

Barriers to Internal Rotation, Ultraviolet Spectra, and Conformations of *N,N*-Dimethyl-*N'*-arylthioureas and *N,N,N'*-Trimethylthioureas

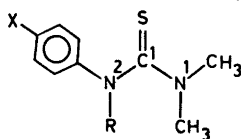
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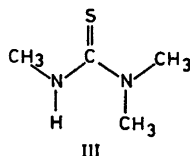
The barriers to rotation of the dimethylamino group in a series of *p*-substituted *N,N*-dimethyl-*N'*-phenylthioureas have been measured by the NMR lineshape technique, and good Hammett correlations with σ_p were obtained. The barrier-lowering effect of an *N'*-methyl group, and possible conformations of dimethyl- and trimethylarylthioureas are discussed with arguments from ultraviolet, infrared, and NMR spectra. Molecular orbital calculations give good correlations with barriers and ultraviolet spectra. The possible effect of thione-thiol tautomerism on barriers in dimethylarylthioureas is discussed.

Attempts to measure the barrier to internal rotation in tetramethylthiourea, as well as that in tetramethylselenourea,¹ by the NMR lineshape method have failed, since these compounds give only one signal down to -120°C . This is quite different from other *N,N*-dimethylthioamides, which have ΔG^\ddagger values for rotation of the dimethylamino group in the range 15–24

- I R=H
 a, X=NO₂
 b, X=CH₃CO
 c, X=CH₃OCO
 d, X=Cl
 e, X=F
 f, X=H
 g, X=CH₃
 h, X=CH₃O
 i, X=(CH₃)₂N



- II R=CH₃
 a, X=NO₂
 b, X=H



kcal/mole.² In R-CS-N(CH₃)₂, the barrier decreases with increasing conjugating capacity of R, and the low barrier of tetramethylthiourea must at least partly be due to the strong electron-donating effect of the dimethylamino group.² This is supported by the ΔG^\ddagger value of *N,N*-dimethyl-*N'*-acetylthiourea, which is 16.1 kcal/mole.² However, model studies and also structure investigations³ show that the dimethylamino groups in tetramethylurea and tetramethylthiourea cannot be in the molecular plane, and the steric effect will lower the barrier. The importance of the steric effect is well substantiated by the recent work of Brown and Katekar,⁴ who report a ΔG^\ddagger value of 10.8 kcal/mole for *N,N*-dibenzyl-*N'*-methylthiourea. In this molecule planarity is possible.

One would expect the introduction of a phenyl group on one amino group to diminish the conjugating capacity of the nitrogen atom and thereby increase the barrier to rotation of the other amino group, and a preliminary ΔG^\ddagger value of 11.5 kcal/mole for *N,N*-dimethyl-*N'*-phenylthiourea seemed to support this expectation.² Brown and Katekar⁴ report $\Delta G^\ddagger = 11.3$ kcal/mole for *N,N*-dibenzyl-*N'*-phenylthiourea, in agreement with this picture, whereas the value of 10.7 kcal/mole for *N,N*-dimethyl-*N'*-phenylthiourea reported by Siddall and Stewart⁵ seems to be too low.

If the conjugating capacity of the phenyl group is of importance for increasing the barrier, it should be possible to modify its effect by introducing electron-attracting or electron-donating substituents in the *para* position. We now wish to report the results of an investigation of the barriers in compounds Ia–Ii and IIa and b. For comparison, we have also studied *N,N,N'*-trimethylthiourea (III). The measured barriers are discussed together with other NMR data as well as ultraviolet and infrared spectra with reference to possible conformations of I and II.

PREPARATIVE PART

Compounds Id, Ie, If, Ig and Ii were prepared according to Ho *et al.*⁶

N,N-Dimethyl-*N'*-anisyl-thiourea (Ih) was prepared using the same method,⁶ and a 44 % yield of colourless prisms was obtained, m.p. 126–126.5°. (Found: C 57.8; H 6.29; N 13.2; S 15.1. C₁₀H₁₄N₂OS (210.30) requires C 57.1; H 6.71; N 13.3; S 15.2).

N,N-Dimethyl-*N'*-*p*-nitrophenylthiourea (Ia) was prepared by dissolving *p*-nitroaniline (0.2 mole) in ethanol (600 ml), and adding carbon disulphide (0.72 mole) and N NaOH (15 ml) to the cooled solution. Dimethylamine (0.66 mole) in ethanol (180 ml) was added, and the mixture was refluxed for four days. Even after this time the reaction was far from complete, but the desired product was extracted from unchanged *p*-nitroaniline with N NaOH. On acidification of the alkaline extract, Ia separated as yellow prisms (7 % yield), m.p. 176–177.5° after recrystallization from toluene. (Found: C 48.3; H 5.02; N 18.8; S 14.1. C₉H₁₁N₂O₂S (225.28) requires C 48.0; H 4.92; N 18.7; S 14.2). Ho *et al.*⁶ claim to have prepared this compound but give m.p. 124–125°. Their product is probably a mixture of Ia and much *p*-nitroaniline.

N,N-Dimethyl-*N'*-*p*-acetylphenyl-thiourea (Ib) was prepared in an analogous way. The crude product consisted of a mixture of Ib and unreacted amine. Extraction of the latter with N HCl gave Ib as yellow prisms (5 % yield), m.p. 167–169° after recrystallization from toluene. (Found: C 59.5; H 6.17; N 12.6; S 14.4. C₁₁H₁₃N₂OS (222.32) requires C 59.5; H 6.35; N 12.6; S 14.4).

N,N-Dimethyl-*N'*-*p*-carbomethoxyphenyl-thiourea (Ic) was prepared by the standard method of Ref. 6 (43 % yield) as colourless prisms, m.p. 175.5–176.5° after recrystallization from toluene. (Found: C 55.4; H 5.78; N 11.9; S 13.5. C₁₁H₁₄N₂O₂S (238.32) requires C 55.4; H 5.92; N 11.8; S 13.5).

N,N,N'-Trimethyl-*N'*-*p*-nitrophenyl-thiourea (IIa). *N,N*-Dimethylthiocarbamoyl chloride (8 mmole) and *N*-methyl-*p*-nitroaniline⁷ (4 mmole) were refluxed in xylene (10 ml) for 12 h. Then triethylamine (8 mmole) was added, and the mixture was refluxed for another 12 h. After cooling, the triethylammonium chloride was removed by filtration, and evaporation of the filtrate gave yellow prisms (35 % yield), m.p. 120–122° after recrystallization from butanol. (Found: C 50.4; H 5.65; N 17.5; S 13.4. C₁₀H₁₃N₃O₂S (239.30) requires C 50.2; H 5.48; N 17.6; S 13.4).

N,N,N'-Trimethyl-*N'*-phenylthiourea (IIb). *N,N*-Dimethylthiocarbamoyl chloride (0.012 mole) in benzene was added dropwise to a solution of *N*-methylaniline (0.024 mole) in benzene (25 ml) and the mixture was refluxed for 24 h. After extraction with water the benzene solution was evaporated, and the solid residue (96 % yield) was recrystallized from heptane to give colourless prisms, m.p. 76–77°. (Found: C 62.1; H 7.14; N 14.4; S 16.6. C₁₀H₁₄N₂S (194.31) requires C 61.8; H 7.26; N 14.4; S 16.5).

N,N,S-Trimethyl-*N'*-*p*-tolyl-isothiourea (Vb). Sodium ethoxide (0.05 mole) in absolute ethanol (50 ml) was added to a solution of Ig (0.05 mole) in absolute ethanol (20 ml), followed by methyl iodide (0.05 mole). The reaction was completed at room temperature over night, and the product was vacuum distilled, b.p. 158–160° at 6 Torr (1.6 g, 15 % yield). The purity was checked by gas chromatography. (Found: C 63.1; H 7.64; N 13.5; S 15.4. C₁₁H₁₆N₂S (208.33) requires C 63.4; H 7.74; N 13.5; S 15.4).

NMR SPECTRA AND EVALUATION OF RATE CONSTANTS

The spectra were recorded on a Varian A-60 spectrometer equipped with a Varian V-6031 variable-temperature probe and temperature controller. It was our intention to evaluate the rate constants by a complete lineshape treatment.⁸ Uncertainties in the determination of the transverse relaxation time (T_2), caused by the low temperature (–35 to –65°), have compelled us to work in a temperature range rather close to coalescence, where the lineshape is not strongly affected by moderate changes in T_2 . We have therefore been content to study ΔG^\ddagger in this region. Compounds Ie to Ii were measured in deuteriochloroform solution, but Ia to Id were not sufficiently soluble in this solvent, and they were therefore studied in pyridine solution. For comparison, Ie, If, Ih, and Ii were studied in the same solvent. Due to overlapping of signals, Ih in pyridine and Ii in both solvents have only been studied at the coalescence temperature by the approximate method.⁹ The same applies to IIa and IIb, which were studied in dichlorofluoromethane solution. (This solvent is regarded as nearly equivalent to deuteriochloroform in solvating properties.) The con-

Table 1. Concentrations of solutions used for lineshape studies.

Compound	Molarity in CDCl ₃	Molarity in pyridine
Ia		0.9
Ib		0.9
Ic		0.9
Id		2.6
Ie	0.7	1.8, 1.2
If	0.7	1.9
Ig	0.6	
Ih	0.6	1.9
Ii	0.6	1.8

centrations employed are found in Table 1. The high concentrations used in pyridine solution were necessary to prevent solvent crystallization. The temperatures were monitored by the temperature dependent shift differences of suitable mixtures in capillary tubes, placed coaxially in the sample tubes. When pyridine was used as solvent, methanolic hydrochloric acid was employed in the capillary tubes, but with deuteriochloroform the methanol and sample methyl signals overlapped, and instead a mixture of dichloromethane, concentrated hydrochloric acid, and methanol- d_4 was employed. The temperature-dependent shifts as well as other shift data discussed in this work were determined by the sidebands generated by a Hewlett-Packard Model 200 CD oscillator and measured by a Model 3734 A frequency counter from the same company. The shifts were calibrated against the standard Varian methanol sample by the normal substitution method. Since the mixtures are not quite stable, the calibration had to be repeated before each series of measurements. Recently, Van Geet¹⁰ has criticized the Varian temperature standards, and we have therefore calibrated our methanol sample with a copper-constantan thermocouple. Also in this case the substitution technique was used, and a least squares treatment of eleven calibration points gave a good linear relation in the region -70 to $+4^\circ$. The deviations were less than those found by Van Geet. At -65°C the Varian sample gave 0.9° and at -34°C 1.6° too low temperature.

The transverse relaxation time was determined as described in Ref. 1. However, this treatment requires that broadening due to longitudinal relaxation can be neglected. That this condition may not always be fulfilled can be inferred from a slightly dissymmetric appearance of the doublets at low temperatures. The high-field *N*-methyl signal is slightly broader than the other one, possibly due to different relaxation conditions. This effect has also been observed by Siddall and Stewart⁵ in the case of If.

The evaluation of the rate constants was performed as described in Ref. 1, though with one change. From temperatures just below coalescence and upwards, a covariation can be observed between τ and the nonexchanging chemical shift $\Delta\nu_0$. Therefore, the latter parameter was not treated as disposable in this temperature region, but the mean of the values obtained at lower temperatures was used. No pronounced temperature dependence of $\Delta\nu_0$ was observed.

Molecular orbital calculations. In order to make possible a comparison with the MO data discussed in Ref. 2, a calculation with a modified ω -method with β -variation¹¹ was performed on system If (IIb) employing parameter set 4 from Ref.¹¹.

The ultraviolet spectra were recorded on a Unicam Model S.P. 800 recording spectrophotometer.

The infrared spectra were recorded at 25°C on a Perkin-Elmer Model 221 prism-grating instrument. The cells consisted of calcium fluoride plates separated by teflon spacers, and cell thicknesses were measured by the interference technique. At low concentrations, where no associated forms were present, the extinction coefficients of forms A and B (assumed to be equal, *vide infra*) were estimated. These were used at higher concentrations to measure the concentrations of A and B, and the concentration of associated forms was obtained as the difference $C_{\text{total}} - (C_A + C_B)$.

Table 2. NMR and rate data for I, II, and III.

Compound	Solvent	<i>T</i> K	τ sec	ΔG^\ddagger kcal/ mole	$\Delta\nu_0$ Hz ^a
Ia	pyridine	222.3	0.0410	11.5	23.0
		223.6	0.0360	11.5	21.6
		224.3	0.0285	11.4	22.2
		225.4	0.0260	11.4	21.2
		225.8	0.0230	11.4	21.6
Ib	pyridine	213.5	0.064	11.2	25.4
		217.6	0.0275	11.1	24.6
		218.2	0.0255	11.0	23.1
		227.0	0.0064	10.9	24.4
Ic	pyridine	210.3	0.0540	10.9	27.8
		215.2	0.0208	10.8	29.4
		220.1	0.0175	11.0	26.2
		229.0	0.0047	10.8	27.8
Id	pyridine	210.1	0.0206	10.5	33.0
		215.7	0.0168	10.7	32.2
		227.0	0.0050	10.8	32.6
		238.1	0.0020	10.9	32.6
Ie	pyridine <i>c</i> =1.2	215.0	0.0124	10.6	31.4
		228.5	0.0036	10.7	31.4
		236.2	0.00175	10.7	31.4
		211.4	0.0222	10.6	32.2
Ie	pyridine <i>c</i> =1.8	213.8	0.0193	10.7	32.0
		217.6	0.0136	10.7	30.8
		224.5	0.0064	10.8	31.6
		228.4	0.0034	10.7	31.6
Ie	CDCl ₃	223.0	0.0551	11.6	20.8
		225.3	0.0451	11.7	20.6
		229.5	0.0267	11.7	19.8
		233.7	0.0140	11.6	20.4
If	pyridine	207.6	0.0207	10.4	36.0
		212.1	0.0147	10.5	36.2
		215.7	0.0104	10.5	34.4
		220.3	0.0062	10.5	35.6
		223.6	0.00396	10.5	35.6
If	CDCl ₃	217.2	0.088	11.5	27.4
		228.0	0.0344	11.7	26.4
		232.0	0.0227	11.7	25.8
		237.6	0.0080	11.5	26.6
Ig	CDCl ₃	219.3	0.123	11.8	22.0
		224.3	0.0570	11.7	21.2
		228.4	0.0254	11.6	21.2
		232.2	0.0116	11.4	21.6
Ih	CDCl ₃	237.1	0.0052	11.3	21.6
		212.1	0.0810	11.2	21.6
		217.2	0.0614	11.4	21.8
		224.5	0.0317	11.5	22.1
		228.0	0.0184	11.4	21.6
		230.2	0.0171	11.5	20.2
Ih	pyridine	208		10.3 ^b	
Ii	pyridine	205		9.9 ^b	
Ii	CDCl ₃	223		11.1 ^b	
IIa	CHCl ₂ F	170		8.3 ^b	
IIb	CHCl ₂ F	193		9.5 ^b	
III	CDCl ₃	211		10.6 ^b	

^a Non-exchanging chemical shifts, as obtained from the lineshape treatment.^b By the approximate method at the coalescence temperature.

DISCUSSION OF BARRIERS AND CHEMICAL SHIFTS

The NMR data, mean life times, τ , and free energies of activation for the rotations are given in Table 2.

A thiourea with negligible steric effects and without extra conjugation was desirable as reference compound, and *N,N,N'*-trimethylthiourea was chosen for this purpose. In deuteriochloroform at room temperature this compound shows a singlet for the dimethylamino group, whereas the third methyl group appears as a doublet due to coupling with the NH group ($J = 4.6$ Hz). The dimethylamino signal broadens at lower temperatures and splits into a doublet at -62° ($\Delta\nu_0 = 18$ Hz). The resulting $\Delta G^\ddagger = 10.6$ kcal is slightly lower than the value reported for *N,N*-dibenzyl-*N'*-methylthiourea.⁴

It is evident that the ΔG^\ddagger values of compounds I show no significant temperature dependence within the limits of accuracy of this treatment. This is also in agreement with the trend in recent more accurate studies of hindered rotation in amide-type molecules,¹²⁻¹⁴ according to which the activation entropies are close to zero. In order to make a Hammett correlation, we used the mean values of ΔG^\ddagger and the Eyring equation¹⁵ to calculate rate constants

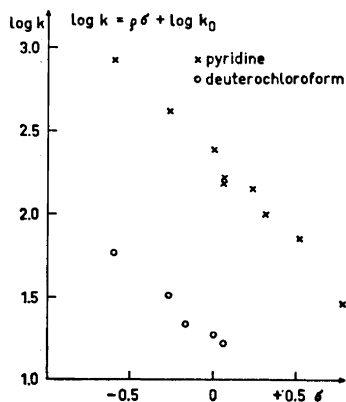


Fig. 1. Hammett correlation for compounds Ia—Ii.

for the rotations of compounds Ia to Ii at 223 K. The Hammett σ_p -values are taken from the compilation of Jaffé,¹⁶ except for the value for CO_2CH_3 , which is that given in Ref. 17. Good linear correlations are obtained (Fig. 1), for which ρ -values and regression coefficients are presented in Table 3. These correlations demonstrate the correctness of the initial assumption of a barrier-increasing conjugation between the aryl group and the thiourea group. The magnitudes of the ρ -values can profitably be compared with the value of -1.17 calculated from the results of Jackman *et al.*¹⁸ for the rotation in *p*-substituted *N,N*-dimethylbenzamides, a reaction with the same electronic requirements as the one studied in the present work. Our somewhat lower value is quite reasonable in view of the greater distance between substituent and reaction center.

Table 3. Hammett correlations for compounds Ia to Ii.

Solvent	ρ^a	R'	ρ^c	R
CDCl ₃	-0.82	0.9858	-0.74	0.9428
Pyridine	-1.04	0.9918	-1.06	0.9787

^a With all barriers.

^b Regression coefficient.

^c With the exception of barriers determined at the coalescence temperature only.

The main reason for the lower barriers in pyridine solution is probably hydrogen bonding between pyridine molecules and NH groups, which increases the electron density around the nitrogen atom N² and makes its lone pair electrons more available for a conjugation, which competes with that of the dimethylamino group. This effect will increase the bond order in the C¹-N² bond, thereby increasing the interaction between the aromatic ring and the reaction center, which also explains the more negative ρ -value in pyridine.

Table 4. Concentration dependency of ΔG^\ddagger for If in CDCl₃.

c in CDCl ₃	T _c K	$\Delta\nu_0$ Hz	ΔG^\ddagger kcal/mole
0.06	222	20.2	11.2
0.12	224	22.6	11.3
0.19	225	24.0	11.3
0.37	228	26.6	11.4
0.56	230	27.8	11.5
0.76	231	30.0	11.5

As will be further discussed in the sections on chemical shifts and infrared spectra, compounds I are partly associated in deuteriochloroform solution. In order to study the effect of this association on the barriers, we have performed a crude coalescence temperature investigation of If in deuteriochloroform at six concentrations in the range 0.06 to 0.76 (molal). The coalescence temperature increased by ten degrees in this region, and even if this was partly compensated by an increase in $\Delta\nu_0$, a significant increase in ΔG^\ddagger with concentration was observed (Table 4). In this case, the result of association is opposite to what was found in pyridine. The effect on the NH group and N² electrons should work in the same direction in both cases. However, pyridine is a far stronger base than thiourea ($pK_a = 5.17$ ¹⁹ and -1.19 ²⁰ respectively), and the hydrogen bond and its effect on the barrier should be stronger in the former case. This is also supported by the infrared shifts of the NH band

in the two solvents. In deuteriochloroform, the thiocarbonyl group is also involved, and hydrogen bonding will increase the polarity of this group, thereby increasing the mesomeric interaction of the amino groups and thus the barrier.

In compounds IIa and IIb the barriers are about 3 kcal/mole lower than in the corresponding compounds Ia and If. A possible rationalization for this will be discussed in connection with the conformations of I and II.

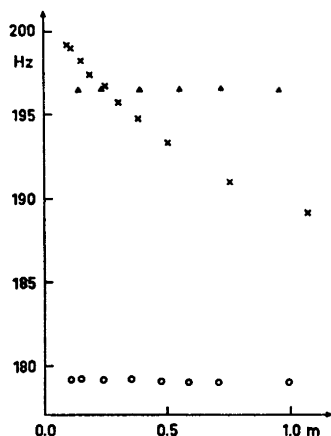


Fig. 2a. ν_{NMe_2} -values for If (\times), IIf (\circ) and III (Δ) in CDCl_3 , as function of concentration.

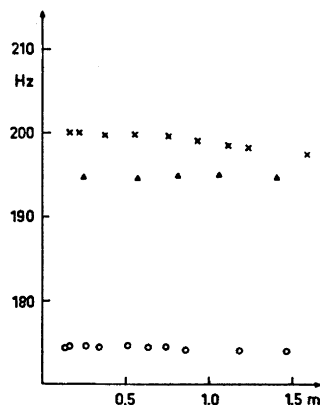


Fig. 2b. ν_{NMe_2} -values for the same compounds in pyridine.

The chemical shifts of the dimethylamino group (ν_{NMe_2}) in If, IIf, and III have been studied with reference to solvent and concentration effects at room temperature, and that of If in deuteriochloroform also at temperatures well below coalescence. The ν_{NMe_2} -values of IIf and III show only a small concentration dependence in deuteriochloroform at room temperature, whereas that of If decreases strongly with increasing concentration, its value approaching that of IIf (Fig. 2a). In pyridine, no strong concentration dependence was observed (Fig. 2b), and also in this solvent ν_{NMe_2} was considerably smaller for IIf than for If or III. At a temperature where the rotation of the dimethylamino group was slow (-77°C), both *N*-methyl signals of If in deuteriochloroform moved upfield with increasing concentration, but the high field signal, which is probably *trans* to the thiocarbonyl group,²¹ showed the largest shifts (Fig. 3).

DISCUSSION OF ULTRAVIOLET SPECTRA

The UV spectra are recorded in Tables 5 and 6 together with the spectra of pertinent parent substances. Compounds Ia to Ii display two strong absorption bands in the wavelength region above 240 nm. The long wavelength band is

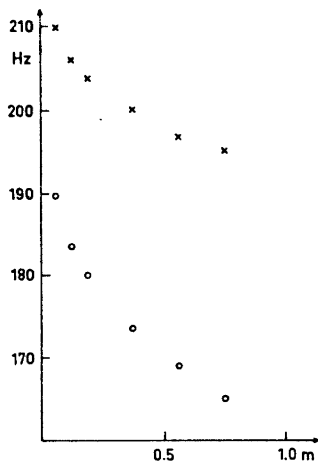


Fig. 3. Chemical shift values for the *N*-methyl signals of If (below coalescence).

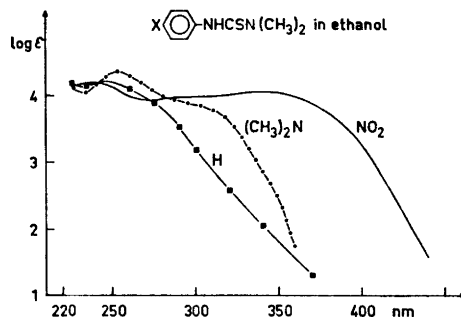


Fig. 4.

highly substituent dependent, and in compounds Id to Ii it is only visible as a shoulder. It is shifted to longer wavelengths by substituents with strong +M and -M effect, most strikingly by the latter type (Fig. 4). In Ia, Ib, and Ic the long wavelength band shows a red shift with increasing solvent polarity, which indicates that it is caused by a transition of charge transfer type, localized mainly in the *para*-substituted aniline chromophore. It can be observed that this transition occurs with higher energy in the thioureas than in the free amines, which is reasonable since the lone pair of the amino group is engaged in a conjugation with the thiocarbonyl group, which opposes the charge transfer. The same kind of difference is found between *p*-nitroaniline and its *N*-acetyl derivative, where the latter has λ_{\max} 318 nm ($\log \epsilon = 4.15$) in ethanol.²²

In the other compounds of type I, the long wavelength band shows a blue shift with increasing solvent polarity, most pronounced in If, where this band is so strongly displaced that it is completely covered by the second band in ethanol solution. This type of solvent dependence is characteristic of thioureas.³⁵

In heptane solution If shows a weaker band at 325 nm. This undergoes a strong blue shift with increasing solvent polarity, and it is in all probability an $n \rightarrow \pi^*$ band. Its ϵ -value is about ten times higher than in simple thioamides, which can be ascribed to a twisting of the conjugated system. This causes the n and π^* orbitals to mix and removes the prohibition which normally applies to $n \rightarrow \pi^*$ transitions.

The spectrum of IIb shows only one $\pi \rightarrow \pi^*$ band above 240 nm. This band undergoes a blue shift with increasing solvent polarity, but much smaller than that shown by If (Fig. 5). The solvent dependence of IIb is much more similar to that of a simple thioamide. As previously discussed,³⁶ the difference between

Table 5. Ultraviolet spectra of Ia-i and the parent amines.

X-C ₆ H ₄ -NHCSN(CH ₃) ₂						X-C ₆ H ₄ -NH ₂					
X	Solvent	λ_{\max}	$\log \epsilon$	λ_{\max}	$\log \epsilon$	Solvent	λ_{\max}	$\log \epsilon$	λ_{\max}	$\log \epsilon$	Ref.
NO ₂	C ₂ H ₅ OH	295	3.98	339	4.04	C ₂ H ₅ OH	227	3.86	375	4.19	22
	CH ₂ Cl ₂	295	4.00	330	4.02	C ₇ H ₁₆	226	3.90	319	4.8	23
COCH ₃	C ₂ H ₅ OH	273	4.21	308	4.13	C ₂ H ₅ OH	316	4.30			24
	CH ₂ Cl ₂	273	4.28	298	4.18	C ₆ H ₁₂	285	4.28			25
COOCH ₃	C ₂ H ₅ OH	267	4.29	298	4.11	C ₂ H ₅ OH	294	4.30			26
	CH ₂ Cl ₂	269	4.31	288	4.18	CH ₂ Cl ₂	279	4.28			
Cl	C ₂ H ₅ OH	247	4.29			C ₂ H ₅ OH	244.5	4.10			27
	CH ₂ Cl ₂	250	4.26			C ₆ H ₁₄	241.4	4.10			27
F	C ₂ H ₅ OH	243	4.16			C ₂ H ₅ OH	233.4	3.85			27
	CH ₂ Cl ₂	248	4.15			C ₆ H ₁₄	230.5	3.85			27
H	C ₂ H ₅ OH	247	4.2 ^o			C ₂ H ₅ OH	235	3.99	286	3.24	28
	CH ₂ Cl ₂	251	4.13			C ₆ H ₁₂	233.5	3.96	286	3.28	29
CH ₃	C ₇ H ₁₆	272	4.20	325	2.75						
	C ₂ H ₅ OH	246	4.24			C ₂ H ₅ OH	238	3.9	292	3.3	30
OCH ₃	CH ₂ Cl ₂	250	4.18			i-C ₈ H ₁₈	237	3.98	293	3.28	31
	C ₂ H ₅ OH	244	4.26			C ₂ H ₅ OH	236	3.9	299	3.2	32
N(CH ₃) ₂	CH ₂ Cl ₂	250	4.25			C ₆ H ₁₂	237	3.97	305	3.46	32
	C ₂ H ₅ OH	253	4.36			C ₂ H ₅ OH	250	4.2	313	3.3	33
	CH ₂ Cl ₂	258	4.34			C ₂ H ₅ OC ₂ H ₅	248	4.24	328	3.46	34

Table 6. Ultraviolet spectra of IIa, IIb, III, Vb, and tetramethylthiourea.

	Hydrocarbons				Ethanol				Ref.
	λ_{\max}	$\log \epsilon$	λ_{\max}	$\log \epsilon$	λ_{\max}	$\log \epsilon$	λ_{\max}	$\log \epsilon$	
	Trimethylthiourea (III)	251	4.09	295(Sh)		240	4.14	280(Sh)	
Tetramethylthiourea	262	4.18	330	2.36	256	4.24	305(Sh)	2	35
<i>N,N,N'</i> -Trimethyl- <i>N'</i> -phenyl-thiourea (IIb)	274.5	4.27	335	2.66	270	4.30			
<i>N,N,N'</i> -Trimethyl- <i>N'</i> - <i>p</i> -nitrophenyl-thiourea (IIa)	259	3.9	337	4.13	265	4.11	350	4.06	
<i>N,N,S</i> -Trimethyl- <i>N'</i> - <i>p</i> -tolyl-isothiourea (Vb)	240	4.10	292	3.93					

simple thioamides and thiourea in this respect is due to the larger decrease in the polarity of the thiocarbonyl group on excitation in thioureas. Compound IIb also displays an $n \rightarrow \pi^*$ band in heptane solution.

Compound IIa shows a strong, broad band at 350 nm in ethanol. This band appears at longer wavelength than in Ia, indicating a stronger *p*-nitroaniline character in the former compound.

DISCUSSION OF INFRARED SPECTRA

Several authors³⁷⁻³⁹ have shown that the NH stretching frequency of an amide with the NH and C=O groups in the *trans* configuration is 20–40 cm^{-1} higher than that of the *cis* isomer. The identification is based on the influence of substituent size on the *cis/trans* ratio, and Siddall *et al.*³⁹, who isolated pure *cis* and *trans* isomers of formanilide, which were identified by NMR

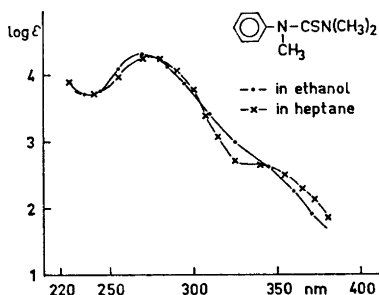


Fig. 5.

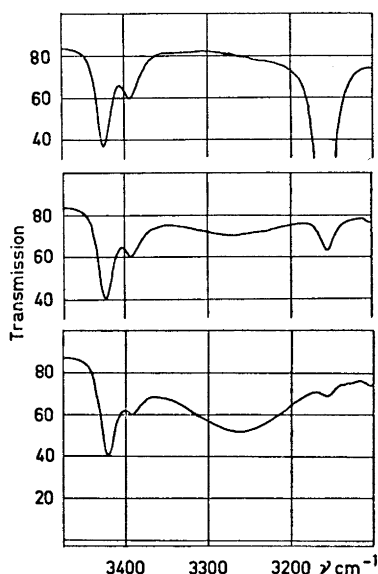
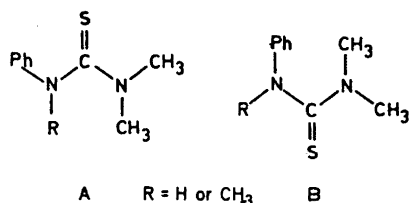


Fig. 6. Infrared spectra of IIa in 0.04 (cell thickness 0.05 cm, top), 0.4 (0.0056 cm, middle), and 1.0 molar (0.0271 cm, bottom) CDCl_3 solutions. A solvent peak appears at 3155 cm^{-1} .

spectroscopy, could confirm this assignment. Gosavi *et al.*⁴⁰ also found two unassociated NH stretching bands in *N,N'*-dialkylthioureas with alkyl groups large enough to upset the dominance of the conformer with both alkyl groups *cis* to the thiocarbonyl group. Recently, Walter and Ruess⁴¹ have shown that IIa exists in carbon tetrachloride solution ($C = 10^{-3}$) as a mixture of the conformers with the phenyl group *cis* (A) and *trans* (B) to the thiocarbonyl group in the ratio 1:1.28, with no associated form observable. The two forms are characterized by NH stretching frequencies of 3428 and 3392 cm^{-1} , respectively. In this case, the assignment was confirmed by the influence of *ortho* substituents



on the *cis-trans* ratio. We have repeated their results with If, and we have observed the same two absorption bands, although with a different intensity ratio, in deuteriochloroform solution. With increasing concentration, a broad, intense band appears at 3265 cm^{-1} (Fig. 6).

A quantitative estimation of the different forms requires a knowledge of the ratio of the extinction coefficients of the *cis* and *trans* monomer NH stretching bands. Russell and Thompson³⁷ assumed that these coefficients to a first approximation are equal, and this usage has more or less tacitly been followed by later authors. We have found two cases, where the reliability of the approximation can be tested. According to NMR measurements, *N*-methylthioformamide exists in various solvents in the form with the methyl group *cis* to the thiocarbonyl group to the extent of 87–88%,⁴² and from a published infrared spectrum⁴³ a value of 90% can be calculated for carbon tetrachloride solution.* For thioacetanilide in the same solvent, 60% of the form corresponding to A is obtained from the infrared spectrum,³⁷ whereas NMR⁴⁴ gives 53.8%. It therefore seems permissible to use the approximation for crude estimates of isomer ratios. Analysis of the infrared spectra in Fig. 6 gives the concentrations of A, B and associated forms presented in Table 7.

Table 7. Infrared analysis of If in CDCl_3 solution (from spectra in Fig. 6).

Molarity	% A	% B	% associated
0.04	75	25	—
0.4	55	20	25
1.0	45	15	40

In pyridine, no monomer bands are visible. A strong, broad band with maximum at 3225 cm^{-1} must be ascribed to one or more associated forms, whereas a much weaker band at 3125 cm^{-1} may be due to a different type of association or to an overtone or combination band similar to the one found at 3080 cm^{-1} in the spectra of anilides and thioanilides.³⁸

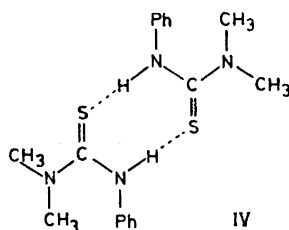
* Added in proof: W. Walter (personal communication) has separated the Z and E forms of *N*-methylthioacetamide and found ϵ -values of 258 and 142, respectively.

DISCUSSION OF THE CONFORMATIONS OF THE *N*-ARYLTHIOUREAS

Inspection of molecular models clearly shows that the conjugated systems in I and II cannot be planar, neither in conformation A nor in conformation B, and that the deviations from planarity must be greater in the latter form. As discussed in the section on infrared spectra, If consists of a mixture of monomers of conformations A and B, together with associated forms at higher concentrations. The dominating conformation among the associated forms can be inferred from the concentration dependence of the chemical shifts of the *N*-methyl NMR signals of If at temperatures below coalescence (Fig. 3). The large upfield shift of the high-field signal with increasing concentration can only be explained by a conformational change, which places the dimethylamino group, and in particular the methyl group *trans* to the thiocarbonyl group, in a region of stronger shielding. The only reasonable source of strong diamagnetic effects is the benzene ring, and it can be seen on models that the methyl group in question must be situated above the plane of the benzene ring in B (Fig. 7). This change is quite acceptable if the dominant associated form is a dimer, (IV).



Fig. 7. Conformations A and B from Dreiding models.



The small concentration dependence of ν_{NMe_3} for If in pyridine is in agreement with a hydrogen-bonded molecule with a constant *cis-trans* ratio. The large ν_{NMe_3} -value indicates a large proportion of form A (Fig. 2b).

NMR and ultraviolet spectra and studies of molecular models show that the A-B equilibrium must be displaced towards form B in II. As in the associated form of If, the small ν_{NMe_3} -value of IIb is best explained by a large proportion of form B. It is possible to calculate the shielding effect of the benzene ring in this conformation by the method by Bovey and Johnson,⁴⁵ if the geometry of the molecule is known. We have used the shift data tabulated in Appendix B of

Ref. 46 and several reasonable geometries to calculate the difference between ν_{NMe_3} for forms A and B. We obtained values in the range 20–30 Hz (mean for six protons), which may be compared with the difference of 22 Hz between the ν_{NMe_3} -values of If and IIb in deuteriochloroform solution, the former extrapolated to zero concentration (Fig. 2a). Analysis of the infrared spectra of If in deuteriochloroform shows an A to B ratio of about 3:1 (Table 7), which means that the proportion of B in If at low concentrations is too low to affect the comparison.

The non-exchanging chemical shift difference, $\Delta\nu_0$, has been measured for If and IIb in dichlorofluoromethane solution (*C* about 0.1) below coalescence. The values, 24.6 and 44.0 Hz, are in good agreement with a picture, in which one methyl group in IIb is in a strongly shielded position.

The signals of the aromatic protons have not been subjected to a general study. One could expect that the thiocarbonyl group should have a deshielding effect on the *ortho* protons in form A. It is of interest, therefore, to note that the centres of the "doublets" of Ia fall at 492 and 447 Hz downfield from TMS, whereas those of IIa fall at 492 and 418 Hz, all in deuteriochloroform. This means that $|\nu_{\text{meta}} - \nu_{\text{ortho}}|$ for Ia is 45 Hz, and for IIa 74 Hz. The difference $\delta\nu$ between these two values, 29 Hz, agrees remarkably well with the corresponding difference for the *exo* and *endo* forms of formamides reported by Carter.⁴⁷ The present case, however, is not quite as clearcut as that of the formamides. The larger $|\nu_{\text{ortho}} - \nu_{\text{meta}}|$ value for IIa may in part be due to the weaker conjugation between N^2 and the thiocarbonyl group, which increases the electron transport into the aromatic ring. On the other hand, the infrared spectrum of Ia in deuteriochloroform shows an A to B ratio of 2:1. The presence of form B decreases the difference $\delta\nu$ to a value smaller than that expected if Ia had been pure A and IIa pure B.

Models show that the phenyl group is subject to stronger steric interferences in form B than in form A, and that these can be relieved by simultaneous rotations around the $\text{C}^1 - \text{N}^2$ and $\text{N}^2 - \text{aryl}$ bonds (Fig. 7). The importance of the rotation around the $\text{C}^1 - \text{N}^2$ bond is shown by the ultraviolet spectra, though these have been recorded in other solvents.

The first $\pi \rightarrow \pi^*$ transitions of Ia, IIa, and *p*-nitroaniline (in ethanol) fall at 339 nm, 350 nm, and 375 nm, respectively (Tables 5 and 6). The larger *p*-nitroaniline character in IIa than in Ia is in agreement with a larger $\text{C}^1 - \text{N}^2$ twist in the former and therefore also with a larger proportion of form B. The same conclusion is reached by a comparison of the solvent shifts of If and IIb. The stronger thioamide character of the latter (see discussion of ultraviolet spectra) is in agreement with a larger $\text{C}^1 - \text{N}^2$ twist in this compound.

From the available data a picture emerges, according to which form A dominates in dilute solutions of compounds I in deuteriochloroform, and form B in compounds II under all conditions. The very constant ν_{NMe_3} of IIb in deuteriochloroform solution at different concentrations indicates (Fig. 2a) that the A–B equilibrium in this compound is unaffected by association processes.

The difference of about 3 kcal/mole in the $\text{C}^1 - \text{N}^1$ barrier between compounds Ia* and IIa or If and IIb cannot be due to a complete orthogonality

* Corrected to deuteriochloroform solution.

between the thiourea group and the benzene ring in II. The barriers of III, 10.6 kcal/mole, and of *N,N*-dibenzyl-*N'*-methylthiourea, 10.8 kcal/mole,⁴ show that conjugation with the phenyl ring can only raise the barrier by about 1 kcal/mole. Otherwise, orthogonality could be a tempting explanation, since Pedersen⁴⁸ has shown that *N*-methylacetanilide in the solid state as well as in solution exists almost entirely in the conformation corresponding to B and with the phenyl ring orthogonal to the amide group. On the other hand, acetanilide exists in the conformation corresponding to A, with the benzene ring twisted only about 17° from the amide plane.^{49,50} Furthermore, an orthogonal conformation cannot explain the observation that the increasing effect of a nitro group on the barrier is as large (about 1 kcal/mole) for II as for I. Also, the ultraviolet spectra of IIa and IIb require considerable conjugation through the N²-aryl bond. Instead, the lower barriers in IIa and IIb must be due mainly to the steric strain in the molecule, caused by the methyl group on N². This strain, which originates in interferences with the dimethylamino group in the initial state, is relieved in the transition state, and therefore it serves to lower the barrier, just as proposed for tetramethylthiourea.

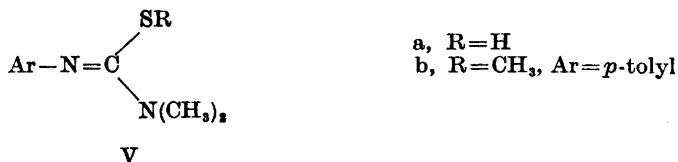
MOLECULAR ORBITAL CALCULATIONS

In Ref. 2 a reasonable linear correlation between ΔG^\ddagger values and calculated π -electron contributions, ΔE_π , to the barriers was observed. We have now calculated ΔE_π for the *N*-phenylthiourea system with the same parameter set (Set 4, Ref. 11), and obtained a value of 0.496 β , compared to 0.488 β for the simple thiourea system. Both values compare favourably with the experimental barriers of 11.5 kcal/mole for If and 10.8 kcal/mole for III. A least-squares linear correlation line for these compounds and the thioamides in Ref. 2 has the equation $\Delta G^\ddagger = 80.0 \Delta E_\pi / \beta - 27.8$ with a correlation coefficient of 0.933, valid for systems without strong steric interferences.

The calculated transition energies for the phenylthiourea system are for the first $\pi \rightarrow \pi^*$ transition 0.995 β and for the $n \rightarrow \pi^*$ transition 0.905 β . The corresponding values for the simple thiourea system are 1.067 β and 0.974 β . The ratios between the experimental transition energies, If/III, are 0.923 for the $\pi \rightarrow \pi^*$ and 0.908 for the $n \rightarrow \pi^*$ transition in heptane solution, and the corresponding theoretical ratios are 0.933 and 0.929. Obviously, the effect of the phenyl group is quite satisfactorily reproduced by the calculations.

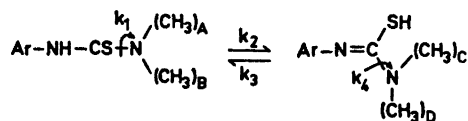
ON THE QUESTION OF A THIONE-THIOL TAUTOMERISM

It could be argued that the difference in rotational barrier between compounds of types I and II is in fact caused by a dominant thiol form (Va) in the former group of compounds. Compounds of type V are *N,N*-dimethyl-*N'*-arylamidines, and analogous formamidines have shown quite high barriers to rotation around the C¹-N¹ bond.^{51,52} However, even if the existence of large proportions of thiol tautomers of different thioamides has been advocated by some authors, no authenticated case of an open-chain thioamide with a measurable concentration of thiol form is known. Walter *et al.*⁵³ have recently shown



that some pyridinecarbothioamides are not thiols, as proposed by other authors. Rae⁴⁴ has discussed the possibility of a thiol form in thioanilides and concludes from NMR spectra that little or none of this tautomer can exist in solution.

In the present case, the infrared spectra of I_f in carbon tetrachloride and chloroform solutions show only NH bands and no bands around 2500 cm⁻¹, which could be ascribed to SH stretching vibrations. This at least speaks against a large concentration of thiol form. For comparison, we have prepared the S-methyl derivative of I_g (Vb). The ultraviolet spectrum of this compound (Table 6) is rather different from that of I_g. The maximum at 292 nm in Vb has no counterpart in the spectrum of I_g (λ_{max}: 250 nm), and a comparison of the extinction coefficients for the two compounds in the region 290–300 nm shows that at most only a small proportion (less than 10 %) of the thiol form can be present. This argument requires that Va and Vb have fairly similar absorption spectra, which seems to be a reasonable assumption. Compound Vb shows only one signal for the dimethylamino group down to -100°C in carbon disulphide as well as in pyridine-dichloromethane solution. The analogous formamidine has Δ*G*[‡]=14 kcal/mole,⁵¹ and it is obvious that a methylthio group has a similar barrier-lowering effect in amidines as in thioamides, where Δ*G*[‡] changes from 24.5 kcal/mole for dimethylthioformamide to 15.6 kcal/mole for methyl *N,N*-dimethyldithiocarbamate.² The barrier for Vb is probably less than 8.5 kcal/mole, since no exchange broadening was visible at -100°. The effect of a possible thiol tautomer on the observed rate constants and barriers can be discussed, if the exchanging system is treated as a four-site case:



The spectrum will be characterised by four chemical shifts, ν_A to ν_D , four rate constants, k_1 to k_4 , four transverse relaxation times, T_{2A} to T_{2D} , and the fractional populations P_{thione} and P_{thiol} ($P_{\text{thione}} + P_{\text{thiol}} = 1$). The lineshape can be calculated from the Bloch equations for the four sites, modified by the appropriate exchanges. If all rate constants are small, four lines will appear at ν_A to ν_D . This is not observed even at low temperatures, which may be due either to a small proportion of thiol form or to the rate constants k_2 and k_3 being large, or to a combination of both. If k_2 and k_3 are large, *i.e.* if the thione-thiol interconversion is rapid, the observed rate constant, k_{obs} , will be obtained from (1) and (2).

$$k_{\text{obs}} = k_1 \times P_{\text{thione}} + k_4 \times P_{\text{thiol}} \quad (1)$$

$$P_{\text{thione}} \times k_2 = P_{\text{thiol}} \times k_3 \quad (2)$$

In this case, the thiol form can quite well have a considerable influence on k_{obs} even if P_{thiol} is small, provided k_4 is large compared to k_1 , which appears to be the case in the present system. However, this can only lower the barrier, and therefore the presence of a thiol form cannot explain why the barriers of I are higher than those of II. If, on the other hand, k_2 and k_3 are small, the spectrum will consist of two independent exchanging doublets, A–B and C–D, of which only A–B has been observed, and to which the measured rates and barriers apply.

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