The School of Molecular and Life Sciences

The Photochemical Investigation of Manganese and Rhenium Tricarbonyl Complexes

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Declaration

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made.

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

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Abstract

This thesis contains two published chapters, the first was the photochemical investigation and synthesis of ten Manganese(I) Tricarbonyl complexes bound to variably functionalised 5-aryl-tetrazolato ligands. When irradiated with light between 365 – 555 nm, all 10 of the complexes simultaneously released three CO ligands, degrading into their original components and MnO_2. A representative Mn complex was tested for its antibacterial activity against gram-negative Escherichia coli. The compound was not active when the bacterial growth was conducted in the dark. When pre-irradiated with 365 nm light, the compounds degradation products inhibited bacterial growth. Further studies revealed that the anti-bacterial activity was due to the release of 1,10- phenanthroline, which was not active when bound to the Manganese complex.

The second chapter consists of the study of three Re(I) tricarbonyl complexes, with the general formulation $Re(N\text{^}L)(CO)_3X$ (where N^L is a bidentate ligand containing a pyridine functionalized at position 2 with a thione or a thiazol-2-ylidene group and X is either chloro or bromo) with the aim of exploring their photophysical and photochemical properties. Re(I) tricarbonyl diim complexes have been explored extensively for their photochemical and photophysical properties, however, N-heterocyclic carbenes that bind to Rhenium through a pyridyl N atom and a carbene C atom have only began to be explored more recently. The two complexes bound to the thione ligand were found to undergo ligand exchange with solvent when dissolved in acetonitrile, forming $Re(NCMe)_2(CO)_3X$. This was reversible when precipitated with diethyl ether, resulting in the reformation of the original complex. Conversely, the complexes were stable in dichloromethane and acetone. The complex bound to the thiazole-2-ylidene ligand didn't undergo ligand exchange in acetonitrile. Upon excitation to its lowest metal to ligand charge transfer state resulted in ligand substitution and the formation of multiple products, including Re(I) tricarbonyl and dicarbonyl solvato complexes as well as free thiazol-2-ylidene ligand.

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I would like to thank my supervisors Professor Max Massi and Dr Peter Simpson for all your time, patience, teachings and editing on my journey. I have learnt an incredible amount about Chemistry under your teachings and I am very grateful for the opportunities you provided me with.

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Copyright statement

Abbreviations

APAP	acetaminophen
CORM	carbon monoxide releasing molecule
DeoxyMb	deoxymyoglobin
E. coli	escherichia coli
Hb	haemoglobin
HbCO	carboxy haemoglobin
HO	haemoxygenase
IONP	iron oxide nanoparticle
Mb	myoglobin
MbCO	carbonmonoxy myoglobin
MLCT	metal to ligand charge transfer
NADPH	nicotinamide Adenine Dinucleotide Phosphate Hydrogen
NHC	N-heterocyclic carbene
NIR	near infrared
UV	ultraviolet

Table of Contents

Chapter 1: Introduction

1.1 Carbon Monoxide

Carbon monoxide (CO), commonly referred to as the "silent killer", is a colourless, odourless, tasteless gas, well known for its adverse environmental effects and toxicity.[1] This toxicity is due to the ability of CO to bind to the iron (III) centre in haemoglobin (Hb) ~200 times more effectively than oxygen (O_2).[2] Hb is responsible for transferring inhaled O_2 to internal tissues, however, since CO preferentially binds and is much slower to release from Hb, a small increase in CO concentration dramatically reduces O_2 delivery to areas of low oxygen partial pressure, eventually leading to asphyxiation.[2-4] Paradoxically, CO, along with nitrous oxide (NO) and dihydrogen sulphide (H_2S), is also endogenously produced in higher organisms in the transmission of chemical signals that induce certain physiological and biochemical processes in tissues and cells.[5]

1.2 Endogenously Produced CO in the Human Body

Under normal conditions the rate of endogenously produced CO in the human body is ~20 μmol h^{-1}. One of the three isoforms of haem oxygenase, HO-2 is responsible for the base level of CO in body; however, when under stress another isoform of haem oxygenase, known as HO-1, is highly upregulated. This HO-1 upregulation leads to a large increase in endogenously produced CO, which can even be detected in the human breath. Levels of CO detected in the human breath can be used to track the severity of disease states including asthma, bronchitis, cystic fibrosis, diabetes, and rhinitis. The discovery of the role that HO-1 induced CO plays in responding to stress and the cytoprotection they provide to affected tissues led to significant research in further understanding what processes they regulate within the human body. The first known HO-1 regulated stress response was discovered in 1969 and accounts for 86% of the endogenously produced CO in the human body. This CO is formed via the oxidation of haem, catalysed by HO-1. A common example of this process is the colouration changes observed during bruise repair (Figure 2). Upon impact, toxic free haem is released from damaged red blood cells, resulting in dark red/purple discolouration under the skin (Figure 1 and 2a). This haem is oxidised to reaction intermediate α-meso-hydroxyhaem, consuming one equivalent of NADPH and O_2 in the process (Figure 1). α-Meso-hydroxyhaem further reacts with O_2 releasing 1 equivalent of CO and forming verohaem, which oxidises once more to form biliverdin, again consuming NADPH and O_2 (figure 1). During this process the tetrapyrrol ring is cleaved and

the iron centre reduced from iron(III) to iron(II) before being released from the tetrapyrrol coordination sphere. This consumption of oxygen leads to a blue colour whilst green is observed due to the formation of pigment biliverdin (Figure 1 and 2b). Finally, biliverdin is reduced to bilirubin by biliverdin reductase, producing a yellow colour, which finally fades upon the excretion of bilirubin bound glucuronic acid (Figure 1 and 2c). Much of the CO produced during this process is bound to the released iron from haem creating a bright red colour in the final stages of repair. (Figure 2d).[4-7]

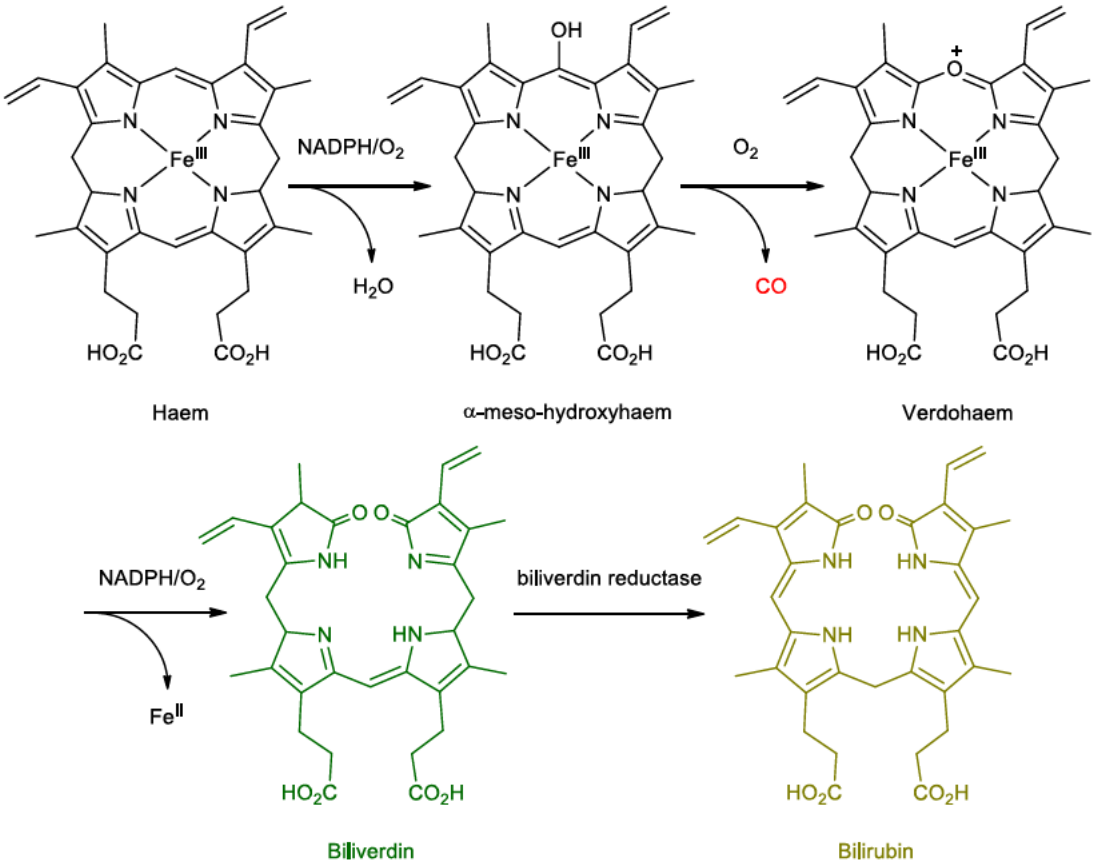


Figure 1: HO catalysed break down of free haem to bilirubin, Fe(II) and CO.

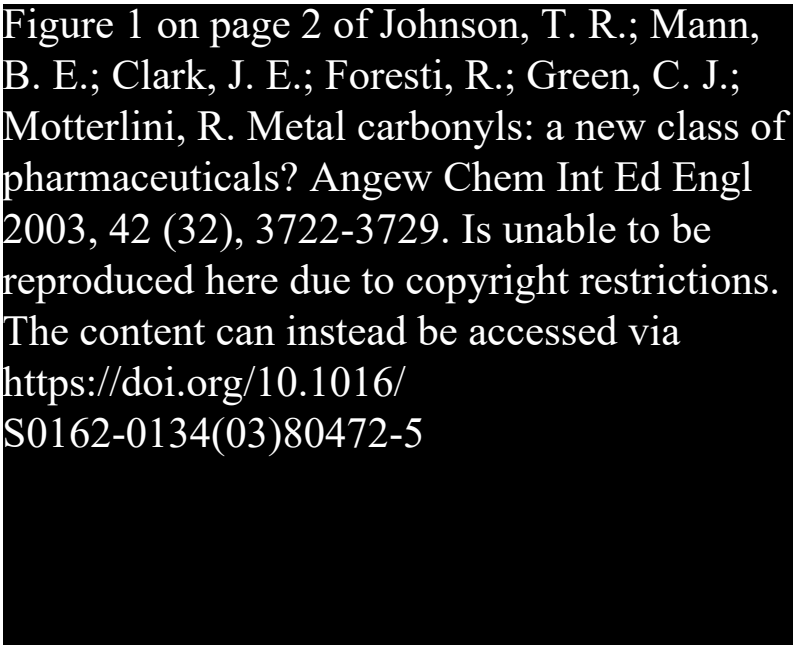


Figure 2: Different colour changes observed during the HO catalysed degradation of free haem; a) initial damage freeing haem, b) break down to biliverdin, c) reduction to bilirubin, d) final stage of repair with free CO binding to free Fe^{2+}. Figure obtained with permission from published work by Johnson *et al.*[5]

1.3 Medicinal Properties of CO

Initial attempts to study the medicinal effects of CO mostly consisted of the use of CO gas.[7] Early research into the physiological properties of CO discovered many beneficial medicinal properties, some of which are listed below, with examples:[5]

- ***anti-inflammatory*** - mice exposed to CO inhalation exhibited lower tumour necrosis factor-α concentration located in plasma whilst also producing increased levels of IL-10 (an anti-inflammatory cytokine).[8]
- ***reduction of transplanted organ rejection*** - a mouse heart was transferred to a rat with the graft lasting 50 days when exposed to 400 ppm of CO gas for 2 days, as opposed to only 5-7 days when only exposed to air.[9]
- ***hyperoxia protection*** - rats pre-exposed to CO inhalation were protected from oxidative lung injury.[10]
- ***ischemia protection*** - pre-exposure to CO minimised damage in a liver that was deoxygenated then reoxygenated (ischemia/reperfusion).[11]
- ***modulation of perfusion pressure*** - CO decreased perfusion pressure in isolated human placenta.[12]
- ***lung protection*** - CO exposure protected against septic shock and lung injury.[13]

- ***regulation of vascular smooth muscle tone and blood pressure under stress conditions***.[14]

After the discovery of the exciting medicinal properties of CO, attempts have been made to deliver CO exogenously to humans. Ikaria *et al.* developed the first device, known as the Covox DS to investigate the delivery of CO through inhalation.[15] The Covox DS administers CO proportional to body weight (mg kg^{-1} h^{-1}) irrespective of respiration rate. CO is able to be delivered via injection into the ventilation circuit of the device or through a nasal cannula. Unfortunately this method of administering CO has significant drawbacks; CO is very difficult to store safely, devices such as the Covox DS are very expensive, it is not target selective to areas within the body and most notably, it is very hard to delivery CO safely through inhalation without effecting oxygen transportation throughout the body.[4-7] In order to circumvent the issues of CO inhalation, founding research by Motterlini *et al*. postulated that CO could be stored in a stable chemical form. This stored CO could be supplied to targeted cells or tissues where, upon activation, CO would be released *in-situ* in a controllable manner. Upon searching the literature, they identified transition metals as the best method of storage as they can bind to CO to form stable metal carbonyl complexes. The term CO-releasing molecule (CORM) was coined to describe this new mode of CO delivery. Ground breaking research by Motterlini *et al.* tested the first CORMs in various biological applications with significant success. Research in the field has rapidly grown to this day with four major modes of triggering CO release from the metal coordination sphere so far explored. These include, ligand-exchange with solvent, enzyme triggered bond cleavage and subsequent oxidation (ET-CORMs), photoactivation (photoCORMs) and most recently, heating via exposure to an alternating current.

1.4 Birth of CO Releasing Molecules

1.4.1 First photoactivatable CO-releasing molecules

The first transition metal complexes Motterlini decided to test for a biological environment was manganese decacarbonyl $Mn_2(CO)_{10}$ and ironpentacarbonyl $Fe(CO)_5$ (Figure 3), as the literature revealed photoexcitation of the complexes lead to the dissociative loss of CO. Of particular interest was $Mn_2(CO)_{10}$, which released CO at a ratio of 1 mol CO per 1 mol $Mn_2(CO)_{10}$ with a half-life <1 minute when exposed to 365 nm light. This was quantified by monitoring the conversion of deoxymyoglobin (deoxyMb) to carbonmonoxy myoglobin (MbCO) in DMSO by UV-Visible spectroscopy. *Ex-vivo* biological studies were performed by perfusing $Mn_2(CO)_{10}$ into isolated rat hearts. Interestingly, hearts dosed with L-nitro-arginine methyl ester (a NO synthase inhibitor that causes coronary constriction) showed significantly

reduced coronary vasoconstriction when also dosed with $Mn_2(CO)_{10}$. Most importantly, this reduction in vasoconstriction was only observed after irradiation with light, with no effect on hearts dosed under darkness. This was the first evidence that a transition metal carbonyl complex could be used to deliver CO to tissue with positive medicinal effect and the complex was named CORM-1. Although CORM-1 showed promising therapeutic application and mode of activation, it required DMSO for solubility in aqueous solution and for photodissociation to occur, as well as being highly toxic. This resulted in the search for water soluble complexes with different activation modes of CO release.[6]

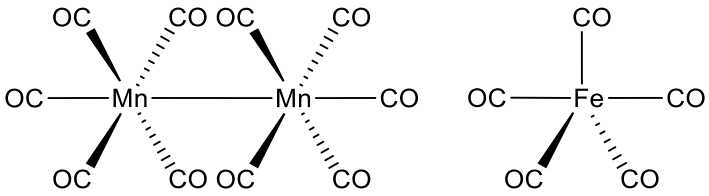


Figure 3: First photoCORMs test for biological application $Mn_2(CO)_{10}$ (CORM-1) and $Fe(CO)_5$.

1.4.2 Ligand Exchange Triggered CO-releasing molecules CORM-2, CORM-3 and ALF-794

The group shifted its focus to studying ruthenium based CORMs as many ruthenium based compounds were being tested as anti-inflammatory and cancer killing prodrugs. Tricarbonyldichlororuthenium (II) dimer $(Ru(CO)_3Cl_2)_2$, later termed CORM-2 (Figure 4), was chosen from a wide range of ruthenium carbonyls as literature research indicated the complex would react reversibly with DMSO to liberate CO. CORM-2 was dissolved in a DMSO/phosphate buffered saline (PBS) solution containing Mb, which converted to MbCO in <1 minute. Isolated rate aortae dosed with DMSO/PBS containing CORM-2 were found to produce profound vasodilation. The vasoactive properties of CORM-2 were further supported when rats, dosed with CORM-2, showed no increase in mean arterial pressure when exposed to acute hypertension. Although a new mode of solvent induced CORM activation was discovered, CORM-2 (as observed in CORM-1) also suffered from poor solubility in aqueous media requiring significant DMSO.

The next CORM selected for trials was tricarbonylchloro(glycinato) ruthenium(II), [$Ru(CO)_3Cl$(glycinate)], later termed CORM-3. The addition of glycinate provided water solubility to CORM-3, which dissolved in PBS containing Mb, without any DMSO. CORM-3 underwent ligand exchange releasing CO at a rate of 1 mol CO per 1 mol CORM-3 with a half-life of 1 minute. CORM-3 was then tested for its vasodilatory effect on isolated aortic rings from rats. These aortic rings were precontracted with phenylephrine, then dosed with CORM-3, resulting in a profound relaxation within minutes. The liberation of CO from CORM-3 led to the formation of an inactivated CORM (later termed iCORM) which was used as a negative control. The CO depleted iCORM had no vasodilatory effect thus proving that CO was directly responsible for the vasorelaxation properties observed from treatment with CORM-3.[16]

A more recent ligand exchange triggered CORM, $Mo(CO)_3(CNCMe_2CO_2Me)_3$, termed ALF-794, was synthesised by Romao *et al*.[17] The isocyanide ligands were modulated in order to form similar complexes with increased water solubility and target specificity. These complexes were designed by Alfama and tested for treatment against acetaminophen(APAP)-induced liver failure. Variations in the number of methyl substituents on the isocyanide ligand [$N{\equiv}C\text{-}C(CH_3)nH_2\text{-}n\text{-}COOH$] affected the amount of CORM uptake in the liver. When compared to blood CO level, liver CO concentration increased by a factor of 0.3 for n = 0, 1 for n =1 and 5.3 for n = 2. In addition, n = 2 complex was found to accumulate in the liver more than the kidneys, providing specificity. In contrast, when the isocyanide ligands contained two anionic carboxylates, the complex preferentially targeted the kidneys over the liver. The complexes were then tested for their biological activity in mice. CO release was triggered by rat liver microsomes, with ALF-794 reducing alanine aminotransferase (ALT) levels when compared to an untreated control. Increased levels of ALT are an indicator for hepatocellular carcinoma (the most common form of liver cancer).

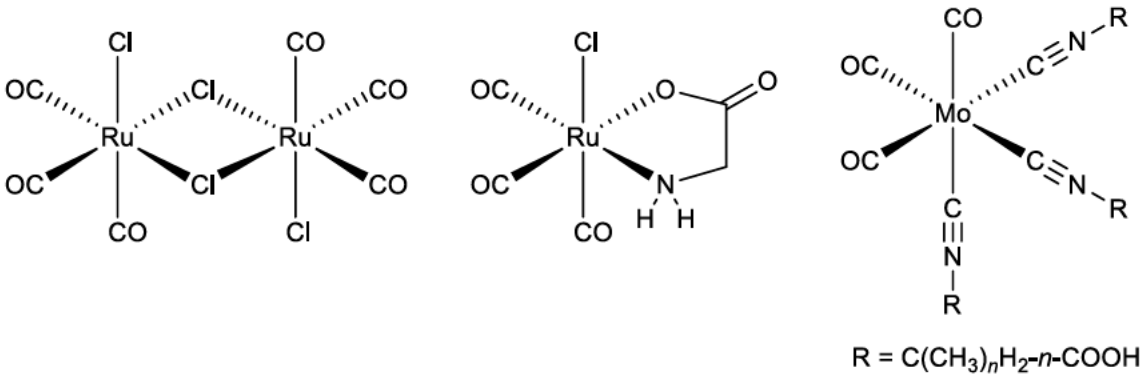


Figure 4: Important ligand exchange CORMs tested for biological application $(Ru(CO)_3Cl_2)_2$ (CORM-2), $Ru(CO)_3$(glycinate)Cl (CORM-3) and $Mo(CO)_3(CNCMe_2CO_2Me)_3$ (ALF-794).

1.4.3 pH/Ligand Exchange CO-releasing molecule CORM-A1

Upon further investigation, the group of Motterlini *et al.* discovered that certain radio imaging compounds bound to CO could be prepared using a boron-based carbonylating CO source, potassium boranocarbonate. A similar compound, sodium boranocarbonate $Na_2H_3BCO_2$, was selected for testing as the first non-transition metal based CORM, and later named CORM-A1 (Figure 5). CORM-A1 was water soluble and dissolved in PBS (Phosphate-buffered saline) containing Mb, releasing 1 mol CO per mol of CORM-A1 with a relatively slow half-life, when compared to CORM-3, of 21 minutes. When the pH of the PBS solution was lowered it was found that the half

-life of CO formation decreased, while conversely, when the temperature of the solution was decreased the half-life of CO formation increased, revealing the mode of activation to be both pH and temperature dependant. CORM-A1 was perfused into isolated rate aortic rings pre-constricted with phenylephrine and the resulting vasodilation properties compared to that of CORM-3. The rates of relaxation reflected the differing release rates of CO, with CORM-A1 producing a much slower and sustained relaxation over 30 minutes. This provided evidence for the importance of dosage control and the profound effect CO release rate can have on vasoactive properties.[18]

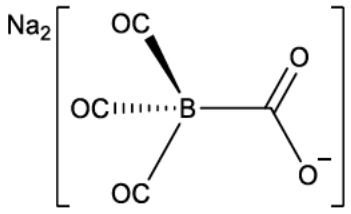


Figure 5: First pH/ligand exchange triggered CORM tested for biological application $Na_2H_3BCO_2$ (CORM-A1).

1.4.4 Enzyme Triggered CO-releasing molecule

To circumvent the issues of immediate CO release in media observed with pH and substitution triggered CORMs, Schmalz *et al.* created a novel class of enzyme triggered CORMs (ET-CORMs). The most prominent structure was an iron(0) tricarbonyl bound to a dienol coligand. The dienol was functionalised with esters and phosphates, which stabilised the dienolate form (Figure 6). When esterases or phosphatases were introduced an enzymatic cleavage of the C-O or P-O bonds occurred resulting in the production of the enolate form. The resulting enone was very labile, decomposing immediately in air via oxidation, releasing iron(III) and three units of CO per complex. Not only do these ET-CORMs provide control over the rate of CO release, but they are also easily functionalised for targeted tissue specificity.

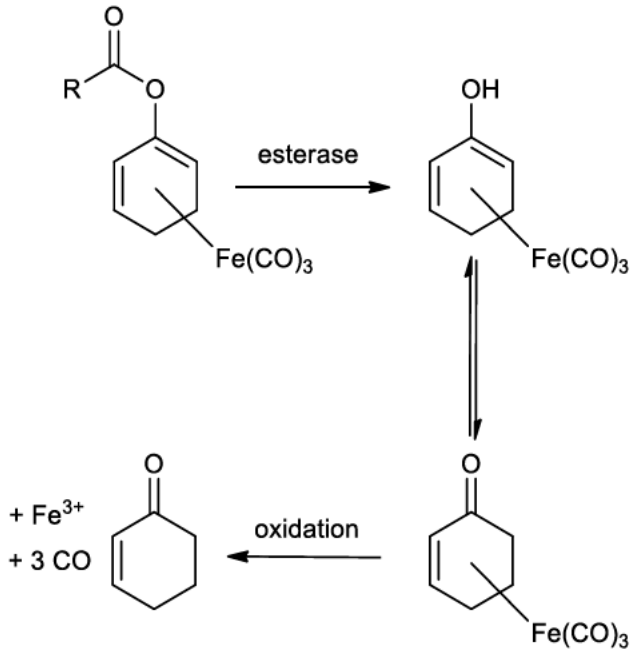


Figure 6: First oxidation triggered CORMs based on iron dienyl(phosphate/ester stabilised) tricarbonyl complexes (ET-CORMs).

1.4.5 Magnetic Field Triggered CO-releasing molecule

Another novel method of triggering CORM release at a desire time and location is heating produced from an alternating magnetic field. Janiak *et al.* synthesised various dicarbonylchlorido(imidazole-2-carbaldehydeoxime)(alkoxycarbonyl) ruthenium(II) complexes (oximeCORMs) (Figure 7).[19] These oximeCORMs were immobilised by binding to a catechol-modified backbone on the surface of maghemite iron oxide nanoparticles (IONPs). The oximeCORM-IONPs were coated with dextran, providing water solubility, then placed inside protective polymer alginate shell to allow monitoring of the aliginate-dextran-oximeCORM-IONPs CO release in a Mb assay via UV-VIS absorption. The aliginate-dextran-oximeCORM-IONPs CO release half-lives were determined to be ~814 min at 20 °C, 346 min at 37 °C and 73 min at 50 °C. Even though the aliginate-dextran-oximeCORM-IONPs released some CO in field free conditions, the half-lives significantly decreased when an alternating magnetic field (31.7 kA m^{-1}, 247 kHz, 39.9 mTesla) was applied.[19]

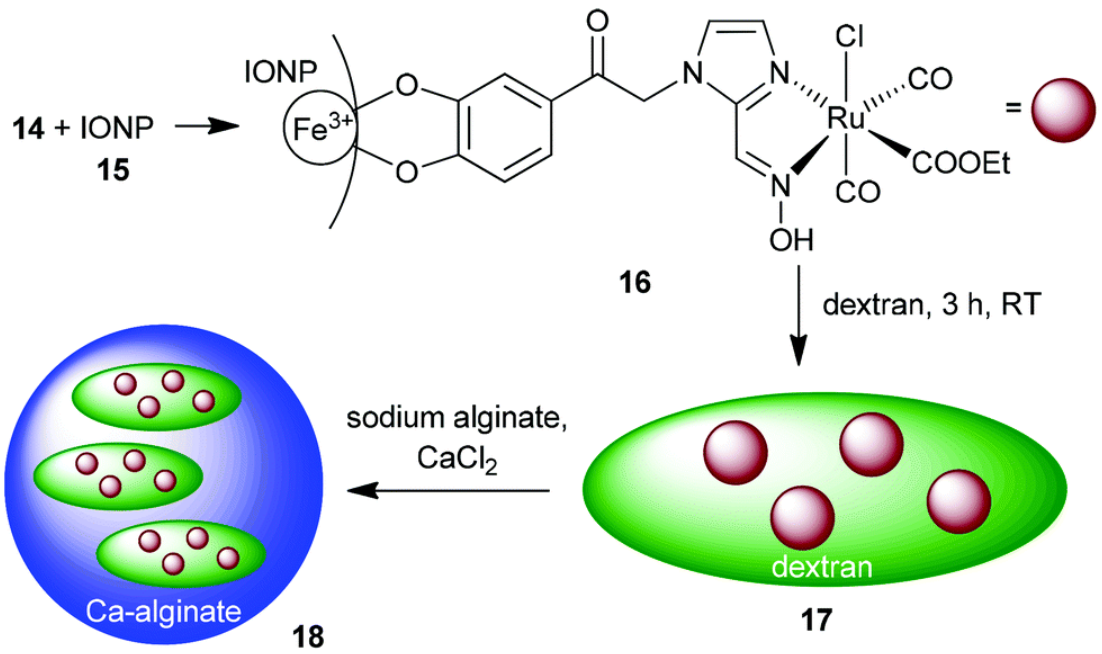


Figure 7: Preparation of magnetic field triggered aliginate-dextran-oximeCORM IONP. Image taken with permission from publication by Janiak *et al.*[19]

1.5 Early Ultra-Violet Activated photoCORMs

For a CORM to be most effective it needs to be soluble in aqueous media and break down to non-toxic products that will not further react within the human body to form unknown species. Being able to functionalise the CORM to have targeted specificity is also important to have a desired response. Due to the instant release of CO from many ligand exchange or pH triggered CORMs; they have limited ability to target specific areas within the body. CORMs that can be activated by light are currently extensively being explored by many research groups, as they ideally allow for precise spatial and temporal control of CO release in biological systems. Using light as a trigger provides dosage control through exposure time and the ability to active the CORM at a targeted location. Although Motterlini *et al.* were the first to use photoCORMs as a CO delivery method to biological targets, Schatzschneider *et al.* are widely credited as the first to design new photoCORMs for this purpose. The first photoCORM developed by this group was tris(pyrazolyl)methanetricarbonyl manganese(I) hexafluorophosphate, $[Mn(tpm)(CO)_3]PF_6$. Photolysis of $[Mn(tpm)(CO)_3]PF_6$ at 365 nm yielded 2 mol CO per mol $[Mn(tpm)(CO)_3]PF_6$ in a DMSO/PBS solution as quantified by the conversion Mb to MbCO. $[Mn(tpm)(CO)_3]PF_6$ dissolved in DMSO was tested for its photo induced cytotoxicity on HT29 human colon cancer cells *in vitro*. Illumination with 365 nm light was applied to the cells, resulting in significant photoinduced toxicity. This raised questions about the purpose of CO delivery. Previous studies showed that CO delivery resulted in wound healing and cytoprotective properties, suggesting that CO improves cell growth and motility, yet in this case the opposite was observed. This result indicated that photoCORMs could also be used as anti-tumour agents. The Jekyll and Hyde character of endogenously produced CO makes controlling timing, location and dosage extremely important.[20-22] Berends and Kurz published a new tripodal based *fac*-$Mn(CO)_3^+$ photoCORM where the pyrazole ring was substituted with acetate, resulting in the neutral complex $Mn(CO)_3$(bpzaa). $Mn(CO)_3$(bpzaa) was compared to $[Mn(tpm)(CO)_3]PF_6$ with both releasing three CO molecules per complex when exposed to UV light for long time periods. They were also able to determine that this CO loss was sequential with the first CO lost due to photo-irradiation whilst the second and third CO ligands were lost due to sequential oxidation of the Manganese centre from Mn(I) to Mn(II) and Mn(II) to Mn(III) respectively.[23] With $[Mn(tpm)(CO)_3]PF_6$ photochemical properties now understood, Schatzschneider *et al.* began to explore a synthetic method to attach peptides to functionalised versions of the complex. The rational of attaching the peptides was to form bioconjugate photoCORMs that accumulate in targeted tissue and only exert cytotoxic activity upon

irradiation at a well-defined area. Initially, the tpa ligand was reacted to incorporate a terminal alkene which, subsequently, was used to form the analogous complex $[Mn(tpm\text{-}L1)(CO)_3]PF_6$. The Sonogashira cross-coupling reaction used to bind $[Mn(tpm\text{-}L1)(CO)_3]PF_6$ to a 4-iodophenylalanine residue in the middle of the amino acid sequence or, in a separate reaction, a *N*-terminal iodobenzoic acid. A copper catalysed 1,3-dipolar cycloaddition "click" reaction (CuAAC) was also successfully performed between $[Mn(tpm\text{-}L1)(CO)_3]PF_6$ and a *N*-terminal azido acetic acid on the amino acid. In addition, the reactions were unsuccessful when attempting to bind the tpm-L1 ligand to the peptide, enforcing a "post labelling strategy". These three reactions provided, for the first time, peptide bioconjugates of a CO releasing molecule. All three peptide bound complexes were soluble in aqueous Mb assays, found to be dark stable and released CO when exposed to 365 nm light.[24-28]

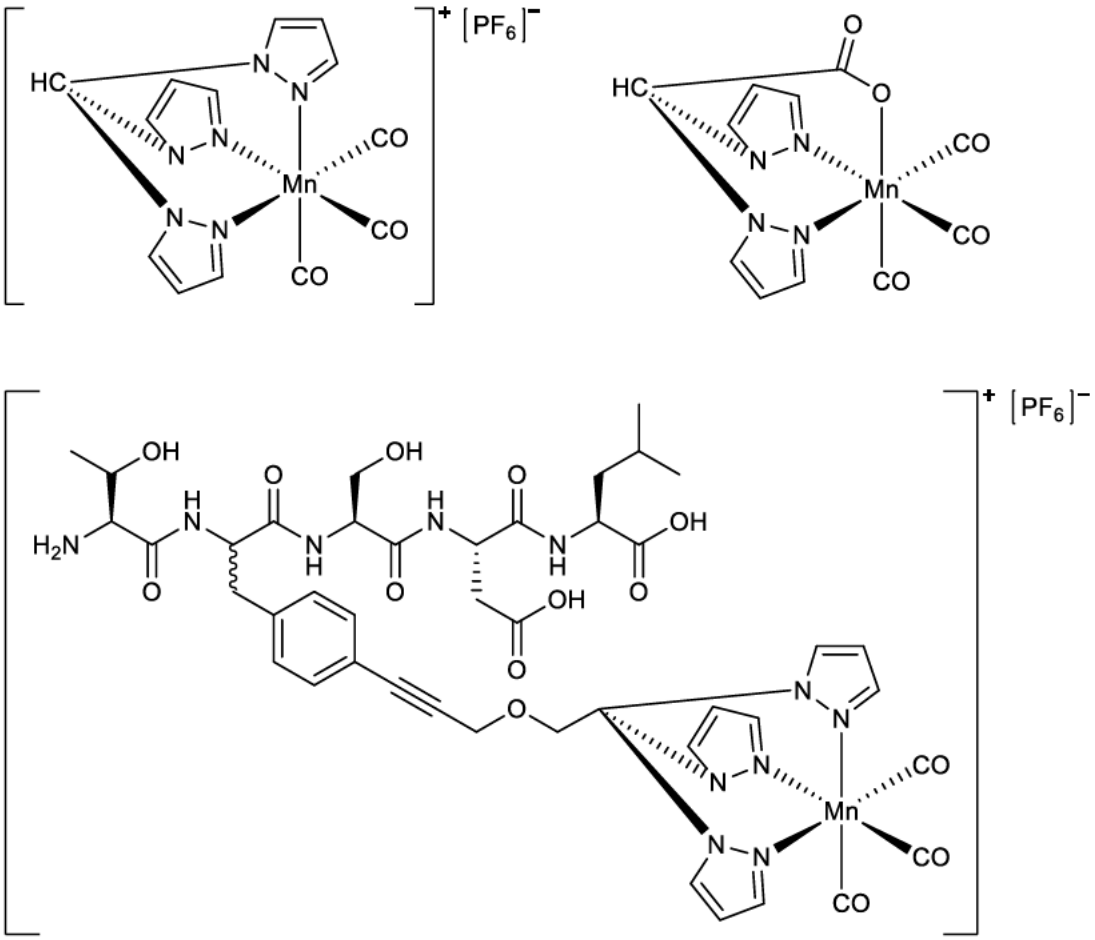


Figure 8: Early UV light activated photoCORMs $[Mn(tpm)(CO)_3]PF_6$, $Mn(CO)_3(bpzaa)$ and $[Mn(tpm\text{-}L1)(CO)_3]PF_6$ bound to a side-chain functionalised peptide bioconjugate.

1.6 Ideal Properties for a photoCORM

A significant drawback associated with the majority of early manganese photoCORMs is that they require ultraviolet (UV) or blue shifted visible light in order to trigger the release of CO. Besides the obvious issue of UV light causing damage to DNA in cells, both these frequencies of light transmit poorly through biological fluids and tissues reducing many of the early studied photoCORMs to surface applications. For example, oxygenated whole blood (Figure 9) absorbs most of the source light between wavelengths 200-600 nm. The optimal irradiation window to maximise transmittance through the body lies between 650-1350 nm. This has created considerable interest in producing photoCORMs that can be activated with tissue penetrating red to near infra-red light.[29-31]

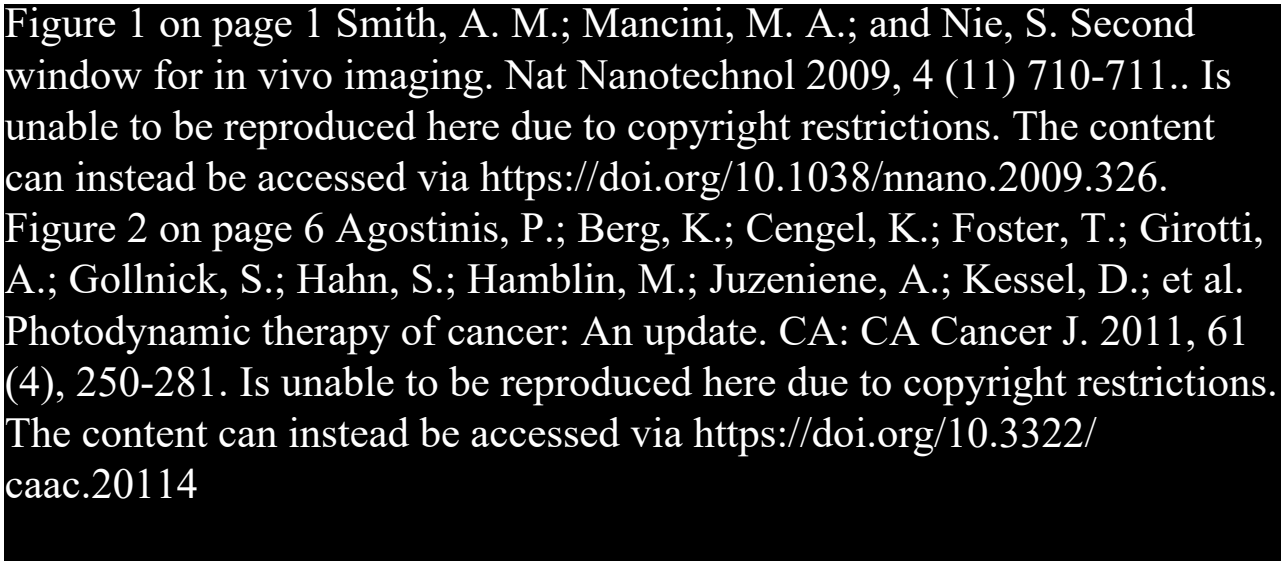


Figure 9: Effective attenuation of different wavelengths of light through biological fluids and tissues. Images taken with permission from Smith *et al.* and Agostinis *et al.*[32]

1.7 Visible and Near Infrared Activated PhotoCORMs

In order to overcome the issues associated with UV activated photoCORMs Mascharak *et al.* investigated the effect of ligand design to red-shift the MLCT absorbance band of Mn(I) centred photoCORMs. They began with the ligand tris(pryridyl)amine (tpa) synthesising the complex $[Mn(tpa)(CO)_3]ClO_4$ which had an MLCT λ_{max} absorbance of 330 nm (UV). In order to red shift the MLCT band a new complex was synthesised from N,N-bis(2-pyridylmethyl)amine (dpa), $[Mn(dpa)(CO)_3]ClO_4$. Due to the increased conjugation of the dpa ligand, the MLCT λ_{max} absorbance of $Mn(dpa)(CO)_3(Br)$ redshifted 20 nm to 350 nm. To build on this proof of concept pyridylmethyl(2-quinolylmethyl)amine (pqa), a ligand with further increased conjugation, was used to form $[Mn(pqa)(CO)_3]ClO_4$ redshifting the MLCT λ_{max} absorbance to 360 nm.[33, 34]

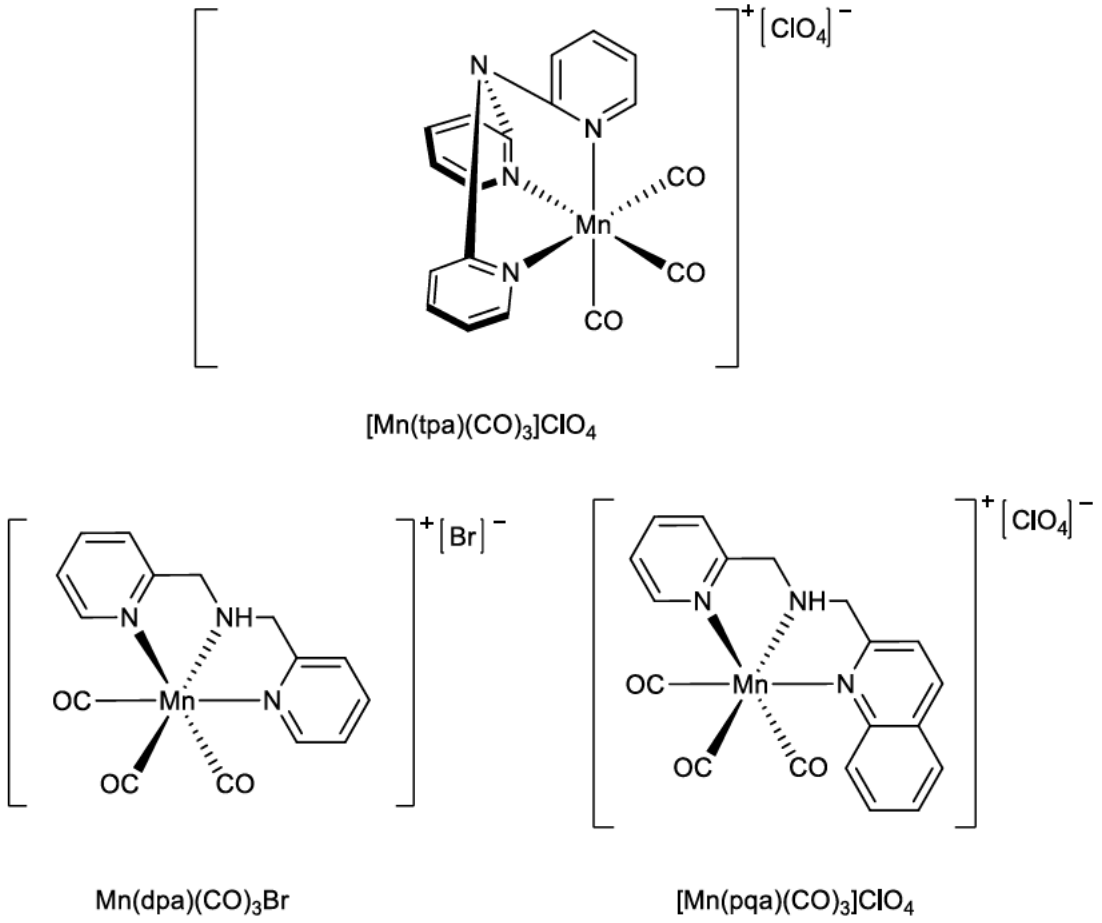


Figure 10: Mascharak's first generation of polypyridine Mn(I) carbonyl complexes.

Mascharak *et al.* then synthesised a new set of Mn(I) carbonyl complexes from ligands 2-(phenyliminomethyl)quinoline (pimq), 2-quinoline-N-(2-methylthiophenyl)-methylenimine

(qmtpm) and 2-pyridyl-N-(2-methylthiophenyl) methylenimine (pmtpm). These three ligands contained aromatic N-donors to further increase conjugation and therefore further redshift the MLCT band as observed in the first generation of Mn(I) carbonyl complexes. A $–SCH_3$ group was incorporated in ligands qmtpm and pmtpm to facilitate CO release by potentially forming a five membered ring to fill the coordination sphere. Thirdly, the ancillary ligand was studied by replacing acetonitrile with bromide as it was theorised that the strong σ-donation properties of the bromide would destabilise the occupied molecular orbitals and therefore lower the energy of the MLCT transition. Four complexes $Mn(pmtpm)(CO)_3Br$, $[Mn(pmtpm)(CO)_3(MeCN)]ClO_4$, $Mn(qmtpm)(CO)_3Br$ and $[Mn(qmtpm)(CO)_3(MeCN)]ClO_4$ were synthesised in order to explore these variations. Electronic absorption studies were conducted on all four complexes. Increase in conjugation resulted in a significant redshift in MLCT λ_{max} absorbance between complexes $[Mn(pmtpm)(CO)_3(MeCN)]ClO_4$ (λ_{max} = 390 nm) and $[Mn(qmtpm)(CO)_3(MeCN)]ClO_4$ (λ_{max} = 435 nm). In addition, the strong σ donating bromide ancillary ligand further redshifted MLCT λ_{max} absorbance for complexes $Mn(pmtpm)(CO)_3Br$ (λ_{max} = 500 nm) and $Mn(qmtpm)(CO)_3Br$ (λ_{max} = 535 nm). This research highlighted design strategies to create photoCORMs that can be activated by visible light which continue to be employed in current research in the field.[33, 34]

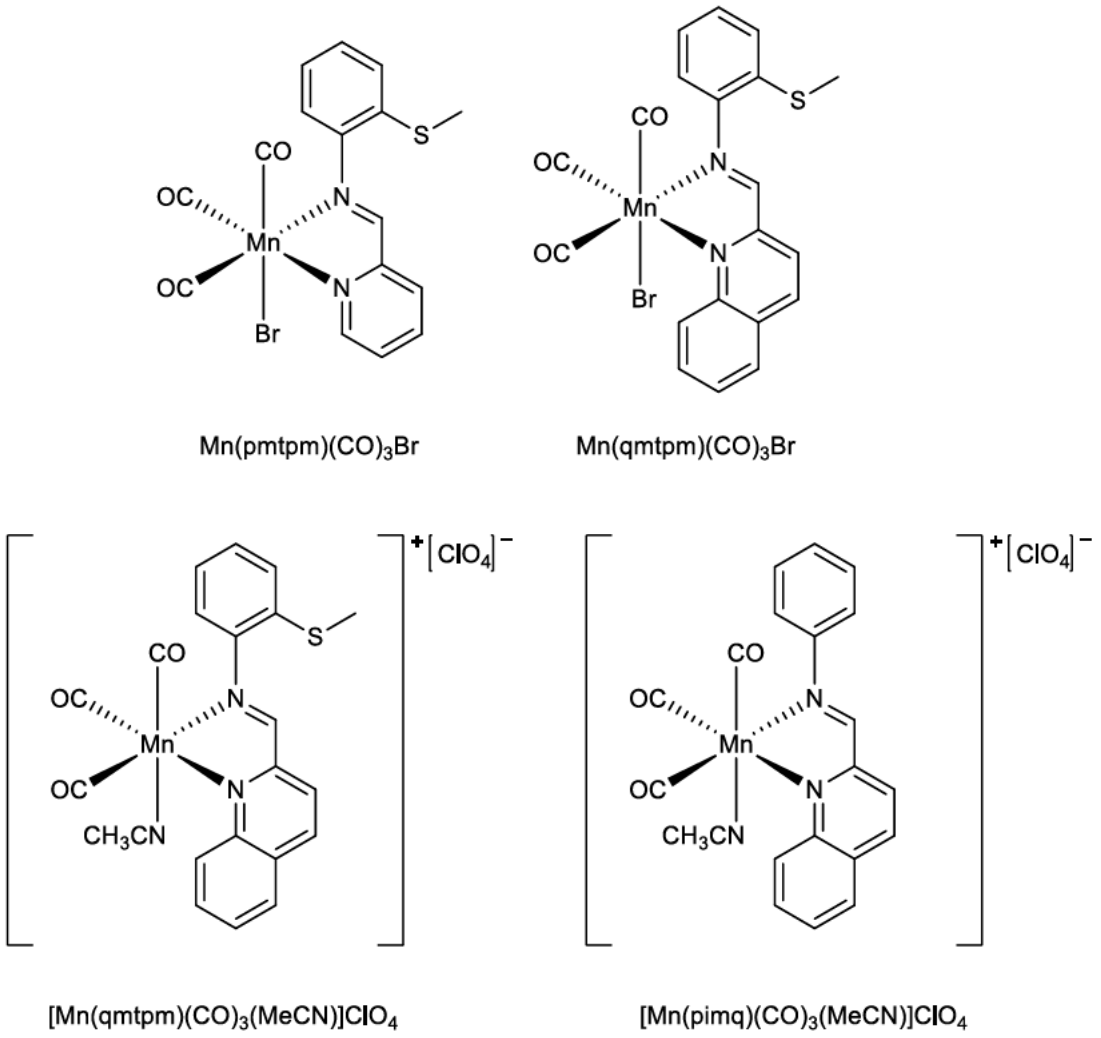


Figure 11: Mascharak's second generation of conjugated bidentate pyridine/imine Mn(I) carbonyl complexes.

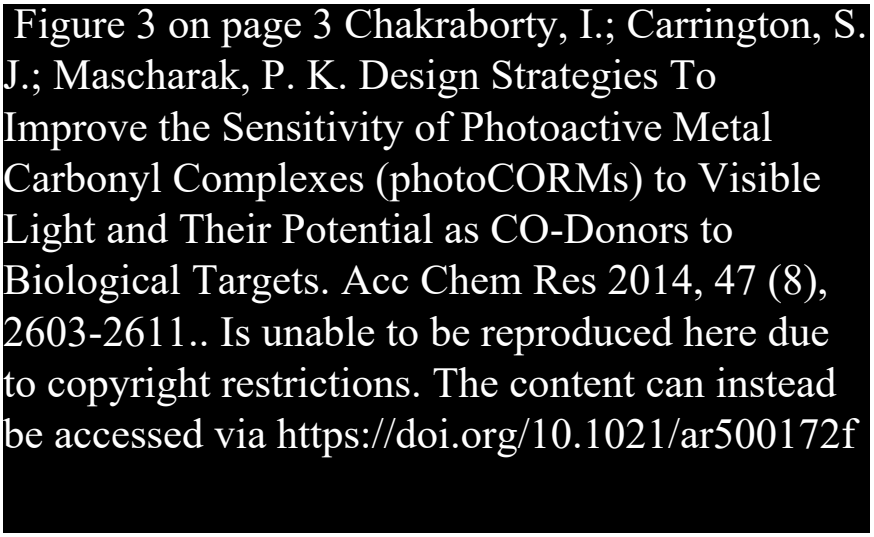
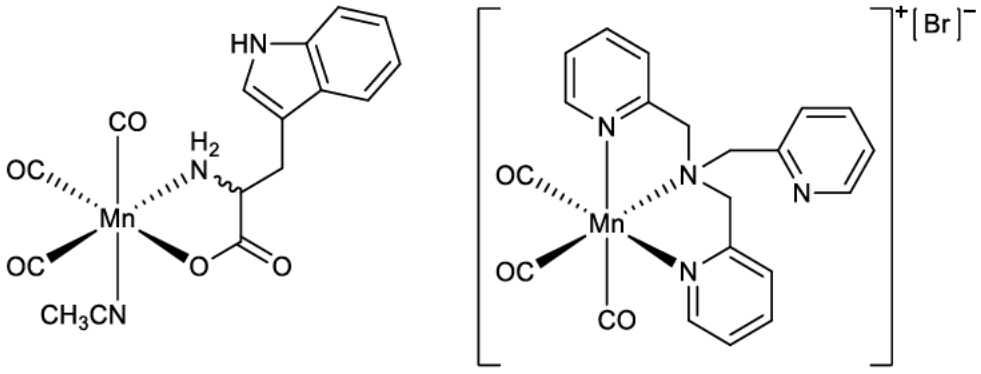


Figure 12: Electronic absorption spectra of Mn(pmtpm)$(CO)_3$Br (blue trace), [Mn(pmtpm$(CO)_3$(MeCN)]ClO_4 (green trace), Mn(qmtpm)$(CO)_3$Br (pink trace), and [Mn(qmtpm$(CO)_3$(MeCN)]ClO_4 (red trace). Image taken from publication by Mascharak *et al.*[34]

1.8 PhotoCORMs as Anti-bacterial Agents

With growing global concern over the rate of new bacterial strains and the reduction of anti-biotics able to treat them significant research has been conducted to find new drugs. PhotoCORMs are one such pro-drug currently being investigated, for example research by Fairlamb *et al.*[35] described a tryptophan dervived Mn(I) carbonyl complex known as TryptoCORM (Figure 13). TryptoCORM released 2 moles of CO per mol of CORM when exposed to 400 nm light, as well as tryptophan and an unknown Mn species. The complex exhibited low toxicity against mammalian cells yet reduced the growth of *Escherichia coli* (*E. coli*). The inhibition of *E. coli* growth only occurred when the complex was exposed to 400 nm light and was attributed to CO release as similar tests with the iCORM showed no effect on bacterial growth.[35-37] Another photoCORM tested for its anti-bacterial activity was [Mn$(CO)_3$(tpa- κ^3 *N*)]Br (tpa = tris(2-pyridylmethyl)amine) published by Poole and Schatzschneider *et al.*[38] [Mn$(CO)_3$(tpa-κ^3 *N*)]Br had no effect on *E. coli* growth in the dark yet inhibited growth when the complex was irradiated with 365 nm light. ICP-MS studies indicated a large amount of metal-carbonyl complex internalised in the *E. coli* cells.[38-41]

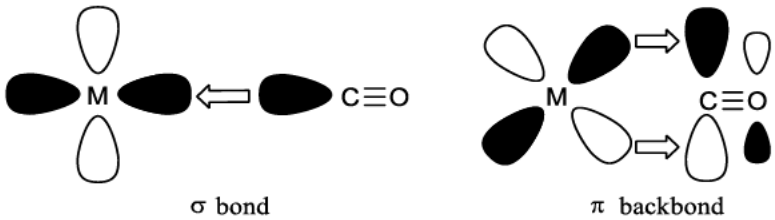


TryptoCORM Mn(tpa-κ^3*N*)$(CO)_3$Br

Figure 13: Antibacterial photoCORMs TryptoCORM and $Mn(CO)_3$(tpa- κ^3 *N*)Br.

1.9 Photochemistry of Manganese CO PhotoCORMs

Manganese complexes are widely studied in this field as they have highly favourable and tuneable electronic and photochemical properties. Manganese(I) carbonyl PhotoCORMs exhibit a metal to ligand charge transfer (MLCT) absorbance band when excited with light. An MLCT transition is the transfer of an electron from a d orbital of the metal centre to the unoccupied anti-bonding pi molecular orbital (π* MO) of a conjugated ligand, such as phenanthroline. MLCT transitions are more likely to occur in complexes that contain low oxidation state metal centres, and, ligands with easily accessible unoccupied π* MO's, making manganese-(I) an ideal metal centre for a photoCORM.[42] A d-metal CO bond can be described in two parts: a sigma bond (σ) between an electron pair of carbon in CO and an empty d orbital of the metal, and, a pi (π) bond between the filled d orbitals of the metal and the empty π* MO's of CO (more commonly known as back bonding).[43]



σ bond π backbond

Figure 14: σ donation and π back bonding between d metal and CO.

In reality, d-metal CO bonding is a resonance between the two following forms:

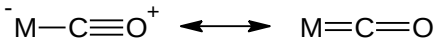


Figure 15: Resonance forms of metal carbonyl bond.

The structure on the left occurs without back bonding, weakening the M-CO bond. Whilst the structure on the right is a result of total back bonding strengthening the M-CO bond. When a manganese carbonyl PhotoCORM complex is excited to the ^{1}MLCT excited state, electron density is transferred from the metal centre to the empty π* MO of a polypyridyl based coordinated ligand. This shift in electron density from the metal to the ligand reduces the amount of back bonding, shifting the resonance form to the left and labilising the Mn-CO bond resulting in CO release. [20, 30, 34, 44]

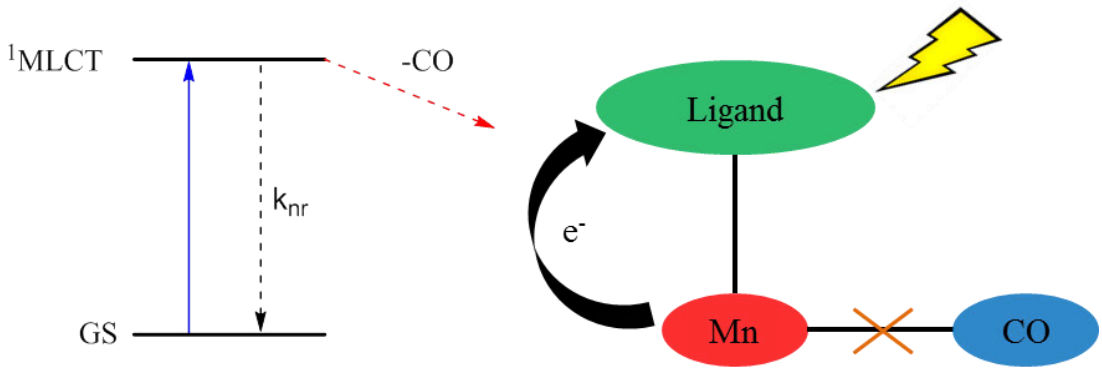


Figure 16: Jablonkski diagram (left) and general system (right) of a Mn PhotoCORMs excitation induced ^{1}MLCTand subsequent CO loss.

1.10 Tetrazoles

Tetrazoles are a class of aromatic heterocyclic compounds composed of a five membered ring containing four nitrogen atoms and one carbon atom. They are isosteres[45] of carboxylic acid and have a similar pK_a, ~5.[46] Tetrazoles are metabolically more stable than carboxylic analogues, and as a result, are used in medicinal chemistry as an isosteric substitute for carboxylic acid substituents in biologically active molecules. Biological properties of various tetrazoles include antibacterial, antifungal, antiinflammatory, antiviral, antituberculosis, cyclo-

oxygenase inhibition and anticancer.[47-49] Tetrazoles have two tautomeric structures differentiated by the location of tetrazolic proton being on either the N1 or N2 atom (Figure 17). The two tautomers can be identified via ^{13}C-NMR as the tetrazolic carbon (C_T) has a different chemical shift for each. The C_t chemical shift for the N_1 tautomer ranges from 152-156 ppm whilst the C_t chemical shift for the N2 tautomer is between 162- 165 ppm.[50, 51]

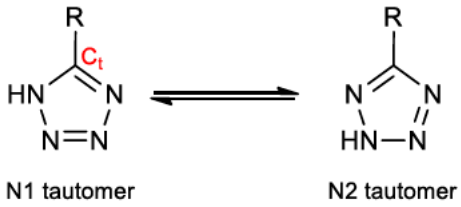


Figure 17: N1 and N2 tautomers of tetrazoles.

1.11 N-Heterocyclic Carbenes

A singlet carbene is divalent sp^2 hybridised neutral carbon atom with two single bonds, a lone pair of valence electrons in a sp^2 orbital and an empty 2p orbital (Figure 18).

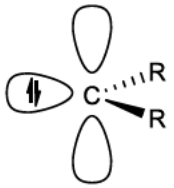


Figure 18: Simplified representation of a singlet carbene.

Carbenes are extremely reactive and tend to form dimers making them very difficult to isolate.[52] The search to isolate a carbene was started over 150 years ago by French Chemist Jean Baptiste André Dumas. Even though he was unsuccessful, it led to an explosion of research and growth in knowledge about the illusive molecule over the next century. Despite this expansion in understanding, carbenes were viewed as shorted lived highly reactive intermediates until 1968 where founding research by Wanzlick *et al.* discovered that carbenes adjacent to heteroatoms (in particular nitrogen), were significantly more stable than traditional carbenes.[53] This increased stability was attributed to the ability of the adjacent nitrogen atoms to donate electron

density to the empty 2p orbital of the carbon atom. The two lone pair π electrons of the nitrogen atoms are also shared between the carbon and nitrogen atoms resulting in an overall resonance stabilisation of the carbene (Figure 19).

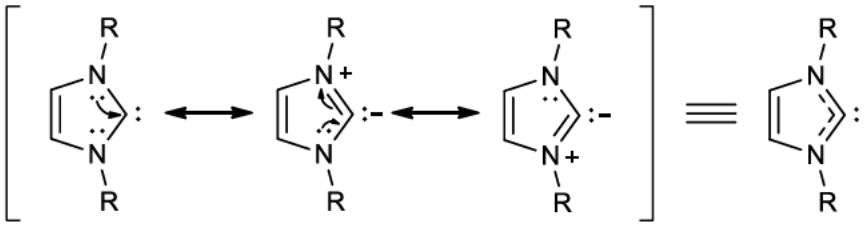


Figure 19: Electron donation from adjacent nitrogen atoms stabilising the carbene carbon atom.

Carbenes next to heteroatoms are known as persistent carbenes due their increased stability compared to traditional hydrocarbon based carbenes. The most common persistent carbene consists of two adjacent nitrogen atoms (diaminos) but other heteroatoms including sulphur and oxygen also have been isolated. Of the diamino based carbenes, the most well-known are N-heterocyclic carbenes (NHC) containing a cyclic ring as observed in Figure 19.

1.12 Donor Properties of N-Heterocyclic Carbenes

Like phosphine ligands NHC carbene ligands are strong σ donors and generally poor to moderate π acceptors. However, NHCs are easier to synthesise and modulate than phosphines making them a useful alternative as a ligand. NHCs have several modes of binding and can act as bis or tris- chelators. They can also be used in pincer, tripodal and bridging motifs, allowing NHCs to form many coordination geometries and the ability to bind to a variety of metal centres. Because NHCs form stable metal complexes, they have been used as ligands in a wide range of fields such as catalysis (both homo- and heterogeneous),[54, 55] medicinal studies,[56, 57] electrochemistry,[58] radiochemistry,[59] enantiomeric separation,[60] and cellular imaging (diagnostics).[61, 62]

1.13 Luminescence of Rhenium(I) Complexes

Transition metal complexes have been researched extensively for their luminescence properties ever since early studies on the emission of tris(bipyridine)ruthenium(II) $[Ru(bpy)_3]^{2+}$.[63-65] Some of the potential applications of these heavy metal based complexes include photocatalysis, optics, sensors and diagnostic agents. Out of the widely researched transitions metals used to form luminescent complexes, Re(I) has the most unique chemical properties. Elemental Re can form complexes in a variety of oxidation states which is typical of elements in group VII of the periodic table. However, it is complexes containing Re(I) that are the most heavly researched in the field of heavy metal complex luminescence.[66]

A standard Re(I) complex for luminescence has the general formula $[Re(diim)(CO)_3L]^{0/+}$, where the diim represents a diamine ligand, such as phenanthroline, and the L an ancillary ligand of neutral or cationic charge. These complexes have a low spin $5d^6$ valence electronic configuration resulting in a ground state with singlet multiplicity. As a result, electronic excitation of the complexes results in a singlet manifold of excited states with a ligand centred π- π^* character (LC) or a metal-to-ligand charge transfer (MLCT), where the Re to diim MLCT states are generally lower in energy than the LC states. These transitions are easily determined in UV-Vis absorption spectra of $[Re(diim)(CO)_3L]^{0/+}$ complexes with MLCT transitions appearing as broad bands or shoulders of lower intensity generally between 350-410 nm. Conversely, LC transitions exhibit intense bands between 250-350 nm. Upon population of the singlet manifold (S_n), the excited electronic configuration undergoes internal conversion (IC) with complex vibrationally relaxing to the lowest energy excited configuration (S_1). The strong spin-orbit coupling of the heavy metal Re results in a mixing of singlet and triplet spin multiply states. This relaxes the spin selection rule allowing for intersystem crossing (ISC) between the lowest in energy singlet and highest in energy triplet spin multiplicity states, typical of heavy metal containing complexes.[67] The excited triplet electronic configuration again undergoes IC to the lowest in energy excited triplet configuration (T_1). This fast population of the lowest in energy triplet excited state, in general ^{3}MLCT, is the source of the luminescence properties of $[Re(CO)_3(diim)L]^{0/+}$ complexes. The spin forbidden character of phosphoresce decay from the populated ^{3}MLCT to the singlet ground state results in longer excited state lifetime decays in the range of hundreds of nanoseconds to few microseconds. The phosphoresce of $[Re(CO)_3(diim)L]^{0/+}$ complexes, which depends upon the relative energy between the LC and MLCT excited states, has been explored extensively with more advanced ligands systems over the years.[68-70]

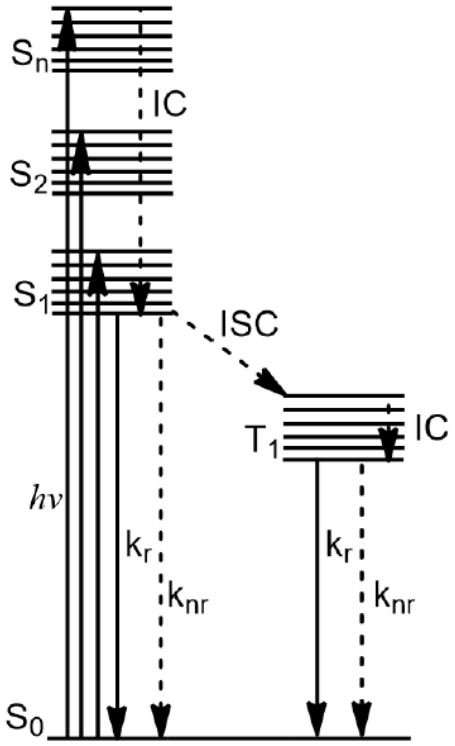


Figure 20: Jablonski diagram of general electronic transitions.

1.14 Energy modulation of excited states

In order to expand upon the early research on $[Re(CO)_3(diim)L]^{0/+}$ the chemical identity of the diim ligand began to be modified via the addition of electron withdrawing or donating functional groups and/or increasing the π conjugation on the diim ligand. With the excited state being MLCT in character, it can be explained with a simple electronic configuration where an electron in the 5d orbitals of the Re(I) centre is excited to the empty anti-bonding π^* orbitals located on the diim ligand. By adding an electron donating functional group to the diim ligand, the MLCT states of the Re(I) complex generally increases in energy. Conversely, if an electron withdrawing functional group is added to the diim, the MLCT states decrease in energy. In addition, the 5d orbitals of the Re(I) centre can also be stabilised by using an electron poor ancillary ligand or destabilised with an electron rich ancillary ligand. Destabilising the 5d orbitals of the Re(I) centre results in a lowering of energy of the MLCT states whilst stabilising the 5d orbitals causes an increase in energy of the MLCT states. As a result complexes of the general formula $[Re(CO)_3(diim)L]^{0/+}$ could have their emissions tuned by chemical altering the diim or L ligands.

In addition to the number of photons emitted, changing the energy of the excited states also effects the quantum yield and excited state lifetime decay. The energy gap law[71] highly

influences the phosphorescence of $[Re(CO)_3(diim)L]^{0/+}$ with the non-radiative decay constant (k_{nr}) exponentially increasing as the difference in energy between the ^{3}MLCT state and the ground state decreases. In general, orange to red emissive Re(I) complexes have shorter excited state lifetime decays and smaller quantum yields in comparison to ideal green emitting complexes.

1.15 Photochemistry

Most $[Re(CO)_3(diim)L]^{0/+}$ complexes are photochemically stable due to excited ligand field states (LF) generally playing a minor role in the phosphorescence of $[Re(CO)_3(diim)L]^{0/+}$ complexes. This is attributed to Re being a heavy metal and CO a strong field ligand, resulting in an increase in energy of LF states relative to both LC and MLCT states. However, in cases where Re(I) complexes are also bound to ligands with a strong trans effect, the population of LF states is involved in the photochemical substitution of CO.

1.16 Early Re(I)–NHC complexes Photophysical studies

Over a decade ago, our research group began an investigation into the photophysical properties of Re(I) complexes bound to NHC ligands. Re(I) NHC complexes had been synthesised and explored in the past, however, comprehensive photophysical studies were limited. The initial complexes synthesised by our group[72] **1Cl** and **1Br** were isolated through the substitution of two CO ligands in $ReCO_5X$ (X = Cl or Br) with benzimidazole salts (Figure 21). Absorption spectra of the complexes in diluted dichloromethane solutions displayed typical LC (250-300 nm) and metal to ligand to ligand transfer (MLLCT, 320-400 nm) transitions. Emission profiles of the two complexes were structureless peaking between 500-510 nm. When placed in a frozen matrix, rigidochromism occurred with a blueshift of the emission maxima. The emissive transition state was attributed as an ^{3}MLCT whilst the blue-shift observed in emission maxima, when compared to $Re(phen)(CO_3)Cl$, was justified by a lowering of π conjugation when replacing phen with the NHC ligand.

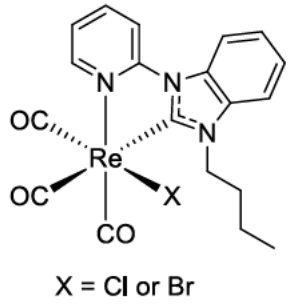


Figure 21: Complexes **1Cl and 1Br**.

Interestingly, when the two complexes were analysed in dilute acetonitrile after irradiation at 365 nm, the absorption spectra revealed a gradual change in profile. Over time the original ^{3}MLLCT band for both complexes disappeared whilst simultaneously forming a new red-shifted ^{3}MLLCT band. However, when analysed over the same timeframe (~ 60 min) in the dark, no change was observed in the absorption spectra for both complexes.

Not long after this discovery, Zeng and co-workers[73] published a library of Re(I)(NHC) complexes (Figure 22) synthesised using silver transfer reactions with Ag_2O. These complexes varied the NHC ligand by replacing the pyridyl substituent with pyrimidyl and the imidazole with benzimidazole whilst also inserting a methylene spacer between the two heterocycles. The pyridyl-NHC Re complex without the methylene spacer produced photophysical results in line with analogous complexes **1X** in diluted dichloromethane solutions exhibiting a shorter excited state lifetime decay and lower quantum yields in comparison to $Re(phen)(CO)_3Cl$. This was rationalised by the population of lower lying ^{3}LF excited states or the presence of non-radiative pathways. Comparatively, the complexes with a methylene spacer were non emissive due to the lowering of NHC ligand rigidity. Surprisingly, the MLCT emission maxima in diluted dichloromethane solutions of the pyrimidyl-NHC complex red-shifted 60 nm compared to the pyridyl-NHC complex. The excited state lifetime decays and the quantum yield were found to be longer and higher, respectively, for the pyrimidyl-NHC complex relative to the exchanged pyridyl-NHC complex. These interesting results were opposite to the trend expected due to the energy gap law.

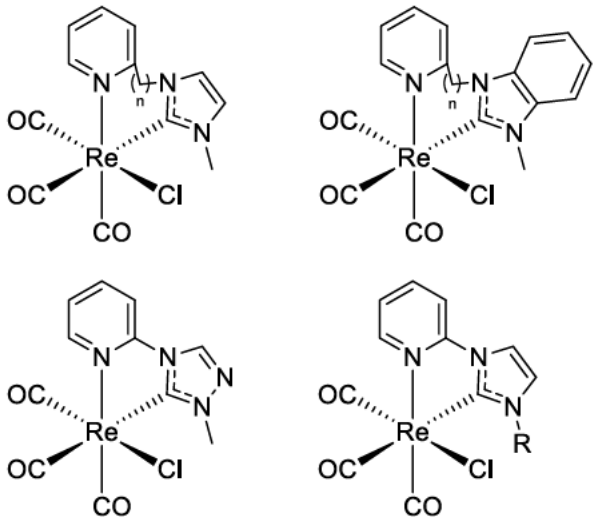


Figure 22: Library of Re(I)-NHC complexes investigated by Zheng and co-workers (n = 0 or 1; R = methyl, n butyl, benzyl and mesityl)

Zeng and co-workers did not explore the photophysical properties of the complexes in acetonitrile which our group decided to explore due to the analogous **1X** complex being photochemically active when exciting in the MLCT region. Our group set out to relate small variations in the Re(I)-NHC complexes structures (Figure 23) to their photophysical and photochemical properties.[74-76] Most of the complexes photophysical data followed the same previously observed trend with complexes in the **2(R)X** series producing short, excited state lifetime decays and low quantum yields. This suggested that changing the chemical identity of the R group or adding a benzimidazole ring to the imidazole had no observable effect on the energy of the ^{3}MLCT state which was further supported with TD-DFT studies.[76] These complexes were also found to be photochemically active in diluted acetonitrile solutions undergoing the same changes observed for the **1X** complexes in our previous study. The photochemical changes of the **2(R)X** series was monitored with sequential ^{1}H-NMR and IR spectra in deuterated acetonitrile solutions. Interestingly, the **2(R)X** complexes broke down to form three clear products. The three products were identified as a tricarbonyl solvato complex, which are also photochemically active and possibly the origin of the other two products. The two other products were identified as a dicarbonyl solvato complex and a dicarbonyl solvato halogen complex (Figure 24).

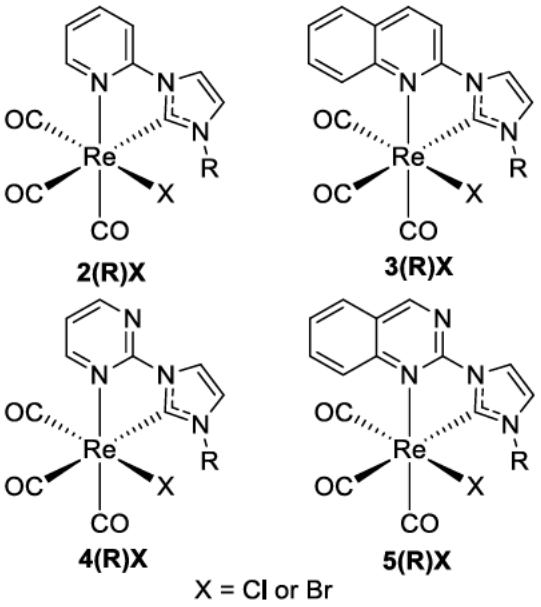


Figure 23: Re(I)-NHC complexes investigated by our group **2(R)X** (R = n-butyl, phenyl, mesityl; X = Cl, Br), quinolinyl-functionalised series **3(R)X** (R = phenyl; X = Cl, Br), pyrimidyl-functionalised series **4(R)X** (R = phenyl, mesityl; X = Cl, Br), and quinoxyl-functionalised series **5(R)X** (R = phenyl, mesityl; X = Cl, Br).

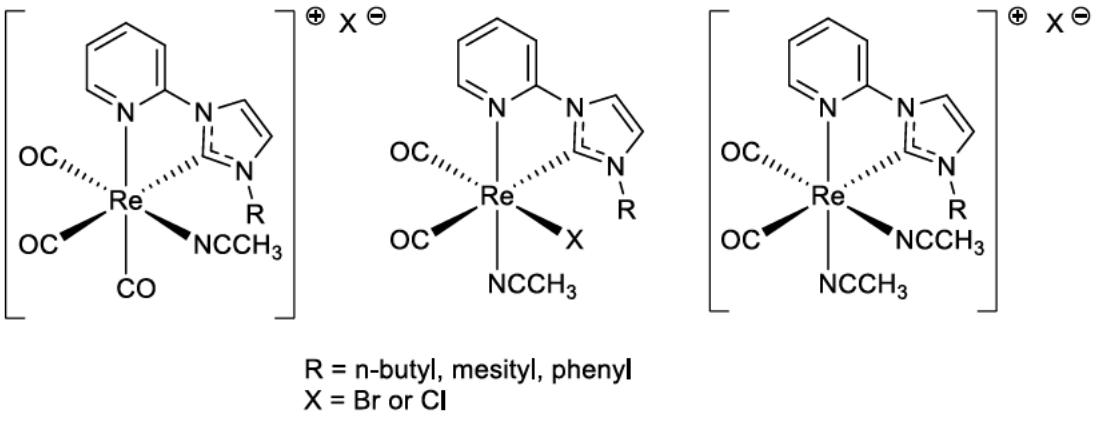


Figure 24; Photoproducts *fac*-[Re(NHC)(CO)$_3$ACN]$^+$, *fac*-[Re(NHC)(CO)$_2$(ACN)X] and *fac*-[Re(NHC)(CO)$_2$(ACN)$_2$] when irradiated in acetonitrile.

1.17 Aims

The aims of my project are to create manganese photo-CORMs with tetrazole bidentate ligands and tetrazole ancillary ligands, as tetrazoles coordinated to manganese were lacking in literature. Early in my research it was discovered the manganese based tetrazoles were not ideal photo-CORMs as they broke down to their original ligands and a manganese oxide when exposed the visible light. As a result, I focused my project on making anti-bacterial agents activated by light, with modulation to the tetrazole ligands to redshift the complexes MLCT maxima.

In addition to the manganese project, I worked on expanding the research previously conducted within our group on Re(I)-NHC carbonyls complexes. Studies conducted by Strassner *et al*.[77, 78] outlined a synthetic pathway to prepare a broad range of *N*-arylthiazole-2-thiones, which were further reacted to form corresponding *N*-arylthiazolium salts. Using this method, I synthesised pyridyl NHC complex and thione complexes using the precursors ligands. These complexes were characterised and explored both photochemically and photophysically with comparison to the analogous complexes previously explored in our group.

1.18 References

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Chapter 2: Synthesis and Photochemical Properties of Manganese(I) Tricarbonyl Diimine Complexes Bound to Tetrazolato Ligands

2.1 Context

Ten manganese(I) tricarbonyl diimine complexes bound to variably functionalised 5-aryl-tetrazolato ligands were prepared, and their photochemical properties were investigated. Upon exposure to light at 365 nm, each complex decomposed to its free diimine and tetrazolato ligands, simultaneously dissociating three CO ligands, as evidenced by changes in the IR spectra of the irradiated complexes over time. The anti-bacterial properties of one of these complexes were tested against Escherichia coli. While the complex displayed no effect on the bacterial growth in the dark, pre-irradiated solutions inhibited bacterial growth. Comparative studies revealed that the antibacterial properties originate from the presence of free 1,10-phenanthroline.

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Signatures of all co-authors on this paper to confirm the primary contribution from Mr Matthew J Stout can be found below.

To whom it may concern I, [Matthew Joshua Stout) contributed (full synthesis and characterisation of all complexes via H-NMR, IR, photochemical studies, as well as writing entire transcript) to the paper/publication entitled "Synthesis and Photochemical Properties of Manganese(I) Tricarbonyl Diimine Complexes Bound to Tetrazolato Ligands. *European Journal of Inorganic Chemistry*"

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Chapter 3: Synthesis and Photochemical Properties of Re(I) Tricarbonyl Complexes Bound to Thione and Thiazol-2-ylidene Ligands

3.1 Context

Three Re(I) tricarbonyl complexes, with the general formulation $Re(N^{\wedge}L)(CO)_3X$ (where N^L is a bidentate ligand containing a pyridine functionalized at position 2 with a thione or a thiazol-2-ylidene group and X is either chloro or bromo), were synthesized and their reactivities explored in terms of solvent dependent ligand substitution, in both the ground and excited states. When they were dissolved in acetonitrile, the complexes bound to the thione ligand underwent reversible ligand exchange with the solvent, resulting in the formation of $Re(NCMe)_2(CO)_3X$; the starting complex could be re-formed by precipitation following addition of diethyl ether. On the other hand, the complexes appeared to be inert in dichloromethane or acetone. Conversely, the complex bound to the thiazol-2-ylidene ligand did not display any ligand exchange reaction in the dark but underwent photoactivated ligand substitution on excitation to its lowest metal to ligand charge transfer manifold. Photolysis of this complex in acetonitrile generated multiple products, including Re(I) tricarbonyl and dicarbonyl solvato complexes as well as free thiazol-2-ylidene ligand.

Signatures of all co-authors on this paper to confirm the primary contribution from Mr Matthew J Stout can be found below.

To whom it may concern I, [Matthew Joshua Stout) contributed (full synthesis and characterisation of all complexes via H-NMR, IR, photochemical studies, photophysical studies as well as writing entire transcript) to the paper/publication entitled "Synthesis and Photochemical Properties of Re(I) Tricarbonyl Complexes Bound to Thione and Thiazole-2-ylidene Ligand"

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Chapter 4: Summary and Future Work

The research conducted on ten manganese(I) tetrazole complexes in chapter 2 of this thesis was undertaken to expand upon our previously published work on analogous rhenium complexes. The ten manganese(I) complexes were synthesised and fully characterised, including X-ray crystal structure analysis for the five complexes bound to the phenanthroline. All the complexes were stable as a solid and when dissolved in darkness, however, when exposed to visible light, all three carbonyls were lost simultaneously, leading to the release of phenanthroline or bathocuproine and the corresponding tetrazolato ligand. This phenomenon is not common in literature with most manganese carbonyl complexes releasing one or two carbonyls before stabilising to form a new manganese complex. As a result, the manganese complexes studied in this thesis were deemed unsuitable as potential photoCORMs as originally targeted. The complexes were then activated with a variety of light source from low power artificial lab light to a high power PoliLight, ranging from wavelengths 365-555 nm. The complexes were activated in the UV to blue region with no difference observed in activation wavelength between the bathocuproine and phenanthroline diimine ligands or between the 5 tetrazole auxiliary ligands. It was hoped that exchanging the phenanthroline for the more conjugated bathocuproine diimine ligand would result in a redshift of activation energy in the complexes, however, when the complexes were activated, no difference was observed in activation wavelength or rate of CO release between the bathocuproine and phenanthroline diimine ligands or between the 5 tetrazole auxiliary ligands. This result was attributed to the phenyl rings in bathocuproine being able to rotate removing the increased conjugation desired in the complexes. With the aim of creating photoCORMs that could be activated by a range of light not met, our attention was turned to exploring the anti-bacterial properties of the complexes. A significant amount of research has been put into finding new anti-bacterial drugs in recent years and some promising research had shown manganese CORMs to be effective anti-bacterial agents. Bacterial growth inhibition was tested using solutions containing either the intact or the photolysed complex $Mn(phen)(CO)_3$**4**., with inhibition of E. coli observed for the latter. This effect seemed to be caused by the presence of phenanthroline since phenanthroline alone inhibited bacterial growth to a similar level observed in the presence of the pre-irradited $Mn(phen)(CO)_3$**4**. Although not meeting the initial aims set out, the simultaneous release of all three carbonyls when irradiated with UV to blue light

and the antibacterial properties of phenanthroline, only when released from the complex, were remarkably interesting results. Ideas for future projects on these complexes would be to use analogous phenanthroline complexes with electron withdrawing groups attached such as CN in order to increased conjugation and therefore redshift the light required for activation. In addition, if an analogous complex or complex with a completely different dimmine system could be isolated which releases only 1 or 2 carbonyls to form a stable iCORM, they could be explored in cells with the tetrazole ancillary ligands now able to target different cellular compartments for biological studies.

The research presented in chapter 3 of this thesis on three Rhenium(I) NHC tricarbonyl complexes was conducted to expand upon our groups previously published work which investigated the effect of exchanging a diim for a NHC ligand had on the reactivity and luminescent properties of Re(I) tricarbonyl complexes. In addition, studies conducted by Strassner *et al*.[77, 78] outlined a synthetic pathway to prepare a broad range of *N*-arylthiazole-2-thiones, which were further reacted to form the corresponding *N*-arylthiazolium salts. We believed that this synthetic pathway could be modified to provide access to 3-(pyrid-2-yl)-4,5-dimethylthiazole-2-thione (**1**) and 3-(pyrid-2-yl)-4,5-dimethylthiazolium hexafluorophosphate (**2**H[PF_6]) (Scheme 1). In addition, the *N*-arylthiazole-2-thione precursors were not explored as bidentate ligands for the Pt(II) complexes. Initially thione and thiazole ligands **1** and **2** were synthesised and characterised using Strassner's synthetic method. Numerous attempts were made to use the same procedure to synthesise the analogous 4, 5-dimethyl-3-(2-pyrimidyl)-thiazoline-2-thione using the commercially available 2-aminopyrimidine however, it was unfortunately never able to be isolated. The reaction was then modified to try and modulate the thione via the ketone instead of the pyridine ring with 3-chloro-2-butanone replaced with 2-bromo-1,2-diphenylethanone in an attempt to synthesise 4, 5-diphethyl-3-(2-pyridyl)thiazoline-2-thione. Although a possible desired product was observed via ^{1}H-NMR countless attempts to isolate it were unsuccessful. We therefore sought to investigate the thione and thiazole Re(I) tricarbonyl NHC complexes as a comparative study to our previously established Re(I) NHC complexes. Both the thiazole and thione ligands **1** and **2** as well as the three Rhenium tricarbonyl NHC/NCS complexes Re(**1**)$(CO)_3$Br, Re(**1**)$(CO)_3$Cl and Re(**2**)$(CO)_3$Br were synthesised and fully characterised. All three complexes reacted instantly in acetonitrile-d_3 and dimethylsulfoxide-d_6 with Re(**1**)$(CO)_3$Cl reacting faster than its bromide counterpart.

Photolysis at 365 nm had no effect on the rate of the reactions which was identified as solvent exchange with dissociated ligand **1** confirmed via UV-Vis and FT-IR studies. Comparatively, Re(**2**)$(CO)_3$Br exhibited similar photochemical and photophysical properties previously reported by Vaughan *et al.*, forming two photo unstable dicarbonyl complexes, one photo unstable tricarbonyl complex and free ligand **2**[X] upon photolysis with 365 nm light. Ideas for future projects on these complexes are to further explore synthesising a range of analogous thione and thiazole by modifying the identity of the pyrid-2-yl amine or the ketone used at the start of reaction published by Strassner *et al*. These complexes can then further be compared to the photophysical and photochemical properties of the complexes published by Vaughan *et al.*

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