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A Correlation Analysis of C=N ^{13}C Chemical Shifts. The Use of Substituted Benzaldehyde (2-Hydroxycyclohexyl)hydrazones as Probes

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The C=N ^{13}C chemical shifts of two series of substituted benzaldehyde (2-hydroxycyclohexyl)hydrazones were measured. The aromatic ring-substituent chemical shifts (SCS) of hydrazones were for the first time analyzed in terms of separate resonance and inductive effects through use of the dual substituent parameter (DSP) approach. The SCS values showed that electron-donating substituents cause downfield and electron acceptors upfield shifts, thus following the reverse trend. The inductive effects of the substituents are predominant, the inductive transmission coefficient ϱ_I for both *para*- and *meta*-substituted benzaldehyde (2-hydroxycyclohexyl)hydrazones having a general value of -6.0 ± 0.2. This reverse inductive contribution is consistent with the π-polarization mechanism. The resonance contribution to SCS varies from case to case and as expected is higher in the *para* series than in the *meta* series. The C=N ^{13}C chemical shifts of hydrazones are appreciably more susceptible to substituent-induced electronic changes than those of imines, although both are more sensitive than the α-carbon ^{13}C chemical shifts of styrenes, phenylacetylenes, benzonitriles, or the side-chain carbonyl derivatives of benzene to substituent effects.

Introduction

The mechanism by which substituents modify the electronic environment of the azomethine carbon is very important because of the prominent role of the carbon−nitrogen double bond in chemistry. Scrutiny of the variation in ^{13}C chemical shifts in a series of substituted compounds helps in understanding the transmission of these substituent effects.[1,2] Taking into account, for example, the biological importance of hydrazones,[3] relatively little attention has been focused on their ^{13}C chemical shifts. Only two systematic investigations have been reported.[4,5] The correlation of the azomethine ^{13}C chemical shifts with the Hammett constants has been used to study the structure and electronic environments of imines, but only one attempt has been performed on hydrazones.[5] The goal of this work was to investigate the correlations between ^{13}C chemical shifts and substituent parameters and also to provide better insight into the transmission mechanism of substituent effects through a comparison of the behavior of imines and hydrazones.

Using a series of substituted benzaldehyde (2-hydroxycyclohexyl)hydrazones (**3** and **4** in Scheme 1) as probes, we have focused on the substituent chemical shifts (SCS) on the azomethine carbon induced by aromatic ring substituents. These compounds were selected because they possess a large shift range, which improves the reliability of measurements. Two different series, *i.e.* *N*-methyl (**3**) and *N*-benzyl (**4**) substituted derivatives, have been used to confirm the results obtained. It is to be emphasized that both *para* and *meta* substituents are included. Besides these two series, five series from the literature are now included. The SCS data are analyzed by the dual substituent parameter (DSP) equation developed by Ehrenson *et al.*[6] It is nowadays well understood that a substituent can affect a system to which it is bonded by two basic mechanisms of electronic transmission, *i.e.* through both polar and resonance effects.[1,2,6-8] It has been shown that, in particular, NMR data should be analyzed by using the two-parameter equation.[2] The DSP equation (1) separates substituent effects into

$$\mathrm{SCS} = \varrho_I \sigma_I + \varrho_R \sigma_R \tag{1}$$

inductive ($\varrho_I\sigma_I$) and resonance ($\varrho_R\sigma_R$) components. In this equation, SCS means the ^{13}C chemical shift (in ppm) for a substituted compound relative to the unsubstituted compound. One of four different resonance scales (σ_R^+, σ_R^o, σ_R^{BA}, or σ_R^-) is used, depending on the electron demand.

Scheme 1

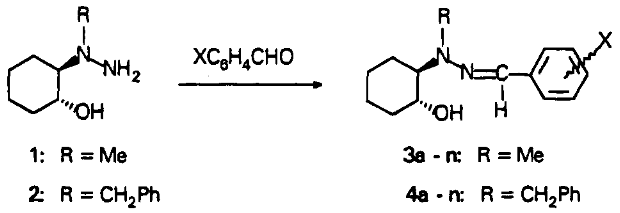

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Table 1. Analytical Data on Methyl-Substituted Cyclohexylhydrazones 3a–n

				anal.					
		mp (°C)	formula	C		H		N	
no.	X	solvent	M_w	calcd	found	calcd	found	calcd	found
3a	*p*-NO$_2$	158–159 ethanol	$C_{14}H_{19}N_3O_3$ 277.33	60.63	60.47	6.91	7.09	15.15	15.02
3b	*m*-NO$_2$	91–93 hexane	$C_{14}H_{19}N_3O_3$ 277.33	60.63	60.50	6.91	6.98	15.15	15.36
3c	*p*-CN	148–149 hexane	$C_{15}H_{19}N_3O$ 257.34	70.01	70.12	7.44	7.29	16.33	16.45
3d	*m*-CF$_3$	oil	$C_{15}H_{19}F_3N_2O$ 300.33						
3e	*p*-Cl	100–102 hexane	$C_{14}H_{19}ClN_2O$ 266.77	63.03	63.27	7.19	7.30	10.50	10.73
3f	*m*-Cl	oil	$C_{14}H_{19}ClN_2O$ 266.77						
3g	*p*-F	oil	$C_{14}H_{19}FN_2O$ 250.32						
3h	*m*-F	oil	$C_{14}H_{19}FN_2O$ 250.32						
3i	H	oil	$C_{14}H_{20}N_2O$ 232.33						
3j	*p*-Me	70–72 hexane	$C_{15}H_{22}N_2O$ 246.36	73.13	73.32	9.00	9.23	11.37	11.24
3k	*m*-Me	83–84 hexane	$C_{15}H_{22}N_2O$ 246.36	73.13	73.21	9.00	9.19	11.37	11.47
3l	*p*-OMe	94–95 hexane	$C_{15}H_{22}N_2O_2$ 262.36	68.67	68.56	8.45	8.60	10.68	11.02
3m	*m*-OMe	oil	$C_{15}H_{22}N_2O_2$ 312.33						
3n	*p*-NMe$_2$	oil	$C_{16}H_{25}N_3O$ 275.40						

Experimental Section

Melting points were determined on an Electrothermal Digital melting point apparatus and are uncorrected. Noise-decoupled ^{13}C NMR spectra were recorded for 0.2 M solutions in CDCl$_3$ (used as a field-frequency lock signal) at ambient temperature on a JEOL GX-400 spectrometer operating at 100.54 MHz. To aid shift assignments, proton-coupled ^{13}C NMR spectra with NOE were also recorded.

Cyclohexene oxide and aromatic aldehydes were commercial products. *trans*-Hydrazino alcohols **1** and **2** were prepared by ring opening of cyclohexene oxide with methylamine or benzylamine, followed by nitrosation and reduction.[9,10] The N^2-methyl derivative **1** could also be prepared directly, in about 85% purity, by the ring opening of cyclohexene oxide with methylhydrazine.[9]

General Procedure for Reactions between Hydrazino Alcohol 1 or 2 and Aromatic Aldehydes. Hydrazino alcohol **1** or **2** (1 mmol) was dissolved in 10 mL of ethanol, and aromatic aldehyde (1 mmol) was added. The mixture was left to stand for 2 h at room temperature, the solvent was evaporated off, and the products were crystallized on treatment with ether. In the case of oily products, the evaporation was repeated once, with addition of 10 mL of benzene, and the oils were dried in a vacuum desiccator for 24 h. All crystalline products gave correct elementary analyses (C, H, N). For the characterization of the prepared derivatives, see Tables 1 and 2.

Results and Discussion

Syntheses. Compound **1** or **2** reacts smoothly with aromatic aldehydes at room temperature in an ethanolic solution and gives hydrazones **3** or **4** in nearly quantitative yields within 15–60 min. NMR (400 MHz) measurements revealed no sign of hydrazone–1,3,4-benzoxadiazine ring–chain tautomerism[11] either in CDCl$_3$ or in DMSO-d_6 solution.[12,13]

General. Table 3 lists the azomethine carbon ^{13}C chemical shifts of the prepared compounds [set A includes the *N*-methyl derivatives (compounds **3a–n**) and set B the *N*-benzyl derivatives (compounds **4a–n**)]. The data can be compared with those measured by Gordon *et al.*[5] for phenylhydrazones (set C) or N^2-unsubstituted hydrazones (set D), with those measured for *N*-benzylideneanilines by Kawasaki[14] (set E) or Akaba *et al.*[15] (set F) and with those measured for *N*-benzylidenebenzylamines by Arrowsmith *et al.*[16] (set G). The different sets are specified in Table 4. Characteristic differences appear in the behavior of hydrazones (sets A, B, C, and D) and azomethines (sets E, F, and G). First, the shift range is essentially larger for hydrazones (~7 ppm for sets A and B, ~5 ppm for set C, and ~4.5 ppm for set D) than for azomethines (~3 ppm for set E, ~2.5 ppm for set F, and ~3 ppm for set G). Second, the resonances for different hydrazones (around 130 ppm for sets A and B, around 135 ppm for set C, and around 140 ppm for set D) appear at appreciably higher field than those for *N*-benzylideneanilines and *N*-benzylidenebenzylamines (around 160 ppm).

The values in Table 3 reveal that all substituents except *m*-Me, *p*-Me, *p*-OMe, and *p*-NMe$_2$ cause upfield shifts of the azomethine carbon signal. This means an unexpected trend in SCS: the electron-withdrawing substituents cause upfield shifts, while donors cause downfield shifts. However, similar "reverse" SCS effects have been detected earlier both on the azomethine carbon of phenylhydrazones,[5] N^2-unsubstituted hydrazones,[5] *N*-

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(16) Arrowsmith, J. E.; Cook, M. J.; Hardstone, D. J. *Org. Magn. Res.* **1978**, *11*, 160.

Table 2. **Analytical Data on Benzyl-Substituted Cyclohexylhydrazones 4a–n**

				anal.					
				C		H		N	
no.	X	mp (°C) solvent	formula M_w	calcd	found	calcd	found	calcd	found
4a	*p*-NO$_2$	144–145 ethanol	$C_{20}H_{23}N_3O_3$ 353.43	67.97	67.88	6.56	6.47	11.89	12.00
4b	*m*-NO$_2$	132–133 hexane	$C_{20}H_{23}N_3O_3$ 353.43	67.97	67.90	6.56	6.67	11.89	11.77
4c	*p*-CN	131–133 ether	$C_{21}H_{23}N_3O$ 312.33	75.65	75.44	6.95	7.08	12.60	12.72
4d	*m*-CF$_3$	oil	$C_{21}H_{23}F_3N_2O$ 376.43						
4e	*p*-Cl	139–140 ethanol	$C_{20}H_{23}ClN_2O$ 342.87	70.06	70.12	6.76	6.94	8.17	8.23
4f	*m*-Cl	114–115 hexane	$C_{20}H_{23}ClN_2O$ 342.87	70.06	70.01	6.76	6.87	8.17	8.30
4g	*p*-F	116–118 hexane	$C_{20}H_{23}FN_2O$ 326.42	73.59	73.45	7.10	7.31	8.58	8.67
4h	*m*-F	117–119 hexane	$C_{20}H_{23}FN_2O$ 326.42	73.59	73.60	7.10	7.34	8.58	8.46
4i	H	120–121.5 hexane	$C_{20}H_{24}N_2O$ 308.43	77.89	77.67	7.84	7.98	9.08	9.01
4j	*p*-Me	128–129 hexane	$C_{21}H_{26}N_2O$ 322.46	78.22	78.10	8.13	8.43	8.69	8.53
4k	*m*-Me	134–135 ethanol	$C_{21}H_{26}N_2O$ 322.46	78.22	78.12	8.13	8.25	8.69	8.60
4l	*p*-OMe	110–111 hexane	$C_{21}H_{26}N_2O_2$ 338.46	74.53	74.60	7.74	7.96	8.28	8.02
4m	*m*-OMe	97–99 hexane	$C_{21}H_{26}N_2O_2$ 338.46	74.53	74.41	7.74	7.69	8.28	8.11
4n	*p*-NMe$_2$	118–119 hexane	$C_{22}H_{29}N_3O$ 351.50	75.18	75.31	8.32	8.51	11.95	12.07

Table 3. C=N ^{13}C Chemical Shifts of the Prepared Benzaldehyde (2-Hydroxycyclohexyl)hydrazones in CDCl$_3$ [Solvent Resonance (77.10 ppm from TMS) Was Used as a Reference]

	substituent X	*N*-methyl derivatives **3a–n**	*N*-benzyl derivatives **4a–n**
a	*p*-NO$_2$	127.14	127.46
b	*m*-NO$_2$	127.88	127.31
c	*p*-CN	127.60	128.02
d	*m*-CF$_3$	129.28	128.89
e	*p*-Cl	130.30	130.28
f	*m*-Cl	129.21	129.80
g	*p*-F	130.38	130.78
h	*m*-F	129.36	130.00
i	H	131.89	131.91
j	*p*-Me	132.45	132.38
k	*m*-Me	132.35	132.24
l	*p*-OMe	132.59	132.45
m	*m*-OMe	131.22	131.60
n	*p*-NMe$_2$	133.93	134.34

benzylideneanilines,[14,15] or *N*-benzylidenebenzylamines[16] and on the α-carbon of styrenes, benzonitriles, or the side-chain carbonyl groups of benzene derivatives.[2,8] A linear correlation is obtained over the total range when the ^{13}C chemical shifts of our benzyl derivatives (set B) are plotted *vs* those of the methyl derivatives (set A), as shown in Figure 1. The slope of 0.95 (r = 0.9845) indicates that the *N*-benzyl derivatives are somewhat less sensitive than the *N*-methyl derivatives to the substituent effects.

The single-parameter correlation of the ^{13}C NMR shift data with the Hammett substituent constants has usually been used when analyzing the substituent effects on the azomethine carbon, but with poor success.[5,14-16] On the other hand, the DSP analyses carried out on the substituent effects on the α-carbon chemical shifts of benzonitriles and the side-chain carbonyl sites of benzene derivatives have been very successful.[2,8,17,18] We found first the correlation of the azomethine carbon shifts *vs* the substituent constants σ or σ^+ to be poor (*cf.* Figure 2). Phenomenologically, a breakpoint could be observed at σ or $\sigma^+ = 0$, dividing the correlation into two separate lines. Figure 2 shows these plots for the C=N ^{13}C chemical shifts of the hydrazones in question *vs* σ or σ^+. Satisfactory correlations are given by both lines. Kawasaki[14] interpreted an analogous behavior of azomethine carbon shifts for *N*-benzylideneanilines by a combination of two mechanisms, *i.e.* the SCS values are controlled by electron-donating conjugation and polarization of the C=N bond. Accordingly, electron-withdrawing substituents cause large high-field shifts by suppressing the polarization effect [see Scheme 2, **5** ↔ **6**, $\varrho^+ = -4.35$] on the ^{13}C chemical shift.[14] On the other hand, electron-releasing substituents operate through two opposite mechanisms: a major contribution of electron donation

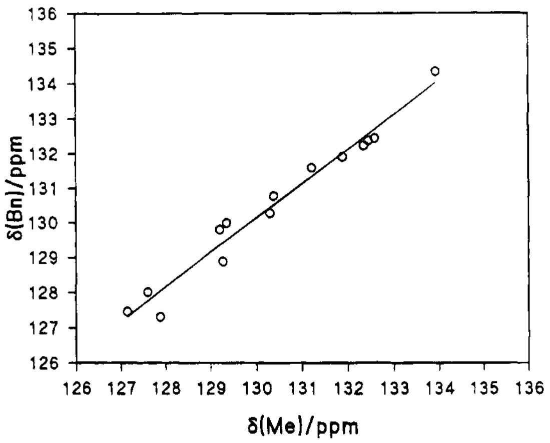

Figure 1. Cross-correlation between the C=N ^{13}C chemical shifts of benzaldehyde benzyl(2-hydroxycyclohexyl)hydrazones **4a–n** and benzaldehyde methyl(2-hydroxycyclohexyl)hydrazones **3a–n**.

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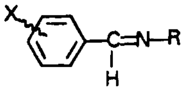
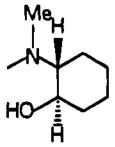
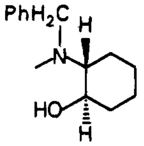
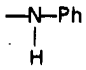
Table 4. Structures of the Different Hydrazone and Imine Sets Analyzed by the DSP Approach (*cf.* Tables 5 and 6)



Set	R	Ref.
A		this work
B		this work
C	 $-\mathrm{NH}-\mathrm{Ph}$	5
D	$-\mathrm{NH_2}$	5
E	—Ph	14
F	—Ph	15
G	$-\mathrm{CH_2}-\mathrm{Ph}$	16

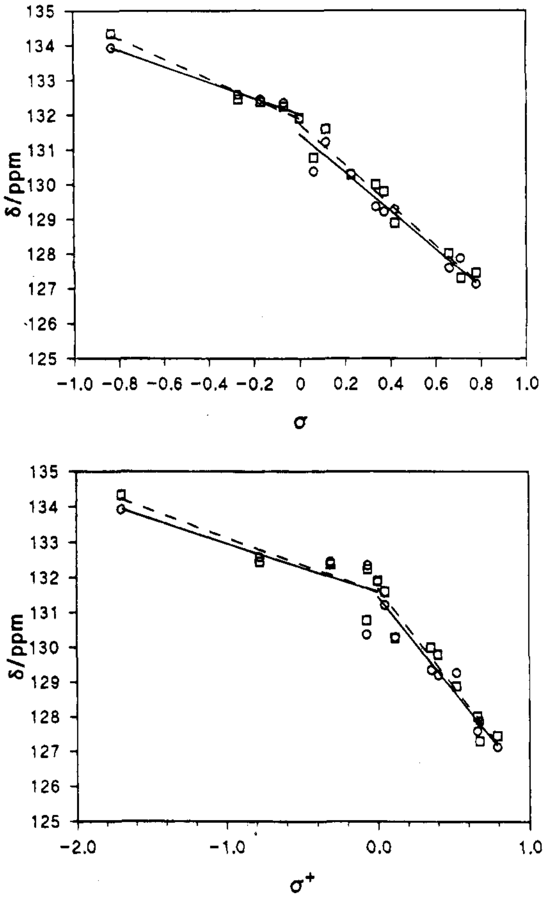
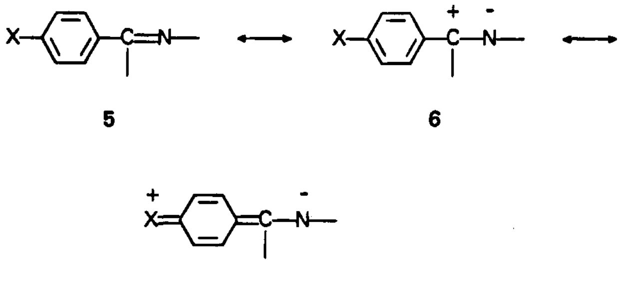


Figure 2. Correlation of the C=N ^{13}C chemical shifts of benzaldehyde methyl(2-hydroxycyclohexyl)hydrazones **3a–n** (○) or benzyl(2-hydroxycyclohexyl)hydrazones **4a–n** (□) *vs* σ or σ^+.

Scheme 2



5 **6** **7**

Table 5. DSP Analysis of the Azomethine Carbon SCS Data for Set A (Compounds 3a–n) and Set B (Compounds 4a–n) According to Eq 1

	set A		set B	
	para series	*meta* series	*para* series	*meta* series
ϱ_I	−6.2	−6.0	−5.8	−6.2
ϱ_R	−4.9	−0.84	−5.0	−3.2
scale[a]	0	+	0	0
ϱ_R/ϱ_I	0.79	0.14	0.86	0.52
SD[b]	0.16	0.13	0.17	0.14
f^c	0.06	0.06	0.07	0.06

[a] The correlation was examined for each of the four resonance scales (σ_R^-, σ_R°, σ_R^{BA}, and σ_R^+) and the results for the one with the lowest SD are shown. [b] Standard deviation of the correlation. [c] f = SD/RMS, where RMS = root mean square of the data.

through resonance [**7** in Scheme 2, $\varrho^+ = 5.36$, tentatively] and a minor contribution of enhanced polarization [**6** in Scheme 2, $\varrho^+ = -4.35$, tentatively). According to Kawasaki,[14] the net result is the appearance of small high-field shift effects. Two important points (corresponding the *p-N,N*-dimethylamino and *p*-chloro derivatives) were, however, neglected without justification.[14] Even if the basic idea of Kawasaki,[14] *i.e.* the lack of a simple relationship between the azomethine chemical shifts and σ or σ^+, seems correct, the situation for simple imines is complicated by the experimentally narrow shift range in the case of electron-releasing substituents. Further, this explanation appears illogical because it means two simultaneous but distinct dependences between the measured values (SCS) and the combined substituent constants (σ or σ^+ includes both the polar and the resonance components). The single-parameter Hammett-type analyses are often inadequate because they restrict the inductive and resonance parameters to fixed proportions. Therefore, DSP analyses by eq 1 should be preferred.[2,19] The DSP correlation parameters obtained in this work are given in Table 5. Due to the greater shift range and a wide substituent scale, the present compounds are more reliable for study of the substituent effect correlations at the C=N site than those in the earlier investigations.[5,14-16] The "goodness of fit" of a DSP correlation is judged by the parameter f = SD/RMS. Here, SD is the standard deviation of the fit and RMS is the root mean square of the experimental data. Values <0.1 for f represent excellent correlations.[6] The good fits obtained (Table 5) show that the chemical shifts are systematic and electronic in origin. The DSP analysis also reveals that the ratio of resonance to inductive effects ($\lambda = \varrho_R/\varrho_I$) changes from one series to another. As

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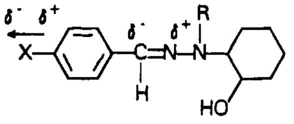
(19) (a) Brownlee, R. T. C.; Topsom, R. D. *Tetrahedron Letters* **1972**, 5187. (b) Bromilow, J.; Brownlee, R. T. C. *J. Org. Chem.* **1979**, *44*, 1261.

discussed later, the earlier results[5,14-16] can also be treated satisfactorily in terms of the DSP equation.

Inductive Effects. High negative values are observed for ϱ_I in all cases (*cf.* Table 5). This "reverse" direction of the inductive SCS effect is best explained by the π-polarization mechanism. The concept of π-polarization is well established and has been extensively discussed elsewhere.[1b,2,8,17] According to this theory, the substituent dipole polarizes each π-unit separately as a localized system, as shown in **8** for the present compounds. The



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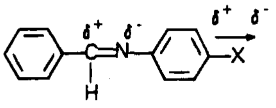
polarization of the C=N system in the side chain by an electron-withdrawing substituent results in an increase in π-electron density at the α-carbon. The increased shielding of the carbon then corresponds to the upfield shift of the ^{13}C chemical shift. In other words, the SCS effects are normal, but the changes in the electron density at the α-carbon are "reversed", *i.e.* electron acceptors increase the electron density and donors decrease it. The high negative values of ϱ_I indicate that the inductive effects are mainly controlled by localized π-polarization, and the polarization of the entire conjugated π-unit must make only a minor contribution. The negative ϱ_I values for the α-carbon chemical shifts of *N*-benzylideneanilines and *N*-benzylidenebenzylamines and also those for the α-carbon chemical shifts of styrenes, of benzonitriles, and of benzene derivatives with a carbonyl group in the side chain have previously been interpreted in terms of the π-polarization mechanism.[2,8,17,18] The π-electron density calculations performed for some of these cases support the NMR data.[2,17] Further, the DSP analyses of the ^{15}N shifts for *N*-benzylideneanilines substituted at the benzylidene moiety and for series **9** confirmed the concept of π-polarization for these compounds.[2,20] In the former case the ϱ_I value is positive (14.5), whereas for the series **9** where the nitrogen atom is at the other end of the polarized C=N π-system, ϱ_I has a negative value (−6.8).



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For comparison, Table 6 gives DSP correlation parameters calculated by us from eq 1 for phenylhydrazones and N^2-unsubstituted hydrazones with the data of Gordon *et al.*[5] (sets C and D, respectively) and for *N*-benzylideneanilines with the data of Kawasaki[14] (set E) and Akaba *et al.*[15] (set F), together with those calculated by Bromilow *et al.*[8] for *N*-benzylidenebenzylamines with the data of Arrowsmith *et al.*[16] (set G). All these series contain only *para*-substituted derivatives.

Table 6. DSP Analysis of the Azomethine Carbon SCS Data for *Para*-Substituted Phenylhydrazones (Set C[a]), N^2-Unsubstituted Hydrazones (Set D[a]), *N*-Benzylideneanilines (Sets E[b] and F[c]), and *N*-Benzylidenebenzylamines (Set G[d]) According to Eq 1

	set C	set D	set E	set F	set G
ϱ_I	−4.6	−5.5	−4.1	−3.9	−3.6
ϱ_R	−3.1	−2.7	−0.71	−0.53	−0.7
scale[e]	0	BA	–	–	0
ϱ_R/ϱ_I	0.67	0.49	0.17	0.14	0.2
SD[f]	0.095	0.16	0.24	0.21	0.11
f[g]	0.06	0.07	0.16	0.13	0.09

[a-c] Calculated with the aid of data from the following sources: [a]ref 5, [b]ref 14, and [c]ref 15. [d] From ref 8. [e] The correlation was examined for each of the four resonance scales (σ_R^-, σ_R^o, σ_R^{BA}, and σ_R^+) and the results for the one with the lowest SD are shown. [f] Standard deviation of the correlation. [g] f = SD/RMS, where RMS = root mean square of the data.

The ϱ_I value for a *meta* series is often somewhat higher than that for the *para* series, which is interpreted as reflecting the through-space transmission of the π-polarization effect.[2] In the present case, $|\varrho_I(meta)| > |\varrho_I(para)|$ for set B, but the opposite holds for set A (Table 5). The differences, however, are small, and a general value of -6.0 ± 0.2 is obtained for ϱ_I. A constant ϱ_I value of -2.7 ± 0.3 has been found for a wide range of *para*-substituted compounds containing a C=C, C=O, C≡C, or C≡N system.[2] Although the ϱ_I values given in Table 6 are smaller than those for the hydrazones (Table 5), it is seen that ϱ_I for a C=N system is generally higher than the values observed for styrenes, phenylacetylenes, carbonyl compounds, or benzonitriles.[2] It is noteworthy that the value −5.5 calculated for N^2-unsubstituted hydrazones (set D) is close to the present ϱ_I values. Although the substitution range of the aromatic ring is not too wide in set D, the fit of the correlation is good (f = 0.07) and the result can be regarded as reliable. Accordingly, appreciably more negative ϱ_I values than those for imines seem to be characteristic for N^2-unsubstituted and N^2-alkyl-substituted hydrazones. The ϱ_I values are practically the same for the two slightly modified structures of (2-hydroxycyclohexyl)hydrazones (sets A and B). Accordingly, they can be considered to be reliable parameters of the hydrazone structure in question. For phenylhydrazones (set C), the aromatic N^2-substitution is seen to change the ϱ_I value less negative so that it is closer to the typical values for imines (sets E, F, and G). The observed SCS values are a combination of two factors, the changes in the electron distribution of the π-electron system and the sensitivity of the chemical shifts at the probe site to these changes (shift−charge ratio). The highly negative ϱ_I values for C=N carbons may therefore reflect one or both of these factors. Increased negative ϱ_I values at C-α have been observed with increasing conjugation of the side chain, as for β-nitrostyrenes, benzylidenemalononitriles (β,β-dicyanostyrenes), or chalcones.[2] In these cases, the extended polarization in addition to the localized polarization is presumed to contribute to the inductive transmission coefficient ϱ_I. A significantly negative ϱ_I value (−4.6) has also been observed for benzaldoximes in which oxygen is attached to the nitrogen of the C=N bond, and this obviously reflects the increased polarizability of the carbon−nitrogen double bond in that case.[2] The differentiation of the factors determining the inductive transmission is a complex question. However, the highly negative ϱ_I values for hydrazones obviously illustrate the easier polarization of the C=N bond as compared with that in imines. Further, for hydrazones ϱ_I seems to be very sensitive to electronic alteration at N^1/N^2, induced by substitution at N^2. The sequence of the ϱ_I values, −6.0 for N^2-alkyl-substituted hydrazones (−CH=N−NH−R), −5.5 for N^2-unsubstituted hydrazones (−CH=N−NH$_2$), and −4.6 for N^2-phenyl-substituted hydrazones (−CH=N−NH−Ph) (see Tables 5 and 6), probably re-

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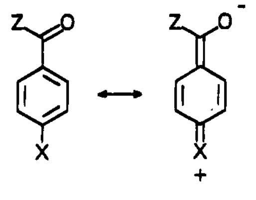
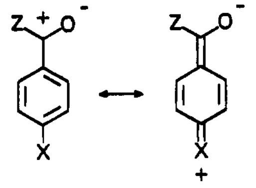
(20) Westerman, P. W.; Botto, R. E.; Roberts, J. D. *J. Org. Chem.* **1978**, *43*, 2590.

Scheme 3



10 11

Scheme 4

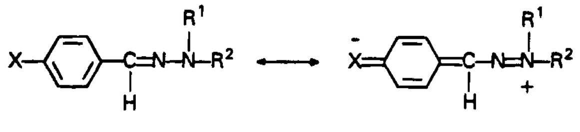


12 11

flects the availability of the free electron pair of N^2 for interaction with the conjugated π-electron system.

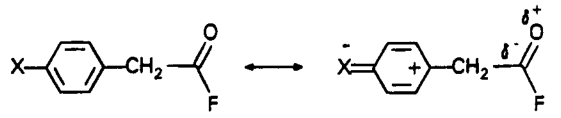
Resonance Effects. Resonance effects are expected to be smaller for *meta* derivatives than for *para* derivatives and this tendency is clearly seen from the ϱ_R values in Table 5. The total azomethine ^{13}C chemical shifts depend on the relative contributions of structures **5** and **6** (Scheme 2), analogously with the behavior of the carbonyl shifts.[21] It is obvious that the resonance effects of substituents are sensitive to the relative importance of these contributing structures, too. It has been suggested for side-chain carbonyl benzene derivatives that the interaction **10** ↔ **11** (Scheme 3) results in negative ϱ_R, as observed in our case, whereas interaction of the type **12** ↔ **11** (Scheme 4) results in positive ϱ_R values.[8] This has been explained as follows. In the substituent interaction **10** ↔ **11** π-charge density is transferred to the oxygen, while in the interaction **12** ↔ **11** π-electron density is transferred directly from the substituent to the carbon site.[8] With carbonyl compounds, the group Z modifies the relative importance of structures **10** and **12**, thereby affecting the ϱ_R values. The ratio ϱ_R/ϱ_I may vary, *e.g.* from 0.42 for Z = OEt to −0.33 for Z = H.[8] There is a distinct analogy between these side-chain carbonyl benzene derivatives and our compounds, structure **10** corresponding to the nonpolarized form (**5**) and structure **12** to the polarized form (**6**) (see Scheme 2). Although it is evident that several factors contribute to the total ^{13}C chemical shifts of the azomethine carbon, it is interesting to realize that for *para*-substituted hydrazones (sets A, B, C, and D) the observed shifts are at higher field than those for *para*-substituted simple imines, *N*-benzylideneanilines, or *N*-benzylidenebenzylamines (sets E, F, and G). In other words, the structures with upfield azomethine carbon shifts have a greater "reverse" resonance contribution (more negative ϱ_R values and greater ϱ_R/ϱ_I values) to the SCS values than those with downfield shifts. This is consistent with the idea that the negative ϱ_R is a consequence of the increased contribution of the nonpolarized form (**5**). Further, for hydrazones, substituent interactions such as **13** ↔ **14** (Scheme 5) are possible, and the increased contribution of the nonpolarized form obviously leads to the negative ϱ_R values.

Scheme 5



13 14

Scheme 6



15 16

We have so far discussed the primary resonance effect of substituents. It has been suggested, however, that a field-transmitted resonance-polar effect may occur too.[2,22] A dipole is induced in the aromatic ring by resonance delocalization and this dipole is able to polarize the distant π-unit. The observed component is proportional to σ_R, even though the polarization effect is transmitted through space, because the magnitude of the dipole set up in the benzene ring is proportional to the σ_R values of the substituents. This has been demonstrated, for example, with systems such as **15** ↔ **16** (Scheme 6), where the polarizable π-unit is isolated from the benzene ring.[22] This kind of secondary resonance effect has been used in part to explain the negative $\varrho_R(meta)$ values for side-chain carbonyl benzene derivatives[2] and it can operate for the C=N system too.

Conclusions

The present study is the first attempt to analyze the aromatic ring-substituent effects on the C=N ^{13}C chemical shifts of hydrazones in terms of separate polar and resonance effects. Characteristic parameters were obtained, which are relevant in light of those typical for imines or C=O systems. For the two examined series of substituted benzaldehyde (2-hydroxycyclohexyl)hydrazones, the SCS data excellently fitted the DSP equation, indicating that the substituent-induced changes in the C=N ^{13}C chemical shifts are systematic and electronic in origin. The inductive effects of the substituents are predominant and the reverse inductive contribution is obviously largely determined by localized π-polarization of the C=N π-electrons. The present study clearly shows that changes induced in the ^{13}C chemical shifts of a C=N carbon at the α-site by the polar and resonance effects of distant ring substituents are markedly greater than those of a C=C, C≡C, C≡N, or C=O carbon at the α-site of benzene derivatives. Further, there seems to be a distinct difference in behavior of hydrazones and imines, the C=N ^{13}C chemical shifts of hydrazones being significantly more sensitive to substituent effects.

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