**1.Introduction**

Organic compounds can be prepared with structural variation in the vicinity of a reaction centre and thus it is possible to allow an almost continuous variation in its electrophilic or nucleophilic character. This capacity may then be used as a delicate probe into the effects caused by electronic perturbation upon reaction and from which the electronic demands of the reaction may be inferred. Many rate constants and equilibrium constants for organic reactions in solution have been measured and the spectra (IR, UV, NMR etc.) of thousands of organic compounds have been recorded. As this body of quantitative results has been enormous, it becomes important to summarize and analyze data. The summarizing has involved the development and application of empirical correlations by means of which one body of data can be related to another. At the same time, the data may be analyzed to reveal the fundamental factors underlying the phenomena in question. This general approach is commonly known as correlation analysis.

One of the most successful and intensively investigated empirical relationships towards quantitative exploration of reactivity in organic chemistry is the famous Hammett equation.1-15 The Hammett equation describes linear relationship involving log k or log K of substituted benzoic acids. Such correlations may be described as rate-rate, equilibrium-equilibrium or rate-equilibrium relationships. These relationships are usually referred to as Linear Free Energy Relationships (LFER). The term LFER has often been used to cover the whole correlation analysis in organic chemistry. A brief account of correlation analysis is given below:

**1.1 The Hammett equation**

The Hammett equation3,12,14,15 is usually expressed in the form of equations (1.1) and (1.2), where k or K is the rate or equilibrium constant respectively for a side-chain reaction of *meta*- or *para*-substituted benzene derivative.

log k = log ko + *ρ*σ (1.1)

log K = log Ko + *ρ*σ (1.2)

The symbol ko or Ko denotes the statistical quantity approximating to k or K for the unsubstituted or parent compound. The empirical constant σ, known as substituent constant, measures the polar effect relative to hydrogen as a substituent in the *meta*- or *para*- position and is, in principle, independent of the reaction. The other constant *ρ*, known as reaction constant, depends on the nature of the reaction and measures the susceptibility of the reaction to polar effects. The value of *ρ* is determined by the reaction and its condition such as a reagent, solvent, catalyst and temperature and is independent of the nature of the substituents. The ionization of benzoic acids in water at 25o C is taken as the standard reaction for which *ρ* is defined as 1.00. The value of σ for a given substituent is thus log (K/Ko), where Ko is the ionization constant of the substituted benzoic acid itself. The magnitude of *ρ* measures the extent of transmission of the electronic effect of substituents. The validity of the above equations (1.1) and (1.2) is restricted to substituents in the *meta*- and *para-* positions of the benzene ring. These equations (1.1) and (1.2) were tested by Hammett15 on fifty-two reaction series and found to express a large body of experimental data with a mean deviation of about ±15 percent.

The electron density at the reaction site is determined by the ability of the substituent to withdraw or donate electrons and is measured by σ constants. Electron-attracting substituents have positive values of σ and electron-releasing substituents have negative values of σ. The σ scale covers roughly the numerical range 0 ± 1.0.

A reaction which is facilitated by reducing the electron density at the reaction centre has a positive value of *ρ* and one facilitated by increasing the electron density at the reaction centre has a negative value. The *ρ* scale covers roughly 0 ± 4. The sign of *ρ* in radical reactions cannot easily be predicted. However, the electron distribution in the transition state of radical reactions can be inferred from the experimental value. The dependence of *ρ* on temperature has the form16,17 of equation (1.3).

*ρ* = constant (1- β/T) (1.3)

The slope of *ρ* vs T-1 plot is usually positive,8 so that *ρ* decreases with temperature. The slope is usually small even almost zero18,19 but steep dependence20 and even reversal ones8 have also been described.

The dependence of *ρ* on solvent21-23 is very marked but is not well understood theoretically. It seems that the effect of solvent cannot be described by a single parameter equation.

Of the factors controlling the absolute values of *ρ*, the distance of the substituents from the reaction centre is the most important, more exactly it is the length and nature of the side chain. When the side-chain is extended by inserting in it a group Y, the constant *ρ* decreases in the ratio Лy (the transmission factor) defined in equation (1.4)

Лy = *ρ*yz / *ρ*z (1.4)

Where *ρ*yz is the reaction constant for the compound of the type Ar-Y-Z and *ρ*z is the reaction constant for the compound of the type Ar-Z.

The value of Л indicates the ability of the chain to transmit polar effects;24-27 however, in order to obtain results of general validity, π must be independent of the reaction centre chosen (Z), as indicated in Eq. (1.5).

*ρ*yz / *ρ*z = *ρ*yz ’ / *ρ*z ’ (1.5)

The equation (1.5), the so called *ρ* – *ρ* relationship, has been shown to hold in the dissociation of carboxylic acids, their reactions with diazodiphenylmethane and hydrolysis of their esters.25-29 For the insertion of a CH2 group in Ar-Z, π corresponds to the value of about 0.419,30 and with two CH2 groups it decreases to ca. 0.2.8,27,29 Replacing one CH2 group by a hetero atom (oxygen27,31,32 or Sulphur31,33,34), a sulphoxy,31,33 a sulphonyl group31,33 or an amino group35,36 has little effect on the value of π.

Conjugated chains transmit polar effects much better than saturated chains. A CH=CH group is approximately equivalent to one CH2 group.25,27,37,38

Transmission through the C≡C group is similar39 to that of the C=C bond but it is weaker than through the CH=CH group.27,40,41 Even longer conjugated chains transmit electronic influence effectively.42-45

As early as 1953, Jaffe8 examined the application of the Hammett equation to about 400 reaction series and on the basis of correlation coefficient concluded that about 70% of the correlations were satisfactory (r > 0.95) or excellent (r > 0.99). This suggests that about 30 % of the rate or equilibrium data are outside the scope of the Hammett equation in its original form and mode of application.

Deviations are commonly shown by *para*-substituents of considerable +R or -R effect. When σ values based on the ionization of benzoic acids are used, deviations may occur with highly electron-withdrawing *para*-substituents (+R substituents) for reactions involving -R electron-rich reaction centres are with highly electron-releasing substituents (-R substituents) for reactions involving +R electron-poor reaction centers. These deviations, have been explained in terms of ‘cross conjugation’ i.e., conjugation involving substituent and reaction center. In each case, ‘exalted’ σ values are required for conformity to the Hammett equation. The special substituent constants for +R substituents are denoted by σ – and those for -R substituents are denoted by σ +.46 The values of σ – are based on the ionization of either anilinium ions or phenols in water. The values of σ + are based on the rates of solvolysis of t-cumyl chlorides in 90 % acetone-water at 25o C.

The use of σ + and σ –  greatly extends the range of applicability of the Hammett equation.47-49 However, the contribution of the resonance effect of a substituent relative to its inductive effect must, in principle, vary continuously as the electron-demanding quality of the reaction center varies, i.e., demanding upon whether it is electron-rich or electron-poor. Hence for each substituent having a resonance effect, a sliding scale of substituent constants would be expected and not just a pair of discrete values of σ + and σ for -R substituents or σ –  and σ for +R substituents. This tends towards the situation in which the substituent constant becomes reaction dependent. Therefore, various multimeter extensions of the Hammett equation appeared, notably the Yukawa-Tsuno equation,50,51 the Taft-Lewis equation,52-56 and the Swain-Lupton equation.57

**1.2 Multiparameter extensions of the Hammett equation**

Yukawa and Tsuno50 proposed a method for dealing with -R substituents in their influence on reactions which are more electron-demanding than the ionization of benzoic acids. They suggested that values of (σ+- σ) would provide a scale of enhanced resonance effects and they modified the Hammett equation as

log k = log ko + *ρ*[σ +r (σ+ - σ ) ] (1.6)

The equation (1.6) implies the multiple linear correlations of log k with σ and (σ+- σ).

The quantity r is a proportionality constant giving the contribution of the enhanced resonance effect for -R substituents. If r = 0 the equation is reduced to the simple Hammett equation and if r = 1, it corresponds to a straight forward correlation with σ +.

A corresponding equation with σ – constants to deal with the influence of +R substituents on reactions which are less electron-demanding than the ionization of benzoic acids was formulated by Yoshika *et al*.51

log k = log ko + *ρ*[σ +r ( σ -- σ ) ] (1.7)

According to Taft52-54, the Hammett σ values are quantitatively separable into inductive and resonance contributions through the following equations:

σm = σI + ασR (1.8)

σp = σI + σR (1.9)

The inductive effect is given by σI is assumed to operate equally from the *meta*- and *para*-positions. The resonance effect given by σR, contributes to σm indirectly, α being the “relay coefficient”. Taft and Lewis53,54 set up a σI scale based on alicyclic and aliphatic reactivities. Based on the ionization of benzoic acid, a value for α of 0.33 was suggested.

Exner58 carried out a modified analysis based on the following equations:

σm = σI + 0.33 σR  (1.10)

σp = λσI + σR (1.11)

The coefficient λ expresses any differences in the operation of the inductive effect as between the *meta*- and the *para*- position. Exner58 was in favour of λ = 1.14 i.e., the inductive effect operates more powerfully from the *para-*position. The dissection of parameters into σI and σR- type contributions gives the possibility of a ‘dual substituent parameter’ treatment for reaction series through an equation.53,54

log (k/ko) = *ρ*I σI + *ρ*R σR (1.12)

In Taft’s treatment, each substituent is characterized by position-independent σI and σR values, but the susceptibility to inductive and to resonance effect is to be expressed separately through position-dependent *ρ*I  and *ρ*R values. The separation into inductive and resonance effects has been performed for σ+, σ- and σo (based on ‘insulated’ system) constants to give σR+, σR- and σRo respectively.

Swain and co-workers57,59 have expressed the polar effect of any given substituent in terms of two basic characteristics: a field constant, F, and a resonance constant, R. All the various σ constants are the linear combinations for F and R of the form, Eq. (1.13)

σ = f F + r R (1.13)

The field, f, and resonance, r, are weighting factors which give the blend of field and resonance effects for the systems used to define the particular σ scale. This treatment has found extensive application in the correlation analysis of NMR data. Application to chemical reactivity seems to be restricted to a few instances.

**1.3 *ortho*-Effect**

Linear free energy relationship to the Hammett type that has been used to correlate vast numbers of rate (k) and equilibrium constant (K) for reactions of *meta-* and *para*- substituted derivatives. Since the Hammett equation has been so successful in the treatment of the effects of groups in the *meta-* and *para-* position, it is not surprising that attempts have been made to apply it to *ortho-*positions also.60,61 The effect on a reaction rate or equilibrium constant of a group in the *ortho-*position is called *ortho-* effect. The *ortho-*substituents are bound to the adjacent position of the side-chain, various kinds of proximity effects, such as steric and proximity electric effects, which are otherwise insignificant, generally operate on the side chain functions. Hydrogen bonding and other intramolecular interactions of *ortho-*substituents may sometimes play significant roles in reactivities of *ortho*-substituted derivatives. Unfortunately, these proximity effects contribute in varying degrees in different systems. Thus, the reactivities of *ortho-*substituted compounds are not explained by a single, generally applicable set of parameters. However, a correlation can be achieved in one of the following ways3.

log k = *ρ*\*σ\*o + h (1.14)

σ\* is the *ortho-*substituent constant and ρ\* is the susceptibility constant.

log k = δ Es + h (1.15)

Es is the steric substituent constant and δ is the susceptibility constant. The ratio of the rate constant for an *ortho-* to that of corresponding *para-*substituted benzene derivatives, ko/kp may frequently be taken as an approximate measure of the steric effect of the *ortho-*substituents.62

log (k/ko) = = *ρ*\*σ\*o + δ Es (1.16)

The above equations (1.14), (1.15) and (1.16) are due to the work of Taft.

Charton’s treatment, on the *ortho-*substituent effect, is considered to be a better treatment because of its wider applicability in understanding the nature of the *ortho-*effect. He derives two multiparameter equations. They are as follows,

log k = α σI + β σR + h (1.17)

where σI and σR are the inductive and resonance substituent constants α and β are the localized and delocalized compounds and h is the intercept.

log k = α σI + β σR + φ ν + h (1.18)

where ν is the parameter for the steric effect and φ is the coefficient of the steric term. Thus, the separation of polar, resonance and steric effect has received much attention in recent years.

**1.4 Correlation with spectroscopic data**

Though correlation of the substituent constant σ was originally proposed to equilibria and reaction rates, the substituent constants have also been applied to optical spectroscopy,63 NMR spectroscopy6,7 and to mass spectroscopy of organic compounds.64 Thus correlations of infrared frequencies65-68 with substituent constants and also of 1H and 13C NMR substituent-induced chemical shifts (SCS)69-77  have received considerable attention. Substituent effects in the mass spectra of organic compounds are also often explained with the Hammett σ constants.64,78-81

**1.5 Investigation of Substituent Effects by 1H and 13C NMR Spectra**

Soon after the first systematic studies of the 13C NMR of aromatic  
compounds it became evident that 13C SCS are likely to be useful for the three reasons.

i) The inherently high dispersion of 13C SCS means that data would be obtained with fairly high precision, ii) There appears to be a close relationship between the 13C chemical shift of a nucleus and the calculated charge density at that atom, thereby reinforcing the supposed parallelism with substituent electronic perturbations, iii) The ,13C probe does not itself introduce any perturbation. Consequently, 13C chemical shifts have been used extensively as monitors of molecular structure and electronic distribution.

l3C NMR chemical shift measurements are increasingly used for the investigation of the electronic effects of the substituents and their mode of transmission through aromatic and other unsaturated systems. In benzene derivatives, a substituent exerts a characteristic substituent effect on the chemical shifts of the ring carbon atoms. The carbon shielding and the chemical reactivity parameter are reflecting the changes in local charge density arising from the electronic influence of the substituent and hence these two quantities can be correlated.

The substituents may affect the local charge density of an aromatic carbon by various effects (Iσ, F, πσ, πF, R, πorbital and σπ*).* These changes in charge density at the aromatic carbons affect the paramagnetic shielding term.82 Electron releasing substituents delocalize their lone pair of electrons into the π*-* system and increase the charge density at the *o-* and *p-* carbons of benzene derivatives. Electron attracting substituents can delocalize the π*-*electrons of the ring and thereby reduce the charge density at the *o-* and *p-* carbons. Thus, electron releasing substituents shield the *o-* and *p-* carbons while electron attracting substituents have deshielding influence.

The effect of substituents in the ring on the chemical shifts of side-chain carbons is of obvious interest, especially in those cases where the side-chain carbon is conjugated with the ring. This allows resonance interaction with substituents to take place and the effect of distance on the extent of such interactions can be explored. The chemical shifts of sp2 and sp carbons directly bonded to the ring have been observed to show ‘reverse’ substituent effects83,84, i.e. electron attracting substituents apparently increase the electron density on the carbon concerned whereas electron releasing substituent decrease it. This phenomenon has been attributed to the polarization of the π- system of the side chain.

Correlation of the chemical shift with substituent constant (e.g. Hammett σ) has been widely used to investigate the nature of the effect of the substituent of the physical properties of compounds. Electron density around the nucleus of interest (C, H) is mostly affected by the electron donating and electron withdrawing ability of the substituent. Therefore, a correlation between the observed chemical shift and any parameter representing such ability seems to be well-founded, would indicate that the effect of any other rate would be satisfactorily predicted by simply measuring the chemical shift of a given derivative, and there are numerous reports on the subject.85 Correlation of these parameters has now been applied, originally proposed to equilibria and reaction rates, to spectroscopic properties such as 1H and 13C NMR substituent induced chemical shifts (SCS) in recent years.85- 92

The proton chemical shifts are influenced by magnetic anisotropies of neighbouring groups and by intermolecular (e.g. solvent) effects. In contrast with 1H NMR chemical shifts, 13C chemical shifts are relatively insensitive to the magnetic anisotropy effects93 and to solvent and concentration effects.94

Extensive correlations of 13C chemical shifts in mono-substituted benzenes with Hammett σconstants were first reported by Spieseck and Schneider95, following the pioneering studies of Lauterbur.96 It was observed that the chemical shifts measured for the *para*-ring carbons δ (Cp)of a series of mono-substituted benzenes were approximately related to the *σ+*pvalues of the substituents.94,97 Attempts to find analogous relationships for δ(Cm)of mono substituted benzenes have met with varied success.95,97,98 Schulman *et al*.97 have shown that δ (Cm) values of the substituents with non-bonding electron pairs correlate well with σ+m, but those of the remaining substituents give less satisfactory correlations.

A report on the correlation of NMR chemical shifts with Hammett values and analogous parameters99 has been given as,

δ= *⍴* σ + δo (1.19)

In Eq. (1.19), δis the chemical shift; σis an appropriate reactivity (Hammett) parameter such as σ*+*p, σ*-*p*,* σm*,* σI, σR (BA), σoR, σ+R, σ-R. *⍴* is a proportionality constant and δo is the intercept. For several chemical structures, single parameter relationship does not give satisfactory correlations. Therefore, several dual substituent parameter (DSP) extensions of the Hammett approach have been developed. Among them, the most important are Swain and Lupton22 (Eq.1.20) and Ehrenson *et al.*100 (Eq.1.21).

δ =ƒ F+ r R + δ*°* (1.20)  
 δ *= ⍴*I σI *+ ⍴*R σR +δ*°*  (1.21)

The important difference between the two is that Swain and Lupton apply a single set of F and R values whereas Ehrenson *et al*.101 allow a choice of four distinct σR scales (σR (BA), σ°R, σ-R and σ+R). Yukawa and Tsuno102 proposed equation (1.6) for dealing with the enhanced resonance effects and they modified the Hammett equation as follows (Eq. 1.22),

δ *= ⍴*σ + r (σ+ - σ) + δo (1.22)

the quantity 'r' is a proportionality constant giving the contribution of the enhanced resonance effects for +M substituents.

The DSP analysis of sterically congested systems has been improved by TSP by using Charton’s steric parameter using Eq. (1.23).

δ *= ⍴*I σI*+⍴*R σR + φν+δ*°* (1.23)

The DSP equation (1.21) is the most generally useful treatment and is well suited for the analysis of spectroscopic data. In equation (1.21), the derived *⍴*I and *⍴*Rvalues which are position-dependent, give a direct measure of the relative transmission of inductive and resonance effects. The DSP method represents a general approach for the correlation of substituent effects over a large range of different datasets. The generality is due to the independence of the *⍴*Iand *⍴*Rtransmission coefficients. Since inductive and resonance effects are transmitted by different mechanisms103 their relative importance may change from one system to another. This feature cannot be accommodated104 in a single parameter approach. The answer to the question whether a DSP method or a single parameter equation will best describe the SCS of the various systems is a subject of controversy. Last two decades papers may be mentioned to exemplify this. Cornelis *et al*.105 and Bottino *et al.*106 by an examination of a number of styrene derivatives reached the conclusion that the DSP treatment, in general, is not significantly superior to the simpler single parameter treatment. But Cornelis data enabled Craik and Co-workers104  to show the power of the DSP method. Anu *et al****.***107also have proved the power of the DSP method. It may be concluded that,

i) while in some situations there might be no significant importance in fits obtained by the DSP method compared with single parameter treatment, this is not so in the general case, and

ii) the *⍴*Iand *⍴*Rvalues obtained from the DSP analysis are extremely useful in assigning mechanistic significance to proposed pathways for the transmission of substituent effects.

The relative importance of the resonance and inductive effects is expressed by blending factor (λ) obtained as the ratio of the coefficients r and ƒ or *⍴*Iand *⍴*R.

**1.6 The Nature and Mechanism of Transmission of Electronic Effects**

In order to assess the influence of substituents on the chemical shift of organic molecules a clear understanding of the nature and transmission of the different types of substituent effects is necessary.

**1.6.1 The Inductive Effect**

The basis of this electronic perturbation is originating in part from differences in electro negativity which causes polarization of both σ- and π- bonds and also from electrostatic effects experienced at the reaction center due to charges and dipoles resident on the substituent. A polarization of both σ- and π- bond by the substituent group is known as inductive effect Fig. (1.1), becoming progressively attenuated. The other, known as a field effect Fig. (1.2) is propagated through space and depends more on its intensity on proximity than on the number of bonds separating source and receptor. The electronic dipole field of the polar substituent-substrate bond can influence the reaction center across space and this is called field effect.108-112



Fig. 1.1



Fig. 1.2

The substituent effects in various aromatic systems act through polarization of π-electrons whether the polar nature of a substituent or substituent-carbon bond can polarize a π-system without charge transfer. This has been generally referred to as a π- inductive effect113, which can arise in two ways, i) induction of charge differences on the underlying σ- framework may lead to compensating changes in the π- electronic distribution and is designated as πσ effect.108,114,115 The partial charges on CH2-X, which in turn cause a redistribution of charge by an alternate polarization of π- electrons as in Fig. (1.3). ii) the π-system may also be polarized by a through-space electrostatic interaction with a remote dipole and this effect is termed as πF effect.



Fig 1.3

The π- system may also be perturbed by repulsive interactions with a neighbouring filled orbital on the substituent. This orbital repulsion effect is designated as πorbital Fig. (1.4).



Fig 1.4

The π-electron system may also be polarized as in Fig. (1.5) by charge or   
dipoles located on the substituent. This effect called **π**-polarization is basically  
different from π-inductive effect in the magnitude of charge density reorganization at the *ortho*- and *meta-* positions.



Fig. 1.5

**1.6.2 The Resonance Effect:**

The interaction of substituent orbitals of suitable systems with the π-orbitals of the ring can lead to charge transfer either to or from the substituent and this is called resonance effect (R). In order to exercise a resonance effect, a substituent must possess a p- or π- orbital which is available to conjugate with the π-MOs of the aromatic system.

(i) X- is a donor group and typically possesses an unshared electron pair or **π-**electrons on atom directly attached to the ring.  
 -NR2, -OR, -SR2, -Cl, -CH= CH2  
 (ii) substituents Z have a π*-* acceptor centre adjacent to the ring.



This effect, important in systems such as C6H5-X, is transmitted to a remote probe site (Fig. 1.6) through the π-systems in appropriate molecules such as biphenyls etc.,



Fig. 1.6

In systems like C6H5-CH2-Y, hyperconjugation116 (Fig. 1.7) involving σ-π  
bond interaction accounts for the resonance properties. A final possible effect is  
any perturbation of σ-electron populations arising from a change occurring in the  
π-system and this has been designated as σ- πeffect (σπ).



Fig. 1.7

Of the various modes of transmission of electronic effects, the Iσ, F, πσ, and πF effects depend on substituent polarity, while R and σπ, effects depends on charge transfer ability.

**1.7 Correlation with electrochemical properties**

The free energy relationship obtained by polarographic studies differs from that obtained from most other physical methods.117,118 The half-wave potentials of reversible systems are equivalent to logarithms of equilibrium constants, whereas those of irreversible systems are proportional to logarithms of rate constants. Hence the application of half-wave potentials in extra thermodynamic relationships is not merely empirical but is a logical extension of the treatment of kinetic and equilibrium data.

Cyclic voltammetry, a popular tool in the last thirty-five years for studying electrochemical reactions has been employed by organic chemists in the study of biosynthetic reaction pathways119 and studies of electrochemically generated free radicals.120 An increasing number of inorganic chemists have been using cyclic voltammetry to evaluate the effects of ligands on the oxidation/reduction potentials of the central metal ion in complexes and multinuclear clusters.121 This type of information plays an integral part in many of the approaches directed toward solar energy conversion122 and in model studies of enzymatic catalysis.123 Knowledge of the electrochemistry of a metal complex can be useful in the selection of the proper oxidizing agent to put the metal complex in an intermediate oxidation state.124 Electrochemical methodology has also been exploited as a novel means of introducing functional groups and removing blocking agents.125

In the reaction series of the type x-Ar-R, if R is the electroactive group and X is the substituent in *meta*- or *para*- position, it is possible to write the equation (1.20).126

(E1/2 )XR = *ρ*R σX + (E1/2 ) HR (1.24)

In the equation (1.24), (E1/2 )XR  is the half-peak potential of the substituted compound and (E1/2 ) HR is that of the parent compound. *ρ*R is the proportionality constant, called the reaction constant, expressed in volts, that characterizes the susceptibility of the electroactive group R on a benzenoid ring to the effect of substituents placed in *meta*- or *para*- positions on the ring. Its value is dependent on the nature of the electroactive group, R, on the composition of the supporting electrolyte, on temperature and on other experimental conditions. It is independent of the kind and position of the substituent. σX is the Hammett substituent constant.3

There are many articles that deal with the theory and practice of modern voltammetry in-depth.127-129 Many authors have reported the substituent effects on peak potential measured by cyclic voltammetry.130-135