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NOTE

Polynuclear Magnetic Resonance of Substituted Thiobenzanilides and Benzanilides: Transmission of Substituent Effects through the Thiocarboxamide Group

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The ^{1}H, ^{13}C and ^{19}F NMR spectra of 3′- and 4′-substituted 3- and 4-fluorobenzanilides and thiobenzanilides are reported. According to the ^{19}F substituent-induced shifts (SCS), transmission of substituent effects through the NHCS group is less efficient than that through NHCO groups. On the other hand, in thioanilides a greater part of the substituent effect remains on the functional group itself, as follows mainly from ^{13}C SCS of the central carbon. An explanation is possible in terms of the greater polarizability of sulfur, which accommodates charge better than oxygen. Comparison with the isomers studied previously reveals that transmission depends slightly on the direction. It is more efficient through the NHCX group than through the CXNH group: the nitrogen atom as donor interacts more strongly than carbonyl with the substituent effects of acceptor groups. © **1997 by John Wiley & Sons, Ltd.**

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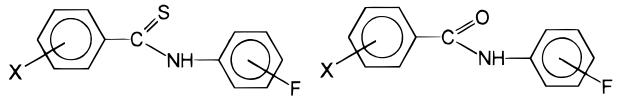
INTRODUCTION

Within the framework of a broader program on aromatic thioamides,[1,2] we investigated the fundamental properties of the thioamide groups with respect to use in correlation analysis and in quantitative structure–activity relationships (QSAR). In these investigations, the thioamide group can act (i) as a substituent,[3–6] characterized by a substituent constant σ in a broad sense, (ii) as a functional group influenced by variable substitution[7–10] and (iii) as an indifferent group transmitting the substituent effects from the substituent to the functional centre.[11] Whenever possible, we compared the physical properties of thioamides with those of similar amides whose properties are better known.

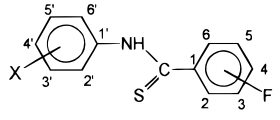
The present work deals mainly with the last-named aspect, viz. transmitting substituent effects through the thiocarboxamide group. In a previous study,[11] we estimated the transmission ability of the CSNH group on compounds **1** and **2** in which the fluorine atom served as probe and its ^{19}F substituent-induced chemical shifts (SCS) were monitored. Comparison with amides **3** and **4** revealed that the thioamide group transfers the effects less efficiently than the amide group, while a relatively greater part of the change in electron density remains on the CSNH group itself. This can be rationalized in a simplified manner by the greater polarizability of sulfur compared with oxygen, or by its greater ability to accommodate a charge.[10]



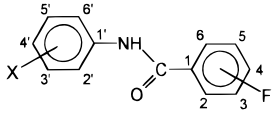
1 3-F
2 4-F

3 3-F
4 4-F

In this work we are investigated thioamides of reversed structure, **5** and **6**, in comparison with the analogous amides **7** and **8**. The choice of substituents X was the same as previously:[11] it was dictated by the suitability of the same compounds for biological tests. Fluorine ^{19}F NMR shifts as probe have the merit of great sensitivity. In addition, they are believed to be controlled by the substituent inductive and mesomeric effects in a regular way.[12] Several series of compounds $XC_6H_4YC_6H_4F$ have already been investigated with the



5 3-F
6 4-F



7 3-F
8 4-F

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aim of comparing the transmitting abilities of the group Y.[13–16] A problem of theoretical interest may be whether the substituent effects are transferred in either direction (say in **1** and **5**) with the same intensity. In principle, there is no reason why it should be so, since the term 'transmission' must be understood only as a model. Any analogy, e.g. with the electric current, may be misleading: certain interposed groups can even enhance the transmission instead of reducing it.[13] As previously,[11] we report here also the ^{13}C and ^{1}H NMR spectra. Some of their SCS may serve as a probe of electron density on the CSNH or CONH groups themselves.

RESULTS AND DISCUSSION

The measured SCS of compounds **5–8** (Tables 1–3) were subjected systematically to correlation analysis. Of the various correlations we tried, only those which show any regularity and can be interpreted in a reasonable way are reported. For evaluating the transmission of substituent effects, the ^{19}F SCS listed in Table 1 are decisive. Most important is a comparison of thioamides **5** and **6** with amides **7** and **8**. Their ^{19}F SCS are linearly dependent with good accuracy, comparable to the experimental error, as can be seen from the statistics in Table 4, line 1. Transmission through the NHCS group is less effective than through the NHCO group. The same result was obtained previously[11] for the reversed groups CSNH (**1** and **2**) and CONH (**3** and **4**): even the ratios 0.81 and 0.80, respectively, are virtually equal (Table 4, line 2). A plot is not shown. In contradistinction to the previous case (Fig. 1 in Ref. 11), a linear dependence is valid now even for the substituent $N(CH_3)_2$. Its deviation observed previously[11] was evidently caused by through-conjugation with the C=O or C=S bonds (compare lines 1 and 2 in Table 4).

In all correlations we prefer a direct comparison of the two relevant series. In the literature,[13–16] correlations with substituent constants σ were preferred and discussed in terms of the proportionality constants ρ. Since the latter constants may have appreciable errors, the results are less reliable. This reasoning applies particularly to comparisons of transmission in either direction. The statistics given in lines 3 (for thioamides) and 4 (for amides) in Table 4 reveal good linearity: the slopes are not different from each other but are only slightly greater than unity (not significantly so in the former case). More telling is the plot shown in Fig. 1. Comparison with the line of unit slope seems convincing but this result depends strongly on the four nitro derivatives. There is no difference between amides and thioamides. One has to conclude that transmission is stronger when the substituent is on the side of the NH group. This can be rationalized by noting that the nitrogen atom, as a good donor, interacts better with the acceptor substituents. This effect is much stronger with NH as a bridging group, i.e. in derivatives of diphenylamine.[13]

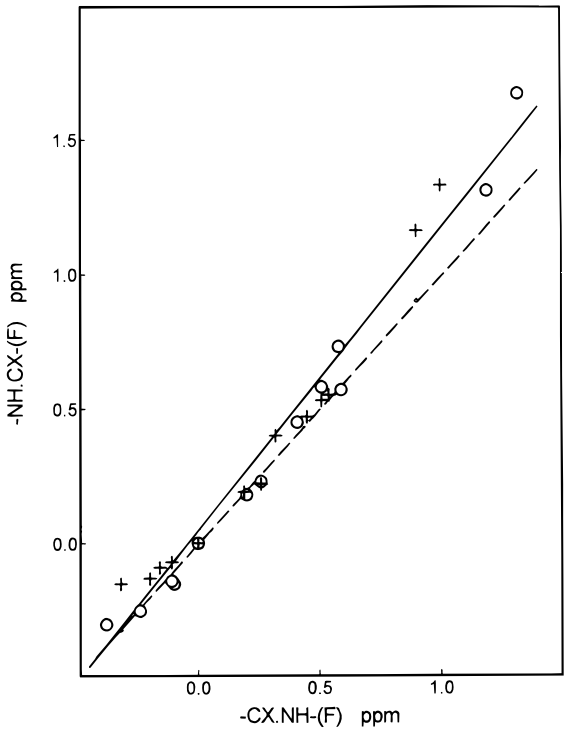

Figure 1. Transmission of substituent effects through the CONH and CSNH groups in either direction: *x*-axis,[19]F SCS in **1–4**; *y*-axis in **5–8**. ○, Amides, + thioamides; the full line is the regression line and the dashed line a slope of unity.

Table 1. Fluorine-19 NMR chemical shifts δ(F) and substituent effects Δδ(F) in 3- and 4-fluorothiobenzanilides 5 and 6 and 3- and 4-fluorobenzanilides 7 and 8 in $CDCl_3$

	5		6		7		8	
R	δ(F)	Δδ(F)	δ(F)	Δδ(F)	δ(F)	Δδ(F)	δ(F)	Δδ(F)
H	-112.20	—	-109.21	—	-111.88	—	-108.07	—
3-Cl	-111.98	0.22	-108.68	0.53	-111.65	0.23	-107.50	0.57
3-NO_2	-111.73	0.47	-108.05	1.16	-111.30	0.58	-106.76	1.31
3-OMe	—[a]	—[a]	-109.25	-0.04	-111.87	0.01	-108.04	0.03
4-Cl	-112.01	0.19	-108.81	0.40	-111.70	0.18	-107.62	0.45
4-Br	-111.99	0.21	-108.79	0.42	-111.66	0.22	-107.58	0.49
4-Me	-112.27	-0.07	-109.34	-0.13	-112.03	-0.15	-108.32	-0.25
4-NO_2	-111.65	0.55	-107.88	1.33	-111.15	0.73	-106.40	1.67
4-OMe	-112.29	-0.09	-109.36	-0.15	-112.02	-0.14	-108.37	-0.30
4-NMe_2	-112.49	-0.29	-109.84	-0.63	-112.26	-0.38	-108.82	-0.75

[a] The compound was not synthesized.

Table 2. Carbon-13 NMR chemical shifts (ppm) in 3- and 4-fluorothiobenzanilides 5 and 6 and 3- and 4-fluorobenzanilides 7 and 8 in $CDCl_3$

Compounds	R	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C=X	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)	C(6′)	R
5	H	145.15	114.52	162.57	118.08	130.23	121.80	196.63	138.81	123.67	129.12	127.17	129.12	123.67	—
	3-Cl	144.81	114.55	162.60	118.30	130.34	121.75	197.00	139.84	123.68	134.76	127.18	130.10	121.73	—
	3-NO_2	144.42	114.60	162.63	118.65	130.46	121.85	197.69	139.77	118.68	148.52	121.59	129.89	129.47	—
	4-Cl	144.94	114.53	162.60	118.28	130.32	121.80	196.86	137.31	124.99	129.27	132.39	129.27	124.99	—
	4-Br	144.91	114.52	162.58	118.27	130.31	121.80	196.71	137.79	125.20	132.22	120.17	132.22	125.20	—
	4-Me	145.11	114.50	162.58	118.02	130.22	121.81	196.51	136.32	123.76	129.69	137.24	129.69	123.76	21.12
	4-NO_2	144.80	114.56	162.65	118.68	130.50	121.85	197.46	144.20	124.86	122.80	145.19	122.80	124.86	—
	4-OMe	144.94	114.50	162.57	118.00	130.20	121.83	196.49	131.83	125.54	114.25	158.42	114.25	125.54	55.48
	4-NMe_2	145.17	114.48	162.54	117.74	130.11	121.83	195.35	128.15	125.02	112.10	149.43	112.10	125.02	40.44
6	H	139.30	129.04	115.55	164.61	115.55	129.04	197.10	138.98	123.80	129.11	127.07	129.11	123.80	—
	3-Cl	138.98	129.09	115.66	164.73	115.66	129.09	197.50	140.00	123.81	134.71	127.07	130.06	121.87	—
	3-NO_2	138.63	129.10	115.83	164.95	115.83	129.10	198.08	139.94	118.77	148.54	121.50	129.86	129.58	—
	3-OMe	139.50	128.98	115.54	164.57	115.54	128.98	196.90	140.10	109.24	160.12	112.82	129.81	115.72	55.42
	4-Cl	139.10	129.03	115.67	164.73	115.67	129.03	197.31	137.47	125.11	129.26	132.30	129.26	125.11	—
	4-Br	139.08	129.02	115.69	164.74	115.69	129.02	197.28	137.99	125.32	132.24	120.10	132.24	125.32	—
	4-Me	139.26	128.94	115.51	164.61	115.51	128.94	196.94	136.48	123.89	129.66	137.14	129.66	123.89	21.08
	4-NO2	139.08	129.11	115.87	164.96	115.87	129.11	197.91	144.40	124.84	122.86	145.12	122.86	124.84	—
	4-OMe	139.07	128.95	115.53	164.61	115.53	128.95	196.96	131.98	125.68	114.25	158.38	114.25	125.68	55.46
	4-NMe_2	139.37	128.90	115.49	164.50	115.49	128.90	195.97	128.30	125.18	112.15	149.46	112.15	125.18	40.47
7	H	137.31	114.54	162.89	118.85	130.46	122.45	164.47	137.64	120.38	129.14	124.88	129.14	120.38	—
	3-Cl	136.84	114.57	162.92	119.16	130.59	122.42	164.43	138.77	120.45	134.87	124.94	130.12	118.26	—
	3-NO_2	136.32	114.68	163.00	119.57	130.76	122.49	164.58	138.80	115.06	148.76	119.44	130.06	125.91	—
	3-OMe	137.31	114.52	162.92	118.89	130.50	122.40	164.40	138.86	106.03	160.35	110.81	129.82	112.39	55.35
	4-Cl	136.93	114.55	162.91	119.09	130.56	122.42	164.41	136.20	121.60	129.19	129.97	129.19	121.60	—
	4-Br	136.92	114.55	162.93	119.11	130.58	122.42	164.39	136.72	121.88	132.16	117.56	132.16	121.88	—
	4-Me	137.43	114.52	162.91	118.74	130.43	122.41	164.34	134.60	120.44	129.65	135.08	129.65	120.44	20.86
	4-NO_2	136.28	114.71	162.99	119.72	130.81	122.52	164.48	143.10	119.61	125.20	144.07	125.20	119.61	—
	4-OMe	137.38	114.51	162.91	118.70	130.42	122.41	164.35	130.70	122.27	114.34	156.93	114.34	122.27	55.50
	4-NMe_2	137.65	114.15	162.88	118.44	130.31	122.37	164.16	127.31	122.30	112.98	148.41	112.98	122.20	40.79
8	H	131.23	129.42	115.89	164.98	115.89	129.42	164.68	137.82	120.31	129.16	124.75	129.16	120.31	—
	3-Cl	130.75	129.46	115.98	165.10	115.98	129.46	164.69	138.95	120.42	134.84	124.78	130.10	118.24	—
	3-NO_2	130.24	129.58	116.17	165.33	116.17	129.58	164.79	138.97	115.00	148.75	119.27	130.03	125.89	—
	3-OMe	131.19	129.40	115.87	164.97	115.87	129.40	164.69	139.04	106.03	160.34	110.66	129.79	112.38	55.34
	4-Cl	130.83	129.44	115.95	165.07	115.95	129.44	164.68	136.37	121.57	129.16	129.81	129.16	121.57	—
	4-Br	130.84	129.45	115.98	165.09	115.98	129.45	164.64	136.89	121.85	132.14	117.39	132.14	121.85	—
	4-Me	131.30	129.39	115.79	164.89	115.79	129.39	164.66	135.26	120.45	129.62	134.44	129.62	120.45	20.84
	4-NO_2	130.21	129.66	116.20	165.39	116.20	129.66	164.77	143.67	119.56	125.17	143.90	125.17	119.56	—
	4-OMe	131.27	129.36	115.83	164.90	115.83	129.36	164.62	130.87	122.25	114.35	156.86	114.35	122.25	55.52
	4-NMe_2	131.53	129.30	115.73	164.78	115.73	129.30	164.45	127.50	122.21	113.05	148.38	113.05	122.21	40.83

[a] The signals of carbon atoms C(1)–C(6) are split into doublets in: thiobenzanilides **5**: J[C(1),F]=6.8–7.8 Hz, J[C(2),F]=23.4–24.4 Hz, J[C(3),F]=247.1–249.0 Hz, J[C(4),F]=20.5–21.5 Hz, J[C(5),F]=7.8–8.8 Hz, J[C(6),F]≈2.9 Hz; thiobenzanilides **6**: J[C(2),F]=J[C(6),F]=8.8–9.8 Hz, J[C(3),F]=J[C(5),F]=21.5–22.5 Hz, J[C(4),F]=252.9–257.9 Hz; benzanilides **7**: J[C(1),F]=6.5–6.8 Hz, J[C(2),F]=22.5–23.4 Hz, J[C(3),F]=248.0–250.5 Hz, J[C(4),F]=20.5–21.5 Hz, J[C(5),F]≈7.8 Hz, J[C(6),F]=2.9 Hz, J[C(=O),F]=2.5 Hz; benzanilides **8**: J[C(1),F]=2.8–3.2 Hz, J[C(2),F]=J[C(6),F]=8.8–9.8 Hz, J[C(3),F]=–J[C(5),F]=21.5–22.5 Hz, J[C(4),F]=252.0–254.9 Hz

Table 3. Proton NMR chemical shifts (ppm) in 3- and 4-fluorothiobenzanilides 5 and 6 and 3- and 4-fluorobenzanilides 7 and 8 in $CDCl_3$

Compounds	R	H(2)	H(3)	H(4)	H(5)	H(6)	NH	H(2′)	H(3′)	H(4′)	H(5′)	H(6′)	R
5	H	~7.574	—	7.182	~7.39	~7.574	9.00	7.741	7.434	7.299	7.434	7.741	—
	3-Cl	~7.55	—	7.198	7.395	~7.55	8.96	7.862	—	7.273	7.356	7.610	—
	3-NO_2	~7.583	—	7.228	7.426	~7.583	9.16	8.660	—	8.143	7.615	~8.15	—
	4-Cl	~7.564	—	7.197	~7.40	~7.564	8.94	7.710	~7.40	—	~7.40	7.710	—
	4-Br	~7.55	—	7.192	7.390	~7.55	8.95	~7.65	~7.55	—	~7.55	~7.65	—
	4-Me	~7.58	—	7.181	7.389	~7.58	8.94	~7.60	7.240	—	7.240	~7.60	2.38
	4-NO_2	7.557	—	7.232	7.425	7.573	9.21	8.034	8.292	—	8.292	8.034	—
	4-OMe	~7.573	—	7.177	7.383	~7.573	8.94	7.607	6.984	—	6.984	7.607	3.83
	4-NMe_2	7.572	—	7.155	7.368	7.563	8.93	7.553	6.727	—	6.727	7.553	2.98
6	H	7.866	7.101	—	7.101	7.866	8.94	7.741	7.435	7.296	7.435	7.741	—
	3-Cl	7.820	7.093	—	7.093	7.820	8.94	7.820	—	7.260	7.340	7.570	—
	3-NO_2	7.860	7.137	—	7.137	7.860	9.07	8.630	—	8.146	7.614	8.146	—
	3-OMe	7.850	7.094	—	7.094	7.850	8.93	7.198	—	6.834	7.317	7.580	3.82
	4-Cl	7.855	7.110	—	7.110	7.855	8.89	7.698	7.399	—	7.399	7.698	—
	4-Br	7.852	7.110	—	7.110	7.852	8.87	7.649	7.551	—	7.551	7.649	—
	4-Me	7.850	7.085	—	7.085	7.850	8.93	7.574	7.226	—	7.226	7.574	2.37
	4-NO_2	7.857	7.139	—	7.139	7.857	9.09	8.010	8.303	—	8.303	8.010	—
	4-OMe	7.872	7.103	—	7.103	7.872	8.88	7.602	6.958	—	6.958	7.602	3.84
	4-NMe_2	7.866	7.092	—	7.092	7.866	8.86	7.545	6.740	—	6.740	7.545	2.98
7	H	7.594	—	7.252	7.470	7.628	7.74	7.628	7.384	7.174	7.384	7.628	—
	3-Cl	7.565	—	7.251	7.456	7.604	7.85	7.746	—	7.138	7.282	7.472	—
	3-NO_2	7.619	—	7.303	7.511	7.654	7.95	8.488	—	8.030	7.566	8.083	—
	3-OMe	7.573	—	7.237	7.448	7.611	7.81	7.090	—	6.720	7.255	7.397	3.82
	4-Cl	7.567	—	7.250	7.455	7.606	7.83	7.576	7.329	—	7.329	7.576	—
	4-Br	7.579	—	7.263	7.473	7.613	7.74	7.537	7.491	—	7.491	7.537	—
	4-Me	7.571	—	7.227	7.439	7.608	7.77	7.495	7.166	—	7.166	7.495	2.34
	4-NO_2	7.613	—	7.311	7.516	7.650	8.01	7.840	8.279	—	8.279	7.840	—
	4-OMe	7.579	—	7.234	7.450	7.613	7.70	7.521	6.910	—	6.910	7.521	3.82
	4-NMe_2	7.569	—	7.206	7.424	7.602	7.69	7.454	6.727	—	6.727	7.454	2.94
8	H	7.890	7.174	—	7.174	7.890	7.70	7.619	7.381	7.165	7.381	7.619	—
	3-Cl	7.864	7.153	—	7.153	7.864	7.83	7.738	—	7.129	7.276	7.464	—
	3-NO_2	7.920	7.207	—	7.207	7.920	7.94	8.478	—	8.079	7.558	8.018	—
	3-OMe	7.868	7.146	—	7.146	7.868	7.79	7.080	—	6.712	7.250	7.395	3.82
	4-Cl	7.866	7.157	—	7.157	7.866	7.79	7.571	7.327	—	7.327	7.571	—
	4-Br	7.876	7.176	—	7.176	7.876	7.70	7.532	7.488	—	7.488	7.532	—
	4-Me	7.871	7.150	—	7.150	7.871	7.70	7.491	7.171	—	7.171	7.491	2.34
	4-NO_2	7.911	7.194	—	7.194	7.911	8.12	7.833	8.251	—	8.251	7.833	—
	4-OMe	7.875	7.161	—	7.161	7.875	7.62	7.514	6.914	—	6.914	7.514	3.82
	4-NMe_2	7.866	7.142	—	7.142	7.866	7.59	7.450	6.740	—	6.740	7.450	2.94

Transmission of substituent effects can be followed also from the ^{13}C SCS of the *para* and *ipso* carbon atoms, but less efficiently than from ^{19}F. For compounds **1–4** we obtained the result[11] that CSNH transmits worse than CONH (Table 4, line 6): the slope was equal for C(1) and C(4) and not significantly different from that obtained from ^{19}F (compare with line 2). Extending this correlation to compounds **5–8**, we

Table 4. Correlations of SCS in substituted benzamides and thiobenzamides 1–8

		Group (compounds)					
Entry	SCS	*x*	*y*	Slope	*R*	SD	*N*
1	^{19}F	NHCO (**7**, **8**)	NHCS (**5**, **6**)	0.81(0.06	0.9958	0.046	18
2		CONH (**3**, **4**)[a]	CSNH (**1**, **2**)[a]	0.80(0.02	0.9940	0.045	14[b]
3		NHCS (**5**, **6**)	CSNH (**1**, **2**)	1.12(0.07	0.9789	0.102	13[b]
4		NHCO (**7**, **8**)	CONH (**3**, **4**)	1.15(0.05	0.9918	0.080	13[b]
5	$^{13}C(4)$	NHCO (**7**, **8**)	NHCS (**5**, **6**)	0.73(0.03	0.9882	0.037	18[c]
6	$^{13}C(1)(4)$	CONH (**3**, **4**)[a]	CSNH (**1**, **2**)[a]	0.74(0.02	0.9931	0.039	27[d]
7	$^{13}C{=}X$	NHCO (**7**, **8**)	NHCS (**5**, **6**)	~7			18
8		CONH (**3**, **4**)[a]	CSNH (**1**, **2**)[a]	~1.3			13[b]

[a] Correlations reported previously, corresponding to Figs 1–3, respectively, in Ref. 11.
[b] Compounds with substituent $N(CH_3)_2$ omitted.
[c] Only the position C(4′).
[d] Positions C(1) and C(4) together, substituent $N(CH_3)_2$ omitted.

obtained a scattered plot and elimination of several strong substituents [NO_2, $N(CH_3)_2$, OCH_3] in the series C(1) would be required. For this reason, we restricted the correlation only to the C(4) atom. Then the result was the same as previously (Table 4, line 5). The deviations were evidently due to strong resonance effects of some substituents when present in the *para* position to the NH group.[17]

From a different point of view, we can consider the thioamido or amido groups as substituents. In this case, our results offer an opportunity to calculate the pertinent inductive constants σ_I and resonance constants σ_R according to Taft's DSP model.[18] According to the defining equations,[12,18] σ_I is determined from the ^{19}F SCS of **5** or **7** with reference to fluorobenzene as the unsubstituted compound; σ_R is defined from the differences between **6** and **5** or **8** and **7**, respectively. We obtain for the substituent $CSNHC_6H_5$ $\sigma_I = 0.20$ and $\sigma_R = 0.10$, for $CONHC_6H_5$ $\sigma_I = 0.25$ and $\sigma_R = 0.13$. The constants σ for amide substituents are generally obtainable with difficulty owing to solubility problems. Recent quantum chemical calculations[19] gave for $CSNH_2$ $\sigma_I = 0.28$, $\sigma_R = 0.11$ and for $CONH_2$ $\sigma_I = 0.21$, $\sigma_R = 0.07$; the values are not very different but the sequence is reversed. The DSP treatment has been broadly used for correlations of SCS but also subjected to criticism.[11,20] Note also that the experimental σ of $CSNHC_6H_5$ relate to the mixture of *E* and *Z* conformers,[21] while amides are virtually all in the *Z* conformation.

Finally, as the third possible point of view, we take the thioamido and amido groups as a reaction center. Then we can attempt to evaluate their relative sensitivity to substitution according to some ^{13}C and ^{1}H shifts. Significant results were obtained previously[11] with $^{13}C(=S)$ and $^{13}C(=O)$ SCS of **1**–**4** (Table 4, line 8). Since the SCS in thioamides were greater, it was concluded that a relatively greater part of the electron density remains on the functional group and a relatively smaller part is transmitted further. When we try to apply this test to compounds **5**–**8** (Table 4, line 7), we find that the SCS of $^{13}C(=O)$ in **7** and **8** are almost constant within the scatter of the correlation. The slope in this correlation would be fairly high, hence the previous finding is qualitatively supported. Another possibility is offered by ^{1}H SCS in the NH group. For compounds **1**–**4** a scattered plot was obtained[11] but its slope was greater than unity (*ca* 1.6), showing again the greater effect on the thioamide than on the amide group. For **5**–**8** the scatter is still greater and its slope cannot be determined with any reliability.

Generally, the scatter of all plots with compounds **5**–**8** is worse than that with **1**–**4**. This could be expected since in **5**–**8** the substituent can be conjugated with the amino group whereas in **1**–**4** it is with the carbonyl or thiocarbonyl group. Correlations of the Hammett type were originally based on benzoic acids and correlations with anilines are less regular.[17] With the C=X group only the substituent $N(CH_3)_2$ can be strongly conjugated (as observed in lines 2, 3, 4, 8 in Table 4). In the case of the NH group as reaction center, this can occur with several acceptor substituents. The result is then a generally larger scatter.

We can conclude that all the results are compatible with the picture that in thioamides there is a stronger n–π conjugation inside the functional group than in amides, transmission of substituent effects through the group is weaker, and the effects on the group itself are stronger. This can all be interpreted in terms of the greater polarizability of sulfur or its greater ability to accommodate a negative charge.[10]

EXPERIMENTAL

Synthesis of compounds

Compounds **5**–**8** were prepared by standard procedures;[22] their physical properties will be reported in connection with their biological activities.[23] Identities and purities were checked via the NMR spectra (see Tables 1–3).

NMR measurements

NMR spectra were measured on a Varian UNITY 500 Fourier transform NMR spectrometer (^{1}H at 500 MHz, ^{13}C at 125.7 MHz and ^{19}F at 470.3 MHz). For each of the compounds **5**–**8**, the spectra (^{1}H, ^{19}F and ^{13}C) were run with the same solution (about 10 mg in 0.5 ml of $CDCl_3$) at 30 °C and referenced to internal tetramethylsilane (^{1}H and ^{13}C) or $CFCl_3$ (^{19}F). Carbon-13 NMR spectra were accumulated with broad-band proton decoupling. The structural assignment of carbon signals was done on the basis of chemical shifts (C=O, C=S and CH_3 signals), signal intensities, molecular symmetry, characteristic fluorine–carbon coupling constants and known substituent effects in the benzene ring (aromatic carbons). Whereas all carbon atoms of benzanilides **7** and **8** give sharp lines, in thiobenzanilides **5** and **6** the signals of C=S and the neighboring carbon atom C(1) are significantly broadened and smaller line broadening is observed also for signals of carbons C(2) and C(6). The ^{19}F NMR spectra of benzanilides generally showed multiplets due to *J*(F,H) with aromatic protons {doublet of doublets of doublets with J[F,H(2)] $\approx$ 8.2 Hz, J[F,H(4)] $\approx$ 9.3 Hz and J[F,H(5)] $\approx$ 5.4 Hz in benzanilides **7** and triplet of triplets with J[F,H(2)] = J[F,H(6)] $\approx$ 5.2 Hz and J[F,H(3)] = J[F,H(5)] $\approx$ 5.2 Hz in benzanilides **8**}. Similar splitting was observed for some thiobenzanilides **5** and **6** (with 3-NO_2, 4-NO_2, 4-OMe and 4-NMe_2) while the others showed a broad unresolved peak. Proton NMR spectra of all benzanilides **8** and **9** showed narrow lines and easily analyzable multiplets resulting from *J*(H,H) and *J*(F,H) couplings, whereas the spectra of thiobenzanilides **5** and **6** manifested line broadening effects to different extents for individual compounds and individual structural positions of the given proton.

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