



Steric hindrance and electronic effects of sulfonatepropyl chain on gold center. An experimental and DFT study

Gabriela A. Fernández, Viviana Dorn^{*1}, Alicia B. Chopa², Gustavo F. Silbestri^{**1}

Instituto de Química del Sur (INQUISUR), Departamento de Química, Universidad Nacional del Sur, Av. Alem 1253, B8000CPB Bahía Blanca, Argentina

ARTICLE INFO

Article history:

Received 6 June 2017

Received in revised form

2 September 2017

Accepted 27 September 2017

Available online 5 October 2017

Keywords:

Water-soluble Au(I)

N-heterocyclic carbene

DFT methods

ABSTRACT

Density Functional Theories (DFT) methods were applied to describe the catalytic effect of a series of sulfonated NHC gold(I) complexes. In order to explain the experimental results obtained in the hydration of phenylacetylene in aqueous media. The complexes [1,3-bis(2,6-diisopropyl-4-sodiumsulfonatophenyl)imidazol-2-ylidene]gold(I) chloride (**C1**) and [(3-sulfonatepropyl)imidazol-2-ylidene]gold(I) chloride (**C5**) were considered representative compounds based on their structure and reactivity. In accordance to the experimental results, the DFT studies show that the alkyl chain folds generate a strong steric hindrance and electronic effects on the metal center causing a decrease of the catalytic activity.

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1. Introduction

Only a very small percentage of synthetic organic reactions were carried out in the presence of water. In the past, in the last decades there have been notable advances in the field of organic chemistry in aqueous media [1]. Moreover, water insolubility of many organic products facilitates the separation process and, in the case of water-soluble catalysts, it opens the way for their recycling and reuse.

The N-heterocyclic carbenes (NHCs) were first reported in 1968 by Wanzlick [2] and Öfele [3]. Since the first synthesis of a free stable NHC by Arduengo in 1991 [4], NHC-metal compounds revolutionized the field of catalysis, gradually displacing the typical phosphine and amine-type ligands in view of their higher stability and reactivity [5]. Even though most of the transition metals are coordinated with NHC ligands and the majority of the resulting complexes were used in organometallic catalysis [6]; only a small number of them, predominantly Ru and Pd and, in a few examples, Ag, Cu, Rh, Pt and Ir have been investigated in aqueous phase [1,7]. It is worth noting that, although the chemistry of water soluble NHC-gold(I) complexes is still a relatively young field, it has provided successful results in various application areas such as catalysis, medicine and luminescence [8].

The synthesis of new water soluble NHC-gold complexes, the study of their physicochemical properties as well as their application to several chemical transformations -including their potential recovery-is a very significant contribution to organometallic catalysis and to sustainable organic chemistry in general.

In previous studies, we synthesized water-soluble gold(I) complexes -supporting sulfonated NHC ligands-from the corresponding imidazolium salts [8b]. Recently, we have shown that complexes **C1** to **C5** (Fig. 1) are active and recyclable catalysts in the alkyne hydration in water:methanol (1:1), even in the absence of silver salts. Moreover, we have found that the bulkiness of the ligands influences the catalytic properties and higher yields in shortest times were obtained with bulkier NHC ligands. Kinetic information on the influence of the steric bulk around the metal center was obtained by monitoring the reaction (GC) over time. As Fig. 2 shows, the 100% conversion of phenylacetylene to acetophenone was obtained after induction periods that differed notably: 30 min for **C1** and 100 h for **C5** [9]. These results are consistent with those reported by other authors on different reactions carried out in conventional organic solvents [10]. Interestingly, the introduction of a less bulky structural moiety, such as 3-sulfonatepropyl (**C5**), caused long reaction times.

It is important to mention that the computational results obtained by Mazzone et al. [12] were consistent with the experimental observation of Leyva and Corma [13] for gold(I) catalyzed hydration of alkynes. The mechanism proposed is summarized in Scheme 1. The first step is the coordination of the triple bond to the Au(I) phosphine complex and subsequent attack of the nucleophile

* Corresponding author.

** Corresponding author.

E-mail addresses: vdorn@edu.ar (V. Dorn), gsilbestri@uns.edu.ar (G.F. Silbestri).

¹ Member of CONICET.

² Member of CIC.

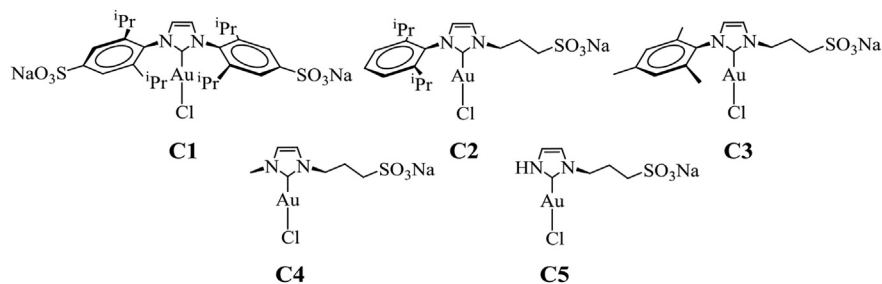


Fig. 1. Structure of sulfonated NHC-gold(I) complexes.

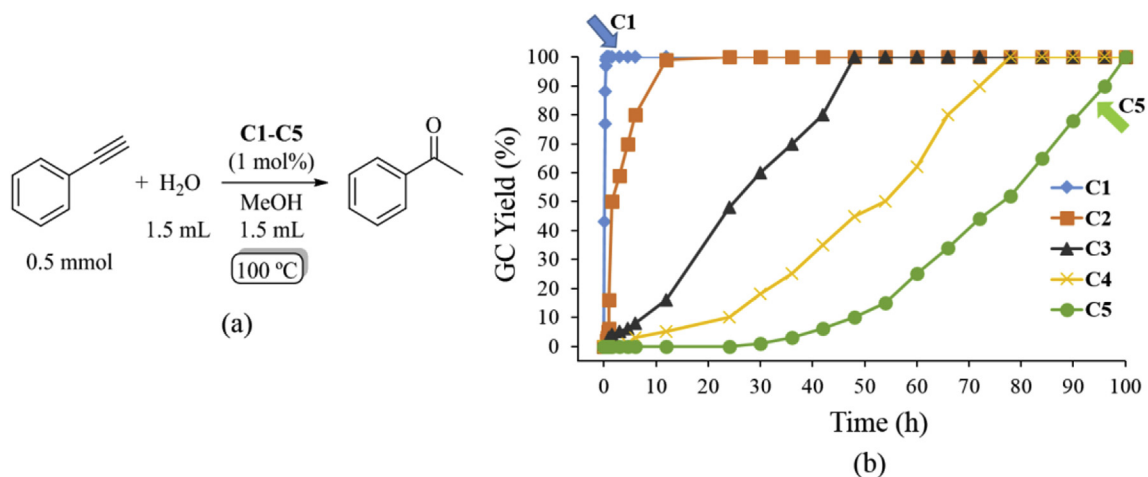
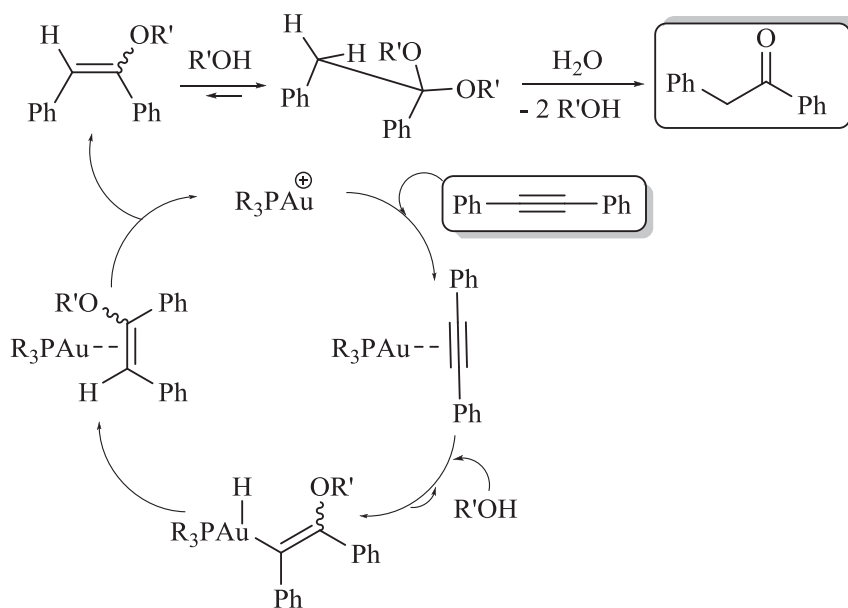


Fig. 2. (a) Hydration of phenylacetylene; (b) Comparison of reaction progress: **C1** (0.5 h); **C2** (13 h); **C3** (48 h); **C4** (72 h) and **C5** (100 h) [11].



Scheme 1. Representation of Au(I)phosphine-catalyzed hydration.

(H₂O or MeOH). Finally a protodeauration affords the enolic product together with the release of the catalyst. The addition of a second molecule of H₂O (MeOH) forms the corresponding ketal and subsequent reaction with water leads to the formation of the ketone final product [13].

Continuing with our research and aiming to explain the different catalytic activities found, herein we performed a computational analysis applying DFT methods.

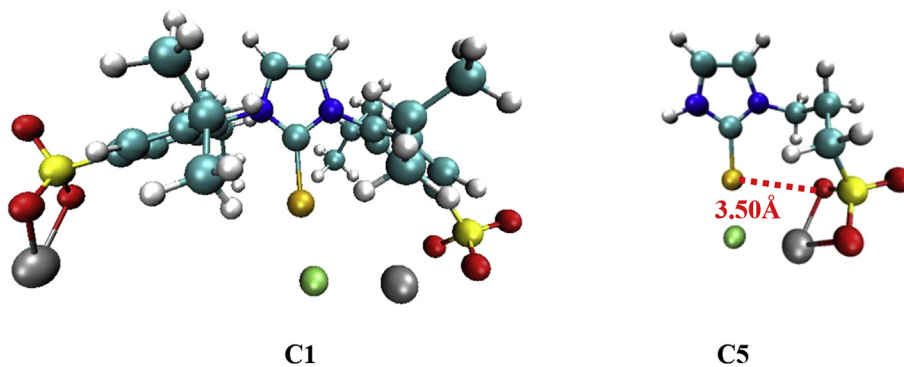


Fig. 3. Geometries of neutral **C1** and **C5**.

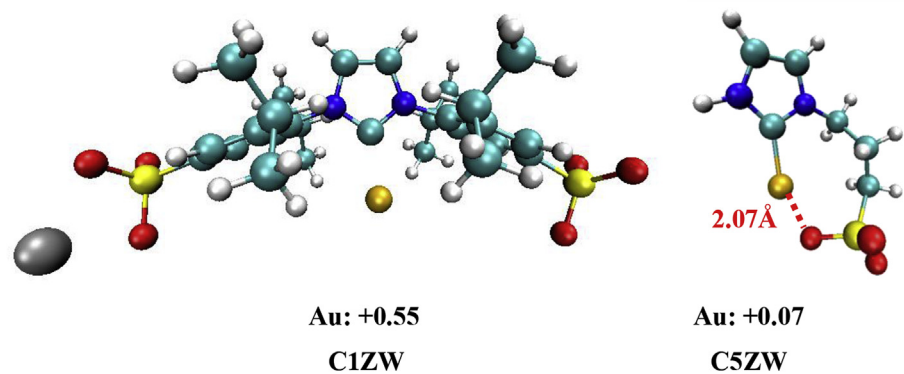


Fig. 4. Geometries and ESP charges of Au(+1) for **C1ZW** and **C5ZW**.

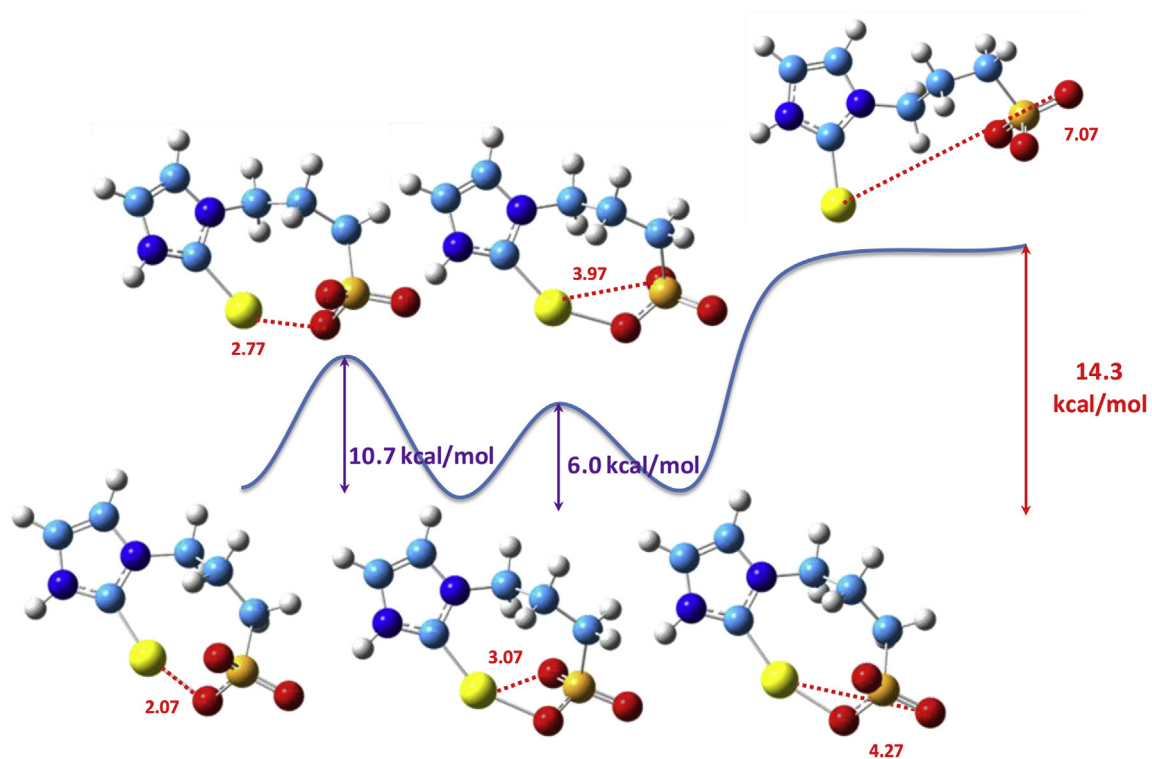


Fig. 5. Energy profile of the Au-O bond elongation (red dashes line) in **C5ZW**. All energies are ΔE (solvated) values (in kcal/mol) and all distances are in Å. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

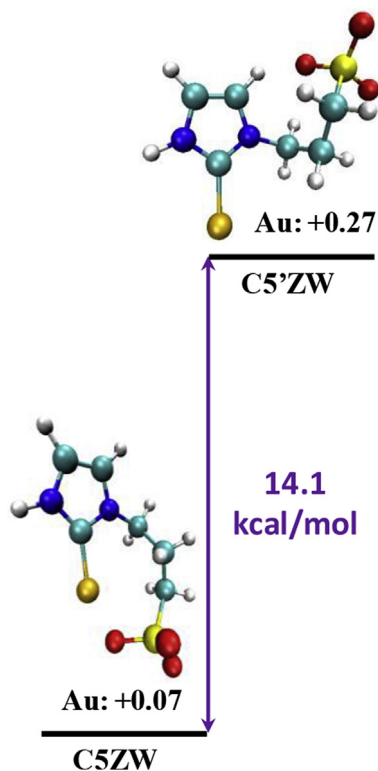


Fig. 6. Geometries and ESP charges of Au(+1) for two conformers of **C5ZW** evaluated by B3LYP/6-31 + G* and LANL2DZ (Au) in the presence of a continuum solvent (water). Energy difference is a ΔE (solvated) value (in kcal/mol).

2. Results and discussion

Experimental observations during the catalysis prompted us to study those complexes that showed the most different reactivities (**C1** and **C5**) through computational calculations. Our initial exploration began by modeling neutral complexes corresponding to **C1** and **C5**, applying DFT [14] with the B3LYP [15] functional, the LANL2DZ [16] pseudopotential for the Au atom and 6-31 + G* basis set for the other atoms, which is known to be an appropriate methodology for the theoretical study of these reactive systems

[12,17]. Final energies in solution (water) were obtained within the Tomasi's polarized continuum model (PCM) [18] as implemented in Gaussian09.

As shown in Fig. 3, no structural peculiarities for **C1** were observed, whereas in **C5** the alkyl chain was folded up around the metal center.

Considering that the metal of the complex must be Au(+1), so as to the hydration of alkynes takes place [19], we modeled zwitterion complexes (ZW) **C1** and **C5**. In this sense, we showed the geometries corresponding to **C1ZW** and **C5ZW** in Fig. 4; besides, we computed the atomic charges by fitting the electrostatic potential (ESP charges) [20]. The DFT calculations showed significant differences between both complexes. In **C1**, the geometric parameters between the neutral and zwitterion species remained without changes, but **C5** showed a strong interaction between the metal and the oxygen atom of the sulfonate group (red dashed line in **C5ZW**, Fig. 4). The distance Au-O in the neutral **C5** was 3.50 Å and it was shortened to 2.07 Å in the zwitterion complex, giving evidence of the strong interaction aforementioned. Moreover, the strong interaction between the gold and oxygen atom of the sulfonate group in **C5ZW** directly affected the distribution of the positive charge on gold center, being lower in **C5ZW** (+0.07) than in **C1ZW** (+0.55).

Based on these results, we calculated the required energy to extend the alkyl chain in **C5ZW**. We elongated the Au-O bond (steps of 0.01 Å each, red dashes line) at B3LYP/6-31 + G* level using the PCM method for introducing the solvent effects (water), with full optimization for the remainder degrees of freedom and we obtained the energy profile shown in Fig. 5.

First we observed two barriers similar in energy (10.7 and 6.0 kcal/mol), that were associated to the interaction of gold and the different oxygen atoms of the sulphonated group. However, the system required 13.3 kcal/mol to move away the alkyl chain from the metal center. Then, we optimized the last structure of this energy profile at 6-31 + G*/LANL2DZ level, to obtain the **C5ZW** conformer with the alkyl chain elongating away from metal. We named this structure **C5'ZW**. As it can be seen on Fig. 6, DFT calculations showed that **C5'ZW** is less stable than **C5ZW** with a difference of 14.1 kcal/mol. Besides, the lack of interaction between the metal and oxygen atom of the sulfonate group in **C5'ZW**, increased the distribution of the positive charge on the gold center, being higher in **C5'ZW** (+0.27) than in **C5ZW** (+0.07). Thus, steric and electronic factors produced by the folded up of alkyl chain over the metal center generate a significant steric hindrance and

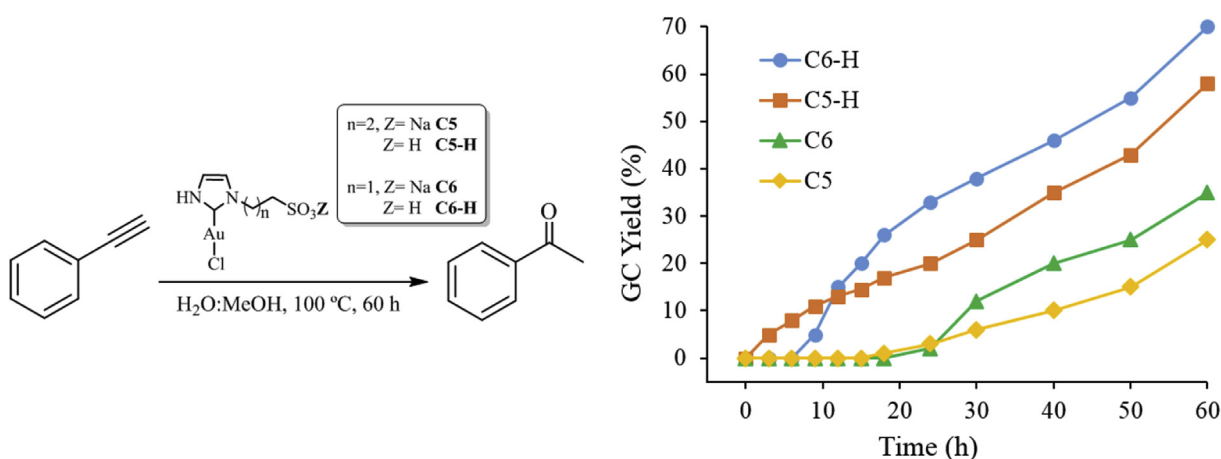


Fig. 7. Comparison of reaction progress: **C5** (◆) and **C6** (▲) vs **C5-H** (■) and **C6-H** (●). Reactions were run in water:methanol (1:1) at 100 °C. (■ and ●, reaction carried out in acid medium, pH = 2).

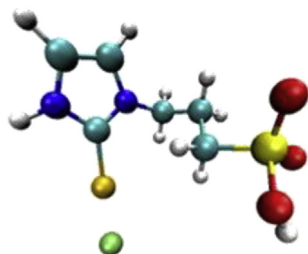


Fig. 8. Geometries for C5-H.

decrease the metal charge in the **C5ZW** conformer. Based on the aforementioned observations, we could assume that the lower reactivity of **C5ZW** compared to that of **C1ZW**, would be related to the high energy that **C5ZW** required to get the more reactive conformer **C5'ZW**.

On the other hand, and taking into account that the effect of the less effective catalyst **C5** could be improved at acid pH (pH = 2) [21], as shown in Fig. 7 [**C5** (◆) vs **C5-H** (■)], being **C5-H** the product obtained when the reaction was carried out in acid medium, see Supporting Information], we modeled the protonated complex **C5-H** for the same conversion (25% conversion, 60 h and 30 h, respectively), following the described calculating methodology. As shown in Fig. 8, the alkyl chain was not folded up around the metal center unlike **C5**. This could be the reason why the complex **C5-H** is more reactive than **C5** (see Fig. 7).

In order to study the effect produced by decreasing the length of the alkyl chain, we synthesized the 2-sulfonatoethyl-complexes **C6** and **C6-H**, and studied their catalytic effects. Fig. 7 shows that the induction time is reduced, improving the catalytic effect [25% conversion, 60 h for **C5** (◆) and 50 h for **C6** (▲)]. Once again, the reaction carried out in acid medium [**C6-H**, (●)] was more efficient (25% conversion in 20 h). It is important to mention that the reaction in the absence of catalyst was negative.

Finally, in order to explain these results, we modeled the -sulfonatoethyl side chain of the neutral complex **C6** and found that the alkyl chain was folded up around the metal center again (Fig. 9). Continuing with the calculating methodology applied to **C5** complex, we modeled the active species -the zwitterion **C6ZW**- and observed that the calculated ESP charge was +0.21 and the distance Au-O was 2.21 Å (Fig. 9). Following the procedures performed on **C5ZW**, we elongated the Au-O bond to get the energy profile for **C6ZW** (see Electronic Supporting Information) and optimized the

last structure to obtain the **C6'ZW** conformer with the alkyl chain elongating away from the metal, and named this structure as **C6'ZW**. As it can be seen in Fig. 9, DFT calculations showed that **C6'ZW** is only 1.1 kcal/mol less stable than **C6ZW**, while the distribution of positive charge on the gold center was higher in **C6'ZW** (+0.49) than in **C6ZW** (+0.21).

We observed a lower energy barrier associated to the conformational interchange in **C6ZW**, which is 13 kcal/mol less than that required for **C5ZW**. This, in conjunction with the higher charge on the metal, and the greater distance Au-O for **C6ZW** compared to **C5ZW**, could justify the higher reactivity of **C6** (see Fig. 7). Based on these results we suggest that the sulfonatoethyl chain (**C6**) is more flexible than the sulfonatepropyl chain (**C5**). Accordingly, **C6ZW** could be more reactive than the zwitterion complex **C5ZW**.

As Fig. 9 shows, according to that observed for the **C5** complex, when the sulfonate group of **C6** was protonated (**C6-H**) the alkyl chain elongated away from metal -the sulfonic acid group was located farther from metal-making it more efficient for catalysis than **C6ZW** (see Fig. 7).

With the aim to complete this theoretical study, we calculated the first step of the catalytic cycle, namely, the coordination of the gold center to the triple bond of the alkyne (Scheme 1) with catalysts **C1ZW** and two conformers of **C5ZW**.

As shown in Fig. 10, this step is energetically favorable for all the studied complexes, being much more exothermic (-91.1 kcal/mol) for the **C1ZW-complex**, which showed the shorter distance between the gold center and the triple bond (2.13 Å). Besides, the formation of **C5ZW**- and **C5'ZW**-complexes, is less energetically favorable than that for **C1ZW**, in agree with the reactivity observed.

3. Conclusions

In summary, based on DFT calculations, we could explain the lowest catalytic effect -in the hydration of phenylacetylene in aqueous media-of **C5** complex compared to **C1** complex in terms of steric arrangement of the 3-sulfonatepropyl chain and ESP charge of the metal center. These calculations also explained the advantageous effect, over the catalysis, of protonating the ligands of **C5-H** and **C6-H** complexes. Finally, and in agree with the reactivity observed, the first step of the catalytic cycle was more energetically favorable for **C1ZW** than for **C5ZW**- and **C5'ZW**-complexes. This work shows that DFT is a successful computational approach for studying these reactive systems.

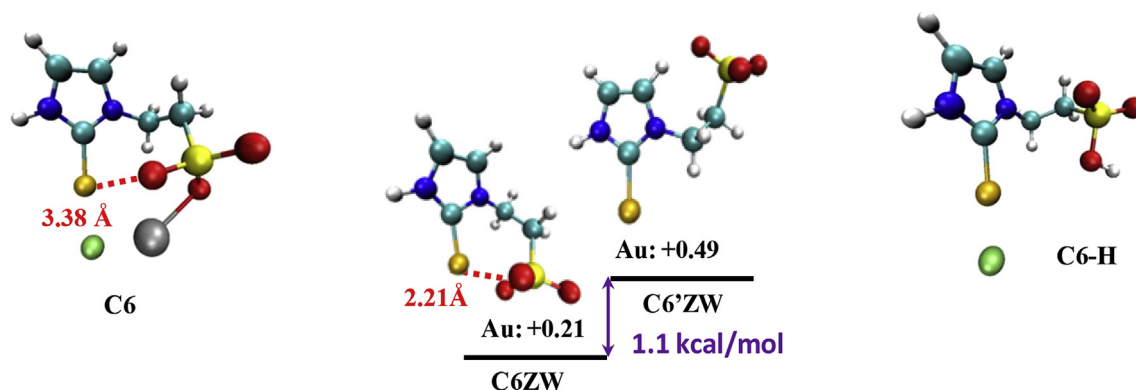


Fig. 9. Geometries for **C6**, **C6ZW**, **C6'ZW**, **C6-H** and ESP charges of Au(+1) for **C6ZW** and **C6'ZW** evaluated by B3LYP/6-31 + G* and LANL2DZ (Au) in the presence of a continuum solvent (water). Energy difference is a ΔE (solvated) value (in kcal/mol).

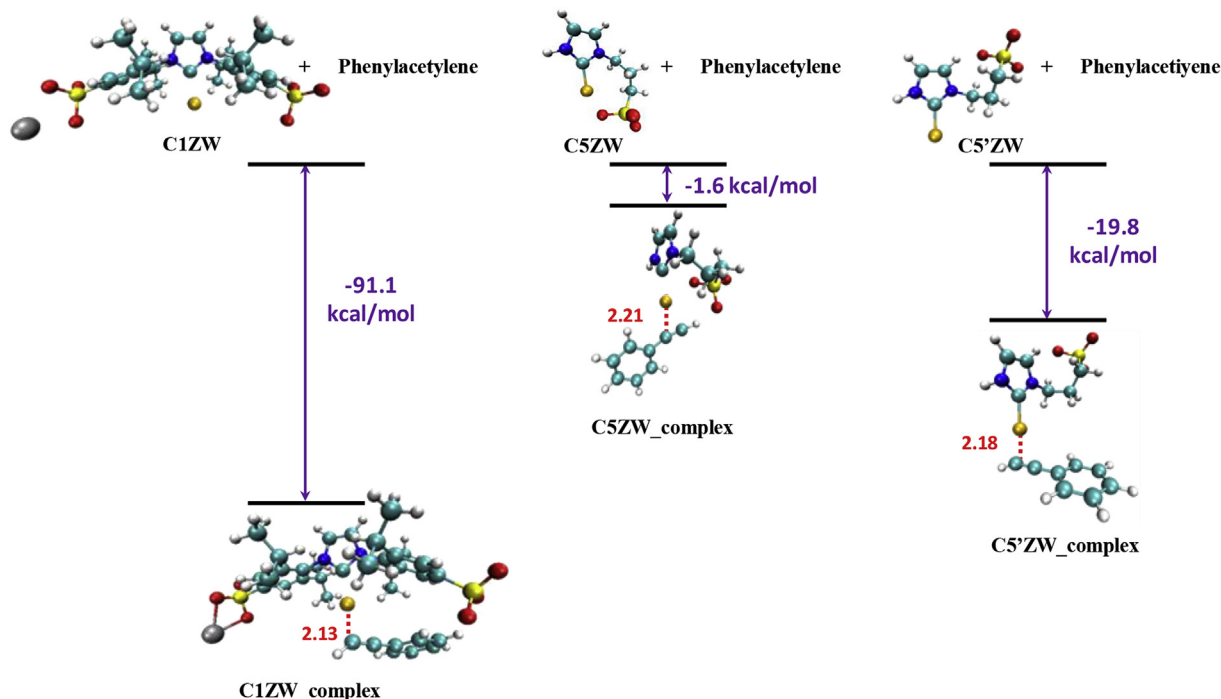


Fig. 10. Geometries for **C1ZW-**, **C5ZW-** and **C5'ZW-complex** evaluated by B3LYP/6-31 + G* and LANL2DZ (Au) in the presence of a continuum solvent (water). Energy difference is a ΔE (solvated) value (in kcal/mol) and all distances Au-C are in Å.

Author contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Acknowledgments

This work was partially supported by ANPCYT (PICT 2010-1830 and PICT 2012-1449), and Universidad Nacional del Sur (PGI 24/Q074). The authors thank Professor Ernesto de Jesús for helpful discussion and comments. CONICET is thanked for a research fellowship to G. A. F.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.jorganchem.2017.09.040>.

References

- [1] E. Levin, E. Ivry, C.E. Diesendruck, N.G. Lemcoff, Water in N-Heterocyclic carbene-assisted catalysis, *Chem. Rev.* 115 (2015) 4607–4692.
- [2] H.-W. Wanzlick, H.-J. Schönherr, Direct synthesis of a mercury salt-carbene complex, *Angew. Chem. Int. Ed.* 7 (1968) 141–142.
- [3] (a) K. Öfele, 1,3-Dimethyl-4-imidazolinyliiden-(2)-pentacarbonylchrom ein neuer Übergangsmetall-carben-komplex, *J. Organometal. Chem.* 12 (1968) 42–43; (b) K. Öfele, M. Herberhold, Tetracarbonylbis(1,3-dimethyl-4-imidazol-2-ylidene)chromium(0), *Angew. Chem. Int. Ed.* 9 (1970) 739–740.
- [4] A.J. Arduengo, R.L. Harlow, M. Kline, A Stable Crystalline Carbene, *J. Am. Chem. Soc.* 113(1991) 361–363.
- [5] (a) S.P. Nolan (Ed.), *N-Heterocyclic Carbenes in Synthesis*, Wiley-VCH, Weinheim, 2006; (b) F. Glorius (Ed.), *N-Heterocyclic Carbenes in Transition-metal Catalysis*, Springer, Berlin/Heidelberg, 2007; (c) , in: *N- S. Heterocyclic Carbenes: from Laboratory Curiosities to Efficient Synthetic Tools*, RSC Catalysis Series, Diez-gonzalez, The Royal Society of Chemistry, 2011.
- [6] (a) M.C. Jahnke, F.E. Hahn, in: R. Chauvin, Y. Canac (Eds.), *Transition Metal Complexes of Neutral η^1 -Carbon Ligands*, Topics in Organometallic Chemistry vol. 30, Springer-Verlag, Berlin/Heidelberg, 2010, pp. 95–129; (b) M.N. Hopkinson, C. Richter, M. Schedler, F. Glorius, An overview of N-heterocyclic carbenes, *Nature* 510 (2014) 485–496.
- [7] (a) H.D. Velazquez, F. Verpoort, N-heterocyclic carbene transition metal complexes for catalysis in aqueous media, *Chem. Soc. Rev.* 41 (2012) 7032–7060; (b) L.-A. Schaper, S.J. Hock, W.A. Herrmann, F. Kühn, Synthesis and application of water-soluble NHC transition-metal complexes, *Angew. Chem. Int. Ed.* 51 (2012) 2–22.
- [8] (a) F. Joó, A.C. Bényei, C.E. Nagy, A. Almássy, Novel sulfonated N-heterocyclic carbene gold(I) complexes: homogeneous gold catalysis for the hydration of terminal alkynes in aqueous media, *Organometallics* 29 (2010) 2484–2490; (b) G.A. Fernández, A.S. Picco, M.R. Ceolín, A.B. Chopa, G.F. Silbestri, Synthesis and structural characterization of water-soluble Gold(I) N-Heterocyclic carbene complexes. An x-ray absorption fine structure spectroscopy (XAFS) study, *Organometallics* 32 (2013) 6315–6323; (c) Y.R. Hristova, B. Kemper, P. Besenius, Water-soluble Au (I) complexes, their synthesis and applications, *Tetrahedron* 69 (2013) 10525–10533.
- [9] G.A. Fernández, A.B. Chopa, G.F. Silbestri, A structure/catalytic activity study of gold(I)-NHC complexes, as well as their recyclability and reusability, in the hydration of alkynes in aqueous medium, *Catal. Sci. Technol.* 6 (2016) 1921–1929.
- [10] (a) A.R. Martin, Y. Makida, S. Meiries, A.M.Z. Slawin, S.P. Nolan, Enhanced activity of [Ni(NHC)CpCl] complexes in arylation catalysis, *Organometallics* 32 (2013) 6265–6270; (b) A. Collado, J. Balogh, S. Meiries, A.M.Z. Slawin, L. Falivene, L. Cavallo, S.P. Nolan, Steric and electronic parameters of a bulky yet flexible N-Heterocyclic carbene: 1,3-Bis(2,6-bis(1-ethylpropyl)phenyl)imidazol-2-ylidene (IPent), *Organometallics* 32 (2013) 3249–3252; (c) U. Jacquemard, P. Harpaiter, S. Roland, Introduction of bulky tert-butyl substituents on the core of N,N'-diaryl N-heterocyclic carbenes through the corresponding vicinal diamines, *Tetrahedron Lett.* 54 (2013) 4793–4795; (d) S.G. Weber, D. Zahner, F. Rominger, B.F. Straub, Mechanistic investigations of a stable, highly active, extremely sterically shielded molecular gold catalyst, *ChemCatChem* 5 (2013) 2330–2335; (e) E. Tomás-Mendivil, P.Y. Toullec, J. Borge, S. Conejero, V. Michelet, V. Cadierno, 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, *ACS Catal.* 3 (2013) 3086–3098; (f) A. Gómez-Suárez, R.S. Ramón, O. Songis, A.M.Z. Slawin, C.S.J. Cazin, S.P. Nolan, Influence of a very bulky N-Heterocyclic carbene in gold-mediated catalysis, *Organometallics* 30 (2011) 5463–5470.
- [11] NOTE: It should be mentioned that the generation of Au nanoparticles (violet coloration of the solution) was not detected. See Ref 9.

- [12] G. Mazzone, N. Russo, E. Sicilia, Homogeneous gold catalysis: hydration of 1,2-diphenylacetylene with methanol in aqueous media. A theoretical viewpoint, *Organometallics* 31 (2012) 3074–3080.
- [13] A. Leyva, A. Corma, Isolable Gold(I) complexes having one low-coordinating ligand as catalysts for the selective hydration of substituted alkynes at room temperature without acidic promoters, *J. Organometal. Chem.* 74 (2009) 2067–2074.
- [14] W. Kohn, I. Sham, Self-consistent equations including exchange and correlation effects, *J. Phys. Rev. A* 140 (1965) 1133–1138.
- [15] (a) C. Lee, W. Yang, R.G. Parr, Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density, *Phys. Rev. B* 37 (1988) 785–789;
(b) A.D. Becke, Density-functional exchange-energy approximation with correct asymptotic behavior, *Phys. Rev. A* 38 (1988) 3098–3100;
(c) E. Miehlich, A. Savin, H. Stoll, H. Preuss, Results obtained with the correlation energy density functionals of Becke and Lee, Yang and Parr, *Chem. Phys. Lett.* 157 (1989) 200–206.
- [16] W.R. Wadt, P.J. Hay, Ab initio effective core potentials for molecular calculations. Potentials for the transition metal atoms Sc to Hg, *J. Chem. Phys.* 82 (270) (1985) 284–299.
- [17] X.-H. Zhang, K.-T. Wang, Theoretical investigation of the mechanism of gold(I)-catalyzed hydrothiolation of alkynes and alkenes with phenanthroline, *RSC Adv.* 5 (2015) 34439–34446 and references therein.
- [18] (a) S. Miertus, E. Scrocco, J. Tomasi, Electrostatic interaction of a solute with a continuum. A direct utilization of Ab initio molecular potentials for the prevision of solvent effects, *Chem. Phys.* 55 (1981) 117–129;
(b) S. Miertus, J. Tomasi, Approximate evaluations of the electrostatic free energy and internal energy changes in solution processes, *Chem. Phys.* 65 (1982) 239–245;
(c) M. Cossi, V. Barone, R. Cammi, J. Tomasi, Ab initio study of solvated molecules: a new implementation of the polarizable continuum model, *Chem. Phys. Lett.* 255 (1996) 327–335.
- [19] The active species are often generated in situ by chloride abstraction from [LAuCl] upon treatment with a silver salt bearing a weakly coordinating anion.
- [20] (a) S.P. Fisher, A. El-Hellani, F.S. Tham, V. Lavallo, Anionic and zwitterionic carboranyl N-heterocyclic carbene Au(I) complexes, *Dalton Trans.* 45 (2016) 9762–9765;
(b) S. Bastin, C. Barthes, N. Lugan, G. Lavigne, V. César, Anionic N-Heterocyclic carbene complexes of Gold(I) as precatalysts for silver-free cycloisomerization of enynes, *Eur. J. Inorg. Chem.* (2015) 2216–2221;
(c) V. Lavallo, J.H. Wright II, F.S. Tham, S. Quinlivan, Perhalogenated carba-closo-dodecaborate anions as ligand substituents: applications in gold catalysis, *Angew. Chem. Int. Ed.* 52 (2013) 3172–3176;
(d) S. Kronig, E. Theuergarten, C.G. Daniliuc, P.G. Jones, M. Tamm, Anionic N-Heterocyclic carbenes that contain a weakly coordinating borate moiety, *Angew. Chem. Int. Ed.* 51 (2012) 3240–3244.
- [21] pKs of complexes C1–C5 is between 6.4 and 7.2, “The sulfonated moiety which is flexible enough to coordinate the metal or to interfere with the reaction center. Such coordination could be eliminated working at an acidic pH.”, See Ref 9.