Hindawi Publishing Corporation
Bioinorganic Chemistry and Applications
Volume 2006, Article ID 60291, Pages 1–10
DOI 10.1155/BCA/2006/60291

Interaction of Thioamides, Selenoamides, and Amides With Diiodine

Sotiris K. Hadjikakou and Nick Hadjiliadis

Section of Inorganic and Analytical Chemistry, Department of Chemistry, University of Ioannina, 45110 Ioannina, Greece

Received 25 June 2006; Revised 27 August 2006; Accepted 8 September 2006

We review the results of our work on the iodine interaction with thioamides, selenoamides, and amides. Complexes with (i) "spoke" or "extended spoke" structures, $D \cdot I_2$ and $D \cdot I_2 \cdot I_2$, respectively, (D is the ligand donor) (ii) iodonium salts of $\{[D_2 - I]^+[I_n]^-\}$ ($n = 3, 7$) and $\{[D_2 - I]^+[FeCl_4]^-\}$ formulae and (iii) disulfides of the categories (a) [D − D], (b) $\{[D - DH]^+[I_3]^-\}$ have been isolated and characterized. A compound of formula $\{[D_2 - I]^+[I_3]^-[D \cdot I_2]\}$ containing both types of complexes (i) and (ii) was also isolated. The interaction of diiodine with selenium analogs of the antithyroid drug 6-*n*-propyl-2-thiouracil (PTU), of formulae RSeU (6-alkyl-2-Selenouracil) results in the formation of complexes with formulae $[(RSeU)I_2]$. All these results are correlated with the mechanism of action of antithyroid drugs. Finally, we review here our work on the diiodine interaction with the amides (LO).

INTRODUCTION

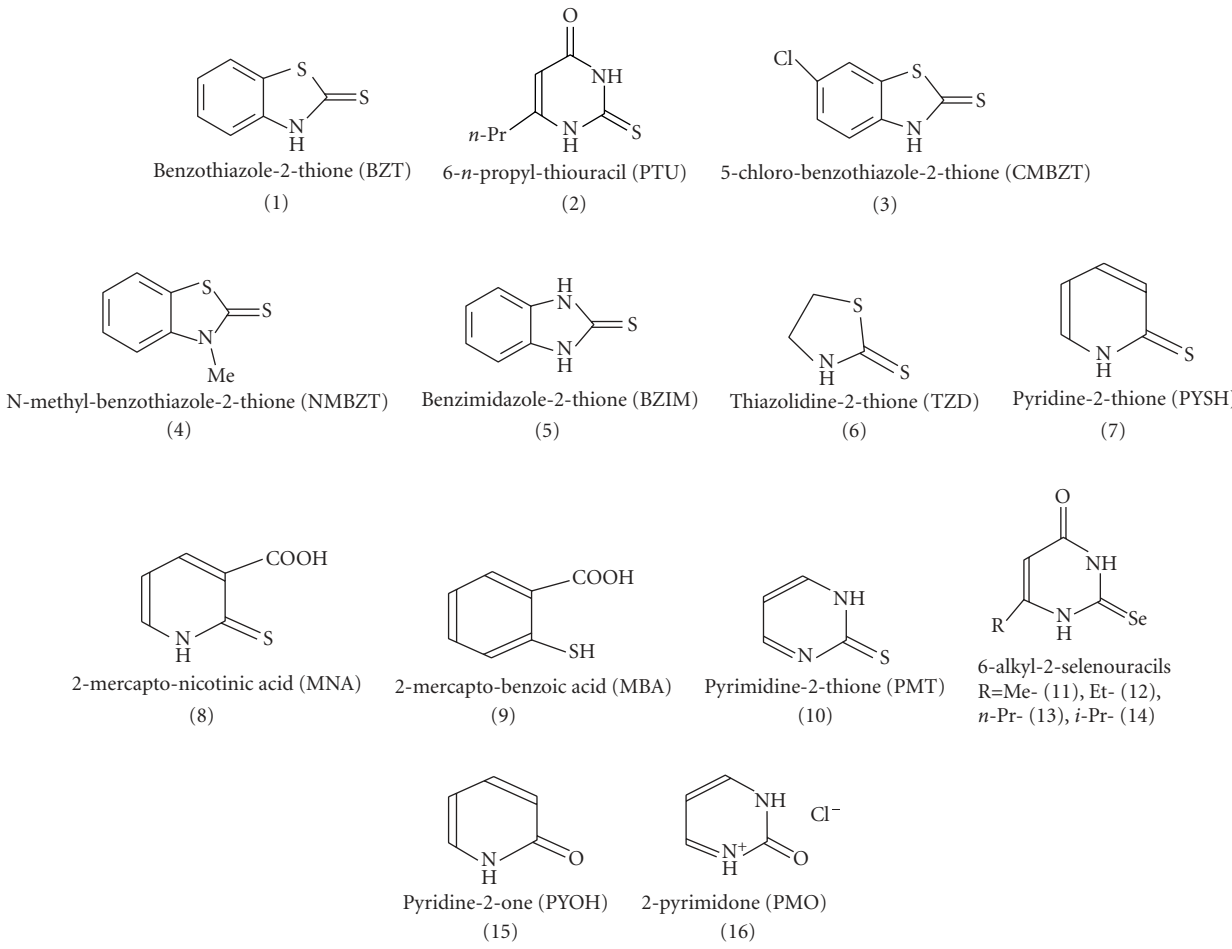
The perturbation of the I−I bond when diiodine binds to heterocycles such as thioamides or selonoamides results to novel complexes containing iodine [1–13]. Various types of such complexes have been obtained thus far, including charge transfer (ct) complexes with the so-called "spoke" or "extended spoke" structures ($DS \cdot I_2$ or $DS \cdot I_2 \cdot I_2$) (D is the ligand donor) [6], the "T-shape" structures, iodine(I) coordinated to two thioamides to form "iodonium salts" ($[DS{-}I{-}DS]^+ \cdot (I_3)^-$) [6], oxidation products of formulae $(DS{-}I)^+$ [6], dications of formulae ($[DS{-}SD]^{2+}(I_n^-)_2$), [6] and monocations of formulae ($[DS{-}SDH]^+(I_3)^-$) [6] (DS or D=S, a thioamide ligand donor).

The interest in studying I_2 interaction with thioamides and selenoamides arises from their application in both biological chemistry and material sciences. Thus,

(i) thioamides, like 6-*n*-propyl-thiouracil (PTU), N-methyl-imidazoline-2-thione (methimazole, MMI), 3-methyl-2-thioxo-4-imidazoline-1-carboxylate (carbimazole) (CBZ), are known antithyroid drugs [14] against hyperthyroidism, while thiazolidine-2-thione (TZD) and 1,3-bis(hydroxymethyl)-benzimidazoline-2-thione (BHBZIM) were also used as such, in the past. Hyperthyroidism (Grave's disease) is characterized by the overproduction of *T*4 and *T*3 hormones. The way that the above and other similar thioamides interact with I_2 is of great importance, in an attempt to approximate the elucidation of their mechanism of action, since I_2 is involved in the synthesis of both *T*4 and *T*3 hormones [15–17];

(ii) iodine chemistry is recently proving to be of considerable interest because of the discovery of low-temperature, semi- and superconducting polyiodides, which quickly led to the deliberate doping of conjugated polymers with elemental iodine [13]. The ability of iodine to catenate leads to the formation of polyiodides of various structures [13] reviewed recently by Boyle et al, Deplano et al, and Svensson et al [10–13]. The structural variety of polyiodides ranges from the simple I_3^- through the linear I_4^{2-}, the V-shaped I_5^-, three-pronged structures of I_7^-, I_9^-, I_{10}^{2-}, and I_{12}^{2-}, the Z-shaped I_7^-, I_8^{2-}, the branched I_{16}^{2-}, and the S-shaped and linear I_{16}^{4-} species to infinite chains [5]. The size and shape of the polyiodide ions have been found to depend in an unpredictable way on the size and shape of the counter ion.

In this paper, we review the results of our work on the iodine interaction with thioamides. Complexes of the so-called "spoke" and "extended spoke" structures, $D \cdot I_2$ and $D \cdot I_2 \cdot I_2$, respectively, (D is the ligand donor) (ii) iodonium salts of $\{[D_2{-}I]^+[I_n]^-\}$ ($n = 3, 7$) and $\{[D_2{-}I]^+[FeCl_4]^-\}$



Scheme 1: Ligands used in our work.

formulae and (iii) disulfides of the categories (a) [D−D] and (b) $\{[D-DH]^+[I_3]^-\}$ produced by oxidation action of I_2, have been isolated and characterized. A compound of formula $\{[D_2-I]^+[I_3]^-[D \cdot I_2]\}$ containing both types of complexes (i) and (ii) was also isolated.

In addition the results on interaction between diiodine with selenium analogs of the antithyroid drug 6-*n*-propyl-2-thiouracil (PTU) of formulae RSeU have also been included. Complexes of formulae $[(RSeU)I_2]$ with "spoke" structures have been isolated. These complexes are stable in nonpolar solvents, but they decompose in polar solvents, producing diselenide compounds or undertaking deselenation. All these results are well correlated with the mechanism of action of antithyroid drugs. Finally, we review here our work on the diiodine interaction with the amides (LO) (L = organic framework), 2-hydroxy-pyridine and 2-hydroxy-pyrimidine. Complexes of formulae $\{(LO)_3[(LO)]^+ \cdot I_3^-\}$, $\{(LO)_6 \cdot [(LO)_2]^{2+} \cdot ((1/2)I^-) \cdot ((3/2)I_7^-) \cdot (I_2)\}$, as well as $\{[LOH]^+Cl^-I_2\}$ have been isolated and characterized.

The ligands used in the present study are summarized in Scheme 1.

RESULTS AND DISCUSSION

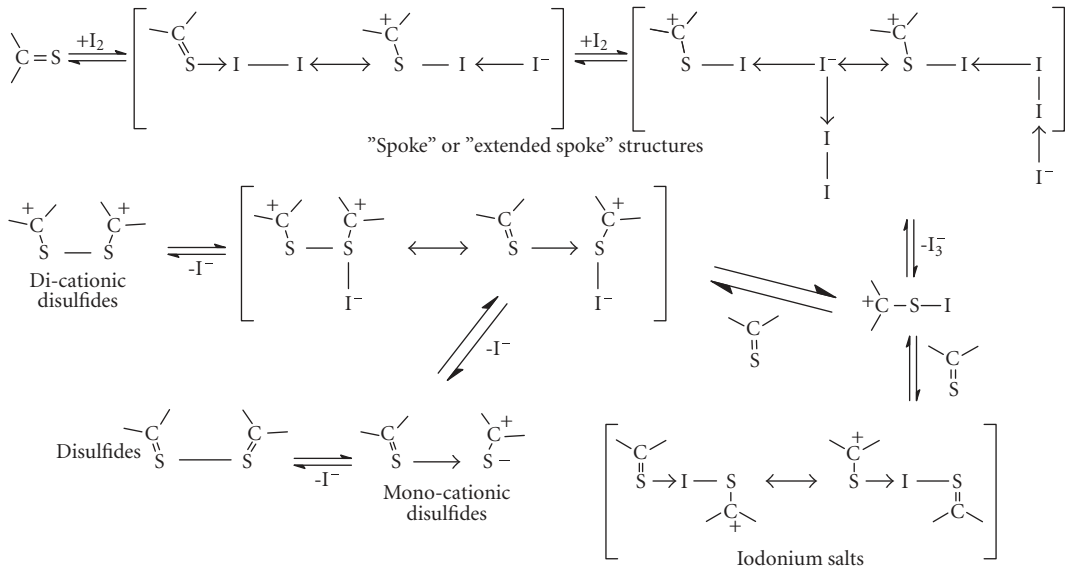
Synthesis of thioamide-diiodine complexes

Charge transfer complexes with "spoke" or "extended spoke" structures

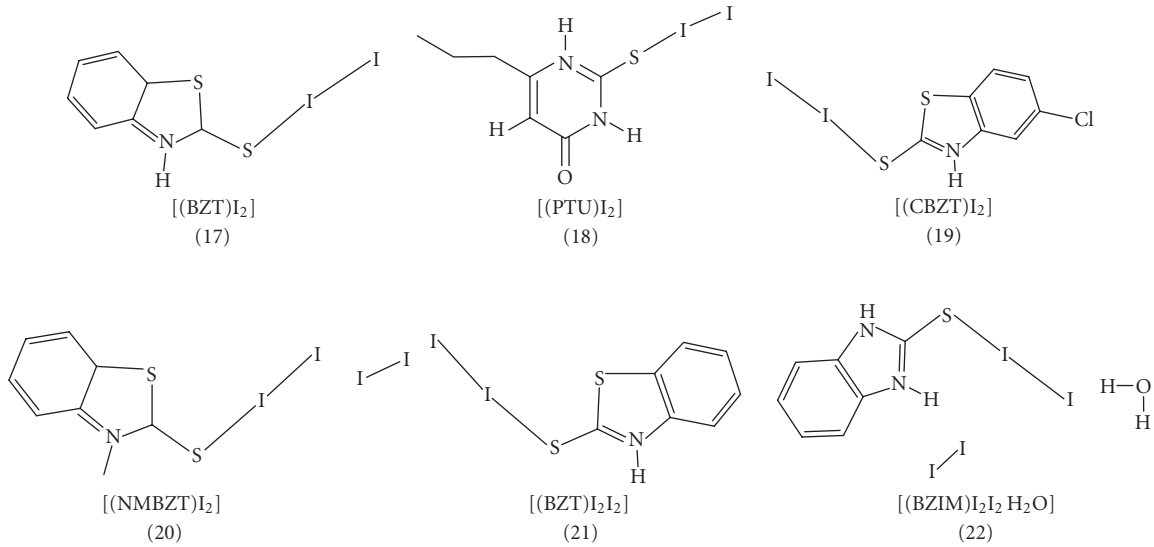
Reactions between diiodine and the thioamides (1)–(5) (Scheme 1) lead to the formation of charge transfer (ct) complexes with the so-called "spoke" or "extended spoke" structures ($DS \cdot I_2$ or $DS \cdot I_2 \cdots I_2$) according to the general reaction shown in Scheme 2.

Thus, reaction of diiodine with (1), (2), (3), or (4) in a molar ratio 1 : 1 (I_2 : L) results to the formation of ct complexes of formulae $[(BZT)I_2]$ (17) [1], $[(PTU)I_2]$ (18) [3], $[(CBZT)I_2]$ (19) [3], and $[(NMBZT)I_2]$ (20) [6] with spoke structures (Scheme 3). Reactions of diiodine with (1) or (5) in 2 : 1 (I_2 : L) molar ratio form ct complexes of extended spoke structures with formulae $[(BZT)I_2I_2]$ (21) [1] and $[(BZIM)I_2I_2H_2O]$ (22) [1] (Scheme 3).

Table 1 summarizes bond distances and angles of importance of our ct complexes with spoke and extended spoke structures.



Scheme 2



Scheme 3: Molecular diagrams of ct complexes with spoke and extended spoke structures.

The I−I bond distances are varying from 2.79 Å, in case of complexes with weak I−S interaction, to 3.08 Å, as a result of a strong I−S interaction. The corresponding I−I bond is subsequently elongated with respect to the corresponding distance in free I−I in the solid state [19] (2.717 Å at 110 K [20]). Bigoli et al [21] has classified iodine adducts of sulfur donors into three classes, depending on I−I bond order (n), calculated from Pauling's equation $d(I-I) = d_0 - 0.85 \cdot \log(n)$ (1) [where d is I−I interatomic distance of the adduct, d_0 is the I−I bond distance of gas phase I_2 (2.67 Å), and n is the I−I bond order] [18]. When $n \geq 0.6$ and $d(I-I) < 2.85$ Å, the adduct is type A, and when $n \leq 0.4$ and $d(I-I) > 3.01$ Å, it is type C. Compounds with intermediate values were classified as type B. Thus, compounds (18) and (20) are classified into A type, compounds (19), (21), and (22) into B type, whereas compound (17) is C type.

Figure 1 correlates d(I−I) versus d(I−S). A linear correlation is observed with the exception of complex (17). This behavior has been already explained [22].

The S−I−I group has a linear structure with an angle of almost 180°. The N−C−S−I torsion angle is also found almost equal to 180° indicating an almost coplanar arrangement of the I_2 towards > C=S bond except the case of $[(PTU)I_2]$ complex, where it is found to be −95.93°. In fact, $[(PTU)I_2]$ complex is the first ct complex with perpendicular arrangement of I_2 towards > C=S characterized by X-ray crystallography [3].

Table 1: Selected bond distances and angles of spoke and extended ct complexes.

Complex	I−I(I_2) (Å)	I−I(S) (Å)	I−S (Å)	I−I−S (∘)	N−C−S−I−(∘)	n (e)* bond order	Type
[(BZT)I_2] (17)	—	3.077(2)	2.728(6)	174.18(14)	166.40	0.33	C
[(PTU)I_2] (18)	—	2.826(1)	2.780(1)	175.85(2)	−95.93	0.65	A
[(CBZT)I_2] (19)	—	2.920(1)	2.633(1)	173.78(4)	167.88	0.51	B
[(NMBZT)I_2] (20)	—	2.7912(1)	2.808(3)	176.94(7)	172.90	0.72	A
[(BZT)I_2I_2] (21)	2.7504(18)	2.969(2)	2.587(5)	177.78(13)	174.71	0.44	B
[(BZIM)$I_2I_2H_2O$] (22)	2.767(3)	2.989(2)	2.571(6)	176.76(14)	2.95	0.42	B

*The I−I bond order calculated from Pauling's equation $d(I-I) = d_0 - 0.85 \cdot \log(n)$ (where d is I−I interatomic distance of the adduct, d_0 is the I−I bond distance of gas phase I_2 (2.67 Å), and n is the I−I bond order) [18].

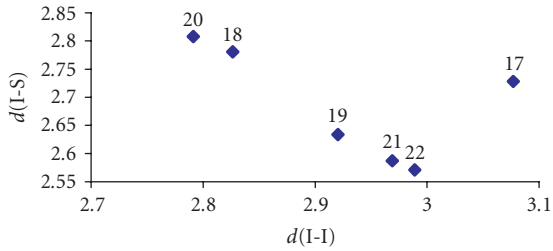
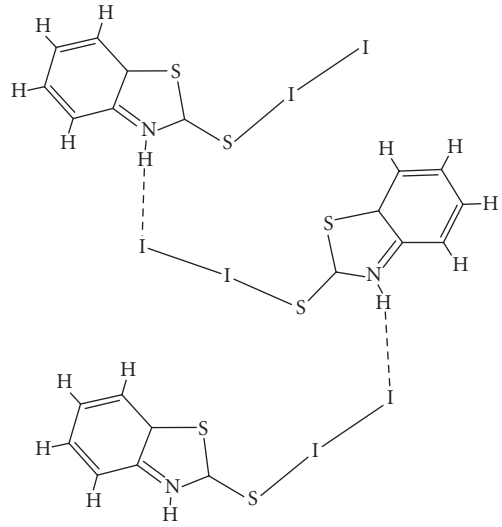


Figure 1: Correlation between d(I−S) and d(I−I) found for spoke and extended spoke ct complexes of diiodine, [(BZT)I_2] (17), [(PTU)I_2] (18), [(CBZT)I_2] (19), [(NMBZT)I_2] (20), [(BZT)I_2I_2] (21), and [(BZIM)$I_2I_2H_2O$] (22).



Scheme 4: 1D intermolecular network of complex [(BZT)I_2].

An extended intermolecular 1D network through hydrogen bonding interaction is also formed in complex [(BZT)I_2] (17) with N · · · I = 3.597(18) Å (Scheme 4).

Iodonium salt complexes

Reaction between diiodine and thioamides such as TZD (6) or BZIM (5) leads to the formation of iodonium salt complexes of $[\{(TZD)_2I^+\}\cdot I_3^- \cdot 2I_2]$ (23) (Scheme 5) and $\{[(BZIM)_2I^+]I_3^-\}\{[(BZIM)I_2]\}$ (24) (Scheme 5) formulae according to the reaction in Scheme 2.

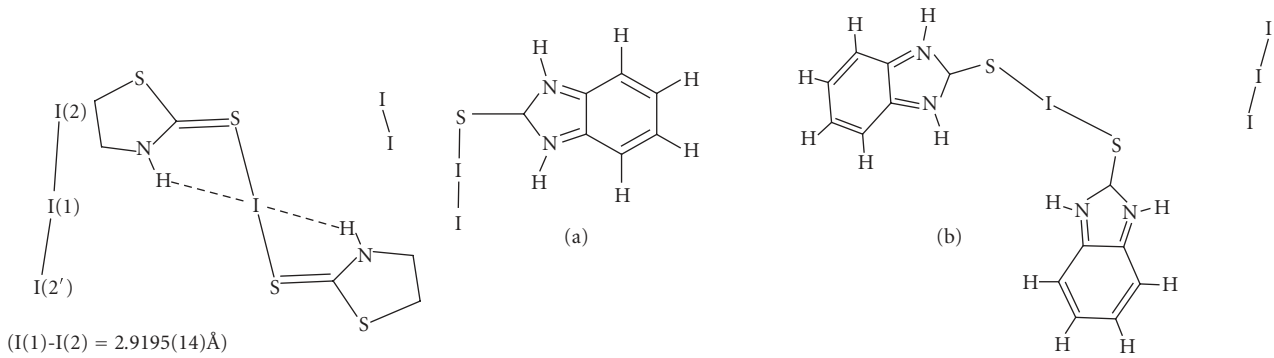
The two I−S bond distances are 2.654(6) Å in (23) and in case of (24) they are 2.597(4) Å and 2.702(4) Å, respectively. The I−I bond distances in I_3^- counter anions are found to be equal (I−I = 2.9195(14) Å) in case of (23). In case of (24) two types of I_3^- counter anions are observed, one is symmetric with I(1)−I(2) = 2.9300(12) Å while the other is not since it participates in hydrogen bonding (I(1A)−I(2A)= 2.880(6) Å and I(1A)−I(3A) = 3.058(5) Å, resp) and better described as I^-, interacting with $I_2(I \cdots I_2)$ [11]. The two hydrogen bonding interactions are taking place between the I^+ and the hydrogen atoms of the amide nitrogen atoms (H[N] · · · I = 2.9336(6) Å) in case of (23) (Scheme 5) and I(11)· · ·H−N(11)″ of 3.20 Å in case of (24) (Scheme 6). *Ab initio* quantum mechanical methods and density functional theory (DFT) techniques applied on the iodonium part of (24) suggested that the conformations obtained in the crystalline state result from an intermolecular electrostatic interaction between the positively charged iodine and the negatively charged NH (total group (NH) charges calculated −0.005 e for N(11)″, −0.014 e for N(21)″, −0.004 e for N(13)″, and −0.012 e for N(23)″) [6] (Scheme 6).

When (NMBZT) (4) reacts with diiodine in the presence of $FeCl_3$ in a molar ratio of 3 : 6 : 1 (NMBZT : I_2 : $FeCl_3$) (1), complex $\{[(NMBZT)_2I]^+ \cdot [FeCl_4]^-\}$ (25) (Scheme 7) together with $\{[(NMBZT)_2I^+]\}\cdot[I_7]^-$ were formed [6]. The I−S bond distances are I−S = 2.5961(15) Å and 2.6596(14) Å, respectively, with an almost linear S−I^+−S arrangement (S−I−S = 177.77(5)°)

$$3\text{NMBZT} + 6I_2 + FeCl_3 \longrightarrow \left(\frac{1}{2}\right)\{[(\text{NMBZT})_2I^+[FeCl_4]^-]\} + \{[(\text{NMBZT})_2I^+]^\bullet[I_7^-]\} + \text{unidentified products.} \quad (1)$$

Monocationic and neutral disulfides

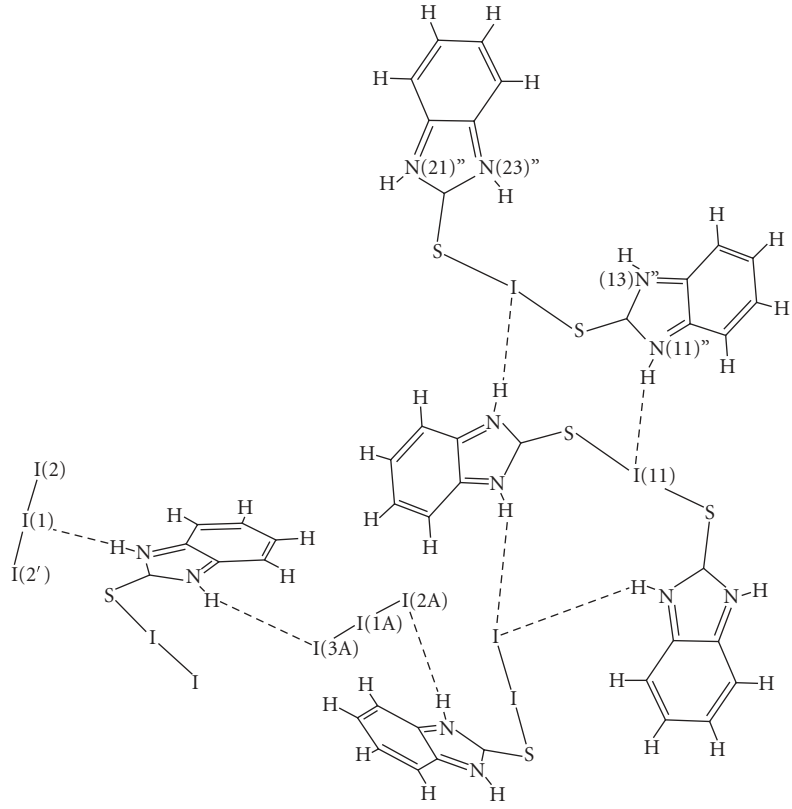
The reaction of 2-mercaptopyridine (PYSH) (7) with diiodine in a molar ratio of 1 : 2 led to the oxidation and dimerization of the ligand and produced $\{(PYS-PYSH)^+ \cdot I_3^-\}$ (26) (Scheme 8). The structure of the compound consists of two residues; one cationic $(PYS-PYSH)^+$, containing the S−S bond linking the two 2-mercapto-pyridine molecules



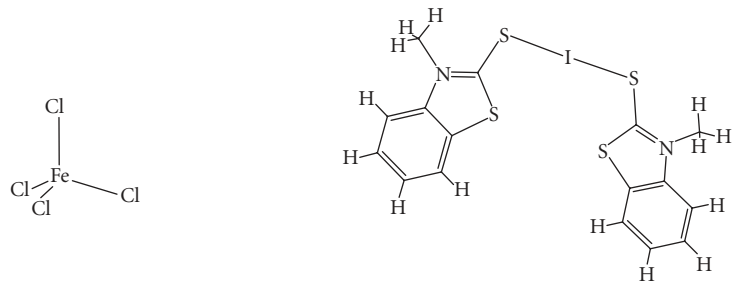
$[\{(TZD)_2I^+\} \cdot I_3^- \cdot 2I_2]$
(23)

$\{[(BZIM)_2I^+] \cdot I_3^-\} \cdot \{[(BZIM)I_2]\}$
(24)

Scheme 5

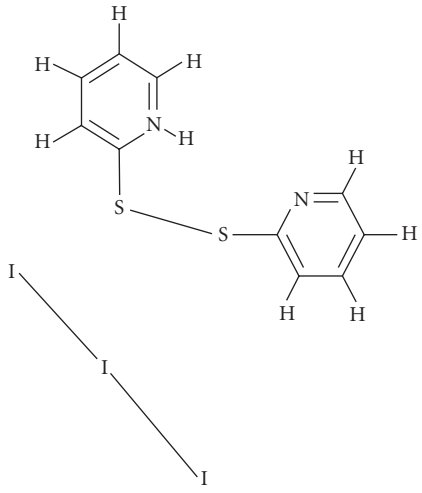


Scheme 6: Hydrogen bonding interactions taking place in (24).



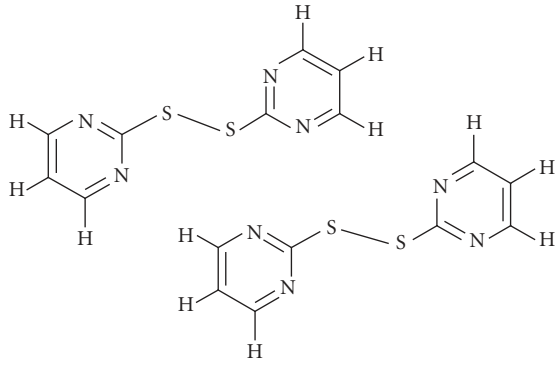
$\{[(NMBZT)_2I]^+ \cdot [FeCl_4]^-\}$
(25)

Scheme 7: $\{[(NMBZT)_2I]^+ \cdot [FeCl_4]^-\}$(25).



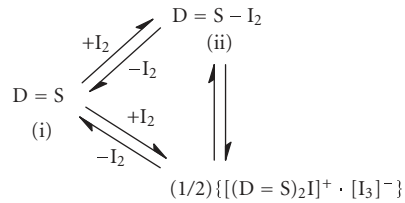
$\{(\text{PYS-PYSH})^+ \cdot I_3^-\}$
(26)

Scheme 8: $\{(\text{PYS-PYSH})^+ \cdot I_3^-\}$(26).



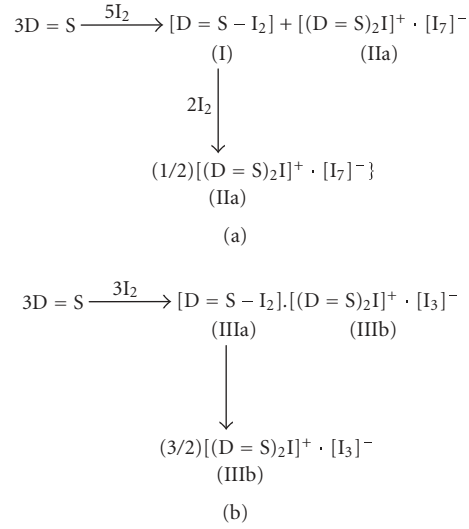
$[(\text{PMT})_2]$
(29)

Scheme 9: $[(\text{PMT})_2]$(29).



Scheme 10

one of which is protonated, and one I_3^- counter anion. In the crystal lattice there are four symmetry-independent cation-anion pairs. There are only a few crystal structures reported in the literature containing open chain stable cations of DS-SD dimers, such as the monocationic: $\{[(C_4H_6N_2S{-}SN_2C_4H_5)_2]^{2+} \cdot (I_3^-) \cdot (I_5^-)\}$ [15]. The two I−I bond distances of the I_3^- in the four components of complex (26) are 2.887(4) Å and 2.944(3) Å in component a, 2.874(4) Å and 2.957(3) Å in b, 2.968(3) Å and 2.862(3) Å in c, and 2.855(4) Å and 2.927(3) Å in d, respectively, indicating a slight asymmetry of I_3^- in this complex (covalent linear asymmetric).



Scheme 11

Moreover, when MNA (8), MBA (9), or PMT (10) reacts with diiodine under the same experimental conditions as in the case of the preparation of complex (7), (see above), neutral disulfides were produced with formulae $[(\text{MNA})_2]$ (27), $[(\text{MBA})_2]$ (28), and $[(\text{PMT})_2]$ (29) according to the reaction shown in Scheme 2. Scheme 9 shows the disulfide formed in case of (10) with formula $[(\text{PMT})_2]$ (29).

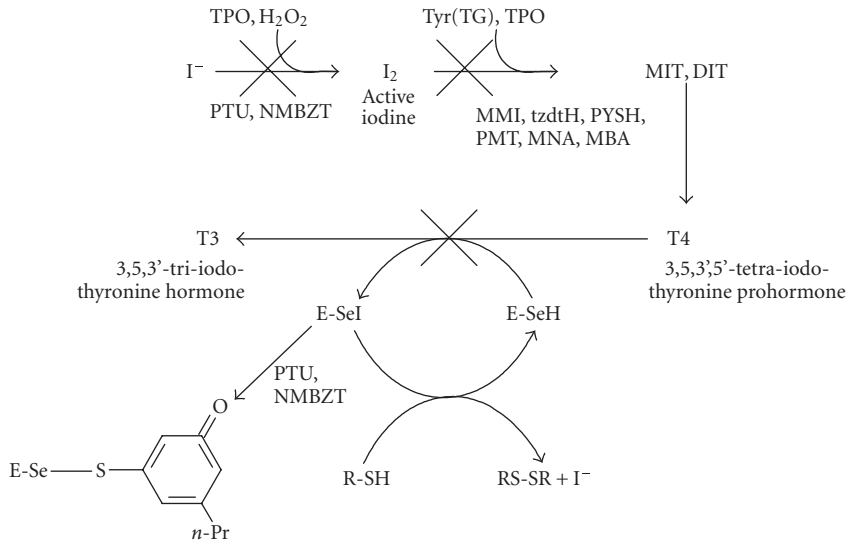
Complex (24) isolated from the reaction of (5) and I_2 reveals the cocrystallization of both a "spoke" structure and an iodonium salt structure. This leads to the conclusion that the equilibrium of Scheme 10 is established in solution.

It has also been shown that the disproportionation reaction, with the generation of the ionic compound from thioamide-iodine complexes, exhibits pressure dependence [2]. A pressure increase leads to the ionic iodonium salt (iii) from (ii) (Scheme 10). The favoring of $\{[(\text{MBZIM})_2\text{I}]^+[I_3]^-\}$ (24a) formation is also proved by computational studies, based on energetic grounds [6].

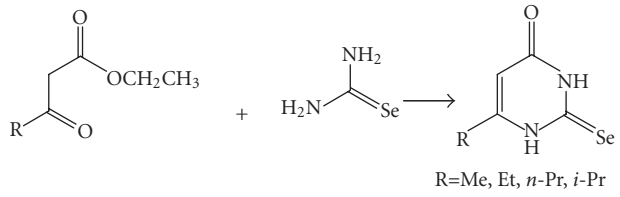
The conductivity measurements indicate that when diiodine is added to a solution of BZIM (5) (D=S), initially both the neutral (I) and the ionic (IIa) compounds are formed as it is shown in Scheme 11(a). Further addition of diiodine results to the ionic complex (IIa). In the case of NMBZT (Scheme 11(b)) a cocrystallization of both the spoke and iodonium complexes takes place producing only the iodonium complex, in excess of I_2.

For the mechanism of action of antithyroid drugs the reaction scheme shown in Scheme 12 is followed.

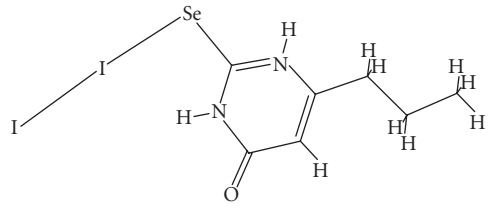
Our results strongly indicate that the antithyroid drugs PTU (2) and N-Methyl-2-mercapto-imidazoline (MMI) have a different way of action. Thus, (2) together with NMBZT (4) forming weak S−I ct complexes (Table 1) may interfere either by inhibiting TPO activity [26] or by inhibiting deiodinase (ID-1) enzyme which is responsible for the formation of $T3$ from $T4$ hormone.



Scheme 12



Scheme 13: Synthesis of 6-alkyl-2-selenouracil ligands (11)–(14).



Scheme 14: Molecular structure of $[(n\text{-PrSeU})I_2]$(30).

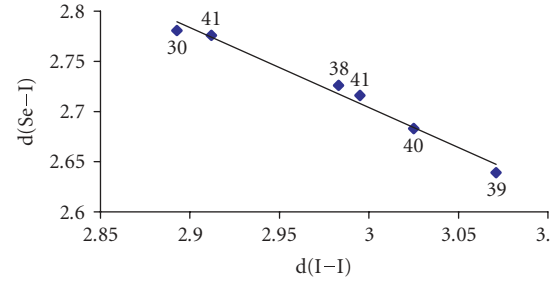


Figure 2: Graphical plot of d(Se−I) versus d(I−I) for $[(n\text{-PrSeU})I_2]$ (30), $(tzSeMe)\cdot I_2$, (38) (tzSeMe = N-Methyl-thiazolidine-2(3H)-selone) [23], $(btSeMe)\cdot 2I_2$, (39) (btSeMe = N-Methyl-benzothiazole-2(3H)-selone) [23], $\{(L\cdot I_2)\cdot (L_2)^+\cdot 2I_3^-\}$ (40) (L = bis(N,N′-Dimethyl-imidazolidin-2-yl)-di-selenone) [24], $(mbis)\cdot 2I_2$, (41) (mbis = 1,1′-bis(3-Methyl-4-imidazolin-2-selenone)methane) [25].

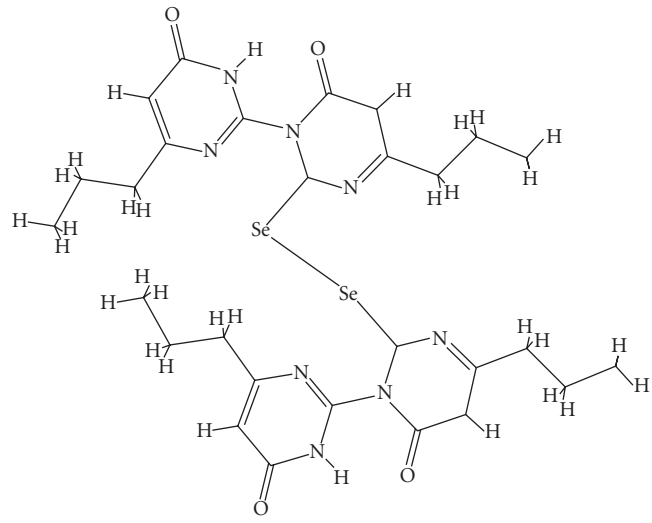
MMI, TZD (6), PYSH (7), PMT (10), MNA (8), and MBA (9), on the other hand, that strongly bind to I_2 or are oxidized to disulfides [15] most probably interfere in the formation of monoiodotyrosine (MIT), diiodotyrosine (DIT) by the tyrosine residues of thyroglobulin Tyr(TG), competing with active iodine.

Synthesis of selenoamide-diiodine complexes

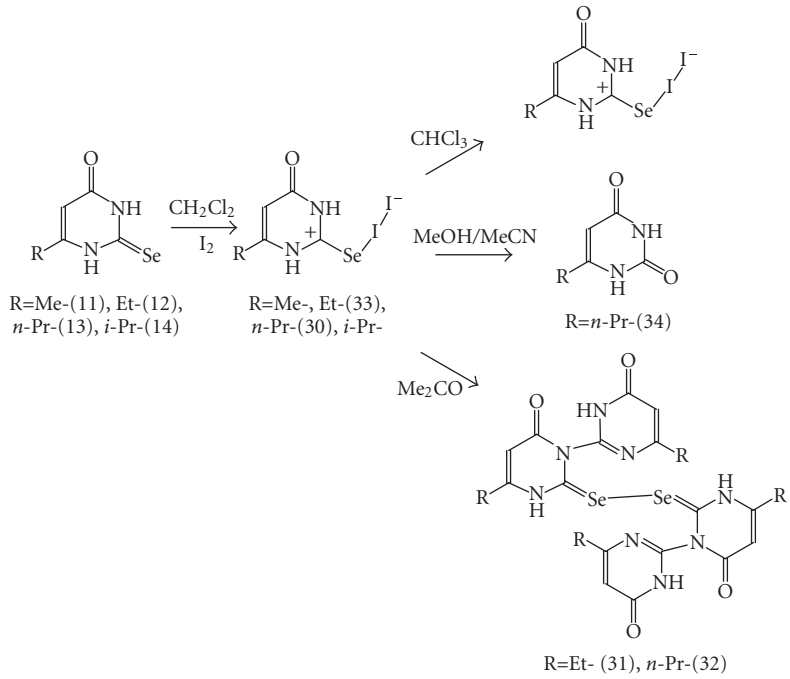
Since thyroid deiodinase contains selenocysteine [27], the seleno-analog of PTU (PSeU) is expected to exhibit a higher antithyroid activity than PTU, because of the easier formation of Enzyme-Se-Se-PSeU species than Enzyme-Se-S-PTU due to the higher nucleophilicity of Se. To examine this possibility we have extended our studies to the interaction of I_2 with selenoamides. Scheme 1 shows the ligand used in this work. Ligands (11)–(14) were synthesized according the reactions shown in Scheme 13.

Reactions of alkyl-selenoamides with diiodine in a 1 : 1 molar ratio in dichloromethane solutions result in the formation of $[(RSeU)I_2]$ [R = methyl-, ethyl-, *n*-propyl-, and *i*-propyl-] (Scheme 14).

$[(n\text{-PrSeU})I_2]$ (30) was found to be a charge transfer complex with an Se−I bond. The I−I interatomic distance of 2.8928(10) Å is longer than that in either the gas phase (2.677 Å) or crystalline diiodine (2.717 Å at 110 K) presumably owing to the Se · · · I interaction. It is, however, the shortest such distance measured for a diiodine-selenoamide complexes suggesting a minimal perturbation resulting from the Se · · · I contact, which is the longest measured thus far [7]. The I−I bond order of 0.547 calculated for $[(n\text{-PrSeU})I_2]$ from Pauling's equation $d(I-I) = d_0 - 0.85\cdot\log(n)$ (1) (where



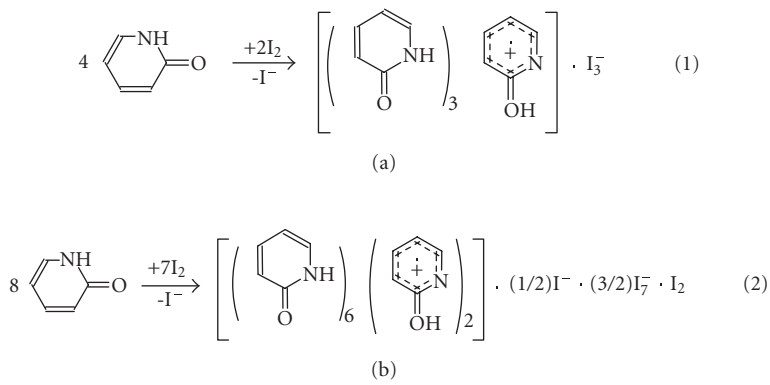
Scheme 15: [N-(6-*n*-Pr-4-pyrimidone)(6-*n*-Pr-SeU)$_2$](32).



Scheme 16

d is I−I interatomic distance of the adduct, d_0 is the I−I bond distance of gas phase I_2 (2.67 Å) and n is the I−I bond order) [18] is the highest such bond order for selenoamide-diiodine complexes. All these data are consistent with a weak Se · · · I interaction, the weakest ever found. According to Bigoli et al classification, complex (30) is classified in the B type of adduct. It is interesting to note that the corresponding [(PTU)I_2] complex forms a weaker ct complex, with an I−I bond order of 0.65e [3] compared to the 0.547e found for [(n-Pr−SeU)I_2] which implies a weaker S · · · I interaction. With the same classification the former complex is of A type, while the latter of B type. Interestingly, there is a linear correlation between the Se · · · I and I−I distances (see Table 1 and Figure 2).

The diselenides [N-(6-Et-4-pyrimidone)(6-Et-SeU)$_2$] (31) and [N-(6-*n*-Pr-4-pyrimidone)(6-*n*-Pr−SeU)$_2$] (32) (Scheme 15) were produced upon recrystallization of [(n-PrSeU)I_2] (30) and [(n-EtSeU)I_2] (33) from acetone, as oxidation products. On the other hand, deselenation with the formation of 6-*n*-propyl-2-uracil (n-Pr−U) (34) was observed when (30) was recrystallized from methanol/acetonitrile solutions [7].



Scheme 17

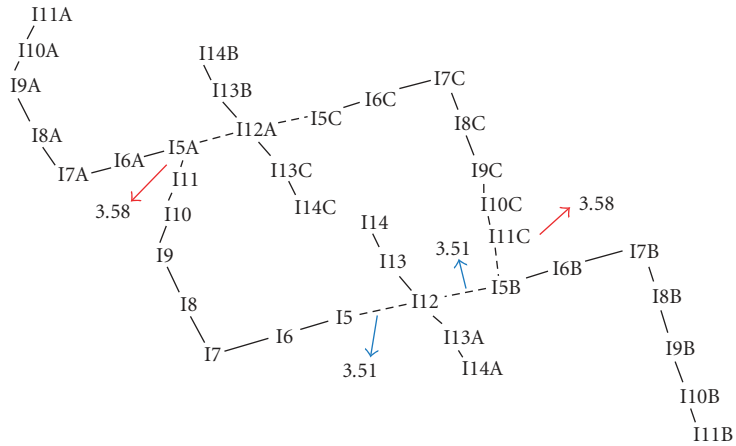


Figure 3: Polyiodine network established by weak halogen-halogen interactions, in the distance range 3.51 Å–3.58 Å, between I_7^- and $I_2 \cdots I^- \cdots I_2$ ions in the $\{(PYOH)_6 \cdot [(PYOH)_2]^{2+} \cdot ((1/2)I^-) \cdot ((3/2)I_7^-) \cdot (I_2)\}$.

In conclusion, while 6-alkyl-2-selenouracil compounds (RSeU) (Scheme 16) are stable in various solvents, including water and other polar or nonpolar solvents, "spoke" ct complexes of formulae $[(RSeU)I_2]$ are formed in dichloromethane solutions, but are unstable in methanol/acetonitrile and/or acetone solutions (Scheme 16). $[(RSeU)I_2]$ is transformed to 6-alkyl-2-uracil in methanolic/acetonitrile solutions (Scheme 16). Upon recrystallization of the compound in acetone the diselenides containing also a covalent C−N bond with an adjacent PTU molecule are formed possibly through the formation of a substituted selenouracil as indicated by ^{1}H, ^{13}C NMR spectra, and ESI-MS spectra. The whole process may be hydrolytic (Scheme 16).

Synthesis of amide-diiodine complexes

The reaction of 2-pyridone (PYOH) (15) with diiodine in a molar ratio of 2 : 1 and 1 : 2, respectively, resulted to the formation of $\{(PYOH)_3[(PYOH)]^+I_3^-\}$ (35) and $\{(PYOH)_6 \cdot [(PYOH)_2]^{2+} \cdot ((1/2)I^-) \cdot ((3/2)I_7^-) \cdot (I_2)\}$ (36) complexes (Scheme 17). The reactions were carried out in dichloromethane solutions.

The reaction of 2-pyrimidone ($PMOH_2^+Cl^-$) (15) with diiodine in a molar ratio of 1 : 1 resulted to the formation of $\{[LOH]^+Cl^-I_2\}$ (37) complex.

In case of complex (36) the counter anions form a polyiodine network. Figure 3 shows the polyiodine network established by weak halogen-halogen interactions, in the distance range 3.51 Å–3.58 Å, between I_7^- and $I_2 \cdots I^- \cdots I_2$ ions forming an infinite chain.

In conclusion, structures containing polyiodide anions with cationic aromatic ligands as counterparts of formulae $\{[(L)(HL^+)] \cdot (I^-_n)\}$ are known to be synthesized by the treatment of the appropriate amide with HI [28–30]. In contrast, the complexes with PYOH, in the present case, were formed by the direct reaction of 2-hydroxypyridine with diiodine in a molar ratio of 2 : 1 and 1 : 2. This is a redox reaction, where 2-hydroxy-pyridine firstly is oxidized to pyridinone-2 radical cation. In the case of 2-hydroxypyridine, however, peroxide structures are not formed like disulfides in the case of PYSH. Polyiodide anions are simultaneously produced in this case. This should be a consequence of redox differences between −SH and OH groups and may be proven a useful pathway for the synthesis of polyiodide materials.

REFERENCES

[1] Daga V, Hadjikakou SK, Hadjiliadis N, Kubicki M, dos Santos JHZ, Butler IS. 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). *European Journal of Inorganic Chemistry.* 2002;2002(7):1718–1728.

[2] dos Santos JHZ, Butler IS, Daga V, Hadjikakou SK, Hadjiliadis N. High-pressure Fourier transform micro-Raman spectroscopic investigation of diiodine-heterocyclic thioamide adducts. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy.* 2002;58(12):2725–2735.

[3] Antoniadis CD, Corban G, Hadjikakou SK, et al. Synthesis and characterization of (PTU) I_2 (PTU = 6-*n*-propyl-2-thiouracil) and (CMBZT)I_2 (CMBZT = 5-chloro-2-mercaptobenzothiazole) and possible implications for the mechanism of action of anti-thyroid drugs. *European Journal of Inorganic Chemistry.* 2003;2003(8):1635–1640.

[4] Antoniadis CD, Hadjikakou SK, Hadjiliadis N, Kubicki M, Butler IS. Synthesis, X-ray characterisation and studies of the new ionic complex [Bis(pyridin-2-yl) disulfide] triiodide, obtained by oxidation of 2-mercaptopyridine with I_2 - implications in the mechanism of action of antithyroid drugs. *European Journal of Inorganic Chemistry.* 2004;2004(21):4324–4329.

[5] Antoniadis CD, Hadjikakou SK, Hadjiliadis N, Kubicki M, Butler IS. Synthesis, X-ray characterization and study of new ionic complexes of 2-pyridone, obtained by oxidation with I_2. *New Journal of Chemistry.* 2005;29:714–720.

[6] Corban GJ, Hadjikakou SK, Hadjiliadis N, et al. Synthesis, structural characterization, and computational studies of novel diiodine adducts with the heterocyclic thioamides *N*-methylbenzothiazole-2-thione and benzimidazole-2-thione: implications with the mechanism of action of antithyroid drugs. *Inorganic Chemistry.* 2005;44(23):8617–8627.

[7] Antoniadis CD, Hadjikakou SK, Hadjiliadis N, Papakyriakou A, Baril M, Butler IS. Synthesis and structures of Se analogues of the antithyroid drug 6-n-propyl-2-thiouracil and its alkyl derivatives: Formation of dimeric Se-Se compounds and deselenation reactions of charge-transfer adducts of diiodine. *Chemistry - A European Journal.* 2006;12(26):6888–6897.

[8] Antoniadis CD, Blake AJ, Hadjikakou SK, et al. Structural characterization of selenium and selenium-diiodine analogues of the antithyroid drug 6-n-propyl-2-thiouracil and its alkyl derivatives. *Acta Crystallographica. Section B.* 2006;62(Pt 4):580–591.

[9] Corban GJ, Antoniadis C, Hadjikakou SK, Hadjiliadis N, Meng J-F, Butler IS. Pressure-Tuning Raman Spectra of Diiodine Thioamide Compounds: Models for Antithyroid Drug Activity. *Bioinorganic Chemistry and Applications.* 2006;2006: Article ID 68542, 5 pages.

[10] Boyle PD, Godfrey SM. The reactions of sulfur and selenium donor molecules with dihalogens and interhalogens. *Coordination Chemistry Reviews.* 2001;223(1):265–299.

[11] Deplano P, Ferraro JR, Mercuri ML, Trogu EF. Structural and Raman spectroscopic studies as complementary tools in elucidating the nature of the bonding in polyiodides and in donor-I_2 adducts. *Coordination Chemistry Reviews.* 1999;188(1):71–95.

[12] Aragoni MC, Arca M, Devillanova FA, et al. Charge-transfer adducts between donorscontaining chalcogens (S and Se) and di-iodine: solution studies. *Coordination Chemistry Reviews.* 1999;184(1):271–290.

[13] Svensson PH, Kloo L. Synthesis, structure, and bonding in polyiodide and metal iodide-iodine systems. *Chemical Reviews.* 2003;103(5):1649–1684.

[14] Reynolds JEF, Prasad AB, eds. *Martindale: The Extra Pharmacopoeia.* 28th ed. London, UK: The Pharmaceutical Press; 1982.

[15] Aragoni MC, Arca M, Demartin F, et al. Anti-thyroid drug methimazole: X-ray characterization of two novel ionic disulfides obtained from its chemical oxidation by I_2. *Journal of the American Chemical Society.* 2002;124(17):4538–4539.

[16] du Mont W-W, Mugesh G, Wismach C, Jones PG. Reactions of organoselenenyl iodides with thiouracil drugs: an enzyme mimetic study on the inhibition of iodothyronine deiodinase. *Angewandte Chemie International Edition.* 2001;40(13):2486–2489.

[17] Taurog A. *Endocrinology.* London, UK: Academic Press; 1979. Edited by DeGroot L; vol 1.

[18] Pauling L. *The Nature of the Chemical Bond.* 3rd ed. Ithaca, NY: Cornell University Press; 1960.

[19] Purcell KF, Kotz JC. *An Introduction to Inorganic Chemistry.* Philadelphia, Pa: Saunders College; 1980.

[20] van Bolhuis F, Koster PB, Migchelsen T. Refinement of the crystal structure of iodine at 110° K. *Acta Crystallographica.* 1967;23(1):90–91.

[21] Bigoli F, Deplano P, Ienco A, et al. Structure and bonding of diiodine adducts of the sulfur-rich donors 1,3-dithiacyclohexane-2-thione (ptc) and 4,5-ethylenedithio-1,3-dithiole-2-thione (ttb). *Inorganic Chemistry.* 1999;38(21):4626–4636.

[22] Aragoni MC, Arca M, Demartin F, et al. DFT calculations, structural and spectroscopic studies on the products formed between IBr and N,N'-dimethylbenzoimidazole-2(3*H*)-thione and -2(3*H*)-selone. *Journal of the Chemical Society, Dalton Transactions.* 2005;(13):2252–2258.

[23] Cristiani F, Demartin F, Devillanova FA, Isaia F, Lippolis V, Verani G. Charge-transfer complexes of *N*-methylthiazolidine-2(3*H*)-selone (1) and *N*-methylbenzothiazole-2(3*H*)-selone (2) with I_2 and IBr: crystal structures of $1 \cdot I_2$, $I_{1.25}Br_{0.75}$, $2 \cdot 2I_2$, and 2.2IBr. *Inorganic Chemistry.* 1994;33(26):6315–6324.

[24] Demartin F, Devillanova FA, Isaia F, Lippolis V, Verani G. Reaction of N,N'-dimethylimidazolidine-2-selone (L) with I_2. Crystal structure of the mixed-valence $(L.I_2)(L_2)^{2+}.2I_3$-compound. *Inorganica Chimica Acta.* 1997;255(1):203–205.

[25] Aragoni MC, Arca M, Demartin F, et al. C.T.complexes and related compounds between S and Se containing donors and I_2, Br_2, IBr, ICl. *Trends in Inorganic Chemistry.* 1999;6:1–18.

[26] Corban G, Hadjikakou SK, Hadjiliadis N. In preparation.

[27] Berry MJ, Banu L, Larsen R. Type I iodothyronine deiodinase is a selenocysteine-containing enzyme. *Nature.* 1991;349(6308):438–440.

[28] Herbstein FH, Kapon M, Schwotzer W. Crystal structure of tetrakis (phenacetin) dihydrogentetraiodide dihydrate $\{[H_5C_2OC_6H_4N(H)C(CH_3) = O]_4 \cdot H_2I_4 \cdot 2H_2O\}$. *Helvetica Chimica Acta.* 1983;66(1):35–43.

[29] Herbstein FH, Kapon M. The crystal structures of the polyiodide salts $(\text{phenacetin})_2 \cdot HI_5$ and $(\text{theobromine})_2 \cdot H_2I_8$. *Philosophical Transactions of the Royal Society of London. Series A.* 1979;291(1379):199–218.

[30] Reddy JM, Knox K, Robin MB. Crystal structure of $HI_3 \cdot 2C_6H_5CONH_2$: a model of the starch—iodine complex. *The Journal of Chemical Physics.* 1964;40(4):1082–1089.