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Converting between the oxides of nitrogen using metal-ligand coordination complexes

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Converting Between the Oxides of Nitrogen Using Metal-Ligand Coordination Complexes

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The oxides of nitrogen (chiefly NO, NO_3^-, NO_2^- and N_2O) are key components of the natural nitrogen cycle and are intermediates in a range of processes of enormous biological, environmental and industrial importance. Nature has evolved numerous enzymes which handle the conversion of these oxides to/from other small nitrogen-containing species and there also exist a number of heterogeneous catalysts that can mediate similar reactions. In the chemical space between these two extremes exist metal-ligand coordination complexes that are easier to interrogate than heterogeneous systems and simpler in structure than enzymes. In this tutorial review, we will examine catalysts for the inter-conversions of the various nitrogen oxides that are based on such complexes, looking in particular at more recent examples that take inspiration from the natural systems.

Key Learning Points

1. The key role of nitrogen oxides (especially nitrite) in the nitrogen cycle.
2. The coordination chemistry in the active sites of the various nitrogen oxide reductase enzymes.
3. How nitrite binds to, and is reduced at, metal ligand coordination complexes.
4. The various platforms that have been used for NO reduction.
5. Nitrate reduction with metal ligand coordination complexes.

1. Introduction

Nitrogen is present in most of the building blocks of life and can be found in almost every major product of the chemical and pharmaceutical industries. It can exist in a number of oxidation states in various compounds (from +5 in nitrate to −3 in ammonia), but N_2 itself is extremely inert on account of its strong N≡N triple bond. It must therefore be "fixed" prior to incorporation into larger molecules. The most prevalent route of fixation is *via* conversion of N_2 to ammonia, which is achieved industrially through the Haber Bosch process. The analogous transformation in natural systems (N_2 reduction to ammonium using nitrogenase) is also a major contributor to total global nitrogen fixation.[1]

Regardless of how N_2 is fixed, there is a constant flux of nitrogen from one oxidation state to another mediated by a range of natural systems: this is the *nitrogen cycle* (Fig. 1). Inspection of Fig. 1 reveals the critical importance of the oxides of nitrogen and their inter-conversions in the nitrogen cycle. The delicate balance maintained by these competing processes is readily disturbed by anthropogenic nitrogen-cycle activity, such as excessive use of nitrate fertilisers. As shown in Fig. 1, nitrite stands out as the common intermediate in a number of nitrogen conversion reactions of major importance, and it can thus be viewed as the key to catalysis in the nitrogen cycle.[1] Fig. 1 also gives examples of some of the enzymes responsible for catalysing the transformation of nitrogen from one oxidation state to another. These enzymes contain transition metal coordination complexes in their active sites, the structures of many of which have been elucidated. In the following section, we will examine the structures of some of these enzymes and what is known of their mechanisms of action.

To the best of our knowledge, there has been no comprehensive review of metal-ligand coordination complexes for the catalytic interconversion of the nitrogen oxides since Karlin's review in 2002.[2] The aim of this review is therefore to provide an introduction to this fascinating field post-2002 that will give the interested reader an idea of the current state-of-the-art. Furthermore, we shall restrict ourselves as far as possible to a discussion of functional systems able to mediate conversions of the nitrogen oxides, rather than those systems that merely bind these oxides. Finally, this review will address only small, artificial metal-ligand coordination complexes for the nitrogen oxide transformations summarised by Fig. 1. Readers interested in heterogeneous catalysts and electrocatalysts are directed to an excellent review by Koper on this subject.[3]

2. Natural Systems for the Inter-conversions of the Nitrogen Oxides

N_2 enters the nitrogen cycle not only through the fixation of N_2 to ammonia but also in the form of nitrate and nitrite from mineral sources and physical events such as lightning strikes. Biological systems are then able to convert between the various

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oxidation states of nitrogen with high specificity using a handful of generic classes of enzymes, effectively allowing any oxidation state of nitrogen to be accessed. Where a single enzyme cannot carry out the desired transformation, sequences of enzymes are used.[1] For example, nitrate conversion to ammonia can be achieved through a combination of molybdenum-dependent nitrate reductases (reducing nitrate to nitrite) and sirohaem-containing nitrite reductases (reducing nitrite to ammonia). All the enzymes featured in Fig. 1 contain metal-ligand coordination complexes in their active sites. In this section, we will examine the structures of these active sites, which lend such obvious inspiration to many of the metal-ligand complexes that we shall explore in this review.
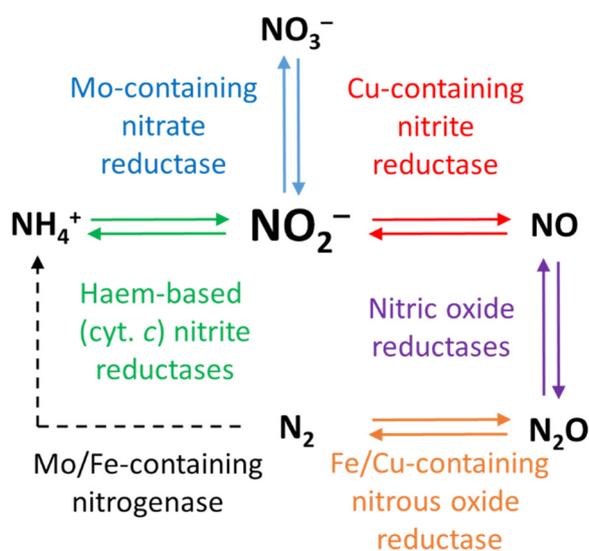

Fig. 1 Overview of the nitrogen cycle, showing the prominent positions occupied by the nitrogen oxides (especially nitrite). Examples of some of the enzymes involved are given (more details on these can be found later in the text). All the reaction pathways shown with bold arrows will be addressed in this review. Processes shown by dashed arrows are not reviewed herein.

2.1 Nitrite reduction to ammonium with haem-based nitrite reductases

The 6-electron reduction of nitrite to ammonia is catalysed by a number of nitrite reductases that use haems as their active centres. The general equation for this reaction is:

$$NO_2^- + 6e^- + 8H^+ \rightarrow NH_4^+ + 2H_2O \qquad \text{(Eq. 1)}$$
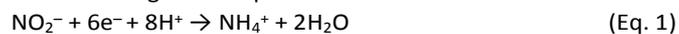
We shall look here at the example of cytochrome *c* nitrite reductase, which is possibly the best characterised of these haem-based systems. Remarkably, this enzyme is able to mediate this multi-electron, multi-proton reduction without the release of less reduced potential intermediates such as NO. Neese and co-workers have proposed a mechanism of action for cytochrome *c* nitrite reductase based on the crystal structures of reaction intermediates and Density Functional Theory (DFT) calculations,[4,5] and this putative catalytic cycle is summarised in Fig. 2.

Upon binding of nitrite to the Fe(II) centre of the haem, N-O bond heterolysis occurs to generate a haem-nitrosyl ({Fe-NO}) complex. This is facilitated by a high degree of back-bonding from the filled d_{xz} orbital of the Fe(II) to an empty π* orbital on the bound nitrite.[4] This back-bonding serves to both strengthen the Fe-N bond and weaken the N-O bonds, promoting heterolysis. Successive electron and proton transfers then result in the formation of the {Fe-NH(O)} adduct, where the nitrogen coordinated to iron is protonated in preference to the remaining oxygen. Further proton-coupled-electron transfers then lead to the formation of a putative iron-hydroxylamine complex ({Fe-NH₂OH}), which is then itself protonated and reduced to break the final N-O bond, liberating water and giving the {Fe-NH₃} intermediate. Further protonation then causes release of ammonium, allowing a second molecule of nitrite to bind and permitting the enzyme to enter the next catalytic cycle.[1,4]
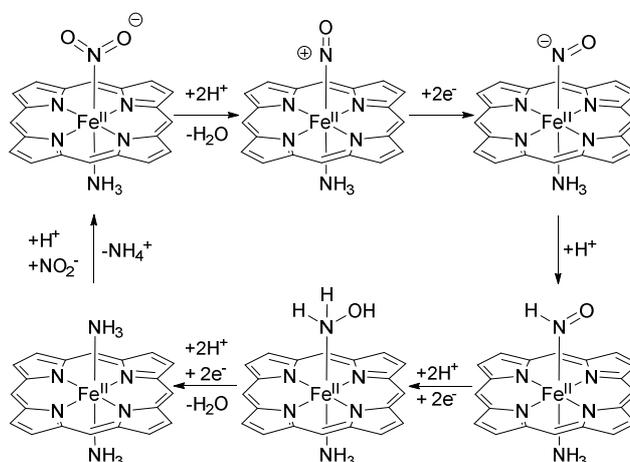

Fig. 2 Mechanism of nitrite reduction by cytochrome *c* nitrite reductase according to Neese and co-workers.[4]

2.2 Nitrite reduction to nitric oxide with copper-based nitrite reductases

Various bacteria remove nitrogen from their systems using the process of denitrification. This involves reduction of nitrite ions to NO and nitrous oxide (N₂O) followed by a further, final reduction to dinitrogen gas. The first step in this denitrification pathway is the reduction of nitrite to NO:

$$NO_2^- + e^- + 2H^+ \rightarrow NO + H_2O \qquad \text{(Eq. 2)}$$

Again, haem-containing enzymes can be used to effect this conversion.[1] However, molybdenum and copper-based enzymes also exist that can perform this reaction. In the case of copper, the reaction catalysed by copper-containing nitrite reductase (CuNIR) can be expressed as:

$$Cu(I) + NO_2^- + 2H^+ \rightarrow Cu(II) + NO + H_2O \qquad \text{(Eq. 3)}$$

CuNIR actually contains two copper centres: the type-1 Cu centre is surrounded by two histidine (imidazole-type) ligands, a cysteine ligand and a methionine ligand (these latter both coordinate through sulfur), whilst the distorted tetrahedral type-2 Cu centre is coordinated by 3 histidine ligands and a single water molecule.[6] Nitrite is thought to be reduced on the type-2 Cu centre using electrons donated by the type-1 centre

to the type-2 centre. Numerous studies have contributed to the current level of understanding with respect to the mechanism of action of the type-2 centre in CuNIR,[1,7] which is presented in Fig. 3.
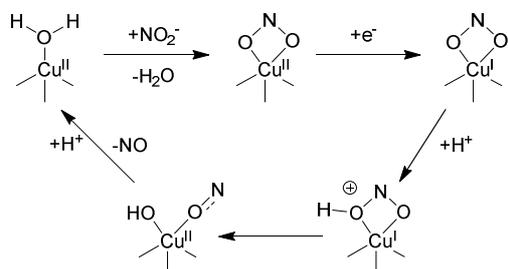

Fig. 3 The proposed mechanism (simplified) of nitrite reduction to NO in CuNIR.

In this proposed mechanism, nitrite displaces water and binds to the Cu(II) centre of CuNIR through its two oxygen atoms, producing a distorted square-based pyramidal geometry at the copper. Reduction of the Cu(II) centre then occurs as a result of electron transfer from a type-1 centre. There is currently some debate as to the ordering of the binding and reduction events, and it is possible that reduction precedes binding.[1] In any case, the bound nitrite is then protonated at the oxygen that is to be abstracted, after which N-OH bond lysis occurs. This bond scission is facilitated by back-bonding from the HOMO (the copper d_{x2-y2} orbital) into the N-OH σ^* orbital. This interaction between the Cu and the oxygen atoms of the nitrite arises as a consequence of the bidentate binding mode of the NO_2^-.[7] After the N-OH is broken, protonation of the {Cu-OH} species thus formed leads to NO liberation and the generation of a Cu(II)-aqua complex. This aqua complex can then re-enter the catalytic cycle by binding to nitrite followed by reduction (or *vice-versa*).

2.3 Nitrite oxidation to nitrate

The biological processes that underlie the interconversion of NO_2^- and NO_3^- are less well understood than the aforementioned reductions of nitrite. The dissimilatory pathway for conversion of nitrite to nitrate is performed using the molybdenum-containing nitrite oxidoreductase (MoNiOR) enzymes, in which two thiolate-bearing pyranopterin cofactors enforce a distorted trigonal prismatic geometry on the Mo centre, with the thiolates defining one rectangular face of the prism.[8] The general reaction for nitrite oxidation is given in Equation 4:

$$NO_2^- + H_2O \rightarrow NO_3^- + 2H^+ + 2e^- \tag{Eq. 4}$$
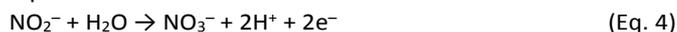
Little is known about the mechanism of action of MoNiOR, although the oxygen atom that is added to nitrite to give nitrate is probably derived from water as suggested by Equation 4. The dissimilatory nitrate reductases are members of the DMSO reductase family, and so may share structural and mechanistic similarities with other enzymes within this subclass.[9] However, we shall content ourselves here by simply noting the likely active site structure of MoNiOR, which is shown in simplified fashion in Fig. 4a.
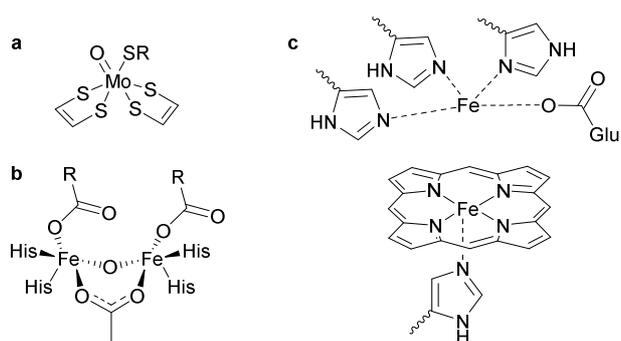

Fig. 4 a) Simplified active site structure of the dissimilatory nitrate reductases, showing the primary coordination environment around the Mo centre. SR is typically cysteine. Alternatively, this ligand could be present as –OR in the form of serine. b) Active site structure of flavodiiron nitric oxide reductase, FNOR. The R-groups on FNOR are either aspartate or glutamate. His = histidine. c) Simplified active site structure of nitric oxide reductase. Glu = glutamate.

2.4 Nitric oxide reduction

Two types of enzymes exist for the conversion of NO to N_2O: Nitric oxide reductase (which contains two iron centres, one as haem and the other coordinated to a glutamate and three histidine ligands)[10] and the non-haem flavodiiron nitric oxide reductase (FNOR, see structures b and c in Fig. 4).[11] In both cases, the general reaction is given by:

$$2NO + 2e^- + 2H^+ \rightarrow N_2O + H_2O \tag{Eq. 5}$$

Caranto *et al* recently undertook an in-depth study of the mechanism of action of flavodiiron nitric oxide reductase,[11] and postulated the following mechanism for NO reduction to N_2O. Starting from the reduced Fe(II)-Fe(II) state, NO binds rapidly to one Fe(II) centre, with a second NO (if NO is present in excess) adding subsequently to the other Fe(II) to give the {(NO)Fe(II)-Fe(II)(NO)} complex. Elimination of N_2O (which is the rate determining step) then occurs, with concomitant oxidation of both the iron centres to Fe(III). In the enzyme, these Fe(III) centres are then rapidly reduced back to the Fe(II) state by internal electron transfer, allowing the enzyme to bind and turn-over more NO. A detailed understanding of the N-O bond cleavage and N-N bond formation reactions remains elusive at time of writing, and clearly this is an area which warrants further examination.

3. Artificial Metal-Ligand Coordination Complexes for Nitrite Reduction

3.1 Nitrite reduction with copper complexes

Copper coordination complexes have been developed as mimics of CuNIR in order to effect the reduction of nitrite to NO according to Equation 3 (see section 2.2). The underlying mechanism for Equation 3 with reference to copper coordination complexes is generally thought to proceed as proposed by Averill,[12] whereby nitrite binds to a reduced Cu(I) centre, with subsequent protonation yielding water and a Cu(I)-bound NO^+ ligand. According to this postulated mechanism, binding of nitrite to a more oxidized Cu(II) centre would not lead

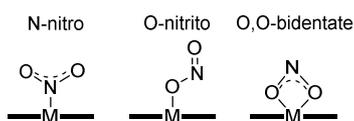to NO production, but might do so upon reduction of the metal centre.

Fig. 5 Common modes for binding of nitrite to metal centres.

Various modes for the binding of nitrite to transition metal complexes have been observed (Fig. 5), including η^1-NO_2 (N-nitro), η^1-ONO (O-nitrito), and η^2-O-N-O (O,O-bidentate). In 1996, Tolman reported a functional, mononuclear model complex of CuNIR containing a Cu(I) centre supported by a sterically hindered triazacyclononane ligand that was somewhat reminiscent of the active site of enzyme.[13] The nitrite was bound to the metal through its nitrogen atom (N-nitro), producing a distorted tetrahedral geometry at copper. Upon addition of acetic acid to this Cu(I)-nitrite adduct, NO was evolved according to Equation 3, with concomitant generation of the corresponding Cu(II) di-acetate complex. Since this report, numerous other Cu complexes featuring tripodal ligands have shown activity for nitrite reduction to NO (see, for example, references 2 and 14). Here, we shall focus on a few of the more illustrative examples from the last decade.

The first of these recent examples that we shall consider was reported by Kujime *et al* in 2008,[15] who studied several copper(I) nitrite complexes with various tridentate ligands (see Fig. 6) in order to determine the steric and electronic effects of the ligands on CuNIR-type activity. As with Tolman's CuNIR mimic, all five Cu(I)-nitrite complexes reacted with acetic acid to liberate NO and to form the corresponding Cu(II)-acetate complexes. However, there was a marked difference in the activity of the various complexes as a function of the tripodal ligand used, on account of both steric and electronic factors.

In terms of electronics, CuNIR-type activity was found to increase with increasing electron donation by the tridentate ligand. Upon coordination to the copper centre, the nitrite ion accepts electrons from the copper's occupied $3d_\pi$-orbital into its p_π^*-orbital (π-back-bonding), whilst donating electrons from its occupied p_σ-orbital into the unoccupied 4s orbital of copper (σ-donation). As the π-back-bonding from the copper centre is less significant than the σ-donation from the nitrite ion, the electron density of nitrite when bound to Cu is smaller than in the free anion. The use of electron-donating ligands on the Cu centre should then act to push electron density onto the copper, increasing the π-back-bonding effect and therefore leading to a higher electron density on the nitrite when it is bound to Cu than might otherwise be expected. This means that the electron density on both the nitrite and copper, and therefore the energy of the HOMO, can be controlled by careful choice of ligand.

For both (TIC)Cu(NO_2) and (TPM)Cu(NO_2)-type complexes (Fig. 6), the HOMO is formed by a combination of interactions between the 4s-orbital of the Cu and the p_σ-orbital of NO_2^-. It is the HOMO of the copper complex which interacts with the

protons during the reaction (allowing one oxygen of the bound nitrite to be lost as water, see Equation 3), and the initial protonation of the copper-bound nitrite is the rate determining step.[15] Hence the higher the energy of the HOMO, the faster initial protonation of the nitrite and hence the greater the reactivity observed. Kujime *et al* found that the HOMO of the (TIC)Cu(NO_2) complexes was about 0.5 eV higher than that of their (TPM)Cu(NO_2) analogues, leading to enhanced reactivity for the TIC-Cu complexes. Moreover, Kujime *et al* also showed that steric effects have a large influence on reactivity. When more bulky ligand R-groups were used, X-ray crystallography revealed that the Cu-N_{ligand} bond lengths (between the copper centre and the tripodal ligand) increased. This reduced electron donation from the tripodal ligand to the Cu, and hence decreased the overall electron density on the nitrite (due to decreased π-back-bonding from the Cu to the bound nitrite). This in turn led to slower nitrite reduction. Hence the authors concluded that less sterically encumbered complexes exhibited superior catalysis.
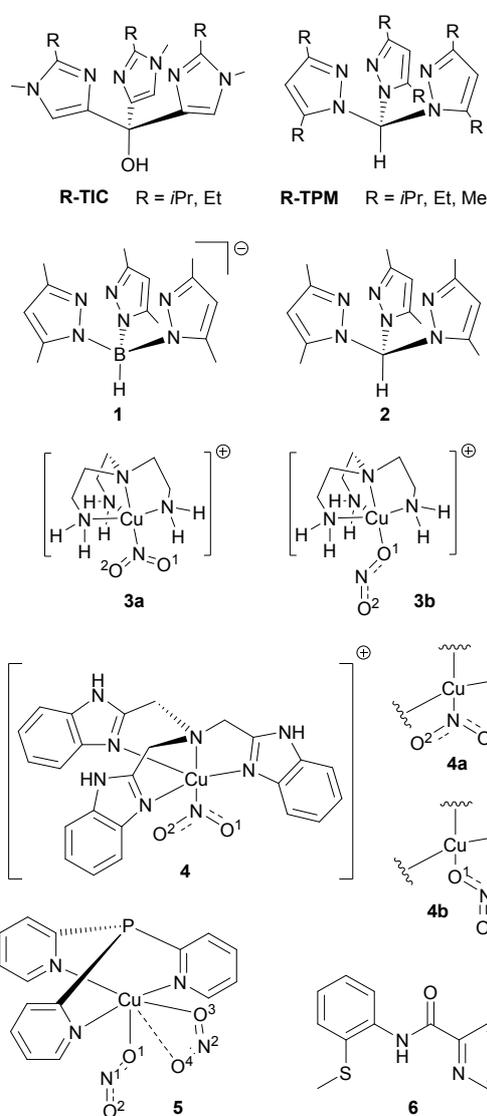

Fig. 6 Chemical structures of the various ligands and complexes discussed in the text in relation to nitrite reduction with copper complexes.

A distinct tripodal ligand for supporting Cu(I) was recently reported by Hsu and co-workers based on the scorpionate ligand hydrotris(3,5-dimethylpyrazolyl)borate (**1**, Fig. 6).[16] The activity of the Cu(I)-NO_2 complex of this ligand was compared to that of its C-bridged analogue (**2**), revealing that in both cases protonation was not the rate determining step during reaction with acetic acid to liberate NO (in contrast to the RDS observed by Kujime *et al* with their complexes[15]). The more electron-rich B-bridged tripodal complex was found to be a more effective catalyst for nitrite reduction to NO than the C-bridged tripod complex, which the authors suggested could be due to greater electron density on the nitro ligand in the case of the B-bridged complex.

An alternative set of structurally-related copper-tripodal ligand complexes (based on Cu(II)) that are competent for nitrite reduction to NO and N_2O was reported recently by Woollard-Shore *et al*.[17] The structures of some of these complexes are shown in Fig. 6. The complexes of generic formula ([Cu(NO_2)(Tren][PF_6]) (where Tren is tris-(2-aminoethyl)amine) and the complexes of formula ([Cu(NO_2)(Tris-[(benzimidazol-2-yl)methyl]amine)][NO_2]) were found to be a mixture of η^1-NO_2 and η^1-ONO isomers. X-ray crystallography revealed that the η^1-NO_2 bound isomer of complex **3** (**3a**) displays two roughly equal nitrite N-O bond lengths (1.246 Å and 1.239 Å). In contrast, the η^1-ONO bound isomer complex **3b** showed unequal N-O bond lengths with r(N-O1) = 1.317 Å and r(N-O2) = 1.214 Å (where O1 is bound to the Cu centre). A disparity between N-O bond lengths may be expected for the η^1-ONO bound isomers of each complex, but a significant difference in N-O bond lengths of the η^1-NO_2 bound isomer of complex **4** (**4a**) was also observed: r(N-O1) = 1.217 Å and r(N-O2) = 1.318 Å. This disparity in N-O bond lengths for complex **4a** (which is not observed in the analogous isomer complex **3a**) suggests that there is a difference in the distribution of electron density between the Cu^{2+} centre and the coordinated NO_2^- in complexes **3** and **4** brought about by the different ligand environments.[17] In complex **4a**, the d_{xz} and d_{yz} orbitals of the Cu^{2+} centre which are involved in bonding to the NO_2^- donate more strongly through back-bonding into the empty π^*-orbital of NO_2^- than in complex **3a**, causing the overall electron density on the Cu^{2+} ion in **4a** to be lower. This is reflected in a difference in the position of the Cu(I)/Cu(II) redox couples: **4a** has a more positive reduction potential (and hence is easier to reduce) than is complex **3a**.

The η^1-ONO bound isomer complex **4b** showed an elongation of the r(N-O1) bond (1.361 Å) (O1 is bound to Cu centre) with contraction of the r(N-O2) bond (1.210 Å) which is characteristic of the η^1-ONO bound mode. Density functional theory calculations showed that the η^1-NO_2 isomers were lower in energy than the η^1-ONO isomers by −5.2 kJ mol^{-1} and −3.8 kJ mol^{-1} for complexes **3** and **4** respectively in the gas-phase. This small difference in calculated energies helps to explain why both the η^1-ONO and η^1-NO_2 linkage isomers were observed. Complex **4** demonstrated better catalytic properties on almost all fronts, including percentage of NO_2^- converted, reaction time, initial NO_2^- conversion rate and percentage of NO present in the final gas mixture.

Two different binding modes for nitrite were also observed for compound **5** ([Cu(NO_2)(Tris-(4-phenyl-3-aza-3-butenyl)amine)][BF_4]) with both an end-on η^1-ONO ligand and a bidentate η^2-ONO ligand. Comparison of the bond lengths in these complexes suggests that the bonding between the Cu^{2+} centre and the η^1-ONO ligand is stronger than the interaction with the bidentate η^2-ONO ligand. Complex **5** was found to have very selective catalytic properties - converting 88% of NO_2^- into NO with no trace of N_2O. However, it remains unclear whether it is the η^1-ONO, the η^2-ONO, or possibly both nitrites, which are reduced and hence no correlation can be drawn between binding mode and reactivity with this complex.

CuNIR-type activity can also be observed in Cu-tripodal ligands that coordinate to the copper centre through heteroatoms other than solely nitrogen. A good example of this was published by Patra and co-workers in 2013, wherein the tridentate N,N,S ligand N-2-methylthiophenyl-2'-pyridinecarboxamide (**6**, Fig. 6) was used to synthesise both Cu(I) and Cu(II) complexes which were then coordinated to nitrite.[18] The Cu(I)-nitrite adduct was found to evolve NO when exposed to acid, whilst the Cu(II)-nitrite adduct liberated only nitrite under the same conditions. The Cu(II)-nitrite adduct could, however, be electro-reduced to its Cu(I) form, from which NO could be evolved upon treatment with acid, in agreement with the proposed mechanism of nitrite reduction proposed by Averill.[12]

Electrochemical methods for reducing nitrite using copper complexes attached to electrodes have also been explored. Yamaguchi and co-workers used the tripodal N,N,N ligand (bis(6-methyl-2-pyridylmethyl)amine ethyl sulfide to coordinate to a Cu(I) centre and attached this to the surface of gold electrodes using the thiol tether.[19] Under acidic conditions (pH 5.3), an electrocatalytic wave for the reduction of NO_2^- to NO was observed, but no such wave was observed in the presence of nitrite at higher pH. This underlines the fact that the reduction of nitrite as shown in Equation 3 requires protons. In a similar fashion, Orain *et al* have attached Cu(I) complexes based on the ligand tris(2-pyridylmethyl)amine to gold electrodes and have also observed a requirement for acidic conditions in order to evolve NO from nitrite solutions.[20] Approaches such as this are now being exploited in the development of prototype NO-release systems for biomedical applications.[21]

3.2 Nitrite reduction with mono-nuclear iron complexes

An early example of nitrite reduction mediated by iron coordination complexes was supplied by Meyer and co-workers, who used the water-soluble porphyrin [Fe^{III}(H_2O)(*meso*-tetrakis(*p*-sulfonatophenyl)porphyrin)]$^{3-}$ in mildly acidic aqueous solution to reduce nitrite to ammonia, with significant amounts of N_2O and hydroxylamine also being produced.[22] The authors determined that the nitrosyl complex [Fe^{II}(NO^+)(*meso*-tetrakis(*p*-sulfonatophenyl)porphyrin)]$^{3-}$ was an intermediate in this reaction pathway, a complex which itself formed *via* reaction of the reduced Fe(II) porphyrin complex with HONO. This nitrosyl complex was then in turn reduced

electrochemically by sequential 1-electron processes to generate NH_3, *via* the NH_2OH adduct as an intermediate. Thus this work constituted both a structural and functional model of the natural cytochrome *c* nitrite reductases (see Equation 1).

Iron porphyrins have also been employed for the generation of NO from nitrite. For example, Chi and co-workers used iron *meso*-tetrakis (4-*N*-methylpyridiniumyl) porphyrin ([$Fe^{III}(TMPyP)$]$^{5+}$) to generate NO from nitrite solutions electrochemically.[23] In order to obtain free NO gas, both cathodic and anodic processes were required. In the first step, the Fe(III)-porphyrin complex was reduced in the presence of nitrite to give the bis-nitrito Fe(II)-porphyrin complex [$Fe^{II}(NO_2^-)_2(TMPyP)$]$^{2+}$ which subsequently disproportionated to give the [$Fe^{III}(TMPyP)$]$^{5+}$ starting material and the mono-nitrosyl complex [$Fe^{II}(NO)(TMPyP)$]$^{4+}$. This mono-nitrosyl complex was then subjected to an electrochemical oxidation to re-generate [$Fe^{III}(TMPyP)$]$^{5+}$ and release NO gas. The authors combined these two electrochemical processes in a flow-cell apparatus in order to generate a constant stream of NO by this method.

Another example of nitrite reduction to NO with iron porphyrins that is of particular relevance to NO formation in biological systems was reported recently by Ford and co-workers.[24] Using the water soluble Fe(III)(TPPS) complex (TPPS = tetrakis(sulfonatomesityl)porphyrinato), the authors were able to observe oxygen atom transfer from nitrite to species of biological relevance such as cysteine and glutathione, with simultaneous formation of the Fe(II)(TPPS)(NO) complex. However, despite the high stability commonly exhibited by such ferrous nitrosyl adducts (*cf.* Chi *et al*, who could liberate NO from their analogous Fe(II)-NO complex only by electrochemical oxidation of the iron centre[23]), Ford's team observed what they describe as "a matrix of redox transformations" that lead to spontaneous regeneration of the Fe(III)(TPPS) starting material with concomitant production of N_2O and NO at pH 6. HNO (nitroxyl) was suggested as the most likely precursor for N_2O formation on the basis of trapping experiments. Meanwhile, NO liberation was proposed to occur *via* coordination of a second equivalent of nitrite at the proximal site of Fe(II)(TPPS)(NO), giving first Fe(II)(TPPS)(NO)(NO_2^-) and then the oxidised complex Fe(III)(TPPS)(NO), from which NO can dissociate. Although the precise mechanism for NO liberation from Fe(II)(TPPS)(NO) remains somewhat unclear, what is obvious is that ferrous nitrosyls such Fe(II)(TPPS)(NO) may not be as inert as commonly assumed at pH values around 6.

Very recently, Harrop and co-workers have reported the first example of a non-heme complex ([$Fe(LN_4^{Im})(NO_2)_2$], see Fig. 7) with trans-coordinated nitrite ligands that is capable of reducing nitrite to NO in a catalytic fashion.[25] The reaction chemistry of this iron complex was investigated using thiols as these are able to function both as proton and electron sources for the reduction of the coordinated nitro ligands (*cf*. the use of thiols in reference 24). Using *p*-chlorobenzenethiol (*p*-ClArSH) as a sacrificial reductant in conjunction with *p*-toluene sulfonic acid (*p*-TsOH) as a proton source, NO was produced selectively from this complex with no evidence for the formation of other nitrogen oxides such as N_2O or NO_2. In the presence of excess nitrite, catalytic turnover was demonstrated and the active

complex could be isolated in 80% yield after 3 cycles (see Fig. 7). The selectivity of this catalyst is impressive, and bodes well for the development of systems that can generate NO to the exclusion of other nitrogen oxides.
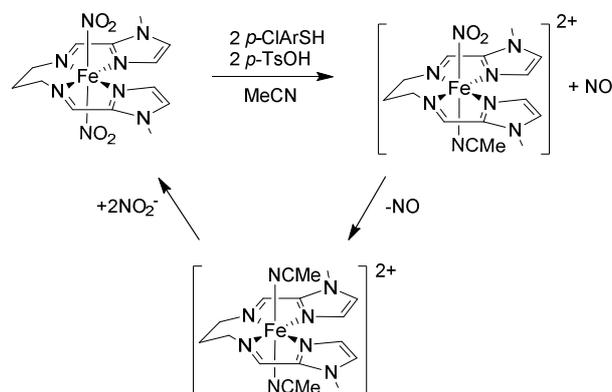

Fig. 7 The structure of complex [$Fe(LN_4^{Im})(NO_2)_2$] and details of its reaction with nitrite in the presence of *p*-chlorobenzenethiol and *p*-toluene sulfonic acid as reported by Harrop.[25]

Iron phthalocyanine complexes also display interesting activity with regard to nitrite reduction. Kudrik and van Eldik have studied the reactions of Fe(III) tetrasulfophthalocyanine with nitrite in the presence of both dithionite and sulfoxylate.[26] With dithionite, NO was the dominant product observed, but when sulfoxylate was used as the reductant the main product was ammonia. This difference in reactivity was attributed to the different structures of the intermediate complexes formed during reduction by these two reagents: nitrite reduction by sulfoxylate (the stronger reducing agent) proceeds *via* an intermediate in which nitrite is coordinated to a highly reduced Fe(I) centre through nitrogen, whereas nitrite reduction by dithionite occurs through an intermediate in which an η^1-ONO nitrite coordinates to an Fe(II) centre. As expected, the stronger reductant then leads to a greater degree of reduction of the nitrite – in this case the 6-electron reduction to NH_3. Meanwhile, the less strong reducing agent is only able to effect the loss of one of the oxygen atoms of the nitrite (as water), leading to NO as the reduced product.

As a final example of the use of mono-nuclear iron complexes in the reduction of nitrite, we shall consider the system recently reported by Fout in which the role of hydrogen bonding in nitrite reduction is explicitly addressed.[27] The Fe(II) complex [$N(afa^{Cy})_3Fe(OTf)$]$^+$ (see Fig. 8) was observed to react cleanly with nitrite to yield the iron(III)-oxo species, [$N(afa^{Cy})_3Fe(O)$]$^+$ and NO gas. The presence of a single hydrogen bond between the ligand and nitrite causes preferential binding of the nitrite to the metal centre in an η^1-ONO fashion, which then in turn leads to the observed products of reduction: NO gas and an Fe(III)-oxo species that has retained the Fe-O bond from the η^1-ONO-bound nitrite. Given the prominent role of hydrogen bonding in the natural nitrite reduction systems,[1] investigation of the effects of hydrogen bonding in artificial systems is an area that offers great promise for altering binding orientations and hence product selectivity.
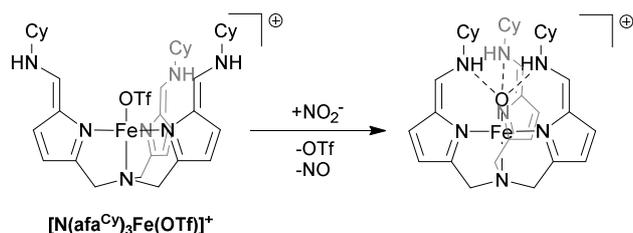
Fig. 8 The structure of complex $[N(afa^{Cy})_3Fe(OTf)]^+$ and its reaction with nitrite to generate NO.

3.3 Nitrite reduction using other metal-ligand systems

There are a few other notable examples of metal-ligand coordination complexes that can reduce nitrite. Meyer has reported the reduction of nitrite and NO bound to metal centres to ammonia, using complexes of the form $[M(terpyridine)(bipyridine)NO_x]^{n+}$, where M = Ru or Os.[28] However, in neither case was catalysis possible, as the M-NH$_3$ adducts were inert to substitution and hence NH$_3$ formation inhibited turnover.

Bimetallic systems have emerged as promising platforms for nitrite reduction. Uyeda and Peters have demonstrated selective conversion of NO$_2^-$ to N$_2$O using a heterobimetallic Co-Mg complex supported by diamine-dioxime ligands (Fig. 9).[29] On the basis of data procured from cyclic voltammetry and electrolysis experiments, Uyeda and Peters devised a plausible electrocatalytic cycle for the reduction of nitrite based on the pre-catalyst depicted in Fig. 9.
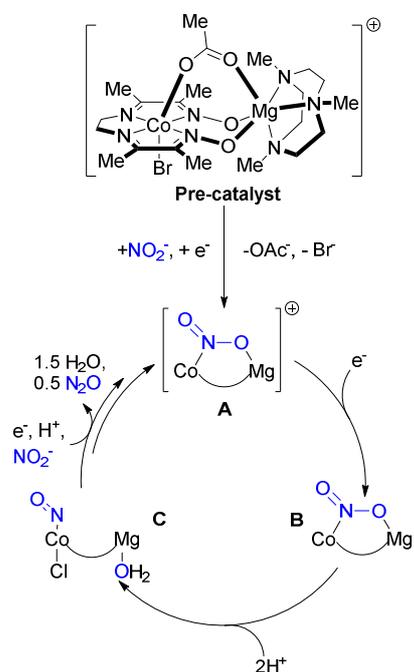

Fig. 9 The mechanism of N$_2$O production from nitrite with Uyeda and Peters' bimetallic Co-Mg catalyst.[29]

The proposed cycle begins with reduction of the pre-catalyst by 1 electron, which is followed by the loss of bromide and displacement of the OAc$^-$ ligand by nitrite to give the cationic complex **A**. Single electron reduction of complex **A** gives

complex **B**, then subsequent protonation with two equivalents of acid yields nitrosyl complex **C** which, after further reduction and protonation steps, eliminates nitrous oxide and leaves a vacant site on the bimetallic catalyst to which NO$_2^-$ can bind, regenerating complex **A**. Incorporation of the redox-innocent, Lewis-acidic Mg^{2+} centre into the framework was found to increase the stability of the Co-NO$_2^-$ adduct sufficiently under acidic conditions that addition of the acid [Et$_3$NH][BPh$_4$] to complex **B**, did not produce hydrogen (as normally observed with such Co complexes in the absence of Mg), but instead led to N$_2$O production *via* complex **C**. Although further mechanistic investigation is required to validate this proposed electrocatalytic cycle, it is consistent with the reactivity of the various intermediates isolated by the authors. The impressive selectivity for production of N$_2$O over H$_2$, NH$_2$OH or NH$_3$ makes this system attractive for further research and development.

Karlin has also reported a bimetallic catalyst for nitrite reduction, in this case a system that combines iron porphyrins and tripodal copper complexes to mediate the reversible interconversion of nitrite and NO.[30] Upon addition of an Fe(II)-porphyrin to the Cu(II)-nitrite complex $[(tmpa)Cu^{II}(NO_2)]^+$, the (Fe^{II})-haem-nitrosyl adduct was obtained, along with the oxygen-bridged $[(porphyrin)Fe^{III}-O-Cu^{II}(tmpa)]^+$ complex (Fig. 10).
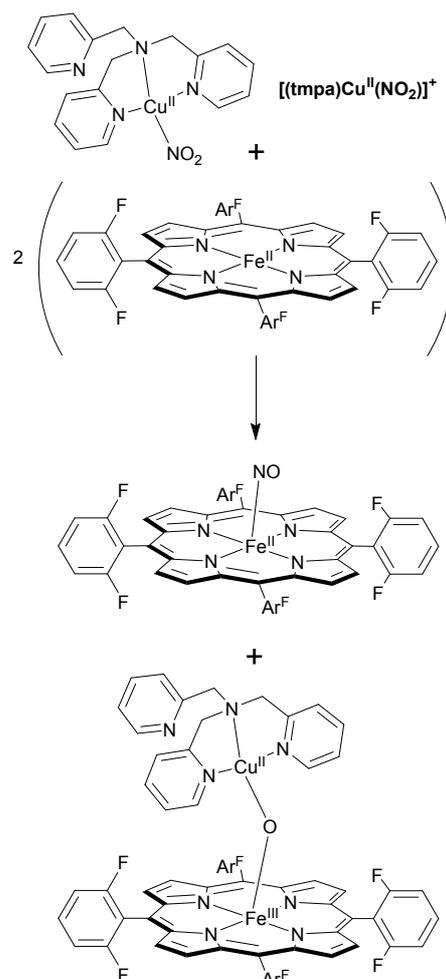
Fig. 10 Nitrite reduction to NO using Karlin's bimetallic haem-Cu tripod system.[30]

From this, the authors deduced that the haem played the role of the reductant whilst the Cu(II) ion provided a Lewis acid interaction (*cf.* Uyeda and Peters, reference 29), facilitating N-O bond cleavage in nitrite and stabilising the oxo anion in the heterobimetallic oxygen-bridged product. Importantly, the authors were able to demonstrate that the reverse process (in this case the addition of two equivalents of NO to [(porphyrin)Fe^{III}–O–Cu^{II}(tmpa)]$^+$ to generate the (Fe^{II})-haem-nitrosyl adduct and the [(tmpa)Cu^{II}(NO$_2$)]$^+$ starting material) was also possible, capturing some of the function of the haem$_{a3}$/Cu$_B$ active site of cytochrome *c* oxidase, which is able to reduce nitrite to NO reversibly.

4. Nitric Oxide Reduction with Artificial Metal-Ligand Coordination Complexes

The reactions of nitric oxide with transition metal complexes were comprehensively reviewed by Ford in 2002.[31] This section will look at examples of NO reduction with metal-ligand coordination complexes since that time, concentrating largely on complexes with aromatic heterocyclic ligands. Readers interested in NO reduction to N$_2$O using somewhat simpler metal-ligand complexes will find a useful overview of these in the first sections of reference 32.

Onishi and co-workers demonstrated N-N coupling of two nitrosyl ligands on bimetallic ruthenium clusters to produce N$_2$O in 2007.[33] Dimerisation of the ruthenium-nitrosyl complex TpRuCl$_2$(NO) (complex **7**, where Tp= hydrotris(pyrazolyl)borate; see Fig. 11) was achieved by refluxing complex **7** with stoichiometric amounts of pyrazole and excess Et$_3$N in CH$_2$Cl$_2$ to give bimetallic complex **8** in 29% yield. Oxidation of **8** by AgBF$_4$ in acetonitrile resulted in cleavage of the N-N bond to give dinitrosyl complex **9** ([{TpRu(NO)}$_2$(μ-Cl)(μ-pyrazolyl)](BF$_4$)$_2$) in 56% yield. Cleavage of the N(=O)-N(=O) bond was confirmed by X-ray crystallography of complex **9** which revealed a N···N distance of 3.006 Å. Comparison of the N-O bond distances in complex **9** (1.169 Å and 1.131 Å) shows significant shortening when compared to the N-O bond lengths of complex **8**, indicating an increase in bond order as would be expected after N-N bond scission. Interestingly, when treated with zinc metal, complex **9** reductively reformed the N-N bond to afford the starting material in 70% yield. Treatment of complex **8** with HBF$_4$.OEt$_2$ in CH$_2$Cl$_2$ yielded bimetallic complex **10** ([(TpRu)$_2$(μ-Cl)(μ-pyrazolyl)(μ-O)]; 21% yield), complex **9** (43% yield) and N$_2$O gas (25% yield based on complex **8**). Hence this system displays a range of interesting and reversible N-N bond formation and cleavage reactions.

Collman and co-workers reported the first functional synthetic nitric oxide reductase model complex in 2008, by decorating a porphyrin unit with imidazole appendages, such that metallation with iron gave rise to a complex containing both haem and non-haem iron centres, highly reminiscent of the active site of nitric oxide reductase (see Fig. 4c).[34] When both irons were present as Fe(II), addition of NO gas led to the production of N$_2$O. Detailed electronic, EPR and infra-red

analysis allowed aspects of the mechanism of action to be determined. It was found that one molecule of NO binds to each Fe(II) centre (as opposed to both molecules binding to only one iron), and that production of N$_2$O was achieved with simultaneous oxidation of both metal centres to the Fe(III) state. Mixed-valence complexes (where the haem iron was in the 3+ oxidation state and the non-haem iron in the 2+ state) were not competent for N$_2$O production from NO.
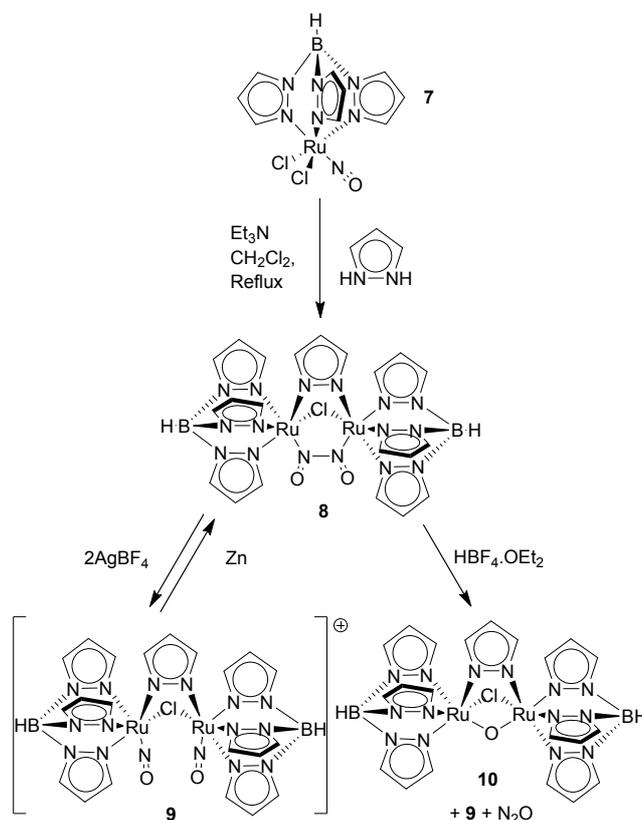

Fig. 11 Onishi's di-ruthenium platform for NO reduction to N$_2$O.[33]

A similar approach was taken by Karlin and co-workers, who reported NO reduction by a hetero-bimetallic complex containing tethered haem and copper centres analogous to those shown in Fig. 10.[35] The activity of this system was investigated starting from the complex containing a haem iron, but no copper centre. Upon addition of excess NO to this mono-metallic complex, the dinitrosyl {Fe(NO)$_2$} complex formed, wherein NO was bound to the iron centre both above and below the plane of the porphyrin ring, as confirmed by UV-vis and EPR spectroscopies. Addition of [Cu^I(MeCN)$_4$]$^+$ and 2 equivalents of acid to this dinitrosyl complex resulted in the production of nitrous oxide in >80% yield, with both metal centres undergoing oxidation in the process (Fe(II)→Fe(III) and Cu(I)→Cu(II)). In the absence of copper, addition of acid to the dinitrosyl complex yielded only the mono-nitrosyl adduct. On the other hand, addition of [Cu^I(MeCN)$_4$]$^+$ but no acid resulted in a haem-copper complex in which the haem iron remained bound to only one NO molecule (and also remained in the Fe(II) state), whilst the copper centre was oxidised to Cu(II) and found to be

coordinated to nitrite. Meanwhile, N_2O was evolved. The authors attributed the presence of both NO_2 and N_2O in this instance to disproportionation of the NO released from the $\{Fe(NO)_2\}$ complex *via* the process: $3NO \rightarrow NO_2 + N_2O$. The yield of N_2O by this disproportionation reaction was significantly below that expected on the basis of Equation 5, which describes the selective conversion of NO to N_2O as the sole nitrogen-containing product. Hence the authors reasoned that a haem centre, a copper ion and two equivalents of both acid and NO were all necessary in order to reduce NO to N_2O in the same fashion as the cytochrome *c* oxidases (shown in Equation 5).

Around the same time as this article by Karlin and co-workers, Xu *et al* reported the production of N_2O by protonation of a system comprising two haem units bridged by an N_2O_2 moiety (generated by the treatment of 2 equivalents of the haem precursor with hyponitrous acid, $H_2N_2O_2$).[36] This study constituted the first iron-porphyrin hyponitrite complex ever isolated and established that the binding to iron in such complexes is through oxygen (as Fe-O-N-N-O-Fe), in contrast to the complexes described by Collman and Karlin, where NO binding to the metal centre was proposed to be through nitrogen. Thus, it seems that there may be more than one generic mechanism by which NO can be reduced to N_2O using bimetallic haem-based complexes.

Entirely non-haem di-iron complexes have also been reported as being competent for NO reduction, in an analogous fashion to the flavodiiron nitric oxide reductases (FNORs). In 2013, Lehnert and co-workers described the rapid and quantitative production of N_2O from NO and complex **11** (Fig. 12).[37] NO was found to bind to both the iron centres in this complex to give a pseudo-octahedral coordination geometry at each iron. No N_2O production was detected, but two-electron reduction of this complex by either chemical or electrochemical means resulted in fast and clean production of N_2O in almost 100% yield. Monomeric complexes analogous to complex **11** but containing only a single iron centre did not mediate N_2O production. Surprisingly (given Equation 5), N_2O formation by the di-iron complex was found not to be proton-dependent. The authors proposed that NO reduction in the absence of protons might proceed *via* the formation of a *μ*-oxo bridged di-iron unit, according to the equation: $2Fe^{II}\text{-}NO + 2e^- \rightarrow N_2O + Fe^{II}\text{-}O\text{-}Fe^{II}$ and some spectroscopic evidence was found supporting this hypothesis.

Jiang *et al* recently reported the photo-driven production of N_2O from a non-haem iron-nitrosyl dimer that also bears similarities to the flavodiiron nitric oxide reductases.[38] In this case, irradiation of complex **12** (Fig. 12) with white light at both room temperature and 15 K produced N_2O (up to 90% yield at 15 K). By detailed spectroscopic analysis of the low-temperature reaction, the authors established that irradiation of complex **12** leads to dissociation of at least one of the coordinated NO ligands. This dissociated NO might then bind in a side-on mode to a still coordinated NO ligand to produce a transient hyponitrite complex, which in turn then decomposes to liberate N_2O upon further irradiation.
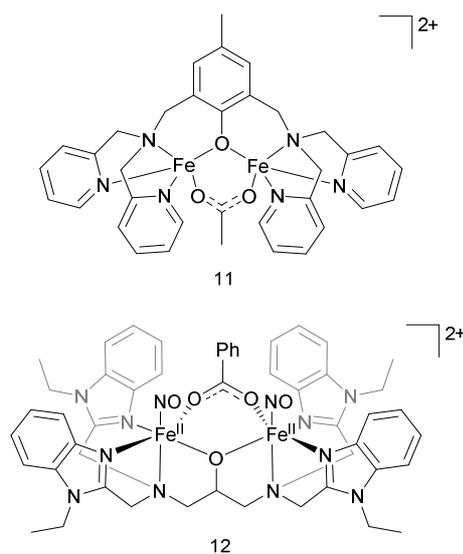

Fig. 12 The structures of non-haem di-iron NO-reducing complexes **11** and **12**.

The final example we shall consider concerns the production of N_2O and water from the reaction of $[Ni(NO)(bipy)_2][PF_6]$ (bipy = 2,2-bipyridine) with acetylacetone (H-acac).[39] This reaction was observed to give rise to ligand re-arrangements at nickel, producing $[Ni(bipy)_3][PF_6]_2$ and the complex $[Ni(bipy)N_2O_2]$. This latter complex (which could be isolated and characterised crystallographically) exhibited a square-planar Ni(II) centre coordinated to one bipy ligand and one *cis*-$[N_2O_2]^{2-}$ (hyponitrite) ligand. This hyponitrite was symmetrically coordinated to the Ni centre through its two oxygen atoms (both Ni-O bonds were found to be 1.800(1) Å), whilst the N-N bond length (1.240(3) Å) was consistent with a double bond. The hyponitrite complex then reacted further with H-acac, giving the complex $[Ni(acac)_2(bipy)]$ with concomitant N-O bond cleavage and N_2O production. This work was the first well-characterised report of NO reduction mediated by nickel.

5. Nitrous Oxide Reduction with Artificial Metal-Ligand Coordination Complexes

The 2-electron, 2-proton reduction of nitrous oxide to nitrogen is mediated in nature by the copper-containing metallo-enzyme nitrous oxide reductase during the last step of bacterial denitrification according to the equation:[1]

$$N_2O + 2H^+ + 2e^- \rightarrow N_2 + H_2O \tag{Eq. 6}$$

The active site in nitrous oxide reductase is believed to contain a tetra-copper site with a μ_4-bridging sulfide ligand in between these copper centres. Well-defined metal-ligand coordination complexes that are functional analogues of nitrous oxide reductase are somewhat rare, and we shall restrict ourselves here to looking at two of the more pertinent recent examples of such complexes. The first of these was described by Bar-Nahum *et al* in 2009.[40] In this work, tri-copper complex **13** (Fig. 13), containing a $\{Cu_3S_2\}^{2+}$ core incorporating a bridging disulfide $(S_2)^{2-}$ moiety, was synthesised and found to react slowly with excess N_2O to give N_2. On the basis of spectroscopic and mass spectrometric analyses, the authors proposed that

the first step in N₂O reduction was the reversible generation of a di-copper cluster (complex **14**, Fig. 13) as the active species for N₂O conversion:

$$\{Cu_3S_2\}^{2+} \rightarrow \{Cu_2S_2\}^+ + \{Cu\}^+$$
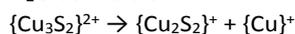
This di-copper cluster was then suggested to reduce N₂O *via* a transition state in which N₂O bridges between the copper centres by way of its oxygen, although the authors noted that such a mechanism was not analogous to that believed to operate in the enzyme.
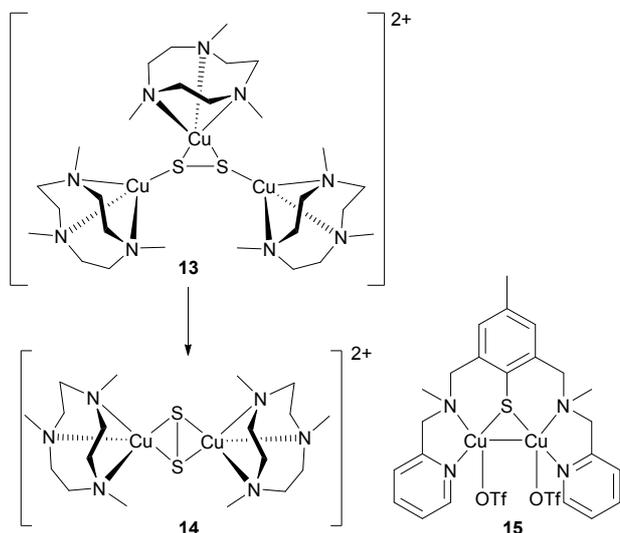

Fig. 13 The structures of the N₂O reduction mediators reported by Bar-Nahum *et al*[40] and Esmieu *et al*.[41]

Very recently, Torelli and co-workers published an account of an alternative mixed-valence di-copper complex (**15**, Fig. 13) containing a {Cu₂S} core that is competent for N₂O reduction to N₂ in acetone.[41] The proposed mechanism calls for exchange of one of the labile trifluoromethanesulfonate ligands on the complex for N₂O, leading to N₂ evolution with the formation of a bridging Cu-O-Cu unit (where this oxygen is postulated to originate from N₂O). Meanwhile, a second molecule of the di-copper complex that has undergone exchange of one of the labile trifluoromethanesulfonate ligands on the complex for N₂O undergoes displacement of this N₂O ligand by water, and then reacts with the Cu-O-Cu complex to generate the Cu-OH-Cu complex, which was found to be the final copper-containing product of the reaction.

Given nitrous oxide's potency as a greenhouse gas and ozone-depleter, catalysts able to mediate the selective removal of N₂O from exhaust gas streams by conversion to N₂ are attractive targets. Hence we can expect many more functional N₂O-reducing platforms to be reported in the coming years.

6. Nitrate Reduction with Artificial Metal-Ligand Coordination Complexes

6.1 Nitrate reduction to nitrite and *vice versa*

Structural models of the oxotransferase enzymes (of which both the assimilatory and the dissimilatory enzymes are members)

are numerous,[42,43] but those competent for nitrate reduction are comparatively rare. In this subsection, we shall examine coordination complexes that are functional for nitrate reduction to nitrite or nitrite oxidation to nitrate (see Equation 4).

Seminal work in this area has been conducted by Holm and co-workers, who reported the first well-characterised reduction of NO₃⁻ to NO₂⁻ by molybdenum-mediated oxygen atom transfer in 1989.[44] The metal-ligand complex in question was synthesised before the structure of any molybdoenzyme had been determined and was based on an S,N,S pincer. Hence it does not bear close structural analogy to the dithiolene-based active sites in the natural nitrate reductases. In later work, however, Holm modelled the active site structure of the dissimilatory nitrate reductases more closely and was able to synthesise a range of metal-ligand coordination complexes capable of oxygen atom transfer reactions (see Fig. 14).[45]
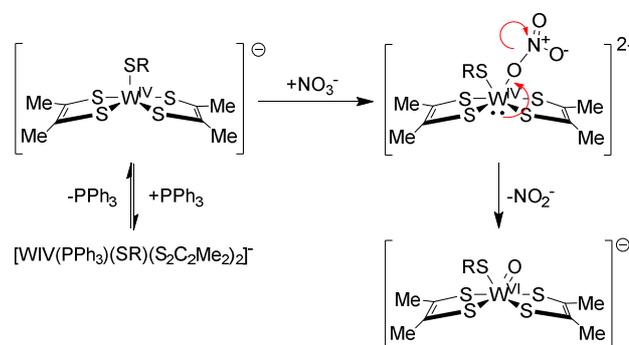

Fig. 14 Mechanism of nitrate reduction to nitrite with Holm's tungsten-centred catalysts as reported in reference 45.

On the basis of kinetic measurements, Holm proposed an associative pathway for nitrate reduction by the tungsten-based complexes reported in reference 45 (the Mo-based complexes were insufficiently stable to be interrogated in such detail), as summarised in Fig. 14. The mechanism built on Holm's earlier work[44] by suggesting that nitrate reduction by direct oxo transfer to the metal centre (with the metal undergoing W^IV to W^VI oxidation in the process) is a viable route to nitrate reduction in these systems.

A similar approach was taken by Sarkar and co-workers, who reported catalytic nitrate reduction to nitrite using Mo-centred catalysts bearing 1,2-dicyanoethylenedithiolate (mnt²⁻), SPh and PPh₃ ligands.[46,47] The first step in the proposed catalytic cycle (Fig. 15) is dissociation of the triphenylphosphine ligand, giving a penta-coordinated intermediate species able to undergo reaction with nitrate to generate nitrite, along with oxygen atom transfer to the molybdenum centre and concomitant Mo^IV to Mo^VI oxidation (*cf.* Holm's proposed mechanism for nitrate reduction at W centres in Fig. 14). The free PPh₃ previously released then reacts with the molybdenum-oxo species to give O=PPh₃ and re-generate the active penta-coordinated Mo^IV complex. This complex can either react with more nitrate, or else re-combine with free PPh₃ to form the catalytically-inert starting complex. Turn-over

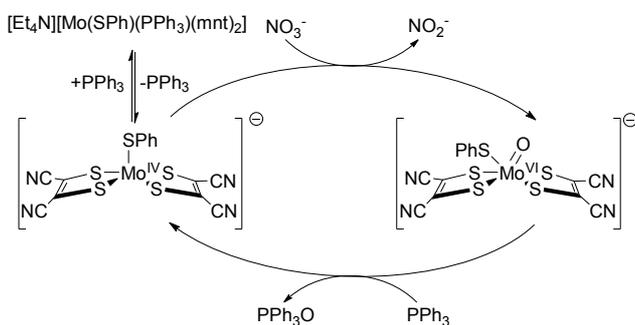numbers of 50 $mmol^{-1}$ s^{-1} (based on the amount of nitrite, $O=PPh_3$ and PPh_3 recovered) were obtained.[46]

Fig. 15 The catalytic cycle for the reduction of nitrate to nitrite using $[Et_4N][Mo(SPh)(mnt)_2]$ and a triphenyl phosphine reducing agent as reported by Sarkar and co-workers.[46,47]

An example of the *oxidation* of nitrite to nitrate is provided by Man *et al*, who employed a *trans*-dioxoruthenium(VI) complex to mediate oxygen atom transfer from the metal-oxo to NO_2^-.[48] Reaction of the *trans*-dioxoruthenium(VI) complex with nitrite was observed to lead to the reduced *trans*-$\{Ru^{IV}(ONO_2)\}^+$ species (where the nitrate ligand was bound to Ru through oxygen), as determined by spectrophotometric, mass spectroscopic and crystallographic analyses. Nitrate was then released by this Ru^{IV} complex upon reaction with water in stoichiometric yield after around 2 hours. ^{18}O labelling studies showed that the oxygen transferred to the nitrite originated from the *trans*-dioxoruthenium(VI) complex *via* a reversible oxygen atom transfer reaction, rather than by an outer-sphere reaction involving solvent water.

6.2 Nitrate reduction to other nitrogen oxides

Nitrate reduction with metal-ligand coordination complexes to species other than nitrite has also been reported. An interesting dinitrosyl-iron complex which mediates the conversion of nitrate to first NO_2 and then nitric oxide was reported in 2013 by Tsai *et al*.[49] The thermally-unstable iron-centred complex 16 (Fig. 16) was formed by reaction between $[(OAc)_2Fe(NO)_2]^-$ and 2 equivalents of nitric acid and was found to react with bis-(diethylthiocarbamoyl)disulfide $((S_2CNEt_2)_2)$ to form complex 18 (*via* intermediate 17) with release of N_2O_4. This N_2O_4 exists in equilibrium with NO_2, and one equivalent of the NO_2 thus formed then oxidises complex 18 to give the $\{Fe(NO_2)(NO)\}$ adduct 19 (Fig. 16). Reaction of complex 19 with dimethyl sulfide then re-generates complex 18, and also produces NO and dimethyl sulfoxide.

The electrochemically-catalysed reduction of nitrate to hydroxylamine using metal-cyclams (cyclam = 1,4,8,11-tetra-azacyclotetradecane) was investigated by several groups in the 1980s and 1990s, as detailed in reference 3. Whether the metal cyclam complexes were used directly in aqueous solution or absorbed on the electrode surface, the reduction reactions mediated by the metal-ligand complexes were six-electron processes: $NO_3^- + 5H_2O + 6e^- \rightarrow NH_2OH + 7OH^-$. Depending on

the underlying electrode material, hydroxylamine was sometimes the final product (*e.g.* when the cathode was Hg), whilst the use of other cathode materials (such as Ag, Cu or Pb) caused the hydroxylamine produced to be further reduced to ammonia at the potentials used.
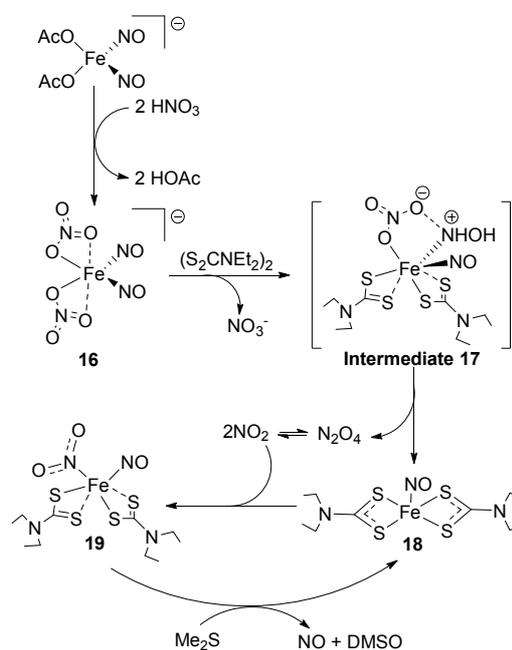

Fig. 16 Nitrate reduction to NO_2 and nitric oxide as reported by Tsai *et al*.[49]

As a final example, Kudrik *et al* have used cobalt-phthalocyanines to mediate the conversion of nitrate to N_2 and N_2O by dithionite.[50] Cobalt-phthalocyanine-nitrite complexes were identified as intermediates in these nitrate reduction reactions. However, when nitrite itself was used as the substrate, the final reaction product was found to be ammonia, and not N_2 or N_2O. These apparently contradictory results were rationalised by the authors by considering the different possible binding modes of nitrite to the cobalt centre during reaction (see Fig. 5 and section 3.1). In all cases, the proposed mechanism of reaction called for the reduction of the initial Co(II)-phthalocyanine complex to the Co(I) oxidation state by dithionite, followed by coordination to and reaction with nitrate or nitrite. When nitrite was the substrate, the authors suggested that coordination was through nitrogen (η^1-NO_2) and that reduction and protonation then led to the Co(II)-NO adduct (bound through nitrogen), which then in turn gave ammonia upon further reduction and protonation. On the other hand, nitrate coordinated to the Co(I)-phthalocyanine complex through oxygen (η^1-ONO), which upon reduction and protonation of the nitrogen oxide then gave the Co(II)-ON adduct (where the bond to cobalt was though oxygen). Further reduction of this intermediate was then held to give $O=N^-$, which dimerised to give N_2O, which could in turn be further reduced to dinitrogen. Differences in the electrophilicity of nitrate and nitrite were held to account for the different binding

preferences of these two substrates. This work has obvious parallels with the same authors' work on nitrite reduction with iron-phthalocyanine complexes (see section 3.2)[26] and serves to emphasise the importance that nitrite binding mode can have in determining the products of reduction.

7. Conclusions and Outlook

In this tutorial review, we have presented an overview of the metal-ligand coordination complexes able to mediate the inter-conversions of the various nitrogen oxides. Many of these complexes bear similarities to the active sites of enzymes that perform the same transformations. Whilst intended in no way to be a comprehensive review of the topic, we believe that the examples presented herein represent a sufficiently broad cross-section of the recent research in this fascinating field to enable the reader to gain a ready understanding of the status of, and remaining challenges in, this area.

The nitrogen oxides are a class of molecules central to biology, geochemistry and modern life. Nitrate fertilisers are essential for feeding the world's growing population, and their misuse constitutes a major environmental hazard. Species such as N_2O and NO_2 are produced by air-breathing internal combustion engines and are implicated in atmospheric pollution and the greenhouse effect. NO is an important signalling molecule in the body and a potent vasodilator. Converting between the oxides of nitrogen is thus an area of tremendous, and increasing, importance. The ability to selectively convert from one oxide to another would allow, for instance, the safe removal of excess nitrate from groundwater by conversion to nitrogen gas, the *in situ* generation of NO from nitrate salts in the bloodstream, or the efficient removal of N_2O from exhaust gases. Nature possesses enzymes that can mediate these transformations with high specificity and high efficiency, but synthetic systems lag behind in both these respects. Some of the publications reviewed in this tutorial article perhaps suggest how synthetic catalysts could be improved in order to capture some of Nature's reactivity. For example, the explicit inclusion of hydrogen bonding by Fout[27] shows how substrate binding and orientation can be tuned by weak non-covalent interactions, just as in the active sites of the corresponding enzymes.[1] Kudrik and van Eldik's work shows how different binding modes can then lead to very different products during reduction.[26,50] Meanwhile, Kujime *et al* and Woollard-Shore *et al* have shown elegantly how subtle variations in electronics and sterics can have big effects on catalysis.[15,17] Hence by applying the principles of metal-ligand coordination chemistry, we can hope to produce more selective and efficient catalysts for the conversions of the nitrogen oxides. We hope that this review might in some small way inspire a new generation of scientists to strive to develop improved catalysts for these vital and challenging processes.

Biographies

Andrew J. Timmons was born in Edinburgh in 1993 and attended George Watson's College where he first developed an interest in science. In 2011, he started a BSc (Hons) degree in Chemistry and Medicinal Chemistry at the University of Glasgow. His interests lie in renewable energy, small molecule activation and catalysis, which led him to undertake a final year project with Dr. Mark Symes. At the time of writing, Andrew is focussed on his final year examinations and has aspirations to continue his education by pursuing a PhD after graduation.

Mark D. Symes was born in London in 1982 and graduated from the University of Cambridge in 2005. After a PhD at the University of Edinburgh with David A. Leigh (FRS), he was a postdoctoral researcher in the group of Daniel G. Nocera at MIT. He returned to the UK as a postdoctoral research associate at the University of Glasgow in 2011, and he joined the faculty at Glasgow in 2013. His research interests span energy conversion, small molecule activations, electrochemistry and coordination chemistry.

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