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Structural studies of *N*-2-(3-picolyl)- and *N*-2-(4-picolyl)-*N′*-tolylthioureas

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Reactions of 2-aminopicolines with 2- and 4-tolyl isothiocyanates yielded *N*-2-(4-picolyl)-*N′*-4-tolylthiourea, **1**, *N*-2-(3-picolyl)-*N′*-4-tolylthiourea, **2**, and *N*-2-(4-picolyl)-*N′*-2-tolylthiourea, **3**. Compound **1** is monoclinic, of space group $P2_1/c$ with $a = 7.456(1)$ Å, $b = 13.135(3)$ Å, $c = 13.959(3)$ Å, $\beta = 104.99(3)^\circ$, and $V = 1320.\underline{5}(5)$ Å^3 with $Z = 4$, for $d_{\mathrm{calc}} = 1.294$ g/cm^3. Compound **2** is triclinic, of space group $P\bar{1}$ with $a = 6.877(3)$ Å, $b = 7.590(5)$ Å, $c = 13.213(9)$ Å, $\alpha = 78.38(2)^\circ$, $\beta = 77.96(4)^\circ$, $\gamma = 86.36(4)^\circ$, and $V = 660.5(7)$ Å^3 with $Z = 2$, for $d_{\mathrm{calc}} = 1.294$ g/cm^3. Compound **3** is monoclinic, of space group $P2_1/c$ with $a = 12.604(2)$ Å, $b = 15.592(3)$ Å, $c = 6.875(2)$ Å, $\beta = 91.05(2)^\circ$, and $V = 1350.9(2)$ Å^3 with $Z = 4$, for $d_{\mathrm{calc}} = 1.265$ g/cm^3. The three thioureas are found in both solid state and solution in a conformation resulting from intramolecular N—H$\cdots$N hydrogen bonding. Compounds **1** and **3** present an intermolecular hydrogen bond involving the thione sulfur and the NH hydrogen, which is not present in **2** owing to the steric hindrance of the methyl group in the phenyl ring. The geometry of the molecule is affected by the position of the methyl groups on the pyridine and aryl rings.

KEY WORDS: Thiourea; pyridine; hydrogen bonding.

Introduction

The ^{1}H NMR spectra of 2-pyridyl thioureas indicate the presence of an intramolecular hydrogen bond between N′H and the pyridyl nitrogen in solution.[1] The solid-state structures of 2-pyridyl thiourea[2] and substituted *N*-(2-pyridyl)-*N′*-arylthioureas[3–6] show the presence of this intramolecular hydrogen bond. Also present in the solid state is an intermolecular NH hydrogen bond to a sulfur of a neighboring molecule (Fig. 1).

In order to study the influence of substituents on the aryl and pyridyl rings on the geometry of the molecules and on the intra- and intermolecular hydrogen bonds, in this paper we present the ^{1}H NMR spectra and crystal structures of *N*-2-(4-picolyl)-*N′*-4-tolylthiourea, **1**, *N*-2-(3-picolyl)-*N′*-4-tolylthiourea, **2**, and *N*-2-(4-picolyl)-*N′*-2-tolylthiourea, **3**. In **1** the methyl groups are away from the thiourea moieties, but in **2** and **3** there are methyl groups alpha to the carbon bonded to the nitrogen on the pyridine ring (**2**) or

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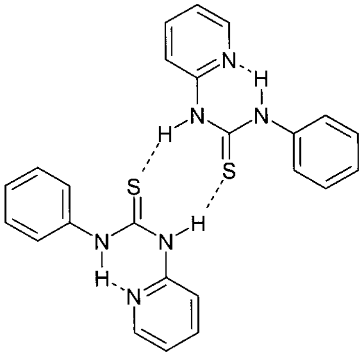


Fig. 1. Intra- and intermolecular hydrogen bonding found in *N*-2-picolyl-*N*′-tolylthioureas.

the phenyl ring (**3**), and these may have a steric influence on the geometry of the molecule and, in **2** on the intermolecular hydrogen bonding (Fig. 2).

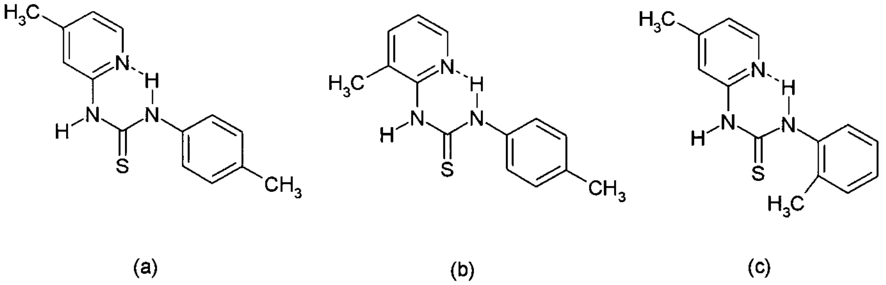
Experimental

2-Amino-3-picoline and 2-amino-4-picoline, as well as 2-tolyl- and 4-tolyl isothiocyanate, were purchased from Aldrich and used as received. 2-Aminopicoline was mixed with a tolyl isothiocyanate in a 1:1 molar ratio (e.g., 2 mmol) in 30 mL of 95% ethanol, and the mixture was stirred with gentle warming for a minimum of 1 h. On cooling and slowly evaporating the reactant mixture (35°C), the thioureas crystallized from solution. The crystals were filtered, washed with cold 2-propanol, and dried. The yields were approx. 70% for each of the thioureas and the melting points are as follows: **3**, 189–191°C; **2**, 116–118°C; and **1**, 184–186°C. The ^{1}H NMR spectra were recorded in $CDCl_3$ with a Bruker 300-MHz spectrometer and the enthalpies of fusion were obtained with approximately 3-mg samples at a heating rate of 10°C/min using a Perkin-Elmer differential scanning calorimeter, DSC7.

Crystals were grown by slow evaporation of acetone–anhydrous ethanolic mixtures (1:1 by volume) at room temperature. The colorless thiourea crystals were mounted in random orientation on a glass fiber, and the structures were solved by direct methods and missing atoms were found by difference Fourier synthesis. The nonhydrogen atoms were refined with anisotropic temperature factors. Hydrogens attached to nitrogens and ring carbons were refined isotropically, and the methyl hydrogens were allowed to ride on their carbons and assigned a fixed isotropic temperature factor, $U = 0.05$ Å^2. For **1**, scattering factors were taken from International Tables for X-ray Crystallography (1974, Vol. IV)[8] and calculations were done with the SHELXTL PC™ program package.[9] Scattering factors for **3** and **2** are from Wassmaier and Kirfel,[10] and calculations were done by MaXus, version 2.0.[11] Table 1 summarizes the crystal data, collection information, and refinement data for these thioureas.

Results

The thermal ellipsoid plots of **1–3** are shown in Fig. 3. Selected bond distances and angles are in Table 2 and hydrogen-bonding geometries are in



(a) (b) (c)

Fig. 2. Drawings of (a) **1**, (b) **2**, and (c) **3**.

Table 1. Crystallographic Data for **1**, **2**, and **3**

Crystal data	**1**	**2**	**3**
CCDC no.	163123	163124	163125
Crystal color, habit	Colorless, prism	Colorless, prism	Colorless, prism
Empirical formula	$C_{14}H_{15}N_3S$	$C_{14}H_{15}N_3S$	$C_{14}H_{15}N_3S$
Formula weight	257.35	257.35	257.35
Temperature, K	293(2)	130(2)	293(2)
Crystal size, mm	0.32 × 0.28 × 0.20	0.26 × 0.17 × 0.05	0.32 × 0.20 × 0.20
Crystal system	Monoclinic	Triclinic	Monoclinic
Space group	$P2_1/c$	$P\bar{1}$ (No. 2)	$P2_1/c$
a, Å	12.604(2)	6.877(3)	7.456(1)
b, Å	15.592(3)	7.590(5)	13.135(3)
c, Å	6.875(2)	13.213(9)	13.959(3)
α, deg	90	78.38(2)	90
β, deg	91.05(2)	77.96(4)	104.99(3)
γ, deg	90	86.36(4)	90
Volume, Å^3	1350.9(6)	660.5(7)	1320.5(5)
Z	4	2	4
Density (calcd.), Mg/m^3	1.265	1.294	1.294
Absorption coefficients, mm^{-1}	0.225	0.230	2.047
Diffractometer	Nonius MACH3	Nonius Kappa CCD	Siemens P4
θ range for data collection, deg	1.61–27.39	5.16–21.95	4.7–55.04
Reflections measured	3249	2289	1701
Independent reflections (R_{int})	2985 (0.0205)	1416 (0.1413)	1550 (0.0433)
Observed reflections	1437 [$I > 2.0\sigma(I)$]	628 [$I > 2.0\sigma(I)$]	1295 [$F > 3.0\sigma(F)$]
Data/restraints/parameters	2985/0/202	1416/0/201	1550/0/170
Extinction coefficient	0.00605	0	0.0017(5)
Goodness of fit	1.136	0.703	1.45
R, wR	0.0589, 0.0963	0.0530, 0.0950	0.0462, 0.1306
R, wR (all data)	0.1436, 0.1448	0.1587, 0.1337	0.0553, 0.1367

Table 3. The conformation of the thioureas is such that the C2 of the pyridine ring and the S atom are *anti* with respect to the N2—C7, and C8 from the phenyl ring and the S atom are *syn* with respect to C7—N3. An intramolecular hydrogen bond between N3—H and N1 is present in **1–3**, with a N3—N1 distance equal to 2.630(3), 2.631(8), and 2.646(4) Å, respectively (Fig. 4). The angle between the pyridine ring and the thiourea moiety (N2—C7—S1—N3) in **1–3** is 4.5(1), 8.1(2), and 9.7(1)°, respectively, and the angle between the phenyl ring and the thiourea moiety is 21.7(1), 8.0(2), and 73.4(1)° respectively.

The molecules in **1** and **3** form self-complimentary NH $\cdots$ S hydrogen bonds, N2—S1$^{(1-x,-y,-z)}$ $= 3.438(3)$ Å and N2—S1$^{(1-x,-y,2-z)}$ $= 3.437(3)$ Å, respectively. In **2** instead of this N—H $\cdots$ S hydrogen bonds two C—H $\cdots$ S interactions are present, as shown in Fig. 4.

The DSC plots of these thioureas show a sharp peak due to melting, followed immediately by a broader peak representing decomposition. The enthalpies of fusion are as follows: **1**, 44.6 kJ/mol; **2**, 22.5 kJ/mol; and **3**, 53.7 kJ/mol.

Discussion

Compounds **1–3** were synthesized in good yields from the reaction between the appropriate 2-aminopicoline and tolyl isothiocyanate. The ^{1}H NMR spectra of **1–3** show that N3$\underline{\mathrm{H}}$ is downfield from the rest of the signals, 13.477, 13.777, and 13.571 ppm, respectively, indicating its involvement in intramolecular hydrogen bond.

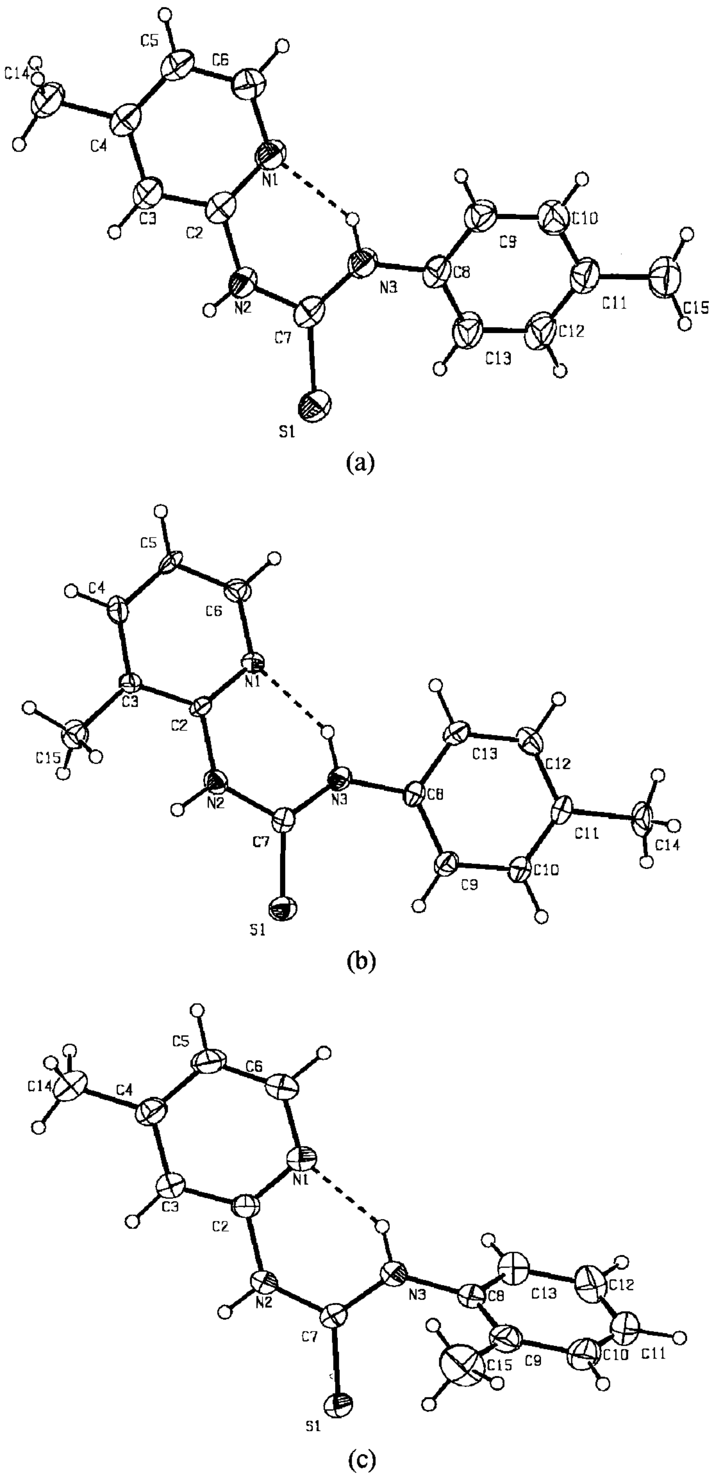


Fig. 3. Thermal ellipsoid diagram showing intramolecular hydrogen bonding for (a) **1**, (b) **2**, and (c) **3**, with atom numbering scheme and displacement ellipsoids at 30% probability level.

Table 2. Selected Bond Distances (Å) and Angles (Deg) for **1**, **2**, and **3**

	1	**2**	**3**
Bond distances			
S1—C7	1.683(3)	1.666(7)	1.680(3)
N1—C2	1.328(4)	1.319(7)	1.321(4)
N1—C6	1.349(4)	1.351(7)	1.338(4)
N2—C2	1.411(4)	1.400(7)	1.404(4)
N2—C7	1.369(4)	1.410(7)	1.368(4)
N3—C7	1.327(4)	1.334(7)	1.323(4)
N3—C8	1.431(4)	1.410(7)	1.417(4)
Bond angles			
C2—N2—C7	129.7(3)	130.3(5)	130.9(3)
C7—N3—C8	126.0(3)	133.1(6)	131.8(3)
N1—C2—N2	118.5(3)	118.5(5)	118.1(3)
N2—C2—C3	117.9(3)	117.3(6)	118.3(3)
S1—C7—N2	118.9(3)	117.1(5)	117.3(2)
S1—C7—N3	124.2(3)	128.8(5)	127.1(2)
N2—C7—N3	116.8(3)	114.2(5)	115.6(3)
N3—C8—C9	121.7(4)	125.9(6)	116.8(3)
N3—C8—C13	117.0(4)	115.1(6)	125.2(3)

The three thioureas reported here, like other 2-pyridyl thioureas,[2–6] are found in a conformation resulting from intramolecular hydrogen bonding. This result is in agreement with Etter's hydrogen-bond rules, which indicate that intramolecular hydrogen-bonded six-membered rings are favored as compared to rings with intermolecular hydrogen bond[12]. Because of this hydrogen bond, the angle between the pyridine ring and the thiourea moiety mean planes is less than 15°.[2–4,6,7] This hydrogen bond locks the pyridine ring and it cannot rotate freely: this has an important influence on the intermolecular hydrogen bonding, as will be seeing.

Thioureas tend to form intermolecular N—H···S hydrogen bonds. In cyclic thioureas the intermolecular N—H···S hydrogen bonds produce tapes and force molecules on one side of the tape to reside in a plane that is parallel to, but separated (∼1 Å) from, the plane occupied by the molecules on the other side of the tape.[13] In the crystal structure of **1**, **2**, and **3**, there are two molecules in parallel planes that may form self-complimentary N—H···S interactions, but in each one the step between the molecules is very different. In **1** the height of the step is ∼1.40 Å, higher than that observed in cyclic thioureas, but distances and angles are within the accepted values for N—H···S hydrogen bonds. In **2**, owing to the steric hindrance of the methyl group in the phenyl ring, the height of the step is 2.50 Å, and no N—H···S bond is formed; instead C—H···S hydrogen bonds are present. In **3** the height of the step is only 0.35 Å, and the self-complimentary N—H···S as well as C(3)—H(3)···S(1) are present, as shown in Fig. 5.

The present 2-pyridyl thioureas have similar bond distances and angles, with the most notable difference being the longer N2—C7 bond distance for **2** and the shorter C7—N3—C8 and S1—C7—N3 bond angles for **3**. The previously reported *N*-2-(3-picolyl)- and *N*-2-(4-picolyl)-*N*′-2-phenylthioureas have bond distances and angles similar to those found here.[6] There is a

Table 3. Hydrogen Bond Parameters for **1**, **2**, and **3**

D—H···A	D—H (Å)	H···A (Å)	D···A (Å)	D—H···A (deg)	Symmetry code
1					
N3—H3A···N1	0.81(3)	1.95(3)	2.630(4)	141(3)	
N2—H2···S1	0.79(3)	2.72(3)	3.437(3)	152(3)	$1-x, -y, -z$
2					
N3—H3N···N1	0.8801	1.8570	2.631(7)	145.70	
C13—H13···S1	0.9506	2.8566	3.687(8)	146.52	$x, -1+y, z$
C15—H15C···S1	0.9798	2.7921	3.752(7)	166.49	$-x, 2-y, -z$
3					
N3—H3A···N1	0.90(5)	1.88(4)	2.646(4)	142(4)	
N2—H2A···S1	0.88(3)	2.57(4)	3.437(3)	167(3)	$1-x, -y, 2-z$
C(3)—H(3)···S(1)	0.95(3)	2.84(3)	3.674(4)	147(2)	$1-x, -y, 2-z$

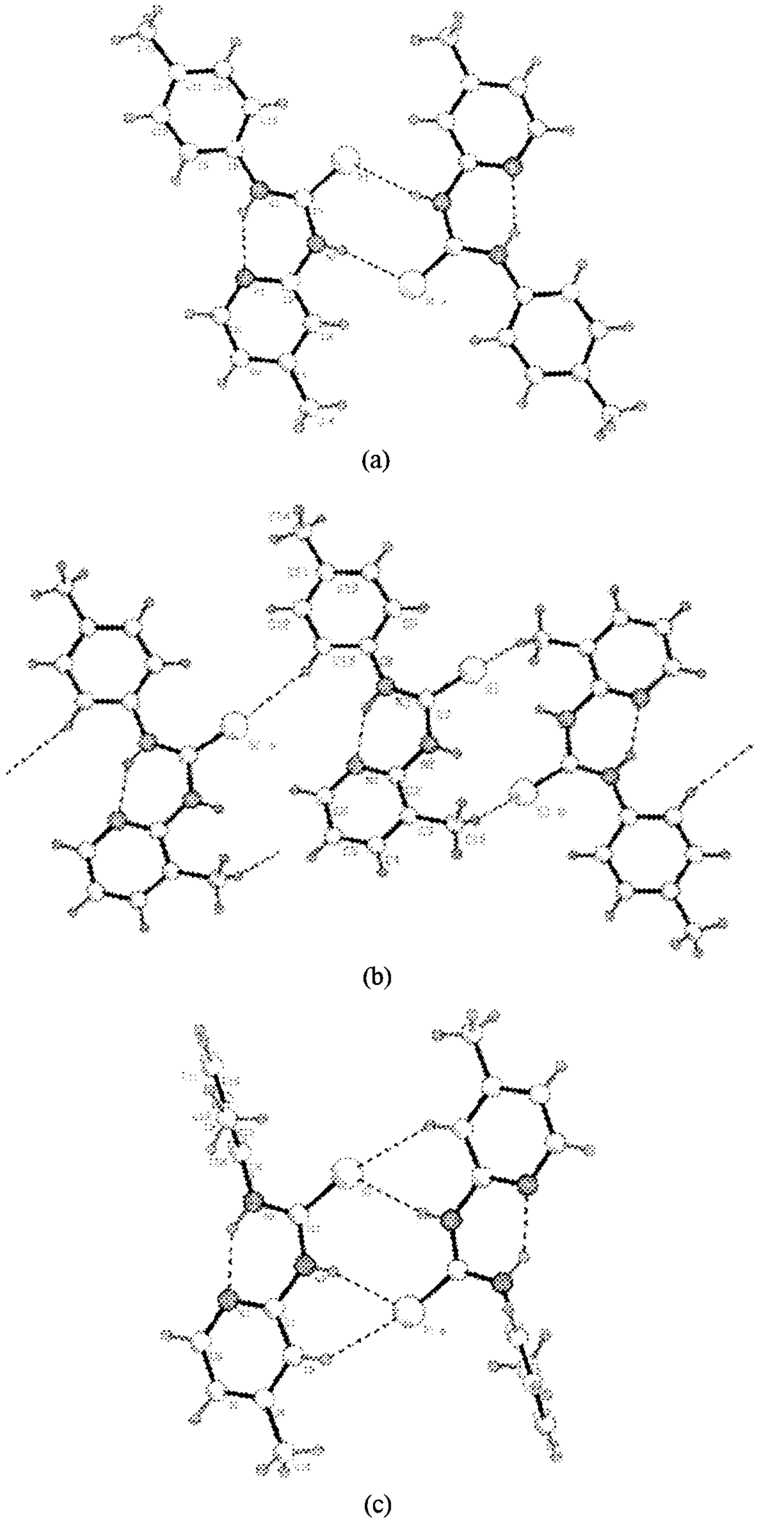
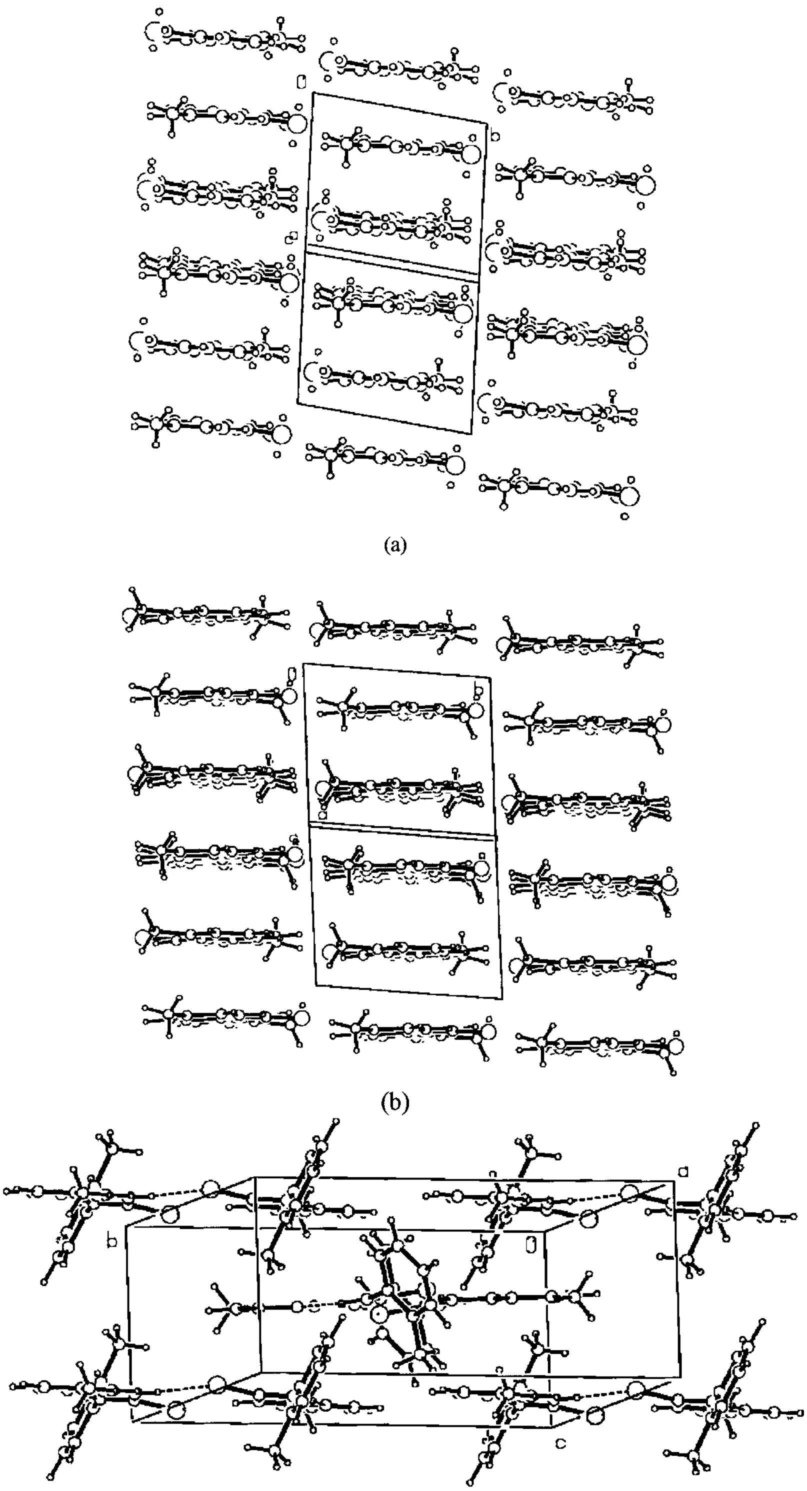


Fig. 4. Intermolecular hydrogen bonding for (a) **1** and (b) **3**.


(a)

(b)

(c)

Fig. 5. Packing diagrams for (a) **1**, (b) **2**, and (c) **3**.

considerable difference in the angle between the phenyl ring and the thiourea moiety in **3** as compared to that in **1** and **2**, **3** being the most distorted molecule. Among the 2-pyridyl thioureas with methyl groups on one or both rings,[2–4,6,7] **2** is the least distorted and *N*-(2-pyridyl)-*N*′-3-tolylthiourea is the most distorted.[6] In **3** and *N*-(2-pyridyl)-*N*′-3-tolylthiourea the distortion may be due to the steric hindrance of the methyl group in the phenyl ring. The tilt of the phenyl ring in **3** affects the way the molecules pack in the crystal, as shown in Fig. 5.

Conclusions

The methyl groups on the aryl and pyridyl rings have no influence on the intramolecular bond between N3─H and N1. This intramolecular hydrogen bond is favored in comparison to intermolecular hydrogen bond, and is present in solution and in the solid state. The methyl substitution on the pyridyl ring causes the N2─H bond to become considerably less polar in solution. The methyl group alpha to the carbon bonded to the nitrogen affects the intermolecular N2H $\cdots$ S hydrogen bond and the geometry of the molecule.

Supplementary material

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center. Copies of available material can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB21EZ, UK (Fax: +44-(0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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