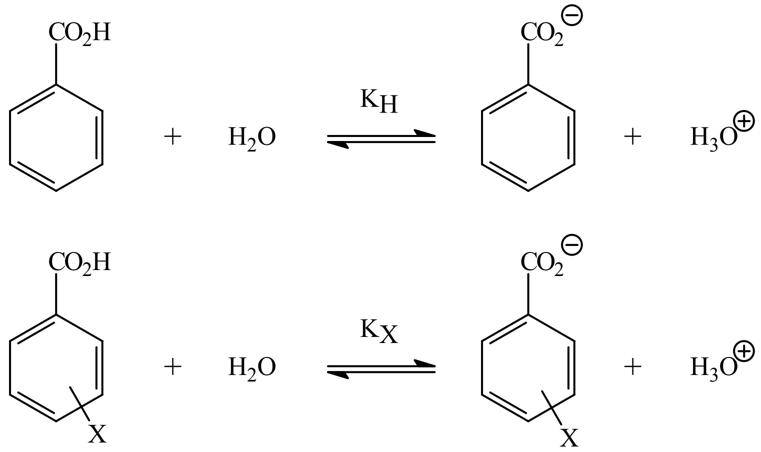
Linear Free Energy Relationships (LFERs): Applying the Hammett Equation to a Series of Substituted Benzoic Acids

Background:

A linear free-energy relationship is said to exist if 'the same series of changes in conditions affects the rate or equilibrium of a second reaction in exactly the same way as the first'. Hammett was the first to illustrate this relationship (*1*). He noted that a particular substituent on a benzoic acid ring would effect it's degree of ionization (pK_a) in a similar manner as it would effect other reactions. By way of an 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.

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

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 value and electron donating substituents will be negative;

(e.g., σ_{para} (NO_2) = 0.78 , σ_{para} (OCH_3) = -0.27)

A particular substituent will exert differing effects depending on their proximity to the reaction centre and their ability to 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 σ_I and resonance σ_R effects. 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 be generally greater for meta than para substitution.

A number of modified substituent constants have been defined for specific cases. Some of these are listed in the table below. For meta-substitued 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	-0.2	-0.78
-H	0.00	0.00		
-Ph	0.06	-0.01		-0.17
-Cl	0.37	0.23		0.11
-Br	0.39	0.23		0.15
-I	0.35	0.18	0.13	
$-CO_2R$	0.37	0.45		0.48
$-CF_3$	0.43	0.54		
-CN	0.56	0.66	0.90	0.66
$-NO_2$	0.71	0.78	1.24	0.79

A similar linear free energy treatment using the same substituent constants has been applied to rate constants and provides valuable mechanistic information about the extent of charge build up at the transition state of the rate determining step (*1-5, 8*).

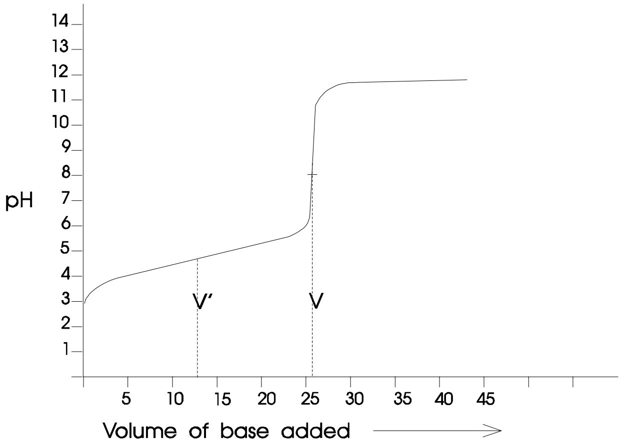
This experiment investigates the Hammett Equation by looking at various meta and para substituted benzoic acids and determing their respective σ constants. The σ constants will be determined by measuring the pK_a of the substituted benzoic acids and comparing these to the pK_a of benzoic acid.

In this experiment, you will need to determine the K_a for the various benzoic acid derivatives from their titration curves. The procedure is as follows, using the generic acid RCO_2H. The titration reaction is:

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

At the beginning of the titration, there is the 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. The pH at this point can be shown to equal pK_a.

A typical titration curve is shown below:



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 $[RCO_2H] = [RCO_2^{-}]$;

$$K_a = [H_3O^{+}]$$

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

EXPERIMENTAL

Objectives:

- Experimentally determine the acid dissociation constant (K_a) of a series of substituted benzoic acids.
- Correlate the K_a values with known substituent constants (σ_x).
- Use the correlation generated above to calculate the substituent constants for 'unknown' substituted benzoic acid compounds.

Procedure:

This lab requires numerous titrations. Please refresh yourself with proper titration techniques. Those would include proper handling of a pipette, the use and calibration of a pH meter and the importance of endpoint and the pH at the half endpoint (which is equal to the pK_a).

Ensure the pH meter is calibrated and recheck the calibration between each titration. For detailed instructions on the use of pH meters, see an instruction sheets provided in the laboratory and speak to your lab instructor.

Into each beaker, place 4.0×10^{-4} mol of the various acids. Pipette 25 mL of 70:30 ethanol-water solution into each beaker. Stir the contents to completely dissolve the benzoic acid BEFORE you begin the titration.

The titration will be carried out using 5.0×10^{-2} M NaOH in 70:30 ethanol-water. Calculate the volume of titrant required to reach the endpoint of the titrations. Record the initial pH of the acid solution and begin titrating, recording the pH with every addition of ~0.25 mL of titrant. As the pH begins to increase rapidly, record the pH after each addition of ~ 0.1 mL of titrant.

The following benzoic acid derivatives will be available in the laboratory;

benzoic acid	*m*-chlorobenzoic acid	*p*-aminobenzoic acid
	m-iodobenzoic acid	*p*-chlorobenzoic acid
	m-methoxybenzoic acid	*p*-bromoobenzoic acid
	m-nitrobenzoic acid	*p*-iodobenzoic acid
	m-toluic acid	*p*-hydroxybenzoic acid
		p-methoxybenzoic acid
	3,5-dinitrobenzoic acid	*p*-nitrobenzoic acid
	m-unknown acid I	*p*-unknown acid II

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.
- For each benzoic acid, tabulate the K_a and $pK_H - pK_X$
- Plot $pK_H - pK_X$ versus the literature σ values and determine the value of ρ you obtained for this experiment.
- Using this calculated value of ρ, determine the σ values of the two unknowns.

Questions:

- With your understanding of resonance, electron withdrawing and electron donating characteristics, rationalize the observed effects of each of the substituents in the meta and para position. Are there any surprises.
- Determine the substituent constants for the two unknowns. Compare your results with literature values (*1–5*).
- Explain detail how and why the two 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 a similar experiment analyzing the acidity of substituted phenols, the substituent constants σ^- were used *(1,7)*. Explain.

References:

(1) Jaffe, H.H. A Re-examination of the Hammett equation, *Chem. Rev.,* **1953**, 53, 191.

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(3) **The Physical Basis of Organic Chemistry**, H. Maskill, Oxford Science Publications 1985,chapter 5, pp 202-211, 442-459.

(4) **Environmental Organic Chemistry, 2nd Ed.**, R.P. Schwarzenbach; P.M. Gschwend; D.M. Imboden, Wiley-Interscience Publishers, 2003, chapter 8, pp 253-268.

(5) **Mechanism and Theory in Organic Chemistry,** T. Lowry; K.S. Richardson, Harper and Row Publishers, Inc., 1987, chapter 2, pp 143-159.

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(8) Mullins, R.J.; Vedernikov, A.; Viswanathan, R. Competition Experiments as a Means of Evaluating Linear Free Energy Relationships, *J. Chem. Educ.*, **2004**, 81, 1357-1361.