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# Hindered Internal Rotations in *N*-Arylthioncarbamates and *N*-Aryldithiocarbamates

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The thioamide type rotation in some *p*-substituted *N*-arylthion- and *N*-aryldithiocarbamates has been studied by monitoring the temperature-dependent $^1$H-NMR spectra of the aryl and alkoxy (alkylthio) protons. The evaluation of the rate constants was carried out by approximate methods, the validity of which for the aromatic protons was checked by calculations with the density matrix program DNMR 3. The *N*-aryl groups are barrier-lowering compared to methyl groups. The identification of the spectra of *Z* and *E* isomers was made on the basis of the expected effects of the anisotropy of the thiocarbonyl group.

The comparatively high barriers to rotation of the amino group in amides and thioamides, which have been extensively studied by NMR lineshape methods,[1] are ascribed to an electronic interaction between the nitrogen lone pair and the carbonyl (thiocarbonyl) group, which stabilizes the initial state but is absent in the transition state of the rotation. Substituents that interfere with this interaction also affect the barrier. Thus, substituents with double bonds [2] or hetero atoms with lone pairs [3,4] attached to the (thio)amide carbon atom lower the barrier, because they conjugate with the (thio)carbonyl group. As discussed in Ref. 3, the main reason for the lowering of the barrier is that the substituents interact more strongly with the (thio)carbonyl group in the transition state than in the initial state, where a competing cross-conjugation with the amino group is operative.

A similar effect should be expected when a substituent with double bonds or an aromatic ring is attached to the nitrogen atom. Gehring *et al.*[5] reported a considerable lowering in barrier on going from *N*,*N*-dialkylamides to *N*-alkyl-*N*-vinylamides. However, the great differences in $E_a$ (6.2 – 14.3 kcal/mol for formamides, 6.2 – 8.7 kcal/mol for acetamides) are probably mostly due to the method of evaluation. The line-separation method [6] was used, and the log *A* values vary from 11.4 to 17.4. However, when the $\Delta G^{\ddagger}$ values at coalescence are calculated from the given coalescence temperatures and non-exchanging

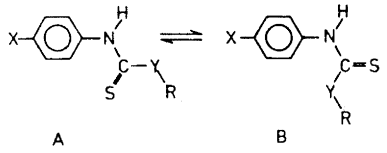
chemical shifts ($\Delta\nu_0$), smaller but probably more significant differences in the expected direction are obtained (*ca.* 1.5 kcal/mol for both formamides and acetamides).

A study of the effect of an *N*-aryl group is rendered difficult by steric factors. In *N*-alkylanilides [7] and in *ortho*-substituted anilides [8] the aromatic ring is perpendicular to the amide plane, and in *N*-unsubstituted anilides without *ortho* substituents the *E*/*Z* ratio is often unfavourable for NMR lineshape studies.[9] Carter [10] has measured the amide type rotational barriers by NMR technique in a series of para-substituted formanilides with an *E*/*Z* ratio close to unity, and he has found $\Delta G^{\ddagger}$ values at the coalescence temperature in the range 17.7 – 18.3 kcal/mol. These barriers are not much different from that reported for formamide, 17.8 kcal/mol.[11]

However, it should be noted that the effect of the vinyl group in the *N*-vinylamides [5] is compared to that of a methyl group, whereas the effect of an aryl group is compared to that of a hydrogen atom. Since *N*-methyl groups in amides are barrier-increasing relative to hydrogen, the aryl group, like the vinyl group, is barrier-decreasing relative to a methyl group. The choice of reference barriers will be further discussed in connection with the results of the present investigation.

The small effect of *N*-aryl substitution in formamide cannot be due to a nearly perpendicular arrangement of the aromatic ring and the amide group, since the angle between these two planes in crystalline acetanilide is 17.6°[12,13] and there is no reason to expect a larger angle in formanilide.

The present work was undertaken because some *para*-substituted thioanilides with favourable *E*/*Z* ratios became available (Ia – e), and the temperature-dependence of the aromatic proton NMR signals provided an extra opportunity to measure the barriers. It was anticipated that the results would give information on the effect of *N*-aryl substitution in thioamides.



A B

I

a. X = $(CH_3)_2N$, Y = S, R = $CH_3$.
b. X = $(CH_3)_2N$, Y = O, R = $CH_3$.
c. X = $(CH_3)_2N$, Y = O, R = $C_2H_5$.
d. X = $(CH_3)_2N$, Y = O, R = i-$C_3H_7$.
e. X = $CH_3O$, Y = S, R = $CH_3$.

## EXPERIMENTAL

*Preparative part.* The preparation of Ia has been described previously,[14] and Ie was prepared as described in Ref. 15.

*Methyl* p-*dimethylaminophenylthioncarbamate (Ib).* Methyl chlorothionformate [16] (0.04 mol) was added dropwise with stirring and external cooling to a solution of *N*,*N*-dimethyl-*p*-phenylenediamine (0.04 mol) in dry acetone (50 ml). The solution was left overnight at +5°, and the resulting pale yellow crystals (hydrochloride of Ib) were filtered off and treated with sodium bicarbonate solution to give colourless crystals (2.61

g, 31 % yield), m.p. 137 – 138° after recrystallization from chloroform-ligroin (b.p. 80 – 100°). (Found: C 57.1; H 6.92; N 13.2; S 15.3. $C_{10}H_{14}N_2OS$ (210.30) requires C 57.1; H 6.71; N 13.3; S 15.3).

*Ethyl* p-*dimethylaminophenylthioncarbamate (Ic)* was prepared in an analogous fashion. However, ethyl chlorothionformate could not be prepared as described in Ref. 16. Instead, the preparation of Ic was performed as follows. Sodium ethoxide (0.05 mol) in absolute ethanol was added dropwise with stirring to a solution of thiophosgene (0.05 mol) in absolute ethanol (3 ml) under nitrogen with external cooling to −20°. The mixture was allowed to warm to room temperature, and the precipitated sodium chloride was removed by filtration. *N,N*-Dimethyl-*p*-phenylenediamine (0.05 mol) in absolute ethanol (50 ml) was added dropwise with stirring under nitrogen.

On the following day the ethanol was removed by evaporation, and the residue was brought to crystallization by trituration with acetone. The product (hydrochloride of Ic) was dissolved in water, and addition of sodium acetate precipitated colourless prisms (4.5 g, 40 % yield), m.p. 100 – 101° after recrystallization from toluene-ligroin (b.p. 80 – 100°). (Found: C 59.3; H 7.36; N 12.5; S 14.4. $C_{11}H_{16}N_2O_5$ (224.33) requires C 58.9; H 7.19; N 12.5; S 14.3).

*2-Propyl* p-*dimethylaminophenylthioncarbamate (Id)*. *p*-Dimethylaminophenyl isothiocyanate [17] (0.02 mol) in hexamethylphosphoric triamide (HMPT, 100 ml) was added dropwise with stirring and cooling to −10° to a solution of sodium 2-propoxide (0.02 mol) in 2-propanol (200 ml). The mixture was left overnight at −20° and then poured onto ice. After extraction with chloroform and washing of the chloroform solution with dilute hydrochloric acid, bicarbonate solution, and water, some HMPT still remained. This was removed by evaporation, dissolution of the residue in benzene, and repeated extractions with water. Evaporation of the benzene solution gave a pale brown crystalline residue (0.29 g, 6 % yield), which crystallized from toluene-ligroin (b.p. 80 – 100°) as colourless prisms, m.p. 105 – 106°. (Found: C 60.1; H 7.69; N 11.7; S 13.5. $C_{12}H_{18}N_2OS$ (238.35) requires C 60.5; H 7.61; N 11.8; S 13.5).

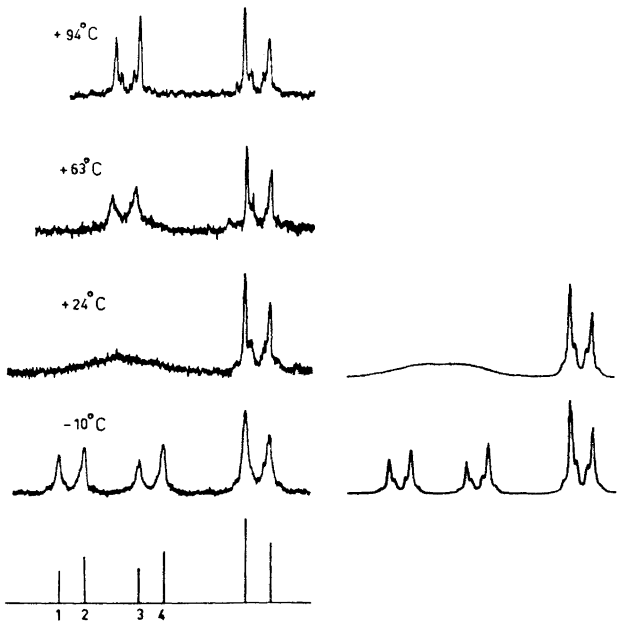



*Fig. 1.* Experimental and calculated spectra of the aromatic protons of Ia (in pyridine-$d_5$).

*NMR spectra and evaluation of rate constants.* The spectra were recorded on Varian Models A-60 and XL-100 NMR spectrometers equipped with variable temperature probes and V-6040 temperature controllers. The temperatures were measured from the internal chemical shifts of capillaries filled with methanol (low temperature) or ethylene glycol (high temperature) and placed concentrically in the sample tubes. The capillaries were calibrated with a copper-constantan thermocouple as previously described.[18] The samples were measured in 0.5 M solutions.

The evaluation of the rate constants from the lineshape of the *S*- and *O*-methyl proton signals was carried out by the approximate method developed by Shanan-Atidi and Bar-Eli [19] for uncoupled two-site cases with unequal populations. In Ic the ethyl methylene proton signals were observed with simultaneous decoupling of the methyl protons.

In the evaluation of the rate constants from the aromatic proton signals, the latter were treated as two AB spectra with different populations in the slow exchange limit, which change to one AB spectrum in the fast exchange limit. The chemical shift differences between the protons *meta* to the thiocarbamoyl group in the *E* and *Z* forms is quite small, and therefore the exchange has been treated as one between site 1 and site 3 and between site 2 and site 4 (Fig. 1). To check the validity of this approximation, the lineshape of the AA'BB' $\rightleftharpoons$ CC'DD' exchange system in Ia was calculated by the density matrix method (program DNMR 3).[20] The rate constant used was that found by the approximate method at coalescence; the chemical shifts ($\nu_A$ to $\nu_D$) and the population ratio were obtained from the low temperature spectrum, and the appropriate coupling constants ($J_{ortho} = 8.0$ Hz, $J_{meta} = 2.5$ Hz, $J_{para} = 0.5$ Hz,) were taken from the literature.[21] As can be seen in Fig. 1, the agreement between the calculated and the experimental lineshapes is quite satisfactory, and the approximate method can be regarded as reliable. The rate constants and $\Delta G^{\ddagger}$ and $\Delta\nu_0$ values are summarized in Table 1.

*Table 1.*

| Compound | Solvent | $p_A$[a] | $\Delta\nu_0$ Hz | $T_c$ K | $\Delta G^{\ddagger}_{B\rightarrow A}$ kcal/mol | Frequency MHz | $^1$H signals observed |
|---|---|---|---|---|---|---|---|
| Ia | Pyridine-$d_5$ | 0.48 | 29.5 | 297 | 15.0 | 60 | Aromatic |
| Ia | $CDCl_3$ | 0.14 | 11.4 | 267 | 14.8 | 100 | *S*-Methyl |
| Ib | Pyridine-$d_5$ | 0.44 | 24.9 | 314 | 16.1 | 60 | Aromatic |
| Ib | $CDCl_3$ | 0.25 | 3.5 | 288 | 16.3 | 60 | *O*-Methyl |
| Ic | Pyridine-$d_5$ | 0.46 | 23.1 | 316 | 16.2 | 60 | Aromatic |
| Ic | Pyridine-$d_5$ | 0.46 | 7.5 | 307 | 16.3 | 100 | *O*-Methylene |
| Id | Pyridine-$d_5$ | 0.41 | 23.5 | 319 | 16.5 | 60 | Aromatic |
| Ie | Pyridine-$d_5$ | 0.67 | 26.5 | 288 | 14.9 | 60 | Aromatic |
| Ie | $CDCl_3$ | 0.10 | 10.8 | 256 | 14.4 | 100 | *S*-Methyl |

[a] Mol fraction of form A.

## RESULTS AND DISCUSSION

A possible set of reference compounds for I is the corresponding *N*-methylthion- and dithiocarbamates (II), in which case the effect of the aryl group is compared with that of a methyl group. Whereas the barriers for II are still unknown, those for the corresponding *N*,*N*-dimethylthioamides (III) are 17.7 and 15.6 kcal/mol, respectively [3] (in *ortho*-dichlorobenzene). The difference between IIa and IIIa, and between IIb and IIIb, may be estimated by a comparison with the pair *N*-methylthioacetamide and *N*,*N*-dimethylthioacetamide. The first of these compounds has been extensively studied by Walter and Schaumann.[22] These authors could separate the *E* and *Z* forms

II III

IIa, IIIa. Y = O.
IIb, IIIb. Y = S.

by TLC and follow their isomerization by IR and UV spectroscopy. In chloroform solution a UV-kinetic investigation gave $\Delta G^{\ddagger}_{E\rightarrow Z} = 21.2$ kcal/mol, $\Delta G^{\ddagger}_{Z\rightarrow E} = 23.4$ kcal/mol. A complicating factor in this comparison is the relatively larger stabilization of the *Z* forms. This is found also in amides [23] and esters,[24] and a recent *ab initio* calculation on methyl formate indicates that it is due to electrostatic attraction between the oxygen and the methyl hydrogen atoms.[25] On the other hand, the *E* form of *N*-methylthioacetamide is destabilized by about 1 kcal/mol by a repulsive interaction between the methyl groups.[26] A similar repulsion must be expected in the *Z* form of IIb, since the van der Waals radii of methyl and sulphur are rather similar, and a somewhat smaller repulsion is expected in the *E* form of IIa.* For *N*,*N*-dimethylthioacetamide $\Delta G^{\ddagger}$ values of 21.6 [3] and 21.8 kcal/mol [28] have been reported, both in *ortho*-dichlorobenzene. Roughly, the difference between the $\Delta G^{\ddagger}$ values for *N*,*N*-dimethylthioacetamide and the *E* form of *N*-mehylthioacetamide, 0.4 – 0.6 kcal/mol, can be used as a correction from compounds III to the corresponding compounds II, *i.e.* $\Delta G^{\ddagger}_{E\rightarrow Z}$ should be $17.2 \pm 0.1$ and $15.1 \pm 0.1$ kcal/mol for IIa and IIb, respectively. The real deviations may of course be somewhat larger than $\pm 0.1$ kcal/mol.

An inspection of the $\Delta G^{\ddagger}$ values in Table 1 reveals in most cases slightly higher values in pyridine-$d_5$ than in deuteriochloroform solution. This is at variance with the behavior of the *N*,*N*-dimethyl-*N'*-arylthioureas, where the barriers to rotation of the dimethylamino group were found to be *ca.* 1 kcal/mol lower in pyridine than in deuteriochloroform.[18] The solvent effect in the latter example was explained by hydrogen bonding between NH protons and pyridine nitrogen atoms, which should lead to a strengthening of the (Ar)N – C = S interaction in competition with the $(CH_3)_2$N – C = S interaction. The same mechanism can evidently account for the solvent effect in the present work, since the rotation observed is around the (Ar)N – C = S bond.

Comparison of the $\Delta G^{\ddagger}$ values in deuteriochloroform in Table 1 with the assumed values for IIa and IIb shows a small barrier-lowering effect (*ca.* 0.3 kcal/mol) of the *p*-dimethylaminophenyl group in the dithiocarbamates, and a somewhat larger effect of the *p*-methoxyphenyl group, as expected from the electron-donating effects of the dimethylamino and methoxy groups. The barrier-lowering effect of the *p*-dimethylamino group is larger (*ca.* 0.9 kcal/mol) in the thioncarbamate series.

* The *E*–*Z* nomenclature [27] is slightly confusing in systems I and II, since the *Z* form when Y = O is the *E* form when Y = S. Therefore, the symbols A and B are used for I in the present work.

Surprisingly, the effect of increasing the size of the group R (Ib – Id) is an increased stabilization of form B. (For assignments of forms A and B, *vide infra.)* No explanation for this effect can be offered at present.

It has been found in several anilides and thioanilides that the aromatic protons *ortho* to the anilide nitrogen atom are considerably more deshielded in the *Z* (A) form than in the *E* (B) form, due to the anisotropy of the carbonyl or thiocarbonyl group.[29] In the present case, therefore, the group of aromatic proton signals found at lowest field is assigned to the *ortho* protons in form A. With the approximation that the aromatic proton spin systems in the slow exchange limit can be treated as two AB spectra, the effect of the anisotropy of the thiocarbonyl group can be measured by the difference, $\Delta$, between the internal chemical shifts $|\nu_A - \nu_B|$ for the A and B forms. The pertinent data are recorded in Table 2. It is apparent that the $\Delta$ values are much smaller for

*Table 2.* Internal chemical shifts and shift differences (at 60 MHz) for I, forms A and B.

| Compound | Solvent | $\lvert\nu_A - \nu_B\rvert$ Hz[a] A | B | $\Delta^b$ Hz |
|---|---|---|---|---|
| Ia | Pyridine-$d_5$ | 69.2 | 39.0 | 30.2 |
| Ia | $CDCl_3$ | 38.8 | 29.0 | 9.8 |
| Ib | Pyridine-$d_5$ | 63.4 | 38.4 | 25.0 |
| Ib | $CDCl_3$ | 38.4 | 27.8 | 10.6 |
| Ic | Pyridine-$d_5$ | 64.2 | 42.6 | 21.6 |
| Id | Pyridine-$d_5$ | 63.8 | 41.8 | 22.0 |
| Ie | Pyridine-$d_5$ | 52.2 | 24.4 | 27.8 |
| Ie | $CDCl_3$ | 29.8 | 19.7 | 10.1 |

[a] Note that A and B here are the common NMR symbols. [b] $\Delta = |\nu_A - \nu_B|_A - |\nu_A - \nu_B|_B$ ($c = 0.5$).

deuteriochloroform than for pyridine-$d_5$ solution. This may be due to the orientation of solvating pyridine molecules by the molecular electric dipole moment (ASIS effect [30]). In A, the negative end of the dipole is close to the *ortho* hydrogen atoms, and consequently a solvating pyridine molecule should preferentially shield the *meta* protons. In form B the negative end of the dipole is directed away from the aromatic ring, and shielding of the *ortho* protons becomes possible. The effect of hydrogen bonded pyridine molecules should to a first approximation be the same in forms A and B.

The $\Delta$ values observed in deuteriochloroform solution are less than half of the values observed for *N*,*N*-dimethyl-*N'*-arylthioureas,[18] and also for formanilides.[10] For *p*-nitrothioformanilide in acetone solution Rae [31] has observed a $\Delta$ value of 39 Hz. The lower values in the compounds studied here must reflect a difference in the anisotropy of the thiocarbonyl group.

Since it was found that the aryl groups in I are barrier-lowering compared to a methyl group, it was of interest to perform a similar comparison for the formanilides discussed in Ref. 10. For these, the reference is the $E \rightarrow Z$ barrier in *N*-methylformamide, 18.0 kcal/mol in 1,2-dichloroethane.[32] Evidently, the aryl groups are not significantly barrier-lowering compared to a methyl group

in the formanilides. The *p*-methoxyphenyl and *p*-dimethylaminophenyl groups are even slightly barrier-raising. A possible explanation for the difference between the formanilides and compounds I may be that the thiocarbonyl group is more polarizable in both directions by substituents on the nitrogen atom than the carbonyl group.

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