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# Hydrogen bonding interactions with the thiocarbonyl $\pi$ -system<sup>†</sup>

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Hydrogen bonding interactions with the  $\pi$ -system of thiocarbonyls are evident in the X-ray crystal structures of a range of thiourea derivatives and from an analysis of the CSD.

# Introduction

Supramolecular interactions involving  $\pi$ -electron density are a fundamental class of supramolecular synthon<sup>1</sup> with  $\pi$ - $\pi$ stacking and  $CH \cdots \pi$  interactions being perhaps the most well known examples.<sup>2-6</sup> The OH… $\pi$  and NH… $\pi$  interactions are also now well recognised in aromatic systems.7-10 Supramolecular interactions involving carbonyl and thiocarbonyl X=C (X=O, S) bonding  $\pi$ -electron density are less well understood and generally not used as reliable synthons. Despite this comparative scarcity one of the earliest examples of the interaction between hydrogen bonds and the  $\pi$ -electrons of carbonyls occurs in the well-known crystal structure of  $\beta$ -urea.<sup>11–14</sup> The urea oxygen atom is involved in four hydrogen bonds: two through the nonbonding lone pairs on the oxygen atom and two through the  $\pi$ -electrons of the carbonyl double bond. The  $\pi$ -bonded hydrogen bond donors are situated out of the O=C-N plane and the angle to the carbonyl C=O bond of 106° is more acute than conventional hydrogen bonding to the oxygen lone pairs. The presence of four hydrogen bond acidic NH protons and only one carbonyl acceptor in urea means that every possible potential hydrogen bond acceptor is involved in the structure. The situation is the same in the analogous thiourea which displays several polymorphs,<sup>15,16</sup> however four hydrogen bonds are consistently observed in each structure: two bonded to the lone pairs and two others situated out of the S=C-N plane. The angle between the thiocarbonyl bond and the two out of plane hydrogen atoms is close to  $90^{\circ}$  in all forms.

Urea derivatives display different hydrogen bonding patterns to thiourea derivatives due to differing conformational preferences arising from the differing availability of the sulfur and oxygen atoms as hydrogen bond acceptors, and the different X=C bond lengths. The *syn*- and *anti*-conformations of disubstituted ureas are shown in Fig. 1.<sup>17</sup> While the *syn*-conformation is most common in urea derivatives, the *anti*-conformation is

most common in thiourea derivatives. The hydrogen bonding motifs that arise from these preferences are chains formed by the tape motif of the *syn*-conformation, and centrosymmetric dimers formed the *anti*-conformation.

The difference between hydrogen bonding to carbonyl and thiocarbonyl bonds has been only sparsely discussed. One important study into the differences of hydrogen bonding to carbonyl and thiocarbonyl fragments utilized the Cambridge Structural Database (CSD) to compare the metrics of crystal structures from the literature.<sup>18</sup> It was shown that hydrogen bonds to C=S bonds are weaker than to C=O bonds, and that C=S fragments are more likely to accept more than one hydrogen bond donor. Interestingly, in the orientation distribution of H-bond donors it is observed that the distribution out of the plane of the lone pairs is more diffuse for thiocarbonyls, extending from the ideal  $0^{\circ}$  to a plane...H angle of  $70^{\circ}$ , whereas interactions with the carbonyl bond tend to occur within the range of 0 to 20°. Within the lone pair plane, the hydrogen bonding is more directional than in thiocarbonyl bonds. Crucially thiocarbonyl groups only act as effective hydrogen bond acceptors if they are attached to groups they delocalise the double bond electron density, as is the case in thioureas.



**Fig. 1** *syn* and *anti* conformations adopted by disubstituted urea and thiourea derivatives in the solid-state. The *syn*-tape hydrogen bonding motif is common for urea derivatives, whereas the *anti*-centrosymmetric dimer formation is common for thiourea derivatives.<sup>17</sup>

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Some work has been carried out on the electron density of the lone pairs on the sulfur atom in a thioureido group.<sup>19</sup> Bogdanović and co-workers identified that the sulfur atom in the crystal structure of salicylaldehyde thiosemicarbazone has three different hydrogen bonds to it, Fig. 2. One hydrogen bond is from an NH of a thioureido group of another molecule of salicylaldehyde thiosemicarbazone in a centrosymmetric dimer fashion based on  $H(2N)\cdots S(1)$ , while there is hydrogen bonding from an NH from another molecule,  $H(3A)\cdots S(1)$ . Both of these interactions are in the thioureido plane. There is also a weak C–H donation from a third molecule, which is out of the lone pair plane. This latter interaction is a relatively long hydrogen bond with  $H(7)\cdots S(1)$  distance of 3.008(8) Å and a  $C(7)-H(7)\cdots S(1)$  angle of 124.64(7)°. The final NH group, H(3B), hydrogen bonds to O(1).

A survey of the CSD found that 495 out of a total of 835 N– H hydrogen bond interactions to the thioureido group in its crystal structures exist as part of centrosymmetric dimers. These dimers were compared to 3630 more general hydrogen bonding interactions to thioureido functional groups, D–H···S=C (D = C, O, N). For the dimers, the average C=S···H bond angle is in the region of 110 to 115°, whereas a wider distribution is observed for the non-dimer interactions, with an average in the region of 80–100°. A lack of directionality in C=S···H bonding is attributed to the torus of the lone pair electrons around the sulfur atom being equally polarisable in or out of the plane.<sup>19</sup>

In the present paper we present the structures of six new thiourea derivatives bearing multiple NH hydrogen bond donor groups. Steric hindrance of the thiourea groups in these types of system is a significant factor in the availability of the hydrogen bond donor and acceptor groups.<sup>20</sup> We correlate this structural data with data obtained from the CSD to show that the thiocarbonyl group in thiourea derivatives acts as an effective hydrogen bond acceptor *via* the  $\pi$ -electron density. The incidence and metrics of the thiocarbonyl– $\pi$  hydrogen bond interaction are presented.



Fig. 2 X-Ray crystal structure of salicylaldehyde thiosemicarbazone displaying hydrogen bonding.<sup>19</sup>

# **Results and discussion**

#### Crystal structures

Compounds 2-6 are all readily prepared from reaction of a diamine with an isothiocyanate in solution. Compounds 3-6 have been reported previously within the context of a study on anion complexation by their ruthenium(II) derivatives.<sup>21</sup> 1-(2-Amino-phenylene)-3-methyl-thiourea (1) and 1-(2-aminophenylene)-3-tert-butyl-thiourea (2) were synthesised as part of this work (see Experimental section). We also attempted the preparation of all six compounds mechanochemically<sup>22,23</sup> by grinding either the neat solid or liquid starting materials in the appropriate stoichiometric ratio in a Retsch MM200 ball mill. Mechanochemistry has proved effective previously in amineisocvanate reactions.<sup>24</sup> In the case of compounds 2 and 6 the starting materials failed to react. Compounds 3 and 5 were successfully prepared mechanochemically. Mechanochemistry also proved to be the only effective way to isolate compound 1. The slower kinetics of the mechanochemical reaction proved effective at producing the monosubstituted product. In the case of the isopropyl analogue a mixture of the monosubstituted product and disubstituted 5 was produced, however this converted to 5 upon recrystallisation.

The X-ray crystal structures of **1–6** were determined in order to examine the distribution of hydrogen bonding involving the thiourea groups. The X-ray crystal structures of **1** and **2**, which, like thiourea itself, are rich in hydrogen bond donor NH groups, are shown in Fig. 3.



For both compounds the molecular bond lengths and angles are within expected ranges. Centrosymmetric dimer formation through hydrogen bonded thiourea groups is common for thioureas<sup>15,17</sup> and is observed in **2** for S(1) and H(2A), Fig. 3b. The short H···S contact of 2.53 Å, the obtuse C=S···H angle of 107.3°, as well as the low torsional angle between N(2)– C=S(1)···H(2A) of 11.1° with the thiocarbonyl bond are typical of conventional hydrogen bonding with the nonbonding sulfur



Fig. 3 (a) X-Ray crystal structure of 1 showing the two independent molecules based on S(1) and S(2). The two conventional hydrogen bonding interactions to S(2) are shown. The third interaction is orthogonal. The molecule based on S(1) exhibits a conventional hydrogen bond and an N–H $\cdots\pi$  interaction. (b) X-Ray crystal structure of 2 showing one centrosymmetric dimer pair, while a second molecule hydrogen bonds through N–H into the  $\pi$ -electron density of the thiocarbonyl bond. (c) Hirshfield surface<sup>25,26</sup> derived from the X-ray structure of 2 showing the three hydrogen bonding interactions to the C=S bond as the three red regions.

lone pair. However, in the structure of **2** one of the hydrogen atoms on the primary amine, H(1B), is directed towards the thiocarbonyl bond. In contrast to conventional hydrogen bonds, an acute angle of the hydrogen atom donor with the thiocarbonyl bond of 83.6° is observed. This brings the hydrogen close to the centre of the double bond (the distance to the double bond centroid is 2.83, compared to an H…S distance of 2.80 Å). Furthermore, the torsional angle between the hydrogen, the thiocarbonyl bond and the adjacent nitrogen atom (N-C=S… H) is 100.1°; well out of the conventional lone pair hydrogen bonding plane (which has an ideal value of 0°). The interaction is longer than the conventional hydrogen bond involving S(1) and H(2A), with an H(1B)…S(1) distance of 2.79(2) Å.

These parameters give a strong indication of interaction between the hydrogen and the  $\pi$ -electron density of the double bond, and thus evidence that  $\pi$ -electrons of thiocarbonyl bonds act as hydrogen-bond acceptors, Fig. 4. The presence of three strong hydrogen bonding interactions involving the thiourea group is confirmed by Hirshfield surface analysis<sup>25,26</sup> (Fig. 3c) which shows the principal interactions in red. The two hydrogen bonds that form the hydrogen bonded dimer are evident as the two largest red regions of the surface, while the NH $\cdots\pi$  interaction is also clearly evident. Interestingly, there appears to be no interaction with other molecules from the remaining two hydrogen bond donor NH groups. The hydrogen atom from the other thioureido NH group, N(3), appears to be sterically hindered by the tertiary butyl group and aryl ring within the same molecule, although there may be a weak N–H··· $\pi$  aromatic interaction. The other free NH hydrogen atom is also turned towards the aryl ring of another molecule, presumably from the interaction of the other hydrogen on the amine with the thiourea sulfur atom. Therefore the lack of hydrogen bonding in these two NH groups is most likely attributable to the surrounding steric bulk and dominance of the other hydrogen-bonding interactions. Similarly the remaining thiourea lone pair is also sterically hindered by the tert-butyl group.

The structure of 1 is more complicated than that of 2 and exhibits two crystallographically independent molecules (Z' = 2, ref. 27). The molecule based on S(2) exhibits two conventional hydrogen bonds to the thiocarbonyl group with interactions from thioamide and amine type NH donors approximately along the lone pair directions, although one of these interactions is





H?

H?

Lone pairs in N-C-X plane [overhead view]

 $\pi$ -electrons orthogonal to N-C-X plane [side view]



relatively long. In addition a third interaction is of the NH… $\pi$ type involving amine N(4)–H(4) and is positioned orthogonally to the plane of the conventional hydrogen bonds. The N(4)…S(2) distance of 3.453(2) Å is considerably shorter than the conventional N(1)…S(2) distance, 3.6739(17) Å. The molecule based on S(1) accepts hydrogen bonds from thiourea NH proton H(6) to a lone pair, but from H(3A) *via* the thiocarbonyl  $\pi$ -electron density. A more conventional approach to the remaining lone pair is apparently sterically hindered by the aromatic ring, Fig. 3a. The structure of **1** also exhibits an unusual  $R_2^2(9)$ hydrogen bonded ring involving the thiourea acceptor on one molecule and the primary amine on the another. A final unusual feature is one of the primary amine NH groups not engaged in any significant hydrogen bonding interaction.

The structure of 1-methyl-3-[2-(3-methyl-thioureido)-ethyl]thiourea (3) was also determined by X-ray crystallography, and it forms hydrogen bonds with very similar interactions to 2, Fig. 5.

A centrosymmetric dimer is present, as well as an interaction with the  $\pi$ -electrons of the thiocarbonyl bond. Again, the two different types of interaction display markedly different metrics, in particular the C=S···H angle is 109.0° for the centrosymmetric dimer pattern, whereas a C=S···H angle of 85.7° is found for the hydrogen-bond donor that is out of the thioureido plane, Tables 1 and 2.

The crystal structures of **4–6** similarly show a range of interesting hydrogen bonding interactions including short contacts to the C=S  $\pi$ -electron density in some, but not in all cases. The crystal structure of 1-methyl-3-[2-(3-methyl-thioureido)-phenyl]thiourea (**4**) exhibits one thiourea group arranged in the *anti* conformation, consistent with centrosymmetric dimer formation, while the other is arranged in the *syn* conformation. However, in contrast to the structures of **2** and **3**, compound **4** does not exhibit the centrosymmetric dimerisation typical of



**Fig. 5** X-Ray crystal structure of **3** showing similar H-bond interactions to those found in compound **2**. The compound has crystallographic twofold symmetry.

	Hydrogen atom					
	H(3A)–S(1) 2.62 84.5 104.4 3.3685(18) 81.1 96.4	H(6)–S(1) 2.81 117.9 22.8 3.4788(17) 108.3 26.3	H(2)–S(2) 2.57 112.4 22.1 3.3040(17) 117.4 13.5	H(4A)–S(2) 2.55 77.9 97.9 3.453(2) 76.4 98.3	H(1B)–S(2) 2.90 115.5 171.9 3.6739(17) 119.5 173.7	
		Hydr	rogen atom			
$\begin{array}{l} 2\\ S\cdots H/\mathring{A}\\ C=S\cdots H/^{\circ}\\ N-C=S\cdots H/^{\circ}\\ S\cdots N/\mathring{A}\\ C=S\cdots N/^{\circ}\\ N-C=S\cdots N/^{\circ} \end{array}$	H(1N)-S(1) 2.53 107.3 11.2 3.3551(11) 111.5 173.7			H(3N)–S1 2.79(2) 83.6 100.1 3.6130(15) 88.4 95.8		
		H	ydrogen atom			
$\begin{array}{c} 3\\ S\cdots H/\mathring{A}\\ C=S\cdots H/^{\circ}\\ N-C=S\cdots H/^{\circ}\\ S\cdots N/\mathring{A}\\ C=S\cdots N/^{\circ}\\ N-C=S\cdots N/^{\circ} \end{array}$	H(1)-S1 2.49 109.0 11.2 3.353(3) 112.6 10.1				H(2)–S1 2.73 85.7 74.3 3.547(3) 87.1 68.4	

Table 1 H-Bond metrics for the structures of 1, 2, and 3

thioureas. Each molecule, in fact, forms hydrogen bond dimers of various types with three other molecules, Fig. 6.

The structure of 1-isopropyl-3-[2-(3-isopropyl-thioureido)phenyl]-thiourea (5) does exhibit the centrosymmetric dimer synthon,  $H(2N)\cdots S(1)$ , Fig. 7. The hydrogen atom of the *anti* thiourea group that is not involved in dimer formation, H(1N), exhibits an intramolecular hydrogen-bond to the sulfur atom of the thiourea group in the *syn* conformation, S(2). The hydrogen atoms of this *syn* thiourea group bond to a sulfur atom of an adjacent molecule, and while one, H(4N), is reasonably in the plane of the thiourea group with a torsional angle of  $24^\circ$ , the other, H(3N), is more out of the plane with a torsional angle of 55°, Table 1. There is a significant difference in the C=S···H angle observed for these two hydrogen bonds as well: the C=S···H (3N) angle is 120°, whereas for the H atom that is out of the plane the C=S···H(4N) angle is 88°.

The crystal structure of 1-methyl-3-[6-(3-methyl-thioureido)pyridin-2-yl]-thiourea (6) is shown in Fig. 8. Each thiourea group forms centrosymmetric dimer involving H(2) and H(4), while the remaining NH hydrogen atoms, H(1) and H(5), form intramolecular hydrogen bonds with the pyridyl nitrogen atom, N(3). As each arm forms a centrosymmetric dimer with another

 Table 2
 Hydrogen bonding metrics for 4 and 5

	Hydrogen atom			
	H(3N)–S1	H(4N)-S1	H(2N)-S2	H(1N)-S2
	2.841(17)	2.477(19)	2.551(18)	2.620(19)
	125.4	117.0	113.0	124.0
	36.1	15.1	60.3	91.6
	3.5205(11)	3.2848(11)	3.3232(11)	3.3250(11)
	133.1	122.1	107.3	131.4
	149.3	16.1	62.0	95.8
	Hydrogen atom			
5	H(3N)–S1	H(4N)-S1	H(1N)-S2	H(2N)–S1
$S \cdots H/Å$	2.52	2.81	2.38	2.63
$C = S \cdots H/°$	88.3	119.8	81.1	105.8
$N - C = S \cdots H/°$	57.0	23.7	54.9	29.8
$S \cdots N/Å$	3.2840(17)	3.4948(18)	3.1082(15)	3.3949(16)
$C = S \cdots N/°$	95.2	123.9	74.2	111.0
$N - C = S \cdots N/°$	116.7	144.8	47.1	23.0



Fig. 6 X-Ray crystal structure of 4 showing hydrogen bonded dimer formation in three different ways (a–c), and (d) the eight hydrogen bonding interactions to a single molecule of 4 (red) from the three hydrogen bond dimers (green, blue and orange).

molecule, which in turn is forming a further dimer with the other thiourea group, one-dimensional chains are formed. The presence of the additional pyridyl group in this compounds means that there is no dearth of strong hydrogen bond acceptors, however steric interactions between H(1) and H(5) cause the urea groups to lie out of the plane of the pyridyl rings resulting in inter-chain hydrogen bonds in which both sulfur atoms act as bifurcated acceptors. While these additional interactions are not to the S=C  $\pi$  electron density, they are out of the environment around the sulfur acceptors.

# CSD comparison of carbonyl and thiocarbonyl H-bond interactions

To further investigate hydrogen bonding interactions with the S=C  $\pi$ -electron density, a search of the CSD was undertaken to explore hydrogen atoms bonded to good hydrogen bond donors Q (Q = N, O) that were bonded to hydrogen atoms within the sum of the van der Waals radii of the acceptor of both thiocarbonyl and carbonyl moieties (Fig. 9). A comparative study was undertaken to investigate the torsional angle from the hydrogen through the C=X bond (X = O, S) and to an adjacent atom. It is expected that interactions with the carbonyl or thiocarbonyl lone pair will be in the plane of S-C-N fragment since the S and O atoms are sp<sup>2</sup> hybridised. Therefore deviation away from a torsional angle of zero degrees will reduce the lone pair character of an interaction whilst increasing interaction with the orthogonal  $\pi$ -electrons of the thiocarbonyl double bond.

For the case of NM–C=S···H–Q (NM = any non-metal), 1623 hits were generated in the CSD constituting 3146 fragments, while for NM–C=O···H–Q, a very large number of hits (38 179) were generated. A scatter plot of the torsional angle distribution displays typical behaviour for bonding to lone pairs with interactions clustering around 0 and  $180^{\circ}$ .

However, a plot of the ratio of distances from the hydrogen to carbon and sulfur atoms,  $H \cdots C/H \cdots S$ , Fig. 10 (orange line denotes moving average), in thiocarbonyls shows that as the torsional angle increases from zero, this ratio decreases in magnitude. In other words, the hydrogen atom moves towards the centre of the C=S bond as it moves out of the lone pair plane. This behaviour is not observed in the C=O case, where a constant average ratio is maintained throughout the torsional range, Fig. 10.

Further evidence is given by the distribution of the hydrogen atoms about the thiocarbonyl bond. A distribution plot of hydrogen bond donors about the X=C-N fragment (for X=S, O) for all entries in the CSD with Q-H…X=C-N contacts was generated using ISOSTAR.<sup>28</sup> It is clear that the hydrogen bond donation to the lone pairs is the dominant form of hydrogen bonding to both of these fragments. However, if the search is limited to a torsional angle range of 60 to 120° for the H…X=C-N,



**Fig.** 7 X-Ray crystal structure of **5** showing hydrogen bonding interactions.

a large difference in the distribution of hydrogen bond donors around the central X=C-N fragment is observed. Contour plots of these distributions are shown in Fig. 11. For the carbonyl case, the distribution is centered at an angle of 135° to the carbonyl bond and with an elongated 'tail' down to 180° to the bond. The distance from the oxygen atom to the area most densely populated by donor atoms is the region of 3.0 Å. In contrast, the thiocarbonyl distribution is more spherical and centered at 95° to the thiocarbonyl bond, with an S–Q distance in the region of 4.0 Å. The distances and angles from the maximum density of the donor atoms to the double



Fig. 9 Schematic showing the  $H \cdots C$  and  $H \cdots X$  bond distances. The ratio  $H \cdots C/H \cdots X$  indicates the relative position of the hydrogen atom to the C=X bond, so that a decrease in the ratio is indicative of the hydrogen atom moving closer to the carbon atom.

bond were also found. For the carbonyl case, the maximum donor atom (Q) density was found at a distance of 2.9 Å from the oxygen atom and at an angle of 135° to the carbonyl bond. The maximum density of the donor atom Q was found to be somewhat further from the acceptor S atom of the thiocarbonyl than in the carbonyl case at a distance of 3.8 Å, but at an angle of 89° to the thiocarbonyl bond.

As can be observed from the contour plots, there is a striking difference in the distribution of H-bond donors to the two bonds within this torsional angle range. The examples reported in the present work (1, 2 and 3) lie close to the carbon atom in the most populated (blue) region with a C=S…N angles of  $81.1^{\circ}$ ,  $88.4^{\circ}$  and  $87.1^{\circ}$  and S…N distances of 3.3685(18), 3.6130(15) and 3.547(3) Å, for 1, 2 and 3, respectively. They also possess a very similar angle to the thiocarbonyl bond as the maximum donor density, with a slightly shorter S…N distance.

The metrics for the general carbonyl and thiocarbonyl cases are summarized in Table 3. It can be seen that the H-bond distance to carbonyls is generally stronger than to the thiocarbonyl bonds with X····H distances of 1.90 and 2.63 Å, respectively. While for carbonyls the bonding to hydrogen atoms is relatively weakened in the cases where the torsional angle is between 60 and 120° from the general case (1.90 to 2.06 Å), a slightly stronger interaction is observed for examples at torsional angles between 60 and 120° (2.63 to 2.59 Å). It is also possible to see that for both carbonyl and thiocarbonyl general



Fig. 8 X-Ray crystal structure of 6 showing hydrogen bonding interactions. Hydrogen bond distances: N(1)…N(3) 2.702(4), N(5)…N(3) 2.715(4), N(5)…S(2)' 3.367(3), N(1)…S(1)'' 3.380(3), N(4)…S(2)' 3.434(3), and N(2)…S(1)'' 3.417(3) Å.



**Fig. 10** Graphs of torsional angle *vs.* ratio of H···C and H···X distance in hydrogen bonding to C=X (X = O, S). While for the carbonyl bond (X=O) there is no variation in this ratio over the torsional angle range, there is a significant reduction in H–C/H–S for the thiocarbonyl range around 90 and  $-90^{\circ}$ .

cases the C=X···H bond angle is similar at 117° and 115° for the carbonyl and thiocarbonyl bonds respectively. However, at high torsional angles, the angle between the H atom and the carbonyl bond increases to 134°, whereas the thiocarbonyl decreases to 107°. Due to the positioning of the H-bond density donor over the sulfur atom, at C=S···H angles in the region of 90°, it is likely that the  $\pi$ -electrons of the thiocarbonyl bond are more

involved in this type of hydrogen bonding than is suggested by Bogdanović and coworkers.<sup>19</sup>

Limiting the search to hydrogen contacts with a C=X···H angle of less than  $90^{\circ}$  for all torsional angles gives another interesting result. For carbonyls the predominant contact is at low (around 0 or  $180^{\circ}$ ) torsional angle, indicative of lone pair bonding. It should be noted that a small proportion of the



Fig. 11 Contour plots created from entries in the CSD for the density of H-bond donors within the torsional angle range of  $60-120^{\circ}$  from the acceptor fragment: (a) NM–C=O carbonyl bond and (b) NM–C=S thiocarbonyl bond.

**Table 3** Hydrogen bond metrics for the general carbonyl (NM–C=O) and thiocarbonyl cases (NM–C=S) from entries in the CSD. Average bond distances and angles are given for each using the full data range (Full) and limiting data to those at a torsional range of 60–120° to the NM–C=X fragment (Tor 60–120°)

NM-C=O			NM-C=S		
	Full	Tor 60–120°		Full	Tor 60–120°
O…H/Å	1.90	2.06	S–H	2.63	2.59
C=O····H/°	117	134	C=S-H	115	107
N−C=O····H/°	0	108	N-C=S-H	0	97
O…O/Å	2.55	2.92	S–O	3.63	3.36
$C = O \cdots O/^{\circ}$	125	134	C=S-O	114	85
N–C=O····Q/°	0	92	N-C=S-Q	0	107



Fig. 12 Contour plots created from entries in the CSD for the density of H-bond donors which are less than  $90^{\circ}$  to the C=X bond for (a) N-C=O carbonyl bond and (b) N-C=S thiocarbonyl bond.

hydrogen bond donors are involved in  $\pi$ -type bonding. However, for thiocarbonyls the majority of H-bond donors that possess a hydrogen at less than 90° to the C=S bond are in the torsional angle range of 60 to  $120^{\circ}$ , indicative of  $\pi$ -type bonding. A minor fraction of the donors bond through the lone pairs as exhibited by the small contour in the N–C=S plane, Fig. 12.

#### Conclusions

In conclusion we give evidence that the  $\pi$ -electron density from thiocarbonyls is an effective H-bond acceptor, particularly in cases where there is a paucity of other, conventional hydrogen bond acceptors. Interactions to the  $\pi$ -electron density of thiocarbonyls are markedly more prevalent than the oxygen analogues. While the present examples 1-3 exhibit a slightly weaker than average interaction, the parameters of torsional angle and donor to acceptor angle show typical directional behaviour towards the  $\pi$ -electrons.

# **Experimental**

### **Synthesis**

Compounds 3-6 were prepared by previously published procedures.21

Preparation of 1-(2-amino-phenylene)-3-methyl-thiourea (1). 1,2-Phenylenediamine (0.22 g, 2.05 mmol) and methylisothiocyanate (0.32 g, 4.4 mmol) were ground in a 5 mL chamber with a ball bearing at 30 Hz for 1 hour. Recrystallisation from methanol produced crystals which were isolated by filtration and washed with diethyl ether. Yield = 0.067 g, 0.4mmol, 20%. IR (v, cm<sup>-1</sup>) 3376 (w, N–H), 3299 (m, N–H), 3194 (s, N-H) 1620 (m, Ph-NH<sub>2</sub>). EI-MS: 182.1 (100%, [M + H]<sup>+</sup>). <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>) 8.83 (1H, s, N-H), 7.13 (1H, s, N-H), 6.96 (1H, t, J 7.6, Ar-H), 6.92 (1H, d, J 7.7, Ar-H), 6.72 (1H, d, J7.3, Ar-H), 6.54 (1H, t, J7.6), 4.79 (2H, s, NH<sub>2</sub>), 2.85 (3H, d, J 4.1, CH<sub>3</sub>). { $^{1}$ H}- $^{13}$ C NMR (126 MHz, DMSO- $d_{6}$ ) 182.24, 144.95, 128.76, 128.08, 123.56, 117.17, 116.46, 32.27. Anal. Calcd for C<sub>8</sub>H<sub>11</sub>N<sub>3</sub>S: C 53.01, H 6.12, N 23.18%; found: C 52.78, H 6.10, N 23.14%.

Preparation of 1-(2-amino-phenylene)-3-tert-butyl-thiourea (2). 1,2-Phenylenediamine (0.6 g, 5.5 mmol) and tert-butyl isothiocyanate (1.3 g, 11.3 mmol) were dissolved in 30 mL of methanol and the mixture refluxed for 2 hours. The solvent was removed in vacuo and the white precipitate washed with hexane. The product could be isolated by recrystallising the crude product in toluene. Yield = 0.6 g, 2.7 mmol, 49%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, J/Hz): 1.43 (9H, s, C-(CH<sub>3</sub>)<sub>3</sub>), 4.00 (2H, br, NH<sub>2</sub>), 5.78 (1H, br, NH), 6.71 (1H, dd,  ${}^{3}J = 8.0$ , CH<sub>Ar</sub>), 6.77  $(1H, d, {}^{3}J = 8.0, CH_{Ar}), 7.00 (1H, d, {}^{3}J = 8.0, CH_{Ar}), 7.10$  $(1H, dd, {}^{3}J = 8.0, CH_{Ar}), 7.66 (1H, br, NH). {}^{1}H}^{-13}C NMR$ (CDCl<sub>3</sub>, 400 MHz): 28.66, 53.68, 116.46, 118.82, 121.10, 128.19, 129.32, 143.25, 179.46. ESI-MS: 224.1 (100%, [M + H]<sup>+</sup>). Anal. Calcd for C<sub>11</sub>H<sub>17</sub>N<sub>3</sub>S: C 59.19, H 7.67, N 18.81%; found: C 59.12, H 7.72, N 18.81%.

### **X-Ray diffraction**

Diffraction quality single crystals were obtained by slow evaporation of ethanol solutions, with the exception of 4, which were obtained from MeOH/H2O solution. The diffraction experiments were carried out on Gemini, SMART 1000, 6000 or KappaCCD diffractometer. The crystals were cooled using Cryostream (Oxford Cryosystems) open-flow N2 cryostats. The structures were solved by direct methods and refined by fullmatrix least-squares on  $F^2$  for all the data using SHELX software<sup>29</sup> with the aid of X-Seed.<sup>30,31</sup>

1-(2-Amino-phenylene)-3-methyl-thiourea (1).  $C_8H_{11}N_3S$ , M =181.26, colourless block,  $0.74 \times 0.33 \times 0.23$  mm<sup>3</sup>, monoclinic, space group  $P2_1/n$  (no. 14), a = 14.7266(6), b = 7.6637(3), c = 16.2667(7) Å,  $\beta = 105.323(4)^{\circ}$ , V = 1770.61(12) Å<sup>3</sup>, Z = 8,  $D_{\rm c} = 1.360 \text{ g cm}^{-3}$ ,  $F_{000} = 768$ , Gemini, MoK $\alpha$  radiation,  $\lambda =$ 0.71073 Å, T = 120(2) K,  $2\theta_{max} = 58.06^{\circ}$ , 8107 reflections collected, 4136 unique ( $R_{int} = 0.0635$ ). Final GooF = 1.064, R1 = 0.0531, wR2 = 0.1373, R indices based on 3508 reflections with  $I > 2\sigma(I)$  (refinement on  $F^2$ ), 235 parameters, 0 restraints.  $L_p$ and absorption corrections applied,  $\mu = 0.312 \text{ mm}^{-1}$ .

1-(2-Amino-phenylene)-3-tert-butyl-thiourea (2).  $C_{11}H_{17}N_3S$ , M = 223.34, colourless block,  $0.39 \times 0.19 \times 0.18$  mm<sup>3</sup>, monoclinic, space group  $P2_1/n$  (no. 14), a = 10.6285(4), b = 9.7517(4), c = 12.8232(5) Å,  $\beta = 109.7120(10)^{\circ}$ , V = 1251.19(9) Å<sup>3</sup>, Z = 4,  $D_{\rm c} = 1.186 \text{ g cm}^{-3}, F_{000} = 480, \text{SMART 1000}, \text{MoK}\alpha \text{ radiation},$  $\lambda = 0.71073$  Å, T = 120(2) K,  $2\theta_{\text{max}} = 60.8^{\circ}$ , 11 735 reflections collected, 3477 unique ( $R_{int} = 0.0598$ ). Final GooF = 1.042, R1 = 0.0373, wR2 = 0.0922, R indices based on 2825 reflections with  $I > 2\sigma(I)$  (refinement on  $F^2$ ), 144 parameters, 0 restraints.  $L_p$ and absorption corrections applied,  $\mu = 0.233 \text{ mm}^{-1}$ .

1-Methyl-3-[2-(3-methyl-thioureido)-ethyl]-thiourea (3). C<sub>6</sub>H<sub>14</sub>  $N_4S_2$ , M = 206.33, colourless block,  $0.09 \times 0.08 \times 0.05 \text{ mm}^3$ , tetragonal, space group  $P4_2/n$  (no. 86), a = b = 9.5098(5), c = 10.8333(7) Å, V = 979.72(10) Å<sup>3</sup>, Z = 4,  $D_c = 1.399$  g cm<sup>-3</sup>,  $F_{000} = 440$ , SMART 6000, MoK $\alpha$  radiation,  $\lambda = 0.71073$  Å, T = 200(2) K,  $2\theta_{\text{max}} = 52.7^{\circ}$ , 6601 reflections collected, 1002 unique ( $R_{int} = 0.0608$ ). Final GooF = 0.921, R1 = 0.0296, wR2 = 0.0625, R indices based on 716 reflections with  $I > 2\sigma(I)$ (refinement on  $F^2$ ), 56 parameters, 0 restraints.  $L_p$  and absorption corrections applied,  $\mu = 0.498 \text{ mm}^{-1}$ .

1-Methyl-3-[2-(3-methyl-thioureido)-phenyl]-thiourea (4).  $C_{10}H_{14}N_4S_2$ , M = 254.37, colourless block,  $0.28 \times 0.24 \times 0.10$ mm<sup>3</sup>, monoclinic, space group C2/c (no. 15), a = 18.0632(8), b =7.5649(3), c = 19.4089(8) Å,  $\beta = 116.0840(10)^{\circ}$ , V = 2382.03(17)Å<sup>3</sup>, Z = 8,  $D_c = 1.419$  g cm<sup>-3</sup>,  $F_{000} = 1072$ , SMART 1000, MoK $\alpha$ radiation,  $\lambda = 0.71073$  Å, T = 120(2) K,  $2\theta_{\text{max}} = 60.7^{\circ}$ , 13 725 reflections collected, 3395 unique ( $R_{int} = 0.0269$ ). Final GooF = 1.054, R1 = 0.0296, wR2 = 0.0735, R indices based on 2966 reflections with  $I > 2\sigma(I)$  (refinement on  $F^2$ ), 201 parameters, 0 restraints.  $L_p$  and absorption corrections applied,  $\mu = 0.425$  $mm^{-1}$ .

1-Isopropyl-3-[2-(3-isopropyl-thioureido)-phenyl]-thiourea (5).  $C_{14}H_{22}N_4S_2$ , M = 310.48, colourless block,  $0.28 \times 0.21 \times 0.12$ mm<sup>3</sup>, triclinic, space group P1 (no. 2), a = 9.4599(6), b =9.5946(6), c = 11.0971(7) A,  $\alpha = 78.9840(10)$ ,  $\beta = 66.4850(10)$ ,  $\gamma = 65.0450(10)^{\circ}, V = 837.03(9) \text{ Å}^3, Z = 2, D_c = 1.232 \text{ g cm}^{-3},$  $F_{000} = 332$ , SMART 1000, MoK $\alpha$  radiation,  $\lambda = 0.71073$  Å, T =120(2) K,  $2\theta_{\text{max}} = 60.1^{\circ}$ , 8785 reflections collected, 4507 unique  $(R_{int} = 0.0439)$ . Final GooF = 1.018, R1 = 0.0392, wR2 = 0.0918, R indices based on 3673 reflections with  $I > 2\sigma(I)$ (refinement on  $F^2$ ), 181 parameters, 0 restraints.  $L_p$  and absorption corrections applied,  $\mu = 0.315 \text{ mm}^{-1}$ .

**1-Methyl-3-[6-(3-methyl-thioureido)-pyridin-2-yl]-thiourea (6).**   $C_9H_{13}N_5S_2$ , M = 255.36, colourless block,  $0.24 \times 0.10 \times 0.01$ mm<sup>3</sup>, triclinic, space group  $P\overline{1}$  (no. 2), a = 5.798(2), b = 9.447(4), c = 11.167(4) Å,  $\alpha = 87.646(7)$ ,  $\beta = 75.043(6)$ ,  $\gamma = 75.422(6)^\circ$ , V = 571.7(4) Å<sup>3</sup>, Z = 2,  $D_c = 1.483$  g cm<sup>-3</sup>,  $F_{000} = 268$ , SMART 6000, MoK $\alpha$  radiation,  $\lambda = 0.71073$  Å, T = 120(2) K,  $2\theta_{max} = 55.0^\circ$ , 4141 unique reflections (see CIF† for discussion of twinning). Final GooF = 1.070, R1 = 0.0450, wR2 = 0.1149, Rindices based on 3349 reflections with  $I > 2\sigma(I)$  (refinement on  $F^2$ ), 148 parameters, 0 restraints.  $L_p$  and absorption corrections applied,  $\mu = 0.446$  mm<sup>-1</sup>.

#### CSD search

**CSD search and Isogen plot method.** A search of the CSD<sup>32-34</sup> was undertaken using the central fragment of NM–C=X (NM = any non-metal atom, X = S, O) and a contact group of H–Q (Q = N,O) where an X···H contact (distance between atoms no larger than sum of van der Waals radii) existed. Similar searches were conducted applying one of the following two constraints: NM–C=X···H torsional angles limited to between 60° and 120°, or C=X···H angle no greater than 90°. The parameters and coordinate files were saved for these searches and used to generate scatter plots in the Isogen program. Contour scatter plots of the donor atom, Q, were generated in Rasmol with an internal scaling of 20 (red), 40 (green), and 80 (blue). The maximum density was found by setting all scales to 99, and measurements were taken using the tools provided by the program.

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