Synthesis, Spectroscopic and Structural Characterization of Novel Diiodine Adducts with the Heterocyclic Thioamides, Thiazolidine-2-thione (tzdtH), Benzothiazole-2-thione (bztzdtH) and Benzimidazole-2-thione (bzimtH)

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Direct reaction of thiazolidine-2-thione (tzdtH), an anti-thyroidal agent with diiodine in a molar ratio of 1:2 caused the heterolytic cleavage of diiodine and formation of [{(tzdtH)$_2$I$^+$}·I$_3^-$·2I$_2$] (**1**), whereas the reaction of benzothiazole-2-thione (bztzdtH) with diiodine in a molar ratio of 1:2 and 1:1 resulted in the formation of the [{(bztzdtH)I$_2$}·I$_2$] (**2**) and [(bztzdtH)I$_2$] (**3**) charge-transfer (c.t.) complexes. In addition, the reaction between benzimidazole-2-thione (bzimtH) with diiodine in a molar ratio 1:2 yielded the c.t. complex [{(bzimtH)I$_2$}$_2$·I$_2$·2H$_2$O] (**4**). All reactions were carried out in dichloromethane. The molecules have been characterized by m.p., elemental analyses, and FT-Raman, FT-IR, UV/Vis and ^{1}H NMR spectroscopy. Crystal structures of the named complexes have been determined by X-ray diffraction at –103 °C (**1**), 20 °C (**2** and **3**) and –168 °C (**4**). The charge-transfer nature of the bonds of the adducts (**1**–**4**) has been verified by the lengthening of the I–I bond lengths as compared to the S–I bond lengths, by the characteristic c.t. bands observed in the UV spectra and by the shifts of frequencies measured for the I–I bond vibration in the FT-Raman spectra of the complexes. Compound **1** (C$_3$H$_5$NS$_2$I$_4$) is monoclinic with a space group $P2_1/n$ and a = 9.145(2) Å, b = 13.259(2) Å, c = 10.615(2) Å, β = 106.30(2)°, Z = 4. The complex is ionic, containing an S–I$^+$–S linkage and an I$_3^-$ counter anion. Compound **2** [C$_7$H$_5$NS$_2$I$_4$, monoclinic, space group $P2_1/n$, a = 8.357(2) Å, b = 17.829(4) Å, c = 9.603(2) Å, Z = 4, β = 94.39(3)°] consists of a benzothiazole-2-thione ligand bonded with an iodine atom through a sulfur atom. A neutral diiodine molecule is also cocrystallized. A benzothiazole-2-thione ligand is also bonded through its sulfur atom to an iodine atom in molecule **3** [C$_7$H$_5$NS$_2$I$_2$, orthorhombic, space group $P2_12_12_1$, a = 4.189(1) Å, b = 9.770(3) Å, c = 27.704(8) Å, Z = 4]. Extended intramolecular N–H···I contacts link the molecules forming a supramolecular assembly. The crystal structure of **4** (C$_7$H$_6$N$_2$SI$_3$·H$_2$O) reveals a monoclinic space group $P2_1/c$ and a = 13.4828(14) Å, b = 4.6704(4) Å, c = 21.267(2) Å, β = 101.029(8)°, Z = 4. It consists of a benzimidazole-2-thione ligand bonded to an iodine atom through a sulfur atom. An extended intramolecular linkage via I(2)···H(4)[C(4)] leads to the formation of dimers, while an extended hydrogen-bonding network {H(12w)[O(12)w]···N(3), O(1w)···N(3)} links the alternate parallel dimers forming a supramolecular assembly. Attempts to draw conclusions on the behavior of a thione, when used as an anti-thyroidal agent, towards diiodine have been made.
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1. Introduction

Among the most widely anti-thyroidal agents used for the treatment of hyper-thyroidism (Graves' decease) over the years are thioamides such as *N*-methylimidazoline-2-thione (methimazole), 3-methyl-2-thioxo-4-imidazoline-1-carboxylate (carbimazole) and propylthiouracil.[1] Mercaptothiazoline (thiazolidine-2-thione) has also been used[1] for this purpose. Thioamides inhibit the formation of 3,5,3′-triiodothyronine (T3) and 3,5,3′,5′-tetraiodothyronine (T4) hormones by depressing the incorporation of oxidized iodides to tyrosine, a precursor of T3 and T4 hormones.[2] In addition, a good correlation between the anti-thyroid activity in vivo and the formation constants of diiodine complexes with organic bases has been found.[2c] Therefore, there is an increasing interest in the study of the charge transfer complexes of iodine with thioamides or thiones [3−18] not

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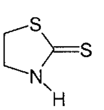
only for the clarification of the iodine-binding mechanism but also for the development of new anti-thyroidal agents as well. Moreover, the sulfur−iodine charge transfer complexes have been shown to possess promising electrical properties such as superconducting ability.[14,16,19]

The adduct bond formation between a donor (sulfur atom in the present case) and diiodine stabilizes the lone pair of electrons of the donor by mixing its orbital with the σ* anti-bonding orbital of I_2.[20] As a result a sulfur−iodine dative bond forms and the double bond of the thione group and also the iodine−iodine bonds[4,6] are lengthened. A direct relationship was found to exist between these three bond lengths: if *d*(S−I) is short, then *d*(C−S) and *d*(I−I) will be long and the donation is considered strong; for weak complexes, the situation is reversed.[4,6] In addition the ν(I−I) frequencies are linearly correlated with *d*(I−I) bond lengths.[12]

It is also worth noting that a partial positive charge is imparted to the rest of the molecule by the lengthening of the double bond of the thione group *d*(C−S).[4] Therefore, thioamides are particularly good donors; the positive charge is easily supported by nitrogen atoms (especially if it contains alkyl groups). Generally, the greater the stabilizing ability of the *N*-alkyl or -aryl groups, the stronger the resulting diiodine complex will be.[4] Similar behavior is expected in the case of molecules containing 1,3-dithiole sulfur atoms, such that the positive charge is delocalized over the S−C−S fragment of the ring, forming a 6π pseudo-aromatic system.[7]

In this paper, we report the structural and spectroscopic characterization of four new diiodine complexes with the heterocyclic thioamides, thiazolidine-2-thione or mercaptothiazoline (tzdtH, **I**), benzothiazole-2-thione (bztzdtH, **II**) and benzimidazole-2-thione (bzimtH, **III**) of formulae $[\{(tzdtH)_2I^+\}\cdot I_3^-\cdot 2I_2]$ (**1**), $[\{(bztzdtH)I_2\}\cdot I_2]$ (**2**), $[(bztzdtH)I_2]$ (**3**) and $[\{(bzimtH)I_2\}_2\cdot I_2\cdot 2H_2O]$ (**4**).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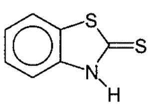
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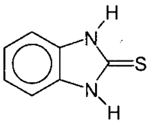

III

TzdtH (**I**) has been used in the treatment of hyper-thyroidism and our aim was to investigate its behavior in the reaction with diiodine. The ligands bztzdtH (**II**) and bzimtH (**III**), on the other hand, were also used for comparison purposes. Formation constant measurements of all these ligands with diiodine have been reported previously[8,9,21,22] in organic solvents, but always assuming the formation of 1:1 complexes in solution. No structural and/or spectroscopic studies have ever been reported previously. The structure of compound **1** shows that the ligand tzdtH, with anti-thyroidal activity, easily forms iodonium salts and is able to retain a total of four diiodine molecules per ligand molecule, thus acting as an iodine sponge. This is the first anti-thyroidal agent ever reported which contains an I_3^- counterion and interacts and retains two more diiodine molecules.

2. Results and Discussion

2.1. General Aspects

Studies on the interaction of thione donors with diiodine have established three types of adducts in the solid state, as proposed by Deplano et al.[5,10,23] These are type D···I−I (**A**) with long D···I and short I−I bond lengths,[24,25] type D−I−I (**B**) with comparable D−I and I−I distances[14,26] and type $D-I^+\cdots I^-$ (**C**) with short D−I and long I···I distances.[16] In type **A**,[5,10] the UV/Vis spectra show both the known charge-transfer band and the blue-shifted diiodine and donor bands, while the Raman ν(I−I) band appears in the range 180−140 cm^{-1}. In type **B**,[5,10] two peaks due to $\nu_{asym}(I-I)$ and $\nu_{sym}(I-I)$ are observed in the Raman spectra while in type **C** there is only one peak due to the ν(D−I) vibration.

In addition, reduction of iodine to polyiodides by electron transfer to the diiodine from the donor may also take place, together with the formation of iodonium salts with I^+ linearly bound to two donor molecules.[11,12,17] $D\cdot nI_2$ complexes may also form where the bonded I_2 molecule interacts with the other diiodine molecules.[11,16,27,28]

In our case, thiazolidine-2-thione causes the heterolytic cleavage of the I−I bond resulting in the formation of the $S-I^+-S$ and I_3^- as a counter anion. This is a rather rare structure and the second according to the best of our knowledge of an anti-thyroidal agent, the first being the one with thiourea (tu).[29] The two other ligands, benzothiazole-2-thione and benzimidazole-2-thione form compounds of stoichiometry DI_2 and $(DI_2)I_2$ (D is the thione donor) of **B** and **C** types.

Thiazolidine-2-thione could be considered as a strong donor towards diiodine, while benzothiazole-2-thione or benzimidazole-2-thione as weaker such donors. This is expected,[8] since in the last two cases, the sulfur atom is part of an aromatic system.

The formulae of the synthesized complexes **1**, **2**, **3** and **4** were first deduced from elemental analyses and spectroscopic data. All complexes were highly soluble in organic solvents and their crystals were stable in air but were stored in darkness in a refrigerator.

2.2. Crystal and Molecular Structures

$[\{(tzdtH)_2I^+\}\cdot I_3^-\cdot 2I_2]$ (1)

An ORTEP diagram of compound **1** is shown in Figure 1 while selected bond lengths and angles are given in Table 1. There are only a few crystal structures reported in the literature containing $S-I^+-S$ dimers. These include 1,3-dimethyl-2-thiourea (dmtu), ethylenethiouria (etu) thiourea (tu) and *N*-methylbenzothiazole-2-thione (mbzttH).[4,12,16,29]

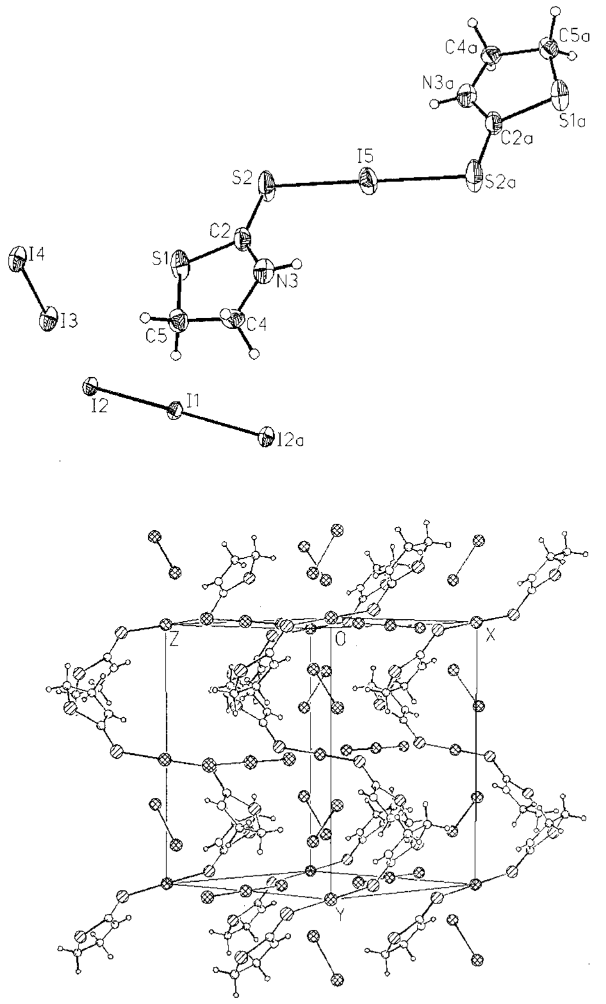


Figure 1. ORTEP diagram and unit cell of **1** together with the atomic numbering scheme

Table 1. Selected bond lengths [Å] and angles [°] for **1** with e.s.d. values in parentheses

Bond lengths:	
I(1)−I(2)	2.9195(14)
I(3)−I(4)	2.741(2)
I(5)−S(2)	2.654(6)
N(3)···I(4)[a]	3.82(2)
N(3)−H(3)	0.860(19)
H(3)[N(3)]···I(5)	2.9336(6)
N(3)···I(5)	3.495(19)
Bond angles:	
I(2)−I(1)−I(2)[b]	180.0
S(2)−I(5)−S(2)[c]	180.0
N(3)−H(3)···I(4)[a]	140

[a] $x + 1, y, z$. [b] $-x, -y, -z + 1$. [c] $-x + 1, -y + 1, -z + 1$.

The structure of compound **1** consists of three residues, one cationic {$(tzdtH)_2I^+$}, containing the linear $S-I^+-S$ linkage, one I_3^- counter anion and two independent diiodine molecules, shown only in the packing diagram of Figure 1. More similar structures including metal complexes have also been reported.[12] Comparison of various structural parameters of known iodonium complexes are reported in Table 2.

Both S−I bond lengths are equal to 2.654(6) Å. These bond lengths compare well with the corresponding distances found in {$[(dmtu)_2I]$} [2.602(4) and 2.654(4) Å],[4] in $[(tu)_2I^+]$ 2.629 Å [29] and in $[(mbzttH)_2I^+]$ [I−S = 2.600(2) and 2.634(2) Å].[12] They are, however, significantly longer than the ones in $(etu)\cdot I^+$ of 2.487(3) Å.[16] The S(2)−C(2) bond length of the complex **1** (Figure 1) is only 1.65(3) Å which is among the shortest such distances ever reported (Table 2).

The N(3)−C(2)−S(2)−I(5) torsion angle (Figure 1) is 9(3)° indicating an almost co-planar arrangement of the iodine atom towards the plane of N−C=S bond. The corresponding torsion angle found in {$[(tu)_2I^+]I^-$} is 17°, again almost co-planar, presumably due to the short intramolecular I···H or I···N distances.[29]

An intramolecular hydrogen bond between the imino NH proton and the sulfur atom coordinated to the iodine atom is formed in **1** (Figure 1) {H(3)[N(3)]···I(5) = 2.9336(6) and N(3)···I(5) = 3.495(19) Å}.[30] This hydrogen bonding favors the planar structure.[9]

The I(1)−I(2) bond length (Figure 1) of the linear I_3^- counter anion is 2.9195(14) Å, slightly longer than the corresponding bond lengths measured in {$[(dmtu)_2I][I_3^-]$} [I−I = 2.8874(14) and 2.9082(14) Å[4]]. Two diiodine mole-

Table 2. Structural parameters of known iodonium complexes

Compound	Counterion	S−I [Å]	C=S [Å]	I−I−I [Å]	I−I [Å]	$I_3^-\cdots I_2$ or $I^-\cdots I_2$ [Å]	S−I−S [°]	X−C−S−I [°]	Ref.
$(tzdtH)_2I^+$	$I_3^-\cdot 2I_2$	2.654(6)	1.65(3)	2.9195(14)	2.741(2)	3.4220 3.4120	180.00	9(3) (X = N) 169.7(12) (X = S)	[a]
$(dmtu)_2\cdot I^+]$[b]	I_3^-	2.602(4)/ 2.654(4)	1.728(13)/ 1.715(14)	2.8874(14)/ 2.9440(13)	–		177.77(4)	–	[4]
$(etu)\cdot I^+]$[b]	I_3^-	2.487(3)	1.73(1)	3.004(1)/ 2.850(1)	–		–	–	[16]
$[(tu)_2I^+)$[b]	I^-	2.629	1.723	–	–		180.0	17	[31]
$(mbzttH)_2I^+$ [b]	$I^-\cdot 3I_2$	2.600(2)/ 2634(2)	1.694(7)/ 1.682(7)		2.771(1)/ 2.746(1)/ 2.766(1)	3.237(1) 3.260(1) 3.242(1)	174.97(7)	–	[12]

[a] This work. [b] dmtu = 1,3-dimethyl-2-thiourea, etu = ethylenethiourea, tu = thiourea, mbzttH = *N*-methylbenzothiazole-2-thione.

cules are also co-crystallized with an I(3)−I(4) bond length of 2.741(2) Å (Figure 1). Weak intermolecular interactions (I_3^-···I_2), shorter than the sum of iodine van der Waals radii have been measured[30] between I(3)···I(2) (3.4220 Å) and I(4)···I(2) (3.4120 Å) and are longer than the corresponding I^-···I interactions between I^- and I_2 species found in {[(mbzttH)$_2$I$^+$][I$^-$·3I$_2$]} [3.237(1), 3.260(1) and 3.242(1) Å].[12]

[{(bztzdtH)I_2}·I_2] (2), [(bztzdtH)I_2] (3) and [{(bzimtH)I_2}$_2$·I_2·H_2O] (4)

ORTEP diagrams of molecules **2**, **3** and **4** are shown in Figures 2−4, respectively, while selected bond lengths and angles are given in Tables 3−5.

The crystal structures of molecules **2**, **3** and **4** consist of a thione ligand, bonded with a diiodine atom through a sulfur atom with S−I = 2.587(5) Å in **2** (Figure 2), S−I = 2.728(6) Å in **3** (Figure 3) and 2.571(6) Å in **4** (Figure 4), respectively. The corresponding I−I bonds are lengthened with values of I−I = 2.969(2) Å in **2** (Figure 2), I−I = 3.077(2) Å in **3** (Figure 3) and I−I = 2.989(2) Å in **4** (Figure 4) as compared with the I−I distances in the gas phase (2.677 Å),[14,31] or in crystalline diiodine (2.717 Å at 110 K),[14,32] as a result of the S···I interaction. Table 6 compares structural parameters of compounds **2**, **3** and **4** with other compounds of similar structures.

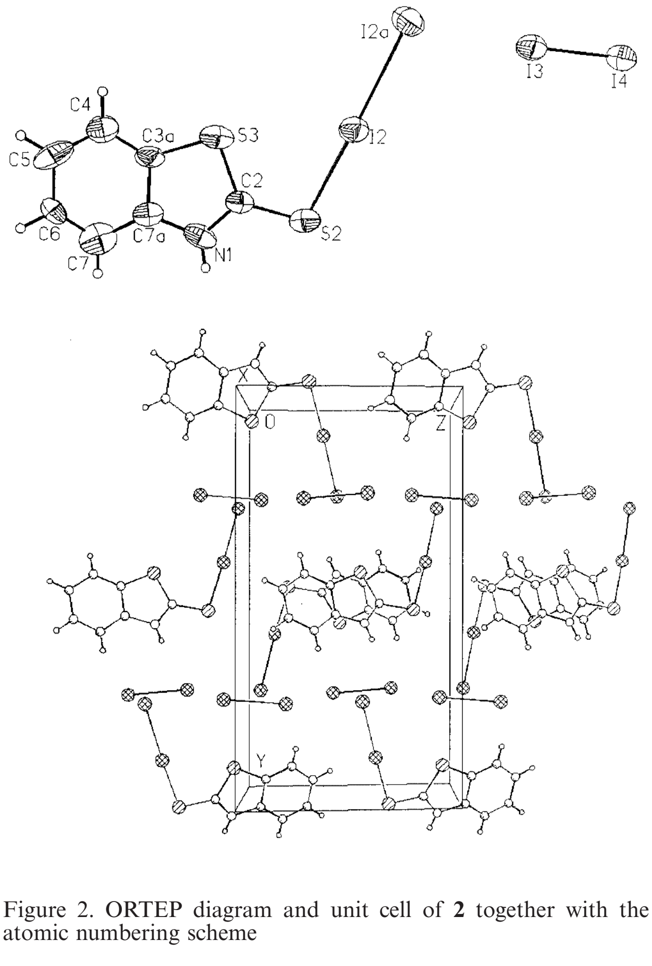


Figure 2. ORTEP diagram and unit cell of **2** together with the atomic numbering scheme

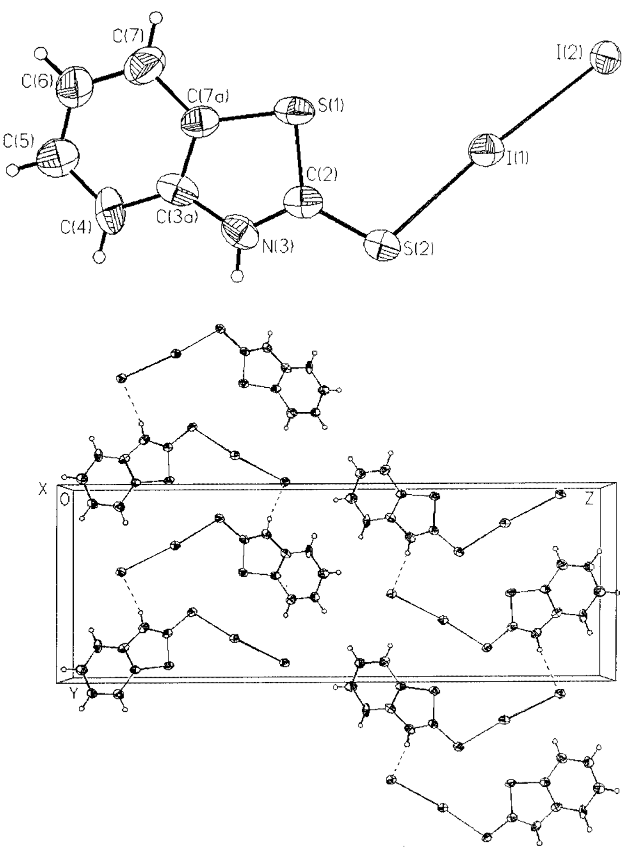


Figure 3. ORTEP diagram and unit cell of **3** together with the atomic numbering scheme

All bond lengths are within the expected ranges, however, the S−I bond length of molecule **2** is the shortest ever reported. The ligand donation leads to the formation of a neutral complex. The I−I bond lengths, all longer than the corresponding distance in free diiodine, are the longest ever measured for compounds **3** and **4**.

An extended intramolecular hydrogen bonding H(3)[N(3)]···I(2) = 2.7865(16) with N(3)···I(2) = 3.597(19) Å (Figure 3) is also formed in complex **3**. In the case of complex **4**, an intramolecular I(2)···H(4)[C(4)] = 3.2540 Å interaction[30] (Figure 4) leads to the formation of dimers, while an extended hydrogen-bonding network H(12w)[O(12)w]··· N(3) = 1.9033 Å, O(1w)··· N(3) = 2.846(19) Å[30] (Figure 4) links the alternate parallel dimers forming a supramolecular assembly.

The X−C=S···I torsion angles for the complexes were S(3)−C(2)−S(2)−I(2) = −2.3(12)° for **2** , S(1)−C(2)−S(2)−I(2) = −15.6(14)° for **3** and N(1)−C(2)−S(1)−I(3) = 3.0(19)° for **4**. Thus, all compounds, including **1** can be considered of almost coplanar arrangements of iodine atoms towards the N−C=S bond planes.

Finally, the values for the S−I−I angles (Table 6) also imply an almost linear arrangement.

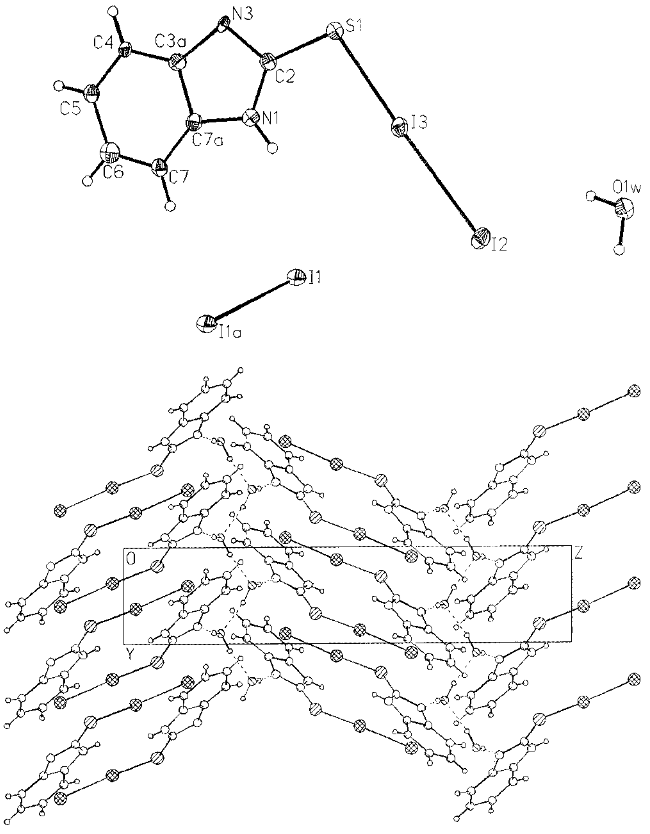


Figure 4. ORTEP diagram and unit cell of **4** together with the atomic numbering scheme

Table 3. Selected bond lengths [Å] and angles [°] for **2** with e.s.d. values in parentheses

Bond lengths:	
I(3)−I(4)	2.7504(18)
I(2)−I(2A)	2.969(2)
S(2)−I(2)	2.587(5)
N(1)···I(3)[a]	3.76(2)
Bond angles:	
C(2)−S(2)−I(2)	101.4(6)
S(2)−I(2)−I(2A)	177.78(13)
N(1)−H(1)···I(3)[a]	145

[a] $-x + 1, -y, -z + 1$.

Table 4. Selected bond lengths [Å] and angles [°] for **3** with e.s.d. values in parentheses

Bond lengths:	
I(1)−I(2)	3.077(2)
I(1)−S(2)	2.728(6)
N(3)···I(2)[a]	3.597(18)
Bond angles:	
S(2)−I(1)−I(2)	174.18(14)
C(2)−S(2)−I(1)	109.2(7)
N(3)−H(3)···I(2)[a]	158

[a] $-x + 1, y + 1/2, -z + 3/2$.

Table 5. Selected bond lengths [Å] and angles [°] for **4** with e.s.d. values in parentheses

Bond lengths:	
I(1)−I(1)[a]	2.767(3)
I(2)−I(3)	2.989(2)
I(3)−S(1)	2.571(6)
N(1)···I(3)	3.471(8)
O(1)W···O(1)W[b]	2.78(2)
O(1)W···N(3)[c]	2.77(3)
Bond angles:	
S(1)−I(3)−I(2)	176.76(14)
C(2)−S(1)−I(3)	102.3(8)
N(1)−H(1)···I(3)	119
O(1)W−H(1)W(1)···O(1)W[b]	171
O(1)W−H(1)W(2)···N(3)[c]	170

[a] $-x, -y + 1, -z + 1$. [b] $1 - x, -1/2 + y, 3/2 - z$. [c] $x, 3/2 - y, 1/2 + z$.

2.3. Spectroscopy

UV/Vis

The visible spectra of the thione−diiodine adducts in dichloromethane or chloroform exhibit one distinct absorption band at 495−505 nm which is assigned to the "blue-shift" band of I_2,[18] which occurs at 504 nm in free I_2 in CH_2Cl_2.[14] A shoulder in the range of 310−360 nm could be assigned to a charge-transfer band from the HOMO of the donor to the diiodine LUMO (σ_{π}*)[5,8−10,17]. Complex **1** exhibits a c.t. band at 317 nm, while complex **4** shows a c.t. band at 356 nm. It should be noted that the c.t. bands are not recognizable for complexes **2−3**, most probably as a result of interference from the intraligand transitions occurring at almost the same wavelength. The bands, however, are enhanced in intensity, increasing their coefficients, in the complexes.

According to the assumption of Laurence et al.,[9] c.t. absorption bands of I_2−thioamide complexes have been correlated with an in-plane or a perpendicular arrangement of the I_2 moiety towards the plane of N−C=S and this hypothesis is also followed by the thiocarbonyl−I_2 adduct studied by Essefar et al.[3] Thus, complexes of thiocarbonyl−I_2 or I_2−thioamide with in-plane conformation, where the X−C=S···I torsion angle was close to 0°, have shown the c.t. band at 295−305 nm while those with perpendicular arrangements with the angle near 90° have shown this band around 320−350 nm.[3,9] Generally, perpendicular complexes are expected when the substituents around the thiocarbonyl group are bulky[9] while a planar arrangement is expected when an NH group *cis* to the thiocarbonyl group exists.[3] Thus, for all our complexes coplanar arrangements are expected since they all contain the *cis*-NH group, able to form hydrogen bonds with I_2.

Since the X−C=S···I torsion angle for compound **1** is 9(3)° and for **4** is 3.0(19)°, the results of Laurence et al.[9] as well as Esseffar et al.[3] seem to be confirmed for **1** but unexpectedly not for **4**. The absorption band at 283 nm in the spectrum of complex **1**, at 329 nm in the case of complex **2**, at 329.5 nm for **3** and at 309.5 nm for **4** are attributed to intraligand (π→π*) transitions.

Vibrational Spectroscopy

Characteristic infrared bands of the complexes and the ligands are listed in Table 7. The spectra of the complexes

Table 6. Structural parameters of known iodine complexes

Compound	S−I [Å]	N−H [Å]	H(N)···I [Å]	N···I [Å]	C=S [Å]	I−I [Å] coord./ uncoord.	I···I [Å]	S−I−I [°]	X−C−S−I [°]	Ref.
[{(bztzdtH)I_2}·I_2]	2.587(5)	0.8595	–	–	1.706(18)	2.969(2)/ 2.7504(18)	3.423(2)/ 3.445(2)	177.79(13)	−2.3(12) (X = S) 174.7(13) (X = N)	[a]
[(bztzdtH)I_2]	2.728(6)	0.861(19)	2.7865(16)	3.597(19)	1.75(2)	3.077(2)	–	174.19(14)	−15.6(14) (X = S) 166.5(15) (X = N)	[a]
[{(bzimtH)I_2}$_2$·I_2·H_2O]	2.571(6)	0.8603	3.0397	3.545(8)	1.722(19)	2.989(2)/ 2.767(3)	3.4464(19)	176.84(13)	3.0(19) (X = N) −179.7(13) (X = N)	[a]
[ptc·I_2][b]	2.755(2)	–	–	–	1.690(6)	2.812(1)	–	175.42(4)	–	[5]
[ttb·I_2][b]	2.805(3)	–	–	–	1.663(8)	2.812(2)	–	175.43(6)	–	[5]
[mdtt·I_2][b]	2.716(3)	–	–	–	1.666(11)	2.8083(14)	–	177.46(7)	−1.5(9)	[7]
mbit·I_2][b]	2.683(2)	–	–	–	1.721(4)	2.897(1)	–	175.71(3)	−96.4(4)	[10]
bzoxtH·I_2][b]	2.874(2)		3.09	–	1.689(7)	2.769(1)	3.453(1)	178.44(4)	–	[11]
dmimdtH ·I_2][b]	2.748(1)	–	–	–	1.678(3)	2.817(1)	–	176.89(2)	–	[13]

[a] This work. [b] ptc = 1,3-dithiacyclohexane-2-thione, ttb = 4,5-ethylenedithio-1,3-dithiole-2-thione, mdtt = 4,5-bis(methylsulfanyl)-1,3-dithiole-2-thione, mbit = 1,1-methylenebis(3-methyl-4-imidazoline-2-thione), bzoxtH = benzoxazole-2-thione and dmimdtH = 5,5-dimethylimidazoline-2,4-dithione.

Table 7. Characteristic vibration bands [cm^{-1}] in infrared spectra of complexes or ligands

Complex	ν(N−H) solid state	ν(N−H) CH_2Cl_2 solution	Thioamide I	Thioamide II	Thioamide III	Thioamide IV	FT-Raman free I_2	Coordinated I_2	I_3^- ions	Ref.
[{(tzdtH)$_2I^+$} I_3^-·2I2] (**1**)	3296	3325	1512	1300	994	–	181.5, 178.5,		116.8	[a]
[{(bztzdtH)I_2}·I_2] (**2**)	3271	3372	1480	1329	1010	845	172.8	143.7		[a]
[(bztzdtH)I_2] (**3**)	3116	3372	1489	1327	1011	848		147		[a]
[{(bzimtH)I_2}$_2$·I_2·H_2O] (**4**)	3325	3379	1508	1212	–	747	170			[a]
ThzdtH	3131	3396, 3233	1490	1245	990	650−690				[33a]
BzthzdtH	3108	3379, 3204	1490	1320	1010	860				[33b−33c]
BzimtH	3155	3434	1513	1339	1016	743				[33d−33e]

[a] This work.

show distinct vibrational bands between 1520−1480 and 1330−1210 cm^{-1}, which can be assigned to ν(CN) vibrations (thioamide I and II bands) and 1020−990 and 850−740 cm^{-1}, which can be attributed to the ν(CS) vibrations (thioamide III and IV bands). Amide N−H bond vibrations were observed at 3434−3204 cm^{-1} in CH_2Cl_2. According to Laurence et al.,[9] the ν(NH) band of I_2−thioamide complexes in CH_2Cl_2 shifts to lower wavenumbers and it is more intense in the planar complexes than in the perpendicular ones (torsion angle X−C=S···I). This is due to the amphoteric behavior of I^+, which can simultaneously accept electrons from the sulfur atom and offer electrons to the hydrogen atom of the N−H group, thus forming an intramolecular hydrogen bond.[9]

In our case, N−H···I hydrogen bonds exist in complexes **1**, **3** and **4**. In CH_2Cl_2 solutions, the band assignable to ν(N−H) appears in the IR spectrum of complex **1** at 3325 cm^{-1}, while the ligand tzdtH shows also two bands for the same vibration at 3396, and 3233 cm^{-1} assigned to its free and associated forms.[9] The band of the free form shifts by 71 cm^{-1} to lower wavenumbers in **1**. In **4** the shift of 55 cm^{-1} is towards lower wavenumbers (3379 cm^{-1} for **4**, 3434 cm^{-1} for bzimtH), in accordance with its structure. However, the ν(N−H) band of the free form of the ligand bztzdtH at 3379 cm^{-1} ν(N−H) appears as a unique band at 3372 cm^{-1} in both **2** and **3** complexes shifted again to lower wavenumbers (7 cm^{-1}) in accordance with the literature.[9] In the solid state the situation is even more complicated, since all bands shift to higher wavenumbers on passing from the free ligands to the complexes.

New bands appearing at 155 cm^{-1} in the far-IR spectra of the compounds may be assigned to the ν(I−I) stretching vibration modes.[34] The corresponding ν(I−S) bond vibration for the dithian−I_2 complex, was observed at 212 cm^{-1}.[34] In our compounds, new bands appear around 281−280 cm^{-1} and 255−254 cm^{-1} which can be similarly assigned (Figure 5).

Characteristic Raman frequencies of the compounds are also included in Table 7. Diiodine vapor gives a strong band at 216 cm^{-1} ν(I−I) which appears at 180 cm^{-1} in the solid state.[35] This shifts to lower wavenumbers upon coordination to a donor atom, reflecting the reduction in the I−I bond order and the strengthening of the complex formed.[5,10,12]

Thus, the Raman spectrum of complex **1**, recorded in the 300−50 cm^{-1} region, shows a doublet at 181.5 and 178.0

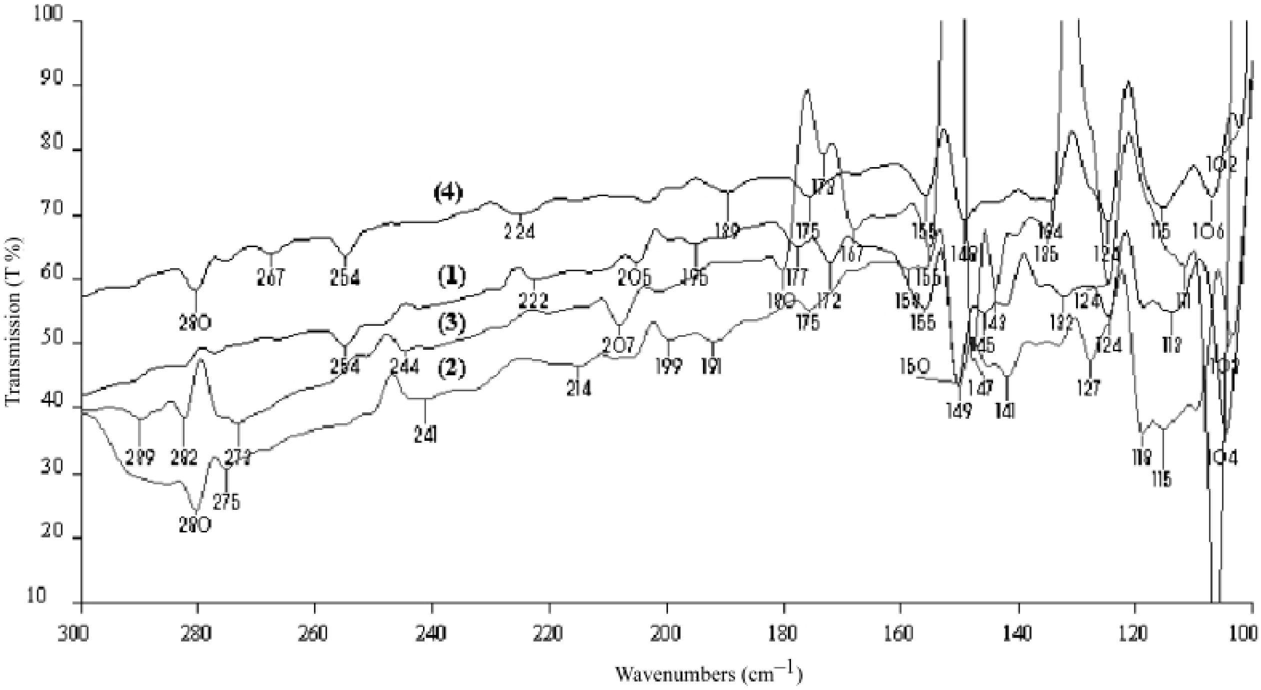


Figure 5. Far-IR spectra of the complexes

cm^{-1}, very close to that usually reported for the symmetric stretching [ν_1(I−I)] of I_2 in the solid state, which may be attributed to the uncoordinated I_2 that cocrystallizes. The I−I bond length of 2.715 Å, measured in free diiodine,[32] is slightly lengthened to 2.741 Å in **1**, justifying this shifting (Table 2). It is worth mentioning that bands around 110 cm^{-1} are normally attributed to the ν_1 symmetric stretching of I_3^-, which being a symmetrical ion normally exhibits only one Raman-active band. Antisymmetric stretching and bending is only infrared-active. When a distortion of I_3^- occurs, the antisymmetric stretching may become Raman-active and additional bands of medium intensity near 140−130 and 80−70 cm^{-1} can be observed, assigned to antisymmetric stretching (ν_3) and ν_2 deformation, respectively.[24,26] Thus, the intense band at 116.8 cm^{-1} is indicative of the presence of I_3^- ions. Similar assignments have also been reported in the literature: 172 cm^{-1} [strong, ν(I−I)], 150 (medium) and 105cm^{-1} [strong, $\nu(I_3^-)$][15,36] for interacting I_3^- and I_2 units. Furthermore the shoulder at 153.3 cm^{-1} might be attributed to the δ(C−S−I) bend, which has already been reported at 150 cm^{-1}.[37] Moreover, δ(C−S−I) bends are reported to be less intense than [ν_1(I−I)]. Therefore, it is very likely that the shoulder at 153.5 cm^{-1} might also be attributed to I, bridging both of the (tzdtH) moieties, in our case.

The Raman spectrum of complex **2** is characterized by an intense band at 172.8 cm^{-1}, attributed to ν_1(I−I) of the I_2 counterpart [I(3)−I(4), Figure 2]. The band at 143.7 cm^{-1} may also be attributed, to coordinated I_2 moieties (Figure 2). Structural assignments from Raman spectra indicate that complex **2** follows the pattern of the D−I−I (**B**-type) adducts[5] which is also in agreement with the relatively shorter S−I and longer I−I bonds measured for **2** by X-ray crystallography (see section 2.2).

The Raman spectrum of complex **3** shows a band at 147 cm^{-1} which can be attributed to ν_1(I−I) symmetric stretching. Considering the magnitude of the shift from free I_2 of 33 cm^{-1} for complex **3** and of 36.3 cm^{-1} for complex **2**, it can be said that the species generated in adduct formation are much effective.

Bands around 150 cm^{-1} were also reported in the literature for I_2 adducts: 152 cm^{-1} (5,5-dimethylimidazolidine-2,4-dithionediiodine),[24] 147 cm^{-1} {4,5,6,7-tetrathiocino[1,2-*b*:3,4-*b′*]diimidazolyl-1,3,8,10-tetraethyl-2,9-dithionebis(diiodine)},[38] 158 cm^{-1} (5,5-dimethyl-4-oxoimidazolidine-2-thionediiodine),[24] 152 and 158 cm^{-1} (5,5-dimethylimidazoline-2,4-dithione and 5,5-dimethyl-4-oxo-2-thioxoimidazolidium, respectively).[24] Finally, the presence of free I_2 is detected in the Raman spectrum of complex **4** as a shoulder at 170 cm^{-1}.

Resonance Raman (RR) uses visible laser excitation sources − which may induce fluorescence, sample pyrolysis, and photoreactions − and spurious peaks, could appear in the spectrum.[39a] Studies comparing FT-Raman and RR spectroscopy have shown remarkable advantages of the former since it eliminates or strongly reduces the pyrolysis of the samples.[39b]

The RR spectra of complex **1** were obtained, using laser sources, 488.0 and 514.5 nm. Bands at 220 cm^{-1} observed in RR have been attributed to I_2 in the gas phase arising from decomposition.[39c] The band observed in the present case (256.8 cm^{-1}) at a much higher frequency, is attributed to I_2 (vapor).

The large band centered at 100 cm^{-1} can be attributed to I_3^- species. In the case of the 514.5 nm line, the spectrum is dominated by a peak at 112.6 cm^{-1} (I_3^-). A large band centered at 167.9 cm^{-1} might be attributed to an I_2 interacting species. The high intensity observed for the 112.6 cm^{-1} band could be due to I_2 disproportionation. Nevertheless, enhancement of this band has already been reported in the literature and attributed to the resonance effect.[39c]

The RR spectra of complex **2** at 488.0 nm showed very low intensity, presenting a cut-off below 50 cm^{-1}. At 514.5 cm^{-1}, we observed an enhancement of the peak at 107 cm^{-1} ($2\nu = 212$ cm^{-1}), and a shoulder at 158.2 cm^{-1}. Once again, the detection of a band relating to I_3^- could either be considered as an RR effect or as the generation of I_3^- species by decomposition. As in the previous case, the RR spectrum using the 488.0-nm line led to a very low intensity spectrum in the case of complex **3**, presenting a cut-off below 50 cm^{-1}. In the case of 514.5-nm excitation, bands at 172 cm^{-1} and 107 cm^{-1} dominate the spectrum in the low-frequency region. It is worth noting the presence of the band at 172 cm^{-1} attributed to I_2, which was absent when an NIR source was used. For this system, the ν(C−H) region as well as the skeleton region (not shown) seemed to be unaffected. The spectra of complex **4** showed no band in the case of the 488.0-nm source. With the 514.5-nm line, an intense band was observed at 107.0 cm^{-1} ($2\nu = 214.9$ cm^{-1}; $3\nu = 328.3$ cm^{-1}), attributable to an I_3^- species which may be generated by the decomposition of complex **4**. As in the previous case, a cut-off below 50 cm^{-1} was shown in the case of 663 nm line.

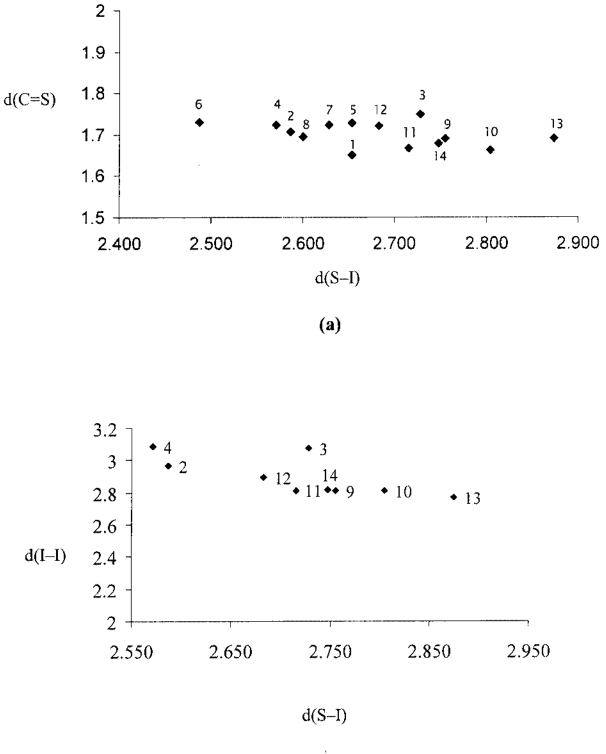
2.4. Correlations

The S−I bond strength of the iodine charge transfer complexes could be classified by the graphical plots of d(C=S) vs. d(S−I) [see (a) in Figure 6] or d(I−I) vs. d(S−I) [see (b) in Figure 6].[4] Ionic complexes exhibit short S−I bond lengths, due to the strong interaction between the iodine and sulfur atoms [see (a) in Figure 6], which seems to be independent from the C=S bond length. For charge transfer complexes with an S−I−I structure, a hyperbolic correlation between d(S−I) vs. d(I−I) has been proposed[16] which is also confirmed for the complexes **2** and **4** but not for **3** [see (b) in Figure 6]. Additionally d(I−I) is linearly correlated to the FT-Raman ν(I−I) frequencies[24] confirmed for complexes **2** and **3** (Figure 7).

According to the value of the I−I bond order (n) defined by the Pauling Equation,[31] where d_o is the I−I bond length of I_2 in the gas phase, which is 2.67 Å,[40] Deplano et al.[24] and Bigoli et al.[5] classified I_2 adducts in three classes, type **A** (D···I−I), **B** (D−I−I) and **C** (D−I···I).[10,24]

$$d(\mathrm{I-I}) = d_o - 0.85\cdot\log(n)$$

If the value of the I−I bond order $n \geq 0.6$ [$d(\mathrm{I-I}) < 2.85$ Å] the adduct could be classified as a type **A**, while if $n \leq 0.4$ [$d(\mathrm{I-I}) > 3.01$ Å] as a type **C**. The I−I bond order values calculated for the complexes studied in this work are 0.445, 0.332 and 0.421 for the complexes **2**, **3**, and **4**, re-



(a)

(b)

Figure 6. Plot of d(S−C) against d(S−I) (a) and d(I−I) against d(S−I) (b) for thione−iodine adducts **5** [{$(dmtu)_2\cdot I^+$}$\cdot I_3^-$][4] (dmtu = 1,3-dimethyl-2-thiourea), **6** [{$(etu)\cdot I^+$}$\cdot I_3^-$][16] (etu = ethylenethiouria), **7** [{$(tu)_2I^+$}$\cdot I^-$][29] (tu = thiourea), **8** [$(mbzttH)_2I^+\cdot I^-\cdot 3I_2$][12] (mbzttH = N-methylbenzothiazole-2-thione), **9** [$ptc\cdot I_2$][5] (ptc = 1,3-dithiacyclohexane-2-thione), **10** [$ttb\cdot I_2$],[5] (ttb = 4,5-ethylenedithio-1,3-dithiole-2-thione), **11** [$mdtt\cdot I_2$][7] [mdtt = 4,5-bis(methylsulfanyl)-1,3-dithiole-2-thione], **12** [$mbit\cdot I_2$][10] [mbit = 1,1-methylenebis(3-methyl-4-imidazoline-2-thione)], **13** [$bzoxtH\cdot I_2$][11] (bzoxtH = benzoxazole-2-thione), **14** [$dmimdtH\cdot I_2$][13] (dmimdtH = 5,5-dimethylimidazoline-2,4-dithione), including our compounds **1**−**4**

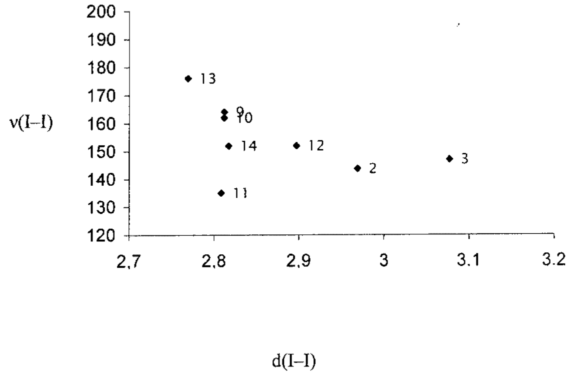


Figure 7. Correlation between ν(I−I) Raman bands of the adducts **9** [$ptc\cdot I_2$][5] (ptc = 1,3-dithiacyclohexane-2-thione) [ν(I−I) = 164 cm^{-1}], **10** [$ttb\cdot I_2$][5] (ttb = 4,5-ethylenedithio-1,3-dithiole-2-thione) [ν(I−I) = 162 cm^{-1}], **11** [$mdtt\cdot I_2$][7] [mdtt = 4,5-bis(methylsulfanyl)-1,3-dithiole-2-thione] [ν(I−I) = 136 cm^{-1}], **12** [$mbit\cdot I_2$][10] [mbit = 1,1-methylenebis(3-methyl-4-imidazoline-2-thione] [ν(I−I) = 152 cm^{-1}], **13** [$bzoxtH\cdot I_2$][11] (bzoxtH = benzoxazole-2-thione) [ν(I−I) = 176 cm^{-1}], **14** [$dmimdtH\cdot I_2$][13] (dmimdtH = 5,5-dimethylimidazoline-2,4-dithione) [ν(I−I) = 152 cm^{-1}], including compounds **2**−**4**

spectively. Therefore, complex **3** could be classified as a type **C** adduct, and complexes **2** and **4** as types **B**.

3. Conclusions

Using the anti-thyroidal agent thiazolidine-2-thione, together with benzothiazole-2-thione or benzimidazole-2-thione, we have tried to compare their behavior towards I_2 coordination and possibly throw some light on the anti-thyroidal activity and mechanism of reaction of these types of molecules. The structure of compound **1** is the second such example of an anti-thyroidal agent.

Laurence et al.[9] also tried to reach similar conclusions by using the anti-thyroidal drugs methimazole, carbimazole and propylthiouracil. No crystal structure of their I_2 adducts was reported, however.[9,41] These authors[9,41] concluded that the action of the anti-thyroidal drugs involved diiodine sponges trapping I_2, I^+ or HOI[42] which were produced during the oxidation of iodide ions taken up by the thyroid. Thus, the agents should be able to form stable complexes with diiodine, diverting iodides from their second oxidation step ($I_2 \rightarrow 2\ I^+ + 2\ e^-$) and in this way prevent the electrophilic substitution of I^+ on the tyrosine residue of thyroglobulin.[2c,43]

This conclusion seems to be substantiated in our work, because (i) like methimazole,[9] thiazolidine-2-thione forms the most stable complexes with I_2 in CH_2Cl_2 solution, compared with the other two ligands[8,9,22] assuming the formation of 1:1 complexes; (ii) the data shows that thiazolidine-2-thione can be classified as a strong donor ligand, in contrast to the non-anti-thyroidal activity of the two other ligands; (iii) thiazolidine-2-thione is such a strong donor that it causes heterolytic cleavage of the diiodine molecule to form $[\{D_2I^+\}I_3^-{\cdot}2I_2]$ species and is able to carry two more neutral I_2 molecules in the solid state, which the two other ligands cannot.

Therefore, new anti-thyroidal agents might be found among the strong donors towards diiodine, having the ability to absorb as many molecules of diiodine as possible. Also, these agents should be able to reduce iodine to polyiodides by causing cleavage of the I−I bond.

4. Experimental Section

4.1. Materials and Instruments: All solvents used were reagent grade. Diiodine (Aldrich), thiazolidine-2-thione, benzothiazole-2-thione and benzimidazole-2-thione (Merck) were used with no further purification. Elemental analyses for C,H,N,S were carried out with a Carlo−Erba EA model 1108 elemental analyzer. Melting points were measured in open tubes with a Stuart scientific apparatus and are uncorrected. Infra-red spectra in the region of 4000−370 cm^{-1} were obtained from KBr discs while far-infrared spectra in the region of 400−50 cm^{-1} were obtained from polyethylene discs, with a Perkin−Elmer Spectrum GX FT-IR spectrophotometer. A Jasco UV/Vis/NIR V 570 series spectrophotometer was used to obtain the electronic absorption spectra. The ^1H NMR spectra were recorded with a Bruker AC250 MHFT NMR instrument in $CDCl_3$ solutions. Chemical shifts δ are given in ppm referenced to internal TMS (^1H).

4.2. Synthesis and Crystallization of the Molecules: Complexes $[\{(tzdtH)_2I^+\}{\cdot}I_3^-{\cdot}2I_2]$ (**1**), $[\{(bztzdtH)I_2\}{\cdot}I_2]$ (**2**), $[(bztzdtH)I_2]$ (**3**) and $[\{(bzimtH)I_2\}_2{\cdot}I_2{\cdot}2H_2O]$ (**4**) were prepared by mixing dichloromethane solutions of diiodine with dichloromethane solution of the appropriate thione in molar ratios of 2:1 in the case of complexes **1**, **2** and **4** or 1:1 for complex **3** in air at 0 °C under continuous stirring for 2−3 h. The solutions were then filtered and the resulting clear solutions were kept in the refrigerator for several days. Dark crystals of the complexes suitable for single-crystal analysis by X-ray crystallography were then grown and filtered off.

Complex 1: Yield 0.060 g, (20%); m.p. 50−52 °C. UV/Vis (CH_2Cl_2): λ_{max} (logε) = 497 (3.59), 283 (4.50), 227.5 (4.39). ^1H NMR ($CDCl_3$): δ = 7.9441 [s, 1 H, HN−C(5)], 4.1884−4.1481 [t, CH_2−C(4)], 3.7081−3.6688 [t, 2 H, CH_2−C(5)]. $C_6H_{10}IN_2S_4{\cdot}I_3{\cdot}2I_2$ (1253.60): calcd. C 5.75, H 0.80, N 2.23, S 10.23; found C 5.57, H 0.50, N 2.09; S 9.46.

Complex 2: Yield 0.105 g (30%); m.p. 112 °C. UV/Vis (CH_2Cl_2): λ_{max} (logε) = 503 (2.82), 329 (3.90), 229 (3.92). ^1H NMR ($CDCl_3$): δ = 10.542 [s, 1 H, HN−C(2) of bztzdtH], 7.597−7.384 (m, 4 H, bz of bztzdtH). $C_7H_5I_2NS_2{\cdot}I_2$ (674.84): calcd. C 12.46, H 0.75, N 2.08, S 9.50; found C 12.96, H 0.47, N 1.91, S 6.28.

Complex 3: Yield 0.256 g (61%), m.p. 110 °C. UV/Vis (CH_2Cl_2): λ_{max} (logε) = 506.5 (3.02), 329.5 (4.46), 229 (4.30). ^1H NMR ($CDCl_3$): δ = 10.6 [br, 1 H, HN−C(2) of bztzdtH], 7.935−7.379 (m, 4 H, bz of bztzdtH). $C_7H_5I_2NS_2$ (421.06): calcd. C 19.97, H 1.20, N 3.33; S 15.23; found C 19.78; H 1.12, N 3.19, S 15.68.

Complex 4: Yield 0.045 g (12%); m.p. 165 °C. UV/Vis ($CHCl_3$): λ_{max} (logε) = 499, (3.56), 309.5, (4.91), 239 (4.60). ^1H NMR ($CDCl_3$): δ = 7.4055−7.3099 (m, 4 H, bz of bzimtH). $C_{14}H_{12}I_6N_4S_2{\cdot}2H_2O$ (1097.83): calcd. C 15.32, H 1.47, N 5.10, S 5.84; found C 15.91, H 0.94, N 5.11, S 6.74.

4.3. Raman Measurements: Micro FT-Raman measurements were carried out by using near-infrared laser radiation (Nd^{3+}:YAG, 1064.1 nm). FT-Raman spectra (2.6 cm^{-1} resolution) were recorded with a Bruker IFS-88 FT-IR/FRA-105 Raman module fitted with a Ge proprietary detector and coupled via two 1.0-m photooptic cables to a Nikon Optiphot-II optical microscope equipped with a Nikon 20X, super long-range objective. Near-IR laser radiation was directed onto the sample through the objective and collected along the same optical pathway in a 180° backscattering mode. Samples were measured as solid powders dispersed on a glass slide. Resonance Raman spectra were measured by means of a Renishaw 3000 Ramanscope spectrometer. A typical acquisition time was 10 s, with a slit of 25 μ. Measurements were performed using 488.0- and 514.5-nm sources.

4.4. X-ray Structure Determination: Data were collected by the ω-scan technique in the range $3° < 2\theta < 23°$ for **1** and **4**, and $3° < 2\theta < 25°$ for **2** and **3** with a KUMA KM4CCD four-circle diffractometer[44a] with CCD detector, using graphite-monochromated Mo-K_α (λ = 0.71073Å) at −103 °C (**1**), 20 °C (**2** and **3**) and −168 °C (**4**). Cell parameters were determined by a least-squares fit[44b] of 655, 444, 807, and 3156 reflections for **1**, **2**, **3** and **4**, respectively. All data were corrected for Lorentz-polarization effects and absorption.[44b] Totals of 4672 (**1**), 5771 (**2**), 4699 (**3**) and 6939 (**4**) reflections were collected of which 1603, 2207, 1484 and 1691, respectively, were unique; of these 1175, 1159, 1311 and 1631 were observed [$I > 2\sigma(I)$]. The structures were solved with direct

Table 8. Crystal data and the structure refinement details for complexes **1**, **2**, **3** and **4**

	1	**2**	**3**	**4**
Empirical formula	$C_3H_5I_4NS_2$	$C_7H_5I_4NS_2$	$C_7H_5I_2NS_2$	$C_7H_6I_3N_2S \cdot H_2O$
Formula mass	626.80	674.84	421.04	548.91
Crystal size [mm]	0.3 × 0.15 × 0.1	0.4 × 0.2 × 0.1	0.2 × 0.2 × 0.1	0.3 × 0.2 × 0.05
Crystal system	monoclinic	monoclinic	orthorhombic	monoclinic
Space group	$P2_1/n$	$P2_1/n$	$P2_12_12_1$	$P2_1/c$
a [Å]	9.145(2)	8.357(2)	4.189(1)	13.4828(14)
b [Å]	13.259(2)	17.829(4)	9.770(3)	4.6704(4)
c [Å]	10.615(2)	9.603(2)	27.704(8)	21.267(2)
β [°]	106.30(2)	94.39(3)		101.029(8)
V [Å^3]	1235.4(5)	1426.6(6)	1133.8(5)	1376.3(2)
Z	4	4	4	4
$\rho_{calcd.}$ [g cm^{-3}]	3.37	3.14	2.47	2.64
μ [mm^{-1}]	10.38	9.00	5.87	6.94
R[a], $wR2$[b] [$I > 2\sigma(I)$] (%)	5.06, 13.49	6.54, 12.76	6.33, 13.05	6.53, 14.50

[a] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$.

methods using SHELXS97[45] and refined by full-matrix least-squares procedures on F^2. All non-hydrogen atoms were refined anisotropically, hydrogen atoms were located at calculated positions and refined as a "riding model" with isotropic thermal parameters fixed at 1.2 times the U_{eq} values of the appropriate carrier atom. Selected crystal data are listed in Table 8. Bond lengths and angles for the complexes are given in Tables 2−5, while the displacement ellipsoid representation of the complexes and their unit cell diagrams are shown in Figures 1−4. CCDC-172151 (**1**), -172154 (**2**), -172153 (**3**) and -172152 (**4**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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