^{13}C and ^{1}H NMR of α-Arylnitrones. Substituent Effects on the α-Position of α-(*p*-Substituted Phenyl)nitrones

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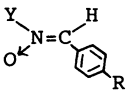
Substituent effects on the ^{13}C and ^{1}H NMR chemical shifts of the α-position of various α-(*p*-substituted phenyl)nitrones, α-phenyl-*N*-(1-cyano-2-methylpropyl)nitrones (**1**), α-phenyl-*N*-methylnitrones (**2**), and α-phenyl-*N*-phenylnitrones (**3**), have been investigated and the obtained results have been compared with data related to *N*-(*p*-substituted benzylidene)anilines (**4**) and reported data for *p*-substituted styrenes (**5**). The chemical shifts of the α-arylnitrones are well correlated with substituent constants by means of a linear combination of two empirical parameters, σ_i and σ_π. Inductive effects predominate at the α-carbon but resonance effects predominate at the α-hydrogen.

Much attention has been paid to the chemistry of nitrones because of their widely applicable reactivities.[1—3] 1,3-Dipolar cycloadditions of nitrones and their functionalizations at the α-position have great synthetic utilities.[3]

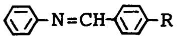
Nitrones have a positive charge on the nitrogen atom which can be delocalized between the nitrogen atom and the α-carbon atom.[1] The extent of the delocalization is naturally influenced by substituents on the α-carbon and the nitrogen. An understanding of the electronic behavior of the α-position is, therefore, one of the essential subjects in nitrone chemistry.

NMR spectroscopy is a powerfull tool for studying the electronic behavior of the nitrone function and a few attempts have been made to correlate electronic substituent constants with the chemical shifts of nitrones.[4] However, they are still lacking an adequate explanation regarding this subject. In a recent study of substituent effects on the ^{1}H and ^{13}C NMR spectra of α, *N*-diarylnitrones, Arumugam et al.[5] found a linear correlation between the chemical shifts of the α-proton (^{1}H$_\alpha$) and the Hammett σ_p parameters or the Swain–Lupton *F* and *R* parameters. Their analyses, however, have left some important problems, especially concerning the correlation with the chemical shifts of the α-carbon of a series of α-arylnitrones: the parameters they used showed no correlation with these chemical shifts which would give more direct information about the mechanisms of the transmission of substituent effects on the α-position. As a primary approach, it is necessary to decide whether this is due to the use of inappropriate parameters or to contributions from substituent effects other than inductive and resonance ones.

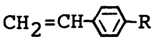
The present work is concerned with a systematic investigation of the effects of substituents in the phenyl ring on the α-position of various α-arylnitrones, α-(*p*-substituted phenyl)-*N*-(1-cyano-2-methylpropyl)nitrones (**1**), α-(*p*-substituted phenyl)-*N*-methylnitrones (**2**) and α-(*p*-substituted phenyl)-*N*-phenylnitrones (**3**), by means of ^{13}C and ^{1}H NMR spectroscopy. For a comparison, *N*-(*p*-substituted benzylidene)anilines (**4**) and *p*-substituted styrenes (**5**) have been investigated.



$Y = i\text{-}Pr\text{-}\overset{CN}{CH}$ (**1**)
Me (**2**)
Ph (**3**)



(**4**)



(**5**)

Experimental

Materials. 2-(Hydroxyamino)valeronitrile[6] and *N*-phenylhydroxylamine[7] were prepared and purified according to procedures described in the literature. *N*-Methylhydroxylamine was synthesized according to a reported method[8] with a little modification.

The nitrones used were generally prepared by the condensation of an apporopriate *N*-substituted hydroxylamine with *p*-substituted benzaldehydes in ethanol and purified by recrystallization from ethanol, ethanol–hexane or benzene–hexane.

N-(*p*-Substituted benzylidene)anilines were prepared by the literature method.[9]

Melting points (uncorrected, °C) of the compounds prepared are as follows. **1a**, 154.5—155.5; **1b**, 135—136; **1c**, 114—115; **1d**, 112.5—113.5; **1e**, 93—93.5; **1f**, 114—114.5; **1g**, 139; **1h**, 117.5—118.5; **1i**, 125—126; **2a**, 106—107 (lit, 105[10]); **2b**, 123.5—124, (lit, 120.5[11]); **2c**, 82.5—83; **2d**, 109—110; **2e**, 130—131, (lit, 127.5—128[11]); **2f**, 129.5—130; **2g**, 193—193.5 (lit, 187[11]); **2h**, 222—223, (lit, 206—207[11]); **3a**, 142—143; **3b**, 116—117; **3c**, 165—166; **3d**, 89—90, (lit, 95,[12] 85—87[4b]); **3e**, 105—106, (lit, 114,[12] 113—113.5[4b]); **3f**, 136—137; **3g**, 154—155; **3h**, 169—170, (lit, 165,[12] 161.5—162[4b]); **3i**, 133—134, (lit, 155.5—156[4b]); **3j**, 157—158, (lit, 147—149[4b]); **3k**, 193—194, (lit. 187,[12] 186—186.5[4b]); **4a**, 98—99; **4b**, 56—57, (lit, 63—64[13]); **4c**, 78—79; **4d**, 43.5—44.5, (lit, 146—147/3 mmHg[13] (1 mmHg=133.322 Pa)); **4e**, 50.5—51.5; **4f**, 42—43; **4g**, 64—65; **4h**, 73.5—74; **4i**, 76—77, (lit, 125.5—126.5[13]); **4j**, 97—98; **4k**, 91—92.

Compounds, **1a**, **1e**, **1g**, **2d**, **3c**, **3f**, **4c**, **4f**, and **4j** are new and their elemental analyses are as follows:

(**1a**) Found: C, 68.45; H, 8.01; N, 16.72%. Calcd for $C_{14}H_{19}N_3O$: C, 68.54; H, 7.81; N, 17.13%.

(**1e**) Found: C, 65.26 H, 5.95; N, 12.59%. Calcd for $C_{12}H_{13}FN_2O$: C, 65.43; H, 5.96; N, 12.72%.

(**1g**) Found: C, 51.22; H, 4.66; N, 9.91%. Calcd for $C_{12}H_{13}BrN_2O$: C, 51.25; H, 4.67; N, 9.96%.

(**2d**) Found: C, 63.01; H, 5.21; N, 9.21%. Calcd for C_8H_8FNO: C, 62.73; H, 5.28; N, 9.15%.

(**3c**) Found: C, 69.08; H, 5.20; N, 5.65%. Calcd for $C_{14}H_{13}NOS$: C, 69.11; H, 5.39; N, 5.75%.

(**3f**) Found: C, 72.58; H, 4.53; N, 6.48%. Calcd for $C_{13}H_{10}FNO$: C, 72.54; H, 4.68; N, 6.51%.

(**4c**) Found: C, 73.86; H, 5.65; N, 6.16%. Calcd for $C_{14}H_{13}NS$: C, 73.99; H, 5.77; N, 6.16%.

(**4f**) Found: C, 78.13; H, 4.79; N, 7.00%. Calcd for $C_{13}H_{10}FN$: C, 78.37; H, 5.06; N, 7.03%.

(**4j**) Found: C, 81.60; H, 4.70; N, 13.48%. Calcd for $C_{14}H_{10}N_2$: C, 81.53; H, 4.89; N, 13.58%.

NMR Measurement. The ^{13}C NMR spectra were measured at 67.8 MHz on a JEOL GX-270 spectrometer under a pulse Fourier transform mode. A spectral width of 17000—18000 Hz was used with 16K (resolution 2.4 Hz) data points. ^1H NMR spectra were obtained on a JEOL PS-100 NMR spectrometer operating at 100 MHz for **1**, at 270 MHz on a JEOL GX-270 NMR spectrometer for **2**, and at 90 MHz on a Hitachi Perkin Elmer R-22 NMR spectrometer for **3** and **4**. Sample solutions were prepared in a concentration of ca. 0.5 M (mol dm^{-3}) for ^{13}C NMR and 0.25 M for ^1H NMR spectra with $CDCl_3$ (99.8%, Merck) containing 1% TMS (tetramethylsilane) as an internal standard. Sample tubes with a 5-mm diameter were used and the probe was at room temperature.

$^{13}C_\alpha$ signals were assigned on the basis of their peak heights and the off-resonance decoupling method. $^1H_\alpha$ signals were either assigned on the basis of an integration of their peak areas or identified by a comparison of their chemical shifts with the spectral data of authentic samples.[4b,10,13]

Parametrizations of the simple HMO method were carried out on an NEC personal computer, PC-9801E, using a modified Tominaga's program.[14]

Results and Discussion

The observed ^{13}C and ^1H chemical shifts (δ) for the α-position of α-arylnitrones **1**—**3** and their substituent-induced chemical shifts (SCS) are summarized in Table 1 together with the corresponding chemical shifts and the SCS data for imines **4** and styrenes **5**.[15]

Although two geometrical isomers, *E* and *Z*, are known in several alkylnitrones,[1,16] all the nitrones used were exclusively in a *Z* configuration at room temperature and the two ortho hydrogens in the α-phenyl group situated syn to the nitrone oxygen appeared at a field lower than the rest of the aromatic hydrogens.

The chemical shifts were independent of the concentrations of the compounds used over a range of 0.1 to 2.0 M (with a smaller error than 0.05 ppm).

Table 1. $^{13}C_\alpha$ and $^1H_\alpha$ Chemical Shifts (δ) and SCS Values of α-Arylnitrones (**1**—**3**), Imines (**4**) and Styrenes (**5**)

Compound	R	^{13}C NMR		^1H NMR	
		δ[a)]	SCS[b)]	δ[a)]	SCS[b)]
1a	NMe_2	135.14	0.40	7.431	−0.195
b	OMe	134.46	−0.28	7.549	−0.077
c	Me	134.80	0.06	7.570	−0.056
d	H	134.74	0.0	7.626	0.0
e	F	133.61	−1.13	7.612	−0.014
f	Cl	133.64	−1.10	7.616	−0.010
g	Br	133.70	−1.04	7.597	−0.029
h	CN	133.09	−1.65	7.718	0.092
i	NO_2	132.48	−2.26	7.795	0.169
2a	SMe	134.90	−0.30	7.314	−0.057
b	Me	135.26	0.06	7.326	−0.045
c	H	135.20	0.0	7.371	0.0
d	F	134.04	−1.16	7.357	−0.014
e	Cl	134.10	−1.10	7.357	−0.014
f	Br	134.13	−1.07	7.344	−0.027
g	CN	133.52	−1.68	7.455	0.084
h	NO_2	133.15	−2.05	7.528	0.157
3a	NMe_2			7.772	−0.106
b	OMe	134.13	−0.46	7.823	−0.055
c	SMe	134.07	−0.52	7.850	−0.028
d	Me	134.59	0.00	7.864	−0.014
e	H	134.59	0.0	7.878	0.0
f	F	133.36	−1.22	7.874	−0.004
g	Cl	133.33	−1.25		
h	Br	133.42	−1.16	7.876	−0.011
i	COOMe	133.52	−1.07	7.890	0.012
j	CN	132.69	−1.90	7.997	0.119
k	NO_2	132.32	−2.26	8.033	0.155
4a	NMe_2	160.23	−0.12	8.297	−0.142
b	OMe	159.64	−0.71	8.366	−0.073
c	SMe	159.55	−0.80	8.371	−0.068
d	Me	160.29	−0.06	8.396	−0.043
e	H	160.35	0.0	8.439	0.0
f	F	158.76	−1.59	8.398	−0.041
g	Cl	158.73	−1.62	8.389	−0.050
h	Br	158.91	−1.44	8.443	0.004
i	COOMe	159.00	−1.35		
j	CN	157.80	−2.54	8.471	0.032
k	NO_2	157.32	−3.03	8.540	0.101
5a[c)]	NMe_2	136.67	−0.29	6.503	−0.126
b	NH_2			6.494	−0.135
c	OMe	136.29	−0.67	6.561	−0.068
d	SMe			6.562	−0.067
e	Me	136.73	−0.23	6.574	−0.055
f	H	136.96	0.0	6.629	0.0
g	F	136.11	−0.85	6.591	−0.038
h	Cl	135.69	−1.27	6.582	−0.047
i	Br	135.76	−1.20	6.568	−0.061
j	I	135.84	−1.12	6.550	−0.079
k	COMe	136.07	−0.89	6.664	0.035
l	COOMe			6.655	0.026
m	CN	135.39	−1.57	6.630	0.001
n	NO_2	135.03	−1.93	6.701	0.072

a) δ: In ppm downfield from internal TMS. b) SCS $=\delta(X\text{-}R)-\delta(X\text{-}H)$. c) Ref. 15.

The $^{13}C_\alpha$ signals of nitrones **1**—**3** appeared in a spectral region close to one another, and they were slightly upfield from the corresponding signals of styrenes **5** but more than 25 ppm upfield from those of imines **4**. Table 1 reveals that as the electron-withdrawing ability of substituents increases, the $^{13}C_\alpha$ signal of the nitrones moves upfield. The upfield shift caused by electron-donating *p*-substituents with a higher electronegative atom, such as OMe and SMe, is also noticeable. Such a behavior is, however, not a characteristic of nitrones alone and also observed in the corresponding chemical shifts of imines **4**[17] and styrenes **5**.[15,18]

In aromatic systems with a conjugated side chain, the range of the substituent chemical shift for the α-carbon, $^{13}C_\alpha$ SCS, is generally much narrower than that of the $^{13}C_\beta$ SCS. In the present investigation, the ranges of the $^{13}C_\alpha$ SCS for compounds **1**—**5** were all within a width of 3 ppm (Table 1).

The plots of the $^{13}C_\alpha$ SCS values of **1**—**4** against the values for styrenes exhibited good linear correlations (Fig. 1). The slopes are all larger than unity (Table 2). The magnitude of a slope should be a measure of the relative sensitivity of the α-carbon toward substituents.

The large slope for **4** may be explained by the participation of a lone pair on the nitrogen atom. The lone pair could shift the electron cloud around the C=N bond toward the α-carbon according to the requirement of the electron-withdrawing ability of *p*-substituents in the α-phenyl ring. The carbanionic character at the α-carbon increases with an increase in the electron-withdrawing ability of the substituent. The increased shielding at the α-carbon results in an upfield shift of the $^{13}C_\alpha$ signal.

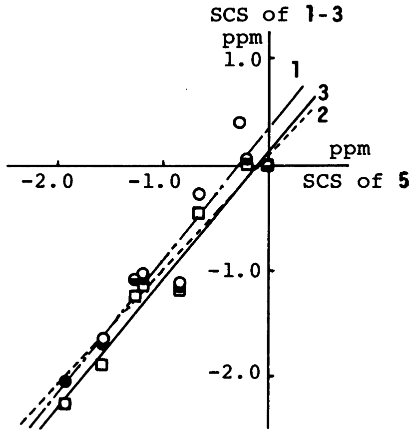
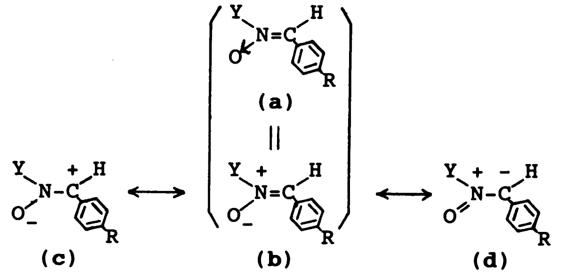


Fig. 1. Correlations of $^{13}C_\alpha$ SCS's of **1** (—○—), **2** (--●--), and **3** (—□—) with $^{13}C_\alpha$ SCS of **5**.

Table 2. Relative Susceptibility of **1**—**5** to Substituent Effects

X	SCS(X)/SCS(styrene)	
	^{13}C NMR	^{1}H NMR
1	1.28	1.78
2	1.09	1.47
3	1.23	1.34
4	1.64	1.17
5	1.00	1.00

Although nitrones are usually represented by a structure, **a** or **b**, the positive charge on the nitrogen atom is essentially delocalized between the nitrogen and the α-carbon atoms, as represented by an additional canonical structure **c**. However, the upfield shift of the $^{13}C_\alpha$ signals of nitrones **1**—**3**, which was caused by electron-withdrawing substituents, can not be rationalized by the structure of **c**. This behavior requires an explanation that the introduction of electron-withdrawing susbtituents and electron-donating substituents with an electronegative atom into the α-phenyl ring predominantly induces a "back polarized" structure **d** from **b**, or the concept of "π-polarization,"[19] in which an electron cloud around the C=N bond of **b** is withdrawn toward the α-carbon by electron-withdrawing substituents introduced in the α-phenyl group.



Although the net substituent effect at the α-carbon is smaller than that for imine **4**, this can be rationalized by the charge compensation between the normally-localized structure **c** and the "back polarized" structure **d**.

Table 3 shows the results of an HMO calculation. The Coulomb integral and the resonance integral values used for **3** and **4** are as follows: **3**[20]: $h_N=0.6$, $h_O=1.0$, $k_{CN}=1.0$, $k_{NO}=1.5$; **4**[21]: $h_N=0.5$, $k_{CN}=1.0$.

If these values used for pyridine *N*-oxides are truly applicable to a calculation for **3**, the order obtained for the α-carbon charge density, **3**>**5**>**4**, can explain

Table 3. Charge Densities and Bond Orders for **3**—**5**

	Charge density[a)]	Bond order[a)]	
	C_α	C_α=N or C_α=C	N→O
3	1.269	0.628	0.639
4	0.835	0.795	
5	1.000	0.911	

a) Calculated by the HMO method.

the largest upfield shift of the $^{13}C_\alpha$ chemical shift of **3**. On the other hand, the bond order for the C_α=N bond of **3** is smaller than those for the corresponding double bonds of **4** and **5**. These two estimations suggest a considerable contribution of the canonical form **d** in the structure of nitrones.

In Hammett plots of $^{13}C_\alpha$ chemical shifts vs. σ values, the slopes for α-arylnitrones **1**—**3** and imine **4** are larger than that of styrene **5** (Table 4), and the correlations are much better with σ_m than with σ_p. This and the order, $\rho_m > \rho_p$, obtained for all the compounds indicate that inductive effects are predominant at the α-carbon atom.

As shown in Table 4 and Figs. 2—4, the $^{13}C_\alpha$ SCS values for the nitrones are, expectedly, correlated much better with a linear combination of σ_i and σ_π, namely a correlation with $\rho_i\sigma_i+\rho_\pi\sigma_\pi$, than with σ_m. ρ_i and ρ_π represent empirical coefficients, and σ_π corresponds to resonance substituent constants, σ_π^+ and σ_π^-, presented by Yukawa and Tsuno,[22] having negative and positive signs for electron-donating groups and electron-withdrawing groups, respectively. The ρ_π values estimated for **1**—**5** were essentially equal to the arithmetic means of the corresponding coefficients of σ_π^+ and σ_π^- and, thus, the use of the linear combination of σ_i and σ_π is appropriate as a multivariate parameter analysis for the nitrones. Our dual-parameter analyses clealy show that inductive effects are the predominant factors in the $^{13}C_\alpha$ chemical shifts.

The relative importance of factors operating in the delocalization of the nitrone function can be estimated from the ratio, ρ_π/ρ_i (Table 5). The magnitude of the ratio, $\rho_\pi/\rho_i < 0.5$, means that inductive effects are always stronger than resonance effects at the α-carbon.

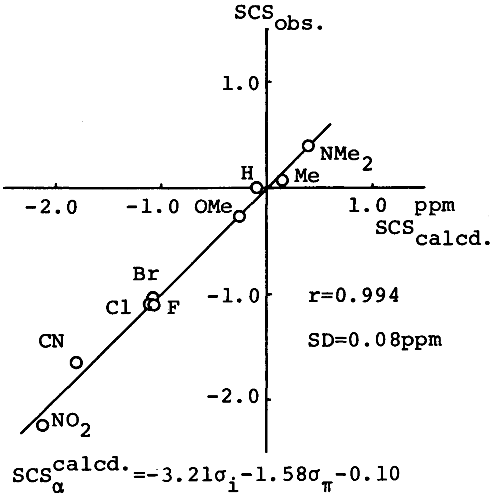


Fig. 2. Correlation between observed and calculated SCS_α for **1**.

Table 4. Correlation Analyses of SCS Values for Compounds **1**—**5**

		SCS = $\rho_p\sigma_p+C$				SCS = $\rho_m\sigma_m+C$				SCS = $\rho_i\sigma_i+\rho_\pi\sigma_\pi+C$				
	n[a]	ρ_p	C	SD[b]	r[c]	ρ_m	C	SD[b]	r[c]	ρ_i	ρ_π	C	SD[b]	r[c]
1 ^{13}C NMR	9	−1.92	−0.59	0.76	0.937	−2.69	−0.08	0.20	0.984	−3.21	−1.58	−0.10	0.08	0.994
		±0.64	±0.32			±0.44	±0.17			±0.61	±0.45	±0.19		
^{1}H NMR	9	0.23	−0.04	0.01	0.961	0.28	−0.08	0.02	0.871	0.09	0.36	−0.01	0.00	0.988
		±0.06	±0.02			±0.14	±0.06			±0.10	±0.07	±0.03		
2 ^{13}C NMR	8	−2.14	−0.46	0.62	0.922	−2.65	−0.06	0.12	0.986	−3.23	−1.23	−0.09	0.03	0.997
		±0.89	±0.34			±0.45	±0.19			±0.42	±0.41	±0.13		
^{1}H NMR	8	0.20	−0.03	0.01	0.942	0.20	−0.05	0.01	0.794	0.07	0.32	−0.01	0.00	0.967
		±0.08	±0.03			±0.15	±0.06			±0.13	±0.12	±0.04		
3 ^{13}C NMR	10	−1.88	−0.62	1.20	0.873	−2.85	−0.13	0.09	0.991	−3.57	−1.11	−0.12	0.09	0.991
		±0.85	±0.33			±0.31	±0.12			±0.57	±0.47	±0.17		
^{1}H NMR	10	0.16	−0.01	0.01	0.918	0.22	−0.05	0.01	0.881	0.12	0.22	−0.01	0.01	0.931
		±0.06	±0.02			±0.10	±0.04			±0.17	±0.11	±0.05		
4 ^{13}C NMR	11	−2.09	−0.95	2.52	0.862	−3.32	−0.37	0.52	0.973	−4.66	−1.25	−0.19	0.32	0.983
		±0.93	±0.38			±0.59	±0.22			±1.00	±0.66	±0.29		
^{1}H NMR	10	0.15	−0.04	0.11	0.922	0.17	−0.07	0.01	0.801	0.01	0.25	−0.01	0.00	0.966
		±0.05	±0.02			±0.11	±0.04			±0.01	±0.07	±0.03		
5 ^{13}C NMR	11	−1.18	−0.73	1.17	0.814	−1.92	−0.39	0.37	0.945	−2.95	−0.51	−0.20	0.30	0.956
		±0.63	±0.26			±0.50	±0.19			±0.96	±0.64	±0.28		
^{1}H NMR	14	0.12	−0.05	0.01	0.870	0.15	−0.07	0.02	0.692	−0.02	0.22	−0.02	0.01	0.943
		±0.04	±0.02			±0.10	±0.03			±0.10	±0.06	±0.03		

a) The number of data. b) Standard deviations. c) Correlation coefficients.

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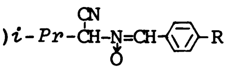

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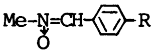

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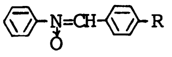

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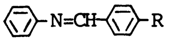

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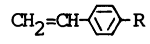


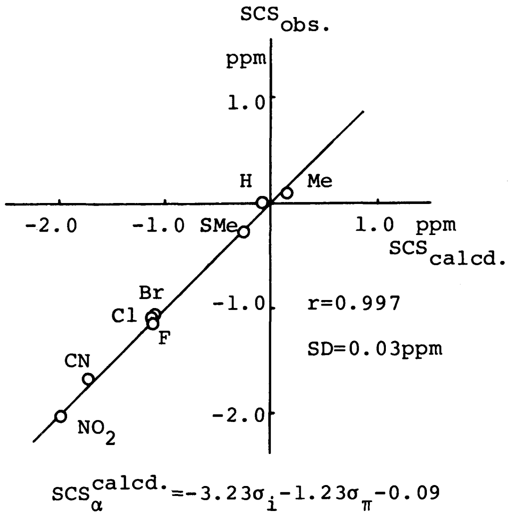


Fig. 3. Correlation between observed and calculated SCS_α for **2**.

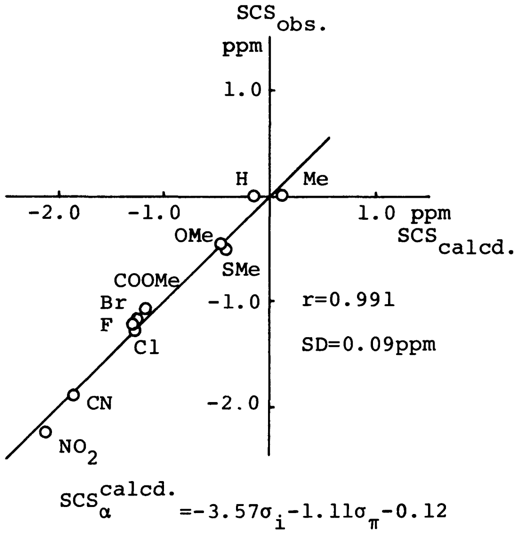


Fig. 4. Correlation between observed and calculated SCS_α for **3**.

The substituent effects of R on to the para and ipso positions, i.e. effects on to the ring carbons next and para to the C_α of nitrones, respectively, are essentially the same as those for monosubstituted benzenes.[23] The plots of SCS_1 vs. SCS_{Bz} showed a good linearity,

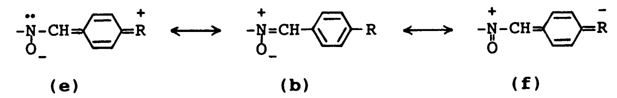
$$SCS_{1,\mathrm{para}} = 0.96(SCS_{Bz}) - 0.24 \qquad (r=0.996)$$

$$SCS_{1,\mathrm{ipso}} = 0.92(SCS_{Bz}) + 0.21 \qquad (r=0.997)$$

where SCS_1 and SCS_{Bz} represent the ^{13}C SCS of nitrones **1** and monosubstituted benzenes, respectively. On the other hand, no correlation was observed between $SCS_{1,\mathrm{ipso}}$ and $SCS_{1,\alpha}$. These findings again support the above conclusion that resonance effects on the C_α through a conjugation system of a phenyl ring are minor. However, we do not suggest that the resonance effects are unimportant. The effects are rather important in nitrones, but the negative ρ_π values can not be rationalized by the canonical forms **c** and **d**. The negative ρ_π values probably result from resonance interactions of R with the nitrone function in structure **b**.

Table 5. Relative Contribution of Resonance Effects and Inductive Effects on the α-Position of **1**—**5**

X	ρ_π/ρ_i	
	^{13}C NMR	^1H NMR
1	0.49	4.0
2	0.38	4.6
3	0.31	1.8
4	0.27	25.0
5	0.17	11.0



For nitrones with an electron-donating substituent, the charge transfer between the nitrogen atom and R (**b**↔**e**) results in a decrease in the net charge density of the shortened conjugation system. On the other hand, for nitrones with an electron-withdrawing substituent, the charge transfer between the oxygen atom and R (**b**↔**f**) increases the net charge density of the extended conjugation system. These interactions result in a relatively small negative ρ_π value at the C_α since it is a nonconjugating site. The resonance effects in nitrones **1**—**3** are, therefore, more important than those in imines **4** and styrenes **5**.

The region of $^1H_\alpha$ signals of nitrones **1**—**3** lies between the corresponding signal regions of **4** and **5**, i.e., in a lower field than that of **5** but in an upper field than that of **4**. The phenomenon also can be explained by the compensating contribution of structures **c** and **d**.

In contrast with the $^{13}C_\alpha$ chemical shifts, the $^1H_\alpha$ signals of compounds **1**—**5** normally move downfield as the electron-withdrawing ability of substituents increases. This opposite behavior results from a change in the causative factors of the ^{13}C and ^1H chemical shifts. It is well accepted that for a particular nucleus the total shielding constant, σ^t, can be approximated by a sum of three terms[24]: diamagnetic contribution (σ^d), paramagnetic contribution (σ^p), and the contribution from neighboring groups per nuclei (σ'). The first term, σ^p, has been shown to contribute to 90% of total screening of a ^{13}C nucleus, and the change in the chemical shift as a function of structure may be attributed to the change in σ^p. The second term, σ^d, on the other hand, dominates the proton chemical shift.

The correlations between $^1H_\alpha$ SCS and σ values are much better with σ_p than with σ_m in all the compounds (Table 4). This suggests that resonance effects are stronger than inductive effects at the α-hydrogen. The slopes are, however, very small and nearly one-tenth of the Hammett slopes for the $^{13}C_\alpha$ chemical shifts, reflecting intervention of one carbon between the H_α and the α-phenyl ring. Correlation analyses with $\rho_i\sigma_i+\rho_\pi\sigma_\pi$ also suggest the predominance of resonance effects in $^1H_\alpha$ chemical shifts.

The observed substituent effects on the $^1H_\alpha$ chemical shifts of nitrones **1**—**3** are larger than those for imine **4** and styrene **5** (Table 2). A resonance measure ρ_π is nearly constant in all the compounds but the order of the magnitude of an inductive measure ρ_i is $\rho_{i\,\mathrm{nitrone}}>\rho_{i\,\mathrm{imine}}$ and $\rho_{i\,\mathrm{styrene}}\simeq 0$. Thus, the ratio ρ_π/ρ_i for the nitrones is smaller than those for imine **4** and styrene **5** (Table 5).

In summary, the $^{13}C_\alpha$ signal of α-arylnitrones shifts upfield as the electron-withdrawing ability of substituents in the α-phenyl ring increases, but the $^1H_\alpha$ signal downfield. The $^{13}C_\alpha$ chemical shifts are well correlated with a linear combination of σ_i and σ_π. Inductive effects predominate at the α-carbon and the contribution of the canonical structure **d** is the largest although its contribution is known to be small in many chemical reactions. The importance of this structure will increase with the electron-withdrawing ability of the substituent R. For the α-hydrogen, resonance effects predominate instead of inductive effects.

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References

1) E. Breuer, "The Chemistry of Functional Groups," Supplement F (The Chemistry of Amino, Nitroso and Nitro Compounds and Their Derivatives Part 1), ed by S. Patai, John Wiley & Sons, New York (1982), Chap. 13.

2) A. Albini and M. Alpegiani, *Chem. Rev.*, **84**, 43 (1984).

3) D. St. C. Black, R. A. Crozier, and V. C. Davis, *Synthesis*, **1975**, 205.

4) a) K. Koyano and H. Suzuki, *Tetrahedron Lett.*, **1968**, 1859; b) *Bull. Chem. Soc. Jpn.*, **42**, 3306 (1969).

5) N. Arumugam, P. Manisankar, S. Sivasubramanian, and D. A. Wilson, *Org. Magn. Reson.*, **22**, 592 (1984).

6) L. Neelakantan and W. H. Hartung, *J. Org. Chem.*, **23**, 964 (1958).

7) L. Gattermann and T. Wieland, "Die Praxis des Organishen Chemikers," Walter de Gruyter and Co., Berlin (1961), p. 154.

8) E. Beckmann, *Ann.*, **365**, 201 (1909).

9) H. Gilman and A. H. Blatt, "Organic Syntheses," 2nd ed, John Wiley & Sons, New York (1961), Coll. Vol. I, p. 80.

10) V. I. Minkin, E. A. Medyantseva, I. M. Andreeva, and G. V. Gorshkova, *J. Org. Chem. USSR*, **9**, 148 (1973).

11) T. Kubota and H. Miyazaki, *Bull. Chem. Soc. Jpn.*, **40**, 245 (1967).

12) E. A. Medyantseva, I. M. Andreeva, and V. I. Minkin, *J. Org. Chem. USSR*, **8**, 149 (1972).

13) K. Tabei and E. Saitou, *Bull. Chem. Soc. Jpn.*, **42**, 1140 (1969).

14) N. Tominaga, *Kagaku No Ryoiki*, **36**, 724 (1982).

15) G. K. Hamer, I. R. Peat, and W. F. Reynolds, *Can. J. Chem.*, **51**, 897 (1973).

16) J. Bjorgo, D. R. Boyd, D. C. Niell, and W. B. Jennings, *J. Chem. Soc., Perkin Trans. 1*, **1977**, 254.

17) N. Inamoto, S. Masuda, K. Tokumaru, and M. Yoshida, *Tetrahedron Lett.*, **1975**, 3697.

18) D. A. R. Happer, *J. Chem. Soc., Perkin Trans. 2*, **1984**, 1637.

19) a) J. Bromilow, R. T. C. Brownlee, D. J. Craik, P. R. Fiske, J. E. Rowe, and M. J. Sadek, *J. Chem. Soc., Perkin Trans. 2*, **1981**, 753; b) D. J. Craik and R. T. C. Brownlee, "Progress in Physical Organic Chemistry," ed by R. W. Taft, John Wiley & Sons, New York (1983), Vol. 14, pp. 1—73.

20) R. A. Barnes, *J. Am. Chem. Soc.*, **81**, 1935 (1959).

21) a) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," John Willey & Sons, New York (1961), Chap. 5; b) T. Kubota and M. Yamakawa, *Bull. Chem. Soc. Jpn.*, **36**, 1564 (1963).

22) a) Y. Yukawa and Y. Tsuno, *Nippon Kagaku Zasshi*, **86**, 873 (1965); b) M. Sawada, M. Ichihara, Y. Yukawa, T. Nakachi, and Y. Tsuno, *Bull. Chem. Soc. Jpn.*, **53**, 2055 (1980).

We may analyze the substituent effects by the use of Linear Aromatic Substituent Reactivity (LArSR: $\log k/k_0=\rho_i\sigma_i+\rho_\pi^+\sigma_\pi^++\rho_\pi^-\sigma_\pi^-$) relationship, though the data have been treated as shown in the present text for the limited number of substituents. A part of the analyses is shown as follows, where substituent constants cited in ref. 22b have been used:

1: $^{13}C_\alpha$ SCS$=-3.14(\pm0.74)\sigma_i-1.47(\pm0.67)\sigma_\pi^+-1.82(\pm1.12)\sigma_\pi^--0.09(\pm0.22)$, $r=0.994$, SD$=0.07$ ppm, $n=9$

2: $^{13}C_\alpha$ SCS$=-3.15(\pm0.49)\sigma_i-0.93(\pm0.93)\sigma_\pi^+-1.48(\pm0.80)\sigma_\pi^--0.07(\pm0.15)$, $r=0.998$, SD$=0.02$ ppm, $n=8$

3: $^{13}C_\alpha$ SCS$=-3.43(\pm0.56)\sigma_i-0.58(\pm0.88)\sigma_\pi^+-1.64(\pm0.87)\sigma_\pi^--0.06(\pm0.17)$, $r=0.994$, SD$=0.06$ ppm, $n=10$

An alternative analysis of the $^{13}C_\alpha$ chemical shift of compounds **1**—**5** by means of Dual Substituent Parameter equation (DSP, $\log k/k_0=\rho_I\sigma_I+\rho_R\sigma_R$) paralleled the analysis done in the present text with comparable precisions. Some of the results are shown as follows:

1: $^{13}C_\alpha$ SCS$=-2.84(\pm0.46)\sigma_I-0.85(\pm0.36)\sigma_R-0.06(\pm0.22)$ $r=0.992$, SD$=0.10$ ppm, $n=9$.

2: $^{13}C_\alpha$ SCS$=-2.81(\pm0.37)\sigma_I-0.84(\pm0.43)\sigma_R-0.04(\pm0.17)$ $r=0.995$, SD$=0.04$ ppm, $n=8$

23) a) Miyajima, Y. Sasaki, and M. Suzuki, *Chem. Pharm. Bull. (Tokyo)*, **19**, 2301 (1971); b) D. F. Ewing, *Org. Magn. Reson.*, **12**, 499 (1979).

24) For example a) R. J. Abraham and P. Loftus, "Proton and Carbon-13 NMR Spectroscopy: An Integrated Approach," Heyden and Son, London (1978); b) G. C. Levy and R. L. Lichter, "Nitrogen-15 Nuclear Magnetic Resonance Spectroscopy," John Wiley & Sons, New York (1979); c) G. J. Martin and M. L. Martin, *Org. Magn. Reson.*, **7**, 2 (1975).