^{13}C and ^{1}H NMR of Arylnitrones. Substituent Effects of α-Phenyl-*N*-(*p*-substituted phenyl)nitrones

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Substituent effects on the chemical shifts of the conjugation sites in α-phenyl-*N*-arylnitrones (**2**) have been investigated. Resonance effects predominate at these positions. The electronic effects of the substituents should be treated separately between electron-donating groups and electron-withdrawing ones. A plausible mechanism for the transmission of the substituent effects in **2** has been proposed.

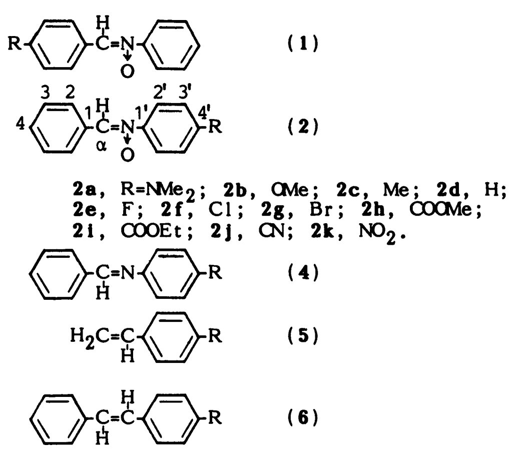
Recently, the substituent effects of α,*N*-diarylnitrones (**1** and **2**) were investigated by means of ^{13}C and ^{1}H NMR spectroscopy.[1)] The analyses, however, seem to be insufficient with regard to the mechanisms of the transmission of the substituent effects. For example, the previous investigators have reported that, while the chemical shifts of C-4′ in α-aryl-*N*-phenylnitrones (**1**) and those of C_α in α-phenyl-*N*-arylnitrones (**2**) are properly correlated with the Hammett σ_p or the Swain-Lupton *F* and *R* parameters, there are poor correlations between these parameters and the chemical shifts of C_α in **1** and those of C-4 in **2**. These results obtained for the conjugation sites of **1** and **2** are inconsistent with their explanation that there are through-resonance effects between the α- and *N*-phenyl rings via the nitrone function; thus, some reasonable explanations of the mechanisms are required.

In a previous paper,[2)] the present authors have systematically investigated the substituent effects of **1** and α-aryl-*N*-alkylnitrones, especially the effect of the 4-substituents on the α-position, by means of ^{13}C and ^{1}H NMR spectroscopy. From the good correlations obtained in correlation analyses, we have concluded that 1) inductive effects are predominant at the α-carbon, and 2) a "back-polarized" structure of nitrones is responsible for the anomalous upfield shift of the C_α signals.

The aim of the present work is to understand the nature of the nitrone function and to give an appropriate explanation of the mechanism of the transmission of the substituent effects by assessing the substituent effects of **2**.

Experimental

Materials. α-Phenyl-*N*-(*p*-substituted phenyl)nitrones (**2**): Nitrones **2a**[3)] and **2b**[3,4)] were synthesized from the corresponding nitrosobenzenes and *N*-benzylpyridinium chloride; they were purified by recrystallization from ethanol-hexane and then from benzene-hexane. Nitrones, **2c**—**k**, were prepared by the condensation of the appropriate phenylhydrox-



Scheme 1.

Table 1. ^{13}C and ^{1}H SCS Values[a)] of α-Phenyl-*N*-(*p*-substituted phenyl)nitrones (**2**)

	R	^{13}C NMR					^{1}H NMR
		C_α	C-1	C-4	C-1′	C-4′	H_α
a	NMe_2	−2.37	0.57	−0.75	−10.80	21.26	−0.08
b	OMe	−0.94	0.19	−0.26	−6.71	30.68	−0.06
c	Me	−0.54	0.10	−0.19	−2.32	10.19	−0.03
d	H	(134.52)[b)]	(130.71)[b)]	(130.90)[b)]	(149.11)[b)]	(129.90)[b)]	(7.92)[b)]
		0.0	0.0	0.0	0.0	0.0	0.0
e	F	−0.08	−0.13	0.16	−3.83	33.16	−0.04
f	Cl	−0.01	−0.21	0.28	−1.61	5.91	−0.02
g	Br	−0.04	−0.24	0.30	−1.16	1.74	−0.02
h	COOMe	0.65	−0.29	0.48	2.88	1.61	0.06
i	COOEt	0.61	−0.27	0.43	2.75	1.92	0.07
j	CN	0.91	−0.58	0.82	2.43	−16.13	0.06
k	NO_2	1.34	−0.64	1.01	3.76	18.35	0.09

a) SCS=δ(X−R)−δ(X−H). b) Chemical shifts δ: in ppm downfield from internal TMS.

ylamines (**3**)[5,6] with benzaldehyde in ethanol and were purified by recrystallization from ethanol-hexane or benzene-hexane. To our knowledge, although nitrones **2a**—**g**, **2i**, and **2k** are known,[1,7] the physical constants of the following nitrones have not been reported: **2b**, mp 129—130 °C (uncorrected), **2e**, 173—175 °C, **2i**, 130—131 °C, **2k**, 191.5—192 °C. Nitrones **2h** and **2j** are new compounds: **2h** mp 195 °C, Found: C, 70.40; H, 4.94; N, 5.49%. Calcd for $C_{15}H_{13}O_3N$: C, 70.58; H, 5.13; N, 5.49%. **2j** mp 164.5—165 °C, Found: C, 75.47; H, 4.25; N, 12.85%. Calcd for $C_{14}H_{10}ON_2$: C, 75.65; H, 4.54; N, 12.61%. All the compounds obtained were characterized as *Z*-isomers by means of their physical constants and spectral data.[2]

NMR Measurement. The ^{13}C NMR spectra of **2a**—**d** were measured at 100.4 MHz on a JEOL GX-400 spectrometer under a pulse Fourier transform mode. A spectral width of 25000 Hz was used with 64 K (digital resolution 0.76 Hz) data points. The ^{13}C NMR spectra of **2c**—**k** were measured at 67.8 MHz on a JEOL GX-270 spectrometer under a pulse Fourier transform mode. A spectral width of 18000 Hz was used with 32 K (digital resolution 1.10 Hz) data points. The ^{1}H NMR spectra were obtained on the JEOL GX-400 NMR spectrometer operating at 400 MHz for **2a**—**d** and on the JEOL GX-270 NMR spectrometer for **2c**—**k** at 270 MHz.

Sample solutions were prepared in a concentration of 0.4 M (mol dm^{-3}), except for **2f**—**h** and **2k** (0.16 M), with $CDCl_3$ (99.8%, Merck) containing 1% TMS (tetramethylsilane) as the internal standard. Sample tubes with a 5-mm diameter were used, and the probe temperature was 20—25 °C. The chemical shifts were independent of the concentrations of the compounds used within a range of 0.15 to 0.5 M (with a deviation smaller than 5 and 3% in ppm for the ^{13}C and ^{1}H spectra respectively). The ^{13}C and $^{1}H_\alpha$ signals of **2** were assigned in a similar manner as described in the previous paper.[2]

Results and Discussion

It is well-accepted that the nitrone function is flush with the two phenyl rings in **1** and **2**.[7a,b] Since C-1′, C_α, and C-4 in **2** are, in contrast to the case of **1**, conjugation sites of the 4′-substituents, we will mainly discuss the substituent effects on these sites. The chemical shifts and substituent-induced chemical shifts (SCS) for C_α, C-1, C-4, C-1′, C-4′, and H_α in **2** are shown in Table 1. All the C_α chemical shifts appear ca. 25 ppm upfield and ca. 20 ppm downfield from the corresponding carbon chemical shifts of imines **4**[8] and styrenes **5**[9] respectively, while they are very close to the corresponding carbon chemical shifts of *trans*-stilbenes **6**.[10] Table 1 reveals that the C_α, C-4, C-1′, and H_α signals of **2** shift downfield as the electron-withdrawing ability of the substituents increases, whereas the C-1 signals shift upfield, showing a reverse substituent effect. This behavior at C-1 is, however, not the characteristic of the nitrone alone; it is also observed in the ^{13}C NMR spectra of **4** and **6**.[8,10]

To ascertain the mechanisms and the extent of the transmission of the substituent effects in **2**, the SCS values for the requisite positions were compared with those for the corresponding sites of **4**, **5**, **6**, and mono-

Table 2. ^{13}C SCS–SCS Correlations between **2** and Reference Systems[a)]

Refernce system	Monosubstituted benzenes					**4**					**5**					**6**				
	$SCS=\rho_{Bz}\cdot\delta_{Bz}+C$					$SCS=\rho_{Im}\cdot\delta_{Im}+C$					$SCS=\rho_{Sy}\cdot\delta_{Sy}+C$					$SCS=\rho_{Sb}\cdot\delta_{Sb}+C$				
Position in **2**	*n*	ρ_{Bz}	C	SD	*r*	*n*	ρ_{Im}	C	SD	*r*	*n*	ρ_{Sy}	C	SD	*r*	*n*	ρ_{Sb}	C	SD	*r*
C_α	10	0.18 ±0.04	0.12 ±0.22	0.08	0.965[b)]	8	0.52 ±0.06	0.03 ±0.12	0.02	0.994	10	0.36 ±0.07	−0.29 ±0.18	0.06	0.974	10	0.38 ±0.07	−0.30 ±0.18	0.06	0.976
C-1						8	0.60 ±0.18	−0.17 ±0.10	0.01	0.960						10	0.59 ±0.05	−0.01 ±0.03	0.00	0.996
C-4	10	0.09 ±0.03	0.30 ±0.15	0.04	0.935[b)]	8	0.88 ±0.16	0.00 ±0.09	0.01	0.984						10	0.76 ±0.09	0.03 ±0.06	0.01	0.989
C-1′	10	0.80 ±0.08	−0.70 ±0.45	0.36	0.992[b)]	8	0.88 ±0.10	−0.64 ±0.54	0.34	0.994	9	0.88 ±0.09	−0.54 ±0.47	0.30	0.993					
C-4′	10	0.92 ±0.11	0.89 ±2.05	5.37	0.990[c)]	8	0.92 ±0.04	0.35 ±0.90	0.43	0.999	9	0.91 ±0.13	1.22 ±2.56	7.03	0.988					

a) *n*: The number of data, SD: standard deviations, and *r*: correlation coefficients. The SCS values for the reference systems were obtained from the reported δ values.[8—11] b) Correlations with the $^{13}C_{para}$ SCS of monosubstituted benzenes. c) Correlations with the $^{13}C_{ipso}$ SCS of monosubstituted benzenes.

substituted benzenes.[11] As is shown in Table 2, the SCS-SCS plots gave fairly good correlations with the correlation coefficients of $r > 0.960$ at these positions.

However, the slopes, ρ_{Bz}, ρ_{Im}, and ρ_{Sb}, are small, especially at C_α, C-4, and a nonconjugation site, C-1, with the exception of the ρ_{Im} at C-4. Since the magnitude of the rho values is a measure of the relative sensitivity of substituent effects, such smaller values than unity in **2** can be explained by the lower double-bond order of the nitrone function compared with the corresponding side-chain double bonds in **4**, **5**, and **6**.[2] Furthermore, among the SCS-SCS correlations at C_α, the correlation between **2** and a non-planar system **4**,[8a–c] in which the *N*-phenyl ring is twisted from the molecular plane containing the C=N bond, is much better (r=0.994) than the correlations between **2** and the comparable planar molecules, such as monosubstituted benzenes, **5**, and **6** (r=0.965—0.976). In the latter correlations, electron-donating and electron-withdrawing groups have apparently different slopes, as is illustrated in Fig. 1. These findings suggest that the mechanisms of the transmission of substituent effects through the side-chain double bond in **2** are considerably different from those for **5** and **6**.

In the analysis of the substituent effects of **2**, the previous investigators have reported[1] that 1) there is an excellent correlation between the chemical shifts at C_α and Hammett σ_p or Swain-Lupton F and R parameters, 2) the chemical shifts at C-1′ have a poor correlation with the σ_p, but a fair correlation with the σ^+, parameters, and 3) there is no correlation between the chemical shifts at C-4 and these parameters. The present analyses by the use of our own spectral data are, however, inconsistent with their results at these positions in **2**. As is illustrated in Fig. 2, the SCS values at C_α show an excellent linear relationship with the σ^+ constants, with a correlation coefficient of 0.991, whereas the correlation coefficient with σ_p constants is, at most, 0.976. This can be best interpreted in terms of an enhanced electron density at C_α caused by the electron-donating groups. This also means that the nitrone function is capable of acting either as an electron-donating group or as an electron-withdrawing group, depending on the nature of the substituents on the *N*-phenyl ring, i.e., the electronically amphoteric character of the nitrone function being ascertained. The deviation of halogens from the correlation shown in Fig. 2 might be caused by the well-known electronically amphoteric character of these atoms. Indeed, a principal component analysis of the ^{13}C SCS of monosubstituted benzenes has recently shown that the substituents cluster into four groups: alkyl, halogens, donors, and acceptors; thus, the omission of halogens might be appropriate in the correlation analyses of nitrones.[12]

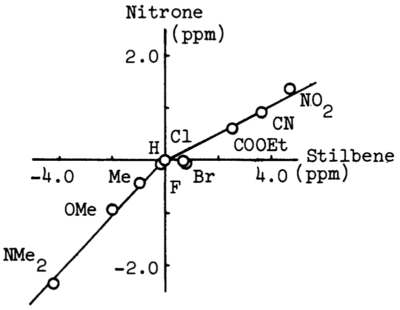


Fig. 1. SCS-SCS correlation at C_α.

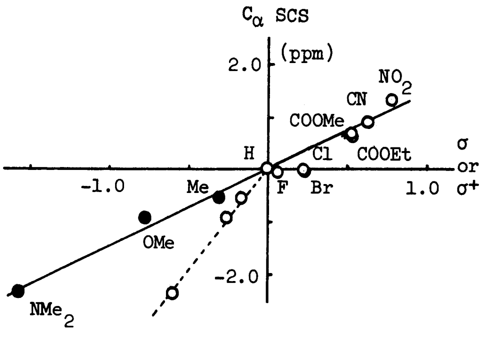


Fig. 2. Plot of C_α SCS vs. Hammett σ (○) or σ^+ (●) constants in **2**.

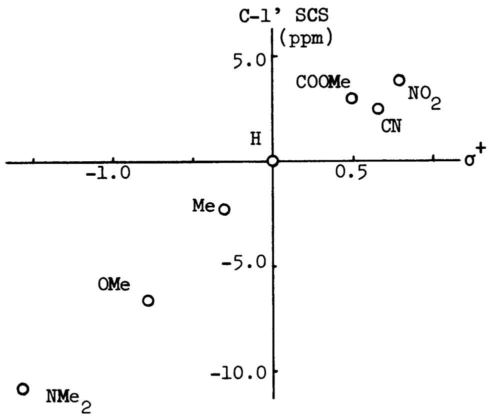


Fig. 3. Plot of C-1′ SCS vs. Hammett σ^+ constants in **2**.

Although the SCS values at C-1′ in **2** can be correlated fairly well with the σ_p constants (r=0.937), the correlation with the σ^+ constants is much better (r=0.971), and the best correlation coefficient (0.990) is obtained when halogen atoms are omitted from the consideration (Fig. 3). Accordingly, the SCS-SCS correlation between C-1′ and C_α also gives a good linear relationship (r=0.978) when halogens are omitted from the plot.

The SCS values of C-4 in **2** showed a good correlation with σ_p. This supports the idea that the electronic effects of the 4′-substituents are virtually transmitted from the *N*-phenyl ring to the *C*-phenyl ring through the whole conjugation system in **2**. The low sensitivity to resonance effects at C-4 is probably responsible for the lower double bond-order of the nitrone function compared with those of the reference systems, **5** and **6**.[2] The SCS-SCS correlation between C_α and C-4 in **2**, however, gave different slopes between electron-

Table 3. Correlations of ^{13}C SCS Values with Hammett σ_p or Yukawa-Tsuno σ_i and σ_π Constants at Representative Positions in **2**[a)]

	n	SCS=$\rho_p\cdot\sigma_p$+C				SCS=$\rho_\pi^+\cdot\sigma_\pi^+ + \rho_\pi^-\cdot\sigma_\pi^-$+C					SCS=$\rho_i\cdot\sigma_i + \rho_\pi^+\cdot\sigma_\pi^+ + \rho_\pi^-\cdot\sigma_\pi^-$+C					
		ρ_p	C	SD	r	ρ_π^+	ρ_π^-	C	SD	r	ρ_i	ρ_π^+	ρ_π^-	C	SD	r
C$_\alpha$	11	2.31 ±0.48	−0.45 ±0.21	0.08	0.965	4.41 ±1.12	3.05 ±1.45	0.14 ±0.27	0.05	0.980	1.27 ±0.54	4.34 ±0.53	2.26 ±0.76	−0.10 ±0.16	0.01	0.996
C-1	11	−0.80 ±0.14	0.00 ±0.06	0.01	0.973	−1.28 ±0.75	−1.18 ±0.97	−0.16 ±0.18	0.02	0.920	−0.90 ±0.25	−1.23 ±0.25	−0.62 ±0.36	0.01 ±0.08	0.00	0.993
C-4	11	1.17 ±0.16	0.00 ±0.07	0.01	0.984	1.65 ±1.02	2.04 ±1.31	0.19 ±0.24	0.04	0.931	1.23 ±0.31	1.59 ±0.30	1.28 ±0.43	−0.04 ±0.09	0.00	0.995
C-1′	11	10.00 ±2.80	−3.09 ±1.23	2.72	0.937	20.02 ±2.81	13.58 ±3.63	−0.47 ±0.66	0.32	0.994						
H$_\alpha$	11	0.13 ±0.04	−0.02 ±0.02	0.00	0.935	0.14 ±0.04	0.33 ±0.06	−0.01 ±0.01	0.00	0.991						

a) n: The number of data, SD: standard deviations, and r: correlation coefficients.

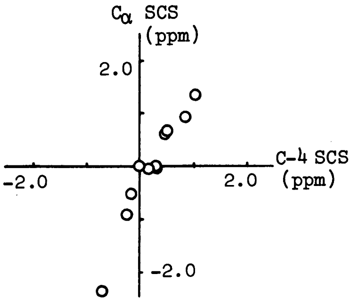


Fig. 4. Plot of C$_\alpha$ SCS vs. C-4 SCS in **2**.

donating and electron-withdrawing substituents (Fig. 4), reflecting different substituent effects at the two sites. Hence, dual parameter analyses will be a better approach to give quantitative information on the balance of electronic substituent effects.

Excellent correlations were obtained between the SCS values and the Yukawa-Tsuno σ_i and σ_π[13)] parameters at the positions in **2** being discussed (Table 3).[††] The resonance effects are, as was expected, predominant at the conjugation sites, C-1′ and C$_\alpha$, except in the case of C-4. The inductive effects can essentially be ignored at C-1′. It should be noticed that the slopes (ρ_π^+) for the electron-donating substituents are much larger than those (ρ_π^-) for the electron-withdrawing substituents at the two positions: $\rho_\pi^+/\rho_\pi^-=1.5$ and 2 at C-1′ and C$_\alpha$ respectively.

The resonance effects are, however, depressed at C-4 and are comparable to inductive effects. Since the ρ_π/ρ_i ratio will be a measure of the relative contribution of resonance effects to inductive effects, we next compared these ratios at C$_\alpha$ and C-4 in **2** with those for the corresponding sites in a reference system **6**. For **6**, the ρ_π^+/ρ_i and ρ_π^-/ρ_i values are nearly constant; i.e., they are 2.3 and 2.5 at C$_\alpha$, and 1.8 and 2.2 at C-4, respectively. On the other hand, these values in **2** are 3.4 and 1.8 at C$_\alpha$, and 1.3 and 1.0 at C-4, respectively. It is thus obvious that the resonance effects in **2** are anomalously enhanced at C$_\alpha$ by the electron-donating groups (but depressed by the electron-withdrawing groups), while at C-4 they are much more depressed, especially by electron-withdrawing groups. Therefore, the electronic effects of the 4′-substituents are transmitted to C$_\alpha$ and C-4 in a different fashion in **2**.

On the basis of the above observations of the electronic substituent effects at C-1′, C$_\alpha$, C-1, and C-4 in **2**, we may propose the mechanisms shown in Scheme 2.

The nitrone function takes a coplanar conformation with the two phenyl groups in **2**, and the double-bond order is lower than those of the corresponding double bonds in **5** and **6**. The observed large shielding at C$_\alpha$ in **2** is best attributable to a "back-polarized" structure, **d**, which predominates over the alternative canonical form, **c**; thus, the positive charge on the nitrone function should be localized mainly on the nitrogen atom. In such situations, resonance effects caused by the electron-donating substituents on the *N*-phenyl ring will be important. The effects are illustrated by the structures shown in the right column of Scheme 2. Among the resonance structures, **g** and **h**, in which a negative charge donated by the substituent R is located on the carbons (i.e., C$_\alpha$ and/or C-1′) next to the positive nitrogen, electrically predominate over such a structure as **i**, in which the negative charge donated by R is delocalized over all the conjugation sites of the molecule (i.e., normal resonance effects are to be expected at the sites). On the other hand, among the resonance structures caused by electron-withdrawing groups, such as **e** and **f**, the **f** structure will show a negligible contribution because of the repulsion between the two neighboring positive charges on the

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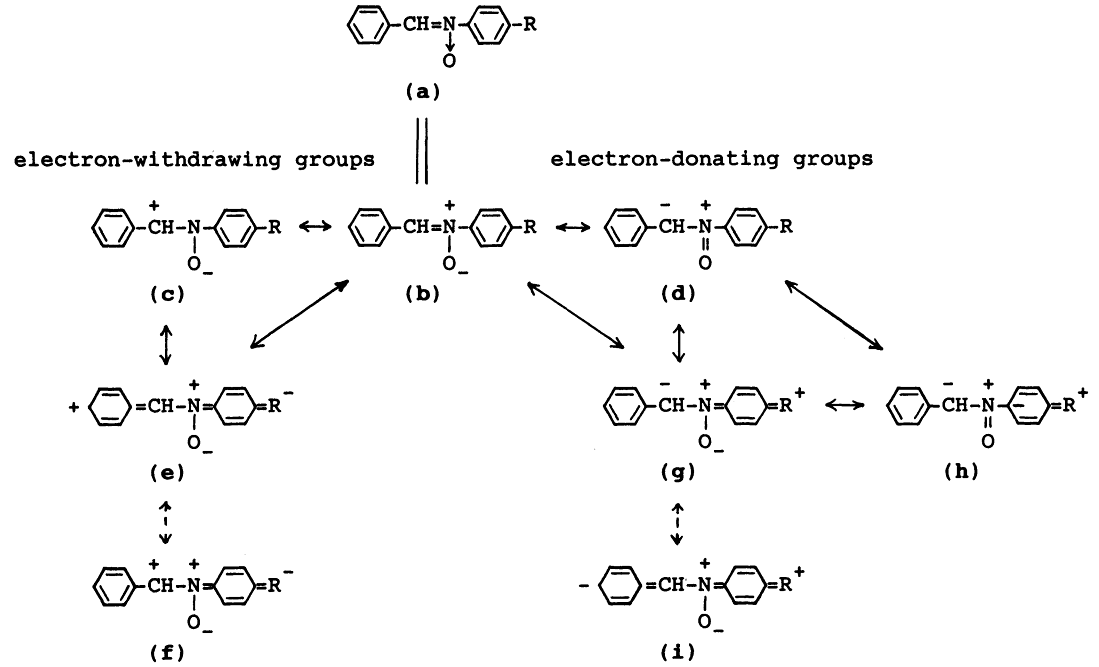
[††] A combined treatment of the σ_π^+ and σ_π^- parameters, such as was attempted in the previous paper,[2)] is inappropriate in a situation such as this where resonance effects are predominant. Our data also give an excellent correlation with the Swain-Lupton F and R parameters: r=0.993 at C-1; r=0.991 at C$_\alpha$; and r=0.995 at C-4.



Scheme 2.

carbon and nitrogen atoms; thus, a positive charge is, as is shown by the canonical structure **e**, delocalized over all the conjugation sites of the molecule according to the electron demand of the electron-withdrawing substituents on the C-4′. Resonance effects caused by electron-withdrawing substituents are, hence, normal but depressed at C_α and C-4.

The H_α chemical shifts of **2** appear between the corresponding proton chemical shifts of **4** and **6**. This also supports the idea that the canonical structure **d** predominates over the alternative structure **c** in **2**. The SCS values at H_α also show a fairly good correlation (r=0.935) with the σ_p constants, and a better correlation coefficient of r=0.990 can be estimated when halogens are omitted from the correlation. The resonance effects of the substituents are, therefore, predominant at H_α. However, the sensitivity of H_α SCS is much lower than that of C_α SCS; therefore, correlation analysis based on H_α SCS seems to be less valuable for discussing the precise mechanism of the transmission of substituent effects.

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