CHEM 331
Problem Set #3: Substitutent Effects and LFERs

1. Consider the following substituent constants (σ values) 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 benzoic acids, where appropriate.

| Substituent	σ_{meta}	σ_{para}
-OH	0.13	-0.38
-COCH$_3$	0.38	0.50
- C$_6$H$_2$(NO$_2$)$_3$	0.43	0.41

    a) Why is σ_{meta} for the hydroxyl group (–OH) positive, whereas the value for σ_{para} is negative?
    b) Why is the acetyl group (-COCH$_3$) a more electron withdrawing in the para vs meta position?
    c) Why does the picryl substituent - C$_6$H$_2$(NO$_2$)$_3$ have nearly the same electron withdrawing ability in both the meta and para position?

2. Using the information in Table 1 and 2 (attached), estimate the pK$_a$ values of the following compounds at 25°C and use Excel to plot the fractional abundance of each acid and conjugate base over a pH range of 2 – 12.
    a) 4-nitrophenol (4-NP)
    b) the conjugate acid of 4-methyloxyaniline (4-MA)
    e) 2,4-dinitrophenoxy acetic acid (2,4-DNPA)

3. The pK$_a$'s and reaction constants (susceptibility factors) ρ for the acid dissociation of substituted 1-naphthylamines and quinolines are given below.
    a) Explain why the quinoline is much more susceptible to electronic substituent effects than 1-naphthylamine.
    b) Predict the fraction of each compound present in the protonated form at pH = 6.00

1-naphthylamine
pK$_a$ = 3.85
ρ = 2.81

quinoline
pK$_a$ = 4.88
ρ = 5.90
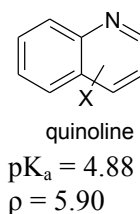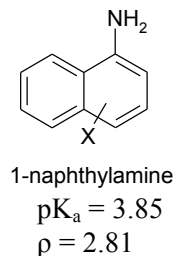
4. The relative rates of alkaline hydrolysis of substituted benzamides in water at 100°C are as follows below. Demonstrate the applicability of the Hammett equation to this reaction, calculate the ρ value, and comment on any deviations from the correlation.

| 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

5. For the following mechanisms:
a) Explain the value of the reaction (susceptibility) constant in terms of the *Hammond postulate*.
b) Specify which σ values are used (σ, σ⁺, σ⁻, or $\sigma_{ortho}^{phenols}$) in obtaining the susceptibility constant and indicate if the reaction centre is in direct resonance with the substituents. Illustrate with an example.

i) hydrolysis of substituted benzyl chlorides; ρ = –4.45
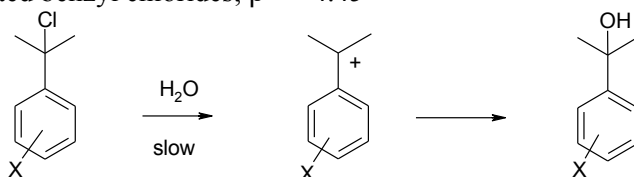
ii) addition of cyanide ion to substituted benzaldehydes; ρ = 2.55
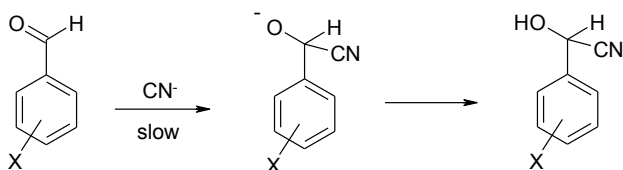
6. The neutral hydrolysis of 2,4-dinitrophenyl acetate (2,4-DNPA) has a measured pseudo first order rate constant of 4.4×10^{-5} s^{-1} at 22.5 °C.
a) If the reaction constant for a series of substituted phenyl acetates is determined to be 0.87, what is rate constant for the neutral hydrolysis of the unsubstituted phenyl acetate at this temperature.
b) Suggest a substituted phenyl acetate that will have a hydrolysis half-life greater than one week.

7. The base catalyzed hydrolysis of phenyl N-phenyl carbamates occurs by the elimination of PhO⁻ group as the rate determining step.
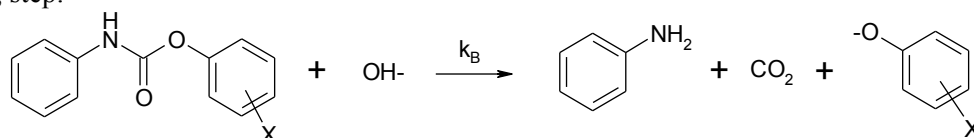
a) Determine the reaction constant (ρ) for this reaction using the using the second order rate constant (k_B) values given in the Table below for other substituted phenyl N-phenyl carbamates.
b) Calculate the second order rate constant for 3-trifloromethylphenyl N-phenyl carbamate.

X	k_B (M^{-1} s^{-1})	X	k_B (M^{-1} s^{-1})
p-CH₃	3.0×10^1	*m*-Cl	1.8×10^3
p-OCH₃	2.5×10^1	*m*-NO₂	1.3×10^4
p-Cl	4.2×10^2	*p*-NO₂	2.7×10^5

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.
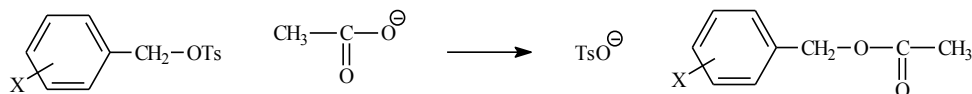
a) Why are the modified σ⁺ values are used instead of σ
b) Explain the magnitude and sign of each of the two reaction constants and provide mechanism/s consistent with these observations.

Table 1: Hammett constants for some common substituents

Substituent	σ_{meta}	σ_{para}	$\sigma-$	σ^+	$\sigma_0^{phenols}$
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: $\sigma-$ and σ^+ apply to *para* substituted groups only

Table 2: Reaction and acidity constants for aromatic acids in water at 25°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

Hammett Plot for Question 8