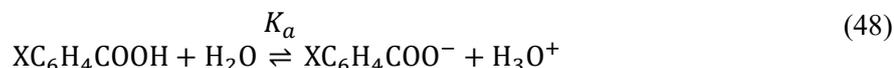


❖ Substituent and Reaction Constants

To discuss the substituent and reaction constants, we need to recall the quantitative relationship between the structure and reactivity first. To do so, we need to find some mathematical parameter that can be used to represent the combined magnitude of inductive and resonance effects of different substituents. This can be achieved by considering the hydrolysis of a series of different benzoic acids as given below.



Where X is a substituent at the *m*- or *p*-position and K_a is the dissociation constant. As expected, the dissociation constant was found to be different for differently substituted substrates.

Since an electron-withdrawing group will better stabilize the conjugate base (i.e., $\text{XC}_6\text{H}_4\text{COO}^-$), resulting in a larger magnitude of K_a (lower pK_a). On the other hand, an electron-donating group will destabilize the conjugate base (i.e., $\text{XC}_6\text{H}_4\text{COO}^-$), resulting in a smaller magnitude of K_a (higher pK_a). Therefore, we can say that the electronic effect (inductive plus mesomeric effect) of a substituent can be represented as the difference between the pK_a value of its benzoic acid derivative and the pK_a value of benzoic acid itself; mathematically, we can say

$$\sigma_X = \log(K_a) - \log(K_a)_0 = -p(K_a) + p(K_a)_0 \quad (49)$$

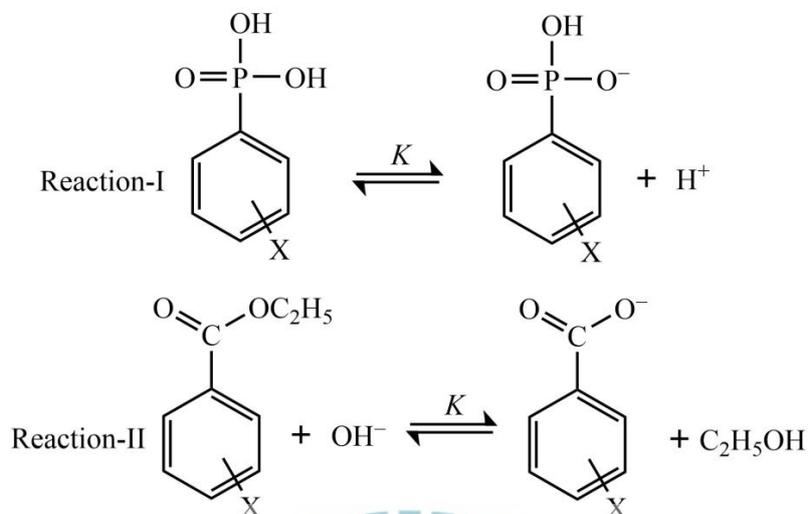
Where the parameter σ_X (or simply σ) is called as substituent constant; and was found for several different groups just subtracting its benzoic acid derivative's pK_a value from pK_a value of benzoic acid. Using $\log m - \log n = \log m/n$, equation (49) can also be written as

$$\log \frac{(K_a)}{(K_a)_0} = \sigma \quad (50)$$

Now if we plot a curve between $\log(K_a)/(K_a)_0$ vs σ , we will definitely get a straight line with a slope which is equal to unity.

Now we need to check if these σ values (i.e., of substituted benzoic acids) can also be used for other meta- or para-substituted benzene derivatives. To do so, consider two series of reactions; the first one is the acid dissociation of phenyl phosphonic acid, and the second one is the base hydrolysis of substituted ethyl benzoate.

Here we will find if different substituents affect their dissociation constants or rates in the same manner as affected in the case of substituted benzoic acid. Also, we did not use ortho-substituents or substituents in the aliphatic system because they also contain steric factors and don't not linear variation.



When plotted the experimental $\log(K_a)/(K_a)_0$ for the reaction-I and experimental $\log k/k_0$ for reaction-II vs the substituent constants obtained for the substituted benzoic acids, we get the following curves. It is obvious that the plots will still be linear like but the slope will be changed. This implies that the order and relative effects for different substituents on both reactions remain the same though the magnitude has been changed which can be attributed to the different nature reaction considers from 'base reaction'.

Therefore, our aim, in this case, should be the determination of the slope (let us say ρ). Since on the vertical side we have ' $[\log(K_a)/(K_a)_0]_{sppa}$ ' for reaction-I (acid dissociation of phenyl phosphonic acid) and on the horizontal side we have ' σ or $[\log(K_a)/(K_a)_0]_{sba}$ ' for base reaction (hydrolysis of substituted benzoic acid), the slope should be

But from equation (50), we know that $[\log(K_a)/\log(K_a)_0]_{sba} = \sigma$; and therefore, we get

$$\left[\log \frac{(K_a)}{(K_a)_0} \right]_{sppa} = \rho \sigma \quad (51)$$

For any reactions,

$$\log K_a = \rho \sigma - \log (K_a)_0 \quad (52)$$

Similarly, on the vertical side we have ' $\log k/k_0$ ' for reaction-II (base hydrolysis of substituted ethyl benzoate) and on the horizontal side we have ' σ or $[\log(K_a)/(K_a)_0]_{sba}$ ' for base reaction (hydrolysis of substituted benzoic acid), the slope should be

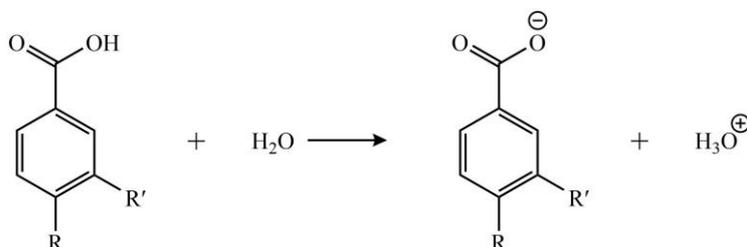
But from equation (50), we know that $[\log(K_a)/\log(K_a)_0]_{sba} = \sigma$; and therefore, we get

$$\left[\log \frac{k}{k_0} \right]_{sppa} = \rho \sigma \quad (53)$$

Equation (51, 53) are Hammett equations where ρ and σ are the substituent and reaction constants.

➤ **Substituent Constants (σ)**

From the derivation of Hammett's equation, we know that the substituent constants can be collected by finding the change in the pK_a value of substituted benzoic acid in water at 25 °C. The reaction constant for this 'base reaction' will simply be equal unity.

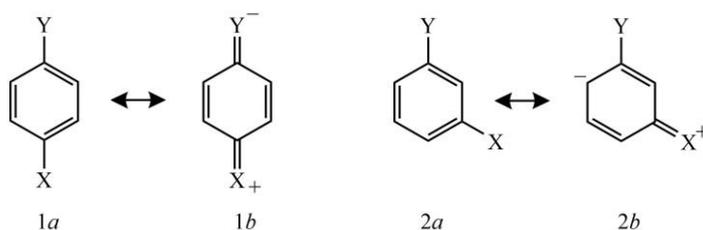


Since an electron-withdrawing group will better stabilize the conjugate base (i.e., $XC_6H_4COO^-$), resulting in a larger magnitude of K_a (lower pK_a). On the other hand, an electron-donating group will destabilize the conjugate base (i.e., $XC_6H_4COO^-$), resulting in a smaller magnitude of K_a (higher pK_a). Therefore, we can say that the electronic effect (inductive plus mesomeric effect) of a substituent can be represented as the difference between the pK_a value of its benzoic acid derivative and the pK_a value of benzoic acid itself.

Various substituent effects can be concluded by looking at σ values displayed in Table 1. With $\rho = 1$, the group of substituents with increasing positive values (such as nitro) makes the equilibrium constant increase relative to the hydrogen as the substituent, which in turn, means that the acidity of the benzoic acid has been increased. This is because the substituents like NO_2 stabilize the negative charge on the carboxylate ion by an inductive effect ($-I$) and also by a negative resonance effect ($-R$).

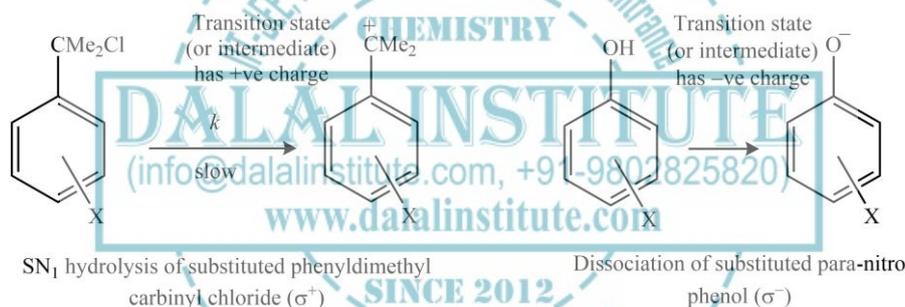
The second kind of substituents is the halo- groups, for which the substituent effect is modestly positive. This can be attributed to the fact that even though the inductive effect is still negative, the resonance effect is positive ($+R$), canceling the former partially. Experimental data also demonstrated that for these substituents, the m -effect is much bigger than the p -effect, because the resonance effect is largely reduced in the m -substituent. In the case of m -substituted substrates, a C atom with the negative charge is further away from the COOH group.

The behavior of resonance effect in the perspective of substituent constants can be understood by the given below, where, in a p -substituted arene (1a), one resonance structure (1b) is a quinoid with the positive charge on the substituent X, freeing electrons and so destabilizing the Y group. This kind of destabilizing outcome is not likely to happen when X is at the m -site.



Furthermore, groups such as ethoxy and methoxy can even show opposite signs for the substituent constant due to the opposing nature of the inductive and resonance effects. It's just the aryl and alkyl substituents like methyl are electron-donating in w.r.t. inductive as well as resonance effects. Finally, If the reaction constant's sign is negative, substituents with a negative substituent constant will raise K_a values.

Now although the substituent constants derived from substituted benzoic acid were quite accurate in predicting $\log(K_a)/(K_a)_0$ or $\log k/k_0$ for several reactions, cases where the rates or dissociations constants predicted were not in line if the substituent is either strongly electron-withdrawing or strongly electron-donating in nature. For instance, $\log(K_a)/(K_a)_0$ of substituted phenols for *p*-CN and *p*-NO₂ are above the line indicating that systems with these substituents act as stronger acids than expectations. This is because if electron-withdrawal arising from mesomeric effects is extended to the reaction site via 'through conjugation', the conjugated acid will be exceptionally stable. Since the substituent is developing a negative charge during this process, the modified substituent constant will be labeled as σ_p^- . Similarly, if the electron-donating arising from mesomeric effects is extended to the reaction site via 'through conjugation', the conjugated acid will be less stable. Since the substituent is developing a positive charge during this process, the modified substituent constant will be labeled as σ_p^+ .



The magnitude by which $\log(K_a)/(K_a)_0$ or $\log k/k_0$ deviate from σ value is added to produce a new scale of substituent constants. The same is true for the *m*-site excepting the fact that values of σ_m^+ will be the same as the σ_m values.

Table 3. Substituent constants: para and meta substituted benzene rings.

Group	σ_p	σ_m	σ_p^+	σ_m^+	σ_p^-
COOH	0.44	0.35	0.42	0.32	0.73
COOR	0.44	0.35	0.48	0.37	0.48
CN	0.70	0.62	0.66	0.56	1.00
NO ₂	0.81	0.71	0.79	0.73	1.27
Cl	0.24	0.37	0.11	0.40	–

➤ **Reaction Constants (ρ)**

After knowing the values of substituent constants, the reaction constant (ρ) can be obtained for an extensive range of reactions. The ‘prototype or base’ reaction is the alkaline hydrolysis of ethyl benzoate in a water mixture at 25 °C. For instance, plotting experimental values of $\log(K_a)/(K_a)_0$ and $\log k/k_0$ for the acid dissociation of phenyl phosphonic acid and base hydrolysis of substituted ethyl benzoates vs substituent constants yielded the ρ values equal to 0.76 and 2.4, respectively.

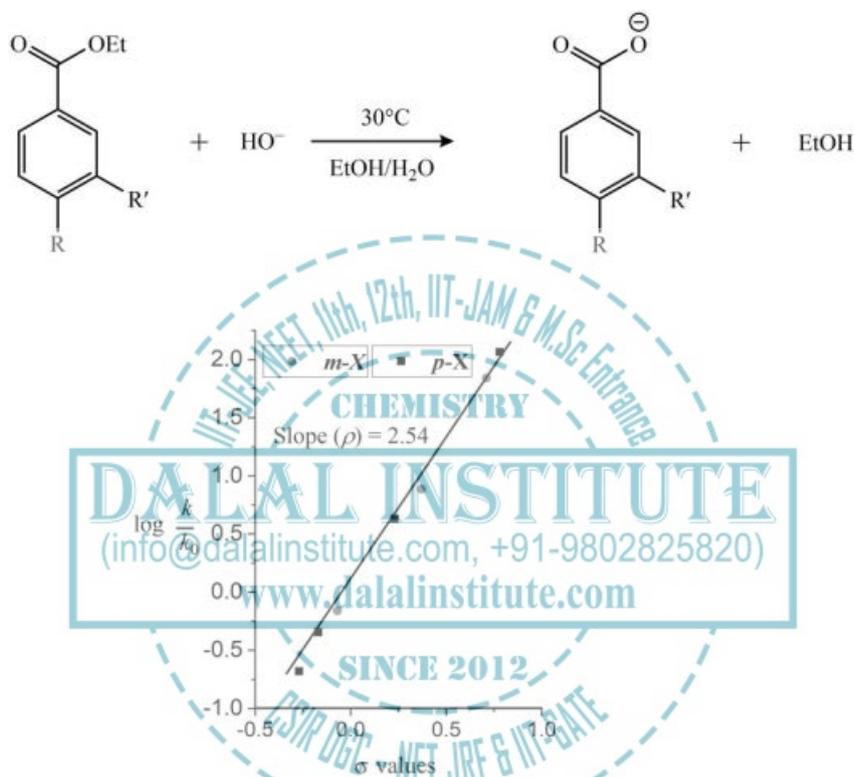


Figure 19. $\log k/k_0$ vs σ for alkaline hydrolysis of substituted ethyl benzoate.

Reaction constants or ρ values for many other reactions and equilibria have been obtained over years. P-values for some of the important reactions provided by Hammett himself are given below.

- i) Hydrolysis of substituted cinnamic acid ester in water /ethanol (+1.267).
- ii) Acid-catalyzed esterification of substituted benzoic esters in C₂H₅OH (-0.085).
- iii) Ionization of substituted phenols in H₂O (+2.008).
- iv) Substituted benzyl chlorides' hydrolysis in H₂O-acetone at 69.8 °C (-1.875).
- v) The acid-catalyzed bromination of substituted acetophenones in CH₃COOH (acetic acid) or water or hydrochloric acid (+0.417).

Now, as far as the significance is concerned, the sensitivity constant (i.e. reaction constant ρ), defines the reaction's susceptibility to different substituents, relative to the ionization of benzoic acid; and is equal to the slope of the Hammett's equation or plot. The reaction's information and the mechanism involved can be found using the value of ρ as given below.

Case 1: if $\rho > 1$, the reaction has a greater sensitivity to substituents than the benzoic acid and a negative charge will accumulate (or a loss of positive charge) in the course of the reaction.

Case 2: if $0 < \rho < 1$, the reaction will be less sensitive to substituents than the benzoic acid and a negative will accumulate (or a loss of positive charge).

Case 3: if $\rho = 0$, the reaction will show no sensitivity to substituents, and no charge will be lost or built.

Case 4: if $\rho < 0$, a positive will accumulate (or a loss of negative charge) during the reaction.

The correlations given above can be used to explain the mechanism of an organic reaction. Since the ρ -value is connected to the charge in the course of the rate-limiting step, the mechanism involved can be developed using the data obtained. For instance, if an aromatic compound's reaction is believed to happen via one of two routes, the organic compound can simply be modified with substituents with dissimilar σ values and then the shortlisting can be done by taking kinetic measurements. After the measurements we mentioned, the Hammett plot can be raised to find the ρ value. Now, if the mechanisms we believe to be true encompass the charge formation, the ρ value will easily confirm our predictions. On the other hand, if the Hammett plot demonstrates that no charge is created during the reaction (i.e., slope or $\rho = 0$), the mechanism with the charge development can simply be neglected.

It is also worthy to note that the Hammett plots may not always be flawlessly linear. For example, a plot may have an unexpected or rapid change in the ρ value or slope. A case like this means that the mechanism responsible for the reaction has simply been changed due to the addition of different substituents. Some other kinds of deviations from linear variation may be attributed to a change in the site of the transition state. A situation like this means that certain substituents may cause the transition state to form later (or earlier) during the mechanism involved.

Table 4. The reaction constants (ρ -values) for a relative analysis for some typical organic chemical reaction types.

Reaction type	ρ -value
Ionization of acids	1.464
Alkaline hydrolysis of ethyl esters	2.494
Acids with diphenyldiazomethane	0.937
Acid dissociation of phenyl phosphonic acid	0.76

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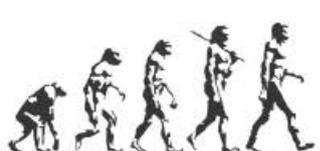
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A TEXTBOOK OF ORGANIC CHEMISTRY

Volume I

MANDEEP DALAL



First Edition

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