Synthesis, structural characterization and in vitro cytotoxicity of new Au(III) and Au(I) complexes with thioamides†


Received 14th May 2009, Accepted 18th September 2009
First published as an Advance Article on the web 13th October 2009
DOI: 10.1039/b909587j

The reactions of tetrachloroauric(III) acid (HAuCl₄) with the thioamides; 2-mercapto-benzothiazole (mbztH) and 5-ethoxy-2-mercapto-benzimidazole (EtmbzimH) lead to the desulfuration of the ligands and the formation of the ionic complexes \{[AuCl₄][bztH₂]⁺\} (1), and \{[AuCl₄][EtmbzimH₂⁺][H₂O]\} (2) (where bztH₂⁺ and EtmbzimH₂⁺ are the desulfurated cations of the starting ligands). The reaction of HAuCl₄ with 2-mercapto-nicotinic acid (mnaH₂), however results in the formation of 2-sulfonate-nicotininc acid (C₆H₅NO₅S) (3) with the simultaneous oxidation of the sulfur atom. On the other hand, the reactions of the gold(I) complex [Au(tpp)Cl] (4) (tpp = triphenylphosphine (Ph₃P)) with the thioamides; 2-mercaptop-thiazolidine (mtzdH), 2-mercapto-benzothiazole (mbztH) and 5-chloro-2-mercapto-benzothiazole (ClmbztH) in the presence of potassium hydroxide resulted in the formation of the gold(I) complexes of formulae [Au(tpp)(mtzd)] (5), [Au(tpp)(mbzt)] (6) and [Au(tpp)(Clmbzt)] (7) without ligand desulfuration. All complexes have been characterized by elemental analysis, FT-IR, far-FT-IR, ¹H-NMR, spectroscopic techniques and X-Ray crystallography. The electrochemical behavior of 1, 2 and 4-7 complexes and the ligands EtmbzimH, mbztH and mnaH₂ was also studied in acetonitrile and DMF using cyclic voltammetry. The results are in support of a mechanism of desulfuration of the ligands by Au(III), involving a first oxidation of S to -SO₃⁻, followed by a C-S bond cleavage. This is also supported by PM6 calculations of bond dissociation energies of the various compounds involved. Complexes 1, 2 and 4-7 were tested for in vitro cytotoxicity against leiomysarcoma cells and the results are discussed in relation with the geometry of the complexes and compared with those of cisplatin and other metals. Complexes 1 and 5 showed higher activity than that of cisplatin, while HAuCl₄ was inactive against sarcoma cells.

Introduction

Chrysotherapy, is the use of gold compounds in medicine with many applications. Gold thiolates are used clinically against rheumatoid arthritis. Recently, many gold(III) and gold(I) compounds were tested for their anti-tumor activity against various cancerous cell lines and the results have been reviewed by Tiekink. A commonly cited reason for the anti-tumor investigation of gold compounds relates to the square-planar geometry, also found for platinum in cisplatin, since gold(III) is isoelectronic with platinum(II) and forms similar square-planar complexes. Given the generally reducing mammalian environment, compounds containing gold(III) may be expected to be reduced in vivo to gold(I) and this led to the investigation of possible antitumor properties of gold(I) compounds as well. However, appropriate selection of the ligand donor set (e.g. N or O) can serve to stabilize gold(III) and consequently there is a rich literature of anti-tumour/cytotoxicity investigations of such species.

In the course of our studies on metalotherapeutics we synthesized and structurally characterized new gold(III) complexes with the thioamides 2-mercapto-benzothiazole (mbztH) and 5-ethoxy-2-mercapto-benzimidazole (EtmbzimH) of formulae \{[AuCl₄][bztH₂]⁺\} (1), and \{[AuCl₄][EtmbzimH₂⁺][H₂O]\} (2) (where bztH₂⁺ and EtmbzimH₂⁺ are the desulfurated cations of the starting ligands) (Scheme 1). Also for gold(I) mixed ligand complexes of [Au(tpp)Cl] (4) with the thioamides 2-mercaptop-thiazolidine (mtzdH), 2-mercapto-benzothiazole (mbztH) and 5-chloro-2-mercapto-benzothiazole (ClmbztH) and tri-phenylphosphine (tpp) of formulae [Au(tpp)(mtzd)] (5), [Au(tpp)(mbzt)] (6) and [Au(tpp)(Clmbzt)] (7) (Scheme 1). Moreover in the reaction of HAuCl₄ with 2-mercapto-nicotinic acid (mnaH₂) the ligand is oxidized to 2-sulfonate-nicotininc acid (C₆H₅NO₅S) (3).
The use of \( \text{AuCl}_4^- \) as a counter ion in complexes 1 and 2 and the isolation of 2-sulfonate-nicotinic acid (\( \text{C}_6\text{H}_5\text{NO}_5\text{S} \); (3)), strongly indicates that \( \text{AuCl}_4^- \) acts rather as a catalyst, while the oxidation is taking place with atmospheric \( \text{O}_2 \) as it was also found in the case of the oxidation of thioethers by this anion. Electromechanical and computational studies on the other hand, strongly indicate that oxidation of the ligands at \( \text{S} \), takes place prior of the breaking of the C-S bonds in the final products. Based on these results, a possible mechanism of the reaction taking place was proposed.

The electrochemical properties of gold(III) complexes with \( \text{N,N-dimethylthiocarbamate (DMDT)} \) and ethylsarcosinedithiocarbamate (ESDT) in acetonitrile have been previously investigated by cyclic voltammetry.\(^a\) The reduction of the gold(III) compounds followed two separated \( \text{Au(III)}/\text{Au(II)} \) and \( \text{Au(II)}/\text{Au(I)} \) steps leading to the formation of a dimeric gold(II) species with bridging chlorine atoms.\(^a\) This is different than the behavior of the complexes in the present study, which involves the \( \text{Au(III)}/\text{Au(I)} \) and \( \text{Au(I)}/\text{Au(0)} \) reduction processes.

The electrochemical behavior of the free ligands \( \text{EtmbzimH, mbztH and mnaH}_2 \) was also evaluated in \( \text{CH}_3\text{CN} \) and \( \text{DMF} \) solutions. The results showed that the easiness of ligand's oxidation changes in the order: \( \text{EtmbzimH} > \text{mbztH} > \text{mnaH}_2 \). The desulfurated product of \( \text{mnaH}_2 \) by means of the controlled potential electrolyses which was performed in acetonitrile were achieved at the first anodic wave potential of \( E = 1.3 \text{ V} \). This support the assumption that the oxidation of \( \text{mnaH}_2 \) ligand also proceeds the desulfuration step.

Finally, the \textit{in vitro} cytotoxicity of complexes 1-2 and 4-7 and \( \text{HAuCl}_4 \) against leiomyosarcoma cells were also evaluated and the results were compared with analogous Sn(IV), Ag(I), Sb(III) complexes, reported by our group earlier\(^a\) and cisplatin.

## Results and discussion

### General aspects

Tetrachlorauric(III) acid (\( \text{HAuCl}_4 \)) solution was prepared according to the literature by dissolving Au foil into a mixture of concentrated hydrochloric acid and nitric acid 4:1.\(^7\) Complexes 1 and 2 were obtained by reacting 1 mmol of the appropriate thioamides 2-mercapto-benzothiazole (mbztH) and 5-ethoxy-2-mercapto-benzimidazole (EtmbzimH) with 0.5 mmol of \( \text{HAuCl}_4 \) solution in methanol/acetonitrile under reflux for 3 h (Scheme 2, reaction I). The reaction of 0.5 mmol \( \text{HAuCl}_4 \) with 1 mmol 2-mercapto-nicotinic acid (\( \text{mnaH}_2 \)) on the other hand, treated with an equimolar amount of KOH, resulted in the formation of 2-sulfonate-nicotininc acid (\( \text{C}_6\text{H}_5\text{NO}_5\text{S} \)) with simultaneous oxidation of the sulfur atom (Scheme 2, reaction II). \( \text{Au(I)} \) complexes 5, 6 and 7 were synthesized by reacting 1 mmol of \( [\text{Au(ppy)}\text{Cl}]^+ \) (4) with 1 mmol of the appropriate thioamide 2-mercapto-thiazolidine (mtzdH), 2-mercapto-benzothiazole (mbztH) or 5-chloro-2-mercapto-benzothiazole (ClmbztH) in the presence of an equimolar amount of KOH, in methanol/water solution (Scheme 2, reaction III).

All complexes are air stable powders. Crystals of compounds 1, 2 and 3, suitable for X-ray analysis, were obtained by slow evaporation of a methanol/acetonitrile (1:1) solution. Crystals of 5, 6 and 7 were grown from a dichloromethane/toluene (1:1) solution.
The crystal structures of 4 and 5 were also re-determined here and found identical to the ones previously reported.  

Vibrational spectroscopy

The infrared spectra of complexes 1 and 2 show strong vibrational bands at 3211 (1) and 3279 (2) cm⁻¹, respectively, which are assigned to v(N-H) stretching vibrations, while no such bands were observed in the spectra of complexes 5, 6 and 7 indicating the de-protonation of their ligands. The corresponding v(N-H) vibration bands are observed at 3111 cm⁻¹ (mbztH), 3084 cm⁻¹ (EtmbzimH), 3107 cm⁻¹ (ClmbzH) and at 3133 cm⁻¹ (mtzdH).⁹⁻¹⁹ The vibrational thioamide bands 1 and II, appear at 1446-1496 cm⁻¹ and 1514-1525 cm⁻¹, respectively, in the Far-IR spectra of complexes 1 and 2, indicating the desulfuration of the 2-mercapto-benzothiazole (mbztH) or 5-ethoxy-2-mercapto-benzimidazole (EtmbzimH) ligands upon their reaction with Au(III).

The new bands at 365 and 360 cm⁻¹ in the far-IR spectra of complexes 1 and 2 show strong vibrational bands at 1024-1075 cm⁻¹ and 634-789 cm⁻¹, respectively, in the spectra of the free ligands mbztH, EtmbzimH, mtzdH and ClbztH shown at 1496-1514 cm⁻¹ and 1248-1319 cm⁻¹ respectively.⁵⁻¹⁹ Thioamide bands III-IV, observed at 995-1173 cm⁻¹ and at 652-811 cm⁻¹, in the spectra of the free ligands,⁵⁻¹⁹ appear at 1024-1075 cm⁻¹ and 634-789 cm⁻¹ respectively in the spectra of complexes 5, 6 and 7. The absence of the thioamide bands in the spectra of complexes 1 and 2 indicate the desulfuration of the 2-mercaptopenzothiazole (mbztH) or 5-ethoxy-2-mercapto-benzimidazole (EtmbzimH) ligands upon their reaction with Au(III).

The new bands at 365 and 360 cm⁻¹ in the far-IR spectra of complexes 1 and 2 have been assigned to the v(Au-Cl) vibrations, ¹⁰⁻²² while bands appearing at 279 and 180 (5), 280 and 179 (6) and 279 and 171 (7) cm⁻¹ in the far-IR spectra of complexes 5-7 are attributed to the v(Au-S) vibrations. ¹⁰⁻²²

Crystal and molecular structures of [AuCl₄][bzth₂]⁺ (1), [AuCl₄][EtmbzimH][bztH₂]^+ (2), the 2-sulfonate-nicotinic acid (3), [Au(tpp)(mbzt)] (6) and [Au(tpp)(Clmbzt)] (7) (A) Anisotropic ellipsoid representation of the building block of complex 1. The ellipsoids are drawn at 50% probability level. (B) Strong hydrogen bonding interactions.

Complexes 1 and 2 are ionic salts containing an [AuCl₄]⁻ counter anion neutralized by a protonated fragment of the free ligand. The absence of the thioamide bands in the spectra of complexes 1 and 2 indicate the desulfuration of the 2-mercaptopenzothiazole (mbztH) or 5-ethoxy-2-mercapto-benzimidazole (EtmbzimH) ligands upon their reaction with Au(III).

The new bands at 365 and 360 cm⁻¹ in the far-IR spectra of complexes 1 and 2 have been assigned to the v(Au-Cl) vibrations, ¹⁰⁻²² while bands appearing at 279 and 180 (5), 280 and 179 (6) and 279 and 171 (7) cm⁻¹ in the far-IR spectra of complexes 5-7 are attributed to the v(Au-S) and v(Au-P) vibrations. ¹⁰⁻²²

Crystal and molecular structures of [AuCl₄][bzth₂]⁺ (1), [AuCl₄][EtmbzimH][bztH₂]^+ (2), the 2-sulfonate-nicotinic acid (3), [Au(tpp)(mbzt)] (6) and [Au(tpp)(Clmbzt)] (7) The structures of compounds 1-3 and 6, 7 were solved by X-ray diffraction at 120(2) K for 1 and 2, and at r.t. (293(2) K) for 3 and 7.

Table 1 Selected bond lengths (Å) and angles (deg) of compounds 1-3 and 6-7

<table>
<thead>
<tr>
<th>Complex 1 (Å) bond lengths</th>
<th>Complex 2 (Å) bond lengths</th>
<th>Compound 3 (Å) bond lengths</th>
<th>Complex 6 (Å) bond lengths</th>
<th>Complex 7 (Å) bond lengths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Au1 C14</td>
<td>2.2808(13)</td>
<td>Au1 S22</td>
<td>2.2960(13)</td>
<td>Au1 S22</td>
</tr>
<tr>
<td>Au1 Cl2</td>
<td>2.2816(12)</td>
<td>Au1 C2i</td>
<td>2.2765(16)</td>
<td>Au1-P1</td>
</tr>
<tr>
<td>Au1 Cl3</td>
<td>2.287(13)</td>
<td>Au1 Cl2i</td>
<td>2.2765(16)</td>
<td>Au1-P1</td>
</tr>
<tr>
<td>Au1 Cl4</td>
<td>2.287(13)</td>
<td>Au1 Cl1i</td>
<td>2.2799(16)</td>
<td>1.437(3)</td>
</tr>
<tr>
<td>C1 N1</td>
<td>1.308(7)</td>
<td>C1 N2</td>
<td>1.322(7)</td>
<td>1.808(3)</td>
</tr>
<tr>
<td>C7 N1</td>
<td>1.398(6)</td>
<td>C3 N2</td>
<td>1.389(6)</td>
<td>N2-C3</td>
</tr>
<tr>
<td>C1 S1</td>
<td>1.684(5)</td>
<td>C2 N1</td>
<td>1.388(6)</td>
<td>N2-C3</td>
</tr>
<tr>
<td>(b) angles</td>
<td></td>
<td>(b) angles</td>
<td></td>
<td>(b) angles</td>
</tr>
<tr>
<td>C4 Au1 Cl3</td>
<td>90.31(4)</td>
<td>S1-C1-C6</td>
<td>126.8(3)</td>
<td>S22-Au1-P1</td>
</tr>
<tr>
<td>C4 Au1 Cl2</td>
<td>178.81(4)</td>
<td>S1-C1-N2</td>
<td>114.7(2)</td>
<td>176.25(5)</td>
</tr>
<tr>
<td>C3 Au1 Cl2</td>
<td>89.14(4)</td>
<td>N2-C1-C6</td>
<td>118.4(3)</td>
<td>S22-Au1-P1</td>
</tr>
<tr>
<td>C4 Au1 Cl1</td>
<td>90.45(5)</td>
<td>S22-C2-C22</td>
<td>115.9(4)</td>
<td>S22-Au1-P1</td>
</tr>
<tr>
<td>C2 Au1 Cl1</td>
<td>90.11(5)</td>
<td>S22-C22-C23</td>
<td>126.6(4)</td>
<td>S22-Au1-P1</td>
</tr>
<tr>
<td>N1 C1 S1</td>
<td>114.4(4)</td>
<td>N2 C23A</td>
<td></td>
<td>176.11(9)</td>
</tr>
</tbody>
</table>

Symmetry transformations used to generate equivalent atoms: (i) -x+1,-y,-z+1.
Fig. 2 (A) Anisotropic ellipsoid representation of the building block of complex 2. The ellipsoids are drawn at 50% probability level. The chloride and oxonium ions and water molecules are not shown for clarity. (B) Strong hydrogen bonding interactions.

Fig. 3 Anisotropic ellipsoid representation of complex 3. The ellipsoids are drawn at 50% probability level.

Fig. 4 (A) Anisotropic ellipsoid representation of complex 6. The ellipsoids are drawn at 50% probability level. (B) Packing diagram of 6 with short contacts.

desulfurated thioamide counter part. The Au-Cl bond distances of 2.28-2.29 Å agree with those found in other [AuCl₄⁻] anions (2.27-2.28 Å in [C₆H₁₁N₂][AuCl₄] ([C₆H₁₁N₂]=1-ethyl-3-methylimidazolium), 23a 2.27-2.29 Å in [C₈H₁₅N₂][AuCl₄] (C₈H₁₅N₂]=1-butyl-3-methylimidazolium) 23a and average 2.29 Å in [C₅SCNmim][AuCl₄] (C₅SCNmim= 1-thiocyanomethyl-3-methylimidazolium chloride). 23b The C-N bond distances in the desulfurated counter parts of complexes 1 and 2 are C₁-N₁= 1.308(7) Å and C₇-N₁= 1.398(6) Å (1) and C₁-N₂= 1.322(7) Å and C₃-N₂= 1.389(6) Å (2) respectively indicating that nitrogen participates in a partial double bond. 17,19 Moreover the angles around the C₁ atoms were H₁-C₁-N₁= 122.8°, H₁-C₁-S₁= 122.8° and S₁-C₁-N₁= 114.4 (4)° in 1 and H₁-C₁-N₂= 124.9°, H₁-C₁-N₁= 124.8° and N₁-C₁-N₂= 110.4(4)° in 2 indicating sp² hybridization of the C atom confirming the existence of a double bond character between C and protonated N atoms in both complexes (Scheme 3).

\[
\text{X= S and Y= H (1) or X= NH and Y= EtO (2)}
\]

Scheme 3
and 2 and the isolation of compound 3. Thus, in case of complexes 1 and 2, the tetrachloroauronic anion is present in the complex as a counter anion since the desulfurated thione is protonated. The stability due to the charge delocalization in case of compound 3 leads to its isolation (see below). Therefore, a reasonable mechanism for the desulfuration of thione ligands could involve first the oxidation of thiones by di-oxygen, catalyzed by the presence of tetrachloroauroic(III) anion followed by the C-S bond cleavage (in the cases of the ligands mbztH and EthmbzimH). In case of compound 3 the 2-sulfonate-nicotinamic acid (C,H,NO,S) is more stable than the other ligands, due to delocalization of the charge density, making the bond cleavage more difficult than in the other two ones. This is confirmed by the electrochemical and computational studies (see below). This indicates that both of the other two ligands produce similar intermediates, however ending up to 1 and 2 complexes, as less stable than 3.

The reactions of 4 with the 2-mercapto-thiazolidine (mtzdH), 2-mercapto-benzothiazole (mbztH) and 5-chloro-2-mercapto-benzothiazole (ClmbztH) in the presence of potassium hydroxide produced mixed ligand complexes of formulae [Au(tpp)(mtzd)] (5), [Au(tpp)(mbzt)] (6) and [Au(tpp)(Clmbzt)] (7). One triphosphine and one thioamide ligand are coordinated to Au(I) through their P and S atoms respectively. The geometry around Au(I) is linear with Au-P bond distances of 2.296(3) Å (6) and 2.259(3) Å (7) respectively and Au-S bond lengths of 2.296(13) Å (6) and 2.296(3) Å (7) respectively. The S-Au-P angle is almost 180° (176.25(5)° for (6) and 176.11(9)° for (7), respectively). The variation from 180° may be due to the packing of the molecules in the crystal lattice. Fig. 4B for (6): C133 · · · C22_e = 3.496(7), C126 · · · C135_f = 3.562(7) Å, Translation of Symmetry Code to Equiv. Pos: e = 3−x,1−y,1−z, f = 3−2−x,−1−2+y,1−2−z (stacking interactions) and Fig. 5B for (7): C125 · · · C132_b = 3.369(13), N23 · · · C115_d = 3.355(19) Å, Translation of Symmetry Code to Equiv. Pos: b = 3−x,1−y,1−z, d = 3−x,1−y,2−z (hydrogen bondings).

Computational studies

The proposed desulfuration mechanism through the formation of a sulfonate intermediate derivative in the case of complexes 1 and 2 (Reaction IV), is further supported by PM6 calculations for the determination of the Bond Dissociation Energy of the C-SO₃H bond.

\[
\text{NH} = \text{S} \rightarrow \text{N} = \text{SH} \rightarrow \text{N} = \text{O} \rightarrow \text{N} = \text{H}
\]

(IV)

The Bond Dissociation Enthalpies (BDE) for the C-S bond were obtained from the enthalpies of the different species using the expression: \( \Delta H_{\text{BDE}}(\text{R}_1 - \text{R}_2) = [\Delta H_{\text{SO}_3}(\text{R}_1) + \Delta H_{\text{SO}_3}(\text{R}_2)] - \Delta H_{\text{SO}_3}(\text{R}_1 - \text{R}_2) \) where (R₁, R₂) are the sulfur oxidized forms of the ligands, R₁ are the free ligands and R₂ the desulfurized forms of the ligands (see Scheme 2, Reaction II). Semi-empirical theoretical methods are especially designed to obtain enthalpy of formation of chemical systems with minimum computational cost and recent work has shown their reliability in BDE estimations.²⁵ PM6 gave the best results in our preliminary testing runs and therefore it was selected for the calculations. The calculated BDE values for the

Fig. 5 (A) Anisotropic ellipsoid representation of complex 7. The ellipsoids are drawn at 50% probability level. (B) Packing diagram of 7 with the short contacts.

Hydrogen bonding interactions N1[H1A]···Cl₃= 3.257(4) Å (1) and N2[H2]···Cl₃= 3.050(5) Å (2) (symmetry transformations: (i) −x+1/2, y−1/2, z and (ii) x, y, z+1) stabilize the supramolecular assemblies of complexes 1 and 2 (Figs. 1B and 2B).

Compound 3 is a zwitterion. The C-S bond distance is 1.808(3) Å indicating a single C-S bond while the C-N (1.34 Å) and the S-O distance of 1.444 Å (stacking interactions) and Fig. 4B for (3) = 3.257(4) Å, Translation of Symmetry Code to Equiv. Pos: e = 3−x,1−y,1−z, f = 3−2−x,−1−2+y,1−2−z (stacking interactions) and Fig. 5B for (7): C125 · · · C132_b = 3.369(13), N23 · · · C115_d = 3.355(19) Å, Translation of Symmetry Code to Equiv. Pos: b = 3−x,1−y,1−z, d = 3−x,1−y,2−z (hydrogen bondings).

Computational studies

The proposed desulfuration mechanism through the formation of a sulfonate intermediate derivative in the case of complexes 1 and 2 (Reaction IV), is further supported by PM6 calculations for the determination of the Bond Dissociation Energy of the C-SO₃H bond.

\[
\text{NH} = \text{S} \rightarrow \text{N} = \text{SH} \rightarrow \text{N} = \text{O} \rightarrow \text{N} = \text{H}
\]

(IV)

The Bond Dissociation Enthalpies (BDE) for the C-S bond were obtained from the enthalpies of the different species using the expression: \( \Delta H_{\text{BDE}}(\text{R}_1 - \text{R}_2) = [\Delta H_{\text{SO}_3}(\text{R}_1) + \Delta H_{\text{SO}_3}(\text{R}_2)] - \Delta H_{\text{SO}_3}(\text{R}_1 - \text{R}_2) \) where (R₁, R₂) are the sulfur oxidized forms of the ligands, R₁ are the free ligands and R₂ the desulfurized forms of the ligands (see Scheme 2, Reaction II). Semi-empirical theoretical methods are especially designed to obtain enthalpy of formation of chemical systems with minimum computational cost and recent work has shown their reliability in BDE estimations.²⁵ PM6 gave the best results in our preliminary testing runs and therefore it was selected for the calculations. The calculated BDE values for the
C-S bond (Reaction IV) of compound 3 is +310.16 kJ mol⁻¹, while the corresponding values for 1 and 2 are +148.16 and +111.96 kJ mol⁻¹ respectively, indicating the easier formation of the desulfurated mbzH or EtmzbzimH ligands in contrast to the desulfuration of the 2-sulfonate-nicotinic acid.

**Electrochemical studies**

(i) The complexes 1-2 and 4-7. The electrochemical behavior of 1-2 and 4-7 was studied in acetonitrile and DMF solutions, using cyclic voltammetry. The redox potentials of these complexes are summarized in Table 2. The cyclic voltammogram of the starting compound 4 displays one irreversible wave in acetonitrile controlled by diffusion (the dependence of I vs. v⁰/² has a linear character) in the cathodic range at ~1.79 V, which is in accordance with literature data and corresponds to the reduction of RAuPPh₃ with simultaneous formation of Au(0) and PPh₃. In the anodic range the one-electron irreversible wave at 1.29 V was observed. Cyclic voltammograms of complex 5 show one irreversible cathodic wave. For the oxidative scan, an irreversible wave was observed.

The replacement of the Cl⁻ anion in complex 4 by a thioamide ligand with poorer electron-accepting ability as in the case of 5 leads to the increase in LUMO energy that results in Au(I)/Au(0) redox couple shift to a more negative potential as compared with complex 4. For the anodic scan the one diffusion-controlled irreversible one-electron wave was observed at 0.93 V, which may be assigned to ligand oxidation as it has been shown previously for a series of RAuPPh₃. This results to considerable shift of the metal-centered oxidation potential towards the anodic range and the corresponding metal-centered wave was not observed in the solvent’s potential window. The electrochemical properties of complexes 6 and 7 were not studied in acetonitrile because of their poor solubility.

Cyclic voltammograms of complex 2 in acetonitrile are presented in Fig. 6(A). Three waves in the cathodic range of potentials were observed. The first one is irreversible and shows a diffusion character and corresponds to the transfer of two-electrons, i.e., the reduction process Au(III)→Au(I). The second one is a one-electron irreversible wave and the third one, at highest negative potential, is a one-electron irreversible one. Scheme 4 shows the steps of redox transformation of complex 2. The first wave may be assigned to the reduction of complex 2 (step 1 at 0.05 V), that results to the destruction of the complex, thus forming AuCl, Cl⁻ ions and the oxidized form of the ligand. The second wave at ~0.51 V corresponds to the reduction of Au¹ to Au⁰. The third wave can be ligand-centered and shows reduction of the cationic species to the radical one. After triggering the potential at ~1.8 V the one-electron wave which appears, is assigned to the oxidation of a product formed during the reduction of 2. In the anodic range the reverse scan shows three irreversible waves. The third one at 1.34 V is an one-electron wave and obviously corresponds to Cl⁻/Cl⁰ oxidation. The nature of the first and second waves might be connected with some chemical reactions which take place in the reduction process of the complex.

The reverse scan after triggering the potential at E < ~0.5 V generates the new peak at 1.4 V. The characteristic triangle form and a significant discordance between the concentration of the complex and the current value, indicate the adsorption character of this wave (Fig. 6A). We propose that this peak

<table>
<thead>
<tr>
<th>Compound</th>
<th>Oxidation potentials, (V)</th>
<th>Reduction potentials, (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E⁺</td>
<td>E''⁺</td>
</tr>
<tr>
<td>1</td>
<td>0.57⁰</td>
<td>1.15⁰</td>
</tr>
<tr>
<td>2</td>
<td>0.71⁰</td>
<td>1.34⁰</td>
</tr>
<tr>
<td>4</td>
<td>1.29</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>0.93</td>
<td>—</td>
</tr>
</tbody>
</table>

* Peak potentials (V, vs. Ag/AgCl/KCl) were determined from cyclic voltammetric scans. Experimental conditions: Pt electrode, v = 200 mV/s, 293 K, acetonitrile containing 50 mM TBABF₄. Eᵢ denotes peak potential of a chemically irreversible step. "In reverse anodic scan triggered beyond ~0.5 V."
The electrochemical behavior of complex 1 is similar to that of complex 2 and can also be explained by Scheme 4. In this case the potential of the third peak is shifted to more positive potentials compared with complex 2 (ΔE = 100 mV, Table 2). The more negative reduction potential observed for the third reduction wave in the case of 2 could be readily rationalized by the presence of the electron-donating alkoxyl substituent in 2-mercaptobenzothiazole ligand, which makes it more electron-donor and poorer π-acceptor, and hence reduces its reduction potential. This fact also reinforces the assumption that the nature of this wave is assigned to the ligand reduction. Similar electrochemical behavior was observed in the electrochemical study of the complexes of Au(III) with 2,2'-bipyridine and oxygen containing ligands.

It should be noted that the presence of the electron-accepting Cl substituents in the 2-mercaptobenzothiazole ring results in the shift of peak potentials to more positive values (Table 3). It was shown previously, that the oxidation of complexes Ph3PAuR (R = Me, Ph, MeO, Cl, Br, I) in acetonitrile proceeds through the formation of the Ph3PAuR+ radical-cation. Decomposition of these species leads to unstable compounds RAu and the formation of Au(0) and R, as described in ref. 26. In the case of Ph3PAuCl (4) no distinct waves in the anodic range appear within the limits of the solvent potential window (at ≈ 1.6 V the discharge of solvent molecules begins). In the cathodic scan the one-electron diffusion-controlled the irreversible wave was observed at –0.59 V.

The electrochemical behavior of complexes 1, 2 and 4 in DMF is very similar to the one in acetonitrile: three irreversible waves in the cathodic range were observed. Therefore, the reduction of these compounds may be described as in Scheme 4.

(ii) The ligand. The redox properties of the ligands Etmbz-imH, mbztH and mnaH2 were studied in an attempt to contribute to the elucidation of the mechanism of the desulfuration process, caused by Au(III) ions. As follows from cyclic voltammograms (Fig. 8), all ligands display the irreversible one-electron wave, controlled by diffusion at anodic range of potentials. The irreversibility takes place in the range of scan rate from 50 mV/s to

![Scheme 4](image-url)

Scheme 4 corresponds to the oxidation of adsorbed Au0 on the surface of the electrode.

The electrochemical behavior of complex 1 corresponds to the oxidation of adsorbed Au0 on the surface of the electrode.

The electrochemical behavior of complex 1 is similar to that of complex 2 and can also be explained by Scheme 4. In this case the potential of the third peak is shifted to more positive potentials compared with complex 2 (ΔE = 100 mV, Table 2). The more negative reduction potential observed for the third reduction wave in the case of 2 could be readily rationalized by the presence of the electron-donating alkoxyl substituent in 2-mercaptobenzothiazole ligand, which makes it more electron-donor and poorer π-acceptor, and hence reduces its reduction potential. This fact also reinforces the assumption that the nature of this wave is assigned to the ligand reduction. Similar electrochemical behavior was observed in the electrochemical study of the complexes of Au(III) with 2,2'-bipyridine and oxygen containing ligands.

It should be noted that the presence of the electron-accepting Cl substituents in the 2-mercaptobenzothiazole ring results in the shift of peak potentials to more positive values (Table 3). It was shown previously, that the oxidation of complexes Ph3PAuR (R = Me, Ph, MeO, Cl, Br, I) in acetonitrile proceeds through the formation of the Ph3PAuR+ radical-cation. Decomposition of these species leads to unstable compounds RAu and the formation of Au(0) and R, as described in ref. 26. In the case of Ph3PAuCl (4) no distinct waves in the anodic range appear within the limits of the solvent potential window (at ≈ 1.6 V the discharge of solvent molecules begins). In the cathodic scan the one-electron diffusion-controlled the irreversible wave was observed at –0.59 V.

The electrochemical behavior of complexes 1, 2 and 4 in DMF is very similar to the one in acetonitrile: three irreversible waves in the cathodic range were observed. Therefore, the reduction of these compounds may be described as in Scheme 4.

(ii) The ligand. The redox properties of the ligands Etmbz-imH, mbztH and mnaH2 were studied in an attempt to contribute to the elucidation of the mechanism of the desulfuration process, caused by Au(III) ions. As follows from cyclic voltammograms (Fig. 8), all ligands display the irreversible one-electron wave, controlled by diffusion at anodic range of potentials. The irreversibility takes place in the range of scan rate from 50 mV/s to

![Fig. 7](image-url)

Fig. 7 Cyclic voltammetry curve for 1.1 × 10−3 M complex 7 in DMF. Experimental conditions: Pt working electrode, 50 mM TBABF4, vs. Ag/AgCl/KCl, scan rate v = 0.2 V/s.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Oxidation potentials, (V)</th>
<th>Reduction potentials, (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EⅠ</td>
<td>EⅡ</td>
</tr>
<tr>
<td>1</td>
<td>0.65</td>
<td>1.44</td>
</tr>
<tr>
<td>2</td>
<td>—</td>
<td>1.35</td>
</tr>
<tr>
<td>4</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>0.72</td>
<td>1.1</td>
</tr>
<tr>
<td>6</td>
<td>0.68</td>
<td>1.05</td>
</tr>
<tr>
<td>7</td>
<td>0.82</td>
<td>1.12</td>
</tr>
</tbody>
</table>

* Peak potentials (V, vs. Ag/AgCl/KCl) were determined from cyclic voltammetric scans. Experimental conditions: Pt electrode, v = 200 mV/s, 293 K, acetonitrile containing 50 mM TBABF4, E0 denotes peak potential of a chemically irreversible step.
case of mnaH₂ only the oxidized derivative was isolated and characterized, we made an attempt to obtain the desulfurated product by means of the controlled potential electrolyses which was performed in acetonitrile at the first anodic wave potential of £ = 1.3 V. In the NMR-spectrum of the product, the proton signal of the SH-group disappeared after electrolyses. The signal of the carboxy group proton on the other hand, was shifted to lower fields and a widening was observed, obviously, because of hydrogen bond formation between the carboxy and sulfo groups. These facts support the assumption that the oxidation of mnaH₂ ligand proceeds the desulfuration step.

### Biological tests

Complexes 1-2 and 4-7 and HÄuCl₄ were tested for cytotoxic activity against leiomyosarcoma cells from the Wistar rat, polycyclic aromatic hydrocarbons (PAH, benzo[a]pyrene) carcinogenesis. Cytotoxic activities for complexes 1-2 and 4-7 and HÄuCl₄ were evaluated as percentage of cells surviving after being exposed to multiple concentrations of a test compound for 24 h time period. The IC₅₀ values after treatment for 24 h were 1.3 ± 0.9 (1), 0.7 ± 0.1 (2), inactive (4), 0.8 ± 0.4 (5), 2.1 ± 1.3 (6) and 1.1 ± 0.5 (7) µM respectively, while HÄuCl₄ was found to be inactive against leiomyosarcoma cells (IC₅₀ = 4.5 ± µM²), for cisplatin. Consequently, complexes 2 and 5, containing Au(III) and Au(I) respectively, were the more active among 1-2 and 4-7. The IC₅₀ values of these complexes, cisplatin and other metals, against leiomyosarcoma cells are compared in Table 5. Gold complexes 2 and 5, are less active than the tin complexes {[(Ph₂Sn)(MNA) (Me₂CO)]} and Ph₃Sn(PMT) with IC₅₀ values 0.005 and 0.1 µM respectively but they show comparable activity with that of silver(I) complexes (Table 5). Among complexes of the same ligands 5-chloro-2-mercapto-benzothiazole, (7, Me₃Sn(CMBZT), (n-Bu)₂Sn(CMBZT), Ph₃Sn(CMBZT) and Ph₃Sn(CMBZT)) the diorganotin complex Ph₃Sn(CMBZT) show higher activity and the same order is followed between gold(I) and organotin complexes 6 and Ph₃Sn(MBZT) of 2-mercapto-benzothiazole ligand (Table 5).

### Conclusions

Based on crystallographic and computational results a possible mechanism for the desulfuration of thioamide ligands upon their reaction with [ÄuCl₄]⁻ ions was proposed. The isolation of the stable enough compound 3 and the final desulfurated complexes 1 and 2 strongly indicate that the AuCl₄⁻ ions, which catalyzes the oxidation of S to -SO₃⁻ by atmospheric O₂, regenerates and acts as a counter ion in 1 and 2. Both electrochemical and computational results indicate that the oxidation of S takes place prior to C-S breakage and desulfuration and justifies the stability of 3, as compared to the sulfonate derivatives of the other ligands.

The catalytic role of AuCl₄⁻ in the oxidation of thiouthers by atmospheric O₂ had also been proposed earlier by Natâle et al.³ Au(II) is most probably first reduced to Au(I) and re-oxidized back to Au(III). This is the case of the electrochemical behavior of the complexes in this study, where a two electron process for the reduction of Au(III) to Au(I) was detected. It should be noted however, that kinetic data would be required to allow a more definitive conclusion on any proposed mechanism, to be made.

---

**Table 4** Electrochemical properties of the ligands EtnbzmH, mnbzH and mnaH₂ in acetonitrile (Pt, 200 mV/s, 293 K, acetonitrile containing 50 mM TBABF₆, V, vs. Ag/AgCl/KCl)

<table>
<thead>
<tr>
<th>Ligand</th>
<th>E&lt;sub&gt;ox&lt;/sub&gt;, V</th>
</tr>
</thead>
<tbody>
<tr>
<td>EtnbzmH</td>
<td>1.02</td>
</tr>
<tr>
<td>mnbzH</td>
<td>1.17</td>
</tr>
<tr>
<td>mnaH₂</td>
<td>1.3</td>
</tr>
</tbody>
</table>
The formation of the mixed ligand gold(I) complexes of formulae [Au(tpm)ltzu] (5), [Au(tpm)(mbzt)] (6) and [Au(tpm)(Clmbzt)] (7) where no desulfurization of the ligands takes place emphasizes the possible catalytic role of AuCl₄⁻ in the oxidation and desulfurization of the ligands.

Finally, complexes 2 and 5 containing Au(III) and Au(I) showed the higher in vitro cytotoxicity against leiomyosarcoma cells, although there is no significant differences on the cytotoxic profile between the complexes 1, 2, 5 and 7. These complexes were also found more active than cis-Pt. Complexes 2 and 5 exhibit lower activity than the corresponding [(Ph₃Sn)(MNA)(Me₂CO)] and Ph₃Sn(PMT) complexes, while they show comparable activity with that of silver(I) complexes (Table 5). Among gold and organotin complexes of the same ligand, tin complexes are again more active.

**Experimental**

**Materials and instruments**

All solvents used were of reagent grade, while thioamides and triphenyl-phosphine (Aldrich, Merk) were used with no further purification. The tetrachloroauric(III) acid (HAuCl₄) solution (0.51 M) was prepared by dissolving 1 g Au foil into 10 ml mixture of concentrated hydrochloric acid (12 M) and nitric acid (16 M) 4:1.¹ Elemental analyses for C, H, N, and S were carried out with a Carlo Erba EA MODEL 1108 elemental analyzer. Infra-red spectra in the region of 4000-370 cm⁻¹ were obtained in KBr discs. Far-infra-red spectra in the region of 500-4 cm⁻¹ were obtained in 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 on a Bruker AC 250, 400 MHFT-NMR instrument in CDCl₃ or DMSO-d₆ solutions. Chemical shifts δ are given in ppm using TMS as internal reference. Micro Raman spectra (64 scans) were recorded at room temperature using a low power (~30 mW) green (514.5) nm laser on a Renishaw In Via spectrometer set at 2.0 resolution. Thermal studies were carried out on a Shimadzu DTG-60 simultaneous DTA-TG apparatus, under a N₂ flow (50 cm³ min⁻¹) at a heating rate of 10 °C min⁻¹.

### Synthesis of compounds

- **[AuCl₄] [bztHz⁺]** (1),
- **[AuCl₄][EtHzimH₂][H₂O]** (2), the 2-sulfonate-nicotinic acid (3), [Au(tpm)(mbzt)] (6) and [Au(tpm)(Clmbzt)] (7)

Complexes 1 and 2 were synthesized as follows: 1 mmol of the appropriate thioamide ligand (0.167 g 2-mercapto-benzothiazole and 0.194 g of 5-ethoxy-2-mercapto-benzimidazole) were dissolved in 10 ml methanol. 10 ml acetonitrile solution which contains 0.5 mmol HAuCl₄ 1 ml (0.51 M) was then added to the ligand's methanolic solution. The resulting solution was heated for 3 hours under reflux. After cooling the solution was filtered off. Slow evaporation of the resulting clear solution form crystals of complexes 1 and 2 suitable for X-ray analysis. Crystals of compound 3 were obtained by slow evaporation of the solution resulted from mixing 10 ml acetonitrile solution of 0.5 mmol HAuCl₄ 1 ml (0.51 M) with 10 ml methanolic solution of 1 mmol of 2-mercapto-nicotinic acid (0.155 g) in the presence of 1 mmol KOH (1 ml, 1 N).

The precursor [Au(tpm)Cl] (4) was derived from the reaction between 1 mmol tri-phenyl-phosphine (0.262 g) with 0.5 mmol of HAuCl₄ solution (1 ml, 0.5 M) in 10 ml methanol.⁶ Crystals of complex 4 were grown from a 20 ml dichloromethane solution. Complexes 5, 6 and 7 were synthesized as follows: A suspension of 0.215 mmol of the appropriate thioamide (0.026 g 2-mercapto-thiophene) for 5, 0.034 g 2-mercapto-benzothiazole for 6 and 0.042 g 5-chloro-2-mercapto-benzimidazole for 7 in distilled water (5 ml) was treated with a solution of KOH 1 N (1 cm⁻³, 1 mmol). The resulting clear solution was then added to 5 ml of a methanolic solution of 0.215 mmol [Au(tpm)Cl] (0.106 g) under stirring for 2 hours. The white precipitate was then filtered off and dried. Crystals of complexes 5, 6 and 7 suitable for X-ray analysis were formed from slow evaporation of a dichloromethane/toluene solution (1:1) of the above powders.

**Table 5** Cytotoxic activity of Au(II)/(I), Ag(I) and Sn complexes as IC₅₀ (µM) values against leiomyosarcoma cells

<table>
<thead>
<tr>
<th>Complex</th>
<th>50% inhibitory concentration (IC₅₀) (µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>4.5</td>
</tr>
<tr>
<td>1</td>
<td>1.3 ± 0.9</td>
</tr>
<tr>
<td>2</td>
<td>0.7 ± 0.1</td>
</tr>
<tr>
<td>4</td>
<td>0.8 ± 0.4</td>
</tr>
<tr>
<td>6</td>
<td>2.1 ± 1.3</td>
</tr>
<tr>
<td>7</td>
<td>1.1 ± 0.5</td>
</tr>
<tr>
<td>[(AgCl₂(TPTP)]⁺</td>
<td>0.8</td>
</tr>
<tr>
<td>[AgCl₂(TPTP)]⁺</td>
<td>0.7</td>
</tr>
<tr>
<td>[AgBr₂(TPTP)]⁺</td>
<td>0.8</td>
</tr>
<tr>
<td>[AgI(TPTP)]⁻</td>
<td>0.9</td>
</tr>
<tr>
<td>Me₃Sn(CMBZT)²⁻</td>
<td>5.7-5.8</td>
</tr>
<tr>
<td>(t-Bu)₃Sn(CMBZT)²⁻</td>
<td>0.6-0.8</td>
</tr>
<tr>
<td>Ph₃Sn(CMBZT)³⁻</td>
<td>0.3-0.5</td>
</tr>
<tr>
<td>Ph₃Sn(CMBZT)⁴⁻</td>
<td>0.5-0.8</td>
</tr>
<tr>
<td>Me₃Sn(PMT)¹⁻</td>
<td>20-60</td>
</tr>
<tr>
<td>(t-Bu)₃Sn(PMT)¹⁻</td>
<td>0.7</td>
</tr>
<tr>
<td>Ph₃Sn(PMT)¹⁻</td>
<td>1-2</td>
</tr>
<tr>
<td>Ph₃Sn(PMT)²⁻</td>
<td>1</td>
</tr>
<tr>
<td>Ph₃Sn(BMZO)³⁻</td>
<td>1.3-3</td>
</tr>
<tr>
<td>Ph₃Sn(BMZT)⁴⁻</td>
<td>1.5-3</td>
</tr>
<tr>
<td>[(Ph₃Sn)(MNA)(Me₂CO)]⁻</td>
<td>0.005</td>
</tr>
<tr>
<td>SbBr₅(TU)₂⁻</td>
<td>23.5 (unpublished results)</td>
</tr>
</tbody>
</table>
Crystallography

Intensity data for the crystals of 1 were collected on a Bruker KappaCCD diffractometer and for 2 on a Bruker APEXI CCD diffractometer, both at the windows of a Bruker FR519 rotating anode (\(\phi\) scans and \(\omega\) scans to fill the asymmetric unit) in the range 3.1°–27.5° for 1 and 3.2°–27.5° for 2, using graphite-monochromated MoK\(_\alpha\) radiation (\(\lambda = 0.71073\) Å) at 293(2) K. The structures were solved with SHELXS-97\(^{34}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

Intensity data for the crystals of 3, 4 and 5 were collected on Bruker P4 diffractometer, with graphite monochromatized MoK\(_\alpha\) radiation (\(\lambda = 0.70737\) Å) at 293(2) K. The structures were solved with SHELXSX-97\(^{36}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined using SHELXL-97.\(^{35}\) All non-hydrogen atoms were corrected for Lorentz-polarization effects and absorption.\(^{36,34}\)

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

The structures were solved using SIR92\(^{33}\) (1) and SIR2004 (2)\(^{34}\) and refined using SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically with hydrogen atoms included in idealized positions and refined using a riding model. Each formula unit of 2 contains in total five water molecules, one of which is disordered and one disordered molecule of \(\text{[H}_2\text{O}^+\). There are also four chloride ions. The presence of the \(\text{[H}_2\text{O}^+\) molecule means that the charge in the formula unit is balanced. It was only possible to locate hydrogen atoms for one of the water moieties, O2. For all other water molecules and the \(\text{[H}_2\text{O}^+\) molecule it was found impossible to locate the hydrogen atoms because of the use of X-ray radiation, the presence of the very heavy gold atom and the low occupancies of water at these positions. For this reason it is not possible to assign which of the O4 and O5 atoms belongs to a water molecule and which belongs to the acid, as the assignment of either atom as the acid would give the correct charge balance. It is highly probable that the O3, O4 and O5 moieties are involved in hydrogen bonding, but this is impossible to confirm due to the fact that the hydrogen atoms in these moieties could not be located.

Intensity data for the crystals of 3, 4 and 5 were collected on Bruker P4 diffractometer, with graphite monochromatized MoK\(_\alpha\) radiation (\(\lambda = 0.70737\) Å) at 293(2) K. The structures were solved with SHELXSX-97\(^{36}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.

In these gold structures, the large residual electron density peaks observed are due to the high atomic radius of gold atom. The structure was solved with direct methods with SHELXS97\(^{35}\) and refined with SHELXL-97.\(^{35}\) All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically.
Computational studies

The ground state optimizations on the investigated molecules were carried out without any constraints using the PM6 semiempirical method as this is implemented in MOPAC 2007 program, utilizing the eigenvector following algorithm.

Electrochemical study

All electrochemical measurements were carried out under argon at room temperature. Cyclic voltammetry experiments were performed in classical three-electrode cell in CH3CN solution with 0.05 M TBABF4 as supporting electrolyte using a model IPC-Win potentiostat. The number of electrons transferred were determined by comparing with the height of Fe2+/Fe3+ = 0.45 V wave for the same concentration and coulometrically. A platinum working electrode with diameter 2 mm, platinum wire auxiliary electrode and aqueous Ag/AgCl/KCl (sat.) reference electrode were used. The solvents were routinely distilled and dried prior to use.

Biological tests

These have been described in detail elsewhere.

Acknowledgements

This research was carried out in partial fulfilment of the requirements for the master thesis of K.N.K. under the supervision of S.K.H., within the graduate program in Bioinorganic Chemistry. S.K.H., E.R.M. and N.H. would like to thank a NATO grant for the exchange of scientists. E.R.M. also thanks RFBR grant N09-03-00743

References

32 G. M. Sheldrick, SADABS - Bruker Nonius area detector scaling and absorption correction - V2.10