MAGNETIC RESONANCE IN CHEMISTRY, VOL. 25, 474-479 (1987)

^{1}H and ^{13}C Nuclear Magnetic Resonance Study of 1,3-Dipyridylthioureas for Chemical Shift Assignments and Conformational Analysis

L. V. Sudha and D. N. Sathyanarayana*
Department of Inorganic and Physical Chemistry, Indian Institute of Science, Bangalore-560 012, India

S. Narasimha Bharati
Department of Organic Chemistry, Indian Institute of Science, Bangalore-560 012, India

A study of molecular conformation by ^{1}H and ^{13}C NMR methods of three 1,3-dipyridyl thioureas namely, 1,3-di(2-pyridyl)thiourea (1), 1,3-di(3-pyridyl)thiourea (2), 1-(2-pyridyl)-3-(3-pyridyl)thiourea (3), and also of 1-phenyl-3-(2-pyridyl)thiourea (4) and 1,3-diphenylthiourea (5), included for the sake of comparison, was carried out. Evidence was obtained that 3 and 4 exist in solution solely in one form, in an internally hydrogen bonded *E,Z* conformation, whereas 1, 2 and 5 exist in two (or more) rotamer forms. The data reveal an interesting dynamic exchange phenomenon occurring in 1 between two intramolecularly hydrogen bonded conformers. The ^{1}H and ^{13}C chemical shifts, ^{1}H,^{1}H and ^{13}C,^{1}H coupling constants are reported. The ^{13}C and ^{1}H chemical shifts are correlated with the electron densities calculated by the CNDO method.

KEY WORDS ^{1}H NMR ^{13}C NMR 1,3-Dipyridylthioureas Conformation.

INTRODUCTION

Several studies have been reported concerning the energy barrier restricting the internal rotation and the relative conformer stability of thiourea derivatives. Previous papers have reported studies mainly on alkylated thioureas,[1-8] and there have been few reports on the conformation of arylthiourea derivatives.[1,9-12] For 1,3-disubstituted thioureas four conformational isomers are possible (Fig. 1), the *E,Z* and *Z,E* conformations being equivalent for identical substituents. The *E,E* rotamer is generally excluded on steric grounds. For 1,3-dialkylthioureas, the preferred conformation for less bulky alkyl groups is the *Z,Z* type.[13,14] Pyridylthioureas introduce a group with its own interesting chemistry, and an additional element of geometric isomerism wherein the heterocyclic nitrogen atom may face the sulphur atom or be on the opposite side.

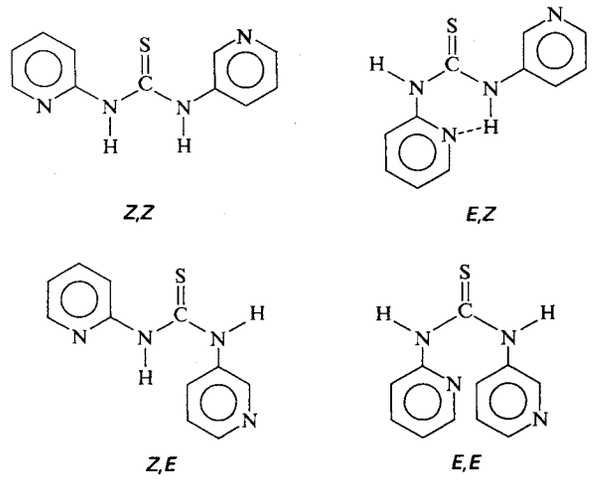

Figure 1. Four conformational isomers of 1,3-disubstituted thiourea; rotamers of **3**.

We have undertaken a study of three model 1,3-dipyridylthioureas, **1-3**, with the aim of analysing the conformational preferences in pyridylthiourea derivatives; also included were 1-phenyl-3-(2-pyridyl)thiourea (**4**) and 1,3-diphenylthiourea (**5**) for the sake of comparison:

$Ar_1NHCSNHAr_2$: (**1**) $Ar_1 = Ar_2 =$ 2-pyridyl;
(**2**) $Ar_1 = Ar_2 =$ 3-pyridyl;
(**3**) $Ar_1 =$ 2-pyridyl, $Ar_2 =$ 3-pyridyl;
(**4**) $Ar_1 =$ 2-pyridyl, $Ar_2 =$ phenyl;
(**5**) $Ar_1 = Ar_2 =$ phenyl.

The conformational analysis of these molecules was carried out by analysing their ^{1}H and ^{13}C NMR spectra; chemical shifts, ^{1}H,^{1}H and ^{13}C,^{1}H coupling constants are also reported. The coalescence temperatures in the ^{1}H and ^{13}C NMR spectra were used for a quantitative estimate of the energy barrier to internal rotation about the thioureide C—N bond. The ^{1}H and ^{13}C chemical shifts of **1** and **3** are correlated with the electron densities obtained by means of the CNDO SCF-MO procedure.[15]

RESULTS AND DISCUSSION

^{1}H NMR Spectra

The ^{1}H chemical shifts (δ values) and the proton–proton coupling constants (Hz) obtained by analysing the

* Author to whom correspondence should be addressed.

0749-1581/87/060474-06$05.00

Received 17 February 1986
Accepted (revised) 11 November 1986

Table 1. Observed ^{1}H NMR parameters

Compound	Solvent	T/K	Chemical shifts, δ ppm					
			(Z)-Pyridyl [(E)-pyridyl]					
			H-2	H-3	H-4	H-5	H-6	(Z)-NH [(E)-NH]
1	$CDCl_3$	213		8.84	7.86	7.21	8.51	9.97
				(7.06)	(7.73)	(7.07)	(8.37)	(14.61)
		253		8.87	7.82	7.18	8.47	9.49
				(6.99)	(7.71)	(7.05)	(8.37)	(14.48)
		273		8.87	7.75	7.10	8.40	9.23
								(14.40)
	$[^2H_6]$DMSO	273		8.03	7.81	7.13	8.36	
2	$[^2H_6]$DMSO	293	8.63		7.94	7.40	7.36	10.12
3	$CDCl_3$	293	8.73		8.35	7.37	8.50	9.13
				(6.91)	(7.73)	(7.06)	(8.27)	(13.90)
	$[^2H_6]$DMSO	293	8.78		8.16	7.40	8.39	
				(7.30)	(7.83)	(7.10)	(8.32)	
4	$CDCl_3$	293						9.38
				(6.96)	(7.70)	(7.03)	(8.23)	(13.73)
5	$CDCl_3$	213			Phenyl group			9.46
								(7.67)
		293			Multiplet centred at 7.38			7.86

			Spin coupling constants, J/Hz, at 293 K								
			J(45)	J(46)	J(56)	J(34)	J(35)	J(36)	J(24)	J(25)	J(26)
1	$CDCl_3$		7.22	1.94	5.12	8.61	0.32	0.25			
2	$[^2H_6]$DMSO		8.25	1.32	4.95				2.53	0	0
3	$CDCl_3$	2-Py:	7.32	1.93	5.09	8.67	0.38	0.27			
		3-Py:	8.25	1.39	4.95				2.06	0	0

experimental spectra with the use of the LAOCOON I and II programs[16] are reported in Table 1. The data refer to [^{2}H]chloroform and [$^2H_6$] dimethyl sulphoxide (DMSO) solutions. Qualitative conclusions on conformational preferences may be drawn by examining the ^{1}H chemical shifts of **1–5**.

The ^{1}H NMR spectra of **1**, **3** and **4** display two NH signals at *ca* 9.0 and 14.0 ppm at ambient temperature, the latter showing concentration-independent behaviour. The two NH signals are different in their nature. The low-field signal is sharp and shows only a small shift (0.32 ppm in the range 213–293 K) towards lower field with decreasing temperature. The high-field signal, on the other hand, is broad and shows a relatively greater shift with temperature (*ca* 1.01 ppm in the range 213–293 K). These facts suggest that the low-field signal arises from a strong intramolecularly hydrogen bonded proton.[17–19] Inspection of the molecular models reveals that the *E,Z* conformation of **1**, **3** and **4** are suitable for N—H···N(pyridyl) hydrogen bonding. This indicates that the low-field signal can be assigned to the NH in the *E* orientation (NH_E) of the CSNH group and the high-field signal to the NH in the *Z* orientation (NH_Z) of the CSNH group. Curiously, the ^{1}H NMR spectrum of **1** at ambient temperature displayed only one set of signals for the pyridyl groups. However, at lower temperatures (below 268 K) separate signals corresponding to the pyridyl group in the *E* and *Z* orientations were observed. This behaviour can be reconciled with a characteristic exchange occurring between two internally hydrogen bonded *E,Z* and *Z,E* conformers (Fig. 2), which is possible only for **1**. Because of the extra stability imparted by the internal hydrogen bonding, the *Z,Z* form will not be populated to any significant extent, and the *E,E* rotamer, as mentioned earlier, is excluded on steric grounds. Over the temperature range 213–323 K, the presence of the extreme low-field signal shows that the (*E*)-NH of **1** is involved in intramolecular hydrogen bonding. Likewise, the spectrum of **3** showed over the temperature range studied eight sets of multiplets in the aromatic region, four sets due to protons of the 2-pyridyl group (in the *E* orientation) and the remaining four sets arising from the 3-pyridyl protons of the *E,Z* isomer. This is consistent with the above suggestion, since no topomerization process (shown in Fig. 2) could be envisaged for **3** and the *Z,E* isomer is thermodynamically less stable. A similar situation exists for **4**.

^{1}H chemical shifts of the pyridyl protons of **3** were assigned with the aid of the subambient temperature spectrum of **1** and the ambient temperature spectrum of **2**. The poor solubility of **2** prevented us from recording its low-temperature spectrum. The ^{1}H spectrum of **2** showed only one signal at 10.12 ppm assignable to the

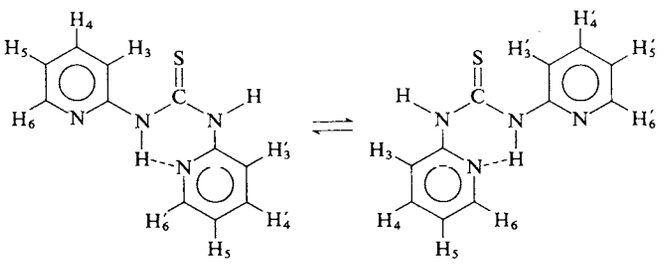

Figure 2. Interconverting forms of **1**.

two NH groups. Similarly, only a single signal was observed at 8.16 ppm at 253 K in the spectrum of **5**. The latter compound exhibited two resonances for the NH groups at 7.67 and 9.46 ppm at 213 K in $CDCl_3$. The low-field signal of **5** could be assigned to the (*Z*)-NH group, which experiences the anisotropic deshielding effect of the C=S moiety, and the other signal to the (*E*)-NH group. A conformational situation is envisaged for **2** and **5** which is different from that of **1**, **3** and **4**. For **2** and **5** it can be argued that the *Z,Z* form is accessible in addition to the *E,Z* and *Z,E* forms. For **1**, **3** and **4** internal hydrogen bonding, contributing to the thermodynamic stability of the *E,Z* (and/or *Z,E*) rotamer, excludes the presence of the *Z,Z* isomer to any significant extent. The ^1H NMR spectra were unsatisfactory in determining the population of the *Z,Z* form in **2** and **5** since **2** is insufficiently soluble and **5** gives a complex spectrum.

Support in favour of the *E,Z* structure for **1**, **3** and **4** can be obtained from the values of the chemical shifts of the aromatic protons. It accounts, for example, for the large low-field shift of H-3 of the (*Z*)-pyridyl group in **1**. The fact that the anisotropic thiocarbonyl group is *cis* and coplanar with the (*Z*)-pyridine ring should result in a maximum deshielding of the H-3 proton. The chemical shift of H-3 of the (*E*)-pyridyl ring is comparable to that of the corresponding proton in simple 2-subsituted pyridines.[20] Data in the literature supports this conclusion.[21–23] For example, in *N*-(2-pyridyl)thioacetamide,[21] which exists as a *Z*-rotamer, H-3 of the (*Z*)-pyridyl group resonates at 8.39 ppm as compared with a value of 6.45 ppm for the H-3 of 2-aminopyridine.[20] Anisotropic effects on protons *meta* and *para* to the amide function are small in comparison with those at the *ortho* position.[23] The assignment of the chemical shift of H-3 of the 2-pyridyl group of **3** and **4** is confirmed by the characteristic value of the *ortho* coupling (*ca* 8 Hz)[24,25] and its assignment in **1** by the observed broadening in the spectrum of **1** because of the dynamic exchange process.

The data in Table 1 show that the pyridyl protons of **1** average at 273 K. The NH signals, however, are not averaged at this temperature. It is anticipated that the NH signals of **1** coalesce near 325–330 K. The NH signals of the analogous oxygen derivative, 1,3-di(2-pyridyl)urea, coalesce[26] at 283 K. Since $CDCl_3$ was employed as the solvent, the spectrum of **1** at the temperature of the coalescing NH signals could not be obtained. For the pyridyl protons of **1**, the data at 273 K for H-4, H-5 and H-6 are clearly the average of the low-temperature data of the (*E*)- and (*Z*)-pyridyl groups. For H-3, however the value at 273 K does not represent such an average. This may be due to the fact that at low temperature H-3 of the (*Z*)-pyridyl group is influenced by the anisotropic effect of the C=S group as much as it is at 293 K, owing the stabilization arising from the intramolecular hydrogen bonding.

The ^1H NMR spectrum of **3** at ambient temperature in $CDCl_3$ shows a doublet at 6.91 ppm which can be assigned to H-3 of the 2-pyridyl group, by analogy with the low-temperature spectrum of **1**. Comparison of the spectrum in [$^2H_6$]DMSO with that in $CDCl_3$ reveals a pronounced low-field shift of the H-3 signal in the more polar solvent (Table 1). This can be attributed to the hydrogen bonding of DMSO with the (*Z*)-NH, while the internal hydrogen bonding with the (*E*)-NH remains intact; molecular models suggest that the low-field shift of the H-3 signal may be attributed to the anisotropic deshielding effect of the DMSO.

^{13}C NMR spectra

The ^{13}C chemical shifts and one-bond ^{13}C–^1H coupling constants (^1J) are given in Table 2. The long-range ^{13}C–^1H coupling constants (^2J, ^3J) are listed in Table 3. The proton-coupled ^{13}C spectra were analysed on a

Table 2. ^{13}C chemical shifts (ppm downfield from Me_4Si) and (in parentheses) coupling constants [^1J(CH)/Hz] of 1,3-disubstituted thioureas

Compound	Solvent	*T*/K	C-2	C-3	C-4	C-5	C-6	
1	$CDCl_3$	213	(*Z*)-py: 152.80	117.25	139.01	120.87	148.34	
			(*E*)-py: 151.87	112.69	137.65	118.73	145.77	
		293	152.74	112.52	138.39	118.61	146.88	
				(169.2)	(163.0)	(164.5)	(180.5)	
	[$^2H_6$]DMSO	293	152.69	113.60	139.51	120.93	148.30	
2	[$^2H_6$]DMSO	293	3-Py: 145.58	136.19	131.32	123.09	145.58	
			(170.1)		(166.0)	(164.5)	(180.7)	
3	$CDCl_3$	293	2-Py: 153.21	112.53	139.35	118.61	148.43	
				(167.2)	(163.0)	(164.6)	(180.5)	
			3-Py: 147.01	135.85	132.02	123.20	145.89	
			(169.1)		(166.0)	(164.5)	(180.7)	
4	$CDCl_3$	293	2-Py: 153.52	112.78	138.98	118.27	145.55	
				(165.1)	(163.3)	(166.9)	(180.5)	
			Ph: 125.00	126.24	128.75	126.24	125.00;	138.85[a]
			(162.5)	(161.8)	(159.5)	(161.8)	(162.5)	
5	$CDCl_3$	213	Ph: 125.92	130.33	127.70	130.32	125.91;	137.61[a]
			125.22	128.91	127.61	128.90	125.24;	135.58[a]
		302	125.28	129.67	127.35	129.67	125.28;	137.35[a]
			(161.1)	(159.0)	(162.2)	(159.0)	(161.1)	

[a] Quaternary carbon.

Table 3. Long-range ^{13}C–^{1}H coupling constants (^2J, ^3J/Hz) in the ^{13}C NMR spectra of 1,3-dipyridylthioureas[a]

	2-Pyridyl			3-Pyridyl	
	1[b]	3	4	2	3
^3J(C-2, H-4)	9.03	9.05	8.83	2.44	2.49
^3J(C-2, H-6)	11.50	11.48	11.77	10.98	10.98
^3J(C-4, H-2)				5.60	5.49
^3J(C-4, H-6)	6.65	6.65	6.62	5.60	5.49
^3J(C-6, H-2)				10.98	10.85
^3J(C-6, H-4)	7.08	7.08	7.36	4.27	4.29
^2J(C-5, H-4)					1.20
^2J(C-5, H-6)			7.52	9.05	9.05
^2J(C-6, H-5)	3.58	3.58	3.68		
^3J(C-3, H-5)	6.98	6.98	7.35		
^3J(C-5, H-3)	6.98	6.98	6.62		

[a] At 293 K in $CDCl_3$, except for **2** (in [$^2H_6$]DMSO).
[b] Average of (*E*)-py and (*Z*)-py.

first-order basis; the absolute values of the direct coupling [J(CH)] were determined. The long-range coupling constants were calculated according to Takeuchi.[27] For this purpose, the low-temperature spectrum of **1** in $CDCl_3$ and the room temperature spectra of **2** and **3** in [$^2H_6$]DMSO were utilized.

The 1,3-homogeneously substituted thiourea **1** undergoes two-site exchange between the two hydrogen-bonded conformers at ambient temperature, which causes some of the carbon signals to broaden and renders the analysis of the coupled spectra difficult. However, **4**, being conformationally rigid, gave well resolved spectra. The values of the direct and long-range coupling constants calculated from these spectra compare well with those from the corresponding 1,3-dipyridyl systems. It is also noted from the ^{1}H and ^{13}C NMR spectra that while the chemical shifts for the *E*-and *Z*-groups differ significantly, the differences in the values of the coupling constants for the groups in *E* and *Z* orientations are negligible.

The assignment of the ^{13}C chemical shifts was made using the fine splitting pattern caused by long-range couplings, and also by using the ^1J values as a diagnostic means. The following features are noteworthy. The signals due to C-2 and C-6 of the 3-pyridyl group overlap in the spectra of **2** and **3** in [$^2H_6$]DMSO. On addition of $CDCl_3$ to the solvent system the signals become separated, exemplifying the effect of solvent on the *ortho*-carbon chemical shift. However, a knowledge of the coupling pattern exhibited by C-2 and C-6 in related 3-pyridyl systems[27] also aided the analysis. For the 2-pyridyl group, the C-5 resonance signal appears as an unsymmetric triplet instead of a quartet owing to its coupling with H-3 and H-6 [^3J(C-5, H-3) and ^2J(C-5, H-6)], since the coupling constants are of nearly equal magnitude. The relatively high values of ^1J for **1**–**4** compared with those for **5** could be attributed to the influence of the nitrogen lone pair.

A comparison of the ^{13}C spectral data of **3**, **4** and **5** clearly shows that the assignments for the phenyl and 2-pyridyl groups (in the *E* orientation) are compatible. Reference to the chemical shifts of **2** aids the assignment of the 3-pyridyl signals of **3**. Relative to the chemical shifts of 2-pyridyl in **4**, the values in **1** are slightly different at the positions *ortho* and *para* to the nitrogen of the pyridine ring. The data recorded in Table 2 show the presence of ^{13}C resonance signals in pairs for **5**, suggesting the presence of at least two rotamer species at subambient temperatures, in accord with the results from the ^{1}H NMR spectra. The formation of the intramolecular hydrogen bond and the geometry of the thioureide group require the (*E*)-pyridyl group to be coplanar with the thioureide skeleton, thereby increasing the conjugative interaction of the (*E*)-pyridyl group with the amide lone pair. This is consistent with the observed high-field shift of the (*E*)-pyridyl protons relative to those of the (*Z*)-pyridyl group (Table 1). Information on the coplanarity of the ring not involved in hydrogen bonding is obtained from the spectrum of **4**. The ^{1}H NMR of spectrum of **4** is complicated and, hence, the ^{13}C spectrum is utilized. The fact that the chemical shifts of C-2 and C-6 are the same excludes the possibility that the N(amide)—Ph ring is present in the plane of the remaining part of the molecule. In a completely planar structure the C-2 signal would be shifted significantly downfield in comparison with that of C-6 owing to the anisotropy of the thiocarbonyl group. In solution, rotation occurs around the N—Ph(Ar_2) bond the rotation is so rapid that an average chemical shift is observed for C-2 and C-6.

Dynamic ^{1}H and ^{13}C NMR measurements[28] in $CDCl_3$ for the coalescing H-4 (T_c 268 K) and C-3 (T_c 283 K) signals of **1** yielded a free energy of activation ($\Delta G^{\ddagger}$) of 51.0 and 53.5 kJ mol^{-1}. The determination, similarly, of $\Delta G^{\ddagger}$ for the coalescing NH (T_c 243 K) and C-*m* (T_c 228 K) signals in the ^{1}H and ^{13}C NMR spectrum of **5** gave 44.9 and 45.0 kJ mol^{-1}, respectively. The errors in the $\Delta G^{\ddagger}$ values were estimated to be less than 1 kJ mol^{-1} in any one method.

The origin of the low-energy barrier about the C—N bond in thioureas relative to thionamides seemingly arises from two complementary effects. These are firstly the competitive conjugative interaction between the two C—N bonds and the C=S group and, secondly, the steric inhibition that prevents the coplanarity of the thiocarbonyl group with the thioureide nitrogen atoms and their substituents. In 1,3-diarylthioureas the aryl groups also compete with the C=S group for the nitrogen lone pair (cross-conjugation), thereby reducing the barrier about the C—N bond in comparison with that for 1,3-dialkylthioureas. The rotational barrier about the C—N bond of **5** is lower than that for 1,3-dimethylthiourea[11] (57.7 kJ mol^{-1}). This decrease, in effect, gives an estimate of the increased conjugation across the N—C(aryl) bond. The rotational barrier about the C—N bond in **1** is higher than in **5**. The energy barrier for the internal rotation about the C—N bond for **1** is energetically affected by the intramolecular hydrogen bond, since the rate of $Z,E \rightleftharpoons E,Z$ interconversion involves the breaking up and formation of hydrogen bonds, with a consequent increase in the free energy of activation.

Calculated electron densities

It is common to relate the ^{1}H and ^{13}C chemical shifts in aromatic systems to the charges at the appropriate

Table 4. Chemical shifts and calculated electron densities

Compound	Parameter	^{13}C chemical shifts, δ/ppm (*Z*)-Pyridyl C-2	C-3	C-4	C-5	C-6	(*E*)-Pyridyl C-2	C-3	C-4	C-5	C-6
1	C.S.	152.8	117.3	139.0	120.9	140.3	151.9	112.9	137.6	118.7	145.8
	q_T	3.756	4.098	3.923	4.071	3.871	3.767	4.101	3.933	4.071	3.881
	q_π	0.903	1.089	0.921	1.073	0.908	0.921	1.104	0.939	1.076	0.923
3	C.S.	147.0	135.9	132.0	123.2	145.9	153.2	112.5	139.4	118.6	148.4
	q_T	3.861	3.985	4.031	4.044	3.882	3.761	4.097	3.927	4.071	3.875
	q_π	0.976	1.014	1.025	1.067	0.977	0.904	1.104	0.910	1.075	0.923
		^{1}H chemical shifts, δ/ppm									
		H-2	H-3	H-4	H-5	H-6	H-2	H-3	H-4	H-5	H-6
3	C.S.	8.73	—	8.35	7.37	8.50	—	6.91	7.73	7.06	8.27
	q_{1s}	0.933	—	0.993	1.039	0.991	—	1.006	0.995	0.981	0.976
		^{1}H chemical shift differences/ppm									
		H-3	H-4	H-5	H-6	H-N					
1	Obsd.	1.78	0.13	0.14	0.14	4.64					
	Calcd.	2.74	0.11	0.19	0.18	1.78					

atoms.[29,30] The ^{1}H and ^{13}C chemical shifts for **1** and **3** are compared with the charge pattern given by the CNDO SCF-MO calculations. The gross atomic charges on the carbon atoms, π and total (q_π and q_T, respectively), are listed in Table 4 for the more stable *E,Z* form. A least-squares fit of the ^{13}C chemical shifts versus the electron densities was made. The correlation was found to be better with total electron densities (correlation coefficient 0.98–0.99) rather than with π-electron densities (correlation coefficient 0.96–0.98), demonstrating the importance of σ electronic contributions in these systems.

A least-squares fit of the 1s electron densities for the pyridyl protons versus the ^{1}H chemical shifts for **1** gave a poor fit. This was expected from our experimental evidence that the anisotropic effect of the C=S moiety is operative for H-3. Instead of comparing the absolute values of the chemical shifts with 1s electron densities, it was thought to be more realistic to compare the differences in the ^{1}H chemical shifts and 1s electron densities for the (*E*) and (*Z*)-pyridyl rings of **1**. The calculated differences in the chemical shifts between the corresponding (*E*)- and (*Z*)-pyridyl protons using the scaling factor of Reynolds[31] are shown in Table 4. The chemical shift differences between the calculated and observed values agree reasonably well for H-4, H-5 and H-6 but not for H-3. This deviation is attributed to the anisotropic effect of the C=S function on H-3 of the (*Z*)-pyridyl group. Likewise, the chemical shift difference between the (*E*)-NH and (*Z*)-NH groups was calculated theoretically from the 1s electron densities using the scaling factor of Sire.[32] It was found that the calculated value (δ 1.78) was much lower than the experimentally observed shift (δ 4.64). Many factors account for this deviation. For example, the (*Z*)-NH group experiences the anisotropic deshielding effect of the C=S group, and the solvent effects are pronounced for the NH chemical shift. The results of the CNDO calculations refer to the isolated gaseous molecules.

A least-squares fit of the 1s electron densities of both the 2- and the 3-pyridyl protons of **3** with the ^{1}H chemical shifts gave a good fit for the 2-pyridyl group (in the *E* orientation, correlation coefficient 0.99) and a poor fit (correlation coefficient 0.92) for 3-pyridyl protons. This is to be expected, since H-2 and H-4 (owing to nearly free rotation over the N—pyridyl bond) of the 3-pyridyl group are affected by the anisotropic deshielding effect of the thiocarbonyl group.

EXPERIMENTAL

Materials

1. The amine (1 M), elemental sulphur (0.025 M) and carbon disulphide (1.5 M) were dissolved in dry ethanol and refluxed for 24 h. The mixture, concentrated at room temperture on a rotary evaporator, was poured into water and the resulting solution was acidified with HCl (2 M). The precipitated sulphur was filtered off, and filtrate neutralized with sodium hydrogen carbonate and the resulting product was extracted with chloroform. The compound obtained after distilling off the solvent was recrystallized from ethanol; m.p. 152–154 °C.

2 and 3. A mixture of the appropriate amines (1 M each) was dissolved in dry ethanol. Carbon disulphide (1.5 M) and NaOH (0.1 M) were added and the mixture refluxed for 36 h. The reaction mixture was acidified at room temperature with HCl (2 M) and the precipitated sulphur, if any, was filtered off. The filtrate was neutralized with sodium hydrogen carbonate and the resulting compound was extracted with chloroform. The residue remaining after the removal of chloroform on a rotary evaporator contained a mixture of three compounds. The required compounds were separated from the mixture by preparative TLC using chloroform–ethyl acetate (4:1) as the solvent: m.p. (**2**) 172–174 °C, (**3**) 182–184 °C.

4. A mixture of phenyl isothiocyanate (1 M) and pyridylamine (1 M) was refluxed in absolute ethanol for

approximately 3 h. The compound which separated on cooling was recrystallized from alcohol–chloroform; m.p. 169 °C.

Compounds **1–4** were identified by elemental analyses for carbon, hydrogen and nitrogen.

5. A commercial sample (E. Merck) was recrystallized from ethanol; m.p. 149–151 °C.

NMR Measurements

^{1}H NMR spectra were recorded on a Bruker WH 270 Fourier transform spectrometer attached to a computer with a 20K memory and operating at 270 MHz. The experimental conditions were spectral width 4000 Hz, pulse width 5 μs, pulse angle 67°, acquisition time 3.0 s and 20–30 acquisitions. The spectra were recorded in $CDCl_3$ or [$^2H_6$]DMSO as solvent, with tetramethylsilane as internal standard.

Fully decoupled and single resonance ^{13}C spectra were obtained with the same instrument, operating at 67.89 MJz. The experimental conditions for single resonance spectra were spectral width 6042 Hz, acquisition time 3.5 s, pulse width 15 μs, pulse angle 67° and 6000–11 000 acquisitions. The experimental conditions for the fully decoupled spectra were spectral width 17420 Hz, acquisition time 3.0 s, pulse width 15 μs, pulse angle 67° and 100–400 pulses. The spectra were obtained in $CDCl_3$ using tetramethylsilane as an internal reference.

Molecular Orbital Studies

Molecular orbital calculations[33] were carried out using the CNDO self-consistent field approximation method.[15] This description includes the effect of both σ and π electron delocalization in determining the final charges. Bond distances and angles for the pyridyl group and thiourea skeleton were taken from the literature.[34,35]

REFERENCES

1. W. E. Stewart and T. H. Siddall, *Chem. Rev.* **70**, 517 (1970).
2. J. S. Hartman and G. S. Schrobilgen, *Can. J. Chem.* **51**, 99 (1973).
3. R. H. Sullivan, P. Nix, E. L. Summers and S. L. Parker, *Org. Magn. Reson.* **21**, 293 (1983).
4. R. H. Sullivan and E. Price, *Org. Magn. Reson.* **7**, 143 (1975).
5. M. L. Martin, M. L. Filleux-Blanchard, G. J. Martin and G. A. Webb, *Org. Magn. Reson.* **13**, 396 (1980).
6. A. M. Giuliani, *J. Chem. Soc., Dalton Trans.* **492**, 497 (1970).
7. M. V. Andreocci, M. Bossa, G. Ramunni, M. Scazzocchio, D. Gattegno and A. M. Giuliani, *J. Chem. Soc., Dalton Trans.* 41 (1974).
8. C. D. Freeman and D. L. Hooper, *J. Phys. Chem.* **78**, 961 (1974).
9. M. L. Filleux-Blanchard, *Org. Magn. Reson.* **9**, 125 (1977).
10. M. L. Filleux-Blanchard and A. Durrand, *Bull. Soc. Chim. Fr.* 4710 (1972).
11. W. Walter and K. P. Ruess, *Justus Liebigs Ann. Chem.* **746**, 54 (1971).
12. H. Kessler and D. Liebfritz, *Tetrahedron Lett.* 1595 (1970).
13. Y. Mido, F. Fujita, H. Matsuura and K. Machida, *Spectrochim. Acta, Part A* **37**, 103 (1981).
14. Y. Mido, *Spectrochim. Acta, Part A* **32**, 1105 (1976).
15. J. A. Pople and D. L. Beveridge, *Approximate Molecular Orbital Theory*. McGraw-Hill, New York (1970).
16. J. D. Swalen, *Prog. Nucl. Magn. Reson. Spectrosc.*, edited by J. W. Emsley, J. Feeney and L. H. Sutcliffe, Pergamon Press, Oxford, **2**, 124 (1966).
17. D. B. Davies and A. Rabczenko, *J. Chem. Soc., Perkin Trans.* 2 82 (1981).
18. B. Brzezinski, *Org. Magn. Reson.* **8**, 283 (1976).
19. J. W. Emsley, J. Feeney and L. H. Sutcliffe, *High Resolution NMR Spectroscopy*, p. 224. Pergamon Press, Oxford (1967).
20. D. W. Aksens and H. Kryvi, *Acta Chem. Scand.* **26**, 2255 (1972).
21. L. V. Sudha and D. N. Sathyanarayana, *J. Coord. Chem.* **13**, 207 (1984).
22. N. Enomoto and M. Kondo, *Bull. Chem. Soc. Jpn.* **45**, 2665 (1972).
23. I. D. Rae, *Can. J. Chem.* **46**, 2589 (1968).
24. J. B. Stothers, *Carbon-13 NMR Spectroscopy*. Academic Press, New York (1972).
25. F. W. Wehrli and T. Wirthlin, *Interpretation of Carbon-13 NMR Spectra*. Heyden, London (1976).
26. N. C. Singha and D. N. Sathyanarayana, unpublished results.
27. Y. Takeuchi, *Org. Magn. Reson.* **7**, 181 (1975).
28. D. K. Dalling, D. M. Grant and L. R. F. Johnson, *J. Am. Chem. Soc.* **93**, 3678 (1971).
29. U. Edlund, B. Eliasson, J. Kowaleski and L. Trogen, *J. Chem. Soc., Perkin Trans.* 2 1260 (1981).
30. G. L. Nelson and E. A. Williams, *Prog. Phys. Org. Chem.* **12**, 229 (1976).
31. W. F. Reynolds, in *Progress in Physical Organic Chemistry*, edited by R. W. Taft, Vol. 14, p. 168. Wiley, New York (1983).
32. J. Sire, *Acta Chem. Scand., Ser. B* **31**, 589 (1977).
33. *Quantum Chemistry Program Exchange*, Program 141. Indiana University, Bloomington, IN.
34. G. O. Sorensen, L. Mahler and N. Rastrup-Andersen, *J. Mol. Struct.* **20**, 119 (1974).
35. G. Marcotrigiano, L. F. Battaglia, A. B. Corradi and M. E. V. Tani, *Cryst. Struct. Commun.* **4**, 361 (1975).