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Substituent effect investigation of 3-(2, 4-dichlorophenyl)-1-(4′-X-phenyl)-2-propen-1-one. Part 1. Correlation analysis of ^{13}C NMR chemical shifts†

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A series of substituted chlorinated chalcones namely, 3-(2,4-dichlorophenyl)-1-(4′-X-phenyl)-2-propen-1-one, have been synthesized, X being H, NH_2, OMe, Me, F, Cl, CO_2Et, CN, and NO_2. Dual substituent parameter (DSP) models of ^{13}C NMR chemical shift (CS) have revealed that π-polarization concept could be utilized to explain the reverse field effect at CO, the enhanced substituent field effect at CO, C-2, and C-5, and the decreased sensitivity of substituent field effect at C-6. Chlorine atoms dipole direction at the benzylidene ring either enhances or reduces substituent effect depending on how they couple with the substituent dipole at the probe site. The correlation of ^{13}C NMR CS of C-2, C-5, and C-6 with σ_P^+ and σ_R^+ indicates that chlorine atoms in the benzylidine ring deplete the ring from charges. Both MSP of Hammett and DSP of Taft ^{13}C NMR CS models give similar trends of substituent effects at C-2, C-5, and C-6. However, the former fail to give a significant correlation for CO and C-6 ^{13}C NMR CS. MSP of σ_q and DSP of Taft and Reynolds models significantly correlated ^{13}C NMR CS of C_β. MSP of σ_q fails to correlate C-1′ ^{13}C NMR CS. Investigation of ^{13}C NMR CS of non-chlorinated chalcones series: 3-phenyl-1-(4′-X-phenyl)-2-propen-1-one has revealed similar trends of substituent effects as in the chlorinated chalcones series for C-1′, CO, C_α, and C_β. In contrast, the substituent effect of the non-chlorinated chalcone series at C-2, C-5, and C-6 did not correlate with any substituent constant. Copyright © 2010 John Wiley & Sons, Ltd.

Supporting information may be found in the online version of this paper.

Keywords: ^{13}C NMR chemical shifts; chalcones; correlation analysis; substituent effect

INTRODUCTION

Chalcones have shown immense chemical and biological applications such as antimalarial,[1] antiplasmodial,[2] anti-HIV,[3–5] anti-cancer,[6,7] and anti-bacterial.[8] Also, chalcones have been objects of a number of theoretical[9,10] and experimental[11,12] structural investigations. Earlier studies on the transmission of substituent effects on substituted chalcones namely 3-phenyl-1-(4′-X-phenyl)-2-propen-1-ones, 3-(4-X-phenyl)-1-(phenyl)-2-propen-1-ones,[13,14] and *trans*-1-phenyl-3-(5-aryl-2-furyl) propenones and *trans*-1-phenyl-3-(5-aryl-2-thienyl) propenones[15] have revealed the electronic nature of substituent effect. These conclusions were based on the correlation of the ^{13}C NMR CS or carbonyl stretching frequencies as represented by P_x for compound with X being the substituent and σ being the Hammett substituent constant. Equation (1) represents the mono substituent parameter model (MSP). There has been some dispute about using the MSP over the dual substituent parameter model (DSP). The former model is simple and gives one weighting factor to interpret the transmission of substituent effect. However, the failure of the MSP in certain cases has encouraged researchers to use the DSP (Eqn 2), which uses σ_R and σ_F substituent resonance and field constants, respectively. Nevertheless, in certain cases the MSP provides better modeling results than the DSP.

$$P_x = \rho\,\sigma + c \qquad (1)$$

$$P_x = \rho_R\,\sigma_R + \rho_F\sigma_F + c \qquad (2)$$

where ρ, ρ_R, and ρ_F are the weighting factors of electronic, resonance, and field substituent effects, respectively, with *c* being the intercept in each model. These models have demonstrated the versatility of both the MSP and DSP in interpreting the mode of transmission of substituent electronic, resonance, and field effects.

Sotomatsu *et al.*[16] found a significant correlation between Hammett's substituent constant and the sum of Mulliken charges of the carboxyl group of various *para* and *meta* substituted benzoic acids calculated by semi-empirical AM1 method. Saleh[17] defined σ_q constant from the sum of calculated Mulliken

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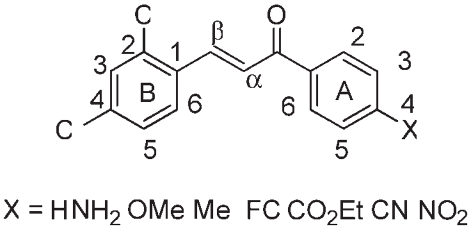
† *In Memoriam the late professor Alexander Perjéssy*

charges[16] of the carboxyl group atoms in *para* or *meta* substituted benzoic acid.

In recent substituent effect studies on ^{13}C NMR CSs and carbonyl stretching frequencies in *E*-2-(X-benzylidene)-1-indanones, *E*-2-(X-benzylidene)-1-tetralone, and *E*-2-(X- benzylidene)-1-benzosuberones,[18,19] each structure contains the α,β-unsaturated ketone functionality. This makes the molecular framework similar to chalcones. It has been concluded[18,19] that the carbon atom α of the side chain, which is next to carbon *para* of the substituted benzene ring, is less sensitive to substituent effect than the β-carbon. However, there was little elaboration on the origins of the field effects in terms of π-polarization.

The π-polarization concept was proposed originally by Hamer *et al.*[20,21] and later was used extensively by Bromilow *et al.*[22] and Brownlee *et al.*[23,24] to rationalize substituent field effect at the side chain of *para* and/or *meta* substituted benzenes. It was also successfully applied to interpret the transmission of substituent effects within 5-substituted indole -2, 3-diones.[25] The π-polarization concept was recently used successfully to interpret the Yukawa–Tsuno model of ^{13}C NMR CS of β-carbon of the vinyl group in *para* substituted styrenes with varying electronic demands at β-carbon.[26] Hence, applying MSP and DSP models to ^{13}C NMR CS and then interpreting the obtained ρ of MSP and ρ_R and ρ_F of DSP – in terms of the electronic effects or resonance and field effects of substituent with the aid of the π-polarization concept – would be a worthwhile analysis to rationalize the mode of transmission of substituent effects through aromatic molecules. Previous structural investigations have not covered chalcones with a chlorinated benzylidine ring.[13–15] These chlorine atoms may alter the substituent effect felt at the benzylidine ring. Hence, the aim of this work is to investigate the mode of transmission of substituent effect and test the quality of MSP and DSP models in modeling ^{13}C NMR CS in 3-(2,4-dichlorophenyl)-1-(4′-X-phenyl)-2-propen-1-ones (Structure 1).



EXPERIMENTAL SECTION

General procedures

Melting points were uncorrected and measured by using Gallenkamp melting point apparatus. Proton NMR spectra were recorded on a Varian VXR 300 NMR spectrometer (299.943 MHz) in $CDCl_3$ at 25 °C with a concentration of $0.02\,ml^{-1}$. ^{13}C NMR spectra were recorded on the same spectrometer at (75.429 MHz) in $CDCl_3$ solvent at 25 °C and referenced with respect to TMS in ppm. The Proton decoupling technique was used to aid the ^{13}C assignment. A concentrated solution in $CDCl_3$ was used. For compounds with X as NH_2, a small amount of CD_3OD was added to increase its solubility in $CDCl_3$. The follow-up of reactions and sample purity were checked by TLC using Merck silica gel 60 F_{254} aluminum sheets and were developed with the solvent mixture indicated in Table S1.

General procedure for the synthesis of 3-(2, 4-dichlorophenyl)-1-(4′-X-phenyl)-2-propen-1-one

Condensation of 2, 4-dichlorobenzaldehyde with 4-X-acetophenone was carried out to prepare the suitable 3-(2, 4-dichlorophenyl)-1-(4′-X-phenyl)-2-propen-1-one (Chalcone). However, two different procedures were employed according to the type of substituent, X, in the acetophenone. Chalcones with substituent X, namely H, NH_2, OMe and Me, were prepared according to the Claisen–Schmidt method[27–29] with a slight modification to the concentration of the base in which 20% of NaOH was used for the preparation of chalcones with substituents H and OMe. Chalcones with substituent X, namely F, CN and NO_2, were prepared by passing HCl gas on ethanolic solution of the 2, 4-dichlorobenzaldehyde and *para* substituted acetophenone in (1:2) mole ratio, respectively.[30] However, chalcone with substituent CO_2Et was prepared *in situ* by hydrolysis and then ethanolysis of the 3-(2, 4-dichlorophenyl)-1-(4′-cyano-phenyl)-2-propen-1-one. Products were recrystalized from ethanol. Table S1 gives the yields percentages, physical properties, uncorrected melting points and retention factors for the prepared compounds. CHN analysis is presented in Table S2.

Proton NMR assignments

Table S3 shows proton NMR spectra. Scheme 1 shows proton designation and carbon atom numbering. Protons on ring B showed an AMX pattern of splitting, while protons on ring A showed an AA′BB′ pattern of splitting. The vinyl protons gave an AB pattern of splitting.

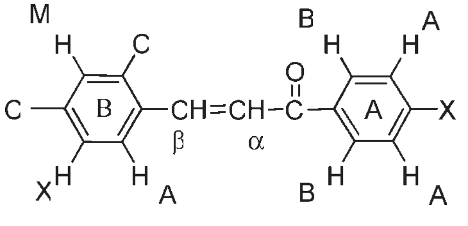
^{13}C NMR spectra assignments

Table 1 presents the measured ^{13}C NMR CS. The calculated ^{13}C NMR CS are presented in parenthesis. Additivity rules of the software ChemBioDraw Ultra 11[31] were used to calculate the expected ^{13}C NMR chemical shifts. ^{13}C NMR CS of the carbonyl, alpha, and beta were assigned according to Reference [14]. Calculated ^{13}C NMR chemical shifts of ring B, CO, C_α, and C_β according to Reference [31] were insensitive to the variation of the substituents. They are given for the unsubstituted compound only; substituted compounds showed the same values of calculated ^{13}C NMR CS. Difference in peak intensities of substituted and unsubstituted carbons aided in peak assignments.

COMPUTATIONS

Statistical calculations

A standard statistical package was used to calculate *r*, *R*, regression coefficient ρs, and standard deviation (SD) of model fit. *f*-statistics[32] was used to judge the quality of the constructed



Scheme 1.

Table 1. ^{13}C NMR CS in ppm of 3-(2, 4-dichlorophenyl)-1-(4′-X-phenyl)-2-propen-1-one

X	C-α	C-β	C-1	C-2	C-3	C-4	C-5	C-6
H	125.01	139.31	131.85	136.07	130.14	136.47	127.56	128.50
	(124.3)	(145.1)	(131.1)	(136.0)	(128.9)	(125.2)	(126.8)	(130.3)
NH_2	124.74	138.05	131.85	135.69	129.83	136.02	127.34	128.33
OCH_3	125.48	138.44	132.07	135.92	130.05	136.18	127.48	128.44
CH_3	125.04	138.88	131.96	136.00	130.09	136.31	127.51	128.46
F	124.54	139.55	131.70	136.10	130.17	136.59	127.58	128.49
Cl	124.39	139.79	131.62	136.03	130.18	136.14	127.59	128.49
CO_2Et	124.76	140.45	131.56	136.22	130.21	136.81	127.63	128.53
NO_2	124.06	141.13	131.14	136.31	130.26	137.18	127.67	128.53

X	CO	C-1′	C-2′,6′	C-3′,5′	C-4′	Others
H	190.07	137.77	128.71	128.60	133.08	
	(189.7)	(137.9)	(128.5)	(129.2)	(134.5)	
NH_2	188.20	128.83	131.05	115.35	149.28	
		(127.9)	(132.0)	(114.7)	(154.2)	
OCH_3	188.20	130.63	130.92	113.90	163.60	55.50 (OCH_3) (55.80)
		(130.2)	(130.9)	(114.8)	(166.4)	
CH_3	189.55	135.15	128.75	129.40	144.00	21.71(CH_3) (21.3)
		(134.9)	(128.8)	(129.5)	(144.2)	
F	188.43	134.09	131.16	115.87	165.74	
		(133.5)	(131.5)	(116.0)	(168.7)	
Cl	188.76	136.67	130.00	129.04	139.55	
		(136.0)	(130.3)	(129.3)	(140.1)	
CO_2Et	189.78	141.04	128.45	129.86	134.15	13.30 (14.1)(CH_3) 61.51(60.9) (OCH_2) 165.74 (165.9)(CO)
		(142.2)	(129.8)	(130.4)	(135.9)	
NO_2	188.63	142.46	129.48	123.88	150.14	
		(144.0)	(130.8)	(124.4)	(153.7)	

$^{1}J(^{13}C,^{19}F) = 255.18$ Hz, $^{ortho}J(^{13}C,^{19}F) = 22.1$ Hz, $^{meta}J\,(^{13}C,^{19}F) = 9.28$ Hz, and $^{para}J\,(^{13}C,^{19}F) = 2.87$ Hz. Bracketed values are calculated CS in ppm.

model, and were calculated by dividing the SD of the model over the root mean square error of data. The lower the *f*-statistics the better is the model. Excluded substituents in modeling due to lack of substituent constant are indicated at the bottom of Tables 2 and 3.

RESULTS AND DISCUSSION

Table 1 shows the variations of ^{13}C NMR CS values when changing the substituent in structure 1. Tables 2 and 3 provide the results of modeling ^{13}C NMR CS via the MSP and DSP models, respectively.

The MSP of σ_q and DSP models were equally significant in modeling $^{13}C_\beta$ NMR CS as indicated by *r*, *R*, and *f*-statistics. None of the MSP models provided significant correlation with ^{13}C-CO NMR CS. Hammett type σ_p^+ was better than σ_q in correlating ^{13}C NMR CS of C-1′, C-2, C-5, and C-6 as concluded from the higher *r* and lower *f*-statistics values for Hammett's model. Similarly, Taft's DSP model selected σ_R^+ as the best substituent constant to correlate ^{13}C NMR CS of C-2, C-5, and C-6. The selection of σ_p^+ and σ_R^+ in MSP and DSP models, respectively, indicates that C-2, C-5, and C-6 may suffer a deficiency of charge. Hence, the failure of Reynolds' DSP model in correlating ^{13}C NMR CS of C-2, C-5, andC-6 can be understood since his model uses $\sigma_R{}^\circ$ as a substituent resonance constant. However, Reynolds' DSP model correlated ^{13}C NMR CS of C-1′ and C_β better than Taft's DSP model, which also uses $\sigma_R{}^\circ$ as a substituent constant. In general, DSP models give better modeling quality than MSP models. ρ_R values for a given carbon responded in a similar fashion in both Reynolds' and Taft's DSP models as long as the latter uses of $\sigma_R{}^\circ$ as the best substituent resonance parameter, and both models had a similar quality of significance as given by R values. This result can be ascribed to the nature of Reynolds' $\sigma_R{}^\circ$. ρ_R in Reynolds' model for ^{13}C-1′ NMR CS is 4.77 times larger than ρ_F for the same atom. This implies more substituent resonance contribution in C-1′ than field effect. This behavior of C-1′ was found previously in *para*-disubstituted benzenes.[33] Taft's DSP model is superior in quality to Reynolds' DSP model in modeling ^{13}C NMR CS of C-CO. The ^{13}C NMR CS of C-CO behaves in a reverse manner to the substituent effect. This means the electron-withdrawing substituent causes an up-field shift to NMR chemical shifts of ^{13}C-CO. Despite that, a positive value of ρ_R was observed in modeling ^{13}C-CO NMR CS by Reynolds' and Taft's DSP models with σ_R^+ being the best substituent resonance constant in the latter model. It has been observed[34] that ^{13}C-CO NMR CS of acetophenone responds normally to substituent resonance effect with ρ_R being positive. The ^{13}C-CO NMR CS in the current study behaves in a similar fashion to that of acetophenone. However, for *para* substituted benzoate the ^{13}C-CO NMR CS gives a

Table 2. Results of ^{13}C NMR CS MSP modeling of chlorinated chalcones

	Hammett's Model[a]				
C-atom	Substituent constant	*c*	ρ	*r*	*f*-statistics
C-1′	σ_p^+	136.59 ± 0.45	6.86 ± 0.72	0.968	0.26
CO	σ_p^+	189.01 ± 0.25	0.53 ± 0.39	0.478	0.54
C-β	σ_p^{BA}	139.46 ± 0.14	2.12 ± 0.33	0.930	0.41
C-2	σ_p^+	136.07 ± 0.02	0.28 ± 0.03	0.972	0.27
C-5	σ_p^+	127.56 ± 0.01	0.15 ± 0.01	0.972	0.27
C-6	σ_p^+	128.48 ± 0.01	0.09 ± 0.01	0.948	0.35

	σ_q Model[b]			
C-atom	*c*	ρ	*r*	*f*-statistics
C-1′	250.99 ± 22.7	267.0 ± 52.2	0.916	0.40
CO	190.37 ± 8.9	3.50 ± 20.4	0.077	0.56
C-β	167.19 ± 1.7	64.20 ± 3.9	0.991	0.15
C-2	140.94 ± 0.8	11.30 ± 1.8	0.942	0.36
C-5	130.19 ± 0.5	6.13 ± 1.2	0.914	0.45
C-6	129.96 ± 0.4	3.46 ± 1.0	0.837	0.59

c is the intercept.

[a] CN was excluded.

[b] CO_2Et and CN were excluded.

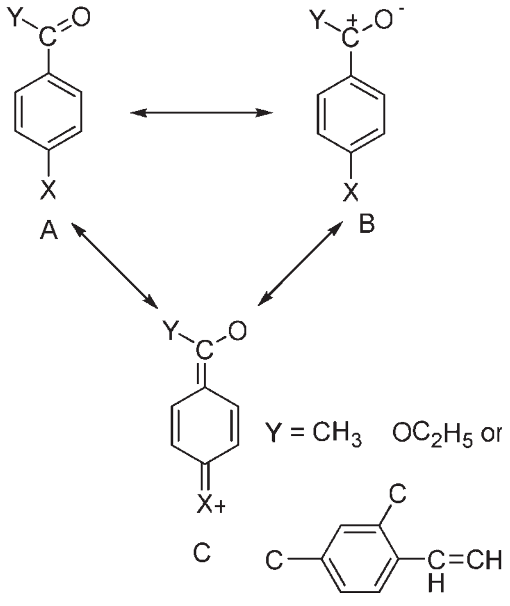
Table 3. Results of ^{13}C NMR CS DSP modeling of chlorinated chalcones

	Taft's Model					
C-atom	Substituent constant	*c*	ρ_I	ρ_R	*R*	*f*-statistics
C-1′	$\sigma_R{}^{\circ}$	137.15 ± 0.46	4.74 ± 1.04	11.90 ± 0.79	0.991	0.15
CO	σ_R^+	189.88 ± 0.14	−2.00 ± 0.29	0.95 ± 0.13	0.976	0.13
C-β	$\sigma_R{}^{\circ}$	139.26 ± 0.07	2.35 ± 0.18	2.96 ± 0.17	0.995	0.12
C-2	σ_R^+	136.06 ± 0.03	0.29 ± 0.07	0.25 ± 0.03	0.981	0.24
C-5	σ_R^+	127.55 ± 0.01	0.17 ± 0.03	0.14 ± 0.01	0.991	0.17
C-6	σ_R^+	128.48 ± 0.02	0.07 ± 0.03	0.09 ± 0.01	0.965	0.30

	Reynolds' Model[a]				
C-atom	*c*	ρ_F	ρ_R	*R*	*f*-statistics
C-1′	137.63 ± 0.29	3.88 ± 0.64	18.50 ± 0.70	0.998	0.07
CO	189.97 ± 0.20	−2.23 ± 0.44	2.59 ± 0.48	0.956	0.18
C-β	139.25 ± 0.08	2.31 ± 0.18	3.04 ± 0.19	0.996	0.10
C-2	136.05 ± 0.06	0.29 ± 0.13	0.63 ± 0.14	0.944	0.40
C-5	127.54 ± 0.04	0.18 ± 0.09	0.32 ± 0.09	0.919	0.48
C-6	128.48 ± 0.03	0.08 ± 0.07	0.21 ± 0.08	0.856	0.60

c is the intercept.

[a] CN was excluded.

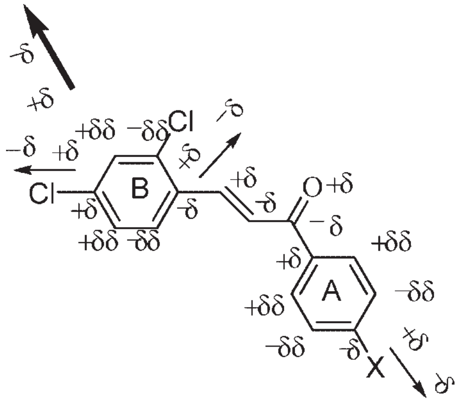


Scheme 2.

negative ρ_R. This phenomenon is called the reverse substituent resonance effect.

The π-polarization along the conjugated π-electron system was found to be under the influence of the substituent at the *para* substituted benzene ring A.[20–24] The π-polarization concept assumes that each π-unit (a double or triple bond, carbonyl, nitrile, or aromatic system) is thought to be polarized separately, the polarization being induced by the substituent dipole in another part of the molecule. This type of π-polarization is called localized or direct π-polarization. The localized π-polarization can be transmitted through either the molecular framework or the solvent continuum. In localized π-polarizations, each π-unit in the side chain polarizes separately.

It has been claimed[35] that in cases of acetophenones resonance, structure C of Scheme 2 is more important than the resonance structure B of Scheme 2. However, in the case of ethyl benzoates, the resonance structure B of Scheme 2 is more important than resonance structure C.



Structure 2.

Thus, in this study we may argue that resonance structure C is more important than structure B because ρ_R is positive. Nonetheless, both DSP models give a reverse substituent field effect i.e. negative values of ρ_I for the ^{13}C-CO NMR CS. Taft's model gives a ρ_I value almost twice ρ_R for ^{13}C-CO NMR CS. Thus, the predominance in the ^{13}C-CO NMR CS value is for the substituent field effect, explaining the reverse behavior of the ^{13}C-CO NMR CS. The reverse substituent field effect (i.e. negative ρ_I) can be rationalized as a result of the π-polarization of the molecular framework. Structure 2 depicts the π-polarization in the studied molecule. A partial negative charge appears at C-CO, reflecting the reverse nature of the substituent field effect felt at that carbon. However, the positive sign of ρ_R for ^{13}C-CO NMR CS indicates a normal substituent effect as explained previously.[35,36]

MSP and DSP models failed to correlate $^{13}C_\alpha$ NMR CS. This failure was observed with other chalcones;[14] it might be related to the insensitivity of $^{13}C_\alpha$ NMR CS to the variation of substituents. In contrast, $^{13}C_\beta$ NMR CS showed a significant correlation in σ_q MSP model. DSP models for $^{13}C_\beta$ NMR CS generated more significant results than MSP models. Reynolds' DSP model was better than Taft's, but both indicated more substituent resonance effect than substituent field effect at C_β. However, the ρ_R/ρ_I and ρ_R/ρ_F of C-1′ are much larger than at C_β. Structure C of Scheme 2 shows that C-1′ is in through resonance, while C_β is not. The correlation of $^{13}C_\beta$ NMR CS with σ_R° of Taft and σ_R° of Reynolds indicates that the substituent is not in direct resonance with C_β. σ_p^+ of Hammett's MSP and σ_R^+ of Taft's DSP significantly correlate ^{13}C NMR CS of C-2, C-5, and C-6, while σ_q and Reynolds' DSP model fail to do so. The selection of σ_p^+ in the MSP model and σ_R^+ in the DSP model as the best substituent parameters may indicate an electron deficiency at C-2, C-5, and C-6. This could be attributed to the chlorine atoms in the benzylidene ring. The $\rho_{R\ C\text{-}2}/\rho_{R\ C\text{-}6}$ being 2.77 and $\rho_{C\text{-}2}/\rho_{C\text{-}6}$ being 3.11 are close results from using different models and confirm the increased substituent resonance effect sensitivity at C-2 over that of C-6, which can be ascribed to the chlorine atom at C-2. The chlorine atom depletes the C-2 from electrons and, hence, the ^{13}C NMR CS of C-2 significantly correlates with σ_p^+ and σ_R^+ with ρ and ρ_R, respectively, and is higher than that of C-6 which lacks a chlorine atom. The $\rho_{R\ C\text{-}5}/\rho_{R\ C\text{-}6}$ and $\rho_{C\text{-}5}/\rho_{C\text{-}6}$ were 1.56 and 1.67, respectively. This trend of $\rho_{R\ C\text{-}5}/\rho_{R\ C\text{-}6}$ and $\rho_{C\text{-}5}/\rho_{C\text{-}6}$ is similar to that observed in C-2 but to a lesser extent because of C-5 being indirectly connected to the chlorine atom as in C-2. The substituent field effect felt at C-2, C-5, and C-6 was normal, i.e. positive values of ρ_j or ρ_F with a rate of fall C-2 > C-5 > C-6. This trend of fall coincides with the rate of fall of ρ_R for the same atoms. Enhanced ρ_F and ρ_R values in Reynolds' DSP model were observed[26] for $^{13}C_\beta$ NMR CS of *para* substituted styrene when the C_β atom becomes bonded to a more electronegative atom or polarizable functional group.

Structure 2 shows the resultant dipole due to chlorine atoms at carbon atoms 2 and 4. The resultant dipole stabilizes the π-polarization at C-2 because of its proximity of partial positive charge and of the resultant chlorine dipole to the partial negative charge generated by the substituent field effect at C-2. However, when a positive charge due to the substituent field effect exists such as at C-5, a lower ρ_I value is observed due to destabilization by similar charge repulsion. A lower ρ_I value than that at C-2 is also observed when the resultant dipole is felt at C-6 in the opposite direction to the substituent field dipole.

The ρ_I/ρ_R for C-2 and C-5 was 1.16 and 1.21, respectively, while the ρ_I/ρ_R for C-6 was 0.78. These rates of fall indicate that ρ_I at C-6 is more sensitive to the destabilizing effect of the resultant dipole of the chlorines atoms C-2 and C-4 than ρ_R, which maintained a higher value than ρ_I.

Table 4. Results of ^{13}C NMR CS MSP modeling of non-chlorinated chalcones[a]

	Hammett's Model				
C-atom	Substituent constant	c	ρ	r	f-statistics
C-1′	σ_p^+	136.49 ± 0.39	7.73 ± 0.80	0.974	0.26
CO	σ_p^+	188.88 ± 0.27	0.26 ± 0.56	0.207	0.54
C-β	σ_p^{BA}	144.75 ± 0.18	2.45 ± 0.43	0.939	0.38
C-2	σ_p^+	128.78 ± 0.05	0.17 ± 0.10	0.605	0.84
C-5	σ_p^+	129.34 ± 0.29	−0.50 ± 0.59	0.352	0.86
C-6	σ_p^+	128.78 ± 0.05	0.17 ± 0.10	0.605	0.86

	σ_q Model			
C-atom	c	ρ	r	f-statistics
C-1′	253.48 ± 27.21	270.0 ± 63.33	0.886	0.53
CO	188.22 ± 9.41	−1.60 ± 21.90	0.032	0.55
C-β	179.72 ± 3.55	80.73 ± 8.25	0.975	0.23
C-2	132.69 ± 1.18	9.06 ± 2.75	0.828	0.59
C-5	127.51 ± 10.47	−4.15 ± 24.38	0.077	0.91
C-6	132.69 ± 1.18	9.06 ± 2.75	0.828	0.59

c is the intercept.

[a] Substituent set: H, CH_3, OCH_3, F, Cl, CN and NO_2.

Table 5. Results of ^{13}C NMR CS DSP modeling of non-chlorinated chalcones[a]

	Taft's Model					
C-atom	Substituent constant	c	ρ_I	ρ_R	R	f-statistics
C-1′	σ_R^{BA}	137.55 ± 0.43	4.85 ± 0.92	12.98 ± 0.88	0.993	0.15
CO	σ_R^+	189.77 ± 0.19	−1.85 ± 0.34	1.15 ± 0.22	0.962	0.17
C-β	σ_R°	144.52 ± 0.08	2.66 ± 0.17	3.19 ± 0.20	0.996	0.09
C-2	σ_R^+	128.66 ± 0.06	0.46 ± 0.13	0.05 ± 0.09	0.877	0.57
C-5	σ_R^+	128.46 ± 0.38	1.43 ± 0.79	−1.27 ± 0.51	0.818	0.59
C-6	σ_R^+	128.66 ± 0.06	0.46 ± 0.13	0.05 ± 0.09	0.877	0.57

	Reynolds' Model				
C-atom	c	ρ_F	ρ_R	R	f-statistics
C-1′	138.01 ± 0.31	3.72 ± 0.64	18.59 ± 0.83	0.997	0.09
CO	189.96 ± 0.96	−2.15 ± 0.30	2.68 ± 0.39	0.974	0.14
C-β	144.49 ± 0.08	2.72 ± 0.16	3.36 ± 0.21	0.997	0.08
C-2	128.66 ± 0.08	0.45 ± 0.16	0.09 ± 0.21	0.838	0.65
C-5	128.44 ± 0.45	1.54 ± 0.94	−2.76 ± 1.23	0.777	0.64
C-6	128.66 ± 0.08	0.45 ± 0.16	0.09 ± 0.21	0.838	0.65

c is the intercept.

[a] Substituent set: H, CH_3, OCH_3, F, Cl, CN, NO_2.

In order to investigate the role of chlorine atoms in the side chain on the transmission of substituent effect, we have investigated the substituent effect on the previously measured[14] ^{13}C NMR CS in 3-phenyl-1-(4′-X-phenyl)-2-propen-1-one as chalcone with non-chlorinated side chain here upon called non-chlorinated chalcone series. Tables 4 and 5 give the MSP and DSP modeling results, respectively. The substituent effect trends for C-1′, CO, C_β, and C_α in the non-chlorinated chalcone series are similar to the chlorinated chalcone series. Nevertheless, carbon atoms of the benzylidine ring B in the non-chlorinated chalcone series failed to correlate with any MSP or DSP model. This finding could be attributed to the generated dipole by the chlorine atoms bonded to carbon atom number 2 and 4 in the chlorinated series. This dipole makes the C-2 and C-4 more sensitive to respond to the substituent at *para* substituted benzene ring A.

CONCLUSION

The π-polarization concept analysis of carbonyl stretching and ^{13}C NMR CS results have aided in explaining successfully the normal and reverse substituent field effect, ρ_F, felt at several substituent sensitive sites. Chlorine atoms in the side chain not only play a significant role in sensitizing carbon atoms of the benzene ring which carries chlorine atoms to the substituent effect, but also the π-polarization and its induced dipoles direction of the remote chlorine atoms play a significant role in determining the substituent field effect felt at probe sites in the vicinity of the chlorine atoms, either enhancing the substituent field effect as in the case of C-2 and C-5 or retarding it as in C-6. The substituent resonance effect is less sensitive than the substituent field effect to the side chain chlorine atoms dipole, as can be inferred from the reverse behavior of ρ_I/ρ_R for C-2 and C-5 from one side and that of C-6 from other side. The choice of certain substituent resonance constant than other helped in detecting that site which is being conjugated such as C-1′, or non-conjugated as in C_β since the former selects σ_R^+, while the latter selects $\sigma_R{}^\circ$. Both MSP and DSP models give conclusive results that the chlorine atoms deplete the benzene ring B from charge as can be inferred from the best selected substituent constant σ_p^+ and σ_R^+ for both models respectively. Trends and interpretation results of ^{13}C NMR CS utilizing the MSP model agree with DSP results as long as ρ_F or ρ_I does not exceed the value of ρ_R as in the case of ^{13}C NMR CS of CO. MSP which uses σ_q gives only one significant result for C_β ^{13}C NMR CS indicating that this substituent constant is useful in the correlation of non-conjugated sites. Calculated ^{13}C NMR CS by ChemBioDraw Ultra11 of side-chain carbon atoms CO, C_α, C_β, and carbons of benzene ring B were insensitive to the variation of substituents.

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