

2010 Symposium on Inorganic Chemistry in Ireland

Programme and Abstracts

Friday 17th September 2010

10.30-11.00 Registration and coffee in the Chemistry Foyer

Session 1 **Chair:** Stuart James

11.00-11.50 Martin Albrecht (University College Dublin)
[Challenging the norm: Catalytic opportunities from abnormal carbene bonding](#)

11.50-12.10 Peter Nockemann (Queen's University Belfast)
[Ionic Liquids for Inorganic and Materials Chemistry](#)

12.10-12.30 Leigh Jones (National University of Ireland, Galway)
[A family of Double-Bowl Metallocalix\[6\]arenes](#)

12:30-12.45 Poster short presentations

Lunch

12.45-13.45 Posters and Sandwiches in LG.201

Session 2 **Chair:** Grace Morgan

13.50-14.20 Patrick C. McGowan (University of Leeds)
[Functionalised Organometallic Molecules as Potential Anticancer Drugs](#)

14.20-14.40 Celine J. Marmion (Royal College of Surgeons in Ireland)
[Exploiting Chromatin as a New Molecular Target for the Development of Novel Metallochemotherapeutics](#)

14:40-15.00 Andrew Kellett (Dublin Institute of Technology)
[Bis-Phenanthroline Copper\(II\) Complexes of Aromatic and Aliphatic Dicarboxylates are Potent *In Vitro* Antitumour Agents with 'Self-Activating' Metallo-Nuclease & DNA Binding Properties](#)

15:00-15.20 John McGinley (National University of Ireland Maynooth)
[Tetrazoles in Macrocyclic and Macromolecular Systems](#)

Afternoon Tea

15.20-15.50 Poster and afternoon tea in LG.201

Session 3 **Chair:** TBC

15.50-16.20 Prof. Sylvia Draper (Trinity College Dublin)
[When Chemistry Stacks-Up: A Bottom-up Approach to Graphene Fragments](#)

16:20-17:30 Robin Perutz (University of York)
[The Detection and Roles of Sigma Bond Complexes of Transition Metals](#)

Drinks Reception and Posters

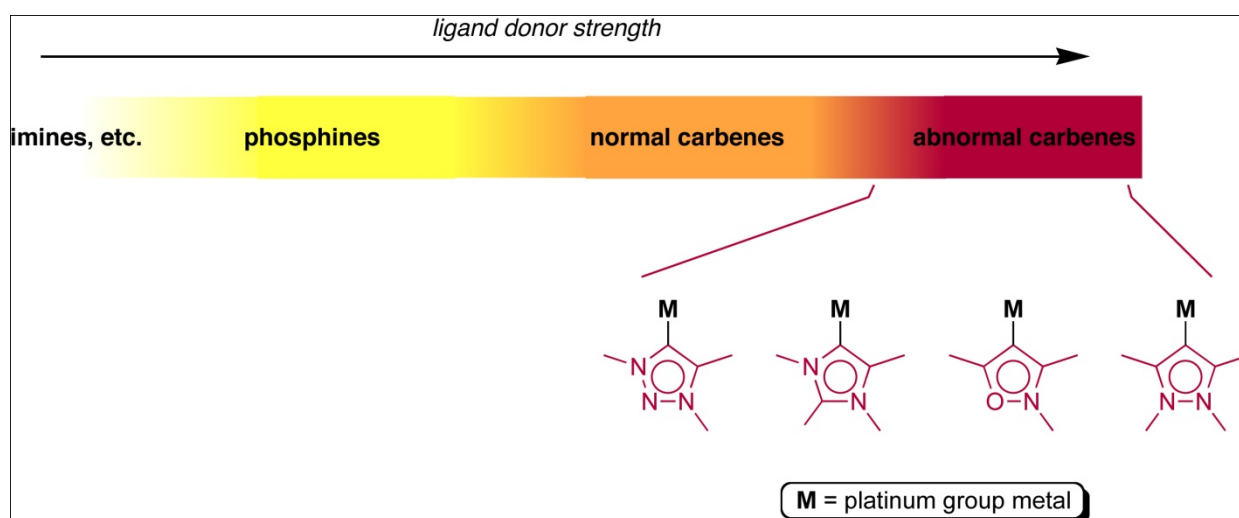
17:30-18.30 Poster and Reception in LG.201

Challenging the norm: Catalytic opportunities from abnormal carbene bonding

M. Albrecht

*School of Chemistry & Chemical Biology, University College Dublin
Belfield, Dublin 4, Ireland
e-mail: martin.albrecht@ucd.ie*

Abnormal N-heterocyclic carbene have become increasingly popular ligands in organometallic chemistry,¹ last but not least because of their exceptionally strong donor ability as compared to other formally neutral ligands such as phosphines and normal carbene ligands (Figure below).²



We will report on our recent progress in expanding the family of abnormal carbenes.³ This class of ligands seems to be tunable over a much broader range than normal N-heterocyclic carbenes, thus approaching the tunability window of classical phosphorus-based ligand systems. In particular, we will focus on the catalytic implications of the abnormal carbene bonding mode, specifically with respect to the activation of less reactive bonds,⁴ including recently discovered activity in C(alkyl)–H and O–H bond cleavage processes.

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Ionic Liquids for Inorganic and Materials Chemistry

Peter Nockemann

Queen's University of Belfast, The QUILL Research Centre, School of Chemistry and Chemical Engineering

E-mail: p.nockemann@qub.ac.uk

Ionic liquids are increasingly attracting the attention of inorganic and materials chemists.^{1,2,3} The incorporation of functional groups in so-called *task-specific ionic liquids* can impart particular capabilities to an ionic liquid, such as the ability to interact with a metal center and an enhanced solubility for metal salts.^{4,5} The solvent properties of ionic liquids are becoming continuously better understood. For applications in catalysis and electrochemistry it is desirable to design specific ionic liquids for complexing metal ions. Dyson and coworkers introduced a range of nitrile functionalized ionic liquids which can bind to metal centers.⁶

We have studied the metal complexing ability of a range of new nitrile-functionalized pyrrolidinium based ionic liquids. Solutions of transition metal and lanthanide salts in these nitrile-functionalized ionic liquids have been studied by IR/Raman, EXAFS, NMR and optical spectroscopic methods. The Ionic liquid solvates of a range of cobalt(II) salts (see Fig. 1) could be crystallized and the crystal structures have been determined.

The number of coordinating nitrile functionalities at the metal center and the strength of the metal-nitrogen bonds depend on the number of carbon atoms between nitrile group and the positive charge of the quaternized nitrogen atoms of the cation. This influence of the charge on the nitrile donor abilities has also been supported by DFT calculations on the ionic liquids. As a result, it has been shown that the coordinating ability of nitrile-functionalized ionic liquids can be tuned by varying the chain length of the nitrile functionality.⁸ In a recent approach we were able to demonstrate the use of metal precursors in such nitrile functionalized ionic liquids for the growth of shaped nanoparticles.

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5. Davis, J. H. Jr., *Chem. Lett.*, 2004, 33, 1072.
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A family of double-bowl metallocalix[6]arenes

Leigh F. Jones

School of Chemistry, National University of Ireland, Galway, Ireland

leigh.jones@nuigalway.ie

Much research in recent years has focused on the development and extension of supramolecular chemistry towards important applications such as catalysis,¹ gas storage,² and medical imaging (MRI contrast agents).³ A rapidly growing research field incorporating supramolecular methods, and the focus of our studies, is that of the development of *host-guest* systems via the targeted structural manipulation of polymetallic complexes and their associated molecular assemblies. Our research has recently focused on the synthesis and characterization of a family of heptanuclear planar discs of general formula $[M_7(OH)_6(L)_6](NO_3)_2$ ($M = Ni^{2+}, Co^{2+}$) (e.g. $[Ni_7]$ complex in Fig. 1), for use as magnetically interesting *host* units; a field of *host-guest* chemistry still in its infancy. The complexes described here consist of a central M^{2+} ion surrounded by a further six M^{2+} ions to give the disc-like topology. These architectures are built (in part) by the Schiff base ligands 2-iminomethyl-6-methoxyphenol (L_1H) or 2-iminomethyl-4-bromo-6-methoxyphenol (L_2H) (Fig. 2), which legate via their imine, phenolic and methoxide functional groups and exhibit a $\eta^1:\eta^2:\eta^1;\mu$ -coordination motif.

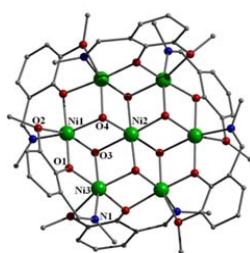


Fig. 1

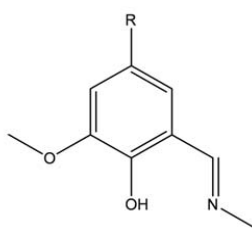


Fig. 2

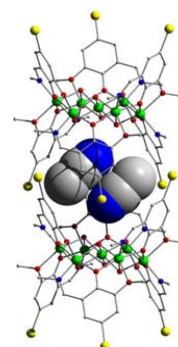


Fig. 3

The individual $[M_7]$ units pack in 1-D columns in their crystal lattices to form double-bowl conformations in which the $[M_7]$ core is the basal plane, akin to the metallocalix[6]arene concave unit. Hydrogen bonding between pairs of $[M_7]$ units result in molecular cavities which allow for the incorporation of a variety of different *guest* molecules (i.e. MeCN *guests* in Fig. 3); demonstrating their effectiveness as inorganic *host* species and thus allowing for direct comparison to supramolecular calix[n]arene behaviour.⁴

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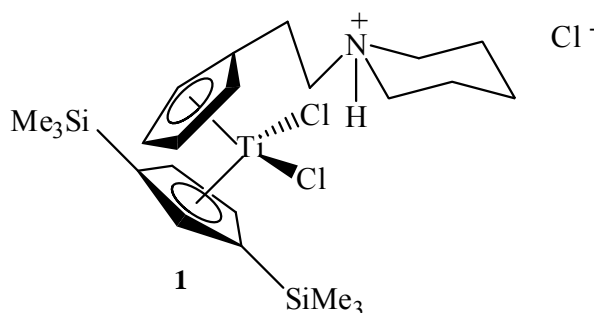
4(a) S. T. Meally, G. Karotsis, E. K. Brechin, G. S. Papaefstathiou, P. W. Dunne, P. McArdle, L. F. Jones., *CrystEngComm* **2010**, 12, 59-63. (b) S. T. Meally, C. McDonald, G. Karotsis, G. S. Papaefstathiou, E. K. Brechin, P. W. Dunne, P. McArdle, N. P. Power, L. F. Jones, *Dalton Trans*, **2010**, 39, 4809 – 4816.

Functionalised Organometallic Molecules as Potential Anticancer Drugs

Patrick C. McGowan, Olivia R. Allen, Andrew L. Gott, Stacey M. Lord and James J. Mannion

University of Leeds, Department of Chemistry, Woodhouse Lane, LS2 9JT, Leeds, England.

We have been interested in the synthesis and structural studies of functionalised ferrocenes for a number of years.¹ We have developed pathways for the synthesis of amino-monofunctionalised ferrocene and ferrocenium salts. We have also developed a library of air stable and water soluble titanium, zirconium and ruthenium organometallic compounds as potential anticancer drugs.²⁻⁴ Following our initial promising results,² one of our lead compounds, a functionalised titanocene **1**, shows excellent *in vitro* activity against number of different cell lines including high activity towards cisplatin resistant cell lines.² A number of *in vivo* range finding experiments have been completed and the results are promising.



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Exploiting Chromatin as a New Molecular Target for the Development of Novel Metallochemotherapeutics

Celine J. Marmion,^a Darren Griffith,^a Maria Morgan,^b Brian Duff,^c Denise Egan,^c James Parker,^a Hassan Nimir,^a Anna Kisova-Halamikova,^d Viktor Brabec^d

^aCentre for Synthesis & Chemical Biology, Department of Pharmaceutical and Medicinal Chemistry, Royal College of Surgeons in Ireland (RCSI), Dublin 2, Ireland (cmarmion@rcsi.ie); ^bDepartment of Molecular & Cellular Therapeutics, RCSI, Dublin 2, Ireland; ^cDepartment of Science, Institute of Technology, Tallaght, Dublin 24, Ireland; ^dInstitute of Biophysics, Academy of Sciences of the Czech Republic, Brno, Czech Republic

Despite the enormous success of platinum drugs as anti-cancer chemotherapeutics, their widespread application and efficacy is hindered by toxic side effects and intrinsic or acquired drug resistance.[1] The cytotoxicity of platinum drugs is attributed to their ability to bind DNA nucleobases and induce apoptosis.[1] The search for new molecular targets beyond DNA which may present unique opportunities for therapeutic exploitation is the subject of intense investigation. The recent correlation between the inhibition of enzymes that regulate chromatin structure/function and tumour growth suppression has, for example, validated chromatin control as a promising new molecular target in contemporary medical oncology. Inhibition of histone deacetylases (HDAC's), for example, enzymes which play a key role in maintaining chromatin structure and thus function, have been shown to cause cell cycle arrest, differentiation and/or apoptosis of tumour cells. While several are currently undergoing clinical trials, already one, suberoylanilide hydroxamic acid, is in clinical use as a treatment for cutaneous T-cell lymphoma. HDAC inhibitors are also known as 'sensitizer drugs' that display synergistic effects with other anti-cancer agents such as cisplatin. Some have also been shown to be selective for cancer cells over normal cells.[2,3]

We have designed, through molecular modeling, and developed novel platinum drug candidates with dual DNA binding and HDAC inhibitory activity.[4,5] The rationale behind their development and their synthesis will be described. A summary of the pharmacological results obtained to date, in which they have been shown to be highly cytotoxic towards cancer cells as well as having enhanced selectivity for cancer cells over normal cells, will also be provided.

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Bis-Phenanthroline Copper(II) Complexes of Aromatic and Aliphatic Dicarboxylates are Potent *In Vitro* Antitumour Agents with ‘Self-Activating’ Metallo-Nuclease & DNA Binding Properties

Andrew Kellett,^{*a} Michael Devereux,^a Mary McNamara,^a Malachy McCann,^b Mark O'Connor,^a Orla Howe,^a Alan Casey,^a Vickie McKee,^c Georgina Rosair^d

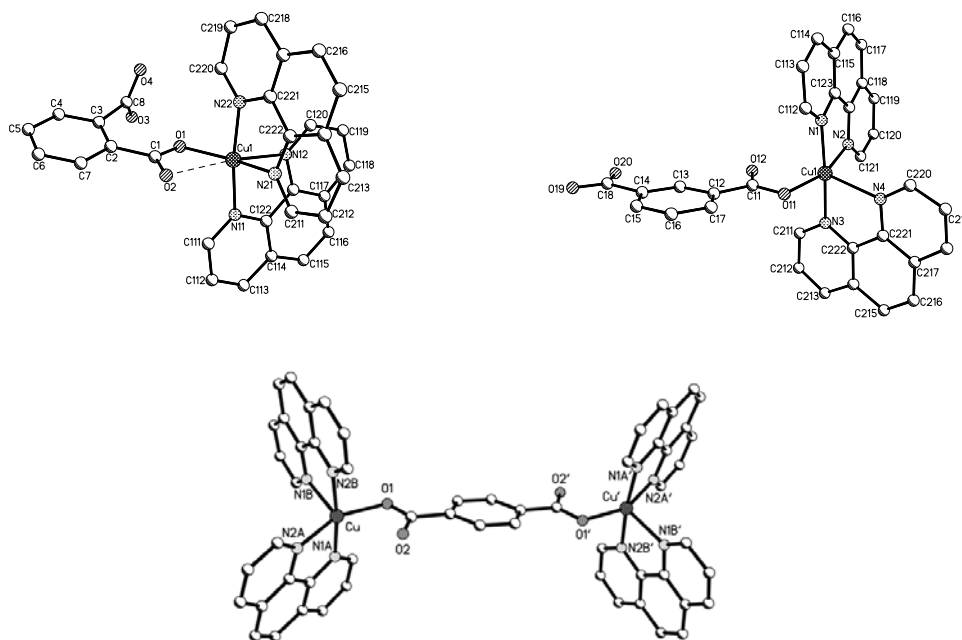
^a Focas Research Institute, Dublin Institute of Technology, Camden Row, Dublin 8, Ireland

^b Chemistry Department, National University of Ireland, Maynooth, Co. Kildare, Ireland

^c Department of Chemistry, Loughborough University, Loughborough, Leicestershire, LE11 3TU, UK

^d School of Engineering and Physical Sciences, Heriot Watt University, Edinburgh, EH14 4AS, UK

The development of ‘self-activating’ chemical nucleases is regarded as the paradigm of redox-active metal-based chemotherapeutics. Complexes of metals such as iron, copper and manganese have been shown to act as effective chemical nucleases through oxidative-induced DNA damage.¹ In the majority of these systems, DNA carbon-hydrogen bond activation requires initiation by an excess of an exogenous agent such as H₂O₂, and/or an appropriate reducing agent, and this effectively limits their *in vivo* application. Only a few self-activating DNA cleavage systems have been reported including Fe(BLM) and Cu(BLM) (BLM = bleomycin) which require the presence of molecular oxygen. Recently this laboratory has produced the first ‘self-activating’ chemical nucleases of the bis-phenanthroline class that induce relaxation of supercoiled plasmid DNA in the absence of external reducing agents.^{2,3} All compounds display rapid, low micromolar and, in some instances sub-micromolar, *in vitro* cytotoxicity against a range of epithelial cancers; breast, colon, prostate and cisplatin-resistant ovarian cancer cell lines. Importantly, the complexes were found to bind DNA efficiently but do not appear to target specific base-paired sequences. Finally, we have observed that nuclearity plays a significant role in terms of both drug toxicity and DNA activation.



¹ M. Pitie and G. Pratviel, *Chem. Rev.*, 2010, **110**, 1018-1059.

² A. Kellett, M. McCann, M. O'Connor, M. McNamara, P. Lynch, G. Rosair, V. McKee, B. Creaven, M. Walsh, S. McClean, A. Foltyn, D. O'Shea, O. Howe, and Michael Devereux, *Chem. Comm.*, Submitted 2010.

³ A. Kellett, M. Devereux, M. McCann and M. McNamara, Patent Filed, 2010.

Tetrazoles in macrocyclic and macromolecular systems

John McGinley

Department of Chemistry, National University of Ireland Maynooth, Maynooth, Ireland

While the use of macrocycles in coordination chemistry has been well established, the use of tetrazole units within such macrocycles is limited. Indeed, there are only a small number of macrocycles reported which contain four tetrazole units [1]. One of the reasons for such a small number is the demanding synthetic pathways required to make such molecules. We have succeeded in synthesising several tetra-tetrazole macrocycles, like that shown in Figure 1, and have looked at their coordination chemistry with various metal ions. The metal ion binding ability of these macrocycles is weak and to try and overcome this, we have looked at macromolecular systems containing four tetrazole molecules as well as macrocycles containing one heterocycle and one phenyl ring, as opposed to the two phenyl rings as shown in Figure 1. The coordination chemistry of both these macromolecular systems and the new macrocycles will be discussed.

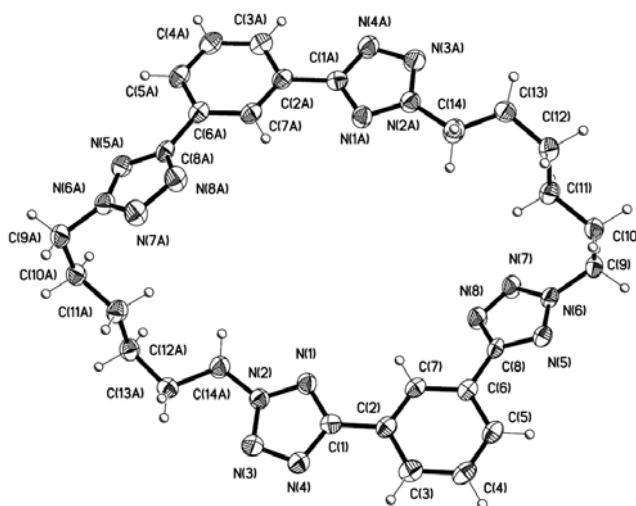


Figure 1.

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When Chemistry Stacks-Up: A Bottom-up Approach to Graphene Fragments

Professor Sylvia Draper

School of Chemistry, University of Dublin, Trinity College Dublin, D2, Ireland

Graphene comprising a single-layer of sp^2 hybridised carbon atoms is being heralded as the new material of the 21st Century.^[1] This is on account of its extraordinary, high electron mobilities and the ease with which its electronic properties can be modulated by externally applied electric fields.^[2] Many novel graphene-based device applications have been predicted or demonstrated e.g. the graphene-based field-effect transistor (FET), gas sensors, biosensors and lateral p-n junctions.^[3]

Most graphene researchers adopt the top-down approach of exfoliating bulk graphite. Comparatively rare is the bottom-up, organic-synthesis of graphene-based fragments, even though these offer the advantages of synthetic purity, lateral control and scope for substituent variation over bulk graphene. Meaningful structure/activity relationships arise ideally from atomically precise graphene and solution processing via printing techniques (e.g. screen or inkjet), desirable for OLED production only becomes a real possibility when solubility issues are overcome. These facts made the generation of soluble N-doped molecular graphenes (N-HSB, scheme 1) (MeOH, THF, MeCN, $CHCl_3$) by the Draper team^[4] a critical advance in a field dominated by generally insoluble all-carbon polyaromatic frameworks based on hexaperi-hexabenzocoronene HBC. This presentation will provide some insight into the synthetic advances that are needed to make useful changes in the functionality, molecular structure and supramolecular order of discrete polyaromatic platforms.

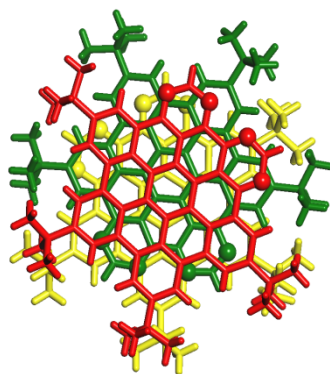


Figure 1 (i) Synchrotron X-ray structure of N-HSB showing helical columnar stacking

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THE DETECTION AND ROLES OF SIGMA BOND COMPLEXES OF TRANSITION METALS

Robin N. Perutz

Department of Chemistry, University of York, York YO10 5DD, UK. rnp1@york.ac.uk

The dihydrogen complex is the best known of the class of σ -complexes, but others are formed by boranes, silanes and alkanes.

Section 1: alkane complexes are the most elusive of σ -complexes, but their role in reaction mechanisms is often apparent. The first section of the lecture describes how laser photochemistry inside the probe of an NMR spectrometer [1] has allowed the observation of σ -alkane complexes of a first row transition metal.

Section 2: This section illustrates an approach for detecting σ -bond complexes that are implicated in rearrangements of conventional complexes. Half-sandwich complexes of the type $\text{Rh}(\eta^5\text{-C}_5\text{H}_5)(\text{H})(\text{E})(\text{L})$ are chiral. By employing a chiral phosphine as the ligand L, new dynamic processes are revealed. When E is a boryl or a silyl ligand, we show by a combination of experiment and theory that the molecule is non-rigid and epimerises via σ -borane or σ -silane transition state [2].

Section 3: Rapid rearrangements have brought about the realisation that σ -complexes can provide the key to interconversion of functional groups at a late transition metal without change of oxidation state. We call this the σ -CAM mechanism and it is quite distinct from the usual mechanisms of metathesis [3].

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