

Received: 4 February 2007,

Revised: 7 August 2007,

Accepted: 7 September 2007,

Published online in Wiley InterScience: 19 December 2007

(www.interscience.wiley.com) DOI 10.1002/poc.1272

Substituent effect study on $^{13}\text{C}_\beta$ SCS of styrene series. A Yukawa–Tsuno model and Reynolds dual substituent parameter model investigation

Basil A. Saleh^a*, Sabih A. Al-Shawi^a and Ghazwan F. Fadhl^b**



The Yukawa–Tsuno (Y–T) and Reynolds dual substituent parameter (DSP) models have been used to model ^{13}C substituent chemical shift (SCS) of the C_β atom of 19 series of *para*-substituted styrenes ($\text{X}-\text{C}_6\text{H}_4\text{CR}=\text{CYW}$) with variable electronic and structural demands in the side-chain. The best fit of the Y–T model was better than that of the Reynolds DSP model for most of the studied series. A high correlation was found between the ρ value of the Y–T model and ρ_F value of the Reynolds DSP model. The ρ value, which reflects the sensitivity of $^{13}\text{C}_\beta$ SCS to the substituent field effect, was found to be influenced by the group W on the C_β atom. A W group that enhances the *para*-substituent π -polarization of the side-chain has a higher ρ value than its counterpart W groups that induce counter π -polarization in the side-chain. The series with W in an *E*-configuration to the aryl ring has higher ρ value than corresponding Z series. A lower ρ value is observed when W induces a counter π -polarization of the side-chain (as with NO_2 and COMe) or when the R substituent imposes a 65° dihedral angle between the side-chain and the *para*-substituted benzene ring (as with *t*-Bu). When the W group is a heterocyclic ring, the closer the heteroatom is to C_β , the lower the ρ value is due to the greater counter π -polarization. The two components of the substituent effect on $^{13}\text{C}_\beta$ SCS, namely the field effect and resonance effect, behave inversely. The resonance demand (r^+ value) increases, as the Y and/or W groups become more electron-withdrawing (EW). The series with W as a heterocyclic ring develop negative charge at the carbon atom of the heterocyclic ring adjacent to C_β (and to which the styryl moiety is attached) and has a lower r^+ value than those which fail to do so. The lowest r^+ value was for those series with a 65° dihedral angle. Copyright © 2007 John Wiley & Sons, Ltd.

Supplementary electronic material for this paper is available in Wiley InterScience at <http://www.mrw.interscience.wiley.com/suppmat/0894-3230/suppmat/>

Keywords: ^{13}C SCS data; substituent effect; correlation analysis; styrenes; Yukawa–Tsuno model; Reynolds DSP model; field and resonance effects; π -polarization

INTRODUCTION

When substitution in one part of an organic molecule is varied, the reorganization of the electronic framework all through the molecule occurs. This can affect the molecule's reactivity, conformation, solubility, equilibrium between the different potential tautomeric forms, acid-base properties, stacking tendency, and so forth. Modeling of substituent effects on the ^{13}C NMR chemical shifts of remote carbons is an effective way to study the changes in electronic states promoted by different phenyl substituents at that carbon.^[1–5]

The substituent-induced changes in the chemical shift (SCS) can be correlated with a single parameter model that uses a mono substituent scale such as the Hammett σ (Eqn 1) or with a dual substituent scale giving a dual substituent parameter (DSP) model such as Eqn 2, which allows variable blends of the inductive (σ_F or σ_I) and resonance (σ_R) contributions.

$$\text{SCS} = \rho\sigma \quad (1)$$

$$\text{SCS} = \rho_F\sigma_F + \rho_I\sigma_I + \rho_R\sigma_R \quad (2)$$

The SCS is the ^{13}C NMR substituent chemical shift for a substituted compound. In Eqn 2, different substituent resonance scales (usually σ_R^+ , σ_R^0 , σ_R^{BA} , σ_R^-) can be tested, and the one that yields the best fit to the experimental data is selected. Even in those cases where a good correlation with Eqn 1 is obtained, the use of Eqn 2 gives more information because it shows the contributions of conjugative (ρ_R) and non-conjugative, that is,

* Department of Chemistry, College of Science, University of Basrah, Basrah, Iraq.
E-mail: basil_saleh2004@yahoo.com

** Department of Chemistry, College of Education, University of Dohuk, Dohuk, Iraq.
E-mail: ghazwan_fadhl@yahoo.co.uk

a B. A. Saleh, S. A. Al-Shawi
Department of Chemistry, College of Science, University of Basrah, Basrah, Iraq

b G. F. Fadhl
Department of Chemistry, College of Education, University of Dohuk, Dohuk, Iraq

field effects (ρ_F or ρ_i). An observed positive ρ value from Eqns Eqn1 and Eqn2 means a normal substituent effect, and a negative one indicates a reverse substituent effect.^[6,7]

Reynolds *et al.*^[8] have derived substituent field σ_F and resonance σ_R° scales from $^{13}\text{C}_\beta$ SCS of *para*- and *meta*-substituted styrenes using an iterative target factor testing technique. In later investigations,^[9–11] it was demonstrated that the Reynolds' σ_F and σ_R° scales are superior to any other commonly used substituent constants whether these were single or dual models in reproducing ^{13}C and ^{19}F SCS of side-chains of *para*-substituted benzenes and 1-X-4-bicyclooctane skeletons, respectively. Yukawa and Tsuno have derived another type of model to study the substituent effect on the side-chain of a disubstituted benzene ring when there is electron deficiency at the reaction site of the side-chain. They have applied their model to modeling kinetic data of solvolysis (e.g., acetolysis) of β -aryltosylates and brosylates.^[12] The Yukawa–Tsuno (Y-T) model takes the form of:

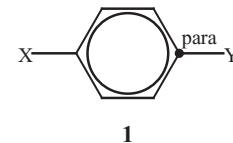
$$\delta P = \rho(\sigma^\circ + r^+ \Delta \sigma_R^\circ) \quad (3)$$

where δP is the substituent effect on the studied kinetic data, σ° is the normal substituent scale, that is, when the *p*-substituted benzene ring is isolated from the side-chain by methylene group so as to prevent any through resonance between the substituent and the side-chain, $\Delta \sigma_R^\circ$ is the substituent resonance scale measuring the capability of π -delocalization of a π -electron donor (ED) substituent and the reaction site of the side-chain. It is defined by $\sigma_P^\circ - \sigma^\circ$. The r^+ (*italic*) is a parameter characteristic for the given reaction and measures the extent of resonance demand, that is, the degree of resonance interaction between the aryl group and the reaction site in the rate-determining transition state. It has been found^[13] that r^+ varies between 0.01 and 1.5.

To understand the transmission of electronic effects in an aromatic framework, the concepts of localized and extended π -polarization should be explained. These concepts were studied by Reynolds *et al.*^[14] and later characterized in more detailed way by Bromilow *et al.*^[15] Each π -unit (a double or triple bond, carbonyl, or aromatic system) is thought to be polarized separately, the polarization being induced by the substituent dipole in another part of the molecule (Fig. 1A). This interaction can be transmitted either through the molecular framework or through the solvent continuum and is exactly called localized or direct polarized because each π -unit in the side-chain is polarized separately. On the other hand, the terminal atoms of a conjugated π -system show some addition polarization (proportional to σ_F) that can best be explained in terms of substituent-induced polarization of the whole π -network. This

component is termed extended polarization (Fig. 1B). Obviously, it can be seen that the terminal atoms (C_β atom in styrene) suffer from a deficit of electron density and thus correlate with σ_R° . Therefore, one can conclude that the Y-T model should be preferable to study substituent effects on these terminal atoms.

In a previous^[16] study, the Y-T model has been used to investigate the substituent effects on ^{13}C SCS of *para* carbon atoms in 15 series of *para*-substituted benzenes. Details of substituents and side-chains are given for **1**.



$X = \text{NMe}_2, \text{OCH}_3, \text{F}, \text{Cl}, \text{Br}, \text{CH}_3, \text{H}, \text{CN}, \text{and } \text{NO}_2$
 $Y = \text{H}, \text{CH}_3, \text{CH}_2\text{Ph}, \text{Ph}, \text{NH}_2, \text{NO}_2, \text{OMe}, \text{COMe}, \text{CH}=\text{CH}_2, \text{C}(\text{Me})=\text{CH}_2, \text{C}(\text{t-Bu})=\text{CH}_2, (\text{E})\text{CH}=\text{CHCN}, (\text{Z})\text{CH}=\text{CHCN}, \text{CH}=\text{CHCOPh}, \text{2,6-dimethyl-4-substituted acetophenone}$

It was found in that study that the sensitivity of substituent effect, ρ , on $^{13}\text{C}_{\text{para}}$ was increased when the benzene ring was attached to an electron-withdrawing (EW) C-4 Y-substituted side-chain. In contrast, the sensitivity of substituent effect on $^{13}\text{C}_{\text{para}}$ atom was decreased when the benzene ring was attached to ED Y side-chain.

The aim of this study is to investigate the applicability of the Y-T method to model $^{13}\text{C}_\beta$ SCS of various *p*-substituted styrenes with differing electronic demands at C_β of the vinyl side-chain. Also, the present study attempts to compare the performance of the Y-T model and Reynolds DSP model in modeling the same $^{13}\text{C}_\beta$ SCS data and to investigate the nature of the Y-T ρ parameter and compare its behavior with Reynolds' ρ_F and ρ_R parameters.

CALCULATIONS

$^{13}\text{C}_\beta$ SCS data in CDCl_3 solvent were taken from the literature^[8,17–19] and are tabulated in electronic supplementary material as Table 3. We have found by using Eqn 3 directly that is, expanding it, the statistical results become less accurate than the below procedure, because of the rounding error which happens due to the multiplication of ρ by r^+ . The $^{13}\text{C}_\beta$ SCS were regressed on the $[\sigma^\circ + r^+ (\sigma_P^\circ - \sigma^\circ)]$ term, after allowing the variation of r^+ from 0.1 to 1.5 for one decimal only. Then the r^+ which gives the best correlation will be chosen to be expanded to two decimals by scanning the best one decimal r^+ higher and lower by 0.01. This process is then repeated with a 0.01 increment till we reach a two decimal r^+ value, which gives the best correlation coefficient between $[\sigma^\circ + r^+ (\sigma_P^\circ - \sigma^\circ)]$ and $^{13}\text{C}_\beta$ SCS. The corresponding ρ and r^+ are then analyzed. If two r^+ values from the same series give the same correlation coefficient then the quality of correlation is judged by taking the best r^+ with the lowest standard deviation of fit. The σ° and σ_P° substituent scales were taken from the literature^[20] and are tabulated in the electronic supplementary material as Table 4. The Reynolds DSP model was obtained by regressing $^{13}\text{C}_\beta$ SCS on σ_F and σ_R° substituent scales derived by Reynolds *et al.*^[8] The Reynolds σ_F and σ_R° substituent scales are tabulated in the electronic supplementary material as Table 4.

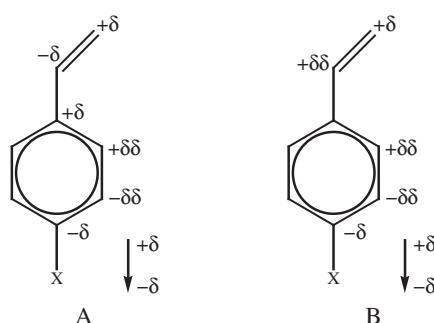


Figure 1. (A): Localized polarization; (B): Extended polarization.

RESULTS AND DISCUSSION

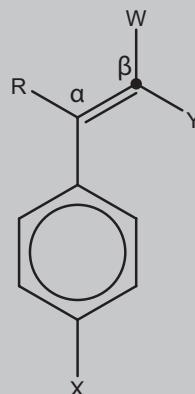
Table 1 shows the structures, the *p*-substituent, and the type of side-chain of the studied series. The correlation coefficients (*r*) and multiple regression coefficients (*R*) of modeling $^{13}\text{C}_\beta$ SCS by the Y-T and the Reynolds substituent scales are given in Table 2. Also shown in Table 2 are the Y-T best chosen ρ and r^+ parameters and Reynolds DSP ρ_F and ρ_R parameters together with the standard error of the tabulated ρ s. The correlation coefficient (*r*), which is used to judge the quality of the correlation in the Y-T model, indicates that series 2–18 have higher *r* values (0.991–0.999) (excellent), while series 1 and 19 gave satisfactory and fair correlation, their *r* values respectively being 0.987 and 0.943. Nevertheless, in the Reynolds DSP model we have found five series with *R* values lower than 0.99 namely series 5, 6, 7, 9, and 10 and their *R* values being respectively 0.989, 0.987, 0.987, 0.980, and 0.970. These correlation results indicate the better modeling capability of the Y-T model than the Reynolds model despite the substituent scales of the Y-T model being derived from non-NMR data, namely kinetic data. The positive values of the correlation parameters of ρ and r^+ mean a normal substituent effect, that is, electron-donating substituent causes shielding while electron-withdrawing (EW) substituent causes deshielding. In order to understand the behavior of the Y-T ρ parameter, we have plotted it against the Reynolds' ρ_F and ρ_R parameters as shown in Figs 2 and 3, respectively. It is clear that there is a reasonable linearity with a significant correlation coefficient (*r*) between ρ and ρ_F parameters, which indicates that the Y-T ρ parameter reflects substituent field effects. However, the correlation between ρ and ρ_R of Reynolds in Fig. 3 shows a high scattering of the plotted data with low correlation coefficient and became even worst (*r*=0.41) when the result of series 19 (Y=H, W=H, R=t-Bu) was deleted. Figure 4 shows the plot between r^+ and ρ_R of Reynolds. It shows some scattering with lower correlation coefficient (*r*) and series 19 deviated from the cluster of points. Also, deletion of series 19 worsens the correlation coefficient (*r*) to become 0.507. The lower quality correlation between r^+ and ρ_R reflects the different nature of σ^+ of Y-T model and σ_R^+ of Reynolds; the latter was derived to reflect the sensitivity of substituent effect felt at the probe site, when there is no direct through conjugation, while r^+ reflects the extent of substituent resonance effect when the probe site is in direct through conjugation.

Effect of Y and W substituents on ρ

As indicated from Eqn 3 that the sensitivity of $^{13}\text{C}_\beta$ SCS to a substituent effect felt at C_β is a function of ρ , it is important to explain the variation of ρ values with the side-chain structure of series 1–19. In all series, the Y and W groups of the side-chain caused a lowering of the ρ value when compared with ρ value of styrene series 17 (Y=H, W=H). An exception to this observation was found in series 2 (Y=H, W=Br) and series 5 (Y=H, W=CN) in which ρ values of these two series were higher than that of the styrene series 17. The disposition of the W group with respect to the *p*-substituted benzene ring plays a great role in determining the polar effect as depicted in the value of ρ . The ρ value of series 3 (Y=Br, W=H) is lower than that of styrene series 17. The π -polarization of series 2 and 3 are shown in Fig. 5.

In Fig. 5A, the dipole generated between the bond Br— C_β coincides with the axis of dipole that goes through the *para*-substituent and the benzene ring since the dihedral angle

Table 1. The styrene series structures



X = H, NMe₂, OCH₃, CH₃, F, Cl, Br, CN and NO₂

Series No.	Y	W	R
1	CH ₃	CH ₃	H
2	H	Br	H
3	Br	H	H
4	H	CO ₂ Me	H
5	H	CN	H
6	CN	H	H
7	H	MeSO ₂	H
8	H	COMe	H
9	H	NO ₂	H
10	MeSO ₂	CO ₂ Et	H
11	H	Ph	H
12	H	2-Furyl	H
13	H	3-Furyl	H
14	H	2-Pyridyl	H
15	H	3-Pyridyl	H
16	H	4-Pyridyl	H
17	H	H	H
18	H	H	CH ₃
19	H	H	t-Bu

(C_{ipso} — C_α — C_β —Br) between the side-chain and the benzene ring is zero. The dipole partial negative charge of the bond Br— C_β stabilizes the partial positive charge at C_β , which is generated by the substituent π -polarization in series 2 more than that of C_β of series 17, which lacks such stabilization. In contrast, Fig. 5B reveals that the angle between the bond dipole of C_β —Br and the axis of dipole that goes through the *para*-substituent and the benzene ring is equal to 60° as can be deduced from Fig. 5B. This dipole non-coincidence destabilizes the polarization of C_β of series 3 when compared with that of series 2 and series 17. Hence, further stabilization occurs to C_β π -polarization in series 2 than that of series 3. The same results were observed for series 5 (Y=H, W=CN) and series 6 (Y=CN, W=H). The former has higher ρ value than the latter due to the coincidence of the axis of dipole that goes through the *para*-substituted benzene ring and the dipole of bond between C_β and CN in series 5. It has been mentioned in the introduction that non-terminal atoms suffer localized (direct) π -polarization whereas terminal atoms suffer from both localized and extended π -polarization. C_β SCS of series 2 and 5 suffer localized and extended π -polarization, whereas C_β of series 3 and 6 suffer only localized π -polarization. Despite these differences in the enhancement in π -polarization in series 2 and 5

Table 2. The results of regression for the C_β atom in styrenes series (1–19) with the Y-T and Reynolds DSP models^a

Series No.	Y-T			Reynolds ^b				n	Ref. ^d
	ρ	r^+	r	ρ_F	ρ_R	R			
1	5.55 (0.345)	0.12	0.987	4.99 (0.536)	7.12 (0.574)	0.993	9	16	
2	6.34 (0.338)	0.27	0.994	5.54 (0.268)	9.79 (0.287)	0.998	9	16	
3	5.30 (0.217)	0.49	0.995	5.01 (0.106)	8.1 (0.139)	0.999	8 ^c	16	
4	5.29 (0.158)	0.48	0.997	5.06 (0.560)	9.42 (0.600)	0.995	9	16	
5	5.80 (0.114)	0.59	0.999	5.93 (0.968)	10.86 (1.03)	0.989	9	16	
6	5.67 (0.115)	0.67	0.999	5.89 (1.05)	11.24 (1.12)	0.987	9	16	
7	5.18 (0.106)	0.65	0.999	5.24 (0.997)	10.24 (1.07)	0.987	9	16	
8	3.96 (0.129)	0.59	0.996	3.78 (0.558)	7.72 (0.598)	0.993	9	16	
9	3.30 (0.074)	0.88	0.998	3.55 (0.902)	7.55 (0.966)	0.980	9	16	
10	4.73 (0.089)	0.95	0.999	5.21 (1.62)	11.01 (1.73)	0.970	9	16	
11	5.65 (0.283)	0.23	0.991	4.99 (0.248)	8.29 (0.266)	0.998	9	17	
12	4.84 (0.219)	0.28	0.993	4.29 (0.221)	7.5 (0.237)	0.998	9	17	
13	5.75 (0.295)	0.21	0.991	5.01 (0.269)	8.38 (0.288)	0.998	9	17	
14	5.14 (0.236)	0.32	0.993	4.56 (0.231)	8.25 (0.247)	0.998	9	17	
15	5.56 (0.242)	0.31	0.993	5.05 (0.245)	8.74 (0.263)	0.998	9	17	
16	5.54 (0.240)	0.35	0.993	5.01 (0.299)	9.05 (0.321)	0.998	9	17	
17	5.77 (0.268)	0.24	0.993	5.11 (0.132)	8.78 (0.142)	0.999	9	8, 18	
18	4.56 (0.188)	0.26	0.994	4.16 (0.145)	6.93 (0.156)	0.999	9	8, 18	
19	1.30 (0.114)	0.01	0.943	2.03 (0.098)	0.86 (0.105)	0.995	9	8, 18	

^a Values in parentheses and under the value of ρ represent standard errors of ρ .

^b Results of Reynolds modeling taken from: S. A. O. Al-Shawi "Models performance assessment and the role of side-chain on the transmission of substituent effect to para, alpha and beta carbon atoms in p-disubstituted benzenes" a PhD thesis (1998) University of Basrah.

^c Series 2 excludes the NMe_2 substituent.

^d References for the ^{13}SCS data.

or the diminishing in π -polarization in series 3 and 6, the π -polarizations localized alone or localized and extended follow the same behavior. Series 9 ($\text{Y}=\text{H}$, $\text{W}=\text{NO}_2$) has the lowest ρ value among the studied series. Figure 6A shows the π -polarization of series 9 due to the dipole of *para*-substituted benzene ring. However, Fig. 6B shows the π -polarization of the vinyl side-chain due to the nitro group. It is clear that this group imposes a partial positive charge on the nitrogen and partial negative charges on both oxygen atoms. These two opposing polarizations lower the stability of the π -polarization due to the *para*-substituted benzene ring at the vinyl side-chain as reflected

by the diminishing ρ value of $^{13}\text{C}_\beta$ SCS, hence reducing the sensitivity of C_β to the substituent field effect.

The next higher ρ value to series 9 ($\text{Y}=\text{H}$, $\text{W}=\text{NO}_2$) is that of series 8 ($\text{Y}=\text{H}$, $\text{W}=\text{COMe}$). Here the acetyl methyl group may contribute to the destabilization of the vinyl side-chain π -polarization by a hyperconjugative effect as shown in Fig. 7. Figure 7A shows the π -polarization effect of the *para*-substituent on the vinyl side-chain. The hyperconjugation effect of the methyl group (Fig. 7B) imposes a π -polarization in the acetyl group, which opposes the π -polarization of the vinyl group due to the *para*-substituted benzene ring (Fig. 7A) that is, opposite

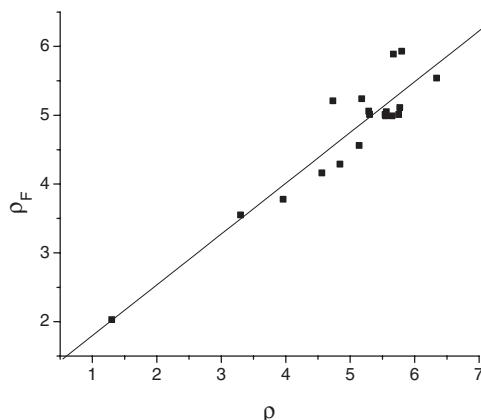


Figure 2. Plot between ρ of Yukawa-Tsuno and ρ_F of Reynolds model ($r=0.932$).

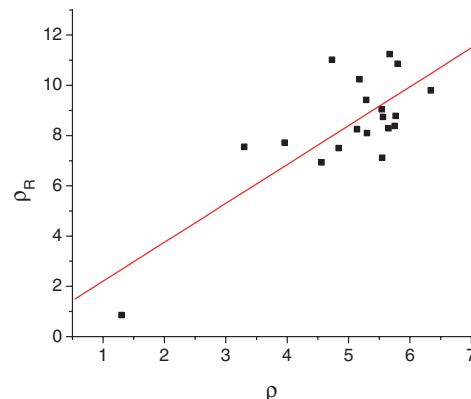


Figure 3. Plot between ρ of Yukawa-Tsuno and ρ_R of Reynolds model ($r=0.788$).

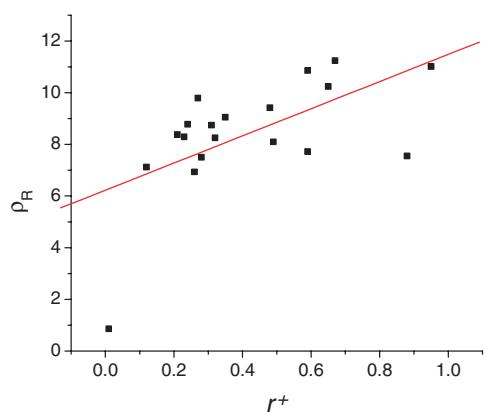


Figure 4. Plot between r^+ of Yukawa-Tsuno and ρ_R of Reynolds model ($r = 0.589$).

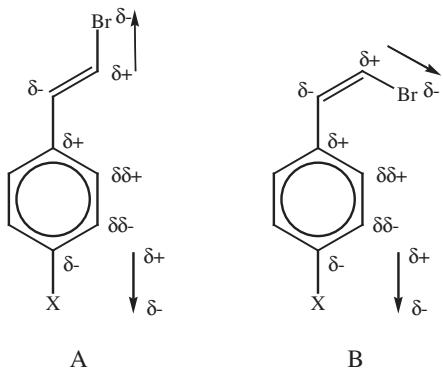


Figure 5. (A): Series 2; (B): Series 3

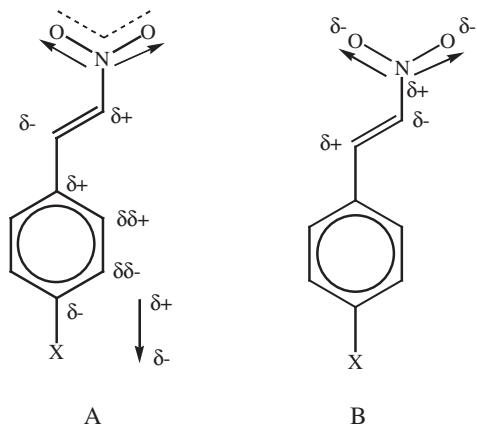


Figure 6. (A): Series 9; (B): NO_2 polarization

partial charges develop on C_β atom. The enhanced π -polarization of the vinyl group side-chain as seen in series 5 ($Y=\text{H}$, $W=\text{CN}$) and series 2 ($Y=\text{H}$, $W=\text{Br}$) is lost here due to an induced opposed π -polarization by the hyperconjugative methyl group.

Series 12 ($Y=\text{H}$, $W=2\text{-furyl}$) and 14 ($Y=\text{H}$, $W=2\text{-pyridyl}$) have a significantly lower ρ than that of styrene series 17. Figure 8A, B represents the π -polarization which takes place in these series. The heteroatom in both structures sets a dipole, which opposes that set by the *para*-substituted benzene ring

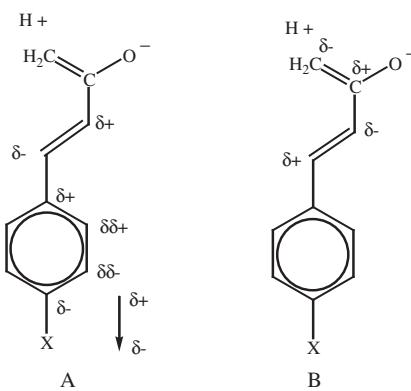


Figure 7. (A): Series 8; (B): Methyl group hyperconjugation

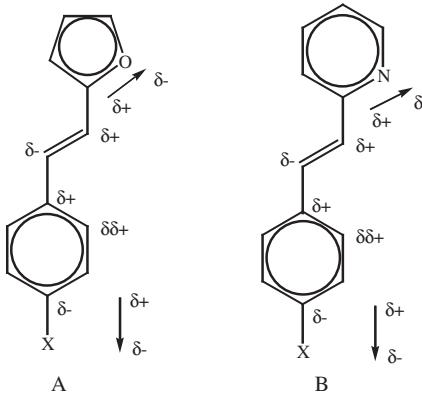


Figure 8. (A): Series 12; (B): Series 14

similar to what happens in series 9 ($Y=\text{H}$, $W=\text{NO}_2$). This opposition in dipoles reduces the $^{13}\text{C}_\beta$ SCS sensitivity to the substituent effect as reflected in the lower ρ of series 12 and 14, when compared with that of styrene series 17. In contrast, the ρ values of series 13 ($Y=\text{H}$, $W=3\text{-furyl}$), 15 ($Y=\text{H}$, $W=3\text{-pyridyl}$), and 16 ($Y=\text{H}$, $W=4\text{-Pyridyl}$) are slightly lower than the ρ value of styrene series 17 due to the dying away of the opposed dipole generated in the heteroaromatic ring of series 13, 15, and 16 since the heteroatom in these series is further away than the heteroatom in series 12 and 14 from C_β .

The effect of the Y and W groups on resonance demand parameter r^+

The r^+ values of all series were larger than that of series 17 ($Y=\text{H}$, $W=\text{H}$) except series 1 ($Y=\text{CH}_3$, $W=\text{CH}_3$), 11 ($Y=\text{H}$, $W=\text{Ph}$), 13 ($Y=\text{H}$, $W=3\text{-furyl}$), and 19 ($Y=\text{H}$, $W=\text{H}$, $R=t\text{-Bu}$). The resonance demand (r^+ value) increases, as the Y and/or W groups become more EW (cf. Table 2, series 2–10). This means increasing EW effect of Y and W would increase the sensitivity of $^{13}\text{C}_\beta$ SCS to the resonance effect of the *para*-substituent in the benzene ring. Hence, the two components of the substituent effect on $^{13}\text{C}_\beta$ SCS, namely the field effect and resonance effect may behave reversely. This reflects what we have seen in structurally related series, for example, series 2 ($Y=\text{H}$, $W=\text{Br}$) and 3 ($Y=\text{Br}$, $W=\text{H}$) in which the ρ value of the former is higher than the latter and vice versa for the r^+ values. Similar trends for series 5 ($Y=\text{H}$, $W=\text{CN}$) and 6 ($Y=\text{CN}$, $W=\text{CN}$) were found. This opposite trend in ρ with respect to r^+ emphasizes the previous

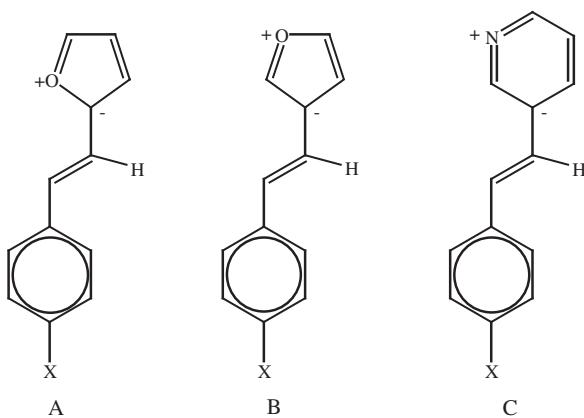


Figure 9. (A): Series 12; (B): Series 13; (C): Series 15

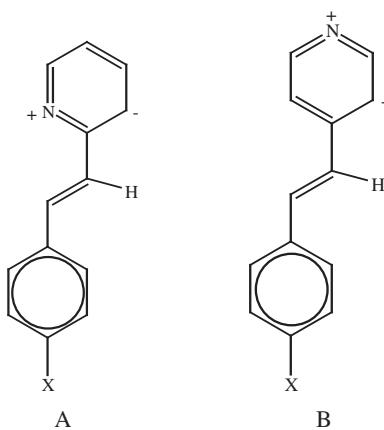


Figure 10. (A): Series 14; (B): Series 16

finding of Figure 2, that ρ reflects pure field effect, not like ρ of Hammett Eqn 1, in which ρ reflects both field and resonance effects simultaneously. The r^+ values of series 14 ($Y=H$, $W=2$ -pyridyl) and 16 ($Y=H$, $W=4$ -pyridyl) are higher than those for series 12 ($Y=H$, $W=2$ -furyl), 13 ($Y=H$, $W=3$ -furyl), and 15 ($Y=H$, $W=3$ -pyridyl). This trend of fall in r^+ value may be attributed to the resonance of the lone pair of the heteroatom in the hetero aromatic ring in which it develops a resonance structure in series 12, 13, and 15 shown by Fig. 9A–C, respectively, in which a negative charge is acquired by the carbon atom at the attachment site of the hetero aromatic ring adjacent to C_β . These resonance structures apparently lower the sensitivity of $^{13}C_\beta$ SCS to the substituent resonance effect as reflected in the lower values of series 12, 13, and 15 when compared with analogous series in which the hetero aromatic rings fail to introduce such a negative charge in the carbon atom of the hetero aromatic ring adjacent to C_β , namely, series 14 and 16 as in Fig. 10, A and B, respectively.

Effect of R group in side-chain on the ρ and r^+

C_β SCS of series 17 ($Y=H$, $W=H$, $R=H$), 18 ($Y=H$, $W=H$, $R=CH_3$), and 19 ($Y=H$, $W=H$, $R=t$ -Bu) suffer localized and extended

π -polarization, since the C_β in these series are terminal atoms only. The transmission of extended π -polarization and resonance effects of the substituent to the side-chain attached to the *p*-substituted benzene ring depends on the dihedral angle between the side-chain and the benzene ring. The dihedral angles between *p*-substituted benzene ring and side-chains of series 17 ($Y=H$, $W=H$, $R=H$), 18 ($Y=H$, $W=H$, $R=CH_3$), and 19 ($Y=H$, $W=H$, $R=t$ -Bu) are 0° , 30° , and 65° , respectively.^[8] Hence, the observed fall of ρ and r^+ values for series 17, 18, and 19 may be attributed to the loss of coplanarity between the *p*-substituted benzene ring and the side-chains in series 19.

Acknowledgements

We are grateful for the referees suggestions and comments.

REFERENCES

- [1] D. J. Craik, R. T. C. Brownlee, *Prog. Phys. Org. Chem.* **1983**, *14*, 1–73.
- [2] W. F. Reynolds, *Prog. Phys. Org. Chem.* **1983**, *14*, 165–203.
- [3] (a) B. Halton, G. M. Dixon, *Org. Biomol. Chem.* **2004**, *2*, 3139–3149; (b) S. M. Bonesi, M. A. Ponce, R. Erra-Balsells, *J. Heterocycl. Chem.* **2004**, *41*, 161–170; (c) E. Mezzina, D. Spinelli, L. Lamartina, S. Buscemi, V. Frenna, G. Macaluso, *Eur. J. Org. Chem.* **2002**, 203–208.
- [4] (a) K. Neuvonen, F. Fülop, H. Neuvonen, K. Pihlaja, *J. Org. Chem.* **1994**, *59*, 5895–5900; (b) K. Neuvonen, F. Fülop, H. Neuvonen, M. Simeonov, K. Pihlaja, *J. Phys. Org. Chem.* **1997**, *10*, 55–66; (c) K. Neuvonen, F. Fülop, H. Neuvonen, A. Koch, E. Kleinpeter, K. Pihlaja, *J. Org. Chem.* **2001**, *66*, 4132–4140; (d) K. Neuvonen, F. Fülop, H. Neuvonen, A. Koch, E. Kleinpeter, K. Pihlaja, *J. Org. Chem.* **2003**, *68*, 2151–2160.
- [5] (a) H. Neuvonen, K. Neuvonen, *J. Chem. Soc., Perkin Trans. 2* **1999**, 1497–1502; (b) H. Neuvonen, K. Neuvonen, A. Koch, E. Kleinpeter, P. Pasanen, *J. Org. Chem.* **2002**, *67*, 6995–7003.
- [6] J. Shorter, in *Similarity Models in Organic Chemistry, Biochemistry and Related Fields, Studies in Organic Chemistry*, Vol. 42 (Eds.: R. I. Zalewski, T. M. Krygowski, J. Shorter), Elsevier Science Publishers, Amsterdam, **1991**.
- [7] S. Ehrenson, R. T. C. Brownlee, R. W. Taft, *Prog. Phys. Org. Chem.* **1973**, *10*, 1–80.
- [8] W. F. Reynolds, A. Gomes, A. Maron, D. W. Macintyre, A. Tanin, G. K. Hamer, I. R. Peat, *Can. J. Chem.* **1983**, *61*, 2376–2384.
- [9] G. F. Fadhl, *Z. Naturforsch.* **1992**, *47a*, 775–780.
- [10] G. F. Fadhl, *Collect. Czech. Chem. Commun.* **1993**, *58*, 385–394.
- [11] N. L. Shihabaldain, H. A. R. Al-Hazam, G. F. Fadhl, *Iraqi Nat. J. Chem.* **2002**, *7*, 422–437.
- [12] Y. Yukawa, Y. Tsuno, *Bull. Chem. Soc. Jpn.* **1959**, *32*, 971–981.
- [13] Y. Tsuno, M. Fujio, *Chem. Soc. Rev.* **1996**, *25*, 129–139.
- [14] (a) G. K. Hamer, I. R. Peat, W. F. Reynolds, *Can. J. Chem.* **1973**, *51*, 897–914; (b) G. K. Hamer, I. R. Peat, W. F. Reynolds, *Can. J. Chem.* **1973**, *51*, 915–926.
- [15] (a) J. Bromilow, R. T. C. Brownlee, D. J. Craik, P. R. Fiske, J. E. Rowe, M. Sadek, *J. Chem. Soc., Perkin Trans. 2* **1981**, 753–759; (b) R. T. C. Brownlee, D. J. Craik, *J. Chem. Soc., Perkin Trans. 2* **1981**, 760–764; (c) R. T. C. Brownlee, D. J. Craik, *J. Org. Magn. Reson.* **1981**, *15*, 248–256.
- [16] B. A. Saleh, *Basrah J. Science* **2003**, *C 21*, 1–9.
- [17] D. A. R. Happer, B. E. Steenson, *J. Chem. Soc., Perkin Trans. 2* **1988**, 19–24.
- [18] C. E. Aun, T. J. Clarkson, D. A. R. Happer, *J. Chem. Soc., Perkin Trans. 2* **1990**, 645–649.
- [19] G. K. Hamer, I. R. Peat, W. F. Reynolds, *Can. J. Chem.* **1973**, *51*, 897–914, 915–926.
- [20] O. Exner, in *Correlation Analysis in Chemistry: Recent Advances* (Eds.: N. B. Chapman, J. Shorter), Plenum, New York, **1978**.