

Benzimidazolene-2-thiones: A New Class of Molecules for the Engineering of Molecular Tapes in the Organic Solid State

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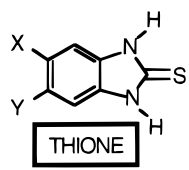
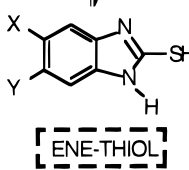
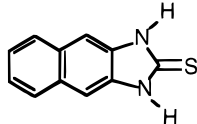
Derivatives of benzimidazolene-2-thione differing in substitution at the 4 and 5 positions have been synthesized and studied by single-crystal X-ray diffraction and/or X-ray powder diffraction. These derivatives include five monosubstituted compounds (**1-SX**; X = Me, F, Cl, Br, I), four disubstituted compounds (**1-SX₂**; X = Me, F, Cl, Br), the parent dihydro compound (**1-SH₂**), and the naphthyl compound (**2-SH₂**). Five of these molecules gave crystals suitable for single-crystal X-ray diffraction. In all of these crystals, the molecules pack as parallel, hydrogen-bonded tapes. Alternate molecules of a tape occupy two different planes that are separated by approximately 1 Å. The resulting structure is named a *stepped* tape. These stepped tapes are divided into two classes based on packing: tapes of **1-SH₂**, **1-SMe₂**, and **1-SF** pack in flat, parallel planes. Tapes of **2-SH₂**, **1-SF₂**, and **1-SCl₂** pack at an angle; of these, two (**2-SH₂** and **1-SF₂**) incorporate molecules of solvent. None of the structures is isomorphous.

Introduction

In this paper we report the crystal structures of five derivatives of benzimidazolene-2-thione and reintroduce the parent compound that has been reported previously.¹ Table 1 shows the molecules that we studied: the series of monosubstituted (**1-SX**) and disubstituted (**1-SX₂**) compounds (X = Me, F, Cl, Br, I); the parent dihydro compound (**1-SH₂**); the naphthyl compound (**2-SH₂**).² Five compounds crystallize in linear hydrogen-bonded arrays that we refer to as stepped tapes (Scheme 1). The molecules comprising these tapes lie in two different planes with one side of the tape translated above the other by ~1 Å, resulting in a bent hydrogen bond. The structures of five other compounds are discussed based on analysis of the lines observed in the powder patterns. Some of these lines appear to be diagnostic for the tapes.

Hydrogen-Bonded Tapes as a Motif for Engineering the Solid State. Our ultimate goal is to understand and control how molecules pack in the three-dimensional solid state. To reduce the complexity of this problem by one dimension, we have investigated tapes:^{3–5} that is, instead of considering how peanuts pack in a box, we consider the simpler problem of how straws

Table 1. Molecules Used in This Study^a

Compound	X	1-SX Y = H	1-SX ₂
	H		1-SH₂
	F	1-SF	1-SF₂
	Me	1-SMe	1-SMe₂
	Cl	1-SCl	1-SCl₂
	Br	1-SBr	1-SBr₂
	I	1-SI	
			
			2-SH₂

^a Compounds that yielded crystals suitable for single-crystal X-ray diffraction appear in boxes. Solid boxes indicate that the compound crystallizes as a thione; dashed boxes indicate an ene-thiol.

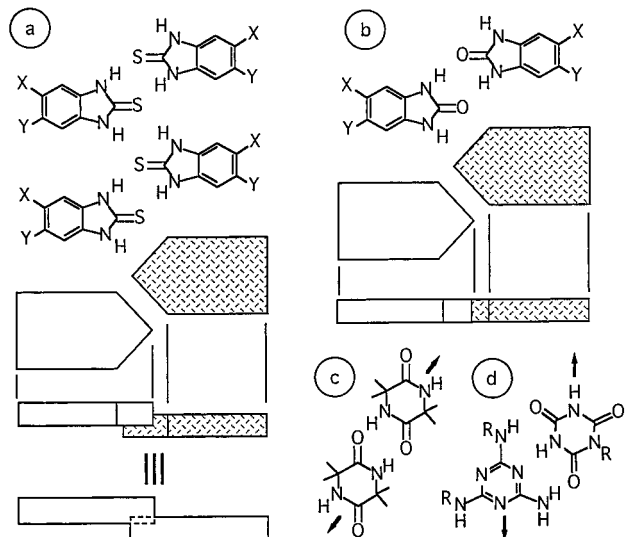
pack. A tape is a linear arrangement of molecules held together by multiple noncovalent interactions resulting in an infinite, quasi-1-D motif.⁶ We use hydrogen bonds for three reasons: they contribute considerable enthalpy

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(2) Throughout this work we will refer back to the oxo analogues using an equivalent nomenclature. For example, the parent benzimidazolone is **1-H₂**—the benzimidazolene-2-thione described here is **1-SH₂**.

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Scheme 1^a

^a (a) Molecules on the left side of the tape of 1-SXY lie on a plane ~ 1 Å above the molecules on the right side of the tape. We refer to these tapes as "stepped". (b) Molecules of a tapes of 1-XY lie on a common plane. We refer to these tapes as planar. (c and d) The diketopiperazines (c) and mixtures of isocyanuric acid and melamine (d) also form tapes connected by hydrogen bonding. Arrows indicate the direction of propagation of the hydrogen-bonding networks.

(1–5 kcal/mol) in the solid state; they are directional; they form between well-defined groups.⁷ For these reasons, extended hydrogen-bonding lattices (chains,⁸ tapes,^{3–6} sheets,⁹ and diamondoids¹⁰) have received much attention as a design motif for engineering the solid state.

Molecules. We have explored three different classes of molecules to probe questions in the organic solid state (Scheme 1): 2-benzimidazolones,³ diketopiperazines,⁴ and derivatives of barbituric acid and melamine.⁵ We pursued the thione analogues of the 2-benzimidazolones for three reasons: (i) they are similar in structure and can be compared; (ii) they are held together by weaker hydrogen bonds and allow the weaker noncovalent interactions (π -H, F-F, and F-H) to assume a bigger role in determining packing; (iii) they are more soluble and more easily crystallized than other molecules that we have explored.¹¹

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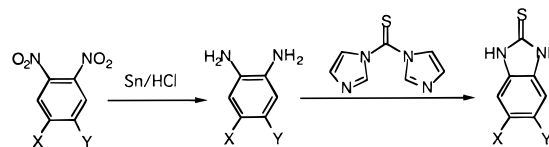
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Synthesis. Most of the compounds in this study are available in one or two steps from the commercially available *o*-diamine or *o*-nitroaniline (eq 1). The dibromobenzimidazolene-2-thione was available through bromination of *N,N*-bistosyl-*o*-phenylenediamine.



Ease of Crystallization. Benzimidazolene-2-thiones yield microcrystalline powders with little effort, but diffraction-quality single crystals remain difficult to obtain. In our hands, only five of the molecules gave crystals suitable for X-ray diffraction. Obtaining diffraction-quality crystals remains the rate-limiting step in studying the physical-organic chemistry of organic crystals in the classes of molecules we have studied (Scheme 1).

Results and Discussion

Crystal Structures of the Benzimidazolene-2-thiones. Similar to the parent compound, all five compounds for which we obtained crystals were tapes (Figures 1 and 2). Table 2 summarizes relevant crystallographic data. We begin with brief discussion of the features common to all the structures before addressing the packing specific to single compounds. We compare these thiones and the benzimidazolones as relevant issues arise. Table 3 summarizes the differences in the packing arrangements for these two classes of molecules.

Thiones Pack as Stepped Tapes with Their Long, Hydrogen-Bonded Axes Parallel. The most important result emerging from this work comes from single-crystal X-ray diffraction: *all* of the thiones that we examined form hydrogen-bonded tapes. In addition, *all* of these tapes pack with their hydrogen-bonded axes in parallel. The aromatic rings of a tape both above and below are offset along the C-S axis perhaps to reduce π - π repulsions or perhaps to relieve steric interactions involving the large sulfur atom (see Figure 1 for details).^{12–14} The magnitude of the offset varies over a short range: the S of one tape appears between the C (of the thiocarbonyl) and C-C bond (common to the 5- and 6-member rings) of the tapes above and below.

In contrast, the benzimidazolones crystallized in three different motifs: three-dimensional networks (non-

(11) The greatest advantage of these compounds over any others that we have studied (2-benzimidazolones, diketopiperazines, barbituric acid-melamine cocrystals) is their high solubility in many organic solvents. This solubility allows us to use conventional silica gel chromatography to purify the products and intermediates and gives us an opportunity to survey many different solvents for crystallization. Crystallization of the benzimidazolones is limited to only a few high boiling solvents including DMF and *N*-methylpyrrolidinone which evaporate very slowly under ambient conditions. We hypothesized that the greater diversity in solvent choice might translate into both a greater chance for success of crystallization, and an opportunity for a more rigorous search for polymorphs.

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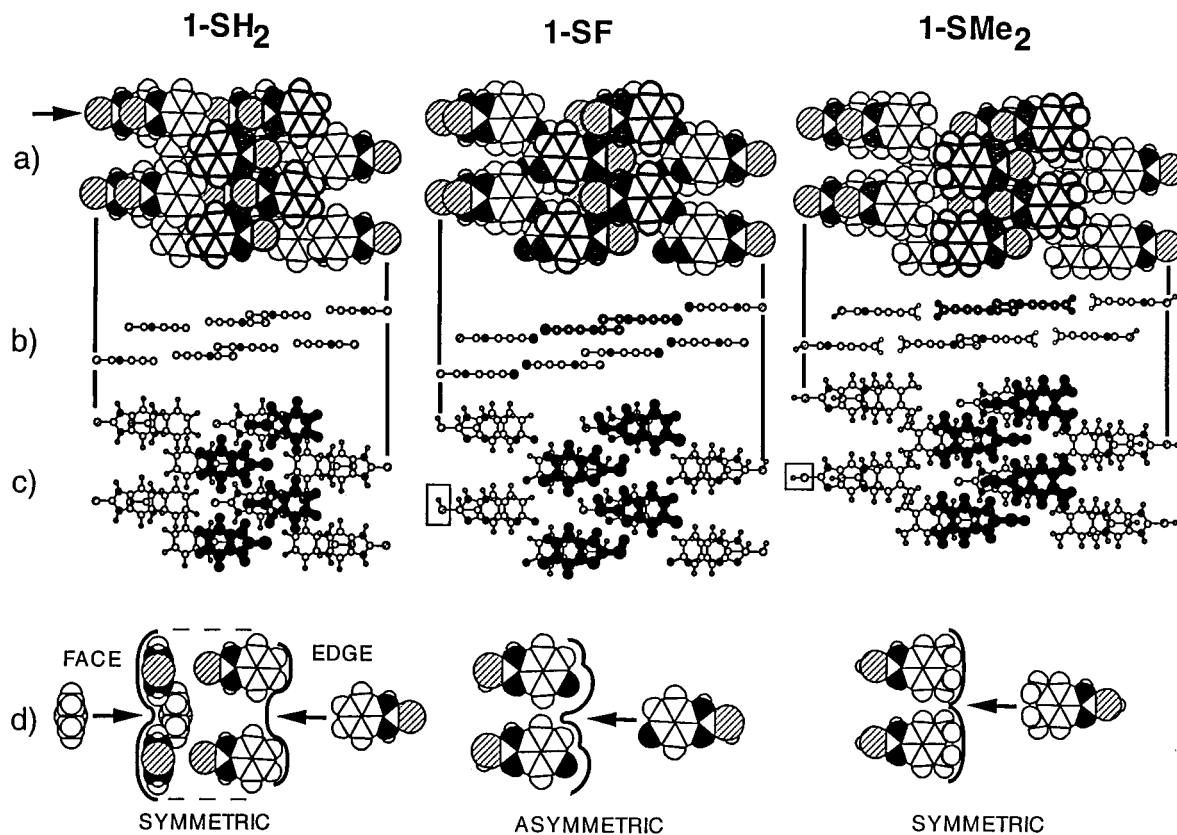


Figure 1. Crystal structures of **1-SH₂**, **1-SF**, and **1-SMe₂**. Two crystallize as the ene-thiols: **1-SMe₂** and **1-SF**. The locations of the protons in these molecules were identified from electron density maps and are shown boxed in (b): the *SH* proton of **1-SF** forms a hydrogen bond with the aromatic nitrogen of an adjacent molecule; the *SH* of **1-SMe₂** is *not* involved in hydrogen bonding—it points into the five-member ring of the tape above or below. These protons are identified with an arrow in (b) and (c). (a) A space-filling model shows a single tape (bold) and adjacent molecules. The arrow shows the alignment of C–S bonds that occurs in all structures. (b) An edge-on view looking down the axis of the tape (bold) highlights the stepped tape. (c) View (a) is reproduced as a ball-and-stick model—with the tape shown in boldface—to indicate the packing of tapes both above and below. (d) The two types of scallops that are found in stepped tapes are shown: scallops on the face (left; side-on view) allows the alignment of C–S bonds; scallops on the edge allow adjacent tapes to interdigitate. See text for more details.

tapes); tapes with their hydrogen-bonded axes packed in parallel; tapes with their hydrogen-bonded axes packed in a nonparallel arrangement. While the aromatic rings are offset in the benzimidazolones, the direction and magnitude of the offset vary.

Hydrogen Bonds in These Crystals Vary in Length and Angle; No Trends in Geometries and Structure Can Be Identified. Table 4 summarizes the relevant distances and angles of the hydrogen bonds in the reported crystal structures. While three different motifs can be identified in the crystalline state (parallel tapes; angled tapes; angled tapes with solvent), we are unable to identify any trend in the hydrogen-bond geometries that correlates with differences in these structures. We were also unable to correlate hydrogen-bond geometry and the structure of the benzimidazolones.

1-SH₂ and 1-SMe₂ Pack Similarly: Both Tapes Have Symmetric Scalloped Edges. We rationalize—and discuss—the packing of tapes in terms of the shape of the tape. That is, the alternating arrangement of molecules produces a tape with a contoured—or scalloped—shape. Figure 1d shows both a top-down and side-on view of these scalloped edges. Arrows indicate how molecules in adjacent tapes pack: tapes packing above and below fill the scallops on the face of the tape (left); tapes packing on the side fill the scallops on

the edge (right). We attribute similarities in the packing of **1-SH₂** and **1-SMe₂** to their common, symmetric edges and faces. The benzimidazolones, **1-H₂** and **1-Me₂**, both form tapes, but these tapes differ in the arrangement of their long axes: nonparallel (**1-H₂**); parallel (**1-Me₂**).

1-SF Displays an Asymmetric Scalloped Edge. Tapes of **1-SF** have scalloped faces and edges: the scalloped edges of **1-SF** are asymmetric in shape. Accordingly, molecules on adjacent tapes interdigitate in a specific orientation: the F atoms of one tape are aligned with the H atoms of the adjacent tapes (Figure 1d). Contact between the fluorine atoms is avoided. Crystals suitable for single-crystal analysis were not obtained for **1-F**.

1-SCl₂. Figure 2 shows the crystal structure of **1-SCl₂**. Adjacent tapes of **1-SCl₂** pack at an angle (~120°). The scalloped edge in these tapes is indicated with an arrow and wavy line in Figure 2b. These edges allow the adjacent tapes to pack in a way that is similar—although angled—to the tapes shown in Figure 1. The benzimidazolones pack as flat tapes as members of a series that are isostructural: **1-Cl₂**, **1-Br₂**, and **1-Me₂** all pack alike. Unlike **1-SCl₂**, the C–Cl bonds between molecules of adjacent tapes in **1-Cl₂** align almost coaxially.

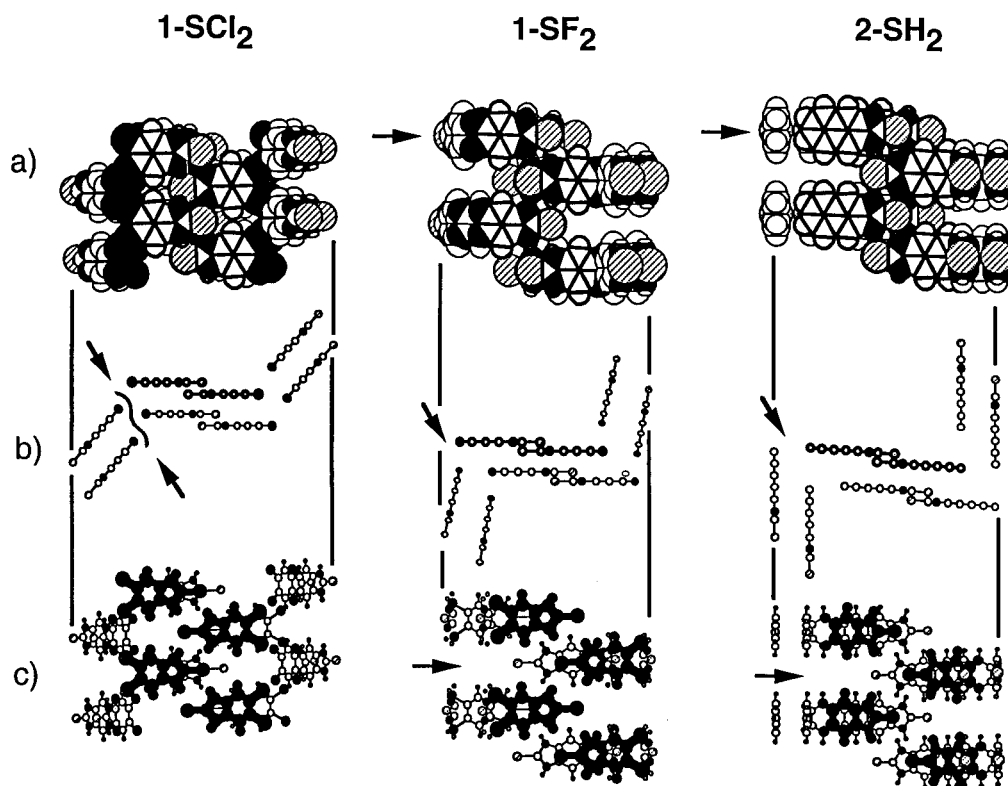


Figure 2. Crystal structures of the **2-SH₂**, **1-SCl₂**, and **1-SF₂**. (a) Space-filling model composed of a single tape and adjacent molecules. (b) Edge-on view looking down the axis of the boldfaced tape. (c) View (a) reproduced as a ball-and-stick model with the tape shown in boldface. Scallops on the face (not shown) allow molecules to pack with C–S bonds aligned. Scallops on the edges are indicated with an arrow and dark wavy line in (b). Arrows in (b, c) indicate the location of molecules of solvent: water in **2-SH₂**; heptane in **1-SF₂**. See text for more details.

Table 2. Crystallographic Data for the Benzimidazolene-2-thiones^a

thione	class	space group	<i>a</i> (Å)	<i>b</i> (Å)	<i>c</i> (Å)	β (deg) ^b	<i>R</i> ₁ ^c	<i>R</i> ₂ ^d	density (g/cm ³) ^e	solvent ^f	crystal shape	melting point (°C)	<i>C</i> _k ^g
1-SH₂		<i>P</i> ₂₁ / <i>m</i>	4.91	8.56	8.29	91.6	10.2	NA	NA	EtOAc	needles	279 (d)	NA
1-SF		<i>P</i> ₂₁	3.9416(12)	8.1477(2)	11.647(3)	93.349(6)	8.0	10.1	1.496	EtOAc	needles	274 (d)	66.3
1-SMe₂		<i>P</i> ₂₁	5.3410(4)	8.3421(7)	10.5205(9)	102.819(2)	8.6	9.6	1.295	EtOAc	needles	>350	67.1
1-SCl₂	V	<i>Pnma</i>	29.5371(5)	8.0059(2)	3.8793(1)	90	5.6	7.3	1.586	EtOAc	needles	349 (d)	63.9
2-SH₂	V _s	<i>Pnma</i>	5.1610(6)	8.4720(9)	25.144(3)	90	6.0	8.3	1.319	wet THF	needles	289 (d)	65.7 (58.9)
1-SF₂	V _s	<i>Pnma</i>	4.5339(4)	8.4698(7)	22.6697(2)	90	6.2	6.9	1.512	EtOH/heptane	needles	>350	74.7 (59.7)

^a Compounds giving single-crystal structures are listed. "Class" indicates the packing arrangement of tapes: parallel (||) or angled (V or V_s). Solvent molecules incorporated into the structure are identified. ^b α and γ are constrained to be 90° by the symmetry of the space group. ^c This value is the crystallographic reliability index, $R_1 = \sum |F_o - F_c| / \sum F_o$ for $F_o > 2\sigma$. ^d $R_2 = \sum |F_o^2 - F_c^2| / \sum F_o^2$ for all σ . ^e Calculated using the Shelx package of programs. ^f Solvent used for the growth of single crystals for X-ray crystallography. ^g C_k is the packing fraction: $C_k = N(V_m/V_c)$, where N is the number of molecules in the unit cell, V_m is the volume of the molecules in the unit cell (calculated with the program Platon rather than using tables of incremental volumes, as done by Kitaigorodski),^{16,17} and V_c is the total volume of the unit cell. Values of C_k appearing in parentheses are calculated after removing the molecules (or atoms) of solvent.

1-SF₂ and 2-SH₂ Crystallize as Solvates. Figure 2 shows the crystal structures of **1-SF₂** and **2-SH₂**. Adjacent tapes pack at an angle (98° for **1-SF₂**; 85° for **2-SH₂**). Unlike **1-SCl₂**, molecules of adjacent tapes lie in register (indicated by the arrow in Figure 2a). This packing arrangement leaves space (indicated with arrows in Figure 2b,c) for molecules of solvent. **1-SF₂** incorporates molecules of heptane into its lattice: these solvent molecules are disordered. **2-SH₂** incorporates molecules of water. We have been unsuccessful in obtaining crystals of these compounds from different solvent systems. The benzimidazolones of pack much differently: one is a 3-D network (**1-F₂**); one is a tape with nonparallel axes (**2-H₂**). Neither of these molecules crystallize as solvates.

Molecules in the Tapes May Exist as Thiones or Ene-Thiols. There is evidence that two of the molecules may crystallize as ene-thiols (**1-SMe₂**; **1-SF**). Contradictory support for these structures is seen in the bond lengths. Unlike the thione tautomer, these ene-thiols (**1-SMe₂**; **1-SF**) have different C–N bond lengths between HS–C–N₁ and HS–C–N₂ (~1.3 Å; ~1.4 Å). The N₁ or 2–C_{arom} bond lengths are also different. Like the thione tautomer, however, the C–S bond lengths of these two molecules fall within a range common to all of these molecules. That is, *all* of these molecules have C–S bond distances of ~1.69 characteristic of a C=S double bond.¹⁵

The space group of the molecules that crystallize as thiones reflects the higher symmetry of these mole-

Table 3. Comparison of the Benzimidazole-2-thiones and the Benzimidazolones^a

BENZIMIDAZOLENE-2-THIONES		
PARALLEL	ANGLED	
1-SH₂	1-SCl₂	
1-SF	1-SF₂ (heptane)	
1-SMe₂	2-SH₂ (water)	
BENZIMIDAZOLONES		
PARALLEL	NONPARALLEL	NETWORKS
		3-D
1-X₂ X=Me,Cl,Br	1-H₂ 2-H₂	1-F₂

^a All of the thiones pack as stepped tapes with their hydrogen-bonding axes in parallel. The corresponding oxo-derivatives pack as flat tapes or 3-D networks. Some tapes pack with their hydrogen-bonding axes parallel, others do not.

cules—defined by the C=S axis—than that of the ene-thiols. While irrelevant for the asymmetric **1-SF**, the loss of this symmetry element for **1-SMe₂** is reflected in its P_{21} space group, instead of P_{21}/m .

The electron density maps differ between thiones and ene-thiols. Both protons of the thiones appear on nitrogen. The protons of the ene-thiols appear on sulfur and a single nitrogen atom.

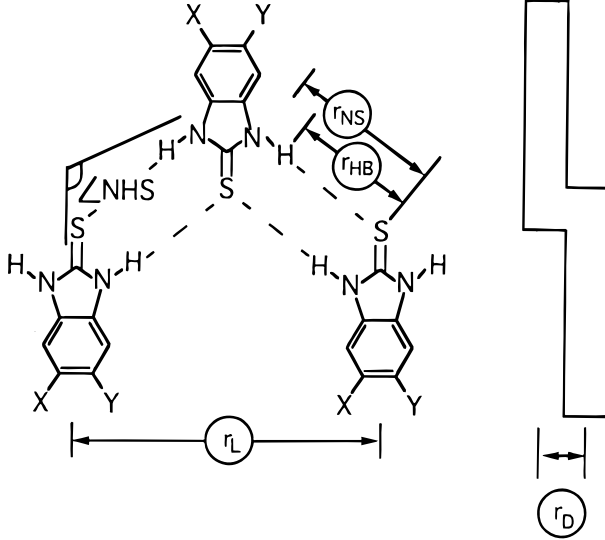
From these data, we cannot state with complete certainty whether **1-SF** and **1-SMe₂** crystallize as thiones or ene-thiols. The ambiguities in bond distances may be the result of the small data sets collected for these molecules. Regardless of the tautomer, however, these molecules still crystallize as tapes.

Powder Patterns. Figure 3 shows the XPD patterns calculated from the structures for which we were able to obtain crystal structures from single-crystal diffraction and measured for those molecules that did not give crystals suitable for single-crystal diffraction.

Thiones Exist in Many Polymorphs but Show Very Similar Patterns of Lines by XPD. To evaluate the extent of polymorphism in these molecules, three representative molecules were studied using XPD: **1-SH₂**, **1-SCl₂**, **1-SF₂**. Powders of each were generated in two ways: thermal annealing; evaporation of solvent.

Powders through thermal annealing. **1-SH₂**, **1-SCl₂**, and **1-SF₂** were heated in open vials at 170 °C for 3 days. The XPD traces of these compounds showed different

Table 4. Hydrogen-Bond Distances (angstroms), Angles (deg), and Other Selected Dimensions



compound	r_{HB}	r_D	$\angle NHS$	r_{NS}	r_L
1-SH₂	2.42	0.8	149	3.37	8.56
1-SF	2.54	1.1	151	3.36	8.15
1-SMe₂	2.44	0.9	173	3.31	8.34
1-SCl₂	2.69	1.2	165	3.32	8.01
1-SF₂	2.52	0.7	162	3.35	8.48
2-SH₂	2.54	0.9	156	3.35	8.47

patterns of lines than those calculated from the known crystal structure or measured from different solvents (discussed below). The overall patterns of lines, however, were similar, and we believe that annealing gives a distinct but potentially related crystal morphology. ¹H NMR spectra (recorded in CDCl₃) for the annealed powders establishes that **1-SCl₂** and **1-SF₂** undergo no decomposition. The ¹H NMR spectrum of **1-SH₂** shows new lines (20% combined area) slightly downfield of those corresponding to **1-SH₂** (80% combined area). The chemical shift of these lines suggests that they correspond to **1-H₂**—the benzimidazolone—and are the result of hydrolysis of **1-SH₂**.

Powders through evaporation of solvent. Powders from 10 different solvents (acetone, benzene, chloroform, dimethylformamide, ethyl acetate, 1:1 ethyl acetate: heptane, ethanol, pyridine, toluene, tetrahydrofuran) through either slow (via open-bottle) or fast (via rotary evaporator) evaporation. Traces of **1-SH₂** and **1-SCl₂** from different solvents gave patterns of lines that appeared very similar: positions of the lines varied by about 1°. The choice of solvent greatly affected the XPD traces of **1-SF₂**—an observation that is intuitively satisfying given the nature (solvated) of the crystal structure. The extensive polymorphism observed in these compounds is not seen in the benzimidazolones.

Lines in the Powder Patterns Are Diagnostic for Some Features of the Packing of Tapes. Analysis¹⁶ of the XPD patterns of molecules for which crystal structures have been obtained shows that lines in these patterns can be attributed to features that are diag-

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(16) Analysis was done using the CERIU₂ package of programs: CERIU₂.1.0 molecular modeling program, MSI: Burlington, MA, 1994. We calculated values of α_k using the program Platon: Platon-92 (Version 28) and Platon-92 (Version 25); Spek, A. L. Bijvoet Center for Biomolecular Research, Vakgroep-Kristal-en Structure-chemie, University of Utrecht.

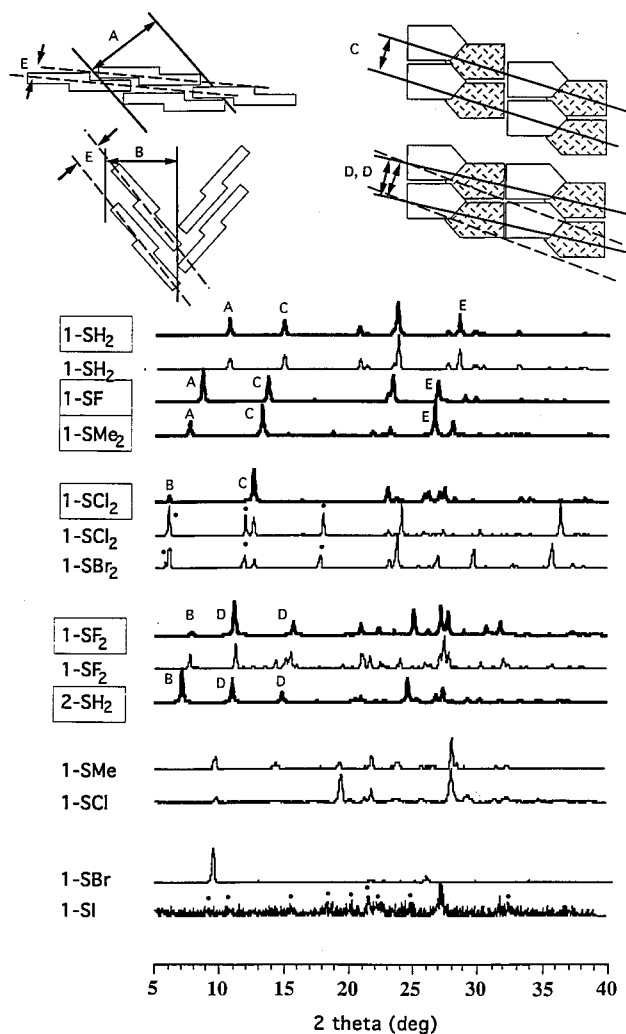


Figure 3. Xpd patterns of the thiones are grouped according to crystal structure class (parallel tapes; angled tapes; angled tapes with solvent). Patterns calculated from known crystal structures are shown in dark lines with their labels in boxes. Patterns measured are shown as light lines. Experimental traces of **1-SH₂**, **1-SCI₂**, and **1-SF₂** are included to illustrate the extent of polymorphism in these compounds. Using the CERIU_S package of programs, we identified structural features of the tapes that produced lines in the XPD patterns. These features are diagnostic for structure and indicated on the top half of the figure. Lines in the calculated patterns are labeled. See the text for a discussion of the value of these lines for the prediction of crystal structures. Lines identified with a ● in **1-SCI₂** and **1-SBr₂** identify peaks corresponding (we believe) to a second polymorph. See the text for more details.

nostic—and potentially predictive—of three-dimensional structure (Figure 3). These patterns are relative simple over significant values of 2θ : we see only one line (labeled A or B) between 6° and 11° ; we see one or two lines (labeled C or D) between 11° and 17° ; we see patterns of lines between 22° and 30° with one line at $\sim 27^\circ$ noted as being specially important.

Lines between 6° and 11° . In all of the crystal structures reported here, the first lines in the calculated XPD patterns (A or B) correspond to the width of a tape projected onto a plane perpendicular to the direction of stacking (Figure 3). As a result of similar stacking, we see a shift toward lower values of 2θ as the tapes get wider (with increasing size of the substituents at the 4- and 5-positions).¹⁷ Changing from parallel tapes to

angled tapes should shift the position of the lines to lower values of 2θ (relative to flat parallel tapes), but the shift is dependent on the angle at which the tapes pack.

Lines between 11° and 17° . Only one line appearing between 11° and 17° in the XPD traces is diagnostic for tapes that pack like **1-SH₂**, **1-SF**, **1-SMe₂**, **1-SCI₂**: that is, for those that interdigitate their scalloped edges. Two lines are observed for **1-SF₂** and **2-SH₂** and reflect the registered alignment of adjacent tapes. The origin of these lines is shown schematically in Figure 3.

Lines between 22° and 30° . The most important line in this region appears around 27° (E). For the parallel tapes, the line is strong, for angled tapes the line is weak and appears among many lines. This line is diagnostic for the presence of a hydrogen-bonded tape: its origin is shown in Figure 3. The complexity of the region and the limited number of crystal structures make further analysis of this region difficult.

Predictions Based on XPD Analysis. We are encouraged by the trends in lines appearing in the XPD trace and suggest (with great caution) that the traces of unknowns with very similar molecular structure may yield important structural information. Two predictions are suggested below. We stress again that the data set with which we are drawing these conclusions is limited. As a result, further study may show that these predictions are erroneous. If, however, XPD analysis proves to be useful in this application, the duration of the rate-limiting step of studying the organic solid state could be markedly reduced.

1-SBr₂ packs as angled tapes that lie in register: the XPD trace is very similar to that of the known structure of 1-SCI₂. The measured powder pattern measured for **1-SCI₂** shows two major polymorphs; one is identical with that calculated from the crystal structure. The XPD pattern measured for **1-SBr₂** also shows two polymorphs and is almost identical with the trace measured for **1-SCI₂**. Both traces show lines at 6° , 13° , 15° , and 18° are common experimental patterns of both **1-SCI₂** and **1-SBr₂**. The lines at 13° and 18° are not observed in the pattern calculated for **1-SCI₂**, and we believe that these belong to the second polymorph.¹⁸ The lines at 15° correspond to the interdigitation of tapes along their scalloped edges. All three traces show complex—but similar—patterns of lines at 27° in the fingerprint region. We infer that one of the polymorphs of **1-SBr₂** crystallizes as stepped tapes. The structure of the related, second polymorphs of **1-SCI₂** and **1-SBr₂** are uncertain.

1-SMe and 1-SCI pack as tapes with similar structures. Three important similarities exist in the XPD traces of the **1-SMe** and **1-SCI** and those of parallel tapes: all show one line between 9° and 10° ; one line at 14° (present in **1-SCI**, but difficult to see in the data shown); a strong line at 28° . We hypothesize that these two molecules crystallize as tapes (9° – 10°), that adjacent tapes pack in a staggered conformation as a result

(17) Kitaigorodskii, A. I. *Molecular Crystals and Molecules*; Academic Press: New York, 1973.

(18) The lines corresponding to the second polymorph (indicated with a dot) appear to pack as **1-SF₂** and **2-SH₂**. Consistent with this solvated packing arrangement, crystals from solutions containing **1-SBr₂** have been observed to change from translucent, high-quality crystals to dried powders.

of their asymmetric scalloped edge (14°), and that these tapes are stepped (28°).

The quality of the data obtained for **1-SBr** and **1-SI** do not allow for predictions of structure. Traces for **1-SBr** and **1-SI** are shown in Figure 3. The quality of the data prevents us from drawing any inferences of structure.

Why Are the Tapes "Stepped"? The tapes in other series that we have described have always been "flat"—not stepped.^{3–5} "Flat" is more descriptive of our conceptual picture of these tapes than of their actual structure. For example, the "flat" tapes of the benzimidazolones are better described as wavy: alternating molecules within a tape lie at a cant between 0° (**1-H₂**) and 15° (**1-Cl₂** and **1-Br₂**). In contrast, the molecules in a tape comprising thiones lie on one of two planes—or steps. The reasons for these packing arrangements are unclear.

Conclusions

Thioureas are a class of molecules that may be interesting for studying packing in the organic solid state for a variety of reasons: consistency in packing; accessibility and solubility of the compounds; extent of polymorphism; limited tautomerization between thione and thiolene; the potential for XPD analysis. We comment on each of these lessons learned below.

Consistency in Packing. We are surprised with the consistency in packing of the thiones given the weakness of the (S··HN) hydrogen bond:¹⁹ they all form stepped tapes that pack with their hydrogen-bonded axes parallel. The reason for this consistent packing is unclear—and surprising in light of our initial motivations for studying these molecules. While all of the thiones studied form tapes—while not all of the benzimidazolones do—both the different composition of the sets of data, and the greater degree of polymorphism observed in the thiones precludes judgment on which series packs in a more consistent manner.

Accessibility and Solubility. Thiones are soluble in a variety of organic solvents, and available in only a few (1–3) steps from commercially available starting materials. This enhanced solubility from the simple substitution of "S" for "O" suggests that thiocarbonyl groups may offer a general solution for working with insoluble, carbonyl-containing molecules.

Polymorphism. These compounds appear to exist in a variety of isostructural crystalline forms: **1-SF₂** (a solvate) demonstrates the greatest polymorphism. We attribute the increased polymorphism of the thiones over the oxo-series to the reduced strength of the hydrogen bond.

Tautomerism: Ene–thiols versus Thiones. The data sets obtained do not allow us to state with certainty whether **1-SMe₂** and **1-SF** crystallize as thiones or ene–thiols. While bond lengths within the five-member ring suggest ene–thiol structures, the C–S bond lengths are identical with molecules that crystallize as thiones. The electronic density maps suggest that **1-SMe₂** and **1-SF** crystallize as ene–thiols: the sulfur and a single

nitrogen are protonated. Regardless of the tautomer, these molecules still form hydrogen-bonded tapes.

Predictions from XPD. Analysis of the XPD traces of a series of compounds with known crystal structures reveal trends in the patterns and positions of lines. With an expanded data set and additional series of compounds, trends for XPD traces might allow for the rapid screening of compounds in order to predict crystal packing arrangements.²⁰

Experimental Section

General Methods. All chemicals were purchased from Aldrich Chemical Co. and used as received. Reagent-grade THF was distilled from sodium benzophenone ketyl. All other solvents were used without purification. Melting points were determined on a Mel-Temp apparatus and are uncorrected. The temperatures at which these compounds decomposed appears in Table 2.

Preparation of Substituted Phenylenediamines by Reduction. SnCl₂·2H₂O (10 eq) was added slowly to a stirring solution of 1:1 water:concentrated HCl. The derivatized nitroaniline was added slowly as a solid. The reaction was stirred for 2 h at reflux. After cooling to room temperature, the reaction was poured onto ice and neutralized slowly (with stirring) with NaOH pellets. The pH was monitored with litmus paper. When the solution was basic (pH 13), ether was added and the aqueous layer was extracted three times. The organic layers were combined and dried over MgSO₄. After filtration, the solvent was evaporated using a rotary evaporator. The resulting crude was taken on without further purification.²¹

Carbonylation of Substituted Phenylenediamines. A solution of 1,1'-thiocarbonyldiimidazole was added dropwise to a stirring solution of diamine (1 equiv) in THF at room temperature. The reaction was stirred overnight. After removing the THF using a rotary evaporator, the residue was suspended in ethyl acetate and washed with water. The organic layer was dried over MgSO₄ and filtered. An equivalent amount of silica gel was added to the dried organics and the solvent was removed using a rotary evaporator. Flash chromatography (eluent identified below) yielded the final product in yields >90%.

Benzimidazolene-2-thione (1-SH₂). As reported.¹ HRMS (CI+) calc (M + H⁺) 151.0330; found 151.0335.

2,3-Naphthimidazolene-2-thione (2-SH₂). Following chromatography with 1:4 ethyl acetate:hexanes (>90%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.64 (s, 2H); δ 7.92 (m, 2H); δ 7.38 (s, 2H); δ 7.36 (m, 2H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 172.08, 132.83, 129.70, 127.44, 124.11, 104.70; HRMS (EI+) calc for (M⁺) 200.0408; found 200.0412.

4,5-Dimethylbenzimidazolene-2-thione (1-SMe₂). Following chromatography using 1:3 ethyl acetate:hexanes as an eluent (>90%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.32 (br s, 2H); δ 6.92 (s, 2H); δ 2.22 (s, 6H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 167.13, 130.56, 130.48; 110.03; 19.56; HRMS (CI+) calc for (M+H⁺) 179.0643; found 179.0641.

4,5-Difluorobenzimidazolene-2-thione (1-SF₂). Following chromatography using 1:3 ethyl acetate:pentane as an eluent (>90%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.71 (br s, 2H); δ 7.20 (t, *J*_{H-F} = 8.6 Hz, 2H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 169.88, 146.24 (*J*_{C-F} = 241.1 Hz), 127.93; 98.30; HRMS (EI+) calc for (M⁺) 1786.0063; found 186.0062.

(20) Similarities between other powder patterns can be made, but their validity is questionable. For example: **1-SMe** and **1-SCI** may pack as tapes with similar structures. Three important similarities exist in the XPD traces of **1-SMe** and **1-SCI** and those of parallel tapes: all show one line between 9° and 10° ; one line at 14° (present in **1-SCI**, but difficult to see in the data shown); a strong line at 28° . We hypothesize that these two molecules crystallize in tapes (9° and 10°), that adjacent tapes pack in a staggered conformation as a result of their asymmetric scalloped edges (14°), and that these tapes are stepped (28°).

(21) Uchida, M.; Morita, S.; Chihiro, M.; Kanbe, T.; Yamasaki, K.; Nakagawa, K. *Chem. Pharm. Bull.* **1989**, *37*, 1517–1523.

(19) For a tabulation of hydrogen bond strengths for a variety of organic molecules see: Leahy, D. E.; Morris, J. J.; Taylor, P. J.; Wait, A. R. *J. Chem. Soc., Perkins Trans.* **2 1992**, 705 and references therein.

4,5-Dichlorobenzimidazolene-2-thione (1-SCl₂). Following chromatography using 1:1 ethyl acetate:hexanes as an eluent (>90%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.77 (br s, 2H); δ 7.32 (s, 2H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 170.28, 132.20, 124.63, 110.54; HRMS (EI⁺) calc 217.9472; found 217.9486.

4,5-Dibromobenzimidazolene-2-thione (1-SBr₂). Prepared by bromination of *N,N*-bis(toluene-*p*-sulfonyl)-*o*-phenylenediamine.²² Following chromatography using 1:2 ethyl acetate:hexanes; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.63 (br s, 2H); δ 7.42 (s, 2H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ; HRMS (EI⁺) calc for (M⁺) 307.8462; found 307.8450.

4-Methylbenzimidazolene-2-thione (1-SMe). Following chromatography using 1:3 ethyl acetate:hexanes as an eluent (>90%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.40 (br s, 2H); δ 7.00 (d, *J* = 7.9 Hz, 1H), δ 6.93 (s, 1H); δ 6.91 (d, *J* = 7.9 Hz, 1H); δ 2.32 (s, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 167.75, 132.43, 131.60, 130.17, 123.14, 109.55, 109.06, 20.91; HRMS (EI⁺) calc for (M + H⁺) 164.0504; found 179.0400.

4-Fluorobenzimidazolene-2-thione (1-SF). Following chromatography using 1:3 ethyl acetate:hexanes as an eluent (>90%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.64 (s, 1H); δ 12.61 (s, 1H), δ 7.12 (m, 1H); δ 6.95 (m, 2H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 167.91, 161.06, 158.70, 133.57, 129.65, 111.85, 111.75, 111.30, 111.03; HRMS (EI⁺) calc for (M + H⁺) 168.0157; found 168.0167.

4-Chlorobenzimidazolene-2-thione (1-SCl). Following chromatography using 1:3 ethyl acetate:hexanes as an eluent (>90%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.68 (s, 1H); δ 12.66 (s, 1H); δ 7.14 (m, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 169.26, 133.22, 131.23, 126.65, 122.20, 110.52, 109.16; HRMS (EI⁺) calc for (M⁺) 183.9862; found 183.9855.

4-Bromobenzimidazolene-2-thione (1-SBr). Following chromatography using 1:3 ethyl acetate:hexanes as an eluent (>90%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.65 (br s, 2H); δ 7.28 (m, 2H), δ 7.11 (s, 1H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 169.12, 133.64, 131.59, 124.96, 114.34, 111.93, 111.10; HRMS (EI⁺) calc for (M + H⁺) 228.9431; found 228.9439.

4-Iodobenzimidazolene-2-thione (1-SI). Prepared by a reported procedure.³ ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.65 (s, 1H); δ 12.59 (s, 1H); δ 7.42 (m, 2H); δ 6.96 (m, 1H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 168.69, 134.00, 131.97, 126.20, 115.43, 111.42; HRMS (EI⁺) calc for (M⁺) 276.9296; found 276.9298.

Determination of the Crystal Structures by Single-Crystal X-ray Diffraction. Data were collected on a Siemens P-4 X-ray diffractometer (Mo Kα₁, λ = 0.710 73) equipped with a CCD detector. Structures were solved and refined using the Siemens SHELXTL-PLUS package of programs.

X-ray Powder Diffraction. The powder diffraction patterns were collected on a Scintag XDS 2000 diffractometer (Cu Kα₁, λ = 1.5405). The samples were prepared by grinding the crystals with a mortar and pestle and spreading the powder on a glass microscope slide.

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Supporting Information Available: Structures, atomic coordinates, and crystal structure data (30 pages). Ordering information given on any current masthead page.

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