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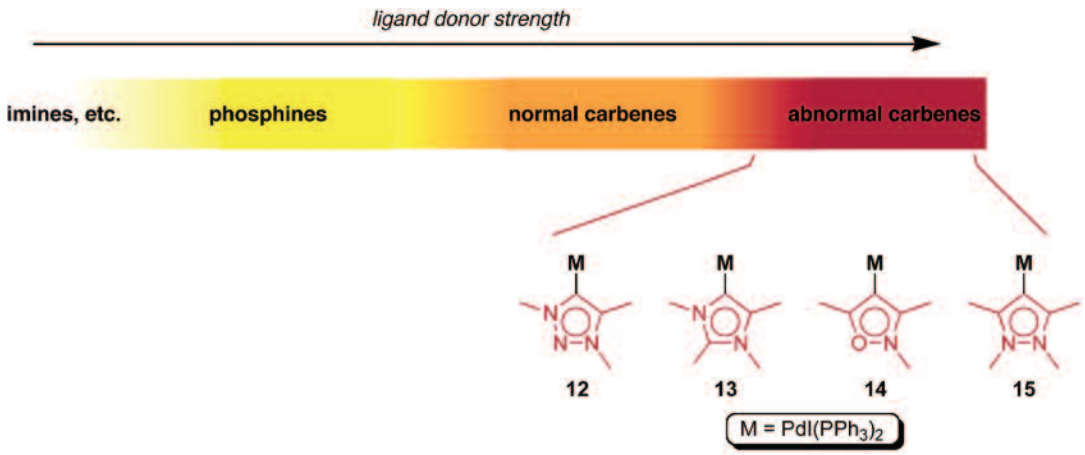
FEATURE :

Challenging the Norm: Abnormal Carbenes as Powerful Ligands in Metal-mediated Transformations



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Editorial

First of all both myself and the council of the ICI would like to wish all of our readers a very merry Christmas and a happy new year. This issue very much has a 'UCD feel' to it as we have received several interesting contributions from members of that institution. Our feature article is from **Prof. Martin Albrecht** – who has recently arrived in Ireland after receiving a prestigious ERC Investigator grant – on the chemistry of very unusual (potentially useful) carbene species. Our School in profile this issue is UCD – **Prof. Rory More O'Ferrall** has kindly submitted an article charting the history of the School from its early days to the present time. Our invited articles come from two very different fields – from the domain of medicinal chemistry and drug design we have a contribution from **Dr. Fawaz Aldabbagh** and **Karen Maher** (UCG) detailing their recent successes in the design of new, potent, anti-cancer compounds, while **Dr. Wolfgang Schmitt** (TCD) has disclosed some of his recent results in the area of inorganic molecular assemblies which are rapidly gaining international attention. Our past president **Dr. Donal Coveney** has kindly contributed the ICN crossword and industry news article once again and **Dr. James O'Sullivan** (UCD) has written a report on the successful ICI congress 2009. **Dr. George Birkett (Henkel)** has provided a teasing Sudoku and we have the usual roundup of highlights from the chemical literature. Finally, on a personal note I am pleased to have the opportunity to publish an obituary of my academic 'grandfather' - the redoubtable former Professor of Chemistry in UCC **Francis Leslie Scott,** written by one of his former students **Prof. Frank Hegarty** (UCD). We welcome comments and suggestions on the balance and direction of the ICN - members are also strongly encouraged to submit essays, articles and correspondence on any issues/developments affecting chemistry, either globally or in Ireland.

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Meeting Report: ECTN4 final meeting in Dresden 8-10/9/09

Dr. Peter E. Childs, Department of Chemical and Environmental Sciences, University of Limerick, Limerick

The 4th. cycle of ECTN funding expires at the end of September 2009. The European Chemistry Thematic Network has been running since 1996 and is the longest running and most successful of the thematic networks set up in the 1990s. It has just received funding for a 5th. cycle from 1/10/09, worth 600,000 Euro, in conjunction with the Chemical Engineering EducationNetwork. The new body will be called the European Chemistry and Chemical Engineering Education Network, EC_2E_2N. This will ensure funding and activity until 2012. The new project will also involve CEFIC. The meeting in Dresden was the final meeting of ECTN4 and focused on the implications of the Bologna Process for chemistry in Europe. 2010 is the deadline for full implementation of Bologna and ECTS in a European Higher Education Area. At present the implementation of Bologna and ECTS is not uniform across Europe, which includes 46 countries – the EU 27 plus 19 others.

The two main aims of the Bologna process are mobility of students **and recognition of educational standards across Europe. The EU has an ambitious target of 20% of graduates to have study or placement abroad by 2020.** At the moment the mobility of students is very patchy: some countries send out a lot of students and others (UK and Ireland for example) send out relatively few. Some of the main problems are language and costs – costs in various countries vary widely. Ireland is much more expensive for students than many European countries. Some countries like Germany pay for their own students to study abroad and for foreign students to attend courses in Germany because they consider it to be an investment in the future. For Irish students a major implication is the need for a second European language to facilitate mobility.

One of the products of ECTN4 was launched at the conference. A working group on Innovation in Chemistry Teaching has produced a book on *Innovation in Teaching and Learning in Chemistry in Higher Education*.
This is published by the RSC and should be essential reading by all university chemistry lecturers. It reviews best practice in a number of areas relevant to teaching chemistry at 3rd. Level.

Under EC_2E_2N the Working Group on Chemical Technology will continue (interface of chemistry and chemical engineering) and the summer schools for new lecturers will also continue. A new group will look at a possible Eurolabel™ for initial science teacher education. See http://ectn-assoc.cpe.fr/network/ectn5.htm for details of activities under the proposed project. All ECTN members are eligible to take part in the working groups.

ECTN has instituted Eurolabels™ in Chemistry at bachelor level (Eurobachelor™) and Master's level (Euromaster™). So far 48 Euobachelors and 24 Euromasters have been approved in 24 countries. This approval indicates that the courses meet specified standards, giving them international currency. Several courses in Ireland have been certified.

There is also discussion of a European model for doctorate education (Salzburg, 2005). The Salzburg principles set a common framework and common goal for doctorate education. Stress is on an original research project not on teaching. There will be a workshop on structuring doctoral education in Zagreb, Dec. 2009; a workshop on research careers in March 2010; an annual conference 4-5 June 2010, Lausanne (Salzburg II); workshop on joint degrees Oct. 2010. (www.eua.be)

ECTN is also considering some form of certification of 3rd. Level teaching, *i.e.* a Eurolabel™ as an indication of quality and achievement.

The 2010 ECTNA annual meeting will be in Montpellier, April 2010 together with the first meeting of EC_2E_2N.

A report was given on the European Research Council (ERC) and its grants for encouraging research in Europe. This is now a major source of significant funding for research grants for young researchers (300 grants per year) and advanced researchers (400 grants per year). www.erc.europa.eu

There was a presentation from SusChem on the future of chemistry and the chemical industry in Europe. Emphasis on new skills for new needs – chemistry is not an old industry that needs managing but a developing industry that is creating new products and new jobs. www.suschem.org

Who cares? Who dares? Recent report on providing skills for an innovative and sustainable Europe. Ireland does quite well in this assessment of skills provision.
http://www.insead.edu/discoverinsead/docs/WhocaresWhodares.pdf

The conference finished with a chemistry magic show given by Herbert Roesky (co-author of *Spectacular Chemistry Experiments, Wiley*).

It is essential for the future for Irish chemistry for Irish universities and chemists to be actively involved in the work of EC_2E_2N. It is an important opportunity for networking across Europe. Details of ECTN activities can be found in the regular newsletter: http://ectn-assoc.cpe.fr/news/index.htm

ICI Congress Report 2009

Dr. James Sullivan, School of Chemistry and Chemical Biology, University College Dublin, Dublin 4

The 2009 Annual Congress of the Institute of Chemistry of Ireland took place in the UCD Centre for Synthesis and Chemical Biology on Friday May 22nd 2009. The Congress, with a theme of 'The Interface between Chemistry and Biology', was attended by over 80 delegates with large numbers of students, researchers and lecturers coming from local and national third level institutions as well as local industry.

The meeting was sponsored by the UCD School of Chemistry and Chemical Biology and several Dublinbased companies, each of whom exhibited materials and apparatus throughout the day. The companies involved were JVA Analytical, Brennan and Co, Agilent Technologies, Labplan and TA/Waters. The meeting was opened by the director of the CSCB, Prof. Pat Guiry of UCD noting that the CSCB was an ideal location to host a symposium entitled the 'Interface between Chemistry and Biology'.

The Centre for Synthesis and Chemical Biology is a PRTLI-funded (Programme for Research in Third Level Institutions) collaboration between UCD, TCD and the Royal College of Surgeons in Ireland. The UCD CSCB building (within which the Congress was held), was officially opened in 2005 and contains 2,200 square metres of research and research support space and fully equipped meeting and seminar rooms. Nine speakers presented their recent research at the meeting. These were drawn from different chemistry schools throughout the island of Ireland where the researcher's interests impinged in some way upon the chemistry – biology interface.

The first session involved talks from Tim Smyth (UL), who discussed the chemistry of Penicillin as a β-lactamase prodrug, Marie Migaud (QUB) who presented her recent research involving therapeutic enzymes which use Nicotinamide Adenine Dinucleotide (NAD) as a co-factor and Isabel Rozas (TCD) who spoke about the synthesis and computational analysis of several guanidinium-like compounds.

Figure 1. Left to right: Dr. Marie Migaud, Dr. Tim Smyth, Dr. Paraic James, Dr. Isabel Rozas, Prof. Pat Guiry.

Following this Humphrey Moynihan (UCC) presented work relating to the preparation and characterisation (using single crystal and powder X-Ray techniques) of different polymorphs that pharmaceuticals can adopt. Subsequently Nick Gathergood (DCU) spoke about the production and application of chiral macrocycles derived from commercially available pharmaceuticals.

Figure 2. Left: Dr. Humphrey Moynihan. Right (left to right): Prof. Michael McGlinchey, Prof. Kevin Nolan. Dr. Paraic James, Dr. Malachy McCann.

A session on inorganic aspects of the chemical-biology interface involved talks from Malachy McCann (NUIM) and Kevin Nolan (RCSI). Malachy, as well as giving a broad introduction to the uses of metals in medicine, gave an overview of recent results from his group involving the medicinal roles of silver-based compounds while Kevin presented work on the translation of inorganic chemical biology into therapeutics

Figure 3. Left: (left to right) Dr. Nick Gathergood, Dr. Humphrey Moynihan, Dr. Paraic James, Prof. Rory More O'Ferrall. Right (left to right): Prof. Stefan Oscarson, Dr. Paraic James, Prof. Paul Murphy.

The final session concerned ongoing research in Ireland in the field of carbohydrate chemistry and presentations were given by Paul Murphy (UCG) who discussed his recent work in synthetic biomimetics and Stefan Oscarson (UCD) who presented work relating to the study of carbohydrate-protein interactions.

The meeting was closed by the new President on the Institute, Dr Paraic James from DCU, who congratulated speakers on the quality of the presentations and made the point that the quality of research ongoing in the Chemical Biology field in Ireland is obviously of a world class standard.

He concluded with an invitation to delegates to provide suggestions and proposals for a host institution and theme for the upcoming Annual Congress of the Institute of Chemistry of Ireland 2010.

News: Three Chemistry Lecturers at DIT Win a National Teaching Award

Dublin Castle hosted the National Excellence in Teaching Awards where the President of Ireland, Mary McAleese, presented five Awards on behalf of the National Academy for the Integration of Research, Teaching and Learning.

More than one hundred guests attended the ceremony on 18th November including Higher Education Authority representatives, senior management of many higher education institutes as well as family and friends of the award winners. Jennifer Murphy, Manager of the National Academy, welcomed the guests and highlighted the significance of the awards programme in recognising and rewarding teaching in Higher Education.

Winners of the five Awards were nominated by senior managers within their institutions and selected by a committee which included international representatives as well as representatives of the Irish University Association, the Institutes of Technology Ireland and the Union of Students in Ireland. The committee was chaired by Prof. Áine Hyland, Chair of the Academy's international advisory board.

Among those receiving awards were a team from the Dublin Institute of Technology - Michael Seery, Claire McDonnell, Christine O'Connor and Sarah Rawe. Despite the diversity of disciplines and Institutions represented, the award winners shared an enthusiasm for teaching that combines with their own research expertise to create an exciting learning environment for students.

The Award comprised a crystal vase, a certificate and ¤5,000, which can be used for further professional development and enhancement of teaching. President McAleese presented the awards highlighting the significant role of integrating research, teaching and learning in the recovery of a sustainable economy. She encouraged teachers to lead by example and to provide innovative and creative teaching and learning opportunities in our higher education institutions. She added that the National Awards were a significant and welcome development in Irish Higher Education.

Michael Kelly, Chairman of the HEA closed the ceremony saying "this morning I was inspired and inspiration runs throughout the approaches adopted by the award winners which make for attention grabbing teaching".

Figure 1. Award winners from DIT (left to right): Dr. Claire McDonnell, Dr. Christine O'Connor, Dr. Michael Seery and Dr. Sarah Rawe.

School Profile: The School of Chemistry and Chemical Biology at University College Dublin

Prof. Rory More O'Ferrall, School of Chemistry and Chemical Biology, University College Dublin, Dublin 4

Now and Then

Like other science departments in Ireland the School of Chemistry and Chemical Biology at UCD has benefited from the investment in science research which has formed part of the government's national development plans of 2000 and 2007. In 2005 an additional chemistry building was completed incorporating state of the art synthetic laboratories and providing for the development of research in 'Synthesis and Chemical Biology'. With the new building came a new level of instrumentation including 600, 500 (2), 400 and 300 MHz NMRs, automated small crystal X-ray crystallography and GC and LC high resolution time of flight and (more recently) MALDI mass spectrometers.

Figure 1. Left: Centre for Synthesis and Chemical Biology. Right: 500 and 600 MHz NMR spectrometers

The new building and its equipment represented a quantum improvement in research facilities. Now in 2009 reconstruction and expansion of the undergraduate and research laboratories of the older building is being undertaken in three phases. This will mean that staff will spend an uncomfortable two years in temporary office accommodation and that over the same period undergraduates will have access to limited laboratory space. However, the prospect of fully modernised and reequipped buildings at the completion of the project in 2011 greatly outweighs any short term inconvenience.

These changes are certainly the most momentous for the department since its transfer to the first buildings on the then new UCD campus at Belfield in 1963. That move was from laboratories in Merrion Street inherited from the Royal College of Science in Ireland in 1926, which indeed had originally been established in 1865 in the Victorian foundation of a Museum of Science and Industry in Dublin. Prior to the move to Belfield these historic laboratories had become quite inadequate to the expanding scientific effort at UCD. For a time they continued to house engineering laboratories until the engineers too moved in 1989. They then received a fitting refurbishment as the Taoiseach's department within an expanded government buildings complex. Undoubtedly, the strategic location of the laboratories next to the Dail was beneficial in UCD's efforts to transfer its faculties to the new campus.

The Professor of Chemistry in 1926 at the time of the move to the Royal College of Science was Hugh Ryan, who has been called 'the father of chemistry' in UCD. He was a graduate of the medical school of the Queen's College in Galway but became interested in chemistry and studied with Emil Fischer in Berlin. He was appointed to University College in 1899, at a time when it retained a direct link with the Catholic University of which John Henry Newman was the first rector in 1854. The buildings of the Catholic University are still intact in St. Stephen's Green, comprising two fine Georgian houses and the remarkable Byzantine University Church squeezed between buildings next to them. In 1882 the faltering institution was affiliated to the newly constituted Royal University with the Queen's Colleges in Cork, Galway and Belfast. Although The Royal University was strictly an examining body, it threw a lifeline to the Catholic University by paying annual salaries of £400 to its thirteen professors who continued teaching in the renamed University College Dublin.

Newman had appointed the distinguished chemist W. K. Sullivan, a Fellow of the Royal Society and subsequently President of the Queen's College in Cork, to the chair of chemistry in the Catholic University's medical school. Hugh Ryan was the third chemist to occupy that chair. In 1908, when University College Dublin was incorporated with the Queen's Colleges in Cork and Galway into the newly founded National University of Ireland, it inherited the imposing buildings of The Royal University in Earlsfort Terrace. Ryan was then able to occupy chemistry laboratories which hitherto had been used only for annual practical examinations.

Earlsfort Terrace remained the principal home of UCD for sixty years. The high standards of examinations and of the scholarship of many of its staff went hand in hand with an informality summed up by the recollection that one joined the College by 'leaning a bicycle against the railings of Earlsfort Terrace'. When the move from 'The Terrace' to Belfield had progressed sufficiently the Aula Maxima of the College was handsomely refurbished and reopened its doors as Dublin's concert hall in 1981. The transformation was a source of astonishment to those who had known the building in its previous incarnation.

Looking back, one can see milestones of development comparable to the current modernisation of the School of Chemistry and Chemical Biology, in the first access to properly constructed laboratories in Earlsfort Terrace in 1908, the acquisition of the laboratories of the Royal College of Science in Merrion Street in 1926 and the move to the Belfield Campus in 1964.

The post war years

A long-standing research area introduced by Hugh Ryan was work on the flavonoid family of natural products. This continued as an interest within the department until after the move to Belfield. It was espoused by T. S. Wheeler who became Professor of Chemistry in 1945. By virtue of their distinctive yellow colouration, unusual among organic compounds, the flavonoids lent themselves to then new techniques of chromatographic separation and characterisation by spectrophotometry.

Tom Wheeler had a major influence on the growth of Chemistry in UCD following the second world war. Apart from vigorously promoting the new campus at Belfield he greatly expanded the scope of the department. Hitherto all professors of chemistry had been organic chemists. Wheeler appointed as an inorganic lecturer David Brown who became the first Professor of Inorganic Chemistry in 1964.

By appointing staff from outside Ireland Wheeler widened the research interests and teaching experience of staff. Satoshi Ushioda a student of the Tokyo alkaloid chemist Shigehiko Sugasawa (who was himself a student of Robert Robinson) joined the department in 1959. Previously he had spent a year in R. B. Woodward's laboratory in Harvard and he brought to UCD the problem-solving seminars made famous by Woodward. These and a final year laboratory course in which students separated chromatographically 300 mgs of an unknown mixture and identified the components by NMR helped maintain a high standard for chemistry degrees in these years. Ushioda got to know his students well. Asked by a colleague for help with a reference he would reply 'I don't recall the name, but if we look up the unknown compounds I will be able to tell you'.

Wheeler actively promoted research and the graduation of PhDs in Chemistry. In this respect he was matched by strong personalities among the heads of chemistry departments in other Irish universities, Leslie Scott in Cork, Wesley Cocker in Trinity College and earlier Tom Dillon in Galway. At first many PhDs worked abroad, but from 1969 an expanded Industrial Development Authority began to attract international fine chemicals and pharmaceutical industries to Ireland. A low corporation tax and, after 1973, access to markets of the (then) European Economic Community were important factors ensuring the success of this endeavour. However, a key ingredient was the availability of a reservoir of PhD chemists many of whom had experience of working in industry abroad and were glad to return to Ireland against the tide of emigration. Undoubtedly, the growth of the chemical and pharmaceutical industries from the late 1960s was a mainstay of the later development of Ireland's 'Celtic Tiger' economy. The contribution of these industries to the economy is of no less significance in the current phase of government investment in scientific research and encouragement to increase the number of PhDs graduating per annum.

David Brown recruited a group of inorganic chemists including Anthony Manning, Kenneth Glass, Noel Fitzpatrick and John Clarke. Although Wheeler died in 1962 his policies were continued by his successors Eva Philbin and Frank Hegarty. In 1970 David Feakins was appointed as the first Professor of Physical Chemistry and brought to UCD wide interests in electrochemistry. Courses in electrochemistry had indeed been taught earlier on a part time basis by De Valera's brother Vivion. Vivion's son Eamon continued the family tradition, working for a PhD under the supervision of David Feakins. He remained a good friend of the department after inheriting from his father ownership of the Irish Press national newspaper. A near contemporary of Eamon who joined Feakins as a post doctoral Fellow and is now head of school was Earle Waghorne. As a son-in-law of Tom Wheeler, Earle Waghorne preserves a link with a predecessor whose influence continued to be felt in Chemistry many years after his early death.

Frank Hegarty joined the department from Cork as Professor of Organic Chemistry in 1980. He had completed a PhD with Leslie Scott and subsequently worked with Jaques-Emile Dubois at the University of Paris during the revolutionary year of 1968. Dubois, a formidable presence in the French scientific establishment, was at that time a director of research at the ministry of defence. Frank Hegarty became UCD's first Vice President for Research. With Rory More O'Ferrall, he developed a school of physical organic chemistry, which graduated more than fifty PhDs and published 300 scientific papers.

The scale of PhD activity at this period is indicated by the fact that both Anthony Manning in Organometallic Chemistry and Dervilla Donnelly in Natural Products Chemistry also graduated more than fifty PhD students. Dervilla Donnelly was the main representative of the continuing interest in flavonoid chemistry, but had wider interests in oxygen-containing natural products and phytochemistry. She also had major interests outside the department including responsibilities as varied as vice chair of the European Science Foundation, President of the Royal Dublin Society and Head of the Custom House Dock's Development Authority responsible for the redevelopment of Dublin's docklands. Her achievements in research and public affairs brought her and the department recognition in the form of honorary doctorates and other awards.

Although Manning's and Donnelly's research groups were among the largest in the department most of the twenty staff in the last quarter of the twentieth century were active in research. In Physical Chemistry Howard Sidebottom attracted considerable funding from the European Union for studies of atmospheric chemistry and was a member of the (large) Intergovernmental Panel on Climate Change which was awarded the Nobel Peace Prize jointly with Al Gore in 2007. Until his retirement in 1996, John Clarke published extensively on surface catalysis including important studies of gold alloys. Earlier, Sean Corish had been appointed from the Department as Professor of Physical Chemistry in TCD.

Since 1970 approximately half the PhDs graduating in chemistry have been employed in industry, many of them in chemical and pharmaceutical companies in and around Dublin, including Schering Plough, Loctite, Wyeth, Astellas and Bristol Myers Squibb, but also in companies located in Cork or elsewhere outside Dublin such as Pfizer, GSK, Eli Lilly or Merck Sharpe and Dohme. Indigenous companies offering custom synthesis such as Topchem in Dublin or ALMAC Chemical Synthesis Services in Belfast also employ Chemistry PhDs. Today, an increasing number of PhDs are widening their experience by taking post-doctoral positions abroad. These help make up the ten percent of PhD graduates taking up teaching and research positions within universities or institutes of technology or, in a few instances, in secondary schools.

Current Research

Following the recession in the economy in the late 1980s the early1990s represented a nadir in the financial fortunes of Chemistry in UCD. In these years the appointment of **Kenneth Dawson** to the chair of physical chemistry, and the earlier appointment of Donald Fitzmaurice in the emerging area of nanochemistry, both coming from Berkeley and with the capacity to raise large external research grants, added an element of glamour as well as increased funding and international contacts for the department. In 2006 Fitzmaurice was head hunted by a Venture Capital company, but a continuing presence of nanochemistry in the department has been assured by a joint appointment between Chemistry and Physics of **Gareth Redmond**, one of his first PhD students, who has brought to UCD his own active research effort in this area. A focus of Kenneth Dawson's research is the interaction of nanomaterials with living systems, especially proteins, which are studied using physicochemical methods including simulation and mathematical modelling.

A biophysics theme is evident in the research of **Gil Lee**, an experienced researcher in physical chemistry, who has joined the school recently as an SFI Stokes Professor from Purdue University. He uses atomic force microscopy to measure intermolecular forces between macromolecules including complementary strands of DNA or streptavidin-biotin complexes and is pioneering the use of magnetophoretic methods for the detection and separation of cells especially of pathogenic bacteria. Returning from TCD to UCD and working on related molecules, **Susan Quinn** studies complexing and photophysical properties of nucleic acids.

Biopolymers and biocolloids are studied by **Vitaly Buckin**, using ultrasonic and other novel spectroscopies. Dynamic simulations of models for biopolymers including their self-assembly are being investigated by **Edward Timoshenko** using computational methods. An active research group designing biosensors for neurotransmitters such as glutamate is headed by **Robert O'Neill.** Methodologies employed include immobilisation of an enzyme such as glutamate oxidase in a polymer/protein composite film on a lipid-coated platinum microcyclinder electrode.

In the 1990s **Wilhelm Risse** brought much needed expertise in polymer chemistry to the department. His main interests are in palladium catalysed olefin polymerisation and he has continuing research contacts with Robert Grubbs in Caltech the Nobel-prize winning doyen of this field. Recently **James Sullivan** has introduced studies of hetereogeneous catalysis, with an emphasis on 'synthesis' of nano-composite iron/barium zeolites to effect removal of nitrogen oxides from exhaust gases of diesel-fueled combustion engines. Other (collaborative) projects include photo-electrocatalytic production of hydrogen and the chemical fixation of carbon dioxide as glucose.

Following the retirement of David Brown the Chair of Inorganic chemistry passed to **Michael McGlinchey** from McMaster University in Ontario, Canada who brought to the school a wealth of experience of reactions at the borderline or organic and organometallic chemistry, an area in which he has published 250 papers. A book with Gerard Jaouen from Paris 6 university introduced the term 'bioorganometallic chemistry'. He oversaw the acquisition of state of the art crystallographic equipment and appointment of a talented crystallographer, **Helge Muller-Bunz**, who in six years has solved fifteen hundered crystal structures including many formal carbocation centres stabilised by coordination with cobalt carbonyls. Emilie Banide, an outstanding PhD student working with McGlinchey last year won the highly competitive international prize for young chemists sponsored by IUPAC (the International Union for Pure and Applied Chemistry).

Michael McGlinchey himself reaches retirement age this year. A new appointment in the field of organometallic, catalytic and medicinal chemistry is **Andrew Phillips**. He has joined the department as an SFI Stokes Lecturer with experience in both transition metal and main group chemistry. His research is focused on new osmium and ruthenium complexes featuring di-azo or tetra-azo ligands. Coordination chemistry is chiefly represented in the school by **Grace Morgan** who is developing libraries of ligands to effect inter alia tuning of metal spin-state stabilisation and cross over and promotion of cluster formation, especially of models of the tetramaganese site of photosystem II.

The interface between organic and inorganic chemistry today is blurred by the extensive use of metals by organic chemists. Fairly squarely in the organic camp is **Paul Evans** who is developing synthetic methodologies for cross-conjugated cyclopentenones for use in prostaglandin synthesis as well as new methods for the preparation of aromatic amine analogues of dopamine and nicotine. **Michael Casey** has interests in asymmetric catalysis and the use of chiral sulfoxides for the preparation of natural products. Currently under investigation is an enantioselective route to podophylotoxin - a precursor of a number of anti cancer agents.

Organophosphorus chemistry represents another borderline with inorganic chemistry. In work unpublished at the time of writing, **Declan Gilheany** and his post doc K. J. Kudavalli from Hyderabad have achieved the first examples of dynamic resolution in the conversion of chiral phosphines to their borane complexes (from which they are easily released). The same researchers have also characterised a long sought-after reactive intermediate in the Appel reaction. Other aspects of organoheteroatom chemistry have been pursued by **Hasim Ibrahim** who studies hypervalent iodine, silicon and phosphorus reagents in addition to methods for enantioselective cyanation and carbonylation.

Synthesis and Chemical Biology

As noted at the beginning of this article, a new building and refurbishment of existing chemistry buildings in UCD has provided modern synthetic laboratories and an aspiration to populate the new area of chemical biology. In 2004 the department was renamed 'School of Chemistry and Chemical Biology'. Chemical Biology is now represented by research in Carbohydrate Chemistry and Chemical Enzymology. Indeed, inspired by funding of a 'Centre for Synthesis and Chemical Biology' (CSCB), embracing chemists, biochemists and chemical engineers in UCD, Trinity College and the Royal College of Surgeons in Ireland, established synthetic chemists have increasingly turned their hands to the synthesis drugs, and with some success.

Francesca Paradisi brings to the school firsthand experience of chemistry and biochemistry. Her research extends from the inhibition of bacterial enzymes for which 2.6-diaminopimelic acid is a substrate to enzymatic catalysis of esterification of triacyl glycerols as an environmentally acceptable route for converting animal and vegetable fats to biodiesel fuels.

Carbohydrate chemistry has suffered a loss in the appointment of Paul Murphy to the Chair of Organic Chemistry in Galway. It has gained however by the appointments of **Stefan Oscarson** from Stockholm and **Xiang Ming Zhu** from the German carbohydrate school of Richard Schmidt. As a senior researcher supported by SFI, Oscarson has an enviable record in the synthesis of complex biologically active carbohydrates including their sulfur and selenium analogues. Current research projects include a search for inhibitors of bacterial binding of *E. coli* and *Heliobacter pylori* to human carbohydrate receptors and development of vaccines against diseases caused by *Haeomophilius influenzae* and *Neisseria meningitides*. Xiang Ming Zhu is primarily interested in glycoconjuates and their analogues with a focus on immunostimulatory glycolipids. Recently he has achieved the synthesis a thioglycoside analogue of galactosylceramide.

In the area of drug synthesis **Matthias Tacke** was recently awarded the Cesar Prize for Translational Anticancer Research at a symposium in the University of Heidelberg for work developing titanocene complexes (including that shown below) as anti cancer agents. These are entering first phase clinical trials, and earlier results from animal models showed encouraging activity against renal cancer, an area which is particularly deficient in drug therapies.

Cancer therapy has also been targeted by **Donal O'Shea** who has been successful in developing a photodynamic anti-cancer therapy using the complex shown attached to a bead below as a fluorescent sensor (first picture) and introducing the bead to a cancer cellular environment (second picture). In a further project, automated multistep synthesis and reactions of 3-hydyroxyindoles have been carried out using a continuous flow micro reactor shown in the third picture below.

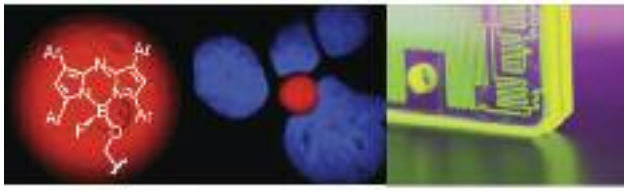
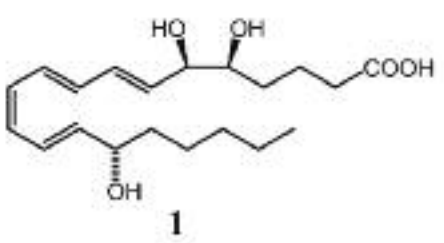
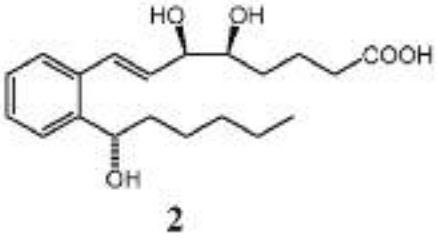


Figure 2. Left and Middle: On-bead fluorescent sensor. Right: Going with the flow

Patrick Guiry has developed synthetic routes to a remarkably simple, more active and much more stable analogue **2** of the biologically active tetraene-containing eicosanoid (oxidised) analogues of prostaglandins the lipoxins illustrated by the structure of lipoxin $A4_1$. This work and Donal O'Shea's work were featured recently in articles in *Chemical & Engineering News*. Patrick Guiry was and still is (in his age bracket!) an international tennis player. Recently he used this interest to illustrate an asymmetric chromium-catalysed homoallenylation of an aldehyde by a tennis simulation on the cover of *Angewandte Chemie* (below).



1



2

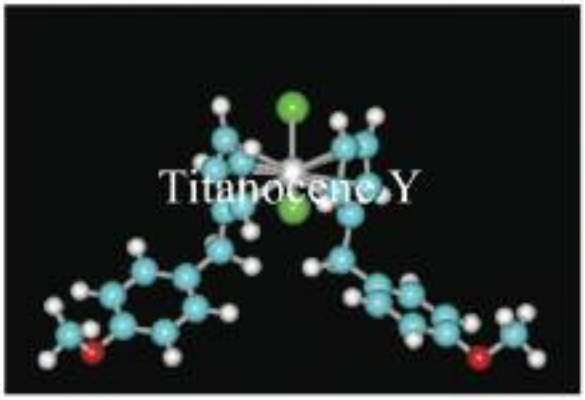


Figure 3. Left: Anti-cancer Candidate for Clinical Trials. Right: Molecules for Tennis?

In 2009 **Martin Albrecht** joined the school bringing an established research group from Fribourg in Switzerland. His interests are in transition metals as active catalytic sites and their modification by ligands, especially heterocyclic carbenes, affecting redox activity, spin state transitions and other properties.
Biological applications of metal carbene complexes including to oxygen metabolism and detoxification with respect to CO have been supported by a European Research Council Starting Grant.

Undergraduate teaching in transition

In this article the research interests of staff have been emphasised rather than undergraduate teaching, not because they are more important but because the undergraduate curriculum remains subject to significant change. In so far as the changes affect other universities and science departments and not only chemistry in UCD, we conclude by briefly reviewing them.

In the past five years undergraduate teaching has adapted to a modular and semester framework based on North American models and using a European credit transfer system. Over the same period an increased fraction of school leavers have embarked on science degrees, partly through encouragement from the government's funding of extra places in science subjects. This has increased the range of interests and levels of preparation of entering students, with consequential changes in the content and presentation of chemistry and other science courses.

In addition there has been a move to increase the 'taught' content of the PhD degree, through formation of a joint graduate programme, Dublin Chemistry, with Trinity College Dublin. This too is having repercussions at undergraduate level.

A further likely influence on the undergraduate curriculum is the pending report of a National Strategy Review Group for Higher Education charged with preparing recommendations to guide Irish higher education over the next ten years. Among possibilities discussed is a revised apportionment of first year science students between the universities and institutes of technology. At present overcrowding of first year science courses in a number of universities, including UCD, is matched by a dearth of qualified students in institutes of technology.

It is probable that these current and potential changes will have found a resolution over the two years during which Chemistry students and staff at UCD wait to occupy their new laboratory accommodation. The possibility of a new deal for undergraduates as they gain access to these laboratories, combined with new appointments of staff and acquisition of a high level of equipment for teaching and research, offer grounds for optimism that the school will go from strength to strength in the second decade of the new millennium.

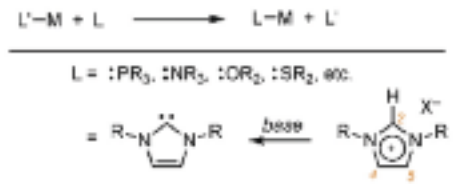
Feature Article

Challenging the Norm: Abnormal Carbenes as Powerful Ligands in Metal-mediated Transformations

Prof. Martin Albrecht, School of Chemistry & Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland

Carbenes in catalysis

Homogeneous catalysis using (transition) metal catalysts is a powerful tool for modern synthesis, in particular because appropriate sets of ligands allow for the adjustment of both activity and selectivity at the metal centre. For a long time, phosphines and their derivatives have been the ligands of choice for most metal-catalysed transformations, despite their drawback of being inherently sensitive to oxidation. Through pioneering work, especially in the laboratories of Bertrand and Arduengo two decades ago, *N*-heterocyclic carbenes (NHCs) have become a promising alternative to the ubiquitous phosphines as ligands for catalytically active transition metals. Indeed, the discovery of NHCs as ligands for transition metals constitutes probably the most influential development in recent organometallic chemistry. Often, the catalytic activity of metal-NHC complexes is extraordinarily high, surpassing the corresponding phosphine analogs by some margin. The success of NHCs as ligands is based on a number of critical features: Firstly, the carbene, typically generated from imidazolium salts through deprotonation, in most cases is stable, allowing it to be used like other neutral ligands for ligand substitution reactions in order to accomplish metal coordination. Secondly, the metal-carbene bond has a significantly larger covalent character than most dative bonds, including M–P bonds. This fact is particularly beneficial for increasing catalyst stability. Thirdly, the NHC ligand is a much stronger donor than even the most basic phosphines. Finally, oxidation of the carbene only occurs under very harsh conditions, thus enabling reactions to be performed under aerobic conditions. However, it is worth noting that the metal-carbene bond is highly susceptible to reductive elimination, which may underline the complementary properties of phosphines and carbenes.



Scheme 1. Utilisation of *N*-heterocyclic carbenes as ligands for transition metals.

Leaving the beaten tracks

The much stronger donor properties of *N*-heterocyclic carbenes has been considered as a key factor in the enhanced catalytic activity of transition metals in C–C and C–N cross-coupling, olefin metathesis, and bond activation processes. However, the donor ability is thwarted to some extent by the inductive effect of the two heteroatoms that are adjacent to the carbene nucleus. This situation can be improved by displacing one or both heteratoms to remote positions, or to eliminate at least one nitrogen entirely from the cycle. Our research has concentrated predominantly on the former approach, which resulted in the creation of so-called abnormal carbenes.[1] The term 'abnormal' indicates that in contrast to the normal NHCs, these carbenes cannot be represented by a M=C double bond without introducing charges on the heterocycle (Scheme 2).[2] The international union of pure and applied chemistry (IUPAC) classifies such species as mesoionic compounds, a terminology that unfortunately omits the genealogical relationship between abnormal and normal carbenes. A broad range of abnormal carbenes are conceivable (Figure 1), and many of these have indeed been studied as ligands for transition metals.

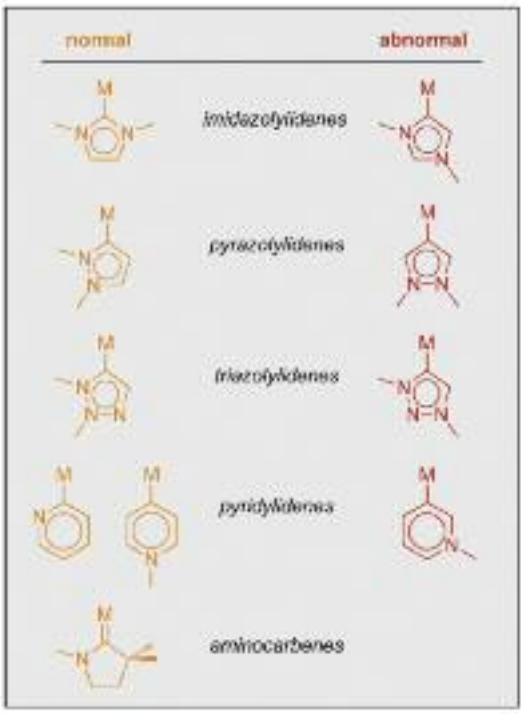
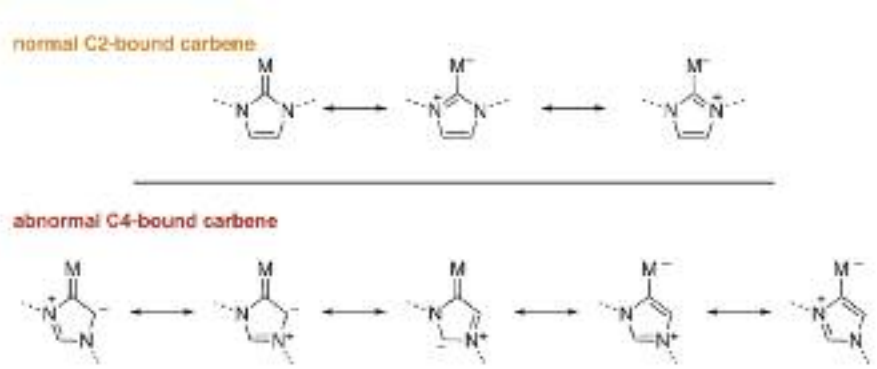


Figure 1. Illustration of normal and abnormal N-heterocyclic carbene ligands coordinated to a metal centre; conceptually, any –NR– fragment may of course be substituted by –PR–, –O–, –S–, or any other isolobal group.



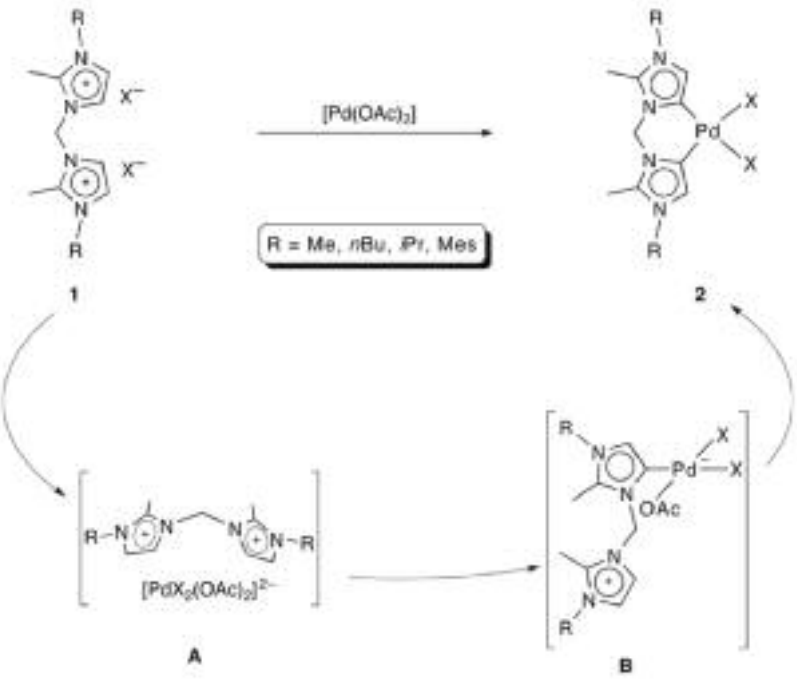
Scheme 2. Abnormal carbene complexes cannot be represented by a neutral resonance form that includes an M=C double bond.

As a consequence of the heteroatom displacement, abnormal carbenes are not well stabilised by inductive and mesomeric effects. In exceptional cases, the free carbene has been isolated, though this route is generally not viable. Recently, different protocols have been developed for the preparation of abnormal carbene complexes. Generally, these routes must suppress the activation of the 'normal' position (C2 in imidazolium salts), which has been achieved by two different strategies. Firstly, it is possible to activate the abnormal site (C_4 or C_5 in imidazolium salts), for example by introducing a halide for subsequent oxidative addition. Alternatively, the C2 position may be deactivated by the incorporation of an alkyl or an aryl substituent. Even though few examples have shown that alkyl protecting groups are not always reliable, this approach has the advantage that protection of the normal position is straightforward. Moreover, C–H bond activation protocols have been established for a number of transition metals, illustrating the flexibility and versatility of this route.

We have been most intrigued by the potential of abnormal carbenes that are bidentate, especially *cis*-coordinating dicarbenes. In chelate complexes derived from these materials, the rotational flexibility of the carbene ligand is restricted, which diminishes the lability of the complex towards reductive elimination. In addition, coordination to a square-planar d^8 platinum group metal affords a complex that has two positions available for ligand/substrate coordination, which are both labilised due to the high *trans* effect of the abnormal carbene ligand. Hence, the electronic impact of the abnormal carbene ligand can be fully exploited in catalytic applications.

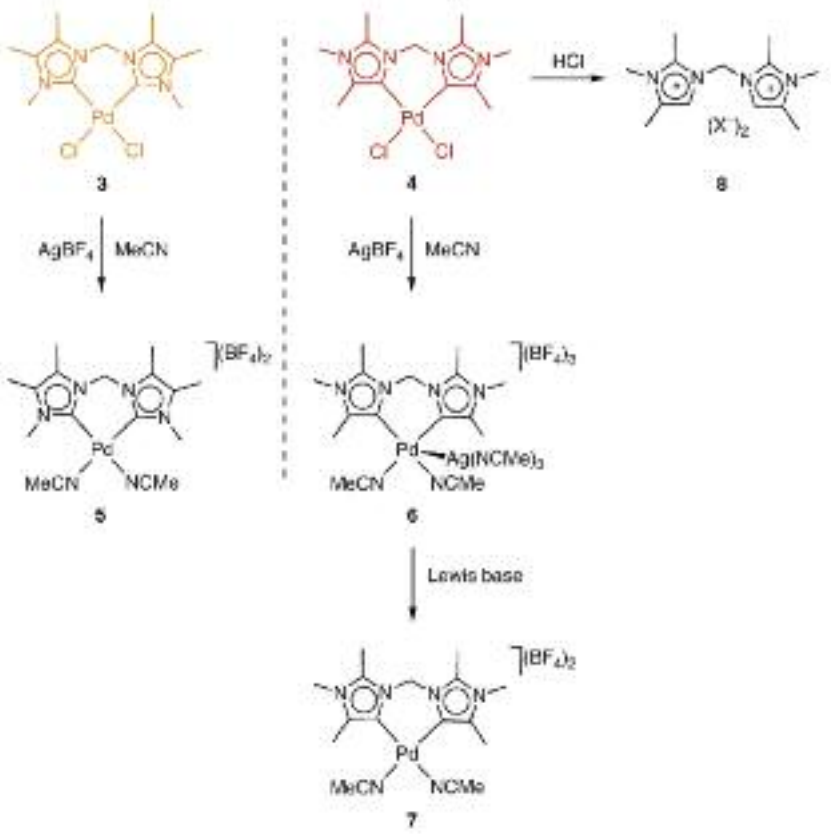
Palladium complexes as useful models

Initial work has concentrated on the evaluation of the donor properties of abnormal carbenes compared to normal analogues. For this purpose, C-2-protected diimidazolium salt **1** has been palladated with $Pd(OAc)_2$, which yields complex **2** comprising a C-4-bound diimidazolylidene ligand (Scheme 3). Variation of the anion X and the substitutents R' in the cationic diimidazolium salt have provided a basic mechanistic understanding of the metallation process. We have surmised that C–H bond activation is initiated by anion coordination to the palladium precursor, thus affording the ion pair [diimidazolium]$^{2+}$[$PdX_2(OAc_2]^{2+}$, **A**. Formation of such an ion pair seems to be essential, as replacing the halides with non-coordinating anions like BF_4^- or PF_6^- suppresses palladation. Subsequent C–H bond activation may proceed much like acetate-mediated cyclometallation, exploiting the dual role of acetate as a base (for imidazolium proton abstraction) and as a ligand (for directing the Palladium centre into close proximity of the potential carbene site). The high selectivity of this bond activation towards the inner C–H bond may arise from tight ion-pairing and appears to be irreversible. The second bond activation from **B**, which leads to chelatation, appears to be a delicate balance between C–H bond lability and nucleophilicity of the palladium centre. In abnormal carbene precursors, the lability of the C-4-bound proton is much lower than C-2–H in the normal system, reflected also in a pK_a difference of about 8 units. The lower reactivity of this proton is compensated by the stronger donor ability of the abnormal carbene in the monocarbene intermediate **B**. This model is supported by results obtained from palladation of a dissymmetric potentially normal-abnormal dicarbene ligand precursor. The reaction stops at the mono-carbene stage, since the abnormal C–H bond is more difficult to activate, yet the normal carbene does not contribute sufficient electron density to the palladium centre to initiate the second bond activation process. This issue is solved by the presence of a labile C-2-H bond in the formation of the normal dicarbene complex, whereas the C-4-bonding mode of the carbene imposes high electron density at the palladium in intermediate **B** for the formation of the dicarbene complex **2**.



Scheme 3. Abnormal dicarbene palladium complex formation via double C–H bond activation.

The electronic impact of abnormal carbenes has been investigated by comparing the reactivity of complexes **3** and **4**. These two complexes comprise a dicarbene ligand with a permethylated periphery. Due to their isostructural relationship, differences in reactivity can be reliably attributed to electronic factors that are imposed by the different carbene bonding modes. Most remarkably, the palladium centre in the abnormal dicarbene complex **4** possesses pronounced Lewis basic character. For example, it serves as a ligand that is competitive with MeCN in the coordination of silver(I) ions, as illustrated by the formation of complex **6** in high yields (*cf.* formation of the solvent complex **5** with normally bound carbene ligands). The Ag–Pd bond in these adducts is 2.8701(6) Å long, one of the closest Ag–Pd contacts known to date, which may reflect the high basicity of the palladium centre in **4**. With Brønsted acids, a similar adduct formation is postulated, yet the hydrogen is not bound in a stable fashion and instead further migrates to the carbon, thus leading to instantaneous Pd–C bond cleavage and formation of the diimidazolium salt **8** at room temperature. In contrast, the normal dicarbene complex **3** is fully stable even when heated in the presence of strong acids. These results indicate that abnormal carbenes exert unique influence on the metal centre. Notably, the typically electrophilic palladium(II) centre becomes nucleophilic when bound to abnormal carbene ligands. As a consequence, new catalytic processes are accessible such as olefin hydrogenation, an area where palladium would not have been necessarily the metal of choice and where the normal analog is essentially inactive.[3]



Scheme 4. Distinctly different reactivity patterns of metal centres bound to abnormal as opposed to normal carbene ligands as a direct consequence of the ligand-induced enhanced nucleophilicity.

Two particularly attractive lines of research have emerged from these preliminary studies. Firstly, the approach may be extended to other transition metals of catalytic interest, such as other platinum group metals. Secondly, the field of mesoionic complexes and abnormal carbenes is not limited to C-4-bound imidazolylidenes, as a variety of other ligand systems are conceivable which have modulated donor properties (see Figure 1).

Variation of the metal

Recent advances in our laboratories have indicated that abnormal carbene bonding can be expanded to a variety of transition metals other than palladium. We have been particularly interested in the complexation of platinum, rhodium, and iridium, since these metals are generally considered to be more nucleophilic than palladium. When these metals are bound to abnormal carbene ligands, their electron density is expected to increase further. Highly basic metal centres are thought to be of great advantage for the metal-mediated activation of typically inert bonds such as C_{alkyl}–H bonds.

This concept has been justified by the preparation and evaluation of rhodium dicarbene complex **9**, which forms a dimeric species through a μ^2-bridging coordination mode of three iodide ligands in the absence of exogenous ligands L (Figure 2). The unique bonding properties of the abnormal carbenes have been exploited for developing an efficient catalytic process for the transfer hydrogenation of ketones using *i*PrOH as dihydrogen source. While typically rhodium(I) precursors are used for such reactions, here the less oxidation sensitive rhodium(III) provides the basis for a suitable catalyst because of the exceptionally strong donor ability of abnormal carbenes. The rhodium(III) centre shows negligible activity in hydrogen transfer catalysis, when less donating C2-bound dicarbenes are used as ligands.

Figure 2. Rhodium(III) complexes comprising abnormally bound carbene ligands and their reactivity in bond activation reactions.

Most remarkably, the extension of the bridge between the two heterocycles in **9** from methylene to propylene induces C–H bond activation of an alkane-type C–H bond to give the tridentate complex **10**.[4] Bond activation occurs under mild conditions (80 °C, aerobic), and is perhaps also facilitated by the geometric constraints imposed by the ligand architecture. However, it is worth noting that when using analogous normal carbene precursors, bidentate coordination without C–H bond activation in the linker group constitutes the predominant reaction pathway, leading to the isolation of complexes such as **11**.

New types of abnormal carbene ligands

As alluded previously, mesoionic ligands are not confined to imidazolium-derived systems. By varying the position of the heteroatom in the heterocycle, a range of different abnormal carbene ligand precursors with specific donor properties can be generated. Much like in phosphine chemistry, where the substituents at phosphorus in PR_3 (R = alkyl, aryl, aryloxy, amide) control the basicity of the ligand, the number of heteratoms and their position appear to be crucial for dictating the donor strength of abnormal NHC ligands, thus providing a methodology to tailor the most basic edge of the ligand donor scale (Figure 3).

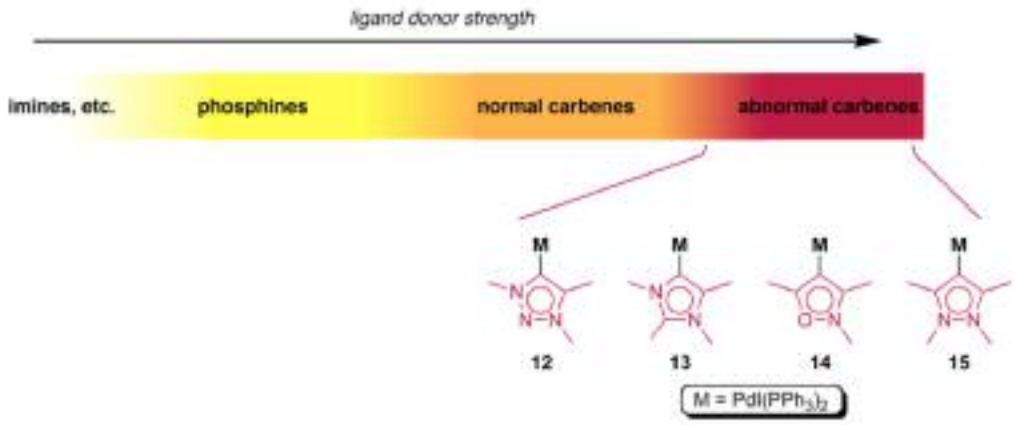


Figure 3. Qualitative donor strength scale for neutral ligands in transition metal chemistry, indicating the remarkable donor ability of abnormal carbene-type ligands in complexes 12–15.

The donor strength of the mesoionic complexes has been estimated, for a series of isostructural complexes **12–15** (M = $PdI(PPh_3)_2$) by using ^{31}P NMR spectroscopy as a probe. These results, paired with analyses from the laboratories of Bertrand, Huynh, and Gusev suggest that 4-pyrazolylidenes (*cf.* **15**) with both heteroatoms positioned remote from the carbene carbon constitute the most basic (formally) neutral donor ligand known to date. The remote location of both heteroatoms minimises inductive effects, yet ensures sufficient charge stabilisation within the heterocycle. Replacing a nitrogen with an oxygen as in complex **14** slightly reduces the donor ability. Shifting one heteratom to a position adjacent to the carbene further reduces the donor strength (*cf.* **13**), as does the introduction of a third nitrogen in triazolylidene complex **12**.

Fine-tuning of the donor properties, for example by the insertion of appropriate electroactive substituents on the heterocycle, enables one to close the gaps between the different ligand systems. The fact that an entire range of highly basic ligands is now available that surpasses the previously ubiquitous phosphines and even classical NHC ligands is particularly attractive in the design of new catalysts. Furthermore, many of these ligand systems are available through a click chemistry approach including dipolar [2+3] cycloadditions.[5] Such facile ligand synthesis considerably adds to the flexibility and versatility of abnormal carbenes and projects exciting perspectives for application in challenging metal-mediated bond activation catalysis and beyond.

Acknowledgments

My most sincere thanks go to the enthusiastic cast of coworkers, past and present, in our laboratories. Our research has been supported financially by the European Research Council through a Starting Grant, by the Swiss National Science Foundation, COST-D40, the Alfred Werner Foundation, and last but not least by IRCSET through ERA-net Chemistry, which provided an initial link between our research and Ireland and the seed for establishing our current research activities at UCD.

References

1. a) M. Albrecht, *Science* **2009**, *326*, 553. b) O. Schuster, L. Yang, H. G. Raubenheimer and M. Albrecht, *Chem. Rev.* **2009**, *109*, 3445. c) M. Albrecht, *Chem. Commun.* **2008**, 3601.
2. It is worth noting that the limiting resonance structures featuring an M=C double contribute only little to the actual description of these complexes. The situation is not much different in normal NHC and in most Fischer carbene complexes and it may be more appropriate to use the term *mesoionic* rather than *carbene* also for these latter complexes.
3. M. Heckenroth, A. Kluser, A. Neels and M. Albrecht, *Angew. Chem. Int. Ed.* **2007**, *46*, 6293.
4. A. Krüger, A. Neels and M. Albrecht, *Chem. Commun*. **2009**, in press.
5. P. Mathew, A. Neels and M. Albrecht, *J. Am. Chem. Soc.* **2008**, *130*, 13534.

Literature Focus

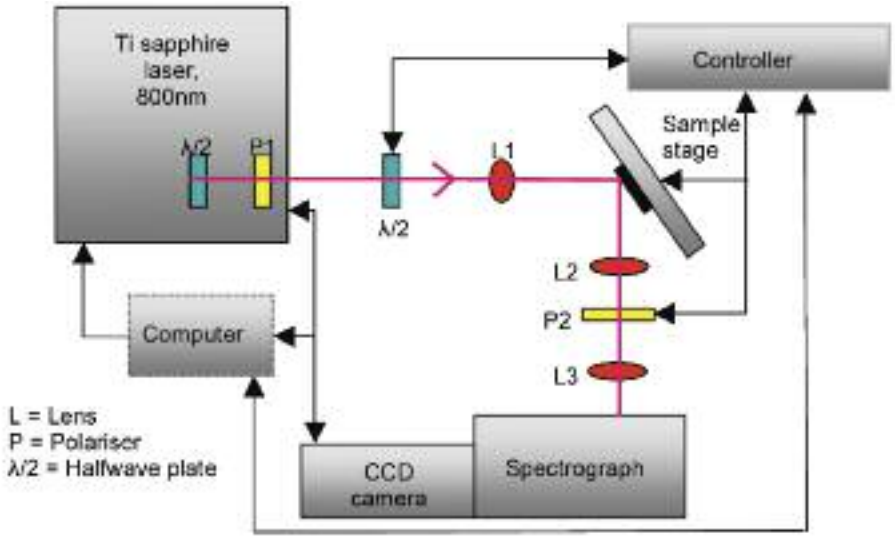
Paul Duffy, Aoife Flood, Francesco Manoni, Deanne Nolan, Aurora Walshe
School of Chemistry, University of Dublin, Trinity College, Dublin 2, Ireland.

Edited by Aoife Flood and Francesco Manoni.
Literature focus is a feature consisting of short abstracts highlighting recent developments of interest in the literature selected by postgraduate researchers.

Polarisation Resolved Spectroscopy

Polarization Resolved Laser-Induced Breakdown Spectroscopy of Al

J. Penczak, Y. Liu and R. Gordon, *J. Phys. Chem. A.* 2009, *113*, 13310

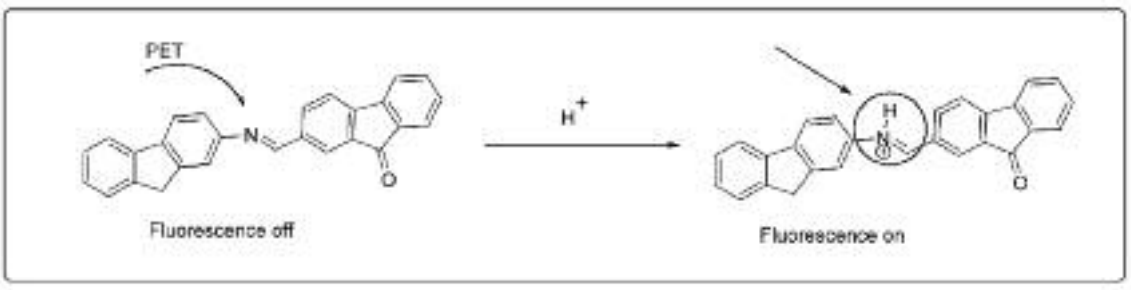


Gordon *et al.* used a polariser to filter out the background, which significantly improved the signal/noise and signal/background ratios of the discrete line spectrum.

Conjugated Fluorenes

Conjugated Fluorenes Prepared From Azomethines Connections-II: The Effect of Alternating Fluorenones and Fluorenes on the Spectroscopic and Electrochemical Properties

S. Dufresne, L. Callaghan and W. Skene, *J. Phys. Chem. B.* 2009, *113*, 15541

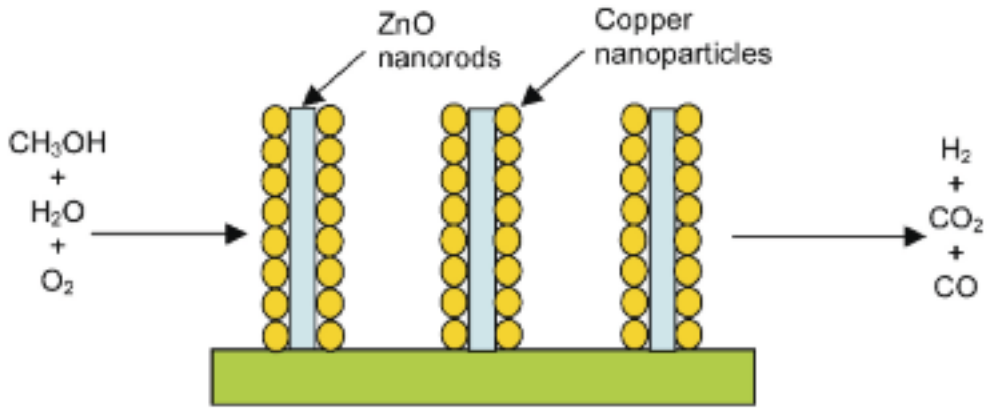


The photophysics and electrochemistry of fluorene and fluorenone azomethine derivatives was examined by Skene and co-workers in order to understand the deactivation pathways responsible for the quenched fluorescence of these compounds.

Methanol to Hydrogen via Microformation Catalysis

Nanostructured Zinc Oxide Nanorods with Copper Nanoparticles as a Microreformation Catalyst

Y. Lin, Y. Hsu, S. Chen, Y. Lin, L. Chen and K. Chen, *Angew. Chem. Int. Ed.* **2009**, *48*, 7586



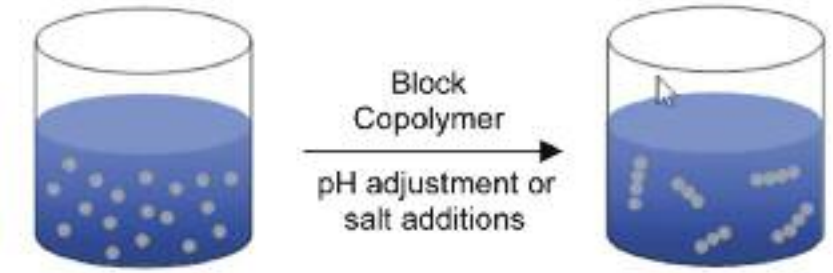
Chen and co-workers arrayed zinc oxide nanorods with copper nanoparticles, which act as an active catalyst for the conversion of methanol into hydrogen.

One Dimensional Silica Nanosphere Arrays

One-Dimensional Assembly of Silica Nanospheres Mediated by Block Copolymer in Liquid Phase

M. Fukao, A. Sugawara, A. Shimojima, W. Fan, M. Arunagirinathan, M. Tsapatsis and T. Okubo A. Russo and A. Lattanzi,

J. Am. Chem. Soc. **2009**, *131*, 16344



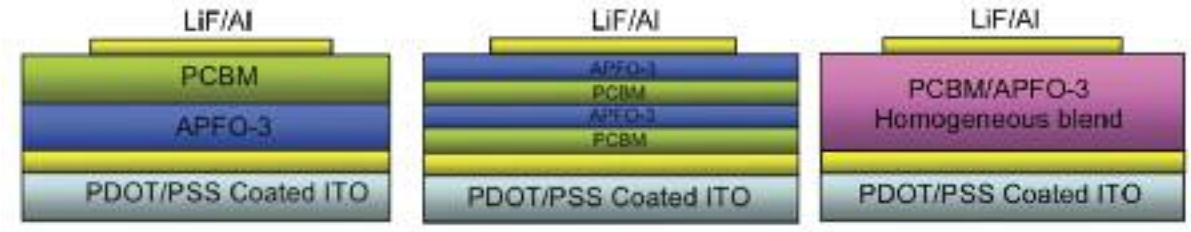
A novel and facile method to prepare highly anisotropic one-dimensional (1D) arrays of silica nanospheres (SNSs) in the liquid phase has been developed by Okubo.

Solar Cell Performance

Device Performance of APFO-3/PCBM Solar Cells with Controlled Morphology

C. Svanstrom, J. Rysz, A. Bernasik, A. Budkowski, F. Zhang, O. Inganas, M. Andersson, K. Magnusson, J. Benson-Smith, J.

Nelson and E. Moons, *Adv. Mater.* **2009**, *21*, 4398

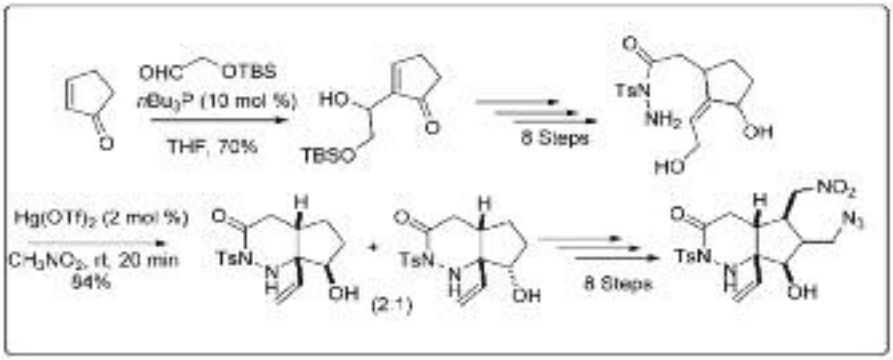


Moons *et* al. investigated photocurrent/voltage performance for polymer/fullerene solar cells with three different device structures.

Synthesis of the Palau'amine Cyclopentane Core

Toward Palau'amine: $Hg(OTf)_2$-Catalyzed Synthesis of the Cyclopentane Core

K. Namba, Y. Kaihara, H. Yamamoto, H. Imagawa, K. Tanino, R. M. Williams and M. Nishizawa, *Chem. Eur. J.* **2009**, *15*, 6560

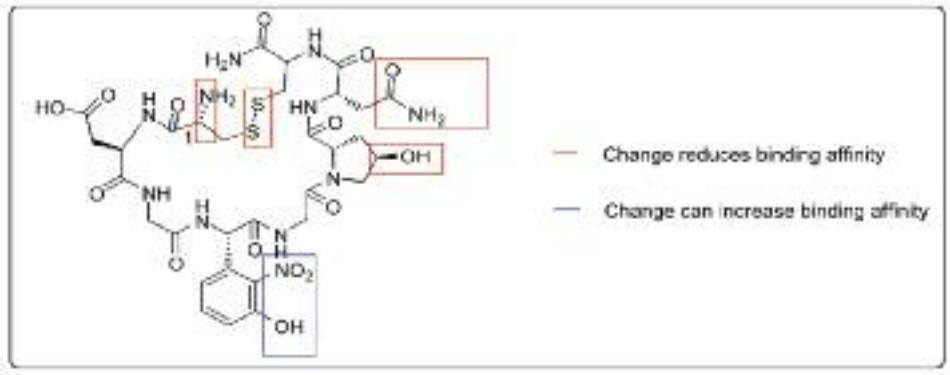


An 18 step synthesis of the cyclopentane core of Palau'amine has been carried out by Namba and co-workers in an overall yield of **4.3%**, incorporating a $Hg(OTf)_2$ catalysed cyclisation reaction as the key step.

Structure Activity Relationship of Breast Cancer Ligands

Structure – Activity Relationship Studies of Targeting Ligands against Breast Cancer Cells

N. Yao, W. Xiao, L. Meza, H. Tseng, M. Chuck and K. S. Lam, *J. Med. Chem.* **2009**, *52*, 6744

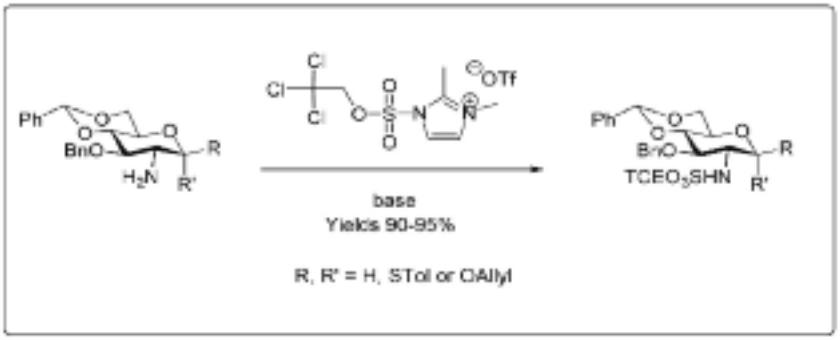


Structure activity relationship analysis of the MDA-MB-231 breast cancer ligand by Lam and co-workers resulted in a ligand with 3.5 fold better binding affinity (IC50: 2.1 μM) than the lead compound.

Carbohydrate *O*-and *N*-Sulfation

O- and *N*-Sulfations of Carbohydrates Using Sulfuryl Imidazolium Salts

L. J. Ingram, A. Desoky, A. M. Ali and S. D. Taylor, *J. Org. Chem.* **2009**, *74*, 6479

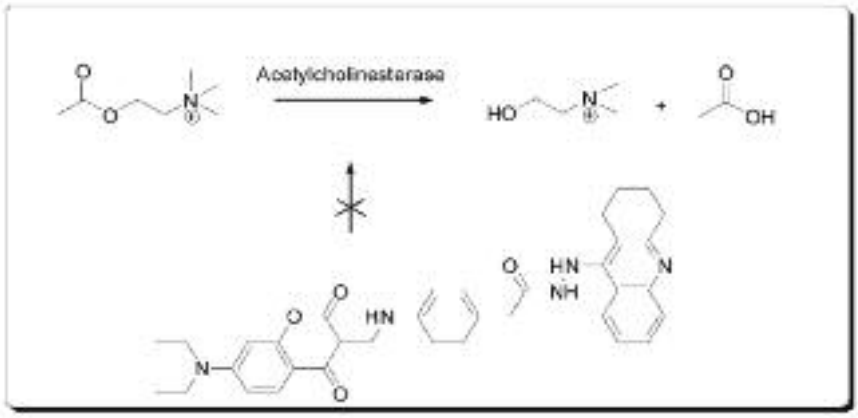


Taylor and co-workers have prepared a sulfuryl imidazolium salt which can be used to incorporate trichloroethyl-protected sulfate esters into carbohydrates. **4 examples: Yields 90-95%.**

Picomolar Cholinesterase Inhibitor

A Gorge-spanning, High-affinity Cholinesterase Inhibitor to Explore β-Amyloid Plaques

P. W. Elsinghorst, W. Härtig, S. Goldhammer, J. Grosche and M. Gütschow, *Org. Biomol. Chem.* **2009**, *7*, 3940

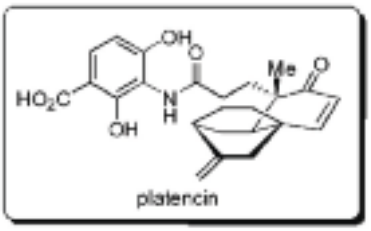


A picomolar **(IC50: 280 ± 10 pM)** fluorescent acetylcholine esterase inhibitor was developed by Gütschow and co-workers as a probe for β-amyloid plaque bound acetylcholinesterase. The inhibitor was shown to bind to β-amyloid plaques directly using competition experiments.

Natural Products

Total Syntheses of (±)-Platencin and (-)-Platencin

K. C. Nicolaou, G. S. Tria, D. J. Edmonds and M. Kar, *J. Am. Chem. Soc.* **2009**, *131*, 15909

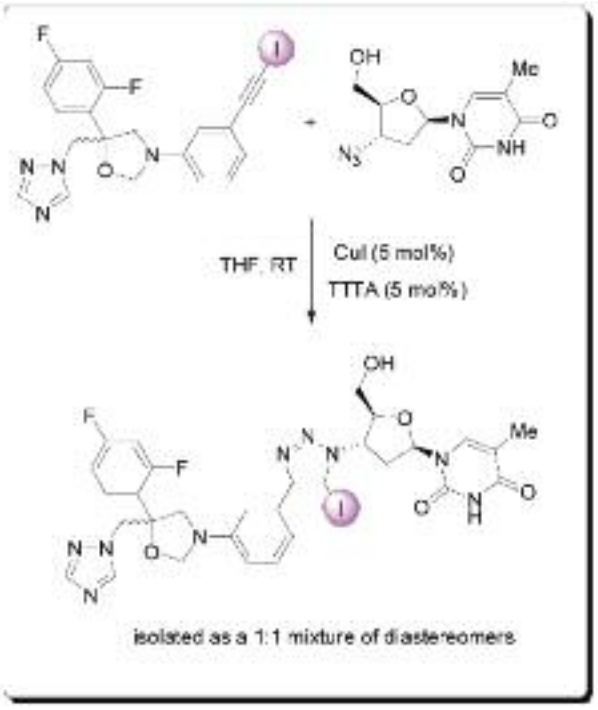


The secondary metabolite platencin, isolated from the bacterial strain *Streptomyces platensis*, represent a novel class of natural product exhibiting unique and potent antibacterial activity. Nicolaou and co-workers have developed both racemic and asymmetric preparations of the natural product.

Click Chemistry

Copper(I)-Catalyzed Cycloaddition of Organic Azides and 1-Iodoalkynes

J. E. Hein, J. C. Tripp, L. B. Krasnova, K. B. Sharpless, V. V. Fokin, *Angew. Chem. Int. Ed.* **2009**, *48*, 8018

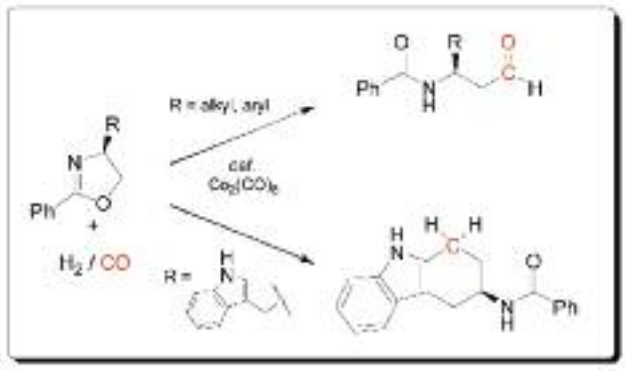


Fokin and co-workers found that 1-Iodoalkynes react rapidly and selectively with organic azides in the presence of copper(I) catalysts. The reaction is compatible with many functional groups and solvents and the products can be further functionalized to give fully substituted 1,2,3-triazoles. **21 examples: Yields 59-99%.**

Catalysis

β-Amidoaldehydes via oxazoline hydroformylation

D. S. Laitar, J. W. Kramer, B. T. Whiting, E. B. Lobkovsky and G. W. Coates, *Chem. Commun.* **2009**, *38*, 5704

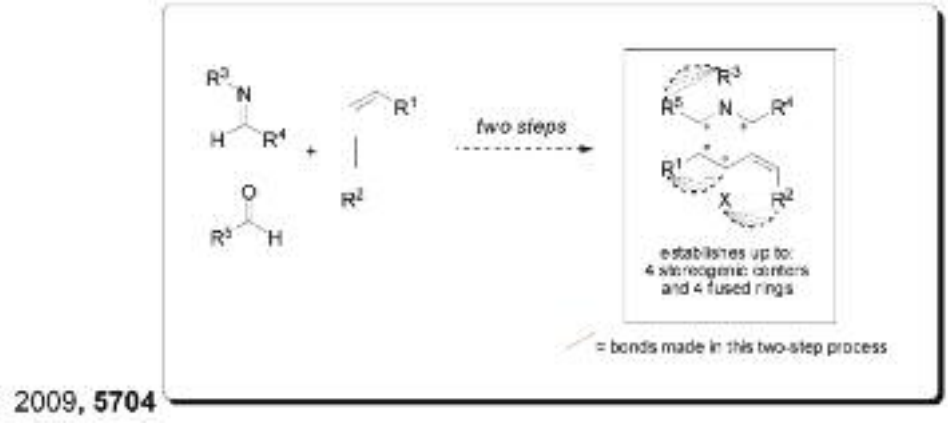


4-Substituted oxazolines, which are readily synthesised from naturally occurring α-amino acids, were converted efficiently and stereospecifically to β-amidoaldehydes by Coates and co-workers in the presence of synthesis gas and catalytic dicobalt octacarbonyl. **11 examples: Yields 63-90%, ee 10-99%.**

Heterocycles

Convergent Synthesis of Piperidines by the Union of Conjugated Alkynes with Imines: A Unique Regioselective Bond Construction for Heterocycle Synthesis

M. Z. Chen and G. C. Micalizio, *Org. Lett.* **2009**, *11*, 4982

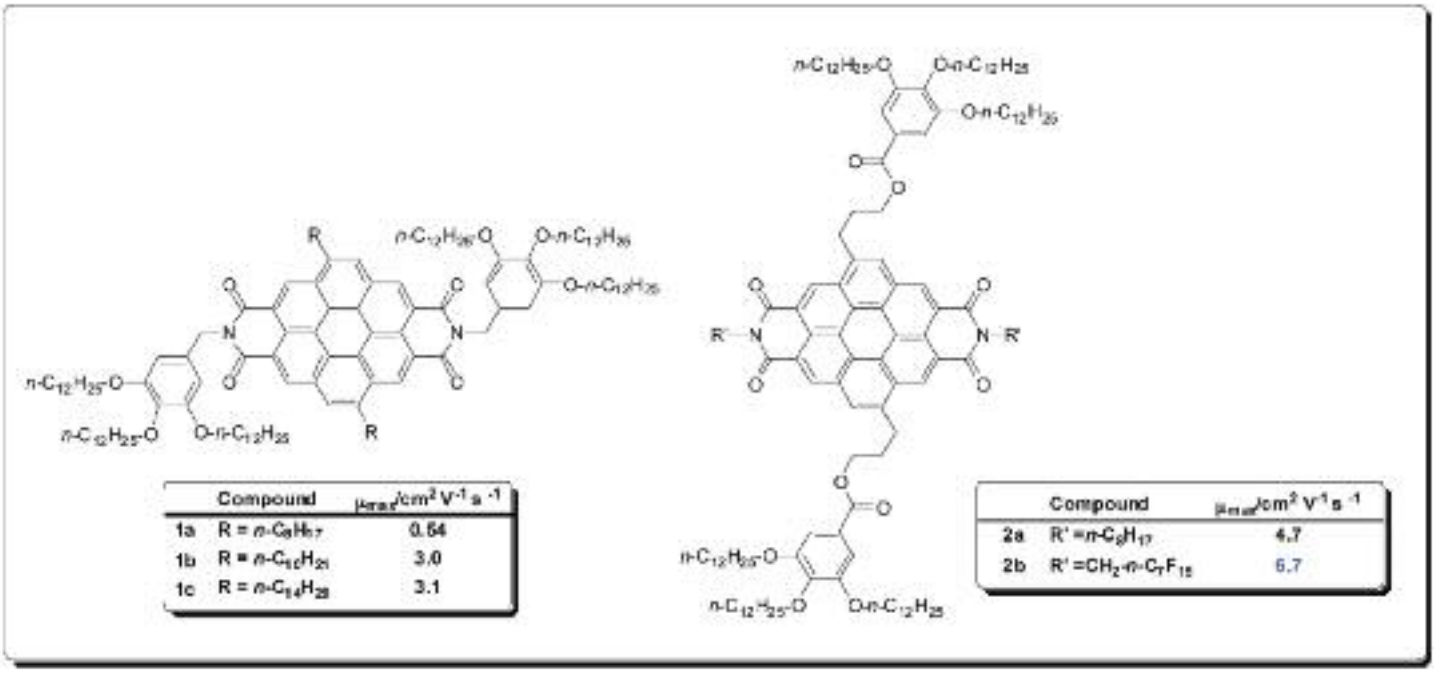


A two-step process is described by Micalizio and co-worker for the union of aromatic imines, conjugated alkynes, and aldehydes that results in a stereoselective synthesis of highly substituted piperidines which can establish up to four stereogenic centers and four fused rings. **11 examples: Yields 63-90%, *ee* 10-99%.**

Discotic Liquid Crystals

Room-temperature discotic liquid-crystalline coronene diimides exhibiting high charge-carrier mobility in air

Z. An, J. Yu, B. Domercq, S. C. Jones, S. Barlow, B. Kippelen and S. R. Marder, *J. Mater. Chem.* **2009**, *19*, 6688

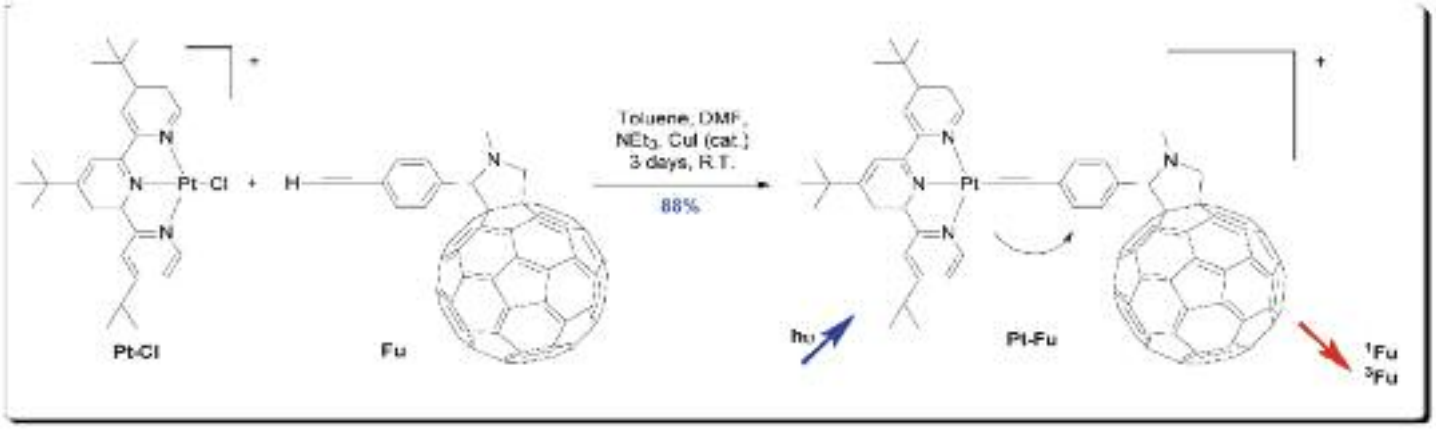


A series of *N,N'*,5,11-tetrasubstituted coronene-2,3,8,9-tetracarboxydiimides were shown by An et al. to form columnar discotic mesophases between room temperature and 200 °C and to exhibit high charge-carrier mobility under ambient conditions. **5 examples: 0.54-6.7 μmax/cm2V-1s-1**

Platinum-Fullerene Dyad

Excited-State Dynamics in a Dyad Comprising Terpyridine-Platinum (II) Ethynylene Linked to Pyrrolidino-[60]Fullerene

B. Ventura, A. Barbieri, A. Zanelli, F. Barigelletti, J. B. Seneclauze, S. Diring and R. Ziessel, *Inorg. Chem.* **2009**, *48*, 6409

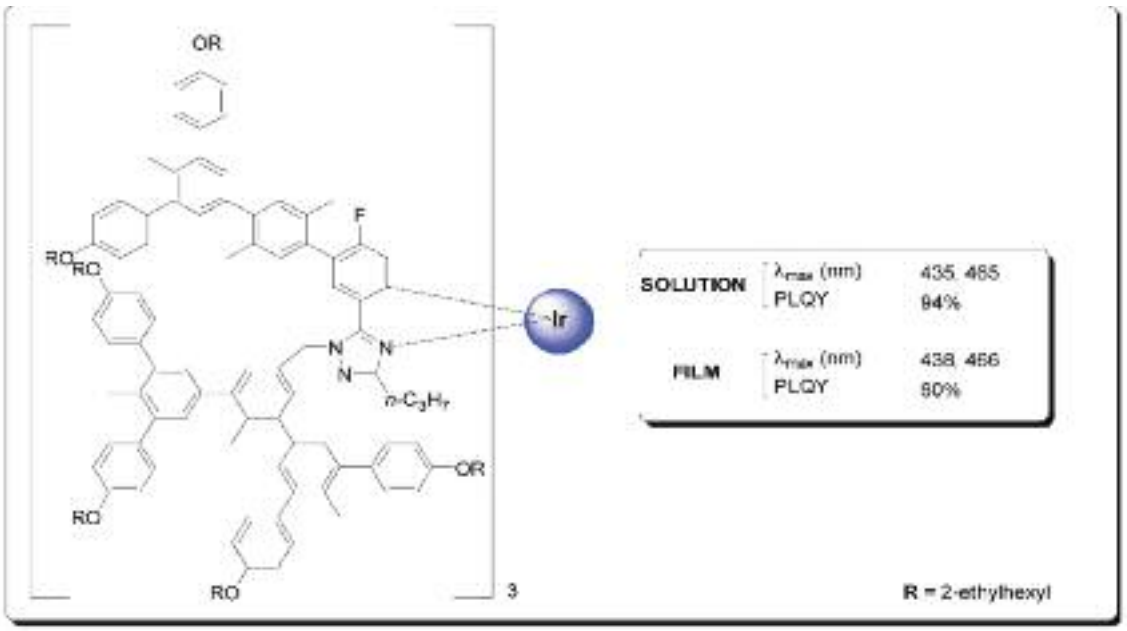


The synthesis and photophysical properties of a fulleropyrrolidine-acetylide-platinum(II)-terpyridyl dyad **(Pt-Fu)** are reported by Ziessel and co-workers. At both room temperature and 77K, complete Pt→Fu energy transfer is observed upon excitation of the Pt centre.

Blue Emitters for OLEDs

High-Triplet-Energy Dendrons: Enhancing the Luminescence of Deep Blue Phosphorescent Iridium(III) Complexes

S. -C. Lo, R. E. Harding, C. P. Shipley, S. G. Stevenson, P. L. Burn and I. D. W. Samuel, *J. Am. Chem. Soc.* **2009**, *131*, 16681

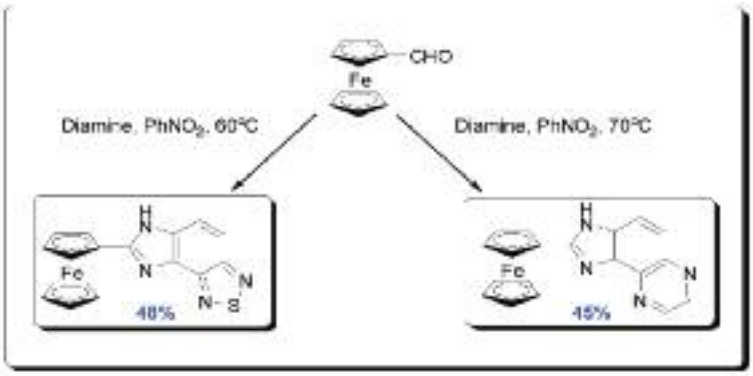


Lo and co workers describe the synthesis of a solution-processable blue phosphorescent iridium(III) dendrimer with a remarkably high solution photoluminescence quantum yield **(PLQY 94%, room temp.)** and its incorporation into single and bilayer OLED devices.

Ion Sensing

Heteroditopic ligands based on ferrocenyl benzimidazoles fused to an additional diaza heterocyclic ring system

M. Alfonso, A. Sola, A. Caballero, A. Tárraga and P. Molina, *Dalton Trans.* 2009, **43**, *9653*

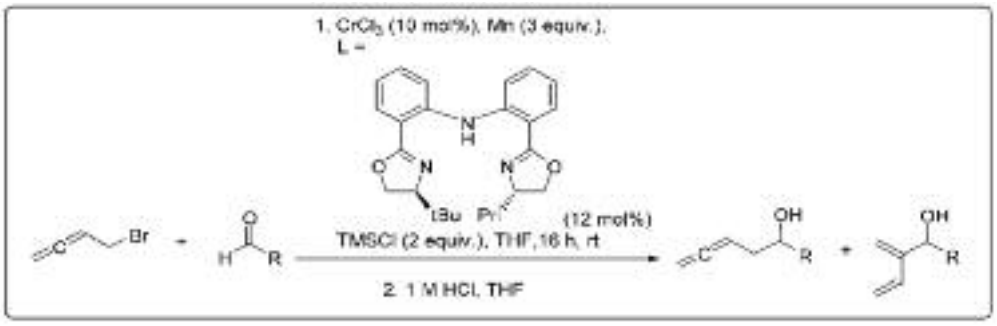


Alfonso et al. described the synthesis of 2 neutral heteroditopic receptors composed of a ferrocene moiety connected to a polyazaheteroaromatic ring system and examined their chemosensor-like behaviour towards various anions and metal cations using spectroscopic and electrochemical methods.

Asymmetric Catalysis

First Regio- and Enantioselective Chromium-Catalyzed Homoallenylation of Aldehydes

V. Coeffard, M. Aylward and P. J. Guiry, *Angew. Chem. Int. Ed.* 2009, *48*, 9152

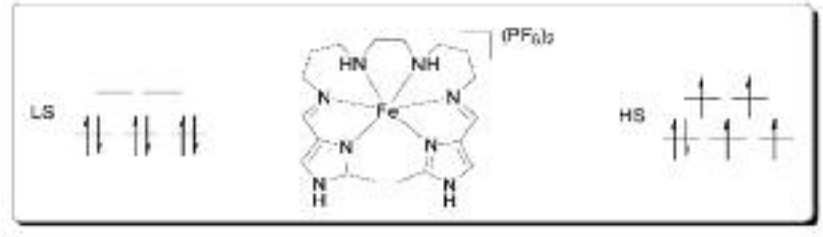


Guiry and co-workers report the first example of regio- and enantioselective Nozaki-Hiyama-Kishi catalytic homoallenylation of aldehydes. They discovered that the bisoxazoline ligand, L, influenced the reactivity, regioselectivity and enantioselectivity of the reaction. **10 examples: *ee* 60-98%**

Spin Crossover

Concerted Spin Crossover and Symmetry Breaking Yield Three Thermally and One Light-Induced Crystallographic Phases of a Molecular Material

N. Bréfuel, H. Watanabe, L. Toupet, J. Come, N. Matsumoto, E. Collet, K. Tanaka and J. P. Tuchagues, *Angew. Chem. Int. Ed.* 2009, *48*, 9304

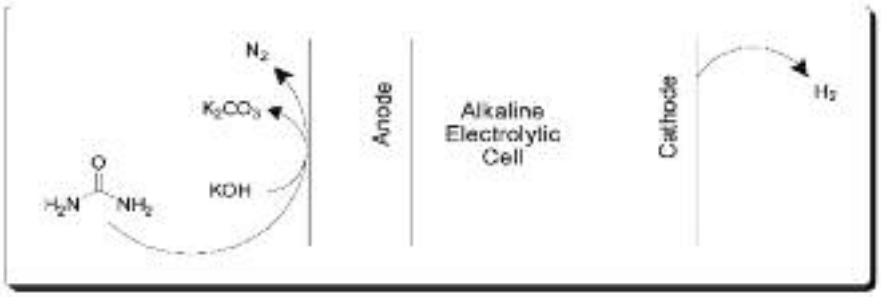


Collet and co-workers have synthesised a molecule with a two-step magnetic susceptibility curve, indicating a two-step spin crossover process. Three separate thermally stable phases were structurally characterised. A fourth, metastable, high spin phase is also possible through light irradiation at low temperature.

H2 Production

Urea Electrolysis: Direct Hydrogen Production From Urine

B. K. Boggs, R. L. King and G. G. Botte, *Chem. Commun.* **2009**, *32*, 4859

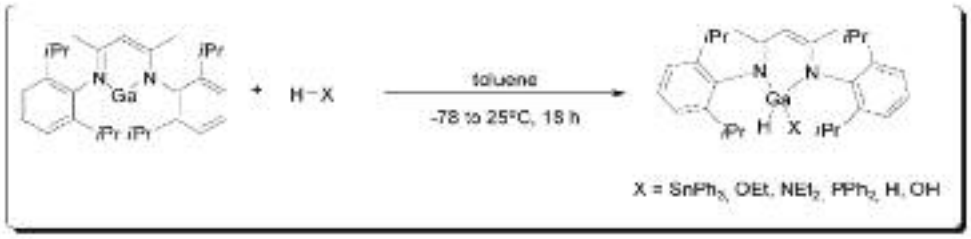


Botte and co-workers have developed a new technology for oxidising urea from wastewater to nitrogen and hydrogen using an inexpensive nickel catalyst at a potential of **0.37V**, theoretically producing **70% cheaper hydrogen**.

New Gallium(I) Chemistry

Oxidative Addition Reactions of Element–Hydrogen Bonds with Different Polarities to a Gallium(I) Compound

A. Seifert, D. Scheid, G. Linti and T. Zessin, *Chem. Eur. J.* **2009**, *15*, 12114

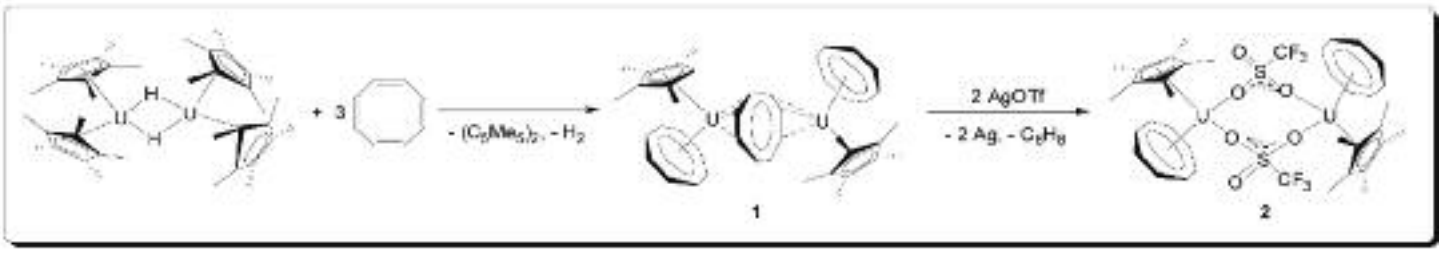


Linti and co-workers demonstrate the activation of various element-hydrogen bonds by oxidative addition to gallium(I) to form gallium(III) hydrides with polarities and concomitant reactivities dependent on X. Dihydrogen reacted at ambient temperature.

Chemistry of Uranium

Synthesis and Insertion Chemistry of Monoalkyl and Monoaryl Uranium(IV) Heteroleptic Metallocene Complexes

W. J. Evans, M. K. Takase, J. W. Ziller and A. L. Rheingold, *Organometallics* **2009**, *28*, 5802

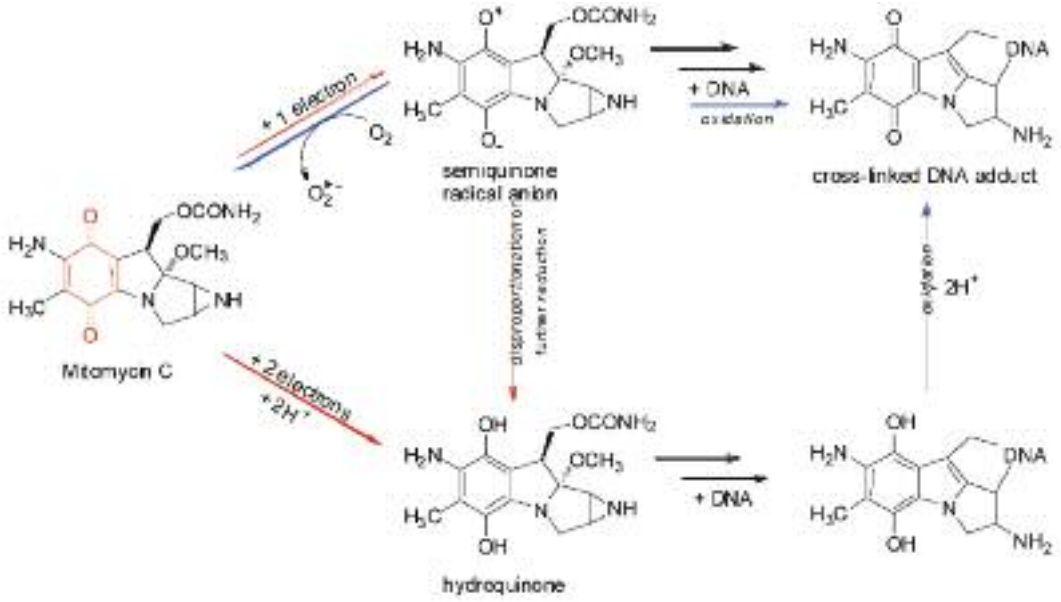


Evans and co-workers used **1** as a precursor for the synthesis of **2**, removing the need for pyrophoric $(C_8H_8)^{2-}$ and $(C_8H_6R_2)^{2-}$ salts for the synthesis. The insertion chemistry of complex **2** was investigated and a series of novel uranocene complexes were characterised.

Highly Potent Bioreductive Benzimidazolequinone Anti-Tumour Agents

Karen Fahey and Dr. Fawaz Aldabbagh, *School of Chemistry, National University of Ireland, Galway, Ireland*

Mitomycin C (MMC) is known as the archetypical bioreductive anti-tumour agent.[1] The cytotoxic effect is exerted through either one or two electron enzymatic reductive activation at the quinone moiety (indicated in red in Scheme 1). Typical one and two-electron reducing enzymes are NADPH-cytochrome P450 oxidoreductase and DT-diaphorase (NQO1) respectively, giving radical anion and hydroquinone reactive intermediates that are alkylated by DNA, resulting in DNA interstrand crosslinks. MMC was first isolated in the 1950s from the bacterium, *Streptomyces caspitosus*,[2] and under its trade names (incl. Mitozytrex and Mutamycin) has long been used in chemotherapy - both intravenously and topically - to treat various solid tumours, including gastrointestinal, breast and bladder cancers.[3] However, like many chemotherapies it can cause severe side-effects, including haemolytic anaemia, irreversible renal failure and bone-marrow suppression, which may contribute to overwhelming infections in an already compromised patient. This makes the discovery of alternative anti-tumour agents a worthwhile endeavor, hence our research over the past decade into synthetic bioreductive benzimidazolequinone alternatives.



Scheme 1. Bioreductive activation of Mitomycin C

The first cancer target of our research was solid tumour hypoxia.[4] Hypoxic or O_2-starved cells make up a significant portion of a solid tumour (Figure 1), and result from inefficient blood oxygen supply, as a tumour rapidly proliferates to outgrow its microvascular system. Anoxic cells will develop on the periphery of the tumour, with hypoxia being profound at distances greater than 100 μm. Hypoxic cells are slow to divide and are resistant to radiotherapy and chemotherapy that kill mainly viable cells in aerobic environments. Untreated hypoxia leads to accelerated malignant cancer progression and metastasis (cancer spread).

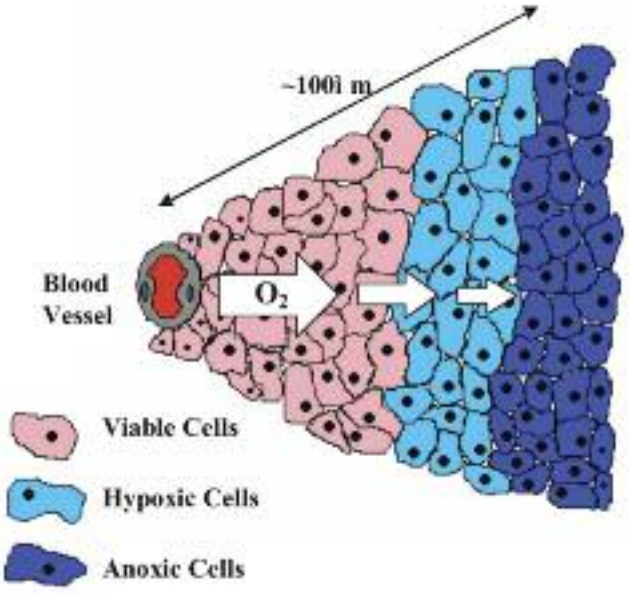


Figure 1. Decreased oxygen concentration as a function of distance from blood vessel.

The chemical basis for replacing the indolequinones (such as MMC) with benzimidazolequinones for hypoxia treatment was the presence of the extra electronegative 3-*N* of the fused imidazole moiety (indicated in blue in Figure 2), facilitating the required single electron bioreductive activation. Semiquinone radical anion formation is associated with hypoxia, and can be reversed by oxygen of viable cells (Scheme 1). Our proposal was supported by reductive potentials for synthesized cyclopropane ring-fused pyrrolo and pyrido[1,2-*a*]benzimidazolequinones **1** and **2**,[5-7] and pyrido[1,2-a]benzimidazolequinone **(3)**[8] (Figure 2) lacking a fused cyclopropane ring, which were all shown to be more easily reduced than MMC (less negative reductive potentials obtained for benzimidazolequinones, Table 1). Nanomolar (10^{-9} M) quantities of benzimidazolequinones **1–3** were cytotoxic towards normal human fibroblast cells (GM00637); compound **3** was found to be more than 300 times more cytotoxic than MMC under hypoxic conditions (Table 1).[8] The rational for synthesising cyclopropane compounds **1** and **2** was that the formation of the activated semiquinone radical anion would induce radical ring-opening to give a highly reactive cyclopropyl radical, capable of exhibiting cytotoxicity through hydrogen abstraction from DNA, leading to strand cleavage. However, the greater activity and selectivity towards hypoxic cells of **3** (despite lacking a DNA-damaging functionality such as a cyclopropane or aziridine ring) indicated that the reversible formation of reactive oxygen radicals (e.g. O_2•-) may be responsible for cytotoxicity (as depicted for MMC in Scheme 1).

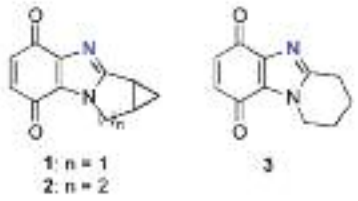


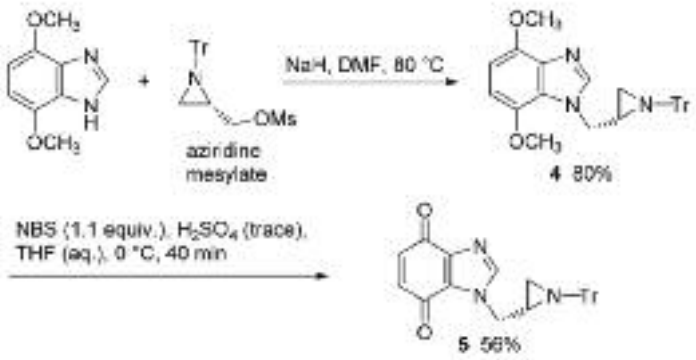
Figure 2. Pyrrolo and pyrido[1,2-*a*]benzimidazolequinones.

Table 1. Reductive potentials and cytotoxicity.[a]

Compound	Eredox [V] versus Fc	IC50(aerobic) [µmol dm^{-3}]	IC50(hypoxia) [µmol dm^{-3}]	HCR
MMC	-1.421	0.9	0.5	1.8
1	-1.052	0.0069	0.0024	2.9
2	-1.074	0.0083	0.0070	1.2
3	-1.080	0.0070	0.0016	4.4

[a] Reductive potentials were obtained by using cyclic voltammetry by dissolving compounds in DMF containing 0.1M tetrabutylammoniumperchlorate as the electrolyte and 1 mM ferrocene (Fc) as reference. E_{redox} (± 0.010 V) calculated as (E_{pc} + E_{pa})/2 from 100 mVs-1 cyclic voltammograms. E_{pc} = cathodic peak potential, *E*pa = anodic peak potential. Cytotoxicity was measured by using the MTT assay on human skin fibroblast cells (GM00637). IC_{50} is the drug concentration required to reduce viability by 50%. Hypoxic cytotoxicity ratio (HCR) is defined as the IC_{50} value for aerobic conditions divided by the IC50 value for hypoxic conditions.[8]

The second cancer target of our research was Fanconi anaemia (FA). FA is a rare human genetic disease characterised by an increased incidence of cancer in early adulthood.[9] At a cellular level, it is diagnosed by hypersensitivity of FA cells to crosslinking agents, in particular MMC. FA cells are mutant in one of a number of genes encoding proteins in the FANC multi-protein complex, which plays a key role in repairing MMC-induced DNA damage. As shown in Scheme 1, the cross-linked DNA adduct is formed through opening of the fused aziridine. This led us to the synthesis of *N*-[(aziridin-2-yl)methyl]benzimidazolequinone **5**, which represents the first example of a benzimidazole and the corresponding benzimidazolequinones had been *N*-substituted with methylaziridines, in order to impart DNA-alkylating ability (Scheme 2).[10]



Scheme 2. Synthesis of *N*-[(aziridin-2*S*-yl)methyl]benzimidazolequinone.

Reaction of 4,7-dimethoxybenzimidazole with aziridine mesylate gave **4** in 80% yield, which then underwent a demethylation-oxidation reaction to yield the desired benzimidazolequinone **5** in 56% yield.[10] Formation of the required benzimidazolequinone **5** from 4,7-dimethoxybenzimidazole **4** was a challenging transformation given the fact that aziridines are prone to ring-opening under acidic conditions, and bromination of benzimidazole with N-bromosuccinamide (NBS) proved a deleterious competitive reaction.

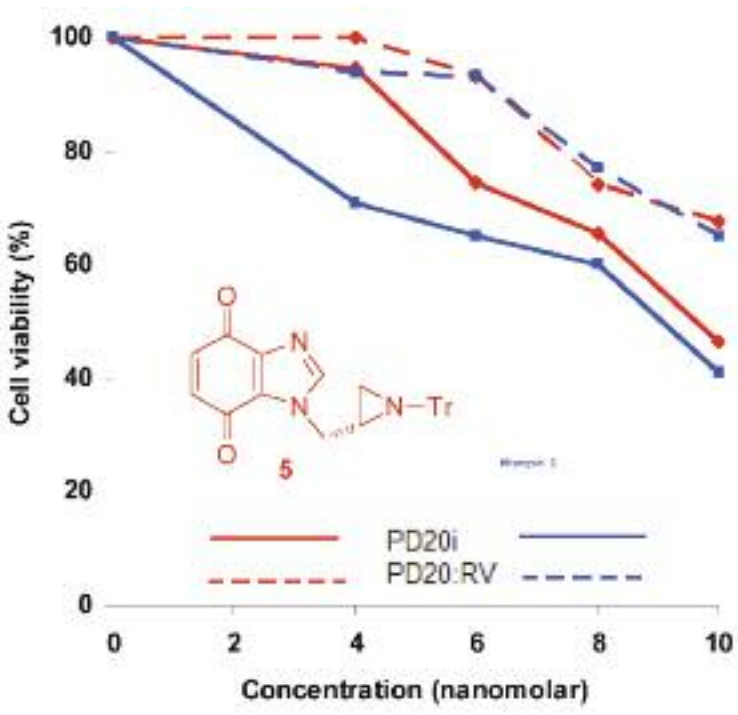


Figure 3. Viability of PD20i and PD20:RV cells determined using the MTT assay to measure the effect of FANCD2 expression on cell viability following treatment with mitomycin C and benzimidazolequinone 5 for 24 h at 37 °C.

Benzimidazolequinone **5** was found to induce hypersensitive killing (at nanomolar (10^{-9} M) concentrations of the drug) of human FA cells (PD20i) lacking FANCD2 in a comparable manner to MMC (Figure 3).[10] As a control, a FA cell line (PD20:RV) expressing wild-type FANCD2 protein from an inserted transgene was also treated with **5** and MMC. These cells expressing FANCD2 were found to be less sensitive, implicating the FANC protein in partial correction of DNA damage. Further, as there is only one position for DNA-alkylation (at the aziridine) in **5**, this indicates that the formation of DNA crosslinks cannot be responsible for hypersensitive cytotoxicity. More recent work has unequivocally asserted the role of the aziridine in hypersensitive killing of FA cells.[11]

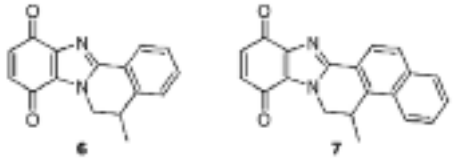


Figure 4. Highly conjugated benzimidazolequinones.

The most recent cancer target of our research is cells expressing high levels of the 2-electron reducing enzyme NQO1 (e.g. cervical (HeLa)[12] and prostate (DU145)[13] cancer cells). Our synthetic targets **6** and **7** are shown in Figure 4: these do not possess recognised DNA-damaging functionality, such as strained aziridine or cyclopropane rings.[14] The strategy behind the design of these molecules was based on stabilising the reduced intermediates of benzimidazolequinones through increased aromatic conjugation, which we speculated would infer greater cytotoxicity and selectivity towards cells containing high levels of NQO1 activity. Our theory was vindicated by the finding that benzimidazolequinone **7** proved to be to be the most potent and selective towards the killing of HeLa and DU145 cells, with normal human fibroblast cells (GM00637) remaining viable using the drug concentrations applied.[15]

Conclusions

We have developed several classes of highly potent bioreductive benzimidazolequinones as potential replacements for the clinically used anti-tumour drug, MMC. For each study, the chemical structure is modified to suit particular cancer targets. It is evident that some benzimidazolequinones prepared are probably too toxic for further development as clinical drugs; however, others hold great promise in future selective targeting of specified cancers.

Acknowledgements

These results have emanated from research conducted with financial support from Science Foundation Ireland (07/RFP/CHEF227) and the Environmental Protection Agency (EPA) Doctoral Scheme (2006-PhD-ET-6). We would also like to acknowledge the receipt of embark initiative postgraduate scholarships for Karen Fahey, Sarah Hehir (PhD 2008) and Liz O'Donovan (PhD 2009) from the Irish Research Council for Science, Engineering and Technology, funded by the National Development Plan. Dr. Aldabbagh is also indebted to the hard work and dedication of other postgraduate and postdoctoral co-workers (past and present) on benzimidazolequinone drug discovery projects, including Sarah Bonham, Dr. Miriam Carr (PDRA), Mary Lynch (PhD 2007), Eoin Moriarty and John O'Shaughnessy (PhD 2005), and to his collaborator Dr. Michael P. Carty (Biochemistry, School of Natural Sciences, NUI, Galway). For postgraduates from the Aldabbagh group, the year of PhD award from NUI, Galway is shown in brackets.

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Hybrid Organic-Inorganic Coordination Assemblies – Molecular Capsules, Porous Networks, Magnetic Materials and Templates for the Preparation of Nanomaterials

Dr. Wolfgang Schmitt, *School of Chemistry, The University of Dublin, Trinity College, Dublin 2*

Hybrid organic–inorganic coordination assemblies represent a class of supramolecular compound whose preparation is a very active area in chemical and materials research. The concept of hybrid organic–inorganic materials presents a means to customise physical and chemical properties by influencing the dimensionality or devolution pattern of inorganic materials within organic matrices. This approach allows a combination of the advantageous properties of inorganic and organic materials. Research areas under this purview include porous materials for gas storage and catalysis or magnetic materials.[1] Other intriguing sub-classes of such hybrid supramolecular compounds are molecular cages and capsules. Depending on their dimension and composition, the cavities in molecular capsules can provide unique chemical environments, serving for instance, as reaction vessels or supramolecular containers.[2] Envisaged applications extend to areas such as enzyme mimetics, artificial photosynthesis, sensors, and drug delivery systems. This article highlights our experimental efforts in the selected areas of supramolecular cages and capsules, metallo-helicates and supramolecular coordination networks.

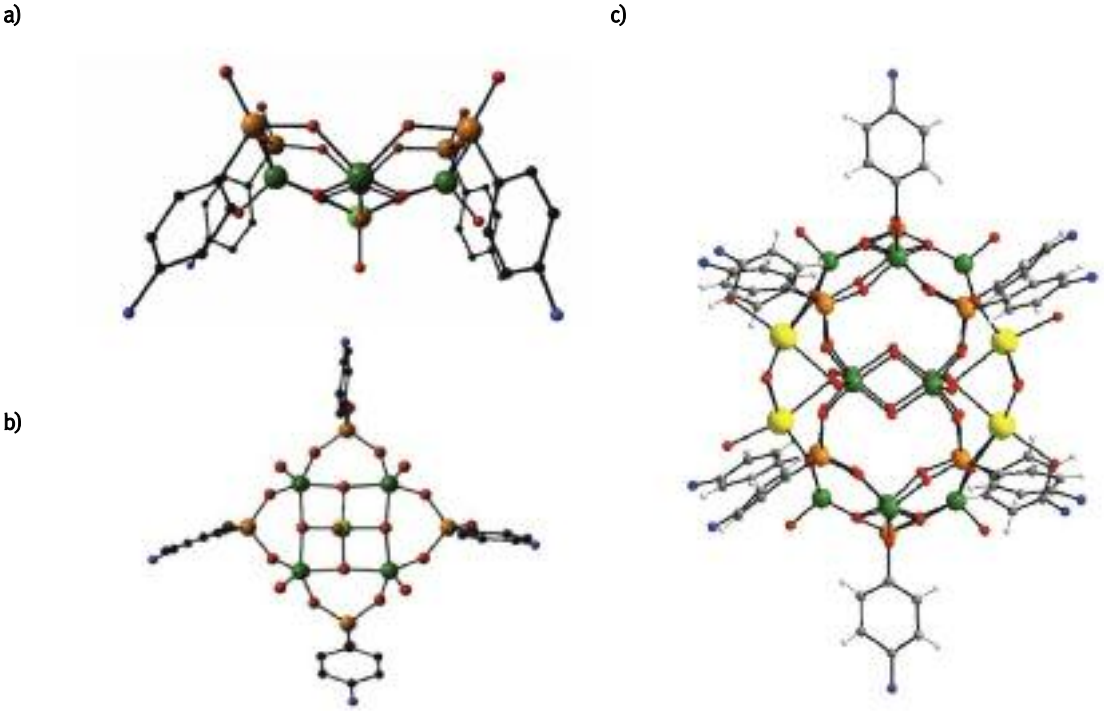


Figure 1. a) and b) Different perspectives of the $[V_5O_9(O_3AsC_6H_4\text{-}4\text{-}NH_2)_4]^{5-}$ 'calix' structure in $Na_5\cdot1\cdot20.5H_2O\cdot3DMF$; H atoms neglected for clarity. c) Structure of the cluster anion in $Na_4(H_2O)_{10}[H_2O\subset2]\cdot1.5DMF$. Color code: V green, As orange, O red, N blue, C dark grey, Na yellow.[6]

Supramolecular cages and molecular capsules

A key issue for the formation of metallosupramolecular entities is the identification of pre-organised, kinetically stable building blocks that provide ligand-accessible coordination sites to direct the assembly process into desired molecules. Polyoxometalates are known to form inorganic capsular entities. Their structures can be rationalised by a set of connection modes and emerge *via* growth reactions from oligonuclear compounds through giant nanosized molecular aggregates[3] into extended 3D structures. Early transition metal ions polarise terminal O^{2-} ligands efficiently resulting in 'closed' clusters in which metal-oxygen bonds point radial to the outside. These short M-O bonds with stabilising dπ-pπ contributions protect the molecular entities but also hamper functionalisation and limit the applications of the desired hybrid organic-inorganic materials. The methodologies used to functionalise polyoxometalates have recently been reviewed[4] and inspired by the synthetic approaches of Zubieta, Clearfield and Müller,[5] we studied the formation of V^V/V^{IV} polyoxometalates in the presence of (4-aminophenyl)arsonic acid, 1,4-benzenebisphosphonic acid and [1,1'-biphenyl]-4,4'-diyl*bis*-phosphonic acid. These experimental efforts resulted in a series of synthetically related, unprecedented polyoxometalates such as $[V_5O_9(O_3AsC_6H_4\text{-}4NH_2)_4]^5$ **(1)**, $[V_{12}O_{14}(OH)_4(H_2O)_2(O_3AsC_6H_4\text{-}4\text{-}NH_2)_{10}]^4$ **(2)**, $[H_2V_{10}O_{18}(O_3PC_6H_4\text{-}PO_3)_4]^8$ **(3)** and $[H_2V_{10}O_{18}(O_3PC_{12}H_8\text{-}PO_3)_4]^8$ **(4)**.[6] We identified a {V-O} building unit in **1** and utilised this pre-organised structural motif to produce a novel class of hybrid capsules, **3** and **4**, whose dimensions can be controlled by the extent of the organic ligands. The compounds form reproducibly in good yields in H_2O/dimethyl

formamide (DMF) mixtures upon partial reduction of sodium meta-vanadates using hydrazine hydrate in the presence of arsonates or phosphonates.

Cluster anion **1**, shown in Figure 1a and b, consists of five vanadium atoms that are surrounded by O donors in a square pyramidal coordination mode. The base of the central $\{V^{V}O_5\}$ pyramid shares common edges with its four surrounding $\{V^{IV}O_5\}$ polyhedra to give the typical convex mixed-valent $\{V^{V}O(\mu_3\text{-}O)_4V^{IV}{}_4O_{12}\}$ unit. The remaining two O donors in the base of each $\{V^{IV}O_5\}$ square pyramid are provided by four (4-aminophenyl)arsonate ligands; each bridging between two V atoms in a O,O'-*syn, syn* coordination mode. The nitrogen functionalities and aromatic ring systems point in the direction of the pyramid tips shaping the appearance of the hybrid organic-inorganic 'calix' structure of **1**. Upon decreasing the pH of the reaction system, the characteristic green colour of the solution of 1 changes into a light blue appearance, effecting the crystallisation of blue cubic crystals of $Na_4(H_2O)_{10}[H_2O\subset\mathbf{2}]\cdot 1.5DMF\cdot 1.25H2O$ (Figure 1c). The polyoxometalate cage **2** contains 12 vanadium atoms and 10 (4-aminophenyl) arsonate ligands. Four solvated sodium ions are incorporated in the framework of the cage and compensate the negative charge of the vanadium cluster anion. The cluster can be visualised as the linkage of two calix clusters **1** *via* 8 arsonate functionalities and two partially hydrated $\{O_4V^{IV}(OH)_2V^{IV}O_4\}$ units in which the V ions share a common edge of their distorted octahedral coordination polyhedra. Within one $\{O_4V^{IV}(OH)_2V^{IV}O_4\}$ unit the O-donors opposite to the common edge are provided by four (4-aminophenyl)arsonate ligands; two of the ligands link to the same calix rim. However, the $\{V^{V}O(\mu_3\text{-}O)_4V^{IV}{}_4O_{12}\}$ motif present in 1 is not exactly replicated in 2; instead of the $\{V^{V}O_5\}$ unit, arsonate groups of the organic ligands extend the apex of the convex caps of the cage. The metal-oxygen core structure of 2 is characterised by dimensions of 11.8 Å x 8.6 Å x 8.2 Å. The accessibility of **1** and our motivation to exploit the observed structural motif for the preparation of hybrid cages and capsules prompted us to use diphosphonates under the same reaction conditions.

The ligands 1,4-benzenebisphosphonic acid and [1,1'-biphenyl]-4,4'-diylbis-phosphonic acid were synthesized by the Michaelis–Arbuzov reaction.[10] This approach resulted in two unprecedented molecular capsules, $[H_2V_{10}O_{18}(O_3PC_6H_4\text{-}PO_3)_4]^{8-}$ **(3)** and $[H_2V_{10}O_{18}(O_3PC_{12}H_8\text{-}PO_3)_4]^{8-}$ **(4)**, shown in Figure 2. In both compounds two convex $\{V^{V}O(\mu_3\text{-}O)_4V^{IV}{}_4O_{12}\}$ motifs are linked intramolecularly via four diphosphonate ligands. The 1,4-benzenediphosphonate ligands in **3** can easily be replaced by their extended homologues and we anticipate that the resulting cages can thus be elongated. **3** has a length of 15.7 Å (polar diameter) and its capsular entity is characterized by intramolecular V^{V}–V^{V} distances of 12.5 Å, a square arrangement of four P atoms with closest P–P distances of 5.5 Å and an average distance of 5.6 Å between the planes of closest parallel aligned aromatic rings. Respective distances in **4** are: 20.1 Å (polar diameter), 16.9 Å (V^{V}–V^{V}) and 5.5 Å (P–P distance). The biphenyl moieties in **4** are slightly disordered, convex curved to the outside of the cages and the distances between the planes of opposite, parallel aligned aromatic rings deviate between 8.2 and 8.4 Å leading to a larger cavity which can accommodate two disordered DMF molecules.

The outlined results demonstrate that we have established an effective synthetic approach to functionalise polyoxovanadates through partial reduction of V^{V} salts in the presence of organic arsonates and phosphonates. We identified a {V-O} motif in **1** that can be utilised to construct a novel class of hybrid capsules. Simple extension of the organic ligands affects the formation of elongated capsules; the preparation of further extended analogues of **3** and **4** that incorporate a variety of guests is the subject of ongoing investigations in our laboratory.

Spin-crossover transitions in metallo-supramolecular structures

Transformations between two labile electronic configurations within molecules can be initiated by light irradiation, temperature or pressure variation and lead to distinctive changes in magnetism, colour and structure. Currently there is an ever increasing interest in such spin crossover (SCO) compounds, partly motivated by their potential application as molecular memory or visual display devices, which has led to a better understanding of the parameters that influence this fascinating phenomenon which can occur in first-row transition metal complexes with d^4-d^7 electronic configurations.[7]

Several Fe^{II} complexes with $3d^6$ configuration and a $\{FeN_6\}$ coordination environment reveal SCO behaviour. These compounds are characterised by a paramagnetic HS state ($^5T_{2g}$, S = 2) which changes to the diamagnetic LS state ($^1A_{1g}$, S = 0) upon cooling (Figure 3a). The transition can be influenced by modification of the organic ligand sphere, considering steric and electronic effects. HS-LS transitions are accompanied by a colour change and a contraction of the coordination sphere. The change in magnetization can be considered as the basis for investigating the phenomenon resulting in a spin-transition curve that describes the concentration of HS molecules, γHS, in relation to the external thermal perturbation. Key characteristics which determine the suitability of the compound with respect to technological applications, are given by *T1/2* (the temperature at which half of the molecules are in the HS state), as well as by the slope and hysteresis width of the transition curve. *T1/2* strongly depends on the metal-ligand bonding characteristics and ligand-field; molecular orbital considerations can be applied to rationalise the influence the ligand.7 Many of the previously reported SCO compounds are mononuclear FeII complexes and in collaboration with the research groups of Paul Kruger and Rodolphe Clérac we are exploring synthetic approaches to multinuclear SCO compounds with the motivation to exploit structural and electronic transitions for sensing applications.

We investigate for instance SCO phenomena in metallo-helicates – supramolecular compounds in which the organic ligand strands rap around a metal–metal axis. The bis-bidentate ligands (L) used in this study were synthesised by Schiff-base condensation from the appropriate carboxaldehydes and diamines and react quantitatively to a set of triple-stranded helicates with the general formula $[Fe_2L_3]^{4+}$ (Figure 3b and c).[8] The structures were characterized by X-ray crystallography, elemental analysis, NMR and UV-VIS spectroscopy. Spin transitions upon temperature variation and light irradiation were studied by magnetic susceptibility, reflectivity and Mössbauer measurements. The initial results exceeded our expectations and are significantly different to observations in related helicates.[8,9]

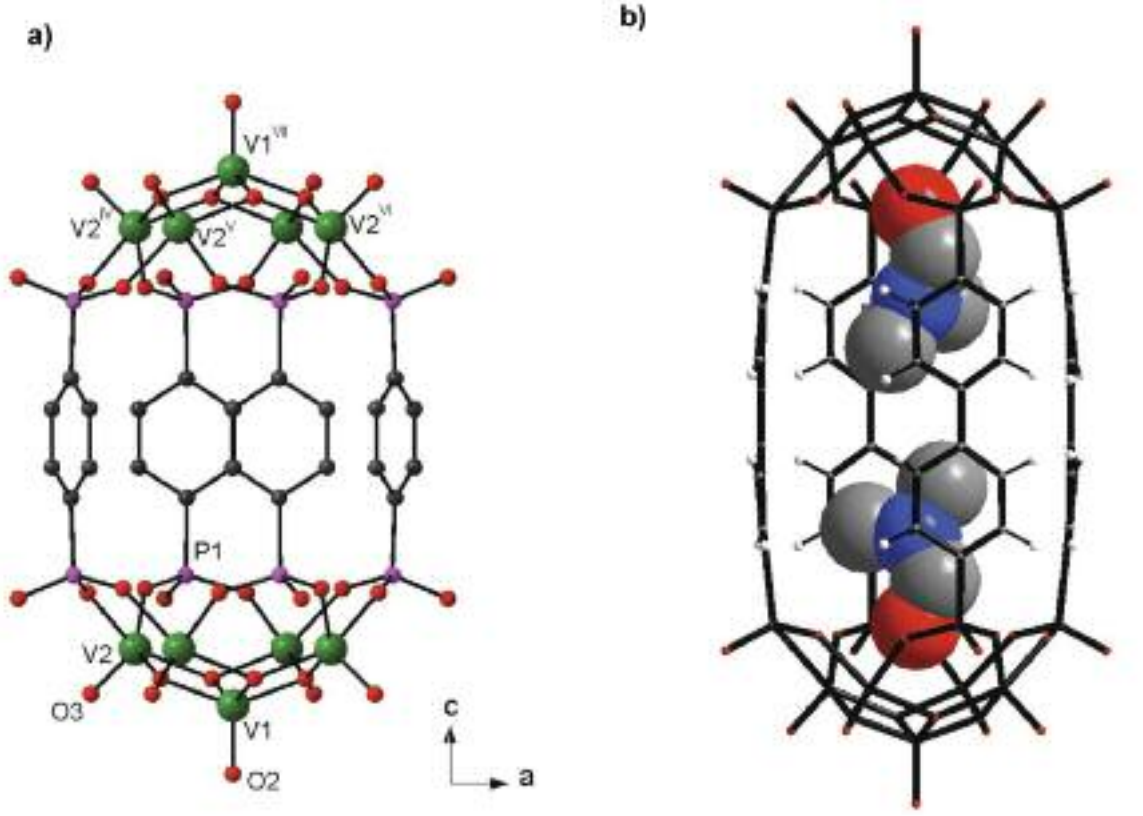
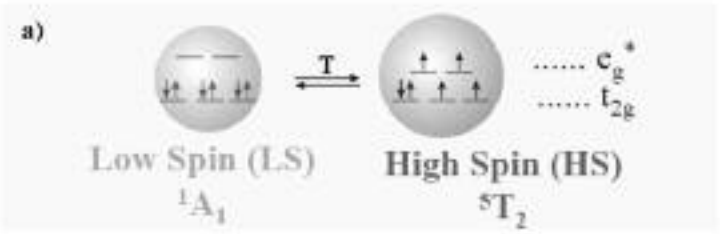
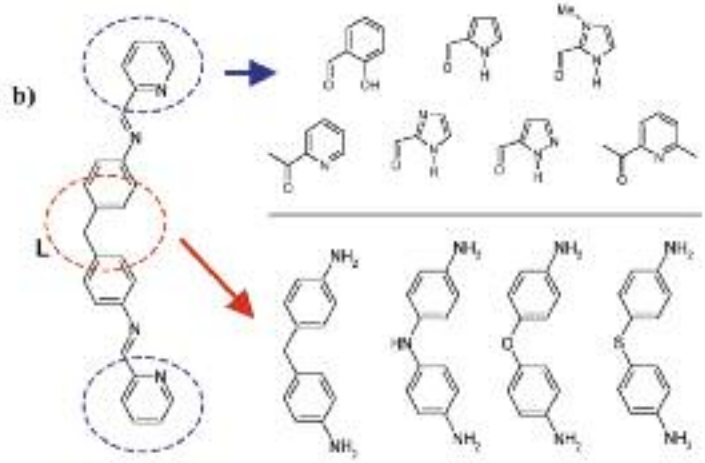
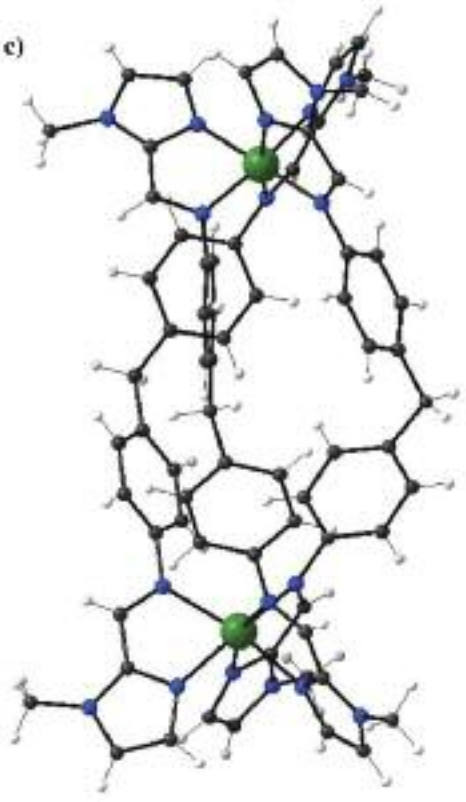


Figure 2. a) Molecular structure of $[H_2V_{10}O_{18}O_3P\text{-}C_6H_4\text{-}PO_3)_4]^{8-}$ (3); b) structure of $[H_2V_{10}O_{18}(O_3P\text{-}C_{12}H_8\text{-}PO_3)_4]^{8-}$ (4) accommodating two DMF molecules within the cage structure. Color code: V green, O red, N blue, C dark grey, P pink.[6]







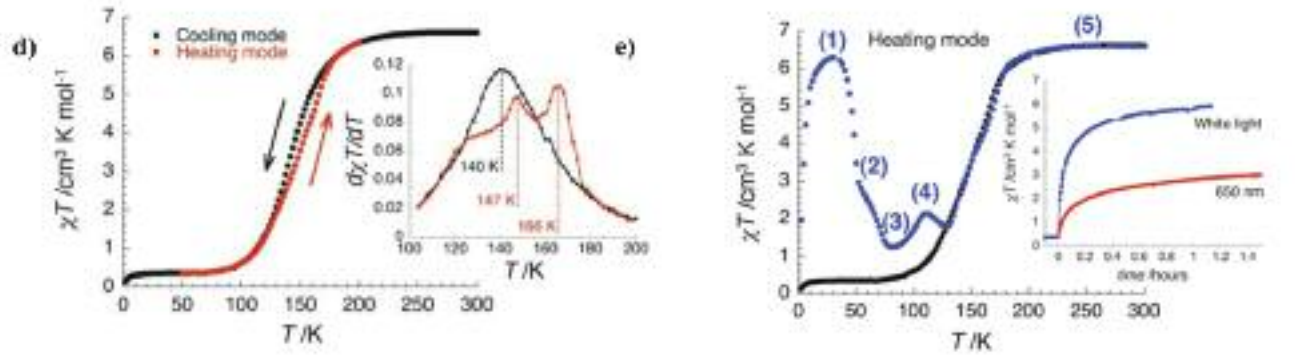
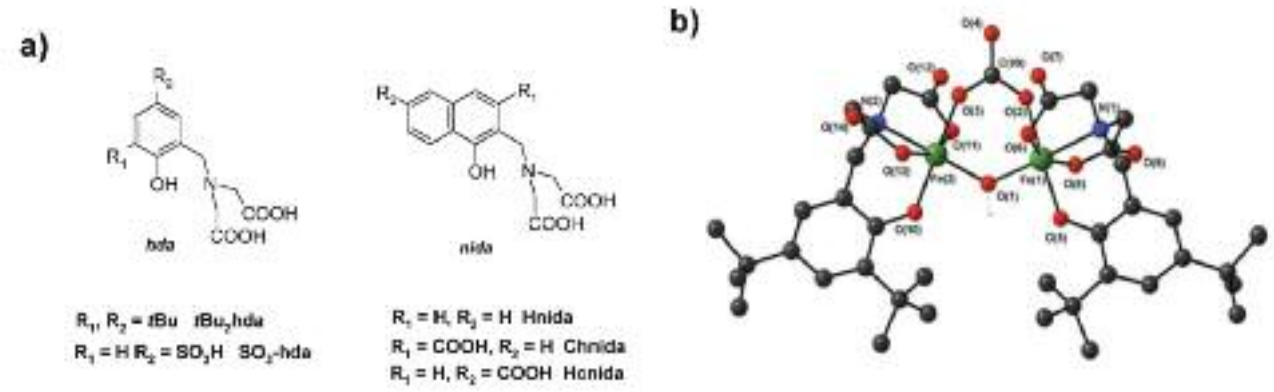


Figure 3. a) SCO in Fe^{II} complexes with $3d^6$ configuration. b) and c) Imine ligands that react to Fe^{II} triple-stranded helicates; Variation of the N-heterocyclic 'head' influences the T range of the SCO; Variation of the bridging group influences the cooperativity between the Fe^{II} centres, thus determines the shape of the spin transition curve. d) *T*-dependence of χT of a selected helicate $[Fe_2(MIOD)_3](ClO_4)_4$ (ligand: imidazolimine groups and oxydianiline bridging moieties), inset $d(\chi T)/dT$; e) LIESST behaviour of $[Fe_2(MIOD)_3](ClO_4)_4$, heating rate after light irradiation = 0.5K/min.).[8]

The modular ligand system allowed us to influence both the temperature range of the observed SCO through the bidentate imine function and the degree of intramolecular cooperativity through the bridging atom of the dianiline moiety of the ligand. Thus, the structural parameters of the ligand system allowed us to modulate between one-step and two-step transitions whilst influencing the temperature range of the spin-crossover and the hysteresis characteristics of the supramolecular compound.[8] Figure 3d illustrates the spin transitions in one selected helicate $[Fe_2(MIOD)_3]^{4+}$ **(5)** that is stabilised by an organic ligand (MIOD) that contains *N*-methyl imidazolimine functional groups which are linked *via* rigid oxydianiline bridging moieties. This dinuclear Fe^{II} helicate crystallises in the presence of perchlorate counterions and the compound undergoes a remarkable asymmetric SCO transition. The first derivative of the χT product relative to the temperature, d χT/dT, in cooling mode leaves no ambiguity regarding the nature of the spin crossover process occurring in one [HS–HS] [LS–LS] step at $T_{1/2}$ = 140K. Nevertheless in the heating mode, the result is reproducibly different suggesting that the Fe^{II} sites switch successively in a two step process within a narrow temperature range of 147–166 K. The temperature dependence of the χT-product is further characterized by weak hysteresis effects. The compound undergoes light-induced transitions (Figure 3e), referred to as LIESST effect (Light Induced Excited Spin State Trapping).[7] The spin transition can be induced almost quantitatively using white light irradiation at 10K and reveals a complicated, reproducible relaxation mechanism of the light-induced magnetic phase. Light irradiation at low temperatures excites the LS $^1A_1$ state to $^1T_1$ and $^1T_2$ states which decay rapidly *via* the spin triplet states $^3T1,2$ to the high-spin $^5T_2$ state. The transformation of the metastable $^5T_2$ to the $^1A_1$ state is forbidden and relies on thermal relaxation processes. Our X-ray crystallographic studies reveal that Fe-N bond distances decrease by ca 12-14% upon switching the electronic state of the Fe^{II} centre from HS to LS configuration. Recently we found structural variations of the compounds allow us to increase $T_{1/2}$ up to 290K – a temperature regime that is desirable for applications. We are currently utilizing related complexes as building units for porous open-framework structures. Light-triggered spin transitions result in electronic and geometrical changes which will be advantageous to control catalytic reactions, gas uptake and release or separation modes of porous materials.



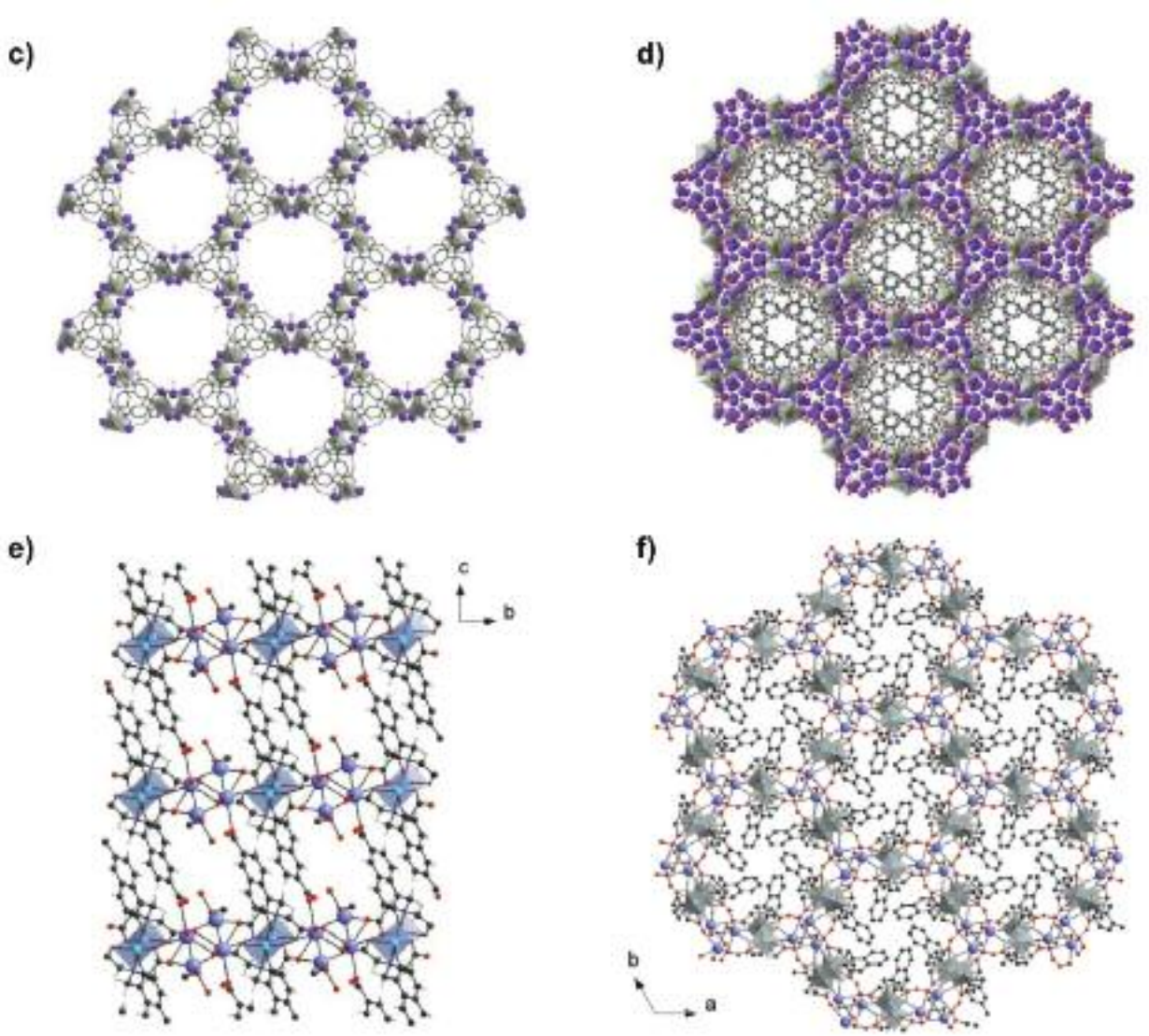


Figure 4. a) Substituted naphthol and phenol ligands; b) Dinuclear Fe^{III} complex $[Fe_2(\mu\text{-}O)(\mu\text{-}CO_3)L_2]^{4-}$ with L = tBu$_2$hda. c) Open-framework structure in $K_6[Fe_2(\mu\text{-}O)(\mu\text{-}CO_3)(SO_3\text{-}hda)_2]\cdot 11H_2O\cdot 9MeOH$ (6). d) Honeycomb structure in $K_6[Fe_2(\mu\text{-}O)(\mu\text{-}CO_3)(Chnida)_2]\cdot 13.5H_2O$ (7). e) Open-framework structure in $K_4[Cu^{II}(Hcnida)]_2\cdot 4H_2O$ (8). f) Honeycomb structure in $K_2[Cu^{II}(hnida)]_2\cdot 2H_2O$ (9). Views in [001]. Fe green, O red, K blue-purple, C dark grey, Cu cyan.

Hybrid organic-inorganic coordination networks

An interesting class of hybrid organic-inorganic materials are coordination networks and metal-organic frameworks (MOFs). MOFs are important crystalline materials consisting of clusters, complexes or metal ions linked through organic ligands and resulting in microporous networks. Many industrial countries have intensified their research to exploit the properties of metal-organic frameworks (MOFs). The interest in these compounds is a result of their advantageous characteristics which include facile synthesis, high porosity, and amenability to chemical modification for targeting purposes. MOFS and hybrid network structures have potentially excellent H_2 storage capabilities and research activities are aiming to provide scientific preconditions to initiate a shift towards more sustainable energy concepts.

We have developed concepts for crystal engineering that yield unique coordination networks where the packing of hydrophilic inorganic and hydrophobic organic portions results in lamellar, double-helical or chiral structures, dense hexagonal arrays or open-framework networks.[10] The work investigated the structure-directing effects of iminodiacetic acid substituted phenols and naphthols (L). These ligands react with FeIII salts in polar solvents to give dinuclear $[Fe_2(\mu\text{-}O)(\mu\text{-}CO_3)L_2]^{4-/6-}$ complexes (Figure 4 a and b). Their alkali and alkali earth counterions bind through carboxylate-, carbonate- or oxo-groups to these negatively charged complexes and are linked to each other forming cross-linked metal-organic frameworks.

Two selected network structures of $K_6[Fe_2(\mu\text{-}O)(\mu\text{-}CO_3)(SO_3\text{-}hda)_2]\cdot 11H_2O\cdot 9MeOH$ **(6)** and $K_6[Fe_2(\mu\text{-}O)(\mu\text{-}CO_3)(Chnida)_2]\cdot 13.5H_2O$ **(7)** are shown in Figure 4c and d.[10] The 3D architectures are determined by the shape and functionality of the organic ligand. Phenolic or naphtholic ligands that contain O-donors opposite to the hydroxyl function promote the formation of porous open-frameworks whilst other ligand topologies result in dense structures. Our approach extends the established reticular synthesis concept to charged transition metal complexes and considers their counterions as an integral part of the resulting frameworks. To develop the synthetic ideas our previous investigations focused mainly on dinuclear iron(III) complexes as a secondary building units (SBUs) of the structures. However the findings are not restricted to this particular SBU, they are valid for a range of negatively charged metal complexes where the stabilising organic ligands, containing separated hydrophilic and hydrophobic moieties, point rigidly in defined directions of space; we have demonstrated that the observed structure directing effects are also valid for related copper complexes $K_4[Cu^{II}(Hcnida)]_2\cdot 2H_2O$ **(8)** and $K_2[Cu^{II}(hnida)]_2\cdot 4H_2O$ **(9)**, shown in Figure 4e and f.[11]

The open framework structures combine promising thermal stabilities with the necessary flexibility to withstand structural changes induced by calcinations or the uptake and release of guest molecules. Whilst the porous networks raise attention as gas storage materials, dense supramolecular structures can be used as templates for the preparation of nanomaterials and we demonstrated this application using ***7*** that consists of nanosized channels that run in the direction of the crystallographic *c*-axis and which are filled with naphthyl moieties of the organic ligands.[11] Upon heating, this compound transforms into hybrid organic-inorganic nanofibres that form within single crystals of the compound and we investigated this by cutting crystals perpendicular to the crystallographic *c*-axis using a focused Ga ion beam. Thermolysis provides a further tool to control the composition of the fibres and at ca. 3700C we obtain high yields of intersected, parallel aligned fibres that are usually contained in micro-capsular entities of amorphous carbon. XRD, EDAX and IR analysis suggest that the fibres are composed of Na_2CO_3 and Fe_2O_3 which react at higher temperatures to give different phases of sodium iron oxides (Fig. 5 a-f). High-surface-area sodium carbonates are industrially used for the removal of NOx, SOx, HF, and HCl pollutants from emissions. The high activity of these sodium carbonates makes them the preferred substances for dry-sorbent injection processes; thus, they are used for flue-gas desulfurisation and scrubbing, effectively decreasing the impact of acid rain on the environment.[12]

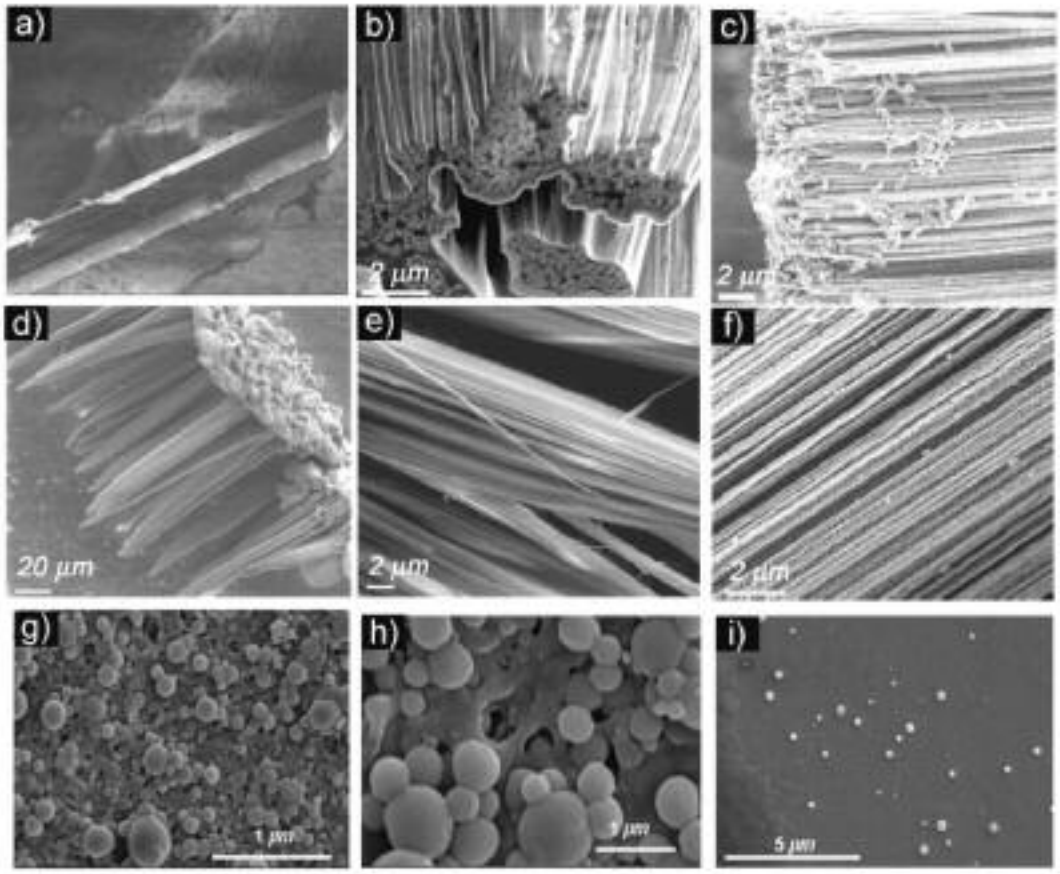


Figure 5. a)-f) Thermolysis of a crystal of $K_6[Fe_2(\mu\text{-}O)(\mu\text{-}CO_3)L_2]\cdot 13.5H_2O$ to give nanosized fibres (hybrid or carbonate/Fe_2O_3 fibres) whose dimensions and composition is determined by the molecular structure of the precursor. g–i) Assembly of mononuclear Fe^{III} complexes into nanosized vesicular spheres.

We recently demonstrated that the investigated reaction system can also be exploited for molecular self-assembly purposes. The outlined results are valid for dinuclear complexes that form under basic reaction conditions. However under neutral conditions monomeric complexes such as $[FeL(H_2O)_2]$ form. As for the dinuclear complexes, the amphiphilic character of the reaction systems, containing hydrophobic organic ligands and hydrophilic metal ions, favours the formation of structures where the areas of different polarities are separated. Whilst the van der Waals forces and related influences of the ligands are still preserved, the absence of alkali metal ions in the crystal structures minimises the dipole–cation interactions. Within the hydrophilic part hydrogen bonded networks of coordination and constitution water molecules become dominant; their arrangement is strongly influenced by the substituents and space requirements of the organic ligand. The hydrophilic parts of the structures incorporate well-defined assemblies of water molecules that mediate between the transition metal complexes and display similarities with solid ice polymorphs. Modification of the ligand structure allows self-assembly of these supramolecular arrangements into nanosized vesicular spheres (Fig. 5 g-f) whose structures have been investigated by X-ray powder diffraction, transmission and scanning electron microscopy.[13] Current research activities involve the investigation of how guests can be incorporated into the spherical aggregates and evaluation of their suitability for drug delivery applications.

Acknowledgements
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Obituary: Francis Leslie Scott

Prof. A. Frank Hegarty, *School of Chemistry and Chemical Biology, University College Dublin, Dublin 4*

Leslie Scott was Professor of Chemistry from 1960 to 1973 at University College Cork during a critical period of its development.

Undergraduate and Postgraduate career at UCC.

He entered UCC in 1945 as an undergraduate having gained first place in Ireland in both Mathematics and Chemistry at Matriculation. He was awarded three Scholarships for entry to UCC, from Cork City Council, the National University of Ireland and the Keliher Foundation. He then graduated top of his class in Chemistry in 1948. One of his lecturers at the time in UCC, Liam Mulcahy, mentioned recently that he was the outstanding student of that time: "if I had set papers to really test Les Scott, then few of the others would have passed!"

He completed an MSc in 1949 on oxyiminotriazines and then a PhD (awarded in January 1952) with Professor Joseph Reilly. During the period 1949 – 1953 at UCC between lecturing and research supervision he estimated that he had co-supervised some 25 MSc and 12 PhDs! One of these was Margaret Kennedy, whom he subsequently married.

UCLA

He then won the very prestigious Travelling Studentship of the NUI (examination and oral set by C.K.Ingold). By the time that he moved to the University of California at Los Angeles (UCLA) in 1953 to work with the renowned Saul Winstein, he had published some 28 papers on Organonitrogen Chemistry.

He spent the period 1953-5 as a Postdoctoral Fellow with Saul Winstein at UCLA and then in 1955-7 he was a Lecturer in Organic Chemistry in UCLA, and taught four undergraduate courses and a postgraduate course in heterocyclic chemistry.

DSc and Publications

He subsequently obtained his DSc from the National University of Ireland while he was still in his twenties, probably the youngest graduate of the NUI to do so. Of the 32 papers that he submitted for his DSc, almost all were in the very best international Journals: five in *Nature*, eight in the *Journal of the American Chemical Society*, six in the *Journal of Organic Chemistry with others in the Journal of the Chemical Society and Angewandte Chemie.* All but four of these were from his period at UCC.

Pennsalt

He moved in 1957 from UCLA into industry working in the research division of Pennsalt Corporation in Philadelphia. He was the Project Leader of the Organic Basic Research Group which involved basic organic mechanism studies together with study of rocket propellants and organic Polymers. Although this was often secret work, it helped to enliven his lectures when he subsequently returned to Ireland.

Professorship of Chemistry at UCC

He returned to academia in the autumn of 1960 when he was appointed Professor of Chemistry at UCC. His application at the time showed that he had widespread support, not only from Winstein and other notable US and European Chemists, but also from Professor Joseph Reilly.

His time at UCC was characterised by extraordinary energy and innovation, leading to significant expansion in undergraduate and postgraduate student numbers, facilities and research publications. These include the new Science Building (opened in 1970) and the appointment of many staff, such as the inaugural Professors of Physical and Inorganic Chemistry.

Teaching at UCC

He was an inspirational teacher both in his own area of Chemistry and the wider scientific world, and for many this was the quality for which he was most renowned. Teaching philosophy and plans formed the major part of his application for the Professorship in 1960. He taught the full first year course each year and his practical demonstrations during these lectures were inventive and interesting. Very many graduates, including those who subsequently majored in subjects other than Chemistry, say that he was the best teacher that they experienced, before and after UCC. Two contrasting comments from students sum this up:

"I was completely bamboozled into doing chemistry by Les Scott – don't know otherwise why I did it!"

"Leslie was, for me, a great apostle for chemistry and was an outstanding teacher of first year chemistry. He dictated his notes by way of a summary at the end of his informal discourse on the topic being covered. I recall him as the most outstanding teacher I ever had the good fortune to experience. He displayed an infectious enthusiasm for his discipline and one just dreamt of being lucky and fortunate enough to be a small feather on an eagle's wing as he soared a chemical sky that seemed so full of promise and potential in the late 60s. By any standard, he was a remarkable scientist and an outstanding advocate of his chosen discipline. And such was his intellect, it could have been any discipline!"

Innovations

- A four-year undergraduate course was introduced, with the first graduates in 1964.
- Introduction of two research projects in final year of undergraduate studies
- Summer Undergraduate Research Programme; begun in the summer of 1961 and continued for 12 years. On average, ten 1st and 2nd year students each year were given a bursary (funded by UCC) to assist in the research laboratories
- Business for Scientists course (with A. J. F. O'Reilly and P. Hayes among the teachers)
- Top External Examiners used; these included C. K. Ingold (University College London), R. A. Raphael (University of Cambridge), R. O. C. Norman (Oxford, then York), and R. S. Nyholm (University College London), all of whom were subsequently knighted in the UK!

Increase in Staff

This led to an exponential increase in student numbers attracted to chemistry. The expansion of the Pharmaceutical Industry in Ireland, which began in the 1970s, then drew on the wide range of people trained in the undergraduate programmes at UCC and its research laboratories. Many of his students also went on to become academics and were critical to the Regional Technical Colleges which were formed at this time. In the period 1960-64, Professor Les Scott, Dr. Sean Teegan, Dr. Noel Mulcahy and Dr. Donal O'Donovan were the academic staff members in the Chemistry Department (with usually one on sabbatical!), while in 1972 the academic staff consisted of four Professors and six Lecturers. There was a similar increase in technical and administrative staff during this period from five to twelve, after many years of stagnation in numbers.

Research Colloquium

At the annual Research Colloquium, he was a noticeable (and sometimes regarded as intimidating!) figure, sitting in the front row and asking searching questions. These were very lively events indeed, and sometimes his own students from UCC were concerned about the reciprocal questions which might then be put to them by academics from other Colleges! During his period, Cork was an enthusiastic organiser of the annual event which was held there in 1964, 1968 and 1972.

City and Gown

Amongst the contributions outside the Department, noticeable were his membership of the Cork Scientific Council, and the Smelter Study Group, which questioned a proposed lead and zinc refinery on Little Island, Cork, near Glanmire. Following a vigorous campaign, he became a member of the Governing Body from 1967 to 1973 and was also active in the UCC Graduates Association and a member of the Royal Irish Academy.

Published work in Chemistry

For the 8 central years as Professor of Chemistry at UCC, he had an average of 12 publications per year (1966 – 1973). There are165 papers in the ISI database with his name and these have over 2000 citations, and his work has the respectable h index of 24. The research areas in Cork included high nitrogen heterocycles, neighbouring group effects, reactive intermediates, 1,3-Dipoles, sulfamic acids and halogenation.

New Building

Due to increased student numbers and in particular the very significant numbers of PhDs, the old Chemistry and Physics Laboratory Building, originally opened in 1911, was clearly inadequate. Planning for a new science building on the recently cleared Cork Jail site was progressed from the mid-1960s. First year students were moved to the recently acquired Lee Maltings in the 1960s and were replaced by more research students in the original fist year laboratories. Following a major fire in this laboratory on the 5th April 1968, all first, second and third years moved to the Lee Maltings. The new building (now the Kane Building), designed by the Boyd Barrett partnership, has received much criticism from its presence on campus, but generally works well internally. The lecture theatres are excellent and the solid teak benches and other storage spaces (designed by a practice well known for its churches!) were particularly appreciated. The building was occupied from 1970.

International Conferences

On the international scene, apart from the publications, his main impact arose from a series of Conferences which he organised in and around Cork. The first, in July 1964, was on 'Organic Reaction Mechanisms', and was sponsored by the Chemical Society. It was the first major conference on this topic and attended by more than 600 over six very full days. All of the internationally renowned practitioners in the field attended the Conference and the social side was equally memorable, with major events in the City Hall, trips down the harbour and a day spent on the Ring of Kerry.

Subsequent conferences (on Inorganic Reaction Mechanisms, Sulphur Chemistry and Structure and Mechanism in Nitrogen Chemistry) were held in Blarney and Kinsale and reflected his own scientific interests. These were run on the Gordon Conference and EUCHEM models. A major book was published by the Chemical Society on 'Organic Reaction Mechanisms', arising from the 1964 Conference.

Legacy

The subsequent careers of the 40 co-authors on his publications give some indication of the impact that the training in research subsequently had. This should also take into account that, in the early 1960s, there were very few positions available in Ireland for which a degree in Chemistry was essential.

- 32% in Universities
- 16% in Institutes of Technology
- 38% in Industry
- 6% in Public Service
- 9% in Second Level Teaching
- Two became Directors of new RTCs within 3 years of completing a PhD
- Very few settled permanently abroad.

As industry expanded, graduates took most of the senior posts. To many it was no coincidence that the Pharmachem Industry targeted Ringaskiddy/Little Island as it took off in the 1970s. Currently the industry has €42.6 billion in exports, and 25,000 in direct employment. Dr. John Lechleiter, the new President and CEO of Eli Lilly, at the sod-turning for their new $400m facility in Kinsale in April 2008 indicated that, while 1% of their 40,000 employees were Irish, 10% of his senior Management Team are from Ireland.

Very many of those who completed a research degree under Les Scott's supervision during the period 1960-1973 attended the first 'Scott Lecture' delivered by Dr. Stephen Connon of TCD in the Kane Building at UCC on April 30th 2009.

Conclusion

While the importance of his work might be seen as the contribution to Irish society in the establishment of a sustainable industrial sector, it also anticipated the significant expansion of education which subsequently occurred. It subsequently provided a firm base for the current active Department of Chemistry and School of Pharmacy at UCC.

Following Margaret's death in 1973, Les Scott left UCC to take his first sabbatical, with Donald Cram (later to be awarded the Noble Prize in Chemistry) at UCLA. He then resigned his Professorship in September 5th 1973 in a letter to the President, to take up a post at the University of Rochester before going to Pennwalt as the Research Director of the Chemical Sciences in Rochester, New York.

In recent years he returned to Cork where he died on January 14th, 2008 and is survived by his daughters Fiona and Anne and his son Spencer.

Advertising Feature

Waters PoraPak Rxn Cartridges for post synthesis cleanup

Waters now offers PoraPak™ Rxn, a family of polymer-based chromatography products for superior cleanup of synthetic reactions. PoraPak Rxn products are available in two chemistries:

- PoraPak Rxn CX, a strong cation-exchange sorbent
- PoraPak Rxn RP, a reversed-phase sorbent.

PoraPak Rxn sorbents are available in fritted syringe-barrel devices in 6, 20 and 60 cc volumes. The resins are also sold in bulk units, and custom configurations are available on request.

NEW SOLUTIONS FOR FASTER RESULTS

PoraPak Rxn sorbents are based on copolymers that exhibit the following properties:

- Hard material that does not develop increasing back pressure with flow.
- Little swelling or shrinking across a range of solvents and pH extremes.
- Low hydraulic resistance enables flow by gravity.
- pH extreme tolerance without dissolution or hydrolysis, both limitations of silica-based sorbents.

This combination of physical and chemical properties makes PoraPak Rxn cartridges ideal for synthesis cleanup. The polymers characteristics and particle size maintain gravity, pressure -or vacuum - assisted flow; even when reaction mixtures contain precipitate that may contribute additional resistance to flow. The sample will still pass through the cartridge.

The polymer used in PoraPak Rxn products is resistant to shrinking or swelling in the organic solvents typically used in synthetic reactions. Tests with the following solvents demonstrate that the packed bed maintains good flow properties:

- DCE
- DCM
- DMSO
- DMF
- THF
- Acetone

Some Medicinal Chemists are familiar with silica-based chromatographic products for reaction cleanup. One of the limitations of these silica-based ion-exchange materials is pH. Silica will dissolve at high pH, while bonded phases are hydrolyzed at low pH; both conditions result in loss of sample and/or impurities (silica and bonded phase) collected in product fractions. PoraPak Rxn polymer-based chromatographic phases are stable at extreme pH. This feature permits using pH as a very powerful tool to create a separation, particularly in ion-exchange mode.

WATERS: A WORLD LEADER IN SEPARATIONS SCIENCE PROVIDING SEPARATIONS SOLUTIONS

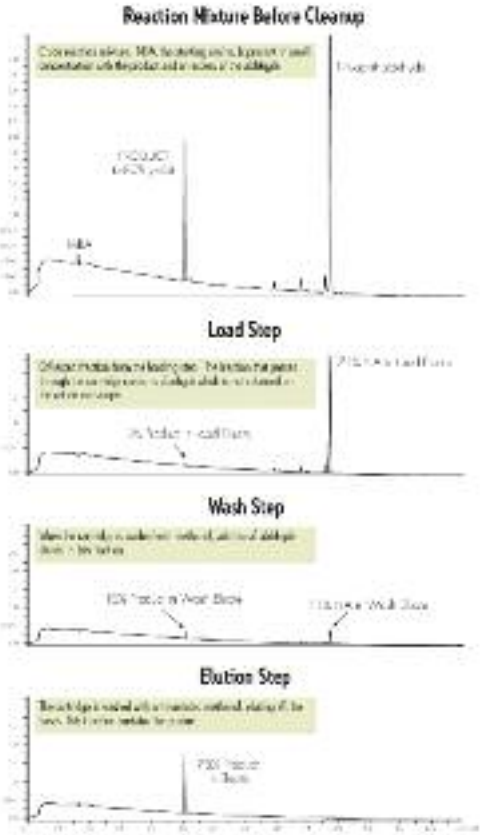
Waters is highly respected world wide for its expertise in chromatography. Coupled with our ability to seamlessly link critical instrumentation, chemistries, separation technologies, and software, this expertise puts us in a unique position to deliver value-added solutions to our customers.

MANUFACTURING

Our world-class manufacturing facilities are continuously expanded and upgraded to keep pace with market demand for our new and existing products. We manufacture under the highest quality standards in the industry, including ISO-9001:2000, ISO 13485:2003 and Current Good Manufacturing Practices (cGMP).

CLEANUP OF A REDUCTIVE AMINATION MIXTURE

Reductive amination is a common reaction carried out in medicinal chemistry laboratories. In this example, a PoraPak Rxn CX cartridge is used to fractionate the reaction mixture.



Using the 'catch-and-elute' procedure to clean up the synthetic mixture enables a quick collection of a limited number of fractions, increasing the certainty of finding the product rapidly. Assay the product fractions for confirmation, then begin the evaporation of the more volatile elution solvent.

[FAST CLEANUP OF SYNTHESIS REACTIONS]

- Efficient Fractionation
- Cost Effective

PoraPak™ Rxn products are designed to ensure fast and thorough cleanup of most synthesis reactions. The polymer used in PoraPak Rxn material is tolerant of pH extremes, shows low hydraulic resistance and displays very little shrinking or swelling in organic solvents. This combination of physical and chemical properties makes PoraPak Rxn an ideal solution for your most challenging synthesis cleanup.

PoraPak™ Rxn
Post Synthesis Cleanup

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Industry News

Dr. Donal Coveney,

TopChem Laboratories Limited, 70 Western Parkway Business Park, Ballymount Drive, Dublin 12, Ireland.

Megamergers

Mergers seem to be back on the agenda after a few quiet years. It doesn't seem that long ago that we saw the formation of GlaxoSmithKline, AstraZeneca, Sanofi-Aventis and Pfizer gobbled up Pharmacia and Warner Lambert in turn.

World number 1 Pfizer has surpassed previous mergers with the acquisition of Wyeth – which itself was No. 10 in the global pecking order. Listening to a senior US Pfizer executive visiting the Enterprise Ireland offices recently, it seems the patent expiry of Lipitor is a key driver for this decision. Lipitor is the world's largest pharmaceutical product with sales running at €12 billion in 2008. The product patent expires in the US and other major markets in 2011 leaving a big hole to fill in revenue. The purchase price of Wyeth of $68 billion is certainly a number that grabs the attention given our Governments tax take is running at €32 billion – equivalent to $48 billion!

Following that trend, Merck and Schering Plough agreed to merge with Merck picking up the $48.1 billion tab on this one. The merged entity will be dubbed Merck and appears to be a natural conclusion to the successful co-marketing of certain products in the US by the two companies.

After every merger comes the cuts and it came as no surprise to hear that Pfizer is cutting R&D by 35%, reducing the number of R&D sites from 20 to 14 and is laying off 19,500 staff. Merck followed suit announcing plans to cut 16,000 employees from their newly merged entity. In both cases numbers are being trimmed by 15%.

It remains to be seen if these mergers have a negative impact on our home turf which leads us neatly on to Domestic News.

Domestic News

We have a few rays of sunshine for beleaguered readers battered by incessant negativity from all quarters.

Servier Ireland officially opened their new facility following an investment of €124 million, a doubling in size and 100 new jobs added. The new facility will serve as a strategic centre for the parent company's pharmaceutical R&D. Servier is a privately owned French company with 20,000 employees and annual sales of €3.7 billion. The Company invests heavily in drug discovery R&D and has a very rich portfolio of proprietary pharmaceutical products.

There have been some developments in Mulhuddart, Co. Dublin recently with Rottapharm announcing a €7 million expansion of manufacturing facilities with the addition of 35 new staff. Helsinn Chemicals Ireland has been sold as a going concern to the Italian company CFM (Co. Farmaceutica Milanese). The Company has been renamed Clarochem Ireland Limited and our best wishes to Dr Brian Keaveney and his colleagues under the new ownership. Helsinn's other pharmaceutical operations in Mulhuddart continue under Helsinn ownership.

Our good friends in Eirgen have announced a €3.3m expansion of their Waterford facility which will increase employment to 40. Eirgen was established in 2005 by Patsy Carney and Tom Brennan and specialises in the development and registration of highly potent drug formulations. While there has been a bit of a bandwagon of high potency API facilities, Eirgen have carved out a niche in the formulation of high potency products.

For those of you unfamiliar with high potency products, these are highly active pharmaceuticals where very low doses are therapeutically active - often at sub milligram levels. As a result, extra precautions are required to protect worker exposure during manufacturing.

Alas the domestic bad news continues with Teva pulling out of Waterford with the loss of 315 citing Irelands "prohibitively high costs". Said jobs are being relocated to Hungary, Czech Republic, Poland and Croatia. If this worrying trend continues one would have to be concerned for the future of manufacturing industry in Ireland. No doubt there will always be "adjustments" but given that we are still seeing expansions let us hope that we at least are holding our own.

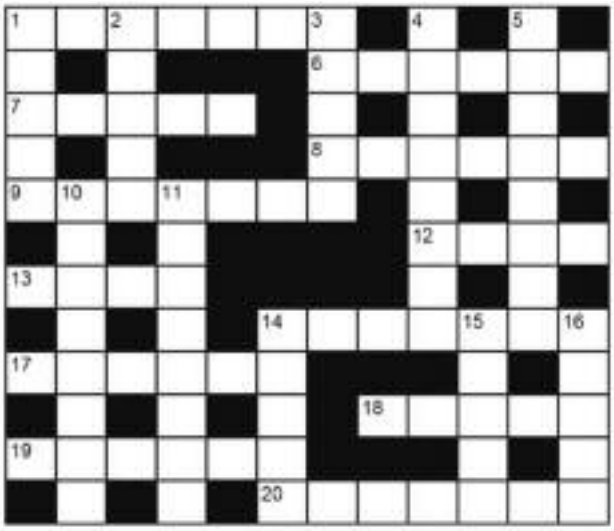
To close, best wishes to those in Corden Pharmachem which closed its doors recently. The site started life in the early seventies as an API manufacturing site for Boehringer Ingeleheim. The facility was sold to private investors in the early nineties and changed ownership to Cambrex and finally Corden Pharmachem which took the decision to close earlier this year. I understand the facility is to be levelled and a similar fate looms for the Pfizer Inchera site. The terms of the EPA licences quite rightly require proper decommissioning of such facilities.

Who would have predicted that such well established pharmaceutical manufacturing sites with highly skilled employees and regulatory approvals could be literally wiped from the landscape?

Let's hope that this is not a trend but a temporary setback for the Pharmachem sector in Ireland.

The ICN Crossword

Dr. Donal Coveney FICI, *TopChem Laboratories Limited, 70 Western Parkway Business Park, Ballymount Drive, Dublin 12, Ireland*



Down

1 Mr. Stokers bat (7)
6 Classic titration indicator (6)
7 Magnification device for watchmakers (5)
8 Divided into three lobes (6)
9 Something added (7)
12 Leave out (4)
13 We don't understand it, but we are all talking about it: A Man (4)
14 Insect sensory appendages (7)
17 Takes a hike on a bee? (6)
18 Abnormal tissue growth (5)
19 Smells (6)
20 Intrinsic nature of something (7)

Across

1 Italian physicist is electrifying (5)
2 Common term for fungi (5)
3 Drive off from column (5)
4 Go sister to stiff hairs or bristles (8)
5 Player of instrument (8)
10 Girls best friend (8)
11 Mull a hit on soft toxic metal(8)
14 Liquorice flavoured plant (5)
15 Makes synthetic tights? (5)
16 Sufficient, plentiful (5)

Previous Solution:

Across.

1. Thunder, 6.Accord 7. Niche, 8. Ionise, 9. Sarcoid,

12. Item 13. Soap 14 Stomata, 17 Barium, 18 Villi,

19 Ritual, 20 Theatre

Down.

1 Tongs, 2 Ulcer, 3 Rabid. 4 Scandium, 5 Crescent,

10 Aromatic, 11 Capsicum, 14 Smelt, 15 Allot, 16 Azide

Gaseous Su Doku

Dr. David Birkett, *Henkel Ireland Ltd., Tallaght Business Park, Whitestown, Dublin 24, Ireland*

F					O			
			Ar			N	H	
				F	H	Ne		
N	Ar		Cl			F		
		F		N		Kr		
		Cl			He		Ar	N
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Notes

Notes

[FAST CLEANUP OF SYNTHESIS REACTIONS]

- Efficient Fractionation
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