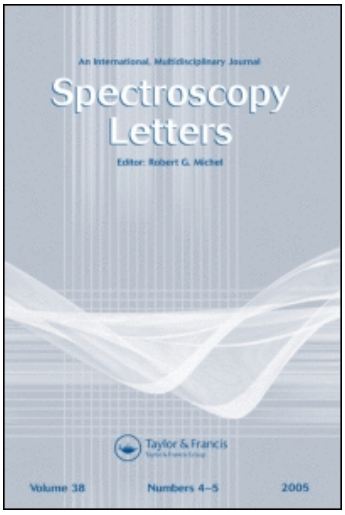

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^{13}C NMR Chemical Shift of β-Alkoxyvinylketones: II. Empirical Substituent Effects in β-Aryl-β-Methoxyvinyltrihalomethylketones

Marcos A. P. Martins[a]; Geonir M. Siqueira[a]; Alex F. C. Flores[a]; Nilo Zanatta[a]
[a] Departamento de Química, Universidade Federal de Santa Maria, Santa Maria, RS, Brazil

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^{13}C NMR CHEMICAL SHIFT OF β-ALKOXYVINYLKETONES: II[Ф]. Empirical Substituent Effects in β-Aryl-β-methoxyvinyltrihalomethylketones

Marcos A.P. Martins*, Geonir M. Siqueira, Alex F.C. Flores and Nilo Zanatta

Departamento de Química, Universidade Federal de Santa Maria
CEP 97.119-900 Santa Maria, RS, Brazil

Key Words: ^{13}C NMR of β-Alkoxyvinylketones
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^{13}C NMR of Trisubstituted alkenes

ABSTRACT

Evaluation by empirically derived equations for the substituent effect (α, β, γ, δ) on the ^{13}C NMR chemical shifts for C-1, C-2, C-3 and C-4 in β-aryl-β-methoxyvinylhalomethylketones **1a-g** to **2a-g** [$R^3C(O)$-CH=C(Ar)-OMe, where R^3 = CCl_3, CF_3 and Ar = *p*-YC_6H_4 (Y = H, Me, MeO, F, Cl, Br, NO_2)], taking as reference the β-ethoxyvinyltrichloromethylketone (**3**), is reported. From the calculated values for the α, β, γ, δ, effects for each substituent it was possible to estimate the chemical shift of each carbon of the compounds **1,2**. The ^{13}C chemical shifts of the C-1, C-2, C-3, C-4 of these compounds, can be estimated with good to rasoable precision: 84% of the calculated chemical shifts are found to be within ±1.0ppm, and 100% are found to be within ±1.5ppm. The Y-*Effects* on C-3 and C-4 are compared with carbon charge densities (q*r*).

Ф For Part I, see Ref. 10.

*Author to whom correspondence should be addressed.

INTRODUCTION

The ^{13}C NMR chemical shifts substituent effects on sp^2 carbon atoms in unsaturated molecules have been widely interpreted in terms of inductive, mesomeric, or other mechanism and correlated with calculated charge densities or physico-chemical parameter such as Hammett constants[1]. However, empirical additive substituent increments obtained by analysis of substituted compounds, have proven to be the most important and useful tool to predict these ^{13}C chemical shifts[1,2].

β-Alcoxyvinylketones functionalized with CX_3-CO and CHX_2-CO groups, with X=F, Cl, groups are interesting precursors for a variety of five and six membered heterocycles[3,4]. Although the synthesis of some of these compounds have been formerly described by Effenberger et al.[5], followed by Hojo et al.[6], only recently our laboratory reported the ^{13}C NMR data of some trihalogenated β-alkoxyvinylhalomethylketones[3,7].

The aim of this work is the evaluation of the ^{13}C chemical shifts of β-aryl-β-methoxyvinylhalomethylketones **1,2** (Scheme), in relation to a reference compound. The empirical substituent increments can be used to create a system of equations that then may allow to calculate the chemical shifts of the carbons 1,2,3 and 4 of similar compounds. The Y-*Effects* on C-3 and C-4 are compared with their respective carbon charge densities (q_r).

EXPERIMENTAL

Compounds

The β-aryl-β-methoxyvinylhalomethylketones **1,2a-g**, were synthesized according to the published techniques developed in our laboratory[7].

^{13}C NMR Spectra

The ^{13}C NMR spectra were recorded on a Bruker AC-80 spectrometer at 20.15 MHz. The experimental conditions on the Bruker AC-80 were: ^{2}D internal lock; pulse width of 30° (1.6μs); acquisition time 1.64s; spectral width 5000 Hz; relaxation delay 2s; number of scans between 3000 and 5000, depending of the type of compound; 16,384 data points giving a digital resolution of 0.61 Hz/point; probe temperature of 35°C.

Chloroform-d_1 solutions with an approximate concentration of 0.5 M and 0.1% of TMS as internal reference were used in 5mm tubes.

Calculations

All calculations were done on a MICROTEC-DX 386 personal computer. The determinations of the carbon charge densities were done by a graphics-based Hückel MO Program[11].

RESULTS AND DISCUSSION

The ^{13}C chemical shift assignments of compounds **1,2** were done by simple comparison among the synthesized compounds[8] and, when necessary, by interpretation of ^{13}C coupled spectra and 2D-NMR techniques such as Heteronuclear Correlated Spectroscopy (COSY CH)[9]. The experimental ^{13}C chemical shifts of compounds **1,2** are shown in Table 1.

From the ^{13}C NMR experimental data of compounds **1,2** (Table 1) the substituent increments were determined, taking β-ethoxyvinyltrichloromethylketone as a reference[1] (Scheme). This reference compound was choosen for the following reasons: (1) specific

TABLE 1

^{13}C chemical shifts of the carbons 1, 2, 3 and 4 of β-aryl-β-methoxy vinyltrihalomethyl ketones **1,2** and the reference compound, β-ethoxy vinyltrichloromethylketone (**3**).

Compound	δ_{C-1}	δ_{C-2}	δ_{C-3}	δ_{C-4}
1a	97.9	178.8	90.8	177.2
1b	97.9	178.5	90.2	177.1
1c	98.2	178.6	89.8	177.0
1d	97.9	178.9	90.8	176.0
1e	97.8	178.7	91.1	175.8
1f	97.7	178.7	91.0	175.7
1g	97.3	178.8	92.2	174.2
2a	116.7	177.2	91.6	178.2
2b	116.8	177.2	91.4	178.3
2c	116.9	177.0	90.7	177.8
2d	116.8	177.1	91.6	176.8
2e	116.7	177.3	91.9	176.7
2f	116.6	177.3	92.1	176.7
2g	116.4	177.5	93.1	175.2
3	96.9	181.1	96.3	167.5

interest on the systematization of the ^{13}C NMR data of halomethyl-substituted β-alkoxyvinylketones[10]; (2) availability of the most complete set of ^{13}C NMR data of compounds with $R^3 = CCl_3$ in our laboratory, thus allowing to calculate the empirical increments of all considered substituents; and finally, (3) the experimental difficulties to synthesize and consequently to acquire ^{13}C NMR data of a standard series of non-substituted compounds.

As previously reported[10], the empirical substituent increments were indicated by Greek letters according to the position occupied by this substituent relative to a given carbon (Scheme). The determination of these increments was done by the Eqs. 1-4.

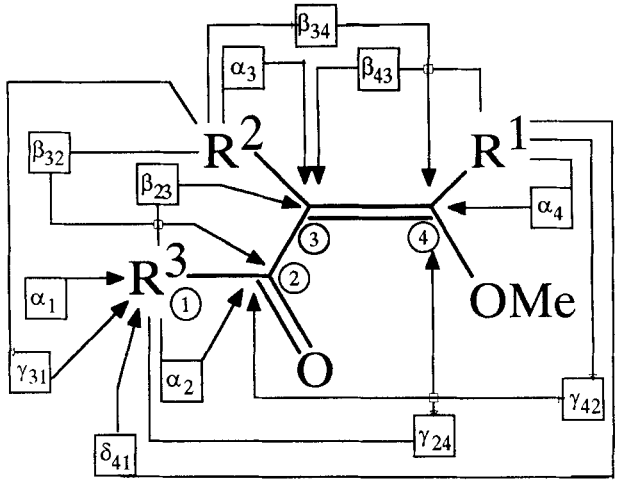
$$\alpha_n = [\delta_{C\text{-}n}(\alpha_R C\text{-}n) - \delta_{C\text{-}n}(REF)] \text{ ppm} \quad (1)$$

$$\beta_{mn} = [\delta_{C\text{-}n}(\beta_R C\text{-}m) - \delta_{C\text{-}n}(REF)] \text{ ppm} \quad (2)$$

$$\gamma_{mn} = [\delta_{C\text{-}n}(\gamma_R C\text{-}m) - \delta_{C\text{-}n}(REF)] \text{ ppm} \quad (3)$$

$$\delta_{mn} = [\delta_{C\text{-}n}(\delta_R C\text{-}m) - \delta_{C\text{-}n}(REF)] \text{ ppm} \quad (4)$$

In Eq. 1, α_n is the effect of the *alpha* substituent on to carbon *n*, i.e. the effect of R^1, R^2, R^3 and halogen on to C-4, C-3, C-2, and C-1, respectively. $\delta_{C\text{-}n}(\alpha_R C\text{-}n)$ is the chemical shift of the *alpha* substituted carbon *n*, and $\delta_{C\text{-}n}(REF)$ is the chemical shift of the carbon *n* of the reference compound (**3**). In Eqs. 2-4, β_{mn}, γ_{mn}, and δ_{mn} are the effect of the substituents bound to a carbon *m*, in position *beta*, *gamma* and *delta*, respectively, relative to the carbon *n*; *n* and *m* are full numbers that in the case of the compounds studied in this work, could vary from 1 to 4. $\delta_{C\text{-}n}$ (β, γ, or $\delta_R C\text{-}m$) is the chemical shift of the carbon *n* that has a substituent on carbon *m*, which could be in *beta*, *gamma*, or *delta* position relative to the carbon *n* (Scheme). The substituent parameters on C-4 and C-3 were determined from the compounds with $R^3 = CCl_3$ and the substituent parameters on C-2 and C-1 were determined from the compounds with R^3 = other substituents. From Eqs. 1-4 were determined parameters for substituents in a series of β-alkoxyvinylhalomethylketones[10]. Thus, for the ^{13}C chemical shift determinations of C-1, C-2, C-3, and C-4 of a series of β-



Compound	R^2	R^1	Compound	R^3
1,2a	H	C_6H_5	**1,3**	CCl_3
b	H	*p*-$CH_3C_6H_4$	**2**	CF_3
c	H	*p*-$CH_3OC_6H_4$		
d	H	*p*-FC_6H_4		
e	H	*p*-ClC_6H_4		
f	H	*p*-BrC_6H_4		
g	H	*p*-$NO_2C_6H_4$		
3	H	H		

Scheme.

alkoxyvinylhalomethylketones, a system of Eqs. 5-8 that uses the data determined from the Eqs. 1-4, was elaborated[10].

$$\delta_{C\text{-}1} = 96{,}9 + \alpha_1 + \gamma_{31} + \delta_{41} \quad (5)$$

$$\delta_{C\text{-}2} = 181{,}1 + \alpha_2 + \beta_{32} + \gamma_{42} \quad (6)$$

$$\delta_{C\text{-}3} = 96{,}3 + \alpha_3 + \beta_{43} + \beta_{23} \quad (7)$$

$$\delta_{C\text{-}4} = 167{,}5 + \alpha_4 + \beta_{34} + \gamma_{24} \quad (8)$$

For β-aryl-β-methoxyvinylhalomethylketones **1,2**, is possible to use the simplyfied equations to adequate the system to the new compound series. In this new series, some substituent parameters[10] are zero, i.e., γ_{31}, β_{32}, α_3, $\beta_{34} = 0$, then we will have the Eqs. 9-12. The parameters determined for Eqs. 9-12 are reported in Table 2.

$$\delta_{C\text{-}1} = 96{,}9 + \alpha_1 + \delta_{41} \quad (9)$$

$$\delta_{C\text{-}2} = 181{,}1 + \alpha_2 + \gamma_{42} \quad (10)$$

$$\delta_{C\text{-}3} = 96{,}3 + \beta_{43} + \beta_{23} \quad (11)$$

$$\delta_{C\text{-}4} = 167{,}5 + \alpha_4 + \gamma_{24} \quad (12)$$

Eqs. 9-12 allow to estimate with high precision the ^{13}C chemical shifts of carbons 1, 2, 3, and 4 for these compounds. We believe this system will also allow to calculate these data in equal accuracy for similar compounds not yet synthesized or evaluated. For example, Table 4 show the calculate ^{13}C chemical shifts of carbons 1, 2, 3, and 4 of β-aryl-β-methoxyvinyldichloromethylketones ($R^3 = CHCl_2$ and $R^2 = H$, Scheme).

TABLE 2

Empirical parameters[a] for Eqs. 9-12.

Substituent R^1	δ_{41}(C-1)	γ_{42}(C-2)	β_{43}(C-3)	α_4(C-4)	q_r(C-3)[b]	q_r(C-4)[b]
H	0	0	0	0	...	...
C_6H_5	1.0	-2.3	-5.5	9.7	-0.087	0.155
p-$CH_3C_6H_4$	1.0	-2.3	-6.1	9.6	-0.087	0.155
p-$OCH_3C_6H_4$	1.0	-2.3	-6.5	9.5	-0.094	0.154
p-FC_6H_4	1.0	-2.3	-5.5	8.5	-0.088	0.155
p-ClC_6H_4	1.0	-2.3	-5.2	8.3	-0.087	0.155
p-BrC_6H_4	1.0	-2.3	-5.3	8.2	-0.087	0.155
p-$NO_2C_6H_4$	1.0	-2.3	-4.1	6.7	-0.015	0.157

Substituent R^2	γ_{31}(C-1)	β_{32}(C-2)	α_3(C-3)	β_{34}(C-4)
H	0	0	0	0

Substituent R^3	α_1(C-1)	α_2(C-2)	β_{23}(C-3)	γ_{24}(C-4)
CCl_3	0	0	0	0
CF_3	19.9	-0.9	2.0	0.8
$CHCl_2$[c]	-27.1	2.9	1.4	-2.0

[a] In ppm.

[b] The carbon charge densities were determined by a graphics-based Hückel MO Program, Ref.11. [q_r (C-3) = $0.033\ \beta_{43} + 0.101$, $r = 0.910$]; [q_r (C-4) = $-0008\ \alpha_4 + 0.162$, $r = 0.920$]

[c] Data from Ref. 10.

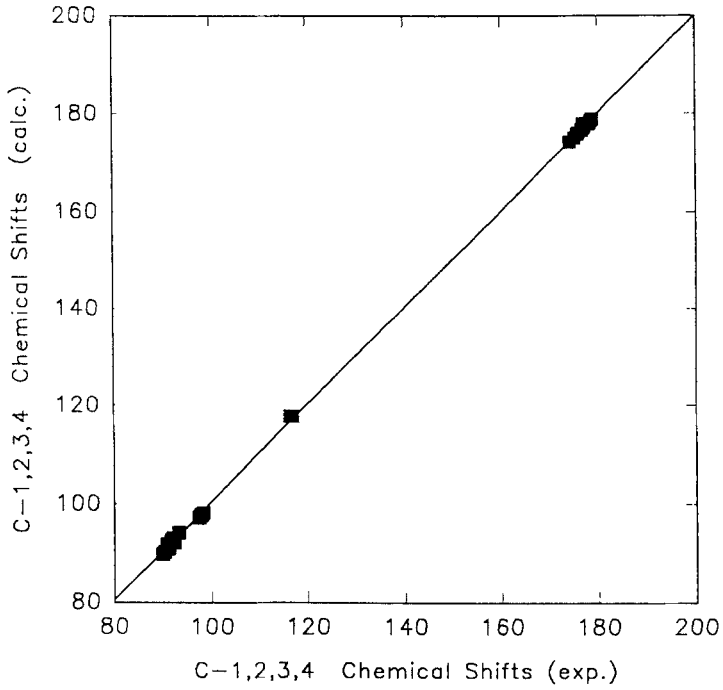


Figure 1. Correlation between the experimental and calculated (Eqs. 9-12) ^{13}C NMR chemical shifts for C-1, C-2, C-3, C-4 of β-aryl-β-methoxyvinyltrihalomethyl ketones **1,2**. ($\delta_{calc.} = 0.9958 \times \delta_{exp.} + 0.9236, r=0.9999$).

Linear correlationship analysis between the experimental and calculated ^{13}C chemical shifts (Eqs. 9-12) of compounds **1,2** were done. For a qualitative observation of the *linear analysis* carried out, Figure 1 shows the exellent relationship of all studied compounds (r =0.999).

However, for a more rigorous analysis of the confidence of the chemical shifts data obtained from the Eqs. 9-12, it is necessary to consider the larger possible number of calculated chemical shifts that fit into the

TABLE 3

Percentage of chemical shifts[a] within the absolute error range for the compounds **1,2**.

Error Range (ppm)	±0.5	±1.0	±1.5
δ (%)	64	84	100

[a] 56 ^{13}C chemical shift values are considered.

TABLE 4

Calculated (Eqs. 9-12) ^{13}C chemical shifts of the carbons 1, 2, 3 and 4 of β-aryl-β-methoxyvinyldichloromethyl ketones (R^3 = $CHCl_2$ and R^2 = H, Scheme).

Compound R^1	δ_{C-1}	δ_{C-2}	δ_{C-3}	δ_{C-4}
C_6H_5	70.8	181.7	92.2	175.2
p-$CH_3C_6H_4$	70.8	181.7	91.6	175.1
p-$OCH_3C_6H_4$	70.8	181.7	91.2	175.0
p-FC_6H_4	70.8	181.7	92.2	174.0
p-ClC_6H_4	70.8	181.7	92.5	173.8
p-BrC_6H_4	70.8	181.7	92.4	173.7
p-$NO_2C_6H_4$	70.8	181.7	93.6	172.2

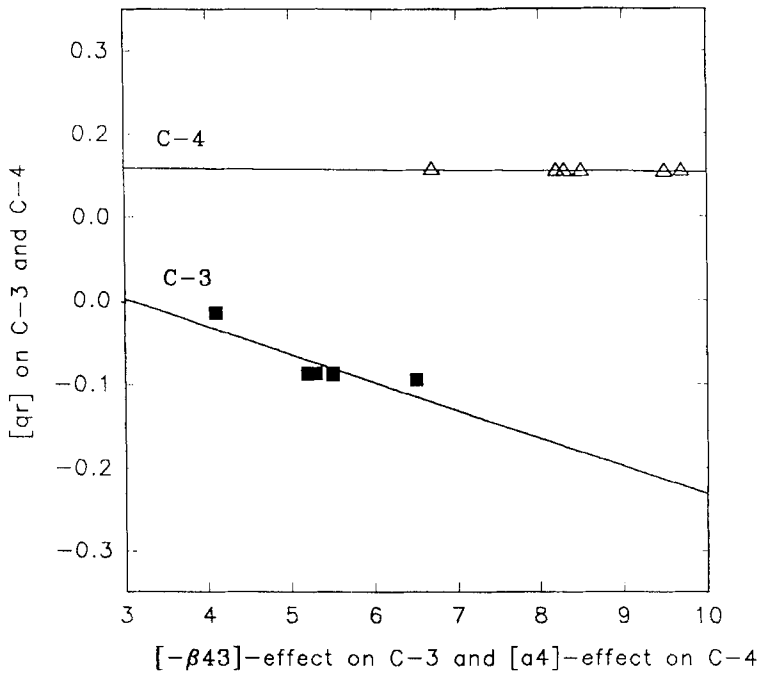


Figure 2. Correlation between the Y-*Effects* (β_{43} and α_4, Table 2) and carbon charge densities (qr, Table 2) on C-3 and C-4 of β-aryl-β-methoxyvinyltrihalomethyl ketones (r=0.910 - 0.920).

ranges of pre-established small absolute errors. For example, in Table 3 are reported the calculated percentages of chemical shifts for the compounds **1,2**, in relation to a given range of absolute error. One can observe that all calculated chemical shifts are within a maximum absolute error range of ±1.5ppm and that 84% of the calculated values deviate less than 1.0ppm from the measured ones.

Thus, considering the correlation coefficient (r, Figure 1), and the chemical shift percentages within the absolute error range (Table 3) one

can affirm that the ^{13}C chemical shifts estimated by the Eqs. 9-12, have a good accuracy.

Linear correlatioship analysis between the Y-*Effects,* β_{43} and α_4 (on C-3 and C-4, respectively) and carbon charge densisties were done[11]. For qualitative observation, the linear analysis carried out, Figure 2 shows the rasoable relatioship of all parameters studied (r=0.910 - 0.920).

CONCLUSION

The model used in this work for the evaluation of the substituent empirical increments (Eqs. 1-4) is very simple and easy to use. The estimation of the ^{13}C NMR chemical shifts of C-1, C-2, C-3, C-4 of compounds **1,2**, from Eqs. 9-12 is simple and accurate. The estimated chemical shifts for the compounds **1,2**, from the Eqs. 9-12, have shown high accuracy, for example, 84% of the chemical shifts are within the absolute error range of ±1.0ppm, and 100% within a range of ±1.5ppm. The model used for the determination of the substituent empirical increments did not account for the limitations resulting of the interaction of neighboring substituent groups. The relationship between Y-*Effects* and carbon charge densities shows a rasoable dependence of ^{13}C NMR chemical shifts for C-3 and C-4 of β-aryl-β-methoxyvinylhalomethylketones **1,2** and parameters obtained from HMO calculations.

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