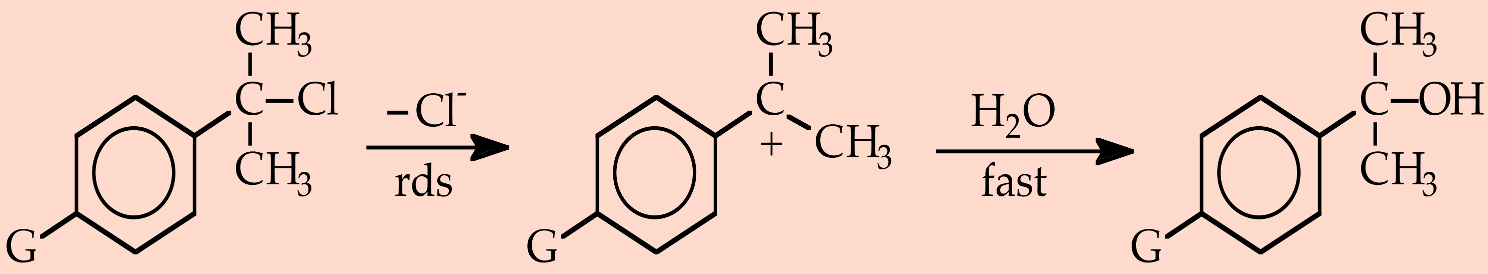
$$\mathrm{Log}\left(\frac{K_X}{K_H}\right)_{\text{any rxn}} \quad \text{or} \quad \mathrm{Log}\left(\frac{k_X}{k_H}\right)_{\text{any rxn}} = \rho\sigma_X$$

Positive rho values indicate reactions that are aided by electron withdrawal from the reaction site.

Negative rho values indicate reactions that are aided by electron donation to the reaction site.

Modification of some Hammett σ-values

Consider the Solvolysis of Benzyl halides



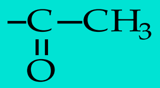
When substituents like -OH, -OR, - NH_2, -NHR, or $-NR_2$ are plotted using normal σ_p-values , they invariably deviate from the linear plot, an indication of an abnormally large substituent effect.

Some Modified σ-Values and their Significance

Examples of Modified Hammett σ-Values

	σ_p	σ_p^+
$-NH_2$	-0.66	-1.70
$-OCH_3$	-0.27	-0.78
$-CH_3$	-0.17	-0.31

σ_p^+ values are used to accommodate substituents that can donate electron density directly to a reaction site.

	σ_p	σ_p^-
$-NO_2$	+0.78	+1.27
$-C{\equiv}N$	+0.63	+1.00
 $-\underset{\underset{O}{\Vert}}{C}-CH_3$	+0.52	+0.87

σ_p^- values are used to accommodate substituents that can withdraw electron density directly from a reaction site.

Significance

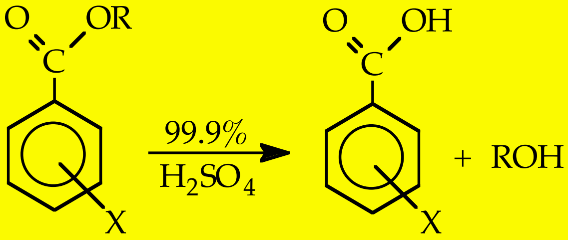
If σ_p^+ values correlate better than σ_p values, then it can be implied that a carbocation conjugated with the benzene ring is being created in the transition state.

If σ_p^- values correlate better than σ_p values, then it can be implied that an anion conjugated with the benzene ring is being created in the transition state.

Deviations from Linearity in Hammett Relationships

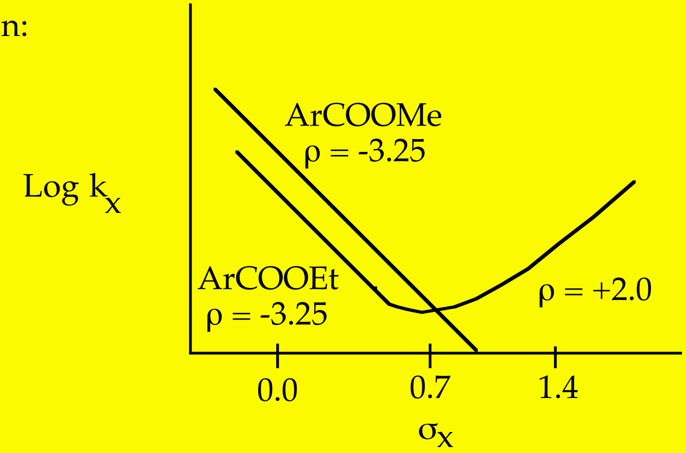
Hydrolysis of Aryl Esters in Sulfuric acid

General Reaction:



(R=Me or Et)

Observation:

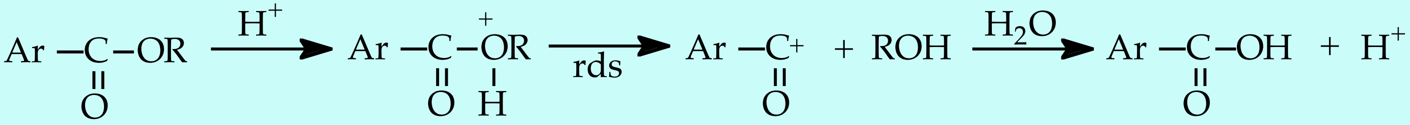


For methyl ester hydrolysis, a typical straight line Hammett plot with a rho value of -3.25 is obtained. Hydrolysis is favored by electron donation in the rds. Initially, the ethyl ester hydrolysis parallels that of the methyl esters. However, for substituents with sigma values greater than ca. +0.6, ethyl ester hydrolysis is favored by electron withdrawal in the rds.

Explanation for Aryl Ester Hydrolyses

For all Methyl esters and Ethyl esters with substituents having σ values < ca. +0.6

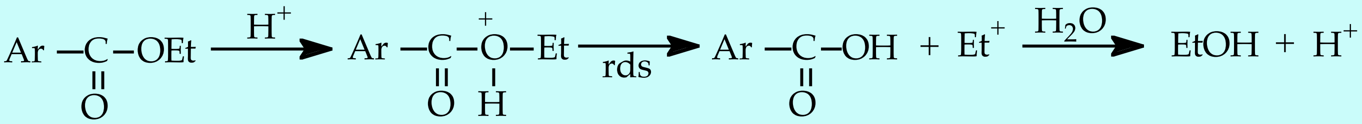
$A_{AC}1$ Pathway Unimolecular acid catalyzed acyl-oxygen cleava



$$\mathrm{Ar-\underset{\underset{\displaystyle O}{\|}}{C}-OR} \xrightarrow{H^{+}} \mathrm{Ar-\underset{\underset{\displaystyle O}{\|}}{C}-\overset{+}{\underset{\underset{\displaystyle H}{|}}{O}}R} \xrightarrow[\text{rds}]{} \mathrm{Ar-\underset{\underset{\displaystyle O}{\|}}{C}{+}} + \mathrm{ROH} \xrightarrow{H_2O} \mathrm{Ar-\underset{\underset{\displaystyle O}{\|}}{C}-OH} + H^{+}$$

For Ethyl esters with substituents having σ values > ca. +0.6

$A_{AL}1$ Pathway Unimolecular acid catalyzed alkyl-oxygen cleav



$$\mathrm{Ar-\underset{\underset{\displaystyle O}{\|}}{C}-OEt} \xrightarrow{H^{+}} \mathrm{Ar-\underset{\underset{\displaystyle O}{\|}}{C}-\overset{+}{\underset{\underset{\displaystyle H}{|}}{O}}-Et} \xrightarrow[\text{rds}]{} \mathrm{Ar-\underset{\underset{\displaystyle O}{\|}}{C}-OH} + \mathrm{Et}^{+} \xrightarrow{H_2O} \mathrm{EtOH} + H^{+}$$

Discussion:

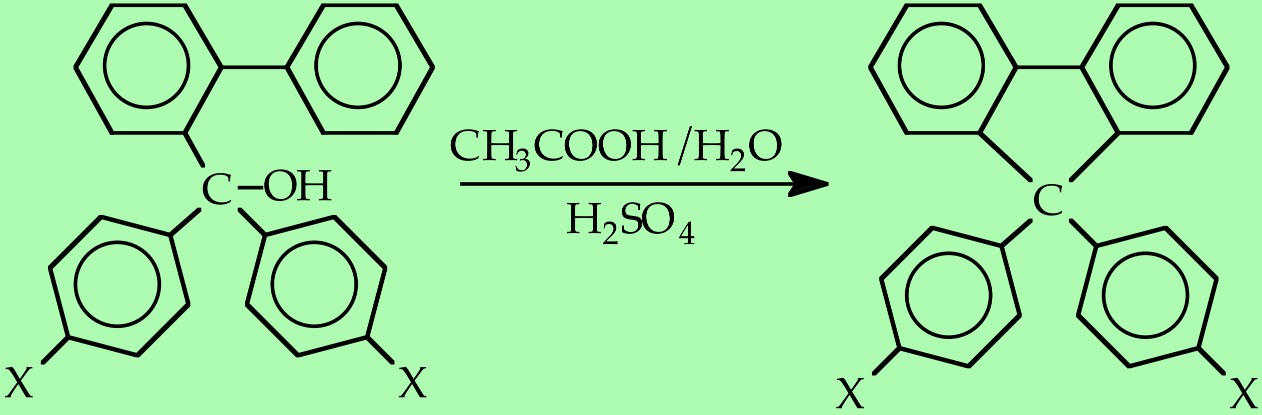
In the unimolecular acyl-oxygen cleavage pathway, the rds involves formation of an acyl cation. Electron donation stabilizes this intermediate and enhances its rate of formation.
In the unimolecular alkyl-oxygen pathway, the rds involves breaking the oxygen-ethyl group bond. Electron withdrawing substituents weaken the oxygen-ethyl carbon bond thereby facilitating the formation of ethyl carbocation.

Comments:

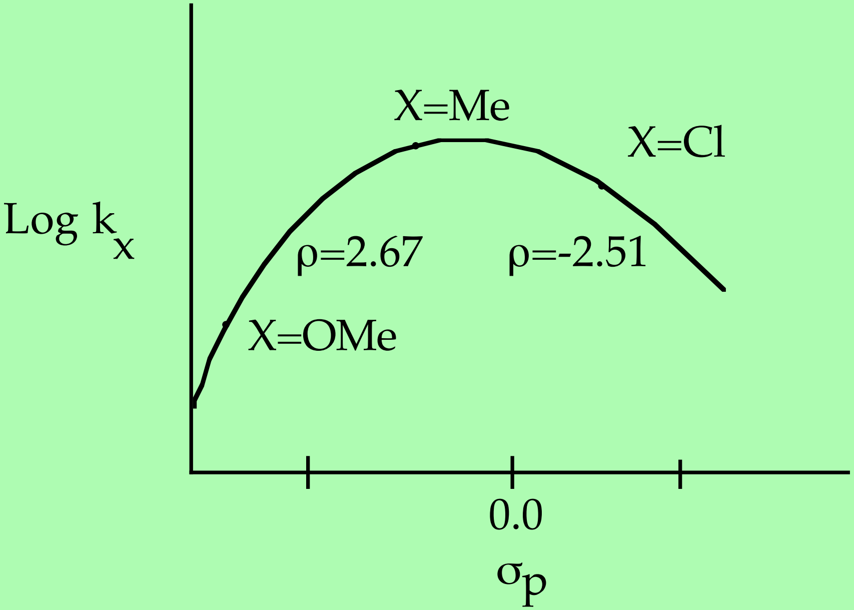
Due to the difference in stability of ethyl carbocation vs. methyl carbocation, the methyl ester hydrolyses **cannot** proceed via the unimolecular alkyl-oxygen cleavage pathway.

Cyclodehydration of 2-Phenyltriarylmethanols

General reaction:

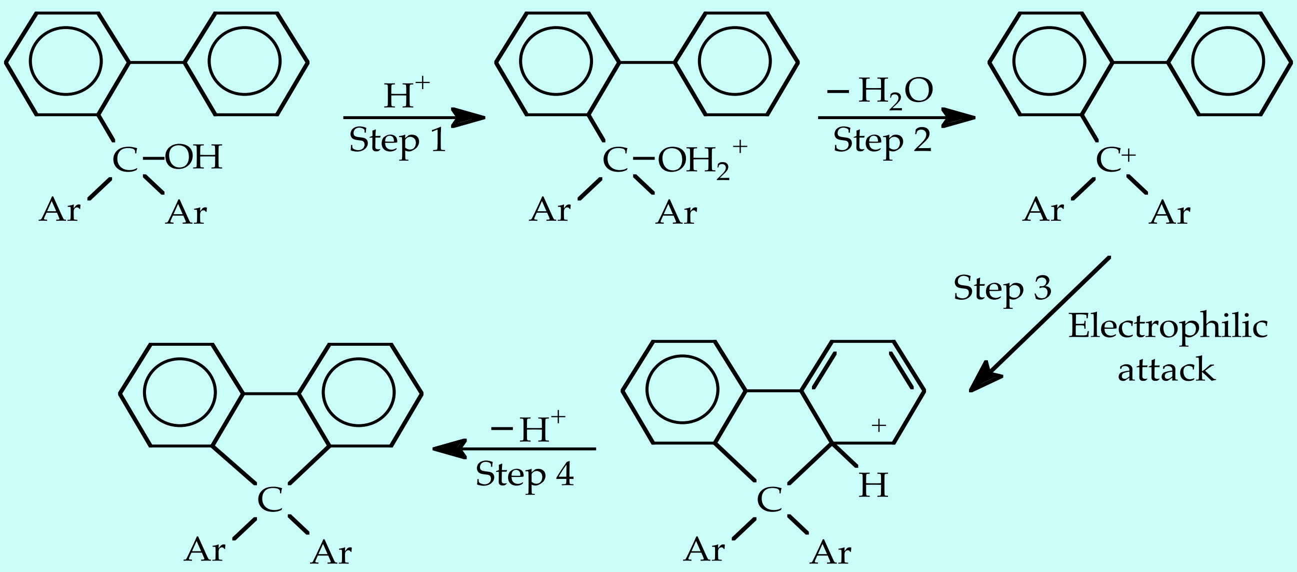


Observation:



Explanation for Cyclodehydration

Rationale:



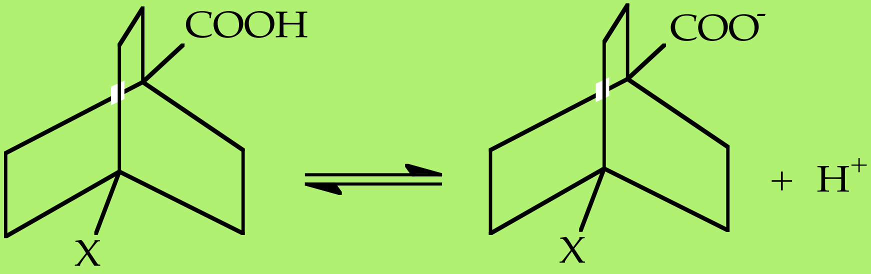
Discussion:

From the concave upward Hammett plot, it will be noted that substituents **less electron donating** than methyl produce a **negative rho** value indicating the slow step involves formation of a carbocation. For substituents **more electron donating** than methyl, a **positive rho** value is obtained indicating that electron withdrawal facilitates the reaction in the slow step.

Thus, for substituents less electron donating than methyl, Step 2, the formation of a carbocationic intermediate is slow. For substituents more electron donating than methyl, Step 2 is fast relative to Step 3 which involves attack by a stabilized carbocation on a nearby benzene ring.

With methyl, one has maximized **both** the rate of formation of carbocation intermediate and its reactivity to give product in the **least amount of time overall**.

Polar Effects in Rigid Aliphatic Systems



$$\text{Log}\,\frac{K_X}{K_H} = \sigma'$$

Typical values for σ'

Substituent	σ'	σ_m	σ_p
H	0.00	0.00	0.00
OH	+0.28	+0.12	-0.37
COOEt	+0.30	+0.37	+0.45
Br	+0.45	+0.39	+0.23
C≡N	+0.58	+0.56	+0.66