ELSEVIER

Coordination Chemistry Reviews
154 (1996) 163–177

COORDINATION CHEMISTRY REVIEWS

From nitrogen fixation to catalysis, diagnosis and therapy [1]

J.R. Dilworth

Department of Biological and Chemical Sciences, Central Campus, University of Essex, Colchester CO4 3SQ, UK

Received 22 November 1995

Contents

Abstract

This review initially traces the development of the coordination chemistry of metals of Groups 16 and 17 with multiply bonded nitrogen or bulky thiolate ligands at the then Unit of Nitrogen Fixation under Joseph Chatt's guidance. A brief outline of the subsequent applications of metal complexes of these ligands in olefin metathesis, methanol carbonylation and radiopharmaceuticals for diagnostic imaging and therapy is then given.

Keywords: Group 16; Group 17; Thiolate ligand; Olefin metathesis; Methanol carbonylation; Radiopharmaceuticals

[1] I am delighted to have the opportunity of contributing this article in honour of Professor Joseph Chatt and the enormous contribution that he made to organometallic and coordination chemistry. On a personal note it also enables me to acknowledge the consistent help and support that he gave me while I was at the then Unit of Nitrogen Fixation and subsequently at the University of Essex. I count myself extremely fortunate to have worked under his guidance, and his encyclopaedic knowledge, enthusiasm and feel for coordination chemistry left a lasting impression.

PII S0010-8545(96)01284-2

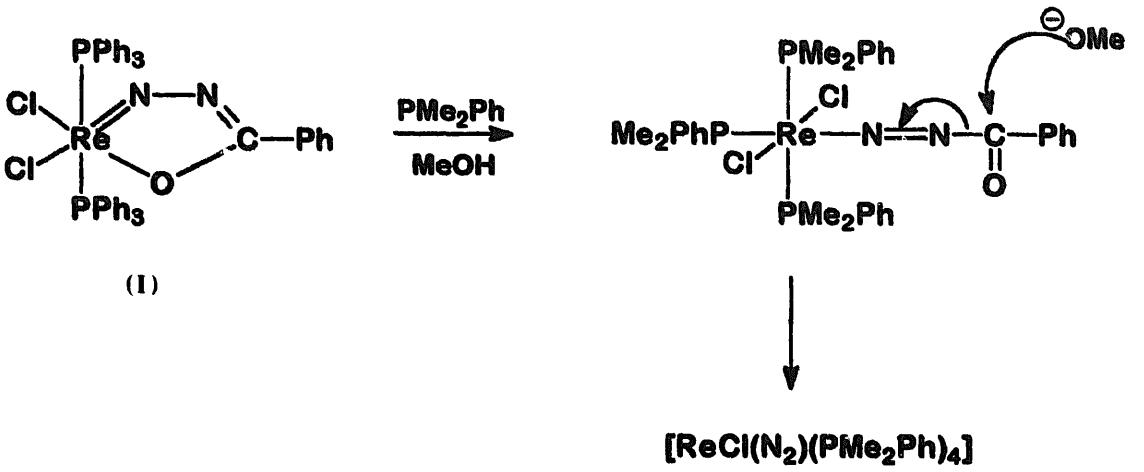
1. Complexes with metal–nitrogen multiple bonds

In the early 1960s while at ICI, Professor Chatt's group had started to open up the chemistry of the then little explored element rhenium. He reported the first preparation of the complex $[ReOCl_3(PPh_3)_2]$ from perrhenate [1] and this is still the precursor of choice for access to rhenium complexes in higher oxidation states. A highlight of this phase of rhenium chemistry was the synthesis of polyhydride complexes of rhenium [2] such as $[ReH_7(PPh_3)_2]$ which continue to attract interest 30 years on. In a typically meticulous reinvestigation of the reaction of hydrazine with $[ReOCl_3(PPh_3)_2]$ Chatt, Johnson et al. showed that the product was in fact the nitride complex $[ReNCl_2(PPh_3)_2]$ [3] and not a Re(II) complex as had been earlier suggested. The same paper that described the nitride complexes also reported the synthesis and characterisation of $[ReCl_3(NPh)(PPh_3)_2]$. This was one of the first examples of an imido-complex, and these are now extensively studied in the field of olefin metathesis catalysis.

As a new Ph.D. student my first project was to follow the work of my predecessor, Rosemary Paske, in establishing the mechanism of cleavage of the N–N bond in the reaction of $[ReOCl_3(PPh_3)_2]$ with hydrazine. We used the strategy of employing substituted hydrazines in an attempt to trap any intermediates that might be formed. Our first efforts did not lead to any species with intact N–N bonds, but we were able to show that 1,2-dialkhydrazines were cleaved on reaction with $[ReOCl_3(PPh_3)_2]$ to give rare examples of alkylimido-complexes $[ReCl_3(NR)(PPh_3)_2]$ (R = Me, Et) [4]. In the case of hydrazines of the type PhCONHNHPh, N–N bond cleavage again occurred to give phenylimido-complexes. We and others [5,6] have subsequently used this route to access the first reported imido-complex of technetium $[TcCl_3(NPh)(PPh_3)_2]$. The role of such Tc and Re complexes in the development of new radiopharmaceutical imaging and therapeutic agents is discussed below.

The first indications that a species with an intact N–N bond could be prepared from a hydrazine came with the preparation of the chelated benzoylhydrazido(3−) complex $[ReCl_2(NNCOPh)(PPh_3)_2]$ (I) from $[ReOCl_3(PPh_3)_2]$ and 1,2-dibenzoylhydrazine. At a time when dinitrogen complexes were still relatively uncommon, we were delighted to find that simple reaction of (I) with mono- or di-tertiary phosphines in methanol to give high yields of Re(I) dinitrogen complexes (II) (Scheme 1). This remains the route of choice for the synthesis of rhenium dinitrogen complexes, and has very recently been used to prepare some novel Re(I) pyridine dinitrogen complexes [7]. The relatively easy loss of the dinitrogen ligand from complexes of the type (II) has provided convenient access to Re(I) complexes with isocyanide and acetylene ligands [8]. It was subsequently shown that the final step of formation of ligated dinitrogen by loss of the COPh group could be reversed by reaction of the monophosphine dinitrogen complexes with PhCOCl. This provided one of the first examples of the formation of an N–C bond from coordinated dinitrogen, and presaged some extensive N–C chemistry with molybdenum and tungsten dinitrogen complexes.

Interest in nitrides and imides within the Chatt group was reinforced with the

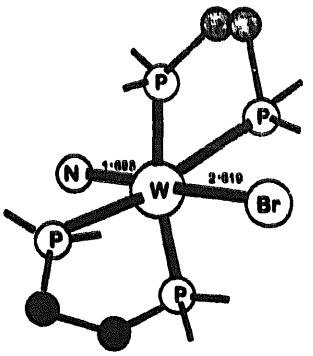


(I)

(II)

Scheme 1.

development of the Chatt cycle for the mechanism of protonation of coordinated dinitrogen which postulated diazenide (NNH), hydrazide (NNH_2) and nitride intermediates. The final step required the protonation of coordinated nitride to ammonia and we embarked on a programme of investigating the reactions of well-defined nitrides with acids. We were able to synthesise the nitride complexes $[MCl(N)(dppe)_2]$ (M = Mo, W; dppe = $Ph_2PCH_2CH_2PPh_2$) which reacted with HCl to give the imides $[MCl(NH)(dppe)_2]Cl$ [9]. A simplified view of the structure of the tungsten complex (**III**), omitting phosphine phenyl groups, shows the trans arrangement of Cl and NH ligands. Further protonation in this instance is inhibited by the stability of the chelated diphosphine ligand.

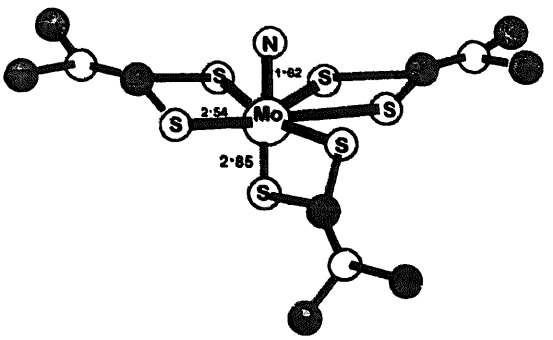


(III)

Under similar conditions the nitride $[MoCl_2N(PPh_3)_2]$ gave a quantitative yield of ammonia. The nucleophilic character of the nitride in $[MoClN(dppe)_2]$ was also exploited in the formation of alkylimido-complexes by reaction with alkyl halides. Subsequent elegant electrochemical studies showed that the coordinated imide could be converted to amine by coupled electrochemical reduction and protonation [10].

We also showed that trimethylsilylazide was a convenient reagent for the synthesis of the polymeric nitrides $\{MCl_3N\}_n$ from $MoCl_5$ and WCl_6. Reaction of $MoCl_3N$

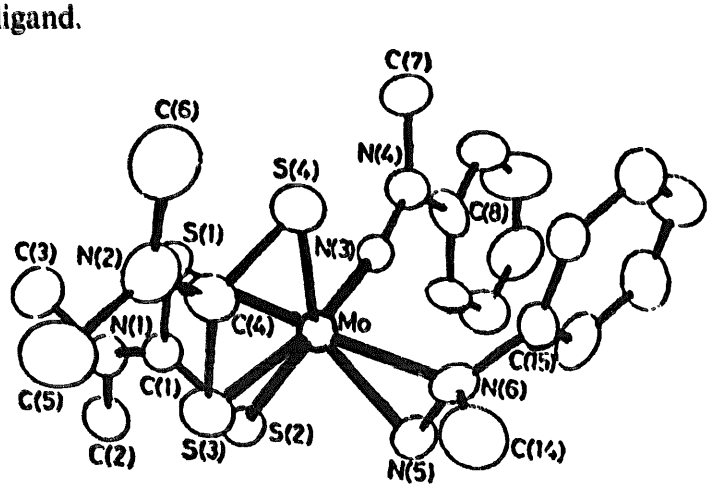
with $Me_3SiS_2CNR_2$ (R = Me, Et) gave the pentagonal bipyramidal (PBP) nitrides $[MoN(dtc)_3]$ ($dtc = S_2CNR_2$). A representation of the structure (**IV**) shows the nitride ligand in an apical site, and significant lengthening of the Mo–S bond in the other apical site due to the strong trans influence of the nitride.



(IV)

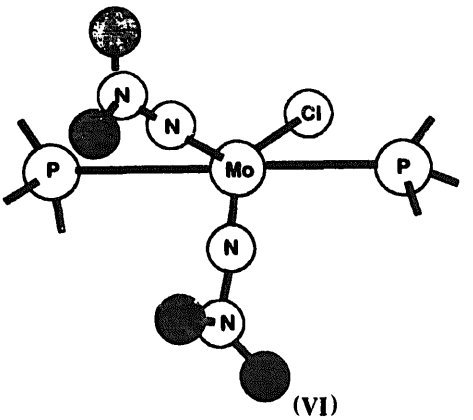
The electron releasing character of the dithiocarbamate ligands enhanced the nucleophilic nature of the nitride ligand to the extent that it reacted with elemental sulphur to give the first reported thionitrosyl complexes $[Mo(NS)(dtc)_3]$ [11]. These were shown to have the same PBP structure as the parent nitride. The range of NS complexes was later extended to other metals by using S_4N_4 as the source of the NS ligand [12]. The deployment of the dithiocarbamate ligand reflects an earlier paper by Chatt et al. [13] in which the ability of dithiocarbamate to stabilise high oxidation states was first rationalised in terms of the canonical form $R_2N^+=CS_2^{2-}$.

Detailed studies of the protonation of coordinated dinitrogen at the Unit of Nitrogen Fixation identified hydrazido(2-), NNH_2, as the key intermediate, and prompted a detailed study of the structures and reactivities of hydrazide ligands, particularly towards protonation. We were able to show that $[MoO_2(dtc)_2]$ reacted readily with 1,1-disubstituted hydrazines to give $[MoO(NNR_2)(dtc)_2]$ (R_2 = Me_2, MePh) and $[Mo(NNR_2)_2(dtc)_2]$ [14]. Protonation of the bis(hydrazido) complexes gave $[Mo(NHNR_2)(NNR_2)(dtc)_2]^+$, the first example of side-on or η^2 coordination of the hydrazide(1-) ligand [15]. An ORTEP view of the structure (**V**) shows that the geometry about the Mo is very distorted from PBP due to the small bite angle of the η^2-hydrazide ligand.



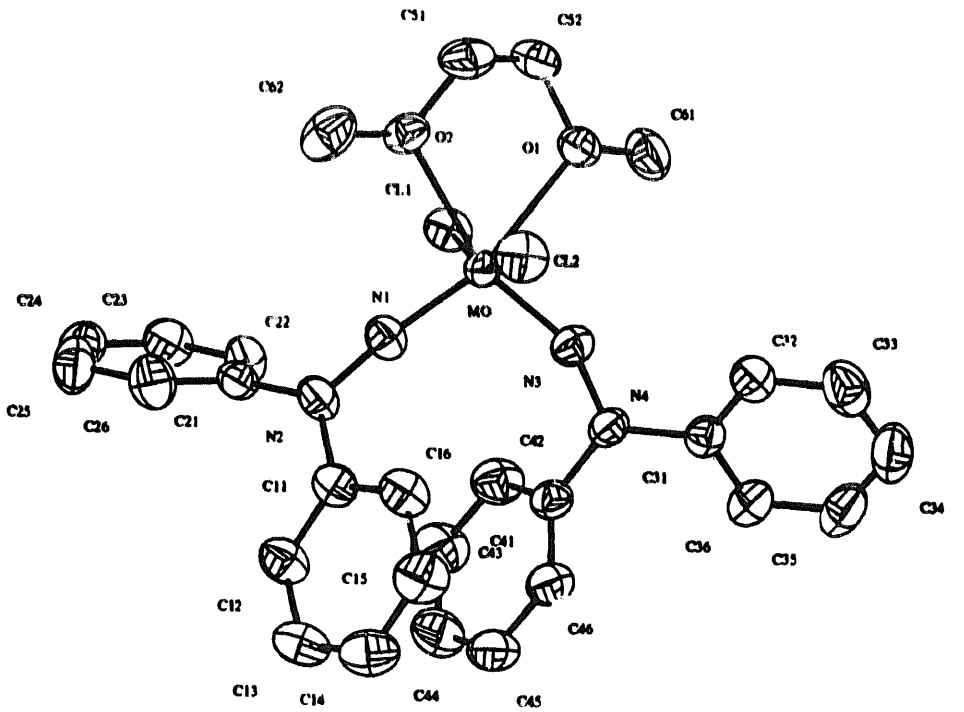
(V)

At the time this was an unexpected type of bonding for $NHNR_2$ ligands, but it was thereafter shown to be preferred to terminal bonding for a wide range of metal sites. This chemistry was later extended to the synthesis of bis(hydrazides) such as $[MoCl(NNR_2)_2(PPh_3)_2]Cl$ [16] (**VI**) by direct reaction of the hydrazine with $[MoCl_4(PPh_3)_2]$. The view of the structure of (**VI**) shows the trigonal bipyramidal structure with the two strictly coplanar NNR_2 units in the equatorial plane, with the bond lengths and geometries consistent with each donating six electrons to the metal.



(VI)

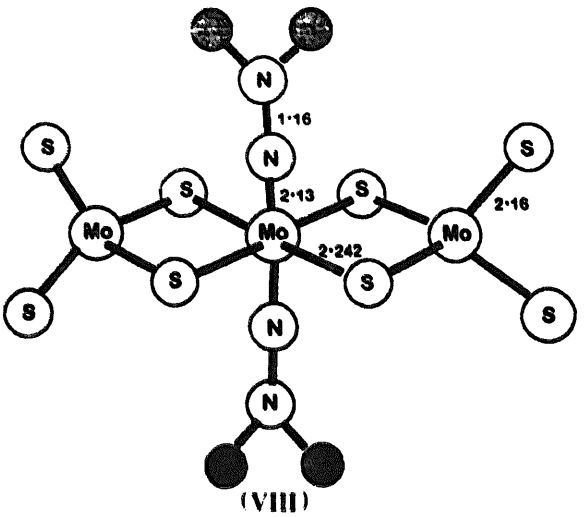
Very recently we have also shown that complexes such as $[MoCl_2(NNR_2)_2)(dme)]$ (**VII**) (dme = 1,2-dimethoxyethane) can conveniently be prepared from $Na_2[MoO_4]$ by reaction with Me_3SiCl and the appropriate hydrazine in dme [17]. The structure of this complex shows the two hydrazido-ligands to be in a cis arrangement.



(VII)

The related rhenium hydrazides, $[ReCl_2(NNR_2)_2(PPh_3)]Cl$ [18] and $[ReCl_3(NNR_2)_2(py)]$ [19] (py = pyridine) have also been prepared in an analogous manner from appropriate hydrazines.

The bonding in bis(imido-)complexes has been discussed in detail [20], and the competition between the *cis*-imido-ligands for available empty metal orbitals in octahedral complexes means that five rather than six electrons are formally donated to the metal. A similar situation pertains with the bis(hydrazide) complexes such as $[Mo(NNR_2)_2(dtc)_2]$ with ten electrons formally donated to the metal by the two ligands. An interesting facet of the bonding of hydrazide(2-) is the ability of the NNR_2 system to transfer electrons from the metal nitrogen multiple bond to the N–N bond. An extreme case of this was found in the complex $[(MoS_4)_2Mo(NNMe_2)_2]$ (**VIII**) where the *trans*-$NNMe_2$ ligands have bond lengths (N–N 1.16(2) Å and Mo–N 2.13(1) Å) indicative of bonding in the iso-diazene, form ($N^- = N^+MePh$) [21].

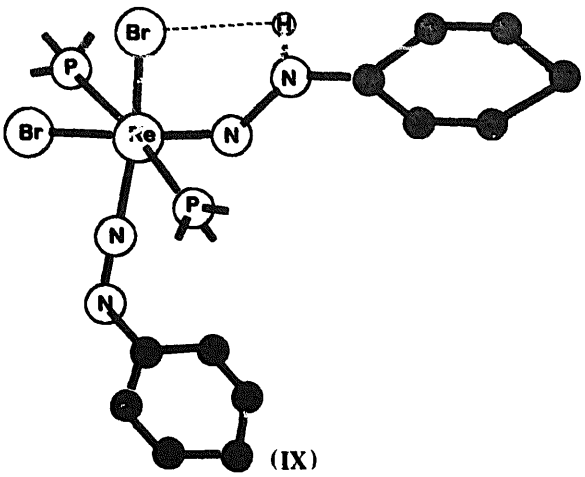


(VIII)

This electronic flexibility of the hydrazido(2-) system is not available to imide(2-) and prompted the investigations of the catalytic activity of hydrazide complexes described below.

The use of phenylhydrazine in place of the 1,1-disubstituted hydrazines enabled us to prepare a wide range of diazenido-complexes such as $[Mo(NNPh)(dtc)_3]$ [22] and $[ReCl(NNPh)_2(PPh_3)_2]$ [23]. The diazenide ligand in these complexes is invariably bound with a linear M–N–N system consistent with the donation of four electrons to the metal. Protonation in these relatively high oxidation state complexes occurred at N_β to give the corresponding hydrazido(2-) complexes. An example of this is provided by the complex $[ReBr_2(NNHPh)(NNPh)(PPh_3)_2]$ (**IX**) [23].

The simplified representation of the structure shows the hydrazido(1–) ligand unusually is bent at N_α as a consequence of the hydrogen bonding of the NH proton to a coordinated bromide. It transpired that hydrazide and diazenide complexes are very much relevant to the development of radiopharmaceutical agents based on technetium and rhenium and our return to this chemistry in the new context is described below.

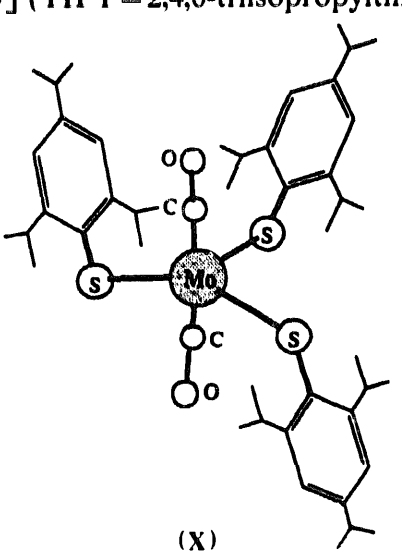


(IX)

2. Metal sulphur coordination chemistry

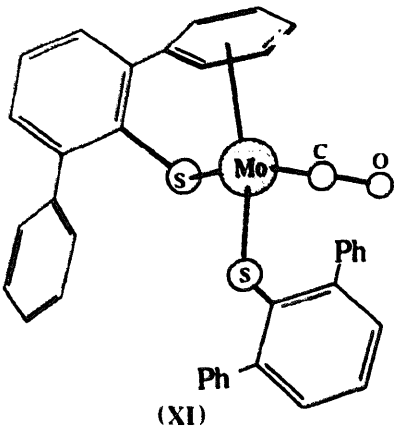
The detailed EXAFS and now the X-ray crystal structure of the Fe–Mo protein from nitrogenase [24] confirmed that both metals are predominantly bound by sulphur. It has therefore long been a goal of those interested in the inorganic chemistry of nitrogen to prepare dinitrogen complexes with a high proportion of sulphur co-ligands. Such complexes have proved hard to come by, and even now there are few authenticated examples.

Our first efforts in this area at Sussex were prompted by reports (subsequently shown to be erroneous) that molybdenum dinitrogen complexes with dithiocarbamate ligands could be prepared. Our subsequent fairly extensive foray into molybdenum dithiocarbamate chemistry was fairly productive in terms of new complexes with metal–nitrogen multiple bonds (see above), but failed to produce a dinitrogen complex. As an alternative we then opted to use the well established strategy of using sterically hindered aromatic thiolate ligands to generate coordinatively unsaturated complexes capable of reacting with small molecules. Our first of many complexes in this area was the stable 14-electron five-coordinate complex $[Mo(CO)_2(TIPT)_3]^-$ (X) [25] (TIPT = 2,4,6-triisopropylthiophenol).



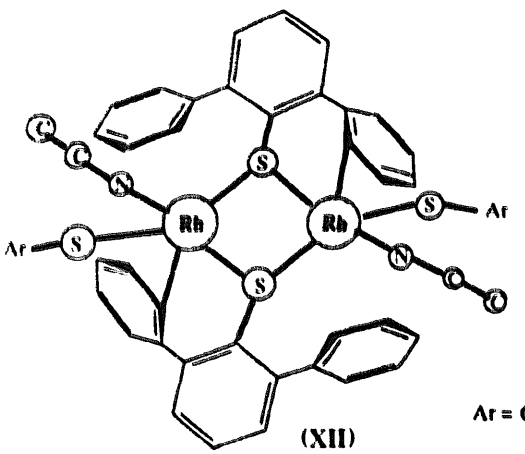
(X)

Thereafter we prepared a number of complexes with a wide variety of thiolate substituents and some of these showed interaction of the substituents with the metal, an example being [Mo(CO)(2-η^6-PhC$_6$H$_4$S–6Ph)(SC$_6$H$_4$Ph$_2$-2,6)] (**XI**) [26].



(XI)

The last complex has a novel structure with an η^6-bonded thiolate phenyl substituent which was readily replaced by three two-electron donor ligands. The same ligand reacted with $RhCl_3$ to give a dimeric complex with bridging thiolate ligands each with one thiolate phenyl group ortho-metallated (**XII**) [27].

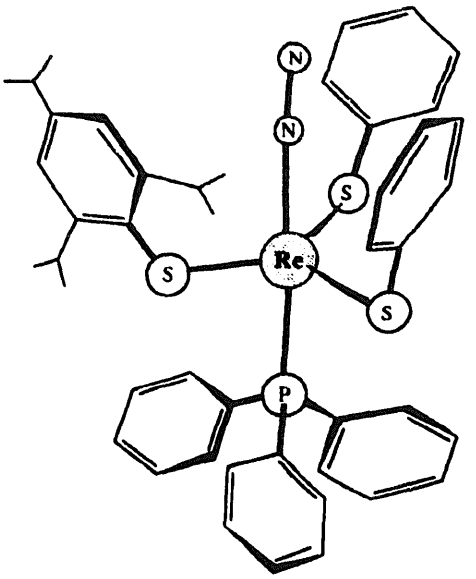


(XII)

Ar = $C_6H_3Ph_2$

This C–H activation parallels one of the first examples of this reaction by Chatt and Davison with a ruthenium diphosphine system [28]. Despite intensive efforts, none of the many thiolate complexes prepared at that time showed any tendency to react with dinitrogen.

However, recently, in our work at Essex, we have returned to the rhenium hydrides such as [$ReH_7(PPh_3)_2$] prepared by Chatt and Coffey in the 1960s and investigated their reaction with bulky aromatic thiolate ligands. The nature of the product is very sensitive to the thiolate substituents; with TIPTH the Re(III) dinitrogen complex [Re(N_2)(TIPT)$_3$(PPh_3)] is formed in high yield [29]. The structure (**XIII**) of the complex showed trigonal bipyramidal geometry with an apical dinitrogen ligand.



(XIII)

The bulky triphenylphosphine molecule in the other apical site causes the thiolate phenyls to orientate on the other side of the trigonal plane, forming a cup-like environment around the bound N_2 molecule. The same complex can also conveniently be obtained in high yield directly from $[ReOCl_3(PPh_3)_2]$, sodium borohydride and thiol in methanol under dinitrogen. With 2,6-dimethylthiophenol (DMTH) a complex of stoichiometry $[Re(DMT)_3(PPh_3)]$ was formed, which has an agostic interaction of the metal with one of the methyl hydrogens [30]. This work parallels that of Richards and co-workers on molybdenum hydride complexes with aromatic thiolate ligands [31]. The target of binding dinitrogen to a sulphide coordinated metal site remains as elusive as ever, but as more information emerges about the structure of the enzyme and model studies continue, this goal will doubtless be realised.

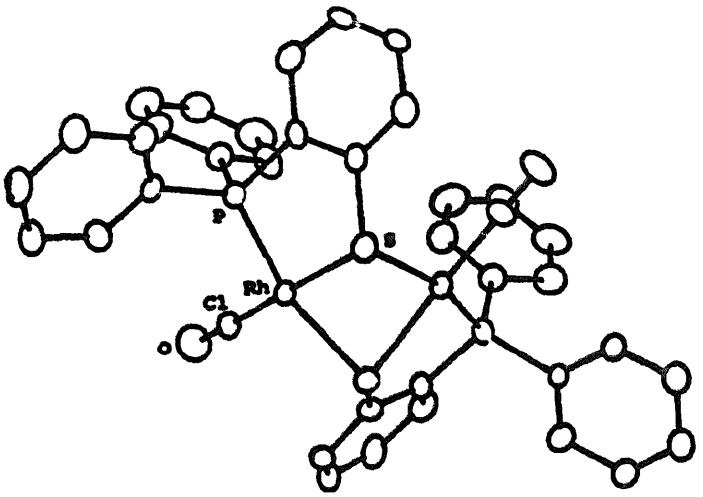
3. Catalytic studies

3.1. Carbonylation studies

Despite the significant number of metalloenzymes involving metal sulphur coordination, there are few examples of homogeneous catalysts involving sulphur ligands. As an extension of our work above on metal thiolate complexes we have of late been investigating the chemistry of 2-diphenylphosphinothiolate ligands. The rationale was that the chelated ligand would be resistant to elimination of the thiol in reactions involving metal hydrides, and that the electron releasing properties of sulphur would enhance electron density at the metal centre.

We found that $[RhCl(PPh_3)_3]$ and other Rh(I) precursors reacted with an excess of 2-$Ph_2PC_6H_4SH$ in the presence of base to give the very stable and unreactive complex $[Rh(SC_6H_4PPh_2\text{-}2)_3]$. However, with one equivalent of the phosphinothiol,

$[\{RhCl(CO)_2\}_2]$ gave the dimeric complex $[Rh_2(SC_6H_4PPh_2\text{-}2)_2(CO)_2]$. The X-ray structure of this complex (**XIV**) shows two square planar Rh(I) units linked by two bridging thiolate sulphurs.



(XIV)

The Rh_2S_2 system is bent, and the Rh–Rh distance of 2.980(1) Å suggests a weak metal–metal interaction. In collaboration with BP Chemicals Ltd. this complex was screened for catalytic activity for the carbonylation of methanol.

The carbonylation of methanol to acetic acid on a rhodium catalyst in the presence of iodide (Monsanto process) is an intensively used industrial process, and the key intermediate has been shown to be $[RhI_2(CO)_2]^-$. Intensive efforts have been made to improve the activity of the catalyst, but the forcing conditions used industrially (180 °C, 30 bar of CO) mean that many complexes degrade in situ to $[RhI_2(CO)_2]^-$. Other complexes with bidentate ligands also fail, as although they undergo oxidative addition of MeI and form acetyls by CO migration/insertion they will not eliminate the COMe group to form acetyl iodide and hence acetic acid.

However complex (**XIV**) was shown [32] to give rates of reaction for carbonylation four to five times higher than $[RhI_2(CO)_2]^-$ and ^{31}P NMR studies of the reaction product confirmed the continued presence of the coordinated phosphinothiolate ligand. The mechanism of the reaction is directly analogous to that for $[RhI_2(CO)_2]^-$. High levels of activity were also found for the complexes $[RhI(CO)(Ph_2PCH_2CH_2SMe)]$ and $[\{Rh(SCH_2CH_2PPh_2)(CO)\}_2]$. We are currently investigating complexes of other P,S donor ligands such as $Ph_2PCH_2CH_2PPhCH_2CH_2SH$ and $Ph_2PCH_2CH_2SCH_2CH_2SH$ in an effort to improve the reaction rates further. This chemistry follows directly from our work at UNF with Professor Chatt using monodentate thiolate ligands and augurs well for the possibility of developing other catalysts based on chelating thiolate systems.

3.2. Metathesis and ring opening metathesis polymerisation (ROMP) of olefins

Olefin metathesis catalysts involving imido co-ligands have been an area of intensive study over the past decade, and a number of highly active systems have been

reported by Schrock [33], Gibson and co-workers [34] and others. As discussed above, the hydrazido(2-) ligand, although formally analogous to imide, does have more electronic flexibility. This prompted us to investigate the potential metathesis activity of a range of hydrazide complexes.

The syntheses of the complexes $[MoCl(NNMePh)_2(PPh_3)_2]Cl$ and $[ReCl_3(NNMePh)_2(py)]$ have been described above. We have recently found [35] that such complexes are highly active precursors for metathesis, and ROMP catalysts with the addition of $EtAlCl_2$ as activator have activities comparable with other reported systems. The Re complex makes an interesting contrast to the corresponding imide which is inactive under the same conditions and the hydrazide is also stereoselective for ROMP reactions of norbornene, giving exclusively the cis polymer. The Mo complex also provides a comparatively rare example of a tertiary phosphine-containing metathesis catalyst. The mechanism of metathesis in other systems has been established to involve a metallocyclobutane intermediate formed from reaction of the olefin with a coordinated alkylidene. Hydrazido alkylidene complexes are presumed intermediates, and we are presently investigating synthetic routes to stable complexes of this type which will be intrinsically active in metathesis reactions. This opens the possibility of reacting olefins which contain functional groups that would be incompatible with the use of the aluminium alkyl activator.

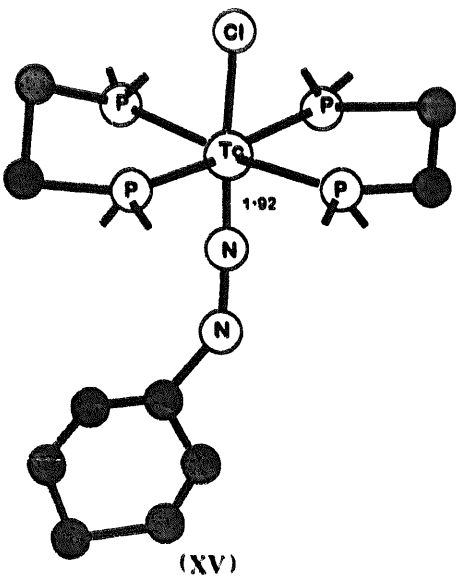
We have also shown that diazenides (e.g. $[ReCl(NNPh)_2(PPh_3)_2]$) and nitride complexes (e.g. $[ReNCl_2(PMe_2Ph)_3]$) are efficient metathesis procatalysts. ^{31}P NMR studies of the reaction mixture after metathesis by the nitride show that the three phosphine ligands are maintained throughout. The work with the nitride complexes very much harks back to the original Chatt paper describing the synthesis of a range of rhenium tertiary phosphine nitrides and subsequent work on organometallic derivatives such as $[ReNPh_2(PPh_3)_2]$ [36]. This research is still very much in its preliminary stages, but it does indicate some interesting differences between hydrazide and imide systems, and suggests that there is an as yet unexplored range of organometallic derivatives of diazenide and hydrazide complexes with potential catalytic applications.

4. Technetium and rhenium complexes with potential radiopharmaceutical applications

Technetium is very much the radioisotope of choice for diagnostic medical imaging owing to the virtually ideal characteristics of the technetium-99m isotope. It is a pure γ emitter, with no damaging β radiation, the energy of the γ-ray is appropriate for detection, and the half life of 6 h is optimal for diagnostic applications. The biodistribution of the technetium species is a function of the charge, size and lipophilicity of the complex, and control of these parameters permits specific targeting to major organs. In the hospital radiopharmacy, technetium is readily available from a generator system as a 10^{-8} M solution of $[TcO_4]^-$ in isotonic saline. The challenge for the coordination chemist in making a viable radiopharmaceutical is to achieve complex yields in excess of 98% at these low concentrations in an aqueous medium

in a 'one-pot' reaction under mild conditions. The synthetic characterisation work for technetium is carried out with the long-lived weak β-emitting isotope ^{99}Tc, typically on a 10–20 mg scale.

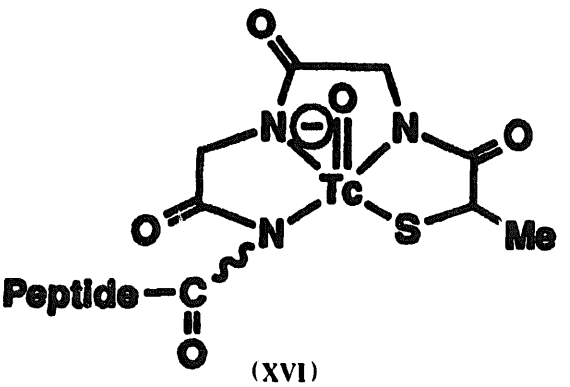
When in 1987 an opportunity rose to explore technetium chemistry in collaboration with Amersham International, we immediately sought to extrapolate some of our chemistry of rhenium with metal–nitrogen multiple bonds to technetium. We [37] and the Davison group at MIT [38] found that the Tc imido-complex $[TcCl_3(NPh)(PPh_3)_2]$ could readily be prepared from $[TcO_4]^-$ by reaction with the hydrazines RCONHNHPh. As expected, the complex was isostructural with the Re analogue described 30 years earlier by Chatt et al. The imido-complexes offered the possibility of fine-tuning the targeting characteristics by altering the imido-core substituents rather than the co-ligands. However, subsequent work with Tc imido-complexes with ligands other than tertiary phosphine, showed that the imido-ligand was not stable under radiopharmaceutically relevant conditions. Thereafter we turned to hydrazido(2−) systems and showed that complexes such as $[Tc(NNMePh)(salen)(PPh_3)]^+$ [39] (salen = *N*,*N*-di(2-hydroxybenzylidene)–ethylenediamine) and $[Tc(NNMePh)_2(dtc)_2]^+$ could readily be prepared from the hydrazine and $[TcO_4]^-$ in semi-aqueous media and were stable. In addition, we have shown that Tc diazenide complexes such as $[TcCl(NNPh)(dppe)_2]^+$ (**XV**) can be prepared directly from pertechnetate, phenylhydrazine hydrochloride and the diphosphine in one step in high yield [40]. A view of the structure of the monodiazenido-complex omitting the phosphine phenyl groups (**XV**) shows a trans arrangement for the chloride and diazenide ligands with the latter having a linear M–N–N system indicative of its acting as a four-electron donor. The Tc–N distance of 1.917(19) Å is somewhat longer than found for other 'singly-bent' diazenide complexes and may reflect the effect of steric repulsions by the phosphorus groups. The synthesis of (**XV**) can also be carried out for the ^{99m}Tc isotope under very dilute conditions.



(XV)

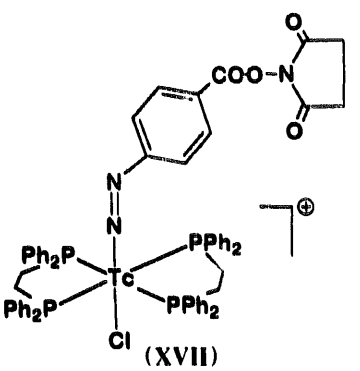
Technetium-based imaging agents are now commercially available for most of the

major organs, and some of this diagnostic role is being increasingly taken up by MRI. Research is now centred on directing technetium complex to more specific sites; this is achieved by conjugation of the technetium complex to small bioactive molecules which provide targeting to specific receptor sites. This is shown in (**XVI**) where the targeting molecule (in this case a peptide) is linked to a tetradentate ligand. Currently attention is focused on small peptides for binding to inter alia surface receptor sites on platelets (for thrombus imaging) or white blood cells (infection site imaging). There is also great interest in the use of monoclonal antibodies or their fragments for a variety of targets including a range of cancer types.



(XVI)

The aryldiazenido-ligand provides the possibility of linking the biomolecule to the diazenide phenyl group, and we have synthesised diazenide complexes such as (**XVII**) with an activated ester group which will bind a molecule such as a peptide via reaction at an NH_2 group.



(XVII)

The complex shown with phenyl phosphine substituents is too lipophilic for use as a radiopharmaceutical, and more hydrophilic analogues with alkyl diphosphines have been prepared. We are currently investigating linking to dopamine-type molecules which bind to D_2 receptor sites in the brain and provide measures of the binding affinity and numbers of such sites. This type of imaging could be particularly valuable to detect the early stages of neurodegenerative diseases and permit more appropriate management regimes, and to monitor the effectiveness of drug treatments.

A further, comparatively recent development in the field of radiopharmaceuticals has been that of rhenium-based agents for therapeutic applications. The rhenium-188

isotope is a β-emitter and if it can be targeted to a cancerous area it could deliver a radiation dose in a specific and efficient manner. This has become feasible with the commercial availability of a ^{188}Re generator which delivers a supply of $[^{188}ReO_4]^-$ analogously to the ^{99m}Tc generator described earlier. The similarity of the chemistry of Tc and Re means that analogous ligand systems and targeting strategies can be deployed for both elements. Recently, we have shown that rhenium diazenide complexes, such as $[Re(NNPh)_2(dtc)_2]^+$ and $[ReCl(NNAr)(dppe)_2]^+$, can be prepared directly from perrhenate, and we are currently looking at methods for conjugation of such complexes to targeting agents such as monoclonal antibody fragments and polyammonium cations, the latter being known to be preferentially taken up by certain types of cancer cell.

5. Postscript

I hope this article will have in some way indicated how the fundamental coordination chemistry developed both in the UNF and earlier underpins a number of exciting current research areas. For my own part, the chemistry I did at Sussex continues to be crucial to several areas of my current research. The chemistry may not always have changed dramatically, but the applications certainly have. In these days of initiatives such as Technology Foresight it is perhaps pertinent to note that there could have been no thought in the 1960s and 1970s of applications such as metathesis catalysis or radiopharmaceuticals. It is nevertheless the case that these areas would probably not have developed as they have without the basic research carried out under Joseph Chatt's guidance and initiative.

References

[1] J. Chatt and G.A. Rowe, J. Chem. Soc., (1962) 4019.
[2] J. Chatt and R.S. Coffey, J. Chem. Soc. A, (1969) 2131.
[3] J. Chatt, J.D. Garforth, N.P. Johnson and G.A. Rowe, J. Chem. Soc., (1964) 1012.
[4] J. Chatt, J.R. Dilworth and G.J Leigh, J. Chem. Soc. A, (1970) 2239.
[5] B. Couthino, J.R. Dilworth, M. Rosser, C.M. Archer and J.D. Kelly, J. Nucl. Med. Biol., 38 (1994) 394.
[6] T. Nicholson, A. Davison and A.G. Jones, J. Nucl. Med Biol., 38 (1994) 421.
[7] J. Barrera, S.D. Orth, M. Sabat and W.D. Harman, J. Nucl. Med. Biol., 38 (1994) 391.
[8] A.J.L. Pombeiro, R.L. Richards and J.R. Dilworth, J. Organomet. Chem., 175 (1979) C17.
[9] J.R. Dilworth, P.L. Dahlstrom, J.R. Hyde and J. Zubieta, Inorg. Chem. Acta, 11 (1982) 21.
[10] M.Y. Mohammed and C.J. Pickett, J. Chem. Soc. Chem. Commun., (1988) 1119.
[11] M.W. Bishop, J. Chatt and J.R. Dilworth, J. Chem. Soc. Dalton Trans., (1979) 1.
[12] J. Anhaus, Z.A. Siddiqui, H.W. Roesky, J.W. Bats and Y. Elerman, Z. Naturforsch. Teil B:, 40 (1985) 740.
[13] J. Chatt, L.A. Duncanson and L.M. Venanzi, Soumen Kemistiehti, B29 (1956) 75.
[14] J. Chatt, B.S.L. Crichton, J.R. Dilworth, P. Dahlstrom, R. Gutkoska and J. Zubieta, J. Organomet. Chem., 4 (1979) 271.
[15] J. Chatt, J.R. Dilworth, P.L. Dahlstrom and J. Zubieta, J. Chem. Soc. Chem. Commun., (1980) 786.
[16] J. Chatt, B.A.L. Crichton, J.R. Dilworth, P. Dahlstrom, R. Gutkoska and J. Zubieta, Inorg. Chem., 21 (1982) 2383.

[17] A. Desai, J.R. Dilworth, V.C. Gibson, C. Redshaw and Y. Zheng, unpublished results, 1996.
[18] J.R. Dilworth, P. Jobanputra, S.J. Parrott, R.M. Thompson, D. Povey and J. Zubieta, Polyhedron, 11 (1992) 147.
[19] B. Coutinho, Ph.D. Thesis, University of Essex, 1995.
[20] W.A. Nugent and B.L. Haymore, Coord. Chem. Rev., 31 (1980) 123.
[21] J.R. Dilworth, J. Zubieta and J.R. Hyde, J. Am. Chem. Soc., 104 (1982) 365.
[22] M.W. Bishop, G. Butler, J. Chatt, J.R. Dilworth and G.J. Leigh, J. Chem. Soc. Dalton Trans., (1979) 1843.
[23] J.R. Dilworth, S.A. Harrison, D.R.M. Walton and E. Schweda, Inorg. Chem., 24 (1985) 2594.
[24] D.C. Rees, M.K. Chan and J. Kim, Adv. Inorg. Chem., 40 (1994) 89.
[25] J.R. Dilworth, J. Hutchinson and J. Zubieta, J. Chem. Soc. Chem. Commun., (1983) 1034.
[26] P.T. Bishop, J.R. Dilworth and J. Zubieta, J. Chem. Soc. Chem. Commun., (1985) 287.
[27] P.T. Bishop, J.R. Dilworth, T. Nicholson and J. Zubieta, J. Chem. Soc. Dalton Trans., (1991) 385.
[28] J. Chatt and J.M. Davison, J. Chem Soc., (1965) 843.
[29] J.R. Dilworth, J. Hu, R.M. Thompson and D.L. Hughes, J. Chem. Soc. Chem. Commun., (1992) 551.
[30] J.R. Dilworth, J. Hu, and J.R. Miller, J. Chem. Soc. Dalton Trans., in press.
[31] T.E. Burrow, A. Hills, D.L. Hughes, J.D. Lowe and R.L Richards, J. Chem. Soc. Dalton Trans., (1991) 1813.
[32] M.J. Baker, J.R. Dilworth, J.R. Miller, G. Sunley and N. Wheatley, J. Chem. Soc. Chem. Commun., (1995) 1579.
[33] R.R. Schrock, Polyhedron, 14 (1995) 3177.
[34] W.J. Feast, V.C. Gibson and E.L. Marshall, J. Chem. Soc. Chem. Commun., (1992) 1157.
[35] A. Desai and J.R. Dilworth, unpublished results, 1995.
[36] J. Chatt, J.D. Garforth and G.A. Rowe, J. Chem. Soc. A. (1996) 1834.
[37] B. Coutinho and J.R. Dilworth, unpublished results, 1995.
[38] T. Nicholson, A. Dawson and A.G. Jones, Inorg. Chem. Acta, 187 (1991) 51.
[39] B. Coutinho, D. Dawson and J.R. Dilworth, unpublished results, 1994.
[40] J.R. Dilworth, P. Jobanputra, R.M. Thompson, D.C. Povey, C.M. Archer and J.D. Kelly, J. Chem. Soc. Dalton Trans., (1994) 1251.