CHEM 331

Problem Set #3: Substitutent Effects and LFERs

Hand in all worked solutions in a neat and organized format. Not all questions will be graded.

Due: Friday, Mar 16th.

1. Consider the following σ values in terms of the electronic character of each group and answer each of the following in terms of the inductive and resonance electronic character of each group (σ_I and σ_R). Illustrate your answer showing resonance structures for substituted phenols, where appropriate.

Substituent	σ_{meta}	σ_{para}	σ-
-OH	0.13	-0.38	
$-COCH_3$	0.38	0.50	0.82
-Cl	0.37	0.23	
$-SO_2CH_3$	0.68	0.72	

a) Why is σ_{meta} for the hydroxyl group (–OH) positive, whereas the value for σ_{para} is negative?
b) Why is the modified σ- value for the actyl group ($-COCH_3$) more positive than either σ_{meta} or σ_{para}?
c) Why is a chloro substituent (-Cl) less electron withdrawing in the para position than the meta position?
d) Why is the methyl sulfonyl group ($-SO_2CH_3$) a more electron withdrawing in the para than the meta position?

2. Derive an expression for the fractional abundance of the protonated (acidic) form of a monoprotic acid in terms of its pK_a and the pH of the solution.

3. Estimate the pK_a values of 4-methyl-2,5-dinitrophenol and 3,4,5-trimethylaniline and calculate the fractional abundance of the conjugate base of each at pH 7.70 at 5.0 ^oC (see Tables 1 and 2).

4. Use Excel to plot an overlay of the fractional abundance of the neutral and both ionized forms of ortho-phthalic acid over a pH range of 2 – 12 at 25^oC (pK_{a1} = 2.89 and pK_{a2} = 5.51).

5. Describe the influence of changing the pH from 4 to 8 on each of the following for 4-ethyl-2,6-dimethyl pyridine (pK_{ow} = -3.70; pK_a = 7.43). Explain using chemical structures and/or mathematical expressions to illustrate your answer.

a) aqueous activity coefficient (γ_w^{sat})
b) air – water partition coefficient (K_{aw})
c) octanol – water partition coefficient (K_{ow})

6. The relative rates of alkaline (base enhanced) hydrolysis of substituted benzamides in water at 100°C are as follows below. Demonstrate the applicability of the Hammett equation to this reaction, calculate the ρ value, and comment on any deviations from the correlation.

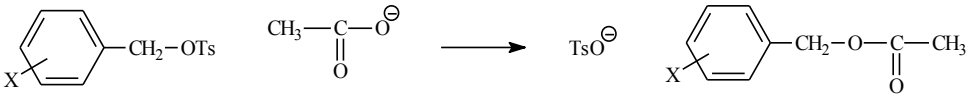
Substituent	Relative Rate	Substituent	Relative Rate	Substituent	Relative Rate
m-I	2.60	*m*-NO_2	5.60	*p*-OCH_3	0.49
p-I	1.69	H	1.00	*m*-NH_2	0.93
m-Br	2.97	*m*-CH_3	0.83	*p*-NH_2	0.20
p-Br	1.91	*p*-CH_3	0.65	*m*-OH	0.19

7. The neutral hydrolysis of 4-nitrophenyl acetate (4-NPA) has a measured *pseudo* first order rate constant of 4.4 x 10^{-5} s^{-1} at room temperature and neutral pH.

a) If the reaction constant for a series of substituted phenyl acetates is determined to be ρ = 0.87, what is the rate constant for the neutral hydrolysis of the unsubstituted phenyl acetate at this temperature?

b) Suggest a substituted phenyl acetate that will have a half life between 1 and 2 days?

8. The acetolysis of substituted benzyl tosylates shown below proceeds via a substitution reaction. The Hammett plot for the rate constants of a series of substituents shows two linear regions, one for EDGs and another for EWGs. Hence there are two reaction (susceptibility) constants (ρ), shown on the figure below.



a) Look up the chemical structure of a tosylate group and indicate if you think it is likely to be a relatively 'good' (i.e., stabilized) leaving group.

b) Why are the modified σ^+ values are used instead of σ in the Hammett plot?

c) Explain the magnitude and sign of each of the two reaction constants and provide mechanism/s consistent with these observations.

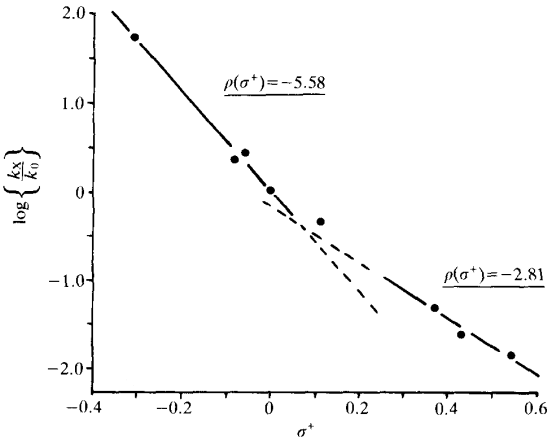


Table 1: Hammett constants for some common substituents

Substituent	σ_{meta}	σ_{para}	σ^-	σ^+	$\sigma_o^{phenols}$
CH_3	-0.07	-0.17		-0.31	-0.13
Ph (C_6H_5)	0.06	0.01			
Cl	0.37	0.23		0.11	0.68
Br	0.39	0.23	0.26	0.15	0.70
I	0.35	0.18		0.13	0.63
OH	0.10	-0.37		-0.92	
OCH_3	0.12	-0.27	-0.12	-0.78	0.0
NO_2	0.71	0.78	1.25	0.79	1.24
CN	0.56	0.66	0.89	0.66	
CO_2CH_3	0.33	0.45	0.66		
$OCOCH_3$	0.36	0.31			
NH_2	-0.16	-0.66		-1.3	
$N(CH_3)_2$	-0.15	-0.83			

Note: σ^- and σ^+ apply to *para* substituted groups only

Table 2: Reaction and acidity constants for aromatic acids in water at 25^{o}C

Acid	ρ	pK_{aH}
Benzoic acid	1.00	4.19
Phenol	2.25	9.92
Phenoxy acetic acid	0.30	3.17
2-chlorophenoxy acetic acid	0.30	3.05
Conjugate acid of aniline	2.89	4.63
Conjugate acid of pyridine	5.90	5.25