Article

A Few Questions about Single-Atom Catalysts: When Modeling Helps

Giovanni Di Liberto, Sergio Tosoni, Luis A. Cipriano, and Gianfranco Pacchioni*

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CONSPECTUS: Single-atom catalysis (SAC) is a fascinating and rapidly growing field in heterogeneous catalysis. In less than 20 years, this has become one of the most widely investigated subjects by the catalytic community for various good reasons: the ability to synthesize active catalysts using a minimum amount of precious metals, the expected higher selectivity of SACs compared to assemblies of nanoparticles of variable sizes, and the fact that SACs represent a bridge between homogeneous and heterogeneous catalysis. The relative simplicity of SAC structures compared to classical heterogeneous catalysts based on supported metal nanoparticles has stimulated an intense simulation activity aimed at predicting new potential catalysts from first principles, often based on machine learning algorithms. This is a very ambitious objective and ultimately represents the final goal of every modeling activity: the possibility to provide realistic predictions of new material properties and catalytic reactivity. However, one of the main reasons that theory is useful is and remains the interpretation and analysis of experimental results, with the no less crucial goal of understanding the basic principles that determine a certain functionality or reactivity. The combination of advanced characterization techniques and theoretical calculations can provide a general conceptual framework to better understand structure−function relationships. In this Account, we will address this aspect in trying to provide answers to some fundamental questions related to the structure, stability, and activity of SACs. We will start by addressing a question that arises every time a new SAC is synthesized: where are the metal atoms? What is their coordination mode with the support? Once we have shown how to address this point, we will move on to the next fundamental question: do the single atoms stay put? How does the chemical environment of a SAC depend on the preparation or reaction conditions? Next, we will analyze the importance of a full characterization of the reaction mechanism to predict reactivity. SACs, due to their analogy to coordination compounds, can form intermediates that do not exist on the surface of metal electrodes. The formation of these intermediates can influence the kinetics of the process and must be considered in the simulation. Finally, we will briefly address a more general question: how does the catalytic activity of SACs compare with that of the corresponding supported metal nanoparticles on the one hand or homogeneous molecular complexes on the other? The final message is that to answer these questions and to take full advantage of quantum chemical modeling, the results of the calculations should be continuously verified with experimental data in a cross-fertilization that is beneficial for both sides.
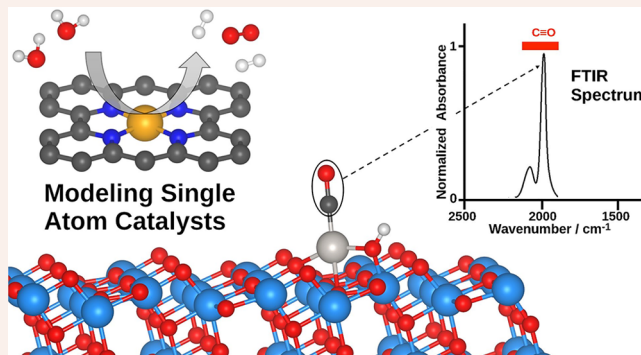
1. INTRODUCTION

There are two main motivations behind the large amount of work devoted in the past 50 years to developing methods and algorithms to solve the Schrödinger equation in materials science and catalysis.[1] One is the possibility to interpret experimental results, mostly spectroscopic measurements, so as to provide a conceptual framework that explains and rationalizes the appearance of a given chemical behavior or physical−chemical property. The second motivation is to predict new systems of potential interest for a given material functionality or catalytic reaction and stimulate experimental activities. There is no question that the second goal is by far more ambitious and challenging than the first one due to the large and often unknown number of variables that contributes to

the overall behavior of a material and, in particular, of a catalyst. However, the first goal, rationalization and understanding, is not of minor importance and practical value.

In this respect, the progress made from the birth of modern quantum chemistry until the present day is amazing.[2] This is due to the development of new theoretical frameworks,[3] the

development of powerful and user-friendly computer codes,[4] and the exponential growth of computing power (at least 8 orders of magnitude in a half century). Nevertheless, the use of theory to provide unexplored routes for the design of novel catalysts remains extremely difficult, probably more than is usually appreciated. Heterogeneous catalysts are complex systems, their functionality depends on several contributions often working in parallel, and their nature changes with time and during the catalytic process, making a clear identification of the structure–properties relationship difficult. In this respect, the advent of catalysts based on single atoms[5] or single sites[6] represents an important step forward because it significantly reduces the complexity with respect to other types of catalysts consisting, for instance, of supported metal nanoparticles on a more or less "inert" support. In this case, in fact, the activity critically depends on the size, shape, composition, fluxionality, and stability of the nanoparticle and often is the result of all of these aspects taken together. Furthermore, supported particles are never monodisperse, and the final activity is the result of the convolution of the activity of each particle involved in the reaction.

The possibility, at least in principle, to deal with a single atomic site greatly reduces the configuration space to explore with first-principles calculations. Thus, it is not surprising that the number of studies dealing with the screening of new potential catalysts has grown very rapidly in parallel with the interest in SACs.[7,8] Furthermore, many examples have been reported where SACs are stabilized on two-dimensional carbon-based matrixes, such as variously doped graphene layers, carbon and boron nitrides, and so forth.[9] Compared to an oxide surface, which exhibits a variety of defects and morphological irregularities, a graphene layer is incomparably easier to model by first principles calculations. Not surprisingly, we assist in the continuous growth of model studies in this area, also based on machine learning algorithms,[10] with the aim of screening large numbers of hypothetical structures to be tested in subsequent experiments.

Things, however, are not so simple. Despite the lower complexity of a SAC compared to supported nanoparticles, there are various elements that make the use of theory delicate. Some of these problems have been recently examined in a dedicated Perspective article.[11] For sure, the most powerful approach to the problem remains the combination of theoretical with experimental studies. Since real catalysts are complex systems in terms of structure and composition, in the past decades a lot of progress was made by considering model systems under controlled conditions, such as oxide single crystals or thin films with supported nanoparticles of known shape and structure.[12] This allowed us to study chemical reactions in special environments (e.g., under UHV conditions) and for well-defined structures of the catalyst, allowing a robust integration of computer modeling with experimental measurements. When information from model systems is not available, a direct comparison with actual catalysts is of course possible, provided that special care is dedicated to making sure that what is computed corresponds to what is measured. When this is the case, theory represents an invaluable tool to complement, integrate, and expand the knowledge obtained from microscopy or spectroscopy.

In the following text, we provide some examples, trying to answer some fundamental questions arising when one is dealing with SACs. The first question is also the simplest one: where are the single atoms on the support? If one wants to model a SAC,

then it is essential to know the local coordination and bonding of the isolated metal atom to the support. This question is more difficult to answer than one may expect. In fact, it is only from the combination of a variety of techniques, including electronic structure calculations, that one can come to a firm assignment of the structure of a SAC.

Identifying the nature of the SAC under static conditions may not be enough. A central question in catalysis deals with the thermal stability and the mobility of the active species. Therefore, the natural question once one has identified the position of a SAC on a surface is, does the SAC stay put when the external conditions change? Once more, answering this question from theory only is difficult. However, the combination of first principles thermodynamics with accurate spectroscopy and microscopy measurements can be very illuminating with respect to the behavior of SACs under different chemical environments.

The third question is related to the role of the intermediates that form in the course of a reaction. In the last few years, a tendency has emerged to apply models and descriptors created or identified for reactions that occur on extended surfaces (metal electrodes, oxide single crystals, etc.) to the case of SACs. However, SACs differ profoundly from metal surfaces and are conceptually closer to coordination complexes and homogeneous catalysts.[13] The very same reaction can follow different mechanisms when performed on a metal electrode or on a coordination compound. We will provide an example showing how this can impact the theoretical predictions.

The final question is also the most ambitious one. SACs are new systems with interesting activity and selectivity and potential use in a variety of processes. Nevertheless, one fundamental question remains: are SACs superior catalysts compared to traditional systems, either homogeneous or heterogeneous? To answer this question, we will consider two examples. In the first one, we will compare the activity of a Au SAC with that of supported Au nanoclusters and nanoparticles. In the second example, we will discuss the performances of Cu-based SACs with those of corresponding homogeneous catalysts. While no general conclusion can be drawn from just two examples, this kind of comparison can be useful to put the chemistry of SACs in a more general context.

2. WHERE ARE THE ATOMS?

2.1. Combine IR, TPD, and DFT for the Unique Identification of SACs

Identifying the exact position of the active site is one of the major challenges in heterogeneous catalysis. SACs are not an exception. The first aspect to deal with is to demonstrate the atomic nature of the species and, when possible, the local coordination with the support.[14] This is a key aspect since the same atom can behave very differently depending on the local coordination. To show this, we recently performed a simple numerical experiment based on density functional theory (DFT).[15] We incorporated 24 transition-metal atoms in a nitrogen-doped graphene support, and we studied the catalytic activity in the hydrogen evolution reaction (HER) as a function of the transition metal. Not surprisingly, the activity, which according to a widely used model is directly related to the free energy of H adsorption, ΔG_H (see below), varies a lot, with some atoms very active and others completely inactive. This corresponds to ΔG_H going from +2.0 to −1.0 eV as a function of the transition metal. The same wide range of reactivity can be obtained by fixing the metal atom, Pt in this case, and changing
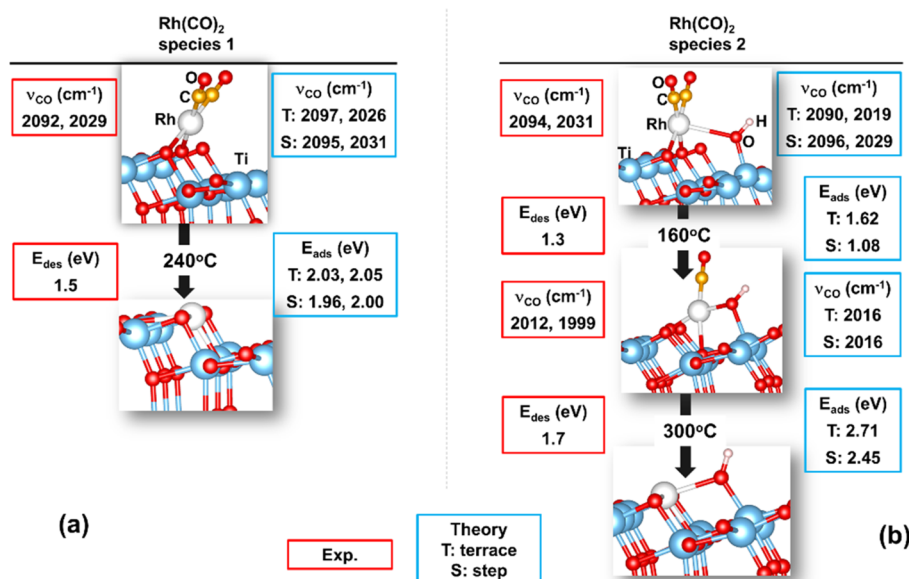
Figure 1. Structure of $Rh(CO)_2$ species identified based on FTIR and TPD spectra and DFT calculations and their evolution with temperature. (a) $(Rh)_{ads}$ and (b) $(RhOH)_{ads}$ species. Red boxes (left): experimental results. Blue boxes (right): DFT results. Reproduced with permission from ref 19. Copyright Royal Society of Chemistry 2020.

the local environment (for instance, by replacing the nitrogen neighbors of Pt with carbon or oxygen atoms).[15] The range of adsorption free energies goes from +1.5 to −1.5 eV, showing that in SACs the metal center is as important as the surroundings. (In this respect, the notion of a single-atom catalyst is a bit misleading.)

This demonstrates the importance of properly identifying the exact coordination of the active center. Some experimental techniques provide evidence of the absence of metal–metal bonds (e.g., extended X-ray absorption fine structure, EXAFS) or of the isolated nature of the atom and the registry with the support (high-resolution transmission electron microscopy, HRTEM). Other information comes from the analysis of the thermal stability of the SAC or from its oxidation state (X-ray photoemission, XPS). All of these data can be matched with theoretical results. But for a throughout and unambiguous analysis of the local bonding, this is not sufficient, and other approaches need to be considered, including electronic structure calculations that are often used to interpret these spectroscopies and microscopies. Another approach consists of the use of adsorbed probe molecules, such as CO, NO, CO_2, phosphines, and so forth. However, CO is the most widely used due to its low reactivity and high sensitivity and can provide important information through the measurement of the CO vibrational frequency and the adsorption energy. These properties are accessible via Fourier transform infrared spectroscopy (FTIR) and temperature-programmed desorption (TPD) spectra, respectively. The resulting spectra can be used to verify the predictions of DFT calculations. When this is the case, this is strong proof that the structure of the SAC used in the calculations coincides with or is very close to that present on the real samples.[16−21]

This approach turned out to be quite successful in the identification of isolated Rh, Ru, and Pt atoms deposited on two representative oxides, anatase TiO_2 (a reducible oxide)[17−19] and tetragonal ZrO_2 (a nonreducible oxide).[16,20] Theory allows one to consider several possible sites. (For a graphical representation of these sites, please consult ref 20.) The metal atom (M) can replace a surface cation, $(M)_{subCat}$, which is equivalent to adsorb M in a cation vacancy, or can replace a lattice O, $(M)_{subO}$ (M adsorption on a O vacancy); it can be simply adsorbed on the surface, $(M)_{ads}$, or form a $(MO)_{ads}$ unit where it is bound to an O atom on the surface. It can also form a $(MO_2)_{ads}$ unit, where M is attached to two extra O atoms, or even $(MOH)_{ads}$ species, where the metal interacts with one or more surface hydroxyl groups. For each of these sites, one can study the interaction with CO and the resulting M–CO, $M(CO)_2$, or, in a few cases, even $M(CO)_3$ surface complexes. In fact, transition-metal atoms can bind more than one CO molecule. The bond strength of CO to the M center varies with the site where M is adsorbed, and an increase in temperature will result in selective CO desorption with consequent changes in the vibrational spectra: while symmetric and antisymmetric CO stretching can be measured (and computed) for geminal $M(CO)_2$ species, only one band is expected for linearly bound CO. Interestingly, from spectroscopic measurements one can also deduce the angle formed by the two CO molecules in $M(CO)_2$ geminal carbonyls, another feature that can be computed and compared with DFT results. But the most relevant property is the CO stretching frequency. This is very sensitive to the nature of the M center and is blue-shifted or red-shifted depending on the nature of the M–CO bond: M atoms in high oxidation states give rise to an increase in the CO frequency,[22] while neutral M centers in zero or low oxidation states result in a decrease in this property due to the occurrence of charge back-donation to the $2\pi^*$ antibonding orbital of CO.[23] The calculation of the CO vibrational shift sometimes presents problems related to the level of the DFT approach used.[24] This, however, is mostly related to CO bound to cation centers where electrostatic contributions dominate. On M atoms or on SACs, the calculation of the CO frequency poses in general fewer problems. For the results discussed in this section, we simply scaled the computed frequencies by a factor 1.01 that takes into account a 1% underestimate of the frequency of free CO in DFT compared to experiment. Thus, the following set of information can be obtained in parallel from theory and experiment:

- oxidation state of the metal;
- thermal stability of the SAC;
- C−O stretching frequency for M(CO) monocarbonyls;
- symmetric and antisymmetric stretching modes for $M(CO)_2$ dicarbonyls;
- more complex IR spectra arising from $M(CO)_3$ complexes (when present);
- CO−M−CO angle for geminal complexes; and
- CO binding energies ($M(CO)_2 \rightarrow M(CO) + CO$; $M(CO) \rightarrow M + CO$).

Real catalyst supports exhibit morphological irregularities, and the characteristics mentioned above can be computed for M atoms on flat terraces as well as on stepped or defective surfaces. This results in a sufficiently large set of data. The logic is stringent: if a particular site exhibits a good level of agreement with the measured data, then it is a likely candidate for the specific location of the SAC.

In a systematic study of Rh, Ru, or Pt atoms on TiO_2 and ZrO_2, we compared data obtained from different experiments and preparation procedures with DFT calculations performed using the same computational setup. A general behavior emerged. Under no circumstance was the M atom found to be in a lattice position, replacing Ti, Zr, or O ions on the oxide surface. Evidence for this is that (1) if CO is adsorbed on M_{sub} sites, then the C−O frequency is off by 100−200 cm^{-1} with respect to the measured one and (2) CO adsorbed on M_{subCat} tends to react with lattice oxygen atoms to form CO_2 that desorbs, an effect that has been explicitly ruled out experimentally. With one exception (Rh on TiO_2), the $(M)_{ads}$ species are also not good candidates to explain the chemistry of these SACs: $(M)_{ads}$ species are in the zero oxidation state, and they give rise to large red shifts of the CO frequency, never observed experimentally. Furthermore, $(M)_{ads}$ species are mobile and tend to aggregate, in contrast with the observed high thermal stability of the SAC.[25]

The best candidates for the local structure of Rh, Ru, and Pt SACs on TiO_2 and ZrO_2 correspond to M atoms adsorbed on the surface and further stabilized by the interaction with one or two OH groups or O adatoms.[16−20] These extra O atoms can result from the direct interaction of the metal atom with a hydroxyl group: $M + OH \rightarrow MO + {}^1/_2 H_2$. These sites, $(MO)_{ads}$, $(MO_2)_{ads}$, and $(MOH)_{ads}$, are interesting for the following reasons: (1) the M atom is in a positive oxidation state, as often observed in XPS; (2) the presence of the extra O atoms or OH groups results in stronger bonding to the surface, consistent with the high thermal stability of these species; (3) the CO adsorption energies; (4) the CO vibrational frequencies are in excellent agreement with the measured ones (Figure 1). While just one of these features could be due to fortuitous agreement with the experiment, the combination of several features for M atoms stabilized at terrace and step sites of the oxides considered represents a strong indication that this is the actual species present on the catalyst. Of course, one should keep in mind the possibility that CO adsorption results in an increased mobility of the M−CO complexes, favoring CO-induced diffusion and/or agglomeration.[26]

To better illustrate this approach, we briefly discuss the interesting case of a Rh single atom supported on anatase $TiO_2(101)$.[19] Strong electrostatic adsorption was used to synthesize atomically dispersed Rh on anatase TiO_2 nanoparticles. The influence of reductive treatments on the Rh local coordination was investigated using CO probe molecule FTIR

and TPD following pretreatment of the sample in H_2 at 100−300 °C or in CO at 300 °C. This resulted in two distinct $Rh(CO)_2$ species with very similar features, depending on the pretreatment. Species 1 exhibits two related bands at 2092 and 2031 cm^{-1} at RT. At 240 °C, both bands disappear, indicating simultaneous CO desorption; this corresponds to a desorption energy of about 1.5 eV. Species 2, observed only in H_2-treated samples, shows two related bands at 2094 and 2031 cm^{-1}, virtually identical to those of species 1, a fact that made the assignment particularly challenging. However, above 160 °C new peaks appear from 1999 to 2012 cm^{-1}, while for temperatures above 300 °C, no CO is present, providing evidence for a sequential CO desorption. In particular, the first desorption (160 °C, $Rh(CO)_2 \rightarrow Rh(CO) + CO$) corresponds to a CO binding energy of 1.3 eV, while the second desorption (300 °C, $Rh(CO) \rightarrow Rh + CO$) indicates a Rh−CO bond of about 1.7 eV.

The origin of this behavior is clear from Figure 1, where the two structures responsible for the features described above are shown. These structures have been selected as indicated above, discarding several candidates due to some inconsistency with the observations (the reader is referred to the original paper for a full account).[19] Species 1 (Figure 1) consists of a Rh atom bound to TiO_2 that forms a geminal carbonyl complex, $Rh(CO)_2$, with features which are fully consistent with the measured ones; notice that an isolated Rh atom is strongly bound to the nondefective $TiO_2(101)$ surface and does not easily diffuse, at variance with the other metal atoms considered (Ru and Pt), thus accounting for the high thermal stability of the SAC. Species 2 corresponds to the same $Rh(CO)_2$ complex bound to a surface OH group which forms when the sample is treated in hydrogen. Despite the different coordination, the two $Rh(CO)_2$ complexes have very similar vibrational spectra, not only when these form on terraces but also when they form on steps (Figure 1), thus explaining the almost identical IR spectra arising from different species! However, the presence of the OH group results in a different stability of the two $Rh(CO)_2$ complexes: while in species 1 the two CO molecules have similar binding energies (about 2.0 eV in DFT), they have clearly distinct binding energies in species 2 (on average 1.3 and 2.6 eV in DFT, Figure 1). This is fully consistent with the observation of a simultaneous CO desorption from species 1 and a sequential CO desorption from species 2. While the computed binding energies are a bit overestimated, the (scaled) IR frequencies are reproduced with surprising accuracy, providing strong proof of the robustness of the assignment.

This shows that only the combined used of the three techniques, IR, TPD, and DFT, can lead to the unambiguous identification of the species present on the catalyst. Using only two of the three approaches would not be sufficient to unravel the nature of the SAC.

3. DO THE ATOMS STAY PUT?

3.1. Dynamic Behavior of SACs: Pt/TiO$_2$

Jack Halpern, a pioneer of homogeneous catalysis, once said that "if you can identify a compound from a catalytic system, it is probably not the catalyst".[27] This statement anticipated something that became clear in the catalysis community in the last two decades: the active site of a catalyst may change or may even form in the course of the reaction. The development of in situ and operando spectroscopies[28] is motivated by the need to identify the temporal evolution of the catalyst under reaction
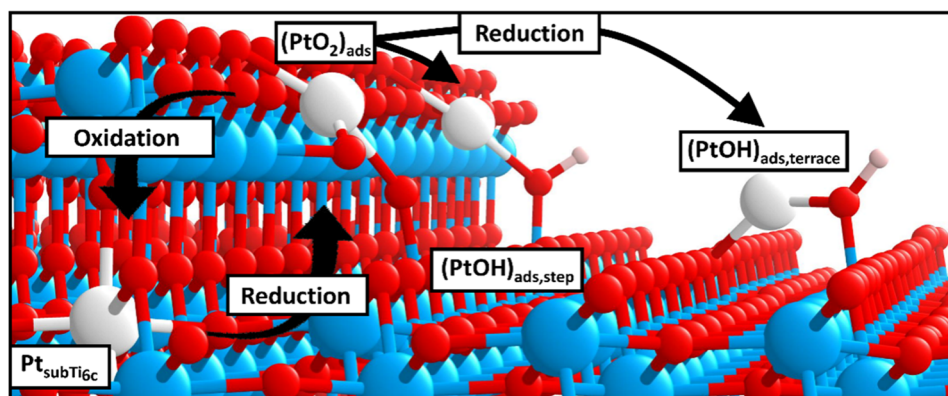
Figure 2. Schematic view of the dynamic evolution of Pt/TiO$_2$ SAC following oxidation, mild reduction, and harsh reduction (shown left to right, respectively). Structures were derived from DFT calculations, consistent with experimental data. Reproduced with permission from ref 30. Copyright Springer Nature 2019.
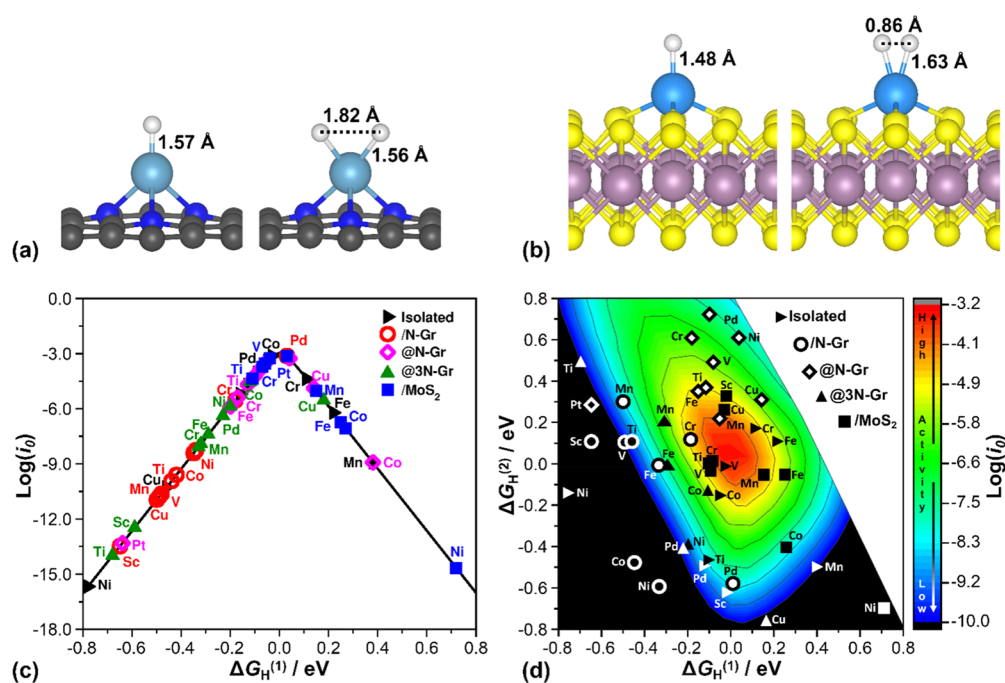
Figure 3. Structures of (a) PdH@3N-Gr and HPdH@3N-Gr and (b) CoH/MoS$_2$ and HCoH/MoS$_2$. (c) Two-dimensional volcano plot derived from numerical DFT results for the case of HER reaction on 55 SACs computed by assuming the formation of a single MH intermediate. (d) Three-dimensional volcano plot derived from numerical DFT results for the case of HER reaction on 55 SACs assuming the formation of MH and HMH intermediates. Red, high activity; blue, low activity. When log(i_0) < −10 (extremely low activity), the color is black. Reproduced with permission from ref 38. Copyright American Chemical Society 2021.

conditions. SACs are not an exception. The stabilization of a specific configuration critically depends on the external conditions, in particular, the oxidizing or reducing nature of the environment during the preparation of the catalyst.

The stability of the possible structures of SACs on oxide supports has been investigated by means of first-principles atomistic thermodynamics as a function of temperature or of the partial pressures of reactive species.[29] Using the oxygen and hydrogen chemical potentials as descriptors, the relative stability of Rh atom positions (adsorbed or substitutional) has been evaluated for Rh/TiO$_2$ SACs, the system described above (Figure 1). The study, confirmed by experimental evidence,[29] clearly demonstrates that Rh single atoms adapt their local coordination and reactivity in response to various redox conditions. In particular, the Rh(OH)$_{ads}$ complexes described previously form when the catalyst is treated in a H$_2$ atmosphere,

while under oxidizing conditions Rh incorporation in the oxide is preferred.

The static or dynamic nature of SACs on oxides has been analyzed in a recent study where in situ atomic-resolution microscopy and spectroscopy characterization supported by first-principles calculations was applied to the case of Pt/TiO$_2$.[30] On the basis of the comparison of experiment and theory, it was found that under oxidizing conditions the Pt atoms replace Ti$_{5c}$ ion positions at step edges; mild reduction pulls these substitutional Pt atoms out of the lattice to form the (PtO$_2$)$_{ads}$ species described in the previous section. Finally, a harsh reduction in H$_2$ induces the formation of (PtOH)$_{ads}$ mobile species adsorbed to both step and terrace sites (Figure 2). The catalytic activity in CO oxidation changes as a function of the local coordination of Pt.[30]

These studies clearly demonstrate that SACs do not have static local coordination but can switch from inactive to active structures under reaction conditions, an aspect that should not be underestimated when models of the reactivity of these systems are proposed or catalytic activities are predicted.

4. PREDICT REACTIVITY: IS THE MODEL COMPLETE?

4.1. Role of "Hidden" Intermediates

To illustrate the specificity of SACs compared to classical catalysts based on extended metal surfaces, we consider the hydrogen evolution reaction (HER) that plays a key role in electrochemical water splitting.[31] The process is based on the formal reduction of two H^+ ions to H_2 on a catalytic surface. Given the importance of the reaction, the number of studies devoted to the theoretical prediction of the HER activity is growing at impressive rate. Similar intense activity is dedicated to the other aspect of water splitting, the oxygen evolution reaction (OER).[32] The screening of potentially good catalysts for HER is normally based on the elegant model proposed by Nørskov and co-workers in 2005.[33] The free energy of adsorption of an H atom on an extended metal surface, ΔG_H, is used to predict the trends in the exchange current for HER. The exchange current in turn is proportional to the amount of hydrogen produced. The activity of SACs in HER is normally studied by adopting the original model based on the formation of just one key intermediate, the MH surface complex.[33] The MH binding energy becomes a simple yet efficient descriptor of the catalytic activity.[34,35] This model has been widely used for metals and recently has been transferred, without modifications, to the case of SACs. However, SACs differ substantially from metal surfaces and can be considered analogues of coordination compounds, more than metal electrodes.

The interaction of H_2 with organometallic complexes was studied a long time ago, and, at variance with metal surfaces, stable dihydride or dihydrogen complexes (HMH) can form when two H atoms, and not just one, interact with a metal center.[36,37] In particular, ligands that withdraw electron density from the metal center such as π-acceptor ligands (e.g., CO) favor the formation of dihydrogen, while electron donor ligands (e.g., phosphines) favor the formation of dihydride complexes. There is no reason that this should not occur also on SACs. In fact, based on DFT calculations, we recently analyzed a set of 55 SACs consisting of transition-metal atoms variously embedded in solid supports (including nitrogen-doped graphene and MoS_2).[38] It turns out that in the large majority of cases SACs form both MH and HMH intermediates and the HMH complexes have either dihydrogen or dihydride character, depending on the metal and on the ligands, by close analogy to inorganic complexes (Figure 3).

This finding has important implications. The neglect of the step related to the formation of the HMH intermediate, in addition to the MH one considered in the original model, may substantially affect the predicted activity of SACs. Extending the original kinetic model to the case where MH and HMH stable intermediates form, one obtains a three-dimensional volcano plot for the HER instead of the classical two-dimensional one (Figure 3).[38] DFT numerical simulations show that the kinetic model accounting for both MH and HMH intermediates may lead to completely different conclusions about the activity of SACs in HER. For a correct prediction of the activity, the formation of nonelectrochemical intermediates must be considered explicitly.

This result not only shows the importance of including all relevant chemical intermediates in a reaction mechanism but also provides an example of the analogies existing between the chemistry of SACs and that of coordination compounds. Furthermore, the proper description of a SAC requires including in the model all of the elements that contribute to the catalytic activity, such as solvent effects and the role of the applied potential. Solvation can be accounted for in several ways, implicitly or explicitly. In the first case, a continuum dielectric is added to the calculation mimicking the effect of the solvent,[39] while in the second case, solvent molecules are explicitly included in the simulation. When the solvent is treated explicitly, one can add enough water molecules to simulate liquid water,[40] or use static approaches based on a single water layer, or even use microsolvation schemes.[41] No matter which model is used, there is no doubt that the solvent is important. At the same time, the role of the external potential is relevant and can have important effects on the electrochemical barriers.[42,43] Predictions of new catalysts that do not include these effects abound but should be considered carefully.

5. SACS, SUPPORTED CLUSTERS, AND HOMOGENEOUS CATALYSTS

The final question is also the most difficult one. In this respect, what we report are just two examples, and their conclusions cannot be generalized to the entire family of reactions on SACs. With respect to more traditional catalysts, SACs offer some obvious advantages: the minor requirement of precious metals, higher selectivity, easier catalyst recovery, and so forth. However, the question of whether SACs are superior to classical catalysts remains open. Here we discuss two cases where extensive experimental studies have been performed and combined with DFT modeling to interpret the reactivity of SACs. The first case, photoactivity under the visible light of Au atoms or Au nanoclusters on N-doped graphene in HER, allows us to compare single atoms with metal nanoaggregates. The other example, the thermal catalysis of Cu SACs on carbon nitride in an organic chemistry reaction, allows us to discuss the performance of SACs in a complex reaction compared to analogous homogeneous catalysts.

5.1. SACs versus Supported Nanoclusters

The HER has been investigated with three catalysts based on Au deposited on nitrogen-doped graphene (N-Gr).[44] The three catalysts, Au single atoms, Au nanoclusters of 0.5−1.0 nm in size, and Au nanoparticles of 20 nm, were prepared by wet chemistry methods and fully characterized at the atomistic level. The experiments showed that under visible light the Au nanocluster photocatalyst exhibits impressive HER activity, followed by Au single atoms and Au nanoparticles. This clear experimental evidence, pointing to a higher activity of Au clusters compared to Au atoms, called for a theoretical interpretation. To this end, the three systems were simulated respectively by a Au isolated atom bound to N-Gr, by a tetrahedral Au_{20} cluster on N-Gr (this structure exists both in the gas phase[45] and on supports[46]), and by an extended Au(111) surface to represent large nanoparticles. The HER reaction was considered using the standard model, i.e., by determining the adsorption free energy of a H atom on the three catalysts.

The results (Figure 4) are consistent with the experimental trend showing a higher activity for the nanoclusters compared to the Au single atoms and the large Au particles and no activity at all for N-doped graphene. This is because an extended Au
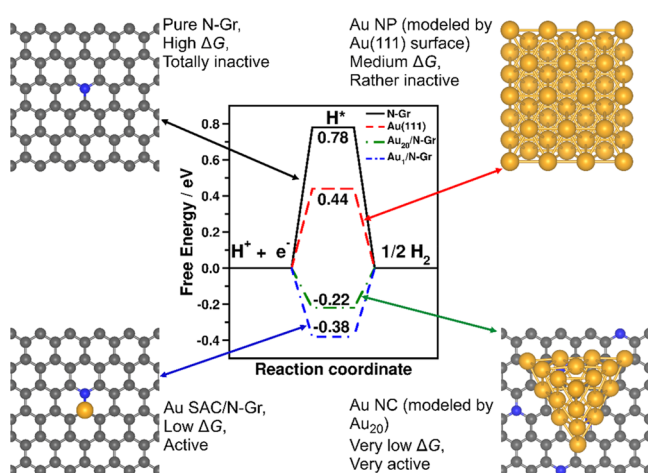
Figure 4. Activity in HER of four different catalysts: N-Gr = pure N-doped graphene; Au NPs/N-Gr = Au nanoparticles on N-Gr modeled by a Au(111) surface; Au NCs/N-Gr = Au nanoclusters on N-Gr modeled by a Au$_{20}$ cluster; and Au SAC/N-Gr = Au single atom on N-Gr. Adapted with permission from ref 44. Copyright The Royal Society of Chemistry 2021.

surface binds hydrogen too weakly ($\Delta G_H > 0$) and a Au atom too strongly ($\Delta G_H < 0$). On Au nanoclusters, on the contrary, the H adsorption free energy is neither too positive nor too negative and results in a higher activity.[44] However, there is clear evidence from the experiments that plasmonic effects also play an important role in capturing the visible light, an effect connected to the size and shape of Au nanoclusters that adds to their intrinsically higher activity. To summarize, Au SACs are active species, but Au nanoclusters have superior activities due to both an intrinsic better catalytic activity and the capability to absorb light; the combination of advanced synthesis and characterization techniques and atomistic modeling allows one to provide a rationale behind the chemistry of these systems. Once more, this is a specific example and cannot be generalized, but it is intended to show that SACs are not necessarily better catalysts than supported nanoclusters or nanoparticles.

5.2. SACs versus Homogeneous Catalysts

SACs are appealing for their high catalytic and photo(electro)-catalytic activity but also for intrinsically yielding the highest activity/mass ratio for metal catalysts. This is pushing toward the study of SACs for applications in organic, industrial, and environmental chemistry. Recently, we have investigated the properties of Cu SACs anchored on C$_3$N$_4$ in a one-pot synthesis of triazoles,[47] a class of compounds useful in pharmaceutical chemistry.[48] A set of spectroscopic techniques were employed, together with first-principles calculations, to unravel the local coordination and oxidation state of the Cu atoms. The absence of signals related to Cu−Cu bonds in EXAFS spectra confirmed the atomically dispersed nature of the Cu species. A complex coordination structure of single Cu atoms emerged from the EXAFS spectra, with Cu bound on average to five first neighbors at 1.9 Å and four second neighbors at 2.9 Å. DFT calculations were performed on various models (Cu deposited in the heptazine pore of carbon nitride, substituted in the framework of carbon nitride, hosted in a vacancy,[49] or entrapped in a sandwich-like arrangement). A different model was used to account for the short (1.9 Å) Cu−N distances evidenced by EXAFS, where Cu is hosted in a C divacancy in N-doped graphene. In none of these models does Cu have as many as five

close neighbors at 1.9 Å, and we thus interpreted the EXAFS results as due to the coexistence of some loosely bound species (such as those coordinated in the pores) and tightly bound ones, for instance, in vacancies. In all of these structures, Cu is in a +1 oxidation state, consistent with XPS measurements.

The proposed reaction mechanism (Figure 5) envisages a first step where acetylene is activated on the Cu SAC, followed by the
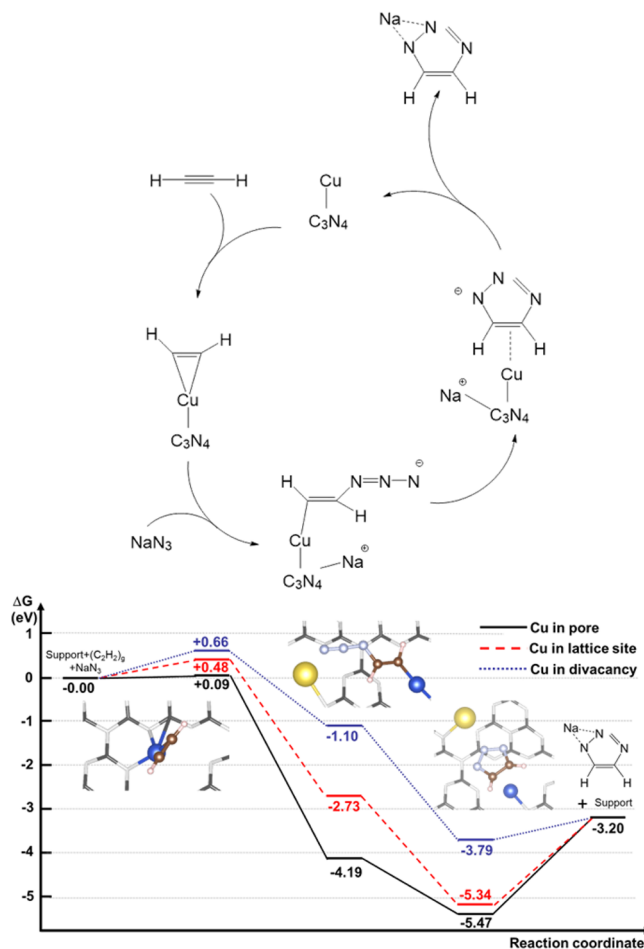
Figure 5. Proposed reaction cycle (top) and energy profile (bottom) for triazole synthesis on Cu/C$_3$N$_4$ SACs. Adapted with permission from ref 47. Copyright American Chemical Society 2022.

coadsorption of an azide molecule and then the cyclization to form a pentacyclic triazolate species. The formation of the cycle is strongly exergonic, but a barrier needs to be overcome to activate the alkine. The entity of the barrier depends on the Cu coordination: loosely bound SACs are more active than strongly bound ones. However, the final desorption of the products to close the catalytic cycle is easier on tightly bound Cu, where the reactants bind less strongly. Overall, the catalytic activity needs a balance, where the reactants are remarkably activated to overcome the initial barrier but the products are promptly released at the end of the cycle.

Experimentally, the Cu SACs embedded in C$_3$N$_4$ displayed higher activity compared to homogeneous catalysts based on CuCl and CuCl$_2$ salts in solution in the presence of organic basic ligands. In particular, after 30 min a reaction rate 3 times larger has been measured for Cu/C$_3$N$_4$ compared to CuCl, while with respect to CuCl$_2$ the difference in the rate is even larger (6 times). It can thus be concluded that Cu$^+$ species outperform

Cu^{2+}, but the charge state of the SAC is not the most important factor. A prominent role is played by the local coordination of Cu. Cu SACs in C_3N_4 are, in this respect, clearly preferable, and the key aspect is their capability to activate the alkine, an effect supported by a comparison at the DFT level of Cu/C_3N_4 structures compared to CuCl molecular complexes as well as the larger turnover frequency with respect to the homogeneous catalyst. On the other side, traditional heterogeneous catalysts for triazole synthesis, based on supported Cu particles, suffer from limited selectivity and stability and do not represent a better alternative to SACs.[50,51] In this context, it is also worth mentioning that there are potential benefits of cooperative effects associated with mixed-valence SACs.[52]

6. CONCLUSIONS AND PERSPECTIVES

From the study of single-atom catalysts on oxide and carbon-based supports, the combination of computational and experimental efforts leads to the following take-home messages:

(1) SACs are inherently less complex than supported nanoparticles, yet their nature is often elusive and the precise identification of their structure is challenging. For theoretical modeling, it is essential to know the exact coordination of a SAC in a support. Even small changes in the coordination may result in different properties and different reactivity.[15] This problem can be addressed only by strengthening the dialogue between theory and experiment and by combining the results obtained from different spectroscopies and microscopies with computational models. Only when all of the parameters considered agree can one be reasonably certain that one of the possible structures of a SAC has been identified. On the other hand, the possibility to tune the catalytic activity by changing not only the metal atom but also its immediate surroundings opens interesting opportunities for the design of new catalysts.

(2) Under reaction conditions, SACs may change their position and become more exposed on the surface of the support. This has been clearly demonstrated for oxide surfaces. Less common are examples of dynamic behavior of SACs on carbon-based supports.[53] The use of ab initio molecular dynamics could provide interesting hints on the structural evolution of SACs.[54]

(3) Too often, simplified but efficient reaction models and schemes derived for metal surfaces in electrochemical reactions are transferred without modification to the study of SACs. However, SACs have little in common with extended surfaces and resemble coordination compounds. In this regard, the formation of non-electrochemical intermediates, of little or no relevance on metals, can be of fundamental importance for SACs. It is desirable that this aspect is taken into account in future screenings of potential candidates for electrocatalytic reactions on SACs.

(4) Many reactions involving SACs occur in a liquid environment. Not surprisingly, the roles of the solvent[55] and of the applied potential[42] are important in defining the final activity. While this can be overlooked for some purposes, e.g., for a comparison of the intrinsic activity of different catalysts, the contributions of the solvent and of the applied potential are important if one is interested in predicting new catalysts from first principles.

(5) The relative simplicity of SACs has led to the possibility to screen large numbers of systems in which a transition-metal atom is stabilized on a support. The same type of screening for small metal clusters would simply be impossible because of the huge number of structures to be explored. This spurred intense but purely computational activity aimed at predicting the "best" catalyst for a given reaction. Although some useful information may emerge from this type of analysis, the most valuable contribution of theory probably remains the ability to integrate and corroborate the results obtained from experimental measurements. This joint approach represents one of the most promising developments in the field of single-atom catalysts and is expected to grow further thanks to more advanced characterization tools and more powerful software and models.

■ AUTHOR INFORMATION

Corresponding Author

Gianfranco Pacchioni − *Dipartimento di Scienza dei Materiali, Università di Milano-Bicocca, 20125 Milano, Italy;* orcid.org/0000-0002-4749-0751; Email: gianfranco.pacchioni@unimib.it

Authors

Giovanni Di Liberto − *Dipartimento di Scienza dei Materiali, Università di Milano-Bicocca, 20125 Milano, Italy;* orcid.org/0000-0003-4289-2732

Sergio Tosoni − *Dipartimento di Scienza dei Materiali, Università di Milano-Bicocca, 20125 Milano, Italy;* orcid.org/0000-0001-5700-4086

Luis A. Cipriano − *Dipartimento di Scienza dei Materiali, Università di Milano-Bicocca, 20125 Milano, Italy;* orcid.org/0000-0002-3801-7751

Complete contact information is available at:
https://pubs.acs.org/10.1021/accountsmr.2c00118

Notes

The authors declare no competing financial interest.

Biographies

Giovanni Di Liberto works on the theoretical modeling of nanomaterials for photo- and electrocatalysis. He received his Ph.D. at the University of Milan and was a visiting scientist at the University of Barcelona in 2019. He received awards in 2018 and 2020 from the Italian Society of Chemistry.

Sergio Tosoni mainly works on the computational description of surfaces and interfaces. He obtained his Ph.D. at the University of Torino in 2007. He worked as postdoctoral researcher at the Humboldt University in Berlin and the University of Barcelona. He was appointed associate professor at the University of Milano-Bicocca in 2022.

Luis A. Cipriano works on theoretical simulations of graphene-supported single-atom catalysts for HER, OER, and semiconductor–oxide interfaces. He received his Ph.D. from the University of Milano-Bicocca in 2022.

Gianfranco Pacchioni is active in the field of heterogeneous catalysis modeling. He worked at the IBM Almaden Research Center, the TU Munich, and the Fritz-Haber Institute (Berlin). He is a professor of chemistry at the University of Milano-Bicocca, where he has been Vice-Rector for Research (2013−2019) and Director of the Department of Materials Science (2003−2009). He is a coauthor of about 550 papers

and has given about 500 invited talks. He received several awards (Humboldt Award, Pascal Medal, etc.) and is a fellow of the Accademia Nazionale dei Lincei, the Academia Europaea, the European Academy of Sciences.

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