



Transferring enzyme features to molecular CO₂ reduction catalysts

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Carbon monoxide dehydrogenases and formate dehydrogenases efficiently catalyze the reduction of CO₂. In both enzymes, CO₂ activation at the metal active site is assisted by proximate amino acids and Fe–S-clusters. Functional features of the enzyme are mimicked in molecular catalysts by redox-active ligands, acidic and charged groups in the ligand periphery, and binuclear scaffolds. These components have all improved the catalytic performance of synthetic systems. Recent studies impart a deeper understanding of the individual contributions of the various functionalities to reactivity and of their combined effects. New catalyst platforms reveal alternate pathways for CO₂ reduction, unique intermediates, and strategies for switching selectivity. Design of a wider array of complexes that combine different functional elements is encouraged to further optimize catalysts for CO₂ reduction, especially for product formation beyond CO. More diverse bimetallic catalysts are needed to better exploit metal–metal interactions for CO₂ conversion.

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Current Opinion in Chemical Biology 2024, 83:102540

This review comes from a themed issue on **Bioorganic Chemistry (2024)**

Edited by **Galia Maayan** and **Clotilde Policar**

For a complete overview see the [Issue](#) and the [Editorial](#)

Available online xxx

<https://doi.org/10.1016/j.cbpa.2024.102540>

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Keywords

CO₂ reduction, Molecular catalysts, Redox-active ligands, Second-sphere interactions, Bimetallic.

Introduction

Biological chemistry and inorganic chemistry are strongly intertwined in the area of small molecule reactivity. Synthetic complexes provide fundamental information regarding the interaction of substrates with transition metal ions, and spectroscopic models to aid in the determination of enzyme mechanisms [1,2].

Enzymatic studies, in turn, have revealed the importance of the wider protein environment in fine-tuning metal active site properties and in governing catalytic efficiency [3]. Consequently, catalyst development for small molecule reactions over the years has steered away from a focus on bio-mimetic complexes to the design of platforms that can capture key features of enzyme active sites beyond the first coordination sphere [4].

Among the most significant small molecule reactions in bioinorganic chemistry — involving H₂, O₂, N₂, and CO₂ — we have chosen to focus this review on recent developments in the design of CO₂ reduction catalysts based on earth-abundant first-row transition metals. The chemistry of CO₂ is of course consequential for the environment, and reduced forms of the molecule can serve as C1 building blocks for the synthesis of organic compounds [5]. In principle, various C1 products can be obtained from the reduction of CO₂ by up to 8 e[−] (whereby further reduction can even lead to C2+ products, such as ethylene or propanal) [6,7]. However, even the two-electron reduction of CO₂, which is the most common research target and which can generate either CO or formate, still presents significant challenges for molecular catalyst development. Contemporary strategies for catalyst design employ key bio-inspired features to enhance the reactivity toward the CO₂ reduction reaction (CO₂RR) [8–10].

In nature, CO and formate can be generated, often reversibly, by carbon monoxide dehydrogenases (CODHs) and formate dehydrogenases (FDHs) [11–13]. CODHs and FDHs are highly complex enzymes that rely on multiple metal ions for function. The active site of the metal-dependent FDHs consists of Mo or W coordinated by a pyranopterin cofactor. Reversible CO₂ reduction by the Ni₂Fe-CODHs occurs at a [NiFe₄S₃]-cluster, the so-called C-cluster [14]. (In contrast, Mo,Cu containing CODHs catalyze only the oxidation of CO to CO₂ [3] and thus are not discussed further herein.) While aspects of the enzyme mechanisms remain to be determined, numerous features are recognized to be essential to their activity and warrant consideration for molecular catalyst development. Both enzyme classes rely on Fe–S clusters to shuttle electrons toward or away from the active site. Amino acids near the metal active site of both enzymes engage in hydrogen bonding interactions and serve as proton relay

sites that are critical for substrate conversion, highlighting the importance of second-sphere interactions for catalysis. For example, formate proton abstraction is facilitated by a His residue adjacent to the Mo center of the Mo-FDHs, while hydrogen bonding interactions involving a selenocysteine further assist in this process. In the CODHs, the metal-bound CO₂ molecule and reduced intermediates are stabilized by hydrogen bonding to lysine and histidine residues in the vicinity of the C-cluster [15]. The CODHs also demonstrate the role of metal–metal cooperativity in CO₂ reduction. The asymmetric geometry of the C-cluster allows the redox-active Ni-center to act as a Lewis base towards the C-atom of the coordinated CO₂, while an Fe-atom plays the role of a Lewis acid and activates one of the O-atoms.

Researchers have recognized the importance of these features — electron transfer sites, second coordination sphere interactions, and metal–metal cooperativity — and sought to incorporate them within synthetic catalysts for the CO₂RR. Several excellent reviews have been written on this topic in recent years [9,10,16–20]. Thus, here, we focus on select current examples of CO₂ reduction catalysts that have advanced our understanding of how the above facets can contribute to catalytic efficiency. The first series of studies described herein convey a deeper understanding of the fundamental role of redox-active ligands in the intricate, multi-electron process of CO₂ reduction. It has long been acknowledged that redox-active ligands can generally be beneficial for catalysis, but their role in proton coupled electron transfer processes is not always straightforward [20]. Second coordination sphere manipulations in molecular catalysts have recently been at the focus of research in small molecule chemistry (*vide supra*), so we only note some of the latest studies that shed further light on this aspect. Finally, we present recent findings concerning bimetallic systems, as new binuclear platforms are continually emerging and reveal different approaches for activation of CO₂.

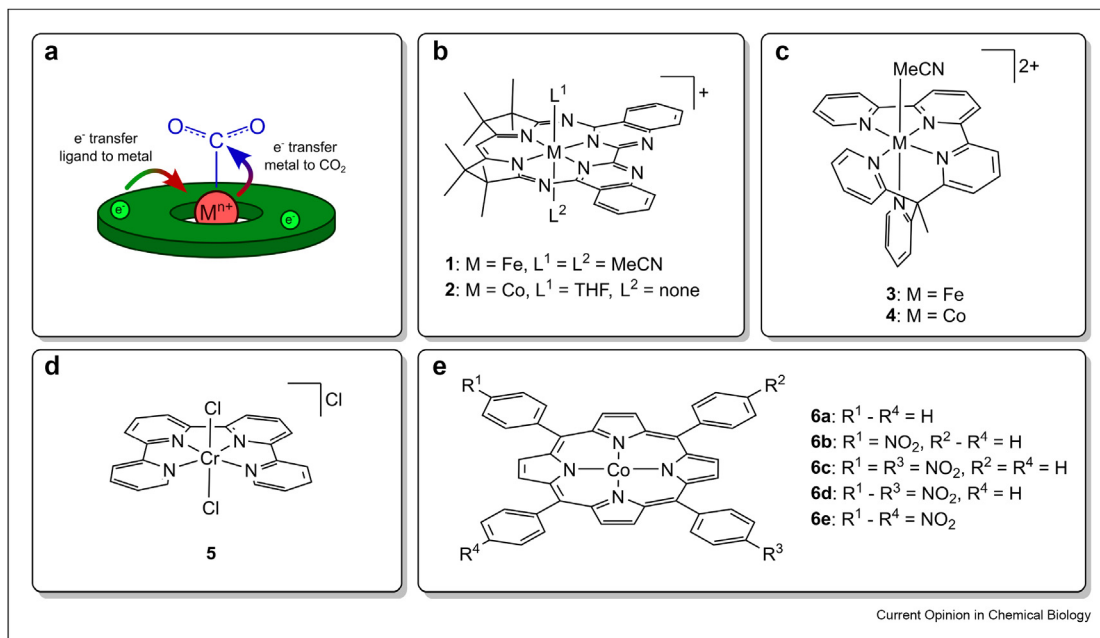
Redox-active ligands

The high activity of Ni,Fe-CODHs in CO₂ reduction is *inter alia* based on multiple Fe–S clusters that shuttle electrons to the C-cluster where CO₂ is activated. Such elaborate electron transfer chains are impractical to duplicate in molecular complexes. Their function, however, can be mimicked to some extent by redox-active ligands that can supply and store electrons in proximity of the metal centers. Redox-active ligands have proven beneficial in various chemical reactions ranging from small molecule activation to organic transformations [21,22]. The key aspects of redox-active ligands with respect to CO₂ reduction have been reviewed elsewhere and therefore will only shortly be summarized here [20]. The ability to reduce the ligand instead of accumulating electrons on the

metal center reduces the Lewis basicity of the metal. Therefore, the formation of a metal hydride is impeded, which also curtails the hydrogen evolution reaction (HER), a common side reaction to CO₂ reduction. Insertion of CO₂ into the metal-hydride bond is believed to be the main pathway to formate production [23], which is consequently also disfavored by redox-active ligands [20]. The use of redox-active ligands thus provides a strategy to achieve high selectivity towards CO. Beyond that, ligand-centered reductions can facilitate the accumulation of negative charge and thereby reduce the overpotential requirement for CO₂ reduction. This effect, however, often correlates with a decreased catalytic activity. Considering these general findings, we focus on recent studies that have expanded our knowledge of the role of redox active ligands in the CO₂RR.

Neese and co-workers recently investigated the CO₂RR for eleven different catalysts containing redox-active ligands using computational methods [28]. Across the diverse series of compounds — with ligands such as TPP and different polypyridines and metals in the first (Cr – Co), second (Ru) and third row (Re) — they identified key common features that underpin their catalytic activity. Apart from inhibiting the production of formate and H₂ as described above, redox-active ligands confer increased stability to the catalyst. Storing the electrons in delocalized, low-energy ligand orbitals precludes formation of reduced intermediates with electron-rich metal centers. This in turn disfavors catalyst deactivation by, e.g., nanoparticle formation or electrode deposition [25,28]. For most complexes, the formal ‘M⁰’ form reacts with CO₂ [28]. However, since the electrons stored in the ligand system are delocalized over an extended π -system, only the metal center can directly coordinate and activate CO₂ *via* orbitals of appropriate symmetry — e.g., the doubly occupied d₂₂ in the formally Fe⁰ form of Fe-tetraphenylporphyrin [Fe^{II}(TPP^{••})]²⁻. Upon coordination and subsequent electron transfer from the metal center to the bound CO₂, a synchronized electron transfer from the ligand to the metal ensures a virtually unchanged electron density at the metal center (Scheme 1a). Keeping the oxidation and spin state of the metal constant throughout the reaction avoids reorganization of the first coordination sphere and the resulting high kinetic barriers. To this end, the orbitals of the metal center and of the redox-active ligand must be well matched in energy and symmetry. The atoms directly coordinated to the metal ion need to mediate electron transfer *via* p-orbitals comprised in the ligand π -system, qualifying, e.g., conjugated N-donors (e.g., imines, porphyrins) or carbenes. Electron transfer is additionally favored by the more diffuse d-orbitals of heavier metals compared to the compact d-orbitals of first-row transition metals.

Scheme 1



a: Schematic representation of the synchronized electron transfer from the reduced ligand to the metal center and from the metal center to the CO₂ ligand; **b-e:** Select examples of CO₂RR catalysts with redox-active ligands [24–27].

The above-described theoretical findings have recently been validated experimentally by studies with various CO₂ reduction catalysts. We recently compared the electrocatalytic CO₂RR by Fe- and Co-complexes (Scheme 1b, **1** and **2**) containing the redox-active Mabiq ligand [24]. The one- and two-electron reductions of these M^{II}-Mabiq complexes are both ligand centered; the metal maintains its +2 oxidation state. Both the Fe and Co complexes selectively generate CO. The high selectivity stems from the Mabiq-centered reduction, which disfavors metal hydride formation. However, the Fe complex has an ~600 mV lower overpotential requirement and operates with a higher Faradaic Efficiency (FE) compared to its Co analog (96 % vs. 60 %). We found these differences to be based on the differing electronic structures. Only the doubly reduced [Fe^{II}(Mabiq^{••})]⁻ possesses a low-lying d₂₂ orbital for CO₂ binding. The electronic structure of this catalytically active species resembles that of the doubly reduced form of Fe^{II}-TPP examined by Neese, described above — except that [Fe^{II}(Mabiq^{••})]⁻ is a triplet species, whereas [Fe^{II}(TPP^{••})]²⁻ has an S = 0 ground state. The Mabiq system is further unique, in that reduction of the ligand leads to protonation of a carbon atom at the diketiminate unit. We hypothesized that the protonated ligand can stabilize CO₂ adducts and act as a proton relay, thereby further enhancing the catalytic performance. The catalytic performance of the Mabiq system is thus benefited by the ‘non-innocence’ of the ligand in several ways.

Similar to our work, the Chang group compared Fe- and Co-complexes based on the redox-active pentadentate polypyridyl ligand tpyPY2Me (Scheme 1c, **3** and **4**) [25]. The one- and two-electron reductions of the ferrous **3** likewise are ligand-centered [29]. Conversely, the first reduction of the Co-containing **4** is metal-centered, triggering HER as a side reaction and thereby reducing the selectivity towards CO to 83 % [25]. Once again, the doubly-reduced forms of **3** and **4** [Fe(tpyPY2Me^{••})] and [Co(tpyPY2Me^{••})], both are described as M²⁺ centers coordinated to a ligand biradical. However, the Co complex is more weakly stabilized by metal–ligand exchange coupling. Therefore, catalyst decomposition occurs for **4** under catalytic conditions, while **3** exhibits high stability and activity in the CO₂RR. In fact, **3** is one of the most active CO₂ reduction catalysts reported to date. Metal–ligand exchange coupling is a critical factor to consider in the design of CO₂ reduction catalysts.

The Cr-quaterpyridine (qpy) complex (Scheme 1d, **5**) illustrates the Neese group’s finding that electron transfer from the ligand to the metal is crucial for high CO₂RR activity [26]. The qpy ligand contains 4 N-donors, while previously reported Cr-based catalysts consisted of N₂O₂- or N₃O-donors based on phenanthroline, bi- or terpyridine ligands containing phenolates [30–32]. The greater number of N-donors increases the electronic coupling between the ligand π-system and the metal center, thereby stabilizing reduced forms of

the compounds and lowering the overpotential requirement [26,28,30]. Indeed, **5** operates at a 200 mV smaller overpotential with an almost 10-fold increase in turnover frequency (TOF) compared to the most active Cr catalyst so far based on an N₂O₂ bipyridyl-ligand [26,32].

Finally, a recent study of the Zhang group showed that the catalytic activity of Co-TPP complexes can be increased by increasing the number of electrons stored in the ligand. This was accomplished by functionalizing the porphyrin ring with nitrophenyl groups (Scheme 1e, **6a-e**) [27]. The researchers examined the effect of these groups on the reductive disproportionation of CO₂ to carbonate and CO, which occurs in the absence of a proton source. By implementing one nitro-group in the TPP scaffold of **6b**, the two-electron reduction of the cobaltous complex to yield a [Co^I(L•)]²⁻ species is shifted to more positive values by >800 mV compared to the parent Co-TPP (**6a**). The reduction no longer occurs at the porphyrin core but on the nitrophenyl moiety. The redox potentials of the ligand-centered reduction remain unchanged with the addition of further nitro-groups to the porphyrin, however, the number of electrons taken up by the ligand increases from one (**6b**) to four (**6e**). For all complexes, CO₂ activation is triggered by reduction of the ligand, resulting in a more than 800 mV smaller overpotential requirement of **6b-e** compared to **6a**. The measured TOFs clearly correlate with the number of nitro-groups of the complexes, i.e., the number of electron storage sites, and **6e** is 27 times more active than **6b**. Although the electrons are stored in the ligand periphery, efficient electron transfer to CO₂ occurs. We envision that strategies such as this may allow greater versatility in tailoring ligand properties and prove particularly useful for generating further reduced CO₂ derivatives.

Modification of the second coordination sphere

Second-sphere interactions are key to the catalytic efficiency of enzyme active sites and likewise have proven to enhance the performance of molecular CO₂ reduction catalysts. Functional groups incorporated within the ligand periphery for this purpose can affect reactivity in multiple ways (Scheme 2a and b) [9,17,39]. First, such 'second-sphere groups' can stabilize the M–CO₂ adducts and thereby increase the binding constant of CO₂. This is realized by hydrogen bonding and electrostatic through-space interactions, as both can stabilize the (partial) negative charge on the O-atoms of the coordinated CO₂. Positively charged groups and H-bonds can further aid C–O bond cleavage by exerting a 'pull effect' on the O-atom.

Second-sphere groups capable of donating hydrogen bonds also can accelerate the protonation of intermediates [9,17,39]. They can act as a pre-positioned

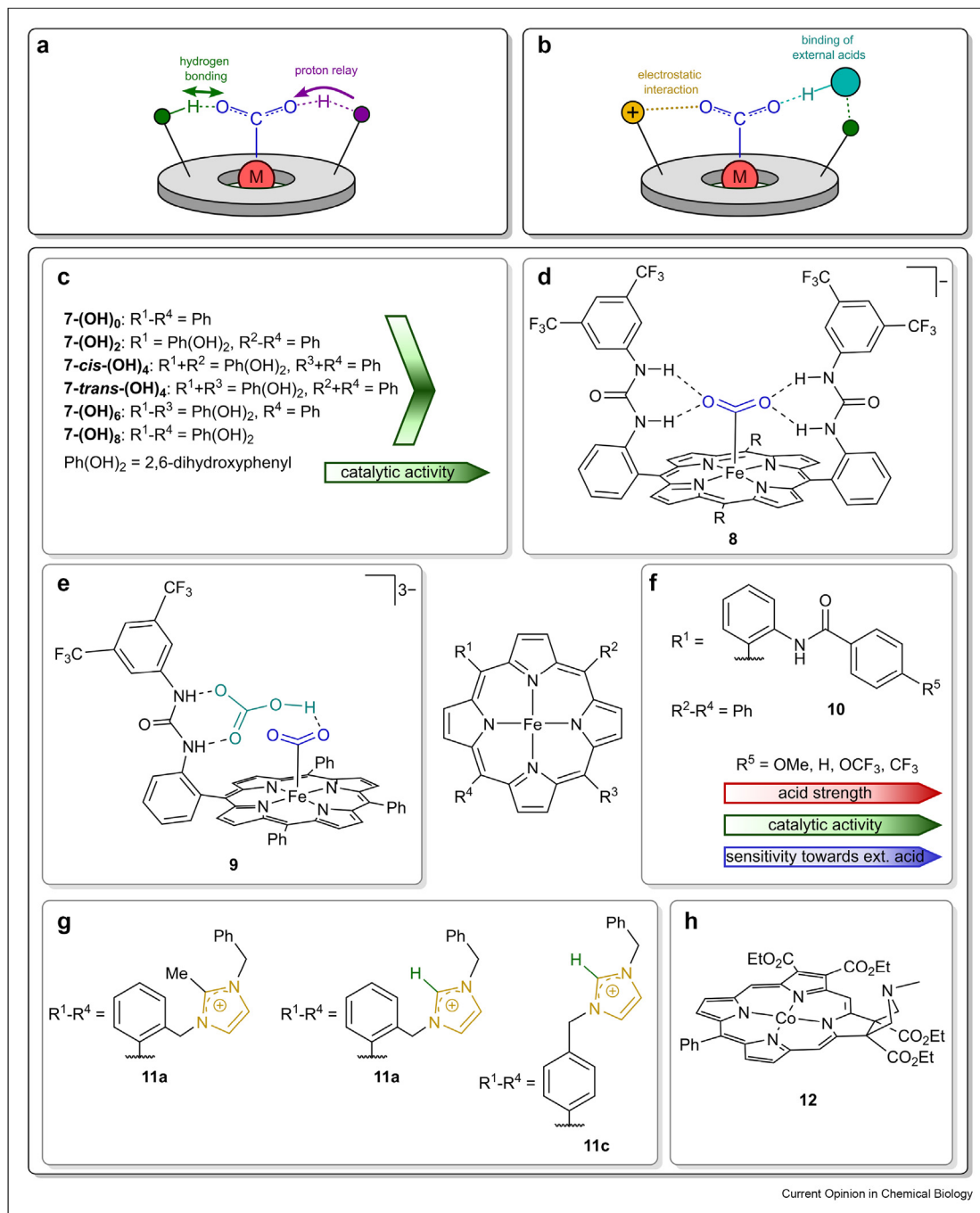
proton donor, which necessitates re-protonation of these groups by the external acid source. Alternatively, such functionalities can interact with the external acid, effectively increasing its local concentration.

Second-sphere groups can also be harnessed to direct the selectivity of the CO₂RR [16,17]. After coordination of CO₂ to the metal center, the selectivity is directed either towards formate production by C-protonation or toward CO formation by O-protonation. The latter process generally is favored by hydrogen bonding to or proton transfer from pendant groups. Formation of a metal hydride — a key intermediate both for formate and H₂ production [23] — can be impeded by making the second-sphere functionality the preferred target for protonation. The resulting acidic, positively charged groups increase the CO₂ affinity of the complex and aid O-protonation (*vide supra*) to yield CO.

Despite the fundamental understanding of second coordination sphere effects, various aspects concerning their role in catalysis remain unclear, with some findings seemingly contradictory. Thus, several recent studies have examined specific facets in greater detail, e.g., the number, orientation, and acidity of pendant groups. Researchers also have combined differing functionalities in a single complex to understand their relative contributions and interplay. In the following section, we present select studies that exemplify the latest findings in this area.

Many of the studies pertaining to the effects of outer sphere interactions on catalytic CO₂ reduction have focused on Fe-porphyrin complexes. The influence of acidic groups within the ligand framework in particular has been the subject of extensive studies [40,41]. The introduction of one phenol group in the ligand periphery of TPP already leads to a drastic increase in catalytic activity [42]. Even higher catalytic activity could be achieved by introducing eight phenolic groups within the scaffold (Scheme 2c, **7-(OH)₈**) [40]. Yet, the activity of Fe-TPP complexes as a function of increasing number of hydroxy groups (Scheme 2c, **7-(OH)_n** with n = 0, 2, 4, 6, 8) has only recently been studied [33]. The **7-(OH)_n** Fe-TPP series also allowed for study of structural effects, i.e., comparison of **7-cis-(OH)₄** vs. **7-trans-(OH)₄**. Among the compounds, **7-trans-(OH)₄** is the most active CO₂RR catalyst in the presence of PhOH as an external proton source. DFT computational studies revealed that **7-(OH)₀** cannot engage in hydrogen bonding, whereas **7-(OH)₂** and **7-cis-(OH)₄** can stabilize the CO₂ ligand with one hydrogen bond. The complexes with two opposing dihydroxyphenyl substituents (**7-trans-(OH)₄**, **7-(OH)₆**, and **7-(OH)₈**) can engage in two hydrogen bonds to the CO₂ ligand, thus further activating the bound substrate. Two adjacent dihydroxyphenyl groups cannot simultaneously

Scheme 2



a-b: Schematic representation of different ways pendant functional groups can influence CO₂ reduction; **c-h**: Select examples of CO₂RR catalysts with pendant functional groups [33–38]. Complex **8** consists of four identical urea groups, but only two are depicted for clarity, i.e., R = urea functionalized phenyl.

engage in hydrogen bonding for steric reasons. However, intramolecular proton transfer by the adjacent, non-interacting OH group then predominates in the **7-*cis*-(OH)₄**, **7-(OH)₆**, **7-(OH)₈** series. The beneficial H-bonding effect of two opposing dihydroxyphenyl groups dominates catalysis in the presence of phenol, while

intramolecular proton transfer becomes significant in the absence of added proton source. Irrespective of the *cis* or *trans* orientation, increasing the number of hydroxy groups alters the electronic structure of the complexes — as evidenced by their UV/vis spectra, formal Fe^{I/0} redox potentials, and calculated Fe–C bond

strengths — such that a decrease in catalytic activity is observed for **7-(OH)₆**, and **7-(OH)₈** compared to **7-trans-(OH)₄**.

The above findings provide a precautionary example that second coordination sphere modification requires careful consideration of potentially competing effects. The reaction conditions (solvent, amount and type of external acid, etc.) require special attention with respect to their impact on proton transfer and hydrogen bonding. Indeed, the incorporation of functional groups meant to provide ‘beneficial’ hydrogen bonding interactions can influence not only the electronic structure of the complexes but can detrimentally influence the sterics around the metal center [43,44]. Overcrowding of the active site can impede the CO₂RR activity and favor an unwanted HER.

Urea groups have also been utilized to stabilize the CO₂-adducts of Fe-TPP complexes through hydrogen bonding interactions. The two urea moieties in UrFe support a quadruple hydrogen bond to the CO₂ ligand (Scheme 2d, **8**) [34]. Notably, in this case, these interactions significantly alter the Fe-TPP CO₂ reduction mechanism, allowing for coordination of CO₂ to the formal Fe^I form rather than to the more electron-rich formal Fe⁰ species. Consequently, an [Fe^{III}-COO]⁻ species is generated, which upon protonation, is readily reduced to [Fe^{II}-COOH]⁻, finally yielding Fe^{II}-CO after transfer of another proton and consequent water formation. The overall result is a lower overpotential requirement for the CO₂RR.

For CO₂ reduction in aqueous solution, the importance of the equilibria between CO₂, carbonic acid, bicarbonate, and carbonate has been recognized; the bicarbonate can act as a proton source. Urea groups are known for their high affinity towards bicarbonate, which inspired the Chang group to investigate Fe-TPP-*ortho*-urea [35]. Indeed, the urea moiety in this compound proved highly effective in capturing bicarbonate through the two H-bonding interactions (Scheme 2e, **9**). Consequently, the acidity of the bound bicarbonate is increased, and the proton source and metal-bound CO₂ are held in proximity to each other. This dual function of the urea leads to a 1500-fold increase in catalytic activity of Fe-TPP-*ortho*-urea compared to the parent Fe-TPP. Yet, the role of bicarbonate is complex, since it can also act as a competing ligand to the metal center, impeding catalytic CO₂ reduction [45]. Further studies would aid our understanding of the differing effects, beneficial or inhibitory, of bicarbonate.

Earlier studies mainly focused on comparing catalysts in the presence or absence of pendent acidic groups. The effect of acid strength of internal proton donors has only recently been evaluated in detail [36,46]. Nichols and co-workers examined amide-functionalized Fe-TPP

complexes (Scheme 2f, **10**) and varied their acidity by implementing electron donating or withdrawing groups in the vicinity (R⁵ in Scheme 2f) [36]. The influence of these groups on the electronic structure of the complexes was negligible, such that the observed effects on catalysis could be correlated to the p*K*_a of the internal proton source. The authors also investigated the influence of the acid strength of external proton sources using phenol derivatives with varying p*K*_as. The complexes containing amides with lower p*K*_a values exhibited higher CO₂RR activities. The same trend was observed for the series of external proton sources. Furthermore, complexes with lower p*K*_a values were more sensitive towards the acidity of the external proton source. The Nichols group’s findings suggest that incorporation of more acidic functionalities should favor catalyst performance. However, opposite trends have been observed in the CO₂RR using compounds containing other types of H-bonding functionalities [46]. Though the reason for the discrepancies remains unclear, as already noted, pendant acidic functionalities can influence catalysis in multiple ways (*vide supra*). Further studies are clearly still needed to disentangle the assorted roles that different functional groups can play under various conditions.

A number of research groups have shown that the introduction of charged groups can drastically influence the catalytic activity [47–50]. While positive charges in the ligand periphery can stabilize coordinated CO₂ and increase the catalytic rates, negative charges are detrimental in that they destabilize this catalytic intermediate. For example, the Fe-TPP derivative with four *ortho*-tetramethylanilinium groups (Fe-*o*-TMA) operates at low overpotential requirements and selectively yields CO with an unprecedented TOF in electrocatalytic CO₂ reduction of up to 10⁶ s⁻¹ [47].

Going beyond the investigation of isolated charge effects, the Chang group recently examined the combination of hydrogen bonding and through-space charge effects using Fe-TPP complexes modified with imidazolium units in the second coordination sphere (Scheme 2g, **11a-c**) [37]. Complex **11a** with a methylated imidazolium moiety is limited to electrostatic effects, while **11b** and **11c** additionally feature a proton for hydrogen bonding. The orientation of the imidazolium units again seems crucial, as **11c** shows low catalytic activity as well as limited stability and selectivity (FE < 30 % in acetonitrile). In contrast, complexes **11a** and **11b** show high selectivity towards CO formation (FE ≈ 100 %) since the imidazolium units are directed toward the Fe-center. The measured TOF of **11b** represents a 14,000-fold increase compared to **11c** and 2000-fold compared to the parent Fe-TPP. Compared to **11a**, the increase in TOF is much smaller (40-fold). The hydrogen bonding ability of **11b** also results in a larger CO₂ binding constant compared to **11a** (5-fold) and **11c**

(20-fold). Through-space charge effects apparently constitute the major contributor to enhanced reactivity, though synergistic hydrogen bonding effects further benefit the reaction.

The Fe complex coordinated by the macrocyclic chlorin ligand, with a pendant amine close to the active site (Scheme 2h, **12**), can selectively catalyze the reduction of CO₂ to formate [38]. The Dey group found that the protonation of the pendant amine allows the coordination of CO₂ to the formal Fe^I complex. Similar to the Fe-TPP derivative **8**, the activation of CO₂ in the formal Fe^I state reduces the overpotential requirements and allows for high TOFs in CO₂ reduction. However, the two complexes differ in that **8** selectively yields CO while the Fe-chlorin complex **12** selectively gives formate. The CO₂ reduction of **12** does not involve metal-hydride formation but proceeds *via* Fe^{III}-COOH and Fe^{II}-COOH intermediates, just as found for **8**. This implies that C-protonation to yield formate occurs rather than the more common O-protonation that would yield CO. The reason for the disparate selectivity of **12** is intriguing and warrants further investigation.

A recent study by the Dey group also demonstrated that an Fe-TPP derivative with a pendant pyridine moiety was capable of reducing CO to methane selectively [51]. The pyridine stabilizes the Fe-CO adduct, allowing for further reduction. This behavior contrasts with that of other Fe-TPP complexes, where fast CO dissociation generally prevents further reduction. Although the reduction of CO₂ with this complex was not reported, the work showcases that second-sphere groups may have the potential to allow CO₂ reductions beyond CO and formate.

Bimetallic activation of CO₂

The synergistic activation of CO₂ at two metal centers partly accounts for the high activity of Ni,Fe-CODH. The cooperative push-pull activation of CO₂ by the Lewis basic Ni in combination with the Lewis acidic Fe facilitates CO₂ binding and accelerates C-O bond cleavage (Scheme 3a) [15,18]. Several synthetic compounds, both homo- and heterobimetallic, have been shown to activate CO₂ *via* this mechanism and show increased catalytic activity versus monometallic analogs [19]. Whereby heterobimetallic and unsymmetric compounds allow for more tailored Lewis acidities. The positioning of the two metal centers in close proximity is essential for their joint reactivity. Another type of bimetallic cooperativity that has been observed in synthetic systems is the so-called tandem mechanism, in which a reaction intermediate (e.g., a hydride, CO₂^{-•} or CO) is transferred from one metal center to another (Scheme 3b). The tandem mechanism in particular has

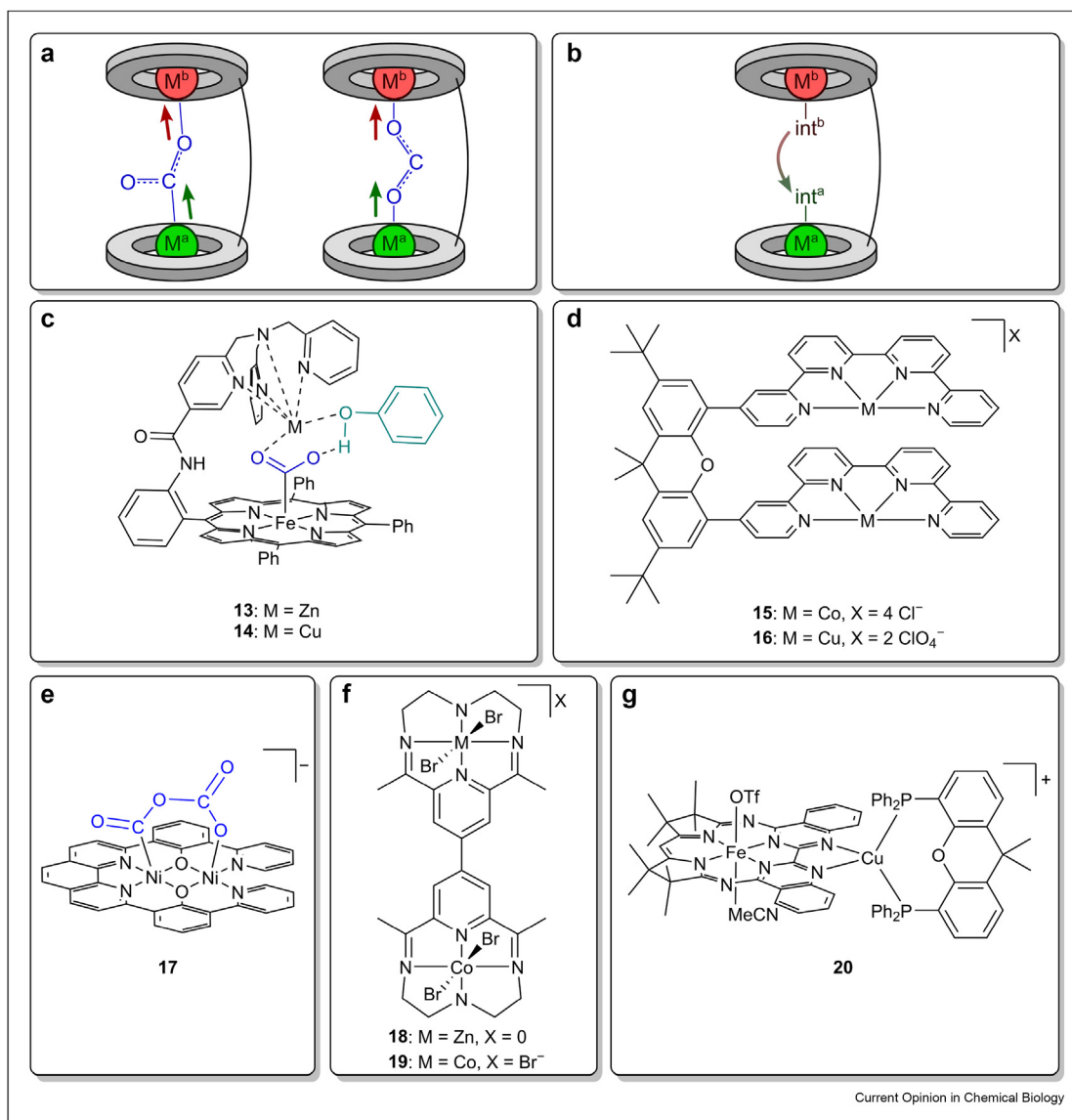
the potential to yield C₁ and C₂ products reduced beyond 2 e⁻.

An excellent and comprehensive review has recently been written on this topic, detailing our current understanding of the different ways that metal-metal cooperativity can be harnessed for CO₂ reduction [19]. Therefore, we herein highlight only select examples that have been reported over the past year, including complexes where the neighboring metals play an alternate role than described above.

Heterobimetallic complexes based on Fe-TPP linked to a metal-tripyrildamine (TPA) moiety (Scheme 3c, M-TPA-Fe-TPP; M = Zn: **13**, M = Cu: **14**, depicted with coordinated CO₂ and phenol) possess unique features that can facilitate the CO₂RR, and illustrate the benefits of the push-pull mechanism outlined above [54]. Both bimetallic Fe/Zn and Fe/Cu complexes show a significant increase in TOF and decreased overpotential requirement for electro- and photocatalytic CO₂ reduction compared to the monometallic Fe-TPP. The TPA moiety of TPA-Fe-TPP led to an increase in the catalytic activity even in the absence of the TPA-bound metal. This was ascribed to hydrogen bonding between the protonated TPA and CO₂. The role of the Zn ion in the bimetallic Zn-TPA-Fe-TPP was further investigated by DFT computational studies. The coordination of CO₂ to the complex, the rate-determining step with Fe-TPP, is strongly favored by the additional coordination of the Lewis acidic Zn²⁺ to the substrate. The neighboring metal also can bind to the proton source (phenol), thereby significantly lowering the activation barrier of the first proton transfer to CO₂ (Scheme 3c). Thus, the Zn serves a role other than a cooperative Lewis acid, and aids in substrate delivery. The unsymmetric TPA/TPP framework offers the potential to investigate other metal ion combinations, as well as to introduce additional second-sphere functionalities.

M₂-bis-quaterpyridine (biqpy) complexes are noteworthy catalyst examples, since CO₂ reduction can proceed by differing mechanisms dependent on reaction conditions or metal centers. The Co₂-biqpy complex (Scheme 3d, **15**) [52] activates CO₂ in a sandwich-type fashion between the two Co centers; this step is followed by either O-protonation to yield CO, or C-protonation to generate formate. The selective formation of CO occurs under acidic conditions, while formate production is favored by basic conditions. Formate also is predominantly generated (60 %) in the photocatalytic CO₂RR by the related bimetallic Cu₂-biqpy complex (Scheme 3d, **16**) alongside smaller amounts of CO and H₂ [53]. However, formate production proceeds *via* a different reaction mechanism than for **15**. The two-electron reduced dicopper

Scheme 3



Schematic representation of the bimetallic activation of CO_2 via **a**: push-pull mechanism, **b**: tandem mechanism ($int = H^-, CO_2^-, CO, \dots$) [19]. **c-g**: Select examples of bimetallic CO_2 reduction catalysts [52–57].

complex, described as $[Cu^0Cu^I(biqpy^\bullet)]$, can form a $Cu_2(\mu-H)$ species. Formate is produced upon binding of CO_2 to this bimetallic hydride species. The small amounts of H_2 produced in the reaction stem from the protonation of $Cu_2(\mu-H)$. CO formation proceeds *via* a pathway involving direct coordination of CO_2 to the Cu centers and without metal-hydride formation. The monometallic analog $Cu(qpy)$ was found to form CO selectively [58]. The results are consistent with previous findings in studies with monometallic compounds, showing that formate production entails the formation of $M-H$ intermediates. The M_2 - $biqpy$ compounds

demonstrate alternate, binuclear pathways for formate formation and suggest strategies to steer product selectivity toward CO or formate.

A recent study by Zhang and co-workers investigated the bimetallic $Ni_2(bphpp)(OAc)_2$ complex (Scheme 3e, 17, depicted with two CO_2 molecules coordinated) with two Ni centers and a redox-active phenanthroline moiety [55]. The complex illustrates push-pull and redox cooperativity by the metal centers, as well as the importance of structural features. The complex catalyzes the reductive disproportionation of CO_2 to CO and

carbonate without the requirement of an added proton source. Three-electron reduction yields a $[\text{Ni}^{\text{I}}\text{Ni}^{\text{I}}(\text{bphpp})]^-$ species, in which both the Ni ions and ligand are reduced. After C-coordination of CO₂ to the primary Ni center, another CO₂ molecule binds to the adjacent Ni center *via* its O-atom to give a cyclic Ni₂(CO₂)₂ intermediate (Scheme 3e, 17). The Lewis acidity of the neighboring Ni center facilitates the C–O bond cleavage, yielding CO and carbonate as products. Comparison with a monometallic analog reveals the additional roles of the second Ni center. It serves as an electron storage site, alongside the phenanthroline moiety, thereby reducing the overpotential requirements. The arrangement of the two metal ions also allows for formation of the cyclic bis-CO₂ intermediate, which reduces key transition state energies.

The varying ways in which two metals can promote reactivity is further highlighted by a recent study comparing the bimetallic pyridylidimine (PDI) based complexes [Co(PDI)-(PDI)Co] and [Zn(PDI)-(PDI)Co] (Scheme 3f, 18 and 19) with the monometallic [Co(PDI)] [57]. The planar geometry of the PDI ligand and the distance between the two metal centers do not allow for synergistic activation of CO₂, yet increased TOFs and decreased overpotential requirements were observed for the bimetallic complexes. Both the homo- and the heterobimetallic complexes selectively form CO, but the Co/Zn compound displayed the highest TOFs. The electrostatic effect of the second metal center represents the major contribution to the increased CO₂RR activity. The redox inactive Zn²⁺ cation bestows a larger electrostatic effect than the Co⁺ cation generated under catalytic conditions in the dicobalt complex. This study again underscores the fundamental ways that an adjacent metal center can modulate the properties of the active site. The authors note that similar strategies to exploit electrostatic interactions could also prove useful in “multidimensional catalyst architectures (e.g., COFs, MOFs, etc.)” [57].

Our group has been investigating bimetallic complexes of the Mabiq ligand (*vide supra*), e.g., complex 20 with a Cu(xantphos) moiety coordinated to an Fe-Mabiq core (Scheme 3g) [56]. The bimetallic complex illustrates how a second metal center can enhance catalysis by modulating redox and photochemical properties of a complex. The neighboring Cu center of CuFe-Mabiq alters the redox potentials for reduction of the Mabiq ligand, as well as the mechanism of CO₂ reduction by the Fe-Mabiq unit. Notably, the ligand-protonation pathway established for the monometallic 2 is not accessible for the bimetallic 20. Both 1 and 20 can photocatalytically reduce CO₂ in the presence of [Ru(bpy)₃]²⁺ as a photosensitizer, with comparable activities. However, only the bimetallic 20 is photocatalytically active when the Ru photosensitizer is omitted, suggesting that the Cu(xantphos)

moiety may be taking over this role. There are few examples of self-sensitized CO₂ photocatalysts [59]. The CuFe-Mabiq complex further highlights the varying roles that a second metal can assume. This includes tuning of redox properties and promotion of different reaction pathways. But the combination of a photosensitizer and a catalyst within a single molecule has distinct advantages and particularly warrants further exploration.

The bimetallic complexes mentioned above exemplify the myriad ways in which a second metal center can enhance catalysis, tune reaction mechanisms, alter selectivity, reduce overpotentials and even facilitate photocatalysis. Many of the abovementioned catalysts contain a redox active ligand, and thus further feature advantages of this ligand class. However, the combination of bimetallic CO₂ activation and second sphere effects remains underexplored, despite the fundamental importance of such interactions in the unprecedented activity of Ni,Fe-CODHs.

Outlook

The complexity of ligand systems, with incorporation of the above-described functionalities, has led to substantial improvements in the performance of synthetic CO₂ reduction catalysts and a greater understanding of how they direct reactivity. Redox-active ligands help circumvent M–H pathways, thus favoring CO formation. The nature of the metal bound to the redox-active ligand is consequent — for the Mabiq and tpyPY2Me complexes, the Fe complexes outperform the Co analogs. In addition to their function as electron reservoirs, the reduced, π -conjugated ligands in these complexes can be prone to protonation [20]. Ligand protonation can yield productive intermediates as well as lead to inefficient pathways in the HER, depending on the protonation site [60]. The impact of proton transfer to differing redox-active ligands on the CO₂RR remains unclear. Placement of electron storage sites in the periphery, as in the nitrophenyl functionalized TPP compounds, may confer similar advantages while avoiding such pitfalls.

Through the many years of enzyme studies and the bioinspired molecular systems that have emerged, we have developed a good understanding of second coordination sphere features. The manifold second-sphere interactions in the active site underpin enzyme catalysis. However, the implementation of pendent groups that exert multiple effects is synthetically challenging. Moreover, many functionalities can perform dual roles and alter metal site properties in ways other than intended. Several complexes have been designed with the purpose of disentangling these effects — particularly to provide an understanding of which steps in the catalytic cycle are impacted, to what extent specific

interactions contribute to the overall performance, and under which conditions. But as illustrated by the recent work discussed herein, further detailed studies are still critically needed.

Bimetallic complexes, in our view, hold the most promise. Homobimetallic complexes represent the majority of the catalysts studied so far still. But as noted above, even in such systems, there are some unique intermediates that hint at new approaches for CO₂RR, as well as interesting findings regarding factors that lead to switching of selectivity. Most enzymes, including CODHs and FDHs, use a combination of different metals, in different environments and with different functions. Heterobimetallic complexes, and those based on unsymmetric ligand scaffolds, are therefore even more attractive. The properties of each metal and metal–ligand interactions at each site can be more readily tuned. The metal centers of heterobinuclear compounds can also adopt diverse roles, but so far, most compounds activate CO₂ by the push–pull mode. Strategies to activate distinct intermediates at two metal centers in a tandem mechanism could yield CO₂ derivatives beyond CO and formate. Within homo- and heterobimetallic systems, additional second-sphere interactions can still be incorporated to further tailor catalytic properties. We look forward to seeing the new developments that will arise in this rapidly moving area of research.

Finally, we note that most catalysts to date seem to favor CO formation — and both redox-active ligands and second-sphere interactions assist this pathway. Formate production still appears to present a greater challenge for catalyst design, not to mention the formation of further reduced CO₂ products. Though aspects of CO formation certainly warrant further studies, intensive efforts should now be directed toward catalyst design for these other reactions.

Funding

Funding is provided by the Deutsch Forschungsgemeinschaft, project number 507868493.

Declaration of competing interest

The authors declare no conflict of interest.

Data availability

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

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