Probing Mechanisms: Hammett Plots and Isotope Effects
February 10, 2020

- Sigma (σ) constants.
- The Hammett reference reaction.
- The reaction constant or Rho (ρ).
- Examples of Hammett studies.
- Isotope effects in the Cr(VI) oxidation of alcohols.

110b Teaching Fellows: Felipe Becerril, Christina Beck, Isabelle Cheng, Junha Gu, Nathalie Hong, Shy Lavasani, Allison Liu, Casey Morrison, Jerusalem Nerayo, Eric Tang, Baili Zhong, Martín Acosta Parra.

Chemistry Seminar! Prof. Doug Grotjahn, San Diego State University, "When Two are Better than One: Bifunctional Catalysts that Move Protons for Organic Chemistry and Energy." Tuesday, February 11, 11:00 am, Seaver North Auditorium.

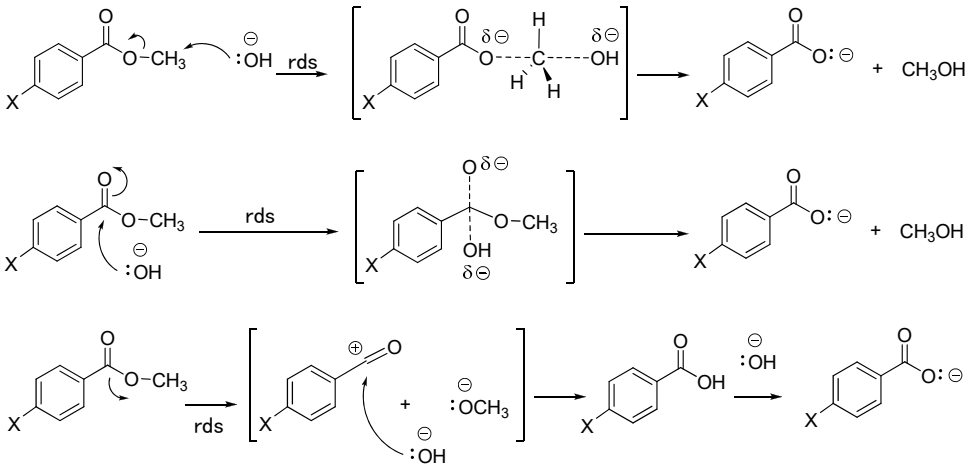
O'Leary office hours: T/Th 9:30-10:00 am, SN 208.

O'Leary's evening review session: Wednesdays 7:00 PM, SN Aud. **Course website**: http://pages.pomona.edu/~djo04747/110/

Suggested Problems for Exam 2. 10e: 16.20, 24, 30, 33, 35, 41, 44, 45, 47. 11e: 16.23, 27, 33, 36, 38, 44, 47, 48, 50. 10e/11e: 17.20, 17.28, 17.31, 17.33, 17.35, 17.38, 17.41, 17.42, 17.47.

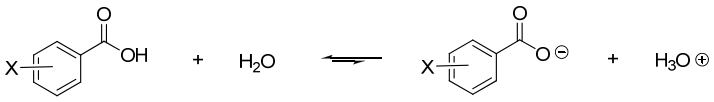
The Big Picture

What tools do we have to differentiate the following mechanistic possibilities?

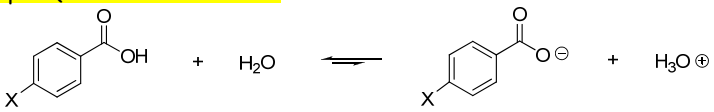


Hammett defined a scale that measured the ability of substituents to influence the acidity of benzoic acid.

The reference reaction (in water at 25 °C):



How $\sigma_{para(Cl)}$ is determined:



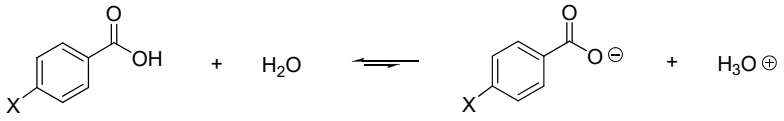
Define:

$$\sigma_{Cl} = \log\left(\frac{K_{Cl}}{K_H}\right) = \log K_{Cl} - \log K_H = pK_H - pK_{Cl}$$

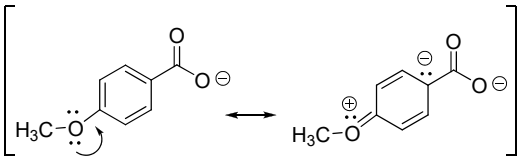
Use known pKa's to compute sigma:

$$pK_H = 4.19 \qquad pK_{Cl} = 3.95 \qquad \sigma_{para(Cl)} = 0.24$$

The trend in σ values follows what we expect from EAS rxns:



X	σ_{para}	type
$-OCH_3$	-0.27	EDG
$-CH_3$	-0.14	EDG
-H	0.00	reference
-Cl	0.24	EWG
-CN	0.70	EWG
$-NO_2$	0.81	EWG



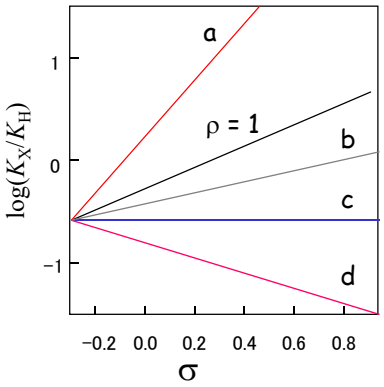
Rho (ρ): the reaction or sensitivity constant

$$\log\left(\frac{K_X}{K_H}\right) = \rho\sigma_X$$

equilibria (thermodynamics)

$$\log\left(\frac{k_X}{k_H}\right) = \rho\sigma_X$$

rates (kinetics)



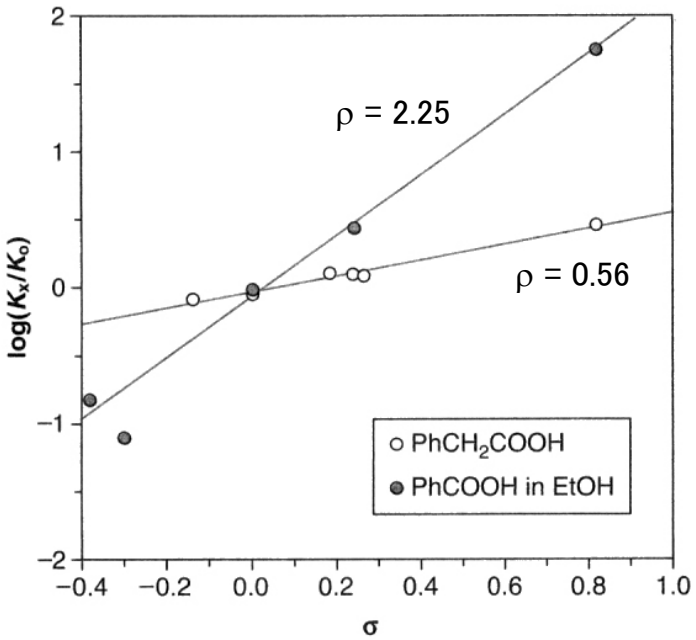
a. When ρ > 1, the reaction under study is more sensitive to substituents than benzoic acid, and negative charge is building during the reaction. (or rate is increased by electron withdrawal)

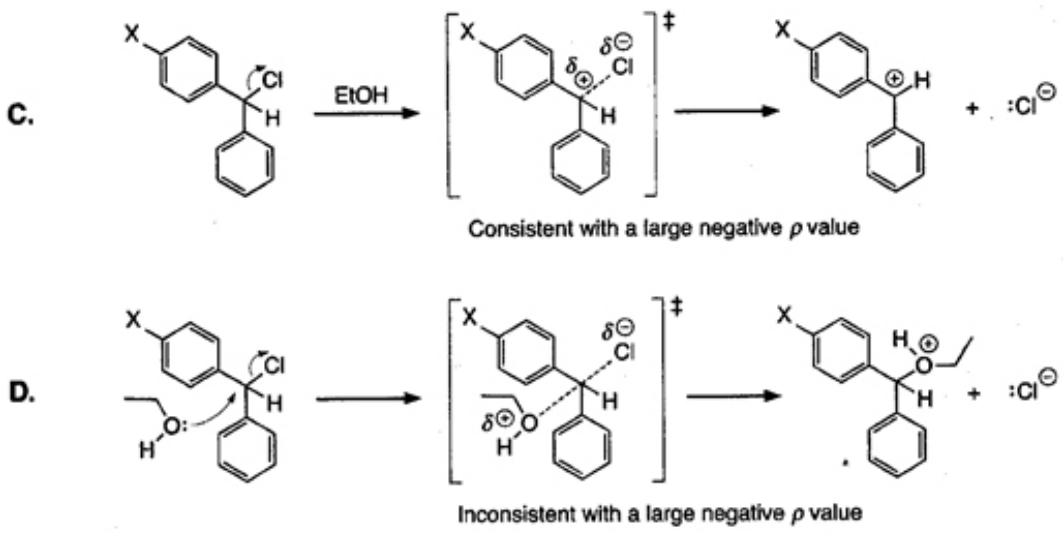
b. When 0 < ρ < 1, the reaction is less sensitive to substituents than benzoic acid, but negative charge is still building during the reaction.

c. When ρ ≈ 0, the reaction shows no substituent effects.

d. When ρ is negative, positive charge is building during the reaction. (or rate is increased by electron donation)

Case Study 1: substituted phenyl acetic acid in H_2O and benzoic acid in EtOH





A ρ value of -5.09 for the first step of the substitution reaction given in **C** and **D** supports alternative **C**.

Anslyn, Dougherty "Modern Physical Organic Chemistry" 2006.

A problem to consider:

Benzaldehyde cyanohydrin formation, shown below, may involve rate-determining attack of either H+ or CN-. From the observed ρ value (2.33) for the rate of formation of cyanohydrins from substituted benzaldehydes, which step do you think is rate determining?

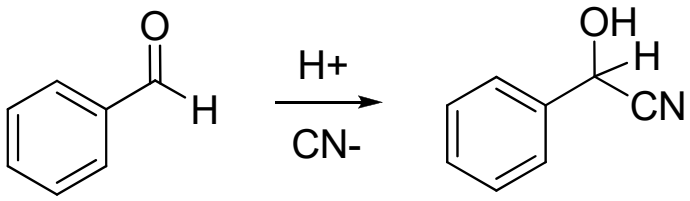


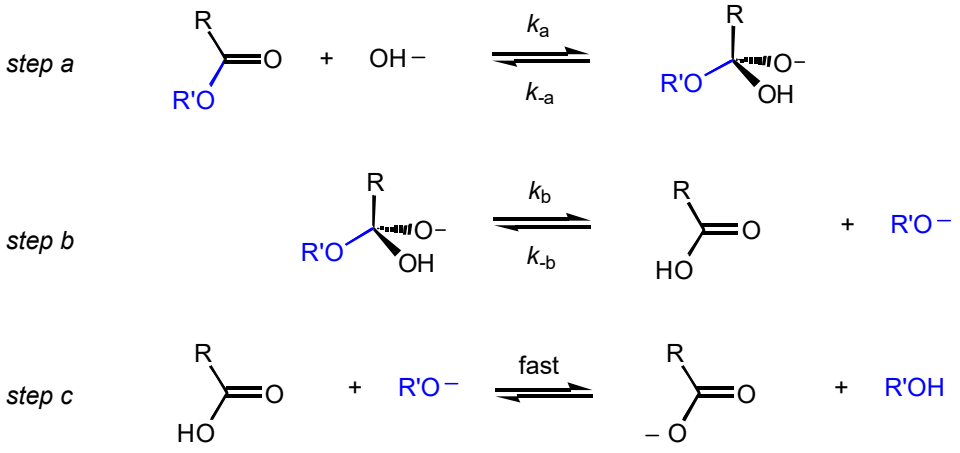
Table 8.2
σ Values for Several Commonly Encountered Substituents*‡

Substituent	σ_{meta}	σ_{para}	σ^+	σ^-
$-NH_2$	−0.09	−0.30	−1.3	
−OH	0.13	−0.38	−0.92	
$-OCH_3$	0.10	−0.12	−0.78	
$-C(CH_3)_3$	−0.09	−0.15	−0.26	
$-CH_3$	−0.06	−0.14	−0.31	
$-Si(CH_3)_3$	−0.04	−0.17		
$-NHC(O)CH_3$	0.14	0.0	−0.6	0.47
−Ph	0.05	0.05	−0.18	0.08
−I	0.35	0.18	0.13	
−Br	0.37	0.26	0.15	
−Cl	0.37	0.24	0.11	
−F	0.34	0.15	−0.07	
$-C(O)CH_3$	0.36	0.47		0.82
$-OC(O)CH_3$	0.39	0.31	0.18	
−C(O)OH	0.35	0.44		0.73
$-CF_3$	0.46	0.53		0.74
−CN	0.62	0.70		0.99
$-NO_2$	0.71	0.81		1.23
$-N(CH_3)_3^+$	0.99	0.96		

*Ritchie, C. D., and Sager, W. F. "An Examination of Structure–Reactivity Relationships." *Prog. Phys. Org. Chem.*, **2**, 323 (1964).
‡σ^+ and σ^- are for para substitution.

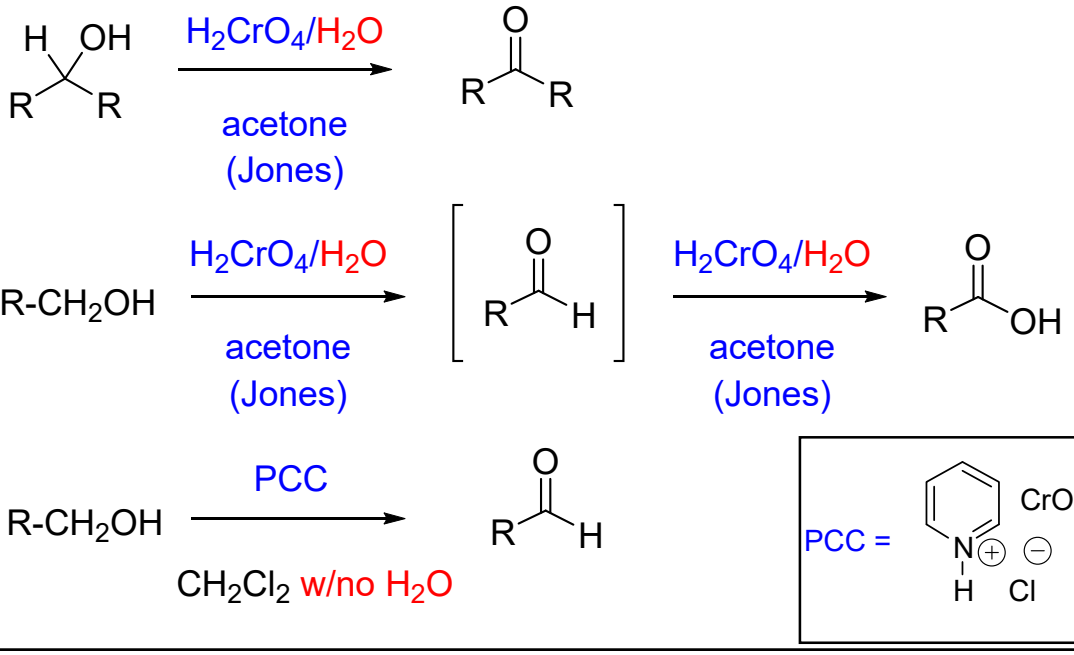
Anslyn, Dougherty "Modern Physical Organic Chemistry" 2006.

Base-Promoted Hydrolysis of Esters

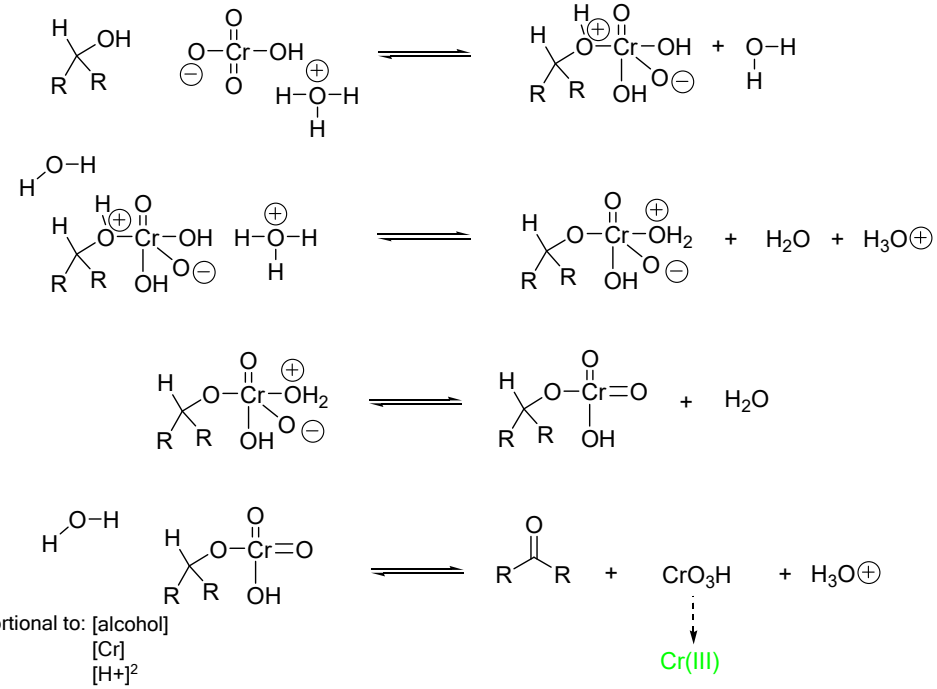


If RO- is a better leaving group than HO-, then the k_b step is fast, k_a is rate determining.

Cr(VI) Oxidation of Alcohols: An Overview of Reagents



Mechanistic Proposal for the Jones Oxidation – Solomons and many other texts.



Rate is proportional to: [alcohol]
[Cr]
$[H+]^2$