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^{1}H, ^{13}C and ^{15}N NMR Spectral and X-ray Structural Studies of 2-Arylsulfonylamino-5-chlorobenzophenones

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Six 2-(4-R-phenylsulfonylamino)-5-chlorobenzophenones were prepared and their ^{1}H, ^{13}C and ^{15}N NMR spectra recorded and assigned. The dependence between the chemical shift of the amide proton and Hammett σ substituent constants is of the V type. Substituent effect on the chemical shift of the amide nitrogen atom was found insignificant. X-ray analysis shows that the terminal benzene rings in 2-(4-nitrophenylsulfonylamino)-5-chlorobenzophenone are located close to each other. They are not, however, parallel, dihedral angle between them being equal to 10.86 deg (MP2/6-31G**//HF/6-31G** *ab initio* calculations show this to be 20.44 deg). This shows that the mutual orientation of two benzene rings in the molecule of this compound is caused by the π-π stacking. It is additionally reinforced by the intramolecular NH…O=C hydrogen bond. Except the dihedral angle between the benzene rings, X-ray determined structure of 2-(4-nitrophenylsulfonylamino)-5-chlorobenzophenone is very similar to this optimized by the *ab initio* calculations.

Key words: sulfonylaminoketones, ^{1}H and ^{13}C NMR, X-ray diffraction, *ab initio* calculations, π-π stacking, hydrogen bonding

A special type of "double" bond between the sulfur and oxygen atoms [1,2] is responsible for an ineffective conjugation of S=O with other double bonds. On the other hand, owing to their strong inductive effect, alkyl and aryl sulfone groups are powerful electron acceptors [3]. Such a group is present in 2-amino-5-chlorobenzophenone, which is a starting material in synthesis of numerous heterocyclic compounds showing the psychotropic properties [4–8]. N-Arylsulfonyl derivatives of 2-amino-5-chlorobenzophenone are almost unknown [4]. Although the related N-(3-benzoylphenyl)methanesulphonamide was studied recently [9], there is no data on the molecular structure of these compounds (Scheme 1) available.

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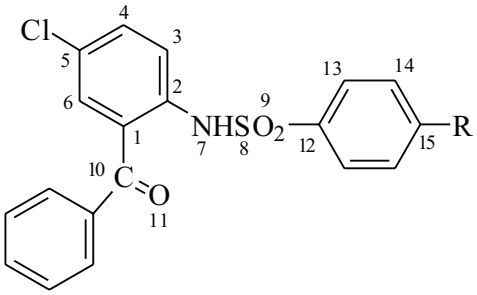
Scheme 1



R = NO_2 (**1**), Br (**2**), Cl (**3**), H (**4**), Me (**5**), OMe (**6**)

EXPERIMENTAL

2-(4-R-Phenylsulfonylamino)-5-chlorobenzophenones {*p*-substituted N-phenyl-sulfonyl-2-amino-5-chlorobenzophenones} were obtained by condensation of 2-amino-5-chlorobenzophenone and substituted benzenesulfonyl chlorides according to [4]. The reaction products (Table 1) were purified by crystallization from ethyl alcohol. Their purity was followed by thin-layer chromatography [Kieselgel 60_{F254}, acetone: *n*-hexane 4:5 (v/v) as an eluent]. Satisfactory analytical data (± 0.3 % for C, H, and N) were obtained for all compounds prepared. Melting points determined on a Boetius table are not corrected.

^{1}H, ^{13}C and ^{15}N NMR experiments were run for 0.1–0.2 M solutions in $CDCl_3$ at 303 K with a Bruker Avance DRX 500 spectrometer equipped with a 5 mm diameter inverse detection probehead and z-gradient accessory working at 500.13 MHz for proton, 125.77 MHz for carbon-13 and 50.69 MHz for nitrogen-15, respectively. ^{1}H and ^{13}C NMR chemical shift assignments are based on homonuclear two-dimensional (2 D) double quantum filtered (DQF) COSY [10,11] and (2 D) heteronuclear pulsed field gradient (PFG) selected ^{1}H,^{13}C HMQC and HMBC [12] experiments as described in our previous papers [13,14]. ^{1}H and ^{13}C NMR chemical shifts are referenced to the trace signal of $CHCl_3$ (δ = 7.26 ppm from TMS) in proton experiments and the centre peak of $CDCl_3$ (δ = 77.00 ppm from TMS) in carbon-13 experiments. ^{15}N NMR chemical shifts are measured from PFG ^{1}H,^{15}N HMBC correlation maps as before [13,14]. A 1 mm diameter capillary of CH_3NO_2 inserted coaxially inside the 5 mm diameter NMR-tube was used as an external reference for nitrogen-15 chemical shifts. Detailed NMR acquisition and processing parameters are available from E.K. on request. IR spectra (KBr discs) were recorded on a Bruker Vector 22 spectrophotometer.

Suitable crystals for X-ray analysis were obtained by slow evaporation of its $CDCl_3$ solution. The X-ray crystallographic data for **1** were recorded with a Nonius Kappa CCD diffractometer. Graphite monochromatised MoK_α radiation [$\lambda(MoK_\alpha)$ = 0.71073 Å] and temperature of 173.0 ± 0.1 K were used. The CCD data were processed with Denzo-SMN v0.93.0 [15] and the structure was solved by direct methods (SHELXS-97 [16]) and refined on F^2 by full-matrix least-squares techniques (SHELXL-97 [17]). The hydrogen atoms were calculated located from the difference Fourier map but the final refinement refined with isotropic temperature factors (1.2 times the carbon temperature factor). M_r ($C_{19}H_{13}ClN_2O_5S$) = 416.82, monoclinic space group P 2_1/c (No. 14), a = 14.9968(3), b = 6.4446(1), c = 19.9241(5) Å, β = 111.185(1)°, V = 1795.49(6) Å^3, Z = 4, D_c = 1.542 g cm^{-3}, μ = 0.365 mm^{-1}. Of 5491 collected reflections 3368 were unique (R_{int} = 0.0278). Final R1 = 0.0398 and wR2 = 0.0788 for $I > 2\sigma I$ (2609 reflections). Crystallographic data excluding structure factors has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-204138. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

All calculation (*in vacuum*) were carried out with Gaussian 98 package [18].

RESULTS AND DISCUSSION

A known method was applied to synthesize 2-(4-R-phenylsulfonylamino)-5-chlorobenzophenones [*p*-substituted N-phenyl-sulfonyl-2-amino-5-chlorobenzophenones] from 2-amino-5-chlorobenzophenone and substituted benzenesulfonyl chlorides [4]. The reaction yields, melting points and IR spectral data for the products are given in Table 1.

Table 1. Reaction yields, melting points and IR spectral data for compounds **1**–**6**.

Compd.	Yield (%)	M.p. (°C)	IR (cm^{-1})			
			N–H	C=O	SO_2 sym.	SO_2 asym.
1	34	181–183	3249	1635	1177	1386
2	39	140–141	3255	1637	1166	1385
3	24	118–122	3256	1637	1166	1385
4	54	57–59	3259	1641	1167	1386
5	34	119–121[a]	3268	1638	1167	1382
6	38	122–123	3280	1650	1158	1384

[a] 120–121°C [4].

Characteristic ^{1}H, ^{13}C and ^{15}N NMR chemical shifts of **1**–**6** are collected in Table 2. Due to limited number of the compounds used, no detailed correlations between their spectral data and the substituent constants could be made. It can be seen, however, that the dependence between the chemical shift of the amide proton and carbonyl carbon atoms and σ substituent constants [19] is of the V type. Substituent effect on the chemical shift of the amide nitrogen atom was found insignificant [due to very small changes in the $\delta(^{15}N)$ values the spectra were recorded only for three selected compounds, carrying the NO_2 and OCH_3 substituents representing the extreme cases by the Hammett constants]. It is obvious, that electron-withdrawing substituents cause the deshielding effect of the ^{15}N NMR signal. It seems noteworthy that the substituent effect on methylene ^{13}C chemical shifts in the NMR spectra of 4-substituted phenyl-4′-methylphenacylsulfones, *p*-Me–C_6H_4–CO–CH_2–SO_2–C_6H_4–R, [20] was "reverse" [$\delta(^{13}\mathbf{C}H_2) = -0.52\sigma^{+} + 63.55$, $\delta(^{13}\mathbf{C}H_2) = -0.39\sigma_I - 1.39\sigma_R + 63.53$].

Table 2. Selected experimental ^{1}H, ^{13}C and ^{15}N NMR chemical shifts (δ) 2-(4-R-phenylsulfonylamino)-5-chlorobenzophenones **1**–**6** for 0.1–0.2 M solution in $CDCl_3$ at 303 K and Hammett σ constants for the respective substituents.

Compd.	N**H**	**C**O	**N**	σ_p[a]
1	9.62	196.44	–267.9[b]	0.78
2	9.65	196.92	c	0.23
3	9.66	196.93	c	0.23
4	9.85	197.09	–267.0	0.00
5	9.67	196.81	c	–0.17
6	9.63	196.93	–266.2	–0.27

[a] Ref. [19]. [b] $\delta(^{15}\mathbf{N}O_2) = -16.7$ ppm. [c] ^{1}H, ^{15}N HMBC spectra for these compounds were not recorded.

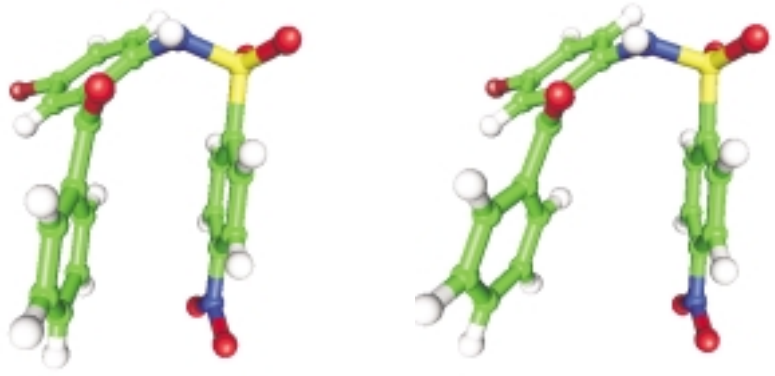
Although both NH and CH_2 are similarly related to the SO_2 group in the respective compounds (they are next to sulfur atom to feel the influence of the substituent). The ^{15}N chemical shift for 2-(4-R-phenylsulfonylamino)-5-chlorobenzophenones decreases when the substituent is getting more electron-withdrawing by character (a "reverse" substituent effect).

In general, the X-ray structure of **1** is very similar to this optimized by the *ab initio* calculations (Fig. 1 and Table 3). It can be seen, however, that the "benzoyl" benzene ring in the calculated structure is much more twisted.

Table 3. Selected calculated (MP2/6-31G**//HF/6-31G**) and X-ray experimental bond lengths [pm] and bond and dihedral angles [deg] for 2-(4-nitrophenylsulfonylamino)-5-chlorobenzophenone.

	Calcd	X-ray
O9C10	502.5	489.7 (3)
O9'C10	478.1	459.0 (3)
O11S8	396.3	381.4 (3)
C10O11	120.1	123.2 (3)
C10C1	150.4	149.8 (3)
C2N7	141.7	143.7 (3)
N7H7	100.0	88 (3)
N7S8	163.9	163.3 (2)
H7...O11	207.0	209 (3)
N7...O11	277.1	274.8 (3)
S8O9	142.5	143.1 (2)
S8O9'	142.7	142.5 (2)
S8C12	178.0	177.2 (2)
C1C10O11	119.8	119.4 (2)
C10C1C2	121.8	120.5 (2)
C1C2N7	121.3	120.3 (2)
C2N7S8	123.3	120.3 (2)
N7S8O9	108.2	108.1 (1)
N7S8O9'	105.1	105.3 (1)
O9S8C12	106.9	107.5 (1)
O9'S8C12	107.6	108.4 (1)
C2N7S8C12	–65.4	–58.3(2)

X-ray analysis (Figs 1 and 2) shows that the nitro group in **1** is twisted by 9.98 deg with respect to the attached benzene ring. This twist is equal to –4.36 deg according to the MP2/6-31G**//HF/6-31G** *ab initio* calculations. Terminal benzene rings in the molecule are not parallel: dihedral angle between them is equal to 10.86 deg (calculations show this to be 20.44 deg). Increase of the C2N7S8C12 dihedral angle from –65.4 deg (X-ray) to –155 and –245 deg causes that the energy of the molecule increases to 20.16 and 20.79 kJ/mol, respectively. This shows that mutual orientation of two benzene rings in the molecule of 2-(4-nitrophenylsulfonylamino)-5-chlorobenzophenone may be caused by the π-π stacking [21]. This conformation is additionally reinforced by intramolecular hydrogen bonding.



a b

Figure 1. The single crystal X-ray (a) and MP2/6-31G**//HF/6-31G**optimized (b) structure of 2-(4-nitrophenylsulfonylamino)-5-chlorobenzophenone.

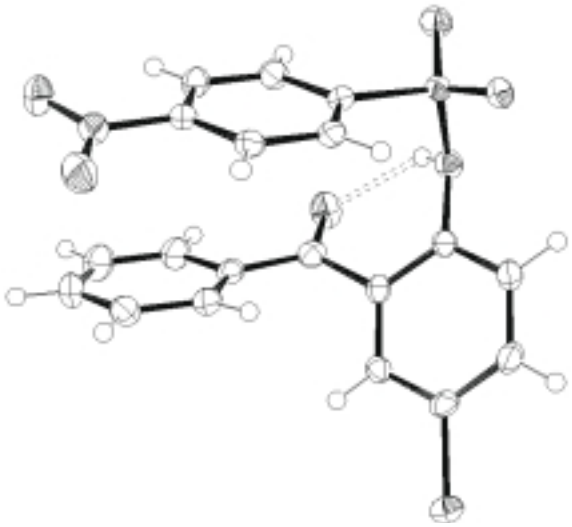


Figure 2. ORTEP plot of (4-nitrophenylsulfonylamino)-5-chlorobenzophenone. Intramolecular hydrogen bond [$d_{N...O}$ = 274.8(3) pm] is shown as broken bar. The thermal ellipsoids are drawn by 50% probability level.

^{1}H chemical shifts for the compounds studied (Table 2) are comparable with these known for N-arylalkanesulfonamides, R–C_6H_4–$NHSO_2$–Alk, where Alk = Me or Et, R = H, *p*-Cl, *p*-Me, *m*-Cl {9.56–10.02 ppm (solutions in DMSO-d_6) [22]}. Low acidity of 2-(phenyl-sulfonylamino)-5-chlorobenzophenones studied is noteworthy. Compounds **1**–**6** are almost insoluble in the alkaline aqueous solutions. It is known that acidity of sulfonamides is usually low and that secondary amides, $ArSO_2NHAr$, are stronger acids than $ArSO_2NH_2$ [23]. Ethyl *o*-phenylsulfonylaminobenzoate, *o*-EtOCO–C_6H_4–$NHSO_2$–Ph, reveals similar behaviour (formation of the sodium salt was possible only when this sulfonamide was treated with sodium in toluene solution [24,25].

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