Substituent Effects in ^{1}H and ^{13}C Nuclear Magnetic Resonance Correlations of Chemical Shifts in *para*-Substituted 5-Arylmethylenehydantoins

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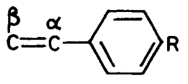
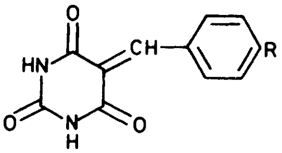
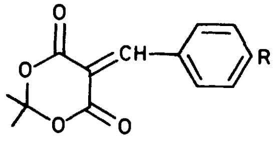
Substituent effects in *para*-substituted 5-arylmethylenehydantoins have been studied by correlations of ^{1}H and ^{13}C chemical shifts with Hammett constants. In addition to the expected correlations for the ^{1}H chemical shift of the vinyl proton and the ^{13}C chemical shift of the β-carbon C-5, good linear correlations are also obtained for the chemical shifts of the N-1 and N-3 protons which are respectively four and five atoms away from the benzene ring as well as for the α-carbon C-6.

Chemical shifts in n.m.r. spectra, being sensitive probes of electron-density distributions, are useful for the study of transmission of electronic effects in organic molecules. Much work has been done on the correlations of ^{1}H and ^{13}C chemical shifts of the vinyl protons and carbons in ring-substituted styrenes with various substituent constants.[1-9] Good linear correlations are generally observed for the ^{1}H shift of the proton at the α-carbon and the ^{13}C shift of the β-carbon. The ^{13}C shift of the α-carbon is usually less affected than that of the β-carbon and often correlates poorly with substituent constants. Comparatively less is known about substituent effects on atoms further along the side-chain. However, excellent correlations between substituent constants σ^+ and ^{13}C shifts not only of the β-carbon but also of the adjacent carbonyl carbons in the series of 5-arylmethylenebarbituric acids (**A**) and 2-arylmethyleneindan-1,3-diones (**B**) were found by Robinson and Irving[6] and by Laszlo *et al.*[9] for Meldrum acid derivatives (**C**). For 5-arylmethylene-2-thiohydantoins (**D**), Ivin *et al.*[7] found good correlations of the ^{1}H shifts of the N(3)–H, which is five atoms away from the benzene ring, with McDaniel–Brown constants and those of the N-1 proton with induction constants. The latter finding appears somewhat surprising as the lone pair on N-1 is clearly conjugated and therefore involved in resonance with the benzylidene group. The (*Z*)-5-arylmethylenehydantoins (**1**)—(**8**) bear obvious structural resemblance to the above mentioned compounds, and it should be interesting to investigate possible correlations of both the ^{1}H and ^{13}C chemical shifts of relevant atoms with substituent constants especially in view of the fact that ring substituted styrene derivatives having electron-releasing substituents such as the NH group attached to β-carbon site have not received much attention.[8]





(**A**)



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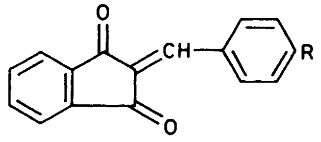

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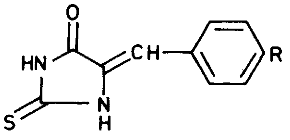
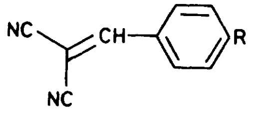
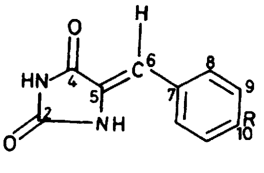


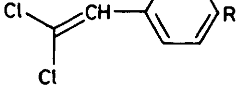
(**D**)



(**E**)



(**1**) R = NMe$_2$
(**2**) R = OH
(**3**) R = OMe
(**4**) R = Me
(**5**) R = H
(**6**) R = Cl
(**7**) R = CN
(**8**) R = NO$_2$



(**F**)

Results and Discussion

The ^{1}H n.m.r. data of the 5-arylmethylenehydantoins (**1**)—(**8**) are listed in Table 1 and their ^{13}C n.m.r. data are given in Table 2. Although the n.m.r. spectra of compounds (**3**)—(**6**) have been reported previously,[10] they are included here for easy comparison and reference. The results of attempted correlations of various ^{1}H and ^{13}C chemical shifts with substituent constants[11] σ, σ^{+}, and σ^{-} are given in Table 3 as correlation coefficients, slopes, and intercepts.

In the ^{1}H n.m.r. spectra, the N-3 proton resonates at lower field than the N-1 proton as the former is deshielded by two carbonyl groups and the latter by only one adjacent carbonyl group. These assignments have further been confirmed by comparison with the spectra of the 1- and 3-methyl-substituted 5-arylmethylenehydantoins which have only an N-3 and N-1 proton respectively.[10]

Figure 1 shows very good linear correlations obtained for the ^{1}H chemical shifts of the protons at both N-1 and N-3. For the N-1 protons, the correlations with σ and σ^{-} are better than with σ^{+}, in agreement with the expected resonance interaction between the N-1 lone pair and the electron-withdrawing aryl substituents. However, the difference among the correlation coefficients is not large. For the N-3 protons, there is no clear preference among the three types of substituent constants. Nevertheless, the excellent correlations of the N-3 proton shifts are significant in view of their long distance from the aryl substituents. The ^{1}H shifts of the vinyl protons at C-6 also correlate fairly well with σ and σ^{-} (Figure 1), although the range of chemical shifts here is even narrower, being only 0.15 p.p.m. Similar narrow ranges have been reported for the corresponding vinyl protons in the arylmethylene derivatives of barbituric and Meldrum acids.[12,13] Analyses of Ivin's ^{1}H n.m.r. data of the 5-arylmethylene-2-thiohydantoins[7] shows that the chemical shifts of both the N-1 and N-3 protons also correlate better with σ and σ^{-} than with σ^{+} values, contrary to his conclusion that only the N(3)–H is conjugated with the aryl substituents. However, the chemical shifts of the C-(6)-H in these thio-derivatives correlate poorly with all three types of substituent constants. The reason for this difference in the correlations of the C-6 protons in the series of oxo- and thio-analogues is unclear.

Studies of ^{13}C chemical shifts complement those of the ^{1}H chemical shifts. The former reflect primary substituent effects transmitted through the bonds, being less sensitive to other effects. This, together with the wider range of ^{13}C chemical shifts, makes them useful probes for electronic effects. From published ^{13}C n.m.r. data on styrene derivatives, the β-carbons are substantially more shielded relative to the α-carbons and ^{13}C chemical shifts of the former correlate well with σ^{+} constants while those of the latter do not. With the series of arylmethylenehydantoins, an interesting observation regarding the relative shieldings of the α- and β-carbons can be made. The assignment of the signal for the α-C-6 in the spectra of compounds (**1**)—(**8**) has been made from the coupled spectra which reveal clear splitting by the attached protons ($^{1}J_{CH}$ *ca.* 160 Hz). The assignment of the signal for the β-C-5 presents some problem since it occurs in the same region as the aromatic carbons. While the *ortho* and *meta* C-8 and C-9 of the benzene ring can be recognized easily from the coupling with attached protons, and the *para* C-10, though without an attached proton, can generally be distinguished as the carbon most affected by the directly attached substituent R, differentiation between the two remaining quaternary C-5 and C-7 is more difficult.

Table 1. ^{1}H Chemical shifts for compounds (**1**)—(**8**) in [^{2}H$_{6}$]DMSO at 35 °C (p.p.m. from Me$_4$Si)

Compd.	N(1)–H	N(3)–H	C(6)–H	Ar–H	Others R
(**1**)	10.19	10.96	6.34	7.50d, 6.70d	2.98
(**2**)	10.28	11.05	6.37	7.48d, 6.79d	
(**3**)	10.37	11.10	6.40	7.58d, 6.95d	3.80
(**4**)	10.42	11.17	6.41	7.52d, 7.22d	2.34
(**5**)	10.47	11.18	6.45	7.64m, 7.40m	
(**6**)	10.56	11.25	6.40	7.65d, 7.42d	
(**7**)	10.76	11.37	6.44	7.80	
(**8**)	10.85	11.40	6.49	8.20d, 7.85d	

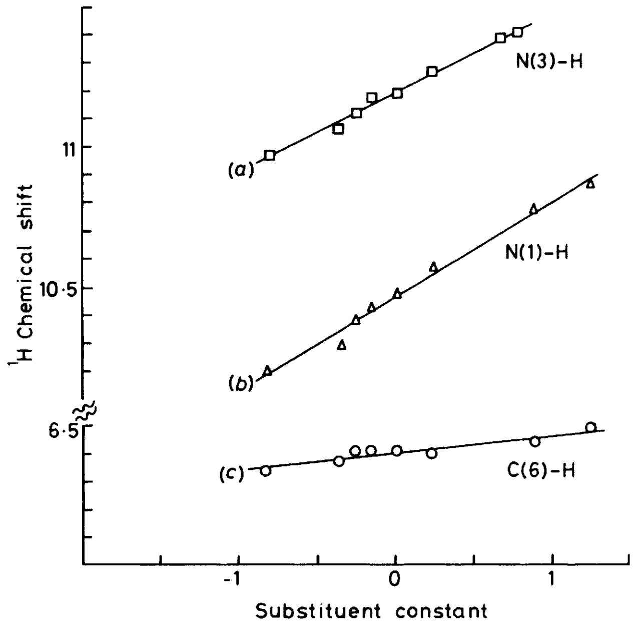


Figure 1. Correlation of ^{1}H chemical shifts (p.p.m. from Me$_4$Si) with *para*-substituent constants. (a) σ; (b), (c) σ^{-}

Table 2. ^{13}C Chemical shifts for compounds (**1**)—(**8**) in [^{2}H$_{6}$]DMSO at 35 °C (p.p.m. from Me$_4$Si)

Compd.	C-2	C-4	C-5	C-6	C-7	C-8	C-9	C-10	Others R
(**1**)	155.5	165.6	123.9	110.3	120.2	130.9	111.9	150.2	39.7
(**2**)	155.4	165.5	125.3	109.2	123.7	131.1	115.6	157.9	
(**3**)	155.7	165.7	126.2	108.9	125.6	131.1	114.3	159.5	55.2
(**4**)	155.5	165.5	127.2	108.5	130.1	129.3	129.3	138.0	20.9
(**5**)	155.7	165.6	128.1	108.3	133.0	129.4	128.8	128.4	
(**6**)	155.6	165.3	128.4	106.7	132.8	130.9	128.6	131.9	
(**7**)	155.6	165.2	130.2	105.8	137.8	132.3	129.7	110.0	118.7
(**8**)	155.6	165.1	130.8	105.0	139.9	130.0	123.6	146.1	

Table 3. Correlation coefficients (γ), slopes (ρ), and intercepts (y) of chemical shifts (p.p.m.) *versus* substituent constants

		N(1)–H	N(3)–H	C(6)–H	C-5	C-6	C-7
σ	γ	0.9896	0.9931	0.9258	0.9875	0.9866	0.9732
	ρ	0.418	0.280	0.076	4.331	−3.32	12.418
	y	10.49	11.18	6.41	127.50	107.84	130.34
σ⁻	γ	0.9934	0.9799	0.9455	0.9695	0.9843	0.9546
	ρ	0.332	0.219	0.062	3.366	−2.62	9.644
	y	10.46	11.17	6.40	127.21	108.06	129.53
σ⁺	γ	0.9607	0.9833	0.9140	0.9929	0.9524	0.9908
	ρ	0.260	0.178	0.049	2.795	−2.04	8.114
	y	10.56	11.23	6.42	128.27	107.31	132.58

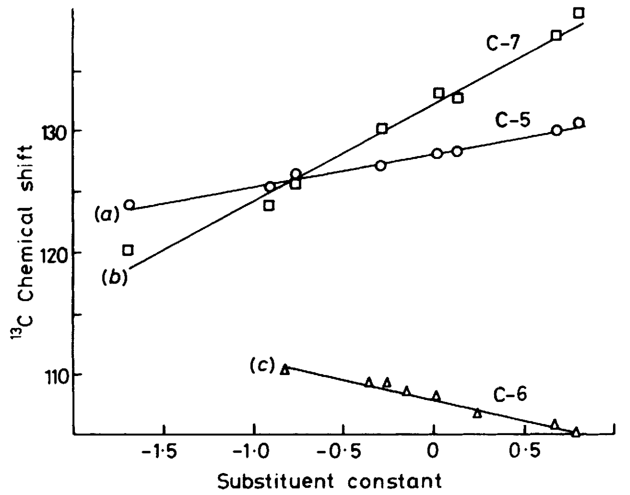


Figure 2. Correlation of ^{13}C chemical shifts (p.p.m. from Me_4Si) with *para*-substituent constants. (a), (b) σ⁺, (c) σ

Assignments of the chemical shifts given in Table 2 have been made largely from the consideration that electronic effects of the substituents are related better to position 7 in the benzene nucleus than to C-5 in the side-chain. These assignments appear to be self-consistent though not unequivocal. However, both sets of ^{13}C chemical shifts show good linear relationships, especially with σ^+ values, as usually found for these two carbons in styrene derivatives (Figure 2).

The ^{13}C chemical shifts of the α-C-6 in the arylmethylenehydantoins show surprisingly good correlations with σ and σ^- values and less so with σ^+, in contrast with the poor correlations commonly found for the ^{13}C shifts of similar α-carbons in styrenes including the arylmethylene derivatives of barbituric acid (**A**), indandione (**B**), and propanedinitrile (**E**). Another notable difference is that the ^{13}C shifts of the carbonyl C-4, which is directly attached to the β-carbon, do not correlate well with any set of substituent constants, and substituent effects are completely attentuated at the carbonyl C-2. Robinson and Irving[6] have suggested that the requirement for obtaining good correlations with the carbonyl groups is the cyclic dicarbonyl structure as present in the barbituric acid and indandione derivatives. The present results seem to be in agreement since in the arylmethylenehydantoins only one carbonyl group is attached to the benzylidene β-carbon, the other attached group being an amino group. The carbonyl and the amino groups may be expected to have opposite conjugative interactions with the benzylidene moiety. The carbonyl group tends to decrease electron density at the C=C bond, resulting in strong resonance interaction of this bond with *para* aryl substituents. It is usually observed with styrene derivatives that such electron density changes are most pronounced at the β-carbon and least at the α-carbon. This general trend is apparently disturbed in the case of the arylmethylenehydantoins. The amino group at N-1 tends to increase electron density at the C=C bond, especially at the α-carbon because of the resonance effect. Hence the ^{13}C shifts of the α-carbon are now found to correlate well with σ or σ^- constants. The amino group therefore causes reversal of the polarization of the C=C bond so that, in the arylmethylenehydantoins, the α-carbon at C-6 is more shielded than the β-carbon at C-5, a trend opposite to that observed in other styrene derivatives studies so far,[1–6] most of which have electron-withdrawing groups at the β-position. It is interesting to note that, in ββ-dichlorostyrenes (**F**),[14] where the chlorine is capable of releasing electrons by resonance, the β-carbon is shielded to a much lesser extent but the general trend still remains the same. Moreover, unlike the arylmethylene derivatives of barbituric acid and indandione, the ^{13}C shifts of the carbonyl carbons in compounds (**1**)—(**8**) show very small changes over the range of aryl substituents and correlate poorly with any set of constants. This, together with the excellent correlation discussed above for the ^1H chemical shifts of the N-1 protons, suggests that between the competitive influences of the carbonyl and amino groups, the dominant interaction appears to be that of the amino with the benzylidene groups.

Experimental

Compounds (**1**)—(**8**) were prepared according to literature procedures.[10] The m.p.s and microanalytical data for the new compounds are: (**1**) m.p. 273 °C (from ethanol) (Found: C, 61.2; H, 5.8; N, 17.6. $C_{12}H_{13}N_3O_2$ requires C, 62.3; H, 5.7; N, 18.2%); (**2**) m.p. 315 °C (from acetic acid) (Found: C, 59.1; H, 3.9; N, 13.5. $C_{10}H_8N_2O_3$ requires C, 58.8; H, 3.9; N, 13.7%); (**7**) m.p. 322 °C (decomp.) (from acetic acid) (Found: C, 61.8; H, 3.3; N, 19.5. $C_{11}H_7N_3O_2$ requires C, 62.0; H, 3.3; N, 19.7%); (**8**) m.p. >300 °C (from ethanol) (Found: C, 51.9; H, 3.2; N, 18.3. $C_{10}H_7N_3O_4$ requires C, 51.5; H, 3.0; N, 18.0%).

^1H N.m.r. spectra were recorded with a Perkin-Elmer R32 spectrometer at 90 MHz and ^{13}C n.m.r. spectra with JEOL FX-90Q spectrometer.

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