

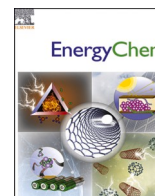


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Structural evolution of artificial water oxidation catalysts: From natural clusters to the design strategies of molecular systems

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ABSTRACT

The development of artificial water oxidation catalysts (WOCs) represents a journey of structural and conceptual evolution. It began with bioinspired explorations of the Mn_4CaO_5 cluster in Photosystem II, establishing core principles of molecular design based on precise control of metal nuclearity and coordination environments, and has now advanced towards a new generation of catalysts centered on earth-abundant metals. Throughout this progression, strategies such as multinuclear cooperativity and metal-ligand interactions have enabled base-metal catalysts to rival and even surpass the performance benchmarks set by their noble counterparts. To bridge the molecular precision of homogeneous catalysts with the operational stability required for practical applications, interfacial engineering has become paramount. Hybrid molecular electrodes, constructed through immobilization strategies that include π - π stacking and covalent anchoring, have emerged as representative paradigms that bridge the molecular and material realms. This review systematically delineates this structural evolution pathway. By integrating biological inspiration, molecular design, and interfacial engineering, it outlines a clear blueprint for developing efficient and stable sustainable water oxidation technologies.

1. Introduction

The escalating global energy demand and the urgent challenge of climate change have intensified the pursuit of sustainable pathways to convert and store renewable electricity in chemical energy [1–4]. Among various energy-conversion routes, electrocatalytic water splitting stands out as one of the most promising strategies to establish a carbon-neutral energy cycle. The oxidation reaction involves the four-electron oxidation of water ($2\text{H}_2\text{O} \rightarrow \text{O}_2 + 4\text{H}^+ + 4\text{e}^-$) and generates energy-rich electrons, which are then used to produce chemical fuels [5]. At the heart of this process lies the anodic oxygen evolution reaction (OER), a kinetically demanding four-electron, four-proton transformation critically hinging on the formation of an O–O bond. Its sluggish kinetics and high overpotential remain the major bottlenecks limiting the overall efficiency of water-electrolysis technologies [6–8].

Among diverse catalytic systems, molecular water oxidation catalysts (WOCs) have emerged as powerful model platforms for elucidating the fundamental principles of multi-electron/proton redox chemistry [9–11]. Their well-defined coordination environments, tunable electronic structures, and mechanistic transparency enable precise

identification of key intermediates and reaction pathways, and rarely attainable advantages in heterogeneous materials. Over the past two decades, research in this field has evolved along two complementary fronts: homogeneous molecular catalysis and electrode-integrated hybrid systems. This structural and applicational evolution serves as the central narrative of this review.

To guide the reader through this structural evolution, a timeline-style schematic (Scheme 1) is presented to summarize representative milestones in the development of molecular WOCs. The scheme captures the progressive transition from mononuclear noble-metal catalysts to multinuclear systems and ultimately to interface-integrated hybrid architectures, illustrating how catalyst design has continuously evolved in response to mechanistic limitations and practical demands.

In homogeneous systems, discrete molecular catalysts have enabled detailed mechanistic dissection of O–O bond formation, typically proceeding through water nucleophilic attack (WNA) or radical coupling (I2M) pathways [12–14]. The field was inaugurated by Meyer's seminal "blue dimer," which provided the first clear evidence that a well-defined molecular species could catalyze water oxidation under electrochemical conditions [15]. This milestone stimulated the development of a wide

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family of Ru- and Ir-based catalysts, deepening the understanding of proton-coupled electron transfer (PCET) and high-valent metal-oxo intermediates in OER catalysis [16–19]. More recently, attention has strategically shifted toward earth-abundant first-row transition metals (Mn, Fe, Co, Ni, Cu) [20–26]. This shift is driven not only by sustainability and cost considerations but also by the new complexities these metals introduce, such as multinuclear cooperativity and spin-state tuning, which open fresh dimensions for controlling catalytic behavior.

Interfacial immobilization strategies have bridged the gap between molecular precision and materials-level robustness required for practical electrochemical operation. The integration of molecular WOCs onto conductive supports not only facilitates catalyst recycling and mechanistic interrogation but also enhances operational stability under oxidative conditions. Through rational interfacial engineering, including π - π stacking, hydrophobic self-assembly, click coupling, phosphonate or silane anchoring, and confinement within conductive porous frameworks, hybrid molecular anodes have been constructed that merge molecular-level reactivity with scalable electrochemical performance [27–30]. These hybrid systems preserve the molecular identity of the active site while promoting efficient charge transport and maintaining structural integrity across the electrode interface.

Although numerous excellent reviews have covered specific aspects of molecular water oxidation, from mechanistic studies of homogeneous complexes to interfacial engineering of hybrid electrodes [31–35], a unified framework that describes how molecular WOCs have evolved structurally in response to mechanistic demands remains scarce. Molecular WOCs have progressed through a sequence of structural evolution, each compelled by specific limitations of the preceding generation. The inability of mononuclear platforms to accumulate multiple oxidative equivalents motivated the emergence of multinuclear systems, and the intrinsic instability of molecular motifs under operational conditions ultimately drove their translation into interface-integrated hybrid anodes in Fig. 1. This review adopts such an evolution-centered perspective, integrating structural progression, catalytic function, and immobilization strategies into a coherent narrative that describes the structural evolution of molecular WOCs. By integrating biological inspiration, molecular design principles, and interfacial engineering, we aim to provide a coherent roadmap that links molecular-level reactivity with the construction of durable, device-ready catalytic architectures.

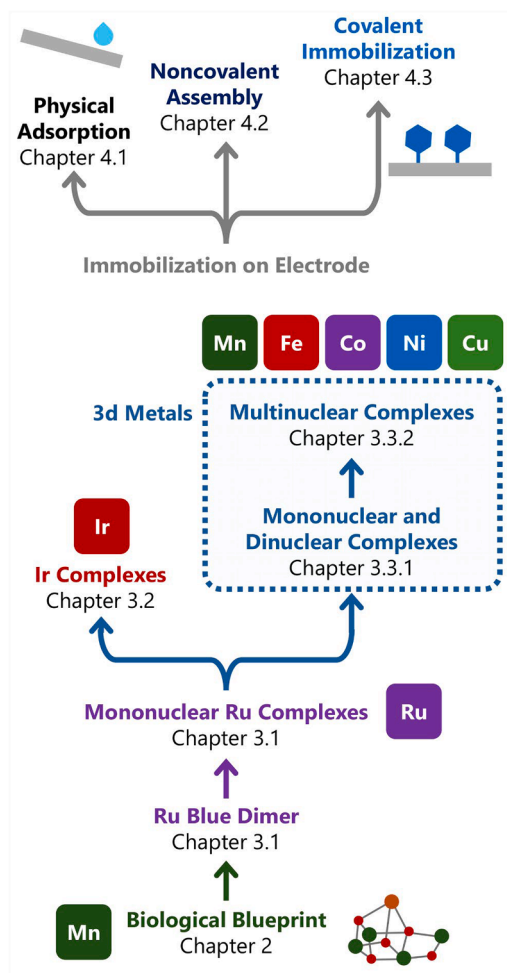
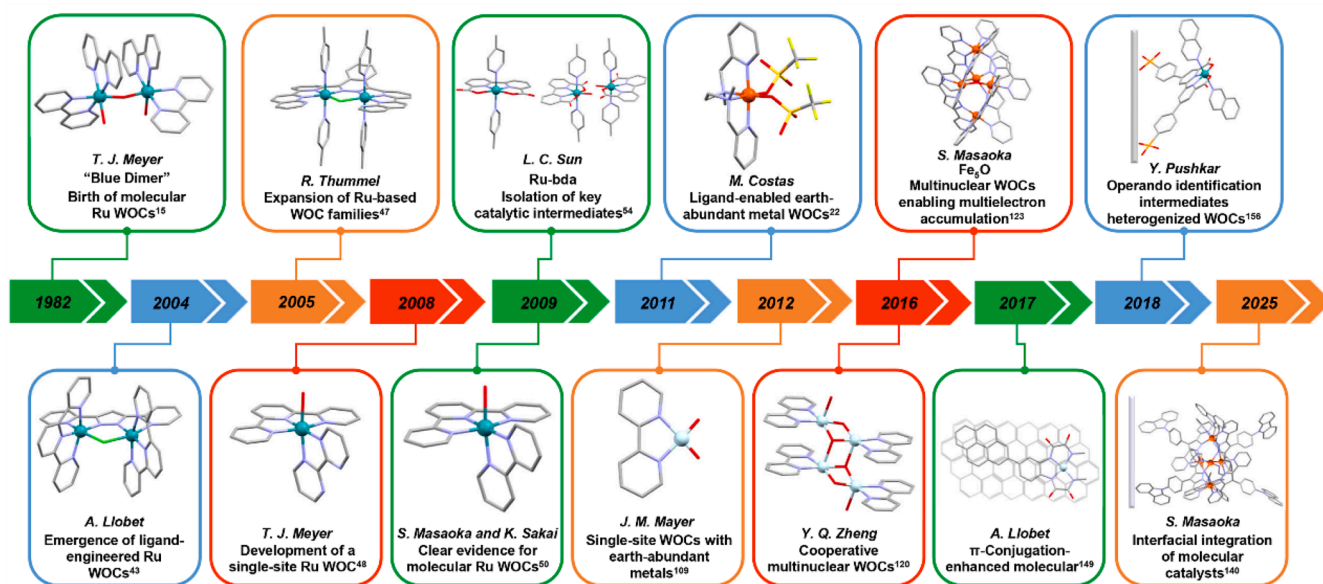


Fig. 1. The evolution in molecular water oxidation catalysts from biological inspiration to molecular design and interfacial immobilization.



Scheme 1. Timeline illustrating the structural evolution of molecular water oxidation catalysts.

2. Natural inspiration: the oxygen-evolving complex (OEC) in photosystem II

In photosystem II (PSII), water oxidation is driven by the chlorophyll special pair P680, whose photoexcitation generates the highly oxidizing species P680⁺ with a potential of about +1.25 V versus NHE. Through the redox-active tyrosine residue D1-Tyr161 (TyrZ), electrons are transferred from the oxygen-evolving complex (OEC), enabling stepwise oxidation of its Mn₄CaO₅ cluster. After four successive charge-separation events through the Kok cycle, the OEC accumulates sufficient oxidizing power to split two water molecules into one dioxygen molecule while releasing four protons.

With advances in structural biology, the molecular architecture of the OEC has been revealed in exquisite detail. The landmark 1.9 Å X-ray crystal structure of PSII reported by Shen and Kamiya resolved the Mn₄CaO₅ cluster and its ligand environment in Fig. 2. The cluster features a distorted cubane-like Mn₃CaO₄ core in which four μ -oxo ligands bridge three Mn ions and one Ca ion, while a fourth dangling Mn is connected via two additional μ -oxo bridges. This geometry can be likened to a distorted chair: the Mn₃CaO₄ cubane forms the seat, and the Mn4 ion with the O4 μ -oxo ligand forms the backrest. Four water molecules are coordinated, two to the dangling Mn and two to the Ca center, providing potential sites for substrate binding or proton transfer [36]. Recent ultrahigh-resolution and time-resolved analyses have visualized key intermediates and proton pathways within the cluster, offering strong evidence that O–O bond formation proceeds through an oxyl/oxo radical-coupling mechanism [37,38]. While gaining a deep understanding of the catalytic mechanisms of molecular water catalysts is crucial, researchers have not neglected the study of the catalytic mechanisms of the PSII system. In 2021, Noguchi monitored the photoactivation process using rapid-scan time-resolved Fourier transform infrared (FTIR) spectroscopy combined with the attenuated total reflection (ATR) technique, pointing out that (Mn^{III})₂Ca complex as the first stable intermediate of the Mn₄CaO₅ cluster, which is generated from the second photooxidation of Mn^{II} [39].

In summary, these insights underscore the finely tuned orchestration of redox relays, multinuclear cooperativity, and PCET processes that underlie the remarkable efficiency of PSII. As such, the OEC serves as a natural blueprint for artificial water oxidation catalysis, inspiring extensive efforts to develop molecular analogues that emulate its essential structural and functional motifs. The following sections will explore how these bioinspired concepts have driven the structural

evolution of artificial WOCs across both homogeneous and heterogeneous systems.

In artificial photosynthetic systems, efficient water oxidation requires catalysts that can operate at relatively low overpotentials while stabilizing high-valent metal intermediates capable of driving multi-electron redox processes. Therefore, the rational design of molecular WOCs fundamentally relies on understanding the elementary steps of the reaction mechanism. Among these steps, O–O bond formation is widely recognized as the most critical and energetically demanding process, accounting for the largest energy barrier in the catalytic cycle and often serving as the rate-determining step [40–42].

To date, two principal mechanistic pathways have been established for O–O bond formation in molecular WOCs: the water nucleophilic attack (WNA) mechanism and the interaction of two metal–oxo units (I2M) mechanism. These two pathways differ fundamentally in their reaction coordinates, proton-electron transfer behavior, and structural requirements of the catalysts. In the WNA pathway, a high-valent metal–oxo intermediate (M=O) is first generated through sequential oxidation and water activation processes. This electrophilic M=O species is then attacked by a water molecule or hydroxide ion acting as a nucleophile, leading to the formation of a metal–hydroperoxo intermediate (M–OOH). This step is typically accompanied by simultaneous proton transfer, often described as atom-proton transfer (APT), which avoids the formation of high-energy charged intermediates and significantly lowers the activation barrier. The subsequent steps involve further proton and electron removal, ultimately resulting in O₂ release and regeneration of the catalytic site. Because the reaction proceeds at a single metal center, WNA-type catalysis generally exhibits first-order kinetics with respect to catalyst concentration.

In contrast, the I2M pathway involves the direct coupling of two high-valent metal–oxo (or oxyl-like) intermediates. In this mechanism, two M–O units possessing radical character approach each other and form an O–O bond via radical coupling, generating a M–O–O–M intermediate, which subsequently evolves into molecular oxygen. Notably, since two water molecules are independently activated at two metal centers, all four protons and four electrons required for water oxidation are typically removed prior to O–O bond formation. As a result, the coupling step itself does not involve additional proton transfer, leading to distinct kinetic behavior and pH dependence compared to the WNA pathway. Due to its requirement for spatial proximity and cooperative interaction between two reactive sites, the I2M mechanism is commonly associated with multinuclear catalysts or systems with flexible ligand frameworks.

Regardless of the pathway, the formation of O–O bonds critically depend on the generation of high-valent metal–oxo intermediates through PCET processes. Depending on the relative redox potentials and acid–base properties (pK_a) of the intermediates, PCET can proceed via either stepwise (s-PCET) or concerted (c-PCET) pathways. The c-PCET mechanism plays a particularly important role in minimizing charge accumulation during multielectron oxidation, enabling multiple redox events to occur within a relatively narrow potential window. This feature has been recognized as a key factor underlying the high efficiency of the natural photosystem II (PSII). In contrast, stepwise electron transfer processes typically show no pH dependence, while PCET processes exhibit characteristic Nernstian behavior, as reflected in Pourbaix diagrams.

In addition to electron transfer, proton transfer dynamics exert a decisive influence on catalytic performance. In the WNA pathway, efficient proton removal during O–O bond formation is essential to avoid kinetic bottlenecks. The presence of external proton acceptors or internal proton relay sites within the ligand framework can significantly accelerate this process. Conversely, when proton transfer relies solely on water molecules, the relatively poor proton-donating and -accepting ability of water leads to sluggish kinetics. These effects can be experimentally probed through pH-dependent activity, kinetic isotope effects, and reaction order analysis, providing valuable insight into the

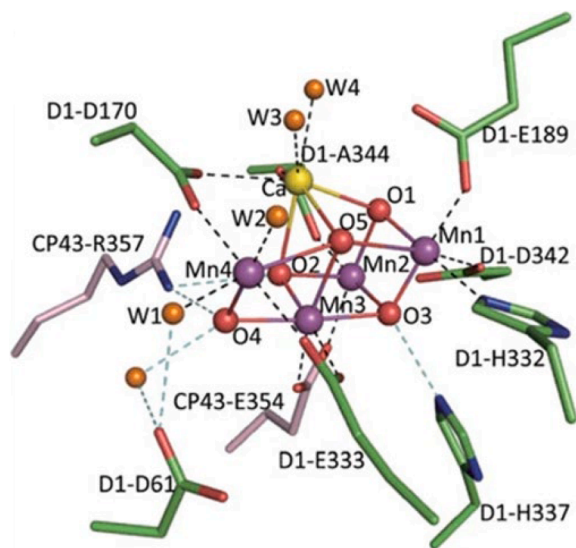


Fig. 2. Stereo view of the Mn₄CaO₅ cluster and its ligand environment. Reproduced with permission [36]. Copyright 2011, Springer.

mechanistic pathways.

Importantly, these mechanistic features are intrinsically correlated with catalyst structure. Mononuclear molecular catalysts, which contain a single active site, generally favor the WNA pathway due to the absence of adjacent reactive centers. In contrast, multinuclear catalysts enable the accumulation and distribution of oxidative equivalents across multiple metal centers, facilitating cooperative interactions and promoting I2M-type O–O bond formation. Furthermore, ligand flexibility, electronic structure tuning, and the incorporation of proton relay functionalities can significantly influence both the preferred reaction pathway and catalytic efficiency.

Therefore, the structural evolution of molecular water oxidation catalysts, from early mononuclear noble-metal systems to multinuclear first-row transition metal complexes and, more recently, to interface-integrated hybrid systems, can be understood as a direct response to these mechanistic requirements. In this sense, advances in catalyst design are not merely empirical optimizations but are fundamentally guided by the need to control PCET processes, stabilize high-valent intermediates, and regulate O–O bond formation pathways.

3. Homogeneous molecular WOCs

Building upon the mechanistic insights gleaned from the natural OEC, researchers have devoted extensive efforts to constructing molecular analogues capable of mediating multielectron, multi-proton transformations under mild conditions. In contrast to the protein-confined Mn_4CaO_5 cluster, synthetic molecular catalysts offer a highly controllable platform in which the metal center, ligand environment, and proton relays can be precisely engineered. Such systems not only provide a molecular-level understanding of the elementary steps governing water oxidation, electron abstraction, O–O bond formation, and proton transfer, but also serve as functional mimics for artificial photosynthetic assemblies. Among these, homogeneous molecular catalysts have played a central role in establishing the fundamental design principles of water oxidation catalysis, owing to their well-defined coordination structures and mechanistic transparency.

3.1. Ruthenium-based molecular WOCs

Ruthenium (Ru) emerged as the earliest and most influential platform for molecular water oxidation catalysis [43–45]. The development of Ru complexes addressed the initial challenge that no synthetic system could yet mimic water oxidation with mechanistic clarity, by providing

strong, structurally well-defined platforms that stabilize high-valent $\text{Ru}=\text{O}$ intermediates and reveal the elementary PCET and O–O bond-forming steps. As illustrated in Fig. 3, Ru-based molecular WOCs have shown a sustained growth in research activity over time, underscoring their foundational role in the field.

Meyer established the field with the μ -oxo-bridged dinuclear Ru complex, the so-called “blue dimer”, complex 1, which provided the first clear evidence that a well-defined molecular species can catalyze multi-electron water oxidation in a homogeneous solution in Fig. 4 [15]. Building on this seminal system, Llobet and Buchholz developed a new class of dinuclear ruthenium complexes $[\text{Ru}^{\text{II}}(\text{bpy})(\text{tpy})_2(\mu\text{-Cl})]^{2+}$ ($\text{Hbpy} = 3,5\text{-bis}(2\text{-pyridyl})\text{pyrazole}$, $\text{tpy} = 2,2':6',2''\text{-terpyridine}$), complex 2, in which the bridging ligand can be transformed into catalytically active aqua sites under acidic conditions [43]. Upon oxidation to the $\text{Ru}^{\text{IV}}\text{-Ru}^{\text{IV}}$ state, these complexes exhibit enhanced catalytic activity for water oxidation with a pseudo-first-order rate constant of $1.4 \times 10^{-2} \text{ s}^{-1}$, exceeding that of earlier Ru–O–Ru systems, along with improved stability. This work represents a crucial step toward structurally tunable dinuclear catalysts, highlighting the importance of ligand exchange dynamics and accessible coordination sites in promoting O–O bond formation. Thummel introduced another rigid polypyridyl-based multidentate ligand and axial pyridine ligands into the catalyst structure to obtain a new family of Ru(II) complexes $\{[\text{Ru}^{\text{II}}(\text{bpy})_2(\mu\text{-Cl})(\mu\text{-bnpdz})]^{3+}(\text{bnpdz} = 3,6\text{-bis}-(1'',8''\text{-naphthyrid-2''-yl})\text{-pyrid-2'-yl})\}$ pyridazine, $\text{bpy} = 2,2'\text{-bipyridine}$), complex 3, with significantly improved stability and activity [46]. Further advancing ligand design, subsequent studies developed a new family of Ru complexes based on naphthyridine-derived bridging frameworks, enabling systematic tuning of both axial ligand electronics and nuclearity (mono- vs dinuclear), complex 3 [47]. Notably, these systems demonstrated efficient catalytic oxygen evolution in Ce^{IV} -driven conditions with turnover numbers up to 3200, highlighting the critical role of axial ligand modulation and coordination environment in governing catalytic performance. This development provided an important structural and functional bridge between early multinuclear architectures and later mechanistically well-defined single-site systems. A landmark advance in labeling the historical transition to single-site systems came in 2008. Meyer reported single-site catalytic water oxidation by the monomeric complexes 4, $[\text{Ru}(\text{tpy})(\text{bpm})(\text{OH}_2)]^{2+}$ ($\text{tpy} = 2,2':6',2''\text{-terpyridine}$; $\text{bpm} = 2,2'\text{-bipyrimidin}$) by a well-defined mechanism involving $\text{Ru}^{\text{V}}=\text{O}$, paving the way toward a family of robust water oxidation catalysts [48]. To gain further insights into the mechanisms of water oxidation catalyzed by molecular catalysts, T. J. Meyer and co-workers first carried out the investigation

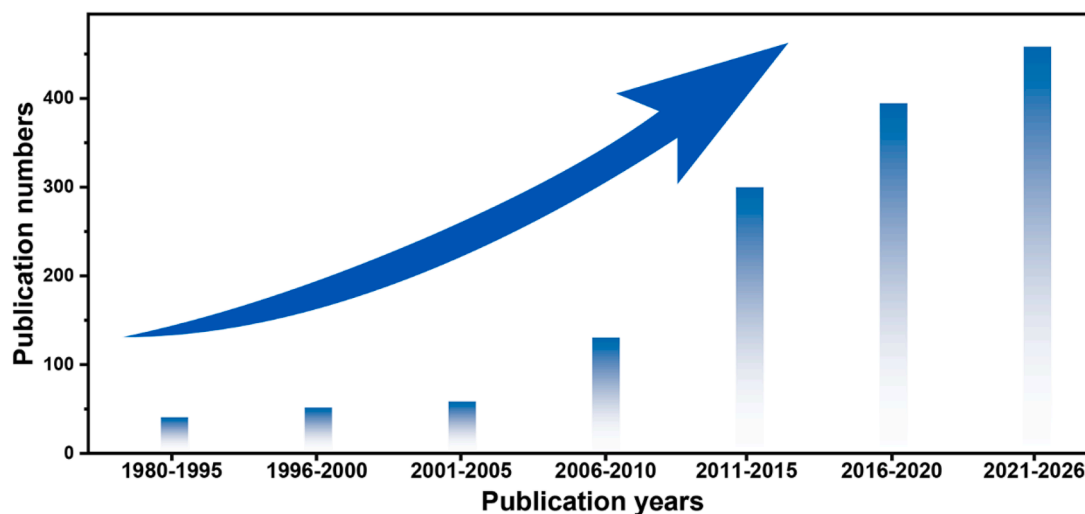


Fig. 3. Publication trends of Ru-based molecular water oxidation catalysts over successive time periods. Data retrieved from the Web of Science core collection database using the search terms “Ru”, “molecular”, and “water oxidation”.

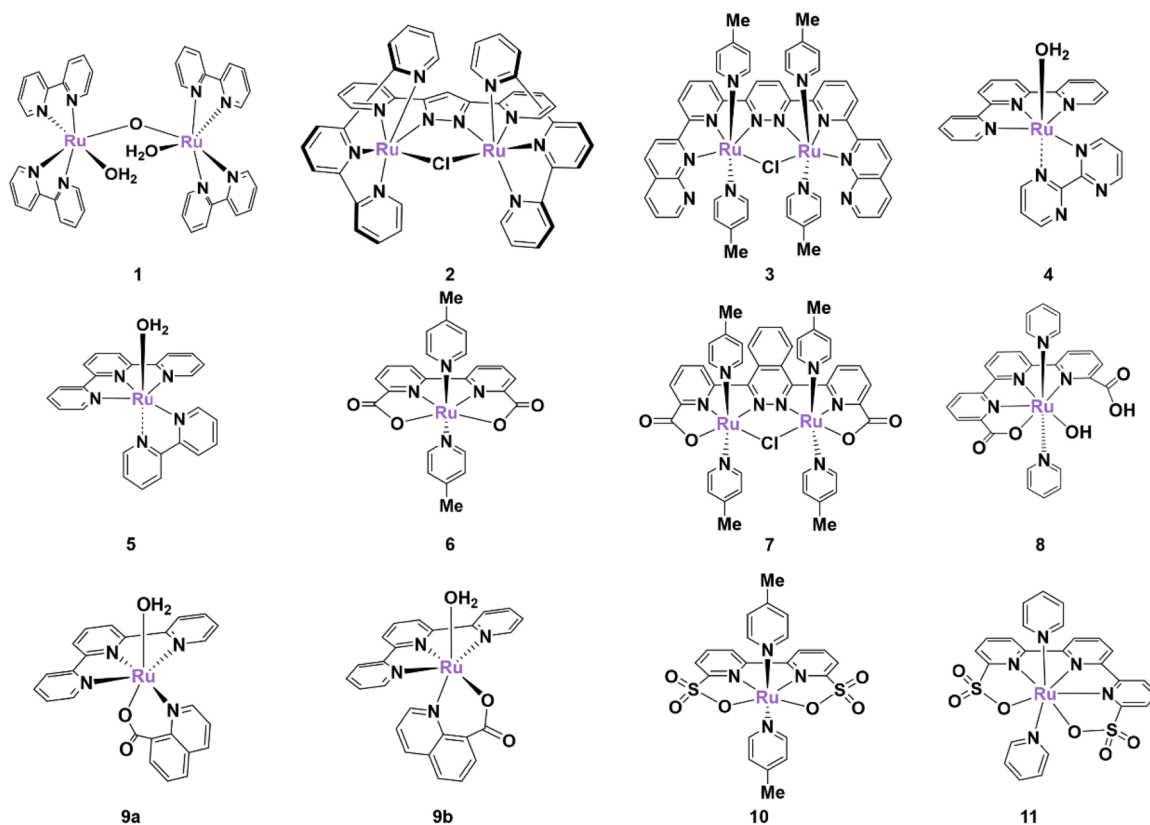


Fig. 4. The structures of Ru complexes.

using $\text{Ru}(\text{tpy})(\text{bpm})(\text{H}_2\text{O})$ as the representative platform of Ru single-atom WOC via time-resolved UV-vis spectra. The results indicated two key steps from $\text{Ru}^{\text{III}}\text{-OH}$ to $\text{Ru}^{\text{III}}\text{-OOH}$, while DFT calculations revealed the existence of three peroxidic intermediates, which were also confirmed by resonance Raman spectrum [49]. In 2009, Sakai and Masaoka provided a clear demonstration of robustness in a mononuclear Ru catalyst $[\text{Ru}(\text{tpy})(\text{bpy})(\text{H}_2\text{O})]^{2+}$, showing that a simple Ru-aqua complex (complex 5) could sustain catalytic turnover under oxidative conditions [50]. Shortly thereafter, Meyer elucidated the mechanistic framework for these systems, establishing the stepwise electron transfer and O–O bond formation pathways [49]. An impressive progress was achieved in 2014 by Pushkar based on $\text{Ru}(\text{bpy})(\text{tpy})(\text{H}_2\text{O})$ WOC, improving the previously proposed mechanism of water splitting catalyzed by Ru WOC. Both EPR measurements and DFT analysis suggested that $\text{Ru}^{\text{V}}=\text{O}$ was not a rate-limiting intermediate [51]. Zhang et al. used in situ MS technique for both chemically and electrochemically driven water oxidation catalyzed by a $\text{Ru}(\text{bpy})(\text{tpy})(\text{OH})$ analogue, indicating a novel pathway by $\text{Ru}^{\text{IV}}=\text{O}$ intermediate instead of $\text{Ru}^{\text{V}}=\text{O}$ [52,53].

Building on the mechanistic insights gained from homogeneous systems, subsequent studies transitioned to electrochemical water oxidation, aiming to evaluate catalyst stability and activity under applied potentials that more closely emulate practical operating environments. A transformative advance was achieved with the development of the Ru-bda ($\text{H}_2\text{bda} = 2,2'$ -bipyridine-6,6'-dicarboxylic acid) platform by Sun and coworkers. The open coordination geometry of Ru(bda)(pic)₂ (pic = 4-picoline), complex 6, was proposed to facilitate O–O bond formation [54]. Further advances in dinuclear systems demonstrated that precise control over ligand geometry and coordination environment can dramatically enhance catalytic efficiency. Sun and co-workers reported a cis-configured dinuclear ruthenium complex featuring carboxylate ligands, complex 7, which exhibits remarkable catalytic activity with turnover numbers exceeding 10 000 and a TOF of 1.2 s^{-1} under Ce^{IV} -driven conditions [55]. Notably, the relatively low

overpotential enables water oxidation to be driven by photogenerated $[\text{Ru}(\text{bpy})_3]^{3+}$, highlighting its potential for integration into light-driven systems. This work underscores the importance of geometric configuration (*cis* vs *trans*) and oxygen-rich ligand environments in promoting catalytic activity and bridging the gap between chemical and photochemical water oxidation. Llobet et al. in 2015, further unraveled the potential of carboxylate ligands by developing $[\text{Ru}(\text{OH})(\text{tda-}\kappa\text{-N}^3\text{O})(\text{py})_2]^+$ (complex 8, tda = (2,2':6',2''-terpyridine)-6,6''-dicarboxylic acid, py = pyridine), which achieved an impressive TOF of 8000 s^{-1} at pH = 7.0 [56]. Llobet et al. reported a comparative study of isomeric ruthenium complexes 9 with the general formula *cis*- and *trans* $[\text{Ru}(\text{trpy})(\text{qc})\text{X}]^{n+}$ (trpy = 2,2':6',2''-terpyridine, qc = 8-quinolinecarboxylate, X = OH₂, n = 1). *Trans* isomers 9a show a lower potential of their redox couple as compared to *cis* isomers 9b due to the different extent of *cis*-*trans* influence of the carboxylate group in the quinolinato or picolinato ligands. The geometry effect of the ligand also contributes to the difference on catalytic performance, with TOF_{max} values of 4.2 s^{-1} for 9a and 6.8 s^{-1} for 9b [57]. Building upon the Ru-bda platform, further ligand engineering led to the development of a sulfonate-substituted analogue, $[\text{Ru}(\text{bds})(\text{pic})_2]$ ($\text{H}_2\text{bds} = 2,2'$ -bipyridine-6,6'-disulfonic acid), complex 10, which exhibits markedly enhanced catalytic activity under both acidic and neutral conditions [58]. Notably, this Ru-bds catalyst achieves turnover frequencies of 160 s^{-1} in acidic media and up to $12,900 \text{ s}^{-1}$ under neutral conditions, significantly outperforming state-of-the-art Ru-bda systems. Mechanistic investigations reveal that high-valent $\text{Ru}=\text{O}$ intermediates with seven-coordinate geometries are involved in O–O bond formation, and that the interaction of two M–O units (I2M) pathway predominates over the water nucleophilic attack (WNA) pathway across different pH conditions. This work highlights how subtle modification of ligand electronic structure can profoundly influence both catalytic activity and mechanistic pathways, representing a key advance in the rational design of molecular water oxidation catalysts. Sun et al. developed a bioinspired Ru-based catalyst with an

adaptive architecture, Ru-tds ($\text{H}_2\text{tds} = (2,2':6',2'')\text{-terpyridine-6,6''-disulfonic acid}$), complex **11**, which enables homogeneous water oxidation at neutral pH with TOFs exceeding 2000 s^{-1} , in 0.1 M phosphate buffer containing 1% $\text{CF}_3\text{CH}_2\text{OH}$ at pH = 7, with a catalytic onset potential of 1.35 V vs NHE, demonstrating enzyme-like efficiency through dynamic stabilization of high-valent Ru intermediates [59]. These advances have established Ru-based molecular catalysts as benchmark systems for elucidating water oxidation mechanisms and for guiding the rational design of next-generation transition-metal catalysts.

3.2. Iridium-based molecular WOCs

Iridium (Ir) complexes emerged as a complementary noble-metal platform to Ru-based systems, seeking alternative noble-metal platforms that could maintain high activity yet offer complementary stability and ligand-field tuning for high-valent oxo chemistry.

The first well-defined Ir-based molecular catalysts were reported by Bernhard et al. in 2007. They demonstrated that cyclometalated Ir^{III} aquo complexes bearing two labile coordination sites could catalyze water oxidation using Ce^{IV} as a sacrificial oxidant [60]. In 2009, Crabtree and Brudvig pioneered the development of mononuclear Cp^*Ir as WOCs, complexes **12** (Fig. 5). Their initial systems demonstrated high activity with $\text{Ce}(\text{IV})$ as a sacrificial oxidant, and H_2^{18}O experiments confirmed water as the oxygen source [61]. Subsequent mechanistic and structural studies further elaborated on the catalytic behavior of these half-sandwich complexes $[\text{Ir}(\text{Cp}^*)(\kappa^2\text{-C}, \text{N})\text{Cl}]$ (**12a**, $\kappa^2\text{-C}$, $\text{N} = 2\text{-phenylpyridine}$; **12b**, $\kappa^2\text{-C}$, $\text{N} = 2\text{-phenylpyrimidine}$), though their stability under oxidative conditions was recognized to be limited under strongly oxidative conditions [62]. These pioneering Ir systems established the chemical foundation for molecular water oxidation and soon inspired the exploration of their electrochemical counterparts under applied potentials.

In parallel with these developments, significant advances have been achieved through the introduction of carbene-based ligand frameworks, particularly triazolydene iridium complexes [63–65]. These systems, extensively developed by Albrecht and co-workers, feature strong σ -donating mesoionic carbene ligands that stabilize multiple oxidation states and facilitate access to high-valent intermediates during catalysis. Notably, these ligands can exhibit non-innocent electronic behavior, enabling PCET processes and enhancing catalytic robustness.

In addition, ligand engineering plays a decisive role in tuning

catalytic activity [66,67]. For example, Macchioni and co-workers demonstrated that subtle modification of ligand substituents can promote the formation of dynamically associated multimetallic species, resulting in order-of-magnitude enhancements in catalytic rates. These findings underscore that catalytic performance is governed not only by molecular structure but also by dynamic aggregation behavior and metal–metal interactions.

In addition to carbene-based systems, a variety of organometallic iridium complexes bearing N,O-, N,N-, and mixed-donor ligands have also been developed as efficient water oxidation catalysts under homogeneous conditions [68–73]. These systems generally operate through molecular catalytic pathways, although their activity and stability are strongly influenced by ligand environment, oxidative conditions, and dynamic catalyst speciation. Notably, some studies have shown that Cp^* -based iridium complexes may undergo ligand degradation without necessarily forming heterogeneous IrO_x species, maintaining a predominantly molecular catalytic regime under certain conditions [74]. Representative examples include pyridinecarboxylate-based iridium catalysts, which were initially identified as highly active molecular systems and subsequently optimized through ligand functionalization strategies enabling pH-responsive activity and enhanced catalytic performance [75]. However, mechanistic investigations have shown that such systems can undergo substantial structural evolution under catalytic conditions, including Cp^* ligand oxidation, dynamic speciation, and even electrodeposition processes under electrochemical conditions [76], highlighting the complex and condition-dependent nature of the active state. Recent studies further suggest that the catalytically active species may retain fragments of the Cp^* ligand and evolve into small iridium clusters or molecular aggregates, highlighting the non-innocent role of ligand degradation in defining the active state [77].

Building on these chemical systems, researchers next turned to electrocatalytic water oxidation, Hetterscheid and Reek in 2011, employed strongly σ -donating N-heterocyclic carbene (NHC) ligands to stabilize high-valent Ir intermediates, leading to $\text{Cp}^*\text{Ir-NHC}$ complex **14** $[\text{Ir}(\text{Cp}^*)(\text{H}_2\text{O})_2(\text{Me}_2\text{-NHC})]$ that exhibited high catalytic performance, with TOF up to 1.5 s^{-1} and TON exceeding 2000 [78]. The Cp^*Ir complex **15** $[\text{Ir}(\text{Cp}^*)(\text{pyalc})]$ [pyalc = 2-(2'-pyridyl)-2-propanolate], developed by Crabtree and Brudvig in 2014, was further electrochemically activated to generate a blue molecular species capable of homogeneous, electrode-driven water oxidation with high Faradaic efficiency, representing a key step toward true Ir-based electrocatalysis [79].

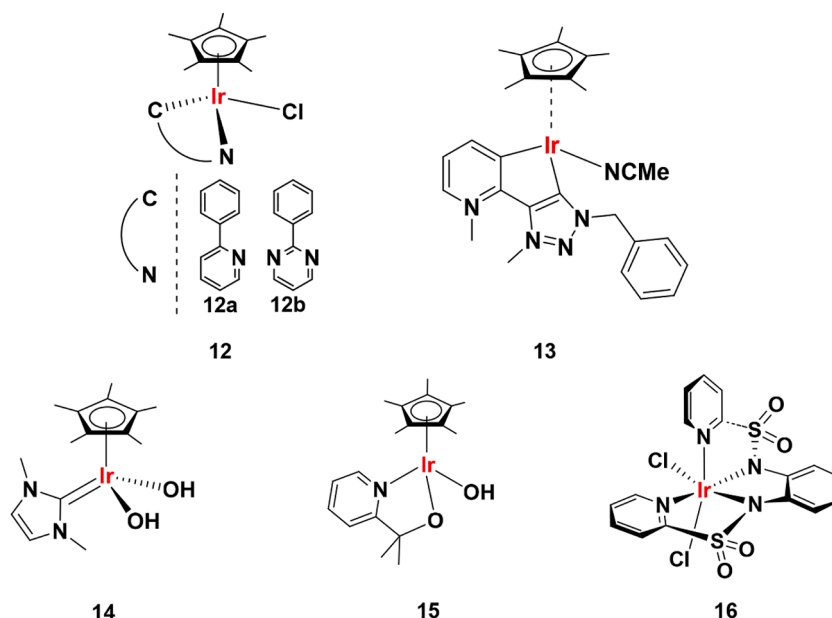


Fig. 5. The structures of Ir complexes.

Building on these Cp*Ir systems, subsequent efforts focused on enhancing the structural rigidity and oxidative robustness of Ir complexes through multidentate ligand frameworks. Bernhard et al. developed a family of Ir^{III} bis(pyridine-2-sulfonamide)(bpsa) complexes (**16**, [Ir(bpsa-pH)Cl₂]) in 2016 featuring robust tetradentate wrap-around ligands that enable durable homogeneous electrocatalytic water oxidation with no IrO_x formation, sustaining thousands of turnovers over 10 days [80].

However, accumulating evidence suggests that many molecular iridium catalysts may undergo further transformation into heterogeneous species under oxidative conditions. Several studies have demonstrated that Cp*-based iridium complexes can evolve into iridium oxide nanoparticles or clusters during catalysis, especially in the presence of strong oxidants such as Ce^{IV}. Spectroscopic and kinetic analyses indicate the existence of two distinct regimes, where molecular species dominate in the initial stages, followed by the gradual formation of IrO_x nanoparticles that become the primary active phase over extended reaction times [68,69].

However, accumulating evidence suggests that many molecular iridium catalysts may undergo further transformation into heterogeneous species under oxidative conditions. Early studies already indicated that Cp*-based iridium catalysts often exhibit a gradual decline in activity under catalytic conditions, suggesting limited long-term stability of the molecular species [81]. In particular, Cp*-based iridium complexes are prone to oxidative degradation of the ligand framework, which can initiate catalyst evolution pathways involving both molecular intermediates and oxide formation [82]. Direct evidence for such evolution has been provided by studies showing that organometallic iridium complexes can rapidly transform into Ir-rich nanoparticles under typical catalytic conditions using Ce^{IV} oxidants, with nanoparticle formation occurring within minutes and even at low oxidant loadings [83]. Several studies have demonstrated that such systems can generate iridium oxide nanoparticles or clusters during catalysis, especially in the presence of strong oxidants such as Ce^{IV}. Detailed spectroscopic and kinetic analyses revealed the existence of two distinct catalytic regimes, where molecular species dominate in the initial stage, followed by the gradual formation of IrO_x nanoparticles that become the primary active phase over extended reaction times [84].

In addition, intermediate species have been identified as small iridium oxide clusters or partially transformed molecular aggregates, bridging the gap between well-defined homogeneous catalysts and heterogeneous IrO_x materials [85]. These findings are further supported by studies showing progressive Cp* ligand degradation and the formation of multiple Ir-containing intermediates under oxidative conditions.

Overall, these observations highlight that the catalytic behavior of iridium systems should be understood as a dynamic continuum, in which molecular complexes, clusters, and oxide phases may coexist and interconvert depending on reaction conditions, rather than as strictly homogeneous or heterogeneous systems.

3.3. First-Row transition metal-based WOCs

Building on the mechanistic foundations established by Ru/Ir platforms, the transition to first-row metal-based WOCs, featuring manganese (Mn), iron (Fe), cobalt (Co), nickel (Ni), and copper (Cu) complexes, represents a pivotal evolutionary step driven by sustainability, biological inspiration, and mechanistic necessity.

This shift directly addresses a central challenge in molecular water oxidation: earth-abundant 3d-metal centers, though inexpensive and conceptually aligned with the OEC, are intrinsically more labile and possess much narrower redox windows than noble metals. As a result, the accumulation of multiple oxidative equivalents at a single metal center is far more difficult to control. As mononuclear platforms matured, the field increasingly recognized that the efficiency of the complexes in nature also derives from cooperative interactions among multiple metal centers. Consequently, attention shifted toward

multinuclear architectures that distribute redox burden across several 3d-metal sites, an essential design principle of the OEC.

3.3.1. Mononuclear and dinuclear systems

Having established the fundamental design logic for stabilizing high-valent 3d-metal centers, the next step in this evolutionary trajectory is to examine mononuclear and dinuclear systems, the most elementary platforms for probing how individual or paired first-row metal sites manage PCET and O–O bond formation. These systems address the central challenge that 3d metals, unlike their noble-metal counterparts, often struggle to accumulate multiple oxidative equivalents without undergoing ligand dissociation or metal-centered decomposition. Although their redox capacity is limited compared with multinuclear architectures, these early studies established the key mechanistic paradigms that later inspired cooperative cluster designs. However, the intrinsic limitations of single or paired metal centers in storing multiple oxidizing equivalents and facilitating efficient O–O bond formation ultimately motivated the development of multinuclear catalytic systems, where cooperative interactions between multiple metal sites enable more efficient multi-electron water oxidation.

In nature, Mn centers were employed as the active center of the OEC in PSII, which has inspired the design of Mn-based WOCs in Fig. 6. In 1994, Naruta et al. reported the first examples of Mn porphyrin dimers **17** capable of catalyzing water oxidation under electrochemical conditions [86]. Among the three Mn porphyrin dimers, the most active one (complex **17c**; Ar = C₆F₅) catalyzed water oxidation, achieving a maximum TON of 9.2 in the presence of nBu₄NOH, illustrating the feasibility of water evolution by a molecular manganese complex despite its modest activity. Although its catalytic activity is limited, the system provided an important platform for understanding how multinuclear manganese centers can cooperate in multi-electron water oxidation. In 2007, Liu, Sun et al. synthesized and spectroscopically characterized two Mn^{IV} corrole-xanthene complexes, which were designed as bio-inspired models for the OEC in PSII [87]. Electrochemical studies revealed that the Mn complexes **18** were capable of catalyzing oxygen evolution at relatively low potential (about 0.80 V), representing a notable advancement in molecular WOCs. In 2014, Smith et al. demonstrated that subtle steric tuning of pyridinophane ligands in high-spin Mn^{II} complexes [(Py₂NR₂)Mn(H₂O)₂]²⁺ (Py = pyridine, R = H, Me, *t*-Bu) (**19**) can switch catalytic behavior from H₂O₂ disproportionation to water oxidation [88]. Complexes with small substituents (**19b**; R = Me) efficiently disproportionate H₂O₂ with their TON up to 58,000, whereas the bulky substituent (**19c**; R = *t*-Bu) is inactive toward H₂O₂ disproportionation but active for OER. This ligand-controlled reactivity switch highlights the decisive role of steric environment in promoting oxidation to high-valent Mn-oxo species. In 2021, Fukuzumi, Nam, and Cao et al. identified a Mn^{IV}-peroxo intermediate during electrocatalytic water oxidation by a Mn^{III} tris(pentafluorophenyl)corrole complex **20**. Kinetic and isotope-labeling studies revealed that both oxygen atoms originate from water, supporting a WNA mechanism via 1e⁻-oxidized Mn^V≡O species. The reaction with OH⁻ (a second-order rate constant, *k*₂ = 7.4 × 10³ M⁻¹ s⁻¹) was orders of magnitude faster than with H₂O (*k*₂ = 4.4 × 10⁻³ M⁻¹ s⁻¹) [89].

Fe complexes have emerged as attractive candidates for homogeneous water oxidation due to the natural abundance and low cost of Fe (Fig. 7). In 2010, Bernhard, Collins et al. reported a series of Fe complexes with a tetra-amido macrocyclic ligand (TAML) as the first example of an Fe-based molecular catalyst for water oxidation (complex **21**) [90]. The investigation of catalytic activities of these complexes was performed at pH 0.7 using ceric ammonium nitrate (CAN) as a chemical oxidant. These complexes show catalytic activities for water oxidation reaction with relatively high reaction rates except for complex **21a**. Although the stability of the catalysts was not so high in acidic media, the study demonstrated that the Fe complexes can serve as water oxidation catalysts and that their catalytic activities can be precisely tuned by modification of the ligand structures. Regarding this

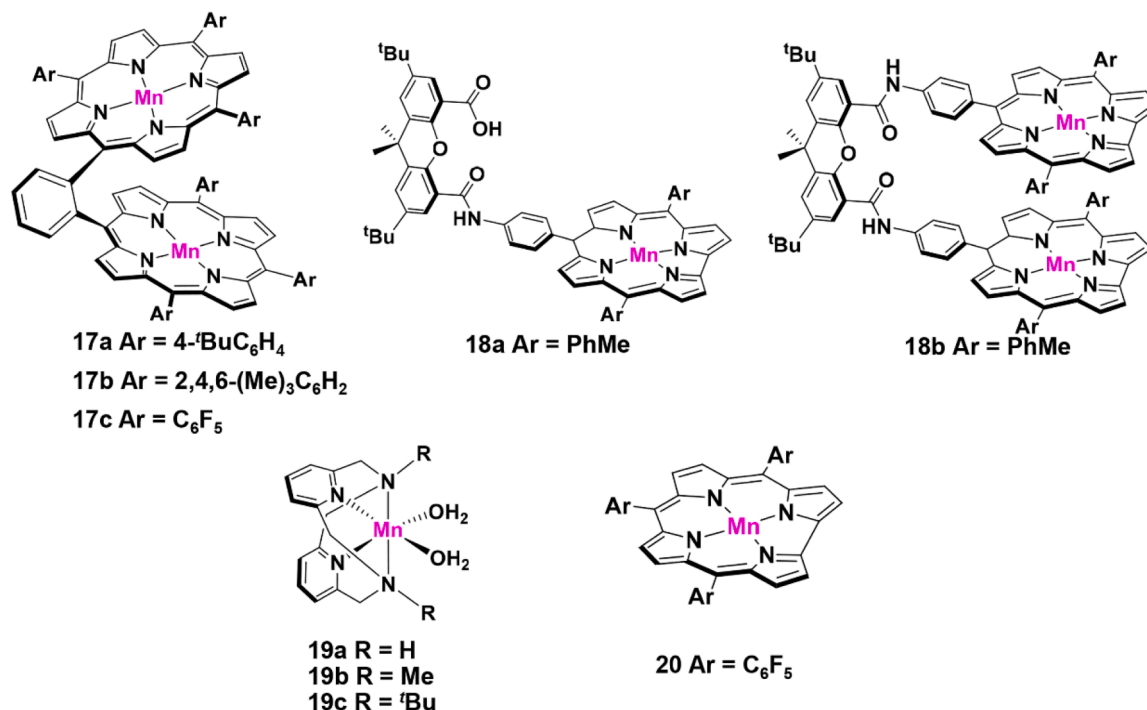


Fig. 6. The structures of Mn mononuclear and dinuclear complexes.

TAML-type complex, Liao, Siegbahn et al. elucidated the reaction mechanism of the complexes using theoretical calculations [91]. In their proposed mechanism, a two-step PCET reaction and one-electron oxidation afford the key $\text{Fe}^{\text{V}}=\text{O}$ intermediate. WNA on these intermediate forms the bond between the two oxygen atoms, and subsequent deprotonation, another PCET reaction, and the release of O_2 regenerate the initial state in the catalytic cycle. Moreover, Gupta, Dhar et al. reported the chemical and photochemical evolution of O_2 catalyzed by Fe complexes with biuret-modified TAML (complex 22a and complex 22b) [92]. They introduced the -NMe group to lower the electron density of the Fe atom, stabilizing the Fe-TAML complexes and solving the problem that Bernhard and Collins et al. had faced. The introduction of an additional -NO₂ moiety in the head aromatic ring further enhanced the stability of the complex. The electrochemical measurements of the complexes in aqueous media indicated the formation of $\text{Fe}^{\text{V}}=\text{O}$ species, which are expected to be important for the water oxidation reaction.

In 2011, Lloret-Fillol, Costas et al. reported the catalytic activities of a series of Fe complexes bearing the tetradentate alkylamine-pyridine (TDAP) type ligands (complex 23–complex 29) [22]. Ligand availability, modularity, and versatility of these complexes allowed systematic study of various structures. In this relevant study in 2019, Lloret-Fillol, Costas et al. succeeded in solving the problem that the oxidation of the alkylamine ligand during the catalytic reaction leads to deactivation of the catalyst [93].

They reported a novel complex 30 similar to complex 24. In this complex, the hydrogen atoms at the benzylic methylene positions were replaced by deuterium, which imparted robustness against C–H oxidation. This study clearly demonstrates that catalytic activity can be improved by the identification of structural limitations at the molecular level and with remediation by rational design. The same group, Costas, Lloret-Fillol, Hetterscheid et al., tried to perform an electrocatalytic reaction for water oxidation using complex 24 and its analogues to investigate the validity of the chemical catalytic reaction mechanism proposed in complex 24, which suggested the involvement of the sacrificial reagents [94]. The results showed that the electrocatalytic reaction proceeded under both acidic and neutral conditions, although the kinetic isotope effect (KIE) values suggested that the

rate-determining step is an electron transfer (ET) under acidic conditions, but the rate-determining step is a PCET under neutral conditions. In 2014, Meyer et al. reported a mononuclear Fe^{III} -aqua complex 31, $[\text{Fe}(\text{dpaq})(\text{H}_2\text{O})]^{2+}$ ($\text{dpaq} = 2\text{-[bis(pyridine-2-ylmethyl)]amino-}N\text{-quinolin-8-yl-acetamido}$), as a molecular electrocatalyst for water oxidation in propylene carbonate–water mixtures. Electrochemical studies suggested a single-site mechanism proceeding via oxidation to $[\text{Fe}^{\text{V}}=\text{O}]^{2+}$. The catalyst exhibited sustained activity for at least 15 h, with a TON of 29 and 45% Faradaic efficiency, without decomposition, representing one of the earliest stable monomeric Fe-based systems that mimics Ru/Ir OER mechanisms [95].

The two PCET reactions, subsequent WNA, another two PCET reactions, and then the ligand exchange between the O_2 and H_2O completed the cycle and regenerated the initial state in the cycle. Moreover, in 2014, Ding, Ma et al. reported the first Fe-based dinuclear complex 32 for water oxidation [96]. Quite high TON ~ 2380 and TOF $\sim 2.2 \text{ s}^{-1}$ were obtained over complex 32 under the optimum conditions. This TON represents the highest value for any homogeneous first-row transition metal-based complex reported to that time. In 2015, Thummel et al. reported the water oxidation reactions catalyzed by complex 33 and complex 34 [97]. Complex 33 is a μ -oxo-bridged dimeric complex with 2-(pyrid-2'-yl)-8-(1'',10''-phenanthrolin-2''-yl)-quinoline (ppq) ligands, and complex 34 is a monomer complex with a bis-phenanthroline amine (dpa) ligand. In the electrochemical measurements of complex 33, the complex exhibited a single two-electron wave, which was attributed to the formation of the $\text{Fe}^{\text{IV}}\text{-Fe}^{\text{IV}}\text{-OH}_2$ species. In 2016, Ott, Thapper et al. reported the new types of Fe-based WOC complex 35a and complex 35b with the pyridine-2,6-diylbis(di(pyridine-2-yl)methanol) (PY5OH) ligand [98].

In this report, CAN and $[\text{Ru}(\text{bpy})_3]^{3+}$ were used as chemical oxidants. Interestingly, under acidic conditions ($\text{pH} \sim 1.5$) and with CAN as the oxidant, complex 35a with a Cl ligand exhibited higher activity than complex 35b without the Cl ligand. In contrast, the catalytic activity of complex 35b was better than that of complex 35a when the reaction was performed at pH 8 using $[\text{Ru}(\text{bpy})_3]^{3+}$ as the oxidant. The TON and TOF of complex 35a at pH 1.5 (with CAN) were 16 and 0.75 s^{-1} , respectively, and those of complex 35b at pH 8 (with Ru^{III}) were 26.5 and 2.2 s^{-1} ,

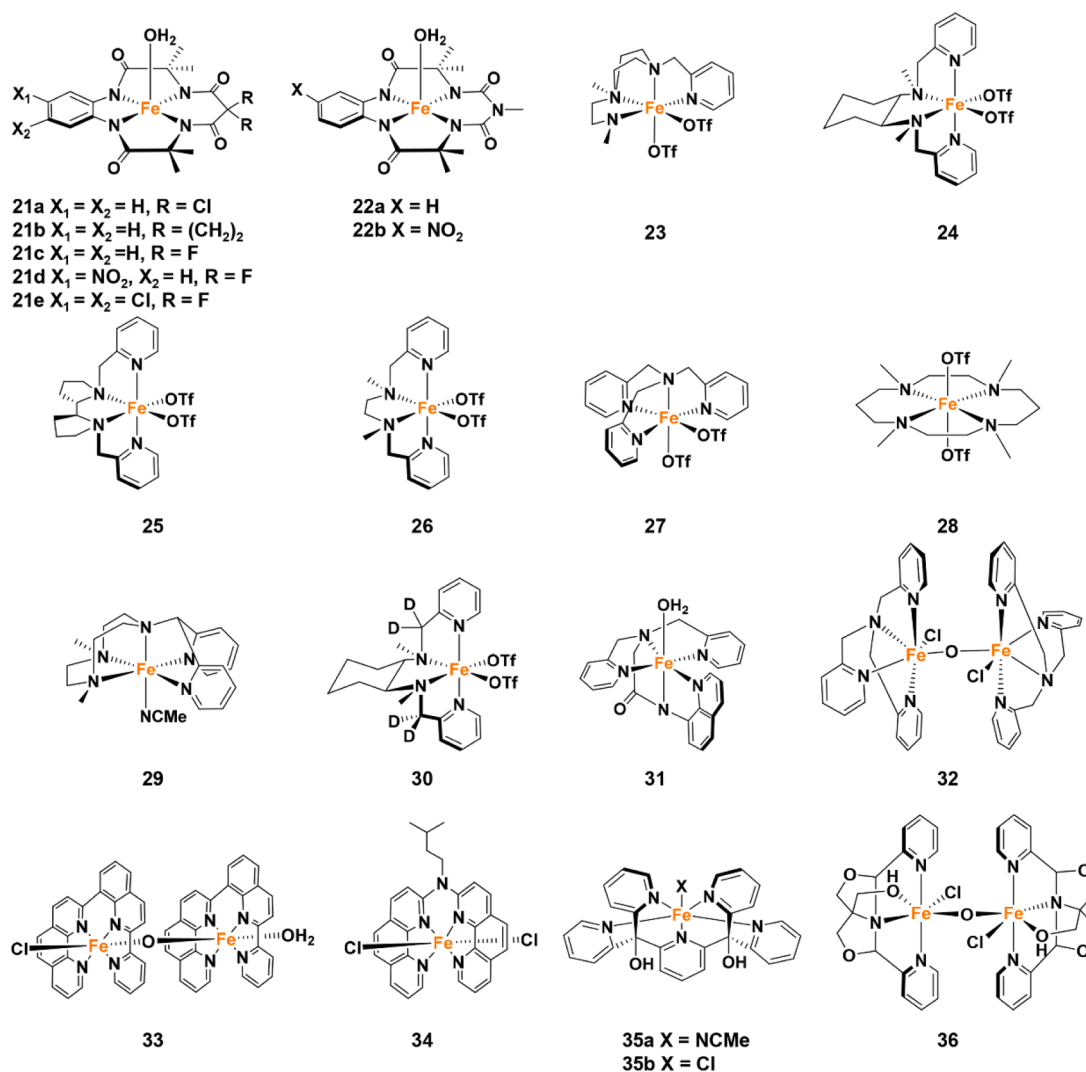


Fig. 7. The structures of Fe mononuclear and dinuclear complexes.

respectively. Notably, complex **35b** also catalyzed light-driven water oxidation at pH 8 relatively high efficiently (TON: 43.5, TOF: 0.6 s^{-1}). In 2020, Das et al. synthesized a dinuclear μ -oxo-bridged Fe complex **36**, $[(\text{FeCl})_2(\mu\text{-O})](\text{FeCl}_4)_2$ ($L = (2\text{-pyridin-2-yl})\text{oxazolidine-4,4-diyl}$) diethanol, poxdiol, and demonstrated its high electrocatalytic activity for homogeneous water oxidation with aqueous NaOH solution. The catalyst exhibited notable stability, achieving its TON of 408 and Faradaic efficiency above 78.6%. Mechanistic studies indicated that the replacement of Cl ligands by OH ligands facilitates O–O bond formation [99].

Co complexes have become the most structurally diverse family of transition metal-based molecular WOCs (Fig. 8). In 2011, Berlinguette et al. reported that the Co^{II} complex **37**, $[\text{Co}(\text{PY5OMe})(\text{OH}_2)](\text{ClO}_4)_2$ [$\text{PY5OMe} = 2,6\text{-bis}(\text{bis-2-pyridyl})\text{methoxymethanepyridine}$], was oxidized via a PCET process to form a high-valent Co^{IV} species mediating water oxidation in basic media [100]. In 2012, Llobet and Stahl et al. constructed dinuclear Co^{III} complexes **38a** and **38b** bridged by 3,5-bis(2-pyridyl)pyrazolate (bpp[−]) ligand, yielding stable dicobalt(III)-peroxo intermediates that catalyze OER at pH ~ 2 [101]. In 2013, Groves et al. developed three cationic Co porphyrins **39** that catalyze OER in neutral media; the most active $\text{Co}^{\text{III}}\text{-5,10,15,20-tetrakis-(1,3-dimethylimidazolium-2-yl)porphyrin}$ ($\text{Co}^{\text{III}}\text{-TDMImP}$) catalyzed OER with $k_{\text{obs}} = 1.4 \times 10^3 \text{ s}^{-1}$ with a Faradaic efficiency near 90%, proceeding through a $\text{Co}^{\text{IV}}\text{-O}$ porphyrin cation-radical formed through buffer-assisted PCET

[102]. In 2018, Jiao and Zhang et al. reported molecular Co^{III} WOCs **40**, $\text{Na}[(L^4)\text{Co}^{\text{III}}]$, where L is a substituted tetraamido macrocyclic ligand. The Co complex in phosphate buffer (pH = 7.0) operates via phosphate-assisted WNA on $\text{Co}^{\text{IV}}=\text{O}$ [103]. Together, these studies established Co-based WOCs as the archetypal PCET-driven system bridging mechanistic precision with operational robustness.

Ni complexes extend the scope of molecular WOCs into neutral aqueous media with excellent durability (Fig. 9). In 2014, Ke, Lu et al. reported a robust homogeneous Ni-based water oxidation catalyst (WOC) **41** that catalyzes OER at neutral buffer (pH = 7.0) with $0.9 \text{ mA}\cdot\text{cm}^{-2}$ current density at a low overpotential of only 170 mV. The O–O bond formation most likely proceeds via an HO–OH coupling pathway from the *cis* isomer of the complex [104]. In 2015, Lai, Cao et al. demonstrated that a water-soluble cationic Ni^{II} porphyrin complex **42** catalyzes water oxidation in neutral aqueous solution (pH = 7.0) with an onset potential of $\sim 1.0 \text{ V}$ vs NHE. The catalyst exhibited durable activity over pH = 2.0 to 8.0 with its TOF of 0.67 s^{-1} at 20°C [105]. A follow-up study in 2016 by the Lu group further confirmed the catalytic relevance of *cis*-configured labile coordination sites in Ni complexes **43**. The investigated complex remained active in aqueous buffer at pH 6.5 and supported the proposed intramolecular O–O coupling mechanism [106]. In 2018, Wang et al. designed two water-soluble Ni^{II} complexes **44a**, $[\text{Ni}(\text{L1})(\text{H}_2\text{O})](\text{BF}_4)_2$ [$\text{L1} = N\text{-benzyl-}N,N',N'\text{-tris}(\text{pyridin-2-ylmethyl})\text{ethylenediamine}$], and **44b**, $[\text{Ni}(\text{L2})(\text{H}_2\text{O})](\text{BF}_4)_2$ [$\text{L2} =$

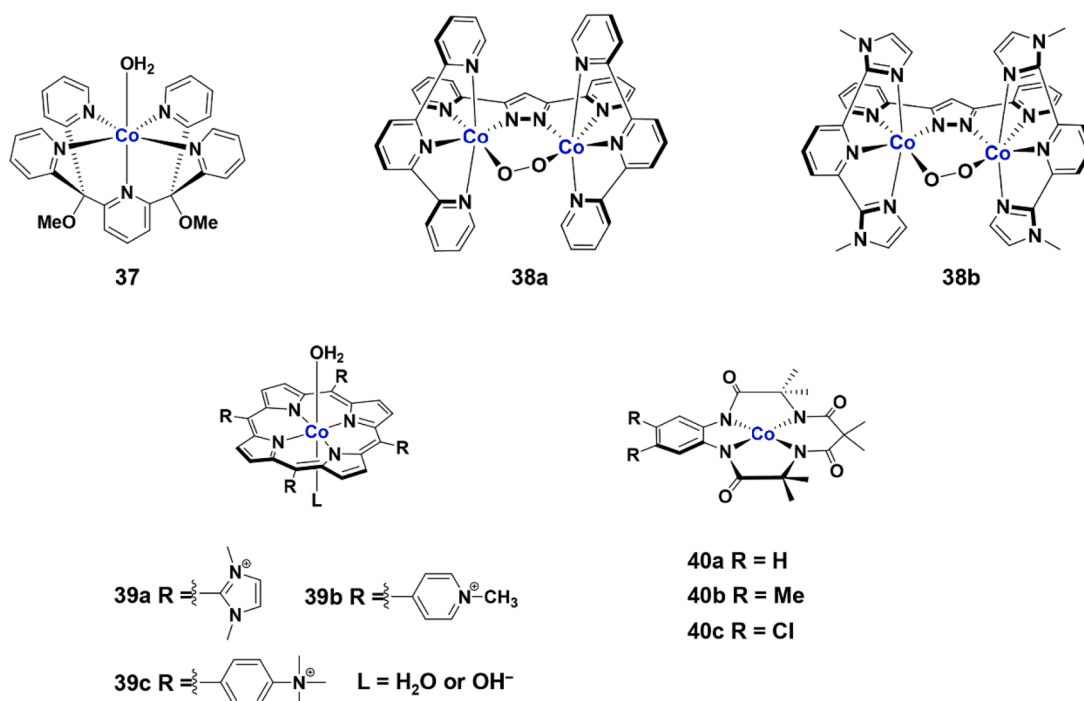


Fig. 8. The structures of Co mononuclear and dinuclear complexes.

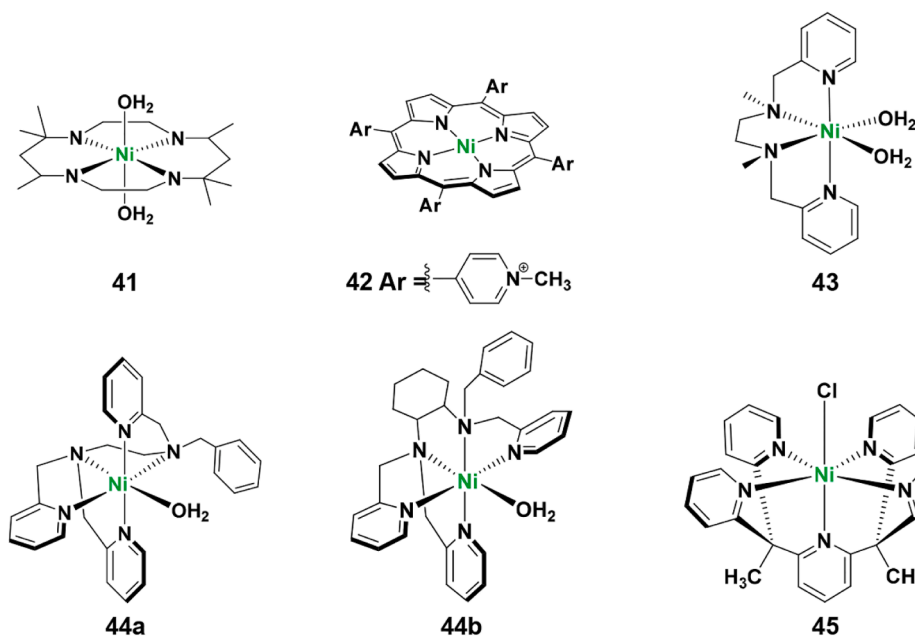


Fig. 9. The structures of Ni mononuclear and dinuclear complexes.

(1*R*, 2*R*)-*N*-benzyl-*N*,*N*',*N*'-tris(pyridin-2-ylmethyl)cyclohexane-1,2-diamine]. Both catalysts promoted electrochemical water oxidation in neutral phosphate buffer (pH = 7), displaying observed rate constants of 3.06 and 4.62 s⁻¹, where rigid backbones improved activity [107]. In 2020, Liao et al. investigated the mononuclear Ni-PY5Me complex 45 [PY5Me = 2,6-bis(1,1-bis(2-pyridyl)ethyl)pyridine] as an efficient molecular catalyst in aqueous phosphate buffer (pH = 10.8) at an applied potential of 1.5 V. DFT calculations revealed a catalytic cycle initiated by two sequential PCET steps forming a high-valent [O=Ni^{IV}-PY5]²⁺ intermediate, followed by WNA on Ni^{IV}=O assisted by a hydrogen phosphate [108]. These findings demonstrate that Ni complexes

combine structural robustness with operational mildness, achieving effective PCET management at near-neutral pH.

Cu-based molecular WOCs have reached the high TOF among first-row transition metals owing to strong metal-ligand cooperation between a metal and ligands (Fig. 10). In 2012, Mayer et al. reported the first mononuclear Cu complex 46 with a bipyridine ligand, exhibiting a remarkably high TOF of ~100 s⁻¹ under electrochemical conditions [109]. In 2014, Lin et al. designed a Cu-based WOC 47 with 6,6'-dihydroxy-2,2'-bipyridine as a ligand, mimicking the assistance of the PCET process in PSII. This biomimetic modification effectively lowered the overpotential for water oxidation while maintaining high catalytic

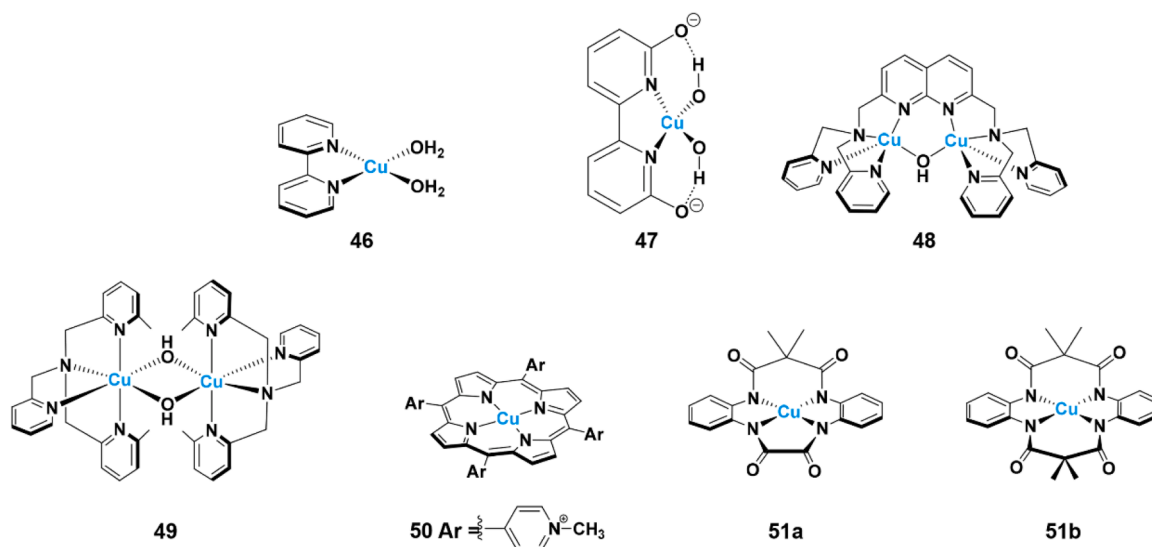


Fig. 10. The structures of Cu mononuclear and dinuclear complexes.

activity, demonstrating how ligand design can facilitate the PCET process [110]. In 2015, Liao and Zhang et al. reported an oxidatively robust 2,7-[bis(2-pyridylmethyl)aminomethyl]-1,8-naphthyridine ligand (BPMAN)-based dinuclear Cu^{II} complex **48**, [Cu₂(BPMAN)(μ-OH)]³⁺, which was the first Cu-based WOC to catalyze water oxidation in neutral aqueous solutions [111]. In 2017, Kieber-Emmons et al. reported a dinuclear Cu^{II} complex **49** that catalyzes water oxidation with high Faradaic efficiency (> 90%) and moderate rates (33 s⁻¹ at ~1 V overpotential, pH = 12.5) via PCET-assisted O–O bond formation [112]. In 2019, Cao et al. reported a water-soluble Cu^{II} porphyrin complex **50**, that catalyzes water oxidation at neutral pH with a low onset potential of 1.13 V vs NHE (corresponds to an onset overpotential of 310 mV) and Faradaic efficiency of >93% [113]. In 2020, Llobet et al. developed a series of Cu complexes **51** supported by a tetra-amidate macrocyclic ligand (TAML). The most delocalized macrocyclic complex **51a** exhibited outstanding activity at neutral pH, achieving $k_{\text{obs}} = 140 \text{ s}^{-1}$ at an overpotential of only 200 mV, owing to delocalized metal-ligand redox cooperativity [114]. Collectively, Cu complexes epitomize the convergence of high TON, structural rigidity, and ligand-assisted multielectron chemistry among first-row transition metal-based systems.

These mononuclear and dinuclear systems collectively elucidate fundamental O–O bond formation mechanisms and ligand-governed redox chemistry, yet their limited capacity for multielectron accumulation motivated the evolution toward multinuclear architectures.

3.3.2. Multinuclear complexes

With the elementary reactivity patterns of mononuclear and dinuclear first-row transition metal-based complexes established, the next

evolutionary step is driven by their inherent limitations in managing the multiple oxidative equivalents required for water oxidation. Although single 3d-metal centers can support M=O-type reactivity, they generally lack sufficient electron-storage capacity and provide limited pathways for distributing oxidative burden. As a result, such systems often favor unproductive one-electron pathways rather than the cooperative multielectron processes required for O–O bond formation. These constraints create a natural impetus to explore multinuclear architectures that more closely emulate the collaborative behavior of the natural OEC in PSII. Multinuclear complexes address this challenge by enabling the sharing of oxidative equivalents across several metal centers via μ-oxo (or hydroxo) bridging sites and rigid multinuclear frameworks. This distributed redox environment suppresses unselective single-site pathways, enhances control over multi-electron processes, and enables concerted PCET processes inaccessible to mono- or dinuclear platforms. Despite their geometric diversity, these systems collectively demonstrate how multinuclear frameworks can unlock new modes of cooperative redox chemistry in 3d metal-based WOCs.

Mn-based complexes have long served as structural blueprints for replicating the Mn₄CaO₅ cluster (OEC) in PSII. Despite extensive bio-inspired efforts, synthetic Mn-based systems have rarely achieved stable high-valent Mn-oxo intermediates capable of supporting the full 4e⁻/4H⁺ O₂-evolution pathway. A recently reported tetranuclear Mn₄O₄ cubane, Mn₃Mn^{III}L₃(OCH₃)Cl₂ [L = 2-(hydroxy(bipyridin-2-yl)methyl)phenol] (complex **52** in Fig. 11), exemplifies this divergence. While maintaining a rigid yet redox-flexible cubane framework, the complex promotes a selective two-electron oxidation of water to hydrogen peroxide rather than oxygen. This behavior highlights a fundamental

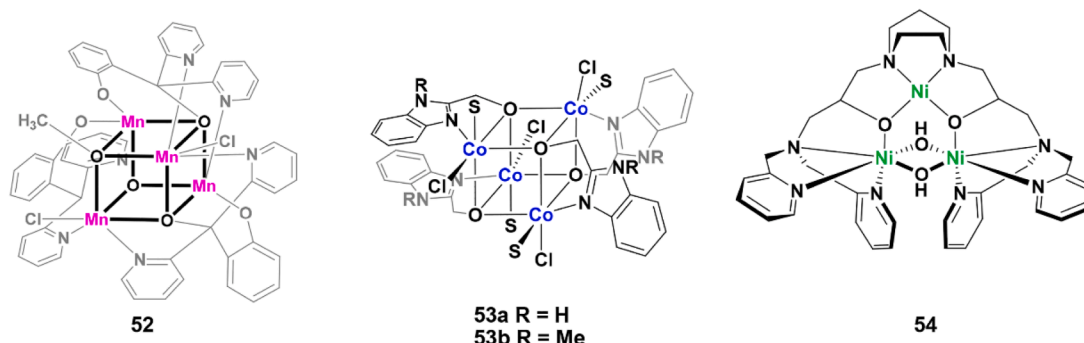


Fig. 11. The structures of Mn, Co, and Ni multinuclear complexes.

limitation of Mn molecular scaffolds: although they can mediate proton-electron transfer with structural fidelity, controlling the formation and stability of the $\text{Mn}^{\text{IV/V}}=\text{O}$ species essential for oxygen evolution remains notably challenging [115].

Co represents the most extensively studied first-row transition metal for cubane-type WOCs. In 2025, Castillo et al. synthesized two cubane-type Co^{II} complexes, $[(\mu_3\text{-L}_1\text{O})\text{CoCl}(\text{MeOH})_4]_4$ (**53a**) and $[(\mu_3\text{-L}_2\text{O})\text{CoCl}(\text{MeOH})_4]_4$ (**53b**) ($\text{L}_1\text{OH} = 1\text{-H-2-benzimidazolylmethanol}$ and $\text{L}_2\text{OH} = 1\text{-methyl-2-benzimidazolylmethanol}$). Both Co_4O_4 cores are stabilized by alkoxide and nitrogen bridges. Complexes catalyze water oxidation in neutral phosphate buffer ($\text{pH} = 7.4$) with onset potentials of 1.65 and 1.68 V vs SHE, TOF values of 1.04 and 1.99 s^{-1} , overpotentials of 710 and 680 mV, and Faradaic efficiencies of 88% and 90%, respectively. Magnetic and DFT studies revealed distinct electronic effects influencing catalytic durability [116]. Meanwhile, the introduction of in situ/operando techniques helped a lot in understanding the mechanism of water oxidation [117]. In 2017, Nocera and co-workers discussed the in-situ characterizations of Co_4O_4 , in which in situ X-ray absorption spectroscopy provided direct evidence of the electronic structure of a Co_2^{IV} site and its role in the mechanism of O–O bond formation [118].

Similar cooperative effects were subsequently observed in nickel clusters. Ni_3O_4 cubane-like **54** have also been explored, with particular emphasis on mechanistic aspects. A trinuclear Ni catalyst was shown to catalyze water oxidation via intramolecular PCET, where cooperative activation across three metal sites triggered O–O bond formation. This study provided clear evidence of trimetallic synergy in PCET-driven catalysis, reinforcing the role of multinuclearity in enabling efficient multi-electron transfer [119].

Cu-based multinuclear complexes have recently emerged as promising alternatives due to their structural diversity and outstanding kinetics. In 2016, Zheng et al. reported the first tetranuclear Cu-based WOCs **55** in Fig. 12, $[\text{Cu}_4(\text{bpy})_4(\mu_2\text{-OH})_2(\mu_3\text{-OH})_2(\text{H}_2\text{O})_2]^{2+}$, which catalyzes water oxidation even in a neutral aqueous solution [120]. In 2018, a bioinspired Cu_4O_4 cubane **56** exhibited efficient electrocatalytic water oxidation in aqueous solution, achieving a TOF of 267 s^{-1} at 1.70 V [121]. Strikingly, another trinuclear Cu-based WOCs **57** has achieved a TOF up to $20,000\text{ s}^{-1}$, 1 M NaHCO_3 aqueous electrolyte at room temperature using a three-electrode configuration, representing the current performance benchmark for molecular WOCs [122]. Control experiments indicated good catalytic stability, as evidenced by unchanged UV–vis spectra before and after electrolysis, the absence of copper oxide deposition on the electrode surface, and a stable catalytic current during controlled potential electrolysis.

The development of multinuclear complexes represents a decisive step from single-site control to cooperative multi-metal activation, enabling simultaneous charge accumulation and PCET distribution reminiscent of the OEC.

Within the landscape of multinuclear first-row systems, the pentanuclear iron complex represents a pivotal evolutionary milestone. In 2016, Masaoka et al. reported a breakthrough with the development of a

pentanuclear Fe (Fe_5) complex in Fig. 13a. This system not only exemplified the power of multinuclear design but also established Fe, the most earth-abundant transition metal, as an active center of one of the most efficient and mechanistically well-defined molecular WOCs. They introduced a μ_3 -oxo-bridged Fe_5 complex, $[\text{Fe}_4^{\text{II}}\text{Fe}^{\text{III}}(\mu_3\text{-O})(\mu\text{-L})_6]^{3+}$ ($\text{HL} = 3,5\text{-bis(2-pyridyl)pyrazole}$), which fundamentally changed the perception of Fe-based catalysts. Before this, mononuclear Fe complexes had been hampered by instability and relatively poor activity. By employing a precisely designed multinuclear scaffold, they demonstrated that the complex shows redox flexibility with multiple Fe centers, facilitating O–O bond formation through cooperative interactions. This work provided a conceptual blueprint for exploiting multinuclearity in first-row transition metal-based WOCs [123]. In a follow-up study, Liao et al. performed DFT calculations to revise the reaction mechanism. The calculations confirmed that Fe_5 promotes O–O coupling through the adjacent two Fe^{IV} centers [124]. Building on these mechanistic insights, Masaoka et al. advanced the structural tunability of Fe_5 in 2019 (Fig. 13b). Depending on whether the ligand is modified by an electron-donating or electron-withdrawing group, the oxidation process differs, and consequently, the onset potential for water oxidation decreases in both processes. One route operated through stepwise one-electron oxidation of Fe ions in the core, while the other route operated through the one-electron reduction of a Fe ion in the apical position upon one-electron oxidation of the overall complex, followed by a water binding reaction coupled with an electron transfer. Importantly, it also pointed to the possibility of introducing a functional group to control the onset potentials of water oxidation [125]. Recently, in situ XAS method was also conducted for Fe_5 WOC in 2023 by Masaoka and Pushkar, revealing the formation of hypervalent $\text{Fe}^{\text{V}}=\text{O}$ and $\text{Fe}^{\text{IV}}=\text{O}$ catalytic intermediates and offering the theoretical basis for proposing possible pathways for Fe_5 -catalyzed water splitting [126]. The Fe_5 system simulates the biomimetic paradigm, embodying a functionally integrated, redox-flexible, and structurally tunable multinuclear framework that sets a new benchmark for earth-abundant molecular WOCs.

To provide a clearer understanding of the origin of multinuclear synergy, we summarize the key cooperative modes in multinuclear molecular WOCs as follows: (i) substrate co-activation, where multiple metal centers jointly interact with the substrate to facilitate bond activation; (ii) electronic regulation, in which adjacent metal sites modulate the electronic structure of the active center, thereby tuning redox potentials and reaction energetics; and (iii) PCET promotion, where spatially distributed sites assist in proton management and lower kinetic barriers.

Beyond these effects, a fundamental distinction between multinuclear and mononuclear catalysts lies in their charge accumulation mechanism. As illustrated in Fig. 14, mononuclear systems, electron transfer typically proceeds in a stepwise manner, often involving the formation of multiple high-energy intermediates. In contrast, multinuclear systems can operate through a fundamentally different

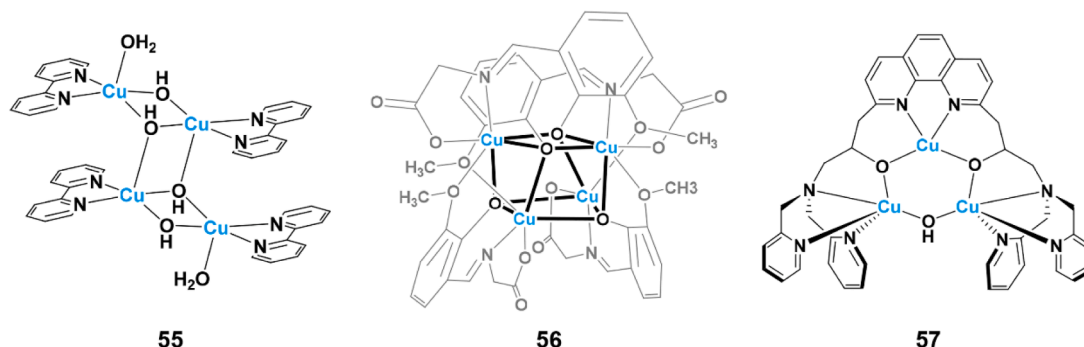


Fig. 12. The structures of Cu-based multinuclear complexes.

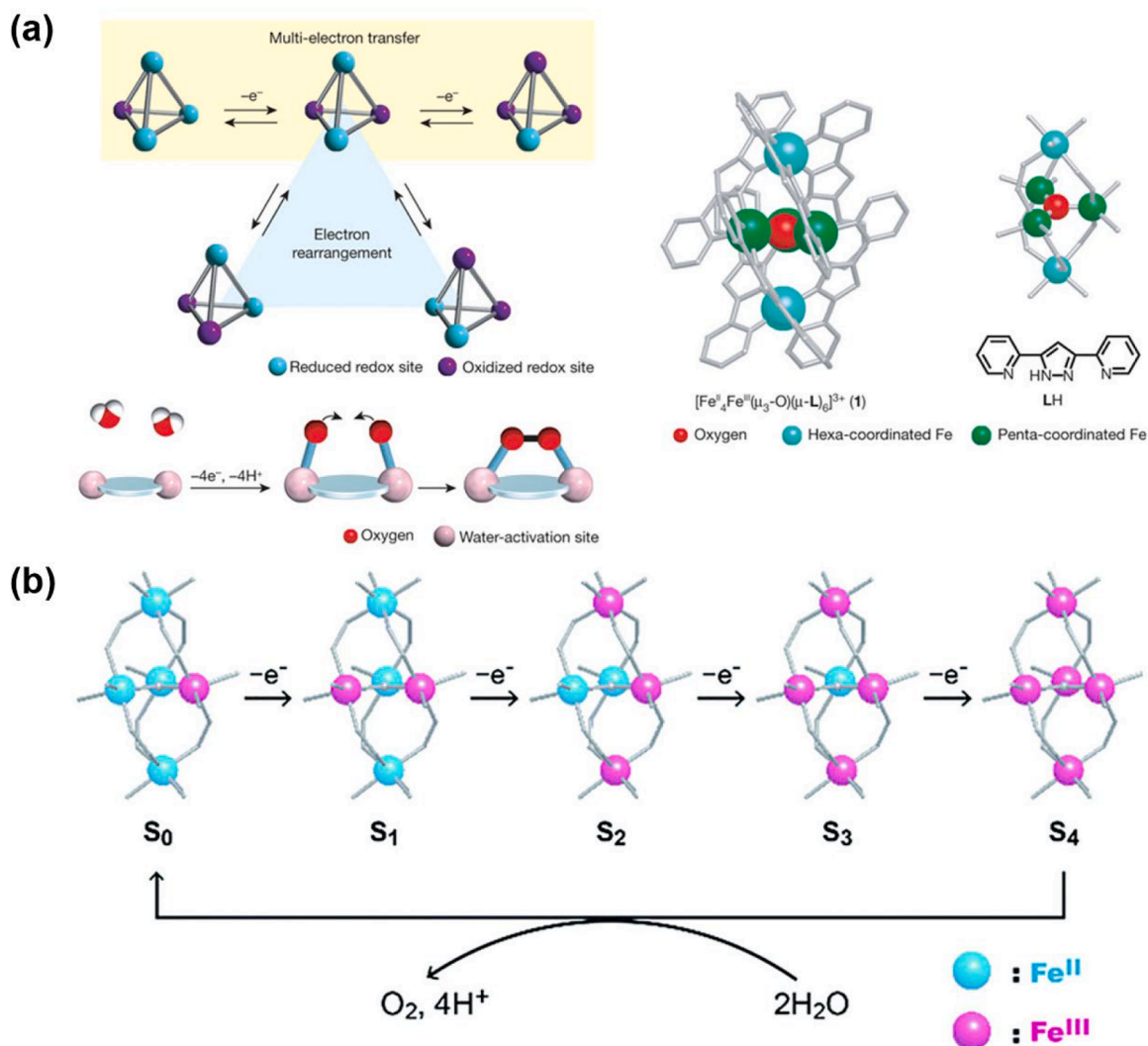


Fig. 13. (a) Redox flexibility arising from a multinuclear core on the Fe_5 core structure of $[Fe_5^II Fe^{III}(\mu_3-O)(\mu-L)_6]^{3+}$ (ball and stick representations on the right side) to realize the accumulation of multiple positive charges required for water oxidation. Reproduced with permission [123]. Copyright 2016, Springer. (b) Sequential oxidation of iron ions in $[Fe_5-H]^{3+}$ and the reaction of the S_4 state to generate O_2 . Reproduced with permission [125]. Copyright 2019, The Royal Society of Chemistry.

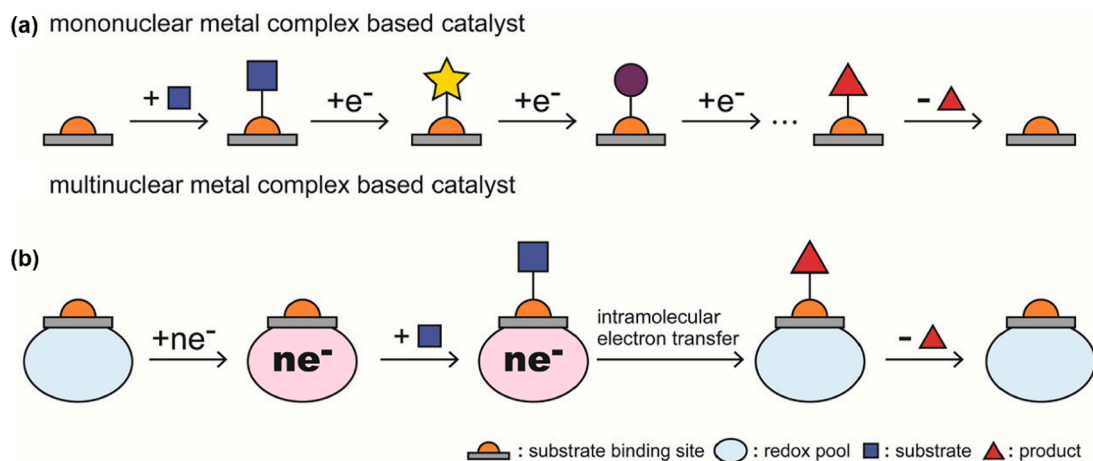


Fig. 14. Schematic of the reaction mechanism for (a) a mononuclear metal complex-based catalyst and (b) a multinuclear metal complex-based catalyst. Reproduced with permission [11]. Copyright 2020, American Chemical Society.

mechanism, where the metal core functions as a redox pool to accumulate multiple charges before catalysis. This accumulated charge

can then be rapidly delivered to the substrate in a concerted manner, thereby facilitating bond transformation with reduced reliance on discrete intermediate states [11]. This enables the rapid injection of accumulated charges into the substrate, thereby facilitating concerted bond rearrangement and avoiding high-energy intermediates.

To quantitatively evaluate the impact of multinuclear synergy on catalytic performance, representative multinuclear systems, particularly well-defined multinuclearity clusters such as pentanuclear complexes, are compared with their mono- and binuclear analogues in Table 1. These selected examples demonstrate that, in specific cases, the redox-pool-enabled charge accumulation and concerted electron transfer can translate into higher TON, lower overpotential, and/or improved reaction kinetics.

4. Strategies for immobilizing molecular water-oxidation catalysts on electrodes

As molecular WOCs have progressed from noble-metal complexes to increasingly capable first-row mono- and multinuclear architectures, their catalytic activity in homogeneous solution has improved substantially. However, these systems often suffer from catalyst leaching, structural instability, and inefficient interfacial charge transfer under electrochemical operating conditions. A parallel limitation has become unmistakable: high intrinsic reactivity in solution does not automatically translate into stability or efficiency at electrode interfaces. When operated under electrochemical conditions, many homogeneous catalysts undergo leaching, structural rearrangement, or experience inefficient charge transfer across the catalyst-electrode boundary. Bridging this molecular-solid gap represents the next evolutionary step in transforming mechanistic insight into practical oxygen-evolution technologies.

Recent studies have demonstrated that heterogenization of molecular catalysts onto oxide supports can effectively address these challenges. For example, immobilization of an Ir-EDTA complex onto TiO₂ yields a robust and highly active catalyst with excellent recyclability, where iridium centers remain atomically dispersed through coordination interactions with surface Ti sites, highlighting the potential of interface-engineered systems to bridge homogeneous and heterogeneous catalysis [127].

To overcome these shortcomings, a broad suite of immobilization strategies has emerged, including physical adsorption, supramolecular/noncovalent assembly, and covalent grafting, each aimed at preserving molecular integrity while establishing durable and efficient electronic coupling with conductive substrates. This section surveys these approaches and illustrates how immobilization extends the structural design principles of molecular WOCs into heterogeneous environments, enabling operation under realistic electrochemical conditions.

4.1. Physical adsorption methods

Physical adsorption methods represent the most fundamental approach to immobilizing molecular WOCs. These strategies address the initial challenge of interfacing molecular catalysts with electrode surfaces while preserving their native coordination structures and avoiding synthetic modification of either the catalyst or the substrate. Although these methods provide a simple and rapid route to forming hybrid interfaces, their reliance on weak adhesion or polymer entrapment often limits long-term stability and efficient charge transport. These limitations motivate the development of more controlled interfacial assembly strategies based on supramolecular interactions. Nonetheless, physical adsorption serves as an essential early step in the evolution of immobilization strategies.

4.1.1. Drop-casting deposition

The drop-casting method is the simplest and most widely used strategy for fabricating molecularly modified electrodes. In this

approach, a catalyst solution is directly deposited onto the electrode surface and subsequently dried to form a thin catalyst layer. Tanaka et al. demonstrated the electrochemical oxidation of water catalyzed by a dinuclear Ru complex drop-cast on an indium-tin oxide (ITO) electrode in Fig. 15a [128,129]. Although this electrode exhibited catalytic activity toward water oxidation, it suffered from poor operational stability due to weak adhesion and partial leaching of the catalyst during operation. Despite these limitations, drop-casting remains valuable for preliminary screening of molecular WOCs and for probing their intrinsic redox and electrocatalytic behaviors under heterogeneous conditions.

4.1.2. Embedding in auxiliary polymer films

4.1.2.1. Polymer embedding strategy for catalyst immobilization. To enhance the mechanical adhesion of molecular catalysts on electrodes, the catalyst can be dispersed within a polymeric matrix and subsequently drop-cast onto the substrate. Upon solvent evaporation, a thin composite film is formed, in which the polymer network provides ionic pathways that facilitate proton and mass transport during catalysis. Yagi et al. reported Nafion-confined molecular catalysts that exhibited improved stability and sustained catalytic activity during water oxidation in Fig. 15b [130]. Subsequent studies extended this concept to various Ru-based and Ir-based WOCs embedded within Nafion or perfluorosulfonic membranes, achieving improved durability under acidic conditions and moderate catalytic activity [131,132]. As a representative non-noble metal example, a bioinspired tetranuclear copper cubane catalyst, Cu₄(LGlu)₄ (LGlu = glutamate-derived ligand), has been immobilized on carbon cloth via physical embedding in a Nafion matrix. The catalyst enables efficient neutral water oxidation (TOF $\approx$ 9.6 s⁻¹ at 0.63 V overpotential, pH = 7.3), where the glutamate ligands act as intramolecular proton relays to promote proton-coupled electron transfer [133].

Nevertheless, because electron transfer between the electrode and the catalytic centers proceeds only through physical contact, such systems often suffer from sluggish charge transport and limited current densities.

4.1.2.2. Mechanistic role of proton/hydroxide conduction. In addition to providing mechanical stabilization and ionic pathways, the proton/hydroxide conduction properties of the polymer matrix play a critical role in modulating the catalytic mechanism [134,135]. Efficient proton transport facilitates PCET, which is central to water oxidation catalysis, by lowering the kinetic barriers associated with proton removal from catalytic intermediates. This effect has been evidenced in Nafion-confined systems, where sulfonic acid groups promote proton transport and thereby enhance PCET kinetics. Conversely, insufficient ionic conduction may lead to the accumulation of high-energy intermediates and increased overpotentials. In neutral or alkaline environments, hydroxide transport can similarly influence reaction pathways by governing local pH and the availability of nucleophilic species. Therefore, the polymer matrix should be regarded not merely as a passive support, but as an active component that regulates the interfacial catalytic microenvironment.

4.1.3. Electropolymerized films

Electropolymerization represents a powerful strategy to immobilize molecular catalysts through the in-situ formation of conductive polymeric networks on electrode surfaces. In contrast to simple physical embedding in insulating matrices such as Nafion, electropolymerized films enable direct electronic communication between adjacent catalytic centers and the underlying electrode.

Llobet and coworkers demonstrated this concept using Ru-Hbpp complexes that undergo potential-driven oxidation to form robust polymeric films on conductive oxide electrodes. Copolymerization of the cationic water-oxidation catalyst [Ru^{II}(μ-bpp)(t-trpy)₂(H₂O)₂]³⁺ with a

Table 1

Summary of Representative Molecular Water Oxidation Catalysts and Their Catalytic Performances.

Cat.	Formula	metal center	Number of the core	Oxidant	TON	TOF /s ⁻¹	η /mV	Condition	Ref.
1	[Ru(H ₂ O)(bpy)] ₂ (μ -O)	Ru	2	CAN	13	0.004	-	pH = 1	15
2	[Ru(H ₂ O)(tpy)] ₂ (μ -bpy)	Ru	2	CAN	512	0.012	-	pH = 1	43
3	[Ru(bpy) ₂] ₂ (μ -Cl)(μ -bnpdz)	Ru	2	CAN	538	0.046	-	pH = 1	46
4	Ru(tpy)(bpm)(H ₂ O)	Ru	1	CAN	310	0.029	-	pH = 1	48
5	Ru(tpy)(bpy)(H ₂ O)	Ru	1	CAN	178	0.004	-	pH = 1	50
6	Ru(bda)(pic) ₂	Ru	1	CAN	>2,000	41	-	pH = 1	54
7	[Ru(pic) ₂] ₂ (μ -cpph)(μ -Cl)	Ru	2	CAN	10,400	1.2	-	pH = 1	55
8	Ru(OH)(tda- κ -N ₃ O)(py) ₂	Ru	1	Electro chemical	2.7 $\times$ 10 ⁷	8,000	610	1.43 V vs. NHE, pH = 7	56
9a	trans-Ru(tpy)(qc)(H ₂ O)	Ru	1	Electro chemical	14.9	4.2	470	1.62 V vs. NHE, pH = 1	57
9b	cis-Ru(tpy)(qc)(H ₂ O)	Ru	1	Electro chemical	-	6.8	540	1.71 V vs. NHE, pH = 1	57
10	Ru(bds)(pic) ₂	Ru	1	Electro chemical	9.3 $\times$ 10 ⁷	12,900	380	1.63 V vs. NHE, pH = 1	58
11	Ru(tds)(py) ₂	Ru	1	CAN	12,000	>2,000	620	1.76 V vs. NHE, pH = 1	59
12a	Ir(Cp*)(ppy)Cl	Ir	1	CAN	-	0.18	-	pH = 1	62
12b	Ir(Cp*)(ppm)Cl	Ir	1	CAN	213	0.024	-	pH = 1	62
13	Ir(Cp*)(MeCN)(py-NHC)	Ir	1	CAN	10,000	0.046	-	pH = 1	63
14	Ir(Cp*)(H ₂ O) ₂ (Me ₂ -NHC)	Ir	1	CAN	>2000	1.5	-	pH = 1	78
15	Ir(Cp*)(pyalc)	Ir	1	Electro chemical	-	-	385	1.45 V vs. NHE, pH = 2.75	79
16	Ir(bpsa-pH)Cl ₂	Ir	1	CAN	2290	0.0075	-	pH = 1	80
17a	Mn ₂ (porphyrin/corrole)	Mn	2	Electro chemical	-	0.0005	-	1.2–2.0 V vs. Ag/Ag ⁺	86
17b	Mn ₂ (porphyrin/corrole)	Mn	2	Electro chemical	-	0.0007	-	1.2–2.0 V vs. Ag/Ag ⁺	86
17c	Mn ₂ (porphyrin/corrole)	Mn	2	Electro chemical	9.2	0.0018	-	1.2–2.0 V vs. Ag/Ag ⁺	86
18a	Mn ₁ (porphyrin/corrole)	Mn	1	Electro chemical	-	-	-	-	87
18b	Mn ₂ (porphyrin/corrole)	Mn	2	Electro chemical	-	-	-	-	87
19a	(Py ₂ NH ₂)Mn(H ₂ O) ₂	Mn	1	Inactive	-	-	-	-	88
19b	(Py ₂ NMe ₂)Mn(H ₂ O) ₂	Mn	1	Inactive	-	-	-	-	88
19c	[Py ₂ N(<i>t</i> -Bu) ₂]Mn(H ₂ O) ₂	Mn	1	Electro chemical	16–24	-	800	1.23 V vs. SHE, pH = 12.2	88
20	Mn tris (pentafluorophenyl) corrole	Mn	1	Electrochemical	6.3	-	-	1.12 V vs. Fe/Fe ⁺	89
21a	Fe-TAML type	Fe	1	Inactive	-	-	-	-	90
21b	Fe-TAML type	Fe	1	CAN	2.5	-	-	pH = 0.7	90
21c	Fe-TAML type	Fe	1	CAN	5.8	-	-	pH = 0.7	90
21d	Fe-TAML type	Fe	1	CAN	7.5	-	-	pH = 0.7	90
21e	Fe-TAML type	Fe	1	CAN	17	>1.3	-	pH = 0.7	90
22a	Fe-TAML type	Fe	1	CAN	10	-	-	pH = 1	92
				Photochemical	220	0.76	-	Photosensitizer: 0.83 mM [Ru(bipy) ₃] ²⁺ , Sacrificial electron donor: 8.30 mM Na ₂ S ₂ O ₈ , pH = 8.7	92
22b	Fe-TAML type	Fe	1	CAN	17	-	-	pH = 1	92
				Photochemical	60	0.21	-	Photosensitizer: [Ru(bipy) ₃] ²⁺ , Sacrificial electron acceptor: Na ₂ S ₂ O ₈ , pH = 8.7	92
23	Fe(Me ₂ Pytacn)	Fe	1	CAN	82	0.063	-	pH = 1	22
24	Fe(mcp)	Fe	1	CAN	360	0.23	-	pH = 1	22
25	Fe(bpbp)	Fe	1	CAN	63	0.046	-	pH = 1	22
26	Fe(mep)	Fe	1	CAN	145	0.14	-	pH = 1	22
27	Fe(tpa)	Fe	1	CAN	40	0.015	-	pH = 1	22
28	Fe(tmc)	Fe	1	Inactive	-	-	-	-	22
29	Fe(NCCH ₃)(^{Me} Py ₂ CH-tacn)	Fe	1	Inactive	-	-	-	-	22
30	Fe(D4-mcp)	Fe	1	CAN	3,800	0.41	-	pH = 1	93
31	Fe(dpaq)(H ₂ O)	Fe	1	Electrochemical	>29	0.15	640	1.58 V vs. NHE	95
32	[Fe(TPA)Cl] ₂ (μ -O)	Fe	2	Oxone	2,380	2.2	-	pH = 4.5	96
33	Fe(ppq)	Fe	2	CAN	-	2.2	-	pH = 1	97
34	Fe(dpa)	Fe	1	CAN	-	0.23	-	pH = 1	97
35a	Fe(PY5OH)(OHMe)	Fe	1	CAN	16	0.75	-	pH ~ 1.5	98
				[Ru(bpy) ₃] (ClO ₄) ₃	7	0.9	-	pH = 8	98
				Photochemical	20	-	-	Photosensitizer: [Ru(bpy) ₃] ²⁺ , Sacrificial electron acceptor: Na ₂ S ₂ O ₈ , pH ~ 8	98
35b	Fe(PY5OH)Cl	Fe	1	CAN	5	0.53	-	pH ~ 1.5	98
				[Ru(bpy) ₃] (ClO ₄) ₃	26.5	2.2	-	pH = 8	98
				Photochemical	43.5	0.6	-	Photosensitizer: [Ru(bpy) ₃] ²⁺ , Sacrificial electron acceptor: Na ₂ S ₂ O ₈ , pH ~ 8	98
36	[Fe(poxdiol)Cl] ₂ (μ -O)	Fe	2	Electro chemical	408	0.11	-	1.0 V vs. Ag/AgCl	99
37	Co(PY5OMe)(OH ₂)	Co	1	Electro chemical	-	79	500	1.59 V vs. NHE, pH = 9.2	100
38a	[Co(tpy)] ₂ (μ -bpy)(μ -O ₂)	Co	2	Electro chemical	-	-	-	pH = 2.1	101
38b	[Co(Me ₂ bimpy)] ₂ (μ -bpy)(μ -O ₂)	Co	2	Electro chemical	-	-	-	pH = 2.1	101
39a	Co(TDMImP)(OH ₂) ₂	Co	1	Electro chemical	-	1,400	-	1.30 V vs. Ag/AgCl, pH = 7	102
39b	Co(TM4PyP)(OH ₂) ₂	Co	1	Electro chemical	-	-	-	-	102
39c	Co(TTMAP)(OH ₂) ₂	Co	1	Electro chemical	-	-	-	-	102

(continued on next page)

Table 1 (continued)

Cat.	Formula	metal center	Number of the core	Oxidant	TON	TOF /s ⁻¹	η /mV	Condition	Ref.
40a	Co-TAML type	Co	1	Electro chemical	-	7.53	380	1.40 V vs. Ag/AgCl, pH = 7.0	103
40b	Co-TAML type	Co	1	Electro chemical	-	7.5	-	1.40 V vs. Ag/AgCl, pH = 7.0	103
40c	Co-TAML type	Co	1	Electro chemical	-	8.81	-	1.40 V vs. Ag/AgCl, pH = 7.0	103
41	Ni(Me ₆ cyclam)(OH) ₂	Ni	1	Electro chemical	15	-	170	1.55 V vs. NHE, pH = 7.0	104
42	Ni-TM4PyP	Ni	1	Electro chemical	-	0.67	-	1.32 V vs. NHE, pH = 7.0	105
43	Ni(mep)	Ni	1	Electro chemical	3.4	-	750	1.60 V vs. NHE, pH = 6.5	106
44a	Ni(Bn-tpa-en)(OH) ₂	Ni	1	Electro chemical	-	3.06	860	1.68 V vs. NHE, pH = 7	107
44b	Ni(Bn-tpa-chda)(OH) ₂	Ni	1	Electro chemical	-	4.62	860	1.68 V vs. NHE, pH = 7	107
45	Ni(PY5OH)Cl	Ni	1	Electro chemical	19	145	800	1.5 V vs. NHE, pH = 10.8	108
46	Cu(bpy)(OH) ₂	Cu	1	Electro chemical	> 30	-100	-750	1.35 V vs. NHE, pH = 12.5	109
47	Cu(OH ₂ bpy)(OH) ₂	Cu	1	Electro chemical	~ 400	0.4	640	1.135 V vs. NHE, pH = 12.4	110
48	Cu ₂ (BPMAN)(μ -OH)	Cu	2	Electro chemical	-	0.6	800	1.87 V vs. NHE, pH = 7	111
49	[Cu(Me ₂ TPMA)] ₂ (μ -OH) ₂	Cu	2	Electro chemical	-	33	1,0	1.62 V vs. NHE, pH = 12.5	112
50	Cu-TM4PyP	Cu	1	Electro chemical	-	30	310	1.30 V vs. NHE, pH = 7.0	113
51a	Cu-TAML type	Cu	1	Electro chemical	79	140	200	1.2 V vs. Fc/Fc ⁺ , pH = 7.0	114
51b	Cu-TAML type	Cu	1	Electro chemical	-	-	100	pH = 7.0	114
52*	Mn ₄ O ₄ (cubane)	Mn	4	Electro chemical	6.9	-	-	0.40 V vs. Fc/Fc ⁺	115
53a	Co ₄ O ₄ (cubane)	Co	4	Electro chemical	2.8	1.04	710	1.65 V vs. SHE, pH = 7.4	116
53b	Co ₄ O ₄ (cubane)	Co	4	Electro chemical	3.5	1.99	680	1.68 V vs. SHE, pH = 7.4	116
54	Ni ₃ O ₂ (OH) ₂	Ni	3	Electro chemical	13	-	-	1.54 V vs. NHE, pH = 7	119
55	Cu ₄ (OH) ₄	Cu	4	Electro chemical	4.6	-	730	1.80 V vs. NHE, pH = 7.0	120
56	Cu ₄ O ₄ (cubane)	Cu	4	Electro chemical	4.74 ±0.10	267	620	1.50 V vs. NHE, pH = 12.0	121
57	Cu ₃ O ₂ (OH)	Cu	3	Electro chemical	34	20,000	910	1.64 V vs. NHE, pH = 8.4	122
58	Fe ₅	Fe	5	Electro chemical	>78	1,900	520	1.42 V vs. Fc/Fc ⁺	123

*This water oxidation reaction produces hydrogen peroxides.

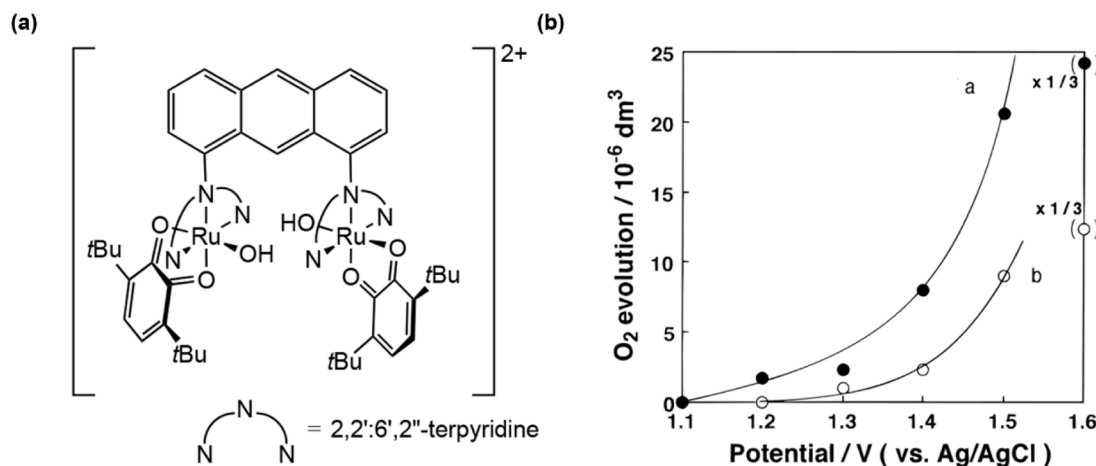


Fig. 15. (a) Structure of a dinuclear ruthenium hydroxo-bridged complex. Reproduced with permission [128]. Copyright 2000, Wiley. (b) Relationship between the amount of O₂ evolved and the applied potential during potentiostatic electrolysis using a Ru complex/Nafion-modified Pt electrode, compared with a Nafion-coated Pt electrode in 0.1 M KNO₃ (pH = 5.5). Reproduced with permission [130]. Copyright 1996, American Chemical Society.

cobaltabisdicarbollide monomer generates a new material. The resulting molecular assemblies exhibited remarkable structural integrity and catalytic stability, establishing the viability of electropolymerization for molecular water-oxidation systems in Fig. 16a [136]. Later, Sun and co-workers designed functionalized Ru-bda WOCs that can be electrochemically polymerized onto basal-plane pyrolytic graphite electrode, forming conjugated hybrid films with efficient charge transport and sustained activity (TOF = 10.47 s⁻¹ at ~700 mV overpotential), maintaining a high TON of up to 31,600 during 1 h of electrolysis in Fig. 16b [137]. More recently, Zhuo and co-workers introduced styrenic comonomers into the polymeric environment of [Ru(bda)]-type WOCs to engineer the second coordination sphere around Ru centers, modulating the hydrophobic microenvironment and fine-tuning O–O bond formation pathways in Fig. 16c [138]. Beyond polymerizing the catalyst itself or its immediate ligands, electropolymerization has also enabled the formation of polymer-integrated molecular architectures, in which the

conducting polymer framework serves as the primary structural scaffold. In this approach, the Sun group developed thiophene-functionalized Ru water-oxidation catalysts that undergo oxidative electropolymerization to form polythiophene networks, in which molecular active sites are covalently embedded, affording electronically wired molecular anodes without direct molecule-electrode grafting [139].

Most recently, in 2025, Kondo and Masaoka reported a breakthrough extension of Fe₅ into aqueous media for efficient water oxidation inspired by PSII. This work demonstrated that the electrochemically polymerized Fe₅ with carbazole moieties catalyzes water oxidation under aqueous media with both high activity and remarkable stability in Fig. 16d, marking an essential step toward the realistic implementation of Fe-based molecular WOCs [140].

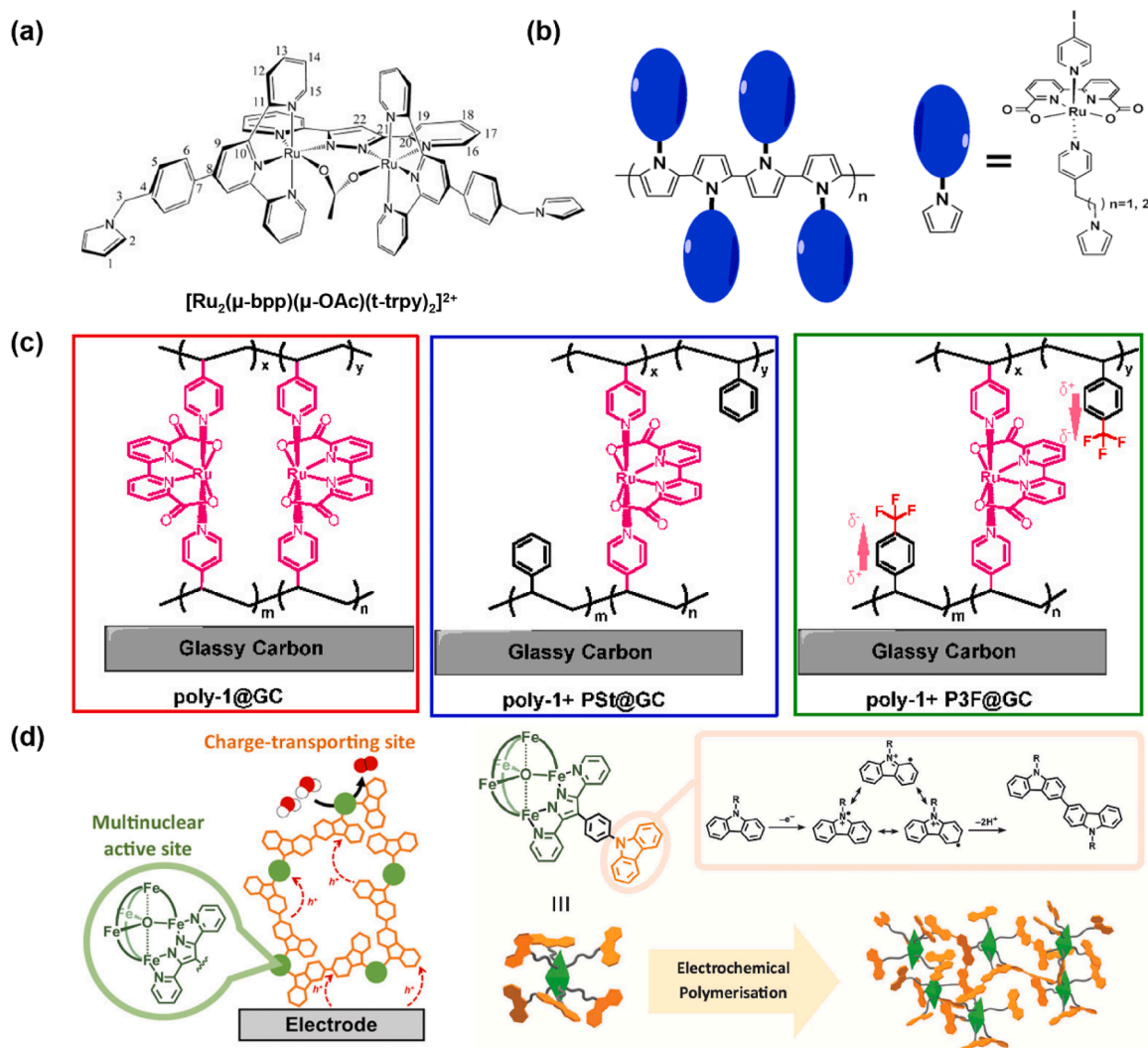


Fig. 16. (a) Structure of the cationic dinuclear complex $[\text{Ru}_2(\mu\text{-bpp})(\mu\text{-OAc})(\text{t-trpy})]^{2+}$ (bpp = bis(2-pyridyl)pyrazolate; t-trpy = tris-terpyridine derivative). Reproduced with permission [136]; Copyright 2008, Wiley. (b) Chemical structure of a Ru-bda complex ($\text{H}_2\text{bda} = 2,2'$ -bipyridine-6,6'-dicarboxylic acid) and a schematic illustration of its electropolymerization. Reproduced with permission [137]. Copyright 2015, The Royal Society of Chemistry. (c) Schematic diagrams of electrodes prepared via electropolymerization of Ru-based molecular catalysts. Reproduced with permission [138]. Copyright 2021, Elsevier. (d) Left: Schematic representation of an artificial catalytic system for water oxidation. Right: Strategy for constructing polymer-based catalytic materials via electropolymerization of a pentanuclear iron complex bearing carbazole moieties, affording multinuclear active sites embedded within charge-transporting polymer networks. Reproduced with permission [140]. Copyright 2025, Springer.

4.1.4. Conducting polymer matrix embedding of molecular WOCs

In addition to electropolymerization on electrode surfaces, conducting polymer matrices can also serve as stabilizing hosts for molecular water-oxidation catalysts through covalent integration within conducting polymer catalysts. Cubane-type Co_4O_4 clusters, which combine features of homogeneous and heterogeneous catalysis and incorporate bioinspired structural motifs, have attracted sustained interest as molecular oxygen evolution catalysts but often suffer from limited stability under operating conditions. To address this challenge, a conductive polymer-hybrid strategy has been developed in which Co_4O_4 cubane oxo clusters are covalently immobilized within a polypyrrole matrix. In this architecture, the p-type conducting polymer facilitates hole transport during oxygen evolution while providing a stabilizing environment for the molecular cluster. Notably, asymmetric coordination of the Co_4O_4 unit within the polymer matrix mitigates catalyst decomposition pathways and enhances catalytic efficiency by exposing a directed cofacial dihydroxide motif during catalysis. This polymer matrix embedding approach extends polymer-based heterogenization beyond surface-confined films and offers an effective route to stabilize

and activate structurally complex molecular clusters for sustained water oxidation [141].

4.2. Noncovalent assembly

Noncovalent assembly methods build upon the limitations of physical adsorption. Approaches based on π - π stacking with carbon supports, hydrophobic organization, and coordination-induced film growth provide greater control over interfacial electronic coupling. These methods address the challenge that physically adsorbed catalysts tend to desorb or reorganize under operating conditions, and therefore require additional stabilizing interactions to maintain structural integrity and catalytic accessibility. By leveraging supramolecular forces and weak coordination motifs, noncovalent assembly enables the formation of more stable and better-organized hybrid interfaces without altering the intrinsic molecular identity of the catalyst. However, because these interactions remain relatively weak under strongly oxidative conditions, further stabilization through direct chemical bonding becomes desirable. These strategies represent enhanced interfacial control while

retaining synthetic versatility.

4.2.1. π - π stacking on carbon-based supports

Noncovalent π - π interactions between aromatic ligands and sp^2 -hybridized carbon materials offer a highly effective means of immobilizing molecular WOCs while ensuring intimate electronic coupling with the conductive substrate. The planar aromatic surfaces of carbon nanotubes (CNTs), graphene, or graphite facilitate van der Waals and charge-transfer interactions with conjugated ligands, providing electronically coherent interfaces that promote rapid interfacial charge transport. In addition, defect sites in carbon materials, such as edge planes or vacancy defects, can interact more strongly with the ligands or metal centers of molecular catalysts, in some cases establishing quasi-covalent interfacial bonding or electronic coupling that further enhances interfacial charge-transfer kinetics and catalyst stability [142].

Sun and co-workers reported a monomeric $\text{Ru}(\text{bpa})(\text{pic})_2$ complex

immobilized on multiwalled carbon nanotubes (MWCNTs) through aromatic π - π interactions (Fig. 16a). The resulting molecular anode exhibited high activity and remarkable structural robustness under electrochemical water oxidation conditions, achieving an overpotential as low as 160 mV at neutral pH in Fig. 17a [143]. Subsequent work by Llobet and co-workers introduced pyrene-functionalized ruthenium complexes of the type $[\text{Ru}(\text{tda})(\text{L})_2]$ [$\text{tda} = (2,2':6',2''\text{-terpyridine})\text{-}6,6''\text{-dicarboxylate}$, $\text{L} = \text{pyrene-functionalized pyridyl ligands}$] that can form stronger π - π interactions with carbon nanotubes. The resulting hybrid molecular anodes exhibited outstanding operational stability, achieving over a million TON at $\text{pH} = 7$ with an applied potential of 1.45 V vs. NHE without any sign of degradation [144]. Theoretical simulations by Zhan and Ahlquist provided molecular-level insight into the interfacial dynamics of $[\text{Ru}^{\text{V}}\text{O}(\text{bda})\text{L}_2]$ catalysts π -stacked on CNTs, revealing diffusion-controlled dimer formation and dynamically resolved O-O bond generation at the carbon-water interface (Fig. 17b)

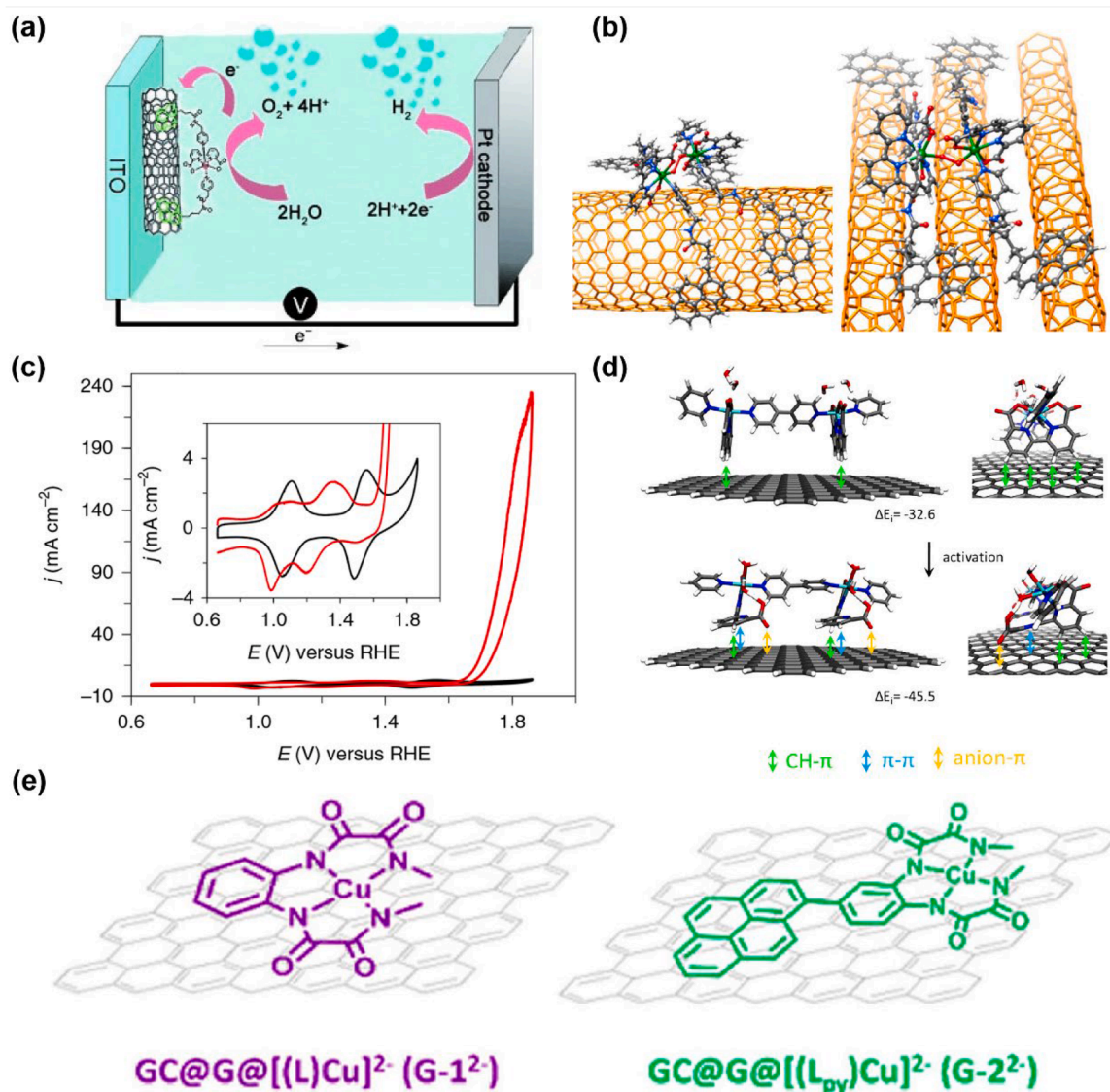


Fig. 17. (a) Schematic illustration of an electrochemical cell for water splitting and the molecular catalyst structure. Reproduced with permission [143]. Copyright 2011, Wiley. (b) Empirical valence bond simulations of the Ru complex, showing the transition-state structures at large (left) and small (right) carbon nanotube-water interfaces. Reproduced with permission [145]. Copyright 2018, American Chemical Society. (c) Cyclic voltammograms before (black line) and after activation (red line) of Ru complex hybrid electrodes recorded in 1.0 M phosphate buffer ($\text{pH} = 7$) at a scan rate of 100 mV s^{-1} . Reproduced with permission [146]. Copyright 2020, Springer. (d) Schematic representation of noncovalent interactions in a dimer-model electrode before (top) and after activation (bottom), with semiempirical calculated interaction energies per Ru center (ΔE_i , kJ mol^{-1}). Reproduced with permission [148]. Copyright 2021, American Chemical Society. (e) Schematic representation of Cu-based complex hybrid materials immobilized via π - π interactions on graphitic supports. Reproduced with permission [149]. Copyright 2017, American Chemical Society.

[145]. Further expanding this concept, Llobet and coworkers reported that functional Ru molecular coordination oligomers that adsorb onto graphitic surfaces such as MWCNTs via aromatic CH- π interactions, enabled the formation of robust hybrid electroanodes capable of sustaining current densities of $\approx 0.3 \text{ A cm}^{-2}$ under neutral conditions (Fig. 17c) [146]. Extending π - π -mediated integration to porous frameworks, the NU-1000-Ru mixed-linker metal-organic framework (MOF) co-assembled with MWCNTs has been shown to form conductive hybrid electrodes in which aromatic linkers engage in interfacial π - π contacts with the carbon scaffold, establishing efficient charge transport across the composite network [147]. Most recently, Würthner and Llobet demonstrated a surface-promoted evolution mechanism in which the Ru-bda-based oligomer [bda = (2,2'-bipyridine)-6,6'-dicarboxylate] of general formula $\{[\text{Ru}^{\text{II}}(\text{bda}-\kappa\text{-N}_2\text{O}_2)(4,4'\text{-bpy})]_{10}(4,4'\text{-bpy})\}$ (4,4'-bpy = 4,4'-bipyridine), has been prepared, isolated, and thoroughly characterized in homogeneous solution. This oligomer engages in CH- π interactions and facilitates its anchoring on MWCNTs in Fig. 17d. This transformation enhances charge delocalization and interfacial coupling, affording hybrid anodes that sustain high water-oxidation current densities in the range of 200 mA cm^{-2} at 1.45 V vs NHE, pH = 7, with remarkable durability, marking a key step toward quasi-covalent, self-assembled molecular electrodes [148]. Heterogenization can transform non-noble metal molecular catalysts from intrinsically redox-limited systems into highly active interfacial architectures. Llobet and co-workers reported a heterogenized copper molecular water oxidation catalyst in Fig. 17e, the complex of general formula $[\text{L}_{\text{py}}\text{Cu}]^{2+}$, $[\text{L}_{\text{py}} = 4\text{-pyrenyl-1,2-phenylenebis(oxamidate)ligand}]$, immobilized on graphene through π - π stacking interactions between pyrene units and the carbon surface, affording an overpotential of 538 mV, a k_{cat} of 540 s^{-1} , and $> 5300 \text{ TON}$ [149].

4.2.2. Hydrophobic interactions

Self-assembly driven by hydrophobic interaction forces provides another noncovalent means of immobilizing molecular catalysts at electrode surfaces. Sun and co-workers employed hydrophobic interactions between a dodecyloxy-substituted Ru complex and MWCNTs to fabricate hybrid molecular electrodes. The resulting system exhibited a TOF of 7.6 s^{-1} and a catalytic current density of 2.2 mA cm^{-2} at an overpotential of $\approx 480 \text{ mV}$, maintaining its activity for over 1 h of electrolysis [150]. Building on the concept of self-assembled monolayers, Concepcion and co-workers developed a self-assembled bilayer anchoring strategy stabilized through noncovalent van der Waals interactions between long alkyl chains. In this approach, alkyl-terminated oxide electrodes interact with functionalized molecular catalysts, forming bilayer assemblies that afford a simple, robust, and broadly applicable platform for immobilizing catalysts, chromophores, and chromophore-catalyst assemblies in Fig. 18a [151]. These studies collectively demonstrate that hydrophobic and electrostatic assembly

can yield stable and well-oriented hybrid films without the need for chemical anchoring.

4.2.3. Coordination-induced film growth on conductive substrates

Beyond carbon-based and hydrophobic assemblies, noncovalent integration can also arise from coordination-driven film growth of MOF on conductive substrates. In the UiO-67- $[\text{RuOH}_2]$ system, a MOF thin film was solvothermally grown on fluorine-doped tin oxide (FTO) and postsynthetically functionalized with $[\text{Ru}(\text{tpy})(\text{dcbpy})(\text{OH})_2]^{2+}$ complexes, yielding a robust hybrid electrode for electrocatalytic water oxidation (Fig. 18b) [152].

4.3. Covalent immobilization methods

Covalent immobilization represents the mature stage in the evolution of hybrid molecular anodes, emerging as a solution to the inherent limitations of noncovalent assembly methods, particularly their vulnerability to desorption or structural reorganization under strongly oxidative conditions. By forming strong chemical bonds between the molecular WOC and the electrode surface, covalent strategies suppress catalyst desorption and allow high-valent intermediates to form without extensive reorganizing the coordination sphere. A key innovation of covalent grafting is that it not only secures molecular identity but also improves interfacial electron-transfer kinetics by establishing well-defined electronic communication channels. Covalent anchoring thus represents a decisive advance in achieving operational durability, enabling molecular WOCs to function under conditions relevant to integrated electrochemical devices.

4.3.1. Click chemistry on carbon electrodes

Click chemistry provides a highly efficient and modular route for covalent immobilization of molecular WOCs on carbon electrodes. Sun and co-workers pioneered a Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) approach to anchor a Ru(II) complex, $[\text{Ru}(\text{pdc})(\text{pic})_3]$ ($\text{pdc} = 2,6\text{-pyridinedicarboxylate}$; $\text{pic} = 4\text{-picoline}$), onto azide-functionalized glassy carbon electrodes (Fig. 19a). The resulting triazole linkage provided exceptional robustness against oxidative potentials and O_2 -rich aqueous environments. The modified electrodes exhibited a TOF of 1.6 s^{-1} at a 700 mV overpotential and retained their activity over extended operation [153]. Building on this concept, Stahl and co-workers developed a modular synthetic route to alkyne-derivatized Ru^{II} polypyridyl complexes via a common alkyne intermediate, enabling late-stage ligand coordination to generate electronically diverse species suitable for click immobilization on electrode surfaces in Fig. 19b [154].

4.3.2. Covalent molecular-surface integration strategies

In contrast to click-based coupling on carbon electrodes, extensive efforts have focused on establishing direct metal-oxide covalent linkages

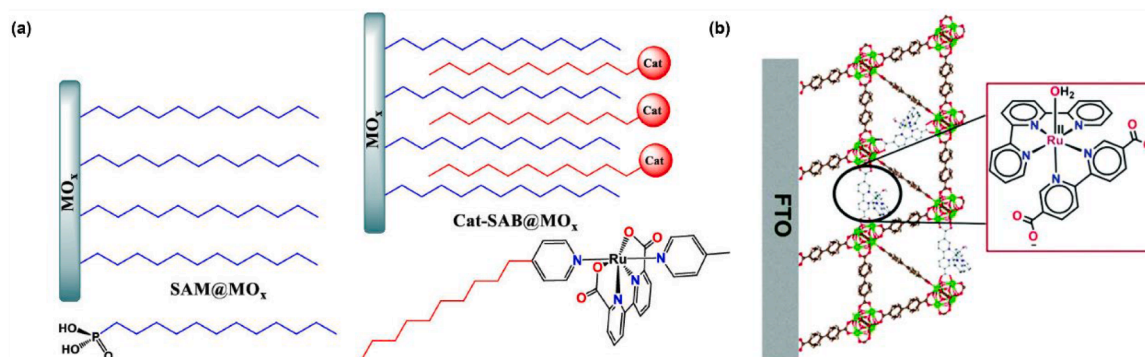


Fig. 18. (a) Left: Self-assembled monolayer on a metal oxide. Right: Self-assembled bilayer on a metal oxide. Reproduced with permission [151]. Copyright 2019, American Chemical Society. (b) Schematic representation of UiO-67- $[\text{RuOH}_2]$ thin films grown on FTO. Reproduced with permission [152]. Copyright 2017, The Royal Society of Chemistry.

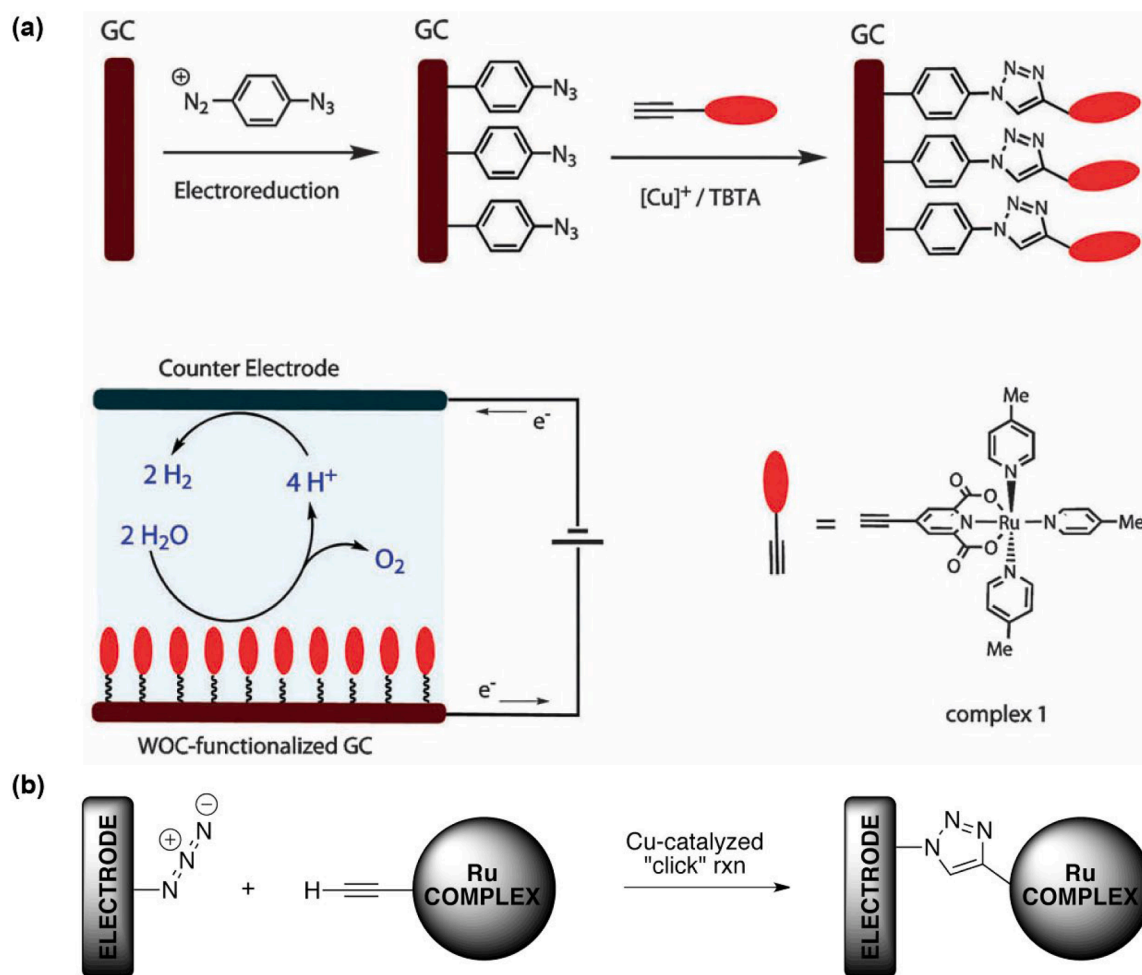


Fig. 19. (a) Schematic illustration of oxygen evolution at a click-functionalized electrode surface. Reproduced with permission [153]. Copyright 2012, The Royal Society of Chemistry. (b) Cu(I)-catalyzed azide-alkyne cycloaddition for covalent attachment of an alkyne-substituted Ru catalyst to an azide-modified electrode. Reproduced with permission [154]. Copyright 2013, American Chemical Society.

to integrate molecular WOCs onto conductive oxide supports such as FTO, ITO, and TiO_2 . Meyer and co-workers extended this strategy by immobilizing a phosphonate-derivatized single-site Ru(II) water oxidation catalyst, $[\text{Ru}(\text{Mebimpy})(4,4'-((\text{HO})_2\text{OPCH}_2)_2\text{bpy})(\text{OH})_2]^{2+}$ [Mebimpy = 2,6-bis(1-methylbenzimidazol-2-yl)pyridine], onto oxide electrodes, including fluorine-doped SnO_2 or $\text{Sn}(\text{IV})$ -doped In_2O_3 electrodes or on nanocrystalline TiO_2 (Fig. 20a). The immobilized complex maintains the homogeneous catalytic mechanism under heterogeneous conditions, operating as a durable surface electrocatalyst for sustained O_2 evolution [155]. Subsequently, in-situ X-ray absorption spectroscopy provided direct evidence for the formation of the key $\text{Ru}^{\text{V}}=\text{O}$ intermediate on a site-isolated Ru-bda typed [bda = (2,2'-bipyridine)-6,6'-dicarboxylate] modified porous ITO electrode, confirming that the molecular mechanism is preserved at the heterogeneous interface in Fig. 20b. The surface-bound catalyst exhibited a short $\text{Ru}=\text{O}$ bond distance of $1.75 \pm 0.02 \text{ \AA}$, consistent with DFT results, and mechanistic analysis indicated that water nucleophilic attack on the $\text{Ru}^{\text{V}}=\text{O}$ species constitutes the rate-determining O–O bond formation step under acidic conditions [156]. Meyer et al. further reported the all-in-one Ru assemblies (Fig. 20c), synthesized by coupling $[\text{Ru}(\text{bpy})_2\text{Cl}_2] \cdot 2\text{H}_2\text{O}$ with $[\text{Ru}(\text{LLL})(\text{bpm})\text{Cl}]^+$ (LLL = tpy or Mebimpy) to afford $[(\text{bpy})_2\text{Ru}(\text{bpm})\text{Ru}(\text{LLL})\text{Cl}]\text{Cl}_3$. Subsequent chloride abstraction with triflic acid and ligand exchange in water yielded the aqua-bridged dinuclear assemblies $[(\text{bpy})_2\text{Ru}(\text{bpm})\text{Ru}(\text{LLL})(\text{H}_2\text{O})]^{4+}$, providing a platform for efficient OER both in solution and on electrode surfaces [157]. Joya et al. reported surface-immobilized mono-iridium complexes $[(\text{L}_2\text{bpy})\text{Ir}(\text{Cp}^*)]$

$(\text{OH}_2)]^{2+}$ (L = $-\text{PO}_3\text{H}_2$ or $-\text{COOH}$; bpy = 2,2'-bipyridine) covalently anchored on ITO electrodes. Phosphonate anchoring afforded markedly enhanced stability and catalytic performance compared to carboxylate linkages in Fig. 20d, achieving TOF = 6.7 s^{-1} , TON > 210,000, and current densities above 1.7 mA cm^{-2} [158].

More recently, a supramolecular self-assembled bilayer strategy has been introduced, in which a silane monolayer bearing long alkyl chains is covalently attached to oxide electrodes and serves as a hydrophobic platform to organize alkyl-functionalized molecular water-oxidation catalysts on top in Fig. 20e. This hierarchical assembly spatially separates the catalyst from the oxide surface, providing excellent structural integrity and long-term stability while maintaining efficient electronic communication for electron transfer. The resulting hybrid anodes operate efficiently at neutral pH, sustaining current densities of $\approx 0.4 \text{ mA cm}^{-2}$ for 15 h with > 33,800 turnovers and > 92% Faradaic efficiency, all while preserving the molecular character of the catalyst [159].

The evolution of immobilization strategies, from simple physisorption to sophisticated covalent integration, completes the conceptual evolution of molecular WOCs from solution to the electrode interface. As summarized schematically in Fig. 21, this development can be viewed as a progressive transition from weak molecular adsorption to structurally rigid interfacial immobilization, accompanied by a gradual enhancement in catalyst stability and interfacial charge-transfer efficiency.

This progression reflects a continuous optimization of the molecular-

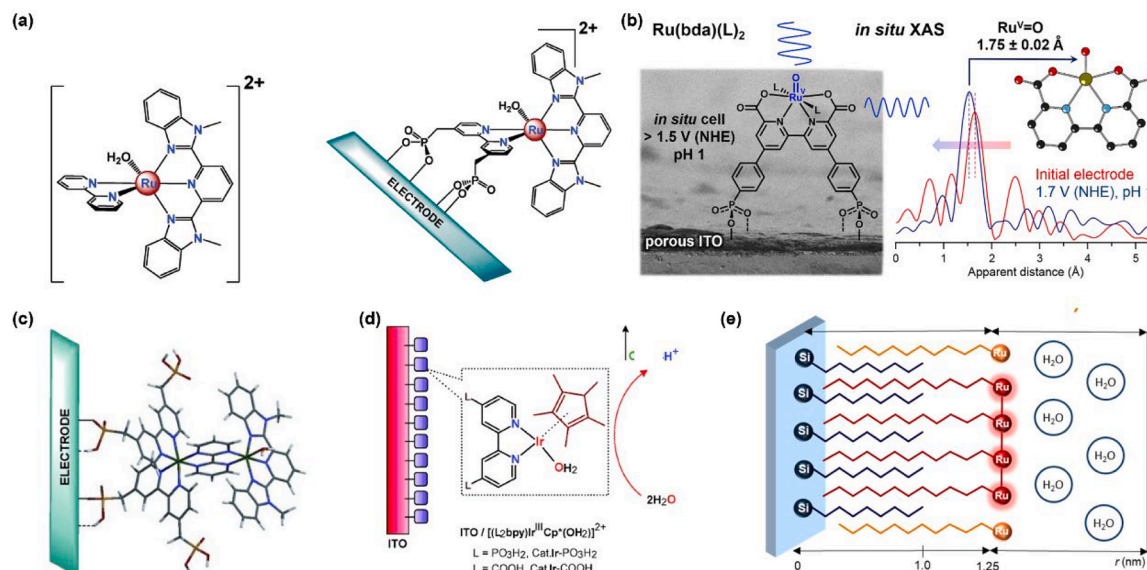


Fig. 20. (a) Schematic representation of a phosphonate-derivatized Ru complex covalently attached to a metal oxide electrode. Reproduced with permission [155]. Copyright 2009, American Chemical Society. (b) Schematic illustration of phosphate-based anchoring of a Ru-bda catalyst on a porous ITO electrode. Reproduced with permission [156]. Copyright 2018, American Chemical Society. (c) All-in-one redox mediator-water oxidation catalyst covalently anchored on a metal oxide electrode. Reproduced with permission [157]. Copyright 2009, Wiley. (d) Schematic representation of surface-immobilized $[(\text{L}_2\text{bpy})\text{Ir}^{\text{III}}\text{Cp}^*(\text{OH}_2)]^{2+}$ on ITO electrodes for electrochemical water oxidation. Reproduced with permission [158]. Copyright 2012, Wiley. (e) Schematic illustration of a hybrid Ru molecular catalyst/oxide interface constructed via self-assembled silane bilayers. Reproduced with permission [159]. Copyright 2025, American Chemical Society.

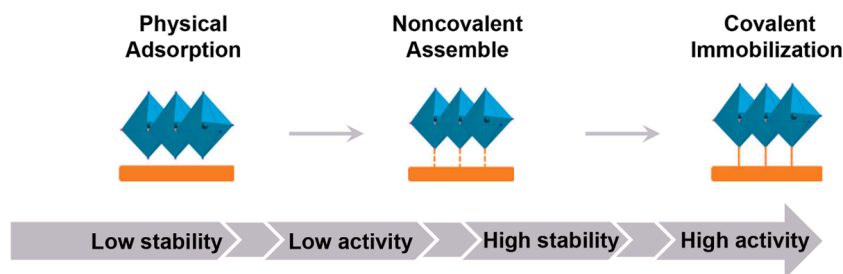


Fig. 21. Evolution of interface immobilization strategies for molecular catalysts on solid supports.

material junction, balancing the preservation of molecular identity against the demands for operational robustness and efficient charge transport. In the early stage, molecular catalysts are typically associated with conductive substrates through weak physisorption or van der Waals interactions, which provide facile synthetic accessibility but often suffer from catalyst leaching and limited electronic coupling. Subsequent strategies introduce stronger noncovalent interactions or interfacial aggregation effects, which partially stabilize the catalyst layer and improve electronic communication with the electrode surface.

A further level of control is achieved through surface anchoring approaches, where coordination bonding or chemical linkage between the molecular catalyst and the substrate establishes more defined interfacial structures. Such anchoring strategies enhance catalyst retention and create more efficient pathways for electron transfer across the molecular-solid interface.

Ultimately, rigid immobilization strategies based on covalent attachment or framework confinement represent the most robust architecture, effectively integrating molecular active sites into solid matrices while maintaining catalytic functionality. These architectures provide superior resistance to catalyst detachment and enable more stable operation under oxidative conditions relevant to water oxidation.

Each class of methods, physical, noncovalent, and covalent, occupies a distinct niche in the design space, offering a different compromise between synthetic accessibility, interfacial stability, and electronic

properties. The comparison of these approaches highlights a central design principle in hybrid catalyst development: increasing degrees of interfacial fixation generally leads to improved operational stability and more efficient charge transport, although often at the cost of increased synthetic complexity.

The development of these strategies has been instrumental in transforming molecular catalysts from homogeneous model systems into functional components of hybrid electrodes, thereby bridging the gap between molecular-level mechanistic understanding and device-level performance requirements. By establishing controllable molecular-material interfaces, these immobilization strategies provide a conceptual framework for integrating well-defined catalytic centers into heterogeneous environments while retaining key mechanistic insights from molecular catalysis. This sets the stage for the final discussion on future perspectives, where the integration of these well-defined active sites into complex, operational systems remain the ultimate challenge.

5. Conclusions and perspectives

Over the past several decades, research on molecular WOCs has undergone a remarkable structural and conceptual evolution, transitioning from soluble homogeneous models to robust, electrode-integrated hybrid systems. This journey, traced in this review, began by drawing inspiration from the atomic-level architecture of the natural

OEC, progressed through the rational design of molecular complexes, first with noble metals, then with earth-abundant alternatives, and culminated in sophisticated interface engineering strategies that anchor these molecular sites to conductive supports. This paradigm shift from discrete molecular design to holistic interface engineering has been pivotal in advancing the field.

Through this evolution, several key design principles have crystallized. The systematic development of noncovalent and covalent immobilization strategies has not only overcome the intrinsic stability bottleneck of molecular catalysts but also enabled precise control over interfacial charge transfer and structural integrity. These advances have successfully translated the atomic-level precision of coordination chemistry into scalable, solid-state electrocatalytic function, blurring the traditional boundary between homogeneous and heterogeneous catalysis and fostering a deep convergence of mechanistic understanding and device-level performance.

Despite remarkable progress, several challenges remain. The foremost issue lies in the absence of standardized evaluation protocols, which hinders quantitative comparison across different systems. Future efforts should aim to establish unified testing frameworks and reporting conventions to enhance data reproducibility and comparability. In addition, operando spectroscopic and electrochemical characterization techniques (e.g., X-ray absorption spectroscopy, Raman spectroscopy, electron paramagnetic resonance) combined with multiscale theoretical simulations are essential for dynamically tracking catalytic intermediates, oxidation-state evolution, and interfacial charge-transport kinetics. Finally, the rational development of sustainable catalytic platforms based on earth-abundant transition metals, while maintaining mechanistic clarity and structural integrity, remains a central mission for the field.

Beyond these general considerations, several critical bottlenecks currently limit the practical advancement of molecular WOCs. First, the synthetic complexity of multinuclear and structurally well-defined catalysts, particularly high-nuclearity clusters, poses significant challenges in terms of scalability, reproducibility, and structural precision. Second, interfacial charge transfer efficiency remains suboptimal in many immobilized systems due to weak electronic coupling or mismatched energy alignment between molecular catalysts and conductive supports. Third, structural degradation during long-term operation, including ligand dissociation, metal leaching, and transformation into heterogeneous oxides, undermines catalytic stability and obscures mechanistic interpretation.

In addition to the conventional four-electron OER, increasing attention has recently been directed toward the alternative two-electron water oxidation pathway for H_2O_2 production. Notably, these two pathways share common surface intermediates, particularly OH^* and OOH^* species, but diverge in their reaction energetics and product selectivity. The competition between the $2e^-$ and $4e^-$ pathways is largely governed by the relative adsorption free energies of key intermediates (e.g., ΔG_{OH} and ΔG_{OOH}), which determine whether the reaction proceeds toward O–O bond retention (H_2O_2) or O–O bond cleavage (O_2 evolution). Therefore, precise tuning of the catalyst electronic structure and adsorption properties offers a promising strategy to regulate reaction selectivity. Incorporating this perspective may open new opportunities for molecular catalyst design beyond conventional OER, particularly for selective and energy-efficient H_2O_2 generation.

Addressing these bottlenecks requires the development of more targeted and innovative strategies. For instance, modular and self-assembly-driven synthetic approaches may offer scalable routes toward well-defined multinuclear architectures with controlled nuclearity and geometry. Meanwhile, advanced interface engineering, such as covalent anchoring, π -conjugated linkers, and electronic coupling layers, can enhance interfacial charge transport and reduce kinetic losses. Furthermore, the design of robust ligand frameworks with enhanced oxidative stability, as well as dynamic self-healing or adaptive catalytic systems, may provide viable pathways to mitigate long-term structural

degradation.

Looking forward, two major and interconnected directions are expected to guide the next wave of breakthroughs, both extending the current evolutionary trajectory:

- (1) The development of advanced functional analogues based on earth-abundant metals. This will require moving beyond simple metal substitution to a deeper electronic-structure tuning and interface engineering, aiming to achieve and surpass noble-metal benchmarks in both activities, crucially, and long-term durability under operating conditions.
- (2) The realization of efficient molecule-solid-photoelectrochemical coupling. The ultimate test for molecular WOCs lies in their integration into functional devices. This demands innovative self-assembly and interface design to seamlessly incorporate these catalysts into photoelectrodes, enabling the practical implementation of molecular catalytic systems in artificial photosynthesis and solar-fuel conversion.

More broadly, future breakthroughs are likely to emerge from the integration of precise molecular design, controlled multimetallic synergy, and dynamic interface engineering, enabling catalytic systems that not only achieve high activity but also maintain long-term operational stability under realistic conditions.

In conclusion, the structural evolution of artificial WOCs exemplifies how bioinspiration, molecular-level control, and materials engineering can synergize to address a key challenge in sustainable energy. Through the continued deep integration of molecular catalysis and interface science, molecular WOCs are poised to transition further from academic model systems into technologically relevant components, holding concrete promise as key anodic materials for the next generation of high-performance and energy-efficient water electrolysis technologies.

CRedit authorship contribution statement

Hui Zeng: Writing – review & editing, Writing – original draft, Conceptualization. **Akira Hasegawa:** Writing – original draft. **Aolun Xu:** Writing – original draft. **Shigeyuki Masaoka:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

No data was used for the research described in the article.

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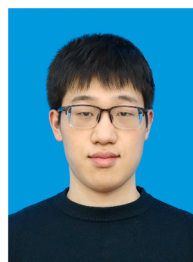
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