A Nuclear Magnetic Resonance Study of Hindered Internal Rotation in Diethylthiourea

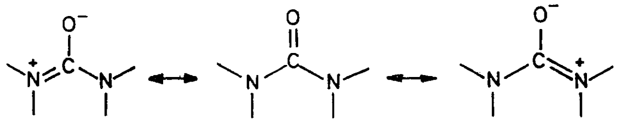
By **A. M. Giuliani**, Laboratorio di Teoria e Struttura Elettronica e Comportamento Spettrochimico dei Composti di Coordinazione del C.N.R., Università di Roma, Italy

Variable-temperature n.m.r. spectra of *NN'*-diethylthiourea have been recorded in acetone and in chloroform solutions. At low temperature the rotation about the thioamide bonds is slow and different rotational isomers can be detected. Only two of the three possible isomers seem to be present; *i.e.* the rotamer with two ethyl groups *cis* and the rotamer with one group *cis* and the other *trans* to the thioamide sulphur atom. The third isomer, with the two alkyl groups *trans* to the sulphur atom, is presumably too sterically hindered to be present in detectable amounts. The effects of solvent and concentration are also discussed.

We are studying the synthesis and properties of complexes formed from metals and sulphur-containing ligands. We report here the n.m.r. behaviour of one such ligand, diethylthiourea; the thioureas have already been the subject of much interest.[1-10]

We have examined the possibility for the existence of different rotamers, because of the partial double-bond character of the thioamide bond. While the hindered internal rotation around the (S=C)–N bond in thioamides has been extensively studied by n.m.r. spectroscopy,[11] it is only recently that restricted rotation about this bond has been observed for thioureas.[12-17]

The low-energy barrier to free rotation in thioureas, as evidenced by the low temperature at which the different rotamers have different resonance frequencies has been attributed [12] to the competition between the two amide bonds for electron delocalization:



Siddall and Stewart [12] first reported n.m.r. evidence for restricted rotation in thioureas, and evaluated the rotation barrier for the (S=C)–N(CH_3)$_2$ group in *N*-phenyl-*N'N'*-dimethylthiourea. They saw no evidence of splitting of the signal of the NH–C_6H_5 group; there-

---

[1] R. L. Carlin and S. L. Holt, jun., *Inorg. Chem.*, 1963, **2**, 849.

[2] F. A. Cotton, O. D. Faut, and J. T. Mague, *Inorg. Chem.*, 1964, **3**, 17.

[3] S. L. Holt, jun., and R. L. Carlin, *J. Amer. Chem. Soc.*, 1964, **86**, 3017.

[4] C. D. Flint and M. Goodgame, *J. Chem. Soc.* (*A*), 1966, 744.

[5] M. Schafer and C. Curran, *Inorg. Chem.*, 1966, **5**, 265.

[6] C. Puglisi and R. Levitus, *J. Inorg. Nuclear Chem.*, 1967, **29**, 1069.

[7] E. Cervone, P. Cancellieri, and C. Furlani, *J. Inorg. Nuclear Chem.*, 1968, **30**, 2431.

[8] T. Tarantelli and C. Furlani, *J. Chem. Soc.* (*A*), 1968, 1717; *Gazzetta*, 1970, **100**, 1012, 1076.

[9] O. Piovesana and C. Furlani, *J. Inorg. Nuclear Chem.*, 1968, **30**, 1249.

[10] O. Piovesana and C. Furlani, *J. Inorg. Nuclear Chem.*, 1970, **32**, 879.

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

[12] T. H. Siddall III and W. E. Stewart, *J. Org. Chem.*, 1967, **32**, 3261.

[13] J. Sandström, *J. Phys. Chem.*, 1967, **71**, 2318.

[14] R. K. Gosavi, U. Agarwala, and C. N. R. Rao, *J. Amer. Chem. Soc.*, 1967, **89**, 235.

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

[16] B. T. Brown and G. F. Katekar, *Tetrahedron Letters*, 1969, 2343.

[17] H. Kessler and D. Leibfritz, *Tetrahedron Letters*, 1970, 1595.

fore, either the rotation about this amide bond is rapid or one isomer predominates over the other.

Assignment of the resonances to the *cis*- and *trans*-rotamers has been reported for *N*-methylthiourea;[15] the methyl group *cis* to the sulphur atom resonates at higher field compared to the *trans*-methyl. The assignment has been made on the basis of the relative areas of the two signals and by considering the anisotropic diamagnetic shielding of the $-C=S$ group.[15]

TABLE 1

Chemical shifts of ettu in $CDCl_3$ and [$^2H_6$]acetone at different concentrations

Solvent	t(°C)	c (g l^{-1})	δ [p.p.m. from tetramethylsilane (internal)]				
			CH_2		NH		
$CDCl_3$	−50	194	3·24m	3·61m	6·207t	7·207t	7·349t
	−60	194	3·24m	3·61m	6·24t	7·30t	7·52t
	−50	122			6·101t	7·20	7·26
	−50	28·8			5·709b,t	6·996b	6·85t
CD_3COCD_3	−60	100	3·22m (32·6%)	3·55m	7·23t	7·42t	7·80t
		60	3·21dq (32·5%)	3·54m	7·20t (36%)	7·39t (32%)	7·64 (31·5%)
		40	3·20dq (30·6%)	3·56m	7·19t (38%)	7·38t	7·58t (31·1%)
		20	3·20m	3·56m	7·19b	7·38	7·44

Here the n.m.r. behaviour of *NN'*-diethylthiourea will be discussed; considerable data for the compound and its complexes have already been published.[9,10]

EXPERIMENTAL

NN'-Diethylthiourea (ettu) was a Fluka pract. product. Merck UVASOL deuteriated solvents were used.

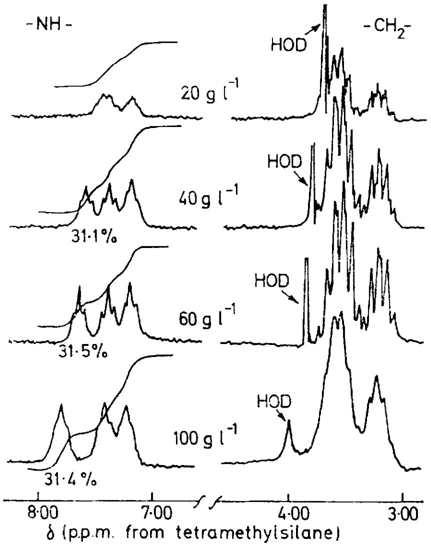


FIGURE 1 NH and methylene protons of ettu in [$^2H_6$] acetone at different concentrations; at 100 MHz, t = −60 °C, with tetramethylsilane as internal standard

Some of the spectra were recorded at 100 MHz (Varian XL-100 and Jeol-PS 100 spectrometers) and some at 90 MHz (Bruker HX-90). Standard tubes of 5 mm o.d. were used. Tetramethylsilane was used as internal reference. Homonuclear spin-decoupling experiments were performed with heteronuclear field stabilization on ^{19}F ($CFCl_3$) and tetramethylsilane as reference.

RESULTS

Series of ^1H n.m.r. spectra at different concentrations of ettu in $CDCl_3$ and CD_3COCD_3 were run at low temperature. In Table 1 chemical shifts and relative areas from integral curves are reported. Some of the results are shown in Figures 1 and 2.

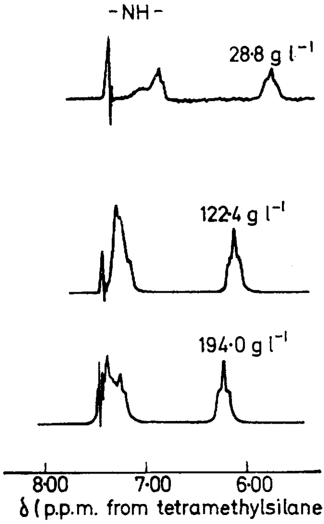


FIGURE 2 NH protons of ettu in $CDCl_3$ at different concentrations; at 100 MHz, t = −50 °C, tetramethylsilane as internal standard

It may be noted (Figure 2), that in $CDCl_3$ the two low-field NH signals interchange their position as the concentration decreases.

Variable-temperature measurements were run both in [$^2H_6$]acetone and in $CDCl_3$; the data are collected in Tables 2 and 3. Some of the spectra are shown in Figures 3 and 4.

The coalescence temperature in $CDCl_3$ is −16° ± 2 °C and in [$^2H_6$]acetone is −30° ± 2 °C. Spin-decoupling experiments have been performed at low temperature (−70 °C) in [$^2H_6$]acetone solution, with a concentration of 80 g l^{-1} of ettu.

The lower-field NH triplet is coupled to the higher-field

TABLE 2

Chemical shifts and coupling constants for NH and methylene protons of ettu in [$^2H_6$]acetone at different temperatures

δ [p.p.m. from tetramethylsilane (internal)]

	CH$_2$			NH				
t (°C)				3	2		1	*J* (Hz)
−10		3·47b			7·01b			
−20		3·49b			7·09b			$J^3_{CH_2-NH} = 4{\cdot}9 \pm 0{\cdot}1$
−25		3·49b			7·12b			
−30		3·52th			7·16b			
(coalescence)								$J^2_{CH_2-NH} = 5{\cdot}3 \pm 0{\cdot}1$
−32		3·55th			7·17tl			
−35	3·55b		3·27s		7·19tl			
−38	3·56b		3·26s	7·40s		7·19b		$J^1_{CH_2-NH} = 5{\cdot}3 \pm 0{\cdot}1$
−40	3·57b		3·25b	7·41s		7·20b		
−45	3·57b		3·23b	7·47b		7·20b		
−50	3·57m		3·22m	7·50b	7·30b		7·13b	$J_{CH_2-CH_3} = 7{\cdot}1 \pm 0{\cdot}1$
−60	3·57m		3·22m	7·61t	7·36t		7·17b	
−70	3·57m		3·22m	7·71t	7·40t		7·22t	
−90	3·57m		3·22m	7·91t	7·52t		7·33t	

At 90 MHz, concentration 50 g l^{-1}; th = tail to high field, tl = tail to low field.

TABLE 3

Chemical shifts and coupling constants for NH and methylene protons of ettu in CDCl$_3$ at different temperatures

δ [p.p.m. from tetramethylsilane (internal)]

	CH$_2$			NH				
t (°C)				1	2		3	*J* * (Hz)
0		3·38b,m			6·36b			
−5		3·40b			6·43b			
−8		3·40b			6·46b			$J^1_{CH_2-NH} = 5{\cdot}1 \pm 0{\cdot}2$
−12		3·41b			6·51b			
−15		3·42b		6·08s		6·63b		
(coalescence)								
−18		3·42th		6·03b		6·68b		$J^2_{CH_2-NH} = 4{\cdot}4 \pm 0{\cdot}2$
−20		3·45th		5·93b		6·71b		
−22		3·48th		5·92b		6·74b		
−25	3·32s		3·53b	5·90b		6·80b		$J^3_{CH_2-NH} = 4{\cdot}8 \pm 0{\cdot}2$
−28	3·31b		3·55	5·88b		6·82b		
−30	3·30b (*ca.* 35%)		3·56	5·84b (34%)		6·83b		
−50	3·26m,b (37·5%)		3·58	5·90b (37%)		7·07b		$J_{CH_2-CH_3} = 7{\cdot}1 \pm 0{\cdot}1$
−70	3·26m,b (36·5%)		3·58	6·08t,b (36·5%)	7·27t,b		7·43t,b	

At 90 MHz, concentration 80 g l^{-1}, * *J* determined at −60 °C.

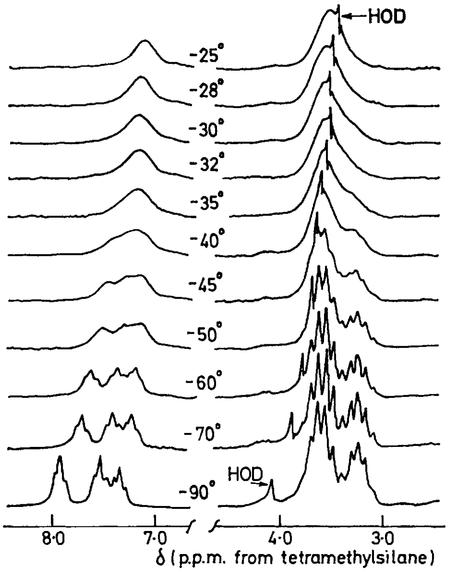


FIGURE 3 NH and methylene protons of ettu in [$^2H_6$]acetone at different temperatures; at 90 MHz, concentration 60 g l^{-1}, with tetramethylsilane as internal standard

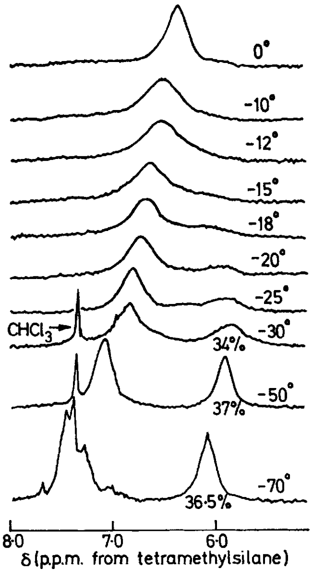


FIGURE 4 NH protons of ettu in CDCl$_3$ at different temperatures; at 90 MHz, concentration 100 g l^{-1}, tetramethylsilane as internal standard

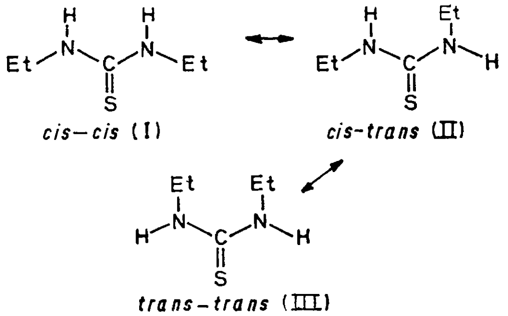
$-CH_2-$ double quartet, while irradiation at the centre of the other two NH triplets modifies the low-field $-CH_2-$ multiplet.

The coupling constants of the three NH triplets, in deuterioacetone, have been precisely determined with a frequency counter. They are: $J = 4{\cdot}9 \pm 0{\cdot}1$ Hz for the low-field triplet and $J = 5{\cdot}3 \pm 0{\cdot}1$ Hz for the two higher-field triplets.

Spin decoupling in $CDCl_3$ solutions (conc. 80 g l^{-1}) shows that the lower-field triplet is coupled to the high-field methylene multiplet, while irradiation of the low-field $-CH_2-$ multiplet causes the collapse of the high-field NH triplets to singlets.

DISCUSSION

Three different conformations are possible for diethylthiourea, given the partial double-bond character of the thioamide C(S)–N bonds.


cis–cis (I)

cis–trans (II)

trans–trans (III)

At low temperatures rotation about the C–N bonds should be slow enough to give forms (I) and (III) which should each give rise to one triplet for the NH protons and a double quartet for the CH_2 group, and to form (II) whose NH protons should appear as two triplets of equal relative area and whose CH_2 protons as two double quartets.

It is fairly well established that for unsymmetrically substituted amides (except formamide) the major isomer has the bulkier group *cis* to the carbonyl oxygen.[18] For *N*-methylthioamides,[19] too, the conformation with methyl group *cis* to sulphur seems to be preferred. It may reasonably be assumed that thioureas should show similar behaviour. Moreover, for *N*-methylthiourea,[15] it has been established that the *cis*-isomer is favoured over the *trans*, because of the steric interaction between *trans*-methyl and *trans*-hydrogen.

Thus, it seems justifiable to suppose that form (III) is present, if at all, only in very small amounts; models show that the *trans–trans*-isomer (III) should be less favoured, because of steric hindrance.

Temperature Effects.—The data of Table 3 show that, at low temperature, ettu in $[^2H_6]$acetone gives rise to three triplets for the NH protons, one at lower field ($J = 4{\cdot}9 \pm 0{\cdot}1$ Hz) and two partly overlapping at higher field ($J = 5{\cdot}3 \pm 0{\cdot}1$ Hz).

The three triplets are attributed to an equilibrium of forms (I) and (II), to the exclusion of form (III). There should then exist one kind of methylene group *trans* to the thiocarbonyl sulphur, and two kinds of CH_2 groups *cis*. The high-field methylene multiplet may, therefore, be tentatively assigned to the group *trans* to sulphur in form (II). It follows that the low-field NH triplet, which is coupled to it, should be assigned to the *cis*-NH group.

The other two, higher-field, NH signals are then assigned to NH protons *trans* to the thiocarbonyl group in forms (I) and (II). The equality of the coupling constants for these triplets supports this tentative assignment. However, this assignment is in contrast with reports for *N*-methylthiourea.[15] However, interchange of the position of the *cis*- and *trans*- resonances is not unusual for this kind of compound.

For example, in dimethylformamide the methyl group *cis* to C=O resonates at higher field than that *trans*, while for the CH_2 and CH groups of diethyl- and di-isopropyl-formamide the reverse is true.[20,21] Moreover, for *NN*-dimethylthioamides,[22] the *cis*-methyl resonates at higher field in dimethylthioformamide, but at lower field in dimethylthioacetamide.

Differential dilution shifts, when the acetone solution is diluted with benzene, are quite unexpected and of no help in assigning the resonances in this case: the high-field methylene signal is almost unaffected, while the low-field multiplet is shifted to lower fields. An analogous effect has been observed for *NN*-dibenzylbenzamide in $CDCl_3$ solutions,[23] and the absence of dilution shifts was tentatively ascribed to steric interference.

However data in $CDCl_3$ solution (Table 3), though quite different, substantiate the assignments made. The NH protons give rise to three triplets, one at higher field and two at lower field, partly overlapping. The CH_2 protons appear as a lower-field multiplet and a higher-field double quartet. The relative areas of the signals are reported in Table 3.

Spin-decoupling experiments show that the high-field $-CH_2-$ resonance is coupled to the low-field $-NH-$ triplet, while the low-field methylene multiplet is coupled to the two higher-field NH protons. The coupling constants are $J = 5{\cdot}1 \pm 0{\cdot}2$ Hz for the high-field NH triplet, $4{\cdot}4 \pm 0{\cdot}2$ Hz for the lower-field triplet, and $4{\cdot}8 \pm 0{\cdot}2$ for the third signal. Dilution with benzene of the chloroform solution shifts the high-field methylene resonance farther upfield than the other. The former can, therefore, be assigned to a methylene *trans* to sulphur. This is in agreement with the assignment made in acetone solution.

---

[18] L. A. La Planche and M. T. Rogers, *J. Amer. Chem. Soc.*, 1963, **85**, 3728.

[19] J. Sandström and B. Uppström, *Acta Chem. Scand.*, 1967, **21**, 2254.

[20] M. Frucht, A. H. Lewin, and F. A. Bovey, *Tetrahedron Letters*, 1970, 3707.

[21] A. Greenville Whittaker, D. W. Moore, and S. Siegel, *J. Phys. Chem.*, 1964, **68**, 3431.

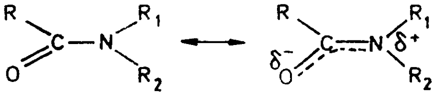
[22] R. C. Neuman, jun., and L. B. Young, *J. Phys. Chem.*, 1965, **69**, 1777.

[23] A. H. Lewin, M. Frucht, and F. A. Bovey, *Tetrahedron Letters*, 1970, 1083.

Of the NH triplets, the low-field one is then assigned to the proton *cis* to sulphur in form (II), and the higher-field triplet to the *trans*-NH in the same molecule (from the relative areas), while the third peak is assigned to form (I).

Effect of Solvent and Concentration.—The dependence of n.m.r. spectra of amides and thioamides on solvent and concentration has been well investigated.[11,13,24-28]

Specific solvent interactions which stabilize the polar ground state (B) of such compounds, have been found to increase the rotational barrier:[27,24]



(A) (B)

However, the origin of the solvent effects is still a controversial matter.

Different solvent and concentration effects have been suggested: formation of hydrogen-bonded dimers,[29] hydrogen bonding to the solvent molecules,[24,27] and dipolar association between the amide molecules [25-27,30] or between solvent and amide molecules, which would enhance the magnetic anisotropy of the carbonyl group.[30,31] Probably, in most cases, all or several of these effects are present at the same time, and the total effect of such interactions is generally unpredictable.

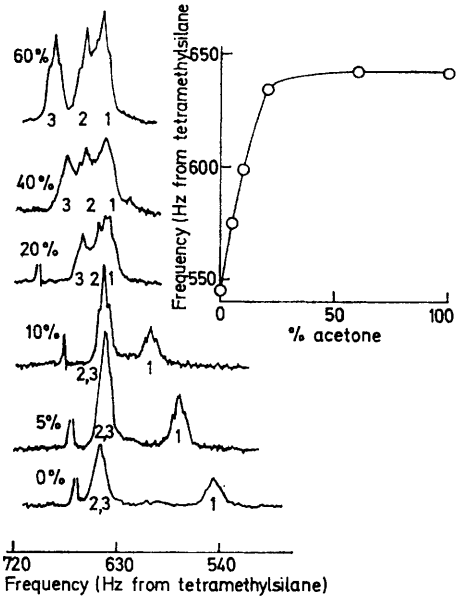


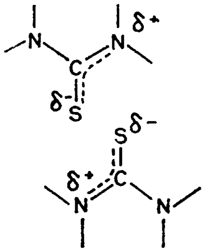
FIGURE 5 NH protons of ettu in mixtures of $CDCl_3$ and [$^2H_6$]-acetone; at 90 MHz, temperature −50 °C, concentration 90 g l^{-1}, tetramethylsilane internal standard, numbers on the curves indicate the percentage of acetone in the solvent mixture

In the case of ettu, it seems reasonable to assume that specific solvent interactions involving hydrogen bonds to solvent would occur to a different extent for NH protons *cis* or *trans* to the sulphur atom, or belonging to different rotamers. The large downfield shift of the higher-field NH triplet going from $CDCl_3$ to acetone (Figure 5) suggests that this group is involved in hydrogen bonding to the solvent to a greater extent than the others and that it is virtually all bound to acetone even in mixtures containing only 20% acetone.

The existence of hydrogen-bonded dimers (or higher polymers) may qualitatively account for the downfield shifts of all the NH resonances with decreasing temperature (Figures 3 and 4). The shift of all the NH signals to higher fields as the concentration decreases (Figures 1 and 2) both in $CDCl_3$ and CD_3COCD_3 solutions, may be qualitatively explained by the same effect.

The total effect of concentration is larger in $CDCl_3$ solutions, than in acetone, because here the strong competition of solvent for hydrogen bonding leaves a smaller net effect.

If dipolar interactions of the type (C) are also present, they should decrease with concentration and be more effective at low temperature. In fact, this dipolar association should enhance the magnetic anisotropy of the C=S group,[25,31] and increase therefore the chemical shift between the *cis*- and *trans*-protons.



(C)

At low temperature, the effect should become more pronounced because the increased viscosity and decreased thermal motion increase the average half-life of a given dipolar interaction. The more polarizable the solvent the larger should be the effect,[25] because a polar solvent would increase the stability of the polar form (B). Therefore the effect of dipolar association should be larger in acetone ($\mu = 2{\cdot}88$ D) than in chloroform ($\mu = 1{\cdot}28$ D). But acetone itself can give rise to dipolar association with the solute, and the carbonyl group can take the place of the thiocarbonyl group of ettu. As a consequence, there is only a small effect on the chemical shifts as concentration decreases. Moreover, hydrogen bonding to the solvent, which is a major effect in acetone, is competitive with the stabilization of dipolar association.

Dipolar association, together with the formation of dimers, may be responsible for the decrease in the

---

[24] R. C. Neuman, jun., and L. B. Young, *J. Phys. Chem.*, 1965, **69**, 2570.

[25] A. Greenville Whittaker and S. Siegel, *J. Chem. Phys.*, 1965, **42**, 3320.

[26] R. C. Neuman, jun., D. N. Roark, and V. Jonas, *J. Amer. Chem. Soc.*, 1967, **89**, 3412.

[27] J. C. Woodbrey and M. T. Rogers, *J. Amer. Chem. Soc.*, 1962, **84**, 13.

[28] M. T. Rogers and J. C. Woodbrey, *J. Phys. Chem.*, 1962, **66**, 540.

[29] B. Summers, L. H. Piette, and W. G. Schneider, *Canad. J. Chem.*, 1960, **38**, 681.

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

[31] P. T. Narasimhan and M. T. Rogers, *J. Phys. Chem.*, 1959, **63**, 1388.

relative chemical shift of *cis*- and *trans*-NH protons, as the concentration decreases. The position of the methylene resonances, on the other hand, is almost unaffected by concentration. A small shift of these resonances to low field and a moderate increase in the internal chemical shift is observed going from acetone to chloroform solutions. At low temperature the CH_2 resonances reach a limiting ' non-exchange ' value of the chemical shift.

The smaller effect of solvent and concentration on the methylene signals as compared to the NH resonances, is easily understood, because the CH_2 groups are not directly involved in hydrogen bonding and dipolar interactions. This is also the reason why a limiting value is reached at low temperature for the internal chemical shift of the methylene groups.

The great number of factors affecting the position of the NH resonances prevents a quantitative computation of their effects. For instance, one would expect a higher coalescence temperature in acetone than in chloroform, because the higher polarity of the former, stabilizing the polar ground state of ettu, should increase the energy barrier of rotation. But coalescence, in acetone, occurs not only because of increased rate of rotation, but also because, with increasing temperature, the hydrogen bonds to the solvent break, thus decreasing the non-exchanging chemical shift and lowering, therefore, the coalescence temperature. Under these conditions, even a rough estimate of the energy barrier to internal rotation appears unreliable.

On the other hand such an estimate based on the shifts and widths of the CH_2 signals is prevented by their high multiplicity and partial overlapping.

In conclusion, the presence in solution of hydrogen-bonded dimers and the strong association with polar solvents suggested by the i.r. data,[10] are confirmed by the present n.m.r. measurements.

The n.m.r. spectra, in addition, suggest also the existence of dipolar association and give useful information about the different isomers which are present in solution.

I am grateful to the Chemistry Department of the University of Padova for the use of the Bruker HX-90 spectrometer, and particularly to Professor G. Rigatti for his kind help.

[1/1205 *Received*, 12*th July*, **1971**]