

Studies on gold(II) complexes with hard and soft donor ligands Part IV*. A reactivity study in solution using EPR spectroscopy

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Abstract

The reactions of Au(II) complexes, *cis*-[Au(mta)₂Cl]Cl (**1a**), *trans*-[Au(mta)₂Cl]Cl (**1b**), [Au(mta)₂Cl]₂Cl₂ (**1c**), Au(pma)Cl (**2a**), Au(pma)Br (**2b**) and Au₂(pma)Cl₄ (**2c**), where mta and pma are the deprotonated ligands of *o*-methylthioaniline (Hmta) and *N*-(2-pyridylmethyl)-2-mercaptoaniline (Hpma), respectively, are reported. When these complexes are reacted with selected ligands containing nitrogen donors, the resulting EPR spectra are indicative of coordination with the nitrogen of the incoming ligand. Both compounds **2a** and **2c** react with cysteine (cys) in DMF solution to produce the stable reaction product [Au(pma)(cys)]₂ (**2e**), the EPR spectrum of which indicates the presence of two interacting gold(II) ions to form a dimeric system. A radical formed during the course of the reaction of **2c** with CN⁻ in DMSO solution which exhibits a multiline EPR spectrum with a *g* value of 2.003 may be due to the formation of pyridine-*N*-oxide anion radical subsequently stabilized by either DMSO complex formation and/or σ -bond formation to the central metal atom.

Introduction

The oxidation state II is dominant in the chemistry of copper, but considerably less common for silver and even rarer for gold. Since gold is a 5d element, the ligand-field splitting of d orbitals is much greater than that in copper. A d⁹ gold(II) complex would be strongly distorted tetragonally and the ninth electron would occupy the highly unfavourable d_{x²-y²} orbital, which will be raised correspondingly higher in energy. Hence Au(II) complexes are expected to be oxidized or to disproportionate readily [1].

However, it has been possible to stabilize the oxidation state II for gold in some cases. In the first case, Au(II) is stabilized by the presence of a strong Au–Au bond in certain dimeric complexes and consequently these are diamagnetic [2, 3]. In the other cases, paramagnetic Au(II) complexes are reported to be stabilized by delocalization of the unpaired electron over the ligands [2–8]. We have reported [3, 7, 8] the synthesis and characterization of paramagnetic gold(II) complexes, some of which are dinuclear, with the ligands *o*-aminobenzenethiol (Habt), *o*-methylthioaniline (Hmta),

1,2-di(*o*-aminophenylthio)ethane (dae) and *N*-(2-pyridylmethyl)-2-mercaptoaniline (Hpma). These complexes are found to be extremely stable in the solid state and reasonably stable in solution. The structures [7, 8] of the compound *cis*-[Au(mta)₂Cl]Cl (**1a**), *trans*-[Au(mta)₂Cl]Cl (**1b**), [Au(mta)₂Cl]₂Cl₂ (**1c**), Au(pma)Cl (**2a**), Au(pma)Br (**2b**) and Au₂(pma)Cl₄ (**2c**) are shown in Fig. 1. Most of these complexes readily react with pyridine, imidazole, purine and pyrimidine bases, cysteine, and anionic ligands such as CN⁻, SeCN⁻, etc. and produce reasonably stable paramagnetic species. We have studied these reactions in solution using EPR spectroscopy. It has been possible to isolate and characterize the reaction product in a few cases. Here we report the results of these reactions.

Experimental

Chemicals

The compounds HAuCl₄·3H₂O was obtained from Johnson Matthey; NaAuCl₄·2H₂O and KAUBr₄·2H₂O were prepared using standard procedures. K¹³CN was obtained from Sigma. All other chemicals were of reagent grade and were used as such. All the solvents were dried and distilled before use.

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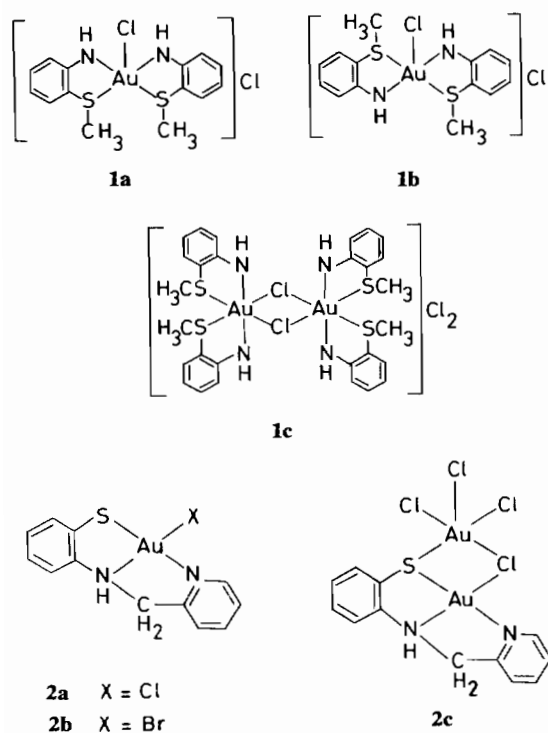


Fig. 1. Structures of the compounds **1a–c** and **2a–c**.

Preparation of starting complexes

The complexes *cis*-[Au(mta)₂Cl]Cl (**1a**), *trans*-[Au(mta)₂Cl]Cl (**1b**), [Au(mta)₂Cl]₂Cl₂ (**1c**), Au(pma)Cl (**2a**), Au(pma)Br (**2b**) and Au₂(pma)Cl₄ (**2c**) were prepared using the methods described in the literature [7, 8].

All reactions of these complexes were carried out in solution at room temperature using deaerated dry solvents with monodentate ligands in the ratio M:L = 1:1. The concentration of the complexes **1a–c** and **2a–c** used for the reactions was about 10⁻⁴ M. The following two reaction products were isolated from the solution.

Au(pma)(py)Cl (**2d**)

50 mg of **2a** were dissolved in a minimum volume of DMF and about 15 mg of pyridine (py) were added to this solution. The solution was stirred at room temperature for 2 h and the solvent was dried *in vacuo*. The compound was recrystallized from dichloromethane. Yield 80%. *Anal.* Found: C, 39.22; H, 3.18; N, 8.20; Au, 36.11. Calc. for C₁₇H₁₆N₃SClAu: C, 38.74; H, 3.03; N, 7.97; Au, 37.41%.

[*Au(pma)(cys)*]₂ (**2e**)

This compound could be synthesized by reacting either **2a** or **2c** with cysteine (cys) in DMF solution as follows. 50 mg of **2c** dissolved in a minimum volume of DMF were stirred with 12 mg of cysteine for 72 h when the solution turned green. The solvent was then evaporated

off *in vacuo* and the solid was washed with water followed by ethanol. The compound was recrystallized from dichloromethane. Yield 30%. *Anal.* Found: C, 34.68; H, 3.31; N, 7.69; Au, 35.87. Calc. for C₃₀H₃₄N₆S₄O₄Au₂: C, 33.83; H, 3.19; N, 7.89; Au, 37.03%.

Physical measurements

Electron paramagnetic resonance spectra were recorded on a Varian E-112 X/Q-band spectrometer. DPPH was used as internal field marker. The simulations of the spectra were performed on a Varian 620L computer and an IBM compatible personnel computer using programs generated in our laboratory. Conductances were determined with a Philips 9500 bridge, using a cell calibrated with 0.02 M KCl solution. IR spectra were measured with a Perkin-Elmer model 783 spectrophotometer using KBr pellets. Microanalyses (C, H, N) were performed in a Perkin-Elmer 240C elemental analyzer.

Results and discussion

A number of reactions have been carried out in solution at room temperature with monodentate ligands, both neutral and anionic, in the ratio 1:1, and the EPR spectra of these solutions have been studied. Most of the reactions are instantaneous and the reaction products are found to be stable. In most cases the EPR spectrum of the reaction product is found to be entirely different from that of the corresponding parent complex. The solution EPR spectra of the parent complexes **1a–c** and **2a–c** are shown in Fig. 2. The blue CH₂Cl₂ solution of the isomeric pair of monomeric gold(II) compounds **1a** and **1b** give identical EPR spectra consisting of four hyperfine lines of equal intensity (*A*_{Au} ≈ 6.5 G) due to the interaction of the unpaired electron with one gold nucleus (100% ¹⁹⁷Au, *I* = 3/2) while the corresponding dimeric compound **1c** in CH₂Cl₂ or DMF exhibits a seven-line EPR multiplet with an intensity ratio of 1:2:3:4:3:2:1 (*A*_{Au} = 4.0 G) indicating its origin from two interacting gold nuclei [7]. The purple nitrobenzene solutions of the mononuclear compounds **2a** and **2b** exhibit identical EPR spectra consisting of four equally spaced equally intense lines (*A*_{Au} = 7.0 g) originating from one gold nucleus [8]. On the other hand, the dinuclear compound **2c** in nitrobenzene exhibits an EPR spectrum consisting of seven unsymmetrical lines originating from the interaction of one unpaired electron with two inequivalent ¹⁹⁷Au nuclei, and this nitrobenzene solution, when allowed to stand at room temperature for about 72 h, gives a four-line pattern of equal intensity which originates from the paramagnetic species Au(pma)Cl [8] generated in the solution due to the

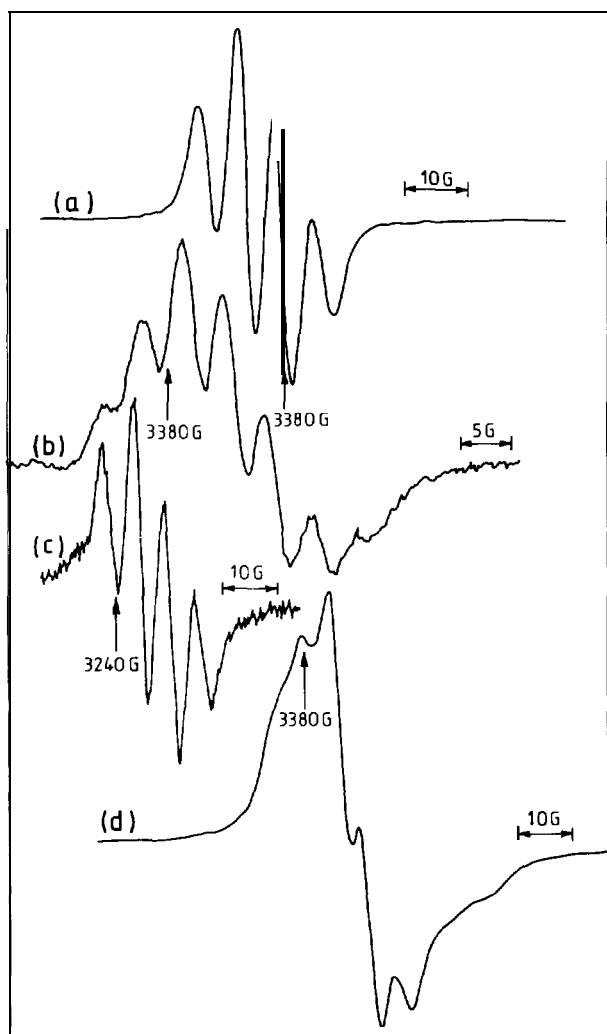


Fig. 2. Solution EPR spectra recorded at X-band frequency ($\nu \approx 9.5$ GHz) at room temperature for the compounds: (a) **1a** in CH_2Cl_2 , (b) **1c** in DMF, (c) **2a** in nitrobenzene, (d) **2c** in nitrobenzene.

spontaneous dissociation of the mixed valent **Au(II)/Au(III)** compound **2c**. However, all three compounds **2a-c** give a four-line pattern in DMF [8]. No super-hyperfine structure originating from the interaction with the nitrogen nucleus/nuclei of the ligand(s) mta or pma is observed in these complexes [7, 8].

Reactions of the complexes **1a-e**

When pyridine or imidazole is added to a dichloromethane solution of any of these compounds **1a-c**, the EPR spectrum is changed from a four-line/seven-line pattern into a simple equal intensity triplet with a hyperfine splitting of approximately 6.5 G (Fig. 3(a)). Similar results are obtained when the same reactions are carried out in DMF solutions. When a DMF solution of **1c** is allowed to react separately with CN^- , SeCN^- and NCO^- , a similar equal intensity three-line pattern

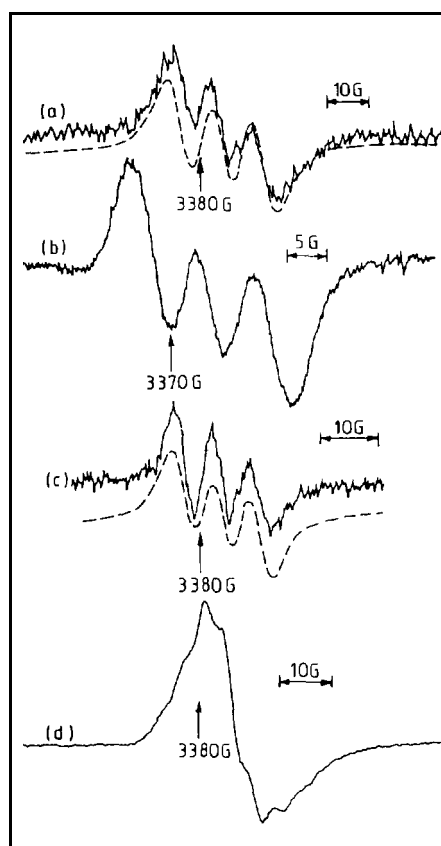


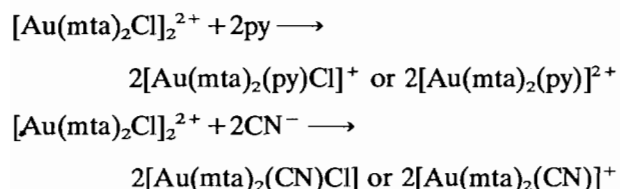
Fig. 3. Solution EPR spectra recorded at X-band frequency ($\nu \approx 9.5$ GHz) at room temperature for the reaction product of: (a) **1a** with imidazole, (b) **1c** with CN^- , (c) **2a** with pyridine, (d) **2c** with cysteine; the corresponding simulated spectrum represented with dotted lines.

is revealed in each case (Fig. 3(b)). Given the experimental condition of compounds and solvents involved, no other nucleus than a single nitrogen would have brought about this pattern of EPR spectra in all these reactions. The simulated spectrum obtained by assuming the interaction of the unpaired electron with a single nitrogen nucleus ($I = 1$) is found to be in good agreement with the experimental one (Fig. 3). Interesting results are also obtained by reacting **1c** in DMF with purine and pyrimidine bases as well as a few nucleosides at room temperature. The addition of adenine, cytosine or cytidine yields a three-line EPR pattern, but the addition of adenosine gives only a single-line EPR spectrum. The original seven-line multiplet of the parent compound **1c** is unchanged with the addition of guanine, uracil or histidine. But with cysteine, **1c** reacts readily and the blue solution of the reaction product gives an intense EPR signal which is not well-resolved.

The presence of a triplet in the EPR spectra of the products of these reactions involving nitrogenous ligands raises the question regarding its origin. Since the addition of new ligand is responsible for the reaction, it

should be part of the newly produced Au(II) complex. At the same time it is unlikely that one of the two bidentate ligands, mta, complexed with Au(II) in **1a** and **1b** could have come out of the coordination sphere during the reaction. So, the most plausible molecular formula for the newly produced complex is either $[\text{Au}(\text{mta})_2\text{YCl}]\text{Cl}$ or $[\text{Au}(\text{mta})_2\text{Y}]\text{Cl}_2$ where Y is the new ligand. In such a case, the hyperfine splitting should not have come from the equivalent nitrogens of the two mta ligands which should have given rise to a quintet with the intensity ratio 1:2:3:2:1 in contrast to our observed equal intensity triplet. This will leave the nitrogen of the incoming ligand in the axial position. The low value for $A_N(\text{iso})$ (e.g. 6.5, 5.5 and 5.5 G for pyridine, imidazole and cyanide adducts of **1c**, respectively) in comparison with the observation of ≈ 14 G for the isotropic splitting due to ^{14}N in nd^9 systems with the rigorous $d_{x^2-y^2}$ ground state indicates the delocalization of the unpaired electron over the whole complex with a low density at the nitrogen site, especially when it is in the axial position.

The occurrence of a three-line EPR spectrum from the solution of any one of the reaction products of the chloro bridged dinuclear compound **1c** indicates that the chloro bridge is split by the incoming ligand, e.g. pyridine (py) or CN^- producing either a six- or a five-coordinate compounds as shown below:



All the reaction products of **1c** with the anionic ligands SeCN^- , NCO^- and CN^- exhibit a three-line spectrum in each case indicating that the nitrogen end of the incoming ligand is coordinated to the metal ion. It is known that in both of its common oxidation states I and III, gold is a 'class b' metal which has been confirmed by studying complexes of gold with ambidentate ligands, in which both gold(I) and gold(III) are almost invariably bound to the softer end of the ligand [9]. In the oxidative addition reactions of diethyldithiocarbamate complex of gold(I) with $(\text{SCN})_2$ and $(\text{SeCN})_2$ it has been confirmed that only the sulfur or selenium end is coordinated to the generated gold(II) ions [10]. But in the present case, the nitrogen end of the SeCN^- is bonded to the metal ion. Cyanide, when bound in a monodentate fashion, is C-bonded in both Au(I) and Au(III) complexes so far known, and hence it is expected that Au(II), having intermediate hardness, would also have C-bound cyanides. The three-line spectrum may have originated from an interaction with the nitrogen nucleus of CN^- since the electron would be considerably de-

localized over the cyanide ligand. Alternatively, it is more probable that the incoming CN^- ligand might have directly bonded to the metal with coordination through its nitrogen end thereby giving rise to a triplet EPR signal. To confirm whether the CN^- ligand is N-bonded or C-bonded in the present cases, we have carried out $^{13}\text{CN}^-$ reactions which yield only a triplet of equal intensity in each case and no ^{13}C superhyperfine splitting is observed. This confirms the presence of N-bonded cyanide in the present cases. Such a nitrogen coordination in CN^- complexes has been earlier observed, for a cobalt cyanide [11]. It may be noted here that **1c**, however, reacting with SCN^- produces a sulfur bridged dimeric compound $[\text{Au}(\text{mta})_2(\text{SCN})]_2(\text{SCN})_2$ (**1d**) which exhibits a seven-line EPR multiplet in solution originating from an interaction with two exchange coupled ^{197}Au nuclei [7].

Reactions of the complexes 2a-c

It has been observed that when pyridine is added to the DMF solutions of the compounds **2a-c**, the EPR spectra are changed from a four/seven-line pattern of the parent complexes into a three-line pattern with equal intensities in each case. This three-line pattern is presumed to arise from an interaction of the unpaired electron with the nitrogen nucleus ($I=1$) of the pyridine ligand. One of these three-line spectra is simulated assuming such an interaction and the agreement between experimental and simulated spectra is satisfactory (Fig. 3(c)). However, the hyperfine splitting due to interaction with the nitrogen nucleus of the incoming ligand is small ($A_N=6$ G) in these cases also, possibly for the same reasons mentioned earlier. The isolated product obtained from the reaction of a concentrated solution of **2a** in DMF with pyridine (py) in the ratio of 1:1.5 at room temperature is found to be $\text{Au}(\text{pma})(\text{py})\text{Cl}$ (**2d**) which is a non-electrolyte in nitromethane. The IR spectrum of this compound clearly shows the presence of the $\nu(\text{Au}-\text{Cl})$ band at 358 cm^{-1} . The observations of $\nu(\text{Au}-\text{Cl})$ at 358 cm^{-1} is consistent with Cl remaining bound to Au and the formation of a five-coordinate Au(II) complex. It may be noted here that the tendency of the metal ion to achieve higher coordination has been observed in previous cases [3, 7, 8].

The purple DMF solution of the reaction product obtained by treating **2a** or **2c** with cysteine (cys) gives a strong EPR signal when recorded immediately after the addition of the reagent in contrast to the four/seven-line multiplet of the parent compound. This purple solution turns greenish-blue on standing for about 48 h, and this solution exhibits a seven-line multiplet. On standing for another 48 h, the solution turns bright green and is stable. This green solution again displays the same EPR spectrum which consists of seven lines (Fig. 3(d)) with an intensity ratio

1:2:3:4:3:2:1 indicating an interaction with two magnetically equivalent ^{197}Au nuclei. The hyperfine coupling ($A_{\text{Au}} \approx 5 \text{ G}$) observed for this compound is quite small. This is strongly indicative of the low metal d character of the highest occupied molecular orbital [12–14]. It

may be recalled here that the compound **2c** when dissolved in DMF exhibits a four-line spectrum originating from the dissociation product $\text{Au}(\text{pma})\text{Cl}$ [8]. The elemental analysis of the cysteine reaction product of **2c** is consistent with the formulation $[\text{Au}(\text{pma})(\text{cys})_2]$

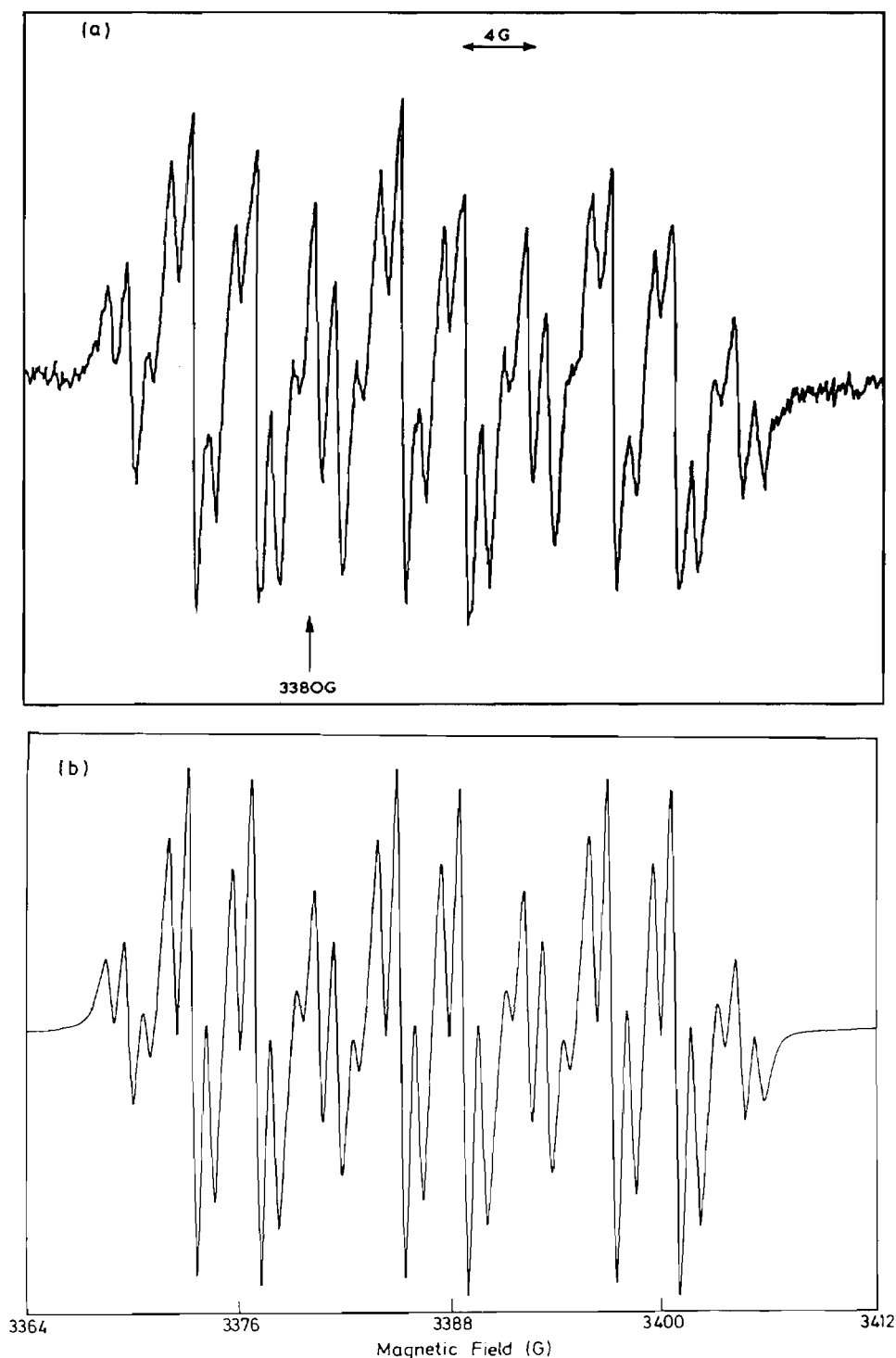


Fig. 4. (a) EPR spectrum of the pyridine-*N*-oxide anion radical generated during the reaction of compound **2c** with CN^- in DMSO solution at room temperature; (b) the corresponding computer simulated spectrum.

(2e). No S–H band is located in the IR spectrum of the compound and since gold has a high tendency to bind to sulfur [3], it is the thiol group of cysteine that is expected to be involved in this reaction. A five-coordinate cysteine thiolato bridged structure is proposed for this dimeric gold(II) compound.

From the study of the mechanism of action of gold-drugs in the treatment of rheumatoid arthritis it has been concluded that gold ion has a high tendency to bind to sulfur-containing groups in enzymes and proteins, and that gold(I)thiol-drugs inhibit enzymes in which a free SH group is necessary for the manifestation of its activity [15]. Thus the reaction of these compounds with cysteine without any reduction may be of biological significance.

Yet another interesting observation is the formation of a radical ion in the reaction of 2c with CN^- in DMSO solution. The brown solution of the reaction product of 2c with CN^- which is quite stable at room temperature for several days exhibits a multiline EPR spectrum as shown in Fig. 4(a). The spectrum is a triplet (intensity ratio, 1:2:1) of a quartet (intensity ratio, 1:3:3:1) of a triplet (intensity ratio, 1:1:1) with a g value of 2.003. It is revealed from the spectrum that a free radical is formed, having a nitrogen nucleus, a set of three equivalent protons ($I=1/2$), and another set of two equivalent protons. The computer simulated spectrum (Fig. 4(b)) with the isotropic hyperfine coupling constants as $A_{\text{N}}=11.9$ G for the 1:1:1 triplet, $A_{\text{H}}=3.6$ G for the quartet and $A_{\text{H}}=1.05$ G for the 1:2:1 triplet is found to be in excellent agreement with the measured EPR spectrum. Given the structure of the gold complex 2c and specially the ligand, the results of simulation indicates that the radical ion may be due to either pyridine anion or pyridine-*N*-oxide anion [16–19]. However, a closer scrutiny of the hyperfine coupling constants of a series of substituted and unsubstituted radical anions of these two types reveals that our observed values for the radical ion compare well with those of pyridine-*N*-oxide anion [19] except for the 4-proton hyperfine coupling constant (3.6 G) as assigned to the three protons at the 2-, 4- and 6-positions of the reaction product in comparison to 8.51 G for the proton at the 4-position (and only 3.01 G for the protons at the 2- and 6-positions) of the pyridine-*N*-oxide anion. So, it is suggested that a pyridine anion must have been initially formed by the cleavage of the pyridyl–methylene bond of the pma ligand followed by a proton addition at the 2-position during the course of the reaction. The pyridine anion radical thus formed is probably oxidized readily (since it is expected to be highly reactive/unstable [16]) in the medium to produce a pyridine-*N*-oxide anion radical which is subsequently stabilized. The unusual stability of this anion could also be due to a possible σ -stabilization later through

bonding with the central metal ion. This could have resulted in a reduced spin density at the proton in 4-position of the anion.

It should be noted that the parent paramagnetic gold(II) complexes themselves exhibited a low hyperfine coupling constant due to ^{197}Au [7, 8] since the highest occupied molecular orbital bearing the unpaired electron has the largest contribution from the sulfur orbitals of the ligand system as proven by the results of SCF- $X\alpha$ -SW calculation on a model compound $\text{Au}(\text{NH}_3)_2(\text{SCH}_3)\text{Cl}$ [8]. Hence, it is not surprising that a further reaction of these Au(II) complexes with an incoming nitrogenous ligand depletes it onto the ligand moiety making the whole complex a metal stabilized radical system. This then would explain our observations of (i) small hyperfine coupling constant for the ^{14}N of the incoming ligand, (ii) the lack of hyperfine splitting due to ^{197}Au in most cases of the reaction product, and (iii) the g value (2.003) being very close to the free radical g value.

Conclusions

The potentially interesting observation in the reactions of these compounds with selective nitrogen donor ligands, and cysteine is that the reaction product is paramagnetic and found to be highly stable most probably due to extensive delocalization of the unpaired electron over the ligands. In most of the cases the product gives a characteristic EPR spectrum from which it is possible to identify the mode of coordination of the incoming ligand. Since most of these compounds readily react with cysteine, a few of these gold(II) compounds may be of potential interest in studying as anti-inflammatory agents. Also the interesting results obtained in the reactions of purine and pyrimidine bases as well as a few nucleosides with some of these complexes indicate that it might be of equal importance to study their applications in biological systems.

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