Catalysis Letters Vol. 98, Nos. 1, October 2004 (© 2004)

Catalysis in chemistry and biochemistry

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Received 28 June 2004; accepted 18 August 2004

Under this title, the Royal Society of London organized a Discussion Meeting in June, 2004. The programme is appended and demonstrates its interdisciplinary nature, both in the presentations and the speakers. It also demonstrates the essential structure of the presentations viz the activation of covalent bonds in dioxygen, hydrocarbons, dihydrogen, carbon monoxide and dinitrogen. Additional emphasis recognized the significant progress that has been made over the past several years in the definition of active sites in heterogeneous, homogeneous and enzymatic catalysis; the description, experimentally and theoretically, of reaction intermediates and transition states in catalysis; and on the opportunities and achievements required for the development of environmentally benign catalysts, based on new science and technology. Bridging the three catalytic systems and their reaction mechanisms are dynamic models of active sites and a recognition of the increasing availability of structures and energetics of intermediates and transition states; the latter provide for the description of reaction pathways and for devising preferred pathways so as to enhance specificity through the promotion/inhibition of particular intermediates.

KEY WORDS: catalysis in chemistry; catalysis in biochemistry; heterogeneous catalysis; homogeneous catalysis; enzyme catalysis.

1. Active sites

It was inevitable that, given the progress that has been made in determining active site structures in homogeneous, heterogeneous and enzyme catalysts, structure–function relationships were explored. It is, salutary, however, to remind oneself that diffraction and spectroscopic studies of active sites are, for the most part, time- and space-averaged and important as they have been in surface science, enzyme chemistry and organometallic/coordination chemistry, they must now be supplemented by convincing evidence of the mobility/lability of active sites in catalytic reactions.

Using scanning tunneling microscopy, G. Ertl, G. A. Somorjai and M. W. Roberts have provided unequivocal evidence for adspecies' mobility and linked it to substrate mobility and surface reconstruction. Earlier Ertl had established disorder–order transitions and reported a robust simulation of mobilities, of the activation of dihydrogen and the role of "steps" as active sites in the dissociative adsorption of nitric oxide and dinitrogen and the mechanism(s) of the catalytic oxidation of carbon monoxide and dihydrogen. Somorjai, using sum frequency generation vibrational spectroscopy to characterize adsorbate structures and scanning tunneling microscopy to monitor surface mobilities, gave a comprehensive account of C-H bond activation in alkenes and alkanes sorbed on a (111) surface of platinum.

Two conclusions were evident

- the surface mobility of adsorbates is essential to produce catalytic activity, and
- the inhibition of surface diffusion by, say, adsorption of carbon monoxide, leads to the formation of ordered structures and a loss of reactivity.

These conclusions are matched by M. W. Roberts' studies of the activation of oxygen at metal surfaces. The evidence for transient species, $O_{\bullet}^{-}$ and,O_2^{-} is clear as is the efficiency of oxydehydrogenation reactions at low temperatures. The reactivity is reduced by thermally induced ordering of oxygen states and accompanying surface reconstruction. Several examples have emerged where surface transients, experimentally undetectable, have been shown to provide low energy reaction pathways to products (vide infra).

Turning to the homogeneous catalytic scene, we noted, in a paper entitled "Non-primary valence interactions in low valent transition metal complexes and some possible implications for the structure of coordinatively unsaturated species" (Bennett, Donaldson, Hitchcock and Mason, *Inorganica Chemica Acta* **12** L9 (1975), that steric interactions between ligands can provide for different stereochemistries of the rhodium(1) ion in tris–triphenylphosphine rhodium chloride (a.k.a Wilkinsons' catalyst); there are pathways for the metal ion to explore which differ little in terms of the total energy of the molecule and, additionally, the ligands' geometrics can exercise preference for the entrance of reactants to the coordination sphere (and for the exit of products).

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Enzymes, like heterogeneous catalysts, allow long-range migration of potential reactants. It is not atypical to observe enzymatic structural changes, over several or more molecular diameters from the active site, as the enzyme passes from a "resting" condition to an activated and activating state following the binding of reactants.

2. Intermediates and transition states

A knowledge of reaction intermediates and transition states is essential to the formulation of catalytic reaction pathways. This point, together with other unifying principles linking the three main sub-divisions of catalysis, were set out in the comprehensive review paper by J. M. Thomas and R. J. P. Williams largely by reference to the usual free energy/reaction-coordinate plots.

T. Poulos discussed intermediates in reactions of cytochrome P450. The Fe(IV)=O oxidant has been established as the intermediate in the heterolytic fission of the dioxygen bond with diffraction studies also providing information on the elaborate network of hydrogen bonds which deliver protons to the iron-linked oxygen. Monooxygenases can be distinguished from peroxidases where the intermediate is relatively inactive. Secondary valence interactions promote the Fe(IV)=O or Fe(IV)—OH intermediates and any synthetic strategy for a model system will need to mimic this observation. Non-heme iron dependent oxygenases and oxidase are involved in metabolism and in the biosynthesis of plant signaling molecules. C. J. Schofield reviewed structural and mechanistic studies on the 2-oxoglutarate-dependent oxygenase and demonstrated the nature of oxidizing intermediates isolated from the environment.

The computational chemistry of oxidases was discussed by Per Siegbahn, the presentation highlighting

- the rapid development of density functional theory and the interplay of experiment with theory, and
- the ease with which short-lived intermediates and transition states can be assessed, always provided that relevant models are available.

The intermediates O_2^-, O_2H^- and $OH^{\cdot}$ commonly feature in mechanistic discussions of catalysis but have only recently been extended by M. W. Roberts' studies of the activation of dioxygen at metal surfaces. Those have identified O^- (and O_2^-) and their reactions with C—H and N—H bonds. The coadsorption of methane and dioxygen at lithium and magnesium surfaces provides for carbonate formation at low temperatures, a result which also follows from the coadsorption of methane and nitric oxide. The control of these oxidation reactions is discussed later.

S. Lippard discussed enzymes which catalyse the hydroxylation of hydrocarbons. A di(-oxo) diiron(IV) species has been characterized as the intermediate which reacts with methane to provide methanol and a bound methyl radical; X-ray analyses also demonstrate the access pathway of substrates to the active site in methanemonoxygenase. The identification of the carboxylate-bridged diiron centres at the active sites has stimulated the syntheses of model complexes (vide infra).

G. Somorjai provided the most complete studies of the activation of C—H bonds at a platinum(111) surface. The experimental strategies of using vibrational spectroscopy to define and characterize the adsorbate structures and high pressure scanning tunneling microscopy to monitor mobility under reaction conditions are combined with an analysis of the activation of alkanes and alkenes as a function of temperature and low and high pressures in the absence or presence of hydrogen. Two important results should be mentioned. The first, which has been commented upon earlier, relates to the reactivity of disordered states at the surface and the disorder–order transition which follows from the adsorption of carbon monoxide or thermal "annealing". Secondly, as might be anticipated, the presence of hydrogen slows down dehydrogenation and, for some of the adsorbed species, influences molecular rearrangements, thus altering reaction *selectivity*.

B. Sharpless reacted to the challenge of transferring more homogeneous and heterogeneous catalytic reactions to aqueous environments with a stimulating discussion of new synthetic methodologies and directions. While R. Catlow, in his paper "Computational approaches to the catalytic activation of C—H bonds", discussed reaction mechanisms in transition metal substituted microporous and oxide catalysts, bringing further emphasis to the point made by Thomas and Williams in their paper, that atypical metal coordination geometries and oxidation states provided for reactivities of importance in several catalytic processes.

The [NiFe]-hydrogenases oxidize H_2 or reduce H^+ in the biological hydrogen cycle and have the group

$$(\mathrm{Cys\ S})_2\mathrm{Ni}^{3+}(\mu - \text{'O'})(\mu \mathrm{S\ Cys})_2\mathrm{Fe}^{2+}(\mathrm{CN})_2(\mathrm{CO})$$

as the active site, 'O', the bridging oxygen species, is either hydroxide or peroxide; both forms are inactive but reduction/activation replaces the 'O' bridging ligand by hydride. The enzyme oxidizes dihydrogen at a rate comparable to a platinum catalyst thus providing an electrochemical probe for studying the active site (Armstrong and Albrecht).

G. Ertl discussed the surface science and intermediates in the activation of CO and N_2 and the implementations for catalysis. There is now widespread agreement on dissociative adsorption and the stepwise reduction of, say, the nitrogen adatoms.

Our understanding of the biofixation of dinitrogen has moved apace with the impressive diffraction studies that have characterized the Mo—Fe protein, the Fe—Mo cofactor that provides the active site for reduction and the Fe-protein that couples ATP hydrolysis to interprotein electron transfer. The elucidation of the mechanism(s) of the nitrogenase reactions has a long way to go (including the identification of a light atom ligand at the centre of the FeMo co-factor) but the present strategies of nitrogenase biochemistry, model chemistry and structural and computational studies are very promising. R. Schrock has shown that dinitrogen can be reduced to ammonia at a single molybdenum centre that is, cleverly, sterically protected against bimetallic decomposition reactions. The isolation and characterizations of eight proposed intermediates in the catalytic reaction (under noncatalytic conditions) which are active as catalyst precursors suggests that dinitrogen is being reduced at a single metal centre which cycles between the +3, +4, +5 and +6 oxidation states of molybdenum.

3. Specificity in and control of catalytic reactions

The selection of a reactant (from many other possible reactants) by an enzyme catalyst has to be completed with high precision. Thomas and Williams' paper cites "the fidelity attainable in enzymatic catalysis often exceeds 1 in 10^5, whereas in non-enzymatic catalysis, selectivites seldom exceed 1 in 10^2 except in enantioselective processes. The most difficult catalysts to control in reactions are metal surfaces".

The demands on accuracy and integrity of enzyme-catalysed reactions can be additionally met with molecular chaperones, which are in part, designed to obviate protein misfolding and the resulting unwanted products. R. Noyori described the rapid, productive and enantioselective hydrogenations of simple ketones which, based on chiraldiphosphine/1,2-diamine-Ru(11) complexes, occurs via a non-classical metal–ligand bifunctional mechanism. The enantiofaces of prochiral ketones are differentiated on the chiral molecular surface of the saturated (18 electron) ruthenium dihydride species. Ligand design and function are all important, supplementing the obvious stereochemical and electronic requirements of the metal.

It may be that the prospects of control of products at metal surface catalysts are not totally bleak. Somorjai's observation that the presence of hydrogen slows dehydrogenation and may influence molecular rearrangements must surely be interpreted as influencing the reaction pathway presumably through selective inhibition or promotion of one or other intermediate. The finding of the effect of coadsorption of carbon monoxide on the mobility of active species has a parallel in Roberts' work where $O_{\bullet}^{-}$ loses its reactivity on thermally induced ordering but, in the disordered states, can rapidly oxidize methane to the carbonate ion. But in other surface reactions that anion radical can "behave" in a more structured way. Starokon *et al.* (2003) have recognized an oxygen species, designated the α-state and present in iron-doped zeolites, with an oxidation chemistry similar to that of the enzyme methanemonoxygenase while Kameoka et al. (2003) have suggested that a "nascent" oxygen transient is present when a N_2O + CH_6 mixture is exposed to an Fe-ion exchanged BEA zeolite responsible for the formation of C_xH_yO species. Carley *et al.* (1998) have suggested $M—OC_3H_6$ and $M—C_3H_6O$ as the respective intermediates in the selective and total oxidation of propene.

The experimental and theoretical definition of intermediates does allow "educated guesses" at directing or favoring particular structures e.g., π-allylic intermediates defined by Somorjai in the activation of C—H bonds. Coadsorption or sequential adsorption could become an invaluable tool in the enhancement of selectivity and specificity in heterogeneous catalysis.

4. Environmentally benign catalysis

Three presentations at the Discussion Meeting were concerned with the science, technology and engineering of catalysts which might fulfill the requirement of environmentally benign processes. Membrane reactor catalytic reactions were described by T. Maschmeyer and deemed to be viable for a number of reactions. P. Ratnasamy described the results of encapsulating a wide variety of transition metal complexes in molecular sieves where enforced structural changes of stereochemistry resulted in significant changes of reactivity–this appears to be an approach of considerable promise. M. Twigg summarized the progress that has been made in the reduction/removal of hydrocarbons, carbon monoxide and nitrogen oxides from automobile exhausts. New challenges to the design of catalysts are flowing from the imperative of improved fuel efficiency in cars e.g., particulate matter control from diesel fuel.

5. Prospects

There can be no doubt that time-resolved diffractions, spectroscopic and microscopic studies of the dynamics of reactants at surfaces will yield data of import to selective catalyst design. The definition of transfer pathways on enzyme surfaces of electrons, protons, atoms and molecules, which are already being described in the conventional time-averaged diffraction experiments and of reactions at the active site will bring entirely new and comprehensive views on catalysis.

Already, we discuss the impact of active site structural determinations on the synthesis of model systems. Compared to the situations of a decade or more ago, the synthetic chemist has clear targets; the synthesis of models for the carboxylate-bridged diiron(11) in methane monooxygenase and toluene monooxygenase are notable for their reactivity, including the generation of reactive intermediates, such as high-valent species capable of hydroxylating or oxidizing C—H bonds. Steric protection against unwanted reactions is also included in the synthetic strategy of the molybdenum complex (Schrock) which has demonstrated several intermediates in the catalytic reduction of dinitrogen. These designer ligands effectively police the active centre(s) with steric control but such channeling may need to be supplemented by other recognition/synthetic methods such as we see so elegantly formulated in the Noyori ruthenium complex; such a development must be necessary to obtain significant improvements in turnover rates in mono-nuclear or, indeed, polynuclear metal complexes. Model synthesis, often based on enzyme-active site structures, must become a productive plank in homogeneous catalysis.

There is some room for optimism for believing that higher levels of selectivity can be achieved in heterogeneous catalysis. A knowledge of intermediates and, perhaps, transition states can obviously provide a strategy for promotion or poisoning/inhibiting reactions. It is interesting to reflect on the traditional views of catalytic reactions which are promoted by, say, alkali metals being sorbed on a transition metal surface:a conventional view would emphasize Lewis base behavior but the recent findings of their effects on a adatom/admolecule mobility must be reckoned with as they might have differential effects on intermediates. We are poised to exploit the present results on C—H bonds and dioxygen to effect novel hydrogenation/dehydrogenation and partial oxidation – complete oxidation reactions. There are, too, the opportunities for tailoring the geometries of coordinatively unsaturated metal ions: from the encapsulation of complexes or ions in cage structures (which have similarities to the mode of action of metalloenzymes); to variable step and kink sites on surfaces, usually designated by high Miller indices; to ligand design which, by their steric and electronic properties, can produce complexes of atypically low coordination number. And the target of benign, environmentally acceptable catalytic reactions can be approached, not at the gallop but at the steady achievements flowing from findings such as those presented in the Discussion Meeting.

APPENDIX

Catalysis in chemistry and biochemistry (An annotated summary of programme)

(i) Principles and activation dioxygen

J. M. Thomas and R.J.P. Williams
Catalyses: Principles, Progress, Prospects

T. Poulos
Intermediates in reactions of cytochrome P-450

C.J. Schofield
Oxidation of non-heme iron systems in catalysis and signaling

Per Siegbahn
Computational catalytic chemistry of oxidases

M.W. Roberts
Activation of oxygen at metal surfaces

(ii) Activation of C—H bonds and of dihydrogen

S. Lippard
Hydroxylation of C—H bonds at carboxylate-bridged diiron centres

G. A. Somorjai
Active sites and states in the heterogeneous catalysis of C—H bonds

R. Noyori
Entiomeric catalysis

B. Sharpless
An asymmetric odyssey leading back to its port of origin

R. Catlow
Computational approaches to the activation of C—H bonds

F. Armstrong and S. Albrecht
[NiFe}-hydrogenases:electrochemical and spectroscopic determination of intermediates

(iii) Activation of carbon monoxide and dinitrogen

G. Ertl
Surface science and intermediates in the activation of CO and N_2:implications for catalysis

R. R. Schrock
Catalytic reduction of dinitrogen at well-defined single metal sites

D. Rees
Biofixation of dinitrogen

(iv) Industrial processes

T. Maschmeyer
Membrane catalytic reactions for processing small molecules

P. Ratnasamy
Novel, benign catalysts for oxidizing hydrocarbons

M. V. Twigg
Controlling automotive exhaust-emissions – successes and underlying science

R. Mason
Summary and concluding remarks