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Gold Catalysts with Polyaromatic-NHC ligands. Enhancement of Activity by Addition of Pyrene

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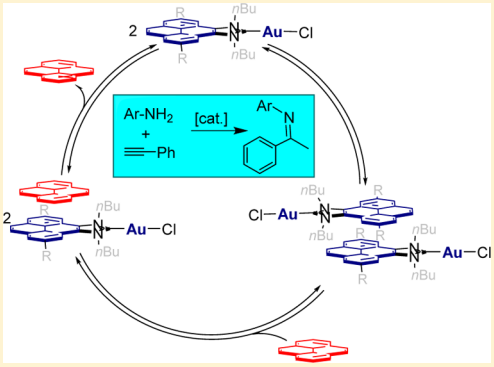
Supporting Information

ABSTRACT: Three Au(I) complexes with N-heterocyclic carbene ligands fused to polycyclic aromatic hydrocarbons (pyrene and phenanthrophenazine) have been obtained and fully characterized. The complexes were tested as catalysts in the hydroamination of terminal alkynes, where they showed moderate to good activity. The addition of a catalytic amount of pyrene to the reaction mixtures produced an improvement in the performance of the catalysts. The study of the reaction order of the catalyst in this reaction indicated that the order is 0.5, indicating that an off-cycle inactive catalyst dimer is formed, as consequence of the self-association of the complex by $\pi-\pi$ stacking interactions. The reaction order in catalyst when pyrene is added to the reaction mixture is $1 > n > 0.5$, therefore being higher than that in the absence of pyrene. Studies made by ^{1}H NMR spectroscopy demonstrate that an important self-association of the catalyst occurs at the concentrations used in the catalytic reactions. The association of pyrene with the catalyst was also observed and quantified by ^{1}H NMR titrations. The studies allowed us to conclude that pyrene influences the activity of the Au(I) catalysts due to reasons related to the modification of the reaction order in the catalyst rather than to allosteric issues.



INTRODUCTION

Originally inspired by enzymatic catalysis, supramolecular catalysis utilizes reversible noncovalent interactions to accelerate reaction rates and/or facilitate highly selective reactions.[1] The development of supramolecular catalysis has been benefited by the advances achieved in the fields of homogeneous catalysis and supramolecular chemistry.[2] As recently defined by Raynal and co-workers, supramolecular catalysis refers to those reactions that involve supramolecular interactions that do not form part of the basic catalytic reaction.[2b] In these types of systems allosteric regulations play an important role, because they determine how the addition of an "effector" may result in an enhancing or inhibiting effect in terms of the activation of a substrate by the catalyst.[3] Inspired by this, many efforts have been made to implement this concept into artificial systems to control chemical reactivity and catalysis. The incorporation of stimuli-responsive features into homogeneous catalysts introduces a new level of control of chemical transformations, allowing these modified systems to perform tasks that cannot be achieved by other means.[4]

Noncovalent interactions such as π-stacking may play an important role in certain types of homogeneously catalyzed reactions. This type of effect has been systematically studied for the case of catalysts containing N-heterocyclic carbene ligands (NHCs).[5] The reason may be that the fan shape of NHCs makes them more prone for establishing effective $\pi-\pi$ interactions with substrates in comparison to cone-shaped phosphines. Some early studies of the influence of π-stacking in reactions catalyzed by NHC-based ligands include the works developed by Grela,[6] Blechert,[7] Collins,[8] Verpoort,[9] and Fürstner[10] and mostly refer to the investigation of olefin metathesis reactions catalyzed by modified Ru-Grubbs type catalysts. An interesting example of the allosteric inhibition of the activity of a Pt(II)-metallocage catalyst by an external additive (pyrene) was described by Peinador, Quintela, and co-workers.[11]

In order to study the influence of π-stacking additives on the catalytic activity of NHC-based metal catalysts, we obtained a series of NHC ligands with fused polycyclic aromatic hydrocarbons.[12] The presence of these extended polyaromatic systems was used to magnify the π-stacking interactions of the ligand with aromatic substrates and with external π-stacking additives, thus boosting the supramolecular effects in the catalytic performances of the catalysts. We observed that the electronic properties of these ligands could be modified upon using suitable π-stacking additives. In particular, we observed that the electron-donating character of the ligands **A**−**C** shown in Chart 1 could be increased by 3 cm^{-1} Tolman Electronic Parameter (TEP) units by simply adding pyrene to a solution of the related metal complexes. On the basis of these results, we performed a number of catalytic studies aiming to determine the influence of the addition of pyrene on the catalytic performances of our complexes bearing NHC ligands with extended polyaromatic systems and, in all cases, we observed

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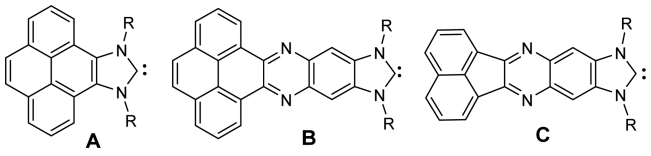
Chart 1. NHC Ligands with Extended Polyaromatic Systems



that the addition of pyrene had an inhibition effect in the activity of our catalysts.[5]

Prompted by these findings, we became interested in obtaining a series of Au(I) complexes with NHC ligands bearing extended polycyclic aromatic systems and in studying the influence of the addition of pyrene on their catalytic properties.

RESULTS AND DISCUSSION

The Au(I) complexes that we obtained in this work were synthesized according to the procedure depicted in Scheme 1. The pyrene-imidazolylidene Au(I) complexes were obtained from the reaction of the corresponding pyrene-imidazolium iodides with silver oxide in methylene chloride to form the corresponding silver-NHC complexes, which we did not isolate. Further addition of [AuCl(SMe_2)] produced the desired Au(I) complexes **1** and **2**, in 63 and 85% yields, respectively. Compound **3** was obtained by deprotonating the phenanthrophenazine-imidazolium salt with NaO*t*Bu and a catalytic amount of NaH in THF at −78 °C. Subsequent addition of [AuCl(SMe_2)] afforded **3** in 54% yield. The NMR spectra of complexes **1**−**3** were in accordance with the 2-fold symmetry of their predicted structures. The ^{13}C NMR spectra revealed the appearance of signals due to the metalated carbene carbons at 177.8, 177.3, and 173.7 ppm for **1**−**3**, respectively.

The molecular structures of **2** and **3** were confirmed by single-crystal X-ray diffraction (Figure 1). The molecular structure of **2** contains a pyrene-imidazolylidene ligand bound to an Au−Cl fragment. The Au−$C_{carbene}$ bond distance is 1.987(3) Å. The Au atom slightly deviates from the plane formed by the extended polycyclic ligand, at a distance of 0.375 Å. Complex **3** contains a phenanthrophenazine-imidazolylidene ligand bound to an Au−Cl fragment. The distance between the Au center and the carbene carbon is 1.982(7) Å. The gold center is on the plane formed by the extended polycyclic ligand,

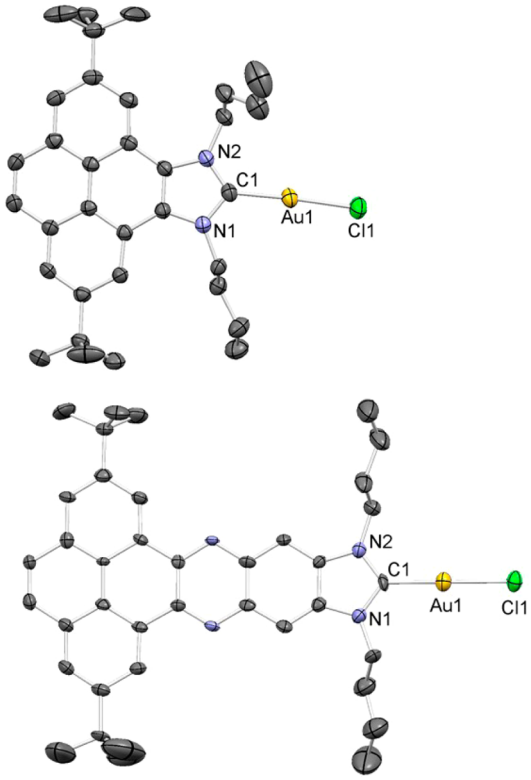
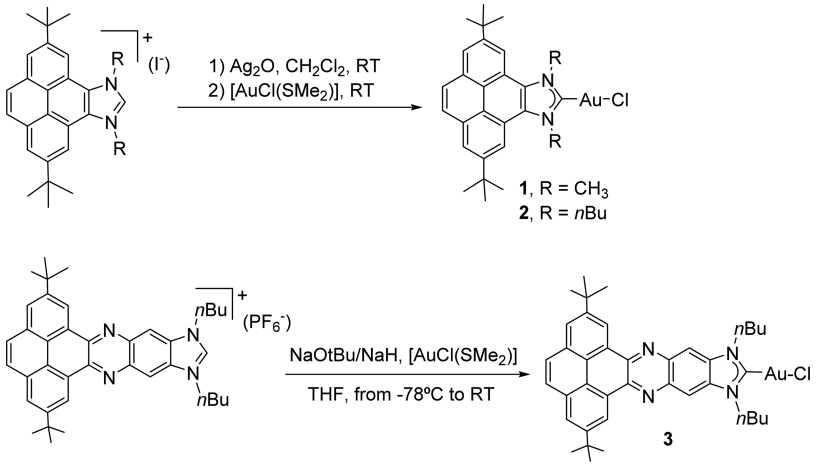


Figure 1. Molecular structures of complexes **2** (above) and **3** (below). Selected bond distances (Å) and angles (deg): complex **2**, Au(1)−Cl(1) 2.2766(8), Au(1)−C(1) 1.987(3), C(1)−Au(1)−Cl(1) 176.30(9); complex **3**, Au(1)−Cl(1) 2.3495(19), Au(1)−C(1) 1.982(7), C(1)−Au(1)−Cl(1) 179.10(2).

and the coordination about the metal center is quasi-linear, as shown by the C−Au−Cl angle of 179.1(2)°.

Complexes **1**−**3** were tested as catalysts in the hydroamination of phenylacetylene, a process for which several Au(I)-based catalysts have shown good activity.[13] The reactions were carried out in acetonitrile at 90 °C, using a catalyst loading of 1 mol %. $AgBF_4$ was added as a chloride scavenger in order to activate the catalyst. The results obtained under these reaction conditions are given in Table 1. From the results shown, it can be observed that catalyst **2** provides the highest yields of the final hydroaminated imine product (product yields

Scheme 1. Synthesis of Au(I) Complexes



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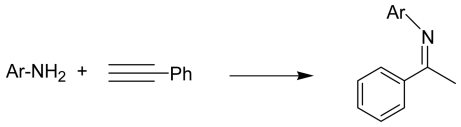
Organometallics 2017, 36, 1447−1451

Table 1. Hydroamination of Phenylacetylene[a]



entry	Ar	catalyst	yield[b]
1	Ph	**1**	44
2	Ph	**2**	88
3	Ph	**2**[c]	99
4	Ph	**3**	21
5	Ph	**3**[c]	36
6	2-MeC_6H_4	**1**	70
7	2-MeC_6H_4	**2**	90
8	2-MeC_6H_4	**2**[c]	92
9	2-MeC_6H_4	**3**	55
10	2-MeC_6H_4	**3**[c]	60
11	4-MeC_6H_4	**1**	50
12	4-MeC_6H_4	**2**	80
13	4-MeC_6H_4	**2**[c]	84
14	4-MeC_6H_4	**3**	29
15	2,4,6-$Me_3C_6H_2$	**1**	41
16	2,4,6-$Me_3C_6H_2$	**2**	68
17	2,4,6-$Me_3C_6H_2$	**2**[c]	82
18	2,4,6-$Me_3C_6H_2$	**3**	37
19	2,4,6-$Me_3C_6H_2$	**3**[c]	40
20	2,6-$iPr_2C_6H_3$	**1**	39
21	2,6-$iPr_2C_6H_3$	**2**	62
22	2,6-$iPr_2C_6H_3$	**2**[c]	77
23	2,6-$iPr_2C_6H_3$	**3**	54

[a]Reaction conditions unless specified otherwise: 0.5 mmol of phenylacetylene, 0.55 mmol of amine, 1 mol % of [cat.], 2 mol % of $AgBF_4$, 1 mL of MeCN, 90 °C, 6 h. [b]Yields determined by GC using anisole (0.5 mmol) as internal standard. [c]Addition of 0.05 mmol of pyrene.

ranging from 62 to 90%). All in all, catalyst **2** is less active than other NHC-Au(I)-based catalysts previously reported by us.[13f] An interesting observation that we can extract from the analysis of the data is that catalyst **3** affords the lowest activity (product yields in the range of 21−55%), a fact that contrasts with the weaker electron-donating character of the phenanthrophenazine-imidazolylidene ligand in comparison to the pyrene-imidazolylidene ligand, which should make us expect a higher activity for **3**, due to the more electrophilic character of its gold center.[14] Prompted by this result, we decided to perform further studies in order to elucidate if supramolecular interactions may have some influence over the catalytic properties of these three catalysts, because catalysts with NHC ligands with polyaromatic fragments are known to be strongly influenced by supramolecular effects on their activities.[5] First, we performed the catalytic reactions adding a catalytic amount of pyrene (10 mol % with respect to the concentration of the substrates) in order to study if the addition of this molecule may have an influence over the outcome of the process. For this study we decided to use catalysts **2** and **3**, these being the most and least active among the three complexes described in this work. The results indicated that, in all cases, the addition of pyrene produced a clear increase in the activity of the catalysts, with benefits within the range of a 5−15% increase in the product yields. This result is remarkable because, in all other cases reported in which pyrene was added into a catalytic reaction, its allosteric effect was always inhibitory, rather than beneficial.[5,11] In order to get a clearer insight into the influence of pyrene on the reaction process, we decided to monitor the reaction by studying the time-dependent reaction profile of the coupling of phenylacetylene with aniline. As can be seen from the profiles shown in Figure 2, the addition of pyrene not only offers higher yields in shorter

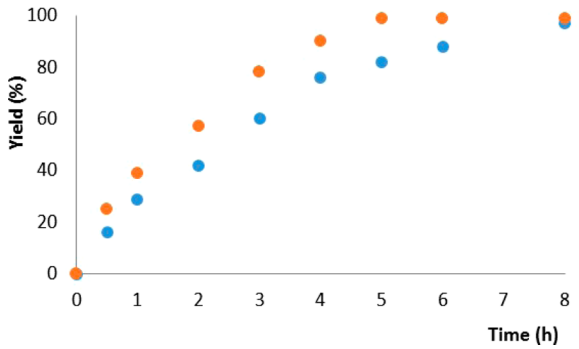


Figure 2. Time-dependent reaction profile of the hydroamination of phenylacetylene with aniline using catalyst **2** (1 mol %) with (orange dots) and without (blue dots) addition of pyrene. All reactions were carried out under the same conditions described in Table 1.

reaction times but also accelerates the reaction from the beginning, thus indicating that the higher activity of the catalyst is due to kinetic reasons, rather than to thermodynamic reasons (i.e., stability of the catalysts).

The study of the reaction profiles of the coupling of phenylacetylene with aniline at different concentrations of the catalyst allowed us to determine the reaction order with respect to the concentration of the catalyst. We used the normalized time scale method for determining the order in catalyst.[15] This method uses a normalized time scale, $t[cat]^n$, where n is the order in catalyst. Figure 3 shows the time-dependent reaction profiles at different catalyst concentrations (Figure 3a), together with a graphic in which the scale is normalized assuming a reaction order of 0.5, which was the value giving the best fit (Figure 3b). This reaction order is consistent with the order that we obtained for other pyrene-functionalized homogeneous catalysts that we recently reported[12d] and is suggestive of the formation of an off-cycle catalytic dimer that is in fast equilibrium with the active monomer species. Owing to this equilibrium, the concentration of monomer is not linearly proportional to the total concentration of catalyst added, and this explains why the order in catalyst is <1. A different situation arises when pyrene is added to the reaction mixture. In this case, the best fitting corresponds to a first order in catalyst, as shown by Figure 3c. This result is very interesting, because it suggests that pyrene associates with **2** and therefore competes with the self-association process, thus partially avoiding the formation of the nonactive dimer. It has to be taken into account that the reaction order of 1 associated with the process performed with the addition of pyrene has to be taken as a crude estimate. A more accurate analysis should indicate that for this case the reaction order "n" should be a fractional number in the range $0.5 < n < 1$, because it is highly unlikely that under the reaction conditions used in these experiments the addition of pyrene results in the 100% formation of pyrene complex **2** aggregates, therefore completely avoiding the self-association of the catalyst.

In order to confirm that self-association of **2** is taking place in acetonitrile, we performed a series of ^1H NMR spectra in

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Organometallics 2017, 36, 1447−1451

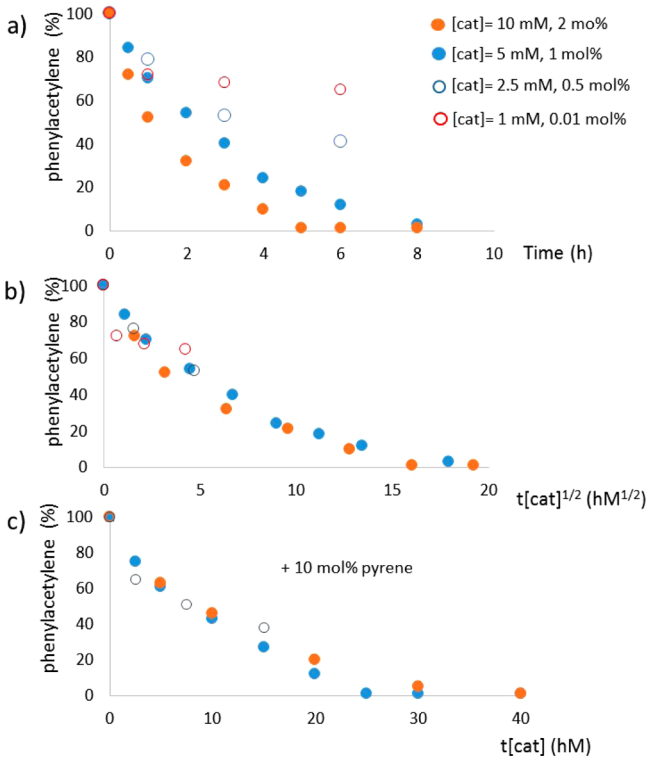

Figure 3. (a) Time-dependent reaction profile of the reaction of phenylacetylene with aniline using catalyst **2**. (b) Reaction profile with normalized time scale assuming a catalyst order of 1/2. (c) Reaction profile for the same reaction with addition of 10 mol % of pyrene and with a normalized time scale assuming a catalyst order of 1. Reaction conditions are the same as those shown in Table 1. In all three graphics the evolution is shown as consumption of phenylacetylene.

CD_3CN at different concentrations of the complex. Figure 4 shows a series of spectra of the complexes at concentrations ranging from 1 to 20 mM. The analysis of the spectra indicates that one of the signals assigned to an aromatic proton of the

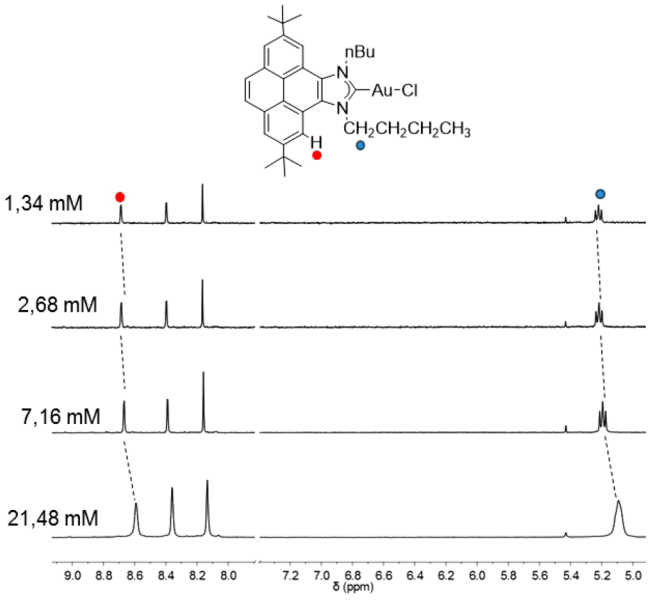

Figure 4. Selected region of a series of ^{1}H NMR spectra (400 MHz) of complex **2** in CD_3CN at different concentrations.

pyrene moiety is shifted upfield by 0.1 ppm upon an increase in the concentration of the complex. The signal due to the protons of the methylene group bound to the nitrogen atoms of the imidazolylidene are also significantly upfield shifted ($\Delta\delta$ = 0.13 ppm). This observation is a clear indication that the complex shows significant self-association in the range of 1−20 mM, which is the concentration range used in our catalytic experiments. The nonlinear regression analysis of the data of this series of spectra indicated that the self-association constant is in the range of 3−5 M^{-1} (a more accurate result could not be given due to the precipitation of the complex at concentrations higher than 20 mM, thus not allowing a study with a sufficient wide range of concentrations). Then we performed ^{1}H NMR studies in order to determine if **2** associates with pyrene in the range of concentrations used in the catalytic experiments. The ^{1}H NMR titrations were performed at constant concentrations of **2** (1 mM) and with monitoring of the variation of the chemical shifts of the signals of the ligand of the complex upon adding increasing amounts of pyrene. The addition of the solution of pyrene induced important perturbations in the ^{1}H NMR spectra of **2**, indicating the formation of aggregates that showed fast kinetics on the NMR time scale. We assumed that these aggregates are formed by $\pi-\pi$ stacking interactions between the molecules of pyrene and the pyrene moiety of complex **2**. As can be observed from the series of spectra shown in Figure 5, the signal due to one of the protons of the pyrene is

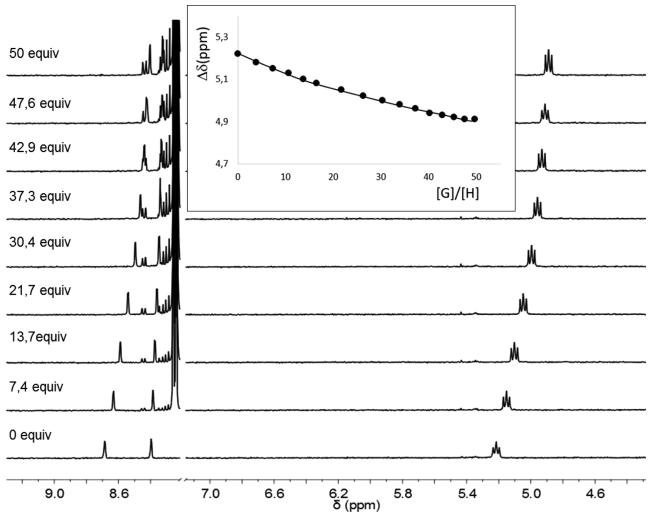

Figure 5. Representative region of the ^{1}H NMR (400 MHz) spectra of the titration of **2** with pyrene in CD_3CN. The spectra were recorded at a constant concentration of **2** (1 mM). The inset plot is the resulting binding isotherm, which returns an association constant of k_{11} = 12 ± 2 M^{-1} (H = **2**; G = pyrene).

shifted upfield by 0.26 ppm, while the signals due to the N−CH_2 protons are shifted by 0.31 ppm. The analysis of the spectra also allowed us to determine that the stoichiometry of the aggregate complex formed by association of pyrene and **2** is 1:1. This assumption is based on the analysis of the binding isotherm resulting from the titration experiment, which gave the lowest residuals for this stoichiometry.[16] A Job plot analysis also supported the formation of the 1:1 complex (see the Supporting Information). The nonlinear regression analysis[16,17] of the curve returned a non-negligible association constant of k_{11} = 12 ± 2 M^{-1}, thus demonstrating the affinity of **2** to form π-stacking aggregates with pyrene in milimolar concentrations.

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Organometallics 2017, 36, 1447−1451

This result indicates that, under the reaction conditions that we used for our catalytic experiments (1 mol % = 5 mM of **2**, 50 mM of pyrene, in CH_3CN), about 35% of the catalyst is forming a host−guest complex with pyrene.

CONCLUSIONS

In summary, we prepared three Au(I) complexes bearing NHC ligands with fused polycyclic aromatic hydrocarbons. The complexes were used as catalysts for the hydroamination of phenylacetylene, where they showed moderate to good activities. The activities of the catalysts were significantly enhanced by addition of a catalytic amount of pyrene. The preliminary kinetic studies indicated that the addition of pyrene produces an increase in the reaction order with respect to the concentration of the catalyst. This increase is attributed to the formation of $\pi-\pi$ stacking aggregates between the molecules of pyrene and the catalyst, which in turn partially avoids self-association of the catalyst. The self-association of the catalyst and the formation of supramolecular aggregates between the catalyst and pyrene were confirmed by ^{1}H NMR titrations and by using well-known host−guest chemistry procedures.

We believe that the results presented in this article are of high importance for the development of new supramolecular catalysts. Our work demonstrates that pyrene influences the activity of a family of homogeneous catalysts of Au(I), due to reasons related to the modification of the reaction order in the catalyst rather than to—probably more intuitive—allosteric issues (i.e., modification of the electronic properties of the catalyst by perturbation of the orbitals of the ligand by π-stacking interactions with the additive).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.7b00172.

Description of synthetic procedures and characterization details, catalytic experiments, spectra of the new complexes, crystallographic data, and ^{1}H NMR spectra from host−guest titrations (PDF)

Crystallographic data (CIF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) *Supramolecular Catalysis*; Van Leeuwen, P. W. N. M., Ed.; Wiley-VCH: Weinheim, Germany, 2008.

(2) (a) Raynal, M.; Ballester, P.; Vidal-Ferran, A.; van Leeuwen, P. W. N. M. *Chem. Soc. Rev.* **2014**, *43*, 1734−1787. (b) Raynal, M.; Ballester, P.; Vidal-Ferran, A.; van Leeuwen, P. W. N. M. *Chem. Soc. Rev.* **2014**, *43*, 1660−1733.

(3) (a) Vlatkovic, M.; Collins, B. S. L.; Feringa, B. L. *Chem. - Eur. J.* **2016**, *22*, 17080−17111. (b) Kumagai, N.; Shibasaki, M. *Catal. Sci. Technol.* **2013**, *3*, 41−57. (c) Kremer, C.; Lutzen, A. *Chem. - Eur. J.* **2013**, *19*, 6162−6196. (d) Goodey, N. M.; Benkovic, S. J. *Nat. Chem. Biol.* **2008**, *4*, 474−482.

(4) (a) Blanco, V.; Leigh, D. A.; Marcos, V. *Chem. Soc. Rev.* **2015**, *44*, 5341−5370. (b) Peris, E. *Chem. Rev.* **2017**, DOI: 10.1021/acs.chemrev.6b00695.

(5) Peris, E. *Chem. Commun.* **2016**, *52*, 5777−5787.

(6) Samojlowicz, C.; Bieniek, M.; Zarecki, A.; Kadyrov, R.; Grela, K. *Chem. Commun.* **2008**, 6282−6284.

(7) Rost, D.; Porta, M.; Gessler, S.; Blechert, S. *Tetrahedron Lett.* **2008**, *49*, 5968−5971.

(8) Grandbois, A.; Collins, S. K. *Chem. - Eur. J.* **2008**, *14*, 9323−9329.

(9) Ledoux, N.; Allaert, B.; Pattyn, S.; Vander Mierde, H.; Vercaemst, C.; Verpoort, F. *Chem. - Eur. J.* **2006**, *12*, 4654−4661.

(10) Fürstner, A.; Ackermann, L.; Gabor, B.; Goddard, R.; Lehmann, C. W.; Mynott, R.; Stelzer, F.; Thiel, O. R. *Chem. - Eur. J.* **2001**, *7*, 3236−3253.

(11) Lopez-Vidal, E. M.; Fernandez-Mato, A.; Garcia, M. D.; Perez-Lorenzo, M.; Peinador, C.; Quintela, J. M. *J. Org. Chem.* **2014**, *79*, 1265−1270.

(12) (a) Valdes, H.; Poyatos, M.; Ujaque, G.; Peris, E. *Chem. - Eur. J.* **2015**, *21*, 1578−1588. (b) Valdes, H.; Poyatos, M.; Peris, E. *Inorg. Chem.* **2015**, *54*, 3654−3659. (c) Valdes, H.; Poyatos, M.; Peris, E. *Organometallics* **2014**, *33*, 394−401. (d) Ruiz-Botella, S.; Peris, E. *Chem. - Eur. J.* **2015**, *21*, 15263−15271.

(13) (a) Pouy, M. J.; Delp, S. A.; Uddin, J.; Ramdeen, V. M.; Cochrane, N. A.; Fortman, G. C.; Gunnoe, T. B.; Cundari, T. R.; Sabat, M.; Myers, W. H. *ACS Catal.* **2012**, *2*, 2182−2193. (b) Katari, M.; Rao, M. N.; Rajaraman, G.; Ghosh, P. *Inorg. Chem.* **2012**, *51*, 5593−5604. (c) Canovese, L.; Visentin, F.; Levi, C.; Santo, C. *Inorg. Chim. Acta* **2012**, *391*, 141−149. (d) Alvarado, E.; Badaj, A. C.; Larocque, T. G.; Lavoie, G. G. *Chem. - Eur. J.* **2012**, *18*, 12112−12121. (e) Gaillard, S.; Bosson, J.; Ramon, R. S.; Nun, P.; Slawin, A. M. Z.; Nolan, S. P. *Chem. - Eur. J.* **2010**, *16*, 13729−13740. (f) Gonell, S.; Poyatos, M.; Peris, E. *Angew. Chem., Int. Ed.* **2013**, *52*, 7009−7013.

(14) Ibañez, S.; Poyatos, M.; Dawe, L. N.; Gusev, D.; Peris, E. *Organometallics* **2016**, *35*, 2747−2758.

(15) Bures, J. *Angew. Chem., Int. Ed.* **2016**, *55*, 2028−2031.

(16) Thordarson, P. *Chem. Soc. Rev.* **2011**, *40*, 1305−1323.

(17) Lowe, A. J.; Pfeffer, F. M.; Thordarson, P. *Supramol. Chem.* **2012**, *24*, 585−594.

DOI: 10.1021/acs.organomet.7b00172
Organometallics 2017, 36, 1447−1451