

DIPOLE MOMENT AND ELECTRON DISTRIBUTION OF THE THIOAMIDE GROUP*

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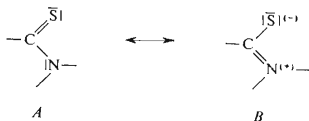
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Dipole moments of seven substituted thiobenzamides *Ia–Ig* and of two *N,N*-dimethylthio-benzamides *IIa, IIb* were measured in dioxan and/or benzene solutions; the infrared spectra proved that association of solutes is negligible under conditions given. The CSNH₂ group moment was estimated to $15.6 \cdot 10^{-30}$ C m at an angle of 75° to the C₍₁₎—C bond, that one of the CSN.(CH₃)₂ group to $16.5 \cdot 10^{-30}$ C m (angle 81°). Analysis in terms of bond moments revealed mesomeric moments m_2 of 6.2 or $8.5 \cdot 10^{-30}$ C m, respectively, which account for the conjugation within the thioamide group. These values are approximately twice greater than in amides and depend similarly on methyl substitution; there are even minor differences in direction. Also the mesomeric moment of the S=C—O group, redetermined now to $3.3 \cdot 10^{-30}$ C m, is greater than in the ester group and even of different direction. The results confirm the importance of $n-\pi$ conjugation for dipole moments.

The electronic structure of the thioamide group can be approximately described in terms of the classical mesomeric formulae *A* and *B*:



The partial double bond character of the C—N bond as required by the formula *B* has been well evidenced¹, most striking was the isolation of stereoisomeric *N*-alkylthioamides². Another consequence of the theory of mesomerism is the charge separation which should be manifested in dipole moment values. Although several measurements in solution are available^{3–10}, an analysis in terms of the mesomeric dipole moments¹¹ is not quite easy for the two following reasons:

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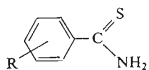
Firstly, the mesomeric moment is defined as the vector difference between the experimental and expected value if the latter is calculated from common bond moments neglecting any conjugation:

$$\mu_m = \mu_{\text{exp}} - \mu_{\text{calc}} \quad (1)$$

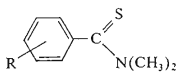
The resulting value may be rather sensitive to the details of calculation, in particular to certain bond moments. Moreover, the direction of μ_{exp} must be known, or alternatively, μ_m must be supposed to lie in a given direction compatible with the mesomeric formulae.

The second problem is specific for unsubstituted thioamides and concerns their association in nonpolar solvents; note that the technique of measurements prevents work at very low concentrations. That is why the mesomeric dipole moment (denoted further m_2) was evaluated mostly for N,N-dialkylthioamides⁴⁻⁶ the association of which is negligible¹². The direction of m_2 was *a priori* assumed from N to S and absolute values obtained for homologous aliphatic N,N-dimethylthioamides ranged from 8.2 to 10.7. (All values of dipole moments in this paper are given in units 10^{-30} C m). The named assumption need not apply since we have found recently¹³ that m_2 in the amide group is oriented from N to C rather than from N to O. The mesomeric dipole moments of secondary thioamides⁴ are still less reliable since the association in benzene solution may be appreciable^{12,14}. Note also that substitution by methyl groups affects the mesomeric dipole moments considerably¹³. In one point, however, the above studies⁴⁻⁶ agree with each other and also with some theoretical calculations¹⁵: m_2 seems to be always greater than in corresponding amides, approximately by a factor of two.

This paper constitutes part of a program dealing with physical properties of thioamides in relation to their antibacterial activity^{16,17}. Its objective was to estimate mesomeric dipole moments in thioamides and N,N-dimethylthioamides. In order to reduce the association of the former as far as possible, we measured the dipole moments in dioxan and controlled the state of solutes by infrared spectroscopy,



- Ia; R = H
 Ib; R = 3-CH₃
 Ic; R = 4-CH₃
 Id; R = 3-Cl
 Ie; R = 4-Cl
 If; R = 3-NO₂
 Ig; R = 4-NO₂



- IIa; R = H
 IIb; R = 4-NO₂

extending thus a recent IR study¹⁴. In contradistinction to Lumbroso and co-workers⁴⁻⁶, we have made no assumption concerning the direction of m_2 . Therefore, we were obliged to determine the direction of the experimental dipole moment, taking advantage of polar substituents in *para* position of the benzene nucleus. Our study has been thus confined to aromatic derivatives: thioamides *Ia-Ig* and N,N-dimethylthioamides *Ila, I Ib*

EXPERIMENTAL

Materials. Substituted thiobenzamides *Ia-Ig* were prepared in connection with a previous communication¹⁷. For the present purpose they were recrystallized once more from a nonpolar solvent and dried *in vacuo* over paraffine and phosphorus pentoxide. N,N-Dimethylthiobenzamide¹⁸ (*Ila*) and N,N-dimethyl-4-nitrothiobenzamide¹⁸ (*I Ib*) have been made available to us by Professor W. Walter.

Physical measurements. The technique has been described recently¹⁹ as well as the properties of dioxan solvent²⁰. The concentration range was $4 \cdot 10^{-3}$ – $3 \cdot 10^{-2}$ mol l⁻¹. The molar refraction R_D was calculated from increments²¹, the increment for the CSNH₂ group conjugated with the benzene nucleus (18.7 cm³) was derived from that for the CS.O group²², replacing the oxygen atom by the primary amino group. Similarly the increment of 28.3 cm³ was derived for the CSN(CH₃)₂ group. Our calculated R_D for compound *Ila* fits reasonably a recent experimental value determined in solution⁹ (54.0 cm³). The calculated values of R_D are listed in Table I, together with the experimental polarization data and dipole moments.

The infrared absorption spectra were registered on a Zeiss Specord 75 IR instrument in dioxan solution (concentration 0.05 mol l⁻¹, 0.6 mm NaCl cells). Calibration was carried out with respect to the literature wavenumbers for thiobenzamide¹⁴. The results are given in Table II.

Calculations. The theoretical dipole moments were calculated with the standard values of bond moments²³ (10^{-30} C m): H_{ar}—C 1, H_{ar}—C 0, C=S 7.2 (see Discussion), C—N 1.50, H—N 4.37, C_{ar}—Cl 5.33, C_{ar}—NO₂ 13.33, mesomeric correction (m_1) for the conjugation of the C=S bond with the aromatic ring 1.5 (see Discussion). The bond angles used for *Ia-Ig* were mean values from two X-ray investigations^{24,25}: C—C=S 120°, C—C—N 112°; the angle H—N—H was taken as 120° because of the large uncertainty in crystallographic values. For *Ila* and *I Ib* we used unchanged values of bond angles considering the more approximate character of our results; the differences compared to a recent X-ray study²⁶ are not essential.

DISCUSSION

Before interpreting the dipole moment data we sought to make sure that the compounds under investigation are present as monomers. According to the thorough infrared investigation of Walter and Vinkler¹⁴, thiobenzamide is present in dioxan solution as a hydrogen bonded complex with two molecules of the solvent, its spectrum displays three N—H stretching bands (denoted $\nu_1^2, \nu_3^2, \nu_4^2$). In mixed solvents, *e.g.* dioxan with dichloromethane, the 1 : 1 complex (bands $\nu_1^1, \nu_3^1, \nu_4^1$) and even unsolved solute molecules (bands ν_a, ν_s) were observed, the complexity of bands being due to Fermi resonance. No association was detected at a solute concentration

$7 \cdot 10^{-2} \text{ mol l}^{-1}$. We extended the measurements to all the compounds *Ia–Ig* (Table II). Under our conditions only the 1 : 2 complex was present and we were able to observe the bands ν_3^2 and ν_4^2 , the former with a shoulder at 3370 cm^{-1} corresponding to ν_1^2 . The dependence on substitution is perceptible. The frequency ν_4^2 decreases with the σ constant of the substituent like the ν_a and ν_s frequencies of non-associated thiobenzamides²⁷, but ν_3^2 rather increases; this behaviour might be explained by the Fermi resonance character of the bands. For further discussion is essential that no additional maximum was observed, so we believe that dimeric forms are virtually absent. Vapor pressure measurement revealed 9% of dimeric 2-pyridone in a $1 \cdot 1 \cdot 10^{-2} \text{ mol l}^{-1}$ dioxan solution while 2-thiopyridon was less dimerized¹². In the case of *N,N*-dimethylthiobenzamides *Ila, I Ib* there were no doubts that they are virtually not associated¹².

Since the hydrogen bonds to dioxan have as a rule small effect on apparent dipole moment^{13,28}, we are justified to treat our dipole moment data as pertaining to an isolated molecule. From the experimental dipole moments of *para* derivatives *Ia, Ic, Ie, and Ig* (Table I), and from the known moments of the substituents we can first derive

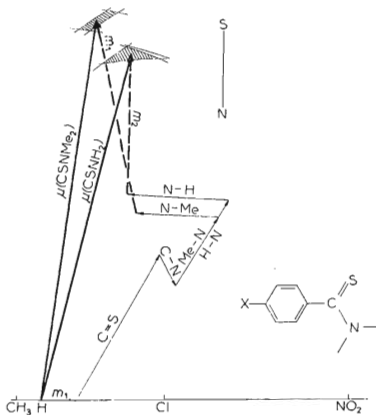


FIG. 1

Determination of the CSNH_2 and CSNMe_2 group moments and their resolution into components. Shown are the component bond moments and the mesomeric contributions for the conjugation $\text{Ar}-\text{CS}$ (m_1) or $\text{S}=\text{C}-\text{N}$ (m_2), respectively

the moment of the CSNH₂ group. In geometrical terms it requires to construe a triangle for each substituent (Fig. 1). The coincidence of the results was reasonable and was further tested by calculating back the expected dipole moments from the mean group moment (Table I, last column). In the case of *meta* derivatives *Ib*, *Id*,

TABLE I

Polarization data and dipole moments of substituted thiobenzamides and N,N-dimethylthio-benzamides (25°C)

Compound	Substituent	Solvent	α^a β^a	$P_{0,}^2, \text{cm}^3$ R_D^b, cm^3	μ (5%) ^c μ (15%) ^c	μ_{calc}^d
<i>Ia</i>	H	Diox	21.11	506	15.8 ^e	15.6
			-0.248	44.0	15.8	
<i>Ib</i>	3-CH ₃	Diox	20.50	535	16.3	15.7 ^f
			-0.418	48.6	16.2	
<i>Ic</i>	4-CH ₃	Diox	20.00	523	16.1	16.0
			-0.396	48.6	16.0	
<i>Id</i>	3-Cl	Diox	15.40	462	15.0	(15.8) ^f
			-0.431	48.9	14.9	
<i>Ie</i>	4-Cl	Diox	15.10	452	14.8 ^g	15.1
			-0.470	48.9	14.7	
<i>If</i>	3-NO ₂	Diox	15.15	486	15.4	(19.1) ^f
			-0.380	50.3	15.3	
<i>Ig</i>	4-NO ₂	Diox	20.65	653	18.1	17.8
			-0.331	50.3	18.0	
<i>IIa</i>	H	Bz	15.77	534	16.1 ^h	16.5
			-0.241	54.7	16.0	
		Diox	19.86	592	17.0	16.5
			-0.100	54.7	16.9	
<i>IIb</i>	4-NO ₂	Bz	18.20	764	19.5	19.6
			-0.414	61.0	19.4	
		Diox	23.20	782	19.8	19.6
			-0.260	61.0	19.7	

^a Slopes of the plots ϵ_{12} vs w_2 and d_{12}^{-1} vs w_2 , respectively; ^b calculated from increments, see Experimental; ^c correction for the atomic polarization 5% or 15% of the R_D value, respectively, units 10^{-30} C m; ^d calculated from the group moments 15.6, or 16.5 · 10^{-30} C m, respectively; ^e ref.⁸ gives 13.1 in benzene; ^f equal population of the two rotamers assumed; ^g ref.⁸ gives 12.7 in benzene; ^h ref.⁵ gives 15.3 (concentration up to 0.16 mol l⁻¹).

and *If* this calculation requires an assumption about the population of the two rotamers with substituent in the position 3 or 5, respectively. According to Table I the population 1 : 1 does not apply exactly, rather the rotamer with the lower dipole moment prevails. This can be expected if the conformation is controlled by the electrostatic interaction²⁹, although the required populations would be somewhat high: 60 and 70% for *Id* and *If*, respectively. Nevertheless, we conclude that our group moment of 15.6 (at an angle of 75° to the C₍₁₎—C bond) fits all the experimental results on the compounds *Ia*—*Ig*. A lower value (13.1) was derived by Pappalardo and Gruttadauria⁸ from only two compounds measured in benzene; its absolute value is then equal to the experimental value of *Ia*. Remarkably, the direction of the vector was the same as found by us. In our opinion the measurement in benzene can be affected by dimerization which has been proven for many thioamides at much lower concentrations^{7,12,14}. A reference⁸ to the Hoecker plot³⁰ is not convincing. This plot is not correct statistically since the concentration appears on both axes; a simple plot of permittivity *vs* concentration¹² would serve as a more sensitive test. We believe that our group moment determined in dioxan is more reliable.

In the next step, the group moment is resolved into bond moments, the residue representing the mesomeric contribution m_2 . Of the component moments, two deserve particular discussion: the C=S bond moment and the correction (denoted m_1) for the conjugation Ar—CS. Both were included in the value of 9.83, used previously^{22,23,31} and based essentially on a comparison of experimental dipole moments of benzophenone and thiobenzophenone. The latter value was, however, in error as revealed by new measurements and by a systematic comparison for a series of thioketones and ketones³². From the compiled table³² it follows that the C=S bond moment is lower than C=O in aliphatic compounds, the difference is reduced in aromatic derivatives. Relatively to our value in use for C=O, the mean value of 7.2 for C=S can be taken; of previous estimates it is near to that tabulated by Minkin, Osipov and Zhdanov³³. In order to account for the experimental dipole moments of aromatic thio ketones, a mesomeric correction $m_1 = 1.5$ is then necessary. The latter value might be tested directly as to their applicability to thioamides, but only in principle, since the uncertainty is too high. If we say in a simplified manner that thioacetamide³ and thiobenzamide in dioxan have approximately equal dipole moments, $m_1 = 1$ would follow with an error of the same order of magnitude.

With the bond moment C=S 7.2 and with $m_1 = 1.5$ we obtained the mesomeric moment $m_2 = 6.2$ as a measure for the conjugation within the thioamide group ($A \leftrightarrow B$). Fig. 1 reveals that the direction of m_2 is almost exactly from N to S (152° to the C—N bond) as suggested by the formula *B*. This direction was assumed *a priori* by Lumbroso in deriving the mesomeric moment of N,N-dimethylthioamides^{4,6}, in this paper it was determined experimentally. The main difference between the two conceptions consists in introducing polar substituents in our work.

This enabled us to determine the direction of the dipole moments on the one hand, and gave the results more statistical weight on the other. Note that such a direction of the mesomeric moment, in agreement with the simplified mesomeric formulae, is not at all self-evident since marked deviations were found with amides¹³, N,N-dimethylamides¹³, and esters³⁴.

A similar treatment as above was applied to N,N-dimethylthiobenzamides. Since it was based only on two derivatives (*Ila*, *Ilb*), the results have less statistical weight. On the other hand, it was possible to carry out the measurements in two solvents with compatible results (Table I). We obtained the group moment $CSN(CH_3)_2$ of 16.5 at an angle of 81° to the $C_{(1)}-C$ bond (Fig. 1) and derived from it the mesomeric moment $m_2 = 8.5$ (164° to the C—N bond). The latter value is distinctly higher than for unsubstituted thiobenzamides, it means that greater basicity of the nitrogen atom favours the mesomeric structure *B*. The small difference in the direction (164° or 152°) need not be significant. Our value is compatible with previous estimates^{4,6} (8.2–10.7 with various aliphatic derivatives) based each on a single derivative, and in our opinion it is more reliable than these. It is further corroborated by processing the dipole moments of substituted N-methyl-N-phenylthiobenzamides⁹ in the same manner. The resulting mesomeric moment is 8.2 (162° to the C—N bond), if *E* configuration is assumed. Comparison of our results to the mesomeric moments of the amide and dimethylamide groups¹³ let conclude that by substituting =S for =O the mesomeric moment is approximately doubled.

With the amended C=S bond moment we are able to redetermine the mesomeric moments within the S=C—O and O=C—S groups in thion esters and thiol esters, respectively. Our previous statements that the former is lower²² than 2, or that their

TABLE II

Wavenumbers of N—H stretching vibration of substituted thiobenzamides in dioxan

Compound	Substituent	1 : 2 Complex	
		ν_3^2	ν_4^2
<i>Ia</i>	H	3 318	3 206
<i>Ib</i>	3-CH ₃	3 317	3 208
<i>Ic</i>	4-CH ₃	3 319	3 210
<i>Id</i>	3-Cl	3 321	3 202
<i>Ie</i>	4-Cl	3 320	3 204
<i>If</i>	3-NO ₂	3 324	3 200
<i>Ig</i>	4-NO ₂	3 324	3 198

existence is not proven³¹, were conditioned by the original, too high C=S bond moment. On the other hand, Lumbroso's estimates³⁵ 3.9 and 0.9, respectively, are impaired similarly as in the case of thioamides, *viz.* by the low statistical weight and by the *a priori* assumed direction of the vector. Referring to our previously published measurements^{22,31} on substituted aromatic derivatives, we can now recalculate the mesomeric moments to 3.3 (at an angle of 6° to the C=S bond) for the S=C—O group and to 1.6 (−10° to the C=O bond) for the O=C—S group. The absolute values do not differ too much from Lumbroso's³⁵ and agree with the general picture, *viz.* the effect of substitution of S for O, but the direction is rather strange.

Summarizing the results obtained hitherto, we conclude that *n*— π conjugation in simple systems (as in amides¹³, thioamides, amidoximes^{36,37}, esters³⁴, thioesters) is of importance and manifests itself in significant values of mesomeric dipole moments. These must be necessarily taken into account as correction terms when calculating expected dipole moments by vector addition of bond moments²³, so much more because they are not constant with respect to substitution or even to configuration³⁷. In other words one can say that the principle of additivity of bond moments breaks down for such conjugated systems. Individual mesomeric moments

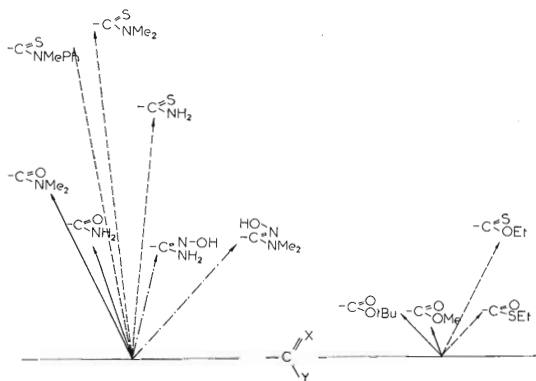


FIG. 2

Mesomeric dipole moments (m_2) resulting from the *n*— π conjugation in various classes of compounds

(m_2) differ appreciably both in absolute value and in direction (Fig. 2). The direction represents the most important contribution of our approach since it was not specified in previous attempts⁴⁻⁶. Although much confidence cannot be given to small differences, several classes of compounds are clearly distinguished in Fig. 2. In thioamides the electron shift takes place approximately in the direction from N to S in accordance with the mesomeric formula *B*. In amides the effective charge transfer is rather from N to C, confirming the view³⁸ that a formula like *B* does not describe quite adequately the actual structure. The very different directions of m_2 in amidoximes and the sensitivity to configuration suggest the importance of oriented lone electron pairs on the imino nitrogen. The differences between esters and thio esters are puzzling, some of the values are rather small and should be confirmed by another approach. As far as the absolute value of m_2 is concerned, two effects are evident in various classes of compounds: the greater polarizability of sulfur as compared to oxygen, and the enhanced basicity of alkyl-substituted nitrogen or oxygen. On the whole, the strong $n-\pi$ conjugation contrasts with the relatively unimportant $\pi-\pi$ conjugation, as found particularly in some aromatic compounds (nitrobenzene³⁹).

We are obliged to Professor W. Walter, University of Hamburg, for kindly providing us with the samples of compounds IIa and IIb. The measurements of permittivities and densities were carried out by Mrs M. Kuthanová under the guidance of Dr V. Jehlička, Department of Physical Chemistry, Institute of Chemical Technology, Prague, some infrared spectral measurements by Dr P. Daněk, Pharmaceutical Faculty, Charles University, Hradec Králové. Their aid is gratefully acknowledged.

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