

Correlation of substituent effects on carbon-13 NMR chemical shifts of side-chain carbons in 5-aryl-2*E*,4*E*-pentadienoic acid derivatives by Taft DSP equation

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Linear Free Energy Equations (LFER) are mainly concerned with relative reactivities in the form of reaction rates and equilibrium data. Theories of structural effects derived from LFER considerations can be expressed in terms of intramolecular and intermolecular interactions. As these interactions influence other quantities, the relationship between the LFER parameters and variations in these quantities such as NMR chemical shifts are of interest. The application of the Hammett equation including its modified forms, to NMR spectroscopy is well-documented¹⁻³. In particular, the Dual Substituent Parameter (DSP) equation of Taft and co-workers⁴ has been widely applied with a considerable amount of success – this approach separates the contributions due to the inductive and resonance effects. The DSP equation of Taft is written as (1) for reaction rates and equilibria. It takes the form (2) for correlating ¹³C NMR chemical shifts. The choice of a specific σ_R scale (σ_R^0 , σ_R^+ , σ_R^- , σ_R^{BA}) for a particular case depends on the electron demand at the reaction centre or detection site (as for NMR chemical shifts). A single substituent parameter treatment would result in comparatively poor correlations in many cases, as it would restrict the inductive and resonance effects to fixed proportions.

$$\log (k/k_0) = \rho_1 \sigma_1 + \rho_R \sigma_R \quad (1)$$

$$\Delta\delta^X - \Delta\delta^H = \rho_1 \sigma_1 + \rho_R \sigma_R \quad (2)$$

¹³C NMR correlations of side-chain carbons : Levy and Nelson correlated substituent effects on *para*-¹³C NMR chemical shifts using the Hammett equation⁵. Though substituent effects are expectedly smaller on the chemical shifts of side-chain carbons, Bromilow *et al.*⁶ correlated these for a number of *meta*- and *para*-disubstituted benzenes, where the side-chains were CN, CF₃, COMe, CO₂Et, Me, OMe and NMe₂ by using the DSP equation (2). Hamer *et al.*⁷ and Happer *et al.*^{8,9} carried out NMR correlation studies using the Hammett equation (single substituent parameter)

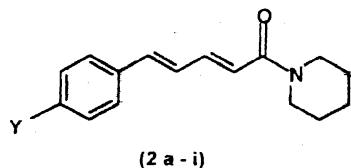
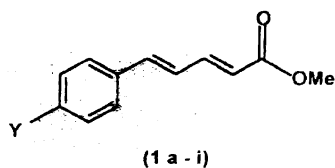
to several styrene derivatives for both the C α - and C β -carbons of the vinyl group. Happer felt that the σ^+ component will be enhanced if a strongly electron-withdrawing substituent such as nitro were placed on the β -carbon atom of the vinyl group. He recorded the ¹³C NMR spectra of 33 *meta*- and *para*-substituted- β -nitrostyrenes. He reported good correlations for the chemical shifts of the β -carbon and Hammett σ^+ constants, except for -R *para*-substituents. Correlations between substituent-induced chemical shifts and the α -carbon were only approximate. These are only to be expected, as the single substituent parameter approach was adopted. Happer extended these correlations to five additional series : cinnamic acids, cinnamate ions, styrenes, β,β -dimethyl- and β,β -dicyanostyrenes⁹.

Aim of present work : We were interested to find out how well substituent effects were transmitted along a diene chain conjugated with a substituted aromatic ring. We investigated this by employing ¹³C NMR spectroscopy as the probe. Wenkert¹⁰ earlier reported detailed assignment techniques for piperine; while Radeaglia *et al.*¹¹ reported studies on a few 5-aryl-2,4-pentadienoic acids, most of which were substituted at the 3-position.

Results and Discussion

We have used Taft's DSP treatment with a considerable degree of success for correlation of side-chain ¹³C NMR chemical shifts where a diene side-chain is conjugated to the aryl nucleus, with two series of 5-aryl-2*E*,4*E*-pentadienoic acid derivatives, viz. the methyl esters (**1a-i**) and piperidides (**2a-i**). Eight *para*-substituents (Cl, Br, F, nitro, NMe₂, OMe, Me, CF₃) of different types covering all types of electron-demand were chosen in addition to the unsubstituted compound to establish the general applicability of the correlation obtained².

These compounds were synthesized by standard reaction protocols (at Calcutta University), where the key steps



- 1, 2
- | | | | |
|---|------------------------|---|-------------------------|
| a | Y = H | f | Y = 4'-CF ₃ |
| b | Y = 4'-F | g | Y = 4'-OCH ₃ |
| c | Y = 4'-Cl | h | Y = 4'-NMe ₂ |
| d | Y = 4'-Br | i | Y = 4'-NO ₂ |
| e | Y = 4'-CH ₃ | | |

were highly stereoselective Wittig-Horner-Emmons^{12,13} reactions of the appropriate aromatic aldehyde with methyl γ -diethyl-phosphono-crotonate to yield compounds **1a-i**. Hydrolysis of these to the dienoic acids, conversion to the acid chlorides with oxalyl chloride, and treatment with piperidine in benzene yielded the piperidides (**2a-i**). Characterization of these compounds were carried out by elemental analyses, IR, ¹H and ¹³C NMR spectroscopy. Their ¹³C NMR spectra were recorded in CDCl₃ at 75.5 MHz with a Bruker AM-300L spectrometer and at 20 MHz with a Varian CFT-20 MHz instrument. Assignments were made with the aid of SFORD, APT and DEPT spectra in addition to coupled spectra (for a few selected compounds), comparison of the chemical shifts with model compounds and inter-comparison among the compounds themselves. The ¹³C NMR chemical shifts for the side-chain carbons only are given in Table 1.

It is expected that *para*-substituents would interact conjugatively with the side-chain of dienoic ester system (compounds of series **1**, L = OMe) or dienamide system (compounds of series **2**, L = *N*-piperidyl) and influence electron densities and hence ¹³C NMR chemical shifts (Fig. 1).

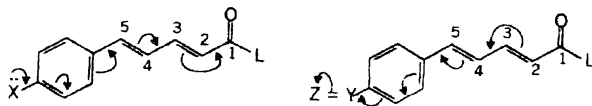


Fig. 1

The side-chain carbons 2 and 4 directly experience the conjugative effect of the *para*-substituent as shown. The carbonyl group is itself a -R group, interacting with the diene system and through it with the aromatic ring. The car-

Table 1. ¹³C NMR chemical shifts of side-chain olefinic carbons of methyl ester series (**1a-i**) and piperidide series (**2a-i**)

Compd. no.	C ₂	C ₃	C ₄	C ₅
1a	120.7	144.6	126.0	140.3
b	120.7	144.4	125.8	139.0
c	121.2	144.1	126.5	138.7
d	121.3	144.1	126.7	138.8
e	119.9	144.8	125.0	140.3
f	122.3	143.8	128.4	138.3
g	119.3	145.0	123.9	140.0
h	117.4	145.8	121.4	141.2
i	123.6	143.2	130.2	137.2
2a	120.4	141.4	126.4	137.6
b	120.8	141.9	126.6	136.9
c	121.2	141.2	127.2	136.2
d	121.3	141.4	127.4	130.5
e	120.0	142.0	125.7	138.0
f	122.4	141.3	129.2	136.3
g	119.5	142.6	124.8	138.0
h	117.7	143.2	122.4	139.0
i	123.8	140.5	131.1	135.0

bonyl group also conjugatively interacts with the alkoxy/amino groups in the ester/amide. It was therefore of interest to find out whether the conjugative interactions of the side-chain carbons in the compound series **1a-i** and **2a-i** would best correlate with which of the four series of substituent parameters (σ_R^0 , σ_R^{BA} , σ_R^+ and σ_R^-) denoting the resonance contributions to the substituent effect. The regression analysis was performed using equation (2) with all four series of substituent parameters. The results of the regression analyses (carried out at J.N.V. University) are given in Table 2.

The two centres that undergo direct conjugative interaction with the aromatic nucleus, viz. C₂ and C₄ showed positive ρ values – electron-withdrawing *para*-substituents caused a downfield shift of the signals. Both ρ_1 and ρ_R were in the order C₄ > C₂, the centre nearer the aromatic ring showing greater susceptibility to substituent effects. However, it was clear that electronic effects were also being effectively transmitted to C₄, which was separated from the aromatic nucleus by a diene chain. Best correlations were obtained for C₂ and C₄ with σ_R^{BA} . The correlations were poorer for the amide series compared with the ester series. Presumably strong delocalization of the carbonyl in the amide function, reduces its conjugative interaction (and hence those of the side-chain carbons) with the aryl moiety. Correlation using σ_R^+ were also poor indicating that strongly positive character was not induced by the carbonyl group on the side-

Table 2. Correlations of chemical shifts of side-chain carbons using Taft's DSP approach

Methyl esters	ρ_1	ρ_R	Best corr. with σ_R scale used	Corr. coeff. R
C_2	3.39 ± 0.16	4.07 ± 0.15	σ_R^{BA}	0.997
	3.14 ± 0.30	5.66 ± 0.42	σ_R^0	0.974
C_3	$-(1.81 \pm 0.21)$	$-(2.09 \pm 0.21)$	σ_R^0	0.991
	$-(1.90 \pm 0.21)$	$-(1.55 \pm 0.23)$	σ_R^{BA}	0.982
C_4	4.69 ± 0.24	5.86 ± 0.23	σ_R^{BA}	0.996
	4.36 ± 0.31	8.21 ± 0.44	σ_R^0	0.993
C_5	$-(4.15 \pm 0.17)$	$-(2.06 \pm 0.23)$	σ_R^0	0.991
	$-(4.22 \pm 0.19)$	$-(1.45 \pm 0.19)$	σ_R^{BA}	0.988
Piperidides				
C_2	5.23 ± 1.30	2.67 ± 1.27	σ_R^{BA}	0.828
	5.03 ± 1.34	3.51 ± 1.8	σ_R^0	0.810
C_3	$-(1.07 \pm 0.21)$	$-(3.06 \pm 0.33)$	σ_R^0	0.976
	$-(1.15 \pm 0.19)$	$-(2.53 \pm 0.27)$	σ_R^{BA}	0.982
C_4	5.04 ± 0.21	7.56 ± 0.24	σ_R^0	0.997
	5.33 ± 0.33	5.34 ± 0.33	σ_R^{BA}	0.992
C_5	$-(3.39 \pm 0.16)$	$-(1.98 \pm 0.16)$	σ_R^{BA}	0.992
	$-(3.26 \pm 0.23)$	$-(2.72 \pm 0.33)$	σ_R^0	0.982

chain carbons. σ_R^- was not expected to give good correlations, as the propensity of negative character developing on the side-chain carbons was ruled out by the presence of the electron-withdrawing carbonyl group. C_3 and C_5 , which were not in direct conjugation with the *para*-substituent, showed a reverse polarization effect, i.e. electron-withdrawing substituents causing a small, but definite, upfield shift. Best correlations for C_3 and C_5 were obtained with σ_R^0 for both series – though the sensitivity to change was much less, this is expected as direct conjugative interactions of the *para*-substituents with these centres were not possible. Again, correlations of C_3 and C_5 were poor with σ^+ . The sensitivity to electronic effects was $C_5 > C_3$, the carbons nearer the aromatic nucleus showing the greater influence.

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