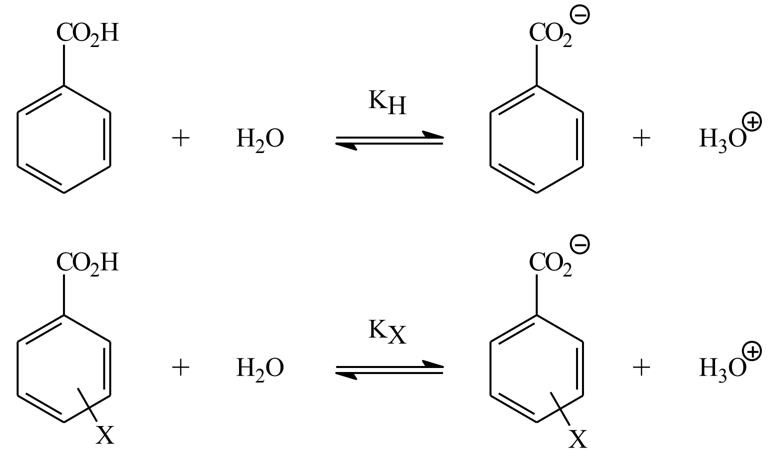
Linear Free Energy Relationships (LFERs): Applying the Hammett Equation to a Series of Substituted Benzoic Acids and Phenols

Background:

The Hammett equation relates observed changes in equilibrium or rate constants to systematic changes in substituents that govern electron donating/withdrawing ability. It is an example of a linear free-energy relationship as changes in log K (log *k*) are linear with substituent effects (*1*). Hammett noted that a particular substituent on the aromatic ring of a benzoic acid would effect it's acidity (ΔpK_a) in a similar manner as it would effect other reactions. For example, a *meta*-chloro group would affect the pK_a of benzoic acid in a manner similar to that of phenylacetic acid (albeit to a differing extent).

Hammett quantified the effect of substituents on any reaction by defining an empirical electronic substituent parameter (σ), which is derived from the acidity constants, K_a's of substituted benzoic acids.



The Hammett Equation relates the relative magnitude of the equilibrium constants to a *reaction constant* ρ and a *substituent constant* σ.

$$\log (K_X / K_H) = \rho \sigma \quad \text{or} \qquad pK_H - pK_X = \rho \sigma$$

For the ionization of benzoic acid in pure water at 25°C (the reference reaction), the constant ρ is defined as 1.00. Thus, the electronic substituent parameter (σ) is defined as:

$$\sigma = \log (K_X / K_H)$$

The reaction constant is a measure of how sensitive a particular reaction is to changes in electronic effects of substituent groups (*1-5*). The reaction constant depends on the nature of the chemical reaction as well as the reaction conditions (solvent, temperature, etc). Both the sign and magnitude of the reaction constant are indicative of the extent of charge build up during the reaction progress. Reactions with $\rho > 0$ are favoured by electron withdrawing groups (i.e., the stabilization of negative charge). Those with $\rho < 0$ are favoured by electron donating groups (i.e., the stabilization of positive charge). The greater the magnitude of ρ, the more sensitive the reaction is to electronic substituent effects.

The substituent constant pertains to the observed electronic (inductive and resonance) effect that a particular substituent imparts to a molecule. Electron withdrawing substituents will have a positive σ value whereas electron donating substituents will have a negative substituent constant;

$$\text{(e.g., } \sigma_{para}\,(NO_2) = 0.78\text{ , } \sigma_{para}\,(OCH_3) = -0.27)$$

A particular substituent will exert differing effects depending on their proximity to the reaction centre and their ability to directly participate in resonance stabilization. The difference between σ_{meta} and σ_{para} of a given substituent are due to the difference in importance between inductive and resonance effects (i.e., σ_I and σ_R). Resonance effects are governed by the ability of a particular substituent to effect electron distribution through resonance structures. Resonance contributions can only occur for ortho and para substituents, although ortho substituents are excluded from the Hammett treatment because steric effects play a complicating role. Meta substituents will have a negligible resonance contribution (σ_R=0) and are almost entirely due to inductive effects (σ_{meta}=σ_I). Inductive effects arise as a result of electronegativity differences and diminish with the distance between the substituent and the reactive centre. Thus, σ_I will generally be greater for meta than para substitution, because of their closer proximity.

A number of modified substituent constants have been defined for specific cases. Some of these are listed in the table below. For meta-substituted benzoic acids the value σ_{meta} should be used. Likewise, when para-substituted benzoic acids are treated the value σ_{para} should be used.

Substituent constants (σ) for Common Substituents (*5*)

Substituent	σ_{meta}	σ_{para}	σ_{para}^{-}	σ_{para}^{+}
$-NH_2$	-0.04	-0.66		-1.3
-OH	0.12	-0.37		-0.92
$-CH_3$	-0.07	-0.17		-0.31
$-OCH_3$	0.12	-0.27	-0.20	-0.78
-H	0.00	0.00		
-Ph	0.06	-0.01		-0.17
-Cl	0.37	0.23	0.19	0.11
-Br	0.39	0.25	0.22	0.15
-I	0.35	0.18	0.13	
$-CO_2R$	0.37	0.45	0.68	0.48
$-CF_3$	0.43	0.54		
-CN	0.56	0.68	0.96	0.66
-CHO		0.22	1.13	
$-NO_2$	0.71	0.78	1.24	0.79

Similar linear free energy treatments using the same substituent constants have been applied to rate constants and can provide valuable mechanistic information about the extent of charge build up at the transition state of the rate determining step (*1-5, 7*).

This experiment investigates the Hammett Equation by measuring the acid dissociation constants of a series of meta and para substituted benzoic acids and phenols. The effect of various substituents on the acid dissociation constants will be determined by measuring the pK_a of the substituted acids and comparing these to the pK_a of parent system (i.e., $\Delta pK_a = pK_{aH} - pK_{aX}$).

In this experiment, you will determine the K_a for the various benzoic acid derivatives from their pH titration curves. The titration reaction is:

$$RCO_2H\ (aq) + OH^-\ (aq) \longrightarrow H_2O + RCO_2^-\ (aq)$$

At the beginning of the titration, there is a maximum concentration of acid and at the equivalence point all of the RCO_2H has been converted to RCO_2^-. However, at the point in the titration when only half of the acid has been titrated, we have the situation where $[RCO_2H] = [RCO_2^-]$. This occurs when the volume of base added is half that required to reach the equivalence point, i.e., V′, where V′ = V/2 (Figure 1). It can be shown, that the pH at the 'half equivalence point' is equal to the pK_a.

For the chemical equilibrium;

$$R\text{-}CO_2H + H_2O ==== H_3O^+ + R\text{-}CO_2^-$$

$$K_a = \frac{[H_3O^+][RCO_2^-]}{[RCO_2H]}$$

Thus, when $[RCO_2H] = [RCO_2^-]$;

$$K_a = [H_3O^+]$$

$$\text{and } pK_a = pH$$

A typical titration curve is shown below:

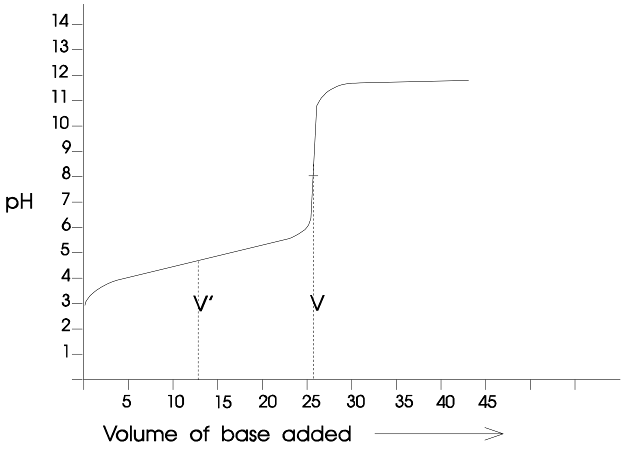


Figure 1: Typical acid/base titration curve for a weak acid – strong base combination.

The pKa of substituted phenols will be determined spectrophotometrically. The proton on the –OH group of a phenol is weakly acidic compared to a carboxylic acid. In their deprotonated form, phenolates (PhO^-) have distinct absorption properties generally absorbing more strongly and at longer wavelengths than the protonated (PhOH) forms (Figure 2). The absorption spectrum of a solution that contains both the protonated and deprotonated forms can be used to determine the fractional abundance of the two forms. If the pH of this solution is known, the fractional abundance can be used to calculate the pK_a (*8*).

$$PhOH \quad + \quad H_2O \quad ==== \quad PhO^- \quad + \quad H_3O^+$$

$$\chi_{PhO-} = \frac{\text{mols } PhO^-}{\text{mols } (PhO^- + PhOH)}$$

The total absorbance of a solution at a pH where both the protonated and deprotonated forms absorb is given by;

$$A_{T,\lambda} = \chi_{PhO-}\ A_{PhO-,\lambda} + \chi_{PhOH}\ A_{PhOH,\lambda} = \chi_{PhO-}\ A_{PhO-,\lambda} + (1-\chi_{PhO-})\ A_{PhOH,\lambda}$$

where χ_{PhO-} is the mole fraction of the deprotonated form and $(1 - \chi_{PhO-})$ is the fraction of the protonated form PhOH; $A_{PhO-,\lambda}$ and $A_{PhOH,\lambda}$ are the absorption of the of the deprotonated and protonated forms at a particular concentration and some specified wavelength, λ. Rearranging this equation for χ_{PhO-} and substituting into the acid dissociation equilibrium expression yields;

$$pK_a = pH + \log\frac{1-\chi_{PhO-}}{\chi_{PhO-}} = pH + \log\left[\left(1-\frac{A_T - A_{PhOH}}{A_{PhO-} - A_{PhOH}}\right) \Bigg/ \left(\frac{A_T - A_{PhOH}}{A_{PhO-} - A_{PhOH}}\right)\right]$$

This calculation can be repeated at several wavelengths where the absorption of the protonated and deprotonated forms are sufficiently different (e.g., λ_1 and λ_2 in Figure 2).

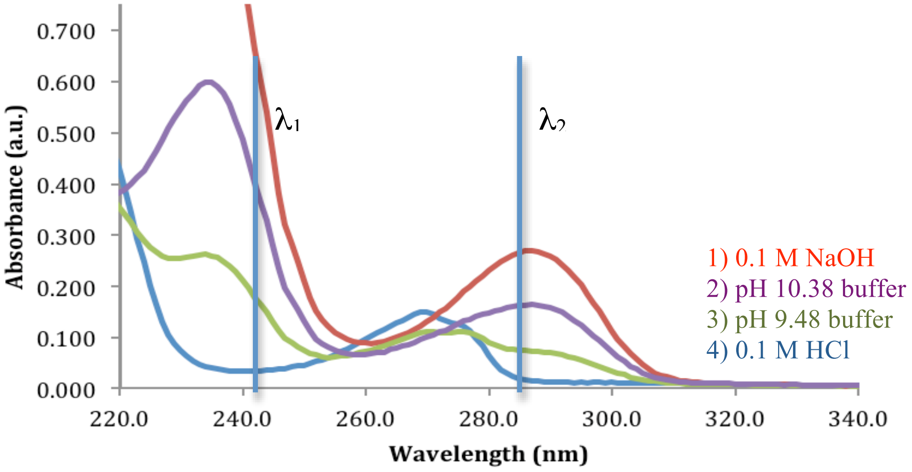


Figure 2: Overlaid Absorbance Spectra of Phenol in water at 0.1 M NaOH, buffer at pH 10.38, buffer at pH 9.48 and 0.1 M HCl.

EXPERIMENTAL

Objectives:

- Experimentally determine the acid dissociation constant (K_a) of a series of substituted benzoic acids and phenols.
- Determine the influence of each substituent on the acidity constant ($\Delta pK_a = pK_{aH} - pK_{aX}$) and correlate these values with known substituent constants (i.e., $\sigma_x, \sigma_p, \sigma_p^-$) to determine the reaction constant ρ.

This lab will require several careful titrations to generate accurate well-described titration curves for benzoic acid derivatives and several uv/vis absorption spectra for phenol derivatives. You will need good technique with each of the following; titration, pH meter calibration, uv/vis spectrophotometry and precise small volume liquid handling.

Procedure for Benzoic Acids:

Ensure the pH meter is calibrated and temperature compensated. Recheck the calibration (pH 7.00 and 10.00) between each titration (For detailed instructions on the use of pH meters, see instruction sheets provided in the laboratory and speak to your lab instructor).

Place roughly 4×10^{-4} mol of benzoic acid in 70:30 ethanol-water solution into a clean dry beaker. Stir the contents and record the initial pH.

Calculate the volume of titrant required to reach the endpoint of the titration, using a 5.0×10^{-2} M NaOH in 70:30 ethanol-water titrant.

Begin titrating after recording the initial pH and record the pH with every addition of ~0.25 mL of titrant. As the pH begins to increase rapidly (near the equivalence point), start to record the pH after each addition of ~ 0.1 mL of titrant.

The following benzoic acids will be available in the laboratory;

Compound	Isomer
Benzoic acid	
Aminobenzoic acid	*para*
Bromobenzoic acid	*meta and para*
Chlorobenzoic acid	*meta and para*
Hydroxybenzoic acid	*para*
Iodobenzoic acid	*meta and para*
Methoxybenzoic acid	*meta and para*
Methylbenzoic acid	*meta and para*
Nitrobenzoic acid	*meta, para and 3,5-di*NO_2

Procedure for Phenols:

Transfer **100.** μL of the ethanol stock solution (using an automated pipettor) of each phenol into 5.00 mL of the following aqueous solutions and record the uv/vis absorption spectrum between 200 – 500 nm in a quartz cuvette after referencing the spectrophotometer on the pure aqueous solution;

- 0.1 M HCl to record the absorption spectrum of the protonated phenol.
- 0.1 M NaOH to record the spectrum of the deprotonated phenolate ion.
- Two buffer solutions close to the expected pK_a to record the absorption spectrum of a solution that contains both the protonated and deprotonated forms.
- Measure the exact pH of the buffers with a calibrated temperature compensated pH meter.

It is important that each solution has the same total concentration of phenol, so ensure that your volume transfers are precise. Export absorption spectra as Excel files for processing and overlay plots. Interrogate your spectra to obtain the absorption at four wavelengths where both forms absorb avoiding wavelengths at or near the isobestic points (same absorbance).

Buffers will be available in 0.5 pH increments between 7.0 and 10.5.

The following substituted phenols will be available as a ~ 5 mM solution (made in ethanol). ***Please handle the phenolic solutions with care, as many of the compounds are toxic and readily absorbed through the skin.*** Please clean any spilled solutions, and take your gloves off when handling either the pH meters or UV-Vis instruments in order to minimize contaminating the equipment.

Compound	Expected ~pK_a	Low pH buffer	High pH buffer
Phenol	10	9.5	10.5
4-bromophenol	9	9.0	10.5
4-chlorophenol	9	9.0	10.5
4-nitrophenol	7	7.0	8.0
4-methoxyphenol	11	9.5	10.5
4-cyanophenol	8	7.0	8.0
4-hydoxybenzaldehyde	7	7.0	8.0
4-hydoxyacetophenone	8	7.5	8.5
methyl 4-hydroxybenzoate	8	7.5	8.5

Data Analysis:

- For each titration, use a spreadsheet to tabulate: buret readings, volume NaOH added, increase in volume after each addition (Δvol), pH after each addition, increase in pH after each addition (ΔpH), change in pH per change in vol (ΔpH/Δvol) and volume of NaOH added x $[H^+]$.
- Graph first derivative plot: volume NaOH added versus ΔpH/Δvol and expand the region showing the maximum to obtain the equivalence point.
- Graph a Gran plot: volume of titrant added versus volume of NaOH added x $[H^+]$ to obtain the equivalence point.
- Use a linear regression approach on the data points around V/2 to determine the pH at V/2 (this region of the titration curve is close to linear).
- Overlay the uv/vis spectra for each phenols at different several different pHs.
- Calculate pK_a of phenols using absorbance of the phenols/phenolates at four wavelengths and report the mean pKa value.
- Tabulate the pK_a (and $pK_H - pK_X$) results for each benzoic acid and phenol measured using shared class data.
- Plot $pK_H - pK_X$ versus the appropriate literature substituent constants (σ values) and determine the sensitivity factor (ρ value) for both the acid dissociation of benzoic acids and phenols used in this experiment.

Questions:

- Rationalize the electron withdrawing/donating characteristics observed for your substituents using your understanding of both inductive and resonance electronic effects.
- Explain why σ_{para} and σ_{meta} for methoxy substitutents have opposite signs.
- The slope of the Hammett plot for substituted benzoic acids in water at 25°C is defined as 1.00. The slope obtained in this experiment is different (i.e., $\rho > 1.00$). Explain (*6*).
- Look up the values of the reaction constant (ρ) for substituted phenyl acetic and 3-phenylpropanoic acids and explain why they are less than 1.00.
- In analyzing the acidity of substituted phenols, the substituent constants σ^- are used *(1,8)*. Explain.

References:

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