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Structure and Hydrogen Bonding of Solid N^1-Alkyl-N^2-arylthioureas. ^{13}C CP/MAS, IR and Semi-Empirical AM1 Studies

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Seven crystalline N^1-alkyl-N^2-arylthioureas were studied by ^{13}C CP/MAS NMR and by IR spectroscopy. The double set of signals in ^{13}C CP/MAS spectra indicates that molecules of N^1-ethyl-N^2-(3-methylphenyl)thiourea and N^1-ethyl-N^2-(4-methylphenyl)thiourea are crystallographically non-equivalent. N^1-Propene-N^2-phenylthiourea forms cyclic dimers with two $N^2—H\cdots S$ hydrogen bonds, as confirmed recently by x-ray diffraction. The broad ν_{NH} maxima at 3175–3295 cm^{-1} in the IR spectra indicate that in other thioureas both N^1-H and N^2-H protons are involved in hydrogen bonding and that the non-bonded N^1-H proton in cyclic dimers of N^1-propenethioureas is probably an exception. Semi-empirical AM1 calculations showed that the N^2-H proton is more positively charged than the N^1-H proton and therefore should be preferentially involved in $N^2—H\cdots S$ hydrogen bonds.

KEY WORDS solid-state ^{13}C CP/MAS NMR; IR; thioureas; hydrogen bonding

INTRODUCTION

The results of our earlier NMR study on N^1-alkyl-N^2-arylthioureas in solution[1] indicated that the preferred orientation of alkyl and aryl substituents with respect to the C=S group is *E*, *Z*. Such a conformation permits the formation of two intermolecular $N—H\cdots S$ hydrogen bonds, especially in cyclic dimers. N^2-H protons are involved in an eight-membered hydrogen-bond ring and N^1-H protons remain free, i.e. not engaged in hydrogen bonding. We expected the existence of such structures in the solid state. Crystallographic data included in the Cambridge Structural Database contain 11 structures with the aryl—N—CS—N— moiety but no N^1-alkyl-N^2-arylthioureas.

It seemed of interest, therefore, to study a set of thioureas in the solid state by means of ^{13}C cross-polarization magic angle spinning (CP/MAS) NMR, vibrational spectroscopy and x-ray diffraction. Four N^2-phenylthioureas were chosen with various alkyl substituents at N^1 and three N^1-ethylthioureas with *p*-CH$_3$, *m*-CH$_3$ and *p*-OCH$_3$ groups at the aromatic ring. Recent results of x-ray measurements confirmed[2] that crystalline N^1-propene-N^2-phenylthiourea forms a cyclic dimer (Fig. 1). This dimer has two equal distances of 0.3333 nm between the nitrogen and sulphur atoms. The question is whether this is an exception or whether such cyclic dimers are typical of N^1-alkyl-N^2-arylthioureas.

One way to check this is given by IR spectra: in cyclic dimers only one *N*-H proton is engaged in hydrogen bonding. The appearance of narrow ν_{NH} band at *ca.* 3450 cm^{-1} can prove the presence of a non-bonded *N*-H proton and confirm, therefore, the cyclic dimer structure. Another way is to use the residual splitting of the C-1 aromatic carbon signal in ^{13}C CP/MAS spectra as an indicator of the geometry at nitrogen atom N^2, directly linked to C-1.

EXPERIMENTAL

N^1-Alkyl-N^2-arylthioureas were synthesized from an alkyl isothiocyanate and aniline (or its substituted derivative) and recrystallized from propan-2-ol.

^{13}C CP/MAS spectra were recorded on a Bruker MSL-300 spectrometer at 75.5 MHz. Powdered samples were placed in a cylindrical rotor and spun at 3–4 kHz. Contact times of 5 ms, repetition times of 8–60 s and spectral widths of 20 kHz were applied for the accumulation of 800–2300 scans. The dipolar-dephased spectra were recorded with a 50 μs delay prior to acquisition. The chemical shifts were referenced indirectly through the glycine carbonyl peak ($\delta = 176.34$ ppm) relative to TMS.

Infrared absorption spectra were recorded from KBr pellets by using a Nicolet Magna IR-550 spectrometer equipped with a data station.

The semi-empirical calculations were carried out using the AM1 program implemented in the MOPAC package version 6.0.[3]

RESULTS AND DISCUSSION

^{13}C NMR spectra of solid, crystalline N^1-alkyl-N^2-arylthioureas were recorded by CP/MAS. A spinning speed of about 3–4 kHz was enough to circumvent sidebands and to assign chemical shifts of aliphatic and aromatic

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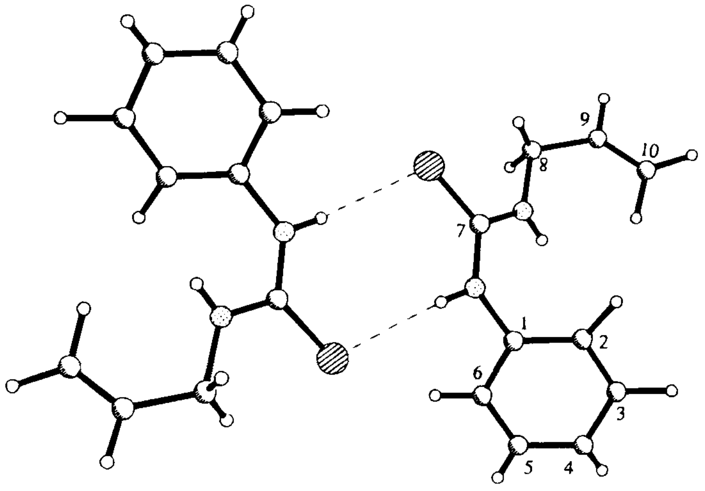


Figure 1. Dimer of N^1-propene-N^2-phenylthiourea.

carbons, but the signal of the thiocarbonyl carbon at 180 ppm was overlapped with rotational peaks. Since we could not increase the speed above 4.5 kHz, we used the dipolar-dephased technique (which exposes quaternary carbons) in order to observe the C=S carbon signal.

^{13}C CP/MAS spectra of N^1,N^1-dimethyl-N^2-phenylthiourea and N^1-isopropyl-N^2-phenylthiourea are illustrated in Figs 2 and 3, respectively. The signals of aromatic C-1 and aliphatic C-8 carbons, which are directly bonded to quadrupolar ^{14}N, show asymmetric doublets with an intensity ratio of approximately 1:2 or/and an increased linewidth. The splitting was helpful in the signal assignment and was used further in the elucidation of geometry at the nitrogen atoms.

The simulation of these lineshapes was carried out using the computer program of Olivieri *et al.*[4] The residual splitting S depends on energetic factors [the dipolar coupling constant D and the quadrupole coupling constant χ, the Zeeman frequency of the ^{14}N Z_N and the asymmetry parameter η of the electric field gradient (EFG) tensor] and geometric factors (the orientation of the internuclear vector r_{C-N} given by the angles α^D and β^D). The orientation of the principal directions of the EFG tensor in the molecular frame and the quadrupolar parameters are needed to predict the splitting. The opposite treatment is also possible, i.e. the measured splitting and determined molecular geometry (x-ray diffraction data) enable one to calculate the sign, magnitude and asymmetry of quadrupole coupling.

For an N^{2}H nitrogen bond to the aromatic ring, the principal z axis is expected to lie along the nitrogen lone-pair orbital and the y axis to be parallel to the C—N bond. Thus, $\beta^D = 90°$ and $\alpha^D = 107°$ (angle C-

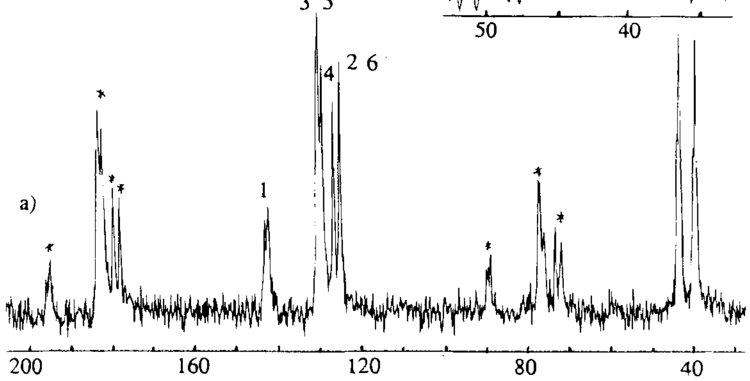


Figure 2. (a) ^{13}C CP/MAS spectrum of N^1-dimethyl-N^2-phenylthiourea. Spinning sidebands are marked with asterisks. The rotation speed was 4008 Hz. (b) Expanded methyl group resonances exhibiting the residual asymmetric splittings caused by dipolar coupling with ^{14}N.

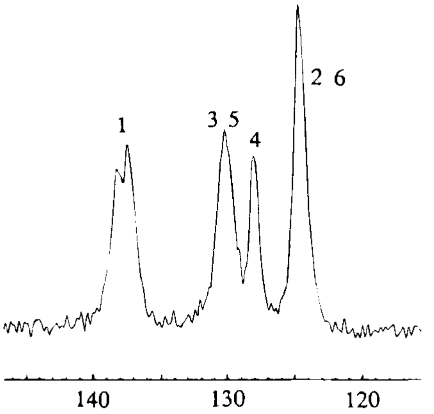


Figure 3. ^{13}C CP/MAS spectrum of N^1-isopropyl-N^2-phenylthiourea in the aromatic carbon region. The residual splitting of the C-1 carbon signal is 53 Hz.

Table 1. NQR values for various compounds

Compound	Nitrogen type	χ (MHz)	η
Urea	NH_2	−3.50	0.323
Dimethylamine	$NHCH_3$	−4.64	0.323
1,3-Dimethylurea	$NHCH_3$	−4.269	0.133
1,1-Dimethylurea	$N(CH_3)_2$	−4.763	0.017
Thiourea	NH_2	−3.10	0.394

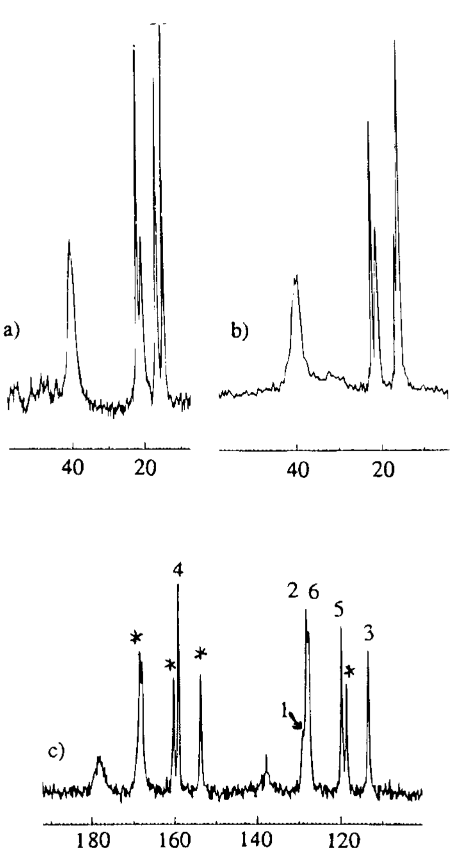


Figure 4. ^{13}C CP/MAS spectrum in the aliphatic carbon region of (a) N^1-ethyl-N^2-(3-methoxyphenyl)thiourea and (b) N^1-ethyl-N^2-(4-methoxyphenyl)thiourea and in the aromatic carbon region of (c) N^1-ethyl-N^2-(4-methoxyphenyl)thiourea.

1—N^2—H) and the length of the C-1—N^2 bond $r = 0.149$ nm are from x-ray data.[2] When using the NQR values similar to those for the peptide ^{14}N in glycylglycine ($\chi = -3.03$ MHz, $\eta = 0.41$) or dialanine ($\chi = -3.20$ MHz, $\eta = 0.31$), we obtain a splitting in the spectra recorded at 75.5 MHz of only 60–62 Hz. It is clear that the quadrupolar parameters for the N^2-phenylthiourea nitrogen should be larger.

The available NQR values[5,6] for similar compounds are given in Table 1.

The simulated C-1 resonances reasonably match those experimentally measured with $\eta = 0.39$ (as for thiourea) and $\chi = -4.77$ MHz. The same value of the residual splitting, $S = 98$ Hz for N^1,N^1-dimethyl- and N^1-propene-N^2-phenylthioureas, suggests that both compounds have the same geometry at the N^2 nitrogen, i.e. they form cyclic dimers, since no significant difference in the quadrupolar parameters for the N^2-phenyl nitrogen can be expected. This supposition can be verified by x-ray diffraction measurements of a single crystal of N^1,N^1-dimethyl-N^2-phenylthiourea.

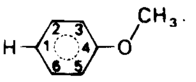
The replacement of hydrogen by a second methyl group in the N^1HCH_3 brings about the decrease in

Table 2. ^{13}C CP/MAS chemical shifts (ppm) for N^1-alkyl-N^2-phenylthioureas [N^1—HR^1 or N^1—$(R^1)_2$]

R^1	C-1	C-2,6	C-3,5	C-4	C=S	C-8	C-9	C-10
CH_3	135.4/136.9	128.8	131.1	128.8	179.5	32.4/33.1		
$CH(CH_3)_2$	137.3/138.0	124.6	130.1	128.0	178.5	48.0	22.8	
$CH_2CH{=}CH_2$	136.2/137.5	124.5	130.9/131.7	128.8	179.4	45.1	134.1	111.4
$(CH_3)_2$	142.1/143.4	125.0	129.2/130.1	126.5	181.0	43.0/43.8 (*Z*) 39.3/40.0 (*E*)		

Table 3. ^{13}C CP/MAS chemical shifts for N^1-ethyl-N^2-arylthioureas (N^2—$C_6H_4R^2$)

R^2	CH_3	C-1	C-2	C-3	C-4	C-5	C-6	C=S	CH_2	CH_3
p-CH_3	20.6/21.83	133.4	126.0	130.9	138.0/139.6	130.9	126.0	180.1	39.8	15.3/16.2
m-CH_3	14.7/16.5	136.8	125.2	138.8/141.0	127.6	129.3	120.7	178.0	40.3	14.7/16.5
p-OCH_3[a]	53.2	127.9	127.5	113.2	158.0	119.6	127.9	177.9	39.1	17.9

[a] Atom numbering: CH_3CH_2—N^1H—CS—N^2H—


electric field asymmetry and another orientation of EFG. Additionally, the two methyl groups in solid N^1-dimethyl-N^2-phenylthiourea are differently oriented with respect to the main directions of the EFG at N^1. Also, the lengths of the two C-8—N^1 bonds are not the same. As a result, various splittings of 63 Hz for $CH_3(E)$ and 58 Hz for $CH_3(Z)$ are observed. Methyl groups are differentiated by the ^{13}C chemical shift values; the separation of resonances of methyl groups *E* and *Z* is 3.2 ppm in CD_2Cl_2 at 221 K^1 and 3.8 ppm in the solid state (Table 2). In solution there is still some averaging of the environment of both methyl groups. In the crystal the positions are rigid, although thermal elipsoids for methyl group atoms are larger than, for example, for aromatic carbons. The above observations could account for various screening of both methyl carbons. However, an effect of 0.6 ppm is produced in the chemical shift of the methyl group $CH_3(E)$, i.e. located *trans* to C=S, whereas the position of methyl group *Z* in the solution and the solid-state spectra does not change.

In the spectrum of N^1-isopropylthiourea (Fig. 3), the splitting of the C-1 signal is 53 Hz and the simulation of the lineshape of the C-1 signal with NQR parameters cited above gives the best fit for $\beta^D = 90°$ and $\alpha^D = 62°$, which suggests a different orientation of N—H with respect to C—N and the *y* axis of EFG than in the case of N^1-propenethiourea.

In the spectra of N^1-ethyl-N^2-arylthioureas, the signal of C-1 is broad but without residual splitting. The CP/MAS spectra of N^1-ethyl-N^2-arylthioureas with *p*-CH_3 and *m*-CH_3 substituents to the aromatic ring (Table 3) are more complicated because the signals of methyl groups and those of substituted aromatic carbons (C-4 or C-3) are clearly seen as unequal doublets [Fig. 4 (a) and (b)] with a splitting of 0.9–1.8 ppm. It is probable, therefore, that it is not a local effect due

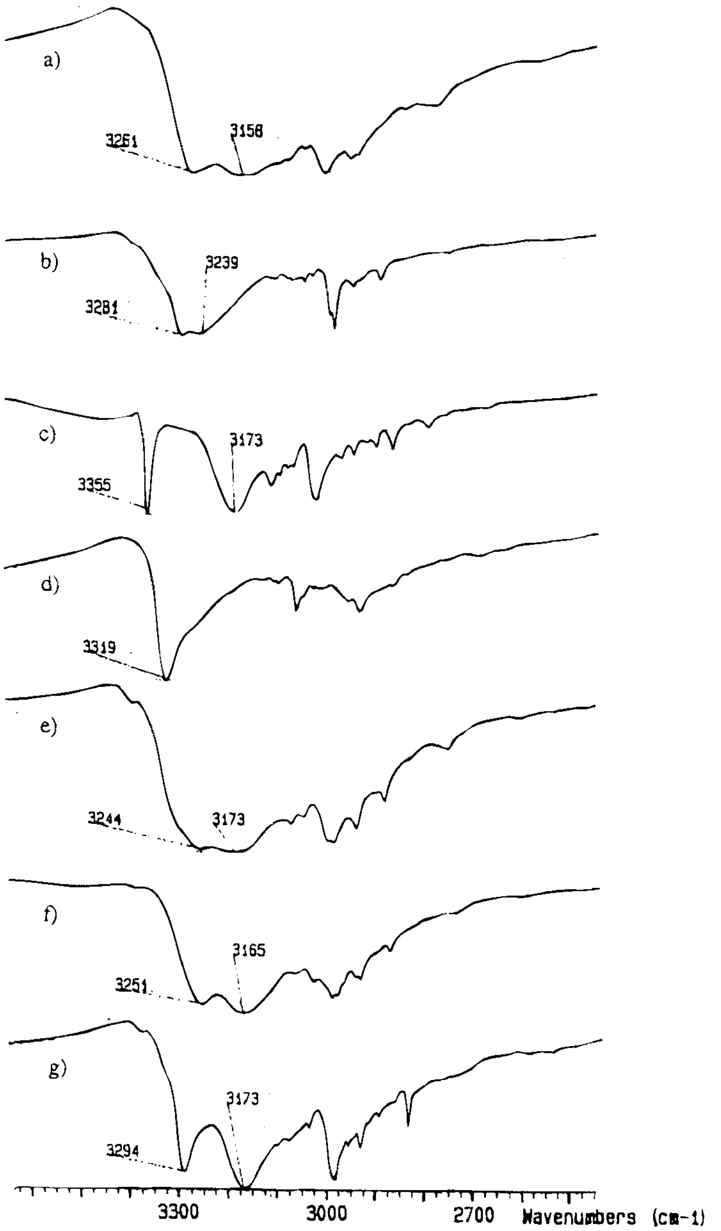


Figure 5. IR spectra in the ν(NH) range of N^1-alkyl-N^2-phenylthioureas with alkyl groups, (a) methyl, (b) isopropyl, (c) propene and (d) dimethyl, and N^1-ethyl-N^2-arylthioureas with substituents at the aromatic ring, (e)*p*-CH_3, (f)*m*-CH_3 and (g)*p*-OCH_3.

Table 4. AM1-optimized bond lengths, selected angles and net charges for N^1-alkyl-N^2-phenylthioureas

Parameter	$N^1-CH_2-CH=CH_2$		$N^1-CH(CH_3)_2$	$N^1-CH_2CH_3$[b]
	AM1	XRD[a]	AM1	AM1
Bond length (nm):				
$C\text{-}1-N^2$	0.1408	0.1429	0.1409	0.1414
$C-N^2$	0.1393	0.1343	0.1394	0.1389
$C-N^1$	0.1375	0.1332	0.1374	0.1378
$C=S$	0.1630	0.1688	0.1634	0.1634
Valence angles (°):				
$C\text{-}1-N^2-C$	126.4	127.4	126.6	126.2
$C'-N^1-C$	120.2	125.8	122.4	122.1
Torsional angles				
$C\text{-}1-N^2-C=S$	177.1	178.6	176.2	
$C\text{-}1-N^2-C-N^1$	−3.5	−0.8	−4.1	
Twist of aromatic ring (°)	38.2	56.0	38.3	44.5
Net charges at:				
N^2	−0.302		−0.302	−0.284
H^2	0.269		0.269	0.262
C	0.169		0.182	0.163
S	−0.321		−0.328	−0.330
N^1	−0.328		−0.328	−0.319
H^1	0.235		0.230	0.254

[a] X-ray diffraction data from Ref. 2.
[b] With p-OCH_3 at the aromatic ring.

to the two frozen conformations of alkyl groups but, more probably, there are two crystallographically non-equivalent types of molecules (with populations 2:1) present in a crystal unit. X-ray diffraction studies of these compounds are in progress.

The differences between chemical shifts, $\Delta\delta = \delta_{liq} - \delta_{sol}$, in $CDCl_3$ solution and in the solid state are within 1 ppm for the majority of carbons. The more significant are those for terminal carbons of alkyl groups, e.g. CH_2(C-10) 5.6 ppm, in N^1-propene-N^2-phenylthiourea and CH_3 −3.5 ppm in N^1-ethyl-N^2-(4-methoxyphenyl) thiourea. This effect can be easily understood. Carbon chemical shifts in solution are the average of various conformations because the molecule in its alkyl part is flexible whereas in the solid state rotation around C—C bonds is frozen and a rigid structure is present.

Significant differences are observed between the solid- and solution-state spectra of N^1-ethylthiourea with a p-OCH_3 substituent at the aromatic ring [Fig. 4(c)]. A single peak was observed for the C-3,5 carbons in solution whereas for the solid two resonances separated by 6.4 ppm are present. This is attributed to the fact that in the solid state the methoxy group exists in a locked, rigid orientation with respect to the aromatic ring, whereas in solution there is fast rotation around the C—O bond, and thus only an averaged value of the chemical shift for C-3 and C-5 is observed. The resonances of C-2 and C-6 are separated by 0.4 ppm but no splitting can be seen at carbons which are far away.

Since the ^1H solid-state NMR spectra were not sufficiently resolved, information about hydrogen bonding was obtained from infrared spectroscopy IR spectra of thiourea and of substituted thioureas in the solid state and in solution have been assigned[7] previously. The spectra of solid N,N-dipyridylthioureas[8] showed NH stretching bands below 3200 cm^{-1} owing to intramolecular hydrogen bonds formed by both NH groups. However, when intermolecular hydrogen bonding was prevented, a narrow band near 3400 cm^{-1} appeared. IR studies of N^1-alkyl-N^2-arylthioureas diluted in $CHCl_3$[9] showed that two ν(NH) absorption maxima are present due to the different conformations of the NH—CS—NH group: the maximum at higher frequency (3407–3423 cm^{-1}) was attributed to the form with NH *trans* to C=S and that at lower frequency (3376–3394 cm^{-1}) to the form with NH *cis*.

IR spectra in the range ν(NH) 2600–3600 cm^{-1} for solid N^1-alkyl-N^2-phenylthioureas and N^1-ethyl-N^2-arylthioureas are presented in Fig. 5. The spectra of the solid compounds exhibit broader bands shifted to lower frequency with respect to those in $CHCl_3$ solutions; this effect is due to association. Only in the case of N^1-propenethiourea is interpretation of the spectrum straightforward because the structure is known from x-ray diffraction: the narrow band at 3355 cm^{-1} is ascribed to non-associated N^1-H protons and the broader band at 3174 cm^{-1} results from $N^2-H\cdots S$ vibrations in the cyclic complex. None of the other thioureas studied show a narrow band at 3350–3400 cm^{-1} which could be connected with N^1-H (or N^2-H) protons not involved in hydrogen bonding. The broad band at 3158–3174 cm^{-1} is present in the spectra of all three N^1-ethyl-N^2-arylthioureas and also of N^1-methyl-N^2-phenylthiourea, suggesting that these compounds might form cyclic dimers. The appearance of a broad band at 3239–3295 cm^{-1} indicates that the N^1-H proton is also involved in hydrogen bonding and probably forms linear associates.

The earlier calculations of the optimum geometry of N^1-alkyl-N^2-phenylthioureas carried out by means of molecular mechanics (program MM2) showed that the E,E and Z,Z structures with both substituents on the same side of C=S are less stable than E,Z and Z,E

structures where phenyl and alkyl groups are far apart (the *E,E* conformation is possible when the twist angle of the aromatic ring is at least 60°). It should be mentioned that the *E,Z* conformation is favoured because it can be additionally stabilized by intermolecular N^2—H···S hydrogen bonds when forming cyclic dimers.

A semi-empirical method (AM1) was used to find electronic and geometric factors which allow the formation of dimers. The geometry was determined by minimizing the energy with respect to all geometrical parameters. The calculations were performed for compounds with ethyl, propene and isopropyl groups at N^1 and for the *E,Z* conformation (Fig. 1), i.e. the same conformation as found by x-ray diffraction of the cyclic dimer.

Replacing the unsaturated (propene) allyl part by ethyl or isopropyl does not change significantly the geometry at N^2, and only an increase of 2° in the angle at N^1 can be noticed (Table 4). Twisting of the aromatic ring by 38° releases the steric interference of both substituents, so the angle found by XRD, 56°, was even larger. The length of the carbon–nitrogen bond decreases in the order C-1—N^2 > C—N^2 > C—N^1 and the short C—N^1 bond indicates relatively strong conjugation of the nitrogen N^1 electron lone pair with the thiocarbonyl π-electron system. If the directions of net charge changes are reproduced properly by AM1, then in both compounds then N^2-H^2 hydrogen is more positively charged than the N^1-H^1 hydrogen and should be preferably involved in N^2—H···S hydrogen bond formation. There are no steric or electronic obstacles which could hinder the formation of cyclic dimers. It can be expected that more such structures will be revealed and evidenced by XRD.

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