**INVESTIGATION OF SUBSTITUENT EFFECTS BY**

**13C NMR SPECTRA**

Transmission of the Substituent Effects Studied by 13C-NMR

Chemical Shifts

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 term30. 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 effects31,32, 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 subject33. 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 years33- 40.

The proton chemical shifts are influenced by magnetic anisotropies of neighboring 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 effects41 and to solvent and concentration effects42.

Extensive correlations of 13C chemical shifts in mono-substituted benzenes with Hammett σconstants were first reported by Spieseck and Schneider45, following the pioneering studies of Lauterbur44. It was observed that the chemical shifts measured for the *para*-ring carbons δ (Cp)of a series of mono-substituted benzenes was approximately related to the *σ+*pvalues of the substituents42,45. Attempts to find analogous relationships for δ(Cm)of mono substituted benzenes have met with varied success43,45,46. Schulman et al.45 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 a less satisfactory correlations.

A report on the correlation of NMR chemical shifts with Hammett values and analogous parameters29 has been given as,

δ= ⍴σ+ δo (15)

In Eq. (15), 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.16) and Ehrenson et al.6 (Eq.17).

δ =ƒ F+ r R + δ*°* (16)  
δ *=* ⍴I σi *+* ⍴r σr +δ*°*  (17)

The important difference between the two is that Swain and Lupton apply a single set of F and R values whereas Ehrenson et al.6 allow a choice of four distinct σR scales (σR (BA), σ°R, σ-R and σ+R). Yukawa and Tsuno16 proposed equation (4) for dealing with the enhanced resonance effects and they modified the Hammett equation (Eq. 18) as follows,

δ *=* ⍴σ + r (σ+ - σ) + δo (18)

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. (19).

δ *=* ⍴I σI*+*⍴r σr + φν+δ*°* (19)

The DSP equation (17) is the most generally useful treatment and is well suited for the analysis of spectroscopic data. In equation (17), 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 data sets. The generality is due to the independence of the ⍴Iand ⍴rtransmission coefficients. Since inductive and resonance effects are transmitted by different mechanisms7 their relative importance may change from one system to another. This feature cannot be accommodated47 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.48 and Bottino et al.49 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-workers47 to show the power of the DSP method. Anu *et al****.***50also have proved the power of the DSP method. It may be concluded that,

i) while in some situations there might be no significant important 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.