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Enantioselective epoxidation of olefins with molecular oxygen catalyzed by gold(III): A dual pathway for oxygen transfer

Avelino Corma [a,*], Irene Domínguez [a], Antonio Doménech [b], Vicente Fornés [a], Carlos J. Gómez-García [c], Tania Ródenas [a], María J. Sabater [a,*]

[a] Instituto de Tecnología Química UPV-CSIC, Avenida Los Naranjos s/n, 46022 Valencia, Spain
[b] Departamento de Química Analítica, Universidad de Valencia, Dr. Moliner 50, 46100 Burjasot, Valencia, Spain
[c] Instituto de Ciencia Molecular (ICMol), Departamento Quimica Inorganica, Universidad de Valencia, C/ Dr. Moliner 50, 46100 Burjasot, Valencia, Spain

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ABSTRACT

A chiral gold(III) complex has been prepared that performs the epoxidation of olefins in the presence of O_2, PhIO, or bleach. Catalytic experiments with ^{18}O show that O_2 is activated on the catalyst and can be directly incorporated into the epoxide through a non-radical mechanism that probably involves formation of gold, oxo, or peroxo species. In addition to this, there is a parallel radical mechanism operating that yields α, β-unsaturated ketones and alcohols as subproducts.

Electrochemical and UV–Vis experiments confirmed the occurrence of a Au(III)/Au(I) redox cycle during the catalytic epoxidation in a mechanism sustained by molecular oxygen.

1. Introduction

The activation of dioxygen by metal complexes is a long sought goal in the field of catalysis [1–3], and there are numerous examples in the literature on catalytic aerobic oxidations with different metals [4–6].

Recently, the number of applications of gold in catalysis has widely expanded [7–13], and in the case of oxidation reactions, heterogeneous gold catalysts have been successful for epoxidation of olefins with "in situ" generated H_2O_2 [14], and for oxidation of alcohols and aldehydes with air [15]. In homogeneous phase, the pioneering work of Natile et al. showed that Au(III) salts were able to act as oxidation reactants and catalysts [16]. In this context, we present here the preparation of a chiral Au(III) complex that is catalytically active and stereoselective for the epoxidation of olefins using classical stoichiometric oxidants such as NaOCl and PhIO, as well as molecular oxygen. By means of isotopic studies it has been found that dioxygen is able to react with olefins through two parallel oxidation mechanisms: A major and selective mechanism that leads to the formation of epoxide, and a minor radical pathway that mainly leads to unsaturated ketones and alcohols.

2. Experimental

2.1. Catalyst preparation (**1Au**)

A solution of 2,6-bis[(4R)-phenyl-2-oxazolin-2-yl]pyridine (1.104 g, 2.98 mmol) in acetonitrile (6 cm^3) was added to an aqueous solution (35 cm^3) of $NaAuCl_4 \times 2H_2O$ (1.18 g, 2.98 mmol) dropwise. The resulting suspension was stirred at room temperature for 24 h and then it was filtered off. The solid was solved in dichloromethane, and the resulting organic solution was washed with water, dried with magnesium sulfate, and concentrated to dryness to give complex **1Au** as a yellow-orange solid. The solid was precipitated from an acetonitrile–water (1:6) solution, recovered by filtration, and dried (1.74 g, 88%), showing the following elemental composition: C, 41.8%; H, 3.12%; N, 6.23%, Cl, 11.45%; $C_{23}H_{20}N_3O_3AuCl_2$ requires C, 42.2%; H, 3.05%; N, 6.42%, Cl, 10.85%; ^{13}C NMR (δ, ppm): 163.8, 163.5, 162.9, 147.7, 147.5, 146.9, 142.5, 139.5, 134.6, 129.6, 129.3, 129.0, 128.0, 127.8, 127.1, 75.2, 69.6, 66.0 and 53.1 ppm; ^1H NMR (δ, ppm): 8.60 (s, 2H), 8.43–8.10 (m, 3H), 7.63–7.28 (m, 8H), 5.5 (dd, 1H; $J = 17$ and 4 Hz), 4.90 (dd, 1H; 19 and 4 Hz), 4.80 (s, 1H), 4.69 (s, 2H), 4.3 (dd, 1H; $J = 17$ and 5 Hz), 3.55 ppm (s, 1H); IR ν_{max}/cm^{-1}: 3500 (br), 1735 (s), 1641 (s), 1578 (s), 1488 (m), 1439 (m), 1293 (s), 1234 (m), 738 (m), 679 (s) cm^{-1}; Raman ν_{max}/cm^{-1}: 1649 (br), 1602 (m), 1577 (m), 1453 (w), 1204 (w), 1029 (w), 1000 (s), 653 (w), 359 (vs), 338 (vs) cm^{-1}; UV–Vis: $\lambda_{max}(CH_2Cl_2)$/nm: 230, 285

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* Corresponding author. Fax: +34 96 3877809.
E-mail address: acorma@itq.upv.es (A. Corma).

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and 330 nm; FAB Mass Spectrometry (*m*/*z*): 620 (M^+–Cl^-), 602 (M^+–Cl^-–OH^-), 584, 388, 370 (M^+–Au–$2Cl^-$–OH^-).

2.2. Starting reagents and catalysts characterization techniques

Most compounds used in this study were commercially available and were of analytical grade: NaOCl solution (10–13% chlorine content), [(4R)-phenyl-2-oxazolin-2-yl]pyridine (pybox), and olefins were purchased by Aldrich. The O_2^{18} (95% O_2^{18}) was purchased by Cambridge Isotope Laboratories. Iodosylbenzene was prepared from iodosylbenzene diacetate following a reported method [17].

Solution NMR spectra were recorded with a Bruker Avance 300 instrument at 300.13 MHz (^{1}H) and 75.47 MHz (^{13}C). ^{1}H and ^{13}C NMR spectra of complex **1Au** were obtained in DMSO-d_6.

IR spectra of pure complexes were recorded within KBr pellets in a Nicolet 710 FT spectrophotometer. Room temperature transmission UV–Vis spectra of transparent dichloromethane solutions were recorded in a Shimadzu UV–Vis scanning spectrophotometer.

FT-Raman spectra were recorded with a Bio-Rad FT-Raman II spectrophotometer. The 1.064 μm line of a Nd:YAG laser was used for excitation along with a germanium detector cooled at liquid nitrogen temperature. The Raman spectra of powdered samples were examined in the 180° scattering configuration using high-quality quartz tubes as cells. The laser power at the samples was $\sim$100 mW. The Raman spectra were corrected for instrumental response using a white light reference spectrum.

Combustion chemical analysis of the samples was carried out using a Fisons EA 1108-CHNS-O analyzer.

Linear potential scan voltammograms (LSVs) were measured with a BAS CV50W equipment using potential scan rates between 10 and 1000 mV/s. A standard three-electrode arrangement was used with a platinum auxiliary electrode and an AgCl (3M NaCl)/Ag reference electrode separated from the bulk solution by a salt bridge, in a thermostated (298 K) cell. Gold (BAS MF 2010, geometrical area 0.018 cm^2) and glassy carbon (BAS MF 2012, geometrical area 0.071 cm^2), working electrodes were used. All electrochemical measurements were performed in well-deaerated solutions under argon atmosphere. Experiments were conducted in acetonitrile using Bu_4NPF_6 (Fluka) in 0.1 M concentration as supporting electrolyte.

2.3. Catalytic experiments

Reactions were carried out at 0 °C in a biphasic system that comprised 2 ml CH_2Cl_2 and 2 ml of an aqueous buffered solution of NaOCl as oxidant (pH 11). The reaction solutions contained 0.30 mmol of olefin, 30% mmol of *n*-undecane as an internal standard, and 0.5% of chiral Au(III) catalyst (molar ratio olefin/catalyst: 20) under oxygen flow (2.4 ml/min). The reactions were monitored by gas chromatography.

Reactions in a monophasic system with PhIO as an oxidant were accomplished as follows: 0.5 mmol of alkene, 30% mmol of undecane (internal standard), 0.5 mmol of PhIO, and 0.5% molar of Au(III) catalyst were added to 2 ml of a dichloromethane solution under oxygen flow (2.4 ml/min). Samples were withdrawn periodically and monitored by gas chromatography and chiral HPLC.

2.4. Experimental procedures used for the O^{18}-analyses

The experimental procedures followed to carry out the O^{18} isotopic labeling experiments were the following:

(a) Reaction with NaOCl was carried out at 0 °C in a biphasic system comprised of 2 ml CH_2Cl_2 and 2 ml of an aqueous buffered solution of NaOCl as oxidant (pH 11). The reaction solutions contained 0.30 mmol of 1-phenylcyclohexene, 30% mmol of *n*-undecane as internal standard and 0.5% of chiral Au(III) catalyst (molar ratio olefin/catalyst: 20 under O_2^{18} flow O_2^{18}, 95%; 2.4 ml/min).

(b) Reaction in a monophasic system with PhIO as oxidant was accomplished as follows: 0.5 mmol of 1-phenylcyclohexene, 30% mmol of undecane (internal standard), 0.5 mmol of PhIO, and 0.5% molar of Au(III) catalyst were added to 2 ml of a dichloromethane solution under O_2^{18} flow (O_2^{18} 95%; 2.4 ml/min).

3. Results and discussion

3.1. Synthesis and characterization

Attempts to prepare a chiral gold complex led us to incorporate an aqueous solution of $NaAuCl_4$ to an acetonitrile solution containing stoichiometric amounts of [(4R)-phenyl-2-oxazolin-2-yl]pyridine (pybox) (see the preparation details in Section 2). A yellow-orange solid was formed which was recovered by filtration, washed exhaustively and analyzed.

After recording ^{1}H and ^{13}C NMR spectra of the complex, it could be observed (Fig. 1) that the interaction of this gold(III) salt with the organic molecule did not lead to the expected complex, but led to a ring-opened complex derivative (**1Au**) as depicted in Scheme 1.

Indeed, the NMR spectra of **1Au** (Fig. 1) confirmed the loss of C_2 symmetry in the original ligand due to a clear ring opening of one of the oxazoline rings.

The ^{13}C NMR spectrum of **1Au** has 19 different signals and just four of them were clearly located in the aliphatic region, with chemical shifts at $\delta^{13}C = 53.1$, 66.0, 69.6, and 75.2 ppm, respectively. Similarly, the ^{1}H NMR spectrum showed five significant signals in the aliphatic region with chemical shifts at $\delta^1H = 4.3$, 4.69, 4.80, 4.90, and 5.5 ppm (see Fig. 1 and characterization data in the experimental section). On the other hand, two of the proton signals in the ^{1}H NMR spectrum (recorded as one-proton singlets) are broad and they were assigned to an OH ($\delta = 3.55$ ppm) with a slow

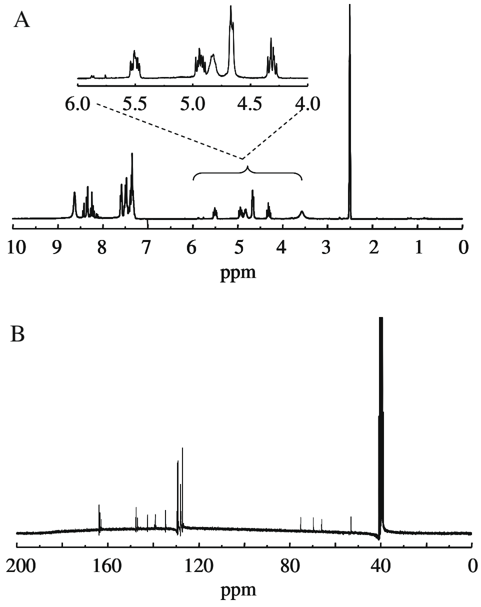
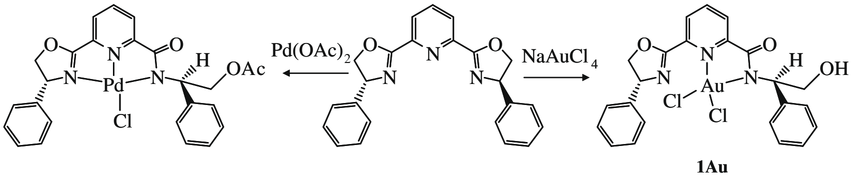


Fig. 1. (A) ^{1}H NMR spectrum of **1Au** recorded in DMSO-d_6; (B) ^{13}C NMR spectrum of **1Au** recorded in DMSO-d_6.



Scheme 1. Schematic representation of the ligand transformation upon reaction with Pd(OAc)$_2$ [17] and NaAuCl$_4$ and tentative structure of **1Au**.

proton exchange with the solvent and a methyne proton CH (δ = 4.80 ppm), which should be adjacent to N.

The formation of a ring-opened complex derivative has a related precedent in the literature, since it has been reported that the instability of a bound pybox ligand toward Pd(OAc)$_2$ produces a ring-opening reaction of the oxazoline ring leading to the formation of a palladium amido complex [18a]. The unexpected formation of this complex from pybox-type ligands reveals the susceptibility of these molecules to react with certain Lewis acids under specific experimental conditions.

We failed to produce **1Au** crystals for their structure to be determined by XRD, and characterization was performed by means of IR, UV–Vis spectroscopies, electrochemistry, and chemical analysis.

Examination of pure **1Au** and the original pybox ligand by UV–Vis spectroscopy showed that the most outstanding difference between both spectra was the dramatic decrease in the 285 nm absorption in the complex as compared with the ligand, coupled with the appearance of the weak absorbance at 330 nm that was exclusive of **1Au** (see Fig. 2).

The IR spectrum of **1Au** given in Fig. 3 shows several intense bands, which can be assigned as follows: (a) a band at 1735 cm^{-1}, which can be assigned to a C=O group, (b) a typical imine vibration band at 1642 cm^{-1}, which is also present in the original ligand and supports the fact that a half of the oxazoline rings have been opened; (c) the stretching vibration typical of C=C bonds at 1578 cm^{-1} and the (d) stretching vibration band at 3500 cm^{-1} typical of OH bonds.

A closer inspection of the IR spectrum also revealed the complete absence of the stretching vibration band typical of N–H bonds at ~3200 cm^{-1}, hence suggesting that nitrogen might be in the form of a tertiary amido group as it was reported for palladium [18] (see Scheme 1). Taking into account these spectroscopic results and the structure of a tertiary amido palladium complex presented in the literature [18a], the structure of **1Au** given in Scheme 1 can be tentatively proposed.

After this and due to the propensity of gold(III) to undergo a chemical reduction, the electrochemical response of **1Au** was studied in acetonitrile solution by linear potential scan voltammetry (LSV), and the electrochemical behavior was compared with that of a reference Au(III) inorganic salt (NaAuCl$_4$) (Fig. 4).

The electrochemistry of both complexes was very similar as both voltammograms showed two well-defined cathodic peaks (I and II), the height of the first peak being approximately twofold of the second one (Fig. 4). These results can be interpreted by considering a two-electron reduction from Au(III) to Au(I) at approximately 0 V vs. AgCl/Ag, the Au(I) being subsequently reduced to Au(0) at more negative potentials (approximately −0.75 V vs. AgCl/Ag in the case of **1Au** and −1.5 V in the case of NaAuCl$_4$ vs. AgCl/Ag). Hence, the 3+ oxidation state of gold in the complex **1Au** was confirmed by electrochemistry.

3.2. Catalytic studies

After characterization, the catalytic activity of **1Au** was explored for the oxidation of various prochiral olefins using NaOCl as oxidant. The complex was active for the epoxidation of 1-phenylcyclohexene, albeit the reaction was rather slow and required more than 64 h for achieving high conversions (see entry 1, Table 1). Under these experimental conditions, the selectivity toward the epoxide was moderate and so was the enantioselectivity, with an enantiomeric excess of 30% (see entry 1 in Table 1).

When oxidation of 1-phenylcyclohexene took place in a monophasic organic system with catalyst **1Au** and PhIO as stoichiometric oxidant under argon atmosphere, the oxidation reaction did not reach completion (51% after 16 h) and selectivity to epoxide was 63%. However, when O$_2$ was bubbled into the reaction mixture (flow O$_2$: 2.4 ml/min) the conversion of the olefin was practically completed in 6 h, whereas the selectivity toward the epoxide was not significantly lowered with respect to that obtained under an inert atmosphere. Indeed, when both experiments were run in parallel, we found that after 4 h reaction time in the presence of PhIO and in the absence of molecular oxygen, only 7% conversion was achieved with the epoxide selectivity being 66% (see entry 2 in Table 1). In striking contrast, 64% of the olefin was converted with PhIO in the presence of oxygen (flow O$_2$: 2.4 ml/min) after 4 h, and selectivity to the epoxide was 63% (see entry 3 in

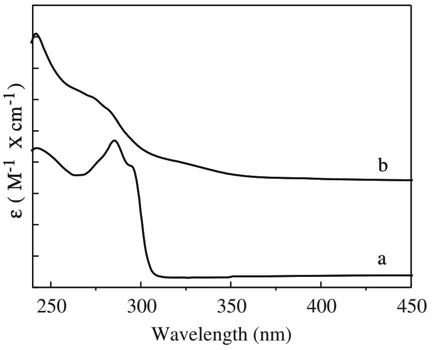


Fig. 2. UV–Vis recorded spectra of (a) bis(oxazolinyl)pyridine ligand (pybox) and (b) complex **1Au** recorded in two different 3.3 × 10^{-6} M dichloromethane solutions.

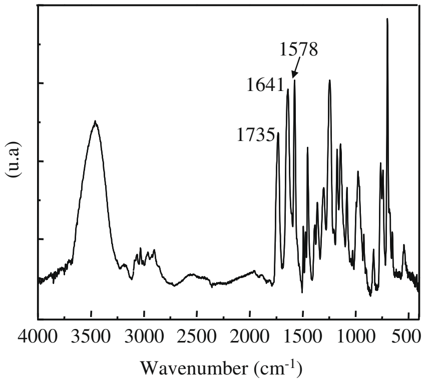


Fig. 3. Infrared spectrum of **1Au** in the range of 4000–400 cm^{-1} obtained in a KBr pellet.

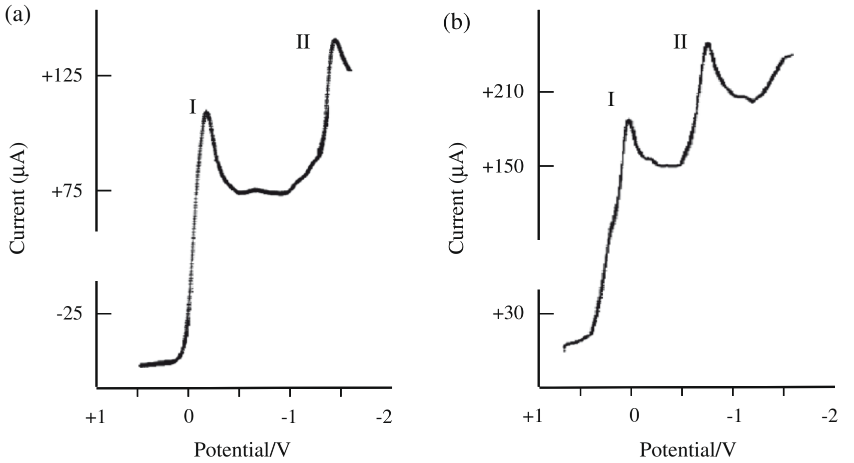


Fig. 4. Linear potential scan voltammograms (LSVs) of (a) $NaAuCl_4$ and (b) gold (III) complex **1Au** in acetonitrile solutions under an argon atmosphere.

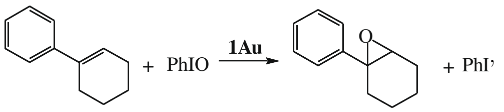
Table 1
Asymmetric epoxidation of alkenes catalyzed by **1Au**.

Alkene	Oxidant	Time (h)	Conversión (%)[a]	Product distribution (%)[b]			ee (%)[c]	TON[d]
				Epoxide	Ketone	Others		
1-Phenylcyclohexene	NaOCl[e]	64	96	56	20	24	30	14
1-Phenylcyclohexene	PhIO[f]	4	7	66	5	–	23	2
1-Phenylcyclohexene	PhIO[g]	4	64	63	27		23	15
1-Phenylcyclohexene	PhIO[h]	6	58	62	25	3	10	12
1-Phenylcyclohexene	NaOCl[i]	6	98	53	24	23	32	5
1-Methylcyclohexene	NaOCl[i]	6	80	8	–	42	8	16
Indene	NaOCl[i]	8	35	40	–	60	45[j]	7
1,2-Dihydronaphtalene	NaOCl[i]	6	70	62	7	1	13[k]	14
α-Methylstyrene	NaOCl[i]	6	30	42	51	7	5[l]	6

[a] Determined by capillary GC and calculated as mmol of substrate transformed.
[b] Determined by capillary GC.
[c] Determined by chiral HPLC (Chiraldex OD-H column) with hexane:ethanol 99:1 mixture of solvents and flow: 0.5 ml/min.
[d] Calculated as mmol of substrate converted/mmol of catalyst.
[e] Reaction was performed at 0 °C by using 0.5% mmol of complex **1Au**, 0.30 mmol of alkene, 30% undecane, and aqueous buffered solution of NaOCl (pH 11).
[f] Reaction was performed at r.t. by using 0.5% mmol of **1Au**, 0.5 mmol of alkene, 30% undecane, and 0.5 mmol of PhIO as oxidant under an inert atmosphere.
[g] Reaction was performed at r.t. by using 0.5% mmol of **1Au**, 0.5 mmol of alkene, 30% undecane, 0.5 mmol of PhIO as oxidant and an oxygen flow of 2.4 ml/min.
[h] Reaction was performed at r.t. by using 0.5% mmol of **1Au**, 0.5 mmol of alkene, 30% undecane, 0.14 mmol of PhIO and an oxygen flow of 2.4 ml/min.
[i] Reaction was performed at 0 °C by using 0.5 mmol of **1Au**, 0.5 mmol of alkene, 30% undecane, aqueous buffered solution of NaOCl (pH 11) and an oxygen flow of 2.4 ml/min.
[j] Determined by chiral HPLC (Chiraldex OB-H column), hexane:ethanol 99:1, flow: 0.5 ml/min.
[k] Determined by chiral HPLC (Chiraldex OB-H column), hexane:ethanol 95:5, flow: 0.5 ml/min.
[l] Determined by chiral GC analysis (Beta-Dex, 30 m).

Table 1). Furthermore, when the epoxidation of 1-phenylcyclohexene was performed with substoichiometric amounts of PhIO (25% mol with respect to the starting alkene), but in the presence of O_2, 58% of the olefin was converted (see entry 4 in Table 1).

To explain the positive role of O_2 in the rate of reaction, one may think that oxygen can be trapped by free radicals, since if the latter were formed during the oxidation process, it will enhance the reaction rate and alkene conversion. However, the fact that dioxygen does not affect the epoxide selectivity values, as usually occurs in typical chain oxidation processes, led us to think of a more selective epoxidation reaction with oxygen catalyzed by gold catalysts. Thus, in order to explain the participation of oxygen in the mechanism we considered a second possibility, in which the oxygen could be involved in the reoxidation of the iodobenzene formed upon oxidation of the olefin with iodosylbenzene (see Eqs. (1) and (2)).



(1)

$$PhI + O_2 \overset{1Au}{\rightarrow} PhIO. \quad (2)$$

Such a process would regenerate the oxidant PhIO, and would explain the practically total oxidation of the olefin with substoichiometric amounts of PhIO. To check this hypothesis, we have tried to reoxidize iodobenzene with O_2 in the presence of **1Au**, but no PhIO was detected in the products. Consequently, the above hypothesis cannot explain the positive role of O_2 in the epoxidation reaction.

At this point and after checking that free-autooxidation with O_2 does not occur in the absence of the catalyst, we considered that oxygen could be activated on the catalyst and oxidize the olefin to give the epoxide. To test this hypothesis, the reaction of iodosylbenzene with 1-phenycyclohexene was carried out in the presence of $^{18}O_2$ (98% enrichment) using complex **1Au** as catalyst, under the same experimental conditions as described above. As expected, the epoxide was obtained once more as the major product at 40% conversion, showing 58% incorporation of ^{18}O as epoxide. This result confirms that in the presence of O_2, the oxygen in the epoxide comes from both iodosylbenzene and dioxygen.

Similarly, we have observed that in the presence of **1Au** and bleach a clear acceleration of the epoxidation, albeit less pronounced than with PhIO, occurs when $^{18}O_2$ was bubbled into the reaction mixture. Again the epoxide was obtained as a major product at 10% conversion, showing 33% incorporation of ^{18}O. Besides the epoxide, α, β-unsaturated ketones, alcohols, and traces of hydroperoxides were also detected during the reaction, and the formation of these products can probably occur through a radical mechanism. To check this, the oxidation of 1-phenylcyclohexene with iodosylbenzene and O_2 was carried out in the presence of catalyst **1Au** and the radical scavenger 2,6-di-tert-butyl-*p*-cresol. The presence of this radical trap in the reaction media strongly inhibited the formation of the above products, while the yield of epoxide was practically not affected. Moreover, when the epoxidation of 1-phenylcyclohexene was performed in CCl_4 as solvent, a complex mixture of oxidized and chlorinated products was observed in detriment of epoxide yield.

In summary, these experimental observations definitively prove the existence of two pathways for the oxygen transfer with chiral Au(III) catalyst **1Au**: (i) a radical allylic oxidation pathway (mainly responsible for the formation of α, β-unsaturated ketones and alcohols, etc.) and (ii) a predominant, more selective, and cleaner process where the metal would mediate in a concerted or nearly concerted transfer of oxygen from the oxidant to the olefin. The isotopic experiments clearly evidenced that a fraction of the oxygen in the epoxide is incorporated from classical stoichiometric oxidant such as PhIO or bleach, whereas the rest of the epoxide is formed from molecular oxygen activated through a gold metal complex during the course of the epoxidation. In close connection to this, it is necessary to remark that control experiments have shown that the epoxidation of 1-phenylcyclohexene with 1Au as a catalyst and molecular oxygen alone as an oxidant does not occur under similar reaction conditions.

Other alkenes were also epoxidized using **1Au** as catalyst, and the results obtained are collected in Table 1. As can be deduced from the Table, there are significant differences in the stereoselectivity of the final epoxide depending on the oxidant used in the experiments (NaOCl or PhIO). In principle, this fact has been already noticed in the literature, where a different range of enantiomeric excesses can be obtained by using different oxygen atom donors in the experiments [18b]. A priori, this fact may suggest that the nature of the active metal intermediate(s) formed in each case used should be different depending on the oxidant itself. In addition to this, it is necessary to take into account that the epoxidation with NaOCl is carried out in a aqueous-organic biphasic system, whereas the epoxidation with PhIO is carried out in the organic solvent such as dichloromethane.

3.3. The role of O_2 and state of gold during the oxidation process

To elucidate the role of O_2 and the oxidation state of gold during the epoxidation process, two potential catalytic pathways for gold were considered: (a) a redox cycle involving different oxidation states of gold (Au(III)/Au(I)) and (b) Au(III) acting simply as a Lewis acid site. To analyze the first possibility, the voltammetric responses of **1Au** were obtained in acetonitrile solutions either in the absence or in the presence of oxygen (see Fig. 5).

Fig. 5 shows the CV response of **1Au** in (a) O_2-free and (b) O_2-saturated 0.1M Bu_4NPF_6 CH_3CN solutions.

As in the case of previous electrochemical experiments (see characterization of **1Au** by linear potential scan voltammetry (LSV)), the voltammetric response of **1Au** under nitrogen showed a prominent reduction process consisting of two overlapping peaks at −0.15 V (peak I) vs. AgCl/Ag, and a weaker wave at −1.2 V (peak II) (see Fig. 5a). Interestingly, when a similar electrochemical experiment was performed in O_2-saturated solution, the CV response of **1Au** showed the previous two overlapping peaks (I) followed by a new peak at ca. −0.9 V (peak III), while the peak at −1.2 V (peak II) disappeared (see Fig. 5b).

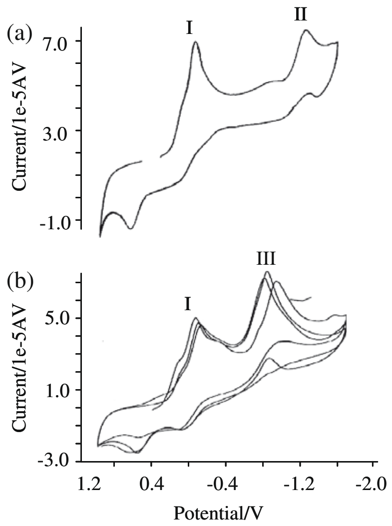


Fig. 5. Cyclic voltammograms of 1.77 mM solution **1Au** in 0.1 M Bu_4NPF_6 CH_3CN solutions: (a) O_2-free and (b) O_2-saturated. Potential scan rate 200 mV/s.

It is well known that molecular oxygen is reduced in aprotic solvents in a reversible one-electron transfer, yielding the peroxide radical, O_2^{-}, at potentials ca. −0.9 V [19], so this peak III was unequivocally assigned to this oxygen reduction process.

As in the case of previous LSVs techniques, the peak I at −0.15 V was assigned to a consecutive one-electron transfer process from Au(III) to afford an intermediate Au(I) complex. However, the disappearance of peak at −1.2 V in the presence of oxygen revealed that complex Au(I) does not undergo reduction to Au(0) as it occurred under an inert atmosphere, but it goes back to the original complex Au(III) (see Fig. 5b). Since upon repetitive cycling, the voltammetric profile remains essentially constant, it can be concluded that complex **1Au** was regenerated during the electrochemical process, hence confirming the occurrence of an Au(III)/Au(I) redox cycle in the presence of oxygen [20].

Besides the electrochemical experiments described above, an "*in situ*" spectroscopic experiment was carried out, searching for changes in the UV–Vis spectrum of the starting Au(III) complex **1Au** after adding the 1-phenylcyclohexene olefin and the oxidant, and looking for similarities with the spectral changes experienced by a related monovalent Au(I) complex under the same experimental conditions.

To do this, a dichloromethane solution of catalyst **1Au** was treated with 1-phenylcyclohexene at 0 °C under air, and spectral changes in the UV–Vis spectrum were not observed. However, the resulting solution turned intense orange upon addition of NaOCl and a new band at 460 nm developed (see inset in Fig. 6).

Attempts were made to isolate and identify this compound on the basis of its Raman spectrum. Thus, as can be seen in Fig. 6, the Raman spectrum of this species recorded at 0 °C shows very similar vibration bands to those of the starting complex **1Au** differing only in the presence of a new band at 262 cm^{-1}, which can be assigned to a gold–oxygen vibration [21]. Moreover, the electrochemical response of this oxygenated metal species (**1Au**–[**O**]) confirmed the trivalent state of gold [22].

Continuing with the above mechanistic experiments, the UV–Vis spectrum of a dichloromethane solution containing stoichiometric amounts of 2,6-bis[(4R)-phenyl-2-oxazolin-2-yl]pyridine and AuCl showed that the stepwise addition of the alkene, 1-phenylcyclohexene, and NaOCl led to the formation of the same compound **1Au**[**O**] with the characteristic spectral band at 460 nm. This experimental fact reveals that a common gold complex intermediate can be formed under oxidizing conditions, regardless of the

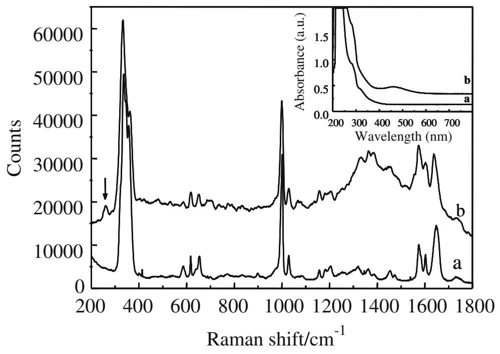


Fig. 6. Raman spectra of pure complex (a) **1Au** and (b) the isolated compound **1Au–O** obtained upon mixing **1Au** and excess NaOCl. The inset shows the absorbance spectra of **1Au** [10^{-4} M] in dichloromethane and (b) the resulting absorbance spectrum upon addition of bleach.

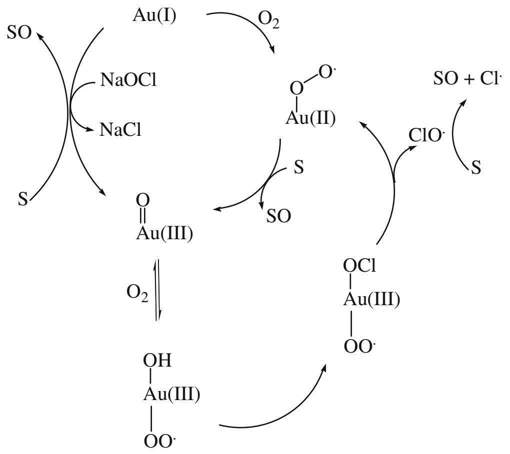


Fig. 7. Possible reaction pathways for the epoxidation of alkenes catalyzed by **1Au** in the presence of classical oxidant NaOCl and O_2.

original oxidation state of the gold species (Au^{1+} or Au^{3+}) used in the reaction, thus indicating that a cyclic transformation within the Au(I)/Au(III) manifold occurs during the epoxidation in the presence of O_2 [23].

Finally, in order to evaluate whether the oxygenated Au(III) complex **1AuO** was the active species, 1-phenylcyclohexene was added to a dichloromethane solution of **1Au**[**O**] at 0 °C under a nitrogen atmosphere. The dark orange color was slowly discharged and 1-phenylcyclohexene oxide together with the α, β-unsaturated ketone was detected by gas chromatography in an approximated ratio of 7:3, respectively. For comparison, 1-phenylcyclohexene was added to a dichloromethane solution of **1Au**[**O**] at 0 °C, but this time under oxygen flow (flow O_2: 2.4 ml/min), and epoxide, α, β-unsaturated ketone, and other minor oxygenated products were formed in a ratio of 4:3:3, respectively. Since the incorporation of oxygen into the reaction mixture does not reproduce the product distribution trends that were attained when the reaction was performed with bleach under aerobic conditions (see Table 1), we concluded that although this gold metal species **1Au**–[**O**] might be one of the possible active oxidants for the alkene epoxidations, this is not the only key intermediate involved in the reaction.

A priori, the simultaneous formation of products derived from allylic attack (alcohol and ketone) and epoxides is consistent with the results of catalytic oxidation of hydrocarbons with *t*-BuOOH and related decomposition reactions of metal alkylhydroperoxides formed by direct interaction of dioxygen with metals (vs. Ru(II),...) [24]. Taking into account that in our case, there is a redox cycle involving the transformation of monovalent Au(I) into Au(III) in the presence of oxygen, the formation of a gold peroxo species can be postulated as one of the possible intermediates involved in the reaction (Fig. 7).

This intermediate could account for the simultaneous formation of allylic oxidation products by means of hydrogen abstraction and epoxidation. In this case, epoxidation should occur through intermediates that imply a radical character at an alkene carbon, hence explaining why the products derived from this route can be scavenged with intermolecular trapping agents.

In close competition with this pathway, formation of an Au(III)oxo complex (Au(III)=O) may afford high yields of epoxides preferably in a concerted or stepwise mechanism in close analogy to other oxo metal complexes (Fig. 7) [25]. This intermediate has been tentatively proposed as reactive intermediate in oxidations of alkanes with gold (III) and H_2O_2 [23].

Coupled with this mechanism, it is possible that Au(III)=O may coordinate with oxygen as depicted in Fig. 7, giving rise to the formation of OH—Au(III)$O_2^{\cdot}$ species (Fig. 7) in close analogy to several oxovanadium complexes [26]. Formation of this metal intermediate may explain why overall the alkene conversion with NaOCl and PhIO is higher and the reaction faster in the presence of oxygen. Notice that a control reaction has shown that monovalent Au(I) catalyst (in the form of AuCl) activates molecular oxygen albeit very slowly (conversion was lower than 10% after 24 h) transforming 1-phenylcyclohexene into epoxide as main product together with typical allylic oxidation products.

Coupled with the above reaction pathway, it is likely that the catalyst in the presence of NaOCl could exchange OH^- with ClO^- (Fig. 7). The homolytic rupture of the Au(III)-OCl bond may give rise to the formation of chloroxyl radical $ClO^{\cdot}$ (a well-known epoxidizing and chlorinating agent) that could easily explain the formation of chlorinated products detected as minor products in some experiments [27] and the closing of the cycle when forming the Au(II) peroxidic intermediate (Fig. 7).

It is clear that the formation of these intermediates has not been detected and consequently this part of the mechanism is speculative. However, what has been experimentally supported is that the epoxide is the main reaction product and that this is not formed through a radical-chain process. Then, it is reasonable to assume that the Au-catalyzed oxidations do not seem to proceed only via a radical mechanism, but gold oxo (or peroxo species) could be presumably involved in parallel as oxidizing species in a more selective oxygen transfer process from an Au(III) intermediate. Cyclic voltammetry undoubtedly confirms that complex **1Au** is regenerated in the presence of oxygen from an intermediate Au(I) complex electrochemically formed during the experiment; hence confirming the occurrence of an Au(III)/Au(I) redox cycle in a mechanism sustained by molecular oxygen.

4. Conclusions

A chiral Au(III) complex based on a oxazoline-containing ligand was prepared in a very simple way from a commercially available chiral ligand. The complex was structurally characterized by different spectroscopic and analytical techniques, whereas electrochemical studies confirmed the prevalence of the +3 valence state of gold in the synthesized complex.

The Au(III) complex is a slow catalyst for the O_2-free oxidation of alkenes with classical oxidants such as PhIO and bleach. The rate of the reaction strongly increases when the oxidation was performed in the presence of oxygen. In this regard, isotopic $^{18}O_2$ labeling experiments have evidenced that the chiral Au(III) complex **1Au** catalyzes the asymmetric epoxidation reaction of prochiral olefins and ^{18}O is incorporated into the epoxide. Similarly, epoxidations carried out in the presence of a radical scavenger definitively prove the existence of a dual pathway for the oxygen transfer with chiral Au(III) catalyst: (A) a radical allylic oxidation pathway (responsible of the formation of α, β-unsaturated ketones an alcohols), and (B) a non-radical process where the metal would mediate in a concerted or a nearly concerted transfer of oxygen from the oxidant to the olefin to form the epoxide.

Electrochemical and UV–Vis experiments confirm that during epoxidation an Au(III)/Au(I) redox cycle occurs with the intervention of molecular oxygen.

This work provides a starting point in the design for aerobic enantioselective epoxidations of olefins without the need of a sacrificial reducing agent.

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