Intramolecular Hydrogen Bonding in *o*-Mercapto-*NN*-dimethylbenzamide †

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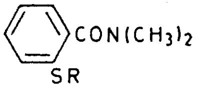
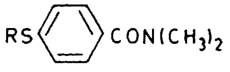
Intramolecular hydrogen bonding in *o*-mercapto-*NN*-dimethylbenzamide is verified from SH and CO i.r. absorptions and n.m.r. chemical shifts of SH protons, in comparison with those of some related compounds. This is confirmed by a solvent influence study and by equilibrium constants for 1 : 1 complex formation with dimethyl sulphoxide.

ALTHOUGH intramolecular hydrogen bonding between mercapto and carbonyl groups was reported for thiosalicyl ester,[1,2] the existence of a hydrogen-bonded system in the corresponding *NN*-dimethylamide has not been described. Hirota and Todokoro, who recently suggested [3] the existence of hydrogen bonding and, thus, a coplanar conformation, for *o*-hydroxy-*NN*-dimethylbenzamide, have indicated the possibility of steric hindrance to coplanarity of the aromatic nucleus and the carbonyl group for some other *ortho*-substituted benzamides. Therefore, it seemed uncertain whether coplanarity is maintained when the hydroxy-group is replaced by the much larger mercapto-group and elucidation of this problem became of interest.

The work reported in this paper deals with *o*-mercapto-*NN*-dimethylbenzamide (1), the related compounds (2)—(6), benzenethiol, and *NN*-dimethylbenzamide.



(1) R = H
(3) R = D
(5) R = CH_3



(2) R = H
(4) R = D
(6) R = CH_3

Some indication of the absence of steric hindrance to coplanarity in the *o*-mercapto-derivative (1) was obtained from the inspection of the n.m.r. spectra. It was observed that, while the spectra of the *o*-mercapto-

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† Presented to the VII Symposium on Organic Sulphur Chemistry, Hamburg, 1976.

[1] N. Mori, S. Kaido, K. Suzuki, M. Nakamura, and Y. Tsusuki, *Bull. Chem. Soc. Japan*, 1971, **44**, 1858.

[2] T. Kobayashi, A. Tamashita, Y. Furuya, R. Horie, and M. Hirota, *Bull. Chem. Soc. Japan*, 1972, **45**, 1494.

[3] M. Hirota and K. Todokoro, *Chem. Letters*, 1974, 777.

derivative (1) and the *para*-derivatives (2) and (6) showed only one NCH_3 signal, that of the *o*-methylthio-derivative (5) exhibited two distinct NCH_3 signals. A plausible explanation for the higher rotational barrier in (5) is steric hindrance to conjugation between the carbonyl group and the aromatic ring, which should strengthen conjugation between the carbonyl group and the lone pair on nitrogen. Conversely, the detection of one NCH_3 signal in (1), (2), and (6), may be considered a consequence of conjugation between the aromatic ring and the carbonyl group, which may greatly suppress that between the carbonyl group and the lone pair on nitrogen and, thus, lower the rotational barrier. Although these qualitative data seemed to suggest a planar system for the *o*-mercapto-derivative (1), they did not show any difference between this compound and the *para*-substituted derivatives (2) and (6), which could be indicative of hydrogen bonding in (1). In order to obtain this information the free energies of activation for the restricted rotation should be determined.

TABLE 1

SH Stretching band frequencies for *o*-mercapto-*NN*-dimethylbenzamide and related compounds

	CCl_4			$CHCl_3$			CCl_4–DMSO (8%)	
Compound	ν/cm^{-1}	$\varepsilon/$ $cm^2\ mol^{-1}$	$\Delta\nu_{\frac{1}{2}}/$ cm^{-1}	ν/cm^{-1}	$\varepsilon/$ $cm^2\ mol^{-1}$	$\Delta\nu_{\frac{1}{2}}/$ cm^{-1}	ν_1/cm^{-1}	ν_2/cm^{-1}
(1)	2 561	13	39	2 571	10.3	32.5	2 486	2 558
	(2 540)	(8)		2 584sh	5.3			
(2)	2 588	3.8	20	2 586	8.3	17	2 478	2 588
Benzenethiol	2 589	1.8	32	2 584	4.6	20	2 493	2 588

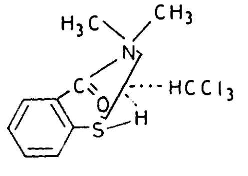
However, more direct evidence for hydrogen bonding in compound (1) could be obtained from the SH and CO i.r. stretching absorptions and chemical shifts of the SH protons. We also report a solvent influence study, as well as the equilibrium constants for association of mercapto-substituted derivatives to dimethyl sulphoxide (DMSO).

RESULTS AND DISCUSSION

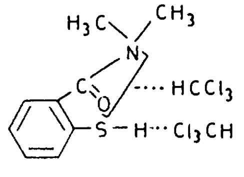
SH *Stretching Absorption*.—Table 1 shows the SH i.r. stretching absorption bands for *o*-mercapto-*NN*-dimethylbenzamide (1), the corresponding *para*-derivative (2), and benzenethiol, in carbon tetrachloride. Intermolecular hydrogen bonding was excluded by measurements in extremely dilute solution. It may be seen that benzenethiol and the *p*-mercapto-derivative (2) exhibit an i.r. band at 2 588 cm^{-1} due to a non-associated SH group. However, this band is absent from the spectrum of the *o*-mercapto derivative (1), which exhibits a strong band at lower frequency (2 561 cm^{-1}), most probably due to SH intramolecularly bonded to the $CON(CH_3)_2$ group. In the spectrum of the *o*-mercapto-derivative (1) a weak shoulder at 2 540 cm^{-1} can also be noticed. However, the fact that it is also present in the spectra of the *o*-methylthio-derivative (5) and does not appear near the SD band, at 1 732 cm^{-1} in the *S*-deuteriated compound (5), suggests that it is of more complex vibrational origin.

Additional evidence for the hydrogen-bonded system in (1) was obtained from a solvent effect study. In contrast to the i.r. spectra of benzenethiol and the *p*-mercapto-derivative (2), which, in chloroform, exhibit an SH band slightly shifted to lower frequency, the spectrum for *o*-mercapto-*NN*-dimethylbenzamide (1), in chloroform, shows the SH band abnormally shifted to higher frequency (2 574 cm^{-1}) and there is an appearance of a shoulder in the normal SH stretching region (2 584 cm^{-1}), which may be assigned to a non-associated SH group. This result suggests that the solvent molecules only partly destroy the hydrogen-bonded system, to give structure (B) in equilibrium with (A).

Interesting results were obtained when the SH stretching frequencies were measured in carbon tetrachloride containing 8% DMSO. The data, included in Table 1, show that, in the case of both benzenethiol and the *p*-mercapto-derivative (2), although the band at 2 588 cm^{-1}, due to free SH (ν_2), still remains, a new band at lower frequency (ν_1) [2 493 cm^{-1} for benzenethiol and 2 478 cm^{-1} for (2)] appears. It may be assigned to SH associated to DMSO (C).



(A)



(B)

$$ArSH --- OS(CH_3)_2$$

(C)

The difference in the positions of the lower frequency bands in benzenethiol and (2) may be attributed to difference in SH acidity. The i.r. spectrum of the *o*-mercapto-derivative (1) in the presence of DMSO contains also two bands in the SH region (Table 1). The band at higher frequency (ν_2) (2 558 cm^{-1}), by comparison with the frequency in carbon tetrachloride, may be assigned to internally bonded SH. The position of the lower frequency band (ν_1) (2 486 cm^{-1}) is very similar to that of the *para*-isomer (2) and, therefore, may be attributed to SH associated to DMSO.

SH *Chemical Shifts*.—The SH i.r. stretching data were confirmed by n.m.r. measurements in carbon tetrachloride, [^{2}H]chloroform, and carbon tetrachloride containing [$^2H_6$]DMSO. They are shown in Table 2.

It may be seen that SH signals for benzenethiol and the *p*-mercapto-derivative (2) do not differ significantly in position. However, the SH resonance signal for *o*-mercapto-*NN*-dimethylbenzamide (1) appears at lower field. It is reasonable to suggest that it is due to internally bonded SH.

The comparison of n.m.r. measurements in [^{2}H]chloroform with those in carbon tetrachloride shows that, in contrast to benzenethiol and the *p*-mercapto-derivative (2), in which the SH signals are shifted to lower fields, the SH signal in the *o*-mercapto-derivative (1) undergoes a shift to higher field. This suggests the contribution of the non-associated SH group and supports our interpretation of i.r. data by equilibrium (A) $\rightleftharpoons$ (B).

TABLE 2

SH Chemical shifts for *o*-mercapto-*NN*-dimethylbenzamide and some related compounds

	ν_{SH}(Hz) [a]				
Compound	CCl_4	$CDCl_3$	CCl_4–[$^2H_6$]DMSO (8%)	$\Delta\nu$ [b]/ Hz	K_{as}/ l mol^{-1}
(1)	235	224	253	18	0.35
(2)	201	212	258	57	0.63
Benzenethiol	196	207	236	40	0.58

[a] From Me_4Si at 60 MHz. [b] $\Delta\nu = \nu(CCl_4\text{–}[^2H_6]DMSO) - \nu(CCl_4)$.

The n.m.r. data in the presence of [$^2H_6$]DMSO (see Table 2) also confirm the corresponding i.r. data, as the $\Delta\nu$ value for the *o*-mercapto-derivative (1) is smaller than that for the *para*-isomer (2). The strength of the association of SH to [$^2H_6$]DMSO in benzenethiol and the *o*- and *p*-mercapto-derivatives (1) and (2) were estimated quantitatively from the equilibrium constants for formation of a 1 : 1 complex (K_{as}) obtained by a graphic method developed by Mathur *et al.*[4] Table 2 shows that the K_{as} value for the *para*-isomer (2) is larger than that for the *ortho*-isomer (1).

TABLE 3

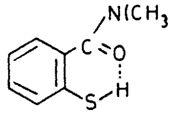
CO Stretching band frequencies for *o*-mercapto-*NN*-dimethylbenzamide and related compounds in CCl_4

Compound	ν_{CO}/cm^{-1}	log ε	$\Delta\nu_{\frac{1}{2}}$/cm^{-1}
(1)	1 641	2.8	c 21
(2)	1 644	2.9	16
(3)	1 640		21
(4)	1 644		16
(5)	1 642	2.9	19
(6)	1 643	2.9	16
NN-Dimethylbenzamide	1 644	2.9	19

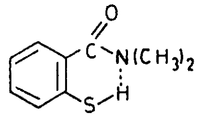
C=O *Stretching Absorption.*—Although the i.r. and n.m.r. data for the SH group provide evidence for the existence of an intramolecular hydrogen-bonded system in *o*-mercapto-*NN*-dimethylbenzamide (1) they do not give any information about the site of association of the SH group. It may be seen (Table 3) that the i.r. spectrum of the *o*-mercapto-derivative (1) exhibits only one ν_{CO} absorption band, which is symmetrical and that there is a shift to lower frequencies of *ca.* 4 cm^{-1} by going from the *para*- (2) and (4) to the *ortho*-derivatives (1) and (3). This suggests that SH is bonded to the carbonyl oxygen (D). The absence of a band at higher frequency than that for *para*-derivatives (2) and (4) or for *NN*-dimethylbenzamide precludes SH bonded to nitrogen (E).

It is noteworthy that the CO_2R and $CON(CH_3)_2$ groups are the only hydrogen accepting substituents which affect the SH stretching frequencies of the *ortho*-substituted benzenethiols studied,[2] as other groups lead only to enhancement of the intensity of SH absorption, without a frequency shift.

o-Mercapto-*NN*-dimethylbenzamide, as shown by the absence of SH and CO stretching bands due to a non-associated form, seems to exist in carbon tetrachloride solution in the hydrogen-bonded form only. This is in contrast with the thiosalicyl ester which, in the same solvent, was shown to be a mixture of two forms, free and hydrogen-bonded.[1]



(D)



(E)

EXPERIMENTAL

Reagents.—All solvents for the spectrometric measurements were spectrograde and were used without any further purification. [^{2}H]Chloroform and [$^2H_6$]DMSO were Stohler Isotopic Chemicals. Benzenethiol was Eastman Organic Chemicals.

NN-*Dimethylbenzamide.*—*NN*-Dimethylbenzamide,[5] *o*-mercapto-,[5,6] *o*-methylthio-,[7,8] and *p*-methylthio-*NN*-dimethylbenzamide[5,9] were prepared by literature procedures. *p*-Mercapto-*NN*-dimethylbenzamide, m.p. 75—81 °C, was prepared by a known method.[5] *S*-Deuteriated *o*- and *p*-mercapto-*NN*-dimethylbenzamide were obtained from the corresponding non-deuteriated compounds on treatment with D_2O (ν_{SD}, *ortho*- 1 732 cm^{-1}, *para*- 1 736 cm^{-1}). All compounds were analysed by g.l.c. to assess their purity.

Spectrometric Measurements.—I.r. spectra were recorded on a Perkin-Elmer model 180 grating spectrometer, at 30°. The spectral slit width was 1.75 cm^{-1}. The SH stretching frequencies were measured over concentration ranges of 0.05—0.002 5M for carbon tetrachloride, 0.05—0.005M for chloroform, and 0.05M for carbon tetrachloride containing DMSO (8%). Quartz matched cells were used of 1.0 cm thickness for 0.05M solutions and 5.0 cm for more dilute solutions. Carbonyl frequencies were measured over a concentration range of 0.002 5—0.001M in carbon tetrachloride, using a pair of potassium bromide 6 mm cells.

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CO and SH stretching frequencies were accurate to ±1 cm^{-1}. N.m.r. spectra were recorded at 60 MHz on a Varian T-60 spectrometer at 35 °C and determined relative to tetramethylsilane as internal standard. NCH_3 Signals were measured for 0.05M solutions in carbon tetrachloride. Chemical shifts of the SH signal were measured over concentration ranges of 0.05—0.01M for carbon tetrachloride and 0.05—0.005M for [^{2}H]chloroform and 0.05M for carbon tetrachloride containing [$^2H_6$]DMSO (8%).

Association Constant Measurements.—Dilution studies of the thiols in carbon tetrachloride were made over concentration ranges of 0.005—0.001M (*o*-mercapto-*NN*-dimethylbenzamide), 0.05—0.005M (*p*-mercapto-*NN*-dimethylbenzamide), and 0.05—0.01M (benzenethiol) and SH chemical shifts were extrapolated to infinite dilution to give ν_0. The chemical shifts of SH in the [$^2H_6$]DMSO–thiol complexes, in carbon tetrachloride, were determined by maintaining the concentration of the thiol (0.01M) constant and varying the molar ratios DMSO : thiol between 10 : 1 and 50 : 1. For each solution five spectra were recorded and the mean value calculated to give ν_1. The values of $\Delta\nu$ ($\nu_1 - \nu_0$) were then calculated for each solution. The association constants (K_{as}) were calculated as described previously.[10,11] All measurements were made at 35 °C and chemical shifts were determined relative to tetramethylsilane as internal standard. The precision of the n.m.r. measurements is ±2 Hz. All plots were treated by appropriate least-square regression analysis to obtain the best straight lines which fit the results. The analysis of the data was accomplished with the aid of a Hewlett–Packard calculator 9820A.

We thank the ' Fundacão de Amparo à Pesquisa do Estado de São Paulo ' for a scholarship (to I. I. M.).

[6/590 *Received*, 29*th March*, 1976]

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