Derivatives of Hydrazine

## II. 1-(*N,N*-Dialkylthiocarbazoyl)imidazoles and Related Compounds. Magnetic Nonequivalence in the ¹H NMR Signals of the Diisopropylamino Group

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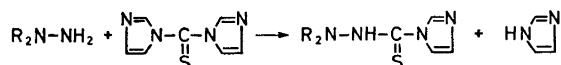
Ten aliphatic N-thiocarbazoylimidazoles have been prepared and characterized by their infrared and NMR spectra. The results show these compounds to be dipolar, monomeric in solution and polymeric in the solid phase. The proof for the dipolar structure, $R_2NH^+-N=C-(C_3H_3N_2)-S^-$, in solution follows unambiguously from the NMR spectrum in which coupling between the NH proton and the protons on the neighbouring carbon atoms has been observed. A consequence of the dipolar structure is the existence of nonequivalent methyl groups in the case R=isopropyl. From the dependence of this non-equivalence on temperature, medium, and concentration it is concluded that it probably originates from preferentially populated conformations around the C=N bonds, but that a "frozen" conformation cannot be excluded. The disappearance of the nonequivalence at 62°C is shown not to be due to an increased rate of inversion at the quaternary nitrogen atom, and it is concluded that the residual asymmetry is below the resolving power of the apparatus.

Part I of this series[1] described routes for the preparation of N- and C-deuterated mono- and dimethylhydrazines. The infrared spectra of these compounds were recorded and an assignment of the main features was proposed. On the basis of this information we have proceeded with an investigation of the spectra of 1-(*N,N*-dialkylthiocarbazoyl)imidazoles and related compounds which are of considerable interest to us as precursors for N-isothiocyanato-dialkylamines.[2] The infrared characteristics of the two major new structural entities present, *i.e.* the thioamide grouping and the imidazole group, are well elucidated by recent studies.[3,4] A total of ten thiocarbazoylimidazoles, I—X (Table 1), were prepared in nearly the same manner from the appropriate 1,1-dialkylhydrazines and N,N'-thiocarbonyldiimidazole. In the same way the C-deuterated 1-(*N,N*-dimethyl-d_6-thiocarbazoyl)imidazole (I—d_6), and the

Table 1. 1-(*N,N*-Dialkylthiocarbazoyl)imidazoles, $R_2N-NH-CS-N\overset{=N}{\underset{}{\Big\lfloor}}$
and related compounds.

R₂N		Yield %	M.p. °C	Formula	Analyses (C, H, N)
(CH₃)₂N	(I)	90	128—129	C₆H₁₀N₄S	Found: 42.12: 5.82 Calc.: 42.33; 5.92
(C₂H₅)₂N	(II)	70	123—124	C₈H₁₄N₄S	Found: 48.30; 7.17 Calc.: 48.47; 7.12
(n-C₃H₇)₂N	(III)	85	101—102	C₁₀H₁₈N₄S	Found: 53.10; 8.14; 24.63 Calc.: 53.06; 8.01; 24.76
(i-C₃H₇)₂N	(IV)	70	129—130	C₁₀H₁₈N₄S	Found: 53.05; 8.34; 24.90 Calc.: 53.06; 8.01; 24.76
(n-C₄H₉)₂N	(V)	10	57—58	C₁₂H₂₂N₄S	Found: 56.85; 8.78; 21.98 Calc.: 56.67; 8.72; 22.03
(i-C₄H₉)₂N	(VI)	55	90—91	C₁₂H₂₂N₄S	Found: 56.85; 8.51; 21.98 Calc.: 56.67; 8.72; 22.03
(C₃H₅)₂N	(VII)	51	82—83	C₁₀H₁₄N₄S	Found: 53.82; 6.64; 25.51 Calc.: 54.02; 6.35; 25.21
Piperidino	(VIII)	85	109—110	C₉H₁₄N₄S	Found: 51.22; 6.56; 26.57 Calc.: 51.42; 6.72; 26.65
2,6-Dimethyl- piperidino	(IX)	60	131—132	C₁₁H₁₈N₄S	Found: 55.65; 7.55; 23.31 Calc.: 55.44; 7.61; 23.52
Morpholino	(X)	90	122—123	C₈H₁₂N₄OS	Found: 45.23; 6.00; 26.21 Calc.: 45.28; 5.70; 26.40

N-deuterated 1-(*N,N*-dimethylthiocarbazoyl-*d*)imidazole (I-*d*) were prepared from the deuterated dimethylhydrazines.

$$R_2N-NH_2 + \underset{S}{\overset{N=}{\Big\lfloor}}N-\overset{}{\underset{\|}{C}}-N\overset{=N}{\Big\lfloor} \longrightarrow R_2N-NH-\overset{}{\underset{\|}{C}}-N\overset{=N}{\Big\lfloor} + HN\overset{=N}{\Big\lfloor}$$

I - X

The infrared spectra of I—X were recorded in KBr pellets and in chloroform solution. A comparison of the spectrum of (I) with those of the deuterated species made it possible to identify the features in the spectra originating from the methyl groups and the NH group, and comparison with the spectra of 1,1-dimethylhydrazine and imidazole allowed an assignment of most of the remaining absorption bands. Many of the assignments made for (I) could be transferred directly to II—X though in a tentative way and with no direct bearing on a discussion of the structure of II—X. Therefore the data given in

Table 2 were selected as the most representative and summarizing all important informations.

The most serious drawback in the evaluation of the infrared spectra of I—X in the solid phase is that these compounds are not monomolecular. Instead they form hydrogen bonded associates, the spectra of which differ from those of the monomers by showing a doubling of many peaks. This effect is most clearly observed in the spectrum of 1-(N,N-dipropylthiocarbazoyl)imidazole (III) which was selected for Table 2 for the same reason. However, molecular weight determinations (in benzene) demonstrated that I—X exist in solution as monomers. In addition it can be deduced from the results in Table 2 that the monomers exist preponderantly in the tautomeric

Table 2. Infrared absorption of 1-(N,N-dimethylthiocarbazoyl)imidazole (I), 1-(N,N-dimethyl-d_6-thiocarbazoyl)imidazole (I-d_6), and 1-(N,N-dipropylthiocarbazoyl)imidazole (III) in KBr pellets and in chloroform solution (cm^{-1}).

Assignment	I		I-d_6		III	
	KBr	CHCl$_3$	KBr	CDCl$_3$	KBr	CHCl$_3$
ν_{im}(C—H)	3144m	3160vw	3144m	3160vw	3160w	3160vw
ν_{im}(C—H)	3105m	3135vw	3105m	3132vw	3134m⎫ 3123m⎭	3134vw
ν_{alk}(C—H)/ (C—D)	3024w	—	2268w	2115vw	2963s 2935m 2877m	2968s 2939m 2879m
ν(N—H)	2946mbr 2720sbr	2600wbr 2450wbr	2920mbr 2710sbr	2680wbr 2590wbr	2768mbr 2700wbr 2658wbr	2670wbr 2600wbr 2490wbr
S$_1$	1525s	1525m	1525s	1526m	1523s ⎫ 1511m⎭	1525m
S$_2$	1478vs⎫ 1468s ⎭	1468vs	1476vs⎫ 1463s ⎭	1468vs	1486vs⎫ 1468vs⎭	1481vsbr
S$_3$	1450s ⎫ 1435m⎭		1448msh⎫ 1438m ⎭	1425vw	1453m⎫ 1441s ⎭	—
δ_{alk}(C—H)/ (C—D)	1424m⎫ 1398w⎭	1398vw	1073w	1082wsh	1423wsh⎫ 1405w ⎭	1411w
S$_4$	1358m	1368m	1360m	1368m	1353m⎫ 1343m⎭	1366m

The following abbreviations have been used: ν=stretching vibration, S=skeletal vibration and δ=deformational vibration. Indexes *im* and *alk* refer to the parts of the molecule constituted by the imidazole ring and the alkyl groups, respectively. The intensities of the absorptions have been given by vs=very strong, s=strong, m=medium, w=weak, vw=very weak, br=broad and sh=shoulder.

dipolar forms (XI). Inspection of a molecular model of XI revealed that intramolecular hydrogen bonding from NH$^+$ to a nitrogen atom in the imidazole ring was sterically unfavourable. This indicates that XI is strongly solvated in solution, since the charged sites are too far apart for intra-molecular forces (N—H···S) to act.

I - X   XI
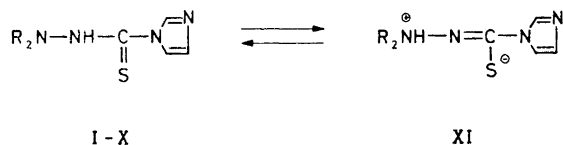
The following arguments in favour of the dipolar structure XI can be deduced from Table 2. Comparison of the spectra of (I) and I-d unambiguously established the absence of absorption due to NH stretching vibration, expected in the range between 3000 and 3500 cm^{-1}. Instead the broad absorption below 3000 cm^{-1} was displaced towards lower wavenumbers in I-d indicating the presence of a hydrogen atom bonded to a positively charged nitrogen atom. The normal location of the NH$^+$ frequency is around 2500 cm^{-1} and is observed only when the spectra are recorded in solution, where the monomeric species are formed. In view of the tendency for I—X to dissociate into imidazole and an N-isothiocyanatoamine on heating one should have expected I—X to adopt the imidazolium structure XII rather than the above alternative XI.
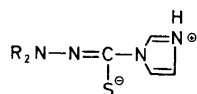
XII

However, a structure analogous to XII (with CH$_3$O- instead of R$_2$N-) has been established in the case of 1-(N-methoxythiocarbamoyl)imidazole [5] and this compound exhibits absorption due to NH$^+$ stretching vibrations very similar to that reported for imidazolium chloride.[4] This feature was not found in the case of I—X, which leaves XI as the only reasonable alternative. It is pertinent to mention that absorption which can be attributed to SH stretching vibration is absent in the spectra of I—X. This excludes the presence of tautomeric thiole forms.

In part I evidence was presented that protonation of the dimethylamino group causes a simplification of the absorption pattern due to CH stretching vibrations of the methyl groups. Only one weak peak with this origin has been found in the spectra of I and I-d_6 and is taken as evidence for the structure XI of the monomer.
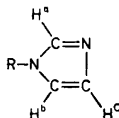
The doubling of the bands in the spectra recorded in KBr, most typically observed in the case of III, shows the existence of strong intermolecular forces between a molecule and its crystal environment. The same phenomenon has been observed in the infrared spectrum of 1-(N,N-dimethylthiocarbazoyl)-

1,2,4-triazole in KBr.[6] In such cases in-phase and out-of-phase vibrations of the same groups in two different molecules can be set up, leading to a splitting of the original single band into two. A similar effect has been reported in the case of imidazole in crystalline phase [4] and attributed to strong hydrogen bonding. To reconcile this explanation with the observation that N-isothio-cyanatoamines are formed [2] from XI on heating to a temperature *ca.* 10°C below the melting points, one is led to assume that association of XI in the solid state occurs from the R_2NH^+ group of one molecule to the basic nitrogen atom of the imidazole group of another molecule. In this way chain associates are formed, in which the strongest hydrogen bonds (*i.e.* the compounds in which most IR bands are observed as doublets) will occur when the forces acting between the chains are small. This explains why this phenomenon is pronounced in the case of III (R=propyl) but at the same time uncorrectly predicts a more extensive splitting for IV (R=isopropyl) and VI (R=iso-butyl). On the other hand, the yield of N-isothiocyanatoamine on pyrolysis of XI appears to increase with the number of split bands in the infrared spectrum. In terms of the model for XI outlined above it is an obvious consequence, since the necessary transfer of hydrogen to the imidazole part of the neighbouring molecule is facilitated by the presence of a strong hydrogen bond.

The bands arising from the skeletal stretching vibrations of I—X correspond quite closely to those expected for the imidazole ring superimposed on those expected for the thiocarbazoyl group. In the case of imidazole in solution [7] the four ring stretching vibrations with the highest frequency have been observed at 1532, 1485, 1428, and 1328 cm^{-1}. This can be compared with the position of S_1—S_4 in Table 2. The C—N and N—N stretching vibrations of 1,1-dimethylhydrazine [1] give rise to the bands at 1060, 1015, and 810 cm^{-1}. The corresponding bands in the spectrum of (I) appear to be displaced to 1035, 967, and 706 cm^{-1}. Three bands have been assigned to the thioamide grouping in the spectra of I—X: one very strong band at 1460—1480 cm^{-1}, one strong band at *ca.* 1300 cm^{-1}, and one strong band at *ca.* 1200 cm^{-1}. The first of these bands, which is in most instances indistinguishable from the S_2 band, originates mainly from a C=N stretching motion and is a counterpart of the B band [3] of thioamides. Consistent with this interpretation this band has been observed in all dipolar thiocarbazoyl compounds so far investigated in the infrared region, *i.e.* in certain dithiocarbazic acids, esters, sulfides, *etc.* The two latter bands are generally observed only in the case of compounds, in which the dipolar thiocarbazoyl group is bonded to nitrogen. Using again the terminology of thioamides, they are most conveniently thought of as displaced C and D bands.[3]

The NMR spectra of I—X together with some analogous compounds were recorded in CDCl$_3$. The chemical shifts of the imidazole protons are summarized in Table 3. The pattern arising from these protons in the case of I—X showed only small variation and is adequately exemplified by the dimethyl compound given in the table. The assignment of the signals to the three individual protons of the imidazole ring is unambiguous only in the case of imidazole where (because of intermolecular hydrogen bonding) the two protons H^b and H^c (Table 3) become magnetically equivalent. The assignments of the protons in the imidazole derivatives have been based on the observation,[8,9] that

Table 3. Chemical shifts[a] (τ, ppm) in $CDCl_3$ (5 % solution, 40°C) of the hydrogen atoms of the imidazole ring in compounds with the general structures
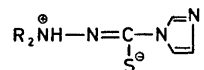

R	H[a]	H[b]	H[c]
H-	2.29	2.86	2.86
(imidazole)N–CO–	1.84	2.47	2.86
$(CH_3)_2N–NH–CS–$	1.50	2.27	2.99
$(CH_3)_2CH–NH–NH–CS–$	1.42	2.21	3.12
$CH_3O–NH–CS–$	0.89	2.08	2.81
(imidazole)N–CS–	1.79	2.48	2.79

[a] Centers of partly resolved multiplets.

conversion of amines to their acyl or thioacyl derivatives causes α-hydrogen atoms to be relatively deshielded. Since it is consistently observed that one of the signals from the imidazole protons is nearly unaffected by N-acylation or N-thioacylation it has been identified as the one originating from H[c]. The two other protons are both deshielded by this substitution and have accordingly been assigned to H[a] (lowest field) and H[b] (highest field). The difference between the chemical shift of H[a] in a thiocarbazoylimidazole ($\tau=1.4-1.5$) and that in 1-(methoxythiocarbamoyl)imidazole ($\tau=0.89$) is in accordance with structure XI for the former compound and a structure analogous to XII for the latter compound.

The signals in the NMR spectrum from the aliphatic protons of I—X consisted (within a first order analysis) of the expected multiplets arising from mutual coupling. It was an intriguing feature of the protons situated on the carbon atom adjacent to the NH^+ group that they appeared as doubled multiplets in the aliphatic series from R=ethyl to isobutyl (Table 4) but not in the two cases R=methyl and R=allyl. One or more of three factors might be held responsible for this extra splitting: (1) coupling with nitrogen (in which case a triple multiplet is expected), (2) coupling with the proton situated on nitrogen, or (except, of course, in the case of the isopropyl derivative), (3) nonequivalence of the CH_2 protons. The latter alternative arises from the attachment of CH_2 to a nitrogen atom carrying three different substituents, but depends (as does the second alternative) on the rate of proton exchange of the NH^+ with the surroundings. The compounds with R=ethyl and R= isopropyl were chosen for closer investigation, and in both cases the second

Table 4. Chemical shifts^a (τ, ppm) and coupling constants (Hz) in $CDCl_3$ (5 % solution, 40°C) of some of the aliphatic protons of 1-(N,N-dialkylthiocarbazoyl)imidazoles with the general structure

$$R_2\overset{\oplus}{N}H-N=\underset{\underset{\ominus}{S}}{C}-N\overset{=N}{\underset{=}{\diagdown}}$$

R	CH_3, CH_2, or CH contiguous to N			NH chemical shift
	Chemical shift	Multiplicity	J	
CH_3	6.97	Singlet	—	0.10
CH_3CH_2	6.77	Quartet	7.0	−0.37
	6.68	Quartet	7.0	
$CH_3CH_2CH_2$	6.91	Triplet	7.4	−0.35
	6.84	Triplet	7.4	
$CH_2=CH-CH_2$	6.22	Doublet	6.0	−0.50
$(CH_3)_2CH$	6.27	Septuplet	6.3	−0.40
	6.19	Septuplet	6.3	
$CH_3CH_2CH_2CH_2$	6.89	Triplet	7.0	−0.38
	6.80	Triplet	6.8	
$(CH_3)_2CHCH_2$	7.06	Doublet	6.5	−0.17
	6.97	Doublet	6.5	

^{a} The centers of the multiplets are given in the table.

alternative, $CH-NH$ coupling, turned out to be the correct explanation. This is based on the following evidence: (1) When the $CDCl_3$ solution was shaken with deuterium oxide the splitting disappeared and only one multiplet resulted. (2) The same results were obtained in double resonance experiments in which the NH frequency was irradiated. (3) When the NMR spectrum of the isopropyl derivative was recorded at 10°C (20 % $CDCl_3$ solution) the signal from the NH proton appeared as a triplet with the same coupling $J_{\text{NH-CH}}=5.5$ Hz as displayed by the septuplet from CH. This is only observed at low temperatures because the signal from the NH proton is broad and because $J_{\text{NH-CH}}$ (*i.e.* the effective coupling constant) increases with decreasing temperature. It must be emphasized that the results obtained here unambiguously verify the structure XI for this class of compound. The absence of $CH-NH$ coupling when R=methyl or allyl is reluctantly attributed to an increased rate of proton exchange in these compounds. In conclusion, in the series from R=ethyl to R=isobutyl the NH proton couples with the neighbouring proton(s) under these conditions, or, in other words, the NH proton may be treated as fixed, measured by the NMR time scale. Accordingly, the necessary condition for the third alternative mentioned above, namely

Table 5. Dependence of the chemical shift^a (τ, ppm) and the coupling constants (Hz) of the aliphatic protons in 1-(N,N-diisopropylthiocarbazoyl)imidazole on the concentration in CDCl$_3$ at 40°C.

Concentration	CH_3		CH		NH
%	Chem. shift	J	Chem. shift	J	Chem. shift
33	8.65	6.4	6.22	6.5	−0.35
	8.59	6.6	6.14	6.6	
5	8.63	6.3	6.27	6.3	−0.40
	8.58	6.4	6.19	6.3	
1	8.61	6.3	—	—	−0.40
	8.56	6.3	—	—	
0.1	8.62	6.5	—	—	—
	8.57	6.5	—	—	

^{a} The centers of the multiplets are given in the table.

attachment to an "asymmetric" atom, is fulfilled, but the absence of non-equivalent methylene protons shows that this condition is not sufficient. This point of view is in accordance with the evidence discussed by Rowsell.[10]

The signals from the methyl protons of 1-(N,N-diisopropylthiocarbazoyl)-imidazole (IV) appeared as two doublets (Table 5) in CDCl$_3$ at 40°C with a chemical shift difference of 0.05—0.06 ppm. Obviously the sufficient conditions for nonequivalence of the methyl groups are fulfilled in this case. The separation of the two doublets is nearly independent of concentration which, in conjunction with the molecular weight determinations mentioned above, substantiates IV as monomeric in solution. To decide whether the non-equivalence is due to local and/or remote shielding differences of the methyl protons, the ^{13}C—H coupling constants between the methyl carbon atoms and the methyl protons were measured for each of the two doublets. In a saturated solution of IV in CDCl$_3$ at 40°C identical values of $J(^{13}C-H)=130.0$ Hz were obtained from both satellites. This shows that inherent asymmetry, as, e.g., different hybridization of the carbon orbitals directed towards the protons, can be neglected. That the coupling constants $J(^{13}C-H)$ are identical for nonequivalent protons is probably the rule rather than the exception[11] but at least one instance has been reported[12] where this is not the case.

The magnetic nonequivalence of the methyl protons of the isopropyl groups must therefore be explained by considering the possible rotamers of IV. Three of these (1—3) are shown in the upper part of Fig. 1. If a rapid rotation (in the sense of the NMR time scale) occurs around each of the two bonds connecting the isopropyl groups with the quaternary nitrogen atom, each of the two isopropyl groups will give rise to identical signals because the same rotamers are experienced in turn. Furthermore, the two methyl groups CH_3^a and CH_3^b will always be in dissimilar environments, i.e. have different chemical
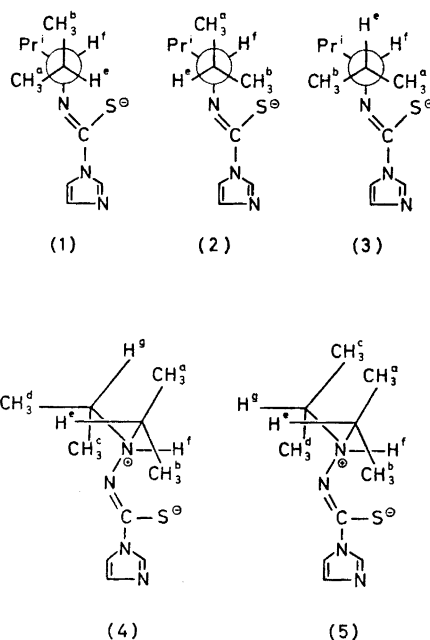
Fig. 1. Upper half: Three rotamers of 1-(N,N-diisopropylthiocarbazoyl)imidazole viewed from the end of an isopropyl group, (1)—(3). (The positively charged nitrogen atom is hidden in the projection). Lower half: Two possible conformations (4) and (5), in which the mutual positions of the isopropyl groups have been taken into account.

shifts even when they are in apparently identical positions. For example, CH_3^b in (1), situated between the groups Pr^i and H^f, is not in the same environment as CH_3^a in (2), also between Pr^i and H^f, because in (1) Pr^i is next to CH_3^a, whilst in (2) Pr^i is next to H^e. Furthermore, the position of the doublet from the CH_3^a group will be different for each of the three rotamers 1—3. Because of the rapid rotation, however, only one doublet is recorded, the averaged position of which depends on the relative populations of 1—3, i.e. is temperature dependent. Since the same argument may be applied to the CH_3^b group we expect two temperature dependent doublets to originate from the three rotamers 1—3. With increasing temperature the magnetic nonequivalence Δ, i.e. the difference between the centers of these doublets, will change until the state of equal populations of 1—3 has been reached; even in this case a residual asymmetry must, of course, remain unless accidental compensation occurs. A careful scanning of the relevant literature shows that a case of residual nonequivalence has never been experimentally established in the case of nonequivalent isopropyl methyl protons. From some papers (e.g. Jakobsen et al.[13]) it can even be concluded that the residual splitting at elevated temperatures is equal to or less than 0.6 Hz, which is close to the limit of resolution of most NMR measurements.

Another possibility is that, due to the bulkiness of the isopropyl groups, both isopropyl groups have effectively fixed conformations, i.e. that the rate of rotation around each of the two bonds connecting the isopropyl groups with the positively charged nitrogen atom either has slowed down to a negligible

value or that the rotation has stopped completely. Inspection of a model shows that the most stable conformation in this case either will be (4) in which the methyl groups are as far from each other as possible or (5) in which neighbouring interactions are minimized. By comparison of the conformations (4) and (2) it can be seen that the position of the methyl groups in the nearest isopropyl group of (4) correspond to that of the rotamer (2). The positions of the methyl groups CH_3^c and CH_3^d in the most distant isopropyl group in (4) viewed from the opposite side of the molecule correspond to the mirror image of the rotamer (3). The conformer (4) would, accordingly, give rise to a total of four doublets in the NMR spectrum, one originating from each of the four methyl groups $CH_3^a - CH_3^d$ (unless, accidentally, some of these methyl groups should be magnetically equivalent, which appears very unlikely). Considering the fact that only two doublets have consistently been observed from the methyl groups in IV, independent of variation in the concentration (Table 5), the temperature (Table 6), or the solvent (Table 7), the possibility of IV occurring with a fixed conformation as (4) can be discarded. If the methyl

Table 6. Temperature dependence (20 % solution in $CDBr_3$) of the chemical shifts[a] (τ, ppm), the coupling constants, and the magnetic nonequivalence (Δ) of the methyl groups (Hz) of the aliphatic protons in 1-(N,N-diisopropylthiocarbazoyl)imidazole.

Temperature °C	CH_3			CH
	Chem. shift	J	Δ	J_{CH-NH}
10	8.490 8.570	6.6 6.6	4.7	5.5
30	8.497 8.570	6.7 6.7	4.4	5.0
40	8.502 8.570	6.8 6.8	4.1	5.0
50	8.508 8.570	6.7 6.7	3.7	4.8
55	8.512 8.567	6.6 6.7	3.3	4.6
60	8.523 8.550	6.8 6.8	1.6	4.0
65	8.535	6.8	0	3.0
70	8.535	6.7	0	0
80	8.535	6.8	0	0

[a] The centers of the multiplets are given in the table.

Table 7. Solvent dependence (5 % solution, 40°C) of the chemical shifts[a] (τ, ppm) and the coupling constants (c/s) of the aliphatic protons in 1-(N,N-diisopropylthiocarbazoyl)-imidazole.

Solvent	CH_3		CH		NH
	Chem. shift	J	Chem. shift	J	Chem. shift
CDCl$_3$	8.63	6.3	6.27	6.3	−0.40
	8.58	6.4	6.19	6.3	
CDBr$_3$	8.58	6.5	6.12	6.5	−0.02
	8.50	6.4	6.04	6.5	
CD$_3$CN	8.68	6.4	6.15	6.4	−0.10
	8.63	6.3	6.07	6.4	
CD$_3$COCD$_3$	8.64	6.5	5.99	6.5	−0.20
	8.57	6.5	5.91	6.5	
Benzene	9.22	6.3	7.08	6.3	−0.35
	9.19	6.3	7.01	6.3	
(CD$_3$)$_2$SO	8.73	6.4	b		+0.10
	8.67	6.5			

[a] The centers of the multiplets are given in the table. [b] Three overlapping systems with $J = 6.3 - 6.5$ Hz.

groups are instead in a position opposite one another conformations as, *e.g.*, (5), shown in the lower half of Fig. 1, are obtained. The end views of the two isopropyl groups in (5) correspond to the conformation (2) and its mirror image, respectively, viewed from in front and from the rear. Since a rotamer and its mirror image must have identical NMR spectra, in this case only two doublets are produced in accordance with what is actually observed in the case of IV.

In conclusion, the magnetic nonequivalence in IV originates probably from a series of differently populated conformations as (1)—(3), but a "frozen" conformation such as (5) is a realistic alternative. To elucidate this point the temperature dependence of the NMR signals was investigated in CDBr$_3$ (Table 6). Owing to the difficulties in obtaining precise values in 5 % solution the concentration was increased to 20 %, but it should be emphasized that the results are within these limits nearly independent of concentration. At approximately 40°C the dissociation of IV into imidazole and N-isothiocyanatodiisopropylamine [2] became apparent in the NMR spectrum by the appearance of the doublet at $\tau = 8.83$ ppm, and at 80°C a total of 15 % had been converted. The temperature dependence was therefore not investigated beyond this temperature.
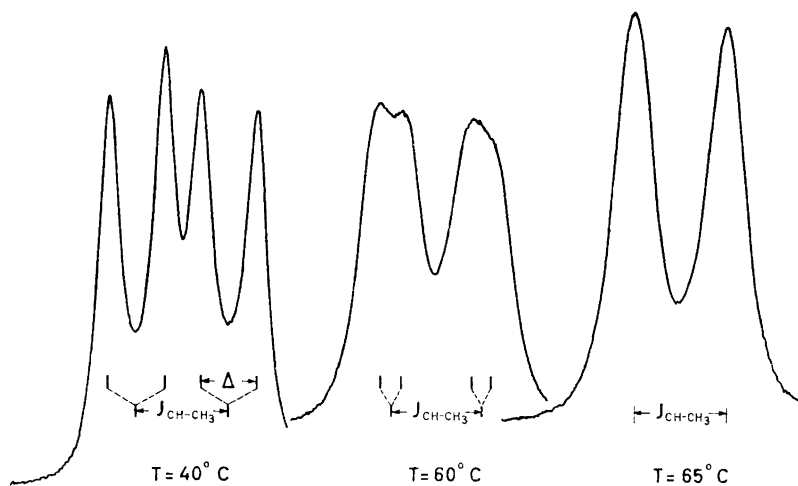
Fig. 2. The methyl proton resonance spectrum of 1-(N,N-diisopropylthiocarbazoyl)-imidazole in $CDBr_3$, showing the dependence of the magnetic nonequivalence, $\varDelta$, on temperature.
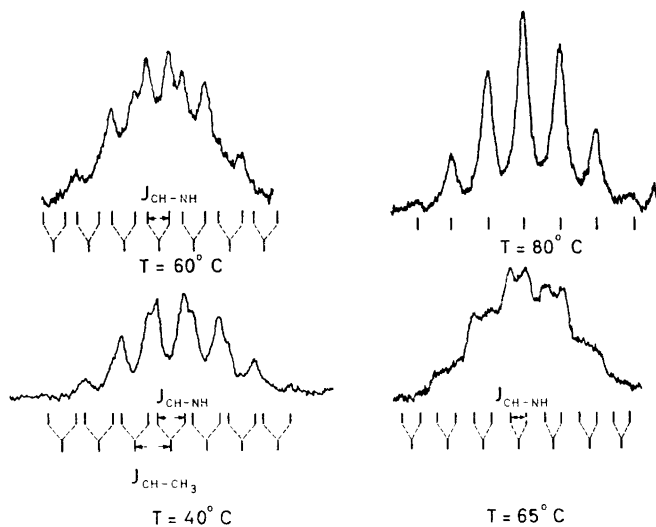

Fig. 3. The NMR spectrum of the methylidyne protons of 1-(N,N-diisopropylthiocarba-zoyl)imidazole in $CDBr_3$, showing the dependence of the coupling with NH on temperature.

The signals obtained for IV at 40°C are shown in Fig. 2 (the methyl protons) and Fig. 3 (the methylidyne protons) together with the interpretation of the splittings. Table 6 lists the results obtained in the temperature interval 10°C—80°C. The data show the most important effects of increasing temperature to be decreasing magnetic nonequivalence (Δ) and decreasing coupling constant $J_{\text{CH-NH}}$ in the interval 10—50°C. The coupling constant $J_{\text{CH-CH3}}$, on the other hand, undergoes no systematic change and may be considered constant. A magnetic nonequivalence, continuously decreasing with increasing temperature, is commonly observed [10,13-17] and can have a twofold explanation in the case of IV. First, the change in Δ with increasing temperature might be attributed to an increased rate of interconversion between a number of rotamers, as (1)—(3) which tend to be equally important. The fact, that Δ varies only because the effective chemical shift of *one* of the methyl groups is changed (Table 6), must then be attributed to an accidental compensation of the shifts introduced by the changing population of the rotamers. In the case of a "frozen" conformation (5) a change of chemical shift with temperature can only happen for a methyl group, the movements of which is limited by an unsymmetrical potential barrier. In the conformation (5) all four methyl groups would be expected to experience unsymmetrical potential walls, but while $CH_3{}^a$ and $CH_3{}^c$ are effectively outside the range of such groups in the molecule which are able to produce long-range shielding effects (*i.e.* the CS bond and the imidazole ring), $CH_3{}^b$ and $CH_3{}^d$ are found in positions which are near the shielding cone of the CS bond. Accordingly, an increase in temperature might give the result, that the doublet originating from $CH_3{}^a$ and $CH_3{}^c$ displays a nearly unchanged chemical shift, whilst the doublet originating from $CH_3{}^b$ and $CH_3{}^d$ is displaced as a result of the altered orientation of the methyl groups relative to the shielding cone. Thus, both models are compatible with the results obtained from this temperature interval.

In the temperature interval 55°C—65°C (very close to 62°C) (Fig. 2) a sudden collapse of the two doublets to one doublet, common to all four methyl groups is observed. From Table 6 it can be seen, that the chemical shift of both doublets change in this interval, but the coupling constant $J_{\text{CH-CH3}}$ again remains almost constant. From the last column in Table 6, and from Fig. 3, it is apparent that the CH-NH coupling is still present, but that it changes somewhat following the changes in the dihedral angles. This means, that the disappearance of the nonequivalence at 65°C cannot be attributed to the increased rate of inversion due to hydrogen exchange at the quaternary nitrogen atom, since this would involve $J_{\text{CH-NH}} = 0$ and not 3.0 Hz as actually observed. Furthermore, Table 6 shows the center of the doublet from the methyl groups to be temperature independent in the interval 65—80°C. The CH—NH coupling disappears at 70°C, but the fact that the remaining spectrum is not changed indicates that the molecule has, from 65—80°C, an unchanged population of the conformations involved, and accordingly a residual asymmetry below the resolving power of the apparatus (parallelling the case mentioned above [13]).

The behaviour of IV in the region 55—80°C is ostensibly at variance with both models outlined above. In an equilibrium between rotamers, a continuous decrease of the nonequivalence with increased temperature, and not a sudden change as observed in the case of IV, should be expected.[10],[13-17] For a "frozen" conformation, as (5), the freedom in rotation necessary to produce a sudden change in chemical shift over a rather small temperature range might be obtained, but it is difficult to see why a temperature-independent doublet should be the result, i.e. why all the conformations involved should have a temperature-independent population.

The most reasonable hypothesis is, that between 55°C and 65°C a series of internal molecular motions, which produce some approximation of symmetry, become possible; that is, symmetry to an extent which prevents the observation of nonequivalence of the methyl protons at 65°C. Inversion at the positively charged nitrogen is excluded (cf. above) but still cis-trans isomerism around the C=N bond (that is, interchange of sulfur and the imidazole ring) or rotation about the N—N bond could be contributing alternatives. Experiments show the chemical shift of the signal due to the $N\overset{+}{H}$ proton to be unaffected by temperature rise from 55°C to 80°C. Accordingly, a change in hydrogen bonding (N—H···S) in this temperature range can play only a minor role for the increased degrees of freedom acquired by the molecule.

The results listed in Table 7 serve mainly to illustrate that the magnetic nonequivalence of the methyl groups does not arise from a specific interaction with the solvent. The case of dimethyl sulfoxide as solvent is interesting in so far as the NMR spectrum displays (at least) three overlapping multiplets from the CH proton, which, in connection with the change of chemical shift value of the NH proton can be taken to indicate partial hydrogen bonding to the solvent. It is also noteworthy that Δ is only 0.03 ppm in benzene. Considering the abnormal shielding of the isopropyl groups in this solvent it is obvious that solvent studies are necessary to get a full understanding of the magnetic nonequivalence of IV. A discussion of this point will, however, be postponed until investigations of other dipolar 1,1-diisopropylthiocarbazoyl derivatives have been finished.

EXPERIMENTAL

Conditions and equipment used for recording the infrared spectra were those reported in part I of this series.[1] The nuclear magnetic resonance (NMR) spectra were obtained on a Varian A-60 instrument with tetramethylsilane as internal reference. The instrument is equipped with a Varian V-6040 variable temperature probe and controller.

Preparation of the thiocarbazoylimidazoles (Table 1). Method A. To a filtered solution of thiocarbonyldiimidazole (1.8 g) in benzene (25 ml) was added the calculated amount of the hydrazine. A slightly exothermic reaction occurred, but the reaction mixture was left for 24 h to complete the reaction. The separated product was filtered off, and recrystallized from benzene to give a colourless, crystalline product. This method was used in the preparation of III, VI, VII, VIII, IX, and X. *Method B.* To a suspension of finely powdered thiocarbonyldiimidazole (1.8 g) in dry ether (50 ml), the hydrazine was added dropwise in the calculated amount with stirring. The mixture was stirred and ground with a spatula for the next ½ h, filtered, and the collected product washed with

ether. Recrystallization from benzene gave a pure, colourless product. This method proved to be superior to that given above in the cases I and V. *Method C*. This method, which uses a mixture of benzene and chloroform for the synthesis, has been reported in an earlier paper [2] for IV, and was used successfully also in the cases I and II.

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Note added in press: An alternate rationalization of these results was suggested by Dr. M. G. Ettlinger in a private discussion. Suppose the following equilibrium with the thiol forms B and C present in amounts too small to be detected: (im = imidazole)
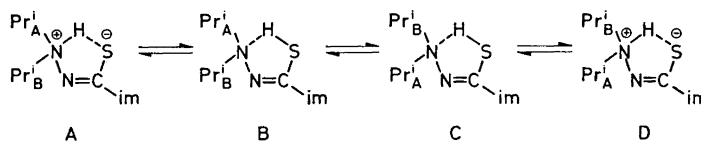
In the intramolecular rearrangement A ⇌ B, hydrogen is transferred from nitrogen to sulfur while in the process B ⇌ C the two isopropyl groups interchange positions with breakage and re-formation of the hydrogen bond. Since translational and vibrational motions are only weakly coupled to the nuclear spin both processes may take place without change in spin orientation of the proton. The effect of transfer between A and B does not eliminate the coupling between the isopropyl groups and the mobile hydrogen; rather it is modified to be the average coupling with contributions from the two sites weighted by the fractional residence times.

The process A ⇌ B, compared to the process B ⇌ C, probably has a much lower activation energy. Below 62°C we could therefore describe A ⇌ B and C ⇌ D as "fast" processes, but B = C as "slow". Accordingly we shall expect nonequivalence of the isopropyl groups and an average coupling to the NH proton. In the temperature interval 62−70°C all processes could be described as "fast". This means that the isopropyl groups become magnetically equivalent, but still coupled to the NH proton. Beyond 70°C an intermolecular hydrogen exchange might gain importance, which means that the coupling disappears.

If this explanation is correct the temperature at which the magnetic nonequivalence of the methyl protons disappears should be almost independent of the concentration of IV. On the other hand, the temperature at which the $CH-NH$ coupling disappears should increase with decreasing concentration of IV. The results obtained with 4−30 % solutions of IV in CDBr$_3$ show these two consequences to be fulfilled. The temperature at which the nonequivalence disappears changes less than 4°C and in the 4 % solution the $CH-NH$ coupling had not disappeared even at 92°C. Other experiments to settle this point will be reported later.

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