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CORRELATION ANALYSIS OF THE ^{13}C CHEMICAL SHIFTS OF SUBSTITUTED BENZALDEHYDE 2-AMINOBENZOYLHYDRAZONES. STUDY OF THE PROPAGATION OF SUBSTITUENT EFFECTS ALONG A HETEROATOMIC CHAIN

KARI NEUVONEN*
Department of Chemistry, University of Turku, FIN-20014 Turku, Finland
FERENC FÜLÖP
Institute of Pharmaceutical Chemistry, Albert Szent-Györgyi Medical University, POB 121 H-6701 Szeged, Hungary
HELMI NEUVONEN
Department of Chemistry, University of Turku, FIN-20014 Turku, Finland
MARIO SIMEONOV
Institute of Organic Chemistry, Bulgarian Academy of Sciences, B6-1040 Sofia, Bulgaria
AND
KALEVI PIHLAJA
Department of Chemistry, University of Turku, FIN-20014 Turku, Finland

The ^{13}C chemical shifts of eight series of *para*- or *meta*-substituted benzaldehyde 2-aminobenzoylhydrazones possessing both amide and imine functionalities were measured. The ^{13}C chemical shifts were used to study the transmission of electronic substituent effects along the heteroaromatic side-chain of the substituted aromatic ring. In addition to the C=N bond, the benzoylhydrazones possess in their side-chain polarizable C=O and phenyl π-units. The benzylidenic ring-substituent chemical shifts were analysed by the dual substituent parameter approach to separate the inductive and resonance effects. The negative ρ_I and ρ_R values observed (*i.e.* reverse substituent effects) indicate a significant π-polarization of the C=N bond. The highly negative ρ_R values, especially those in the case of *meta* substitution, suggest a contribution from a marked secondary field-transmitted resonance effect. The results are compared with those obtained for other hydrazones or imines. Variation of the electron-withdrawing ability of the N^2 substituent is seen to have a systematic effect on the ρ_I values. Reverse substituent effects are also observed at the C-1″ site of the 2-aminobenzoyl ring while C-4″ shifts show normal behaviour, consistent with the general concept of the π-polarization that each π-unit of the side-chain is polarized largely as a localized system. Accordingly, the π-polarization effect is seen efficiently to propagate also along a heteroaromatic chain. On the other hand, the C=O sites exhibit normal, although fairly slight, dependence on the benzylidenic substituent indicating an insignificant role of π-polarization at that site. The effects of the solvent, $CDCl_3$ *vs.* DMSO-d_6, on the ρ_I and ρ_R values are also considered.

INTRODUCTION

There are good possibilities for studying the transmission mechanisms of substituent effects in aromatic compounds by the use of ^{13}C NMR spectroscopy.[1] However, relatively little attention has been paid to the correlations of the C=N ^{13}C chemical shifts *vs* the Hammett or modified substituent constants in the case of other compounds than imines,[2] imines capable of ring–chain tautomerism,[3] or to some extent hydrazones.[4] In a continuation of our investigations concerning the synthesis, transformations and stereochemistry of benzaldehyde aminobenzoylhydrazones,[5] a dual substituent parameter (DSP) analysis of their C=N ^{13}C chemical shifts has now been performed.

* Author for correspondence.

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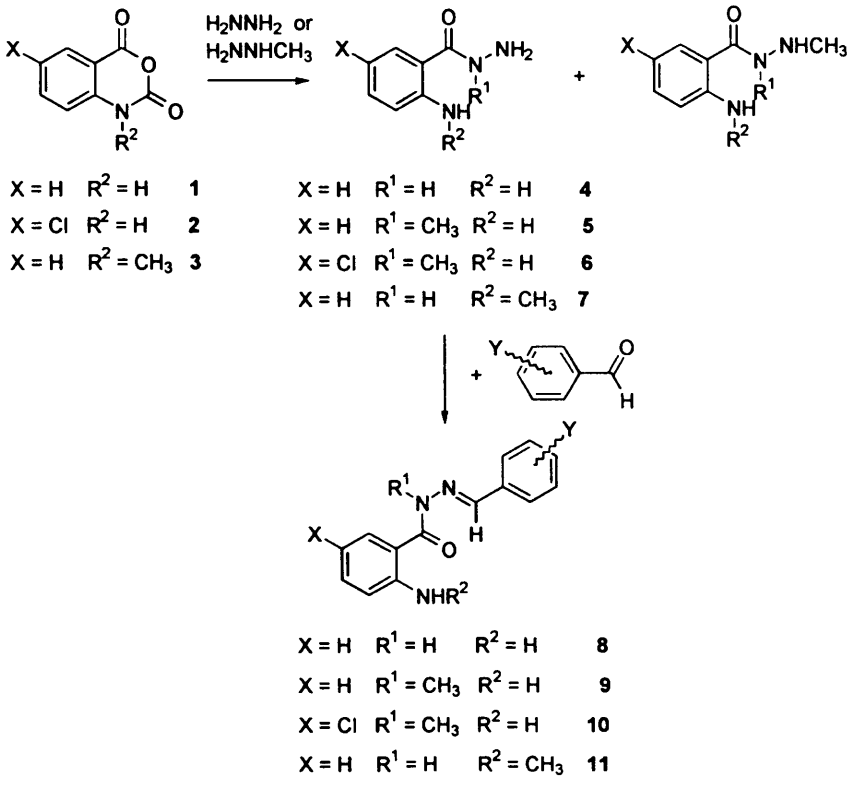
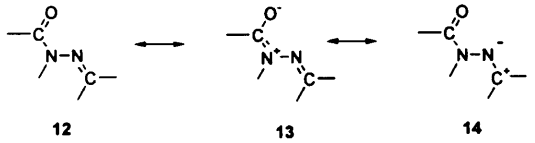


Scheme 1

Benzoylhydrazones (**8–11** in Scheme 1) offer an intriguing case for the study of the ^{13}C chemical shift – substituent correlations because they exhibit functionalities typical of both amides and imines (Scheme 2). These compounds provide a good possibility for studying the transmission of the substituent effects along the side-chain, not only to the C=N site but also to the two more distant π-units, the C=O site and the adjoining phenyl ring. The substituent effects now propagate along a heteroatomic side-chain, contrary to the earlier work[1b] focusing on mainly carbon side-chain systems. Therefore, the C=O ^{13}C chemical shifts and the ^{13}C chemical shifts of the C-1″ and C-4″ sites of the benzoyl ring were also analysed. The relatively large shift ranges for the carbons of the chosen compounds further suggest their use in a ^{13}C chemical shift – substituent correlation



12 13 14

Scheme 2

study. A hydrazone structure is part of many biologically and pharmacologically active compounds, and a scrutiny of electronic effects prevailing in hydrazones could be useful in understanding of the mechanisms of their activities.[6]

The poor suitability of single-parameter treatments in aromatic side-chain systems has been demonstrated in several cases.[1b,2c,4b,c] DSP analysis[1a] [equation (1)] dissects the effects of substituents into inductive ($\rho_I\sigma_I$) and resonance ($\rho_R\sigma_R$) contributions, and it has been found very successful in ^{13}C chemical shift correlations:[1b,1e,4c]

$$SCS = \rho_I\sigma_I + \rho_R\sigma_R \quad (1)$$

where 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^0, σ_R^{BA} and σ_R^-)[1a,b] can be used for σ_R, depending on the electronic demand. The parameter f = SD/RMS is used as a measure of the success of correlations, where SD is the standard deviation of the fit and RMS is the root mean square of the experimental data. Values of f <0·1 represent excellent correlations and f = 0·1–0·2 represent moderately good values.[1a,b]

EXPERIMENTAL SECTION

Melting points were determined on an Electrothermal Digital melting point apparatus and are uncorrected.

Noise-decoupled ^{13}C NMR spectra were recorded in $CDCl_3$ or in DMSO-d_6 (used as a field-frequency lock signal) at 27 °C on a JEOL ALPHA-500 spectrometer operating at 125·65 MHz. Concentrations of 0·1 M were used for series **9** and **10** in $CDCl_3$ and for series **11** in DMSO-d_6. Owing to the poor solubility (<0·1 M) of the compounds of series **8** and **11** in $CDCl_3$, saturated solutions were used. To aid shift assignments, proton-coupled ^{13}C NMR spectra with NOE were recorded when needed.

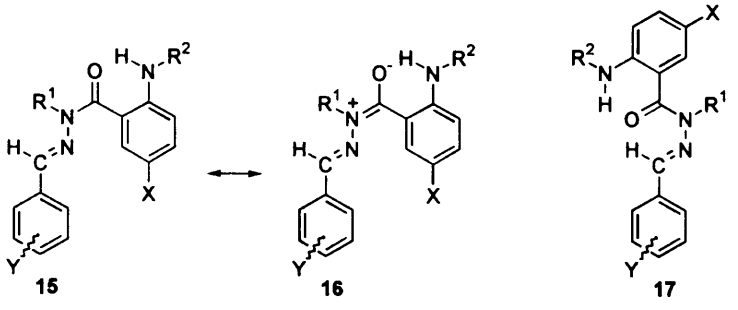
Syntheses. The crystalline starting compounds, 2-aminobenzoylhydrazine (**4**), 1-(2-aminobenzoyl)-1-methylhydrazines (**5** and **6**) and 1-(2-methylaminobenzoyl)hydrazine (**7**), were prepared according to a recently described method[5] from isatoic anhydrides **1**, **2** and **3** and hydrazine or methylhydrazine (Scheme 1). The aldehydes used were commercial products. The aminobenzoylhydrazine **4**, **5**, **6** or **7** (1 mmol) and the appropriate aromatic aldehyde (1 mmol) were dissolved together in ethanol (10 ml) and left to stand overnight. With few exceptions, most of the products crystallized from ethanol and were obtained in crystalline form after evaporation of the solvent. All products gave correct elemental analyses (C, H and N). The yields were 76–92%. M.p. (°C) and the solvents for recrystallization were as follows: **8a**, 242–245 (E = ethanol) (lit.[5c] m.p. 246–248); **8b**, 215–218 (E); **8c**, 178–180 (E); **8d**, 162–164 (D = diisopropyl ether); **8e**, 170–172 (ethyl acetate); **8f**, 197–198 (E) (lit.[5c] m.p. 199–200); **8g**, 150–153 (D); **8h**, 162–164 (D) (lit.[5c] m.p. 166–167); **8i**, 170–172 (E) (lit.[5c] m.p. 178–180); **8j**, 204–206 (E); **8k**, 179–181 (E); **8l**, 186–188 (E); **8m**, 170–171 (E); **8n**, 168–170 (E); **8o**, 169–171 (E); **8p**, 161–163 (E); **9a**, 204–206 (E) (lit.[5d] m.p. 176–178); **9b**, 149–150 (E); **9c**, 120–121 (E); **9d**, 82–84 (D); **9e**, 130–131 (E); **9f**, 132–134 (D) (lit.[5f] m.p. 131–133); **9g**, 159–161 (D) (lit.[5d] m.p. 134–135); **9h**, 139–140 (D) (lit.[5d] m.p. 128–130); **9i**, 187–189 (E); **9j**, 150–151 (E) (lit.[5d] m.p. 129–130); **9k**, 95–98 (D); **9l**, 122–125 (D); **9m**, 124–125 (D) (lit.[5d] m.p. 130–131); **9n**, 107–109 (D); **9o**, 127–128 (D); **9p**, 109–110 (E); **10a**, 209–210 (E); **10b**, 194–196 (E); **10c**, 134–135 (E); **10d**, 154–156 (E); **10e**, 172–174 (E); **10f**, 162–164 (E); **10g**, 189–190 (E); **10h**, 160–162 (E); **10i**, 210–211 (E); **10j**, 134–135 (E); **10k**, 102–105 (D); **10l**, 135–136 (E); **10m**, 147–148 (E); **10n**, 135–136 (E); **10o**, 154–156 (E); **10p**, 104–106 (E); **11a**, 242–245 (E); **11b**, 224–226 (E); **11c**, 217–218 (E); **11d**, 208–209 (E); **11e**, 216–217 (E); **11f**, 192-193 (E); **11g**: 234-235 (E); **11h**: 182-183 (E); **11i**, 218–219 (E); **11j**, 260–262 (ethanol–DMF); **11k**, 253–255 (E); **11l**, 210–203 (E); **11m**, 232–234 (E); **11n**, 253–254 (E); **11o**, 238–239 (E); **11p**, 225–226 (E).

The reactions of 2-aminobenzoylhydrazines with carbonyl compounds can lead to many different heterocycles.[5] Because of the great number of possible products, the structures of certain reaction products were initially reported erroneously, but were later corrected.[5c,e] The reactions of **4**, **5**, **6** and **7** with aromatic aldehydes with different electronic characters led to compounds **8**–**11** exclusively. Interestingly, the NMR spectra revealed no signals relating to hydrazone–benzotriazepinone-type ring–chain tautomerism in either $CDCl_3$ or DMSO-d_6 solutions.

RESULTS AND DISCUSSION

General

Structural characteristics and ^{13}C chemical shifts. Benzoylhydrazones offer an interesting case for study of the correlations between electronic structures and ^{13}C chemical shifts because of the connected carbonyl and hydrazone systems. In principle, benzoylhydrazones can possess *E*/Z configurations in respect of the C=N bond. However, rapid interconversion of the *E* and *Z* forms occurs.[7] Generally, for *N*-substituted hydrazones prepared from aldehydes, the less crowded *E* isomer is thermodynamically so much more stable that its presence can only be observed (*cf.* Scheme 3).[4a,b,6,7]



Scheme 3

Table 1. ^{13}C chemical shifts of the prepared 2-aminobenzoylhydrazones in $CDCl_3$ (TMS as internal standard)[a]

Compound	Substituent Y	Substituent X	C=N	C=O	C-1″	C-4″
8a	*p*-NO_2	H	–	–	–	–
8b	*p*-CN	H	144·4	–	113·5	133·5
8c	*p*-CF_3	H	145·2	–	113·7	133·3
8d	*p*-F	H	146·0	–	114·1	133·1
8e	*p*-Cl	H	145·8	–	114·0	133·1
8f	H	H	147·2	165·8	114·2	133·0
8g	*p*-Me	H	147·4	–	114·4	132·9
8h	*p*-OMe	H	147·3	–	114·4	132·9
8i	*p*-NMe_2	H	148·5	–	114·9	132·6
8j	*m*-NO_2	H	144·3	166·0	113·5	133·4
8k	*m*-CF_3	H	145·4	166·0	113·8	133·3
8l	*m*-F	H	145·7	165·9	113·9	133·2
8m	*m*-Cl	H	145·5	165·9	113·9	133·2
8n	*m*-Br	H	145·4	165·9	113·9	133·2
8o	*m*-Me	H	147·4	165·8	114·2	133·0
8p	*m*-OMe	H	147·3	165·8	114·2	133·1

[a] ^{13}C Chemical shift ranges for other carbons of the benzoyl ring: C-2″ for **8a–i** 149·1–149·7 ppm, for **8j–p** 149·4–149·6 ppm; C-3″ for **8a–i** 116·5–116·7 ppm, for **8j–p** 116·6–116·7 ppm; C-5″ for **8a–i** 117·3–117·7 ppm, for **8j–p** 117·3–117·6 ppm; C-6″ for **8b–i** 127·0–127·3 ppm, for **8j–p** 127·2–127·3 ppm. The assignments between C-3″/C-5″ are tentative.

Table 2. ^{13}C chemical shifts of the prepared N^2-methyl-substituted aminobenzoylhydrazones in $CDCl_3$ (TMS as internal standard)[a]

Compound	Substituent Y	Substituent X	C=N	C=O	C-1″	C-4″
9a	*p*-NO_2	H	135·8	171·5	117·5	131·7
9b	*p*-CN	H	136·4	171·3	117·6	131·6
9c	*p*-CF_3	H	137·1	171·3	118·0	131·4
9d	*p*-F	H	137·8	171·2	118·5	131·2
9e	*p*-Cl	H	137·6	171·2	118·3	131·3
9f	H	H	139·2	171·2	118·5	131·1
9g	*p*-Me	H	139·5	171·2	118·8	131·1
9h	*p*-OMe	H	139·1	170·9	118·9	130·9
9i	*p*-NMe_2	H	140·4	170·8	119·6	130·8
9j	*m*-NO_2	H	135·8	171·3	117·6	131·6
9k	*m*-CF_3	H	136·9	171·3	117·9	131·4
9l	*m*-F	H	137·6	171·3	118·1	131·4
9m	*m*-Cl	H	137·4	171·3	118·1	131·4
9n	*m*-Br	H	137·1	171·2	118·0	131·4
9o	*m*-Me	H	139·4	171·2	118·6	131·1
9p	*m*-OMe	H	138·6	171·2	118·6	131·1
10a	*p*-NO_2	Cl	136·5	170·0	118·1	131·6
10b	*p*-CN	Cl	136·9	169·8	118·2	131·4
10c	*p*-CF_3	Cl	137·6	169·8	118·5	131·3
10d	*p*-F	Cl	138·4	169·6	119·1	131·0
10e	*p*-Cl	Cl	138·2	169·9	118·9	131·1
10f	H	Cl	139·8	169·7	119·3	131·0
10g	*p*-Me	Cl	140·0	169·6	119·5	130·9
10h	*p*-OMe	Cl	139·7	169·6	119·7	130·9
10i	*p*-NMe_2	Cl	140·9	169·3	120·3	130·6
10j	*m*-NO_2	Cl	136·5	169·8	118·3	131·4
10k	*m*-CF_3	Cl	137·6	169·8	118·6	131·3
10l	*m*-F	Cl	138·2	169·8	118·8	131·2
10m	*m*-Cl	Cl	138·0	169·8	118·7	131·3
10n	*m*-Br	Cl	137·7	169·7	118·6	131·2
10o	*m*-Me	Cl	139·8	169·6	119·0	131·0
10p	*m*-OMe	Cl	139·5	169·7	119·2	130·9

[a] ^{13}C Chemical shift ranges for other carbons of the benzoyl ring: C-2″ for **9a-i** 146·8–147·5 ppm, for **9j–p** 147·0–147·3 ppm, for **10a–i** 145·4–146·3 ppm, for **10j–p** 145·7–146·0 ppm; C-3″ for **9a–i** 116·2–116·4 ppm, for **9j–p** 116·1–116·3 ppm, for **10a–i** 117·8–118·1 ppm, for **10j–p** 117·8–118·0 ppm; C-5″ for **9a–i** 116·5–116·8 ppm, for **9j–p** 116·6–116·8 ppm, for **10a–i** 120·7–121·0 ppm, for **10j–p** 120·7–121·0 ppm; C-6″ for **9a–i** 131·8–132·0 ppm, for **9j–p** 131·8–132·0 ppm, for **10a–i** 131·5–131·6 ppm, for **10j–p** 131·4–131·8 ppm· For compounds **9a–p** the assignments between C-3″/C-5″ are tentative.

Table 3. ^{13}C chemical shifts of the prepared $N^{2''}$-methyl-substituted aminobenzoylhydrazones in $CDCl_3$ or DMSO-d_6[a] (TMS as internal standard)[b]

Compound	Substituent Y	Substituent X	C=N	C=O	C-1″	C-4″
11a	*p*-NO_2	H	144·1	165·8	113·4	133·2
11b	*p*-CN	H	144·7	165·7	113·5	133·1
11c	*p*-CF_3	H	145·0	165·8	113·6	133·0
11d	*p*-F	H	145·7	165·5	113·9	132·8
11e	*p*-Cl	H	145·4	165·4	113·8	132·9
11f	H	H	146·9	165·5	113·9	132·8
11g	*p*-Me	H	146·9	165·4	114·1	132·7
11h	*p*-OMe	H	147·0	165·4	114·2	132·6
11i	*p*-NMe_2	H	147·9	165·0	114·5	132·4
11j	*m*-NO_2[c]	H	144·0	–	112·7	134·0
	m-NO_2		144·2	165·7	113·5	133·1
11k	*m*-CF_3[c]	H	145·1	166·4	112·7	133·9
	m-CF_3		144·9	165·7	113·6	133·0
11l	*m*-F[c]	H	145·5	166·5	112·9	133·7
	m-F		145·4	165·6	113·7	132·9
11m	*m*-Cl[c]	H	145·2	166·4	112·8	133·9
	m-Cl		145·0	165·6	113·7	133·0
11n	*m*-Br[c]	H	145·0	166·4	112·8	133·8
	m-Br		144·9	165·6	113·7	133·0
11f	H[c]	H	147·1	166·5	113·2	133·5
	H		146·9	165·5	113·9	132·8
11o	*m*-Me[c]	H	147·1	166·3	113·2	133·6
	m-Me		146·9	165·5	113·9	132·8
11p	*m*-OMe[c]	H	147·0	166·4	113·2	133·6
	m-OMe		146·7	165·5	113·9	132·8

[a] In DMSO-d_6 if not stated otherwise.
[b] ^{13}C chemical shift ranges for other carbons of the benzoyl ring: C-2″ for **11a–i** 150·0–150·4 ppm, for **11j–p** 151·1–151·4 ppm ($CDCl_3$), 150·2–150·3 ppm (DMSO-d_6); C-3″ for **11a–i** 110·4–110·7 ppm, for **11j–p** 111·3–111·6 ppm ($CDCl_3$), 110·5–110·7 ppm (DMSO-d_6); C-5″ for **11a–i** 113·9–114·0 ppm, for **11j–p** 114·4–114·6 ppm ($CDCl_3$), 113·9 ppm (DMSO-d_6); C-6″ for **11a–i** 128·2–128·6 ppm, for **11j–p** 127·3–127·4 ppm ($CDCl_3$), 128·4–128·6 ppm (DMSO-d_6).
[c] In $CDCl_3$.

Further, rotation around the N—N and/or C—N bonds can be restricted, as can the inversion at N^2 (*cf.* Scheme 3). Intramolecular hydrogen bonding between the carbonyl group and the *o*-amino group or the azomethine hydrogen can result in formation of relatively stable planar six-membered ring structures. It is intriguing to see whether the substitution at the benzylidenic moiety can exert electronic/structural effects on and through the —CH=N—N—C(=O)—Ph framework of these molecules.

The C=N carbons of the studied 2-aminobenzoylhydrazones resonate at roughly the same field as those of other known hydrazones and at appreciably higher field than imines, but at slightly lower field compared with cyclohexylhydrazones (Tables 1–3).[2,4] The total C=N shift range (*ca* 3–5 ppm) is about the same as that for other hydrazones.[4] However, it is slightly less than that for cyclohexylhydrazones,[4c] which seem to exhibit exceptionally large C=N shift ranges. In all cases, the substituent effect on the C=O carbon resonance is very small (shift range 0·1–0·8 ppm). The shift range for C-1″ of the benzoyl ring is 0·5–2·2 ppm and that for the C-4″ is 0·5–1·0 ppm.

Owing to the poor solubility of the compounds of set A (**8a–i**), reliable C=O ^{13}C chemical shifts were not obtained in these cases, and for **8a** even no reliable C=N shift could be recorded. The different sets of compounds measured or discussed in this work are specified in Table 4.

C=N shifts

The plots of the C=N ^{13}C chemical shifts against the substituent constants σ^+ were only roughly linear (e.g. for sets C and E, r = −0·895 or −0·896, respectively). However, the linear cross-correlations [Figure 1(a), $r = 0·997$ and (b), $r = 0·997$, respectively] for the C=N shifts between *para*-substituted sets C and A or C and E with a slope of unity (1·01 ± 0·03 and 0·98 ± 0·03, respectively) suggest that the chemical shifts in these cases are determined by similar substituent effects. Thus, N^2-methyl or 5″-chloro substitution does not seem to exert any specific contribution on the transmission of the electronic effects in question. The cross-correlations between the C=N ^{13}C chemical shifts of the *para*-substituted 2-aminobenzoylhydrazones (set C) and the

Table 4. Structures of the different hydrazone and imine sets

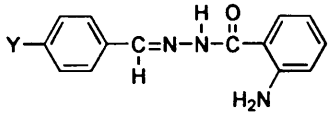
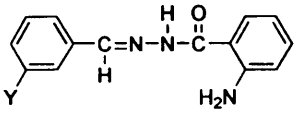
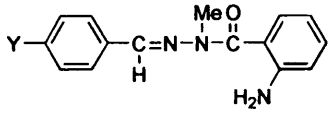
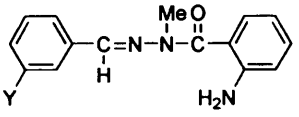
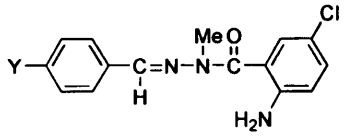
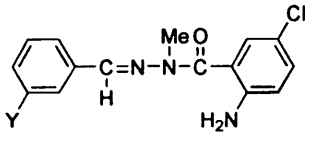
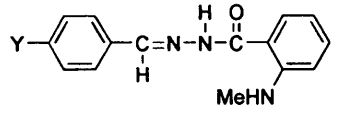
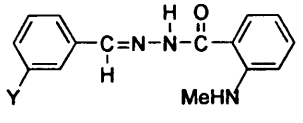
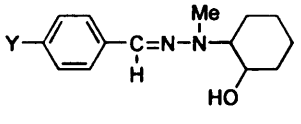
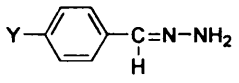
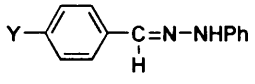
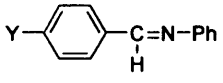
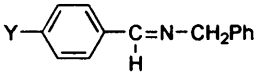
Set		Ref.
A		this work
B		this work
C		this work
D		this work
E		this work
F		this work
G		this work
H		this work
I		4c

Table 4. (*continued*)

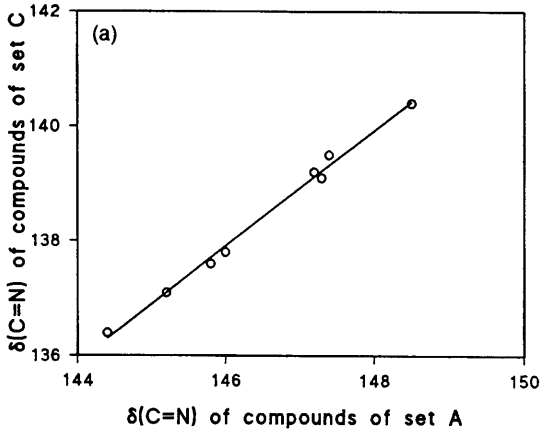
Set		Ref.
J		5b/4c
K		5b/4c; 12/this work
L		2b,c/4c
M		2b,c/4c

N^2-unsubstituted (set J)[4b], or N^2-alkyl-(set I)[4c] or N^2-phenyl (set K)[4b]-substituted hydrazones are given in Figures 2–4. Although the trends are closely similar in every case, it can be seen that the C=N shifts of 2-aminobenzoylhydrazones are less sensitive to substituent effects than those of N^2-unsubstituted or N^2-alkyl-substituted hydrazones [Figures 2 (slope = 0·79 ± 0·03) and 3 (slope = 0·65 ± 0·04)]. Interestingly, in the case of N^2-2-aminobenzoyl- *vs* N^2-phenylhydrazones (Figure 4), the slope is close to unity (0·95 ± 0·03). This suggests that the influence of the phenyl and 2-aminobenzoyl groups on the response of the probe carbon to substituent effects is similar.

To obtain a more detailed insight into the substituent effects prevailing in benzoylhydrazones, a DSP approach was chosen. The DSP equation (1) gave correlations with excellent or good precision (Table 5). Accordingly, it can be deduced that the substituent effects are electronic in origin.

Inductive effects

The high negative ρ_I values (Table 5) mean the reverse behaviour of the inductive SCS effect: electron-withdrawing substituents shield the probe carbon. This is best interpreted by the π-polarization mechanism, which has been explained in detail elsewhere.[1b,1e,8] The substituent dipole induces the localized polarization of each π-unit in the side-chain. An electron-withdrawing substituent of the aromatic ring therefore results in an increase in the π-electron density at some carbon sites, as shown in Scheme 4 for the present compounds. This mechanism agrees with electron density calculations performed for some aromatic side-chain derivatives.[1b,8a,b] The concept of π-polarization does not preclude the extended polarization of a conjugated system. The more negative ρ_I values for the *meta* series compared with the *para* series (set D *vs* set C, set F *vs* set E and set H *vs* set G, Table 5) support the assumed through-space transmission of the π-polarization effect.[1b] The more highly negative values of ρ_I for hydrazones compared with those for imines can be attributed to the easier polarization of the C=N bond in the former case (*cf.* Table 6). Further, according to the data in Table 6, the ρ_I values are sensitive to substitution of hydrazones at N^2. The variation of ρ_I probably reflects the availability of the electron pair of N^2 for interaction with the conjugated π-electron system. A ρ_I value of −4·6 was earlier estimated for substituted benzaldoximes possessing an electron-withdrawing oxygen atom on the 'imine' nitrogen.[1b] For sets A–H and K, the ρ_I values are close to each other. Thus, as expected for the cross-correlation shown in Figure 4, insertion of the carbonyl group between N^2 and the phenyl ring does not seem to change markedly the transmission of the electronic effects to C=N. This suggests that the contributions of the amide resonance structures with partial C=N double bond character are not significant in benzoylhydrazones (see Scheme 2, structure **13**). The effective contribution of structure **13** would undoubtedly affect the electronic environment at the imine carbon. The inductive effect resulting from substitution of the *N*-alkyl group in amides for the more electronegative *N* atom in benzoylhydra-



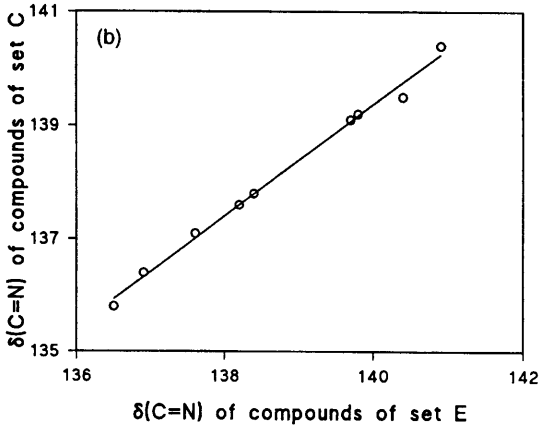


Figure 1. Cross-correlations between C=N ^{13}C chemical shifts of (a) set C and set A and (b) set C and set E

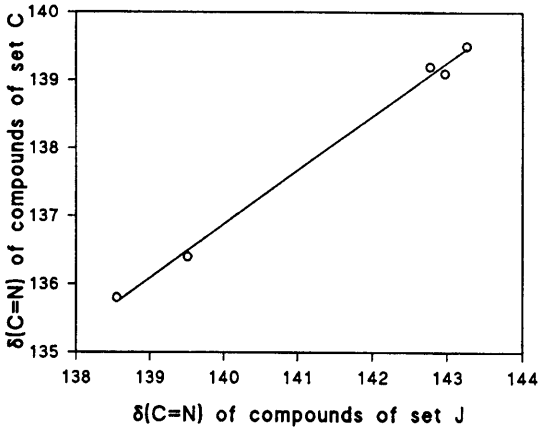


Figure 2. C=N ^{13}C chemical shifts for compounds of set C *vs* those for set J

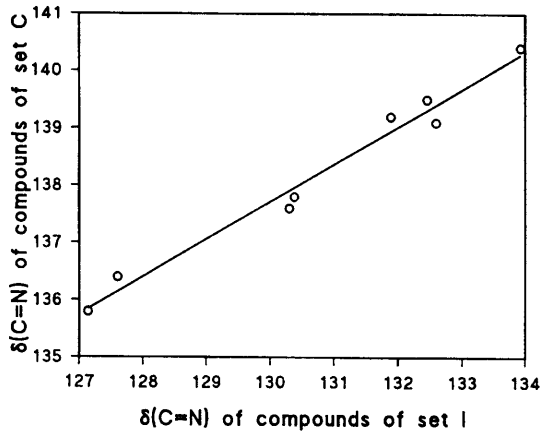


Figure 3. C=N ^{13}C chemical shifts for compounds of set C *vs* those for set I

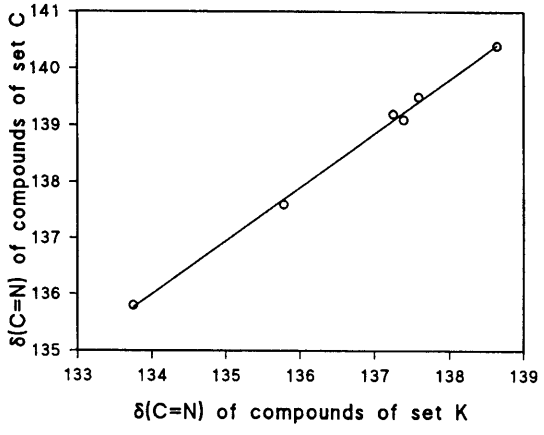


Figure 4. C=N ^{13}C chemical shifts for compounds of set C *vs* those for set K

zones (sets A–H) could be responsible for the destabilization of structures such as **13**.

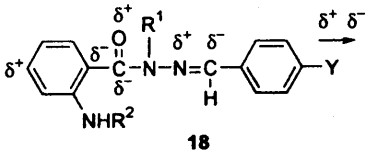
Resonance effects

The ρ_R values obtained for hydrazones are markedly more negative than those obtained for imines (*cf.* Table 7). Further, there seems to be a variation within the hydrazones, and the least negative ρ_R values are observed for benzoylhydrazones. Interpretation of the ρ_R values obtained by DSP analysis is a complicated task. For a wide range of *para*-substituted benzene derivatives containing a C=C, C=O, C≡C or C≡N system with the sp^2 or sp hybridized carbon in the α-position, a nearly constant ρ_I value of $-2{\cdot}7 \pm 0{\cdot}3$ was obtained in $CDCl_3$.[1b] However, it has been found that ρ_R may vary significantly and it may be positive or

Table 5. DSP analysis of side-chain SCS data for sets A (compounds **8a–i**), B (compounds **8f, j–p**), C (compounds **9a–i**), D (compounds **9f, j–o**), E (compounds **10a–i**), F (compounds **10f, j-p**), G (compounds **11a–i**) and H (compounds **11f, j-p**) according to equation (1).[a]

Parameter	Set A	Set B	Set C	Set D	Set E	Set F	Set G[e]	Set H	Set H[e]
C=N carbon									
ρ_I	−4·2	−4·2	−4·6	−4·8	−4·6	−4·7	−3·8	−4·5	−4·2
ρ_R	−2·0	−1·0	−1·8	−1·4	−1·8	−1·5	−1·6	−1·2	−1·0
Scale[b]	BA	+	BA	BA	BA	BA	BA	BA	BA
SD[c]	0·12	0·18	0·088	0·16	0·10	0·20	0·16	0·21	0·22
f[d]	0·08	0·12	0·05	0·08	0·06	0·11	0·11	0·12	0·14
C=O carbon									
ρ_I			0·2		0·3		0·4		
ρ_R			0·3		0·2		0·3		
Scale[b]			+		+		+		
SD[c]			0·070		0·090		0·086		
f[d]			0·35		0·46		0·36		
C-1" carbon									
ρ_I	−1·0	−0·9	−1·2	−1·3	−1·6	−1·5	−0·6	−0·6	−0·6
ρ_R	−0·9	−0·4	−1·3	−0·4	−1·3	−0·4	−0·7	−0·3	−0·2
Scale[b]	BA	BA	BA	+	BA	BA	BA	0	BA
SD[c]	0·048	0·046	0·084	0·039	0·023	0·18	0·042	0·027	0·025
f[d]	0·12	0·13	0·13	0·09	0·03	0·30	0·13	0·08	0·11
C-4" carbon									
ρ_I	0·6	0·5	0·7	0·7	0·6	0·6	0·4	0·8	0·4
ρ_R	0·7	0·1	0·7	0·1	0·8	0·2	0·5	0·2	0·2
Scale[b]	0	−	0	+	0	+	BA	BA	BA
SD[c]	0·043	0·024	0·060	0·039	0·054	0·055	0·024	0·085	0·033
f[d]	0·15	0·11	0·19	0·14	0·18	0·24	0·10	0·28	0·20

[a] In $CDCl_3$ if not stated otherwise.
[b] The correlation was examined for each of the four resonance scales (σ_R^-, σ_R^0, σ_R^{BA} *and* σ_R^+) and the results for that with the lowest SD are shown.
[c] Standard deviation of the correlation.
[d] f = SD/RMS, where RMS = root mean square of the data.
[e] In DMSO-d_6.



18

Scheme 4

negative. For instance, ρ_R is −1·1 for ethyl benzoates[8c] and for benzonitriles,[9] whereas it is +0.8 for acetophenones.[8c] For carbonyl compounds, it has been suggested that a positive ρ_R is observed if the main resonance interaction is **20**↔**21**, while the predominant interaction **19**↔**21** leads to a negative ρ_R (Scheme 5).[8c] In the former case the α-carbon is a conjugating site, whereas in the latter it is a non-conjugating site.

The field-transmitted π-polarization effect has been used to explain the negative ρ_R values obtained for cases where the through-conjugation effect is not possible, but

Table 6. Comparison of ρ_I values of C=N carbon SCS data for condensation products of substituted benzaldehydes (cf. Table 4) resulting in structurally different C=N bonds[a]

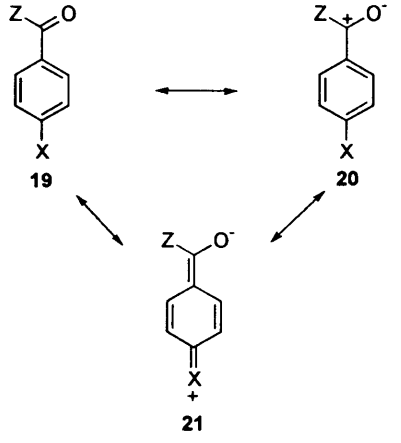
Set	Series	ρ_I
I	N^2-Alkylhydrazones, *para* series	−6·2
J	N^2-Unsubstituted hydrazones, *para* series	−5·5
	N^2-Benzoyl hydrazones	
A	*para* Series	−4·2
C		−4·6
E		−4·6
G		−3·8[b]
B	*meta* Series	−4·2
D		−4·8
F		−4·7
H		−4·5; −4·2[b]
K	N^2Phenylhydrazones, *para* series	−4·6; −3·8[b]
L	Imines, *para* series	−4.1; −3.9
M		-3·6

[a] In $CDCl_3$ if not stated otherwise.
[b] In DMSO-d_6.

Table 7. Comparison of ρ_R values of C=N carbon SCS data for condensation products of substituted benzaldehydes (cf. Table 4) resulting in structurally different C=N bonds[a]

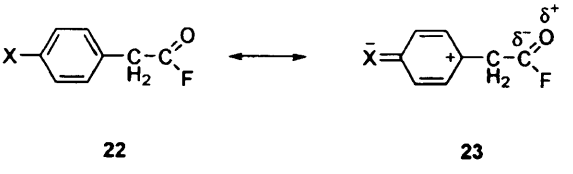
Set	Series	ρ_R
I	N^2-Alkylhydrazones, *para* series	−4·9 (σ_R^0)
J	N^2-Unsubstituted hydrazones, *para* series	−2·7 (σ_R^{BA})
	N^2-Benzoyl hydrazones	
A	*para* Series	−2·0 (σ_R^{BA})
C		−1·8 (σ_R^{BA})
E		−1·8 (σ_R^{BA})
G		−1·6 (σ_R^{BA})[b]
B	*meta* Series	−1.0 (σ_R^+)
D		−1·4 (σ_R^{BA})
F		−1·5 (σ_R^{BA})
H		−1·2 (σ_R^{BA}); −1·0 (σ_R^{BA})[b]
K	N^2-Phenylhydrazones, *para* series	−3·1 (σ_R^0); −1·9 (σ_R^{BA})[b]
L	Imines	−0·71 (σ_R^-); −0·53 (σ_R^-)
M		−0·7 (σ_R^0)

[a] In $CDCl_3$ if not stated otherwise.
[b] In DMSO-d_6.



Scheme 5

a significant negative SCS component proportional to σ_R is observed. Resonance delocalization induces a dipole in an aromatic ring and this is able to polarize the π-unit in question. The magnitude of the dipole induced in the aromatic ring is proportional to σ_R, leading to reverse substituent effects. This secondary resonance effect has been used to explain negative ρ_R values obtained for *meta*-substituted side-chain carbonyl derivatives of benzene[8c] and for *para*-substituted phenylacetyl fluorides, where the polarizable π-unit is isolated from the benzene ring (Scheme 6).[10] Obviously, the variation in the magnitude and sign of the observed ρ_R value is determined by different contributions of the through-conjugation effect and the field-transmitted resonance – polar effect.[11]



22 23

Scheme 6

The highly negative ρ_R values for the C=N site of all hydrazones studied, and especially the somewhat less negative ρ_R values for the *meta* series compared with those of the *para* series (Table 5), suggest that for hydrazones the field-transmitted resonance effect is significant. Further, if the analogy with the carbonyl compounds prevails, an increased contribution of structure **14** in Scheme 2 can be assumed.

Solvent effects

The use of a non-inert solvent is not recommended in electronic transmission studies by means of NMR measurements because of the possibilities of specific solute–solvent interactions.[1b] However, owing to the poor solubility for the compounds not bearing methyl substitution at N^2, besides $CDCl_3$ DMSO-d_6 was also used as solvent in two cases (sets G and H). The values in Table 3 show that the C=N carbons resonate at somewhat higher field in DMSO-d_6 as compared with $CDCl_3$, and the solvent also slightly affects the shift range. The calculated values of ρ_I and ρ_R for set H in DMSO-d_6 are less negative than in $CDCl_3$, indicating a weaker polarization of the C=N bond or a smaller shift–charge ratio in the former, more polar solvent. With the DSP approach, we also analysed the ^{13}C

chemical shift data for the C=N carbons of some *para*-substituted benzaldehyde phenylhydrazones, given by Barchiesi *et al.*[12] in DMSO-d_6. Even if the set in question is not wide (p-NMe_2, p-OMe, H, p-Br and p-NO_2), both electron-donating and electron-withdrawing substituents are included and the fit of the correlation is excellent ($f = 0{\cdot}02$). The values obtained, $\rho_I = -3{\cdot}8$ and $\rho_R = -1{\cdot}9$, may be compared with the values $\rho_I = -4{\cdot}6$ and $\rho_R = -3{\cdot}1$ previously calculated by us[4c] with the aid of the shift data given by Gordon *et al.*[4b] for *para*-substituted benzaldehyde phenylhydrazones in $CDCl_3$ (*cf.* Tables 6 and 7, set K). In that case, the solvent effect is in the same direction as for the present benzoylhydrazones, but the change is more pronounced. Further, for the ^{13}C SCS correlations of the carbonyl carbon of *para*-substituted methyl benzoates in $CDCl_3$, $\rho_I = -2{\cdot}6$ and $\rho_R = -0{\cdot}95$,[11a] whereas in DMSO-d_6, $\rho_I = -2{\cdot}05$ and $\rho_R = -0{\cdot}38$.[11b]

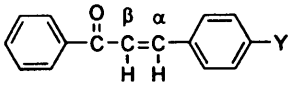
As far as we know, no systematic studies have been reported on the effect of the solvent on π-polarization. Owing to its assumed through-space transmission mechanism, it is understandable that the magnitude of the π-polarization effect may be changed by the dielectric properties of the medium, in harmony with the above results. The good fit of the DSP equation also in DMSO-d_6 (*cf.* Table 5) suggests that there are no specific interactions between the solvent and some single substituent. The solvent used may, however, affect the contribution of intramolecular hydrogen bonds and this can be reflected in the SCS behaviour.

C=O, C-1″ and C-4″ shifts

The shift range of the C=O carbon in a particular series varies from 0·1 ppm to 0·8 ppm (Tables 1–3). Because of the weak substituent effects, a reasonable DSP analysis was possible only for three *para* series (sets C, E and G) and even in these cases the ρ_I and ρ_R values must be considered as tentative only. It is seen that the SCS behaviour is normal, *i.e.* electron-withdrawing substituents cause downfield effects. In other words, the π-polarization mechanism, if present at all, is masked by other effects. Owing to the lack of conjugation, however, extended polarization is not possible at the C=O site. The absence or a minor role of π-polarization suggests a decreased π-bond character of the C=O bond and a direct-field effect involving the interaction of the carbon site in question with the substituent dipole. In contrast with the similar ρ_I values of the C=N ^{13}C chemical shift correlations for N^2-phenylhydrazones and N^2-2-aminobenzoylhydrazones (Table 6), the decreased π-bond order of the C=O bond indicates some contribution of structures such as **13** (Scheme 2). An alternative explanation for the C=O SCS behaviour, suggested by a referee, is that the low positive ρ_I and ρ_R values could be caused by the different orientation of the carbonyl group with respect to the electric field generated by the substituent (*cf.* Structure **17**).

Interestingly, despite the lack of noticeable π-polarization of the C=O bond, the C-1″ probe of the terminal π-unit of the system studied, the phenyl ring of the benzoyl group displays SCS behaviour consistent with the prevailing π-polarization. The polarization of the π-unit leads to negative ρ_I and ρ_R values at C-1″ sites (Table 5). With the exception of one of the *meta* series (set F), the fit of the correlation is good, indicating that the studied substituent effects are electronic in origin. The increased distance of the substituents from the probe site is seen to affect the magnitudes of ρ_I and ρ_R. In the *meta*-substituted series, sets B, D, F and H, a decreased contribution of resonance effect is observed. At the C-4″ site, the expected trend according to the π-polarization mechanism is also clearly seen, *i.e.* the electron-withdrawing substituents cause downfield shifts (*cf.* Scheme 4) and positive ρ_I and ρ_R values are obtained by the DSP analysis (Table 5). Again, the increased distance from the benzylidenic substituent decreases the ρ-values. For the *meta* series very small ρ_R values are observed.

The evaluation of the substituent effects separately on different probe carbons as described above yields valuable information on the transmission of the electronic effects along the hydrazone side-chain. It is interesting to see that a distant benzylidenic substituent may extend its polarizing effect by the π-polarization mechanism up to the phenyl π-unit over two nitrogen atoms along a non-conjugated side-chain. This supports the concept of the through-space transmission of the effect in question.[1b] Previously, comparable results were obtained by ^{13}C chemical shift analysis of the conju-



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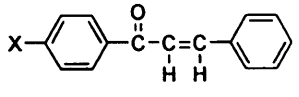

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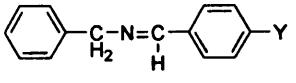

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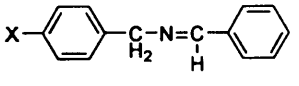

27

gated chalcones **24** and **25**.[8c] For example, negative ρ_I values of −4·0, −1·0 and −0·7 for C-α, C=O and C-1″, respectively, and positive ρ_I values of 4·5 and 0·8 for C-β and C-4″, respectively, were observed in series **24**. Likewise, results obtained with series **26** and **27** are consistent with our data that an intervening π-system is not needed to transmit the π-polarization effect.[8c]

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