Steric Control over Hydrogen Bonding in Crystalline Organic Solids: A Structural Study of *N,N′*-Dialkylthioureas

Radu Custelcean,* Maryna G. Gorbunova, and Peter V. Bonnesen[a]

Abstract: Hydrogen bonding in crystalline *N,N′*-dialkylthioureas was examined with the help of single-crystal X-ray diffraction, DFT calculations, and Cambridge Structural Database (CSD) analysis. A CSD survey indicated that unlike the related urea derivatives, which persistently self-assemble into one-dimensional hydrogen-bonded chains, the analogous thioureas can form two different hydrogen-bonding motifs in the solid state: chains, structurally similar with those found in ureas, and dimers, that further associate into hydrogen-bonded layers. The formation of one motif or another can be manipulated by the bulkiness of the organic substituents on the thiourea group, which provides a clear example of steric control over the hydrogen bonding arrangement in crystalline organic solids.

Keywords: crystal engineering · hydrogen bonds · noncovalent interactions · steric control · thiourea

Introduction

The design of molecular crystals remains an extremely challenging problem despite sustained efforts from numerous groups in the last decade.[1] While in most cases it is still impossible to predict with accuracy the exact crystal structure of a given molecule,[2] a relatively successful approach for the design of crystalline solids with targeted architectures is to employ highly directional and persistent noncovalent interactions such as hydrogen bonds,[3] coordinative bonds,[4] or charge transfer interactions,[5] that are strong enough to control the crystal packing. For example, by employing hydrogen-bonding motifs that are known to form with high probability in various environments,[6] one can build with confidence new materials with desired structure and function. However, there is a very limited number of truly reliable supramolecular motifs available, as the vast majority of functional groups may assume alternative motifs in the solid state, with comparable probability of formation. This being the case, there is a clear need for additional means that one can use to control the assembly of molecular solids. Steric control is an effective tool frequently employed to influence the course of reactions and the product distribution in organic synthesis.[7] In direct contrast, its use as a control element in crystal engineering is far less explored. Most of the examples reported to date focused on steric effects on metal coordination,[8] or on the secondary structures of coordination[9] or hydrogen-bonded solids.[10] Here we illustrate a clear example of steric control over the primary hydrogen bonding structures in crystalline *N,N′*-dialkylthioureas (Scheme 1).[11] We show that the steric bulk of the organic substituents on the thiourea group can be exploited to direct the formation of either chains or dimers, the two hydrogen bonding arrangements typically observed in this class of compounds.[12]

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Results and Discussion

Despite their similar molecular structures, *N,N′*-disubstituted thioureas are significantly different from the analogous urea derivatives with regard to conformer distribution and supramolecular association. While *N,N′*-disubstituted ureas are present predominantly in the *trans-trans* conformation,[13] the corresponding thiourea derivatives typically exist in solution as mixtures of three rotamers: *trans–trans*, *trans–cis*, and *cis–cis* (Scheme 2).[14]

We performed DFT calculations[15] at the B3LYP/6–31G* level,[16] which confirmed the conformational flexibility of various simple *N,N′*-dialkylthioureas (Table 1). The *trans–cis* rotamer was found to be the lowest energy conformation for all compounds studied, with the *trans–trans* rotamer, however, being only slightly higher in energy. The *cis–cis* rotamer,

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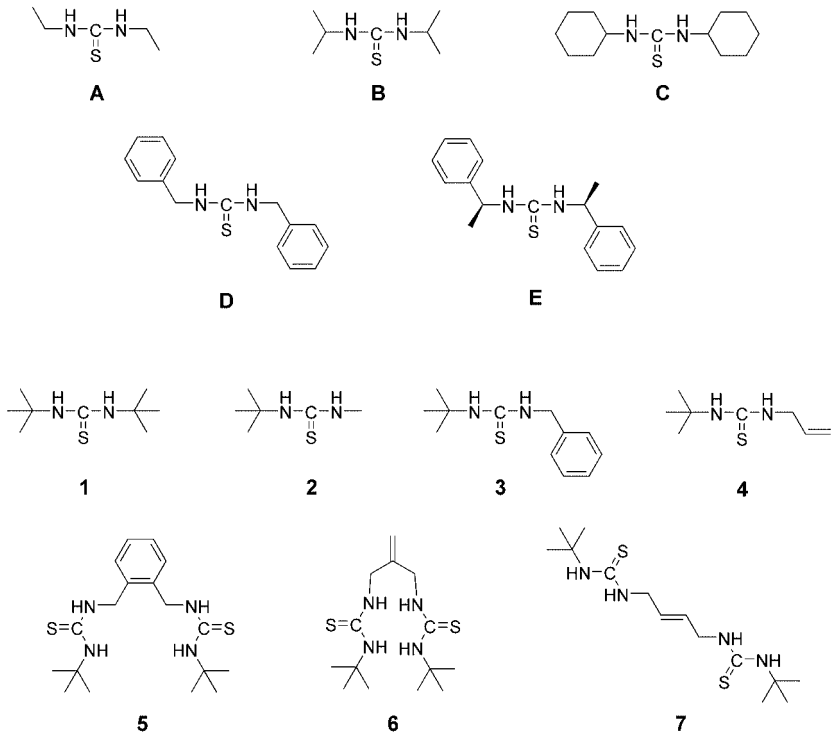
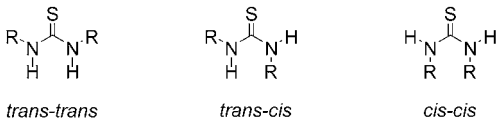


Scheme 1. *N,N′*-Dialkylthioureas considered in this study. Compounds **A**–**E** were retrieved from CSD. Compounds **1**–**7** were structurally characterized as part of this study.



Scheme 2. Observed rotamers of *N,N′*-disubstituted thioureas (defined based on the HNCS dihedral angle).

Table 1. Relative energies (kcal mol^{-1}) of the three rotamers of various *N,N′*-dialkylthioureas (R−NH−C(=S)NH−R), calculated with DFT at the B3LYP/6–31G* level.

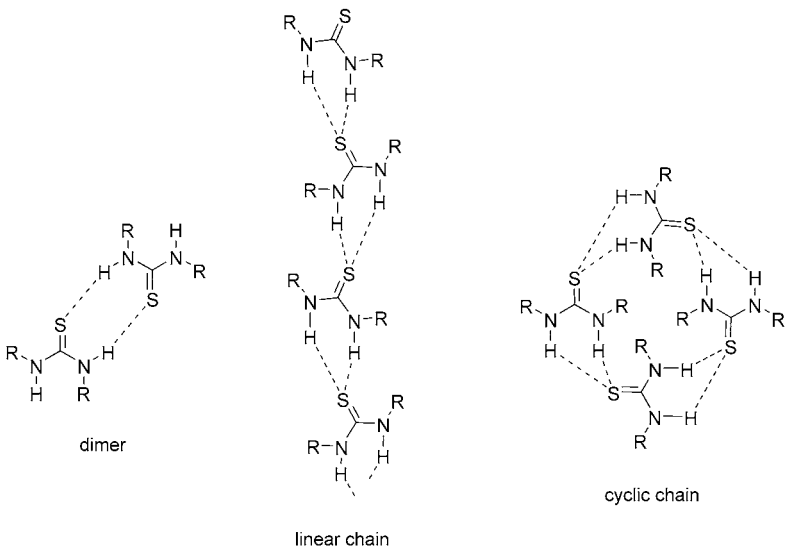
R	*trans–cis*	*trans–trans*	*cis–cis*
Me	0	1.0	5.7
Et	0	0.7	3.9
*i*Pr	0	0.1	4.4
*t*Bu	0	1.4	9.6

on the other hand, was found significantly higher in energy in all cases.

The small energy difference between the *trans–cis* and *trans–trans* rotamers is also reflected in the different self-association behavior of *N,N′*-dialkylthioureas in the solid state, compared to that of analogous ureas. A Cambridge Structural Database survey (CSD, November 03)[17] revealed that *N,N′*-disubstituted thioureas can form two main hydrogen-bonding arrangements in the solid state, depending on the conformation in which the thiourea group is present: the *trans–cis* rotamer forms dimers, whereas the *trans–trans* rotamer forms chains (linear or cyclic) (Scheme 3). The dimers are typically centrosymmetric, whereas the chains are characteristically corrugated, due to the oblique orientation of adjacent *trans-trans* thioureas. Of the total of 23 disubstituted thioureas found in the CSD (only structures with no competing hydrogen-bond donors or acceptors were considered), 12 form dimers and 10 form chains, which correspond to probabilities of formation[6] of 52% and 43%. In addition, one isolated example of *cis–cis* thiourea was identified, which formed hydrogen-bonded tapes, as found in cyclic thioureas.[18] For comparison, *N,N′*-disubstituted ureas form exclusively chains in the solid state.[19]

Since *N,N′*-dialkylthioureas have no preponderant low-energy conformation, we argued that other factors might play decisive roles in determining their hydrogen bonding patterns in the solid state. In an attempt to identify such factors, we analyzed in more detail the crystal structures of the five symmetrical dialkylthioureas found in the CSD: diethyl- (**A**), diisopropyl- (**B**), dicyclohexyl- (**C**), dibenzyl- (**D**), and di-(*S*)-(−)-α-methylbenzylthiourea (**E**). Table 2 summarizes their hydrogen bonding parameters. As shown in Figure 1, compounds **A**–**D** assume the *trans–cis* conformation, and consequently form the dimer motif. Moreover, despite significant variation in the organic groups, they all form similar extended layered networks by further hydrogen bonding between the S and the *trans* H atoms (Figure 2), suggesting that this hydrogen-bonding arrangement is a persistent, highly preferred motif in this homologous series.

In direct contrast to the other members of the series, compound **E** is found in the *trans–trans* conformation in the solid state and forms a hydrogen-bonded helical chain about the 3_1 crystallographic screw axis (Figure 1). DFT calculations indicated that **E**, like other *N,N′*-dialkylthioureas, has no strongly preferred conformational minimum in the gas phase. This suggests that other factors must be responsible for the formation of the alternative chain motif in this particular structure. Examination of the molecular structures of compounds **A**–**E** reveals that of the five compounds, **E** is the most sterically crowded around the NH proton donor groups. Figure 3 depicts the space-filling molecular model of the *trans–cis* rotamer of **E**, optimized at the B3LYP/6–31G* level, which shows that the *trans* NH becomes inaccessible for hydrogen bond formation due to steric congestion from the Me and Ph groups. With no possibility to form the pre-



Scheme 3. Hydrogen-bonding motifs typically observed in *N,N′*-disubstituted thioureas in the solid state.

Table 2. Hydrogen bonding parameters (Å, °) for **A**–**E.**

Compound	*d*(N···S) *cis*/*trans*	*d*(N–H) *cis*/*trans*	*d*(H···S) *cis*/*trans*	<NHS *cis*/*trans*
A	3.458/3.506	0.720/0.821	2.745/2.714	170.3/162.5
B	3.447/3.619	0.740/0.765	2.723/2.891	166.6/159.8
C	3.653/3.753	0.762/0.778	2.920/3.005	162.1/161.8
D	3.498/3.703	0.842/0.830	2.722/3.022	154.0/140.8
E	–/3.411; 3.545	–/0.890; 0.888	–/2.531; 2.708	–/170.2; 157.5

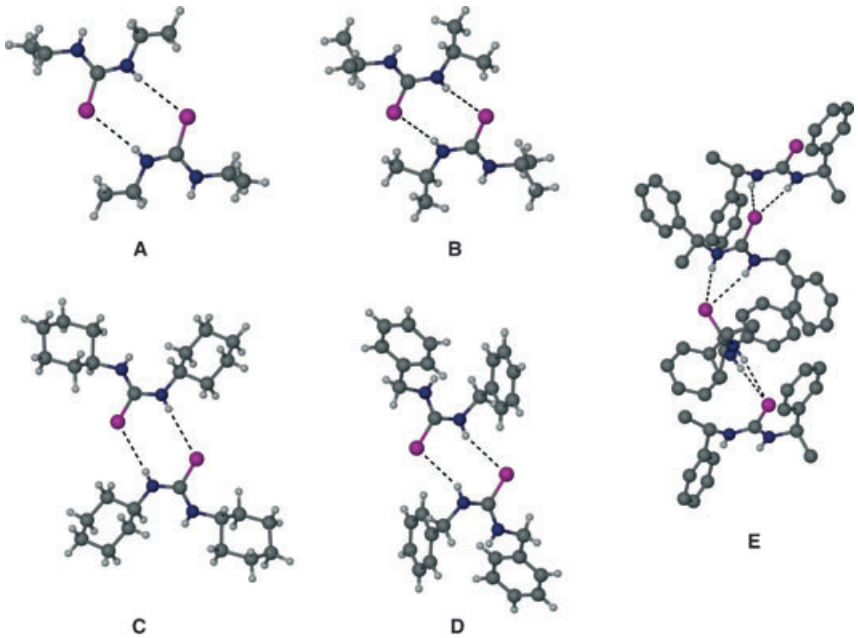


Figure 1. Hydrogen bonding structures in *N,N′*-dialkylthioureas **A**–**E**.

ferred layered hydrogen-bonded network like the other members of the series, **E** is apparently forced to adopt the alternative chain motif.

That the steric bulk of the organic substituents influences the hydrogen bonding of the *trans* NH proton is also indicated by the trend observed in the *trans* H···S intermolecular distances in the series, which monotonically increase as the steric bulk of the organic group increases when going from **A** to **D** (Table 2). The N···S distance in **D** is, however, a little shorter than the corresponding distance in **C**, but that is apparently a result of the significantly sharper NH···S angle observed in **D**, which is another sign of hydrogen bonding weakening.

To further test the steric control hypothesis, we synthesized *N,N′*-di(*t*Bu)thiourea (**1**), and determined its crystal structure. Molecular modeling indicated that, like in **E**, the *trans* NH proton in the *trans–cis* rotamer of **1** would be inaccessible for hydrogen bonding (Figure 4a). This could tip the balance towards the *trans–trans* rotamer and its corresponding chain motif. Figure 4b,c shows that, indeed, **1** adopts the anticipated *trans–trans* conformation and consequently forms hydrogen-bonded chains in the crystalline state. Neighboring thioureas within the chain are twisted relative to each other by 91.3° to minimize intermolecular steric repulsions between the *t*Bu groups. This allows the formation of relatively short hydrogen bonds with non-identical N···S intermolecular distances of 3.469 and 3.503 Å, H···S contact distances of 2.617 and 2.650 Å, and close to linear NH···S angles of 166.1 and 166.9°, respectively.

The asymmetrical *N*-Me-*N′*-*t*Bu-thiourea (**2**), *N*-benzyl-*N′*-*t*Bu-thiourea (**3**), and *N*-allyl-*N′*-*t*Bu-thiourea (**4**) were synthesized and structurally analyzed by single-crystal X-ray diffraction to explore the effects of subtle variations in the steric bulk of the organic substituents on the hydrogen bonding pattern in this class of

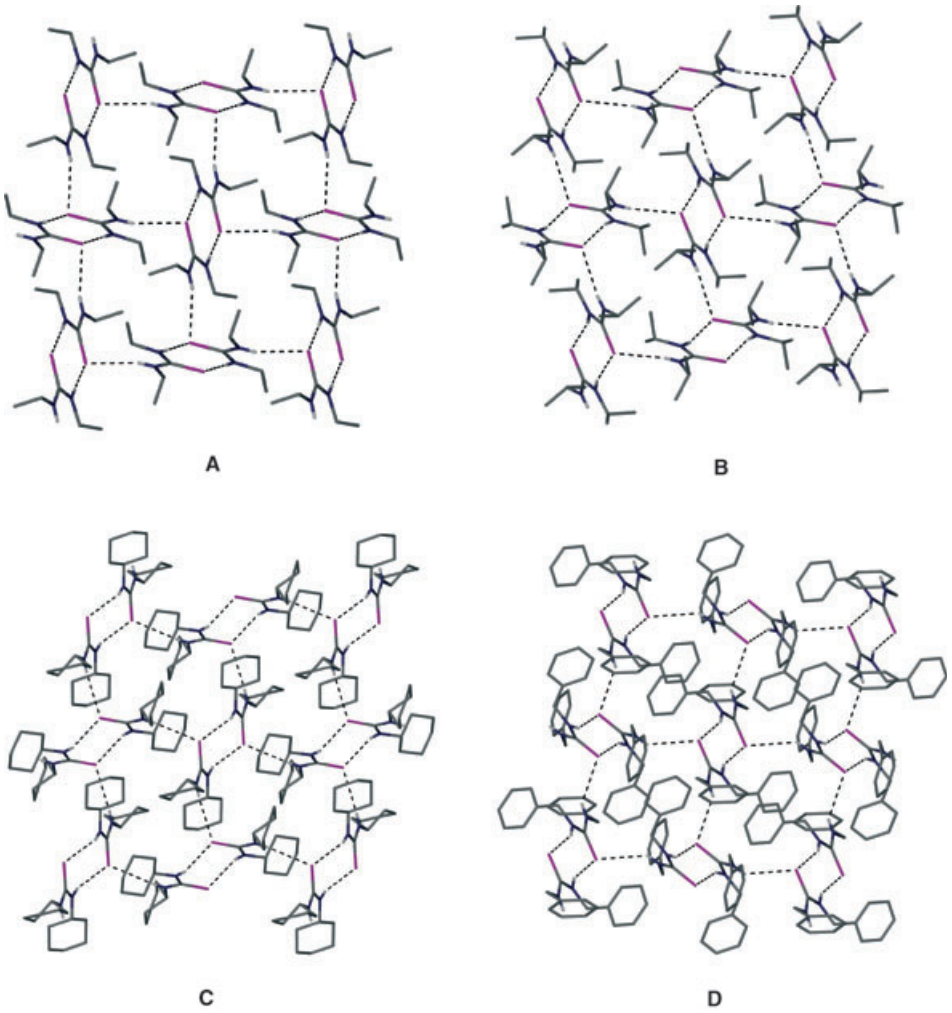


Figure 2. Hydrogen-bonded layers in crystals of *N,N′*-dialkylthioureas **A**–**D**.

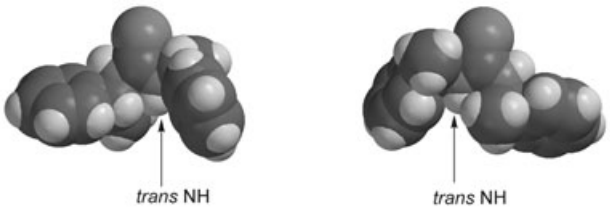


Figure 3. Two views of the molecular model of the *trans–cis* rotamer of **E**.

compounds. DFT calculations showed that, as in the analogous symmetrical thioureas, the *trans–cis* rotamers of **2**–**4** are slightly favored relative to the *trans-trans* rotamers, by 1.2, 1.2, and 1.1 kcal mol^{-1}, respectively. Figure 5 depicts the space-filling models of the *trans–cis* rotamers of **2**–**4**.

Close examination of the molecular model showed that the Me group in **2** is not sufficiently bulky to completely block the access of the hydrogen bond acceptor to the *trans* NH proton, as observed in **E** and **1**. Therefore, the formation of the hydrogen-bonded layers of dimers becomes again a viable option, and indeed, crystal structure analysis showed that **2** exhibits this motif in the solid state (Figure 6), like the symmetrical thioureas **A**–**D**. The hydrogen-bonding parameters in **2** are similar with those found in **A**–**D**: d(N···S) = 3.521 (*cis*), 3.512 Å (*trans*); d(H···S) = 2.775 (*cis*), 2.812 Å (*trans*); < NH···S = 169.2° (*cis*), 146.5° (*trans*).

The larger benzyl and allyl groups in **3** and **4**, on the other hand, are more effective in sterically blocking the *trans* NH proton donors, as shown by the molecular models in Figure 5, thus preventing the formation of the hydrogen bonding layers. Instead, the thiourea groups are forced again to adopt the slightly less favorable *trans-trans* conformation and the alternative chain motif, as illustrated in Figure 7. The thiourea groups are twisted relative to each other along the chain, by 106.0° and 68.2° in **3** and **4**, respectively. The chains are further stabilized by CH···π interactions between the benzyl or allyl

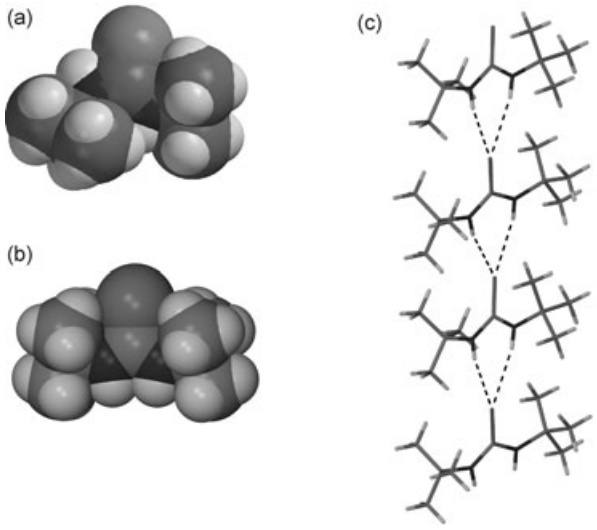


Figure 4. Molecular and crystal structure of **1**. a) Molecular model of the lowest energy *trans–cis* rotamer. b) Observed *trans–trans* rotamer in the crystal. c) Hydrogen-bonded chain in the crystal.

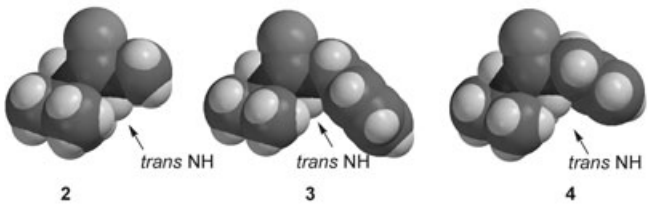


Figure 5. Molecular models of the *trans-cis* rotamers of **2**–**4**.

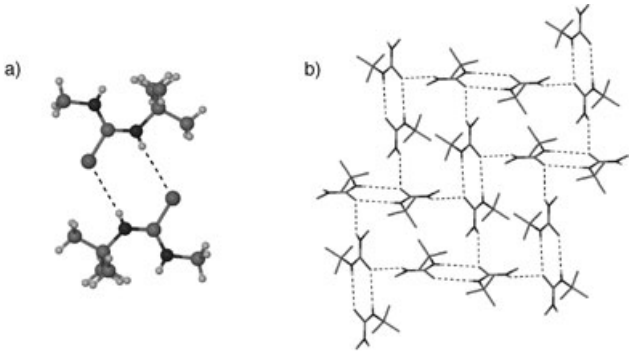


Figure 6. Crystal structure of **2**. a) Hydrogen-bonded dimer. b) Association of dimers into extended hydrogen-bonded layers.

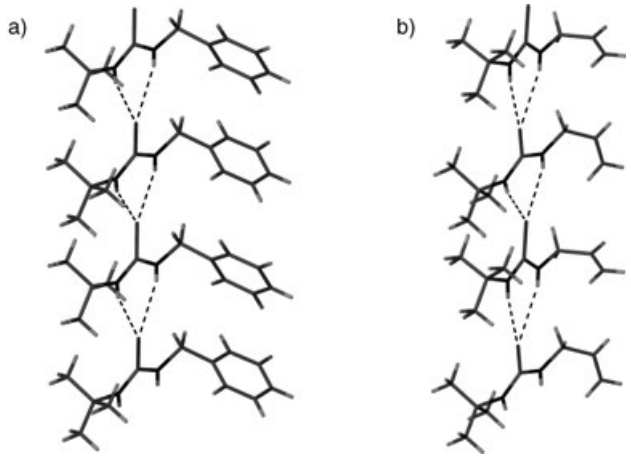


Figure 7. Hydrogen-bonded chains in crystals of **3** (a), and **4** (b).

groups. The hydrogen bonding parameters in **3** and **4** are comparable with those found in **1**. Thus, for **3**, the two non-identical N···S intermolecular separations measure 3.393 and 3.493 Å, while the corresponding H···S contact distances are 2.691 and 2.717 Å, and the NH···S angles are 162.7 and 163.5°, respectively. Similarly, the corresponding geometrical parameters for **4** are: $d(\mathrm{N\cdots S}) = 3.405$ and 3.531 Å; $d(\mathrm{H\cdots S}) = 2.592$ and 2.809 Å; $< \mathrm{NH\cdots S} = 169.3°$ and 158.4°.

The examples presented here demonstrated that by fine-tuning the bulkiness of the organic substituents on the thiourea group, one can predictably switch between the dimer and the chain hydrogen bonding motifs. Now that we have learned how to sterically control the hydrogen bonding connectivity in *N,N′*-dialkylthioureas, we can apply this knowledge to the rational construction of more complex structures. Although initially the thiourea group did not appear as a very reliable building block for crystal design due to its tendency to form alternative hydrogen bonding motifs, the ability to impose one of the two motifs by exercising steric control through appropriate substitution makes now the *N,N′*-dialkylthiourea units more appealing to the crystal engineer. For instance, by employing the *t*Bu substituent as a terminal group, and the benzyl or allyl substituents as linkers, one can build more elaborate structures based on the chain motif. This approach is demonstrated by the bis(thioureas) **5**–**7**, which were synthesized and structurally analyzed in our laboratory.

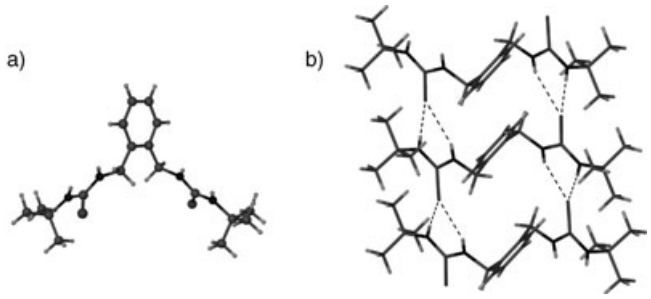


Figure 8. Crystal structure of **5**. a) Molecular structure found in the crystal. b) Packing into hydrogen-bonded ribbons.

The crystal structure of bis(thiourea) **5**, containing the *o*-xylyl group as a linker, is illustrated in Figure 8. The molecules sit on the C_2 crystallographic symmetry axis, with the two thiourea groups pointing to opposite directions. Like in the analogous mono-thiourea **3**, the *t*Bu-substituted thiourea groups self-assemble into hydrogen-bonded chains, which are now connected into ribbons by the *o*-xylyl linker, with the chains assuming an antiparallel orientation in each ribbon. Neighboring thiourea groups within each chain are twisted relative to each other by 86.4°. The measured hydrogen bonding parameters are: $d(\mathrm{N\cdots S}) = 3.385$ and 3.410 Å; $d(\mathrm{H\cdots S}) = 2.620$ and 2.687 Å; $< \mathrm{NH\cdots S} = 159.1°$ and 164.8°.

Similar C_2-symmetric ribbons composed of antiparallel hydrogen-bonded chains were observed in the crystal structure of bis(thiourea) **6**, in which the two thiourea groups are connected by the methallyl linker (Figure 9). The dihedral

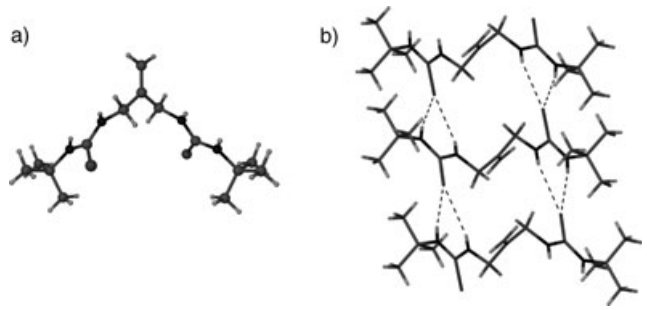


Figure 9. Crystal structure of **6**. a) Molecular structure found in the crystal. b) Packing into hydrogen-bonded ribbons.

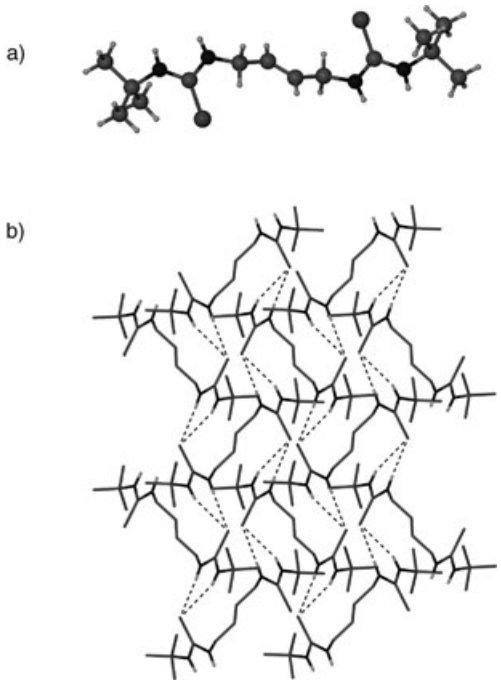


Figure 10. Crystal structure of **7**. a) Molecular structure found in the crystal. b) Packing into hydrogen-bonded layers.

angle between neighboring thioureas along the chain was found to be 72.0° in this structure. The hydrogen bonding parameters fall in the same range as those found in the previous compounds: d(N···S) = 3.422 and 3.433 Å; d(H···S) = 2.642 and 2.731 Å; < NH···S = 167.8 and 158.6°.

When the isomeric *trans*-2-butenyl linker was used, the resulting bis(thiourea) **7** exhibited a centrosymmetric structure in the crystalline state, as illustrated in Figure 10. Intermolecular hydrogen bonding between thiourea groups resulted in the formation of the anticipated chains, in which adjacent thioureas are twisted relative to each other by 83.4°. The salient geometrical features of the chains are: d(N···S) = 3.469 and 3.485 Å; d(H···S) = 2.681 and 2.699 Å; < NH···S = 157.8 and 160.0°. The hydrogen-bonded chains are connected orthogonally by the *trans*-2-butenyl linker into extended layers (Figure 10b).

The ribbons and layers displayed by bis(thiourea) compounds **5**–**7** are just a few examples of more complex architectures that can be built from the primary hydrogen-bonded chain structure of *N,N′*-dialkylthioureas. This study demonstrated that, when used under adequate steric control, this motif may be persistent enough to recommend its use in crystal structure design. By employing various polytopic linkers of different shape and symmetry, many novel materials with targeted structures and functions may become accessible.

Conclusion

This study illustrated a clear example of how one can use steric control to manipulate the primary hydrogen bonding structure of crystalline organic solids. We used *N,N′*-dialkylthioureas as our case study; unlike the analogous disubstituted ureas, *N,N′*-dialkylthioureas can form two different hydrogen bonding motifs with completely different connectivity in the solid state: chains, and dimers. While a CSD survey indicated that statistically the two motifs have very similar probabilities of formation, we found by computer modeling and systematic crystal structure analysis that adequate substitution of thiourea with bulky organic groups strongly favors the formation of the chain motif. This observed selectivity is apparently a result of steric control that operates by disrupting the NH···S hydrogen bonding that normally links the dimers into extended layers. As a result, the one-dimensional hydrogen-bonding chain motif is adopted as the next available low-energy alternative. With the competition eliminated, the thiourea chain motif appears now more attractive for crystal structure design, and we demonstrated its potential by the synthesis of more elaborate solid-state architectures like ribbons and layers. The significance of this study extends beyond just *N,N′*-dialkylthioureas, as it demonstrates how one can increase the incidence of an otherwise improbable hydrogen bonding motif by using steric control.

Experimental Section

Synthesis: *tert*-Butylisothiocyanate, methylisothiocyanate, *tert*-butylamine, benzylamine, and allylamine were purchased from Aldrich and used as received. *o*-Xylylene diamine,[20] 1,3-diamino-2-methylenepropane,[21] and 1,4-diamino-2,3-*trans*-butene[20] were prepared based on literature procedures.

***N,N′*-di-*tert*-butylthiourea (1)**: *tert*-Butylisothiocyanate (0.35 g, 3 mmol) in CH_2Cl_2 (5 mL) was added over *tert*-butylamine (0.22 g, 3 mmol) in CH_2Cl_2 (5 mL), and the resulting solution was stirred under argon at room temperature for 17 h. Subsequently, the solvent was slowly evaporated and the resulting white solid was washed with hexane. Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a CH_2Cl_2 solution. Yield: 0.16 g (28%); ^{1}H NMR (400.13 MHz, $CDCl_3$, 25°C): δ = 1.46 (s, 18H; $C(CH_3)_3$), 5.74 ppm (br s, 2H; NH); ^{13}C NMR (100.61 MHz, $CDCl_3$, 25°C): δ = 29.3 (CH_3), 53.2 ($C(CH_3)_3$), 180.1 ppm (C=S).

***N*-methyl-*N′*-*tert*-butylthiourea (2)**: Methylisothiocyanate (0.22 g, 3 mmol) in CH_2Cl_2 (5 mL) was added over *tert*-butylamine (0.22 g, 3 mmol) in CH_2Cl_2 (5 mL), and the resulting solution was stirred under argon at room temperature for 17 h. Subsequently, the solvent was slowly evaporated and the resulting white solid was washed with hexane. Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a CH_2Cl_2 solution. Yield: 0.32 g (73%); ^{1}H NMR (400.13 MHz, $CDCl_3$, 25°C): δ = 1.40 (s, 9H; $C(CH_3)_3$), 3.08 (br s, 3H; CH_3), 5.73 (br s, 1H; NH) 5.99 ppm (br s, 1H; NH); ^{13}C NMR (100.61 MHz, $CDCl_3$, 25°C): δ = 29.4 ($C(CH_3)_3$), 32.0 (CH_3), 53.7 ($C(CH_3)_3$), 181.9 ppm (C=S).

***N*-benzyl-*N′*-*tert*-butylthiourea (3)**: *tert*-Butylisothiocyanate (0.5 g, 4.4 mmol) and benzylamine (0.48 g, 4.4 mmol) were dissolved in CH_2Cl_2 (25 mL) and the solution was stirred at room temperature for 4 h. Subsequently, the solvent was removed by rotary evaporation and the resulting solid was washed with cold methanol. Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a methanol solution. Yield quantitative; m.p. 94°C; ^{1}H NMR (400.13 MHz, $CDCl_3$, 25°C): δ = 1.38 (s, 9H; $C(CH_3)_3$), 4.77 (br s, 2H; CH_2), 5.87 (br s, 1H; NH) 6.05 (br s, 1H; NH), 7.29–7.35 ppm (m, 5H, Ph); ^{13}C NMR (100.61 MHz, $CDCl_3$, 25°C): δ = 29.5 (CH_3), 49.7 (CH_2), 52.9 ($C(CH_3)_3$), 127.6 (Ph), 127.8 (Ph),

Table 3. Crystallographic data for **1**–**4**.

	1	**2**	**3**	**4**
formula	$C_9H_{20}N_2S$	$C_6H_{14}N_2S$	$C_{12}H_{18}N_2S$	$C_8H_{16}N_2S$
M	188.33	146.25	222.34	172.29
crystal size [mm]	$0.46\times0.06\times0.04$	$0.27\times0.14\times0.03$	$0.26\times0.13\times0.12$	$0.48\times0.23\times0.02$
crystal system	orthorhombic	monoclinic	orthorhombic	monoclinic
space group	*Pbca*	$P2_1/n$	$Pna2_1$	$P2_1/c$
a [Å]	11.778(5)	9.495(6)	9.078(6)	14.806(8)
b [Å]	10.262(4)	8.702(5)	13.088(9)	7.259(4)
c [Å]	18.601(8)	10.842(7)	10.656(7)	9.777(5)
α [°]	90	90	90	90
β [°]	90	105.592(12)	90	105.595(10)
γ [°]	90	90	90	90
V [Å^3]	2248.4(16)	862.8(9)	1266.2(15)	1012.1(10)
Z	8	4	4	4
T [K]	173(2)	173(2)	173(2)	173(2)
ρ_{calcd} [g cm^{-3}]	1.113	1.126	1.166	1.131
$2\theta_{max}$ [°]	56.74	56.96	57.08	56.76
reflns collected	17824	6144	13527	9507
independent reflns	2805	2160	3131	2512
no parameters	123	94	147	123
R_1, wR_2 ($I>2\sigma(I)$)	0.0410, 0.1052	0.0426, 0.1140	0.0320, 0.0805	0.0454, 0.1187
goodness of fit	1.033	1.050	1.020	1.081
residual electron density [eÅ^{-3}]	0.448	0.333	0.208	0.491

128.9 (Ph), 137.2 (Ph), 181.2 ppm (C=S) ppm; elemental analysis calcd (%) for $C_{12}H_{19}N_2S$ (222.35): C 64.82, H 8.16, N 12.60; found: C 65.05, H 8.22, N 12.75.

***N*-allyl-*N'*-*tert*-butylthiourea (4)**: *tert*-Butylisothiocyanate (0.5 g, 4.4 mmol) and allylamine (0.25 g, 4.4 mmol) were dissolved in CH_2Cl_2 (25 mL) and the solution was stirred at room temperature for 4 h. Subsequently, the solvent was removed by rotary evaporation and the resulting white solid was washed with cold methanol. Single crystals suitable for X-ray diffraction were obtained by slow cooling of a methanol solution. Yield quantitative; m.p. 43 °C; ^{1}H NMR (400.13 MHz, $CDCl_3$, 25 °C): $\delta=$ 1.42 (s, 9H; $C(CH_3)_3$), 4.20 (br s, 2H; CH_2), 5.15–5.35 (m, 2H; $=CH_2$), 5.68 (br s, 1H; NH), 5.85–5.95 (m, 1H; CH), 6.05 ppm (br s, 1H; NH); ^{13}C NMR (100.61 MHz, $CDCl_3$, 25 °C): $\delta=$29.4 (CH_3), 47.9 (CH_2), 52.9 ($C(CH_3)_3$), 117.2 ($CH=CH_2$), 133.5 ($CH=CH_2$), 181.2 ppm (C=S); elemental analysis calcd (%) for $C_9H_{16}N_2S$ (172.29): C 55.77, H 9.36, N 16.26; found; C 55.78, H 9.01, N 16.39.

***o*-Xylylene-bis(*tert*-butyl-thiourea) (5)**: *tert*-Butylisothiocyanate (0.5 g, 4.4 mmol) and *o*-xylylene diamine (0.3 g, 2.2 mmol) were dissolved in CH_2Cl_2 (50 mL) and the solution was stirred at room temperature for 4 h. Subsequently, the solvent was removed by rotary evaporation and the resulting white solid was washed with cold methanol. Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a methanol solution. Yield quantitative; m.p. 190 °C; ^{1}H NMR (400.13 MHz, $CDCl_3$, 25 °C): $\delta=$1.38 (s, 18H; $C(CH_3)_3$), 4.84 (d, $J=$ 5.39 Hz, 4H; CH_2), 6.10 (br s, 2H; NH), 6.28 (br s, 2H; NH), 7.27–7.33 (m, 2H; Ph), 7.36–7.43 ppm (m, 2H; Ph); ^{13}C NMR (100.61 MHz, $CDCl_3$, 25 °C): $\delta=$29.5 (CH_3), 46.7 (CH_2), 53.1 ($C(CH_3)_3$), 128.3 (Ph), 129.8 (Ph), 135.6 (Ph), 180.9 ppm (C=S); elemental analysis calcd (%) for $C_{18}H_{30}N_4S_2$ (366.59): C 58.97, H 8.25, N 15.28, S; found: C 59.03, H 8.33, N 15.14.

2-Methylenepropane-1,3-bis(*tert*-butylthiourea) (6): *tert*-Butylisothiocyanate (0.5 g, 4.4 mmol) and 1,3-bis(amino)methylenepropane (0.2 g, 2.2 mmol) were dissolved in CH_2Cl_2 (50 mL) and the solution was stirred at room temperature for 4 h. Subsequently, the solvent was removed by rotary evaporation and the resulting white solid was washed with cold methanol. Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a methanol solution. Yield quantitative; m.p. 159 °C; ^{1}H NMR (400.13 MHz, $CDCl_3$, 25 °C): $\delta=$1.43 (s, 18H; $C(CH_3)_3$), 4.30 (d, $J=$5.91 Hz, 4H; CH_2), 5.20 (s, 2H; $=CH_2$), 6.10 (br s, 2H; NH),

Table 4. Crystallographic data for **5**–**7**.

	5	**6**	**7**
formula	$C_{18}H_{30}N_4S_2$	$C_{14}H_{28}N_4S_2$	$C_{14}H_{28}N_4S_2$
M	366.58	316.52	316.52
crystal size [mm]	$0.34\times0.24\times0.05$	$0.49\times0.36\times0.03$	$0.42\times0.06\times0.02$
crystal system	monoclinic	monoclinic	monoclinic
space group	*C*2/*c*	*C*2/*c*	$P2_1/c$
a [Å]	28.929(17)	27.239(5)	13.263(6)
b [Å]	7.992(5)	7.1286(14)	6.765(3)
c [Å]	9.225(5)	9.798(2)	9.983(4)
α [°]	90	90	90
β [°]	97.284(11)	99.39(3)	94.353(7)
γ [°]	90	90	90
V [Å^3]	2116(2)	1877.0(6)	893.0(6)
Z	4	4	2
T [K]	173(2)	293(2)	173(2)
ρ_{calcd} [g cm^{-3}]	1.151	1.120	1.177
$2\theta_{max}$ [°]	50.0	57.06	50.0
reflns collected	6526	9486	7316
independent reflns	1867	2377	1564
no parameters	120	107	106
R_1, wR_2 ($I>2\sigma(I)$)	0.0638, 0.1511	0.0479, 0.1230	0.0667, 0.1370
goodness of fit	1.148	0.982	1.388
residual electron density [eÅ^{-3}]	0.440	0.304	0.516

6.38 ppm (br t, $J = 5.91$ Hz, 2H; NH); ^{13}C NMR (100.61 MHz, $CDCl_3$, 25 °C): $\delta = 29.5$ (CH_3), 47.9 (CH_2), 52.9 ($C(CH_3)_3$), 116.4 ($C{=}CH_2$), 141.4 ($C{=}CH_2$), 181.0 ppm ($C{=}S$). elemental analysis calcd (%) for $C_{14}H_{29}N_4S_2$ (316.53): C 53.12, H 8.92, N 17.70; found: C 52.99, H 8.69, N 17.84.

***trans*-2-Butene-1,4-bis(*tert*-butylthiourea) (7)**: *tert*-Butylisothiocyanate (0.5 g, 4.4 mmol) and 1,4-diamino-2,3-*trans*-butene (0.2 g, 2.2 mmol) were dissolved in CH_2Cl_2 (50 mL) and the solution was stirred at room temperature for 4 h. Subsequently, the solvent was removed by rotary evaporation and the resulting white solid was washed with cold methanol. Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a methanol/acetone solution. Yield quantitative; m.p. 199 °C; ^{1}H NMR (400.13 MHz, [D_6]DMSO, 25 °C): $\delta = 1.37$ (s, 18H; $C(CH_3)_3$), 3.97 (br s, 4H; CH_2), 5.55 (br s, 2H; =CH), 7.10 (br s, 2H; NH), 7.24 ppm (br t, 2H; NH); ^{13}C NMR (100.61 MHz, [D_6]DMSO, 25 °C): $\delta = 29.3$ (CH_3), 44.6 (CH_2), 52.6 ($C(CH_3)_3$), 128.4 ($CH{=}CH$), 181.5 ppm ($C{=}S$); elemental analysis calcd (%) for $C_{14}H_{29}N_4S_2$ (316.53): C 53.12, H 8.92, N 17.70; found: C 52.03, H 8.38, N 17.64.

X-ray crystallography: Single-crystal X-ray data were collected on a Bruker SMART APEX CCD diffractometer with fine-focus $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å), operated at 50 kV and 30 mA. The structures were solved by direct methods and refined on F^2 using the SHELXTL software package.[22] Absorption corrections were applied using SADABS, part of SHELXTL package. All non-hydrogen atoms were refined anisotropically. The NH hydrogen atoms were located from difference Fourier maps and refined isotropically. The remaining hydrogen atoms were placed in idealized positions, and refined with a riding model. Pertinent crystallographic data for **1**–**7** are listed in Tables 3 and 4. CCDC-249965—CCDC-249971 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44)1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk).

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