Multinuclear (^{1}H, ^{13}C and ^{15}N) Magnetic Resonance Spectroscopy and Substituent Effects on *N*-Phenoxyethylanilines

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^{1}H, ^{13}C and ^{15}N NMR spectra of twenty substituted *N*-phenoxyethylanilines **1–20** were completely and unambiguously assigned using a combination of both homo- and heteronuclear (gs-COSY), ^{1}H detected heteronuclear one-bond (gs-HMQC) and long-range (gs-HMBC) gradient-selected correlation experiments. Correlations between chemical shifts and substituent constants are analyzed separately for both phenyl rings using variable substituents *para* to the fixed substituent -OCH$_2$CH$_2$NHC$_6$H$_5$ (series I) and -NHCH$_2$CH$_2$OC$_6$H$_5$ (series II), respectively. The correlation coefficient for chemical shifts *vs.* a linear combination of inductive and resonance substituent constants is high and improves when only the six values, corresponding to each *para*-monosubstituted series, were used. For nitrogen chemical shifts excellent linear dependences were obtained. The results show that the ethylene chain is not able to transmit the substituent effect from one aromatic ring to the other.

Introduction

Carbon-13 chemical shift measurements have been used extensively for studying the electronic substituent effects of aromatic systems. [1–9] The utility of this technique is based on the linear dependence between the measured substituent-induced chemical shifts (SCS) and the calculated electron densities. Commonly, SCS are analyzed by means of single relationships with the appropriate Hammett substituent constant or another single parameter approach [1] and by means of a dual substituent parameter (DSP) equation [10] (1) where the substituent parameters, σ_I and σ_R, are claimed to reflect the substituent field and resonance effects, respectively. The ϱ_I and ϱ_R terms are susceptibility constants which are characteristic of the measured position. [11]
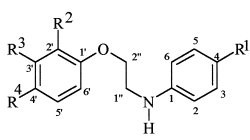
$$\delta_{SCS} = \varrho_I\sigma_I + \varrho_R\sigma_R \qquad (1)$$

For anilines, [12,13] the closely related *N*-arylglycines and their esters, [4] the ^{15}N chemical shift are affected by the substituent present, showing effects similar to those observed for carbon chemical shifts [4] and being linearly dependent of both field/inductive and resonance effects on the substituent.[2–4]

Other spectroscopic methods have been employed to study conformers of *N*-phenoxyethylanilines and homologues in solution. In some nitro-substituted *N*-phenoxyalkylanilines, across-space intramolecular charge-transfer (CT) interaction between the nitrophenyloxy and arylamino groups have been reported. [14] Moreover, to explain the results obtained, some other forces than CT interaction, such as intramolecular hydrogen-bond interaction, were proposed to be preponderant and responsible in bringing the two phenyl groups close together. [14,15]

We were interested in the preparation, acid-base properties and mass spectrometry of *N*-phenoxyethylanilines [16–18] as they show biological activities of various types. [19–22] In the course of NMR studies on such derivatives we report in this paper the complete ^{1}H, ^{13}C and ^{15}N chemical shift assignment obtained from two-dimensional NMR techniques (H,H COSY and H,C COSY) including HMBC and HMQC for substituted *N*-phenoxyethylanilines **1–20** (Figure 1). With the aim to search for evidences of some kind of intramolecular interaction and since no similar studies have

	R^1	R^2	R^3	R^4
1	H	H	H	H
2	H	H	H	OCH$_3$
3	H	H	H	Me
4	H	H	H	Cl
5	H	H	H	Br
6	H	H	H	NO$_2$
7	H	Br	H	Cl
8	H	OCH$_3$	H	H
9	H	Br	H	H
10	H	NO$_2$	H	H
11	H	H	NO$_2$	H
12	OCH$_3$	H	H	H
13	Me	H	H	H
14	Cl	H	H	H
15	NO$_2$	H	H	H
16	OCH$_3$	H	H	Cl
17	OCH$_3$	NO$_2$	H	H
18	Cl	OCH$_3$	H	H
19	Cl	Br	H	H
20	Br	OCH$_3$	H	H

Fig. 1. Structures and numbering of the compounds studied.

been carried out, we made use of their chemical shifts in order to correlate them with substituent effects. Single and dual substituent parameter (DSP) correlations were established and their results are discussed.

Results and Discussion

The 400.1 MHz ^{1}H NMR spectra of *N*-phenoxyethylanilines showed well resolved multiplets for almost every signal, greatly facilitating the proton assignments. For the amino hydrogen a broad singlet is usually present. Aromatic resonance of the *para* derivatives constitute two AA′XX′ spin systems with characteristic multiplet patterns. Their coupling constants were calculated as is outlined in Günther's book. [23] The heteronuclear coupling constants [^{1}J(^{13}C,^{1}H)] of the methylene groups could be easily determined from their satellite signals in the ^{1}H NMR spectrum since these resonances appear in a cleaner area of the spectrum. ^{1}H NMR resonances were completely

and unambiguously assigned on the basis of the proton-proton connectivity network (established from the gs-COSY spectra), homonuclear coupling constants and signal intensities for compounds **1**, **17** and **20**. The ^{13}C NMR assignments of the protonated carbons followed from the analysis of the one-bond heteronuclear correlation data (HMQC) for the same compounds named above (Figure 2). The quaternary carbons were unequivocally determined from the long-range correlation responses observed with the previously assigned ^{1}H signals in the HMBC diagrams. For all other carbons atoms, well-established increment rules were used. Finally attached proton test (APT) spectra were used to distinguish the overlapping resonance of proton-bearing and quaternary carbon in some cases.
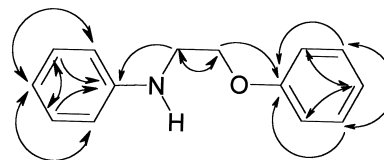

Fig. 2. Long range proton-carbon connectivity network found in the HMBC spectrum of *N*-phenoxyethylaniline **1**; arrows point from H to C; double arrows indicate both H···C correlations.

The ^{1}H, ^{13}C and ^{15}N NMR chemical shifts are summarized in Tables 1, 2 and 3, respectively. In Figure 2 all the connectivities observed in the HMBC spectrum of *N*-phenoxyethylaniline **1** are shown by arrows.

Single and Dual Substituent Parameter (DSP) Correlations

The following substituent constant data were taken from the literature: SCS, [24] σ and σ_I, [25] σ^-, [26] σ^o, [27] σ_R and σ_F, [28] σ_R^o, [2] and σ^-_R. [10]

The ^{13}C chemical shifts for the R^4- (series I; compounds **1–6**) and R^1-monosubstituted *N*-phenoxyethylanilines (series II, compounds **1**, **12–15**) were correlated with the appropriate substituent chemical shifts (SCS) for monosubstituted benzenes (Lynch plots [1]) using variable substituent R^4 (series I) and R^1 (series II) *para* to the fixed substituent -OCH$_2$CH$_2$NHC$_6$H$_5$ and -NHCH$_2$CH$_2$OC$_6$H$_5$, respectively (see Figure 1).

Table 1. ¹H NMR spectral data for N-phenoxyethylanilines **1–20**[a,b,c,d].

	H-2,6	H-3,5	H-4	H-2'	H-3'	H-4'	H-5'	H-6'	2''	1''	NH
1	6.67	7.19	6.74	6.92	7.29	6.96	7.29	6.92	4.15	3.52	ca. 4.1
	d; 8.6	ddd; 8.5, 7.4, 2.1	dt; 7.3, 1.0	d; 8.7	ddd; 8.8, 7.4, 2.4	dt; 7.3, 1.0	ddd; 8.8, 7.4, 2.4	d; 8.7	t; 5.3	t; 5.3	br.s
2	6.67	7.19	6.73	6.84	6.84		6.84	6.84	4.11	3.49	ca. 4.1
	dᵉ; 8.6	ddᵉ; 8.5, 7.4	dt; 7.3, 1.0			–			t; 5.3	t; 5.3	br.s
3	6.66	7.18	6.73	6.81	7.07		7.07	6.81	4.12	3.49	ca. 3.8
	ddᵉ; 8.6, 1.1	ddᵉ; 8.6, 7.3	dt; 7.4, 1.1	9.0, 2.5, 0.6	ddᵉ; 8.8, 0.6	–	ddᵉ; 8.8, 0.6	9.0, 2.5, 0.6	t; 5.3	t; 5.3	br.s
4	6.67	7.20	6.74	6.84	7.23		7.23	6.84	4.12	3.52	4.06
	dᵉ; 8.6	ddᵉ; 8.6, 7.4	dt; 7.4, 1.0	9.7, 2.9, 0.7	9.8, 2.9, 0.6	–	9.8, 2.9, 0.6	9.7, 2.9, 0.7	t; 5.2	t; 5.1	br.s
5	6.67	7.20	6.74	6.79	7.37		7.37	6.79	4.11	3.46	ca. 4.7
	dᵉ; 8.7	ddᵉ; 8.7, 7.3	dt; 7.3, 1.0	9.6, 2.8, 0.7	9.6, 2.8, 0.7	–	9.6, 2.8, 0.7	9.6, 2.8, 0.7	t; 5.3	t; 5.3	br.s
6	6.69	7.21	6.77	6.97	8.19		8.19	6.97	4.24	3.60	4.17
	dᵉ; 8.6	ddᵉ; 8.6, 7.4	dt; 7.4, 1.0	10.1, 2.8, 0.7	10.1, 2.8, 0.7	–	10.1, 2.8, 0.7	10.1, 2.8, 0.7	t; 5.3	t; 5.3	br.s
7	6.69	7.20	6.75		7.53		7.20	6.80	4.17	3.56	4.15
	dᵉ; 8.7	ddᵉ; 8.5, 7.4	dt; 7.3, 1.0	–	d; 2.5	–	dd; 8.8, 2.4	d; 8.8	t; 5.2	t; 5.2	br.s
8	6.67	7.18	6.72		6.90	6.95	6.90	6.92	4.22	3.53	ca. 3.9
	dd; 8.6, 1.0	ddᵉ; 8.5, 7.4	dt; 7.4, 1.0	–					5.3	5.3	br.s
9	6.70	7.20	6.74		7.54	6.85	7.24	6.90	4.21	3.56	4.27
	dᵉ; 8.6	ddᵉ; 8.5, 7.3	dt; 7.3, 1.1	–	dd; 7.9, 1.6	ddd; 7.9, 7.4, 1.4	ddd; 8.2, 7.4, 1.6	dd; 8.2, 1.4	t; 5.3	t; 5.3	br.s
10	6.71	7.20	6.74		7.86	7.05	7.51	7.07	4.30	3.58	4.38
	dᵉ; 8.5	ddᵉ; 8.4, 7.4	br.t; 7.3	–	dd; 8.1, 1.6	br.t; 8.0	ddd; 8.5, 7.4, 1.7	br.d; 8.4	t; 5.1	t; 5.1	br.s
11	6.69	7.21	6.75	7.73		7.83	7.42	7.23	4.22	3.59	4.04
	ddᵉ; 8.6, 1.0	ddᵉ; 8.5, 7.3	dt; 7.4, 1.0	t; 2.3	–	ddd; 8.2, 2.1, 0.9	t; 8.3	ddd; 8.3, 2.1, 0.9	t; 5.2	t; 5.2	br.s
12	6.79	6.65		6.92	7.29	6.94	7.29	6.92	4.15	3.47	ca. 3.8
	9.6, 2.9, 0.7	9.6, 2.9, 0.7	–	dᵉ; 8.8	ddd; 8.8, 7.4, 2.2	dt; 7.3, 1.0	ddd; 8.8, 7.4, 2.2	dᵉ; 8.8	t; 5.2	t; 5.2	br.s
13	6.60	7.00		6.91	7.28	6.97	7.28	6.91	4.14	3.49	3.83
	8.9, 2.3, 0.5	br.d; 7.9	–	ddᵉ; 8.8, 1.0	ddᵉ; 8.8, 7.4	dt; 7.4, 1.0	ddᵉ; 8.8, 7.4	ddᵉ; 8.8, 1.0	t; 5.3	t; 5.3	br.s

	H-2/6	H-3/5	H-2'	H-3'	H-4'	H-5'	H-6'	2''	1''	NH
14	6.59	7.13	6.92	7.29	6.97	7.29	6.92	4.15	3.49	4.12
	9.5, 2.7, 0.6	9.5, 2.7, 0.6	dᵉ; 8.8	ddᵉ; 8.8, 7.4	dd; 7.4, 1.0	ddᵉ; 8.8, 7.4	dᵉ; 8.8	t; 5.2	t; 5.2	br. s
15	6.60	8.09	6.92	7.30	6.99	7.30	6.92	4.19	3.63	4.95
	9.9, 2.7, 0.7	9.9, 2.7, 0.7	d; 8.8	dd; 8.8, 7.4	dt; 7.4, 1.0	dd; 8.8, 7.4	d; 8.8	t; 5.2	t; 5.2	br. s
16	6.79	6.65	6.83	7.23		7.23	6.83	4.10	3.46	ca. 3.7
	9.5, 2.9, 0.6	9.5, 2.9, 0.6	9.6, 2.8, 0.6	9.6, 2.8, 0.6	–	9.6, 2.8, 0.6	9.6, 2.8, 0.6	t; 5.2	t; 5.2	br. s
17	6.80	6.69		7.87	7.05	7.52	7.07	4.29	3.53	4.14
	9.7, 2.9, 0.6	9.7, 2.9, 0.6	–	dd; 8.2, 1.6	ddd; 8.2. 7.4, 1.1	ddd; 8.4, 7.4, 1.6	dd; 8.4, 1.0	t; 5.1	t; 5.0	br. s
18	6.57	7.12		6.90	6.96	6.90	6.91	4.20	3.48	4.31
	9.5, 2.7, 0.6	9.5, 2.7, 0.6	–					t; 5.1	t; 5.0	br. s
19	6.62	7.14		7.54	6.86	7.25	6.90	4.20	3.53	ca. 3.7
	9.5, 2.7, 0.6	9.5, 2.7, 0.6	–	dd; 7.9, 1.6	ddd; 7.9. 7.4, 1.4	ddd; 8.1, 7.4, 1.6	dd; 8.1, 1.4	t; 5.2	t; 5.2	br. s
20	6.53	7.25		6.91	6.97	6.91	6.92	4.20	3.48	4.34
	9.6, 2.7, 0.6	9.6, 2.7, 0.6	–					t; 5.4	br.t; 4.8	br. s

[a] δ(¹H) in ppm relative to TMS; CDCl₃ as solvent; coupling constants [J(¹H,¹H)] in Hz; multiplicities, s: singlet, d: doublet, dd: double doublet, ddd: double double doublet, t: triplet, dt: double triplet, br.s: broad singlet, br.t: broad triplet.

[b] ¹H chemical shifts of the substituents of the *N*-phenoxyethylanilines: **2**, 3.76 (OCH₃); **3**, 2.28 (CH₃); **8**, 3.87 (OCH₃); **12**, 3.75 (OCH₃); **13**, 2.24 (CH₃); **16**, 3.74 (OCH₃); **17**, 3.75 (OCH₃); **18**, 3.86 (OCH₃); **20**, 3.86 (OCH₃).

[c] The aromatic protons of the phenyl ring bearing a OCH₃ substituent in R² or R⁴ positions constitute ABCD (R²) or AA'BB' (R⁴) spin systems which were not analyzed further.

[d] The aromatic protons in the *para*-substituted phenyl ring form AA'XX' spin systems, are described without multiplicity.

[e] Signal with long-range coupling.

Table 2. ^{13}C NMR chemical shifts, heteronuclear coupling constants[a] of methylene groups of compounds **1–20**[bcd].

	C-1	C-2/6	C-3/5	C-4	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′	C-1″	C-2″	$^1J_{C1'-H}$	$^1J_{C2'-H}$
1	147.8	113.2	129.3	117.9	158.6	114.6	129.5	121.1	129.5	114.6	43.4	66.4	136.3	144.2
2	147.9	113.1	129.3	117.8	152.8	115.6	114.7	154.1	114.7	115.6	43.4	67.2	135.9	143.9
3	147.9	113.2	129.3	117.8	156.5	114.4	130.0	130.3	130.0	114.4	43.4	66.6	136.5	143.9
4	147.7	113.2	129.4	118.0	157.2	115.8	129.4	126.0	129.4	115.8	43.2	66.8	136.1	144.2
5	147.7	113.2	129.3	118.0	157.8	116.3	129.3	113.3	129.3	116.3	43.2	66.8	136.3	144.1
6	147.3	113.2	129.4	118.3	163.6	114.5	125.9	141.8	125.9	114.5	43.1	67.3	136.5	145.1
7	147.7	113.4	129.4	118.1	153.9	113.0	132.9	126.6	128.3	114.3	43.1	68.3	136.4	140.2
8	148.1	113.2	129.3	117.7	148.0	150.0	112.1	122.0	120.9	114.9	43.3	68.3	135.2	144.7
9	147.8	113.4	129.3	118.0	154.9	112.5	133.4	122.4	128.5	113.8	43.2	67.9	136.1	145.2
10	147.6	113.5	129.3	118.1	152.1	140.0	125.8	120.8	134.3	114.9	42.9	68.2	136.9	145.7
11	147.3	113.0	129.2	117.9	159.0	108.7	149.0	115.9	129.8	121.4	42.8	67.0	136.4	144.7
12	142.0	114.7	114.9	152.5	158.7	114.6	129.5	121.1	129.5	114.6	44.4	66.5	135.8	143.9
13	144.1	111.9	128.3	125.6	157.2	113.1	128.0	119.6	128.0	113.1	42.3	65.0	135.9	143.9
14	146.5	114.2	129.1	122.4	158.5	114.5	129.6	121.2	129.6	114.5	43.4	66.2	136.9	144.4
15	153.1	111.3	126.4	138.4	158.2	114.5	129.7	121.5	129.7	114.5	42.7	65.9	137.4	144.7
16	141.9	114.7	114.9	152.6	157.3	115.8	129.4	125.9	129.4	115.8	44.3	66.9	135.9	144.2
17	141.7	114.9	115.1	152.7	152.1	139.7	125.8	120.8	134.3	114.8	44.1	68.2	135.9	144.0
18	146.6	114.2	129.1	122.2	147.9	150.0	112.0	122.2	120.9	115.0	43.4	68.2	136.0	144.9
19	146.3	114.6	129.1	122.7	154.9	112.6	133.4	122.6	128.6	113.9	43.4	67.7	135.4	145.0
20	147.0	114.7	131.9	109.2	147.9	150.0	112.0	122.2	120.9	115.0	43.3	68.2	136.4	145.1

[a] Coupling constant in Hz.
[b] $\delta(^{13}C)$ in ppm relative to TMS; CDCl$_3$ as solvent.
[c] ^{13}C chemical shifts of the substituents of the *N*-phenoxyethylanilines: **2**, 55.7 (OCH$_3$); **3**, 20.5 (CH$_3$); **8**, 55.9 (OCH$_3$); **12**, 55.8 (OCH$_3$); **13**, 18.9 (CH$_3$); **16**, 55.8 (OCH$_3$); **17**, 55.8 (OCH$_3$); **18**, 55.8 (OCH$_3$); **20**, 55.8 (OCH$_3$).
[d] Multiplicity of signals of carbon atoms deduced by analysis of ^{13}C APT spectra.

Table 3. ^{15}N NMR spectral data[a,b] for *N*-phenoxyethyl-anilines **1–20**.

	δ(NH)	$\Delta\delta$(NH)	δ(NO$_2$)
1	−319.0	0.0	–
2	−319.5	−0.5	–
3	−319.4	−0.4	–
4	−319.8	−0.8	–
5	−319.9	−0.9	–
6	−319.8	−0.8	−10.61
7	−320.1	−1.1	–
8	−319.0	0.0	–
9	−319.8	−0.8	–
10	−320.3	−1.2	−9.88
11	−320.4	−1.4	−11.1
12	−323.6	−4.6	–
13	−322.1	−3.1	–
14	−319.7	−0.7	–
15	−305.8	13.3	−9.71
16	−324.2	−5.2	–
17	−325.1	−6.1	−10.33
18	−319.6	−0.6	–
19	−320.0	−1.0	–
20	−319.1	−0.1	–

[a] $\delta(^{15}N)$ relative to CH$_3$NO$_2$; solvent: CDCl$_3$.
[b] Due to a fast proton interchange in CDCl$_3$ the determination of $^1J(^{15}N,^1H)$ coupling constant was possible only for **15**: 89.6 Hz.

For carbons *ipso* the *b* values obtained (C-1′, $b = 0.76-0.78$; C-1, $b = 0.80-0.83$) are close to those reported by Lynch [9] for the structurally related -OCH$_3$ ($b = 0.714$) and -NH$_2$ ($b = 0.825$) substituents (Table 4) suggesting that the effect on the aromatic system of the fixed substituents are similar to the parent ones. The chemical shifts of the other carbons at phenyl rings have -with exception of C-2-good linear dependences with the SCS values. The slopes *b* are close to unity showing that the fixed substituent has little effect on the additivity of these shifts. These results were not included in the Tables.

The ^{13}C of *ipso* carbons C-1 and C-1′ and ^{15}N chemical shifts were correlated with other single as well as dual substituent parameters. Hammett substituent constants σ, σ^- and σ° were employed in single correlations (Table 4) while σ_R, σ_R^- and σ_R° along with σ_I parameters were used in dual substituent parameter (DSP) treatments (Table 5). It seemed worth as well to make use of the gas phase field/inductive σ_F and resonance σ_R constant in an extra dual treatment with ^{15}N chemical shifts. For each nucleus two data set were employed (20 and 6 values for C-1 and N atoms and 11 and 6 values for C-1′).

Table 4. Statistical data of the single-substituent parameter correlations $y = \varrho x + c$ at N, C-1, C-1′ atoms for compounds **1–20**.

y *vs.* x	n[a]	ϱ[b]	c[c]	r[d]	EV[e]
δ^{15}N *vs.* σ	20	14.65 ± 1.51	−320.29 ± 0.35	0.916	2.36
δ^{15}N *vs.* σ^f	6	15.95 ± 2.76	−320.29 ± 1.01	0.945	5.41
δ^{15}N *vs.* σ^-	20	11.23 ± 1.12	−320.76 ± 0.35	0.921	2.23
δ^{15}N *vs.* σ^{-f}	6	11.80 ± 1.39	−321.13 ± 0.75	0.973	2.68
δ^{15}N *vs.* σ^o	20	15.23 ± 2.12	−320.70 ± 0.45	0.86	2.23
δ^{15}N *vs.* σ^{of}	6	17.30 ± 3.68	−320.96 ± 1.28	0.920	7.74
δ^{13}C-1 *vs.* σ	20	9.01 ± 1.56	146.40 ± 0.36	0.81	2.52
δ^{13}C-1 *vs.* σ^f	6	9.47 ± 1.64	145.52 ± 0.60	0.945	1.89
δ^{13}C-1 *vs.* σ^-	20	6.27 ± 1.56	145.77 ± 0.49	0.689	4.38
δ^{13}C-1 *vs.* σ^{-f}	6	6.58 ± 1.46	145.13 ± 0.78	0.914	2.91
δ^{13}C-1 *vs.* σ^o	20	8.02 ± 1.95	146.19 ± 0.45	0.696	3.72
δ^{13}C-1 *vs.* σ^{of}	6	9.34 ± 2.07	145.13 ± 0.78	0.914	2.92
δ^{13}C-1 *vs.* SCS	20	0.80 ± 0.03	147.79 ± 0.10	0.988	0.17
δ^{13}C-1 *vs.* SCS^f	6	0.83 ± 0.08	147.78 ± 0.37	0.986	0.65
δ^{13}C-1′ *vs.* σ^g	11	7.90 ± 1.55	157.29 ± 0.42	0.86	1.81
δ^{13}C-1′ *vs.* σ^h	6	8.53 ± 1.86	156.64 ± 0.68	0.917	2.44
δ^{13}C-1′ *vs.* σ^{-g}	11	5.16 ± 1.27	157.16 ± 0.50	0.80	2.48
δ^{13}C-1′ *vs.* σ^{-h}	6	5.90 ± 1.57	156.29 ± 0.84	0.88	3.38
δ^{13}C-1′ *vs.* σ^{og}	11	7.84 ± 2.04	157.18 ± 0.52	0.79	2.67
δ^{13}C-1′ *vs.* σ^{oh}	6	8.96 ± 2.61	156.33 ± 0.90	0.86	3.88
δ^{13}C-1′ *vs.* SCS^g	11	0.76 ± 0.05	158.54 ± 0.17	0.980	0.27
δ^{13}C-1′ *vs.* SCS^h	6	0.78 ± 0.02	158.80 ± 0.07	0.999	0.03

[a] Number of points; [b] slope; [c] intercept; [d] correlation coefficient; [e] estimated variance; [f] series II; [g] R^2-, R^3-substituted values rejected from correlations; [h] series I.

Table 5. Statistical data of the dual-substituent parameter correlations $z = \varrho_x x + \varrho_y y + c$ at N, C-1, C-1′ atoms for compounds **1–20**.

z *vs.* x + y	n[a]	ϱ_x[b]	ϱ_y[b]	c[c]	r[d]	EV[e]	$\lambda = \varrho_y/\varrho_x$
δ^{15}N *vs.* $\sigma_I + \sigma_R$	20	12.15 ± 0.61	30.45 ± 1.12	−319.66 ± 0.16	0.990	0.30	2.51
δ^{15}N *vs.* $\sigma_I + \sigma_R^f$	6	11.49 ± 0.97	30.74 ± 1.67	−319.01 ± 0.42	0.997	0.34	2.67
δ^{15}N *vs.* $\sigma_I + \sigma_R^-$	20	8.99 ± 0.54	16.20 ± 0.56	−319.73 ± 0.15	0.991	0.27	1.80
δ^{15}N *vs.* $\sigma_I + \sigma_R^{-f}$	6	8.91 ± 1.18	15.20 ± 1.02	−319.42 ± 0.48	0.996	0.46	1.70
δ^{15}N *vs.* $\sigma_I + \sigma_R^o$	20	9.20 ± 0.56	16.44 ± 0.58	−319.72 ± 0.15	0.991	0.28	1.79
δ^{15}N *vs.* $\sigma_I + \sigma_R^{of}$	6	8.91 ± 1.18	15.20 ± 1.02	−319.42 ± 0.48	0.996	0.46	1.70
δ^{15}N *vs.* $\sigma_F + \sigma_R$	20	12.31 ± 0.60	29.95 ± 1.09	−319.70 ± 0.16	0.991	0.29	2.43
δ^{15}N *vs.* $\sigma_F + \sigma_R$	6	11.90 ± 1.21	30.22 ± 2.02	−319.22 ± 0.52	0.996	0.49	2.54
δ^{13}C-1 *vs.* $\sigma_I + \sigma_R$	20	4.47 ± 0.85	22.28 ± 1.58	147.52 ± 0.22	0.960	0.60	4.98
δ^{13}C-1 *vs.* $\sigma_I + \sigma_R^f$	6	5.57 ± 2.13	18.89 ± 3.68	146.70 ± 0.92	0.965	1.63	3.39
δ^{13}C-1 *vs.* $\sigma_I + \sigma_R^-$	20	5.17 ± 0.56	15.50 ± 0.69	147.57 ± 0.14	0.983	0.25	3.00
δ^{13}C-1 *vs.* $\sigma_I + \sigma_R^{-f}$	6	6.29 ± 1.47	14.06 ± 1.85	146.85 ± 0.65	0.983	0.79	2.23
δ^{13}C-1 *vs.* $\sigma_I + \sigma_R^o$	20	2.29 ± 0.89	11.92 ± 0.93	147.47 ± 0.24	0.952	0.72	4.90
δ^{13}C-1 *vs.* $\sigma_I + \sigma_R^{of}$	6	4.13 ± 2.41	9.94 ± 2.13	146.45 ± 0.98	0.958	1.93	2.64
δ^{13}C-1′ *vs.* $\sigma_I + \sigma_R^g$	11	4.09 ± 1.00	18.60 ± 2.06	158.17 ± 0.33	0.958	0.65	4.55
δ^{13}C-1′ *vs.* $\sigma_I + \sigma_R^h$	6	3.79 ± 1.84	19.04 ± 3.17	158.24 ± 0.80	0.972	1.21	5.02
δ^{13}C-1′ *vs.* $\sigma_I + \sigma_R^{-g}$	11	2.35 ± 1.01	10.01 ± 1.13	158.10 ± 0.34	0.956	0.68	4.26
δ^{13}C-1′ *vs.* $\sigma_I + \sigma_R^{-h}$	6	2.30 ± 1.96	10.10 ± 1.73	158.01 ± 0.80	0.968	1.27	4.39
δ^{13}C-1′ *vs.* $\sigma_I + \sigma_R^{og}$	11	4.24 ± 0.59	15.87 ± 1.00	158.32 ± 0.20	0.986	0.22	3.74
δ^{13}C-1′ *vs.* $\sigma_I + \sigma_R^{oh}$	6	3.66 ± 0.28	16.47 ± 0.40	158.701 ± 0.12	0.999	0.03	4.50

[a] Number of points; [b] slopes; [c] intercept; [d] correlation coefficient; [e] estimated variance; [f] series II; [g] R^2, R^3 substituted values rejected from correlations; [h] series I.

Since the accuracy of the signal position is not reliable (Table 1), the chemical shift of the amino hydrogen will not be used in correlations. The substituent chemical shift range (ΔSCS) for both methylene carbons C-1″ and C-2″ are only 2.1 and 3.3 ppm, respectively. The linear dependence of these shifts on σ, σ^-, and σ° substituent constants are of low quality (correlation coefficient $r < 0.9$). Dual substituent parameter treatment (DSP) give no improvement of the former results showing that the substituent effect from *N*-phenyl- and *O*-phenyl ring is not transmitted to ethylene carbons. These correlations were excluded from the Tables.

Since special interest has been devoted to study long range substituent effects, the substituent effect at N and C-1 atoms due to the remote phenyloxy ring was investigated. No effect was found. The difference between the stronger electron-acceptor (**6**) and electron-donor (**2**) are only 0.6 ppm for C-1 (Table 2) and 0.4 for N (Table 3).

There is no dependence between $\delta(^{13}$C-1) (ΔSCS 11.1) and σ, σ^-, and σ° ($r = 0.81$; 0.69 and 0.70 respectively). DSP analysis gives much better results: $\delta(^{13}$C-1) *vs.* $\sigma_I + \sigma_R$, $r = 0.960$; $\delta(^{13}$C-1) *vs.* $\sigma_I + \sigma_R^-$, $r = 0.983$; $\delta(^{13}$C-1) *vs.* $\sigma_I + \sigma_R^\circ$, $r = 0.952$. A much better correlation was found taking in account only the R^1 substituted compounds (series II, n = 6, ΔSCS = 11.1). Single linear correlations improve to $r = 0.945$ (σ), 0.914 (σ^-) and 0.914 (σ°), although the estimated variance increase (Table 4). DSP analysis with the same values show no further improvement [$\delta(^{13}$C-1) *vs.* $\sigma_I + \sigma_R$, $r = 0.965$, δ ^{13}C-1 *vs.* $\sigma_I + \sigma_R^-$, $r = 0.983$, δ ^{13}C-1 *vs.* $\sigma_I + \sigma_R^\circ$, $r = 0.958$].

Correlations on the other ring were made on C-1′. The ΔSCS on this atom is 10.8 ppm. *Ortho*-and *meta*-substituted compounds were rejected from the correlations. The remaining eleven compounds show no relationship between δ ^{13}C-1′ and σ, σ^- and σ° ($r < 0.9$) but fair correlations were obtained with DSP analysis: $\delta(^{13}$C-1′) *vs.* $\sigma_I + \sigma_R$, $r = 0.958$; (^{13}C-1′) *vs.* $\sigma_I + \sigma_R^-$, $r = 0.956$; $\delta(^{13}$C-1′) *vs.* $\sigma_I + \sigma_R^\circ$, $r = 0.986$. The quality of the last mentioned linear regression analyses improves when only the six values for the R^4-ring substituted compounds (series I, ΔSCS = 10.8 ppm) are considered: $\delta(^{13}$C-1′) *vs.* $\sigma_I + \sigma_R$, $r = 0.972$; $\delta(^{13}$C-1′) *vs.* $\sigma_I + \sigma_R^-$, $r = 0.968$; $\delta(^{13}$C-1′) *vs.* $\sigma_I + \sigma_R^\circ$, $r = 0.999$. It is noteworthy that the very good linear dependence

of these correlations is in line with the low value of EV of 0.93.

The ΔSCS of the nitrogen atom is 19.3 ppm. Single parameter correlations between $\delta(^{15}$N) and σ, σ^- and σ° improve from $r = 0.916$ to 0.945; 0.921 to 0.973 and 0.86 to 0.920, respectively, when only the six values of series II are considered (ΔSCS = 17.8 ppm). On the other hand, a concomitant increase of variance is registered making the values for σ and σ° unacceptably high.

Very good correlations were obtained by plotting between $\delta(^{15}$N) *vs.* $\sigma_I + \sigma_R$, $\sigma_I + \sigma_R^-$ and $\sigma_I + \sigma_R^\circ$ with both 20 and 6 values. In all cases $r > 0.99$ were obtained.

The resonance coefficient ϱ_R is clearly preponderant (Table 5). The N-atom shows a major dependence on π-delocalization ($1.7 \leq \lambda \leq 2.7$) over the field effects. At the *ipso*-carbons this increase of the dependence on π delocalization ($2.2 \leq \lambda \leq 5.0$) seems to be stronger in C-1′ than in C-1.

These results show good correlations between the atoms studied and the selected parameters. When the series I and II were analyzed, better coefficient correlations were obtained. The assumption that both phenyl ring are independent of each other (as can be seen for the lack of correlations at the ethylene chain carbons or at carbons to the other ring that is being analyzed) allows us to suppose that the neighboring rings act always as not-substituted regardless of the nature of the present substituent. Taking in account the larger data set, the results obtained show no substantial decrease of the quality of the correlations with a concomitant improvement of the EV values (see Tables 4 and 5).

We have not found evidences of any kind of intramolecular interaction like those previously reported. [14] If they were present, changes in the nature of the substituent in one ring should reflect changes at the other. For example, nitro groups at the phenyloxy ring should cause deshielding at carbons in the phenyl amino ring by cross-space intramolecular charge transfer (CT), and hydrogen bond interaction should reflect changes specially in ^{15}N NMR because the nature of the substituent at the phenyloxy ring should modify the capacity of the oxygen to act as base-acceptor.

At this point, the question whether the NMR spectroscopy is unable to detect intramolecular interactions in the compounds studied or whether
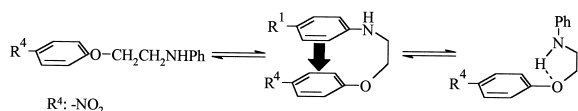
Fig. 3. CT and hydrogen bond intramolecular interaction as proposed by Mutai. [14].

they are not relevant under the conditions employed, remains unclear. Complementary studies will be made in brief using ^{17}O NMR spectroscopy. The general behavior in deuterochloroform solution seems to be structurally similar to that derived from diffraction studies in the solid state. [29]

Experimental

The preparation of the compounds has been reported previously. [16] They were purified by crystallization. Melting points for known compounds agreed with literature values and satisfactory elemental analyses were obtained for the previously unreported compounds.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX-400 spectrometer (400.1 and 100.6 MHz, respectively) and ^{15}N NMR spectra on a Bruker DRX-500 (50.68 MHz) in CDCl$_3$ solutions (15–40 mg in 0,7 ml). Tetramethysilane (δ = 0) was used as standard in both ^{1}H and ^{13}C measurements and nitromethane (δ = 0) for 15 N. Bruker standard software has been used for the 1D and 2D multipulse experiments. ^{15}N parameters were determined by ^{1}H-{^{15}N} detected HMBC spectroscopy.

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