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"The Golden Method": Electrochemical Synthesis Is an Efficient Route to Gold Complexes

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Supporting Information

ABSTRACT: Gold compounds to be obtained by the direct electrochemical oxidation of a noble metal are reported. This achievement provides an alternative procedure to obtaining neutral gold compounds with potential medical or catalytic applications.

Electrochemistry is an important area of chemistry with high applicability on both laboratory and industrial scales.[1] However, it is not widely known that electrochemistry can be used for the synthesis of compounds. The electrochemical technique is one of the simplest and most direct methods to achieve oxidation or reduction. Electrons can be removed from or added to a system without the complications often associated with the presence of redox reagents, thus avoiding the production of additional waste and providing complexes with high purity.[2] Despite these clear advantages, along with the utility of simple reaction setups and the ready availability of commercial power supplies, electrodes and cells, the electrochemical technique is still far from routine.

The main use of electrochemical oxidation or reduction lies in organic synthesis.[3] In contrast, the number of experiments that involve the preparation of inorganic or organometallic compounds is more limited, despite the large amount of available physicochemical information on the behavior of inorganic and organometallic species at electrodes.[4]

The formation of metal complexes with weakly acidic organic ligands, in which the acid group is usually a hydroxide, an amide NH, or a thiol, requires deprotonation of the ligand, which must be facilitated by the addition of a base or by the use of an appropriate metal salt. The major disadvantage of this route lies in the generation of undesirable side products and waste. In these cases, the electrochemical synthesis has significant advantages over classical processes. Electrochemical methods employ simple machinery and pure starting materials. The fact that the metal is employed rather than one of its salts avoids the occurrence of competitive reactions between the anion salts and the ligand to coordinate to the metal ion. Moreover, this approach allows the selective transformation of specific groups in a ligand or in a complex under very mild conditions.

In the last 3 decades, our research group[5] and others[6] have applied the electrochemical synthesis for the isolation of metal complexes by oxidation of a metal anode in a solution containing salicylaldimine (phenol-OH) or thiosemicarbazone/hydrazone-NH ligands. A wide variety of metals have been successfully employed for the synthesis of metal complexes: manganese(II) and -(III), iron(II), cobalt(II), nickel(II), copper(I) and -(II), silver(I), zinc(II), cadmium(II), lead(II), and tin(II).[7,8] However, some transition and main-group metals remain unexplored in terms of the electrochemical synthesis of metal complexes.[4]

Since the early 1980s, the coordination chemistry of gold has expanded continuously because of the development of new innovative approaches that have enabled great diversification in the field of gold research.[9] In this context, different synthetic strategies have been developed for obtaining organogold(I) and coordination gold(I) compounds.[10] In particular, electrochemistry was previously employed by Tuck and coauthors for the synthesis of gold compounds. However, the reported results revealed that this procedure was not useful in the case of gold because the compounds were isolated in very low yield and with serious experimental difficulties.[11]

The interest of achieving a wide range of gold compounds lies in their clinical use for the treatment of rheumatoid arthritis[12] and inflammatory skin disorders such as urticaria and psoriasis.[13] However, the future of the medicinal chemistry of gold may lie in the therapeutic areas related to anticancer[14] and antimicrobial drugs. A second main use for gold compounds is in the field of catalysis:[15] the good performance of gold is well-known in selective and preferential oxidation reactions,[16] and, more recently, it has found potential uses in selective hydrogenation processes.[17] The information outlined above makes it necessary to search for new collections of gold compounds with different structures and properties.

Our group has started to use phosphinothiosemicarbazone ligands to obtain homoleptic calcogenide M^{I} compounds (M = Cu, Ag, Au) by means of a classical chemical synthesis. The results obtained demonstrate that functionalization of a thiosemicarbazone skeleton with a phosphine head by simple

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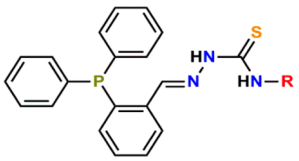
iminic condensation is a suitable strategy to isolate M^I (M = Cu, Ag, Au) complexes.[18−20] These complexes were synthesized using $H[AuCl_4]$ as the starting material, and they exhibit different nuclearities. All of them are ionic and contain Cl ions within the structure acting as ligands or counterions, and, therefore, they have an influence on the global structure of these complexes.

With these precedents in mind, we decided to apply an electrochemical methodology to the synthesis of gold complexes using a family of phosphinothiosemicarbazone ligands. The absence of chloride anions in the electrochemical cell guarantees the isolation of anion-free gold compounds. For our purposes, we chose phosphinothiosemicarbazone ligands substituted by aliphatic (methyl and ethyl) and aromatic (phenyl, methoxyphenyl, and nitrophenyl) groups.

Herein we report the first gold(I) complexes assembled in an efficient manner under mild conditions in an electrochemical cell.

The [NSP] tridentate ligands HL^n [2-[2-(diphenylphosphino)benzylidene]-*N*-R-thiosemicarbazone] (Scheme 1) were synthesized by condensation of 2-(diphenylphosphino)benzaldehyde and the corresponding thiosemicarbazide, and the isolated products were fully characterized.[21]

Scheme 1. Ligands HL^n (n = 1, R = Me; n = 2, R = Et; n = 3, R = Ph; n = 4, R = PhOMe; n = 5, R = $PhNO_2$)



The electrochemical oxidation[22] of a gold plate was performed in a beaker containing a suspension of the ligand HL^n (0.1 g) and tetraethylammonium perchlorate (1 mg) in acetonitrile. All electrochemical reactions were carried out following the same procedure, which can be exemplified by the synthesis of the complex derived from [2-(2-(diphenylphosphino)benzylidene]-*N*-methoxyphenylthiosemicarbazone], HL^4. The electrolysis was performed at 5 mA and 13.5 V for 68 min with magnetic stirring under an argon atmosphere at room temperature (see Figure 1: t = 0 min corresponds to the beginning of the reaction time; t = 30 min is the halfway point; t = 68 min is the end of the reaction). The reaction afforded a clear yellow solution (see Figure 1), from which a yellow solid precipitated upon partial concentration. It should be noted that during the experiment the electrical parameters remained stable (5 mA and 13.5 V) and the formation of undesired gold oxides was not observed.[21] In addition, hydrogen gas evolved from the platinum cathode throughout the whole electrochemical process. The electrochemical efficiency of the process was 0.95, which is compatible with a mechanism involving the transfer of one electron and therefore the formation of Au^I ions in solution.

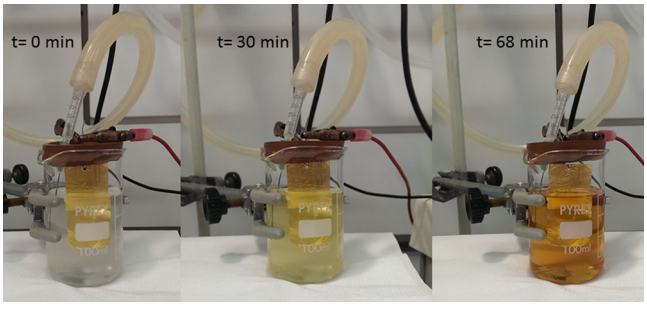


Figure 1. Evolution of the electrochemical synthesis of the complex **2**·$2CH_3CN$ from a colorless suspension of the ligand (t = 0 min) to a clear yellow solution of the complex (t = 68 min).

The electrospray ionization mass spectrometry spectrum and analytical data for the isolated solids are consistent with the formation of the neutral dimeric species $[Au^I_2(L^n)_2]\cdot x CH_3CN$ (x = 0−2),[21] which arises from deprotonation of the ligands HL^n in the electrochemical cell. This fact was confirmed by ^1H NMR spectroscopy by the absence of the characteristic NH signal of the thiosemicarbazone chain, at around 11.86 ppm (Figures S15 and S18),[21] and the appearance of a signal at 34 ppm in the ^{31}P NMR spectrum, which is indicative of the coordination of Au^I to P^{III} (Figures S20−S24). Slow evaporation of the mother liquors afforded yellow crystals for the methyl and methoxyphenyl substituents, from which the molecular structures of the compounds were determined by X-ray crystallography. The structures revealed the formation of neutral dimeric box compounds of the formulas $[Au^I_2(L^1)_2]$ (**1**; Figure 2)[23] and $[Au^I_2(L^4)_2]\cdot 2CH_3CN$ (**2**·$2CH_3CN$, Figure 2).[24]

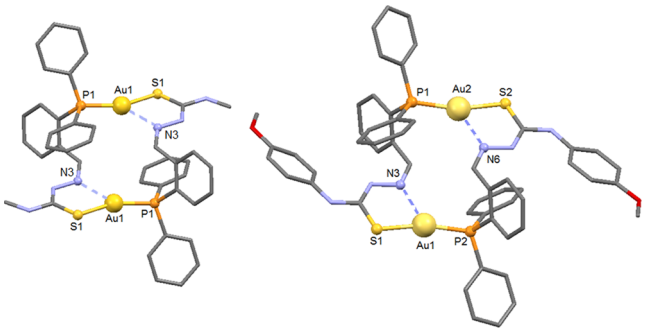


Figure 2. Ball-and-stick representation of **1** and **2**·$2CH_3CN$ obtained by the electrochemical synthesis. Solvated acetonitrile molecules and H atoms are not depicted for clarity.

As can be seen in their X-ray structures, each ligand strand in **1** and **2** uses the thioamide S atom to bind one Au^I center, while the remaining P atom is coordinated to the second Au ion, thus generating a box-type structure. The Au^I ions have distorted linear [PS] kernels. A weak interaction with the imine N atoms (N3 and N6) cannot be ruled out (2.52 Å in **1** and 2.65 Å in **2**). The intramolecular distances between the Au centers (5.5 Å in **1** and 5.8 Å in **2**) precludes any aurophilic interaction. The two ligand threads remain antiparallel in order to avoid unfavorable steric interactions, and this leads to a box-type or mesocate/box structure.

With the exposed results, it is clear that the electrochemical synthesis affords neutral gold compounds with nature different from that of the ionic compounds prepared by traditional chemical methods,[18−20] which display variable stoichiometries and structures, but all of them involve halide ions as ligands or counterions. In addition, isolation of the whole series of five gold(I) compounds demonstrates that the electrochemical synthesis is a reproducible and viable alternative for the isolation of gold(I) compounds.

In summary, an electrochemical procedure has been successfully applied to the efficient isolation of neutral gold(I) compounds for the first time. The absence of counterions, bases,

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or coligands guarantees the assembly of gold complexes whose nature and architectures must differ from those obtained by the traditional chemical synthesis. The main advantages of the electrochemical method to achieve neutral gold complexes in the presence of gold metal as the only consumable material are that (i) it is simple, (ii) it is an inexpensive technique, and (iii) it uses very mild conditions because the reaction takes place at room temperature and in the absence of metal salts, basic reagents, or external catalysts. We are convinced that this achievement will make available to the scientific community a wider variety of gold compounds that are in demand for biomedical or catalytic applications.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.6b01362.

Synthesis and experimental data for ligands and complexes, characterization data and figures, ORTEP diagrams, selected bond distances and angles for the gold complexes, and characterization figures (PDF)

X-ray crystallographic data in CIF format (CIF)

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Notes

The authors declare no competing financial interest.

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(21) See the Supporting Information for detailed characterization data for a new set of complexes obtained by the electrochemical synthesis.

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(23) Crystal data for $[Au_2(L^1)_2]$ (**1**): $C_{42}H_{38}Au_2N_6P_2S_2$, M_w = 1146.78, crystal dimens 0.28 × 0.17 × 0.14 mm^3, monoclinic, $P21/n$, a = 12.8900(7) Å, b = 8.5766(5) Å, c = 18.6133(11) Å, α = 0°, β = 102.501(4)°, γ = 0°, V = 2009.0(2) Å^3, Z = 2, μ = 7.52 mm^{-1}, $F(000)$ = 1104. Radiation λ(Mo Kα) = 0.7107 Å, T = 100(0) K, reflections collected/unique 43623/5869 (R_{int} = 0.050), R1 (all data) = 0.0321, wR2 (all data) = 0.0455, GOF = 1.032, max/min residual density 0.763/−1.167 e/Å^3. CCDC 1476000.

(24) Crystal data for $[Au_2(L^4)_2]\cdot 2CH_3CN$ (**2**·2CH_3CN): $C_{54}H_{46}Au_2N_6O_2P_2S_2\cdot 2C_2H_3N$, M_w = 1413.10, crystal dimens 0.24 × 0.06 × 0.03 mm^3, monoclinic, $P2_1$, a = 10.798(1) Å, b = 22.303(2) Å, c = 11.3535(9) Å, α = 0°, β = 91.038(4)°, γ = 0°, V = 2733(9) Å^3, Z = 2, μ = 5.55 mm^{-1}, $F(000)$ = 1384. Radiation λ(Mo Kα) = 0.7107 Å, T = 100(0) K, reflections collected/unique 44306/12868 (R_{int} = 0.054), R1 (all data) = 0.0781, wR2 (all data) = 0.1442, GOF = 1.048, max/min residual density 3.513/−4.061 e/Å^3. CCDC 1447369.

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