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Addressing Hydrogen Bonding Motifs by Suited Substitution of Thioureas

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Abstract. The possibility to form hydrogen bonds with different motifs is an interesting aspect of the chemistry of thioureas especially regarding catalysis. We present nine new thioureas with different unsymmetric substitution patterns involving aromatic and aliphatic substituents including the structural characterization of four of them. Herein, three different hydrogen bond patterns could be realized. Moreover, DFT calculations were performed to investigate the strength of the hydrogen bonds. Hereby, we show that we can selectively address different hydrogen bonding motifs by the choice of substituents. This enables a correlation of the molecular structure and the bonding motifs. Additionally, by natural resonance theory, we show that the contribution of the thiolate resonance form dominates the electronic structure, which is important for coordination chemistry.

Introduction

Thioureas are important organocatalysts and also ligands for coordination chemistry. Organocatalysts had a large impact on modern chemistry for the last few decades and they are a part of an intensively investigated research field since then.[1–4] They can be environmentally friendly, of only minor toxicity, and cheap.[2,4,5] In many cases, these catalysts offer an easy way to produce asymmetric compounds in an enantiopure manner.[1,6] Here, thiourea derivatives have found to be highly useful. Because of their hydrogen-bonding interactions with other organic molecules they are well-suited for organocatalysis.[7] The hydrogen-bonding mediated catalysis received wide acceptance and is nowadays involved in many enantioselective transformation reactions.[8,9]

Today, different kinds of thiourea catalysts (chiral or achiral, mono- and bifunctional) are known. The growing interest on the hydrogen bonding of thiourea began in the 1970's when *Coiro* et al. analyzed the intermolecular hydrogen bonds of N,N′-dicyclohexylurea.[10] Since 2001 several potential achiral/chiral mono- and bifunctional thiourea and urea derivatives have been synthesized and characterized by many research groups for example by *Schreiner* et al.[11] and other research groups.[8,12,13–17] One of the first remarkable catalysts of this kind was published in 1998 by *Jacobsen* et al.[15] They have synthesized a variety of chiral Schiff base thioureas with broad applications ranging from organic catalysis to textile manufacturing and also extraction of metals.[18] Through different optimization studies, the thiourea derivative and its closely related analogues could be identified as universal and very effective catalysts in Strecker reactions.[15,16] Moreover, a diverse spectrum of reactions[11,14,19–25] is catalyzed by thiourea derivatives, e.g. Diels-Alder,[26] Michael addition,[27–30] Aza-Henry,[27,29] Morita-Baylis-Hillman,[13,17,31,32] and the ring-opening polymerization of lactide.[33–35]

Besides organocatalysis, thiourea based compounds such as antithyroid drugs are useful in the medical field. They have influence on the thyroid hormone, which controls the protein, fat, and carbohydrate metabolism of the human body.[36]

In addition, thiourea serves as a source of sulfide in organic transformations, e.g. for converting alkyl halides to thiols.[37] It has a high industrial potential: in the textile industry it is used as a reductive bleaching agent in combination with hydrogen peroxide.[38] Additionally, thiourea derivatives have also various agricultural applications as herbicides, fungicides and rodenticides.[39]

Herein, we report on nine new thioureas with different substitution patterns involving aromatic and aliphatic residues. By means of molecular structures and theoretical analyses, we show that we can selectively address different hydrogen bonding motifs by the choice of substituents. This enables a correlation of the molecular structure and the bonding motifs without the requirement of a moleculare structure. This is supplemented through theoretical studies e.g. natural resonance theory (NRT), which shows large contribution of the thiolate form.

Results and Discussion

We synthesized nine new unsymmetrically substituted thioureas **1–9** analogous to the research group of *Kong* et al.[40]

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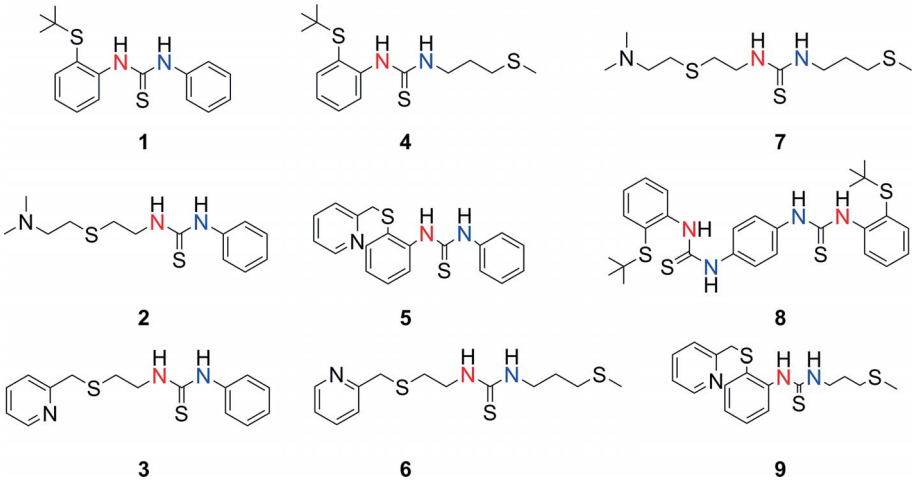
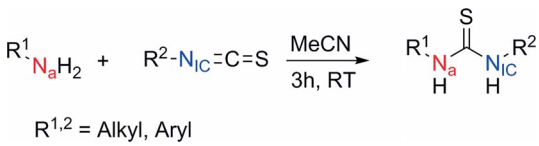


Figure 1. Overview of the new thiourea derivatives.

The desired thiourea derivative is produced by reaction of the corresponding primary amine with an isothiocyanate in acetonitrile (general procedure in Scheme 1).



Scheme 1. General reaction scheme of the synthesis of thioureas (N_a indicates the nitrogen atom from the amine source, whereas N_{IC} indicates the isothiocyanate side).

The synthesized thioureas are shown in Figure 1. The used starting compounds contain three different isothiocyanates and four primary amines. All of these thiourea derivatives exhibit a characteristic resonance in the ^{13}C NMR spectrum of the quaternary carbon atom of the thiourea group at approximately 180 ppm (Table 1). As expected, the two NH protons have different chemical shifts because of the unsymmetric substitution pattern. NH protons in close proximity to aromatic systems appear in low field (ca. 8–9 ppm) and those, which are close to an aliphatic system are found at a higher field (ca. 6–7 ppm) in the NMR spectra. The largest differences appear in molecules with an aromatic and aliphatic residue e.g. compound **2** with signals at 6.70 (aliphatic side) and 8.51 ppm (aromatic side). In most cases the difference is about one ppm as found in compound **1**.

Table 1. Positions of the NH and quaternary carbon signals /ppm of the functional groups.

Ligand	Yield /%	Key position ^1H (NH)		Key position ^{13}C
1	75	8.27	9.23	178.4
2	63	6.70	8.51	180.5
3	76	6.97	8.14	180.3
4	58	6.69	8.47	180.2
5	94	8.76	8.85	180.0
6	60	6.75	7.09	182.0
7	87	6.68	6.80	182.1
8	68	9.22	9.53	179.1
9	63	6.72	8.56	181.1

The thioureas are synthesized in very good yields in the range of 60–95%. Various attempts to purify the respective products revealed that it is beneficial to perform the syntheses with an excess of the primary amine. Hereby the starting materials and the product can be better separated from each other. In order to simplify the following discussions of the unsymmetric substitution pattern of the thioureas, the N atom arising from the amine is called N_a and the other one generated from the isothiocyanate is labelled N_{IC}, respectively.

In the following section we present the molecular structures of the thioureas **1**, **3**, **4**, and **6** in the solid state and the results of the performed DFT calculations. The compounds **1**, **3**, **4**, and **6** were characterized with single-crystal X-ray structure analysis. All structures display a hydrogen-bonding network but with different motifs. The molecular structures show three different motifs. These motifs are displayed in Figure 2. The dimeric motif **A**, which is formed by compound **1** and **3**, contains two N–H···S interactions. The motif **B** consists of an infinite chain with a bifurcated pattern of the hydrogen bonds.

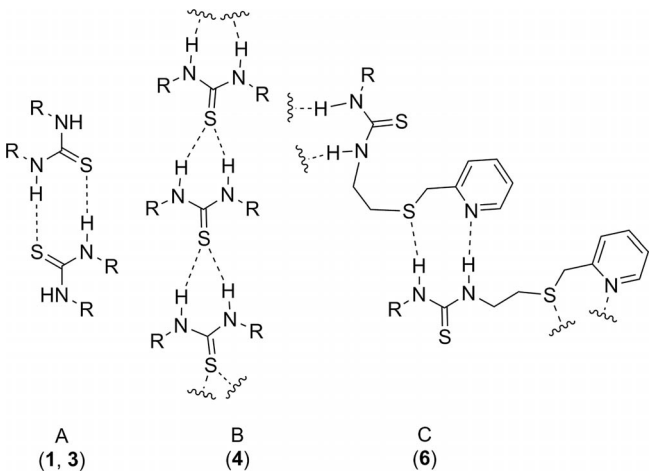


Figure 2. Hydrogen bonding motifs.

Both (N)H functions of one molecule, which form this motif **B**, are connected to the thiourea sulfur of a neighboring mol-

ecule of **4**. The third motif **C** shows hydrogen bonds that do not involve the thiourea sulfur atom. They form a motif with molecules connected to infinite chains via additional S and N donor functions.

The molecular structure of **1** is shown in Figure 3. The substituent of the nitrogen atom N_{IC} of this compound is a phenyl ring and N_a is bound to the *tert*-butyl(phenyl)sulfide residue. The molecular structure exhibits N1–H1···S1# hydrogen bonding motifs with N–H···S of 2.48 Å that connect molecules into non-crystallographic centrosymmetric dimers.

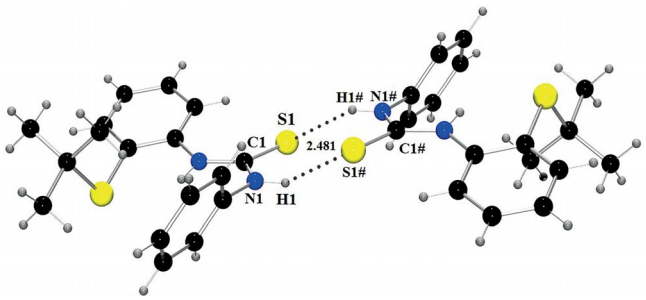


Figure 3. Molecular structure of **1**. Intermolecular hydrogen bonds are shown as dashed lines (motif **A**).

The substituents of **4** are a *tert*-butyl(phenyl)sulfide on one side and a methyl(propyl)sulfide on the other side of the molecule. In compound **4** hydrogen bonding motif **B** is found. It is an infinite chain in the crystal where the units are perpendicular to each other (89.9°) (Figure 4).

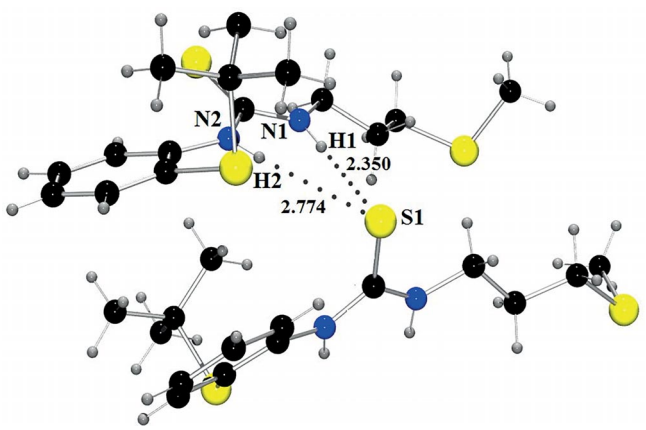


Figure 4. Molecular structure of **4**. Intermolecular hydrogen bonds are shown as dashed lines (motif **B**).

The involved two N–H···S hydrogen bonds are different with 2.35 and 2.77 Å and related C–S···H angles of 95.1° and 107.3°. These two bonding motifs coexist in unsubstituted thiourea (see Figure 5).[41,42]

Its dimeric structure is highlighted with black hydrogen bonds and the infinite chain through blue hydrogen bonds. Selected bond lengths and angles of all molecular structures are shown in Table 2.

In addition to **1**, compound **3** also forms a dimeric structure via hydrogen bonds (Figure 6). The molecular structure has a 2-[(ethylthio)-methyl]pyridine residue at N_a and a phenyl ring at N_{IC}.

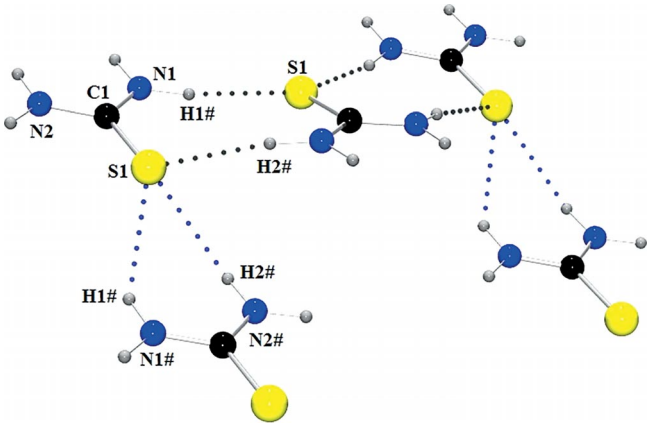


Figure 5. Unsubstituted thiourea (black hydrogen bonds = motif **A** / blue hydrogen bonds = motif **B**).[41]

Table 2. Selected bond lengths /Å and angles /° of **1**, **3**, **4**, and **6** (IC = side of the isothiocyanate residue, a = side of the amine residue).

	1	**3**	**4**	**6**
C=S	1.685(1)	1.699(2)	1.691(2)	1.690(1)
N_{IC}–C(1)	1.353(1)	1.349(3)	1.335(3)	1.348(2)
N_a–C(1)	1.358(1)	1.342(3)	1.361(3)	1.344(2)
N_a–C(1)–N_{IC}	115.2(1)	118.6(2)	114.2(1)	114.9(2)
S–C(1)–N_{IC}	118.3(1)	119.8(2)	121.0(2)	121.6(2)
S–C(1)–N_a	126.5(1)	121.6(2)	124.8(2)	123.6(1)

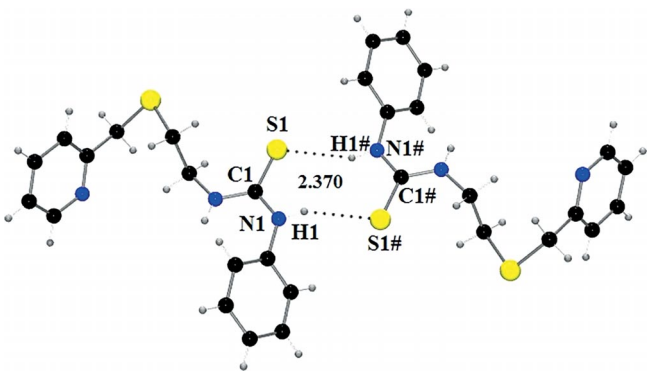


Figure 6. Molecular structure of **3**. Intermolecular hydrogen bonds are shown as dashed lines (motif **A**).

This compound also represents the hydrogen bonding motif **A** as **1**, but with a shorter N–H···S# interaction of 2.37 Å. The molecular structure of compound **6** is shown in Figure 7. It comprises the same [(ethylthio)methyl]pyridine residue as **3** but has a methyl-(propyl)sulfide at N_a. In contrast to the other structures, the N–H···S bond involves the sulfur of the functional group. Additionally, an N–H···$N_{(py)}$ interaction occurs at the pyridine. Similar to **4**, the hydrogen bonds connect the molecules into infinite chains.

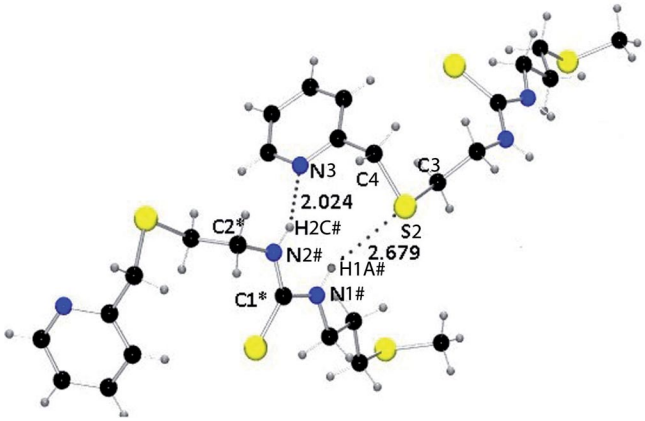


Figure 7. Molecular structure of **6**. Intermolecular hydrogen bonds are shown as dashed lines (motif **C**).

A recent review discusses various hydrogen bonding patterns of (substituted) thioureas[42] and the role of substituents in the structures of thioureas are also described.[43] The results exhibit the possibility for selectively addressing different hydrogen bonding motifs through unsymmetrical substitution patterns at the nitrogen donor atom. Both dimeric structures **1** and **3** have aromatic rings substituted on the nitrogen atom. The infinite chain **4** has one pure aliphatic residue. The hydrogen bonding motif **C** of thiourea **6** is an infinite chain as well and it is constructed with a similar pattern, but it has different hydrogen bonds (Figure 7). This could be one aspect for a directed hydrogen bonding motif and a further step towards a selective synthesis of specific hydrogen bonding motifs for organocatalysis.[8,9,12–17,19–35]

To further investigate these bonding patterns and to clarify the question for the thione or thiolate character of the thiourea, DFT calculations were performed. In the past, large basis sets with diffusion and polarization functions have been found useful for the description of hydrogen bonding systems. *Scheiner* et al. used larger basis set in MP2/aug-cc-pVDZ calculations to describe the interactions between thioureas and imines.[44] In this work, the calculations were carried out with the *triple-zeta* basis set 6-311++G(d,p) and the hybrid functional TPSSh in various solvents and with or without empirical dispersion correction (results are shown in the Tables S1 and S2, Supporting Information).

In contrast to the expensive MP2 method, our method is comparatively efficient. Since the computational costs increase, the DFT offers a good alternative to these methods.[45] The results of the calculations based on two molecules of the respective compounds with the PCM solvent model for acetonitrile without dispersion correction are shown in Table 3. The results of this theoretical description show the best overall agreement with the experimental data of the X-ray analysis. The C=S bond lengths are predicted slightly too long (ca. 0.02 Å), but the C–N bonds are well described. Differences are observed in the hydrogen bond lengths of the dimeric structures of compounds **1** and **3**. The molecular structure of **1** shows the hydrogen bond length with a length of 2.48 Å, but in the calculations it is significantly smaller (2.38 Å) and is on the same level as compound **3**, where the hydrogen bond length is well predicted (exp. 2.37 Å and calcd. 2.38 Å). The hydrogen bonds of compounds **4** and **6**, which could be described as infinite chains, feature a similar accordance with the molecular structure as **1**. The S···H bond lengths of **4** and **6** are displayed too long in the DFT calculations. The second hydrogen bond of **6** (N···H) is well described by the theoretical approach. The angles of all compounds are determined well by the used DFT methods. Remarkable is that the symmetry of compound **1**, **4**, and **6** is broken in the calculations with the PCM model which is identified through slightly unsymmetric atom distances and charge transfer energies. The differences between the atom distances and angles of these compounds are not very large but noticeable. The charge transfer energies of the hydrogen bonding interactions of the dimers are reported in Table 3.

Table 3. Selected bond lengths /Å, angles /° and hydrogen bonding energy /kcal·mol^{-1} of DFT calculations of **1**, **3**, **4**, and **6** [TPSSh/6-311++G(d,p) with PCM for acetonitrile] (IC = side of the isothiocyanate residue, a = side of the amine residue).

	1	**3**	**4**	**6**
C=S	1.701	1.710	1.697	1.709
	1.702		1.701	1.703
N_{IC}–C(1)	1.357	1.357	1.347	1.355
	1.356		1.348	1.350
N_A–C(1)	1.360	1.345	1.374	1.351
	1.360		1.368	1.357
S···H(1)	2.389	2.381	2.472	–
	2.388			
S···H(2)	–	–	3.008	–
S_{te}···H(1)	–	–	–	2.952
N_{py}···H(1)	–	–	–	1.965
N_a–C(1)–N_{ic}	115.29	117.69	113.32	114.57
	115.43		113.37	115.61
S_{tu}–C(1)–N_{ic}	119.61	119.93	121.76	122.27
	119.53		121.02	121.65
S_{tu}–C(1)–N_a	125.04	122.38	124.90	123.16
	124.99		125.58	122.74
C(1)–S_{tu}···H(1)	109.63	109.09	103.19	–
	109.52			
C(1)–S_{tu}···H(2)	–	–	122.60	–
C(1)–S_{te}···H(1)	–	–	–	90.65
				122.57
C–N_{ic}···H(1)	–	–	–	113.44
				127.64
Energy S_{tu}···H–N_{IC}	14.80	15.60	11.55	–
S_{tu}···H–N_a	15.54	15.60	–	–
S_{te}···H–N_{Ic}	–	–	1.22	1.64
N_{Py}···H(1)–N_a	–	–	–	11.69

Except the hydrogen bonds with atom distances of more than 3 Å, the energy of the hydrogen bonds in these thioureas amounts to 11.5–16 kcal·mol^{-1}. These energy values are in a good agreement with the results from *Scheiner* et al. (ca. 16–18 kcal·mol^{-1}).[44] Besides this, NRT (natural resonance theory) calculations were performed to predict the relative contributions of different resonance structures of **1**, **3**, **4**, and **6** to investigate the principle character of the synthesized thioureas, whether they have a thiolate or thione character. We focus on the percentage distribution of the resonance forms with regard to the domination of the thione or thiolate form. Because of

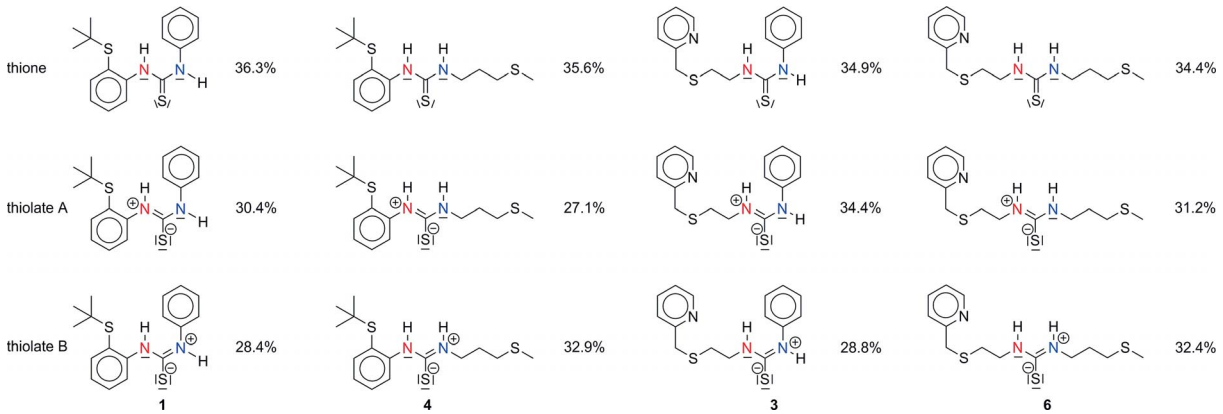


Figure 8. Resonance structures of the compounds **1**, **3**, **4**, and **6** (calculated by NRT).

this, the NRT percentage distributions for all aromatic resonance forms of the same basic structure have been combined.[46] The results are shown in Figure 8. The contribution of the thione form is predicted with 34.4 to 36.3 % for the corresponding compounds. The dominant form is the combination of the two thiolate forms **A** and **B** with in total ca. 60 %. Similar results have been obtained for unsubstituted thioureas.[47] As shown in Figure 8, the **A** and **B** forms are not predicted equally. The form with the highest contribution is the thiolate form **A** of **3**. Generally, the dominant form between these two thiolate forms is the one with the positive charge on the nitrogen atom with an aliphatic group. In compound **6**, with aliphatic groups on both nitrogen atoms, the differences of the distribution is smaller (31.2 % and 32.4 %) as in the other compounds. The preference for the thiolate form is an important aspect with regard to their potential coordination properties.

Conclusions

The possibility to form hydrogen bonds with different motifs is an interesting aspect of the chemistry of thioureas especially regarding catalysis. We have presented nine new substituted thioureas including the structural characterization of four of them. Herein, three different hydrogen bond patterns could be realized. The results show a distinct relation between the substitution pattern and the corresponding bonding motifs. We have found that the substitution of a phenyl group on one of the NH groups results in the dimeric structure motif **A** of **1** and **3**. With a substitution of the aliphatic residue the motif changes to an infinite chain with different types even among themselves [**4** (**B**) and **6** (**C**)]. We can selectively address different hydrogen bonding motifs by the unsymmetrical substitution pattern. The molecular structures are well described by DFT calculations with the *triple-zeta* basis set 6-311++G(d,p) and the hybrid functional TPSSh in various solvents and with and without dispersion correction. Remarkable is that the symmetry of the molecular structure is broken in most cases. Further investigations of the charge transfer energies of the hydrogen bonds show that their energies lie in a range of 11.5 to 16 kcal·mol^{-1} independent of the bonding motif of the thiourea derivatives. With NRT calculations, we investigated the relative contributions of the different resonance structures. The results show a strong preference to the thiolate forms of the compounds, which is an important aspect for coordination chemistry.

Further investigations will be focused on the variation of the thiourea derivatives to confirm the possibility of directed hydrogen bond modification.

Experimental Section

General Methods: All reactions were carried out in a nitrogen atmosphere. Nitrogen was dried by passage through P_2O_5. NMR spectra were recorded with a Bruker Avance 500-spectrometer at 30 °C. ^{1}H and ^{13}C NMR chemical shifts are given relative to TMS (0 ppm). Assignment of NMR signals was done with the help of additional 2D experiments (DEPT-135, DEPT-Q, HMBC, HMQC, COSY). Mass spectra data were measured in acetonitrile with a SYNAPT 2G from Waters (ESI pos/neg; 3 kV; source-T 120 °C; con gas flow 30 L·h^{-1} nitrogen; solvation gas flow 650 L·h^{-1} nitrogen). IR spectra were recorded with a Bruker Vertex 70 FT-IR Spectrometer with ATR technique. CHN analyses were measured with an Elemental Analyzer Modell 240 of PERKIN-ELMER. All chemicals were purchased from Fluka, Sigma Aldrich, Acros Organics, abcr and Merck. All primary amines were synthesized according to literature or analogue to them.[48–50] The solvents were purified by standard literature procedures.[24]

Crystal Structure Analyses: Crystal data for compounds **1**, **3**, **4**, and **6** are presented in Table 4. Data were collected with a Bruker-AXS SMART[51] APEX CCD, using Mo-K_α radiation (λ = 0.71073 Å) and a graphite monochromator. Data reduction and absorption correction were done with SAINT and SADABS.[51] The structures were solved by direct and conventional Fourier methods and all non-hydrogen atoms refined anisotropically with full-matrix least-squares based on F^2 (SHELXTL[51]). Hydrogen atoms were derived from difference Fourier maps and placed at idealized positions, riding on their parent C atoms, with isotropic displacement parameters U_{iso}(H) = 1.2U_{eq}(C) and 1.5U_{eq}(C methyl). All methyl groups were allowed to rotate but not to tip.

Crystallographic data (excluding structure factors) for the structures reported in this study have been deposited with the Cambridge Crystallographic Data Centre, CCDC, 12 Union Road, Cambridge CB21EZ,

Table 4. Crystallographic data and parameters of **1**, **3**, **4**, and **6**.

	1	**3**	**4**	**6**
Empirical formula	$C_{17}H_{20}N_2S_2$	$C_{15}H_{17}N_3S_2$	$C_{15}H_{24}N_2S_3$	$C_{13}H_{21}N_3S_3$
Formula mass /g·mol^{-1}	316.47	303.44	328.54	315.51
Crystal size /mm	0.50 × 0.38 × 0.32	0.20 × 0.08 × 0.04	0.49 × 0.18 × 0.11	0.47 × 0.19 × 0.10
T /K	130(2)	130(2)	130(2)	130(2)
Crystal system	triclinic	monoclinic	monoclinic	orthorhombic
Space group	$P\bar{1}$	$C2/c$	$P2_1/c$	$Aba2$
a /Å	9.3283(11)	19.574(5)	19.453(5)	15.8792(18)
b /Å	9.8195(12)	7.8292(19)	10.019(2)	20.732(3)
c /Å	9.8608(12)	20.210(5)	8.885(2)	9.5760(11)
α /°	74.937(2)	90	90	90
β /°	66.329(2)	100.525(7)	101.916(5)	90
γ /°	82.522(2)	90	90	90
V /Å^3	798.48(17)	3045.0(13)	1694.4(7)	3152.5(7)
Z	2	8	4	8
$\rho_{calc.}$ /mg·m^{-3}	1.316	1.324	1.288	1.330
μ /mm^{-1}	0.328	0.343	0.430	0.461
λ /Å	0.71073	0.71073	0.71073	0.71073
F(000)	336	1280	704	1344
hkl range	–12/12; –9/12; –12/12	–25/22; –10/10; –26/26	–24/25; –13/13; –11/11	–20/20; –22/27; –12/12
Reflections collected	7571	14034	15049	12634
Independent reflections	3766	3633	4028	3755
$R_{int.}$	0.0124	0.0651	0.0832	0.0390
Reflections observed	3766	3633	4028	3755
Number of parameters	190	181	193	173
R_1 [$I \geq 2\sigma(I)$]	0.0300	0.0460	0.0449	0.0330
wR_2 (all data)	0.0832	0.1073	0.0906	0.0738
Goodness-of-fit	1.019	1.006	0.881	1.044
Largest diff. peak, hole /e·Å^{-3}	0.353 and –0.325	0.323 and –0.279	0.402 and –0.362	0.298 and –0.177

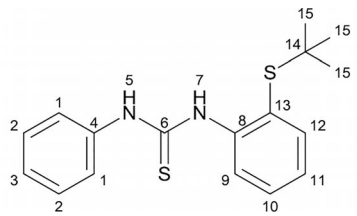
UK. Copies of the data can be obtained free of charge on quoting the depository numbers CCDC-1434770 (**1**), CCDC-1434772 (**3**), CCDC-1434771 (**4**), and CCDC-1434773 (**6**) (Fax: +44-1223-336-033; E-Mail: deposit@ccdc.cam.ac.uk, http://www.ccdc.cam.ac.uk).

Computational Details: Density functional theory (DFT) calculations were performed with the program suite Gaussian 09.[52] The geometries of the complexes were optimized using the nonlocal hybrid meta GGA TPSSh functional[53] and the triple-zeta basis set 6-311++G(d,p) as implemented in Gaussian on all atoms. The starting geometries for the complexes were generated from the molecular structures. Frequency calculations did not show imaginary values verifying local minima on the potential surface. NBO calculations for the complexes were accomplished by use of the program suite NBO 6.0 (includingNRT calculations).[54] As dispersion correction, we used Grimme D3[55] dispersion correction as implemented in Gaussian, Revision D.01 with Becke-Johnson damping factors[56] for TPSSh.

General Solution-phase Synthesis of *N*/*N*′-Thiourea: The general synthesis proceeds comparable to the procedure of *Kong* et al.[40] The corresponding primary amine (12.0 mmol) (depending on the product) was dissolved in anhydrous acetonitrile (120 mL). To this solution the corresponding isothiocyanate (10.9 mmol) was added and the reaction mixture was stirred for 3 h at room temperature. The solvent was removed under reduced pressure. The purification of the crude product is specified at the compound. These purification steps differ from the synthesis protocol of *Kong* et al.[40]

Synthesis of the Starting Material: The primary amines 2-(*tert*-butylthio)aniline (**A1**),[48] 2-[(2-aminoethyl)thio]-*N*,*N*-dimethylethanamine (**A2**),[49] 2-[(pyridin-2-ylmethyl)thio]ethanamine (**A3**)[50] and 2-[(pyridin-2-ylmethyl)thio]aniline (**A4**)[50] were synthesized according to the literature. The isothiocyanates were purchased from Aldrich and directly used.

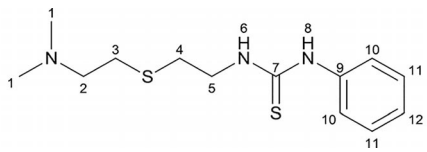
Synthesis of [2-(*tert*-Butylthio)phenyl]-3-phenylthiourea (1): Analogous to the general procedure, amine **A1**[48] (2.17 g, 12 mmol) and phenylisothiocyanate (1.3 mL, 10.9 mmol) were added to anhydrous acetonitrile (120 mL). The reaction mixture was stirred for 3 h at room temperature and the solvent was removed under reduced pressure. The residue was washed with Et_2O and dried under vacuum. The product is a white solid (2.57 g, 8.14 mmol, 74.6 %). Single crystals suitable for X-ray diffraction were obtained through recrystallization from acetonitrile.



^{1}H NMR (500 MHz, $CDCl_3$, 30 °C, ppm): δ = 1.06 (s, 9 H, H15); 7.08 (ddd, 1 H, H11, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 1.4 Hz); 7.35–7.43 (m, 4 H, H1, H3, H10); 7.46 (dd, 1 H, H12, $^3J_{HH}$ = 7.6, $^4J_{HH}$ = 1.6 Hz); 7.49 (m, 2 H, H2); 8.27 (br. s, 1 H, H5); 8.84 (dd, 1 H, H9, $^3J_{HH}$ = 8.2, $^4J_{HH}$ = 0.9 Hz); 9.23 (br. s, 1 H, H7). **^{13}C NMR** (125 MHz, $CDCl_3$, 30 °C, ppm): δ = 30.5 (CH_3, C15); 48.0 (C_q, C14); 122.3 (CH, C9); 123.0 (C_q, C13); 124.3 (CH, C11); 126.6 (CH, C1); 128.0 (CH, C3); 129.8 (CH, C10); 130.2 (CH, C2); 136.0 (C_q, C4); 138.5 (CH, C12); 141.9 (C_q, C8); 178.4 (C_q, C6). **IR** (ATR): $\tilde{\nu}$ = 606 (vw), 627 (w), 658 (m), 696 (m), 735 (m), 760 (s), 773 (m), 808 (vw), 837 (vw), 910 (w), 939 (m), 1003 (w), 1024 (vw), 1035 (w), 1072 (m), 1120 (m), 1165 (m), 1176 (s), 1254 (m), 1288 (m), 1308 (m), 1360 (m), 1390 (vw), 1437 (m), 1448 (m), 1471 (m), 1487 (m), 1512 (s, NH, δ), 1531 (vs, CN, ν), 1577 (m), 2860 (vw), 2896 (vw), 2922 (vw), 2937 (vw), 2958 (w), 2975 (w), 3033 (vw), 3062 (vw), 3089 (vw), 3186 (w), 3242 (w)

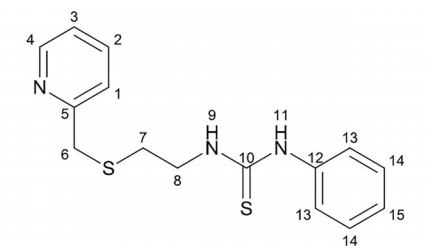
cm^{-1}. **MS-ESI**: [*m/z* (%)]: 317.11 (100) [M^+]; 261.05 (21) [M^+–*t*Bu]; 182.10 (52) [M^+–PhNCS]; 126.03 (73) [M^+–*t*Bu, PhNCS]; **CHN**: calcd. 64.5 % C, 8.9 % N, 6.4 % H, 20.3 % S; found: 64.6 % C, 8.9 % N, 6.3 % H, 20.5 % S.

Synthesis of 1-[2-((2-(Dimethylamino)ethyl)thio)ethyl]-3-phenylthio-urea (2): Amine **A2**[49] (1.77 g, 12 mmol) and phenylisothiocyanate (1.3 mL, 10.9 mmol) were added to anhydrous acetonitrile (120 mL). After 3 h stirring at room temperature the solvent was removed in vacuo. The residue was a pale yellow oil that was poured into water (20 mL) and extracted with DCM (3 × 30 mL). The organic layer was dried with Na_2SO_4, evaporation of the solvent and washing with Et_2O resulted in the product as pale yellow solid **2** (2.17 g, 6.84 mmol, 62.7 %).



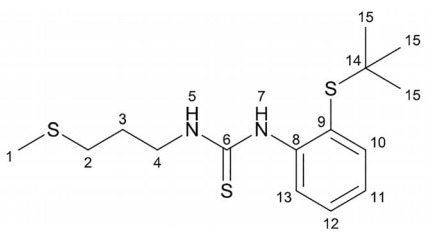
^{1}H NMR (500 MHz, $CDCl_3$, 30 °C, ppm): δ = 2.16 (s, 6 H, H1); 2.44 (t, 2 H, H2, $^3J_{HH}$ = 7.3 Hz); 2.57 (t, 2 H, H3, $^3J_{HH}$ = 7.2 Hz); 2.74 (t, 2 H, H4, $^3J_{HH}$ = 6.4 Hz); 3.77 (dd, 2 H, H5, $^3J_{HH}$ = 6.0 Hz); 6.70 (br. s, 1H, H6/H8); 7.22 (m, 3H, H10+H12); 7.36 (m, 2H, H11); 8.51 (br. s, 1H, H6/H8). **^{13}C NMR** (125 MHz, $CDCl_3$, 30 °C, ppm): δ = 29.4 (CH_2, C3); 31.5 (CH_2, C4); 44.2 (CH_2, C5); 45.2 (CH_3, C1); 59.2 (CH_2, C2); 125.0 (CH, C10/C12); 127.0 (CH, C10/C12); 130.0 (CH, C11); 136.5 (C_q, C9); 180.5 (C_q, C7). **IR** (ATR): $\tilde{\nu}$ = 603 (w), 638 (m), 690 (s), 709 (m), 731 (m), 742 (m), 758 (m), 775 (w), 814 (m), 841 (m), 903 (vw), 918 (vw), 968 (m), 1006 (s), 1031 (s), 1051 (m), 1070 (m), 1093 (s), 1138 (m), 1161 (s), 1195 (m), 1247 (m), 1288 (m), 1315 (s), 1334 (s), 1377 (m), 1408 (m), 1429 (m), 1448 (m), 1458 (m), 1467 (m), 1492 (vs, NH, δ), 1521 (vs, CN, ν), 1593 (m) 2711 (vw), 2777 (m), 2819 (m), 2825 (m), 2862 (m), 2944 (m), 2983 (m), 2993(m), 3058 (w), 3147 (m) cm^{-1}. **MS-ESI**: [*m/z* (%)]: 312.15 (8); 284.12 (100) [M^+]; 211.04 (9); 179.06 (24). **CHN**: calcd. 55.0 % C, 14.8 % N, 7.5 % H, 22.6 % S; found: 55.0 % C, 13.8 % N, 7.2 % H, 21.6 % S.

Synthesis of 1-Phenyl-3-[2-((pyridin-2-ylmethyl)thio)ethyl]-thiourea (3): Amine **A4**[50] (1.98 g, 11.7 mmol) and phenylisothiocyanate (1.3 mL, 10.9 mmol) were added to anhydrous acetonitrile (120 mL). After 3 h stirring at room temperature the solvent was removed in vacuo. The residue was a green oil. Petroleum ether (60–95 °C) was added to the oil and stirred for 1 h at room temperature. The product **3** precipitated as a grey solid (2.54 g, 8.32 mmol, 76.3 %).



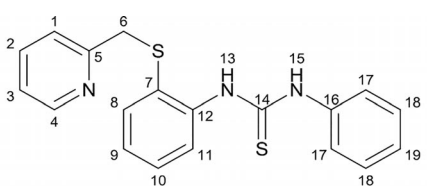
^{1}H NMR (500 MHz, $CDCl_3$, 30 °C, ppm): δ = 2.77 (t, 2 H, H7, $^3J_{HH}$ = 7.2); 3.79 (s, 2 H, H6); 3.83 (dt, 2 H, H8, $^3J_{HH}$ = 6.9 Hz); 6.97 (br. s, 1 H, H9); 7.08 (ddd, 1 H, H3, $^3J_{HH}$ = 7.3, $^4J_{HH}$ = 1.0 Hz); 7.23–7.25 (m, 4 H, H1+H13+H15); 7.35 (dd, 2 H, H14, $^3J_{HH}$ = 7.4 Hz); 7.58 (ddd, 1 H, H2, $^3J_{HH}$ = 7.9, $^4J_{HH}$ = 1.9 Hz); 8.14 (br. s, 1 H, H11); 8.27 (d, 1H, H4, $^3J_{HH}$ = 4.6 Hz). **^{13}C NMR** (125 MHz, $CDCl_3$, 30 °C, ppm): δ = 31.4 (CH_2, C7); 37.7 (CH_2, C6); 44.4 (CH_2, C8); 122.0 (CH, C3); 123.1 (CH, C1); 125.2 (CH, C13); 127.2 (CH, C15); 130.0 (CH, C14); 137.0 (CH, C2); 136.4 (C_q, C12); 149.4 (C_q, C4); 158.5 (C_q, C5); 180.3 (C_q, C10). **IR** (ATR): $\tilde{\nu}$ = 601 (w), 615 (w), 629 (w), 644 (m), 692 (vs), 729 (s), 739 (s), 754 (s), 812 (w), 827 (vw), 842 (vw), 874 (m), 897 (w), 918 (w), 962 (vw), 999 (m), 1024 (w), 1051 (w), 1072 (m), 1086 (m), 1105 (m), 1138 (w), 1155 (m), 1165 (m), 1244 (s), 1294 (m), 1317 (m), 1344 (m), 1384 (w), 1415 (m), 1434 (s), 1448 (m), 1473 (s), 1492 (m, NH, δ), 1529 (vs, CN, ν), 1569 (w), 1589 (m), 2908 (w), 2935 (w), 2953 (w), 2976 (w), 3003 (m), 3018 (m), 3058 (w), 3101 (w), 3159 (m) cm^{-1}. **MS-ESI**: *m/z* (%): 304.09 (42) [M^+]; 211.03 (100) [M^+–$PyCH_3$]; 124.02 (21) [M^+–PhNHCSNH-$(CH_2)_2$]. **CHN**: calcd. 59.4 % C, 13.9 % N, 5.7 % H, 21.1 % S; found: 59.3 % C, 13.7 % N, 5.7 % H, 20.8 % S.

Synthesis of 1-[2-(*tert*-Butylthio)phenyl]-3-[3-(methylthio)propyl]-thiourea (4): Amine **A1**[48] (1.7 g, 9.4 mmol) and 3-(methylthio)propylisothiocyanate (0.8 mL, 6.7 mmol) were added to anhydrous acetonitrile (40 mL). After 3 h stirring at room temperature the solvent was removed in vacuo. The residue was a colorless oil. Petroleum ether (60–95 °C) was added to the oil and stirred for 1 h at room temperature. The product **4** precipitated as white solid (1.28 g, 3.91 mmol, 58.3 %).



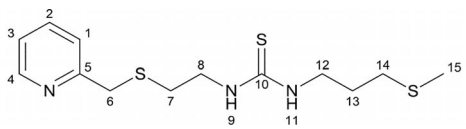
^{1}H NMR (500 MHz, $CDCl_3$, 30 °C, ppm): δ = 1.26 (s, 9 H, H15); 1.92 (tt, 2 H, H3, $^3J_{HH}$ = 7.7 Hz); 2.04 (s, 3 H, H1); 2.53 (t, 2 H, H2, $^3J_{HH}$ = 7.9 Hz); 3.73 (d, 2 H, H4, $^3J_{HH}$ = 5.4 Hz); 6.69 (br. s, 1 H, H5); 7.12 (dd, 1 H, H11 / H12, $^3J_{HH}$ = 8.2 Hz); 7.39 (dd, 1 H, H11 / H12, $^3J_{HH}$ = 8.6 Hz); 7.57 (d, 2 H, H10/H13, $^3J_{HH}$ = 7.3 Hz); 8.47 (br. s, 1H, H7). **^{13}C NMR** (125 MHz, $CDCl_3$, 30 °C, ppm): δ = 15.5 (CH_3, C1); 27.7 (CH_2, C3); 30.8 (CH_3, C 15; 31.8 (CH_2, C2); 44.4 (CH_2, C4); 48.0 (C_q, C14); 122.7 (CH, C10 / C13); 125.1 (CH, C11 / C12); 130.5 (CH, C11 / C12); 139.9 (CH, C10 / C13); 140.9 (C_q, C8, C9); 180.2 (C_q, C6). **IR** (ATR): $\tilde{\nu}$ = 648 (w), 692 (s), 719 (w), 737 (m), 752 (s), 858 (vw), 870 (w), 933 (vw), 956 (w), 1039 (m), 1103 (w), 1126 (w), 1145 (m), 1165 (s), 1207 (m), 1224 (m), 1263 (s), 1294 (s), 1315 (s), 1336 (m), 1359 (w), 1379 (vw), 1443 (m), 1456 (m, NH, δ), 1471 (w), 1531 (vs, CN, ν), 1583 (m), 2860 (vw), 2914 (w), 2937 (vw), 2974 (w), 3120 (vw), 3191 (w), 3246 (w) cm^{-1}. **MS-ESI**: *m/z* (%) 329.11 [M^+] (40), 182.10 (51) [M^+–PhNCS]; 126.03 (100) [M^+–*t*Bu, PhNCS]. **CHN**: calcd. 54.8 % C, 8.5 % N, 7.4 % H, 29.3 % S; found: 55.0 % C, 8.6 % N, 7.2 % H, 29.1 % S.

Synthesis of 1-Phenyl-3-[2-((pyridin-2-ylmethyl)thio)phenyl]-thiourea (5): Amine **A3**[50] (2.59 g, 12 mmol) and phenylisothiocyanate (1.3 mL, 10.9 mmol) were added to anhydrous acetonitrile (120 mL). After 3 h stirring at room temperature the solvent was removed in vacuo. The residue was a yellow oil. Cold Et_2O was added to the oil and product **5** precipitated as a yellow solid (3.6 g, 10.21 mmol, 93.7 %).



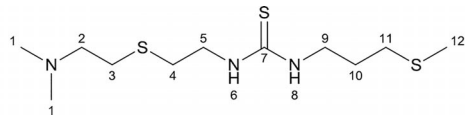
^{1}H NMR (500 MHz, $CDCl_3$, 30 °C, ppm): δ = 4.04 (s, 2 H, H6); 7.02–7.13 (m, 2 H, H1–3/ H8–11/ H17–19); 7.21–7.44 (m, 8 H, H1–3/ H8–11/ H17–19); 7.48–7.52 (m, 1 H, H1–3/ H8–11/ H17–19); 8.03 (d, 1 H, H1–3/ H8–11/ H17–19); 8.35 (dd, 1 H, H4); 8.76 (br. s, 1 H, H15); 8.85 (br. s, 1 H, H13). **^{13}C NMR** (125 MHz, $CDCl_3$, 30 °C, ppm): δ = 41.3 (CH_2, C4); 122.2 (CH, C1–3/ C8–11/ C17–19); 123.2 (CH, C1–3/ C8–11/ C17–19); 125.4 (CH, C1–3/ C8–11/ C17–19); 125.8 (CH, C1–3/ C8–11/ C17–19); 126.3 (CH, C1–3/ C8–11/ C17–19); 127.0 (CH, C1–3/ C8–11/ C17–19); 128.7 (C_q, C7); 128.8 (CH, C1–3/ C8–11/ C17–19); 129.6 (CH, C1–3/ C8–11/ C17–19); 134.4 (CH, C1–3/ C8–11/ C17–19); 136.8 (CH, C1–3/ C8–11/ C17–19); 137.2 (C_q, C16); 139.6 (C_q, C12); 149.1 (CH, C4), 156.9 (C_q, C5); 179.9 (C_q, C14). **IR** (ATR): $\tilde{\nu}$ = 613 (w), 627 (m), 656 (m), 669 (m), 696 (s), 719 (s), 742 (vs), 758 (m), 783 (vw), 796 (w), 841 (w), 864 (vw), 900 (vw), 926 (m), 943 (vw), 960 (vw), 979 (w), 995 (w), 1022 (m), 1035 (w), 1049 (w), 1070 (m), 1130 (m), 1153 (m), 1172 (m), 1199 (m), 1222 (s), 1247 (m), 1272 (m), 1292 (m), 1311 (m), 1357 (m), 1433 (s), 1446 (s), 1468 (s), 1498 (s, NH, δ), 1531 (s, CN, ν), 1568 (m), 1591 (m), 1624 (m), 2858 (vw), 2893 (vw), 2937 (w), 2958 (w), 3002 (w), 3057 (w), 3103 (vw), 3132 (w), 3193 (m), 3244 (w) cm^{-1}. **MS-ESI**: *m/z* (%) 352.09 [M$^+$] (70), 259.03 (51) [M$^+$–PhNH$_2$]; 227.06 (100) [M$^+$–Py-MeSH]. **CHN**: calcd. 64.9% C, 12.0% N, 4.9% H, 18.3% S; found: 65.6% C, 11.9% N, 5.0% H, 18.4% S.

Synthesis of 1-[3-(Methylthio)propyl]-3-[2-((pyridin-2-ylmethyl)-thio)-ethyl]thiourea (6): Amine **A4**[50] (2.03 g, 12 mmol) and 3-(methylthio)propylisothiocyanate (1.45 mL, 10.9 mmol) were added to anhydrous acetonitrile (120 mL). After 3 h stirring at room temperature the solvent was removed in vacuo. The residue was a pale yellow oil. The crude product was dissolved in a few mL of MeOH and cooled down in an ice bath. The product **6** precipitated as a yellow solid and was washed with *n*-pentane (2.07 g, 6.56 mmol, 60.2%).



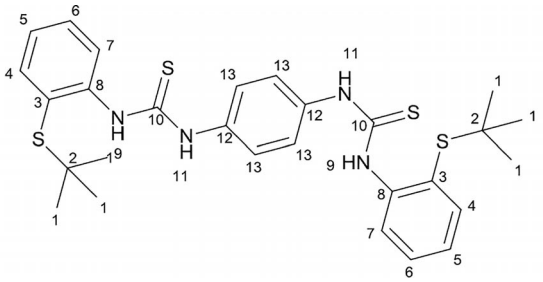
^{1}H NMR (500 MHz, $CDCl_3$, 30 °C, ppm): δ = 1.86 (tt, 2 H, H13, $^3J_{HH}$ = 6.9 Hz); 2.03 (s, 3 H, H15); 2.51 (t, 2 H, H14, $^3J_{HH}$ = 7.5 Hz); 2.71 (t, 2 H, H7, $^3J_{HH}$ = 7.5 Hz); 3.54 (s, 2 H, H12); 3.69 (s, 2 H, H8); 3.82 (s, 2 H, H6); 6.75 (br. s, 1 H, H11); 7.09 (br. s, 1 H, H9); 7.16 (ddd, 1 H, H3, $^3J_{HH}$ = 7.6, $^4J_{HH}$ = 0.9 Hz); 7.31 (d, 1 H, H1, $^3J_{HH}$ = 7.9 Hz); 7.64 (ddd, 1 H, H2, $^3J_{HH}$ = 7.8, $^4J_{HH}$ = 1.7 Hz); 8.47 (m, 1 H, H4). **^{13}C NMR** (125 MHz, $CDCl_3$, 30 °C, ppm): δ = 15.5 (CH_3, C15); 28.2 (CH_2, C13); 31.1 (CH_2, C7); 31.6 (CH_2, C14); 37.5 (CH_2, C6); 44.1 (CH_2, C8, C12); 122.3 (CH, C3); 123.5 (CH, C1); 137.3 (CH, C2); 149.1 (CH, C4); 158.6 (C_q, C5); 182.0 (C_q, C10). **IR** (ATR): $\tilde{\nu}$ = 628 (m), 686 (s), 713 (m), 734 (s), 748 (s), 765 (m), 788 (m), 831 (w), 864 (w), 898 (w), 962 (m), 991 (m), 1003 (m), 1051 (m), 1066 (m), 1086 (m), 1136 (m), 1147 (m), 1176 (m), 1192 (m), 1213 (m), 1224 (m), 1265 (m), 1280 (s), 1319 (s), 1342 (m), 1369 (m), 1412 (m), 1435 (m), 1450 (m), 1473 (m, NH, δ), 1525 (vs, CN, ν), 1568 (m), 1589 (m), 2860 (w), 2916 (m), 2929 (m), 2964 (w), 3022 (m), 3207 (m), 3325 (m) cm^{-1}. **ESI-MS** (*m/z* (%)): 316.09 (100) [M$^+$]; 223.04 (61) [M$^+$– Py-CH$_3$]; 211.03 (57) [M$^+$–NH-(CH$_2$)$_3$SCH$_3$]; 124.02 (24) [M$^+$- (CH$_2$)$_2$-NHCSNH-(CH$_2$)$_3$SCH$_3$)]. **CHN**: calcd. 49.5% C, 13.3% N, 6.7% H, 30.5% S; found: 49.3% C, 13.3% N, 6.4% H, 31.4% S.

Synthesis of 1-[2-((2-(Dimethylamino)ethyl)thio)ethyl]-3-[3-(methyl-thio)propyl]thiourea (7): Amine **A2**[49] (1.77 g, 12 mmol) and 3-(methylthio)propylisothiocyanate (1.45 mL, 10.9 mmol) were added to anhydrous acetonitrile (120 mL). After 3 h stirring at room temperature the solvent was removed in vacuo. The residue was a brown oil that was poured into water (20 mL) and extracted with DCM (3 × 30 mL). The organic layer was dried over Na_2SO_4, evaporation of the solvent and washing with Et_2O resulted in the product as brown oil **7** (1.40 g, 9.42 mmol, 86.5%).



^{1}H NMR (500 MHz, $CDCl_3$, 30 °C, ppm): δ = 1.82 (tt, 2 H, H10, $^3J_{HH}$ = 6.8 Hz); 2.02 (s, 3 H, H12); 2.18 (s, 6 H, H1); 2.46 (m, 2 H, H2); 2.49 (t, 2 H, H3 / H11, $^3J_{HH}$ = 6.9 Hz); 2.59 (m, 2 H, H4), 2.70 (t, 2 H, H3 / H11, $^3J_{HH}$ = 7.1 Hz); 3.64 (m, 4 H, H5, H9); 6.68 (br. s, 1 H, H6 / H8); 6.80 (br. s, 1 H, H6 / H8). **^{13}C NMR** (125 MHz, $CDCl_3$, 30 °C, ppm): δ = 15.4 (CH_3, C12); 28.1 (CH_2, C10); 29.6 (CH_2, C4); 31.5 (CH_2, C3, C11); 43.8 (CH_2, C5, C9); 45.2 (CH_3, C1); 59.0 (CH_2, C2); 182.1 (C_q, C7). **IR** (ATR): $\tilde{\nu}$ = 665 (w), 692 (w), 735 (w), 767 (w), 850 (w), 896 (vw), 958 (w), 1007 (m), 1039 (m), 1053 (m), 1097 (m), 1132 (m), 1170 (m), 1226 (m), 1267 (s), 1292 (m), 1342 (m), 1383 (m), 1435 (m), 1460 (m, NH, δ), 1543 (vs, CN, ν), 2102 (vw), 2179 (vw), 2362 (vw), 2721 (w), 2779 (m), 2821 (m), 2860 (w), 2919 (m), 3062 (vw), 3255 (m) cm^{-1}. **ESI-MS** (*m/z* (%)): 296.12 (63) [M$^+$]; 191.06 (100) [M$^+$–NH-(CH$_2$)$_3$SCH$_3$)]]; 223.03 (41) [M$^+$–(CH$_2$)$_2$N(CH$_3$)$_2$]; 143.06 (37). **CHN**: calcd. 44.7% C, 14.2% N, 8.5% H, 32.6% S; found: 43.6% C, 13.4% N, 8.2% H, 32.2% S.

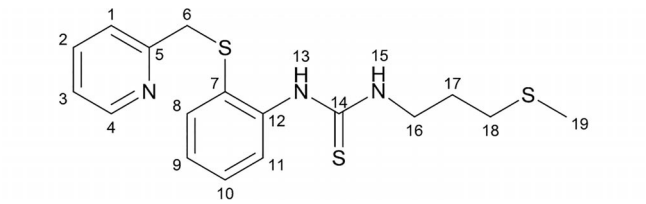
Synthesis of 1,1′-(1,4-Phenylene)bis[3-(2-(*tert*-butylthio)phenyl)-thio-urea] (8): Amine **A1**[48] (1.80 g, 12 mmol) and 1,4-diisothiocyanatobenzene (0.86 g, 4.5 mmol) were added to anhydrous acetonitrile (100 mL). After 3 h stirring at room temperature the solvent was removed in vacuo. The residue was a pale yellow solid **8** (1.70 g, 3.06 mmol, 68.1%).



^{1}H NMR (500 MHz, [D$_8$]THF, 30 °C, ppm): δ = 1.23 (s, 18 H, H1); 7.08 (ddd, 1 H, H5, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 1.1 Hz); 7.39 (dd, 2 H, H7, $^3J_{HH}$ = 7.8, $^4J_{HH}$ = 1.5 Hz); 7.52 (dd, 2 H, H4, $^3J_{HH}$ = 7.4, $^4J_{HH}$ = 1.4 Hz); 7.60 (s, 4 H, H13); 8.76 (m, 2 H, H6); 9.22 (br. s, 2 H, H11); 9.53 (br. s, 2 H, H9). **^{13}C NMR** (125 MHz, [D$_8$]THF, 30 °C, ppm): δ = 30.1 (CH_3, C1); 47.3 (C_q, C2); 122.9 (C_q, C3); 123.4 (CH, C5); 123.4 (CH, C6); 125.6 (CH, C13); 129.2 (CH, C7); 136.1 (C_q, C12); 138.4 (CH, C4); 143.0 (C_q, C8); 179.1 (C_q, C10). **IR** (ATR): $\tilde{\nu}$ = 624 (m), 651 (m), 690 (m), 740 (m), 750 (m), 762 (w), 798, 624 (w), 651 (w), 690 (w), 740 (w), 750 (s), 762 (m), 798 (w), 854 (w), 868 (vw), 937 (w), 953 (vw), 979 (vw), 1022 (m), 1033 (w), 1059 (w), 1093 (m), 1117 (m), 1165 (s), 1190 (s), 1215 (m), 1244 (s), 1288 (m), 1362 (s), 1390 (vw), 1435 (m), 1458 (m), 1469 (m), 1506 (vs, NH, δ), 1533 (s, CN, ν), 1573 (m), 2860 (vw), 2898 (vw), 2922 (w), 2949 (w), 2960 (m), 3130 (m), 3306 (vw) cm^{-1}. **MS-ESI**: *m/z* (%) 555.17 (58) [M$^+$]; 465.12 (17) [M$^+$–*t*BuSH];259.03 (100); 195.05 (18) [*t*BuSPhNHCH$_3$];

227.06 (53) [*t*BuSPhNHCH$_3$SH]. **CHN**: calcd. 60.6 % C, 10.10 % N, 6.2 % H, 23.1 % S; found: 60.5 % C, 9.9 % N, 6.2 % H, 22.5 % S.

Synthesis of 1-[3-(Methylthio)propyl]-3-[2-((pyridin-2-ylmethyl)-thio)-phenyl]thiourea (9): Amine **A3**[50] (2.59 g, 12 mmol) and 3-(methylthio)propylisothiocyanate (1.45 mL, 10.9 mmol) were added to anhydrous acetonitrile (120 mL). The reaction mixture was stirred overnight at room temperature and the solvent was removed in vacuo. The residue was dissolved in acetone and precipitated with petroleum ether (30–70 °C). The product was a pale yellow solid **9** (2.50 g, 6.89 mmol, 63.3 %).



^{1}H NMR (500 MHz, $CDCl_3$, 30 °C, ppm): δ = 1.88 (tt, 2 H, H17, $^3J_{HH}$ = 7.0 Hz); 1.98 (s, 3 H, H19); 2.49 (t, 2 H, H18, $^3J_{HH}$ = 7.0 Hz); 3.69 (dt, 2 H, H16, $^3J_{HH}$ = 6.2 Hz); 4.11 (s, 2 H, H6); 6.72 (br. t, 1 H, H15, $^3J_{HH}$ = 5.1 Hz); 7.05–7.10 (m, 2 H, H3+11); 7.22–7.24 (m, 2 H, H1+H9; 7.37 (dd, 1 H, H10, $^3J_{HH}$ = 7.8, $^4J_{HH}$ = 1.4 Hz); 7.49 (dd, 1 H, H8, $^3J_{HH}$ = 7.7, $^4J_{HH}$ = 1.8 Hz); 7.56 (dd, 1 H, H2, $^3J_{HH}$ = 7.8, $^4J_{HH}$ = 1.7 Hz); 8.46 (dd, 1 H, H4, $^3J_{HH}$ = 4.9, $^4J_{HH}$ = 0.9 Hz), 8.56 (br. s, 1 H, H13). **^{13}C NMR** (125 MHz, $CDCl_3$, 30 °C, ppm): δ = 15.4 (CH_3, C19); 27.9 (CH_2, C17); 31.8 (CH_2, C18); 40.5 (CH_2, C6); 44.4 (CH_2, C16); 122.3 (CH, C11); 123.5 (CH, C1/C9); 126.4 (CH, C8+12); 127.5 (CH, C3); 128.5 (CH, C1/C9); 130.2 (C_q, C7/12); 133.3 (CH, C10); 136.4 (C_q, C7/12); 136.9 (CH, C2); 149.4 (CH, C4); 156.9 (C_q, C5); 181.1 (C_q, C14). **IR** (ATR): $\tilde{\nu}$ = 607 (m), 632 (s), 685 (w), 713 (m), 723 (m), 742 (vs), 762 (w), 785 (w), 812 (m), 843 (w), 885 (vw), 903 (w), 962 (w), 989 (w), 1003 (m), 1024 (m), 1037 (m), 1060 (m), 1085 (m), 1107 (m), 1134 (m), 1151 (m), 1166 (m), 1193 (m), 1207 (m), 1244 (vs), 1273 (m), 1288 (m), 1303 (m), 1315 (m), 1357 (m), 1390 (m), 1421 (m), 1432 (s), 1465 (m), 1477 (m, NH, δ), 1510 (vs, CN, ν), 1540 (m), 1569 (m), 1589 (m), 2912 (m), 2937 (m), 2952 (m), 2983 (m), 3051 (m), 3128 (m) cm^{-1}. **MS-ESI**: *m/z* (%) 364.09 (28) [M$^+$]; 265.14 (100); 259.03 (67) [M$^+$–$NH_2(CH_2)_3SCH_3$]. **CHN**: calcd. 56.2 % C, 11.6 % N, 5.8 % H, 26.5 % S; found: 56.0 % C, 11.5 % N, 5.8 % H, 26.9 % S.

Supporting Information (see footnote on the first page of this article): Structural results of the DFT calculations, NBO charges, and NMR spectra.

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