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ORIGINAL PAPER

Hydrogen-Bonding Networks in Heterocyclic Thioureas

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Abstract The synthesis of heterocyclic thioureas from heterocyclic amines with phenyl- or methylisothiocyanate or CS_2 is described. Seven new X-ray crystal structures are reported: In *N*-(3-pyridyl)-*N*′-phenylthiourea ($Pna2_1$, a = 10.1453(3), b = 17.6183(5), c = 6.4787(2), V = 1158.02(6), Z = 4) hydrogen-bonding results in formation of a 3D network consisting of helices, which form channels parallel to the c-axis. In *N*-(4-pyridyl)-*N*′-phenylthiourea ($P2_1/c$, a = 16.9314(3), b = 10.3554(2), c = 13.5152(3), β = 106.5080 (10), V = 2271.96(8), Z = 4, two independent molecules) hydrogen-bonding results in N–H···S bridged dimers and N–H···Py chains, forming a 2D sheet network. In *N*-(2-pyrimidyl)-*N*′-phenylthiourea ($P2_1/c$, a = 5.45900(10), b = 13.8559(2), c = 14.3356(3), β = 94.9800(10), V = 1080.24(3), Z = 4) and *N*-(2-pyrimidyl)-*N*′-methylthiourea ($P2_1/c$, a = 8.8159(5), b = 11.2386(5), c = 7.7156(4), β = 95.629(2), V = 760.76(7), Z = 4) pairs of intra- and intermolecular N–H···N interactions produce dimers. Dimer formation through N–H···S occurs for *N*-(2-thiazolyl)-*N*′-methylthiourea ($C2/c$, a = 17.9308(3), b = 7.78260(10), c = 10.8686(2), β = 105.3740(10), V = 1462.42(4), Z = 8). Two symmetrically disubstituted thioureas were examined: *N*,*N*′-bis(2-pyridyl)thiourea ($Fdd2$, a = 15.1859(2), b = 30.1654(3), c = 9.44130(10), V = 4324.95(8), Z = 16) forms intra- and intermolecular N–H···Py hydrogen-bonds, forming a 1D zigzag chain and *N*,*N*′-bis(3-pyridyl)thiourea ($P2_1/c$, a = 13.2461(2), b = 6.26170(10), c = 12.3503(2), β = 96.0160(10), V = 1018.73(3), Z = 4) forms intermolecular N–H···Py hydrogen-bonds, resulting in 2D sheets.

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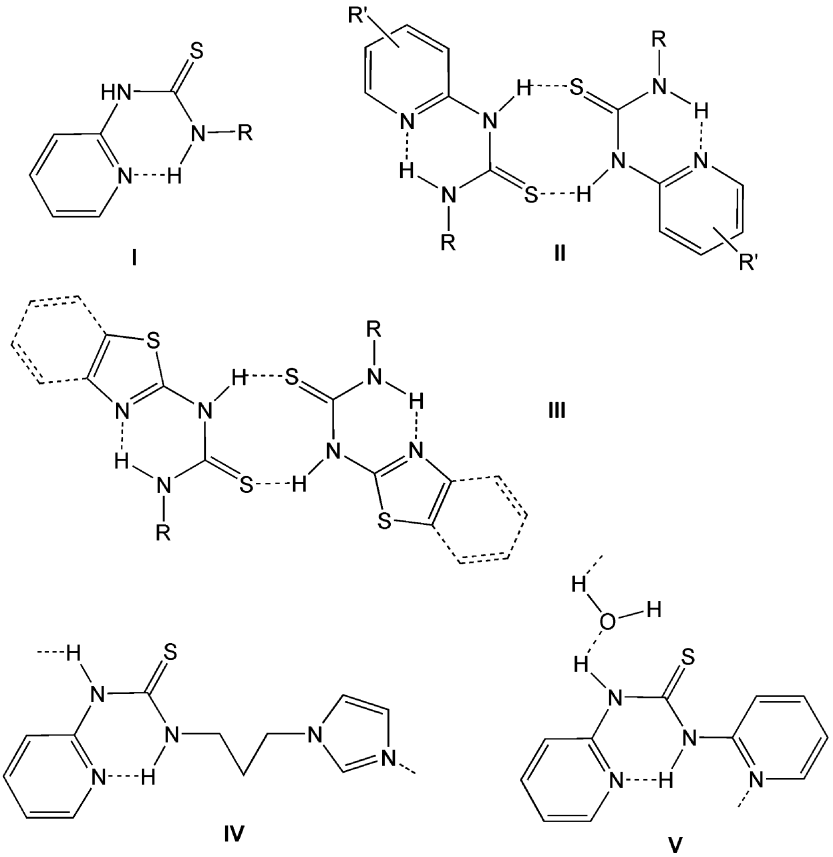
Introduction

Ureas and thioureas are widely recognized for their ability to hydrogen-bond. In addition, they can act as ligands in coordination complexes. This combination has led to their increasing use in an array of self-assembled network materials [1, 2]. It is to be expected that incorporation of heterocyclic rings into thiourea molecules will produce an extended range of possible H-bonding interactions. A number of heterocyclic thiourea crystal structures have been determined [3–9]. However, virtually all of these structures feature a 2-pyridyl or related *ortho*-substituted nitrogen heterocycle. This heteroatom arrangement results in a highly favorable intramolecular H-bond, as illustrated in **I**. A few of the known structures show additional H-bonding, as represented in **II**–**V**. The six known compounds illustrated by **II** and **III** add to the ubiquitous internal H-bond an N–H···S interaction, resulting in dimer formation [3, 5–8]. The "hydrogen-bonded" N···S distances in these species range from 3.256 to 3.379 Å. Although relatively weak, these thiocarbonyl H-bonding interactions are fairly common when the C=S is part of a resonance delocalized system and therefore is relatively long (>*ca.* 1.65 Å) [10]. Compounds **VI** and **V** make use of pendant heteroatom groups to form H-bonded chains, with the latter incorporating an H-bonded water molecule into the chain [6, 9]. Nevertheless, seven compounds that are closely related to **IV**, having pendant furan, thiophene, 2-methylpiperidine, and pyrrolidinone groups, adopt an internal H-bonding only structure, as illustrated by **I** [6]. As part of a study of metal network complexes, we set out to

synthesize and crystallographically characterize a variety of heterocyclic thioureas for use as ligands. The aim of the current study was to identify organic networking patterns resulting from H-bonding.



Experimental

General

All reagents were purchased from Aldrich or Acros and were used as received. Melting point data were recorded on a MelTemp apparatus and are reported uncorrected. C, H, N analyses were carried out by Atlantic Microlabs (Norcross, GA). NMR data were recorded on a Varian Mercury 400 instrument (s = singlet, d = doublet, t = triplet, br = broad, v br = very broad, J = coupling constant; Py = pyridyl, Pym = 2-pyrimidyl, Thz = 2-thiazolyl; for numbering of heterocycles see **1**–**7**). IR spectra were recorded using a Digilab FTS-7000 series FTIR as KBr pellets (s = strong intensity, m = medium, w = weak, br = broad).

Synthesis

*N-(3-Pyridyl)-N′-phenylthiourea (**1**).* 3-Aminopyridine (4.71 g, 50.0 mmol) was dissolved in 60 mL EtOH. Phenyl isothiocyanate (6.76 g, 50.0 mmol) was added, forming a clear, colorless solution. The mixture was stirred overnight under N_2 leading to formation of a precipitate. The white product was isolated by vacuum filtration, was washed with pentane, and was dried in vacuo (9.62 g, 83.9%). m.p.: 156–158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, J = 2.4 Hz, 1H, $H_{Py\text{-}2}$), 8.47 (d, J = 4.7 Hz, 1H, $H_{Py\text{-}4}$), 8.07 (d, J = 8.6 Hz, 1H, $H_{Py\text{-}6}$), 7.94 (s, 1H, NH) 7.62 (s, 1H, NH), 7.50 (7, J = 7.8 Hz, 2H, $H_{Ph\text{-}m}$), 7.36 (m, 4H, $H_{Py\text{-}5}$, $H_{Ph\text{-}o,p}$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.76, 146.19, 145.51, 138.29, 136.07, 132.05, 129.28, 126.23, 124.88, 123.25. Anal. Calcd. for $C_{12}H_{11}N_3S$ C, 62.86; H, 4.84; N, 18.33. Found: C, 62.97; H, 4.87; N, 18.39. IR: 3150 (s, br), 2977 (m, br), 2872 (m, br), 1535 (s), 1511 (s), 1489 (m), 1379 (m), 1231 (m), 1198 (m), 1099 (w), 1024 (m), 735 (m), 710 (m), 691 (m), 647 (m), 615 (m).

*N-(4-Pyridyl)-N′-phenylthiourea (**2**).* 4-Aminopyridine (1.88 g, 20.0 mmol) was dissolved in 20 mL pyridine. Phenyl isothiocyanate (3.38 g, 25.0 mmol) was added, forming a clear, yellow solution. The mixture was stirred overnight under N_2 leading to formation of a precipitate. The white product was isolated by vacuum filtration, stirred in water overnight to remove residual 4-aminopyridine, and was dried in vacuo (3.54 g, 77.1%). m.p.: 139–141 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 br (s, 1H, NH), 8.76 (br s, 1H, NH), 8.46 (d, J = 4.7 Hz, 2H, $H_{Py\text{-}3,5}$), 7.71 (d, J = 4.7 Hz, 2H, $H_{Py\text{-}2,6}$), 7.48, (d, J = 8.6 Hz, 2H, $H_{Ph\text{-}o}$), 7.38 (t, J = 7.4 Hz, 2H, $H_{Ph\text{-}m}$), 7.23 (t, J = 7.4 Hz, 1H, $H_{Ph\text{-}p}$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.75, 130.61, 129.87, 128.35, 127.42, 125.63, 125.53, 116.49. Anal. Calcd. for $C_{12}H_{11}N_3S$ C, 62.86; H, 4.84; N, 18.33. Found: C, 63.05; H, 4.87; N, 18.05. IR: 3160 (s, br), 2992 (m, br), 2951 (m, br), 2926 (m, br), 1593 (s), 1533 (s), 1511 (s), 1485 (s), 1413 (s), 1364 (s), 1287 (m), 1226 (m), 1190 (s), 1004 (w), 777 (s), 692 (m), 642 (m), 628 (m).

N-*(2-Pyrimidyl)*-N′-*phenylthiourea (**3**).* 2-Aminopyrimidine (4.76 g, 50.0 mmol) was dissolved in 20 mL pyridine. Phenyl isothiocyanate (8.12 g, 60.0 mmol) was added, forming a clear, yellow solution. The mixture was stirred overnight under N_2 leading to formation of a precipitate. The white product was isolated by vacuum filtration, washed with diethyl ether, and was dried in vacuo (4.82 g, 41.9%). m.p.: 188–191 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.99 (s, 1H, NH), 9.95 (s, 1H, NH), 8.79 (s, 2H, $H_{Pym\text{-}3,5}$), 7.67 (d, J = 7.8 Hz, 2H, $H_{Ph\text{-}o}$), 7.43 (7, J = 7.4 Hz, 2H, $H_{Ph\text{-}m}$), 7.30 (t, J = 6.3 Hz, 1H, $H_{Pym\text{-}4}$), 7.05 (d, J = 4.7 Hz, 1H, $H_{Ph\text{-}p}$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 179.03, 157.64, 138.70, 129.02, 126.75, 125.15, 115.67. Anal. Calcd. for $C_{11}H_{10}N_4S$ C, 57.37; H, 4.38; N, 24.33. Found: C, 57.58; H, 4.33; N, 24.30. IR: 3209 (m, br), 3173 (m, br), 3028 (m, br), 1593 (m), 1546 (s), 1518 (s), 1443 (m), 1416 (s), 1350 (w), 1195 (m), 1559 (m), 800 (m), 692 (m).

N-*(2-Pyrimidyl)*-N′-*methylthiourea (**4**).* 2-Aminopyrimidine (2.38 g, 25.0 mmol) was dissolved in 25 mL pyridine. Methyl isothiocyanate (2.56 g, 35.0 mmol) was added, forming a clear, yellow solution. The mixture was stirred overnight under N_2. The red-brown solution was concentrated and cooled, producing a precipitate. The off-white product was isolated by vacuum filtration, was washed with diethyl ether, and was dried in vacuo (3.24 g, 76.9%). m.p.: 212–214 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.12 (s, 1H, NH), 9.99 (s, 1H, NH), 8.77, (br s, 2H, $H_{Pym\text{-}3,5}$) 7.00 (t, J = 4.7 Hz, 1H, $H_{Pym\text{-}4}$), 3.29 (t, J = 4.7 Hz, 3H, CH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.78, 157.88, 115.37, 32.66. Anal. Calcd. for $C_6H_8N_4S$ C, 42.84; H, 4.79; N, 33.31. Found: C, 42.94; H, 4.83; N, 33.15. IR: 3230 (m, br), 3165 (w, br), 3071 (m, br), 1578 (s), 1529 (m), 1426 (m), 1359 (w), 1333 (w), 1213 (m), 1143 (w), 1051 (m), 818 (m), 792 (m), 644 (m).

*N-(2-Thiazolyl)-N′-methylthiourea (**5**).* 2-Aminothiazole (2.50 g, 25.0 mmol) was dissolved in 25 mL pyridine. Methyl isothiocyanate (2.19 g, 30.0 mmol) was added, forming a clear, brown solution. The mixture was stirred overnight under N_2. The brown solution was evaporated, leaving a viscous brown oil which solidified under vacuum. The light brown product was washed with diethyl ether, and was dried in vacuo (3.24 g, 76.9%). m.p.: 164–166 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.00 (br s, 1H, NH), 10.81 (br s, 1H, NH), 7.32 (d, J = 3.5 Hz, 1H, $H_{Thz\text{-}5}$), 6.85 (d, J = 3.5 Hz, 1H, $H_{Thz\text{-}4}$), 3.26 (d, J = 4.7 Hz, 3H, CH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 178.61, 162.11, 137.80, 111.52, 32.27. Anal. Calcd. for $C_5H_7N_3S_2$ C, 34.66; H, 4.07; N, 24.25. Found: C, 34.95; H, 4.11; N, 24.06. IR: 3157 (m, br), 3103 (m), 3061 (m, br), 2968 (m, br), 1594 (s), 1561 (s), 1517 (s), 1459 (m), 1359 (w), 1242 (s), 1163 (m), 1112 (w), 1076 (w), 1053 (m), 691 (m), 607 (w).

*N,N′-Bis(2-pyridyl)thiourea (**6**).* 2-Aminopyridine (4.71 g, 50.0 mmol) was dissolved in 20 mL pyridine. Carbon disulfide (7.71 g, 100 mmol) was added, forming a clear, yellow solution. The mixture was refluxed overnight under N_2. The solution was concentrated and cooled, producing a precipitate. The off-white product was isolated by vacuum filtration, stirred in water overnight to remove residual 2-aminopyridine, and was dried in vacuo (4.02 g, 69.8%). m.p.: 155–158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.4 (v br s, 2H, NH), 8.6 (v br s, 2H, $H_{Py\text{-}3}$), 8.40 (br s, 2H, $H_{Py\text{-}4}$), 7.72 (br s, 2H, $H_{Py\text{-}6}$), 7.07 (br s, 2H, $H_{Py\text{-}5}$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 176.28, 151.52, 146.96 & 145.37 (partially coalesced), 136.79 (coalesced, br), 119.24 & 117.86 (partially coalesced), 115.60 & 111.53 (partially coalesced). Anal. Calcd. for $C_{11}H_{10}N_4S_1$ C, 57.37; H, 4.38; N, 24.33. Found: C, 57.65; H, 4.29; N, 24.50. IR: 3462 (s, br), 3235 (m), 1601 (s), 1561 (s), 1524 (s), 1471 (s), 1421 (s), 1351 (s), 1182 (m), 1146 (m), 771 (m).

*N,N′-Bis(3-pyridyl)thiourea (**7**).* 3-Aminopyridine (4.71 g, 50.0 mmol) was dissolved in 20 mL pyridine. Carbon disulfide (7.71 g, 100 mmol) was added, forming a clear, yellow-brown solution. The mixture was stirred overnight under N_2 leading to formation of a precipitate. The white product was isolated by vacuum filtration, washed with diethyl ether, and was dried in vacuo (4.36 g, 75.7%). m.p.: 169–172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 2H, NH), 8.63 (d, J = 2.7 Hz, 2H, $H_{Py\text{-}2}$), 8.36 (d, J = 3.6 Hz, 2H, $H_{Py\text{-}4}$), 7.95 (d, J = 8.2 Hz, 2H, $H_{Py\text{-}6}$), 7.39 (dd, J = 8.2, 4.7 Hz, 2H, $H_{Py\text{-}5}$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.64, 145.32, 145.27, 135.82, 131.38, 123.07. Anal. Calcd. for $C_{11}H_{10}N_4S_1$ C, 57.37; H, 4.38; N, 24.33. Found: C, 57.61; H, 4.39; N, 24.29. IR: 3208 (w), 3166 (w), 3208 (w), 2978 (s, br), 2936 (m, br), 2787 (w, br), 1599 (m), 1582 (m), 1535 (m), 1473 (w),

1417 (s), 1314 (m), 1276 (s), 1254 (m), 1024 (w), 762 (w), 719 (s), 640 (w).

X-ray Crystallography

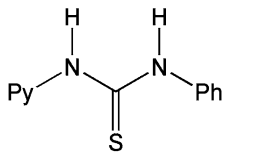
X-ray quality crystals were grown by slow evaporation or diethyl ether layering of acetone solutions. Crystals were mounted on glass fibers. All measurements were made using graphite-monochromated Cu Kα radiation on a Bruker-AXS three-circle diffractometer, equipped with a SMART APEX II CCD detector. Initial space group determination was based on a matrix consisting of 120 frames. The data were reduced using SAINT+ [11], and empirical absorption correction applied using SADABS [12].

Structures were solved using direct methods. Least-squares refinement for all structures was carried out on F^2. The non-hydrogen atoms were refined anisotropically. All hydrogen atoms in each structure were located by standard difference Fourier techniques and were refined with isotropic thermal parameters. Structure solution, refinement and the calculation of derived results were performed using the SHELXTL package of computer programs [13]. Packing diagrams were produced using Mercury [14]. Details of the X-ray experiments and crystal data are summarized in Table 1. Selected bond lengths and bond angles are given in Table 2, a summary of hydrogen-bonds is provided in Table 3, and a summary of interplanar angles is found in Table 4.

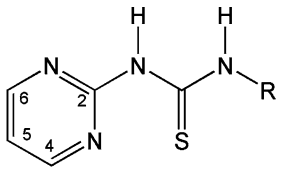
Results and Discussion

Synthesis

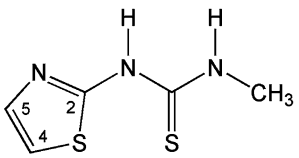
The five heterocyclic-substituted thioureas, **1**–**5** were synthesized through the reactions



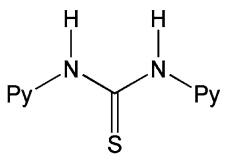
Py = 3-pyridyl, **1**; 4-pyridyl, **2**



R = Ph, **3**; CH_3, **4**



5



Py = 2-pyridyl, **6**; 3-pyridyl, **7**

of phenyl- or methylisothiocyanate with various amino-heterocycles ($ArNH_2$) according to reaction (1) [2, 8, 15–17]. In all cases, good yields were realized. The two homo-substituted thioureas, **6** and **7** were produced by the reaction of aminopyridines with carbon disulfide in pyridine according to reactions (2) and (3) [17, 18]. While 2- and 3-aminopyridine produced compounds **6** and **7**, the attempted reaction with 4-aminopyridine produced a yellow solid that was provisionally identified based upon NMR data as 4-aminopyridinium *N*-(4-pyridyl)dithiocarbamate [16]. Thus, reaction (3) failed to occur presumably due to relatively weak nucleophilicity of 4-aminopyridine.

$$ArNH_2 + RN{=}C{=}S \rightarrow ArNHC(=S)NHR \quad (1)$$

$$PyNH_2 + CS_2 \rightarrow PyNHC(=S)SH \quad (2)$$

$$PyNH_2 + PyNHC(=S)SH \rightarrow (PyNH)_2C{=}S + H_2S \quad (3)$$

N-(3-Pyridyl)-*N*′-phenylthiourea, **1** and *N*-(4-Pyridyl)-*N*′-phenylthiourea, **2**

In contrast to the intramolecular H-bonding behavior uniformly encountered for *ortho*-heterocyclic thioureas, placement of the pyridine nitrogen at the 3- or 4-position produced only intermolecular hydrogen-bonds, resulting in the formation of extended networks. Compound **1** crystallizes in the non-centrosymmetric orthorhombic space group $Pna2_1$ (Flack parameter = 0.022(18)). A molecular diagram is shown in Fig. 1 and a packing diagram emphasizing the 3D H-bonding network is shown in Fig. 2. As is the case with each of the compounds described herein, the molecular structure of **1** is unremarkable. Also, like all but one of the disubstituted thiourea structures reported herein, one thiourea substituent (the phenyl ring) is oriented toward the thiocarbonyl carbon and the other toward the sulfur (EZ conformation). The two ring planes lie at fairly large angles to one another and also to the plane defined by the thiourea core (NC(S)N), see Table 4. The bond lengths and angles within the thiourea core are relatively symmetrical. Two intermolecular H-bonds are seen in **1**: N1–H···N3 (Tu···Py, Tu = thiourea) and N2–H···S1 (Tu···Tu) (see Table 3 for H-bonding distances). The relatively long N···S distances encountered for compounds **1**, **2**, and **5** are facilitated by resonance lengthening of C=S (see Table 2), [10] and are similar to those of previously determined thiourea dimers [3, 5–8]. Helices, consisting of six H-bonded molecules were found to propagate parallel to the *c*-axis forming channels. The phenyl rings lie within

Table 1 Crystal and structure refinement data[a]

	1	2	3	4	5	6	7
CCDC deposit no.	655874	655878	655875	655879	655877	655876	655880
Color and habit	colorless needle	colorless block	colorless block	colorless plate	colorless plate	colorless block	colorless plate
Size, mm	0.41 × 0.04 × 0.04	0.41 × 0.28 × 0.23	0.43 × 0.28 × 0.27	0.21 × 0.20 × 0.05	0.19 × 0.18 × 0.06	0.51 × 0.43 × 0.30	0.25 × 0.08 × 0.02
Formula	$C_{12}H_{11}N_3S$	$C_{12}H_{11}N_3S$	$C_{11}H_{10}N_4S$	$C_6H_8N_4S$	$C_5H_7N_3S_2$	$C_{11}H_{10}N_4S$	$C_{11}H_{10}N_4S$
Formula weight	229.30	229.30	230.29	168.22	173.26	230.29	230.29
Space group	*Pna*2$_1$ (#33)	*P*2$_1$/c (#14)	*P*2$_1$/c (#14)	*P*2$_1$/c (#14)	*C*2/c (#15)	*Fdd*2 (#43)	*P*2$_1$/c (#14)
a (Å)	10.1453(3)	16.9314(3)	5.45900(10)	8.8159(5)	17.9308(3)	15.1859(2)	13.2461(2)
b (Å)	17.6183(5)	10.3554(2)	13.8559(2)	11.2386(5)	7.78260(10)	30.1654(3)	6.26170(10)
c (Å)	6.4787(2)	13.5152(3)	14.3356(3)	7.7156(4)	10.8686(2)	9.44130(10)	12.3503(2)
β (deg)	90	106.5080(10)	94.9800(10)	95.629(2)	105.3740(10)	90	96.0160(10)
Volume (Å^3)	1158.02(6)	2271.96(8)	1080.24(3)	760.76(7)	1462.42(4)	4324.95(8)	1018.73(3)
Z	4	8	4	4	8	16	4
ρ_{calc} (g cm^{-3})	1.315	1.341	1.416	1.469	1.574	1.415	1.501
F_{000}	480	960	480	352	720	1920	480
μ (Cu Kα) (mm^{-1})	2.271	2.315	2.465	3.263	5.970	2.463	2.614
Radiation	CuKα (λ = 1.54178 Å)	CuKα (λ = 1.54178 Å)	CuKα (λ = 1.54178 Å)	CuKα (λ = 1.54178 Å)	CuKα (λ = 1.54178 Å)	CuKα (λ = 1.54178 Å)	CuKα (λ = 1.54178 Å)
Temperature (K)	200	100	100	100	100	100	100
Residuals:[a] R; R_w	0.0276; 0.0544	0.0285; 0.0722	0.0297; 0.0839	0.0255; 0.0731	0.0232; 0.0620	0.0194; 0.0512	0.0266; 0.0714
Goodness of fit	1.081	1.088	1.030	1.046	1.054	1.029	1.022

[a] $R = R_1 = \Sigma||F_o|-|F_c||/(\Sigma|F_o|$ for observed data only. $R_w = wR_2 = \{\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$ for all data

Table 2 Selected bond distances (Å) and angles (°)[a]

	1	2	3	4	5	6	7
C1–S1	1.6990(19)	1.6950(14), 1.6985(14)	1.6813(14)	1.6858(13)	1.6932(15)	1.6736(13)	1.6763(14)
C1–N1	1.332(3)	1.3505(18), 1.3565(17)	1.3807(17)	1.3878(16)	1.375(2)	1.3501(16)	1.3644(18)
C1–N2	1.344(2)	1.3481(18), 1.3375(18)	1.3350(18)	1.3181(17)	1.325(2)	1.3737(16)	1.3654(18)
N1–C2	1.435(2)	1.4144(18), 1.4101(17)	1.3900(18)	1.3842(16)	1.379(2)	1.4010(15)	1.4175(18)
N2–CX	1.424(2)	1.4234(18), 1.4301(18)	1.4264(17)	1.4557(16)	1.452(2)	1.4045(18)	1.4123(18)
N1–C1–N2	118.66(18)	117.30(12), 116.68(12)	116.66(12)	117.40(11)	117.14(13)	114.59(12)	111.55(12)
N1–C1–S1	121.96(15)	123.11(10), 123.60(10)	119.57(10)	118.66(9)	119.00(11)	126.99(10)	124.52(11)
N2–C1–S1	119.36(15)	119.54(10), 119.69(10)	123.76(10)	123.94(9)	123.86(12)	118.42(9)	123.93(11)
C2–N1–C1	122.11(16)	125.48(12), 125.21(12)	129.64(12)	129.54(11)	127.09(13)	131.16(12)	124.41(13)
CX–N2–C1	127.85(19)	129.43(12), 128.30(12)	125.36(12)	124.06(11)	123.57(14)	130.69(11)	123.73(12)

[a] CX = C7 for **1**, **2**, **6**, and **7**; C6 for **3** and **4**; C5 for **5**

Table 3 Hydrogen-bond distances (Å) and Angles (°)

Compound	D–H···A	H···A dist.	D···A dist.	D–H···A angle
1	N2–H2···S1[a]	2.47(2)	3.329(2)	164.7(19)
	N1–H1···N3[b]	2.14(2)	2.936(2)	159(2)
2	N1–H1N···N6[c]	2.109(19)	2.8305(17)	154.1(17)
	N2–H2N···S1[d]	2.527(19)	3.3434(12)	162.0(16)
	N4–H4N···N3	2.059(19)	2.8498(17)	156.6(16)
	N5–H5N···S2[e]	2.449(19)	3.3274(12)	165.2(15)
3	N1–H1···N4[f]	2.265(19)	3.0824(16)	177.8(16)
	N2–H2···N3	1.926(19)	2.6399(16)	140.7(17)
4	N2–H2N···N3	1.966(19)	2.6578(16)	139.3(18)
	N1–H1N···N4[g]	2.302(17)	3.0943(16)	171.1(13)
5	N1–H1N···S1[h]	2.52(2)	3.3184(14)	169.2(18)
	N2–H2N···N3	2.000(19)	2.6911(18)	140.9(17)
6	N2–H2···N3[i]	2.234(19)	3.0779(14)	170.3(16)
	N1–H1···N4	1.87(2)	2.6534(16)	144.7(18)
7	N2–H2N···N4[j]	2.13(2)	2.9526(18)	167.5(17)
	N1–H1N···N3[k]	2.28(2)	3.0728(18)	163.7(16)

Symmetry transformations used to generate equivalent atoms: [a]–*x*, –*y* + 1, *z* + 1/2; [b]*x* + 1/2, –*y* + 1/2, *z*; [c]*x*,*y*–1,*z*; [d]–*x*, –*y* + 1, –*z* + 2; [e]–*x* + 1, –*y* + 2, –*z* + 1; [f]–*x* + 1, –*y* + 2, –*z* + 1; [g]–*x* + 1, –*y*, –*z*; [h]–*x* + 2, *y*, –*z* + 3/2; [i]*x* + 1/4, –*y* + 3/4, *z*–1/4; [j]*x*, –*y* + 3/2, *z*–1/2; [k]*x*, *y* + 1, *z*

Table 4 Interplanar angles (°)

Compound	Ring 1–ring 2[a]	Ring 1–NC(S)N[a]	Ring 2–NC(S)N[a]
1	51.09(6)	86.22(6)	64.62(6)
2	88.58(5), 82.15(5)	46.09(6), 55.62(4)	58.59(4), 48.87(6)
3	68.48(3)	5.91(6)	66.22(3)
4	–	1.94(6)	–
5	–	5.23(7)	–
6	24.16(6)	20.91(5)	8.03(7)
7	72.21(4)	57.73(4)	56.99(4)

[a] Ring 1 is the heterocyclic ring in **1**–**5**. Ring 2 is the phenyl in **1**–**3**

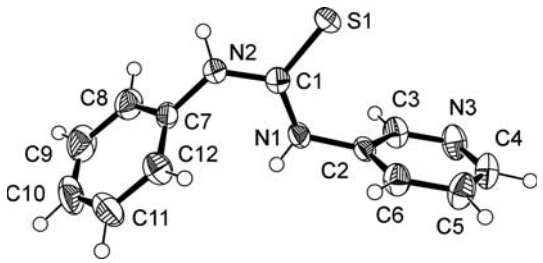
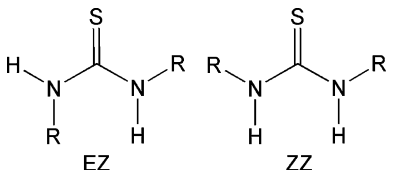


Fig. 1 Molecular structure of **1**. Thermal ellipsoids shown at 50%

these channels. The helices are tiled together with pairs of molecules producing junctions between them. Curiously, the oxygen analog of **1**, *N*-(3-pyridyl)-*N*′-phenylurea reveals a ZZ conformation in the crystal structure and shows no H-bonding [19].



Compound **2** crystallizes in the monoclinic space group $P2_1/c$. A molecular diagram is shown in Fig. 3 and a packing diagram with H-bonding emphasized is shown in Fig. 4. Two independent molecules are present in structure. In similar fashion to **1**, compound **2** forms a symmetrical thiourea core with an EZ conformation (pyridyl is oriented toward sulfur in this case) and shows large interplanar angles between the various combinations of the rings and the thiourea core (Table 4). Pairs of intermolecular H-bonds are formed, one pair for each independent molecule: N1–H···N6, N4–H···N3 (Tu···Py) and N2–H···S1, N5–H···S2 (Tu···Tu). All H-bonds are roughly coplanar, producing a flat 2D sheet structure. The sheets are

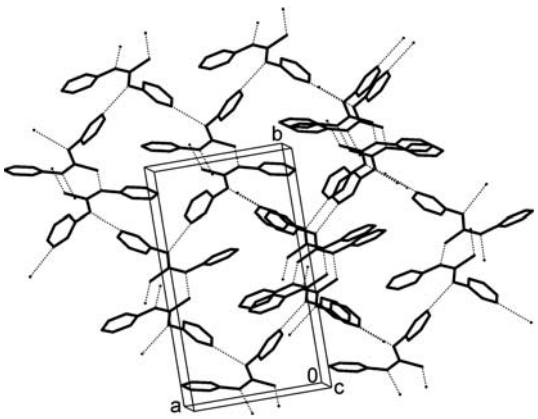


Fig. 2 Hydrogen bonding network and packing diagram for **1**. Hydrogen atoms omitted for clarity

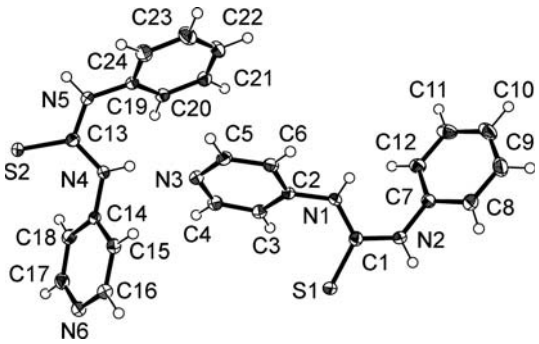


Fig. 3 Molecular structure of **2**. Thermal ellipsoids shown at 50%

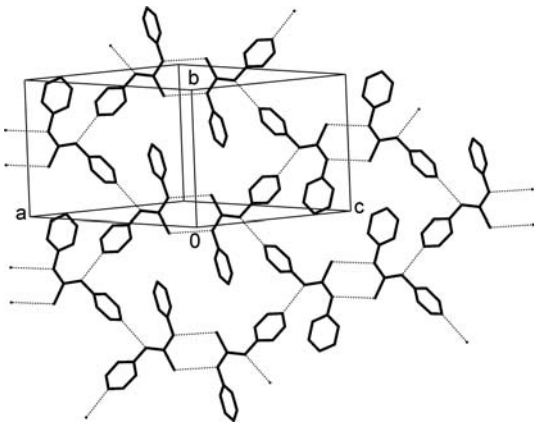


Fig. 4 Hydrogen bonding network and packing diagram for **2**. Hydrogen atoms omitted for clarity

composed of tiled hexagonal rings constructed from six **2** molecules. The sheets run parallel to the crystallographic *b*-axis and the *a*,*c*-diagonal. The analogous urea, *N*-(4-pyridyl)-*N*′-phenylurea, exhibits a Z, Z conformation and shows only a single N–H···N (urea···Py) H-bond, resulting in a chain structure [19].

N-(2-Pyrimidyl)-*N*′-Phenylthiourea, **3**, *N*-(2-Pyrimidyl)-*N*′-Methylthiourea, **4**, and *N*-(2-Thiazolyl)-*N*′-Methylthiourea, **5**

Each of these heterocyclic thioureas features an *ortho*-nitrogen. As a result each compound displays an internal H-bond, such as has been seen for related species (see above). Since intramolecular H-bonding requires an E conformation, all three molecules crystallize as EZ conformers. In contrast to most of the known *ortho*-heterocyclic thioureas, **3**–**5** all form H-bonded dimers. Compound **3** crystallizes in $P2_1/c$. A molecular diagram of the H-bonded dimer, shown in Fig. 5, reveals both an internal H-bond, N2–H···N3 (Tu···Pym) and an intermolecular H-bond, N1–H···N4 (Tu···Pym). An analogous dimeric structure is exhibited by **4**, which crystallizes in $P2_1/c$, see Fig. 6. Dimers are also formed by **5**, which crystallizes in the monoclinic space group *C*2/c. However, in contrast to compounds **3** and **4** which form dimers through N–H···N interactions, compound **5** forms dimers through N2–H···S2 (Tu···Tu), see Fig. 7. The expected internal N1–H···N3 (Tu···Thz) H-bond is also present. In addition, there is a close interaction between S1 and S2 of 3.6279(5) Å. Compound **5** fails to form H-bonds to either of the thiazole ring heteroatoms. Its dimeric structure is very closely related to that of the known thiazole- and benzothiazole-substituted thioureas, **III** [3, 7].

Compounds **3**–**5** stand apart from the other thioureas reported herein with respect to their core bond lengths. As is revealed by the data in Table 2, pairs of thiourea C1–N1 and C1–N2 bonds are of very different lengths in compounds **3**–**5** (1.375–1.388 vs. 1.318–1.335 Å). In addition, the N1–C2 and N2–CX (CX = C6 for **3** and **4**, CX = C5 for **5**) bonds are inequivalent (1.379–1.390 vs. 1.426–1.456 Å). Finally, it will be noted from the data in Table 4 that

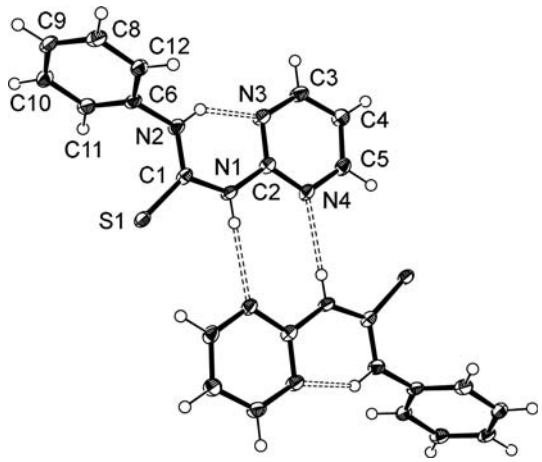


Fig. 5 Molecular structure and hydrogen bonding dimer for **3**. Thermal ellipsoids shown at 50%

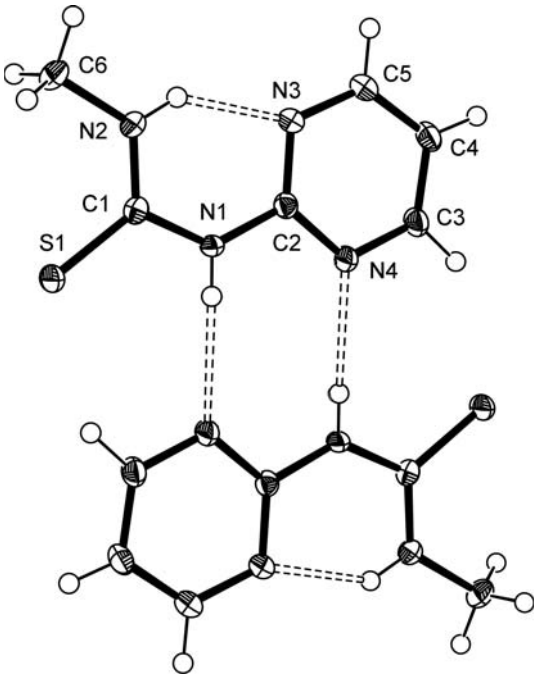


Fig. 6 Molecular structure and hydrogen bonding dimer for **4**. Thermal ellipsoids shown at 50%

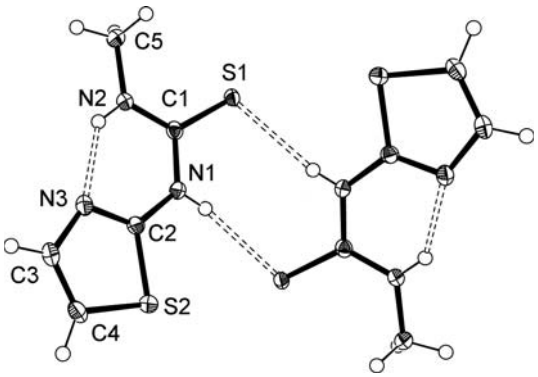
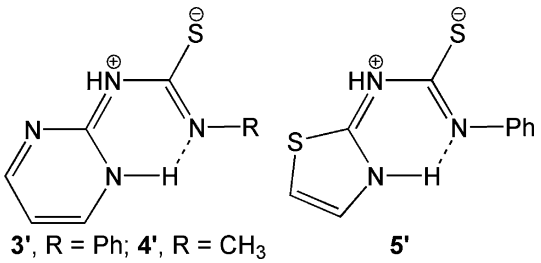


Fig. 7 Molecular structure and hydrogen bonding dimer for **5**. Thermal ellipsoids shown at 50%

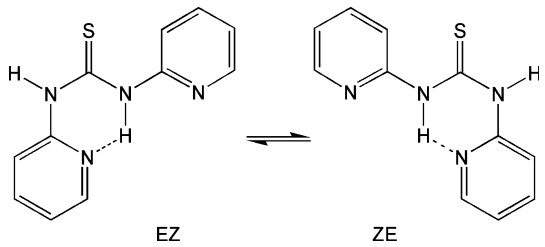
the heterocyclic rings in **3**–**5** are nearly coplanar with the thiourea core. These observations, taken together, are almost certainly the result of contributions from resonance forms **3′**–**5′**. Such resonance contributions are facilitated by the presence of an intramolecular H-bond in each compound.



3', R = Ph; **4'**, R = CH_3 **5'**

N,*N*′-Bis(2-Pyridyl)thiourea, **6**, and *N*,*N*′-Bis(3-Pyridyl) thiourea, **7**

These symmetrical dipyridylthioureas both form extended network structures via H-bonding interactions. Compound **6** crystallized in the non-centrosymmetric orthorhombic space group *F*dd2 (Flack parameter = 0.033(10)). A molecular diagram is shown in Fig. 8 and a packing diagram emphasizing the 2D H-bonding network is shown in Fig. 9. A fairly symmetrical thiourea core is connected to the pyridyl substituents in EZ conformation. Compound **6** shows the expected intramolecular H-bond: N1–H···N4 (Tu···Py). A second, intermolecular, H-bond, N2–H···N3 (Tu···Py) produces a zigzag chain which propagates parallel to the *a*,*c* diagonal. Compound **6** is the only species studied herein that has an *ortho*-substituent on each ring and therefore can form an intramolecular H-bond with either ring. This situation should produce equilibrium between EZ and ZE conformers. Indeed, the ^{1}H and ^{13}C NMR signals (except for those of the thiocarbonyl and *ipso* ring carbons) are greatly broadened at room temperature, indicating that interchange between the conformers is occurring at an intermediate rate in solution at room temperature.



Compound **7** crystallized in $P2_1/c$, forming a H-bonded sheet which propagates parallel to the *b*,*c*-plane. The molecular diagram for **7**, shown in Fig. 10, reveals the only ZZ molecular conformation reported herein. The packing diagram, highlighting H-bonding networking, is shown in Fig. 11. The 2D network structure of **7** results from two sets of Tu···Py interactions analogous to those that produce a 1D chain in **6**: N1–H···N3 and N2–H···N4. However, in the case of **7** both H-bonding interactions are geometrically forced to form intermolecularly and propagate in mutually perpendicular directions: parallel to the *b*- and *c*-axes. The sheets in **7** are not flat since the individual molecules are oriented at an angle of about 70° to the sheet plane. The sheets are comprised of bowl-shaped four-molecule H-bonded units which are tiled together.

A monohydrate of **6** (**6**•H_2O) has previously been reported [9]. It shows an EZ conformation. Interestingly, and in contrast to all of the diarylthioureas reported herein

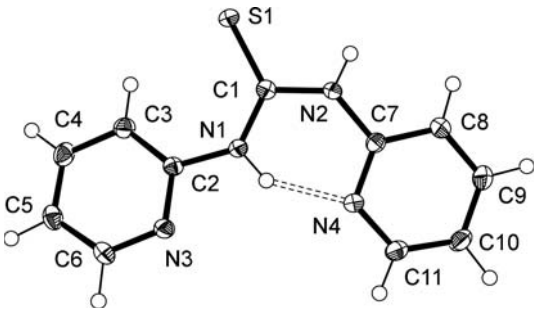


Fig. 8 Molecular structure of **6**. Thermal ellipsoids shown at 50%

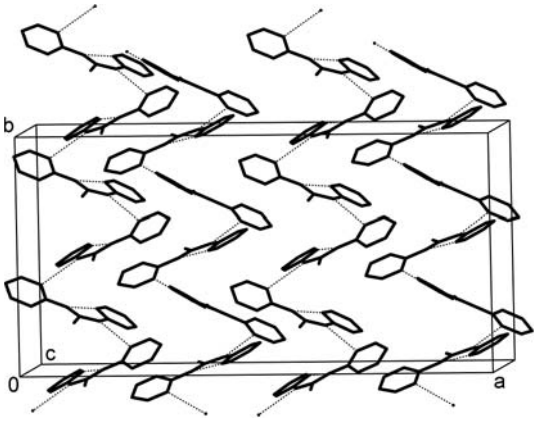


Fig. 9 Hydrogen bonding network and packing diagram for **6**. Hydrogen atoms omitted for clarity

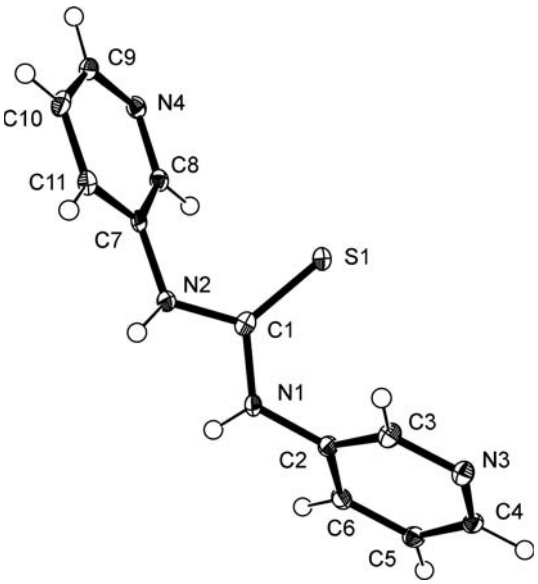


Fig. 10 Molecular structure of **7**. Thermal ellipsoids shown at 50%

(see Table 4), both rings and the thiourea core in **6**•H_2O are virtually coplanar (<5° interplanar angles). The H-bonded structure of **6**•H_2O is analogous to that of **6**,

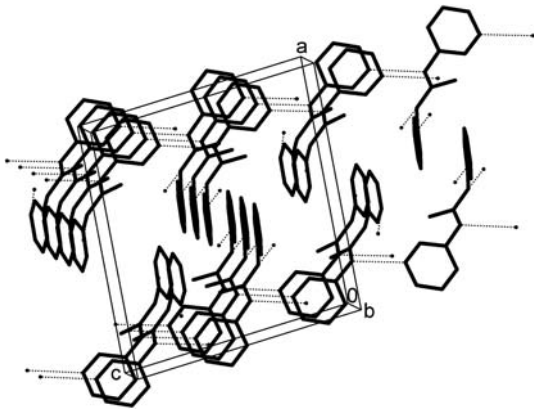


Fig. 11 Hydrogen bonding network and packing diagram for **7**. Hydrogen atoms omitted for clarity

consisting of both intra- and intermolecular H-bonding. However, the latter connects the thiourea nitrogen to the water of hydration, and a second intermolecular H-bond connects the water to a pyridyl ring. Thus, a zigzag chain results, in somewhat analogous fashion to **6**. Like structures **6** and **6**•H_2O, *N*,*N*′-bis(2-pyridyl)urea exists in the EZ conformation and has an internal H-bond [20]. However, in contrast to **6** and **6**•H_2O, it forms dimers via intermolecular N–H···O (urea···urea), instead of producing a chain. Like the thiourea **7**, *N*,*N*′-bis(3-pyridyl)urea adopts a ZZ conformation [21]. Although the interplanar angle between the two rings in the urea is only about 12.2° (versus 72.21(4)° for **7**), nevertheless, like the **7** molecules, the ureas form two sets of urea···Py H-bonds running in roughly perpendicular directions. These interactions result in formation of a sheet structure closely related to that of **7**. The urea molecules lie at an angle of about 45° to the overall H-bonded sheet.

Conclusions

The use of 3- or 4-pyridyl groups in thioureas serves to produce 1D, 2D or 3D networked products through intermolecular hydrogen-bonding. 2-Pyridyl, 2-pyrimidyl, and 2-thiazolyl groups lead to the formation of dimers containing both intra- and intermolecular hydrogen bonds.

Supplementary Material

Tables of atomic coordinates for each structure are available as supplementary material. CCDC 655874–655880 contain the crystallographic data for this paper. These data can be obtained free of charge by e-mailing

data_request@ccdc.cam.ac.uk or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ UK; Fax +44(0)1223-336033; www.ccdc.cam.ac.uk/data_request/cif.

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