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Water-Soluble Gold(I) and Gold(III) Complexes with Sulfonated *N*-Heterocyclic Carbene Ligands: Synthesis, Characterization, and Application in the Catalytic Cycloisomerization of γ-Alkynoic Acids into Enol-Lactones

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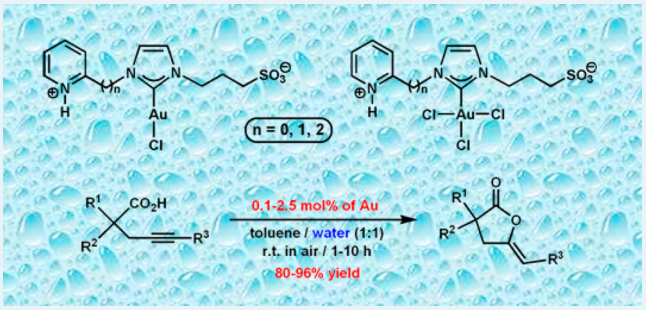
Supporting Information

ABSTRACT: Zwitterionic imidazolium salts bearing 3-sulfonatopropyl, and 2-pyridyl, 2-picolyl, and 2-pyridylethyl substituents have been synthesized and employed as precursors for the preparation of novel water-soluble Au(I)- and Au(III)-NHC complexes of general composition [AuCl(NHC)] and [$AuCl_3$(NHC)] (NHC = *N*-heterocyclic carbene), respectively. These complexes proved to be active, selective, and recyclable catalysts for the intramolecular cyclization of γ-alkynoic acids under biphasic toluene/water conditions, leading to the desired enol-lactones in high yields under mild conditions (r.t.). Remarkably, despite the well-known ability of gold complexes to promote the hydration of C≡C bonds, the competitive hydration process was not observed, even during the cycloisomerization reactions of 1,6-diynes.



KEYWORDS: *gold catalysis, gold complexes, N-heterocyclic carbenes, cycloisomerization, alkynoic acids, enol-lactones, heterocycles*

INTRODUCTION

Gold catalysis is playing an increasing role in organic chemistry for the facile construction of elaborate molecules not readily accessible by standard synthetic methods.[1] The success of this noble metal in catalysis hinges on the exceptional ability of gold compounds to activate π carbon−carbon bonds, specially alkynes and allenes, toward the addition of nucleophiles. Based on this conceptually simple reactivity, a manifold of new synthetically useful reactions have been developed during the past two decades.[2] Like for many other transition metals, the stability, reactivity, and selectivity of gold catalysts greatly depend on the nature of the ligands surrounding the active metal center.[3] In this context, although Au(I) species with tertiary phosphine ligands [$AuCl(PR_3)$] are still the most commonly used for catalytic purposes, gold complexes with *N*-heterocyclic carbenes (NHC) are gaining a great significance because of the higher stability provided by such ligands in comparison to the classical phosphorus-based ones. Some review articles covering the specific use of NHC-containing Au(I) and Au(III) complexes in homogeneous catalysis are already available.[4,5]

On the other hand, because of its obvious economic and environmental advantages, the use of water as a reaction medium for organic synthesis has become one of the major cornerstones in modern chemistry.[6] In the context of metal catalysis, it is also worthy of note that the use of water as solvent is usually associated to an easy catalyst/product separation, thus allowing in some cases the effective recycling of the catalytically active species.[7] The design of metal complexes containing auxiliary ligands with hydrophilic ionic substituents, or able to establish H-bond networks, is the most common approach to develop new catalytic systems active in water or in aqueous-biphasic media.[7] Although the field is clearly dominated by the *P*- and *N*-donor ligands, recent efforts are also being devoted to the preparation of related water-

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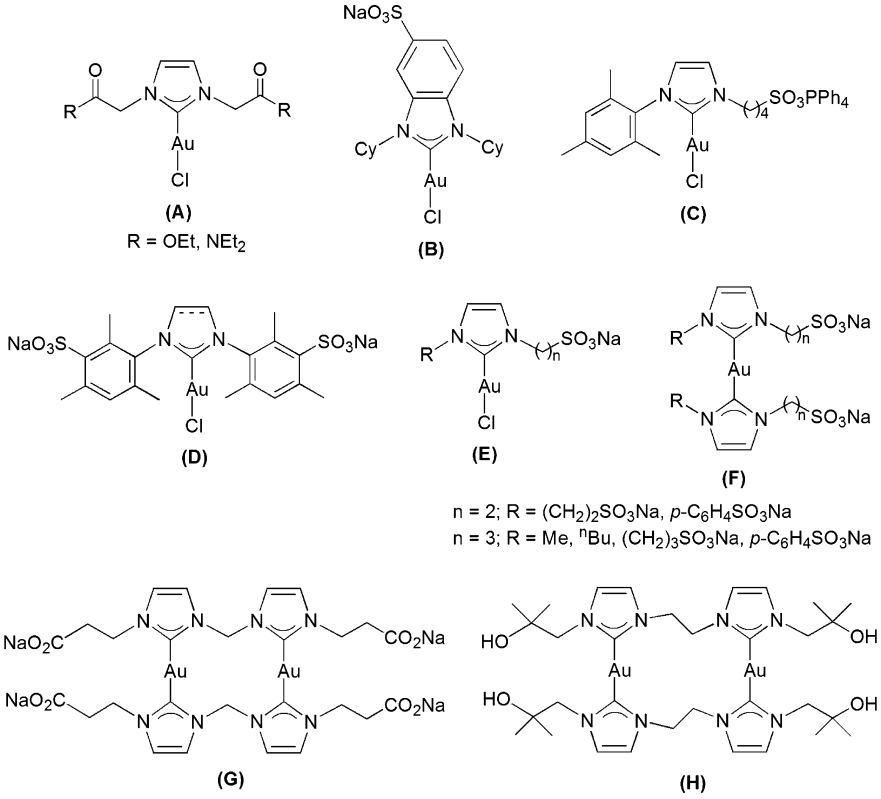


Figure 1. Structure of the Au(I) complexes **A**−**H** containing water-soluble NHC ligands.

soluble NHC derivatives.[8] However, up to date, the number of gold complexes bearing such ligands is still scarce (restricted to the mono- and dinuclear Au(I) species **A**−**H** shown in Figure 1),[9,10] and their catalytic potential remains almost unexplored. Thus, to the best of our knowledge, only the sulfonated derivatives **D**−**F** have been applied by Joó and co-workers as catalysts in the Markovnikov hydration of terminal alkynes in aqueous media.[9b,c,11]

As a significant contribution to this field, we recently communicated that the water-soluble NHC-Au(III) complex **5b** is able to promote a nonhydrative transformation of alkynes in aqueous media, that is, the catalytic cycloisomerization of γ-alkynoic acids (Figure 2).[12] It is worth mentioning that this catalytic transformation provides an easy and atom-economical entry to enol-lactones, an important class of functionalized heterocycles useful as synthetic intermediates. Although a large number of catalysts able to convert γ-alkynoic acids into enol-lactones are already known,[13,14] most of the reported procedures require water-free reaction conditions. In fact, only a few examples, involving Pd-,[15] Pt-,[16] and Cu-based systems,[17] active in aqueous environments have been described to date in the literature.[18]

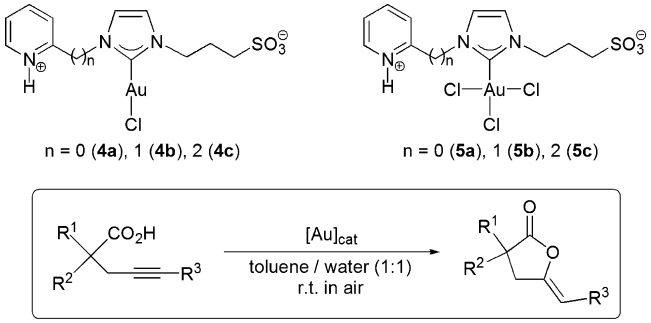


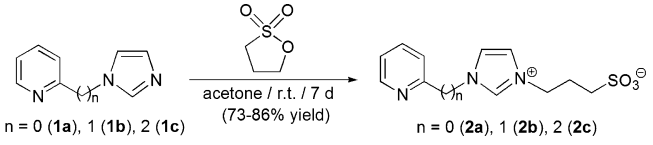
Figure 2. Structure of the gold-NHC complexes described in this work and the cycloisomerization reaction of γ-alkynoic acids.

Following our recent communication,[12] we report herein a comprehensive study involving an improved preparation of complex **5b**, as well as the synthesis and characterization of novel Au(I) and Au(III) derivatives **4a**−**c** and **5a,c**, respectively, containing related water-soluble NHC ligands (Figure 2). A comparative study of the ability of all these systems to promote the cycloisomerization of γ-alkynoic acids in a biphasic toluene/water medium is also presented. Despite the great tendency shown by gold complexes to promote the hydration of C≡C bonds,[9b,c,11,19] competing alkyne hydration processes were not observed using the zwitterionic derivatives **4**−**5a-c** as catalysts, even during the cycloisomerization reaction of 1,6-diyne substrates.

RESULTS AND DISCUSSION

Our investigations started with the preparation of the novel zwitterionic imidazolium salts **2a**−**c** bearing 3-sulfonatopropyl and 2-pyridyl (**2a**), 2-picolyl (**2b**) or 2-pyridylethyl (**2c**) substituents (Scheme 1). They were synthesized in high yields (73−86%) by reacting the known imidazoles **1a**−**c**[20] with 1,3-

Scheme 1. Synthesis of the Zwitterionic Imidazolium Salts 2a−c



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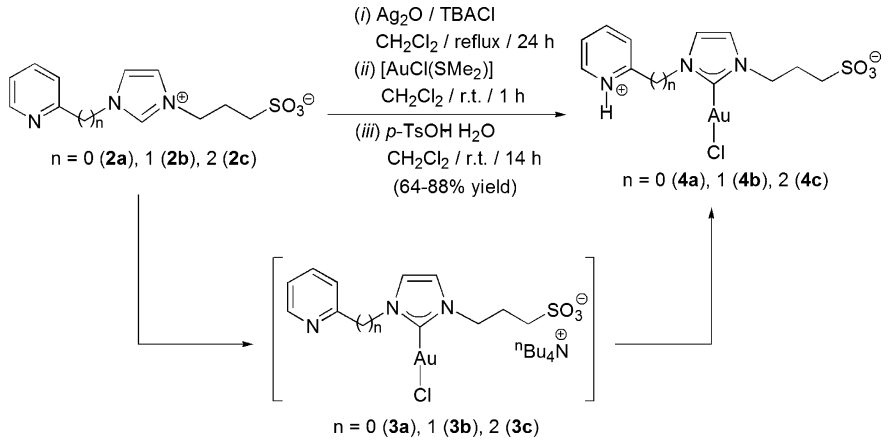
Scheme 2. Synthesis of the Water-Soluble NHC-Au(I) Complexes 4a−c



propane sultone in acetone, at room temperature, for one week.[21] Analytical and spectroscopic data (IR, and ^{1}H and $^{13}C\{^{1}H\}$ NMR) obtained for **2a−c** were in complete accord with the proposed formulations (details are given in the Experimental Section).

The corresponding Au(I)-NHC complexes **4a−c** were then synthesized through a silver-carbene transfer method (Scheme 2). Thus, sequential treatment of dichloromethane solutions of **2a−c** with Ag_2O, in the presence of tetrabutylammonium chloride (TBACl), and [$AuCl(SMe_2)$] resulted in the major formation of the ionic derivatives **3a−c**.[22] However, the difficulties encountered to separate these complexes from the small amounts of TBACl that remained unreacted, because of their similar solubility profiles, made the isolation of **3a−c** in pure form not viable. This fact led us to treat the resulting reaction mixtures with *p*-toluenesulfonic acid. In this way, protonation of the pyridyl unit of **3a−c** occurs, leading to the selective precipitation of the zwitterionic complexes **4a−c**, which were isolated as white air-stable solids in 64−88% yield. As expected, compounds **4a−c** are soluble in water (50 (**4a**), 12 (**4b**) and 10 (**4c**) g/L) at room temperature. However, we must note that their stability in this medium was found to be dependent on the connection between the pyridinium and the imidazol-2-ylidene rings. Thus, in the case of **4a**, where these units are directly connected to each other, a violet coloration of the solution (initially colorless) began to appear after 30 min. Such a color change, previously observed with the related NHC-Au(I) complexes **A** and **E** (Figure 1) in water, is associated with the formation of gold nanoparticles.[9b,e] In contrast, the aqueous solutions containing complexes **4b−c**, in which the pyridinium and imidazol-2-ylidene rings are linked through methylenic chains, remained unchanged for approximately 24 h (at longer times nanoparticles are also formed). This difference in stability is consistent with that observed by Joó and co-workers for compounds **E**, where the presence of aromatic rings directly attached to the sulfonated imidazol-2-ylidene unit led to faster decompositions in comparison with those compounds containing alkyl-substituents.[9b] The higher basic character of the alkyl- vs aryl-substituted NHC ligands seems therefore to confer a greater strength to the Au(I)-carbene bond.

Complexes **4a−c** were characterized by elemental analysis, IR, and ^{1}H and $^{13}C\{^{1}H\}$ NMR spectroscopy (details are given in the Experimental Section). In particular, the $^{13}C\{^{1}H\}$ NMR spectra confirmed the coordination of the imidazol-2-ylidene group to gold by the presence of a typical signal at δ 168.3−169.8 ppm for the carbenic C-2 carbon, similar to the chemical shifts (δ 166.0−172.9 ppm) seen in the related complexes **A−E** (Figure 1).[9a−c,e,f] On the other hand, although the NH hydrogen atom of the pyridinium unit was not observed by ^{1}H NMR spectroscopy, the selective protonation of the pyridyl group of intermediates **3a−c** upon treatment with *p*-TsOH·H_2O (Scheme 2) was fully evidenced by the appearance of a broad absorption band at 2450−2632 cm^{-1} in the IR spectra of compounds **4a−c**.[23] The 2-pyridylethyl-substituted complex **4c** was further characterized by means of a single-crystal X-ray diffraction analysis. X-ray quality crystals of **4c**·$2H_2O$ were obtained by slow diffusion of tetrahydrofuran into a saturated solution of **4c** in water. An ORTEP-type view, along with selected structural parameters, is shown in Figure 3. In the structure, the coordination around the gold center is almost

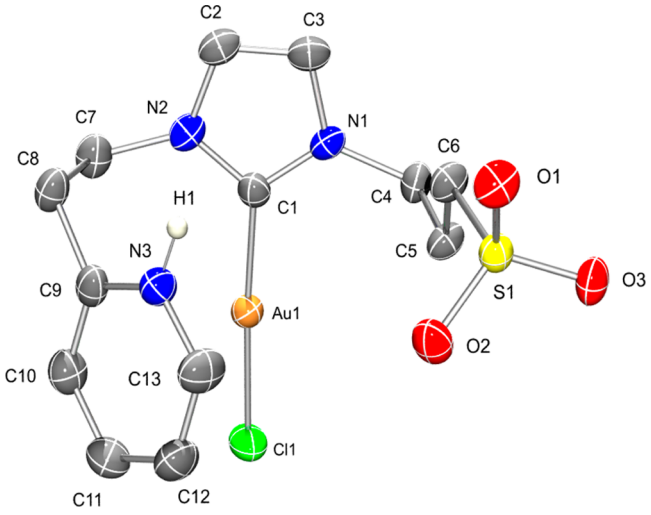


Figure 3. ORTEP-type view of the structure of the NHC-Au(I) complex **4c** showing the crystallographic labeling scheme. Thermal ellipsoids are drawn at 50% probability level. Hydrogen atoms, except that on N(3), have been omitted for clarity. Selected bond distances (Å) and angles (deg): Au(1)−C(1) = 1.988(5); Au(1)−Cl(1) = 2.2856(14); C(1)−N(1) = 1.339(7); C(1)−N(2) = 1.352(6); C(2)−N(2) = 1.387(7); C(2)−C(3) = 1.346(8); C(3)−N(1) = 1.389(7); C(1)−Au(1)−Cl(1) = 176.37(15); N(1)−C(1)−N(2) = 105.3(4); C(1)−N(2)−C(2) = 110.4(4); N(2)−C(2)−C(3) = 106.8(5); C(2)−C(3)−N(1) = 106.5(5); C(3)−N(1)−C(1) = 111.0(4).

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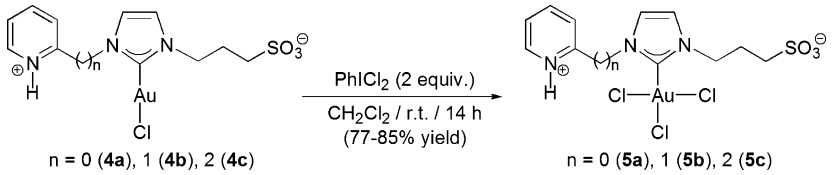
Scheme 3. Synthesis of the NHC-Au(III) Complexes 5a−c



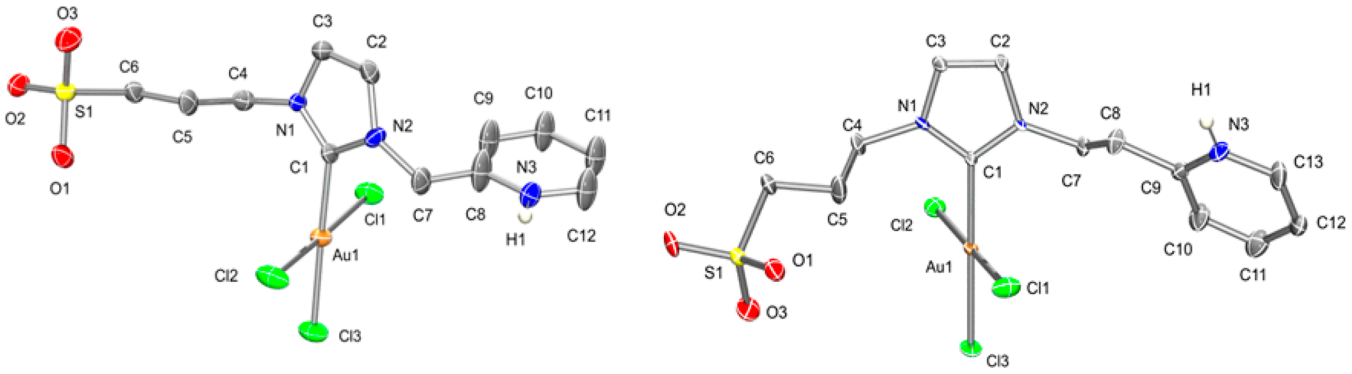


Figure 4. ORTEP-type views of the structures of the NHC-Au(III) complexes **5b** (left) and **5c** (right) showing the crystallographic labeling scheme. Thermal ellipsoids are drawn at 50% (**5b**) and 30% (**5c**) probability level. Hydrogen atoms, except those on the N(3) atoms, have been omitted for clarity.

linear with a C(1)−Au(1)−Cl(1) angle of 176.37(15)°, and Au(1)−C(1) and Au(1)−Cl(1) bond distances of 1.988(5) and 2.2856(14) Å, respectively. These bonding parameters compare well with those previously observed in the solid state structures of the Au(I) compounds **A**−**C** (Figure 1; C−Au−Cl angles, and Au−C and Au−Cl distances in the ranges 178.17(6)−180.0(1)°, 1.976(2)−1.995(4) Å, and 2.2699(6)−2.2871(11) Å, respectively).[9a,e,f] Worthy of note is that, in the crystal packing, two molecules of **4c** were found in the asymmetric unit connected through a weak aurophilic bond (a drawing showing this Au···Au interaction has been included in the Supporting Information).[24] This intermolecular gold−gold contact, which was not noticed in the structures of **A**−**C**, results in a gold···gold distance of 3.4167(3) Å. This value is intermediate to those observed in the solid state structures of the dinuclear derivatives **G** (3.589 Å) and **H** (3.302 Å) (Figure 1) where related intramolecular Au···Au interactions were detected.[9d]

The white NHC-Au(I) complexes **4a−c** were smoothly oxidized to the corresponding yellow Au(III) derivatives **5a−c**, which could be isolated in 77−85% yield, by action of iodobenzene dichloride (Scheme 3).[25] To the best of our knowledge, the air-stable compounds **5a−c** represent the first examples of Au(III) complexes bearing water-soluble sulfonated NHC ligands.

The 2-picolyl- and 2-pyridylethyl-substituted complexes **5b−c** are soluble (33 (**5b**) and 8 (**5c**) g/L) and remarkably stable in water at room temperature. Thus, in contrast to their Au(I) counterparts **4b−c**, nanoparticles formation was only observed after 4 days. Compounds **5b−c** were characterized by the standard spectroscopic techniques (IR and ^{1}H and $^{13}C\{^{1}H\}$ NMR) as well as elemental analyses (details are given in the Experimental Section). Worthy of note is that, while the carbenic carbon of **5b** resonates at exactly the same chemical shift of that of its Au(I) precursor **4b** (δ_C 169.8 ppm), this signal is shifted 15 ppm upfield for complex **5c** (δ_C 153.1 ppm) when compared to that of **4c** (δ_C 168.5 ppm).[26,27]

Confirmation of the structures of these compounds was unambiguously achieved through X-ray diffraction studies on crystals of **5b**·DMSO and **5c**·acetone obtained by slow diffusion of toluene or acetone into saturated solutions of the complexes in DMSO or water, respectively. ORTEP-type views of the molecules are shown in Figure 4, and selected structural parameters are collected in Table 1. As expected, the geometries around the Au atoms are almost ideal square planar, with metal-centered angles within the ranges 86.8(3)−92.56(11)° and 175.66(10)−179.4(3)°. The Au(1)−C(1)

Table 1. Selected Bond Distances (Å) and Bond Angles (deg) for Complexes 5b and 5c

	5b	5c
	Distances	
Au(1)−C(1)	2.002(10)	2.039(9)
Au(1)−Cl(1)	2.282(3)	2.267(3)
Au(1)−Cl(2)	2.272(3)	2.287(3)
Au(1)−Cl(3)	2.314(3)	2.317(3)
C(1)−N(1)	1.303(14)	1.318(12)
C(1)−N(2)	1.376(13)	1.333(13)
C(2)−N(2)	1.376(15)	1.381(13)
C(2)−C(3)	1.319(17)	1.357(14)
C(3)−N(1)	1.409(13)	1.367(12)
	Angles	
C(1)−Au(1)−Cl(1)	86.8(3)	88.4(3)
C(1)−Au(1)−Cl(2)	89.1(3)	89.4(3)
C(1)−Au(1)−Cl(3)	178.8(3)	179.4(3)
Cl(1)−Au(1)−Cl(2)	175.66(10)	177.28(10)
Cl(1)−Au(1)−Cl(3)	92.56(11)	91.03(11)
Cl(2)−Au(1)−Cl(3)	91.54(11)	91.23(10)
N(1)−C(1)−N(2)	108.7(9)	109.9(8)
C(1)−N(2)−C(2)	107.5(9)	107.7(8)
N(2)−C(2)−C(3)	107.8(9)	106.6(8)
C(2)−C(3)−N(1)	108.1(10)	107.8(9)
C(3)−N(1)−C(1)	107.9(9)	108.0(9)

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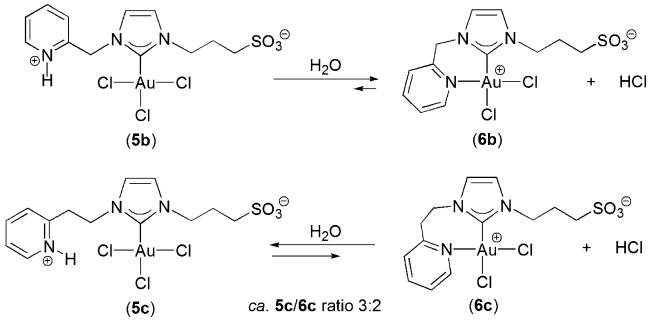
bond distances of 2.002(10) (**5b**) and 2.039(9) Å (**5c**), slightly longer than that found in the structure of the Au(I) complex **4c** (1.988(5) Å; Figure 3), are comparable to those previously reported for related [$AuCl_3$(NHC)] species.[26,27]

Concerning the 2-pyridyl-substituted Au(III)-NHC derivative **5a**, its insolubility in all common laboratory solvents, including water, prevented its characterization by NMR spectroscopy and the possibility of obtaining single crystals. However, we must note that the elemental analysis data obtained for this compound corroborate the proposed formulation.

On the other hand, we have also observed that, when dissolved in water, complexes **5b–c** are in equilibrium with the corresponding chelate derivatives **6b–c**, the latter resulting from the release of HCl and concomitant coordination of the unprotonated pyridyl units to the gold centers (Scheme 4).

Scheme 4. Behavior of the NHC-Au(III) Complexes 5b–c in Water



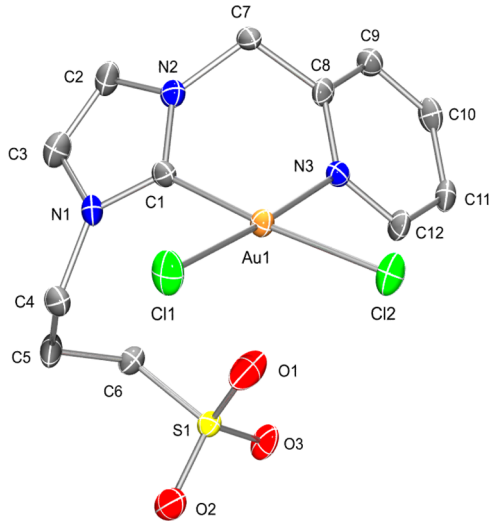


Figure 5. ORTEP-type view of the structure of the NHC-Au(III) complex **6b** showing the crystallographic labeling scheme. Thermal ellipsoids are drawn at 50% probability level. Hydrogen atoms have been omitted for clarity. Selected bond distances (Å) and angles (deg): Au(1)–C(1) = 2.006(6); Au(1)–Cl(1) = 2.2767(13); Au(1)–Cl(2) = 2.23194(14); Au(1)–N(3) = 2.053(4); C(1)–N(1) = 1.347(8); C(1)–N(2) = 1.325(7); C(2)–N(2) = 1.381(7); C(2)–C(3) = 1.351(10); C(3)–N(1) = 1.390(8); C(1)–Au(1)–Cl(1) = 92.42(17); C(1)–Au(1)–Cl(2) = 175.22(17); C(1)–Au(1)–N(3) = 85.7(2); Cl(1)–Au(1)–Cl(2) = 91.83(5); Cl(1)–Au(1)–N(3) = 176.37(13); Cl(2)–Au(1)–N(3) = 89.93(13); N(1)–C(1)–N(2) = 107.8(5); C(1)–N(2)–C(2) = 110.1(5); N(2)–C(2)–C(3) = 106.4(5); C(2)–C(3)–N(1) = 107.5(6); C(3)–N(1)–C(1) = 108.2(5).

Chelation of the NHC ligands in water is readily evidenced by ^{1}H NMR spectroscopy, where the methylenic protons of the 2-picolyl and 2-pyridylethyl moieties become diastereotopic as a consequence of the conformational rigidity associated to the resulting six- and seven-membered metallacycles in **6b–c**. For example, the singlet signal corresponding to the picolyl CH_2 protons in **5b** (δ 5.63 ppm) undergoes an AB splitting in **6b** leading to the appearance of two doublets at δ 5.65 and 5.81 ppm (J = 16.0 Hz). Remarkably, the major species present in solution is not the same in both cases. Thus, while in the case of **5c** a mixture with **6c** in about 3:2 ratio is generated, complex **6b** is almost quantitatively formed when **5b** is dissolved in water. This fact allowed a complete spectroscopic characterization of this chelate compound (see the Experimental Section).[28,29] In addition, slow diffusion of tetrahydrofuran (THF) into the aqueous solution allowed also the selective crystallization of **6b**, which was further characterized by X-ray crystallography (Figure 5). The Au(1)–C(1) bond distance found in this complex (2.006(6) Å) is almost identical to that previously observed in its parent precursor **5c**, reflecting a negligible effect of chelation on the strength of the gold-carbene bond. The observed Au(1)–N(3) distance (2.053(4) Å) also fits well with those reported in the literature for other Au(III) complexes containing *N*-coordinated pyridine units.[29,30]

Once synthesized and characterized, the ability of the soluble complexes **4a–c** and **5b–c** to promote the catalytic cycloisomerization of γ-alkynoic acids was evaluated. Thus, in a first set of experiments, the commercially available 4-pentynoic acid (**7a**) was subjected to the action of the picolyl-Au(III) derivative **5b** (2.5 mol %) in different reaction media, at room temperature (r.t.), and under aerobic conditions (Table 2). The use of biphasic water/organic solvent mixtures led in general to the best results (entries 1–4). In all the mixtures checked, the quantitative formation of the desired 5-methylene-dihydrofuran-2-one (**8a**) was observed after 1–6 h. The toluene/water combination (entry 4), where total conversion of **7a** took place after only 1 h, was particularly effective (TOF = 40 h^{-1}), allowing the formation of **8a** in high yield (81%) after separation of the organic phase, filtration over silica gel and solvent removal.[31] Probably because of the very low solubility of **5b** in the medium, only trace amounts of **8a** were formed when the catalytic reactions were performed in pure acetonitrile, diethyl ether, dichloromethane, or toluene (entries 5–8). In contrast, complete conversion of **7a** into **8a** was observed in methanol after 6 h, a solvent where **5b** is partially soluble (entry 9).[32] As expected, the process was also operative in pure water (entry 10). However, the activity of **5b** in this medium was lower due probably to the low solubility of **7a** in water. In addition, a non selective reaction was observed due to the partial hydrolysis of **8a** to form 3-acetylpropanoic acid. Generation of this byproduct via hydration of the C≡C bond of **7a** was excluded since complex **5b** proved to be unable to hydrate 1-hexyne at room temperature. Only at 100 °C could the hydration of 1-hexyne be observed, the reactions leading to the Markovnikov addition product hexan-2-one in 25% (toluene/water as solvent) or 56% (pure water as solvent) after 24 h of heating. Taking into account that acid-catalyzed hydrolysis of lactones is a well-known process,[33] the HCl released by **5b** when dissolved in water (Scheme 4) may be responsible for the observed partial hydrolysis of **8a**. Under biphasic conditions (entries 1–4), this side reaction was not observed since the product **8a** and HCl are not soluble in the

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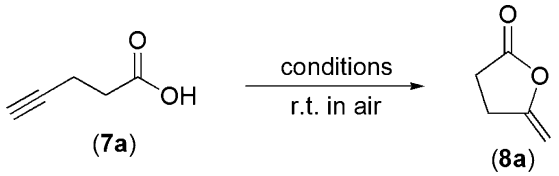
Table 2. Catalytic Cycloisomerization of 4-Pentynoic Acid (7a)[a]



(7a) (8a)

entry	conditions	time (h)	yield (%)[b]	TOF (h^{-1})[c]
1[d]	**5b** (2.5 mol %), MeCN/H_2O	6	>99	7
2[d]	**5b** (2.5 mol %), Et_2O/H_2O	5	>99	8
3[d]	**5b** (2.5 mol %), CH_2Cl_2/H_2O	2	>99	20
4[d]	**5b** (2.5 mol %), toluene/H_2O	1	>99 (81)	40
5[e]	**5b** (2.5 mol %), MeCN	6	traces	<1
6[e]	**5b** (2.5 mol %), Et_2O	5	traces	<1
7[e]	**5b** (2.5 mol %), CH_2Cl_2	2	5	1
8[e]	**5b** (2.5 mol %), toluene	1	traces	<1
9[e]	**5b** (2.5 mol %), MeOH	6	>99	7
10[e]	**5b** (2.5 mol %), H_2O	1	50[e]	20
11[d]	HCl (2.5 mol %), toluene/H_2O	1	1	<1
12[d,g]	**5b** + KOH (2.5 mol %), toluene/H_2O	1	>99	40
13[d]	**2b** (2.5 mol %), toluene/H_2O	1	0	0
14[d,g]	**2b** + KOH (2.5 mol %), toluene/H_2O	1	0	0
15[d]	**5c** (2.5 mol %), toluene/H_2O	1	>99	40
16[d]	**4a** (2.5 mol %), toluene/H_2O	1	>99	40
17[d]	**4b** (2.5 mol %), toluene/H_2O	1	>99	40
18[d]	**4c** (2.5 mol %), toluene/H_2O	1	>99	40
19[d]	$AuCl_3$ (2.5 mol %), toluene/H_2O	4	90[h]	9
20[d]	AuCl (2.5 mol %), toluene/H_2O	6	70[f]	5
21[d]	**I** (2.5 mol %), toluene/H_2O	24	traces	<1
22[d]	**4a** (0.1 mol %), toluene/H_2O	3	>99 (83)	333
23[d]	**4b** (0.1 mol %), toluene/H_2O	3	>99 (85)	333
24[d]	**4c** (0.1 mol %), toluene/H_2O	1.5	>99 (84)	667
25[d]	**5b** (0.1 mol %), toluene/H_2O	3	>99 (81)	333
26[d]	**5c** (0.1 mol %), toluene/H_2O	2	>99 (83)	500

[a]Reactions were performed at r.t. under aerobic conditions starting from 0.3 mmol of **7a**. [b]Determined by TLC or ^{1}H NMR. Isolated yields are given in brackets. [c]Turnover frequencies ((mol product/mol Au)/time) were calculated at the time indicated in each case. [d]1 mL of the corresponding organic solvent and 1 mL of distilled water were employed. [e]2 mL of the corresponding solvent were employed. [f]A mixture of **8a** and 3-acetylpropanoic acid in ca. 3:1 ratio is formed. [g]2.5 mol % of each reagent were employed. [h]A mixture of **8a** and 3-acetylpropanoic acid in *ca.* 5:1 ratio is formed.

same phase. In line with this, we also confirmed that the cycloisomerization of **7a** into **8a** does not result from a Brønsted acid catalysis.[34] Thus, as shown in entries 11−12, no reaction took place using catalytic HCl in the absence of gold, and the activity of **5b** remained unaltered in the presence of KOH. In blank experiments, no catalytic activity was observed employing the zwitterionic imidazolium salt **2b** alone (entry 13) or in combination with KOH (entry 14), thus confirming that the cyclization reaction is promoted by gold.

All the above-commented observations fully support that the intramolecular nucleophilic attack of the carboxylic unit (5-*exo* addition) is taking place upon coordination of the alkyne to the active Au(III) center.[35] In this sense, when the reactions are performed in aqueous environments, the required vacant site is most probably generated by decoordination of the 2-picolyl moiety in the in situ formed complex **6b** (Scheme 4), owing to the known hemilabile character of this group and the behavior shown by **6b** in the presence of NaCl.[28,36] However, when the reaction is performed in methanol (entry 9), coordination of the C≡C bond requires the dissociation of one of the chloride ligands of **5b** since, contrary to what it is observed in water, formation of **6b** does not occur when **5b** is dissolved in CD_3OD, as readily evidenced by ^{1}H NMR spectroscopy. Such a chloride dissociation process would be favored by the high polarity of MeOH. As shown in entries 15−18, the 2-pyridylethyl-substituted Au(III)-NHC complex **5c** (2.5 mol %), as well as the Au(I) derivatives **4a−c** (2.5 mol %), proved to be also active and selective catalysts in the cycloisomerization of **7a** under biphasic toluene/water conditions, leading also to the quantitative formation of **8a** after 1 h (TOF = 40 h^{-1}). The high reactivity of the Au(I) complexes **4a−c** merits to be highlighted since the participation of a chloride abstractor, commonly used in catalytic Au(I) chemistry, was not required. Easy dissociation of the chloride ligand of **4a−c** in the polar aqueous medium, leading to the effective generation of active $[Au(NHC)]^+$ species, can be evoked to explain the catalytic activity observed. Remarkably, the presence of a NHC ligand in the catalysts was crucial, as the efficiency and selectivity of the reaction were markedly lower using simple Au(III) and Au(I) sources, such as $AuCl_3$ and AuCl (entries 19−20). It is also worthy of note that, despite the known ability of silver(I) salts to promote the cycloisomerization of alkynoic acids,[13a] the Ag(I)-NHC derivative **I**[22] proved to be completely ineffective (entry 21).

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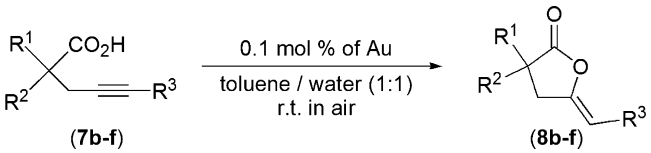
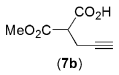
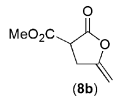
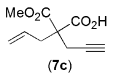
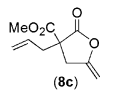
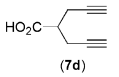
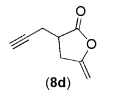
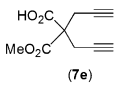
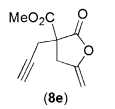
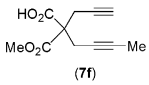
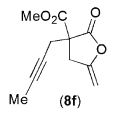
A series of experiments were also performed using a lower metal loading (0.1 instead of 2.5 mol % of Au) and the optimal biphasic toluene/water mixture (entries 22−26). Gratifyingly, this significant reduction in the catalyst loading did not result in a drastic increase of the reaction times (full conversions were in all cases observed within 3 h). These experiments allowed us to identify the Au(I)-NHC complex **4c** as the most active catalyst within this family of compounds, since it was able to generate the desired 5-methylene-dihydrofuran-2-one (**8a**) after only 1.5 h (TOF = 667 h^{-1} and TON = 1000; entry 24). The higher reactivity of **4c** compared to that of the other Au(I) derivatives **4a−b** (entries 22−23) could be related to the lower steric congestion around the active gold center in this complex, that is, the pyridinium and imidazol-2-ylidene units are linked through the longer methylenic chain. This fact would also explain the higher activity found for the Au(III) complex **5c** compared to that of **5b** (entry 26 vs 25).

To define the scope of this catalytic transformation, other γ-alkynoic acids **7b−c** bearing a terminal alkyne unit were subjected to the action of the Au(I) and Au(III) complexes **4a−c** and **5b−c**, respectively (Table 3). The reactions were routinely performed under biphasic toluene/water conditions, that is, by adding the corresponding alkynoic acid (0.5 mmol) and the appropriate gold complex (0.0005 mmol; 0.1 mol %) to a biphasic system composed of 1 mL of toluene and 1 mL of distilled water. The resulting mixture was stirred under air, at room temperature, until complete conversion of the alkynoic acid was observed by thin layer chromatography (TLC). All the complexes were able to convert selectively **7b−c** into the desired five-membered enol-lactones **8b−c** (entries 1−2) The reactions proceeded rapidly (1−6 h), allowing the isolation of **8b−c** in high yields (84−96%) after phase separation. Similarly to **7a**, no traces of the corresponding six-membered lactones, resulting from an *endo* instead of an *exo* cyclization, were detected by ^{1}H NMR spectroscopy in the crude reaction mixtures, and no hydrolysis of **8b−c** or competitive hydration of **7b−c** to form the corresponding keto-acids took place under the biphasic conditions employed. The Au(I)-NHC complex **4c** was found to be, once again, the most active one, allowing to complete the reactions in only 1 h (TOF = 1000 h^{-1}). The same trend was observed in the cycloisomerization of the bispropargylic carboxylic acids **7d−f** (entries 3−5). The reactions led in all the cases to the selective formation of the five-membered enol-lactones **8d−f**, which could be isolated in 80−95% yield. No hydration of the pendant propargylic unit of the products was observed in these reactions.

Remarkably, starting from the nonsymmetrical 1,6-diyne **7f**, exclusive addition of the carboxylic acid unit to the terminal C≡C group took place, the reactions leading to the selective formation of the enol-lactone **8f** (entry 5). The remarkable higher reactivity of terminal vs internal alkyne units was further evidenced in the reactions of the γ-alkynoic acid **7g** and the 1,6-diyne **7h**, both containing internal 2-butynyl units, which, regardless of the catalyst employed, required a higher metal loading (2.5 mol %) to be transformed into the corresponding five-membered enol-lactones **8g−h** in high yield (Scheme 5; times given at total conversion of the substrates by TLC). Interestingly, variable amounts of the corresponding 6-membered ring lactones **9g−h**, resulting from a competing 6-*endo* cyclization, were in all the cases detected in the ^{1}H NMR spectra of the crude reaction mixtures. Attempts to separate these byproducts by column chromatography failed. As in the precedent cases, the Au(I)-NHC complex **4c** proved to be the most active catalyst, leading to the complete consumption of the starting alkynoic acids in shorter times. However, from a selectivity point of view, it led to the worst results with both substrates.

Table 3. Cycloisomerization of the γ-Alkynoic Acids 7b−f under Biphasic Toluene/Water Conditions Using the NHC-Gold Complexes 4a−c and 5b−c[a]



Entry	Substrate	Product	Catalyst	Time (h)[b]	Yield (%)[c]	TOF (h^{-1})[d]
1	 (7b)	 (8b)	**4a**	1	95	1000
			4b	1	94	1000
			4c	1	96	1000
			5b	1	94	1000
			5c	1	93	1000
2	 (7c)	 (8c)	**4a**	3	86	333
			4b	5	84	200
			4c	1	85	1000
			5b	6	86	167
			5c	4	87	250
3	 (7d)	 (8d)	**4a**	6	93	167
			4b	6	92	167
			4c	1	95	1000
			5b	6	94	167
			5c	4	94	250
4	 (7e)	 (8e)	**4a**	8	86	125
			4b	7	83	143
			4c	1	85	1000
			5b	6	86	167
			5c	4	84	250
5	 (7f)	 (8f)	**4a**	10	82	100
			4b	8	84	125
			4c	1	83	1000
			5b	7	80	143
			5c	3	83	333

[a]Reactions were performed in 2 mL of a toluene/water mixture (1:1 v/v), at r.t. under aerobic conditions, starting from 0.5 mmol of **7b−f** and 0.0005 mmol of the corresponding NHC-gold complex (0.1 mol %). [b]Time given at total conversion of the starting alkynoic acid **7b−f** (TLC). [c]Isolated yields. [d]Turnover frequencies ((mol product/mol Au)/time) were calculated at the time indicated in each case.

Finally, their recycling was investigated to determine the lifetime and level of reusability of our gold-NHC complexes, key factors for practical applications of a metal catalyst.[37] The cycloisomerization of 4-pentynoic acid (**7a**) to 5-methylene-dihydrofuran-2-one (**8a**) in the biphasic toluene/water mixture was employed as model reaction, separating the organic phase containing **8a** at the end of each cycle and adding a fresh load of **7a** dissolved in toluene to the aqueous phase in which the gold complexes remain dissolved. To minimize losses of the catalysts during handling, a metal loading of 2.5 mol % was routinely employed. Under these conditions the Au(III)

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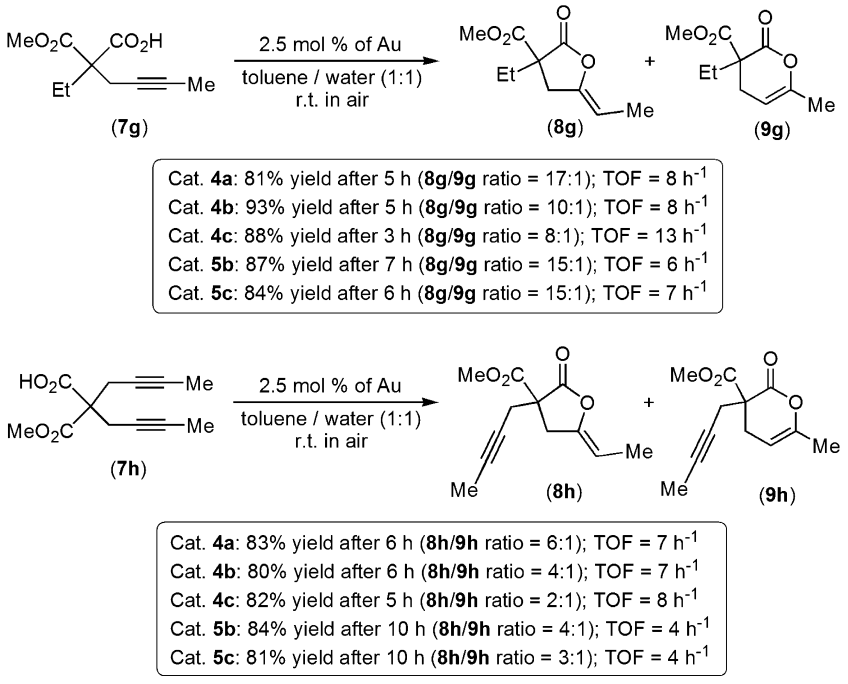
Scheme 5. Catalytic Cycloisomerization of the Alkynoic Acids 7g–h by Complexes 4a–c and 5b–c



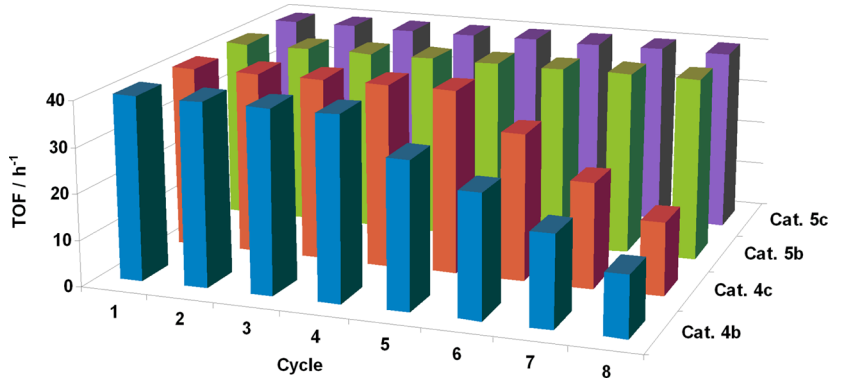


Figure 6. Evolution of the turnover frequency (TOF) of catalysts **4–5b–c** during recycling.

complexes **5b–c** showed an excellent recyclability and could be reused at least 10 times without any loss of activity or selectivity (**8a** was generated in quantitative yield after 1 h at r.t. over the 10 cycles with both catalysts; TOF = 40 h^{-1} in each cycle). In contrast, the efficiency of the recovered aqueous solutions containing their Au(I) counterparts **4b–c** started to decrease after the fourth or fifth run (i.e., longer times were needed to attain the full conversion of **7a** into **8a**). These differences can be visualized in Figure 6, where evolution of the TOF values of catalysts **4–5b–c** during the eight consecutive runs is represented. The decrease in activity of **4b–c** is accompanied by the appearance of a violet tonality in the aqueous solutions indicative of the partial decomposition of the active species into gold nanoparticles (**4a** behaves similarly after the first run). These observations raised the question on the real homogeneous or heterogeneous nature of the catalytic reactions. To shed light on this point, the cycloisomerization of **7a** with complexes **4a–c** was performed in the presence of mercury. No major differences in activity were observed, thus allowing us to discard a heterogeneous catalysis involving gold nanoparticles as the active species. On the other hand, the differences in recyclability observed are in complete accordance with the lower stability of our Au(I) vs Au(III) systems in water commented upon previously.

CONCLUSION

In summary, new gold complexes containing water-soluble *N*-heterocyclic carbene ligands, including the first examples of Au(III) derivatives, have been synthesized, and their utility as recyclable catalysts for the intramolecular cyclization of γ-alkynoic acids clearly demonstrated. In particular, working in a biphasic toluene/water medium, the catalytic reactions proceeded cleanly for a family of representative substrates, delivering selectively the desired five-membered enol-lactones in high yields under remarkably mild conditions (r.t.). We must note that the gold complexes reported herein represent rare examples of catalytic systems able to promote this synthetically useful transformation in aqueous environments.[15−17] It also merits to be highlighted that, despite the well-known ability of gold complexes to promote the hydration of carbon–carbon triple bonds,[9b,c,11,19] competing alkyne hydration processes were never observed, even during the desymmetrization reactions of 1,6-diyne substrates. This fact clearly demonstrates

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the high potential of NHC-gold catalysts for the development of selective transformations of functionalized alkynes in aqueous media.

EXPERIMENTAL SECTION

Synthetic procedures were performed using vacuum-line and standard Schlenk techniques. Solvents were dried by standard methods and distilled under nitrogen before use. Imidazolyl-pyridines **1a**[38] and **1b**,[39] 2-(2-chloroethyl)pyridine,[40] [AuCl(SMe$_2$)],[41] PhICl$_2$,[42] and the alkynoic acids **7b**,[43] **7c**,[16] **7d**,[44] **7e**,[16] **7f**,[12] **7g**,[12] and **7h**,[45] were prepared by following the methods reported in the literature. Flash chromatography was performed using Merck silica gel 60 (230−400 mesh). Infrared spectra were recorded on a Perkin-Elmer 1720-XFT spectrometer. NMR spectra were recorded on a Bruker DPX-300 instrument at 300 MHz (^{1}H) or 75.4 MHz (^{13}C). The chemical shift values (δ) are given in parts per million and are referred to the residual peak of the deuterated solvent employed. DEPT experiments have been carried out for all the compounds reported. Elemental analyses and mass spectra were provided by the Analytical Service of the Instituto de Investigaciones Químicas (IIQ-CSIC).

Synthesis of 2-(2-Imidazol-1-yl-ethyl)pyridine (1c).[20] 2-(2-Chloroethyl)pyridine (1.0 g, 7.1 mmol), imidazole (0.725 g, 10.6 mmol), and NaI (0.106 g, 0.71 mmol) were suspended in a mixture of 25 mL of THF and 25 mL of toluene, and stirred at 100 °C overnight under N$_2$ atmosphere. The solvent was then removed under reduced pressure, and the resulting residue redissolved in 25 mL of dichloromethane and washed with 25 mL of a saturated NaHCO$_3$ aqueous solution. The aqueous phase was recovered and extracted twice with dichloromethane (25 mL). The combined organic layers were dried over anhydrous MgSO$_4$, filtered, and evaporated to dryness. The brownish syrup thus obtained was dissolved in acetone, treated with activated charcoal at room temperature for 15 min and filtered. Evaporation of the volatiles under vacuum afforded **1c** as a pale yellow oil. Yield: 0.71 g (58%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.22 (t, 2H, J = 6.9 Hz), 4.42 (t, 2H, J = 6.9 Hz), 6.85 (s, 1H), 6.98 (d, 1H, J = 7.8 Hz), 7.00 (s, 1H), 7.12−7.18 (m, 1H), 7.36 (s, 1H), 7.57 (td, 1H, J = 7.8, 1.6 Hz), 8.58 (d, 1H, J = 4.8 Hz) ppm. ^{13}C{^{1}H} NMR (75.4 MHz, CDCl$_3$): δ = 39.7, 46.3, 118.8, 122.0, 123.6, 129.3, 136.7, 137.2, 149.7, 157.2 ppm. IR (Nujol): ν = 3113 (w), 3014 (w), 2942 (w), 1653 (w), 1595 (s), 1570 (m), 1510 (s), 1478 (s), 1438 (s), 1395 (w), 1363 (w), 1286 (m), 1232 (m), 1150 (w), 1109 (m), 1080 (s), 1052 (w), 1034 (w), 999 (w), 917 (m), 821 (m), 725 (s), 665 (s) cm^{-1}. HRMS (ESI): m/z = 173.0959, calcd for C$_{10}$H$_{11}$N$_3$: 173.0953.

General Procedure for the Synthesis of the Zwitterionic Imidazolium Derivatives 2a−c. A solution of 1,3-propanesultone (3.67 g, 30 mmol) and the corresponding imidazolyl-pyridine derivative **1a−c** (15 mmol) in dry acetone (40 mL) was stirred at room temperature under N$_2$ atmosphere for a week. The resulting solid precipitate was then filtered, washed with acetone (3 × 15 mL), and dried in vacuo. **(2a):** White solid. Yield: 3.17 g (79%). ^{1}H NMR (300 MHz, D$_2$O): δ = 2.26−2.46 (m, 2H), 2.94 (t, 2H, J = 7.4 Hz), 4.46 (t, 2H, J = 7.2 Hz), 7.56 (dd, 1H, J = 7.5 and 5.0 Hz), 7.70−7.76 (m, 2H), 8.03−8.12 (m, 2H), 8.52 (d, 1H, J = 4.8 Hz), 9.56 (s, 1H) ppm. ^{13}C{^{1}H} NMR (75.4 MHz, D$_2$O): δ = 25.0, 47.2, 48.5, 115.0, 120.0, 123.2, 125.5, 140.9, 146.2, 149.2, 162.3 ppm. IR (KBr): ν = 3159 (m), 3101 (m), 2989 (m), 2937 (w), 2846 (w), 1597 (s), 1548 (s), 1483 (s), 1445 (s), 1417 (m), 1348 (m), 1279 (w), 1235 (s), 1222 (s), 1180 (vs), 1156 (s), 1116 (m), 1082 (m), 1048 (s), 1033 (vs), 994 (m), 886 (w), 865 (m), 793 (s), 775 (s), 756 (s), 718 (m), 640 (m), 581 (m), 529 (s), 515 (m) cm^{-1}. Anal. Calcd for C$_{11}$H$_{13}$N$_3$O$_3$S (%): C, 49.43; H, 4.90; N, 15.72. Found: C, 49.44; H, 4.82; N, 15.53. **(2b):** White solid. Yield: 3.09 g (73%). ^{1}H NMR (300 MHz, D$_2$O): δ = 2.26 (m, 2H), 2.86 (t, 2H, J = 7.2 Hz), 4.33 (t, 2H, J = 7.2 Hz), 5.47 (s, 2H), 7.39−7.54 (m, 4H), 7.87 (t, 1H, J = 7.7 Hz), 8.46 (d, 1H, J = 5.0 Hz), 8.88 (s, 1H) ppm. ^{13}C{^{1}H} NMR (75.4 MHz, D$_2$O): δ = 25.0, 47.2, 48.0, 53.5, 122.7, 123.0, 123.7, 124.6, 139.0, 149.4, 152.0, 162.3 ppm. IR (KBr): ν = 3142 (w), 3105 (w), 1653 (m), 1593 (m), 1570 (m), 1448 (m), 1436 (m), 1353 (w), 1195 (vs), 1041 (s), 859 (w), 765 (m), 646 (m), 606 (m), 531 (m) cm^{-1}. Anal. Calcd for C$_{12}$H$_{15}$N$_3$O$_3$S (%): C, 51.23; H, 5.37; N, 14.94. Found: C, 51.24; H, 5.72; N, 14.77. **(2c):** White solid. Yield: 3.81 g (86%). ^{1}H NMR (300 MHz, D$_2$O): δ = 2.05−2.15 (m, 2H), 2.63 (t, 2H, J = 7.5 Hz), 3.26 (t, 2H, J = 6.4 Hz), 4.17 (t, 2H, J = 6.9 Hz), 4.54 (t, 2H, J = 6.4 Hz), 7.17 (d, 1H, J = 7.8 Hz), 7.25−7.30 (m, 1H), 7.36 (s, 1H), 7.40 (s, 1H), 7.72 (td, 1H, J = 7.8 and 1.6 Hz), 8.37 (d, 1H, J = 4.7 Hz), 8.42 (s, 1H) ppm. ^{13}C{^{1}H} NMR (75.4 MHz, D$_2$O): δ = 25.1, 37.2, 47.0, 47.7, 49.5, 122.6 (2C), 123.1, 124.3, 135.4, 138.6, 148.8, 155.7 ppm. IR (KBr): ν = 3133 (m), 3089 (m), 2973 (w), 2947 (w), 1594 (m), 1564 (s), 1479 (m), 1457 (s), 1441 (m), 1352 (w), 1206 (vs), 1167 (vs), 1034 (vs), 929 (m), 867 (m), 803 (m), 766 (s), 658 (m), 613 (s), 525 (s) cm^{-1}. Anal. Calcd for C$_{13}$H$_{17}$N$_3$O$_3$S (%): C, 52.86; H, 5.80; N, 14.23. Found: C, 53.04; H, 5.71; N, 14.02.

General Procedure for the Synthesis of the NHC-Au(I) Complexes 4a−c. In the absence of light and under N$_2$ atmosphere, the corresponding zwitterionic imidazolium derivative **2a−c** (1.5 mmol), tetrabutylammonium chloride (0.417 g, 1.5 mmol) and Ag$_2$O (0.394 g, 1.7 mmol) were refluxed for 24 h in 30 mL of dichloromethane. The reaction mixture was then filtered through Celite and [AuCl(SMe$_2$)] (0.442 g, 1.5 mmol) was added to the filtrate, leading to the extensive precipitation of AgCl. The mixture was stirred at room temperature for an additional hour and filtered again through Celite. The colorless filtrate was treated overnight at room temperature with p-TsOH·H$_2$O (0.285 g, 1.63 mmol), thus generating a white solid precipitate, which was filtered, washed with dichloromethane (3 × 10 mL) and dried in vacuo. **(4a):** Yield: 0.480 g (64%). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.13−2.26 (m, 2H), 2.52 (t, 2H, J = 7.2 Hz), 4.36 (t, 2H, J = 6.8 Hz), 7.58−7.63 (m, 1H), 7.81 (s, 1H), 7.99 (s, 1H), 8.08−8.17 (m, 1H), 8.23 (d, 1H, J = 8.1 Hz), 8.63 (d, 1H, J = 4.8 Hz) ppm (the signal for the NH proton was not observed). ^{13}C{^{1}H} NMR (75.4 MHz, DMSO-d_6): δ = 27.4, 48.6, 50.9, 118.6, 121.5, 123.2, 124.9, 139.9, 149.5, 150.9, 168.3 ppm. IR (KBr): ν = 3154 (w), 3095 (m), 2939 (w), 2919 (w), 2514 (br), 1617 (s), 1544 (s), 1475 (s), 1434 (s), 1365 (m), 1323 (m), 1275 (m), 1257 (m), 1217 (vs), 1178 (s), 1144 (s), 1032 (vs), 985 (m), 946 (m), 782 (m), 761 (s), 737 (m), 684 (w), 607 (s), 547 (w), 521 (m) cm^{-1}. Anal. Calcd for C$_{11}$H$_{13}$N$_3$O$_3$ClSAu (%): C, 26.44; H, 2.62; N, 8.41. Found: C, 26.92; H, 3.11; N, 8.41. **(4b):** Yield: 0.678 g (88%). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.05−2.16 (m, 2H), 2.44 (t, 2H, J = 7.3 Hz), 4.23 (t, 2H, J = 6.7 Hz), 5.54 (s, 2H), 7.37 (d, 1H, J = 7.8 Hz), 7.55 (br, 2H), 7.60 (s, 1H), 8.02 (t, 1H, J = 7.8 Hz), 8.66 (d, 1H, J = 4.7 Hz) ppm (the signal for the NH proton was not observed). ^{13}C{^{1}H} NMR (75.4 MHz, DMSO-d_6): δ = 27.6, 48.6, 50.3, 55.4, 122.7, 123.0, 123.5, 124.7, 141.1, 147.4, 154.5, 169.8 ppm. IR (KBr): ν = 3158 (m), 3098 (m), 3060 (m), 2963 (m), 2616

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(br), 1647 (m), 1623 (m), 1564 (w), 1547 (w), 1458 (m), 1419 (m), 1358 (w), 1219 (vs), 1160 (vs), 1036 (s), 997 (s), 766 (s), 731 (m), 682 (w), 602 (s), 543 (m), 524 (m) cm^{-1}. Anal. Calcd for $C_{12}H_{15}N_3O_3ClSAu$ (%): C, 28.05; H, 2.94; N, 8.18. Found: C, 28.10; H, 3.10; N, 7.35. **(4c):** Yield: 0.633 g (80%). ^1H NMR (300 MHz, DMSO-d_6): δ = 1.96−2.06 (m, 2H), 2.31 (t, 2H, J = 9.0 Hz), 3.46 (t, 2H, J = 6.0 Hz), 4.08 (t, 2H, J = 6.2 Hz), 4.55 (t, 2H, J = 6.0 Hz), 7.48 (s, 1H), 7.53 (s, 1H), 7.72 (d, 1H, J = 8.1 Hz), 7.84−7.87 (m, 1H), 8.41 (t, 1H, J = 7.4 Hz), 8.83 (d, 1H, J = 5.4 Hz) ppm (the signal for the NH proton was not observed). $^{13}C\{^1H\}$ NMR (75.4 MHz, DMSO-d_6): δ = 27.5, 35.4, 48.6, 50.1, 50.3, 122.0, 123.0, 125.8, 128.1, 143.2, 146.2, 153.7, 168.5 ppm. IR (KBr): ν = 3158 (w), 3097 (m), 2955 (w), 2926 (w), 2880 (w), 2818 (w), 2450 (br), 1642 (s), 1619 (s), 1565 (m), 1543 (m), 1463 (s), 1424 (s), 1352 (m), 1338 (w), 1279 (m), 1216 (vs), 1177 (vs), 1141 (vs), 1031 (vs), 995 (s), 928 (m), 885 (w), 788 (s), 689 (m), 625 (m), 603 (s), 571 (m), 536 (s), 507 (m) cm^{-1}. Anal. Calcd for $C_{13}H_{17}N_3O_3ClSAu$ (%): C, 29.58; H, 3.25; N, 7.96. Found: C, 29.13; H, 3.13; N, 7.52.

General Procedure for the Synthesis of the NHC-Au(III) Complexes 5a−c. A suspension of the corresponding NHC-Au(I) complex **4a−c** (0.5 mmol) in 20 mL of dry dichloromethane was treated overnight at room temperature with an excess of $PhICl_2$ (0.275 g, 1 mmol). The yellow precipitate thus formed was filtered, washed with dichloromethane (3 × 5 mL), and dried in vacuo. **(5a):** Yield: 0.242 g (85%). IR (KBr): ν = 3094 (m), 3073 (m), 3018 (w), 2956 (w), 2928 (w), 1619 (s), 1580 (s), 1502 (vs), 1444 (m), 1373 (m), 1343 (m), 1296 (m), 1264 (w), 1203 (vs), 1186 (vs), 1166 (vs), 1104 (m), 1041 (vs), 968 (w), 952 (w), 889 (w), 816 (w), 782 (s), 728 (m), 655 (w), 607 (s), 542 (m), 523 (m) cm^{-1}. Anal. Calcd for $C_{11}H_{13}Cl_3N_3O_3SAu$ (%): C, 23.15; H, 2.30; N, 7.36. Found: C, 23.46; H, 2.45; N, 7.51. **(5b):** Yield: 0.234 g (80%). ^1H NMR (300 MHz, DMSO-d_6): δ = 2.17 (m, 2H), 2.44 (t, 2H, J = 7.2 Hz), 4.38 (t, 2H, J = 7.2 Hz), 5.46 (br, 1H), 5.63 (s, 2H), 7.45−7.53 (m, 2H), 7.88−7.96 (m, 3H), 8.63 (d, 1H, J = 4.5 Hz) ppm (the signal for the NH proton was not observed). $^{13}C\{^1H\}$ NMR (75.4 MHz, DMSO-d_6): δ = 26.8, 48.2, 49.9, 54.7, 123.9, 124.6, 125.0, 126.3, 137.4, 149.4, 153.5, 169.8 ppm. IR (KBr): ν = 3161 (w), 3100 (m), 2936 (w), 2514 (br), 2093 (w), 1653 (m), 1621 (m), 1575 (w), 1550 (w), 1474 (m), 1431 (w), 1359 (w), 1244 (s), 1222 (s), 1164 (vs), 1148 (vs), 1029 (s), 998 (m), 886 (w), 763 (m), 685 (m), 602 (w), 542 (w), 521 (m), 458 (w) cm^{-1}. Anal. Calcd for $C_{12}H_{15}Cl_3N_3O_3SAu$ (%): C, 24.65; H, 2.59; N, 7.19. Found: C, 24.73; H, 2.74; N, 7.04. **(5c):** Yield: 0.230 g (77%). ^1H NMR (300 MHz, DMSO-d_6): δ = 2.09−2.19 (m, 2H), 2.45 (t, 2H, J = 7.5 Hz), 3.61 (t, 2H, J = 6.9 Hz), 4.33 (t, 2H, J = 7.1 Hz), 4.79 (t, 2H, J = 6.9 Hz), 7.78−7.88 (m, 2H), 7.87 (d, 1H, J = 2.0 Hz), 7.90 (d, 1H, J = 2.0 Hz), 8.39 (t, 1H, J = 7.8 Hz), 8.87 (d, 1H, J = 4.8 Hz) ppm (the signal for the NH proton was not observed). $^{13}C\{^1H\}$ NMR (75.4 MHz, DMSO-d_6): δ = 26.6, 34.4, 48.1, 49.0, 49.7, 124.9, 125.5, 125.8, 127.4, 136.9, 144.4, 145.2, 153.1 ppm. IR (KBr): ν = 3153 (w), 3120 (m), 2935 (m), 2632 (br), 1646 (m), 1623 (m), 1490 (m), 1436 (w), 1387 (w), 1329 (w), 1218 (vs), 1165 (s), 1149 (s), 1035 (s), 998 (w), 848 (w), 780 (m), 764 (m), 739 (m), 678 (m), 626 (w), 597 (m), 543 (m), 523 (m) cm^{-1}. Anal. Calcd for $C_{13}H_{17}Cl_3N_3O_3SAu$ (%): C, 26.08; H, 2.86; N, 7.02. Found: C, 26.16; H, 2.81; N, 6.84.

Characterization Data for the NHC-Au(III) Complex 6b. Complex **6b** is generated almost quantitatively in situ by dissolving **5b** in water at room temperature. Crystals of **6b** can be obtained by slow diffusion of THF into this aqueous solution. ^1H NMR (300 MHz, D_2O): δ = 2.24−2.35 (m, 2H), 2.64−2.71 (m, 1H), 2.84−2.88 (m, 1H), 4.44−4.49 (m, 1H), 4.62−4.66 (m, 1H), 5.65 (d, 1H, J = 16.0 Hz), 5.81 (d, 1H, J = 16.0 Hz), 7.52 (d, 1H, J = 2.1 Hz), 7.63 (d, 1H, J = 2.1 Hz), 7.77 (td, 1H, J = 7.5 and 1.5 Hz), 7.95 (dd, 1H, J = 7.8 and 1.2 Hz), 8.28 (td, 1H, J = 7.8 and 1.2 Hz), 9.1 (d, 1H, J = 7.5 Hz) ppm. $^{13}C\{^1H\}$ NMR (75.4 MHz, D_2O): δ = 25.5, 47.1, 49.0, 54.8, 123.9, 124.2, 127.7, 127.8, 136.4, 144.8, 152.4, 169.6 ppm. IR (KBr): ν = 3183 (w), 3148 (w), 3121 (w), 3092 (w), 3061 (w), 3033 (w), 2998 (w), 2921 (w), 1610 (m), 1566 (w), 1497 (m), 1484 (m), 1467 (m), 1433 (w), 1412 (w), 1333 (w), 1304 (w), 1282 (w), 1203 (vs), 1184 (s), 1143 (m), 1037 (m), 800 (m), 743 (m), 677 (m), 578 (w), 516 (m) cm^{-1}. Anal. Calcd for $C_{12}H_{14}Cl_2N_3O_3SAu$ (%): C, 26.29; H, 2.57; N, 7.67. Found: C, 26.16; H, 2.70; N, 7.83.

General Procedure for the Catalytic Cycloisomerization of Alkynoic Acids. To a biphasic system composed of 1 mL of toluene and 1 mL of distilled water, 0.3 mmol of the corresponding alkynoic acid **7a−h**, and the appropriate gold complex **4a−c** or **5b−c** (0.1 mol % for **7a−f**; 2.5 mol % for **7g−h**) were added. The resulting mixture was stirred under air, at room temperature, until complete conversion of the alkynoic acid was observed by TLC (see Tables 2−3 and Scheme 5). The organic phase was then separated, the aqueous one extracted with diethyl ether (2 × 2 mL), and the combined organic extracts dried over anhydrous $MgSO_4$ and filtered over a short pad of silica gel using CH_2Cl_2 as eluent. The volatiles were removed under vacuum to yield the corresponding lactone in high yield and purity. When required, lactones were further purified by column chromatography over silica gel using hexane:EtOAc (9:1) as eluent. The identity of the known lactones was assessed by comparison of their ^1H and $^{13}C\{^1H\}$ NMR spectroscopic data with those reported in the literature.[12]

Catalyst Recycling. The recyclability of complexes **4a−c** and **5b−c** was investigated using the cycloisomerization of 4-pentynoic acid (**7a**) to 5-methylene-dihydrofuran-2-one (**8a**) as model reaction. Thus, to a biphasic system composed of 1 mL of toluene and 1 mL of distilled water, 29 mg of **7a** (0.3 mmol) and the appropriate gold complex (0.0075 mmol; 2.5 mol %) were added. The resulting mixture was stirred under air at room temperature until complete consumption of **7a** was observed by TLC. The organic phase was then separated and the aqueous one extracted with diethyl ether (2 × 2 mL). To the aqueous layer, 0.3 mmol of fresh 4-pentynoic acid (**7a**) dissolved in 1 mL of toluene were added, and the mixture stirred again under the same conditions for 1 h. This procedure was repeated ten (**5b−c**), eight (**4b−c**), or two (**4a**) times. Analysis by ^1H NMR of organic extracts confirmed that the quantitative transformation of **7a** into **8a** took place in each run.

X-ray Crystal Structure Determination of Complexes 4c, 5b, 5c, and 6b. Crystals of **4c** and **6b** suitable for X-ray diffraction analysis were obtained by slow diffusion of THF into saturated solutions of the complexes in water. For **5b** and **5c** crystals were grown from toluene/DMSO and acetone/water solutions, respectively. The most relevant crystal and refinement data are collected in Supporting Information, Table S1. In all the cases, data collection was performed with an Oxford Diffraction Xcalibur Nova single crystal diffractometer using Cu−Kα radiation (λ = 1.5418 Å). Images were collected at a fixed crystal-detector distance of 63 mm for **4c**, **5c**, and **6b**, and 100 mm for **5b**, using the oscillation method with 1° oscillation

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and 1.5−2.5 s variable exposure time per image for **4c**, 6−40 s for **5b**, and 1.5 s for **5c** and **6b**. Data collection strategy was calculated with the program CrysAlis Pro CCD.[46] Data reduction and cell refinement was performed with the program CrysAlis Pro RED.[46] An empirical absorption correction was applied using the SCALE3 ABSPACK algorithm as implemented in the program CrysAlis Pro RED.[46]

In all the cases the software package WINGX[47] was used for space group determination, structure solution, and refinement. For **4c** the structure was solved by direct methods using SIR92,[48] for **5b** the structure was solved by direct methods using SIR2004,[49] for **6b** the structure was solved by Patterson interpretation and phase expansion using DIRDIF.[50] For **4c**, **5b**, and **6b** isotropic least-squares refinement on F^2 using SHELXL97[51] was performed. For **5c** the structure was solved, with some difficulty, by direct methods using SIR92,[48] but subsequent refinement was not possible. Therefore, experimental data were examined with the program PLATON[52] which detected pseudomerohedral twinning. The twin law proposed (1 0 1/0 −1 0/0 0 −1) is a 2-fold axis which belongs to a higher crystal system (orthorhombic) than the structure (monoclinic). Several restraints on displacement parameters were used during the least-squares refinement with SHELXL97[51] to counterbalance the unsatisfactory effective data to parameter ratio caused by twinning. Final BASF factor was 0.66. The high values of the peak and hole found in the final difference electron density map are a common consequence of a twinned crystal. During the final stages of the refinements, all the positional parameters and the anisotropic temperature factors of all the non-H atoms were refined. The H atoms were geometrically located and their coordinates were refined riding on their parent atoms. In the crystal of **5c** two independent molecules of the complex were found in the asymmetric unit. In the crystal of **4c** two water molecules of solvation per molecule of the complex were found, in the crystal of **5b** one molecule of DMSO per molecule of the complex, and in the crystal of **5c** one molecule of acetone per two molecules of the complex. In all the cases, the maximum residual electron density is located near to heavy atoms. The function minimized was $\{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$ where $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$ (a and b values are given in Supporting Information, Table S1) with $\sigma(F_o^2)$ from counting statistics and $P = (\mathrm{Max}\ (F_o^2,0) + 2F_c^2)/3$. Atomic scattering factors were taken from the International Tables for X-ray Crystallography.[53] Geometrical calculations were made with PARST.[54] The crystallographic plots were made with POV-Ray.[55]

■ ASSOCIATED CONTENT

Supporting Information

A CIF file giving crystallographic data for compounds **4c**, **5b**, **5c**, and **6b**, a table collecting the most relevant crystal and refinement data, a drawing showing the Au(I)···Au(I) interaction in the crystal structure of **4c**, and copies of ^{1}H and ^{13}C{^{1}H} NMR spectra of the zwitterionic imidazolium salts **2a−c** and the enol-lactones synthesized in this work (including COSY analyses of the **8g**/**9g** and **8h**/**9h** mixtures generated using **4c**). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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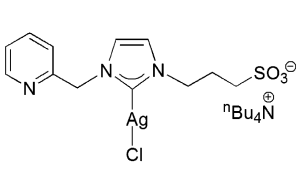
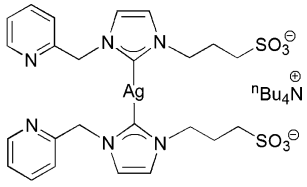
corresponding bis-carbene **J** and unreacted TBACl, that turned out to be inseparable. Spectroscopic data for **I** are as follows: ^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.93 (t, 12H, J = 7.3 Hz), 1.24−1.37 (m, 8H), 1.51−1.62 (m, 8H), 1.99−2.09 (m, 2H), 2.38 (t, 2H, J = 6.9 Hz), 3.14−3.19 (m, 8H), 4.21 (t, 2H, J = 6.9 Hz), 5.43 (s, 2H), 7.26−7.33 (m, 2H), 7.53−7.54 (m, 2H), 7.79 (td, 1H, J = 7.7 and 1.8 Hz), 8.52 (ddd, 1H, J = 4.8, 1.7 and 0.9 Hz) ppm. ^{13}C{^{1}H} NMR (75.4 MHz, DMSO-d_6): δ = 13.9, 19.2, 23.1, 27.7, 47.9, 50.0, 55.8, 57.5, 121.9, 122.0, 122.6, 123.1, 137.3, 149.4, 156.2, 179.3 ppm.



(I)



(J)

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(25) In our preliminary communication (ref 12) the Au(III) complex **5b** had been generated in a lower yield (63 vs 80%) through a not fully reproducible one-pot protocol starting directly from the zwitterionic imidazolium salt **2b**. The method of synthesis given in this article is much more reliable and fully reproducible. On the other hand, we must also indicate that, after a closer examination of its X-ray diffraction data, the formulation of **5b** given in reference 12 (as a sulfonic acid instead of a pyridinium derivative) was erroneous (the observed S-O distances are inconsistent with a SO_3H formulation).

(26) Upfield shift of the carbenic carbon signal is usually observed by ^{13}C{^{1}H} NMR spectroscopy when a NHC-Au(I) complex is oxidized to Au(III). See, for example: (a) Gaillard, S.; Slawin, A. M. Z.; Bonura, A. T.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2010**, *29*, 394−402. (b) Pažický, M.; Loos, A.; Ferreira, M. J.; Serra, D.; Vinokurov, N.; Rominger, F.; Jäkel, C.; Hashmi, A. S. K.; Limbach, M. *Organometallics* **2010**, *29*, 4448−4458.

(27) For [$AuCl_3$(NHC)] complexes, the carbenic carbon signal can resonate within a broad range of chemical shifts (δ_C 130−180 ppm). Representative examples can be found in reference 26 and: Muuronen, M.; Perea-Buceta, J. E.; Patzschke, M.; Helaja, J. *Organometallics* **2012**, *31*, 4320−4330.

(28) (a) Addition of excess NaCl to these aqueous mixtures regenerates the starting complexes **5b−c** quantitatively. (b) All attempts to generate **6c** in a selective manner by treating the aqueous **5c**/**6c** mixture with a base failed (additional uncharacterized products are formed).

(29) Related Au(III) complexes containing κ^2(*C,N*)-coordinated picolyl-NHC ligands have been described in ref 26. and Topf, C.; Hirtenlehner, C.; Fleck, M.; List, M.; Monkowius, U. *Z. Anorg. Allg. Chem.* **2011**, *637*, 2129−2134.

(30) See, for example: (a) Schouteeten, S.; Allen, O. R.; Haley, A. D.; Ong, G. L.; Jones, G. D.; Vicic, D. A. *J. Organomet. Chem.* **2006**, *691*, 4975−4981. (b) Cinellu, M. A.; Maiore, L.; Minghetti, G.; Cocco, F.; Stoccoro, S.; Zucca, A.; Manassero, M.; Manassero, C. *Organometallics* **2009**, *28*, 7015−7024. (c) Segapelo, T. V.; Guzei, I. A.; Spencer, L. C.; Van Zyl, W. E.; Darkwa, J. *Inorg. Chim. Acta* **2009**, *362*, 3314−3324. (d) Orbisaglia, S.; Jacques, B.; Braunstein, P.; Hueber, D.; Pale, P.; Blanc, A.; de Frémont, P. *Organometallics* **2013**, *32*, 4153−4164.

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(32) The cycloisomerization of **7a** was also studied in DMSO, a solvent in which complex **5b** is completely soluble. However, no catalytic activity was observed in this medium due probably to the preferred coordination of DMSO vs the alkyne to the metal.

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(35) As already discussed in our preliminary communication (see ref 12), the intramolecular *exo* attack of the carboxylic unit to the π-coordinate alkyne proceeds in an *anti* fashion as inferred performing the cycloisomerization reactions in a biphasic toluene/D_2O mixture (major incorporation of deuterium in *E* position of the exoxyclic C=C bond of the final enol-lactones was observed).

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