Dipole Moments and Conformations of Arenecarbothioamides

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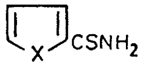
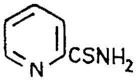
The electric dipole moments of furan-2-carbothioamide, thiophen-2-carbothioamide, pyridine-2- and -3-carbothioamide, thiobenzamide, and 4-chlorothiobenzamide have been measured at 25° in benzene solution. The data obtained have been analysed in terms of molecular solute conformations.

We have previously reported[1] a theoretical study of rotational barriers in pyridinecarbothioamides. Low energy barriers about the ring–thioamide linkage were found, ranging from 2·4 to 4·4 kcal mol^{-1}, which are high enough, however, to prevent the free rotation of the thiocarbamoyl group. These results prompted further experimental investigation on heterocyclic arenecarbothioamides in order to provide additional support for the conclusions reached. To this end, we measured the electric dipole moments in benzene at 25° of the arenecarbothioamides (1)—(6) listed in the Experimental section. The data obtained were used to investigate the rotational equilibrium between the two planar forms of furan-2-carbothioamide, thiophen-2-carbothioamide, and pyridine-2- and -3-carbothioamides.

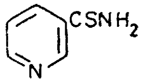


(1) X=O

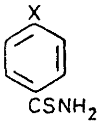
(2) X=S



(3)



(4)



(5) X=H

(6) X=Cl

EXPERIMENTAL

Materials.—Compounds (1)—(6) were prepared by the addition of hydrogen sulphide to the corresponding nitrile in the presence of ammonia, following the general procedures for thioamides.[2,3] Furan-2-carbothioamide had m.p. 131—132°, thiophen-2-carbothioamide 110—111°, pyridine-2-carbothioamide 136—137°, pyridine-3-carbothioamide 190—191°, thiobenzamide 118—119°, and 4-chlorothiobenzamide 129—130°. All compounds were crystallized from water to constant m.p. and $\varepsilon_{max.}$. The purity, as determined by differential scanning calorimetry,[4,5] was $>99·6\%$ for all samples examined.

Physical Measurements.—The electric dipole moments were determined in benzene solution at 25 ± 0·01°, using the apparatus and experimental procedure described in detail elsewhere.[6] The dipole moments were evaluated by the Halverstadt–Kumler method.[7] A Höecker plot[8]

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[3] P. Karrer and J. Schukri, *Helv. Chim. Acta*, 1945, **28**, 820.

[4] E. S. Watson, M. J. O'Neill, J. Justin, and N. Brenner, *Analyt. Chem.*, 1964, **36**, 1233.

[5] Perkin-Elemer Corp., Norwalk, 'Thermal Analysis Newsletter,' nos. 1—6.

[6] G. C. Pappalardo and S. Pistarà, *J. Chem. Eng. Data*, 1972, **17**, 2.

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indicated that no association of the thioamides exists in the range of concentrations used. The experimental results are collected in Table 1.

TABLE 1

Polarization data and dipole moments of arenecarbothioamides in benzene at 25°

Compound	α	ε_{10}	β	v_{10}	R_D/cm^3	$P_{2\infty}$/cm^3	μ/D
(1)	13·38	2·2735	−0·478	1·14250	35·2	344·50	3·87 ±0·01
(2)	14·29	2·2730	−0·545	1·14273	41·3	409·80	4·23 ±0·01
(3)	10·77	2·2728	−0·246	1·14257	43·6	316·33	3·63 ±0·01
(4)	7·13	2·2743	−0·409	1·14252	43·0	215·07	2·88 ±0·05
(5)	12·91	2·2755	−0·342	1·14261	44·1	364·93	3·94 ±0·01
(6)	9·48	2·2723	−0·267	1·14316	51·4	350·53	3·81 ±0·01

$\alpha = d\varepsilon_{12}/dw_2$, $\beta = dv_{12}/dw_2$, $\varepsilon_{10} = \lim_{w_2 \rightarrow 0}\varepsilon_{12}$, $v_{10} = \lim_{w_2 \rightarrow 0} v_{12}$.

RESULTS

The expected dipole moments for the various forms of thioamides (1)—(4) were computed by vector addition of the moment of the heterocyclic ring and the moment of the thiocarbamoyl group. The component group moments of furan (0·67 D), thiophen (0·53 D), and pyridine (2·20 D) were taken from previous measurements in benzene solution.[9] In all these rings the resultant moment was assumed as acting in the direction of the heteroatom along the bisector of the internal angle.[10] The value of the moment of thiocarbamoyl group was taken as the value of the dipole moment of thiobenzamide measured in the present work, *i.e.* 3·94 D. For a group such as this it was necessary to determine the angle α which the vector of the resultant moment makes with the C–C bond axis (see Figure 2). This determination was carried out by comparing the dipole moment of thiobenzamide with that of 4-chlorothiobenzamide (6). By assuming in the calculations that the Cl group moment is 1·56 D,[9] the angle α turned out to be 73·7°. This value is close to that obtained for this angle in the similar compound benzamide.[11]

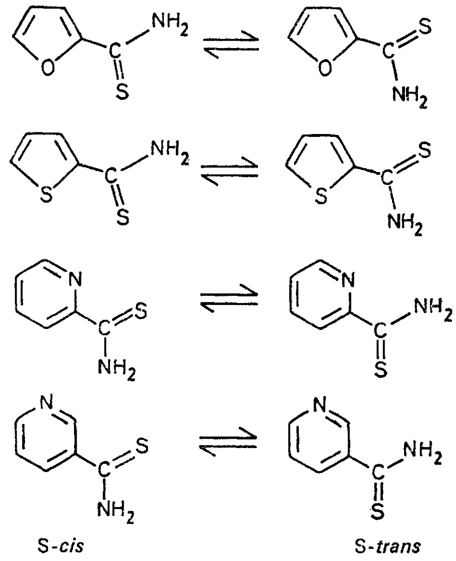

FIGURE 1 The S-*cis*- and S-*trans* conformations of arenecarbothioamides (1)—(4)

TABLE 2

Comparison of calculated and experimental dipole moments

Compound	Conformation	μ_{calc}/D	$\bar{\mu}_{av}$/D	μ_{exp}/D
(1)	S-*cis*	4·61	4·05	3·87
	S-*trans*	3·39		
(2)	S-*cis*	4·47	4·02	4·23
	S-*trans*	3·50		
(3)	S-*cis*	6·10	4·77	3·63
	S-*trans*	2·90		
(4)	S-*cis*	5·69	4·23	2·88
	S-*trans*	1·88		

The total moment of the various conformations of the thioamides was thus calculated by using the relation $\mu = (\mu_x^2 + \mu_y^2 + \mu_z^2)^{\frac{1}{2}}$ in which μ_x, μ_y, and μ_z are the projections, on the axes of an arbitrarily chosen system of coordinates, of the vectors of all the group moments.

TABLE 3

Rotamer populations (mole fraction) and energy differences between conformers

Compound	Conformation	Mole fraction	ΔE/ kcal mol^{-1}
(1)	S-*cis*	0·36	−0·70
	S-*trans*	0·64	
(2)	S-*cis*	0·73	0·20
	S-*trans*	0·27	
(3)	S-*cis*	0·17	−1·31
	S-*trans*	0·83	
(4)	S-*cis*	0·17	−1·31
	S-*trans*	0·83	

The average values of the dipole moments which would result from free rotation of thiocarbamoyl group about the C–C bond ($\bar{\mu}_{av}$) were calculated from the Fuchs–Tiganik formula.[12,13]

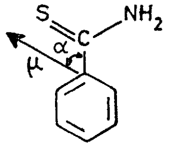

FIGURE 2 Direction of the resultant dipole moment of thiobenzamide (α = 73·7°)

From the entries in Table 2 it is apparent that no single planar conformation of the thioamides agrees with experiment. The measured dipole moments thus provide evidence for an equilibrium mixture of rotational isomers for each compound. Using our experimental values and the dipole moments estimated from group moment calculations, we derived the mole fractions for the S-*cis*- and S-*trans*-conformers, supposing that these were the only ones, and the energy difference $\Delta E(E_{cis} - E_{trans})$ (Table 3).

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[9] A. L. McClellan, ' Tables of Experimental Dipole Moments,' Freeman, San Francisco, 1963.

[10] G. Marino, *J. Heterocyclic Chem.*, 1972, **9**, 817.

[11] W. W. Bates and M. E. Hobbs, *J. Amer. Chem. Soc.*, 1951, **73**, 2151.

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[13] L. Tiganik, *Z. phys. Chem.*, 1932, **14B**, 135.

DISCUSSION

Against the implication in Table **3** that furan-2-carbothioamide has a planar conformation with a small preponderance of the S-*trans*-isomer (S-*trans* : S-*cis* 64 : 36) must be set the following considerations: (i) in the analogous compound furfuraldehyde the O-*cis*-form is the more stable in solution [14] and (ii) as a general rule, in five-membered heterocycles with an *ortho*-formyl group the O-*cis*-form predominates.[15] Now, bearing in mind that accuracy of vector addition is ±0·2 D at best, the calculated $\bar{\mu}_{av}$ value for amide (1) appears to be fairly close to the experimentally determined dipole moment. This may therefore indicate that the thiocarbamoyl group in (1) is freely rotating, *i.e.* several forms are populated with equal probability.

Conversely, the preponderance found for the S-*cis*-conformation for amide (2) cannot be excluded *a priori*, since such a possibility was expectable on the basis of circumstance (ii). Therefore the agreement observable between $\bar{\mu}_{av}$ and μ_{exp} for this molecule may be fortuitous.

In the case of amides (3) and (4) the marked difference between the $\bar{\mu}_{av}$ and μ_{exp} values allow us to exclude the possibility of essentially free rotation of the thiocarbamoyl group about the C–C bond. For pyridine-2-carbothioamide in the equilibrium mixture the molecule is present almost entirely in the S-*trans*-conformation. This conclusion agrees well with results from *X*-ray analysis of the solid [16] and i.r. spectral studies [17,18] which show that the planar S-*trans*-isomer of amide (3) is strongly favoured. It is also apparent that the presence of extensive conjugation between the thiocarbamoyl group and the pyridine ring can be a factor determining the planarity of the molecule, whereas the stability of the S-*trans*-form seems to be controlled by steric effects and intramolecular hydrogen bonding ($N-H\cdots N_{py}$) which disfavour the S-*cis*-form. Moreover, a planar S-*trans*-conformation is a general feature of *o*-formyl derivatives of pyridine.[15]

In the case of amide (4) it can also be inferred that the S-*trans*-conformation is preponderant in the mixture of isomers. Unfortunately, additional information on the preferred conformation of this molecule is not available in the literature. Our present findings do not differ greatly from those from *X*-ray analysis of the analogous compound nicotinamide.[19] In fact, in this molecule the carbamoyl group is twisted 24° out of the planar O-*trans*-arrangement. This experimental evidence, moreover, is also consistent with results of PCILO calculations for nicotinamide.[20]

Finally, it is noteworthy that the ΔE values found for amides (3) and (4) are somewhat less than the calculated energy differences produced by CNDO/2 computations.[1] This discrepancy can be accounted for by considering that the experimental value of ΔE includes the difference in the energies of the isolated rotational isomers and the potential energies due to the interaction of each isomer with neighbouring molecules. Previously [21] an explanation of this solvent effect was given in terms of current theories of solvation. Therein it was also demonstrated that the mole fraction of the rotamer having the highest dipole moment increases on passing from the vapour to the solution state.

[4/118 *Received, 22nd January*, 1974]

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