ChemistryEurope
Excellence in Chemistry Research Worldwide

Perspective
doi.org/10.1002/ceur.202400086

www.journal.chemistry-europe.org

The Reductive Addition–Oxidative Elimination Mechanism

Belén Lerma–Berlanga[a] and Antonio Leyva–Pérez.*[a]

The oxidative addition–reductive elimination (OARE) mechanism of reactive molecules on metal atoms is a cornerstone of modern chemistry. However, the complementary reductive addition–oxidative elimination (RAOE) mechanism is barely considered, despite a first reduction reaction between metal atoms and the incoming organic reactant makes chemical sense in a plethora of processes. Here we show, in a chronological order, early precedents in the literature which indicated the possibility of a general RAOE mechanism, the few systems explicitly reported so far (including a catalytic system) and some other reactions where a RAOE mechanism would satisfactorily explain the mechanistic evidences found. These examples, together, strongly suggest that researchers should consider the RAOE mechanism during their investigations, and not simply adjust their conclusions to the omnipresent OARE mechanism. This new line of thinking might open new avenues in the design of chemical reactions, particularly catalytic ones.

1. Introduction

The first structuration of organometallic reactivity occurred, historically, with the appearance of the oxidative addition–reductive elimination (OARE) mechanism,[1] which served as a starting point to rationalize the different reactions occurring on metal complexes.[2] Although difficult to assign, the first references to the oxidative addition step can be tracked back to the 1960s, and acknowledged to Collman[3] and Vaska[4] during their seminal works on the addition reaction of diatomic molecules (Cl_2, H_2 and others) to $M(CO)_xCl_y(PPh_3)_2$ complexes (M=Ir, Ru; x=1–3; y=0–1). Since them, the OARE mechanism has been used as a basis to explain a plethora of chemical reactions, particularly metal–catalyzed organic reactions, some of them of industrial use such as the production of acetic acid by the carbonylation of methanol (Cativa and Monsanto processes, with Ir and Rh metal catalysts),[5] the hydrogenation reaction of alkenes, alkynes, nitro or keto compounds (purification of ethylene, nutraceuticals and margarine production,…; with Pt, Pd, Ni and Rh catalysts),[6] and the cross–coupling reaction of organic halides with a variety of nucleophiles (Heck, Suzuki, Sonogashira and Buchwald–Hartwig reactions, to name a few; with Pd, Ni, Cu, Fe,… catalysts),[7] among others. The number of reports during the last five decades where the OARE mechanism is mentioned is >22000 (according to Scifinder™), growing year by year and with 920 entries only in 2023. The universality of the OARE mechanism involves not only transition (*d*–block) but also main group (*s*– and *p*–block)[8] and inner transition metals (f–block),[9] and it can be said without any hesitation that the OARE mechanism is a hot topic of research for decades and that modern chemical manufacturing cannot be understood without the OARE mechanism.

In contrast to the OARE mechanism, the reductive addition–oxidative elimination (RAOE) mechanism has barely received any attention. Figure 1 shows that this reaction sequence implies, contrary to the OARE mechanism, a first electronic donation from the adding molecule to the metal atoms of a

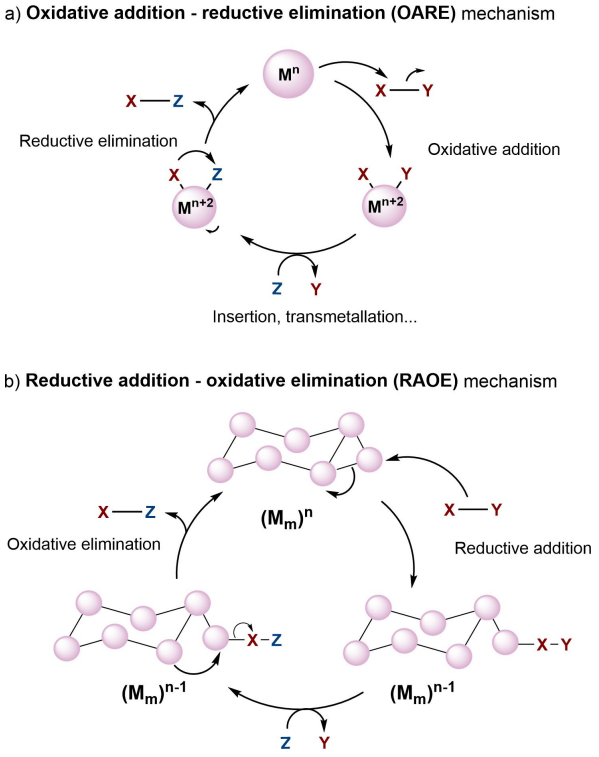

Figure 1. a) Scheme for the classical oxidative addition–reductive elimination (OARE) mechanism. b) Scheme for the proposed reductive addition–oxidative elimination (RAOE) mechanism. Notice that the individual oxidation step for each metal atom in the cluster is not explicitly indicated since the charge of the cluster is shared by all atoms and denoted here as "n", thus the redox events are referred to the overall electronics.

[a] *Dr. B. Lerma–Berlanga, Dr. A. Leyva–Pérez.*
Instituto de Tecnología Química (UPV–CSIC)
Universitat Politècnica de València–Agencia Estatal Consejo Superior de Investigaciones Científicas
Avda. de los Naranjos s/n, 46022 Valencia, Spain
E-mail: anleyva@itq.upv.es

metal aggregation (or to a highly delocalized organic molecule, see ahead), which constitutes the reductive addition reaction. The electron density is then shared by the connected metal atoms in the metal core, which accommodates the two moieties of the breaking starting molecule, typically onto different metal atoms. Then, the same insertion/transmetallation events occurring in the OARE mechanism can operate, to finally trigger the oxidative elimination step and release the reaction product, in a catalytic manner if required.

The lack of RAOE mechanisms in the literature is difficult to accept having in mind that electron–donating molecules are very common reactants in chemical synthesis, and this absence can perhaps be explained by the fact that the classical OARE mechanism was founded on monoelectronic complexes,[10] where the RAOE is not possible. However, RAOE mechanisms could be in operation in some of the catalytic systems reported so far for OARE, circumventing the tendency to adjust (and sometimes force) the experimental evidences to the stablished OARE mechanism. For instance, let us consider three fundamental metal–catalyzed systems adjudicated to the classical OARE mechanisms which might better be depicted by a RAOE mechanism or, at least, would have the same chemical sense: 1) the coupling of benchmark nucleophiles such as NH_3 and H_2O, whereas the literature systematically proposes the electron donation of the metal to the proton (OARE),[11] rather than considering the more feasible donation of the free–pair electrons in the N or O atoms to the metal site (RAOE); 2) the splitting of H_2,[12] which is generally explained by an electron donation from the metal to the unoccupied σ^* orbital of the diatomic molecule, instead of the often equally probable donation from the occupied σ orbital of H_2 to coordinatively unsaturated metal sites; and 3) the activation and breaking of O–O and S–S bonds (i.e. O_2 and disulfides),[13] where, in analogy with H_2, an electronic donation from the occupied π orbitals is as possible as an electron acceptance. This third family of reactions, in concrete with disulfides RS–SR,[14] is indeed one of the few examples reported with both OARE and RAOE mechanisms, and better explained by the latter (see ahead).

This Perspective will describe the three systems reported so far with RAOE mechanisms, one of them catalytic, and will also show other catalytic systems unsatisfactorily explained by the classical OARE mechanism (as recognized in the same references) and which could fit better the RAOE mechanism. Before to that and for the sake of comparison, we will comment on the classical OARE mechanism on metal surfaces, which generated some debate years ago but, as we will show here, seems sufficiently resolved and accepted.

It is noteworthy to remark that the RAOE mechanism has not been disproved for any system in the literature, since, simply, it has not been studied in most cases. Only in those cases where the classical OARE mechanism dramatically deviated from the experimental evidences and any other alternative mechanism (radical, acid, base,…) was also disproved, the RAOE mechanism was studied. In other words, the probability that RAOE mechanisms, when studied, might fit the experimental evidences and explain known and future reactions, is reasonably high. In this way, the RAOE mechanism would expand the limited number of molecular activation types on metals, and provide an alternative pathway to the classical, extremely extended but sometimes assumed OARE mechanism.

2. The Classical Oxidative Addition–Reductive Elimination (OARE) Mechanism on Metal Aggregations

The OARE mechanism on metal cores, including subnano clusters,[15] nanoparticles[16] and macrosized metal surfaces,[17] sometimes formed in–situ from monoatomic metal species,[16f–i] is well stablished after more than three decades of investigation. A mixture of active species during reaction, which has been insightfully named "cocktail catalysis" in some cases, is also common during OARE mechanisms.[18] Figure 2 shows that some of the more important catalytic redox processes with monometallic complexes where an OARE mechanism is claimed to operate, also occur on metal aggregates.[19] As representative examples, we show here the H_2 splitting on metal nanoparticles (hydrogenation reactions),[20] the oxidative addition of iodomethane on a metal surface (i.e. carbonylation of methanol),[21] the cross–coupling reaction of substituted benzenes on sub–nanometer metal clusters,[22] and the hydrogen–borrowing and cross–coupling of aminoderivatives on supported bimetallic nanoalloys,[23] which cover most types of catalytically active metal cores to be encountered.

A recurrent argument against the OARE mechanism on metal aggregates in the liquid phase is the leaching of discrete metal entities (monometallic or perhaps ultrasmall metal clusters of 2–3 atoms),[24,25] which may invalidate the redox mechanism on bound multimetallic entities in solution. However, although the latter can be true for some systems,[26] a battery of evidences confirms the suitability of metal aggregates to undergo the OARE mechanism: 1) leaching studies on many metal–supported solid catalysts confirm that the catalytic activity mainly or exclusively comes from the solid;[27] 2) gas phase oxidative oxidation reactions on metal surfaces, where leaching does not occur, are well known;[21,28] 3) multisite solid

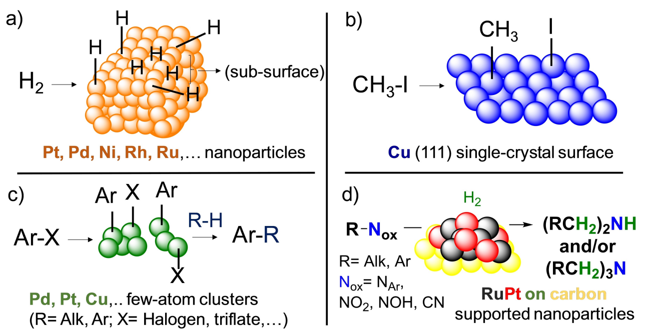

Figure 2. Representative examples of classical OARE mechanisms on different metal aggregations with industrial implementation. a) The H_2 splitting on metal nanoparticles, b) iodomethane oxidative addition for the carbonylation of methanol, c) cross–coupling reaction of halobenzenes on metal clusters, and d) hydrogen–borrowing and cross–coupling of aminoderivatives on supported metal nanoalloys.

Perspective
doi.org/10.1002/ceur.202400086

catalysts are extremely efficient catalysts for a variety of reactions operating through the OARE mechanism, and the concomitant leaching and operational regrouping of the different catalytic elements in solution is highly unlikely;[29] and 4) metal aggregates activated by an external stimulus, i.e. light,[30] plasmon,[31] electricity,[32] and solid supports,[33] are also very active. This body of literature unambiguously confirms the redox activation of a plethora of molecules on different metal aggregates through the OARE mechanism, most of the times in a catalytic fashion.

3. The Reductive Addition–Oxidative Elimination (RAOE) Mechanism

3.1. Precedents in the Literature

Some publications during the 1960s and 1970s already suggested the "gain instead of loss" of electron density on the metal site after the additive breaking of a molecule. Figure 3 shows some of these precedents, which, ironically, involved in some cases the foundational metal complexes of the classical OARE mechanism, i.e. the Vaska's Ir complex **(1)** and a Ru_3 complex **(2)**.[34] The gain of electron density on Ir complexes during reaction with, for instance, H_2,[35] was measured by Fourier transformed infrared spectroscopy (FT–IR), after using carbon monoxide (CO) or the same H_2 molecule as a probe, and the values obtained were incongruent with the values obtained for isolated monometallic complexes where an oxidative addition has occurred, such as complex **(3)**, which of course accounted for a loss of electron density after the oxidation of the monometallic metal site. This inconsistency between the FT–IR values of the isolated monometallic metal complexes (always oxidized) and the FT–IR values obtained during reaction (metal atom apparently reduced) could be accepted at that time with different explanations, such as a distinct coordination mode and back–donation of the CO probe ligands, changes in the coordination sphere during reaction,… In such a way, it was assumed that the Ir complex was still in monometallic form during reaction and it cannot suffer the RAOE mechanism, since the potential agglomeration of the metal atoms into few–atom clusters, to engage into the addition step, was barely considered. Two decades later, investigations by Finke and co–workers[36] demonstrated that the aggregation of the starting monometallic Ir complexes during H_2–mediated hydrogenation reactions indeed occurs, to in–situ generate the catalytically active Ir_4 clusters **(4)**, which activated H_2 during reaction. These two pieces of science, separated through years but connected here, might explain why the monometallic species gain instead of lose electron density during the H_2 reaction, since the in–situ formation of Ir clusters would enable a RAOE mechanism. Indeed, the same anomalous effect of gaining rather than losing electron density was observed for Ru_3 clusters during the H_2 addition, when passing from complex **(4)** to complexes **(5)** and **(6)**.[34]

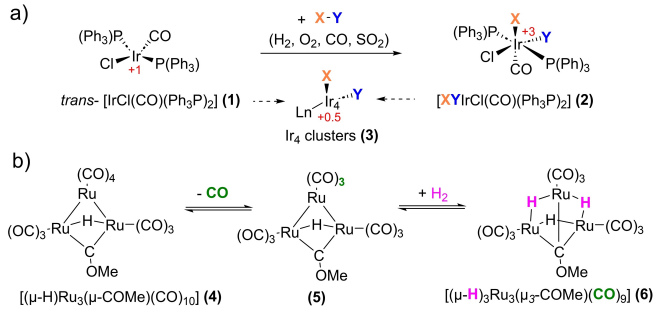

Figure 3. a) Proposed mechanism for a *cis* addition of a diatomic molecule (X–Y) to planar *trans*–[IrCl(CO)($(C_6H_5)_3P)_2$] **(1)**,[4] and the in–situ formation of catalytically active Ir_4 clusters.[35] Formal oxidation states are indicated in red. b) Proposed reaction sequence interconverting [(μ–H)Ru_3(μ–COMe)$(CO)_{10}$] **(4)** to [$(μ–H)_3Ru_3(μ_3–COMe)(CO)_9$] **(6)**.[34]

Finally, the precedents of potential RAOE mechanisms on metal atoms could be expanded to Au atoms, able to move from the −1[37] to the +3 formal oxidation step,[38] and this change in oxidation state can easily occur in clusters when accepting incoming ligands.[39,40]

3.2. Reported Examples of RAOE Mechanisms

3.2.1. Organocatalytic Diborylation of Pyrazine Derivatives

The first publication where we could find the term "reductive addition", in the context here presented, is authorized by Ohmura, Suginome and a co–worker,[41] less than ten years ago, and it is, curiously, a metal–free catalytic reaction. The RAOE mechanism can theoretically occur not only on metal aggregates but also on highly conjugated redox organic molecules, where the electron density can delocalize after the initial reductive addition step. The study shown in Figure 4 involves a 4,4′–bipyridine organocatalyst **(7)**, able to dissociate and incorporate bis(pinacolato)diboron $(Bpin)_2$ **(8)** molecules in a reductive addition step, to catalyze borylation reactions after using pyrazines **(10)** as final oxidation agents. In this way, the 4,4–bipyridine organocatalyst is regenerated after an oxidative elimination pathway, not explicitly mentioned like that in the publication,[41] since the reduced borylated 4,4′–bipyridinyl intermediate **(9)** still requires an external oxidant to be transformed into the final product, or in other words, the oxidative elimination does not occur internally after coupling of the two

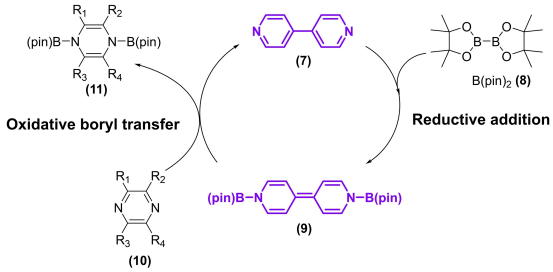

Figure 4. Proposed catalytic cycle involving 4,4′–bipyridine organocatalyst **4**.[41]

Perspective
doi.org/10.1002/ceur.202400086

boryl moieties but after reacting with an external oxidant. Nevertheless, the relevancy of using the concept "reductive addition" in an early example deserves to be remarked.

Figure 5 shows the scope of the reaction, which allowed to prepare a variety of pyrazine derivates **(11)** using the organocatalyst **(12)**.

3.2.2. Stoichiometric Redox Reaction of Thiols on Metal Nanoparticles

The first example that explicitly reports a complete RAOE mechanism was published a couple of years ago by Kumacheva, Liu and co–workers,[42] and it deals with the addition / elimination of thiols to metal nanoparticles (Au, Ag and Pt), as shown in Figure 6. This classical organo–protection of metal nanoparticles, particularly for Au, has been systematically explained in the literature by other mechanisms including the AORE mechanism, but it is here depicted by the RAOE mechanism on the basis of sound experimental evidences.

The dissociation with time of the protecting thiols of Au nanoparticles, structured as self–assembled monolayers (SAM) materials, has traditionally been ascribed to the progressive oxidation of the thiol group with air, to generate less coordinating sulfur oxide species. However, this work demonstrates that the oxidation occurs on the metal atoms of the nanoparticle rather than on the thiol group themselves, thus enabling an "oxidative elimination" process. For that, different peroxides **(13)** (benzoyl or hydrogen peroxide, and also *tert*–butyl hydroperoxide) were used to accelerate the oxidation reaction of the Au–thiol SAM, with the subsequent agglomeration of Au atoms, after creating new Au–Au bonds during the oxidation elimination step. This reaction resembles many other Au cluster (nanoparticle)–catalyzed reactions where oxidant species and thiols participate (i.e. the reversible aerobic oxidation of thiols to disulfides), which we will feature ahead as

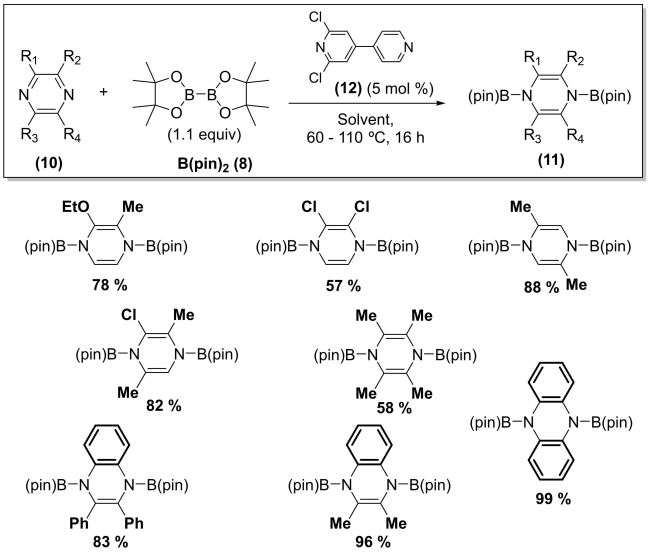

Figure 5. Scope for the organocatalytic diboration of pyrazine derivatives **(11)**.[41]

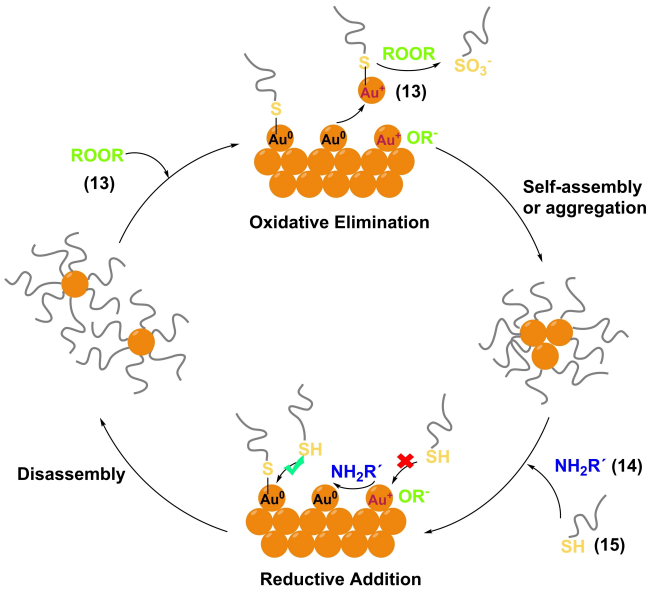

Figure 6. Scheme of the oxidative elimination and reductive addition (OERA) of HS–terminated polymer ligands on the AuNPs.[42] The redox events from Au^0 to Au^+ and vice–versa are indicated with arrows. Different reagents are necessary to close the OERA mechanism, thus a stepwise combination of elementary steps is in operation.

potentially RAOE mechanism–driven reaction. The addition of amines (propylamine, phenylamine or oleylamine) as external reductants **(14)** together with fresh thiols **(15)** (in the form of polymers for a better visualization of the Au nanoparticles by transmission electron microscopy, TEM) completely reversed the process, to obtain the original thiol stabilized Au nanoparticles after a reductive addition step. In this case, a stepwise combination of elementary steps occurs, since the reagents are different for the oxidative elimination (thiols and peroxides) and reductive addition (amines) steps.

Figure 7 shows that the RAOE mechanism occurs with different thiol polymers (polystyrene and polyethylene glycol terminated thiols, PS–SH and PEG–SH respectively), different

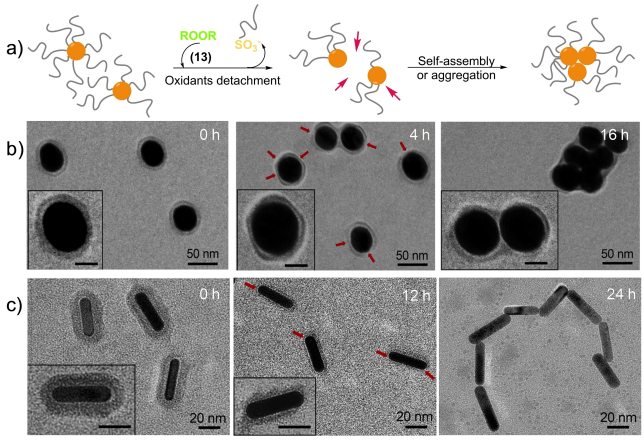

Figure 7. a) Illustration of the self–assembly of Au nanoparticles induced by oxidative elimination. TEM images of time-dependent detachment of thiol ligands from b) Au nanoparticles or c) Au nanorods on polystyrene (AuNP@PS and AuNR@PS, respectively).[42]

Perspective
doi.org/10.1002/ceur.202400086

solvents (tetrahydrofurane, water, ethanol and *N,N'*–dimethylformamide), Au nanoparticles or nanorods of different sizes (7–30 nm), and also different metals (Au, Ag and Pt). Therefore, this study conclusively demonstrates the feasibility of the RAOE mechanism in a stoichiometric manner for a variety of metal nanoparticles, using sacrificial oxidant and reducing agents and, in this case, in the opposite order (oxidative elimination and then reductive addition, called by the same authors an OERA mechanism).[42]

3.2.3. Au_8–catalyzed cross–coupling of Disulfides

The first example of catalytic RAOE mechanism was recently reported by our group.[43a] For that, we leveraged the reported redox interconversion of two well–defined phosphine Au_8 clusters, which require $NaBH_4$ and Cl^-/air as external reducing and oxidizing agents, respectively.[43b] As shown in Figure 8, we envisioned that the reversible transformation of the crystallographically–defined Au cluster **(16)** of formula $[Au_8(dppp)_4Cl_2][(NO_3)_2]$, [dppp = 1,3 bis(diphenylphosphino)propane] into the corresponding $[Au_8(dppp)_4][(NO_3)_2]$ **(17)**[43c] complex might occur after reductive addition and oxidative elimination of a disulfide molecule **(18)** instead of the sacrificial $NaBH_4$ and Cl^-/air agents, in such a way that the system will become cyclic and catalytic if a second disulfide **(19)** is added to the mixture. In this way, the cross–coupling of different disulfides could be achieved. Remarkably, the catalytic approach will bring a stepwise combination of elementary steps (with two different stoichiometric reagents) into a single elementary step (catalytic). The use of crystalline pure Au_8 clusters assured defined spectroscopic values, in order to accurately follow the evolution of the reaction and the Au_8 catalysts by in–situ techniques.

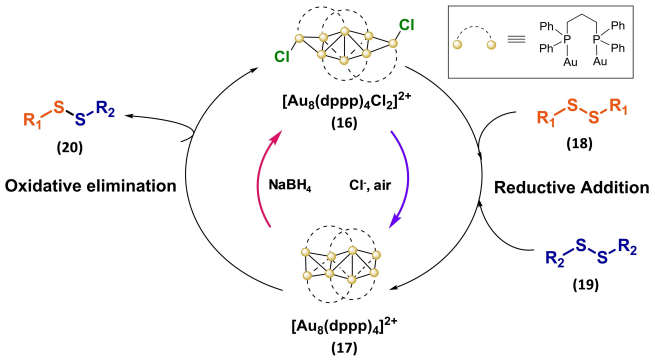

Figure 8. Scheme of the reversible transformation of the Au cluster $[Au_8(dppp)_4Cl_2][(NO_3)_2]$ **(16)** into the corresponding $[Au_8(dppp)_4][(NO_3)_2]$ **(17)**[43c] (notice the increase in $2e^-$ in the cluster after losing $2Cl^-$) by reductive addition and oxidative elimination of a disulfide molecule instead of, as reported,[43b] external sacrificial agents such as $NaBH_4$ or Cl^-/air. For the latter, different reagents are necessary to close the OERA mechanism, thus a stepwise combination of elementary steps is in operation.

Figure 9 shows that the Au_8–catalyzed reaction works well, enabling the synthesis of a variety of disulfides **(20)** in moderate to good yields. The mechanism of the reaction was extensively studied by in–situ ultraviolet–visible absorption spectrophotometry (UV–Vis), ^{31}P nuclear magnetic resonance (NMR) spectra and matrix–assisted laser desorption/ionization–time–of–flight mass spectrometry (MALDI–TOF), showing the interconversion of the redox Au_8 clusters during the process and unveiling some of the expected intermediates for a reaction with a RAOE mechanism. Comparative reactive experiments discarded any OARE mechanism in operation, as well as acid–catalyzed or radical mechanisms, and strongly supported the RAOE pathway. Figure 9 shows the proposed mechanism based not only on the experimental evidences found but also on density functional theory (DFT) calculations. It can be seen that the oxidized Au_8 cluster **(16)** is reduced to the Au_8 cluster **(21)** after addition of two disulfide molecules, with the concomitant breaking of one Au–Au bond, loss of the Cl^- anions (as sulfyl chlorides) and re–structuration of the Au_8 cluster, to give the reduced Au_8 cluster **(22)** containing the activated disulfide as the new ligand. The exchange of thiol moieties on this activated disulfide generates the intermediate **(23)** with the cross–coupling disulfide product

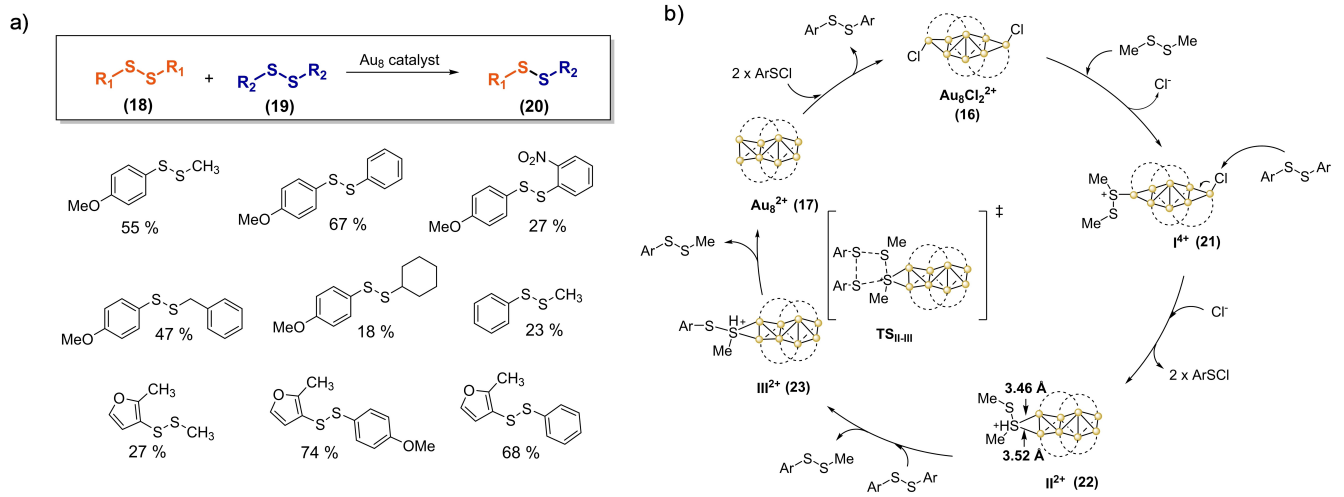

Figure 9. a) Scope for the disulfide metathesis reaction catalyzed by Au_8 cluster **(16)**. b) Proposed RAOE mechanism for the metathesis reaction of disulfides supported by experimental evidences and computational studies. Notice the increase in $2e^-$ in cluster **(16)** after losing $2Cl^-$.

Perspective
doi.org/10.1002/ceur.202400086

(as the typical transmetallation and insertion processes in OARE mechanisms), which is released after a final oxidative elimination event with the sulfyl chlorides left behind, to regenerate the starting oxidized Au_8 complex **(16)** catalyst.

This Au–catalyzed cross–coupling reaction of disulfides, mediated by a RAOE mechanism, is not exclusively catalyzed by the well–defined Au_8 complex **(16)** but also proceeds in the presence of catalytic amounts of supported Au clusters (≈3 nm) on different supports (ZnO, TiO_2, graphene,…).[43a,44] The solid catalyst could be reused, thus showcasing the generality of the mechanism and its potential application in heterogeneous catalysis. The Au–catalyzed reaction significantly improves the catalytic activity of any previously reported metal system for the cross–coupling reaction of disulfides, including $RhH(PPh_3)_4$,[45] $RhCl_3$[46] and $PdCl_2$.[47] Thus, the result might be considered remarkable, if one has in mind the relevancy of the disulfide coupling reaction in biology,[48] its wide application in dynamic covalent/combinatorial chemistry,[49] and that this reaction fulfills the requisites of a modern sustainable organic chemistry, i.e. (reusable) catalysis and full atom economy. The reaction is also applicable to diselenides.[50]

4. Some Reported Reactions Explainable by the Reductive Addition–Oxidative Elimination (RAOE) Mechanism

As said above, the standard in research when studying metal–catalyzed cross–coupling reactions is the adjustment of the reaction mechanism to the classical OARE mechanism. Alternative mechanisms such as radical, acid– or base–catalyzed pathways are considered in some cases; however, these mechanisms are drastically different from the OARE mechanism. This limited mechanistic scenario oversimplifies the study and give a blurred picture of the reaction pathway in some cases. Any detail in the reaction mechanism can be paramount to improve the reaction, much more if a reverse movement of electrons along the pathway occurs, particularly on catalytic sites. In line with this, the study of reversible oxidative addition processes has gained attention in the last years,[51] providing an alternative reaction pathway. However, the reversible oxidative addition still strictly follows the OARE mechanism, just considering the reversibility of the oxidative addition step, i.e. an equilibrium reaction, as key controlling step of the process. The RAOE mechanism proposed here is drastically different to the reversible oxidative addition, since the addition of the incoming substrate to the metal site is accompanied by a decrease rather than an increase in the electron density of the metal atoms, with an overall acceptance of 1 or 2 electrons, to forge the new bond for the coupled product after releasing the extra electrons in an oxidative elimination step. Therefore, the differential outcomes of the RAOE mechanism might be easily spotted for some reported systems if the amount of experimental data is rich enough to analyze and compare. Here we show some examples.

4.1. Organocatalytic Cross–Coupling Reaction of Benzyl Halides and Boronic Acids

Following the same order shown above for the reported RAOE systems, we start this section with an organocatalytic reaction. Figure 10 shows the Suzuki–type coupling of benzyl halides **(24)** and boronic acids **(25)** catalyzed by simple thioethers such as compound **(26)**, to give a variety of diaryl methane products **(27)**, as reported by Huang and co–workers.[52] The reaction is proposed to occur through a zwitterionic boron "ate" intermediate **(28)**, which rearranges to intermediate **(29)** after a 1,2–metalate shift, to afford the Suzuki–type coupling product.

The experimental evidences that support the proposed mechanism in Figure 10 include the lack of Lewis–acidity of the tihioether to catalyze a Friedel–Crafts benzylation reaction, the need of boronic acids rather than boronic esters to make the reaction work, and the intermediacy of an in–situ formed sulfide ylide (which formation is indeed the rate–limiting step for the reaction). All these evidences are compatible with a RAOE mechanism; indeed, one can draw the electronic movement expected for the RAOE mechanism on the very same mechanistic proposal of the organocatalytic reaction, on the intermediates **(28)** and **(29)** (Figure 10b).[52] Besides, the manuscript states that "the selective oxidative addition of transition metals to alkyl halides rather than aryl halides is difficult due to unfavorable transition states and bond strengths", and that is the reason why this study develops and alternative approach. Thus, this system is a potential candidate to proceed through a RAOE mechanism.

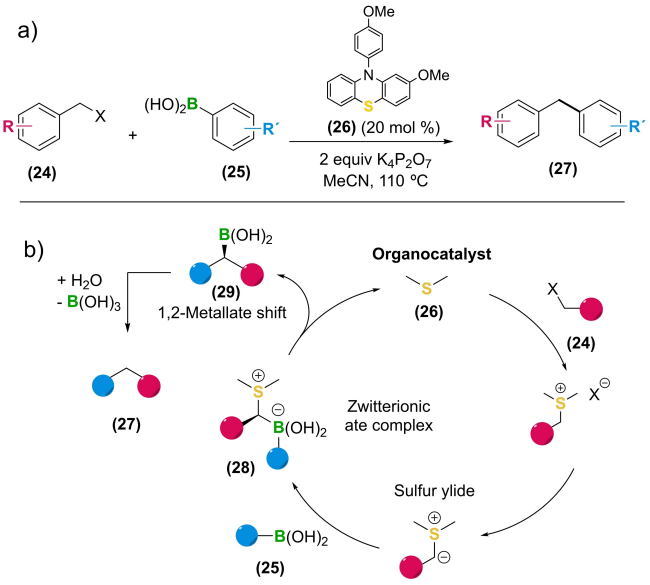

Figure 10. a) Transition–metal–free $C(sp^3) - C(sp^2)$ cross–coupling reaction catalysed by the organic sulfide catalyst **(26)**. b) Scheme of the proposed sulfide–catalysed cross–coupling mechanism.[52]

Perspective
doi.org/10.1002/ceur.202400086

4.2. Reaction of Levamisole Hydrochloride on a Triruthenium (Ru_3) Cluster

Figure 11 shows the chemical structure of levamisole [(−)–2,3,5,6–tetrahydro–6–phenylimidazo[2,1–*b*]thiazole] hydrochloride ([Hlvms]Cl) **(30)**, a well–known drug with immunomodulatory and anticancer properties,[53,54] which consists in a constrained hetero–substituted bicycle compound with different C–N and C–S bonds. Cabeza and co–workes have reported that **(30)** reacts with the commercially available Ru_3 cluster $Ru_3(CO)_{12}$ **(31)** in THF at reflux temperature to build up the new complex **(32)**.[55] This crystallographically characterized Ru_3 complex shows the expected structural features of a reductive addition step, with broken C–S and Ru–Ru bonds,[56] the latter now occupied by the Cl^- anion of the incoming ligand salt, after the addition of the levamisole hydrochloride **(30)**.

The reaction in Figure 11 can be ascribed to a reductive addition step, where the thioether coordinates to the Ru_3 cluster **(31)** in the same way than disulfides coordinate to the Au_8 cluster **(16)** (see Figure 9 above), to break the C–S bond, generate the new C–Ru and S–Ru bonds, transfer the electron density, and break one of the Ru–Ru bonds of the cluster. A RAOE mechanism is more favoured here than a classical OARE mecchanism since $Ru_3(CO)_{12}$ **(31)** has not available coordination positions, thus a direct addtion to generate that coordinating space in the cluster is more likely. However, it could be argued here that the Ru atoms in $Ru_3(CO)_{12}$ are in a too low oxidation step to receive more electron density, but the same study[57] shows reactive experiments where the Cl^- anion bonds to $Ru_3(CO)_{12}$ **(31)** to form a negatively charged Ru_3 cluster. In other words, **(31)** is prone to accept electron density. Analousgy, the reaction of $Ru_3(CO)_{12}$ **(31)** with thiophene or 2–methylthiophene also proceeds via C–S bond cleavage to yield the corresponding complexes $[Ru_2(\mu\text{–}C_4H_4)(CO)_6]$ and $[Ru_4(\mu^3\text{–}S)(\mu\text{–}C_4H_4)(CO)_{11}]$,[57] which could very well come from a RAOE mechanism followed by a disproportion reaction of the resulting Ru_3 addition complex. Phenazine is also operative as a reactant for the reaction with the $Ru_3(CO)_{12}$ **(31)** clusters.[58]

4.3. Aerobic Oxidation of Thiols to Disulfides Catalyzed by Au_5 Clusters

The oxidation of thiols with O_2 to form disulfides is a common process in nature and academic laboratories, however, slow and difficult to control. Corma and co–workers developed a catalyst consisting in sub–nanometric Au clusters deposited on multi-walled carbon nanotubes (MWCNTs), which showed an extraordinary catalytic activity for the aerobic oxidation of thiols (turnover frequency, TOF = $7{\cdot}10^5$ h^{-1}).[59] The Au clusters are formed in–situ, after smooth agglomeration of the initially supported gold salt, which is much less catalytically active. Combined experimental and computational results allowed to propose the reaction mechanism shown in Figure 12. It was observed that the ligation of each molecule of thiophenol **(33)** to the Au cluster **(34)** (exemplified with Au_5 clusters, which showed the highest catalytic activity) is accompanied by a $0.2e^-$ donation from thiophenol **(33)** to the Au cluster, thus with a neat ganancy of electron density on the Au atoms.[60] This step constitutes a reductive addition reaction. After activation and dissociation of O_2 onto the Au_5 cluster containing to two thiophenol molecules, deprotonation of the bonded thiophenol moieties and release of H_2O (without a significant change in the electronics and topology of the Au_5 cluster) occurs, to forge a new Au–Au bond and release the disulfide product **(35)**. This process is essentially the same than the Au_8–catalyzed release of a disulfide product (Figure 9 above), i.e. the oxidative elimination step. The same study[59] shows that the electron movement is completely opposite with the less active single Au atoms, where the density accumulates on the S rather than on the Au atom, which re–inforces the hypothesis of a RAOE mechanism with the few–atom Au clusters.

The Au_5–catalyzed aerobic oxidation of thiols to disulfides is, in our opinion, a clear example of reported reaction where a RAOE mechanism will better explain the reaction mechanism. The key parameter to measure is the relative electronic density of the metal site during reaction, since the overall system will show the same electronic counting than the OARE mechansim. For instance, the levamisole complex **(32)** shown above is a formal $50e^-$ cluster, just $2e^-$ more than the starting $48e^-$ $Ru_3(CO)_{12}$ **(31)** cluster, in accordance with the overall gain of

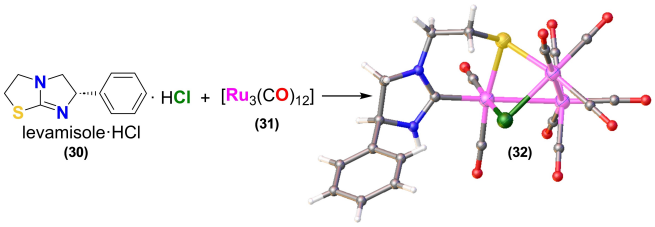

Figure 11. Scheme of the reaction of [Hlvms]Cl **(30)** with $Ru_3(CO)_{12}$ **(31)** to build up the complex **(32)**.[55]

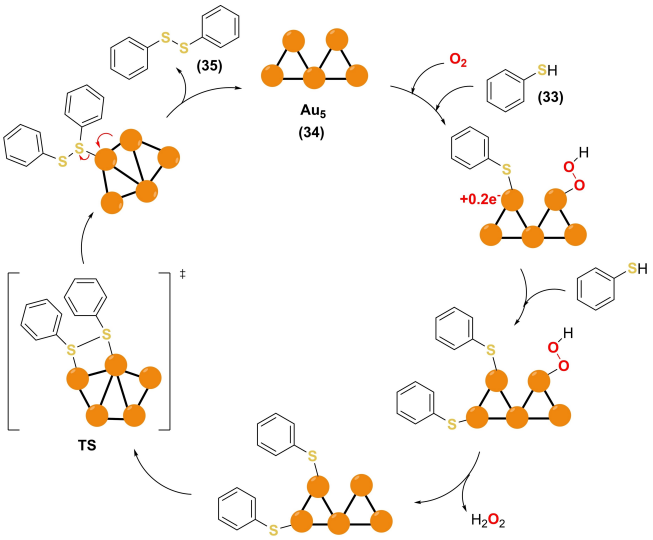

Figure 12. Proposed mechanism of disulfide **(35)** formation catalyzed by an Au_5 cluster, supported by DFT calculations.[59] The increase in electronic density of the Au atom after reductive addition of thiophenol **(33)** and the arrows for the oxidative elimination step are both indicated in red.

Perspective
doi.org/10.1002/ceur.202400086

electron density, but nevertheless the same value would be expected for the OARE mechanism. In the absence of a value for the electron density on the metal core, it is difficult to confirm the RAOE mechanism.

5. Conclusions and Outlook

The RAOE mechanism is a plausible pathway for reactions involving metal aggregations, i.e. clusters from three atoms[61] and above, nanoparticles and extended surfaces, where the approaching molecules donate rather than receive electron density to the metal core, opening up in a reductive addition step. The metal atoms share the electron density, with the possibility of breaking some metal–metal bonds, to accomodate the two moieties of the broken incoming molecule onto different metal atoms.[62] Then, the same intermediate steps than occurs in the classical OARE mechanism, such as transmetallations, insertions, shifts,…, can occur, to finally forge the new bond of the released coupled product with the extra electron density received in the first step, regenerating the broken metal–metal bonds and recuperating the original metal aggregate.

The RAOE mechanism has obvious advantages respect to the OARE mechanism. First, the metal reduces rather than oxidizes to initiate the process, and metals in oxidized form are naturally more stable. Second, donor molecules should better engage in the mechanism, and molecules with available electron density ready to be shared, i.e. on heteroatoms, are extraordinarily common. Third, the interplay of the atoms in the metal core provides a favorable entropic scenario, with much more possibilities of bonding (including the metal–metal breakings and re–boundings), thus favouring the formation of the required transition state to evolve.

We are aware of the transgressive proposal here reported, which supposes a paradigmatic shift in the way of thinking about reaction mechanisms not only on metal aggregates but also in delocalized organic molecules. We do not intend to invalidate the universality of the classical OARE mechanism, neither any of the works previously reported. Most of the systems involving cross–coupled products likely proceed through an OARE mechanism, either with mono– or multi–metallic catalysts. However, our message here is that the RAOE mechanism should be considered during the research studies. In this way, catalyst design may change, and not be exclusively focused on fullfilling the classical OARE mechanism.[63]

Some hints to think for a possible RAOE mechanism during a given reaction might include: 1) reduction of the metal core during the fist stage of the process, 2) involvement of electron donor molecules which prefer to give rather than to receive electron density, and 3) unfeasibility to adjust the experimental evidences to the classical OARE mechanism. All these features are easily quantificable with the current experimental techniques, including in–operando instrumentations such as X–ray photoelectron spectroscopy (XPS), Raman and diffuse reflectance infrared Fourier transform spectroscopy (DRIFTS), to name a few, to follow the electron density of the metal core; NMR and FT–IR to follow the electron density of the incoming molecules; and reactive and kinetic experiments to validate the different mechanistic models. All these experimental tecniques can be accompanied by computational calculations, of high accuracy for small metal clusters.

The understanding of how a wide variety of reactions operate could benefit after including the RAOE mechanism during the mechanstic studies. For instance, paramount reactions such as the hydrogenation reaction with H_2 and the coupling of NH_3 or H_2O (which include ammonium borane decomposition and others)[64] might be revised in some cases, since these molecules possess a low–lying highest ocuppied molecular orbital (HOMO) ready to give electron density, rather than receiving in the antibonding lowest unocuppied molecular orbital (LUMO), and the metal catalysts often employed for the activation of these molecules are metal clusters and nanoparticles.

Acknowledgements

We thank the Ministerio de Ciencia e Innovación Spain (MICIIN), for grant numbers PID2023–148441NB–I00 and Severo Ochoa program CEX2021–001230–S. B. L.–B. thanks Juan de la Cierva grant (JDC2022 – 048323 – I).

Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: reductive addition–oxidative elimination (RAOE) · oxidative addition–reductive elimination (OARE) · catalysis · cross–coupling reactions · metal clusters

[1] J. A. Labinger, *Organometallics* **2015**, *34*, 4784–4795.
[2] a) L. Souillart, N. Cramer, *Chem. Rev.* **2015**, *115*, 9410–9464; b) J. Garcia–Carceles, K. A. Bahou, J. F. Bower, *ACS Catal.* **2020**, *10*, 12738–12759.
[3] J. P. Collman, *Acc. Chem. Res.* **1968**, *1*, 136–143.
[4] L. Vaska, *Acc. Chem. Res.* **1968**, *1*, 335–344.
[5] G. J. Sunley, D. J. Watson, *Catal. Today* **2000**, *58*, 293–307.
[6] E. A. Denisova, A. Yu Kostyukovich, A. N. Fakhrutdinov, V. A. Korabelnikova, A. S. Galushko, V. P. Ananikov, *ACS Catal.* **2022**, *12*, 6980–6996.
[7] P. Ruiz–Castillo, S. L. Buchwald, *Chem. Rev.* **2016**, *116*, 12564–12649.
[8] T. Chu, G. I. Nikonov, *Chem. Rev.* **2018**, *118*, 3608–3680.
[9] B. Gardner, C. E. Kefalidis, E. Lu, D. Patel, E. J. L. McInnes, F. Tuna, A. J. Wooles, L. Maron, S. T. Liddle, *Nat. Commun.* **2017**, *8*, 1898.
[10] a) U. Christmann, R. Vilar, *Angew. Chem. Int. Ed.* **2005**, *44*, 366–374; b) S. Wagschal, L. Alessandro Perego, A. Simon, A. Franco–Espejo, C. Tocqueville, J. Albaneze–Walker, A. Jutand, L. Grimaud, *Chem. Eur. J.* **2019**, *25*, 6980–6987; c) J. Zhang, A. Bellomo, N. Trongsiriwat, T. Jia, P. J. Carroll, S. D. Dreher, M. T. Tudge, H. Yin, J. R. Robinson, E. J. Schelter, P. J. Walsh, *J. Am. Chem. Soc.* **2014**, *136*, 6276–6287.
[11] a) T. Braun, *Angew. Chem. Int. Ed.* **2005**, *44*, 5012–5014; b) S. Doherty, J. G. Knight, Julian, H. Y. Alharbi, R. Paterson, C. Wills, C. Dixon, L. Siller,

T. W. Chamberlain, A. Griffiths, S. M. Collins, K. Wu, M. D. Simmons, R. A. Bourne, K. R. J. Lovelock, J. Seymour, *ChemCatChem* **2022**, *14*, e202101752; c) R. Paterson, A. A. Alharbi, C. Wills, C. Dixon, L. Siller, T. W. Chamberlain, A. Griffiths, S. M. Collins, K. Wu, M. D. Simmons, R. A. Bourne, K. R. J. Lovelock, J. Seymour, J. G. Knight, S. Doherty, *J. Mol. Cat.* **2022**, *528*, 112476; d) T. K. Ghosh, N. N. Nair, *J. Phys. Chem. C* **2011**, *115*, 15403–15409.

[12] a) J. M. Asensio, D. Bouzouita, P. W. N. M. van Leeuwen, B. Chaudret, *Chem. Rev.* **2020**, *120*, 1042–1084; b) D. Adams, B. Captain, *Angew. Chem. Int. Ed.* **2008**, *47*, 252–257.

[13] A. Corma, T. Ródenas, M. J. Sabater, *Chem. Sci.* **2012**, *3*, 398–404.

[14] C. Shen, P. Zhang, Q. Sun, S. Bai, T. S. A. Hor, X. Liu, *Chem. Soc. Rev.* **2015**, *44*, 291–314.

[15] a) F. Garnes–Portolés, R. Greco, J. Oliver–Meseguer, J. Castellanos–Soriano, M. C. Jiménez, M. López–Haro, J. C. Hernández–Garrido, M. Boronat, R. Pérez–Ruiz, A. Leyva–Pérez, *Nat. Catal.* **2021**, *4*, 293–303; b) P. S. D. Robinson, G. N. Khairallah, G. da Silva, H. Lioe, R. A. J. O'Hair, *Angew. Chem. Int. Ed.* **2012**, *51*, 3812–3817; c) M. Boronat, A. Leyva–Perez, A. Corma, *Acc. Chem. Res.* **2014**, *47*, 834–844; d) W. Tu, M. Ghoussoub, C. Veer Singh, C. Veer, Y. C. Chin, *J. Am. Chem. Soc.* **2017**, *139*, 6928–6945; e) K. S. S. V. P. Reddy, P. A. Deshpande, *Mol. Catal.* **2022**, *521*, 112205.

[16] a) B. Chaudret, *Top. Organomet. Chem.* **2005**, *16*, 233–259; b) D. Astruc, Didier, *Inorg. Chem.* **2007**, *46*, 1884–1894; c) C. Deraedt, D. Astruc, *Acc. Chem. Res.* **2014**, *47*, 494–503; d) R. Ricciardi, J. Huskens, W. Verboom, *Org. Biomol. Chem.* **2015**, *13*, 4953–4959; e) A. Palazzolo, S. Carenco, *Chem. Mater.* **2021**, *33*, 7914–7922; f) Z. Huang, Q. P. Sam, G. Dong, *Chem. Sci.* **2015**, *6*, 5491–5498; g) S. Sheokand, M. S. Balakrishna, *Inorg. Chem.* **2023**, *62*, 12317–12328; h) A. M. Trzeciak, J. J. Ziolkowski, *Coord. Chem. Rev.* **2007**, *251*, 1281–1293; i) A. R. Hajipour, G. Azizi, *Synlett* **2013**, *24*, 254–258; j) M. V. Polynski, Y. S. Vlasova, Y. V. Solovev, S. M. Kozlov, V. P. Ananikov, *Chem. Sci.* **2024**, *15*, 9977–9986; k) B. Sun, L. Ning, H. Zeng, *J. Am. Chem. Soc.* **2020**, *142*, 13823–13832; l) A. Gniewek, A. M. Trzeciak, J. J. Ziolkowski, L. Kepinski, J. Wrzyszcz, W. Tylus, *J. Catal.* **2005**, *229*, 332–343; m) D. Guo, K. Jiang, H. Gan, Y. Ren, J. Long, Y. Li, B. Yin, *Angew. Chem. Int. Ed.* **2023**, *62*, e202304662; n) L. Tang, P. Wang, Y. Fan, X. Yang, C. Wan, Z. Zha, *ChemCatChem* **2016**, *8*, 3565–3569; o) K. S. S. V. P. Reddy, A. P. Deshpande, *Appl. Surf. Sci.* **2023**, *614*, 156206; p) A. Leyva–Perez, J. Oliver–Meseguer, J. Cabrero–Antonino, P. Rubio–Marques, P. Serna, P. S. Al–Resayes, A. Corma, *ACS Catal.* **2013**, *3*, 1865–1873; q) G. Budroni, A. Corma, H. Garcia, A. Primo, *J. Catal.* **2007**, *251*, 345–353.

[17] a) J. Lin, H. Abroshan, C. Liu, M. Zhu, G. Li, M. Haruta, *J. Catal.* **2015**, *330*, 354–361; b) S. K. Beaumont, G. Kyriakou, R. M. Lambert, *J. Am. Chem. Soc.* **2010**, *132*, 12246–12248; c) M. Boronat, D. Combita, P. Concepcion, A. Corma, H. Garcia, R. Juarez, S. Laursen, J. Lopez–Castro, *J. Phys. Chem. C* **2012**, *116*, 24855–24867; d) C. Sanchez–Sanchez, F. Yubero, A. R. Gonzalez–Elipe, L. Feria, J. F. Sanz, R. M. Lambert, *J. Phys. Chem. C* **2014**, *118*, 11677–11684; e) N. Candu, A. Dhakshinamoorthy, N. Apostol, C. Teodorescu, A. Corma, H. Garcia, V. I. Parvulescu, *J. Catal.* **2017**, *352*, 59–66; f) Y. Tsuji, M. Yoshida, T. Kamachi, K. Yoshizawa, *J. Am. Chem. Soc.* **2022**, *144*, 18650–18671.

[18] a) M. V. Polynski, V. P. Ananikov, *ACS Catal.* **2019**, *9*, 3991–4005; b) V. M. Chernyshev, V. P. Ananikov, *ACS Catal.* **2022**, *12*, 1180–1200; c) Y. Li, Z. Zhang, T. Fan, X. Li, J. Ji, P. Dong, R. Baines, J. Shen, M. Ye, *ChemPlusChem* **2016**, *81*, 564–573; d) E. E. Ondar, A. Y. Kostyukovich, J. V. Burykina, A. S. Galushko, V. P. Ananikov, *Catal. Sci. Technol.* **2023**, *13*, 6022–6040; e) J. Oliver–Meseguer, I. Dominguez, R. Gavara, A. Leyva–Perez, A. Corma, *ChemCatChem* **2017**, *9*, 1429–1435; f) C. Gonzalez–Arellano, A. Abad, A. Corma, H. Garcia, M. Iglesias, F. Sanchez, *Angew. Chem. Int. Ed.* **2007**, *46*, 1536–1538.

[19] a) R. Chinchilla, C. Najera, *Chem. Soc. Rev.* **2011**, *40*, 5084–5121; b) A. Corma, R. Juarez, M. Boronat, F. Sanchez, M. Iglesias, H. Garcia, Hermenegildo, *Chem. Comm.* **2011**, *47*, 1446–1448; c) A. Elhage, B. Wang, N. Marina, M. L. Marin, M. Cruz, A. E. Lanterna, J. C. Scaiano, *Chem. Sci.* **2018**, *9*, 6844–6852; d) K. Hong, M. Sajjadi, J. M. Suh, K. Zhang, M. Nasrollahzadeh, H. W. Jang, R. S. Varma, M. Shokouhimehr, *ACS Appl. Nano Mater.* **2020**, *3*, 2070–2103; e) A. Corma, H. Garcia, *Chem. Soc. Rev.* **2008**, *37*, 2096–2126; f) G. Li, R. Jin, *Nanotechnol. Rev.* **2013**, *2*, 529–545.

[20] E. M. Fiordaliso, S. Murphy, R. M. Nielsen, S. Dahl, I. Chorkendorff, *Surf. Sci.* **2012**, *606*, 263–272.

[21] J. L. Lin, J. B. E. Bent, *J. Am. Chem. Soc.* **1993**, *115*, 2849–2853.

[22] A. Leyva–Perez, J. Oliver–Meseguer, P. Rubio–Marques, A. Corma, Avelino *Angew. Chem. Int. Ed.* **2013**, *52*, 11554–11559.

[23] M. A. Rivero–Crespo, P. Rubio–Marqués, J. C. Hernández–Garrido, M. Mon, J. Oliver–Meseguer, A. Leyva–Pérez, *Catal. Sci. Technol.* **2023**, *13*, 2508–2516.

[24] N. Jeddi, N. W. J. Scott, I. J. S. Fairlamb, *ACS Catal.* **2022**, *12*, 11615–11638.

[25] K. O. Kirlikovali, E. Cho, T. J. Downard, L. Grigoryan, Z. Han, S. Hong, D. Jung, J. C. Quintana, V. Reynoso, S. Ro, Y. Shen, K. Swartz, E. Ter Sahakyan, A. I. Wixtrom, B. Yoshida, A. L. Rheingold, A. M. Spokoyny, *Dalton Trans.* **2018**, *47*, 3684–3688.

[26] a) E. A. Denisova, D. B. Eremin, E. G. Gordeev, A. M. Tsedilin, V. P. Ananikov, *Inorg. Chem.* **2019**, *58*, 12218–12227; b) E. A. Denisova, A. Y. Kostyukovich, A. N. Fakhrutdinov, V. A. Korabelnikova, A. S. Galushko, V. P. Ananikov, *ACS Catal.* **2022**, *12*, 6980–6996; c) B. D. Briggs, N. M. Bedford, S. Seifert, H. Koerner, H. Ramezani–Dakhel, H. Heinz, R. R. Naik, A. I. Frenkel, M. R. Knecht, *Chem. Sci.* **2015**, *6*, 6413–6419; d) Y. Yang, L. D. Unsworth, N. Semagina, *J. Catal.* **2011**, *281*, 137–146.

[27] a) G. Kyriakou, S. K. Beaumont, S. M. Humphrey, C. Antonetti, R. M. Lambert, *ChemCatChem* **2010**, *2*, 1444–1449; b) N. Norouzi, M. K. Das, A. J. Richard, A. A. Ibrahim, H. M. El–Kaderi, M. S. El–Shall, *Nanoscale* **2020**, *12*, 19191–19202.

[28] J. K. Edwards, J. Pritchard, L. Lu, M. Piccinini, G. Shaw, A. F. Carley, D. J. Morgan, C. J. Kiely, G. J. Hutchings, *Angew. Chem. Int. Ed.* **2014**, *53*, 2381–2384.

[29] a) R. K. Rai, K. Gupta, D. Tyagi, A. Mahata, S. Behrens, X. Yang, Q. Xu, B. Pathak, S. K. Singh, *Catal. Sci. Technol.* **2016**, *6*, 5567–5579; b) B. Boekfa, E. Pahl, N. Gaston, H. Sakurai, J. Limtrakul, M. Ehara, *J. Phys. Chem. C* **2014**, *118*, 22188–22196; c) J. Wang, S. A. Kondrat, Y. Wang, G. L. Brett, C. Giles, J. K. Bartley, L. Lu, Q. Liu, C. J. Kiely, G. J. Hutchings, *ACS Catal.* **2015**, *5*, 3575–3587; d) G. J. Hutchings, C. J. Kiely, *Acc. Chem. Res.* **2013**, *46*, 1759–1772; e) I. N. Francesco, F. Fontaine–Vive, S. Antoniotti, *ChemCatChem* **2014**, *6*, 2784–2791; f) S. U. Son, Y. Jang, J. Park, H. B. Na, H. M. Park, H. J. Yun, J. Lee, T. Hyeon, *J. Am. Chem. Soc.* **2004**, *126*, 5026–5027.

[30] a) F. Raza, D. Yim, J. H. Park, H. Kim, S. Jeon, J. Kim, *J. Am. Chem. Soc.* **2017**, *139*, 14767–14774; b) S. Sarina, H. Zhu, E. Jaatinen, Q. Xiao, H. Liu, J. Jia, C. Chen, J. Zhao, *J. Am. Chem. Soc.* **2013**, *13515*, 5793–5801; c) N. Kang, Q. Wang, R. Djeda, W. Wang, F. Fu, M. M. Moro, M. Ramirez, S. Moya, E. Coy, L. Salmon, *ACS Appl. Mater. Interfaces* **2020**, *12*, 53816–53826; d) A. Singh, M. Kumar, V. Bhalla, *Aggregate* **2023**, *4*, e192; e) S. Zhang, C. Chang, Z. Huang, Y. Ma, W. Gao, J. Li, Y. Qu, *ACS Catal.* **2015**, *5*, 6481–6488.

[31] a) P. Verma, Y. Kuwahara, K. Mori, H. Yamashita, *J. Mater. Chem. A* **2016**, *4*, 10142–10150; b) P. Lyu, R. Espinoza, I. M. Khan, W. C. Spaller, S. Ghosh, S. Nguyen, *iScience* **2022**, *25*, 103737.

[32] a) J. Joy, T. Stuyver, S. Shaik, *J. Am. Chem. Soc.* **2020**, *142*, 3836–3850; b) J. J. Davis, K. S. Coleman, K. L. Busuttil, C. B. Bagshaw, *J. Am. Chem. Soc.* **2005**, *127*, 13082–13083.

[33] a) S. Carrettin, J. Guzman, A. Corma, *Angew. Chem. Int. Ed.* **2005**, *44*, 2242–2245; b) N. G. Willis, J. Guzman, *Appl. Catal. A* **2008**, *339*, 68–75; c) S. Banerjee, C. Basheer, R. N. Zare, *Angew. Chem. Int. Ed.* **2016**, *55*, 12807–12811.

[34] a) L. M. Bavaro, P. Montangero, J. B. Keister, *J. Am. Chem. Soc.* **1983**, *105*, 4977–4981; b) F. J. Safarowic, D. J. Bierdeman, J. B. Keister, *J. Am. Chem. Soc.* **1996**, *118*, 11805–11812.

[35] R. H. Crabtree, S. M. Morehouse, *Inorg. Chem.* **1982**, *21*, 4210–4213.

[36] a) M. A. Watzky, R. G. Finke, *J. Am. Chem. Soc.* **1997**, *119*, 10382–10400; b) L. Starkey Ott, R. G. Finke, *Inorg. Chem.* **2006**, *45*, 8382–8393.

[37] F. Stegemman, C. Benndorf, Y. Zhang, M. Bartsch, H. Zacharias, B. P. T. Fokwa, H. Eckert, O. Janka, *Inorg. Chem.* **2017**, *56*, 1919–1931.

[38] Z. Xia, V. Corce, F. Zhao, C. Przybylski, A. Espagne, L. Jullien, T. Le Saux, Y. Gimbert, H. Dossmann, V. Mouries–Mansuy, C. Ollivier, L. Fensterbank, *Nat. Chem.* **2019**, *11*, 797–805.

[39] J. Oliver–Meseguer, A. Doménech–Carbó, M. Boronat, A. Leyva–Pérez, A. Corma, *Angew. Chem. Int. Ed.* **2017**, *56*, 6435–6439.

[40] J. Oliver–Meseguer, M. Boronat, A. Vidal–Moya, P. Concepción, M. Á Rivero–Crespo, A. Leyva–Pérez, A. Corma, *J. Am. Chem. Soc.* **2018**, *140*, 3215–3218.

[41] T. Ohmura, Y. Morimasa, M. Suginome, *J. Am. Chem. Soc.* **2015**, *137*, 2852–2855.

[42] J. Kang, Y. Wang, F. Peng, N. Zhang, Y. Xue, Y. Yang, E. Kumacheva, K. Liu, *Angew. Chem. Int. Ed.* **2022**, *61*, e202202405.

[43] a) B. Lerma–Berlanga, F. Orlando, E. Merino, A. Leyva–Pérez, *ChemCatChem* **2024**, e202400909; b) Y. Bai, S. He, Y. Lv, M. Zhu, H. Yu, *Inorg. Chem.* **2021**, *60*, 5724–5733; c) Y. Kamei, Y. Shichibu, K. Konishi, *Angew. Chem. Int. Ed.* **2011**, *50*, 7442–7445.

[44] J. Oliver Meseguer, I. Dominguez, R. Gavara, A. Doménech Carbó, J. M. G. Calbet, A. Leyva Pérez, A. Corma, *Chem. Commun.* **2017**, *53*, 1116–1119.
[45] M. Arisawa, M. Yamaguchi, *J. Am. Chem. Soc.* **2003**, *125*, 6624–6625.
[46] M. Arisawa, A. Suwa, M. Yamaguchi, *J. Organomet. Chem.* **2006**, *691*, 1159–1168.
[47] J. Guo, J. Zha, T. Zhang, C. –H Ding, Q. Tan, B. Xu, *Org. Lett.* **2021**, *23*, 3167–3172.
[48] S. Gary, S. Bloom, *ACS Cent. Sci.* **2022**, *8*, 1537–1547.
[49] S. P. Black, J. K. M. Sanders, A. R. Stefankiewicz, *Chem. Soc. Rev.* **2014**, *43*, 186–1872.
[50] a) A. J. Arce, P. Arrojo, Y. De Sanctis, A. J. Deeming, D. J. West, *Polyhedron* **1992**, *11*, 1013–21; b) A. D. Sonawane, R. A. Sonawane, M. Ninomiya, M. Koketsu, *Dalton Trans.* **2021**, *50*, 12764–12790.
[51] D. J. Jones, M. Lautens, G. P. McGlacken, *Nat. Catal.* **2019**, *2*, 843–851.
[52] Z. He, F. Song, H. Sun, Y. Huang, *J. Am. Chem. Soc.* **2018**, *140*, 2693–2699.
[53] J. S. Kovach, P. A. Svingen, D. J. Schaid, *J. Natl. Cancer Inst.* **1992**, *84*, 515–519.
[54] W. K. P. Amery, J. P. J. M. Bruynseels, *Int. J. Immunopharmacol.* **1992**, *14*, 481–486.
[55] J. A. Cabeza, I. del Río, S. García–Granda, V. Riera, M. G. Sánchez–Vega, *Eur. J. Inorg. Chem.* **2002**, *2002*, 2561–2564.
[56] G. Higashihara, M. Terada, A. Inagaki, M. Akita, *Organometallics* **2007**, *26*, 439–444.
[57] A. J. Arce, Y. de Sanctis, A. Karam, A. J. Deeming, *Angew. Chem. Int. Ed.* **1994**, *33*, 1381–1383.
[58] J. A. Cabeza, P. Garcia–Alvarez, V. Pruneda, *Organometallics* **2012**, *31*, 941–946.
[59] A. Corma P Concepción, M. Boronat, M. J. Sabater, J. Navas, M. J. Yacaman, E. Larios, A. Posadas, M. A. López–Quintela, D. Buceta, E. Mendoza, G. Guilera, A. Mayoral Nat, *Chem.* **2013**, *5*, 775–781.
[60] F. Stegemann, C. Benndorf, Y. Zhang, M. Bartsch, H. Zacharias, B. P. T. Fokwa, H. Eckert, O. Janka, *Inorg. Chem.* **2017**, *56*, 1919–1931.
[61] a) E. Fernandez, M. A. Rivero–Crespo, I. Dominguez, P. Rubio–Marques, J. Oliver–Meseguer, L. Liu, M. Cabrero–Antonino, R. Gavara, J. C. Hernandez–Garrido, M. Boronat, A. Leyva Pérez, A. Corma, *J. Am. Chem. Soc.* **2019**, *141*, 1928–1940; b) F. Bigi, D. Cauzzi, N. Della Ca', M. Malacria, R. Maggi, E. Motti, Y. Wang, G. Maestri, *ACS Org. Inorg. Au* **2022**, *2*, 373–385.
[62] L. A. Perego, P. Payard, B. Haddou, I. Ciofini, L. Grimaud, *Chem. Eur. J.* **2018**, *24*, 2192–2199.
[63] a) Z. Xia, V. Corcé, F. Zhao, C. Przybylski, A. Espagne, L. Jullien, T. Le Saux, Y. Gimbert, H. Dossmann, V. Mouriès–Mansuy, C. Ollivier, L. Fensterbank, *Nat. Chem.* **2019**, *11*, 797–805; b) T. McCallum, *Org. Biomol. Chem.* **2023**, *21*, 1629–1646.
[64] C. Wang, J. Tuninetti, Z. Wang, C. Zhang, R. Ciganda, L. Salmon, S. Moya, J. Ruiz, D. Astruc, *J. Am. Chem. Soc.* **2017**, *139*, 11610–11615.

Version of record online: February 3, 2025