Substituted Thioureas. Part I. Study of Trimethylthiourea and its Complexes with Zinc(II)

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The n.m.r. spectra of trimethylthiourea show the presence, both in acetone and in chloroform solutions, of only one conformer with two methyl groups *cis* to the sulphur atom. Hydrogen bonded interactions, intermolecular and to the solvent, have been detected. The spectra of the complexes, in acetone solution, do not reveal the presence of intramolecular hydrogen bonding but only interactions with the solvent.

THE ability of thiourea and substituted thioureas to be co-ordinated through sulphur to various metal cations has been widely investigated by means of electronic and vibrational spectroscopy.[1-14] A relevant number of structures of co-ordination compounds involving such ligands and halogens have been solved to date.[15-23] Very little is known, on the other hand, of the n.m.r. behaviour of such complexes.[24-26]

For many of these thiourea–halogen–metal complexes, *X*-ray data suggest the presence, in the solid state, of intramolecular hydrogen bonding. Such intramolecular interactions have been observed by means of i.r. spectroscopy for some Co^{II} and Zn^{II} complexes in solution, and confirmed by n.m.r. spectroscopy [25] in the case of Zn^{II} complexes with *NN'*-diethylthiourea (detu) and halogens. The large differences in isotropic shifts of *cis* and *trans* NH protons of some thiourea–halogen–Co^{II} complexes have also been ascribed to intra- and inter-molecular hydrogen bonding effects.[24]

Some equilibrium between intramolecularly and solvent bonded species has been suggested [10] on the basis of some i.r. evidence also for Co^{II} complexes with trimethylthiourea (tmtu). The experimental evidence, however, is very limited and the spectral data are not explained unambiguously.

In order to obtain more definite experimental evidence for intramolecular hydrogen bonding in tmtu complexes, it seemed worthwhile to examine the closely similar diamagnetic complexes of Zn^{II} by means of n.m.r. spectroscopy and the results are presented here.

We have supported our experimental study by performing quantum-mechanical calculations to determine the relative stability of the different rotational isomers of thiourea-type ligands. Some of the results obtained are also reported.

EXPERIMENTAL

Preparations.—The ligand tmtu was a Schuchardt product. $Zn(tmtu)_2Cl_2$ was prepared by refluxing an absolute ethanol solution of anhydrous $ZnCl_2$ and the ligand in stoicheiometric ratio, for 1 h; then cooling the reaction mixture in an ice–water bath. The white powder precipitated was filtered, washed, and dried in a vacuum desiccator.

The same procedure was used to obtain $Zn(tmtu)_2Br_2$ using acetone as solvent. The yellowish powder separated was recrystallized from acetone–ethanol and the product obtained as a white crystalline powder.

$Zn(tmtu)_2I_2$ was prepared by refluxing anhydrous ZnI_2 and tmtu in acetone solution, in 1 : 2 mole ratio. The syrup obtained by concentration of the acetone solution yielded the compound as a white amorphous powder, when treated with light petroleum.

Spectral Measurements.—The n.m.r. spectra were recorded with a Bruker HX-90 spectrometer operating at 90 MHz. Standard 5 mm o.d. tubes were used. TMS was present as internal standard and for field stabilization.

Deuteriated Merck UVASOL solvents have been used.

The reading error on the spectra has been estimated as ±0·02 p.p.m. The uncertainty in the calibration of the

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[26] D. Gattegno and A. M. Giuliani, *J.C.S. Dalton*, 1973, in the press.

temperature scale has been evaluated as ±2°. No care was taken to obtain more precise control of temperature, because it was not our purpose to perform a complete kinetic analysis of the spectra obtained.

Calculations.—We have calculated the most stable conformations of the tmtu molecule by means of the quantum-mechanical, semiempirical CNDO/2 method.[27] The computations have been performed on the Univac 1108 of the Centro di Calcolo of the University of Rome, using a programme kindly supplied by the QCPE organization.[28]

A list of the parameters used is reported in Table 1.

TABLE 1

CNDO/2 parameters (energy values in eV)

Atoms	$\frac{1}{2}(I_s + A_s)$	$\frac{1}{2}(I_p + A_p)$	$\frac{1}{2}(I_d + A_d)$	β_0
C	14·051	5·572		−21
N	19·316	7·275		−25
S	17·650	6·989	0·713	−18·15
H	7·176			−9

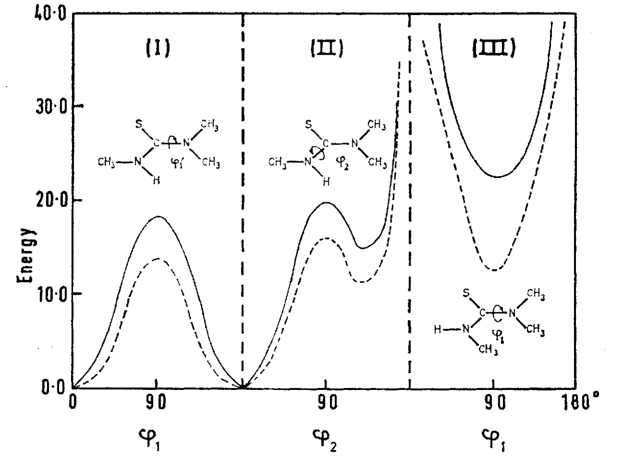
Bond distances and angles are taken from ref. 8 and kept constant for all the conformations studied.

TABLE 2

Energy of the conformations corresponding to the relevant points of the energy profiles for tmtu (kcal mol^{-1}). All the calculations do not include *d*-orbitals in the basis set

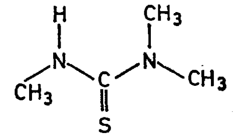
Conformations (ϕ_1, ϕ_2°)	Energy	Conformations (ϕ_1, ϕ_2°)	Energy
(0, 0)	0·00	(0, 180)	620
(90, 0)	13·90	(90, 180)	12·46
(0, 90)	16·12		

The results of these calculations, namely the energy of the system for different conformations obtained by rotating the molecule about the two CN bonds, are given in Table 2 and shown in the Figure. According to these data, only conformation (A), with two methyl groups *cis* to the sulphur atom, should be present in solution. The possibility of tmtu giving complexes in which intramolecular hydrogen bonds are formed has been suggested,[10] but our calculations give a very high energy for conformer (B), which ought to be present in such complexes. To investigate further this possibility, we have calculated the energy of tmtu conformations obtained starting from the planar *trans* conformation (B) and rotating the NMe_2 group about the N–C(S) bond. The results of these calculations are reported in the energy profile of the third section of the Figure; from this curve it can be seen that a rotation of



Energy profiles for tmtu. (I) Energy values as a function of $\phi_1(\phi_2 = 0°)$. (II) Energy values as a function of ϕ_2. (III) Energy values as a function of $\phi_1(\phi_2 = 180°)$. All values in kcal mol^{-1}. (Solid lines: calculation in which *d*-orbitals are included in the basis set; dashed lines: calculations performed without including *d*-orbitals in the basis set)

(A)



(B)

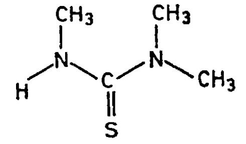


TABLE 3

Chemical shifts of trimethylthiourea protons at variable temperature [a]

Solvent	CD$_3$COCD$_3$				CDCl$_3$			
T/K	$\delta_{NH\text{-}CH_3}$ all (d)	$\delta_{N(CH_3)_2}$		δ_{NH} all broad	$\delta_{NH\text{-}CH_3}$ all (d)	$\delta_{N(CH_3)_2}$		δ_{NH} all broad
301	3·00	3·24 (s)		6·77	3·13	3·28 (d)		5·93
273	2·99	3·24 (s)		6·88				
243	2·97	3·24 (s)		7·03				
223					3·12	3·31 (s)		6·34 (q)
218					3·12	3·34 (s)br		6·36 (q)
213	2·93	3·24 (s)br		7·21	3·12	3·34br		6·40 (q)
211					3·11	3·23br	3·42br	6·41 (q)
208	2·96	3·24 (s)br		7·24	3·12	3·20sh	3·46 (s)br	6·43 (q)
203	2·96	3·23br		7·25	3·14	3·22sh	3·51 (s)	6·49 (q)
201	2·96	3·23br		7·26				
198	2·96	3·15br	3·29br	7·28				
195	2·96	3·12 (s)br	3·32 (s)br	7·29				
193	2·96	3·12 (s)br	3·35 (s)br	7·29 (q)				
188	2·96	3·11 (s)	3·36 (s)	7·31 (q)				
183	2·96	3·10 (s)	3·38 (s)	7·35 (q)				

At 90 MHz, δ in p.p.m. from TMS ± 0·02 p.p.m.; sh = shoulder, br = broad.

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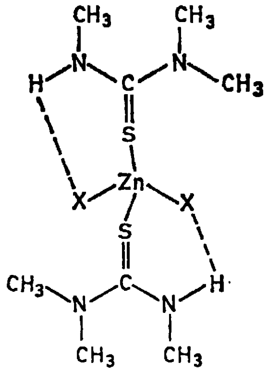
90° about this bond, brings the energy of the molecule 14 kcal mol^{-1} above the value of the most stable conformation of the system and this energy seems too high to be compensated for by hydrogen bond formation.

RESULTS

Variable temperature n.m.r. spectra of tmtu have been recorded both in $[^2H_6]$acetone and in $CDCl_3$ solutions. In Table 3 we report the chemical shifts of the NH and methyl protons in both solvents. At room temperature the spectra consist of a broad resonance for the NH group, a sharp singlet for the NMe_2 methyls, and a sharp doublet for the third methyl, coupled to the NH proton (J 4·2 ± 0·2 Hz in $CDCl_3$ and in acetone).

At lower temperature the sharp methyl singlet broadens and splits eventually in two; the coalescence temperature is 213 ± 2 K in chloroform and 201 ± 2 K in acetone. At 188 K, in acetone solutions, the NMe_2 resonance consists of two sharp signals 25 Hz apart. Dilution with benzene of the chloroform solutions causes a larger upfield shift for the high-field methyl than for the low-field one.[29-31] Each group of the other moiety of the molecule exhibits only one resonance, in the whole temperature range explored, in both solvents. At low temperature the broad NH signal shows some fine structure due to coupling to the methyl group. The signal is shifted to lower field values when the temperature decreases.

We have then taken into consideration the series of complexes $Zn(tmtu)_2X_2$ (X = Cl, Br, and I), to investigate if the potential formation of intramolecular hydrogen bonds could force the ligand in the sterically hindered (B) conformation, as shown in the formula below.



We have therefore examined the n.m.r. behaviour of the above complexes in acetone solutions at variable temperature. The data are collected in Tables 4—6. The limited solubility of the compounds, particularly the chloride complex, prevented the study in other solvents; and even in acetone, the chloride complex is only sparingly soluble.

The $Zn(tmtu)_2Cl_2$ spectrum exhibits, at room temperature, a sharp singlet for the $-NMe_2$ group, which begins to broaden *ca.* 243 K and splits in two at lower temperature (coalescence at 221 ± 2 K). By dilution with benzene, a larger upfield shift is obtained for the high-field signal than for the other. In the whole temperature range from 190 to 308 K the NHMe methyl appears as a doublet [$J(CH_3-NH)$ 3·8 ± 0·2 Hz]. A broad resonance, with no evidence of fine structure, arises from the amide proton. This signal is shifted to higher field as the temperature

TABLE 4

Chemical shifts [a] of $Zn(tmtu)_2Cl_2$ protons in $[^2H_6]$-acetone at variable temperature

T/K	NH–CH_3 [b]	–NMe_2		NH
301	3·10 (d) [c]	3·32 (s)		7·26br
243	3·12 (d)	3·45 (s)		7·62br
233	3·12 (d)	3·33br		7·68br
223	3·12 (d)	3·33br		7·74
(coalescence)				
218	3·12 (d)	3·23	3·42	7·76br
213	3·12 (d) *	3·20br *	3·48br	7·82br
206	*ca.* 3·13 *	3·18 *	3·49 (s)	7·91br
193	*ca.* 3·16 *	3·28 *	3·50 (s)	8·06br

* These peaks are partly overlapping one another.

[a] In p.p.m. from TMS at 90 MHz, TMS as internal standard. [b] $J(CH_3-NH)$ 3·8 ± 0·2 Hz. [c] Overlapping HOD peak.

TABLE 5

Chemical shifts [a] of $Zn(tmtu)_2Br_2$ protons in $[^2H_6]$-acetone at variable temperature

T/K	NHCH_3 [b]	–NMe_2		N–H all broad
301	3·12 (d)	3·32 (s)		7·33
273	3·10 (d)	3·29 (s)		7·50
243	3·13 (d)	3·32 (s)		7·65
235	3·12 (d)	3·32 (s)		7·66
233	3·12 (d)	3·33br		7·73
228	3·12 (d)	3·31br		7·78
(coalescence)				
225	3·13 (d)	3·24 (s)br	3·45 (s)br	7·82
222	3·14 (d)	3·22 (s)br	3·49 (s)br	7·88
213	3·10 (d)	3·19 (s)br	3·47(s)br	7·89
205	3·12 (d)	3·20 (s)br	3·51 (s)br	7·99
198	3·13sh	3·19 (s)	3·52 (s)	8·07
193	3·13sh	3·20 (s)	3·53 (s)	8·10
183	3·13sh	3·18 (s)	3·52 (s)	8·12
173 [c]	3·12 (d)br	3·19 (s)	3·52 (s)	8·21
163 [c]	3·12 (d)br	3·20 (s)	3·53 (s)	8·22

[a] See Table 4. [b] $J(CH_3-NH)$ 4·0 ± 0·2 Hz. [c] Below m.p. of solvent.

TABLE 6

Chemical shifts [a] of $Zn(tmtu)_2I_2$ protons in $[^2H_6]$-acetone at variable temperature

T/K	NH–CH_3 [b]	–NMe_2		NH all broad
301	3·21 (d)	3·40 (s)		7·52
273	3·20 (d)	3·40 (s)		7·71 (q)
253	3·19 (d)	3·40br		7·79 (q)
(coalescence)				
248	3·18 (d)	3·30 (d)	3·47br	7·82 (q)
245	3·18 (d)	3·26br	3·51br	7·83 (q)
243	3·17 (d)	3·24br,sh	3·53 (s)br	7·84 (q)
233	3·17 (d)	3·23 (s)br	3·54 (s)br	7·91 (q)
223	3·17 (d)	3·23 (s)	3·55 (s)	7·97 (q)
213	3·16 (d)	3·23 (s)	3·57 (s)	8·02 (q)
203	3·17 (d)	3·23 (s)	3·57 (s)	8·09 (q)
183	3·14 (d)	3·23 (s)	3·56 (s)	8·21 (q)
173 [c]	3·12	3·21 (s)br	3·54 (s)br	8·26

[a] See Table 4. [b] $J(CH_3-NH)$ 4·2 ± 0·2 Hz. [c] Below m.p. of solvent.

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[29] W. E. Stewart, T. H. Siddall III, *Chem. Rev.*, 1970, **70**, 517, and references therein.

[30] J. V. Hatton and R. E. Richards, *Mol. Phys.*, 1960, **3**, 253.

[31] J. V. Hatton and R. E. Richards, *Mol. Phys.*, 1962, **5**, 139.

increases (Table 4). For this resonance, as for the methyl group bonded to the NH, there is no evidence of splitting, *even at very* low temperature except for a small dipolar broadening near the m.p. of the solvent.

The spectra of $Zn(tmtu)_2Br_2$ and $Zn(tmtu)_2I_2$ follow completely analogous temperature dependences as the chloride complex (see Tables 5 and 6). For the iodide complex the resonance of the NH proton is shifted slightly downfield relative to that of the chloride and bromide complexes, but the temperature shift is the same.

DISCUSSION AND CONCLUSIONS

The variable temperature spectra of tmtu indicate that the rotation about the $C-NMe_2$ bond is hindered, thus giving rise to separate resonances for the methyl groups in the *cis* and *trans* environments. A total lineshape analysis is not possible in the case of chloroform solutions because the ' no-exchange ' limit cannot be reached; and anyway, even in acetone solutions, our data are not suitable for such a kinetic analysis, given the uncertainty on temperature and line-width values. However, the standard free energy of rotation has been calculated, making use of the theory of absolute reaction rates [32] and taking the transmission coefficient equal to unity. We have obtained, at coalescence temperature, $\Delta G^{\ddagger} = 10{\cdot}7 \pm 0{\cdot}2$ kcal mol^{-1} in $CDCl_3$ and $\Delta G^{\ddagger} = 10{\cdot}1 \pm 0{\cdot}2$ kcal mol^{-1} in acetone. The value found in chloroform is in excellent agreement with the value of 10·6 kcal mol^{-1} given by Isaksson and Sandström [33] for tmtu in the same solvent. This value is to be considered in agreement with the energy profile obtained by the calculations and reported in the Figure.

The differential dilution shifts of the signals indicate that the *trans* methyl group resonates at higher field than the *cis*.[29-31] A similar result has been obtained for the methylene resonances of detu,[34] whereas the opposite assignment has been made in the case of *N*-methylthiourea.[35] However, this latter assignment has recently been questioned by Walter and Ruess [36] on the basis of a model for the magnetic anisotropy of the thioamide group [37] and of electrostatic considerations.

The absence of splitting of the resonances of the other moiety of the molecule may indicate either a very fast rotation about this thioamide bond or, in turn, a large predominance of one of the two possible conformers over the other. Because of the steric interaction [29,31] between the two *trans* methyl groups in the (B) form, isomer (A) should be preferred to (B). Moreover, according to the quantum-mechanical calculations reported above, form (B) has a very high energy relative to (A) if a planar molecule is considered. Indeed, also in the case of detu,[34] there is no n.m.r. evidence for the presence in solution of the isomer with the two alkyls *trans* to the sulphur atom. It seems therefore justified to admit a large predominance of isomer (A) in solution, instead of a rapid rotation about the N-C(S) bond, in particular at low temperature. Isaksson and Sandström,[33] too, have shown that form (A) is strongly favoured in the case of trimethylthioureas, on the basis of n.m.r. and u.v. spectra and of studies of molecular models.

The downfield shift of the amide proton resonance with decreasing temperature suggests the existence of specific interactions, like the formation of hydrogen bonded dimers (or higher polymers) or hydrogen bonding to the solvent. The latter effect should be larger in acetone solutions, while the former should be more important in chloroform, owing to its low polarity. In fact, both type of interactions have been observed for the very similar ligand detu,[34] in $CHCl_3$ and acetone solutions. The same interactions, as already pointed out have been suggested on the basis of i.r. spectra.[10]

As for the zinc complexes under investigation, in this case too the splitting observed for the NMe_2 resonance at low temperature indicates a hindered rotation about that CN bond, and from differential dilution shifts the high-field resonance may be assigned to the methyl group *trans* to the sulphur atom, as for the free ligand. Values of the standard free energy of rotation have been calculated for the three complexes with the Eyring equation

$$k_1 = \frac{kT}{h} e^{-\Delta G^{\ddagger}/RT}$$

at coalescence temperature; the values obtained are $\Delta G^{\ddagger} = 11{\cdot}1$, $11{\cdot}4$, and $12{\cdot}6 \pm 0{\cdot}2$ kcal mol^{-1}, for the chloride, bromide, and iodide complex, respectively. The n.m.r. data reported for $Zn(tmtu)_2X_2$ complexes cannot be interpreted supposing that only species with intramolecular $NH \cdots X$ bonds exist in solution, because an almost temperature independent resonance frequency is expected for an intramolecularly hydrogen-bonded proton. The experimental data relative to the $NHCH_3$ moiety of the ligand, are easily and most obviously explained assuming that: (a) only the (A) isomer of the ligand is present in the complexes, and (b) hydrogen bonds to the solvent are formed, to an extent increasing with decreasing temperature. The above explanation agrees well both with n.m.r. data and theoretical calculations. One might alternatively assume a fast equilibrium between solvent-bonded and intramolecularly bonded species. Such an assumption has been made to explain the i.r. spectra of the Co^{II} complexes.[10] However, several considerations based both on theoretical calculations and on n.m.r. evidence allow us to rule this explanation out. The only conformation which would allow intramolecular hydrogen

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[32] S. Glasstone, K. J. Laidler, and H. Eyring, ' The Theory of Rate Processes,' McGraw-Hill, New York, 1941, p. 14.

[33] G. Isaksson and J. Sandström, *Acta Chem. Scand.*, 1970, **24**, 2565.

[34] A. M. Giuliani, *J.C.S. Dalton*, 1972, 493.

[35] A. S. Tompa, R. D. Barefoot, and E. Price, *J. Phys. Chem.*, 1969, **73**, 435.

[36] W. Walter and K. P. Ruess, *Annalen*, 1971, **743**, 167.

[37] W. Walter, E. Schaumann, and H. Paulsen, *Annalen*, 1969, **727**, 61.

bonding, and does not have an energy too high compared to the most stable isomer, is according to our quantum-mechanical calculations (Table 2) a non-planar one, with the dimethylamino-group rotated by 90° relative to the HN–C=S plane. However, the energy difference seems still rather large to be compensated for by the formation of NH $\cdots$ X bonds, even more so if the competition between the solvent and the halogen atom for hydrogen bonding is considered. Such a steric arrangement, in addition, would involve equivalence of the $-NMe_2$ methyls and only one n.m.r. signal should be observed even at low temperature, in complete disagreement with the experimental findings. Moreover the strength of intramolecular NH $\cdots$ X interactions decreases in the order $Cl > Br > I$, and the percentage of intramolecularly bonded species would therefore increase in the order $I < Br < Cl$. The temperature shift of the NH resonance should then be smaller for the chloride than for the bromide and iodide complexes, whereas the same shift has been found for the three complexes.

In addition, we may compare the behaviour of tmtu and detu complexes. One would expect intramolecular interactions to be weaker in the tmtu than in the detu complexes, because of the ligand distortions involved. However, it seems rather unlikely that no sign of ' freezing ' of the equilibrium (broadening or splitting of the resonances) appears down to 163 K, when, in the case of detu complexes, the splitting between intramolecularly bonded and non-bonded NH resonances takes place between 283 and 295 K. The complete agreement between theoretical calculations and n.m.r. experimental data leads to the following conclusions: no intramolecular NH $\cdots$ X bond is present in solutions of $Zn(tmtu)_2X_2$ complexes, and only the conformation with two methyl groups *cis* to sulphur is accessible for tmtu both free and co-ordinated.

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