
Preface—Inorganic reaction mechanisms: insights into chemical challenges

Previous Dalton Discussions were concerned with Inorganic Clusters (Southampton, 1996), Bioinorganic Chemistry (Norwich, 1997), and Inorganic Crystal Engineering (Bologna, 2000). This, the fourth Dalton Discussion, entitled “Inorganic Reaction Mechanisms: Insights into Chemical Challenges” focused on the kinetics and mechanisms of reactions of inorganic species in solution. It was a joint meeting with the Royal Society of Chemistry Inorganic Reaction Mechanisms Group (IRMG),[†] who suggested the appropriateness of a Dalton Discussion in this area. The understanding of the mechanisms of inorganic reactions has increased tremendously over recent years. The present Dalton Discussion was concerned with some of the major techniques now used for acquiring mechanistic information, as well providing a forum for detailed discussion about specific systems. Originally IRMG meetings were held in the UK, but more recently they alternated between the UK and mainland Europe with meetings in Germany, France, Hungary, Croatia, and Ireland. With the large amount of inorganic mechanisms work being done in Germany, it was a very appropriate location for the Dalton Discussion. More than a hundred people from eighteen countries attended the meeting, which was held during 10–13th January 2002, in a former Trappist monastery and summer seat of the von Wittelsbach family on a hill top location at Kloster Banz near Bamberg, which is now run by the Hanns-Seidel Foundation. Each of five main topic areas had a keynote lecture followed by short presentations detailing salient points of papers, so there was ample time for extended discussion after each presentation. This broadly followed the format of a traditional Faraday Discussion with pre-prints of the papers being distributed in advance of the meeting.

Background

The first IRMG meeting was held in Leeds in 1970, and followed an *ad hoc* conference on inorganic reaction mechanisms at Bedford College (London) in 1969. This highlighted the interest in the mechanisms of inorganic reactions, and led to the formation of the IRMG. The extent of understanding at that time had been given in the comprehensive, and particularly influential, second edition of Fred Basolo and Ralph Pearson’s *Mechanisms of Inorganic Reactions*.¹ Several smaller related books were also published around that time,² as was the first volume of the Specialist Periodical Report on Inorganic Reaction Mechanisms edited by John Burgess.³ This critically reported the published literature, and the series went on to provide ongoing coverage into 1979. There then followed *Mechanisms of Inorganic and Organometallic Reactions* which continued a similar critical approach to reporting the mechanistic literature for a further decade.⁴

Three decades ago relatively few photochemical inorganic reactions had been extensively studied, and there was little detailed information about the kinetics of reactions of organometallic compounds. The most widely studied areas were ligand exchange reactions, especially at cobalt(III) and chromium(III) octahedral centres, and at platinum(II) and palladium(II) square-planar centres. These “slow” reactions were usually monitored by visible spectrophotometry, but other techniques were occasionally used. Stopped-flow methods began to be used increasingly for faster substitution reactions at more labile metal centres, while NMR techniques were employed to monitor rapid exchange processes at a variety of metal ions. The basic concepts of associative and dissociative substitution reactions as limiting interchange processes, formalised most notably by Cooper Langford and Harry Gray in *Ligand Substitution Processes*,⁵ began



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to be developed and elaborated in many papers. Rapid base hydrolysis of ammine and amine complexes was interpreted in terms of mechanisms involving very reactive conjugate base species. Redox reactions were well represented. Attention here progressed from inner/outer sphere mechanisms and self-exchange reactions of simple complexes to increasingly larger molecules, in which the distances between redox centres were longer. Biological redox systems, such as metalloproteins, were increasingly studied, and the kinetics and mechanisms of biologically active metal centres attracted a lot of attention. Reactions of organometallic compounds are as important as those of coordination complexes. Processes such as carbonyl substitution and alkyl group migration reactions were studied by traditional infrared or UV/visible methods. Later faster organometallic reactions were followed by

[†] Often referred to as the Inorganic Mechanisms Discussion Group (IMDG).

stopped-flow techniques. Study of fast ligand exchanges and conformational rearrangements made extensive use of NMR methods that became increasingly sophisticated.

Applications of advanced experimental techniques

The first session in the present Dalton Discussion, chaired by Rudi van Eldik (Erlangen), was on advanced experimental techniques, with the keynote lecture by André Merbach⁶ (Lausanne) on high pressure NMR. This technique is now well known, but the overview of the substitution reactions studied in this way over a wide temperature range, and the application to reactions of added gases was most useful. A lengthy debate about the coordination number of Cu^{2+} in aqueous solutions ensued after the presentation of experimental neutron diffraction evidence and first principles molecular dynamics calculations that suggested it is five coordinate.⁷ Istvan Horváth⁸ (Eötvös Lorand) showed that sequential infrared measurements can give a surprising amount of information about the species present in aromatic acylation in the difficult area of low melting ionic fluids. Depending on their enthalpy of activation, some fast reactions can be retarded sufficiently by operating at low temperatures for them to be monitored by readily available techniques. Siegfried Schindler⁹ (Erlangen) nicely described how stopped-flow techniques can be used successfully at low temperatures, but commercially available instruments only operate down to $-40\text{ }^\circ\text{C}$. He also discussed global analysis fitting methods for obtaining rate constants for complex reaction schemes. During discussion there was concern that multiple wavelength analyses might, in some circumstances, give credence to reactions that are not actually present, and modelling of these situations would be worthwhile. Dale Margerum¹⁰ (Purdue) described further developments of the pulsed accelerated flow technique that provides a means of monitoring very fast reactions (up to $5 \times 10^5\text{ s}^{-1}$ and typically $2 \times 10^5\text{ s}^{-1}$). A proper understanding of the reactant mixing process (in a ten-jet mixer) is key to enable meaningful chemical rate constants to be extracted. The application of the technique to the hydrolysis of BrCl was reported. Finally in this session Antonin Vlček¹¹ (Queen Mary and Westfield College) gave an account of picosecond and femtosecond processes in the photo-dissociation of metal carbonyls that was notable for its technical sophistication. With results from ultrafast time-resolved spectra of the photodynamics of organometallic compounds it can be difficult to differentiate between consecutive and parallel reactions, so a combination of techniques is needed. Time-resolved absorption, infra-red, resonance Raman, and fluorescence methods were discussed.

Advanced computational techniques

The second session was chaired by Rob Deeth (Warwick), and dealt with advances in computational chemistry. The keynote lecture by Tom Ziegler¹² (Calgary) was an informative, comprehensive and comprehensible critical overview of the uses and virtues of the different modern methods for calculating molecular energies and rate constants. This area has seen tremendous advances over recent years, and it has become an established tool for considering the viability of various proposed mechanisms and transition states, and for suggesting likely alternatives. Within a few years such computer calculations will surely become as routinely used as the acquisition of kinetic data itself. Michael Hall¹³ (Texas A&M) described the application of density functional calculations to the generation of carbene complexes by methane elimination from tungsten dimethyl-compounds, and here it appears the presence of a strong metal-hydride interaction is important in assisting the process. In an elegant presentation François Rotzinger¹⁴ (Lausanne) revisited the calculation of second order rate constants for the self-exchange reactions that take place *via* outer sphere pathways, and probed the reasons for failures of the Marcus cross-relation in terms of implicitly included relations. The fact that $[\text{Ru}(\text{H}_2\text{O})_6]^{2+}$ seems unusual was mentioned, and the possibility of some metal-metal interaction, and the nature of the second coordination sphere were considered. The computational chemistry section was concluded by Clark Landis¹⁵ (Wisconsin) who reported quantum mechanical modelling of alkene hydroformylation by some rhodium complexes to complement experimental results that, for the examples chosen, are rather sparse. However, the computed activation free energies were much larger than expected, and it was difficult to use these data mechanistically. The origin of this overestimation appears to result from the magnitude of the alkene bonding energy.

Small molecule activation and homogeneous catalysis

The last contribution in the previous section was a bridge into the third section that was on small molecule activation and homogeneous catalysis chaired by Ferenc Joó (Debrecen). Bill Tolman¹⁶ (Minnesota) gave the keynote lecture on the synthesis of sterically hindered benzoates as new models for non-haem di-iron protein oxidative enzymes. This was followed by a technically elegant presentation by Simon Duckett¹⁷ (York) on NMR methods using parahydrogen induced polarisation to detect low concentrations of species present during oxidative addition of hydrogen at iridium(I) centres. Parahydrogen is readily obtained by treating hydrogen with a suitable catalyst at low temperature, and this easily accessible experimental technique could probably be used in a number of other situations to provide evidence to complement computational results. The next two presentations by Walter Leitner¹⁸ (Mulheim) and Morris Bullock¹⁹ (Brookhaven) were concerned with hydrogenation, and provided excellent examples of establishing mechanisms of hydrogenation reactions *via* NMR, and in the latter case with kinetic investigations. Walter Leitner discussed the enantioselective Rh-catalysed alkene reduction of itaconic acid derivatives with formic acid/triethylamine mixtures (transfer hydrogenation) or dihydrogen itself. Deuterium labelling experiments showed that the deuterium pattern in transfer hydrogenation can be different from the vicinal addition with dihydrogen, and that this depends on the nature

of the allylic carboxyl group. The two processes are thought to be essentially similar, with the differences resulting from the relative rates of the steps in the catalytic cycle, compared to the isomerisation rate of the σ -alkyl intermediates. Morris Bullock discussed the slow (days) catalytic hydrogenation of ketones (with dihydrogen) to alcohols at room temperature using molybdenum and tungsten complexes. The ionic mechanism proposed does not require coordination of the ketone to the metal for the hydrogenation, and differs from traditional mechanisms where ketone coordination at the metal centre precedes insertion into an M–H bond. The final paper in this section was by Robin Whyman²⁰ (Liverpool) who focussed on the roles of promoters in the very high-pressure production of chemicals from synthesis gas (mixtures of CO and H₂). The role of the, often thought of as mysterious, but essential industrial “promoters” was described, and in the case of ruthenium promotion of homogeneous iridium-catalysed methanol carbonylation (BP acetic acid process) the use of high pressure NMR provided some additional information to help remove some of the mystery. Here iodide bridged Ru–Ir species were detected and characterised.

Electron and energy transfer processes

The penultimate session was concerned with electron and energy transfer processes, and was chaired by Jim Espenson (Iowa State). The keynote speaker was Fraser Armstrong²¹ (Oxford) who presented results from film cyclic voltammetry of redox-active proteins. With scan rates in excess of 1000 V s⁻¹ the resulting current signals provide considerable information about reactions in the sub-millisecond time domain. The immobilised proteins are tightly bound to the electrode surface, and this might influence the behaviour of the protein. The extent to which this happens is not absolutely clear, but it does not prevent the gathering of very exciting results due to the electron transport being coupled with a variety of chemical reactions such as ion transport. Gábor Lente²² (Debrecen) then showed how the complex mechanism for oxidation of S(IV) species by Fe(III) with excess metal can be elucidated with the help of global spectral analysis. As with the earlier paper by Siegfried Schindler, concerned with multiwavelength analysis, the opinion during debate was divided between those who embraced what computer analysis indicated in terms of the number of significant reactions, and those who advised a degree of considered scepticism. David Stanbury²³ (Auburn) discussed results for the oxidation of thioglycolic acid by hexachloroiridate(IV). This reaction is very susceptible to catalysis by traces of copper, and this was inhibited by addition of bathophenanthrolinedisulfonate so the direct oxidation reaction could be studied. Product analysis showed that the copper mediated and the direct oxidation processes gave different oxidation products. Dave Rorabacher²⁴ (Wayne State) also discussed copper chemistry, this time the electron-transfer kinetics and equilibrium of copper(II/I) complexes with 1,4,7-trithiacyclononane. Here, as in the previous paper, global analysis techniques were not used, but there was great ingenuity in extracting information, changing conditions to test conclusions, and bringing together observations from many sources to test or reinforce a mechanistic hypothesis.

Bioinorganic applications

The last session was on bioinorganic reactions and was chaired by Richard Henderson (Newcastle). The keynote speaker was Larry Que²⁵ (Minnesota) who gave a masterly account of hydrogen peroxide activation to give stereo- and regio-specific attack on alkenes, employing three similar non-haem-iron model complexes. This is of course in marked contrast to the action of Fenton's reagent. The work nicely illustrated the use of isotopic labelling, NMR, kinetic measurements and chemical analysis in a concerted approach to probe the detailed mechanisms of these reactions. The spin state of the iron centres is key to controlling reactivity, and they can be “tuned” by slight ligand modifications to give a family of iron complexes that catalyse a remarkable range of hydrocarbon oxidations. There followed a paper by Suzanne Mayer²⁶ (Virginia Polytechnic) on the mode of action of nitrogenase that employed structural studies, site-directed mutagenesis, and substrates with different steric requirements to probe the most likely site of attack on the Fe–Mo cofactor. In concluding that this is the iron centre, the question remains as to why the molybdenum is present! Sara Goldstein²⁷ (Hebrew University) discussed the reactions of peroxyxynitrite, which has been implicated in biological systems, being formed from reaction between NO and O₂^{-•}. With carbon dioxide an adduct is formed [ONOOC(O)O⁻] that has a half-life of less than 100 ns, and so it does not have any direct role in biological or chemical systems. The concluding contribution by Nick Le Brun²⁸ (East Anglia) again employed a wide range of kinetic and spectroscopic techniques to probe the role of copper ions in promoting the incorporation of iron into the inorganic core of bacterioferritin. In contrast cobalt, zinc, and manganese bind at the iron centres and inhibit iron deposition. It was concluded that copper enhances the rate of oxidation of iron(II), and hence the deposition of insoluble iron. It was noted that preparations of mammalian ferritins, and to a lesser extent bacterioferritins, often contain significant amounts of copper.

Poster sessions

There were some fifty contributions to the poster sessions, and they all reported interesting high quality work. A feature of this meeting was the opportunity for each author to give a brief oral synopsis of their poster. Although space does not permit comment on all of them here, it is worth mentioning a few of the topics covered to convey the scope of the research presented. A collaborative poster from T. Schnepfenseper, A. Wanat and R. van Eldik (Erlangen), E. Bill and K. Wieghardt (Mulheim), and G. Stochel (Jagiellonian University) reported a kinetic and mechanistic analysis of the formation of the classic “brown ring” test reaction for nitrate involving the reaction of NO with [Fe(H₂O)₆]²⁺. On the

basis of evidence from a range of techniques it was concluded the product $[\text{Fe}(\text{H}_2\text{O})_5\text{NO}]^{2+}$ is best described as a high-spin Fe(III) centre antiferromagnetically coupled to NO^- , and not an Fe(I) complex as previously supposed. S. C. Galbraith, C. Robson and D. T. Richens (St. Andrews) reinvestigated anation of $[\text{Rh}(\text{H}_2\text{O})_6]^{3+}$ with Br^- at high pressure. Their results were consistent with a pre-association ion-pair followed by $\text{Br}^-/\text{H}_2\text{O}$ interchange, and support a largely associative mode of activation. A. J. Dunford and R. A. Henderson (Newcastle) developed a method for spectroscopically monitoring the reaction of $^t\text{BuNC}$ with $[\text{Fe}_4\text{S}_4\text{Cl}_4]^{2-}$ that results in only very small spectroscopic changes. After mixing the reactants PhS^- was added in a sequential-mix-stopped-flow apparatus to substitute the terminal chloro-ligands associated with large visible absorption changes. Using this approach the authors obtained evidence that binding to an Fe-S cluster can involve a transient coordination geometry that is different from that in the final product.

Conclusions

At the time of the early IRMG meetings the main experimental variables available to obtain kinetic information were concentration (usually of the incoming ligand) and temperature. Ligand concentration dependence gave reaction orders that sometimes could be used to infer the nature of transition states, while varying temperature provided data to estimate activation enthalpies and entropies. High-pressure techniques developed rapidly to become a powerful general mechanistic tool.²⁹ In marked contrast to the situation today, detection of intermediate species was uncommon, and so mechanistic insight mostly depended on kinetic data coupled with common sense on what might be possible, knowing the nature of the reactants and products. Crystal field considerations were sometimes invoked when considering the nature of transition states, but theoretical computational studies of reaction profiles and likely transition states were essentially non-existent as an aid to understanding mechanistic pathways. This Dalton Discussion clearly showed the huge amount of progress that has been made in all of the areas concerned with elucidating inorganic reaction mechanisms. Several sophisticated experimental techniques are often now used to detect the presence of low concentrations of intermediate species in complex reactions that can be monitored over a wide range of time domains. As a result, ever increasingly complicated systems are being investigated by large multidisciplinary research groups. The major advances made in the computational chemistry area can now be used to provide valuable additional information about the mechanisms of inorganic reactions, and the value of this cannot be over emphasised. It was clear from this meeting that progress is rapid, and the collective use of these approaches means the study of inorganic reaction mechanisms will continue to be a very exciting area in the future.

Acknowledgements

The organising committee and those involved from the Royal Society of Chemistry are to be thanked for their efforts that resulted in a particularly well run and stimulating Dalton Discussion. The organising committee comprised Rudi van Eldik, Michael Davis, Rob Deeth, Lars Elding, James Espenson, István Fábrián, Richard Henderson, Ferenc Joó, André Merbach, Lene Mønsted, Dave Richens, Martyn Twigg, and Neil Winterton. Those from the RSC were John Gibson, Nicole Morgan, and Claire White. Finally special thanks are due to the staff at Kloster Banz for the friendly and efficient way in which they accommodated the constantly changing needs of attendees engrossed in mechanistic discussions.

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