

Effect of substituents on the ^{13}C -NMR chemical shifts of 3-methylene-4-substituted-1,4-pentadienes. Part I.

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Abstract: The principles of linear free energy relationships were applied to the ^{13}C substituent chemical shifts (SCS) of the carbon atoms in the unsaturated chain of 3-methylene-4-substituted-1,4-pentadienes. Correlations of the SCS with the substituent parameters of Swain and Lupton provide a mutually consistent picture of the electronic effects in these compounds. The pattern of the electronic effects can be fully rationalized by a model based on the direct transmission of substituent effects through-space (direct through-space field effects), and *via* conjugative interactions (resonance effects), or by substituent-induced polarization of the π -system in the unsaturated chain (π -polarization effect). Semi-empirical MNDO-PM3 calculations suggest the *s-cis* conformation of 3-methylene-4-substituted-1,4-pentadienes as the one with minimal heat of formation.

Keywords: [3]dendralenes, unsaturated chain carbon ^{13}C SCS, substituent effects, reverse ^{13}C SCS effect, MNDO-PM3 calculations.

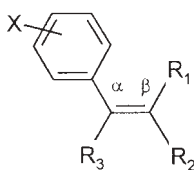
INTRODUCTION

There are two main dual substituent parameter (DSP) scales which are claimed to divide Hammett σ constants into field/inductive and resonance substituent parameters; σ_1 – σ_R scale of Taft and co-workers¹ and the *F*–*R* scale of Swain and Lupton.² These DSP scales have often been used to investigate NMR spectroscopic parameters and to calculate electron densities in aromatic molecules.^{3–5} Styrenes (Scheme 1; $R_1 = R_2 = R_3 = \text{H}$) are well suited for such studies due to their well defined geometry, non-polar side-chain, and easy accessibility to a wide range of groups R_1 , R_2 and R_3 with a reasonably large set of X substituents.^{6–10}

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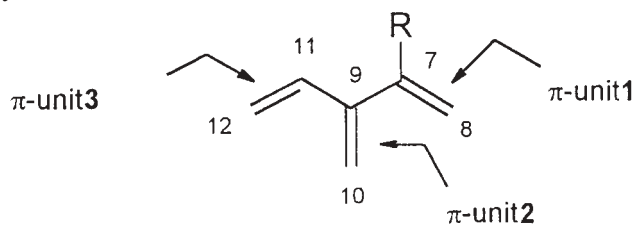
The relative importance of the various transmission modes of substituent effects depends on the particular physical probe under investigation. For example, the specific mechanisms controlling the effect of substituents on ^{13}C -NMR chemical shifts, which are sensitive to π -electron populations, are somewhat different to those found in reactivity studies. The important transmission modes relevant to NMR chemical shift studies are resonance effects, π -polarization and the direct through-space field effect. π -Polarization has the most important polar effect on ^{13}C chemical shifts in unsaturated side-chains.¹¹



1

Scheme 1. Styrene derivatives (1)

In this work linear free energy relationships (LFER) were applied to ^{13}C substituent chemical shifts (SCS) in the unsaturated chain of 3-methylene-4-substituted-1,4-pentadienes, **2-R** (Scheme 2), with the aim of gaining insight into the factors determining NMR chemical shifts and to use the chemical shifts as an empirical estimate of substituent effects in this system.

**2-R**

R = X-C₆H₄ (X = H, *m*-CH₃, *p*-CH₃, *p*-CH₂OH, *p*-OCH₃, *p*-I, 3N, 2N);
2-Thienyl; 2-(Hydroxymethyl)phenyl; 2-Bromopyridin-6-yl

Scheme 2. 3-Methylene-4-substituted-1,4-pentadienes (**2-R**).

Semi-empirical MNDO-PM3 energy minimization calculations suggest that the cross-conjugated triene **2-R** prefers the *s-cis* conformation,¹² which is shown in Fig. 1 for R = C₆H₅. For example, the *s-cis* conformation was previously observed for 3-benzylidene-2,4-bis(trimethylsilyloxy)-1,4-pentadiene which functions as a bis-diene in the multiple Diels-Alder reaction.¹³ In spite of the unusual cross-conjugated properties of **2-R**, the so-called dendralene-type compounds¹⁴ are expected to have geometric characteristics which allow separation of polar and resonance effects.



Fig. 1. The *s-cis* and another two conformers of 3-methylene-4-phenyl-1,4-pentadiene and the corresponding calculated heats of formation.¹²

EXPERIMENTAL

Synthesis of compounds

The eleven investigated 3-methylene-4-substituted-1,4-pentadienes are new compounds,¹⁵ which were prepared by an unpublished procedure¹⁶ using the Heck-type palladium-catalyzed coupling reaction.¹⁷⁻²⁰

Recording of the spectra

The ^{13}C -NMR spectra were obtained in deuterated chloroform (CDCl_3) using a Bruker AM 250 spectrometer operating at 62.9 MHz [^{13}C , additional DEPT (Distortionless Enhancement by Polarization Transfer)] and 25 °C. The central line of the CDCl_3 triplet (77.00 ppm) was used as an internal reference.

Method of calculation

In this work, the MNDO-PM3 method, which is known to be highly reliable for investigating the molecular properties of molecules, ions,²¹⁻²⁹ and zwitterions,³⁰ was used. The MOPAC program package, Version 7.01 was used. The initial structures of the compounds were generated by PC MODEL, version 4.0,³¹ which involves an MMX force field^{32,33} and were saved as MOPAC input files for MNDO-PM3 semi-empirical calculations.^{23,24} The geometries of all the molecular species, corresponding to the energy minima in vacuum, were optimized by the PM3 method. When needed, the obtained structures were refined by the Bartel method (Non-Linear Least Squares gradient minimization routine – NLLSQ), and further proved by vibrational analysis showing only one negative vibration. The simulation of the polar medium was performed using a COSMO facility.^{34,35}

RESULTS AND DISCUSSION

The chemical shifts of the unsaturated chain carbons for the 11 compounds in the series 2-R are given in Table I in terms of the substituent chemical shifts (SCS) with respect to the parent compound. Assignment of these shifts was carried out with the aid of the additivity rule,³⁶ as well as of the estimated chemical shifts of 3-methylene-1,4-pentadiene.^{37,38} In

view of some uncertainty in the assignment of the ^{13}C SCS for carbons C-7 and C-9, these signals are not given in Table I.

TABLE I. ^{13}C substituent chemical shifts (SCS) of the unsaturated chain carbons in 3-methylene-4-substituted-1,4-pentadienes (**2-R**)^a

R	C ₁₁ -SCS	C ₁₂ -SCS	C ₁₀ -SCS	C ₈ -SCS
3-Tolyl	0.05	− 0.13	− 0.05	− 0.18
4-Tolyl	0.08	− 0.14	− 0.07	− 0.84
4-(Hydroxymethyl)phenyl	− 0.05	0.08	0.04	0.05
4-Methoxyphenyl	0.06	− 0.20	− 0.11	− 1.77
4-Iodophenyl	− 0.25	0.39	0.21	0.6
3-Pyridyl ^b	− ^c	0.64	0.42	1.77
2-Pyridyl ^b	− ^c	0.54	0.95	2.59
2-Thienyl ^b	− 0.20	− 0.24	− 0.26	− 1.29
2-(Hydroxymethyl)phenyl	− ^c	− 0.84	− 0.36	2.01
2-Bromopyridin-6-yl ^b	− 0.11	1.92	1.83	2.94
Phenyl ^d	137.27	118.36	117.48	114.86

^a ^{13}C Chemical shifts (in ppm) expressed relative to the unsubstituted compound. Downfield shifts are positive. Solvent is CDCl_3 . ^b Heteroaromatic nuclei were treated as benzenoid structure where one CH or CH:CH fragment is replaced with a heteroatom. ^c In view of their poor sensitivity, these signals are confused with the instrument noise. ^d Chemical shifts of the parent compound relative to Me_4Si .

The unsaturated chain carbon ^{13}C SCS in Table I show that the substituents have a relatively small influence on the ^{13}C chemical shifts. The aromatic ring substituents such as *m*- CH_3 , *p*- CH_3 and *p*- OCH_3 cause a decrease of the electron density at C-11 (downfield shift), while the same substituents increase the electron density at C-8, C-10 and C-12 (upfield shift). Substituents such as *p*- CH_2OH and *p*-I cause an increase of the electron density at C-11, while the same substituents decrease the electron density at C-8, C-10 and C-12. The 2-thienyl group (benzenoid structure where one $\text{CH}=\text{CH}$ fragment is replaced with sulphur) as a heteroatom ring substituent causes an increase of the electron density at all the probe sites (C-8, C-10, C-11 and C-12). The 3-pyridyl, 2-pyridyl and 2-bromopyridin-6-yl groups (benzenoid structures where one CH fragment is replaced with nitrogen) as heteroatom ring substituents decrease the electron density at C-8, C-10 and C-12, while the 2-bromopyridin-6-yl group as a substituent causes an increase of the electron density at C-11. According to the possible proximity effects, the ^{13}C SCS for the *o*-substituted hydroxymethyl group will not be discussed.

The effects of substituents in the aromatic ring on the ^{13}C SCS are customarily analyzed using the Swain-Lupton equation.² In this work this DSP equation was used in the following form:

$$SCS^X = fF + rR + h \quad (1)$$

where SCS^X is the change in chemical shift induced by the substituent X, and F and R are substituent parameters reflecting the field and resonance effects, respectively. The parameters h (the intercept on the ordinate), f and r (measure the sensitivity of the chemical shift to the field and resonance effects of the substituents, respectively), are obtained by polylinear regression analysis.

All available 3-methylene-1,4-pentadiene derivatives were not included in the correlations of the unsaturated chain ^{13}C SCS since F and R values were available for only five substituents ($X = \text{H}, \text{CH}_3, \text{CH}_2\text{OH}, \text{OCH}_3$ and I).^{2,39} Application of multiple linear regression analysis to the observed ^{13}C SCS using the Swain-Lupton Eq. (1), yields the following relationships (2-5):

$$C_{11} - SCS = -0.896 (\pm 0.071)F - 0.605 (\pm 0.062)R - 0.020 \quad (2)$$

$(R = 0.9939, s = 0.021, F = 80.77, n = 5, r/f = 0.675)^{**}$

$$C_{12} - SCS = 1.50 (\pm 0.134)F + 1.19 (\pm 0.115)R + 0.042 \quad (3)$$

$(R = 0.9930, s = 0.039, F = 70.45, n = 5, r/f = 0.793)$

$$C_{10} - SCS = 0.803 (\pm 0.075)F + 0.642 (\pm 0.065)R + 0.023 \quad (4)$$

$(R = 0.9923, s = 0.022, F = 64.46, n = 5, r/f = 0.799)$

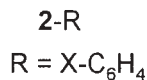
$$C_8 - SCS = 4.40 (\pm 0.205)F + 5.51 (\pm 0.177)R + 0.061 \quad (5)$$

$(R = 0.9990, s = 0.059, F = 486.32, n = 5, r/f = 1.25)$

All the correlations (Eqs. (2–5)) are of good precision indicating that the substituent effects on the chemical shifts in this series are of electronic origin. The observed f and r values in Eqs. (2–4) indicate a prevalent polar effect at carbons C-11, C-12 and C-10, while those in Eq. (5) indicate a dominant resonance effect at carbon C-8. It should be noted that f for C-11 is negative while those for C-12, C-10 and C-8 are positive. A negative sign for f is indicative of a reverse SCS effect, *i.e.*, inductive electron-withdrawing substituents cause an upfield shift. Similar effect have been observed in other conjugated systems, 4-substituted phenylacetylenes,⁴⁰ 1-arylpropynes and 1-arylpropenes,⁴¹ *trans*-1-substituted-1,3-butadienes,⁴² 1-phenyl-1,3-butadienes and phenylalenes,⁴³ *trans*-pyridineacrylic and substituted *trans*-cinnamic acids,⁴⁴ ring substituted styrenes and α -alkyl styrenes,^{6–10} ring substituted β -disubstituted styrene derivatives,^{45–47} 3-aryl-2-cyanoacrylamides,⁴⁸ *N,N*-dimethyl-3-(5-substituted-2-furyl)-acrylamides,⁴⁹ and other systems containing conjugated side-chains.^{11,50} This is consistent with the alternation of the polar effects in the π -unit³ of the investigated series **2-R**. The described effect is based on the π -polarization mechanism involving a through-space-interaction of the substituent dipole and the π -unit³ π -electrons.

^{**} R —regression coefficient; s —standard error of estimate; F —F test for significance of regression; n —number of points in the set.

The structures showed in Scheme 3 illustrate the possible electron withdrawing substituent-induced localized polarization (P_L) of small localized π -units as well as one aspect of extended polarization (P_E) of the conjugated π -system which consists of an aromatic ring and a π -unit¹ in the molecular framework of the investigated series **2-R**.



One important observation is that the *r/f* ratio for non-terminal π -unit³ carbon C-11 (*r/f* = 0.675) is smaller than that for terminal C-12 (*r/f* = 0.795) revealing the larger influence of the resonance effect at the terminal π -unit³ position. The obtained *f* and *r* values for the correlation of the internal carbon ¹³C SCS differences for atoms C-12 and C-11 ($C_{12,11} - \Delta SCS$) with the *F* and *R* substituent parameters indicate that these carbon ¹³C SCS

differences are influenced not only by resonance but also, to an even greater extent, by polar effects. The corresponding relationship is as follows:

$$C_{12,11} - \Delta\text{SCS} = 2.40(\pm 0.201)F + 1.80(\pm 0.173)R + 0.062 \quad (6)$$

$$(R = 0.9935, s = 0.058, F = 76.64, n = 5)$$

We believe that the larger r/f ratio observed in Eq. (3) compared to Eq. (2), together with the relatively larger influence of polar effects on the internal carbon ^{13}C SCS differences for atoms C-12 and C-11, reveals some additional polarization at the π -unit3 terminal atom which could be accounted for by extended polarization contributing to the changes in electron density at this probe center.

It is to be expected that the chemical shifts of the terminal π -unit2 carbon be more affected by the substituent than those at the terminal π -unit3 position according to the locations of carbons C-10 and C-12. The relatively smaller magnitudes of the f and r values observed in Eq. (4) than those in Eq. (3) reveal the peculiarity of the arrangement of the π -electrons in the cross-conjugated chain of the series 2-R. Although the observed f and r values in Eqs. (3 and 4) differ in relative magnitude, they have a very similar pattern. This suggests a similarity in the transmission of electronic effects from the substituents of the aromatic ring to the terminal π -unit carbons. Further evidence for this is obtained from the excellent intercorrelation between the ^{13}C SCS of carbon C-10 and C-12 in the following form:

$$C_{10} - \text{SCS} = 0.536(\pm 0.008)C_{12} - \text{SCS} + 6.52E - 0.5 \quad (7)$$

$$(R = 0.9997, s = 0.004, n = 5)$$

A less accurate, but acceptable intercorrelation was obtained when all 11 3-methylene-4-substituted-1,4-pentadienes were included, as represented by relationship (8):

$$C_{10} - \text{SCS} = 0.859(\pm 0.091)C_{12} - \text{SCS} + 0.079 \quad (8)$$

$$(R = 0.9525, s = 0.205, n = 11)$$

The pattern of the weighting factors f and r in Eq. (5) indicates a dominant resonance effect at the terminal atom of the π -unit1 conjugated to an aromatic ring. This is consistent with the relatively smaller magnitudes of the f and r values observed in Eqs. (2–4), revealing that the chemical shifts of the terminal π -unit1 carbon are more affected by the substituent than are those at more distant π -units.

In Eq. (5), the ratio r/f amounts to 1.25 which is smaller than the ratio $r/f = 2.53$, established for C- β in ring substituted styrenes (Scheme 1; $R_1 = R_2 = R_3 = \text{H}$)⁶ and α -methylstyrenes (AMS) (Scheme 1; $R_3 = \text{CH}_3$, $R_1 = R_2 = \text{H}$)⁷ but bigger than the ratio $r/f = 0.55$ established for C- β in ring substituted α -*t*-butylstyrenes (ATBS) (Scheme 1; $R_3 = \text{C}(\text{CH}_3)_3$, $R_1 = R_2 = \text{H}$).⁷ It is known that the expected magnitudes of the polar and resonance effects in ring substituted styrenes and its α -alkyl substituted derivatives are very sensitive to the geometry assumed by the investigated molecules.^{6,7} While styrene is pla-

nar or nearly planar,⁶ the phenyl-vinyl dihedral angle, θ , for AMS is 30° while that for ATBS is 64°. ⁷ It is apparent for the styrene system that the ratio r/f for C- β decreases dramatically as the vinyl group is twisted out of plane.

The obtained ratio $r/f = 1.25$ for carbon C-8 suggests an increased localization of the resonance effects in the aromatic group of 3-methylene-4-substituted-1,4-pentadienes compared with those for C- β in ring substituted styrenes. Since for 4-substituted styrenes⁶ the vinyl group can be resonance electron donor or acceptor, depending on the nature of the substituent, the localization of the resonance effects in the aromatic group of **2-R** indicates that the π -unit1 is less susceptible to resonance interactions than the vinyl group in styrenes. Thus, the relatively increased field dependence and the decreased resonance dependence for the chemical shifts of the terminal π -unit1 carbon in series **2-R** in comparison with those for C- β in ring substituted styrenes, can be reasonably explained in terms of a conformational effect arising from the disturbed planarity of the extended π -system consisting of the aromatic ring and the π -unit1, caused by the presence of the *cis*-butadiene fragment.

CONCLUSIONS

The excellent correlations of ¹³C SCS with the Swain-Lupton equation suggest that the substituent effects on the ¹³C SCS of the unsaturated chain carbon in the investigated 3-methylene-4-substituted-1,4-pentadienes are electronic in origin. DSP analyses of the data show that resonance effects have a superior influence on the chemical shifts of the unsaturated chain terminal π -unit1 carbon and have an inferior influence on the chemical shifts of the distant unsaturated chain terminal/non-terminal π -unit carbon. The observed alternation of the polar effect in the unsaturated chain of the investigated cross-conjugated trienes bears evidence for a π -polarization mechanism of the transfer of the polar effect operating in this molecular framework.

The results presented in this paper show that the α -substituent on the styrene side chain behaves as a rather isolated *s-cis*-2-butadiene fragment. In an isolated butadiene the terminal carbons bear a higher electron density than the non-terminal ones. This pattern is preserved in the **2-R** compounds. MO calculations show that the effect of the substitution is basically a change of the overall electron population in the butadiene fragment. Depletion or enrichment of the electron population mostly affects the terminal atoms in the 2-butadiene fragment with a smaller change (of opposite sign) on the middle atoms.

In summary, the transmission of the electron effect in 3-methylene-4-substituted-1,4-pentadienes can be well explained in terms of a combination of polar effects (localized and extended π -electron polarization) with resonance effects.

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ИЗВОД

ЕФЕКТИ СУПСТИТУЕНАТА НА ^{13}C -NMR ХЕМИЈСКА ПОМЕРАЊА
3-МЕТИЛЕН-4-СУПСТИТУИСАНИХ-1,4-ПЕНТАДИЕНА. ДЕО IНАТАША В. ВАЛЕНТИЋ,¹ ЖЕЉКО ВИТНИК,² SERGEI KOZHUSHKOV,³ ARMIN DE MEIJERE,³ ГОРДАНА С.
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На ^{13}C супституентска хемијска померања (СХП) угљеникових атома у незасићеном ланцу 3-метилена-4-супституисаних-1,4-пентадиена су примењени принципи линеарне корелације слободне енергије. Корелације СХП са супституентским параметрима Swain-а и Lupton-а пружају усаглашену слику електронских ефеката у овим једињењима. Концепт електронских ефеката може у потпуности бити објашњен моделом који се заснива на директном преношењу ефеката супституената кроз простор (директни ефекти поља кроз простор) и преко конјугационих интеракција (резонанциони ефекти), или путем супституентом изазване поларизације π -система у незасићеном ланцу (ефекти π -поларизације). MNDO-PM3 семи-емпиријска израчунавања упућују на *s-cis* конформацију 3-метилена-4-супституисаних-1,4-пентадиена као конформацију са минималном енергијом образовања.

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