Symposium Organisation Comittee

IT Operator Sameera Wickramarachi Shilawalage Chamil
Book of Abstracts Tobias Krämer
Stationery Lynne Thomas, Derek Middlemiss
Website, Registration and Coordination Thomas Davin
Posterboard Damiano Portinari
Eva Salamanova, Vihar Georgiev, Lorreta Lawton

Coverpicture by courtesy of Photographic Unit, University of Glasgow.
Thanks to Stephen McCann.

Symposium Program

- **9:30** - Registration in Conference Room, Joseph Black Building, conference room (A4-41a)

Chair: Professor John McGrady, University of Glasgow

- **10:25** - Opening Remarks
- **10:30** - Professor Simon Mackay, University of Strathclyde
  "Using Molecular Dynamics Simulations to explore Ligand-DNA interactions"
- **11:00** - Dr Brad Sherborne, Schering-Plough Pharmaceuticals
  "Working with Real HTS data"
- **11:30** - Flash presentations
- **12:00** - LUNCH

Chair: Professor Chick Wilson, University of Glasgow

- **13:00** - Professor Michael Bühl, University of St Andrews
  "From Computational NMR Spectroscopy to Homogeneous Catalysis: Beyond Static Molecules"
- **13:30** - Dr Carole Morrison, University of Edinburgh
  "Adventures in Proton Transport and Migration"
- **14:00** - Dr Martin Paterson, Heriot-Watt University
  "The Challenges Associated With Computing Two-Photon Absorption Properties"
- **14:30** - TEA

Chair: Professor Paul Madden, University of Edinburgh

- **15:00** - Dr Hans Martin Senn, University of Glasgow
  "Insights into Enzymatic Halogenation from QM/MM Calculations"
- **15:30** - Dr Philip Camp, University of Edinburgh
  "Phase Separation in Chemistry and in Biology"
- **16:10** - Closing Remarks
- **16:20** - Posters and wine

Talk Abstracts

Talk 10:30 - 11:00

Using Molecular Dynamics Simulations to explore Ligand-DNA Interactions

Simon Mackay

Strathclyde Institute of Pharmacy and Biomedical Sciences,
University of Strathclyde, Glasgow G4 0NR, Scotland, UK

The University of Strathclyde has historically been successful in the design and development of drug candidates to treat a variety of diseases, and since 2001, we have been applying molecular modelling techniques to aid and augment this process. This lecture will report on our input into one such project, where we have used molecular dynamics simulations in association with biophysical techniques to understand and predict how specifically designed ligands complex with DNA in a sequence-selective manner.

From Computational NMR Spectroscopy to Homogeneous Catalysis: Beyond Static Molecules

Michael Bühl

School of Chemistry, North Haugh, University of St. Andrews, St. Andrews, Fife KY16 9ST, UK

Selected case studies are discussed that illustrate how density functional computations can be used to address current problems in the chemistry of d and f elements. Applications comprise structure and speciation of uranyl complexes in aqueous solution[1], the mechanism of reductive dehalogenation of chloroethylenes catalysed by a vitamin B_{12} model[2], and QM/MM modeling of the ^{51}V NMR chemical shift tensor of a vanadium-dependent chloroperoxidase (VCPO), a vanadium-containing enzyme[3] (see Figure below). In all these cases, molecular dynamics simulations are important ingredients in the computational protocols, be it to describe the dynamic nature of a surrounding protic solvent or to probe for the flexibilty of residues along a peptide backbone.

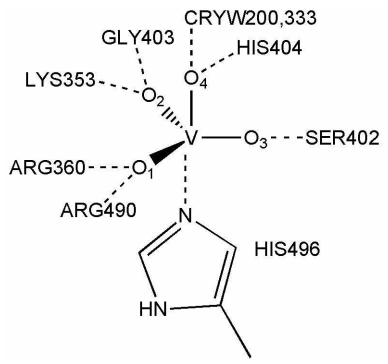


Figure 1: Schematic of the active center in VCPO showing potential hydrogen bonding interactions between the vanadium moiety and the protein environment.

[1] See for instance: M. Bühl, R. Diss, G. Wipff, *Inorg. Chem.*, **2007**, *46*, 5196.
[2] M. Bühl, V. Golubnychiy, *Organometallics*, **2007**, *26*, 6213.
[3] M. P. Waller, M. Bühl, K. R. Geethalakshmi, D. Wang, W. Thiel, *Chem. Eur. J.*, **2007**, *13*, 4723.

Talk 13:30 - 14:00

Adventures in Proton Transport and Proton Migration

Dr Carole A. Morrison

School of Chemistry, University of Edinburgh

Fast proton transport (PT) between hydrogen bond donor and acceptor atoms is of paramount importance in many aspects of chemistry and biology. Applications are diverse and include many technological developments such as hydrogen fuel cells.[1] In nature all reactions that convert energy from one form into another are mediated by PT, which also serves as a vital route to achieve cell pH stabilisation. Proton migration (PM) is a much more subtle effect, where the time-averaged position of the H atom in a short, strong hydrogen bond changes as a function of temperature and pressure.

Our aim is to understand the mechanisms of PT and PM using simulation. This presents something of a challenge for three main reasons. First, bond formation and breaking events are not described by conventional molecular mechanics force fields. Second, owing to the small mass of the hydrogen atom, quantum effects such as tunnelling and zero-point energy contributions can radically alter the reaction landscape. Third, PT is a rare event, meaning that for the majority of the time the system is at rest, with obvious consequences for statistical sampling from molecular dynamics trajectories.

We will present a reaction mechanism for the double PT reaction that occurs spontaneously for the chloroacetic acid dimer system, considering atoms both as classical and quantum particles.[2] We will also present results obtained from molecular dynamics calculations for an adduct of urea and phosphoric acid that go some way towards offering an explanation for the PM phenomenon.

[1] K. D. Kreuer, *Chem. Matter*, **1996**, *8*, 610.

[2] P. Durlac, C. A. Morrison, D. S. Middlemiss and Z. Latajka, *J. Chem. Phys.*, **2007**, *127*, 064304.

Talk 14:00 - 14:30

The Challenges Associated With Computing Two-Photon Absorption Properties

Martin J. Paterson

Heriot-Watt University, Edinburgh

Two-photon absorption is an increasingly important technique in photodynamic anti-cancer treatments due to high-focusing resolution and tissue depth penetration. The theoretical determination of two-photon absorption spectra is important in the development of singlet oxygen photosensitizers, but is complicated by significant electronic correlation effects, one-particle basis set errors, vibrational contributions, solvent effects, and laser-factors. In this talk the use of quadratic response function theory in computing two-photon absorption is discussed. Coupled-cluster response theory is used to benchmark other approaches including density functional response theory for the application to large molecules including tetra-phenyl-porphycenes, which show much promise as photodynamic agents. Solvent effects are investigated *via* a hybrid coupled cluster / molecular mechanics response study of the two-photon absorption of liquid water, including a statistical treatment of the non-linear molecular property *via* a molecular dynamics sampling. Finally, an introduction to the computation of vibrational properties *via* response theory is outlined for the frequency dependent polarizability of formaldehyde *via* the linear response of a full vibrational configuration interaction wavefunction, showing excellent agreement with experiment.

Insights into Enzymatic Halogenation from QM/MM Calculations

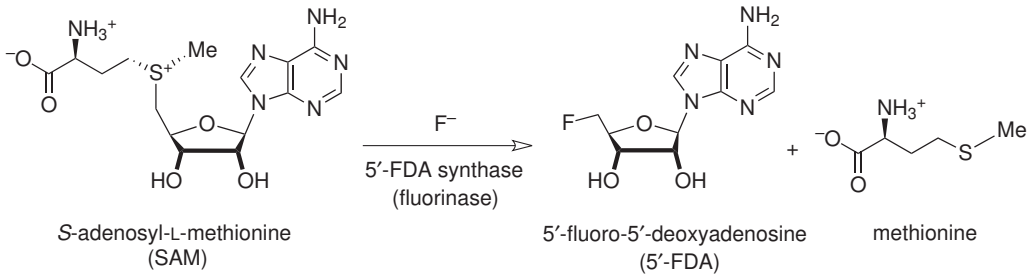
Hans Martin Senn,[a] David O'Hagan,[b] and Walter Thiel[c]

[a] *Department of Chemistry, University of Glasgow, Glasgow G12 8QQ, Scotland, UK* [b] *School of Chemistry and Centre for Biomolecular Sciences, University of St Andrews, St Andrews KY16 9ST, Fife, Scotland, UK* [c] *Max-Planck-Institut fr Kohlenforschung, D-45470 Mülheim an der Ruhr, Germany*

Several thousand natural organohalogens have been identified, produced by organisms from across the phylogenetic tree. Most of them are bioactives, and some halogenated active pharmaceutical ingredients are already produced by fermentation, making use of the capacity of biological systems to form carbonhalogen bonds with exquisite specificity. However, the details of how this is achieved at the chemical level are only just being established. In particular, X-ray structures of three novel enzyme families the first fluorinating enzyme,[1] the flavin-dependent halogenases,[2] and the non-haem iron halogenases[3] have only recently become available.

Our work so far has concentrated on the fluorinase, which catalyses the formation of 5'-fluoro-5'-deoxyadenosine from *S*-adenosyl-L-methionine (SAM) and F^- (Scheme). Fluorinase is the first native enzyme identified to catalyse the formation of CF bonds. We have performed QM/MM studies at the DFT/CHARMM level to gain insight into the C−F bond formation step in the enzyme and compared it to the intrinsic reactivity of the substrates in solution.[4] We will discuss the role of the enzyme in promoting and controlling the reaction, resulting in a rate acceleration relative to solution of 10^8. We will also report on the influence of substrate modifications (other halides, SAM derivatives).

We will give preliminary results and an outlook on future work on the flavindependent and non-haem iron halogenases.



Scheme

[1] C. Dong, F. Huang, H. Deng, C. Schaffrath, J. B. Spencer, D. O'Hagan, J. H. Naismith, *Nature*, **2004**, *427*, 561-565.

[2] C. J. Dong, S. Flecks, S. Unversucht, C. Haupt, K.-H. van Pèe, J. H. Naismith, *Science*, **2005**, *309*, 2216-2219.

[3] L. C. Blasiak, F. H. Vaillancourt, C. T. Walsh, C. L. Drennan, *Nature*, **2006**, *440*, 368-371.

[4] H. M. Senn, D. O'Hagan, W. Thiel, *J. Am. Chem. Soc.*, **2005**, *127*, 13643-13655.

Talk 15:30 - 16:00

Phase Separation in Chemistry and Biology

Philip J. Camp

School of Chemistry, University of Edinburgh

I will discuss two examples of phase separation, one of relevance to colloid chemistry, and the other to the process of pattern formation in certain biominerals. The first example concerns homogeneously magnetised spherical nanoparticles in a colloidal suspension. The magnetic dipole-dipole interactions cause self-assembly of the particles to form chains, rings, and other types of clusters. This aggregation profoundly affects - and may even preclude - a phase transition between dilute and concentrated phases. Recent results from multicanonical and Wang-Landau Monte Carlo simulations will be reviewed; and evidence for the existence of the phase transition will be presented.[1,2] The second example concerns diatoms - unicellular, photosynthetic organisms found in freshwater and marine environments. Diatoms possess ornate, porous skeletons fashioned from amorphous silica. By analogy with the templating synthesis of mesoporous materials, it is thought that fluid-phase structures on the surfaces of diatom cells may provide patterned moulds for the deposition of silica. A simple phase-separation model will be presented which is capable of producing templates for a wide variety of diatom structures.[3]

[1] G. Ganzenmüller and P. J. Camp, *J. Chem. Phys.*, **2007**, *126*, 191104.
[2] G. Ganzenmüller and P. J. Camp, *J. Chem. Phys.*, **2007**, *127*, 154504.
[3] L. Lenoci and P. J. Camp, *Langmuir*, **2008**, *24*, 217–223.

Poster Abstracts

Poster number 1

EPSRC National Service for Computational Chemistry Software (NSCCS)

Helen Tsui

Department of Chemistry, Imperial College London, South Kensington, London, SW7 2AZ, UK

The aim of the NSCCS is to provide UK academics working across all fields of chemistry with access to software packages and hardware resources. Our database of users include both experimentalists who use calculations to complement their practical work, and computational chemists who take advantage of the extensive range of software available.

We also provide support for non-specialists in the form of one-to-one training sessions, software workshops and specialist scientific consultation.

The Service supports a wide range of quantum chemistry, materials chemistry and biological chemistry codes, and state-of-the-art hardware in the form of Magellan, a 224-core SGI Altix 4700 with 896GB of shared memory.

Poster number 2

Periodic Structures of Ammonia Borane Clathrates

Alexander Abramov, Maciej Gutowski

School of Engineering and Physical Sciences - Chemistry, Heriot-Watt University

Recent theoretical research showed that the problem of hydrogen storage might be solved by making use of clathrates of Ammonia Borane (AB). These compounds have promising hydrogen density along with kinetically easily accessible hydrogen.

The structures of the compounds are not known and several possibilities have been suggested. All options are challenging for *ab initio* studies as clathrates normally have large unit cells. We present some periodic systems which can be made of AB molecules and perform screening. The challenges due to the size of the systems are overcome by using linear scaling DFT methods. Relative stabilities and geometrical parameters will be reported.

Poster number 3

Binding Free Energy of DNA Ligands using the MM/PBSA Methodology

N. G. Anthony,[1] K. Wittayanarakul,[1] W. Treesuwan,[2] G. Huchet,[2]
S. Hannongbua,[2] S. P. Mackay.[1]

[1]*Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, 27 Taylor Street, Glasgow G4 0NR, UK* [2]*Chemistry Department, Kasetsart University, Bangkok 10900, Thailand*

Ligands that interact with DNA have the unique ability to affect processes occurring at the genetic level. DNA minor groove binders are such ligands, which are commonly used as molecular probes and have the potential to alleviate problems arising from genetic disorder.[1] The synthesis of such ligands is not trivial, and gaining insights into their molecular aspects of binding to DNA through computer simulation is an important challenge in their development as drug candidates. The University of Strathclyde is at the forefront of chemical novelty in this area, and is currently developing these ligands as a new class of antimicrobial agents.[2] The use of Molecular Dynamics simulations to derive thermodynamic properties of binding events between ligands and DNA has been reported for relative binding free energies for different DNA sequences,[3] but determination of absolute binding free energies has remained elusive. Using the thiazotropsin-A:5'GCGACTAGTCGC system[4] as a test case, we have simulated a binding free energy closely matching that of our analytical calorimetric data. We achieved this by running separate Molecular Dynamics trajectories for the ligand-DNA complex, free DNA duplex and free ligand using the Molecular Mechanics/Poisson-Boltzmann Surface Area (MM/PBSA) methodology within the AMBER suite of software. We are currently applying this protocol to other related sequences to assess its robustness.

[1] Burnett, R., Melander, C., Puckett, J. W., Son, L. S., Wells, R. D. *et al.*, DNA sequence-specific polyamides alleviate transcription inhibition associated with long GAA center dot TTC repeats in Friedreich's ataxia, *Proceedings of the National Academy of Sciences of the United States of America*, **2006**, *103*, 11497–11502.

[2] Anthony, N. G., Breen, D., Clarke, J., Donoghue, G., Drummond, A. J. *et al.*, Antimicrobial lexitropsins containing amide, amidine, and alkene linking groups, *Journal of Medicinal Chemistry*, **2007**, *50*, 6116–6125.

[3] Cheatham, T. E., Simulation and modeling of nucleic acid structure, dynamics and interactions, *Current Opinion in Structural Biology*, **2004**, *14*, 360–367.

[4] Anthony, N. G., Johnston, B. F., Khalaf, A. I., Mackay, S. P., Parkinson, J. A. *et al.*, Short Lexitropsin that Recognizes the DNA Minor Groove at 5 -ACTAGT-3: Understanding the Role of Isopropyl-thiazole, *Journal of the American Chemical Society*, **2004**, *126*, 11338–11349.

Poster number 4

Study of Dense Silicate Phases using NMR Spectroscopy and First-Principles Calculations

Sharon E. Ashbrook,[1] Andrew J. Berry,[2] Chris J. Pickard,[3] Alan Gregorovic,[4] and Stephen Wimperis[4]

[1]*School of Chemistry and EaStCHEM, University of St Andrews, St Andrews, Fife KY16 9ST, UK* [2]*Department of Earth Science and Engineering, Imperial College, London SW7 2AZ, UK* [3]*School of Physics and Astronomy, University of St Andrews, St Andrews, Fife KY16 9SS, UK* [4]*Department of Chemistry and WestCHEM, University of Glasgow, Glasgow G12 8QQ, UK*

Structural studies of dense silicates play an important part in understanding the physical and chemical properties of the Earth's mantle, properties which may be dramatically affected by the incorporation of small amounts of water at defect sites. Natural samples of mantle silicates either contain Fe or are not available, requiring synthesis at high pressures and temperatures, which often yields relatively small amounts of material, hindering the acquisition of NMR data. The study of silicates by NMR is also hampered by the properties of the NMR-active nuclei of the three most abundant elements which make up the silicate Earth, ^{29}Si, ^{17}O and ^{25}Mg. All three have low natural abundances (4.7%, 0.037% and 10%), limiting sensitivity, although this can be overcome synthetically by isotopic enrichment. Furthermore, ^{17}O and ^{25}Mg are quadrupolar, with spectra broadened by the second-order quadrupolar interaction. Complex two-dimensional methods (e.g., MQMAS and STMAS) are consequently required to obtain high-resolution NMR spectra. As a result of these difficulties, we are exploiting first-principles calculations to predict, assign and help interpret high-resolution NMR spectra of isotopically-enriched high-pressure silicates, including the polymorphs of Mg_2SiO_4 and $MgSiO_3$.

We employ the NMR-CASTEP code, a pseudopotential method which utilizes the gauge-including projector-augmented-wave (GIPAW) formalism, allowing calculation of both electric field gradients and NMR chemical shifts. The use of a planewave basis set and periodic boundary conditions make this an ideal method for the study of periodic solids, providing an accurate, yet computationally efficient, approach. We show examples where calculations provide an aid to spectral assignment and interpretation, and also cases where spectral prediction can help experimental acquisition where sensitivity is particularly limiting. Calculations can also aid in determining the correlation of NMR parameters with structural features, providing the possibility of structural insight from materials where diffraction is difficult.

Poster number 5

Mechanistic Analysis of Intermolecular C−H Activation

Amalia I. Poblador-Bahamonde,* Dr. Stuart A. Macgregor

School of Engineering and Physical Sciences, Heriot-Watt University, Riccarton, Edinburgh EH14 4AS, UK; e-mail: aip1@hw.ac.uk

The C−H activation by transition metal complexes is an extremely dynamic area of experimental and theoretical investigation. There has been great progress in the development of new catalysts based on mechanism ranging from *oxidative addition* to *σ-bond metathesis* and *electrophilic activation*. It has been shown that complexes such as **A** are able to catalyse C−H activation, although they require very high temperatures[1a]. Alternatively, complexes such as **B** can perform C−H activation at room temperature, although so far a successful catalyst has not yet been developed. We believe that species such as **B** have certain key design features that facilitate C−H activation.

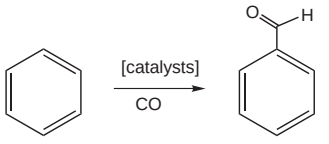
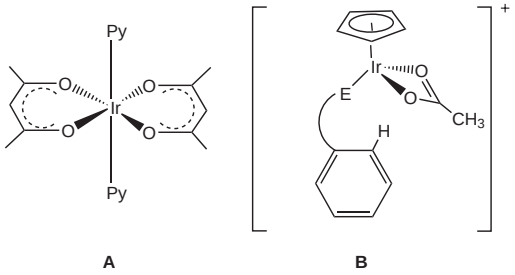
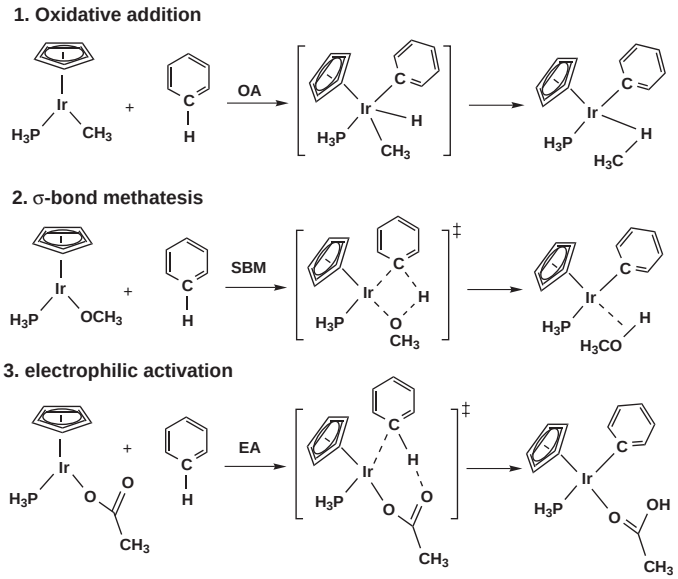


Figure 1



A **B**



A number of general mechanisms have been proposed for C−H activation, however, these are very difficult to distinguish experimentally. Computational chemistry can provide the missing information and through combining experiment and theory Bergman and Hall[1] have proposed an *oxidative addition* process (**1**), while Periana and Goddard[2] have suggested *σ-bond methathesis* (**2**). A third possibility is *electrophilic activation* (**3**) and previous work in our group[3] has suggested that this process is most accessible in complexes such as **B**. This poster will describe the results of density functional calculations (DFT) that model these various possible mechanisms for intermolecular C−H activation.

[1] (a) P. Burger, R. G. Bergman, *J. Am. Chem. Soc.*, **1993**, *115*, 10462. (b) N. Shuqiang, M. B. Hall, *J. Am. Chem. Soc.*, **1998**, *120*, 6169.

[2] J. Oxgaard, R. A. Periana, W. A. Goddard *et al.*, *J. Am. Chem. Soc.*, **2004**, *126*, 11658.

[3] D. L. Davies, S. M. A. Donald, O. Al-Duaij, S. A. Macgregor, M. Polleth, *J. Am. Chem. Soc.*, **2006**, *128*, 4210.

Poster number 6

Distributed Gas-phase and Solid-state Calculations for the Determination of H-Bonded Systems

Julie Bardin, Blair F. Johnston and Alastair J. Florence

Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow G4 0NR

Whilst the determination of molecular crystal structures from powder diffraction data has significantly advanced in the last decade, the location of hydrogen atoms often remains problematic, due to their weak scattering contribution. This is especially of importance when studying hydrogen-bonded systems, such as 2-fluoroethanol and 2,2,2-trifluoroethanol, as the hydroxyl functionality plays a key role in determining the intermolecular interactions in these structures. The use of combined molecular modelling techniques offers a valuable source of additional information to supplement the limited intensity data available from powder diffraction pattern and increase confidence in the location of hydrogen atoms. Firstly, molecular conformations were studied in the gas-phase using Gaussian03[1]; molecules were first optimised at B3LYP 6-31+g(d) and the optimised structural parameters were used for single-point calculations, in which torsion angles of interest were varied. The 648 calculations were performed on our distributed, GridMP[2], computing platform, enabling a quick determination of the relevant potential energy surfaces. The low-energy conformations were then used as input models for experimental crystal structure determination using a global optimisation approach that is also implemented on the GRID-MP system[3]. The hydroxyl H-atom position was held fixed during the global optimisation. The global minimum structure from 500 simulated annealing runs was then geometry optimised using CASTEP[4] to yield DFT-optimised positions for all hydrogen atoms. The optimised structures are confirmed to be consistent with the laboratory X-ray powder diffraction data by Rietveld refinement[5]. From this combined use of gas-phase, periodic and simulated annealing calculations, a degree of uncertainty has been removed in the determination of solid-state structures of crystalline solvents, which would not have been straightforward to solve using experimental data alone.

[1] 1995–2004 Gaussian, Inc.
[2] 2000–2007 United Devices, Inc.
[3] 2004–2008 The Cambridge Crystallographic Data Centre.
[4] 2001–2008 Accelrys Software Inc.
[5] H. M. Rietveld, *J. Appl. Cryst.*, **1969**, *2*, 65–71.

Poster number 7

Calculations of the excited states of biomolecules with CASSCF

Lilianna Bryjko

School of Chemistry, University of St Andrews, St Andrews, Fife KY16 9ST, UK

Complete Active Space Self Consistent Field (CASSCF) calculations for singlet and triplet 2,4-dioxouracil and keto-guanine-7H were done. The basic point for CASSCF calculation is the choice of the active space. Not only the number of active orbitals and electrons but also the number of calculated states has influence upon the results.
Another point of the calculations is the choice of the basis set. The calculations were done with the 6-31G, 6-31G*, cc-pVDZ, cc-pVTZ and aug-cc-pVDZ basis sets. Values such as electronic energy, number of configurations and excitation energy were considered. The ground state dipole moment was compared to the experimental value.

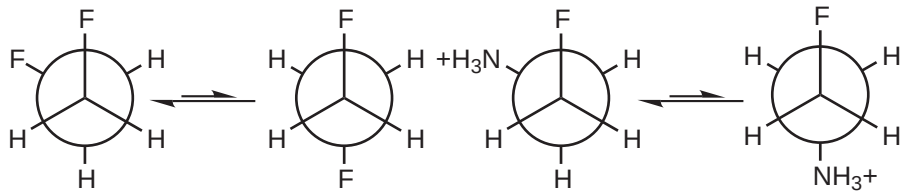
Poster number 8

DFT study of the gauche effect in fluoroethane

D. Buissonneaud,* D. O'Hagan, T. van Mourik

School of Chemistry and Centre for Biomolecular Sciences, University of St Andrews, St Andrews, Fife, KY16 9ST, UK; e-mail: dyb@st-andrews.ac.uk

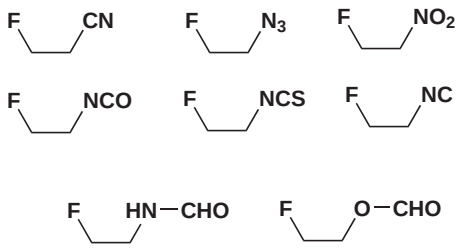
Examples of the gauche effect are found in many molecules, but 1,2-difluoroethane (**1**) is considered the benchmark case for the unexpected gauche conformational preference.[1]



1a **1b** **2a** **2b**

Figure 1: *gauche* (**1a**) and *anti* (**1b**) 1,2-difluoroethane conformers *gauche* (**2a**) and *anti* (**2b**) 2-fluoroethylammonium conformers.

A number of attempts at rationalising the *gauche* preference in 1,2-difluroethane (**1**) have been made; the more common explanation involves hyperconjugation. On the other hand, 2-fluoroethylammonium (**2**) is known to favour the *gauche* conformer due to a strong electrostatic interaction.[2,3] The aim of this research is to study by DFT (density functional theory), neutral molecules which are intermediate between 1,2-difluoroethane (**1**) and 2-fluoroethylammonium (**2**) and to try to understand the relative roles of hyperconjugation or electrostatic effects. The selected molecules are:



[1] L. Goodman, H. Gu, V. Pophristic, *J. Phys. Chem. A*, **2005**, *109*, 1223–1229.
[2] C. R. S. Briggs, M. J. Allen, D. O'Hagan, D. J. Tozer, A. M. Z. Slawin, A. E. Goeta, J. A. K. Howard, *Org. Biomol. Chem.*, **2004**, *2*, 732–740.
[3] N. E. J. Gooseman, D. O'Hagan, M. J. G. Peach, A. M. Z. Slawin, D. J. Tozer, R. J. Young, *Angew. Chem. Int. Ed*, **2007**, *46*, 5904–5908.

Poster number 9

Computer Simulation Studies of Molecular Order in Chromonic Mesophases

F. Chami and M. R. Wilson

Department of Chemistry, Durham University, Science Laboratories, South Road, Durham DH1 3LE, UK

Chromonic liquid crystals occur widely in aqueous dispersions of many formulated products such as pharmaceuticals and the dyes used in inkjet printing. They are also used in material science for fabricating highly ordered thin films and anisotropic carbons. Chromonic mesophases are usually formed in water from disk-like or plate-like molecules. Here, molecular self-assembly occurs into stacks, and the stacks are then able to pack to form liquid crystalline phases. Unlike many lyotropic liquid crystals, self-assembly is not mediated by the hydrophobic effect, *i.e.* entropic interactions but is enthalpy driven.

Molecular order within a chromonic phase is not well understood. From system to system, little is known about how molecules pack. Moreover, we know little about the strength of interactions between molecules in stacks or the ordering of water molecules around the stacks. This paper presents initial results from a simulation study designed to answer some of these fundamental questions. Results are presented from atomistic simulations of a chromonic stack for the molecule edicol (sunset yellow) in water, looking at the ordering of edicol molecules in the columns. Results are also presented looking at quantum predictions of NMR shielding. Here, simulation can be linked to recent experimental measurements in solution, which are aimed at understanding how self-assembly occurs in chromonics.

The Drug Discovery Portal @ Strathclyde: Collation of an Academic Compound Collection

R. L. Clark,[1] C. J. Breslin,[2] S. P. Mackay,[1] B. F. Johnston[1]

[1]*SIPBS, 27 Taylor Street, Glasgow G4 0NR,*
[2]*R & I, 50 George Street, Glasgow G1 1XQ*

The Drug Discovery Portal (DDP) brings together the rich, but currently isolated resources in drug research in academic institutions in Scotland and beyond. It provides an accessible central resource to allow chemists and biologists to boost their current drug discovery research efforts. This is achieved by encouraging chemists to upload structures and biologists to upload targets and both parties to initiate advanced *in silico* screening and hit identification.

The DDP is currently collating the large number of compounds that exist in academic laboratories in Scotland and beyond. Chemists that provide electronic structures of compounds can find a way to repurpose them through the DDP, resulting in increased opportunity for collaborative research in drug discovery.

The University of Strathclyde has a long history of natural products research. Many chemists with varied research interests past and present, have extracted, isolated, identified and synthesised simple and complex natural products to produce a diverse collection of compounds. The design of a compound library enriched with natural-products such as these offers huge potential for the identification of hits for new drug discovery programmes. Recent publications suggest that despite substantial technological developments in combinatorial chemistry generating millions of potentially active compounds, the chemical space that these libraries occupy is small compared with the diversity of a much smaller number of organic natural products.[1]

Here we describe a method for compound collection analysis and compare the growing DDP Academic Compound Collection with some standard virtual screening libraries.

[1] (a) Dobson, C. M., Chemical space and biology, *Nature* **2004**, *432*, 824–828. (b) Feher, M., Schmidt, J. M., Property Distributions: Differences between Drugs, Natural Products, and Molecules from Combinatorial Chemistry, *J. Chem. Inf. Comput. Sci.*, **2003**, *43*, 218–227. (c) Newman, D. J., Cragg, G. M., Natural Products as Sources of New Drugs over the Last 25 Years, *J. Nat. Prod.*, **2007**, *70*, 461–477.

Poster number 11

Virtual Ligand Screening for Riboswitches

Peter Daldrop & Ruth Brenk

College of Life Sciences, University of Dundee, Dundee DD1 5EH

Riboswitches are part of the 5'UTR of mRNAs in certain bacteria (e.g. *B. subtilis*) and several plants (e.g. *A. thaliana*). Dependent on ligand binding they can fold into two different conformations, one of which permits further steps in protein biosynthesis, whereas the other does not. Riboswitches are thus *cis*-acting gene regulatory elements.

In this project a modified G-riboswitch was used as a model system to study the performance of virtual ligand screening.

Virtual ligand docking is used to determine binding properties of chemicals to biological macromolecules. Each chemical is placed into the target crystal structure in multiple orientations and conformations and evaluated with an energy-based scoring function. Whereas this method has been extensively applied in the protein field little is known about its performance with RNA.

The application of virtual ligand screening for the G-riboswitch is described and evaluated by both retrospective and prospective tests.

Poster number 12

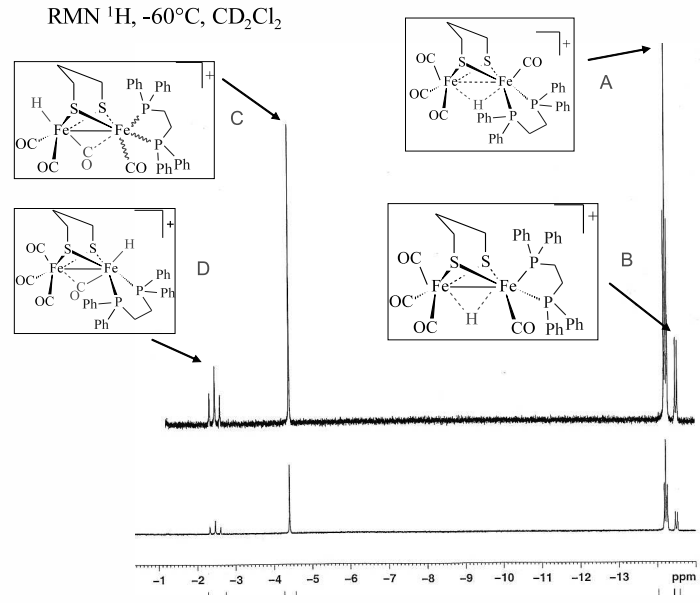
Using DFT-Computed Hydride Chemical Shifts and Coupling Parameters to Identify Species in Solution

Thomas J. Davin,[a] John E. McGrady[a] and Philippe Schollhammer[b]

[a] *The University of Glasgow, Department of Chemistry, University Avenue, Glasgow G12 8QQ* [b] *Université de Bretage Occidentale, UMR 6521, 6, avenue Victor Le Gorgeu - CS93837, 29238, Brest Cedex 3, France; e-mail: thomasd@chem.gla.ac.uk*

The structure of hydride complexes of di-iron clusters is of considerable interest in light of the discovery of the Fe_2 cluster in the active site of hydrogenase enzymes.[1] The identification of these hydrides in solution is typically conducted by ^{1}H NMR spectroscopy, but this does not always provide an unambiguous structural assignement. Thus, a number of candidate structures may be consistent with a given spectroscopic pattern. Density functional theory offers the possibility of calculating NMR spectroscopic parameters (δ, J) for a range of possible structures and then matching these to experiment. This, combined with energetic data, offers a powerful tool for identifying species in solution.

In this poster, we compare calacuted NMR parameters for a series of 4 closely related Fe_2 hydrides recently reported by Schollhammer and co-workers (see Figure).[2] The calculations confirm their structural assignments for 3 of the hydride species (A, C, D), agreement between experiment and theory is less impressive for B.



[1] Evans, D. J. and Pickett, C. J., *Chem. Soc. Rev.*, **2003**, *32*, 268.
[2] Ezzaher, S., Capon, J.-F., Gloaguen, F., Pétillon, F. Y., Schollhammer, P. and Talarmin, *J. Inorg. Chem.*, **2007**, *46*, 3426.

X-ray Absorption Spectroscopy combined with Ligand-field Multiplet Calculations to gain insight in the Coupling between Electronic and Magnetic structures

M. A. de Vries

Laboratory for Quantum Magnetism, Institut Physique Materie Complexe, Ècole Polytechnique Fèdèrale de Lausanne, 1015 Lausanne Switzerland; e-mail: mark.devries@epfl.ch

We have studied the geometrically frustrated antiferromagnet iron jarosite using a combined experimental-theoretical approach. Polarisation dependent X-ray absorption spectra at the Fe L2,3 edges of this compound where measured at the European Synchrotron Radiation Facility (ESRF) in Grenoble and at the Synchrotron Radiation Source in Daresbury. These spectra were used to construct accurate models of the nominally Fe^{3+} ions and their ligand field in iron jarosite using multiconfigurational Hartree-Fock calculations. For these calculations we used the program Hilbert++ which was recently developed at the ESRF. Using this method the experimentally obtained spectra could be reproduced in great detail and calculations yielded accurate numbers for the expectation values of the spin moment, orbital moment, spin-orbit coupling, the magnetic anisotropy energies and the O 2p to Fe 3d charge transfer. The calculated values are in excellent agreement with neutron spectroscopy data and the (high temperature) magnetic susceptibility of the iron jarosite.

Poster number 14

The Gas-Phase Structures of Methylphosphine and Methylphosphine-borane

Robert Noble-Eddy,[a] Sarah L. Masters[a] and Jean-Claude Guillemin[b]

[a]*School of Chemistry, University of Edinbugh, West Mains Road, Edinburgh, UK; e-mail: r.noble-eddy@ed.ac.uk* [b]*Sciences Chimiques de Rennes, École Nationale Supérieure de Chimie de Rennes-CNRS, 35700 Rennes, France*

Recent work in Edinburgh has been focussed towards determining structures of primary phosphines and the complexes they form with borane. Relatively few studies have been conducted on the structure of the primary aliphatic phosphines, ($R-PH_2$), most likely to be due to their unfavourable properties; they are often pyrophoric, toxic, unstable in air and possess an unpleasant odour. However, primary phosphines have potential as starting materials for various applications such as organophosphine ligand design, catalysis and drug design. As such, the development of more stable, *user-friendly* phosphines is of great interest. Stabilisation can be achieved by the addition of a bulky protecting group, for example the mesityl group in mesitylphosphine, or by complexation with a suitable Lewis-base. Complexes with borane have been reported and the chemistry of borane adducts explored but only a few structural studies have been reported.

This poster presents the structures of methylphosphine and methylphosphine-borane determined by gas electron diffraction. As the simplest primary phosphine-borane adduct, this system allows structural study free from the effects of larger substituents, and is sufficiently small that high-level *ab initio* calculations can be performed. The results of these calculations are presented and compared to the experimental structure allowing the accuracy of various theoretical methods to be gauged. Significant structural changes are found around the phosphorus atom upon formation of the complex. These changes, along with the stability they infer, are discussed and rationalised by considering charge transfer within the complex.

Poster number 15

Beyond NBH_x The Importance of Thermodynamics in Materials for Hydrogen Storage

Michael J. Edie, and Maciej Gutowski

Heriot-Watt Unviersity, Chemistry-School of Engineering and Physical Sciences, Edinburgh EH14 4AS, United Kingdom and W. R. Wiley Environmental Molecular Sciences Laboratory, Pacific Northwest National Laboratory, Richland, WA 99352, USA

Boron-nitrogen hydride (BNH_x) materials display exceptionally promising gravimetric and volumetric densities of hydrogen. Hydrogen release from various forms of (BNH_x) compounds is typically slightly exothermic and thus regeneration of the spent materials is challenging form a thermodynamic point of view. We have used density functional calculations to explore a range of approaches aiming to improving the thermodynamic performance of theses materials with respect to hydrogen uptake and release. We recognize that the BN unit is isoelectronic with the CC unit and dehydrogenation of hydrocarbons is typically endothermic. Thus we propose that $(BN)_{(1-y)}C_{2y}H_x$ compounds might display thermodynamics for dehydrogenation intermediate between this for carbon-based and that for BN-based hydrides. We will present promising computational results for molecular and extended $(BN)_{(1-y)}C_{2y}H_x$ compounds.

Poster number 16

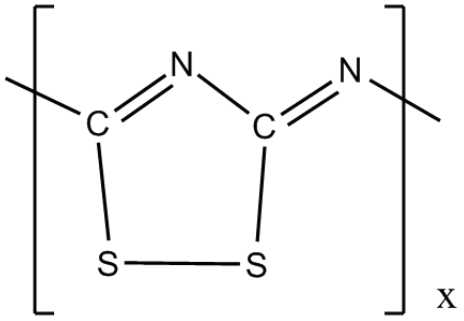
The Structure of the (SCN) Polymer

Herbert Früchtl, Verity Douglas, Tanja van Mourik, Chris J. Pickard
and J. Derek Woollins

School of Chemistry, University of St Andrews, St Andrews, Fife KY16 9ST, UK

Despite its simple composition, the microscopic structure of the (SCN) polymer (polythiocyanogen) is still disputed. Various structures have been proposed in the literature.[1–3] We present a comprehensive computational study of molecular fragments based on these structures. Geometries were optimised at the B3LYP/6-31+g* level, and ^{13}C chemical shifts (computed on with B3LYP/6-311++g(d,p)) were compared to experiment.

In addition, plane-wave DFT calculations were carried out to find a likely crystal structure of the compound. A unit cell of 6 atoms was optimised from random starting positions. Larger cells, made up of the three most stable units found in this search, were then optimised and the ^{13}C NMR parameters calculated at the minimum energy structure.



All calculations point towards a chain of 1,2,4-dithiazole units linked by nitrogen atoms. This is consistent with recent work involving infrared, Raman and NMR techniques.[4]

[1] S. S. Bathnagar, P. L. Kapur, B. D. Koshla, *J. Indian Chem. Soc.*, **1940**, *17*, 529–535.
[2] F. Feher, D. Hirschfeld, K. H. Linke, *Z. Naturforsch. B*, **1962**, *17*, 624–628.
[3] F. Cataldo, Y. Keheyan, *Polyhedron*, **2002**, *21*, 1825–1835.
[4] W. R. Bowman, C. J. Burchell, P. Kilian, A. M. Z. Slawin, P. Wormald, J. D. Woollins, *Chem. Eur. J.*, **2006**, *12*, 6366–6381.

Poster number 17

Intramolecular BSSE and Dispersion in the Tyr-Gly Dipeptide

Grace M. Fullerton* and Tanja van Mourik

School of Chemistry, University of St Andrews, UK

B3LYP /6-31+G(d) and MP2/6-31+G(d) calculations predict a different order of stability for some of the low-lying conformers of the dipeptide tyrosine-glycine (Toroz D. & van Mourik T., *Mol. Phys.*, **2006**, *104*, 559). Structures with a folded peptide backbone ('book' conformers) are more stable at the MP2 level, while structures without this folded arrangement ('extended' conformers), are more stable according to B3LYP. In addition the two methods predict markedly different structures for the book conformers with the MP2 structures having an increased degree of folding of the peptide backbone. Two possible explanations for the different structures predicted by MP2 and B3LYP are intramolecular dispersion interactions (missing in the B3LYP calculations) and intramolecular BSSE (basis set superposition errors), which tend to be large in MP2 calculations. Recently the accurate geometry of the two book conformers that showed the greatest difference between their MP2 and B3LYP optimised structures was computed with df-LMP2 (density-fitting local MP2) (Holroyd L. F., van Mourik T., *Chem. Phys. Lett.*, **2007**, *442*, 42 & Shields A. E., van Mourik T., *J. Phys. Chem. A*, **2007**, *111*, 13272). df-LMP2 is known to be able to overcome the inadequacies in both the MP2 and B3LYP methods as LMP2 describes dispersion but produces much reduced BSSE values as compared to canonical MP2. df-LMP2/aug-cc-pVDZ geometry optimisation of the B3LYP/6-31+G(d) and MP2/6-31+G(d) structures of the remaining four book conformers shows that for three of these conformers the MP2/6-31+G(d) geometry is essentially correct. The more extended B3LYP structures are therefore likely a result of missing dispersion interactions involving the aromatic ring. For the other conformer the df-LMP2 geometry matches neither the MP2 nor the B3LYP structures. The increased degree of folding seen in the MP2 structure is therefore partially due to intramolecular BSSE. The order of stability of all low-lying conformers (both book and extended) has then been established by df-LMP2/aug-cc-pVnZ (n = D, T, Q) single-point energy calculations using book geometries obtained with df-LMP2/aug-cc-pVDZ and the extended geometries from B3LYP/6-31+G(d) optimisations. The most stable book conformer according to MP2/6-31+G(d) remains the most stable with df-LMP2 though the df-LMP2 relative energies of the other book conformers have changed from those calculated with MP2. For the extended conformers df-LMP2/aug-cc-pVTZ and aug-cc-pVQZ calculations both predict that conformations with a H-bonding interaction between the glycine terminal hydroxyl group and the carbonyl oxygen of tyrosine are more stable. df-LMP2 is thus proposed as a suitable method to predict accurate geometries for small peptides containing an aromatic ring due to its reduced BSSE from MP2. Accurate results can be obtained even when using more limited basis sets (aug-cc-pVDZ). However, to obtain accurate df-LMP2 single-point energies when studying these kinds of molecules, larger basis sets (aug-cc-pVTZ, aug-cc-pVQZ) have to be employed.

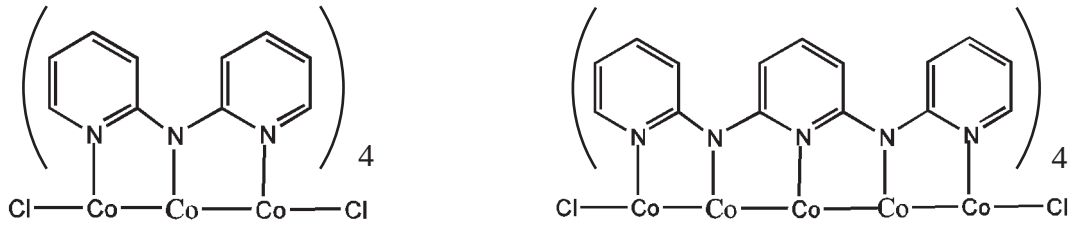
Poster number 18

Electronic Structure/Function Relationship in Metal Nanowires: Components for Molecular Electronics

Vihar Georgiev, John E. McGrady

WestCHEM, Department of Chemistry, University of Glasgow, Glasgow G12 8QQ, Scotland, UK

In the past decade, increasing attention has been given to new class materials-molecular wires and switches. The reason is that these systems are elemental building blocks for future electronic applications. Very promising structures are semiconducting polymers, 1D sandwich molecular wires and extended metal atom chain (EMAC). We concentrate our attention and efforts to EMAC where a helical array of oligo-α-pyridyl ligands (tpda) is used to support a chain of metal centres. These systems, most notably the cobalt chains, exist is symmetric and unsymmetric form, as well as range of intermediate structure. In 2006 Pantazis and McGrady established that of $Co_3(tpda)_4Cl_2$ seems a tristable with three quite distinct low-lying electronic states each which can be populated under particular condition.[1]



(a) $Co_3(tpda)_4Cl_2$ (b) $Co_5(tpda)_4Cl_2$

Figure 1: Structures of Co_3 and Co_5 EMAC.

In order to explore the full potential of these systems as electric wires, we need to understand new this complex behavior evolves as the chain length increases. Herein we repeat the electronic structure of the Co_5 chains and their cation derivates.[2] We also describe preliminary result arranging the behaviour of these systems under the applied voltages typical of electronic devices.

[1] Pantazis,D. A., McGrady, J. E., *J. Am. Chem. Soc.*, **2006**, *128*, 4128.
[2] Pantazis,D. A., Murillo A. C., McGrady, J. E., *Dalton Trans.*, **2008**, *5*, 608–614.

Poster number 19

An Investigation of Structurally-Bound Water Dynamics in High-Pressure Hydrous Magnesium Silicates combining First-Principles DFT Calculations and ^{17}O Solid-State NMR Experimental Data

John Griffin,[1] Caroline E. Pringle,[1] Andrew J. Berry,[2] Stephen Wimperis,[3] Chris J. Pickard,[4] Sharon E. Ashbrook[1]

[1]*School of Chemistry and EaStCHEM, University of St Andrews, St Andrews, Fife KY16 9ST, UK* [2]*Department of Earth Sciences and Engineering, Imperial College, London, SW7 2AZ UK* [3]*Department of Chemistry and WestCHEM, University of Glasgow, Glasgow G12 8QQ, UK* [4]*School of Physics and Astronomy, University of St Andrews, St Andrews, Fife KY16 9SS, UK*

It is estimated that the upper region of the Earth's mantle contains 200–600 ppm of water.[1,2] Indeed, the total water content of the mantle may be many times that of the oceans. However, the exact mechanism of this water storage is not understood. It is thought that nominally anhydrous silicates, such as olivine ($Mg_{2-x}Fe_xSiO_4$), may contain sufficient structurally-bound water at defect sites to account for this amount. Structural studies of inner-Earth silicates are therefore vital for a deeper understanding of how this water incorporation takes place. This work considers members of the humite group, $nMg_2SiO_{48} \cdot Mg(OH)_2$, as possible models of the defect sites accommodating water (or more precisely hydrogen) in olivine. The structures of these minerals, which occur naturally in the Earth's crust, may be described simplistically as n layers of forsterite ($\alpha-Mg_2SiO_4$), separated by a layer of brucite ($Mg(OH)_2$). A previous ^{17}O MAS NMR study[3] of hydroxyl-chondrodite ($n = 2$), hydroxyl-clinohumite ($n = 4$), and forsterite, using two-dimensional MQ-MAS NMR to obtain high-resolution spectra, has allowed determination of isotropic chemical shifts, δ_{iso}, and quadrupolar coupling constants, C_Q, and asymmetry, η_Q. Additionally, high-resolution ST-MAS NMR spectra recorded on the same samples show considerable broadening of resonances corresponding to oxygen sites close to hydrogen atoms in the brucite layers, thus indicating ^{1}H motion with exchange between the two ^{1}H sites H1 and H2 being a possible explanation. This work compares experimental ^{17}O MAS NMR data for hydroxyl-clinohumite and hydroxyl-chondrodite with NMR parameters obtained from calculations performed on geometry-optimised crystal structures using the NMR-CASTEP code. Specifically, results are presented which compare isotropic projections of experimental MQ-MAS NMR data with simulated data based on calculated NMR parameters. For the simulated data, two cases are considered, whereby both static and dynamic disorder of hydrogen atoms in the crystal structure is assumed. NMR-CASTEP calculations also yield ^{2}H NMR parameters, which may compared with potential future experimental ^{2}H NMR studies to probe motion in deuterated samples. However, little work has been done to quantify the accuracy of NMR-CASTEP calculations for this nucleus. Here we present a comparison of experimentally obtained and calculated NMR parameters for some simple model compounds in order to gain an understanding of the accuracy and limitations of NMR-CASTEP for studying ^{2}H.

[1] Bell, D. R., Rossman, G. R., *Science*, **1992**, *255*, 1391.
[2] Wood, B. J., Pawley, A.; Frost, D. R., *Philos. Trans. R. Soc. London A*, **1996**, *354*, 1495.
[3] Ashbrook, S. E., Berry, A. J., Wimperis, S., *J. Am. Chem. Soc.*, **2001**, *123*, 6360.

Poster number 20

Targeted Crystallisation of Novel CBZ Solvates Based on a Retrospective RandomForest Classification

Andrea Johnston,[a] Blair F. Johnston,[a] Alan R. Kennedy[b] and Alastair J. Florence.[a]

[a] *Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, 27 Taylor Street, Glasgow, Scotland G4 0NR* [b] *WestCHEM, Department of Pure and Applied Chemistry, University of Strathclyde, 295 Cathedral Street, Glasgow G1 1XL*

RandomForest[1] (RF) classification has been applied to the results of an automated parallel crystallisation[2] study on the antiepileptic compound carbamazepine (CBZ).[3,4] This work forms part of a of a wider RCUK Basic Technology funded study[5] into crystal structure prediction and the basic science underpinning organic solid-state diversity. The RF analysis utilised 15 physicochemical solvent descriptors, comprising a range of experimental and calculated values; 3 categorical variables describing the experimental conditions from the crystallisation search plus the observed experimental outcome for each crystallisation. 98% of crystallisations that yielded a CBZ solvate were correctly classified by the analysis. A 2-D MDS plot derived from the RF classification proximity matrix identified two clusters, with one of them dominated by those crystallisations that yielded CBZ solvates. However, three solvents that did not yield solvates in the study were also classified within this group and subsequent RF prediction classified these as being more likely to form a solvate than any other outcome. These results provided a rational basis for subsequent targeted crystallisations of CBZ from each solvent that successfully yielded 3 novel crystalline solvates of CBZ (nitromethane, *N*-methylpyrrolidone and *N*, *N*-dimethylacetamide). Analysis of the RF model also provided a rank dependence of the physical form outcome on the solvent descriptors, providing a basis for further investigation of the key factors underlying solvate formation of CBZ and other organic molecular solids. This approach is of particular value to crystallisation studies where the emphasis is on maximising the number of physical forms discovered. A detailed description of the application of RF to crystalline solvate formation, along with crystal structures of the novel forms and full results from the statistical modelling approach are presented.

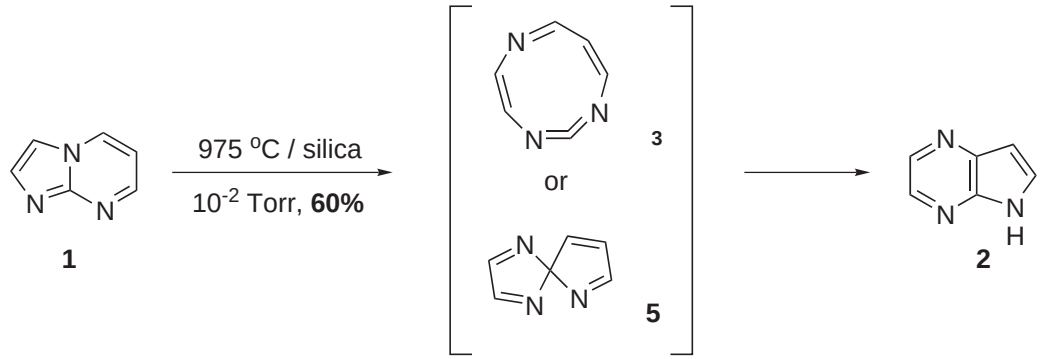
[1] Liaw and Wiener, *R news*, **2002**, *2*, 18–22.
[2] Florence, *et al.*, *J. Appl. Crystallogr.*, **2006**, *39*, 922–924.
[3] Johnston, *et al.*, *CrystEngComm.*, **2007**, *10*, 23–25.
[4] Florence, *et al.*, *J. Pharm. Sci.*, **2006**, *95*, 1918–1930.
[5] Control and Prediction of the Organic Solid-State project (CPOSS) www.cposs.org.uk

Exploring Pyrolysis Mechanisms using *Ab Initio* Calculations

Karen A. Johnston, Hamish McNab,* James Montgomery, William J. O'Neill and Stuart I. Wharton

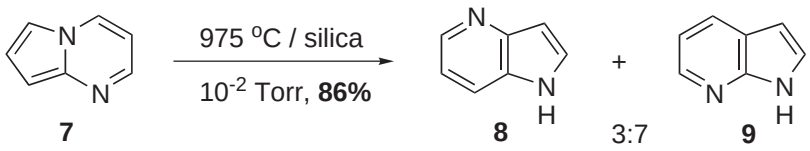
School of Chemistry, The University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ; e-mail: kjohnst2@staffmail.ed.ac.uk

Previous research in our group found that under high temperature flash vacuum pyrolysis (FVP) conditions, imidazo[1,2-*a*]pyrimidine (**1**) rearranges to pyrrolo[2,3-*b*]pyrazine (**2**), Scheme 1.[1] Two mechanisms were postulated for this rearrangement; the first *via* carbodiimide **3**, the other *via* the bicyclic spiro-intermediate **5**. *Ab initio* calculations[2] successfully described the potential energy profiles for both mechanisms although failed to identify the correct mode of rearrangement in this case.



Scheme 1

Pyrolysis of the simpler pyrrolo[1,2-*a*]pyrimidine (**7**) yielded azaindoles **8** and **9** in a 3:7 ratio, Scheme 2. Both of the above suggested mechanisms can yield 4-azaindole (**8**), although only one can successfully access both products.



Scheme 2

[1] Stuart Wharton, Ph.D. Thesis, University of Edinburgh, **2005**.
[2] MP2/6-31G(d,p)

Poster number 22

Structural Characterisation of Perovskites - Combining Diffraction, NMR and First-Principles Calculations

K. E. Johnston, I. S. Kendrick, P. Lightfoot, C. J. Pickard and S. E. Ashbrook

School of Chemistry and EaStCHEM, University of St Andrews, St Andrews, Fife, KY16 9ST, UK; e-mail: kej2@st-andrews.ac.uk

Our current area of research aims to combine experimental solid-state techniques, such as X-ray powder diffraction and solid-state Nuclear Magnetic Resonance (NMR), with Density Functional Theory (DFT) calculations. It is hoped that combining and comparing experimental data with theoretical calculations will aid in the characterisation, and hence structural understanding, of materials.

Our initial work has focussed heavily upon several scandium-based perovskite structures. The relative ease with which the well known perovskite structure can be distorted indicates the importance of such compounds in various areas of materials chemistry. Detailed structural characterisation is therefore essential in identifying any structurally related physical properties. Several scandium-based materials have been synthesised and are currently undergoing X-ray diffraction and ^{45}Sc (I = 7/2) solid-state NMR analysis.

Our computational work uses the NMR-CASTEP[1] code, a planewave pseudopotential method that utilises the gauge-including projector-augmented-wave (GIPAW) formalism and hence enables NMR parameters such as δ_{iso}, C_Q and η_Q to be calculated with relative ease. This, in turn, allows accurate comparisons to be made with the experimental results. Preliminary DFT calculations[2] have been completed for various scandium compounds including Sc_2O_3[3], $LiScO_2$[3], $NaScO_2$[3], $ScVO_4$[3], $ScPO_4$[3], $LaScO_3$[4] and $YScO_3$[5].

All calculations indicate excellent agreement with experimental results. Similar calculations have been extended to one particular solid-solution, $La_{1-x}Y_xScO_3$, in an attempt to model disorder and interpret the NMR spectrum. Different mechanisms for cation substitution on the A-site have been attempted in the structure with relative success.

[1] S. J. Clark, M. D. Segall, C. J. Pickard, P. J. Hasnip, M. J. Probert, K. Refson and M. C. Payne, *Zeitschrift fuer Krystallographie*, **2005**, *220*, 567.
[2] EaStCHEM Research Computing Facility, University of St Andrews.
[3] N. Kim, C. Hsieh and J. F. Stebbins, *Chem. Mater.*, **2006**, *18*, 3855.
[4] R. P. Liferovich and R. H. Mitchell, *J. Solid State Chem.*, **2004**, *177*, 2188.
[5] N. V. Porotnikov, K. I. Petrov, V. N. Tsygankov and M. E. Bogdanova, *Inorg. Mater. (Transl. of Neorg. Mater.)*, **1980**, *16*, 62.

Poster number 23

Antioxidant Activity of Green Tea Polyphenolics

John D. P. Jones

School of Chemistry, Main Building, Park Place, Cardiff University, Wales, UK

The antioxidant activity of green tea is attributed to the flavan-3-ols contained therein with the four phenolic structures found in flavan-3-ols identified as resorcinol, catechol, pyrogallol, and methyl gallate. These compounds and their radicals were investigated computationally using density functional theory and subjected to conformational analysis. The most stable conformers were analysed with isodesmic schemes to obtain relative stabilisation energies for their reaction with phenoxyl radical. Based on the results of this study, the relative free radical scavenging abilities of these compounds may be ranked: resorcinol < catechin < gallate < pyrogallol. Hydrogen bonding interactions, electron donating substituents, and the formation of quinones were found to have a positive effect on radical stabilisation, thus two hypothetical compounds (1,2,3-trihydroxy-4,5,6-trimethyl benzene and 1,2,3,4-tetrahydroxy-5,6-dimethyl benzene) were subjected to the same procedure and compared with the naturally occurring structures. Both hypothetical antioxidants show significantly greater stabilisation than the model compounds.

Poster number 24

A Core Fragment Based Look at HTS Centres around the World

Agata Krasowski, Paul Wyatt, *Ruth Brenk*

University of Dundee, Biological Chemistry and Drug Discovery, Dow Street, Dundee DD1 5EH

High Throughput Screening (HTS) and Virtual Screening (VS) play important roles in modern drug discovery. These methods are used to screen extremely large numbers of compounds against biological targets. New hits selected from HTS and VS can be used as leads for further optimisation and drug development. Recently, several academic groups around the world are setting up screening centres with proprietary compound libraries. Therefore, the question emerges how different the libraries are and if a target should be screened at several centres. To explore the diversity of compounds within the different collections, a core-fragment based approach was developed. Subsequently, the new approach was applied to analyse the similarity between compound libraries of four different screening centres: DDU Dundee, WEHI, NCGC and SJCRH. On a compound level only a small overlap between the different screening sets was observed. However, when the sets were compared on a fragment level the overlap increased but still, there were sufficient differences between the sets to justify screening a target in more than one centre.

Magnetic Coupling in model cubic V, Ni and Cu structures comprised of interlinking HF_2^-, HCl_2^- and $HFCl^-$ ligands

L. M. Lawton, D. S. Middlemiss and C. C. Wilson

Department of Chemistry and WestCHEM Research School, University of Glasgow, Glasgow G12 8QQ, UK

A series of model cubic structures were studied in order to obtain magnetic coupling constants for hydrogen bonds of varying length. Hybrid functional calculations were performed on structures containing V, Ni or Cu transition metals linked by $[FHF]^-$, $[ClHCl]^-$ or $[FHCl]^-$ ligands, in order to ascertain the dependence of coupling strength on exact exchange content, hydrogen bond length and proton position.

The computational code *CRYSTAL06*[1] was used to model these theoretical structures. This code allows for the use of both the Hartree Fock and density functional theory approximations under periodic boundary conditions, and also for the mixed hybrid-exchange calculations that have been shown to yield accurate coupling constants in similar cubic structures.[2] The geometrical options available in *CRYSTAL06* also allowed easy manipulation of the structures, required to extract magnetic coupling constants.

The following basis sets were obtained from the *CRYSTAL* web page and optimised using the *CRYSTAL06* code: the K 86-511G without the d-functions, the transition metal V and Ni 86-411G and Cu 86-4111G, the halogen F 7-311G and Cl 86-311G, and the H 6-311G**. In order to produce an adequate convergence of the total energy, Monkhorst-Pack reciprocal space sampling with a shrinking factor of 8 was implemented and the truncation thresholds for bioelectronic integrals were set at 7,7,7,7.

The dependence of magnetic exchange coupling on proton position and hydrogen bond length was investigated in the Ni systems due to the large coupling values obtained from calculations in which the percentage of HF and DFT exchange were varied. A simple program has also been written in which the numerov method[3] was used to solve the 1D Schrödinger Equation for these systems using the acquired potential energy profiles.

The J_{FHF} of 0.033 K obtained in our Cu system with 35% HF exchange has also been successfully compared to the experimental $[Cu(HF_2)(pyz)_2]BF_4$[4] complex which was shown to possess an antiferromagnetic $J_{Pyrazine}$ coupling of 2.85 K, and a limiting J_{FHF} of 0.03 K. This is encouraging, for the 35%-hybrid functional has been previously shown to yield coupling constants in agreement with experimental values in a wide range of transition metal compounds. Our previous work[2] has also borne the utility of this functional out in studies of a variety of Prussian Blue analogues. It should be noted that our Cu [FHF] compound is Jahn-Teller active, and so a tetragonal distortion of the cubic symmetry manifests in our geometry optimisations, but this does represent the fact that such distortions are to be expected in real materials. Calculations on the experimental $[Cu(HF_2)(pyz)_2]BF_4$ compound have also begun to successfully converge and may also be presented.

[1] V. R. Saunders, R. Dovesi, C. Roetti, R. Orlando, C. M. Zicovich-Wilson, N. M. Harrison, K. Doll, B. Civalleri, I. J. Bush, Ph. D'Arco, M. Llunell, CRYSTAL 2006 User's Manual.

[2] D. S. Middlemiss, C. C. Wilson, A. Harrison and L. M. Lawton, Work in Preparation.

[3] J. L. M. Quiroz Gonzalez and D. Thompson, *Computers in Physics*, **1997**, *11*, 541.

[4] U. Bentrup, K. Harms, W. Massa and J. Pebler, *Solid State Sciences*, **2000**, *2*, 373–376.

Neutral and Ionic Deoxycytidine: New Insights from Theory

Sanliang Ling and Maciej Gutowski

Chemistry-School of Engineering and Physical Sciences, Heriot-Watt University, Edinburgh EH14 4AS, United Kingdom;
e-mail: SL160@hw.ac.uk, M.Gutowski@hw.ac.uk

Nucleosides are basic components of nucleotides, which in turn are building blocks of DNA and RNA. Deoxycytidine (dC) is a nucleoside consisting of cytosine and deoxyribose. Here we present a systematic search across the conformational space of dC at high levels of theory. Numerous local minima are identified at the B3LYP/6-31++G** level, from which the most stable conformers are further reoptimized at the MP2/aug-cc-pvdz level. Our global minimum structure is more stable by 4.8 kcal/mol than the previous structure[1] which was extracted from crystalline X-ray data. Moreover, we found that a hydrogen bond is formed between C2=O2 and O5'-H13' (Figure 1) for all the 8 most stable conformers, and the C2'-*endo*/*anti* conformation turns out to be more stable than the C3'-*endo*/*anti* conformation, in contradiction to previous findings.[1] The IR and Raman spectra are calculated and the results are in reasonable agreements with experiments based on crystalline structures. The vertical ionization potentials (VIP) of the most stable conformers unravel that the lowest energy electron detachment will take place from the sugar site and the calculated value of VIP determined using the electron propagator approach[2] is 8.59 eV. We also analyzed valence- and dipole-bound anionic states that might develop in the course of interaction of dC with low-energy electrons. The calculated electron vertical detachment energy (VDE) for the valence anion of 0.86 eV matches very well the experimental result of 0.87 eV.[3] The calculated value of adiabatic electron affinity (AEA) is 0.42 eV and this property has not been experimentally measured. The VDE values for the several low-lying conformers span a relatively narrow range of 0.68–0.86 eV and overlap with the previous result.[1] We have also identified dipole-bound anionic states of dC (Figure 2). The VDE and AEA values for the anion based on the most stable neutral conformer are 0.074 eV and 0.065 eV, respectively. We conclude that the valence- and dipole-bound anions might coexist in the gas phase.

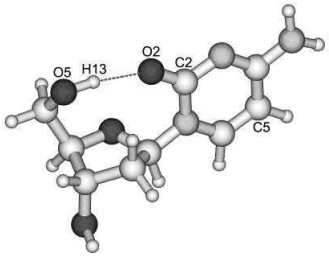


Figure 1: Global minimum of neutral.

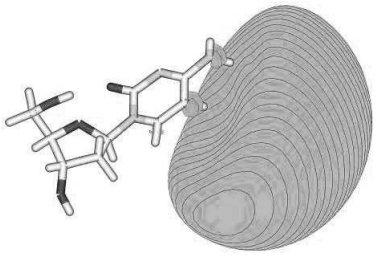


Figure 2: SOMO of the dipole bound anion.

[1] N. A. Richardson, J. Gu, S. Wang, Y. Xie and H. F. Schaefer III., *J. Am. Chem. Soc.*, **2004**, *126*, 4404.
[2] O. Dolgounitcheva, V. G. Zakrzewski and J. V. Ortiz, *Int. J. Quan. Chem.*, **2002**, *90*, 1547.
[3] S. T. Stokes, X. Li, A. Grubisic, Y. J. Ko and K. H. Bowen, *J. Chem. Phys.*, **2007**, *127*, 084321.

Poster number 27

ZrO_2-doped Y_3NbO_7: a combined experimental and theoretical study of the conduction mechanism

Dario Marrocchelli, Stefan Norberg, Paul Madden and Steve Hull

School of Chemistry, University of Edinburgh, Edinburgh EH9 3JJ, UK

My poster will describe the work I have been doing on ZrO_2-doped Y_3NbO_7. Pure Y_3NbO_7 is a good (but not excellent) ionic conductor ($\sigma = 3.1610^{-5}\,\Omega^{-1}\,cm^{-1}$ at 1000 K) and has a cubic fluorite structure with 1/8 of the ideal fluorite structure anion sites empty[1]; it is generally believed that it is these empty sites which are responsible for the ionic conductivity observed in this compound; however, doping this compound with ZrO_2 enhances the ionic conductivity even if we keep this number of vacant sites fixed. There is therefore a different (unknown) mechanism which lowers the conductivity in pure Y_3NbO_7. In order to study this phenomenon and to elucidate the different mechanisms which enhance or lower the conductivity, we carried out Molecular Dynamics simulations and, at the same time, a neutron powder diffraction experiment on $Y_{3-x}Nb_{1-x}Zr_{2x}O_7$ (where x = 0.2, 0.4, 0.6, 0.8, 1). Neutron diffraction experiments can give information on both the crystal structure of the system (Bragg scattering) and on the disorder (diffuse scattering). MD simulations can be incredibly helpful since they can provide information which is not easily accessible experimentally, such the single particle dynamics (experiments almost always provide an averaged picture), high T&P behaviours and more. The first step taken was to develop realistic (DIPPIM) MD potentials for these systems in the way described in ref 2; the reliability of these potentials was tested by comparing the results obtained with a wealth of experimental data: radial distribution functions (obtained by Fourier transform of the neutron data), electrical conductivities and densities were correctly reproduces for many $ZrO_2{-}Y_2O_3{-}Nb_2O_5$ systems. One result worth mentioning is the perfect reproduction of the conductivity vs x curve in $(ZrO_2)_{1-x}{-}(Y_2O_3)_x$; previous studies[3] managed to reproduce the same trend but conductivities were always overestimated. After the reliability of these potentials was proved, we started using the simulations to try to understand what lowers the conductivity in pure Y_3NbO_7; a reasonable guess is that Nb^{5+} traps the oxygen ions with its very high positive charge. To study this, we equalized the anion charges in Y_3NbO_7 to an average value of (3.5+) and then adjusted the short-range potentials so that the radial distribution functions of this system are unchanged; interestingly, such a system shows a much higher conductivity (one order of magnitude higher). This proves that the Nb high ionic charge is detrimental for the conduction process.
I am currently running some simulations on $Y_{3-x}Nb_{1-x}Zr_{2x}O_7$ (with Y, Nb, Zr having all the same charge), and these seems to show a very high, doping-independent conductivity. Again, this is consistent with our picture, because, once charges are equalized, we expect a generally higher conductivity (less anion clustering around Nb) and we do not expect any variation with doping (charges are all the same). In conclusion, we obtained realistic DIPPIM potentials for the $ZrO_2{-}Y_2O_3{-}Nb_2O_5$ systems, checked their reliability by reproducing many experimental data (included our own) and used them to study the conduction mechanism in pure and doped Y_3NbO_7. The results, so far, seems to show that the high charge on Nb is responsible for the lower conductivity in pure Y_3NbO_7 compared with the ZrO_2-doped systems. We plan to do more work on these systems in the future: we are currently analyzing the neutron data *via* a RMC technique and hope to get some information on the oxygen clustering; we will then also calculate the diffuse scattering for a single crystal and the intermediate scattering functions, to see if we can tie up with the neutron data.

I finally want to point out that our work is an example of how theory and experiments can be used together to study certain systems and how these two approaches are complementary; from our work it is evident that, to obtain a complete understanding of a problem, you need information from both experiments and computational chemistry.

[1] Lee J. H. and Yoshimura M., *Solid State Ionics*, **2001**, *139*, 197–203.
[2] Madden P. A., Heaton R. J. *et al.*, *J. Mol. Struct.: THEOCHEM*, **2006**, *771*, 9–18.
[3] Kilo M., Argirusis C. *et al.*, *Phys. Chem. Chem. Phys.*, **2005**, *5*, 2219.

Poster number 28

High-Temperature Gas-Phase Studies of Antimony Oxide - how do Theory and Experiment measure up?

Sarah L. Masters

School of Chemistry, University of Edinburgh, West Mains Road, Edinburgh, EH9 3JJ, UK; e-mail: s.masters@ed.ac.uk

The gaseous molecular structure of antimony oxide (Sb_2O_3) was first investigated by gas electron diffraction (GED) in 1961.[1] At this time, analysis of the scattering patterns obtained from the experiments was performed by eye, and none of the present-day sophisticated methods of data extraction and analysis was available. However, the structure was reported as being a dimer at the experimental temperature (see below), and rSb−O and ∠Sb−O−Sb were recorded, albeit with large errors associated with the parameters.

With the introduction of a new very-high-temperature nozzle to the Edinburgh GED apparatus, the gaseous molecular structure of antimony oxide has been re-investigated at 750 K. As well as using computed force-fields to aid the analysis, the performance of a range of theoretical methods has been assessed, with results reported here. A comparison with the (relatively) more recent solid-state crystal structure[2] is also made.

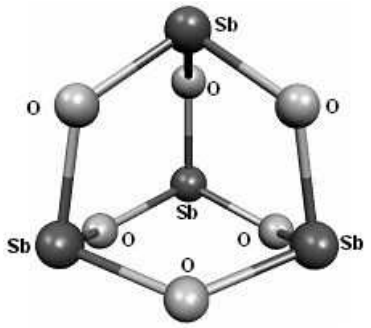


Figure 1: Molecular structure of Antimony Oxide in the gas phase showing the dimeric, tetrahedral, arrangement of the Sb_2O_3 units.

[1] P.A. Akishin, V. P. Spiridonov, *Zh. Strukt. Khimii*, **1961**, *2*, 542.
[2] C. Svensson, *Acta Crystographica*, **1975**, *B31*, 2016.

Poster number 29

Hybrid Functionals for Weak Interactions in Solids

B. Civalleri,[a] D. S. Middlemiss,[b] R. Orlando,[c] C. C. Wilson[b] and P. Ugliengo[a]

[a] *Dipartimento di Chimica IFM e NIS Centre of Excellence, Universitá di Torino, Italy*
[b] *Department of Chemistry and WestCHEM Research School, University of Glasgow, UK*
[c] *Dipartimento di Scienze e Tecnologie Avanzate, Universitá del Piemonte Orientale, Italy*

The Wilson-Levy (WL) correlation functional is combined with the exact Hartree-Fock (HF) exchange in both *a posteriori* (HF+WL) and self-consistent (HFWL) schemes, and applied to a set of weakly bonded extended systems. The solid phases of Ne, Ar, benzene and graphite, and infinite chains of HF and HCl were selected as a set of representative test cases spanning a range of interaction strengths and types. The intermolecular interactions in the benzene crystal were also examined in the light of the suggestion of pairwise additivity made within a previous study. The results obtained from the HF+WL and HFWL approaches are compared with those produced by the pure PBE and hybrid PBE0 functionals. The study confirms the good performance of the WL functional, although we conclude that the weak and long-range components of the interactions are not properly described in some cases.

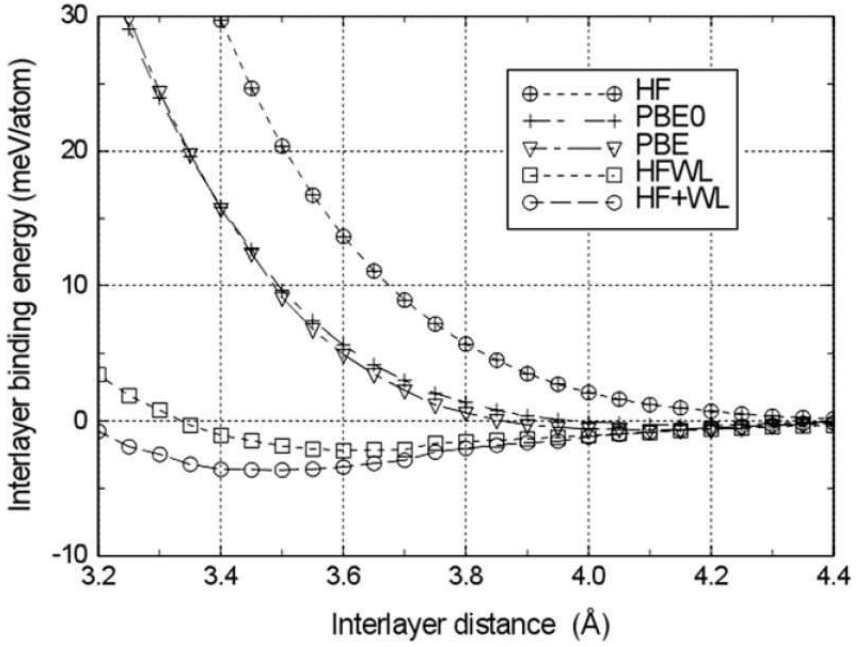


Figure 1: The variation in the interlayer binding energy in graphite with interlayer distance within the various functionals, corrected for basis set superposition.

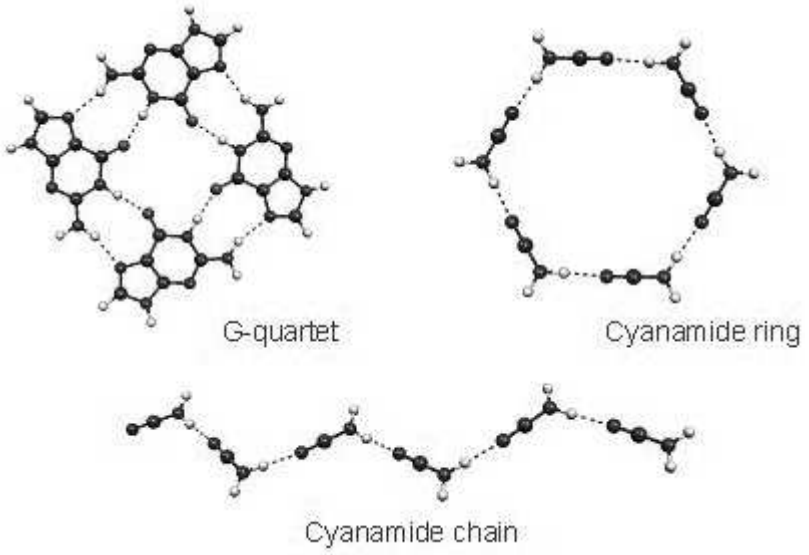
Poster number 30

Characterising the Cooperativity in H-bonded Amino Structures by NMR Calculations

Tanja van Mourik

School of Chemistry, University of St Andrews, UK

Density functional theory was used to examine the effect of hydrogen-bond (H-bond) cooperativity on the NMR parameters in structures containing hydrogen bonds involving amino groups.[1] These included a guanine quartet (G-quartet) and ring and chain structures built from cyanamide monomers.



It is shown that, even in the absence of geometric variations, the magnitude of the NMR parameters changes when H-bonding monomers are progressively added to extending ring or chain structures. In general, the magnitude of the NMR parameters along the H-bond network increases ("positive cooperativity"), whereas the size of the $^{1}J_{NH}$ coupling of the non-H-bonded amino N−H bonds, which are roughly perpendicular to the H-bonding network, decreases in magnitude ("negative cooperativity") when adding more monomers to the rings or chains. These effects are attributed to electron redistribution induced by the presence of nearby H-bonding guanine or cyanamide molecules.

[1] T. van Mourik, A. J. Dingley, *J. Phys. Chem. A*, **2007**, *111*, 11350.

Collisional Removal of OH($X^2\Pi$, $\nu = 0$, J, e) Rotational Angular Momentum Polarization in Collisions with He and Ar

Grant Paterson, Sarantos Marinakis, Robert Tobola, Jacek Kłos, Matthew L. Costen, and Kenneth G. McKendrick

[1]*School of Engineering and Physical Sciences, William H. Perkin Building, Heriot-Watt University, Edinburgh EH14 4AS, UK* [2]*Department of Chemistry and Biochemistry, University of Maryland, College Park, MD 20742, USA*

Polarisation spectroscopy (PS), a third-order non-linear spectroscopic technique, has been developed to study the collisional removal of a prepared rotational angular momentum polarisation (orientation or alignment) in simple systems, namely OH(X) + Ar/He. Experiments which are sensitive to such *vector* properties serve as rigorous tests for *ab initio* potential energy surfaces (PESs). The measured PS signal decay, as a function of pump-probe delay time, is a result of collisions which remove population from an initially prepared quantum state, *i.e.* energy transfer; in this case rotational energy transfer and Λ-doublet changing, and also those hydroxyl radicals which suffer a change in the *plane of rotation* (loss of alignment) or *sense of rotation* (loss of orientation) and remain in the same quantum state. The later is the new information but is not measured directly.
To gain an understanding of these elastic depolarisation events we require prior knowledge of the inelastic contribution to the PS signal loss. As a result, we have performed exact, fully quantum mechanical calculations for the inelastic contributions on a new PES for OH(X)-Ar (presented here for the first time) and on a recent *ab initio* PES for OH(X)-He [*J. Chem. Phys.*, **2002**, *113*, 5736]. We also present m_J-resolved elastic cross-sections which are rarely extracted from the scattering matrix. Current work is focusing on converting these to elastic depolarisation rate constants, which, when summed together with the calculated inelastic contribution will provide a rate constant directly comparable to that experimentally measured. A comparison of the experimental and theoretical results presented here demonstrates the power of this technique to test the interaction potential.

Computational Studies of the Dihydro-Imidazo-Phenanthridinium (DIP) Synthesis Reaction Path

Damiano Portinari, Alexis D. C. Parenty, Chick C. Wilson and Leroy Cronin

Department of Chemistry and WestCHEM Research School, University of Glasgow, Glasgow G12 8QQ, UK

The main area of this research focuses on the theoretical study of a new flexible methodology that allows the production of an unprecedented class of dihydro-imidazo-phenantridinium (DIP) compounds *via* a one-pot three-step reaction that could proceed *via* two theoretical pathways. One pathway (A) is where a primary amine carries out a nucleophilic attack on a phenantridinium moiety, in contrast to pathway (B) where the amine undergoes an S_N2 reaction with a phenantridinium molecule. Density Functional Theory studies have been conducted, with the introduction of one molecule of solvent to the reactant system, with the aim of:

- explaining which is the preferred pathway;
- clarifying the role of the cyclizations involved in determining that preference;
- understanding the substituent effect in the last reaction step, a hydride transfer between a stable intermediate resulting from the cyclization and another reactant molecule.

The calculations clearly show that the rate-determining step is the S_N2 reaction also after inclusion at the stationary points of a continuum solvent model (DMF).
Baldwin (1976) formulated empirical rules to take into account stereoelectronic requirements in cyclization reactions, in which the main parameters considered are the size of the ring that is forming, the ring cyclization mode (exocyclic or endocyclic) and the hybridization of the centre that undergoes a nucleophilic attack. Considering the Baldwin rules, the cyclizations that constitute the second step of the two pathways considered in the reaction studied has been compared. The results show that the 5-*exo*-tet cyclization of pathway A is more favourable than the 5-*endo*-trig of pathway B. Thus, there is agreement with the empirical rules described by Baldwin. However, the reasons that underlie the preference for pathway A should be found in studying the relative energy barriers. The calculations bear this out, clearly indicating the higher activation energy of the first step of path B, a result also found when utilising in those calculations a different primary amine rather than ammonia.

The effect of substituents on the hydride transfer reaction has been carried out utilising electron-donor and electron-attractor groups on the stable intermediate resulting from the cyclization. The utilisation of electron-donor groups renders the hydride transfer quite exothermic with transition states that are reactant-like, in contrast to the situation with more electron-attractor groups, where the reaction became almost thermoneutral and the transition states more product-like. Therefore, it is possible to conclude, on consideration of the Hammond postulate, that the system increases its reactivity by increasing the electron-donating ability of the framework, resulting in a faster reaction under normal reaction conditions.

Poster number 33

A Molecular Dynamics Approach to Equilibrium Structures in Crystals: Nitromethane

Anthony M. Reilly, Derek A. Wann, Carole A. Morrison and David W. H. Rankin

School of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ, UK; e-mail: d.w.h.rankin@ed.ac.uk

The equilibrium structure of a crystal represents the system in a theoretical vibrationless state at the absolute minimum of its potential-energy surface. Such structures can be compared directly between different phases and polymorphs and with theoretical calculations. Structures determined using X-ray and neutron-diffraction experiments are time-averaged over all of the molecular vibrations occurring in the crystal. If these motions are anharmonic or curvilinear then the time-averaged and equilibrium structures will differ.[1] There remains no general and simple method for removing the structural inconsistencies that result.

We have recently developed a new method using molecular dynamics (MD) simulations that allows experimental positions to be corrected to equilibrium positions.[2] The corrections are determined by taking the differences between theoretical equilibrium structures and time-averaged structures obtained from MD trajectories. The application of the method to the crystal structure of nitromethane using an empirical force field will be detailed. Comparisons will be made with experimental data sets.

[1] D. W. J. Cruickshank, *Acta. Crystallogr.*, **1956**, *9*, 757.
[2] A. M. Reilly, D. A. Wann, C. A. Morrison and D. W. H. Rankin, *Chem. Phys. Lett.*, **2007**, *448*, 61.

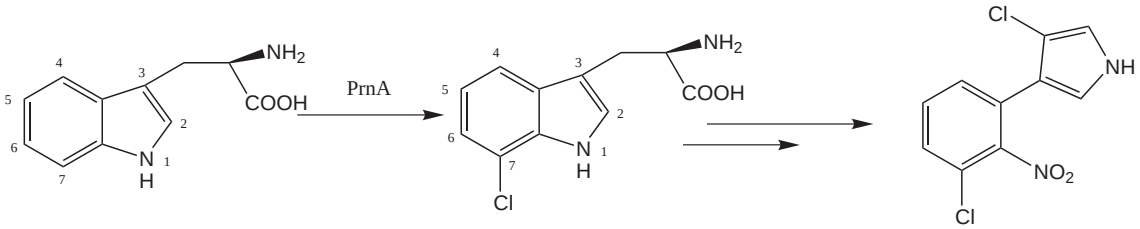
Poster number 34

Flavin-dependent Halogenation

Evdokiya Salamanova, Dr Hans Martin Senn

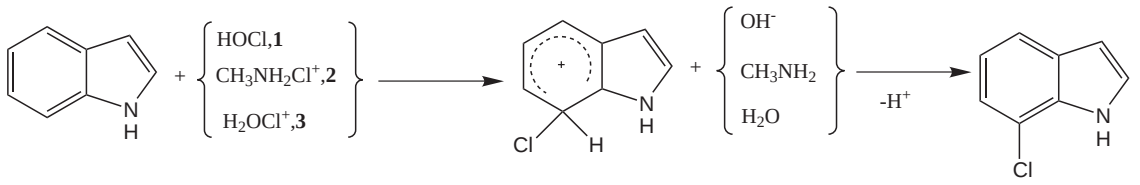
Department of Chemistry, University of Glasgow, Glasgow G12 8QQ, Scotland, UK

PrnA (FAD-dependent tryptophan halogenase) is an enzyme that takes part in the synthesis of the antibiotic pyrrolnitrin. This enzyme is produced by the bacterium *Pseudomonas fluorescens*. It catalyzes the chlorination of tryptophan, the formation of 7-chlorotryptophan.[1] This is the initial step of the synthesis of pyrrolnitrin.



Tryptophan 7-Chlorotryptophan Pyrrolnitrin

We are searching for the exact chlorinating agent, using indole as a model substrate. The chlorinating agent could be hypochlorous acid (HOCl, **1**), (chloroammonio)methane ($CH_3NH_2Cl^+$, **2**) or the chlorooxonium cation (H_2OCl^+, **3**).



Indole σ-complex 7-Chloroindole

1 is formed from in the enzyme hydroperoxyflavin (FADHOOH) and chloride. **2** and **3** could be formed during the reaction because the substrates pass through a tunnel in the enzyme. This tunnel contains a lysine residue, which could donate H^+ to **1** to form **3** or react with **3** to generate **2**. We did geometry optimizations of reactants, intermediates, transition states and products, using Turbomole[2] at TPSS[3]/TZVP level, applying the COSMO solvent model. We made transition state searches with ChemShell[4] to find the energy barrier for the three possible pathways. Our future work will be related to the preparation of the enzyme for MM simulations, MD simulations and QM/MM simulations of the reactions.

[1] Dong, C., Flecks, S., Unversucht, S., Haupt, C., van Pée, K. H., Naismith, J. H., *Science*, **2005**, *309*, 2216–2219.

[2] Treutler, O., Ahlrichs, R., *J. Chem. Phys.*, **1995**, *102*, 346.

[3] Tao, J., Perdew, J. P., Staroverov, V. N., Scuseria, G. E., *Phys. Rev. Lett.*, **2003**, *91*, 146401.

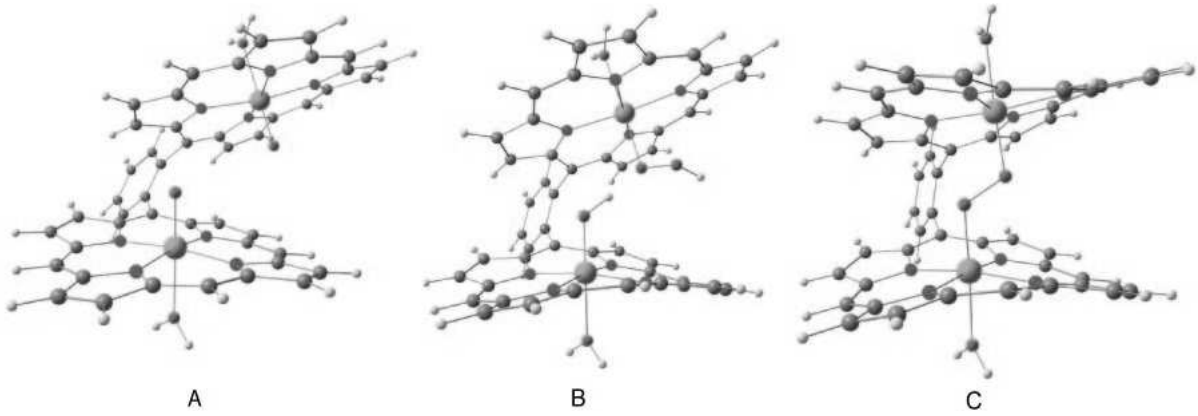
[4] ChemShell, a Computational Chemistry Shell, see www.chemshell.org

A Computational Study of the Oxygen Evolving Mn_2-dimeric Porphyrin Complex: Implications for the Catalytic Oxidation of Water

W. M. C. Sameera, John E. McGrady

WestCHEM, Department of Chemistry, University of Glasgow, G12 8QQ, UK

In photosynthesis, green plants, algae and cyanobacteria produce dioxygen through oxidation of water at a cubane-like Mn_3CaO_4 cluster,[1] the oxygen evolving centre (OEC). Despite recent breakthroughs that have revealed the 3-dimensional structure of the OEC, the mechanism by which it produces O2 remains elusive. In the absence of definitive evidence in the biological system itself, studies of synthetic metal-based model complexes become critical. Quantum chemical calculations, specifically with density functional theory (DFT), have been shown to be useful in exploring the Oxygen evolving complexes. Siegbahn and co-workers have been postulated that the formation of Mn^{IV}-oxyl radical configuration is the key step in the O−O bond formation in photosynthesis.[2,3] Further, DFT studies on the high valent Mn and Ru synthetic oxygen evolving complexes also emphasize the potential importance of metal oxyl radical ($M^{IV}O^{\cdot}$) characteristics, as distinct from metal -oxo ($M^{V}O$), in water oxidation chemistry.[3,4] Our objective is to use density functional theory (DFT) to explore one such model, a Mn_2^{III}-dimeric porphyrin complex, successively catalyze four-electron oxidation of water to evolve molecular Oxygen, synthesized by Naruta and co-workers.[5]



Scheme 1: Computational models for (A) the key intermediate of the proposed reaction pathway for O_2 formation,[5] (B) hydroperoxo intermediate and (C) peroxo intermediate.

In contrast to Siegbahn's proposal, the monomer and the dimer models for the key intermediate (A) prefer Mn^{IV}-porphyrin radical ($Mn^{IV}Porp^{+\cdot}$) configuration rather than Mn^{IV}-oxyl radical ($M^{IV}-O^{\cdot}$) form in their ground state. However, the key step of the mechanism is the formation of active Mn^{IV}-oxyl radical configurations *via* spin state crossing between two distinct potential energy surfaces prior the O−O bond formation. Subtle changes in the Mn-oxo coordination sphere trigger the switch in the electronic structure which, ultimately, lowers the barrier for the reaction. The O−O bond formation can occur either *via* direct coupling between the two MnO groups or by attack of a H_2O-MnO group on a molecule of water, giving rise to hydroperoxo (B) and peroxo (C) intermediates respectively. All these findings have potential implications for O−O bond formation in water oxidation catalysis. In particular Naruta's system perhaps closely mimics the Oxygen evolution mechanism proposed by Hoganson and Babcock[6] for water oxidation in Photosynthesis. These investigations guide the design of catalytically novel and chemically significant second-generation water oxidation catalysts.

[1] Ferreira, K. N., Iverson, T. M., Maghlaoui, K., Barber, J., Iwata, S., *Science*, **2004**, *303*, 1831–1838.
[2] Siegbahn. P. E. M., *Inorg. Chem.*, **2000**, *39*, 2923–2935.
[3] Lundberg, M., Blomberg, R. A., Siegbahn. P. E. M., *Inorg. Chem.*, **2004**, *43*, 264–274.
[4] Yang, X., Baik, M., *J. Am. Chem. Soc.*, **2006**, *128*, 7476–7485.
[5] Yuichi Shimazaki, Y., Nagano, N., Takesue, H., Ye, B. H., Tani, F., Naruta. Y., *Angew. Chem.*, **2004**, *116*, 100–102.
[6] Hoganson, W. C., Babcock, G. T., *Science*, **1997**, *227*, 1953.

Molecular Modelling of MPTP and Cytochrome 2D6 Enzyme Variants

I. M. Shah, K. Wittayanarakul, N. G. Anthony, C. J. Breslin, S. P. Mackay

Strathclyde Institute of Pharmacy and Biomedical Sciences, 27 Taylor Street, University of Strathclyde, Glasgow G4 0NR

Introduction

MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) is a neurotoxic agent which is commonly used to develop animal models of Parkinson's disease (PD). The enzyme cytochrome 2D6 (CYP2D6) displays a protective effect by metabolising MPTP into inactive metabolites.[1] However, *in vitro* studies have demonstrated reduced metabolism of MPTP by mutated CYP2D6 enzymes. We investigated the free energy of binding (ΔG) using molecular modelling studies between MPTP and the wild-type (CYP2D6) and mutant enzyme (CYP2D6*17) structures.

Methods

In the absence of an X-ray structure for the MPTP-CYP2D6 complex, docking methods were used to predict the orientation of the ligand with wild type (pdb code: 2f9q) and mutated CYP2D6 (*in silico* generated from pdb: 2f9q) as the starting structures for molecular dynamics (MD) simulations.[2] In order to validate the docking method *via* AutoDock 4, we also investigated the ΔG values and inhibition constants (K_i) of two clinical drugs, pergolide and ropinirole. MD simulations for 3 ns were then performed on the docked MPTP-CYP2D6 complexes using AMBER 9, with explicit solvent representation. The 100 snapshots from the final 1000z ps were used to calculate the average relative binding free energies using the MM-PBSA method.

Results

The calculated ΔG values obtained from the MD simulations give a good correlation with the experimental values for the different substrates binding to the CYP2D6 enzyme. In addition, it appears that the relative ΔG of the MPTP complex for mutant enzyme (ΔG = -24.27$\pm$5.3 kcal/mol) is higher than the MPTP complexed with wild-type (ΔG = -26.7$\pm$-4.9 kcal/mol). These findings suggest that the lower metabolic activity of CYP2D6*17 could be the result of altered affinity for the ligand caused by the amino acid mutations in the active site.

Conclusion

Our preliminary results show that ΔG of MPTP for the mutant enzyme is higher compared with wild-type CYP2D6, although further analysis is required. This result may explain the experimental findings of reduced substrate metabolism by CYP2D6*17. The starting structures obtained from the docking studies give relatively accurate orientations based on the substrate binding free energies and inhibition constants.

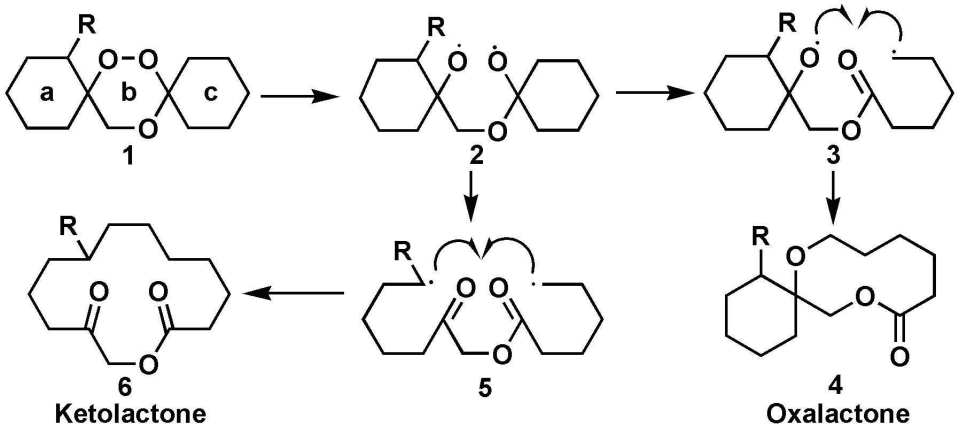
[1] Herraiz, T. *et al.*, *Toxicology and Applied Pharmacology*, **2006**, *216*, 387–398.
[2] Ito, Y. *et al.*, *Journal of Molecular Graphics and Modelling*, **2008**, *26*, 947–956.

The Synthesis and Radical Rearrangement of *Dispiro*-1,2,4-Trioxanes

Benjamin J. Taylor, Kevin J. McCullough and Stuart A. Macgregor

Heriot-Watt University, Edinburgh EH14 4AS, Scotland
e-mail: bjt1@hw.ac.uk

Macrolides with complex substitution patterns have a wide range of pharmaceutical applications, including as antibiotics, anti-tumour agents and anti-HIV agents. In addition structurally simple macrolides are also components of natural musks or fragrances. Thermolysis of *dispiro*-1,2,4-trioxanes (**1**) offers a potentially convenient synthetic route to macrolides as outlined in Scheme 1.



Scheme 1

However, the thermolysis of trioxane (**1**, R = H) produced a mixture of fragmented products and the oxalactone (**4**). In contrast, thermolysis of *dispiro*-1,2,4-trioxanes (**1**, R = OMe) produced the 14-membered macrolide (**6**, R = OMe) as the major isolable product in high yield. This synthetic route has produced a number of novel macrolides in high yield from *dispiro*-1,2,4-trioxanes. Investigation of the mechanism by DFT calculations predicts the rate of opening of ring **a** is significantly slower than that of ring **c** and so is the key step that determines the product obtained. In addition, varying the nature of the R group dramatically lowers the barrier to opening of **a**.

Poster number 38

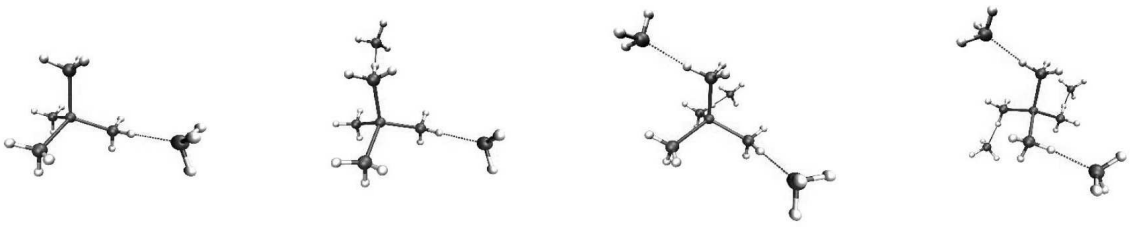
Zinc Ammonia Clusters: A joint Electronic Structure and Mass Spectrometry Study

Andrew R. Turner and Bridgette J. Duncombe

School of Chemistry, The University of Edinburgh, Edinburgh EH9 3JJ, UK

In this work we have used a combination of mass spectrometry techniques and electronic structure calculations to understand the structure and energetics of a series of clusters of the form $[Zn(NH_3)_n]^{2+}$ (n=1...9). The complimentary nature of the experimental and the computational parts of this study allow for a greater understanding than would be available with either technique in isolation. This poster will focus on the computational aspect of this work and show how it compliments the experimental studies.

Both DFT (used in most previous studies of this type of system) and MP2 methods were evaluated for this class of system (with a range of basis sets) and it was found that only MP2/TZVP geometry optimizations consistently generate the lowest energy conformer. DFT calculations always generated a higher energy conformation but would optimize to the lowest energy conformer if started from the MP2/TZVP geometry. The relative stability of different configurations of first and second NH_3 solvation shell arrangements was calculated for various values of n. The most stable first solvation shell configuration corresponds to a tetrahedral $n = 4$ arrangement with higher n values leading to addition of further NH_3 molecules in the second (and eventually third) solvation shells. Ammonia molecules in the second solvation shell are bound to the first solvation shell by a single hydrogen bond with a length in the region of 1.9 Å. Other structures with bifurcated H-bonds also exist and are very close in energy to the minimum energy conformation (< 15 kJ/mol) and we would expect these to be populated under the experimental conditions. At higher coordination numbers ($n > 5$) we see the formation of structures involving secondary solvation in preference to direct coordination; probably due to steric hindrance around the metal ion and the breaking of the tetrahedral binding motif that would be required. The binding energies for different values of n were computed and used to assess the relative stability of different sized clusters. These stabilities agree with results from the experimental studies. The calculations allow for a deeper, molecular level of understanding to be placed on the experimental results while the experiments provide an independent verification of the theoretical results.



Poster number 39

Accurate Structures of $Si_8O_{12}H_8$ and $Si_8O_{12}Me_8$

Derek A. Wann, Anthony M. Reilly and David W. H. Rankin

School of Chemistry, University of Edinburgh, West Mains Road, Edinburgh, EH9 3JJ, UK; e-mail: derek.wann@ed.ac.uk

The molecular structures of $Si_8O_{12}H_8$ and $Si_8O_{12}Me_8$ have been determined using gas electron diffraction (GED) methods. While the determination of the structure of $Si_8O_{12}H_8$ was straightforward, that was not the case for $Si_8O_{12}Me_8$. The use of corrections obtained from SHRINK[1] to account for the effects of vibrations proved inadequate in the case of the methylated silsesquioxane.

We have outlined a method that uses molecular dynamics (MD) simulations with periodic boundary conditions to calculate corrections to interatomic distances so that gas-phase equilibrium structures can be determined. For $Si_8O_{12}Me_8$ a single molecule is placed in a large cell, thus minimising the effects of periodicity. By taking the differences between optimised interatomic distances and those average distances yielded by the MD simulations, corrections for use in GED refinements can be obtained. These corrections are similar in value to those obtained by SHRINK for cases where SHRINK is expected to be correct. However, this method also gives reasonable values in situations where more traditional methods of calculating corrections have significantly over- or underestimated the values.

[1] V. A. Sipachev, *J. Mol. Struct.: THEOCHEM*, **1985**, *22*, 143.

Poster number 40

cis-trans Isomerization of Azobenzenes Studied by NMR Spectroscopy and DFT Calculations

Nuha Wazzan and Anita C. Jones

School of Chemistry, The University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ

Azobenzene and its derivatives have found wide applicability in areas such as dyestuffs, nonlinear optical materials, photostorage and optical switching.[1] It is well known that azobenzene can exist in two different isomeric forms, *trans* and *cis*, in the electronic ground state. The *trans* isomer is the thermodynamically favoured species and azobenzenes are found predominately in this form. The *trans*-to-*cis* isomerisation of azobenzene is induced photochemically, whereas the reverse process can occur thermally or photochemically.

We have investigated the kinetics of *cis-trans* isomerisation of a series of azobenzene derivatives using NMR spectroscopy with *in situ* laser irradiation. The effectiveness of this technique for investigating the photoisomerisation of azo dyes and obtaining structural information on short-lived *cis* isomers has been demonstrated previously.[2,3] We now report the use of this method to investigate the mechanism of the thermal conversion of the photochemically formed *cis* isomer to the more stable *trans* form. The influence of substituents and solvent on the rate constant and the enthalpy and entropy of activation of the isomerisation reaction have been examined. Complementary computational studies have been carried out using density functional theory DFT-B3LYP/6-31G** to predict the structures of the *cis* and *trans* isomers and the activated complex, and to explore the reaction coordinate. The theoretically predicted activation parameters will be compared with those determined experimentally, and the utility of DFT calculations in predicting the effects of molecular structure and solvation on the kinetics of *cis-trans* isomerisation assessed. The mechanism of the isomerisation process will be discussed in terms of the two alternative pathways, rotation about the azo bond and in-plane inversion about one of the azo nitrogens.

[1] L. Wang and X. Wang, An *ab initio* study of stable conformation and thermal isomerization of *p*-aminoazobenzene, *J. Molecular Structure: THEOCHEM*, **2007**, *806*, 179–186.

[2] K. M. Tait, J. A. Parkinson, S. P. Bates, W. J. Ebenezer and A. C. Jones, The novel use of NMR spectroscopy with *in situ* laser irradiation to study azo photoisomerisation, *J. Photochem. Photobiol. A*, **2003**, *154*, 179–188.

[3] K. M. Tait, J. A. Parkinson, D. I. Gibson, P. R. Richardson, W. J. Ebenezer, M. G. Hutchings and A. C. Jones, Structural characterisation of the photoisomers of reactive sulfonated azo dyes by NMR spectroscopy and DFT calculations, *Photochem. Photobiol. Sci.*, **2007**, *6*, 1010–1018.

Charge-Triggered Acid-Base Chemistry

Alexander Whiteside, Maciek Gutowski, Kit Bowen, *et al.*

School of Engineering and Physical Sciences - Chemistry, Heriot-Watt University, Edinburgh EH14 4AS, UK

Addition of an electron to a chemical system can lead to significant geometry changes, as observed in the anion photoelectron spectroscopy of the alkali halides. More significant changes, such as proton transfer in a hydrogen bonded system, can also be triggered in this way. This manifests itself as vibrational band structure in the spectrum. Similar proton transfer processes are of great importance in charge transfer systems, for example in catalysis.

In a recent publication, Gutowski, Bowen and collaborators discuss the transfer of a proton from HCl to NH_3 in the gas phase. Counter-intuitively, this does not occur in an NH_3...HCl hydrogen-bonded complex in isolation - the gas phase proton affinity of Cl^- exceeds that of NH_3. An electron must be bound to the system first. The proton is then transferred in this dipole-bound anion to form a stable $[NH_4^+ \ldots Cl^-]^-$ complex, more accurately described as an NH_4^0 Rydberg radical polarised by Cl^-.

A series of computational studies have been undertaken to expand upon this paper. The proton transfer process is shown to occur in anions of NH_3...HBr, and NH_3...HI. The electronic origin of this transfer process is discussed. This proton transfer is also predicted in cationic hydrogen-bonded complexes. The anion photoelectron spectrum of NH_3HF indicates that it does not behave in the same manner as the other ammonia - hydrogen halide complexes. This is discussed.