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# Chemistry IN NEW ZEALAND

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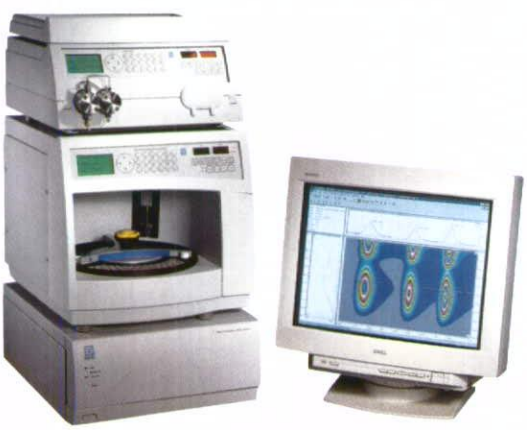

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Chemistry
IN NEW ZEALAND

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**The New Zealand Institute of Chemistry Incorporated**
P O Box 39-283, Howick
Auckland, New Zealand
Phone: +64-9-5356495
Fax: +64-9-5353476
Email: NZICOffice@nzic.org.nz
WWW: http://www.nzic.org.nz

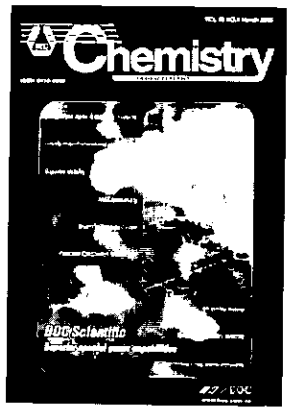
**Managing Editor & Publisher:**
Robert B Lyon
Ancat Holdings Limited
32 Murvale Drive
Bucklands Beach, Auckland
P O Box 38-546
Howick, Auckland, New Zealand
Phone: +64-9-5353475
Fax: 64-9-5353476
Email: chemistry@ancat.co.nz

**Design & Layout:**
Heidi L Brümmer

**Editorial Board:**
Professor B Halton • DSc, FNZIC
Professor L Phillips • DSc, FNZIC
R B Lyon • BSc, MNZIC

**Advertising Sales:**
Ancat Holdings Limited
32 Murvale Drive
Bucklands Beach, Auckland, New Zealand
P O Box 38-546
Howick, Auckland, New Zealand
Phone: +64-9-5353475
Fax: +64-9-5353476
Email: chemistry@ancat.co.nz





# Calibration Gas mixtures

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BOC's Spectraseal cylinder treatment process has assisted organisations all over New Zealand and Australia to meet increasingly strict air emissions legislation and advance with the growing corporate move towards environmental responsibility. Many manufacturing and refining processes produce copious emissions, including environmentally unfriendly ones such as hydrogen sulfide. Scrubbing systems can be used to remove these environmentally unfriendly gases so they do not find their way into the air. But, in order to ensure the scrubbing systems are working, the air exiting the plant must be tested. Most testing instruments require periodic calibration to ensure they're working correctly. The quality of the calibration gas mixtures is crucial to validating the accuracy of these instruments.

BOC's Spectraseal process plays a critical role in an organisation's compliance to tight environmental emission standards because it ensures the quality of the calibration gas mixtures created through this patented cylinder treatment process. These calibration mixtures typically include reactive gases such as $H_2S$, $SO_2$, NO, $NO_2$, $NH_3$ and CO. These gases are so called because they change (react) easily when they contact other things - including air, moisture and the cylinders they are stored in. Several other factors, including time, temperature and residual pressure, can also adversely affect the integrity of gases in cylinders. Some gases react chemically with cylinder walls, while others change concentrations during use as the pressure within the cylinder drops or with variations in storage temperatures. Additionally, as the cylinder pressure decreases through use, there is a growing threat of the desorption of moisture entrained in the cylinder walls, and consequently, a potential degradation of the gas purity. The most common result of these unstable reactions is that part of the gas can stick to the walls of the cylinder, or turn into a different molecule altogether. This means that a mixture containing 8 ppm of a gas may react with the cylinder so that the gas that comes out of the cylinder may only have a concentration of 4 ppm. Spectrasealing a cylinder ensures that the cylinder's interior aluminium surface is enhanced by a special anodising process that renders it chemically inert. A second proprietary process converts this passivation layer into a smooth, unreactive, tightly adherent surface, with negligible adsorptive properties.

*Spectraseal Aluminium Cylinder Features:*

- Special proprietary anodising process renders the internal cylinder surface chemically inert.
- Passivated surface limits the cylinder's potential for adsorption/desorption, and is non-catalytic.
- Spectraseal cylinder guarantees stable shelf-life and 90% product use.
- Cylinder is insensitive to temperature fluctuations from -17.5 to 48.9 °C.
- Cylinder is insensitive to pressure fluctuations from zero to 2200 psig.
- Certified gases retain their original specifications throughout use and extended shelf-lives.

As a result, BOC certified cylinder gas mixtures meet their original certification - both in storage and during use. With the long term stability and accuracy of the calibration gas mixtures quality assured, Spectraseal simplifies the task of complying to the increasingly complex analyses and lower detection levels, down from parts per million to parts per billion, demanded by today's and tomorrow's environmental legislation. BOC has made mixtures of gases with up to 42 components, some of which are highly reactive and/or dangerous, and some which were needed in very low concentrations. If the cylinder containing the mixture is not pacified (*i.e.* won't react with the gases it contains) the quality and shelf-life of the mixture can not be ensured.

The Spectraseal aluminium cylinder is the product of an ongoing effort to optimise the performance of special gases through the development of high quality cylinder packaging technologies. Created specifically for trace level reactive mixtures, the Spectraseal cylinder overcomes the limitations that hamper conventional gas cylinders. Spectraseal mixtures can be made to the user's formulation and concentration and quality and stability assured with mixtures analysed two to four separate times before being released.

As well as being unstable, many of the gases used in special gas mixtures are dangerous, such as the toxic, flammable and carcinogenic gas ethylene oxide, which is used for equipment sterilisation. BOC special gas mixtures can be used to calibrate warning instruments so that any leaks can be detected quickly and accurately.

Other industries that use Spectraseal gas mixtures include mining, petroleum refining, car manufacturing, industrial processes and hospitals. BOC's Spectraseal passivated aluminium cylinders maximise the accuracy, stability, and purity of highly reactive ppb and ppm level calibration gas mixtures. This, in turn, provides more accurate analytical results. All BOC's Spectraseal mixtures for Australia and New Zealand are manufactured at the BOC Special Gases Facility in Wetherill Park, Sydney, Australia.

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## New Fellows of the Royal Society

**Professor Graham Bowmaker (University of Auckland)**

Professor Graham Bowmaker completed his BSc(Hons) and PhD degrees at the University of Sydney, where he was awarded Commonwealth Scholarships for both his undergraduate and postgraduate studies. Since 1968 Graham has been on the staff of the University of Auckland, where he teaches physical and materials chemistry. He is currently head of the Chemistry Department.

He was a senior visitor at the University of Oxford in 1975 and on three occasions (most recently in 1996) has been Alexander von Humboldt Visiting Professor at the Technical University of Munich. In 1996/1997 he was a Visiting Professor at the University of Durham. A Fellow of the New Zealand Institute of Chemistry since 1982, he chaired the Auckland branch of the Institute from 1997 to 1999. He is also a Fellow of the Royal Australian Chemical Institute and a Fellow of the Royal Society of Chemistry.

His main research interest involves the study of molecular structure and bonding by magnetic resonance and vibrational spectroscopic methods. The main systems that he has studied are inorganic-based materials involving the late transition elements (Groups 10, 11, 12) and the main group elements (Groups 15, 16, 17 in particular). He also has an interest in organic materials with unusual physical properties (organic radicals and radical ions; organic conductors and conducting polymers).

The spectroscopic methods that he has employed include electron paramagnetic resonance (EPR), nuclear magnetic resonance (NMR), nuclear quadrupole resonance (NQR), infrared (IR) and Raman spectroscopy. New or previously incompletely characterized species (*e.g.* coordinated halogen cations, polyhalide and poly-pseudohalide anions; copper, silver and gold compounds with unusual metal coordination numbers and structures; nickel, palladium and platinum complexes in unusual oxidation states) have been prepared and characterized by these methods. Where appropriate, structural information deduced from the spectroscopic data has been confirmed in crystallographic studies (joint work with colleagues in Auckland and overseas). This work has generated considerable interest in research groups overseas, and this has led to collaborative studies with colleagues in Australia, Germany, USA, Britain, France and Italy, as well as elsewhere in New Zealand. His most recent research in this area has focussed on the application of solid-state NMR spectroscopy to the study of structure and bonding in inorganic and coordination compounds.

He has also been involved in the application of spectroscopic methods to the study of electrochemical processes and the properties of adsorbed molecules. This work began in the area of EPR spectroelectrochemistry, and has extended more recently to IR and Raman spectroelectrochemistry. The most recent development of this line of research has been a collaborative project with colleagues in the USA and France to measure the IR and far-IR spectra of surface species by using synchrotron radiation. This has involved several visits to the National Synchrotron Light Source at the Brookhaven National Laboratory in New York. The extreme brightness of the synchrotron source, particularly in the far-infrared region, allows the observation of the vibrations of surface species, and this work has resulted in the observation for the first time of far-IR bands due to vibrations of the bonds that bind adsorbed species to an electrode surface.

More recently, his research has involved aspects of materials chemistry. This is a rapidly developing area, as is manifest from the recent appearance of materials chemistry journals published by the two major learned societies in Chemistry (the American Chemical Society and the Royal Society of Chemistry) as well as by the major German publisher VCH. It is an interdisciplinary subject, and two of the major disciplines that it encompasses are physical and inorganic chemistry, both of which are areas in which Professor Bowmaker has had a long-standing interest.

Currently his research is supported by the Public Good Science Fund and the Australian Institute of Nuclear Sciences and Engineering. He has published in excess of 180 research papers, including three major review articles, in international journals.

**Professor Margaret Brimble (University of Auckland)**

Margaret Brimble completed her undergraduate training at the University of Auckland gaining a BSc and MSc (1st Class Hons) degrees in chemistry in 1982 and 1983, respectively. She received the Sir George Grey Scholarship for the most promising research student and the Fowld's Memorial Prize for the top student in the Science Faculty. She was then awarded a UK Commonwealth Scholarship to undertake PhD studies at the University of Southampton, England, from 1983-85 with Professor Ray Baker. In 1986 Margaret then returned to New Zealand to a lectureship at Massey University. In 1992 she was awarded the New Zealand Institute of Chemistry Easterfield Medal and the Royal Society of New Zealand Hamilton Memorial Prize after establishing an independent research group at Massey University working on the chemical synthesis of complex natural products. In 1992 she was an Invited Visiting Professor at the University of California-Berkeley where

she contributed to the undergraduate teaching programme and carried out research with Professor Clayton Heathcock. In 1995 she moved to a Senior Lectureship at the University of Sydney where she was promoted to Reader in Organic Chemistry in 1997.

In 1999 Margaret returned to New Zealand as Professor of Organic and Medicinal Chemistry at the University of Auckland. Despite the difficult financial climate experienced by her Department upon her arrival, Margaret quickly set about revitalizing organic chemistry research at The University of Auckland. She rapidly established an active research group securing funding for her work from several sources. In 2001 her research at The University of Auckland was recognized at an international level when she was awarded the prestigious Distinguished Chemist Award by the Federation of Asian Chemical Societies.

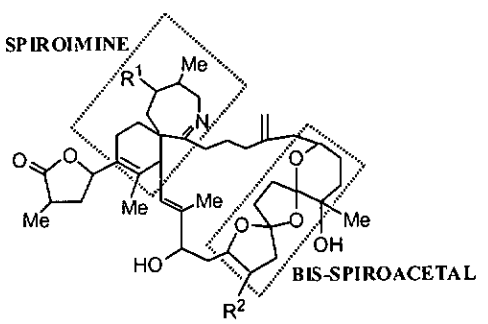
As well as being an active researcher Margaret has always shown a commitment to undergraduate teaching and she taught many of her research students as undergraduates. Recently she introduced a new interdisciplinary BSc Hons degree in Medicinal Chemistry that will commence in 2002. This degree is the first of its kind to be offered in New Zealand and is designed to produce high quality graduates equipped with the multidisciplinary knowledge and skills relevant to the rapidly expanding pharmaceutical and biotechnology industries which form the basis of new global knowledge economies.

Margaret has published over 110 papers in peer reviewed journals and her research interests involve the synthesis of complex natural products that have important biological activity. Natural products have long been regarded as *"nature's medicine chest"* providing a rich source of lead compounds with complex and novel structures which can be synthesized for the development of new pharmaceuticals. It is the synthesis of these complex molecules that tests the existing boundaries of organic synthesis. It demands academic and manipulative rigour, creativity, dedication, persistence and hard work. The tactics and synthetic manoeuvring involved in executing a given synthesis has also been compared to the logic and rationale behind a game of chess.

Natural products synthesis has also been described as an *'enabling science'* in that it provides unlimited opportunity for discovery at the interface with biology and medicine and testimony to this statement is the fact that Margaret also works at the interface of academia with the commercial world in that she is also Head of Medicinal Chemistry for one of New Zealand's new emerging pharmaceutical companies, Neuronz Ltd. Her commercial research team are working on the synthesis of novel peptidomimetics which exhibit neuroactive properties and have potential for commercial development as therapeutic agents for the treatment of neurodegenerative disorders such as Alzheimer's and Parkinson's disease. Margaret exudes enthusiasm for this commercial work and believes that biotechnology companies such as Neuronz Ltd will provide a platform on which to build New Zealand's new knowledge economy. She believes there are many exciting discoveries to be made at the interface of chemistry with biology and that we need to equip chemistry graduates with the necessary skills that will allow them to contribute to a multidisciplinary environment.

Margaret's academic research in synthetic organic chemistry and medicinal chemistry focuses on making and modifying naturally occurring bioactive compounds that have been isolated from plants, animal tissue, microbes or marine and soil organisms, which are rare or hard to isolate in abundance. The target molecules that have succumbed to total synthesis by her research group include the synthesis of the insect antifeedant peramine which is active against one of New Zealand's major insect pests–the argentine stem weevil, the antifungal agents kalafungin, arizonin, actinorhodin and griseusin A, the antileukemia agent medermycin, the polyether antibiotics salinomycin and CP44,161, and the nicotinic acetylcholine receptor antagonist, methyllycaconitine. Margaret also has an active research programme working on the synthesis of new generation antibiotics such as the papulacandins and agents that exhibit selective and potent activity against the peptic ulcer-producing microorganism, *Helicobacter pylori*.

Whilst at The University of Sydney Margaret held the maximum number of highly competitive research grants from the Australian Research Council. Since her return to New Zealand she has been awarded two research grants from the Royal Society of New Zealand Marsden Fund. The Marsden grant she received this year was for her new research project directed towards the synthesis of the shellfish toxins, the spirolides, that are complex macrocyclic compounds produced by the algal blooms that frequently occur in New Zealand coastal waters resulting in closure of shellfish farms. These compounds cause potent and characteristic symptoms in the mouse bioassay and are weak activators of type L calcium channels. The spirolides contain two novel pharmacophores – a spiroimine moiety and a bis-spiroacetal moiety. Both of these heterocyclic arrays have not been synthesized to date and are current synthetic targets for Margaret's research group. The challenge is to establish novel synthetic methodology in order to be able to synthesize these novel pharmacological probes in the laboratory. The spirolides are also useful lead compounds for the development of new therapeutic agents to treat cardiovascular disorders such as hypertension.




**Spirolide B:** $R^1 = H$; $R^2 = Me$
**Spirolide D:** $R^1 = Me$; $R^2 = Me$

Margaret has contributed significantly to her scientific discipline. She is a Fellow of the New Zealand Institute of Chemistry and the Royal Australian Chemical Institute, is an elected member of the International Advisory Board for the International Society of Heterocyclic Chemistry, a Member of the Editorial Boards for several international organic chemistry journals, and has received many invitations to speak at international conferences in her chosen field. She is a Co-Chair for the forthcoming 14th

International Conference on Organic Synthesis that will be held in New Zealand in July 2002, a prestigious international conference that has never before been held outside the northern hemisphere.

Margaret balances her active scientific career with the care of her much treasured three year old daughter Rebecca, who was born just before she took up her appointment as Professor of Organic and Medicinal Chemistry at The University of Auckland in 1999.

## Five Centres Of Research Excellence Chosen By CoRE Fund Committee

The CoRE Fund Committee, chaired by Sir Paul Reeves, has chosen five of the 11 shortlisted proposals to form Centres of Research Excellence. They are:

**Allan Wilson Centre for Molecular Ecology and Evolution**

Host Institution: Massey University, Directors: Professors D. Penny and M. Hendy.
Partners: University of Canterbury, The University of Auckland, University of Otago, Victoria University of Wellington.

The Allan Wilson Centre will undertake studies of the ecology and evolution of New Zealand plants, animals and micro-organisms. Recent research, using new techniques such as sequencing of whole genomes and the study of ancient DNA, has revolutionised our understanding of New Zealand's biodiversity. The simplistic view that New Zealand is a "Moa's Ark" of relic species undergoing "ancient and slow " changes over long periods of time has been overturned by the information obtained with these new techniques. The Centre's vision is to utilise the network of outstanding New Zealand biologists and mathematicians, who have made significant contributions to developing new analytical methods and techniques in this area, to address some of the fundamental questions about our plant and animal life. The Centre will enable a dramatic acceleration in the progress of our understanding of the processes underpinning the ecology and evolution of living systems. The knowledge gained will enable us to contribute internationally to an understanding of the nature of complex biological processes and fragile ecosystems.

**Centre for Molecular Biodiscovery**

Host Institution: The University of Auckland, Director: Professor E. Baker.

The Centre for Molecular Biodiscovery comprises a cluster of five leading research groups at the University of Auckland with complementary expertise in science, engineering and medicine. The Centre will focus on the use of new technology for genomic discovery and on the innovative development of new medicines for infectious disease, diabetes and cancer, based on new findings in molecular biology. Proteins are molecules that perform essential processes in organisms and affecting their function is useful in altering disease states. The structure of key proteins will be determined and used to design and develop new synthetic drugs as well as to enable the development of models that mimic how they function in cells. The Centre's links with major pharmaceutical companies ensure the commercialisation of new discoveries and consequent economic benefits to New Zealand.

**New Zealand Institute of Mathematics and its Applications**

Host Institution: The University of Auckland, Directors: Professors V. Jones and M. Conder.
Partner: New Zealand Mathematics Research Institute.

The New Zealand Institute of Mathematics and its Applications will focus on the use of high-level mathematical and computational techniques to problems in medicine, biology, engineering, industry and commerce, with particular emphasis in areas of emerging importance such as bio-engineering, bio-informatics, medical statistics, optimisation and risk assessment. A key activity of the Institute will be the organisation and presentation of six-monthly programmes on themes of significant and contemporary importance such as mathematical biology and its applications. The rest of the science community will contribute suggestions for these themes. The Institute will accelerate the use of mathematics across the spectrum of science and engineering through its research programmes and intensive periods working on particular themes. In an increasingly complex world, the use of mathematical techniques to enhance good decision-making will provide New Zealanders with a competitive advantage.

**Nga Pae o te Maramatanga (Horizons of Insight) The National Institute of Research Excellence for Maori Development and Advancement**

Host Institution: The University of Auckland, Directors: Professor L. Smith and Associate Professor M. Walker.
Partners: Te Whare Wananga O Awanuiarangi, Te Wananga O Aotearoa, Victoria University of Wellington, University of Otago, University of Waikato, Landcare Research.

The National Institute of Research Excellence for Maori Development and Advancement will focus and build on Maori strengths in education, health and science. It plans to bring together Maori and western intellectual traditions and experience to generate new knowledge that will lead to new technologies and significantly improve socio-economic outcomes for Maori. It will achieve this by (1) drawing on Maori and mainstream knowledge and thought to raise standards of research; (2) improving uptake of research through engagement with Maori social structures; and (3) expanding and deepening both Maori and national research capability. The Institute's planned research programme includes expanding current research activities in (1) new building materials for cheaper, warmer housing; (2) young people's views of schooling and society; and (3) fundamental studies of the processes underlying diseases, such as diabetes, to which Maori are genetically predisposed.

**The MacDiarmid Institute for Advanced Materials and Nanotechnology**

Host Institution: Victoria University of Wellington, Director: Professor P. Callaghan.
Partners: University of Canterbury, Industrial Research Limited, Institute of Geological and Nuclear Sciences.

The MacDiarmid Institute will be the centre for innovation and discovery in fundamental and applied materials science

and technology in New Zealand. Strong international links, coupled with a multi-disciplinary approach, will enable the Institute to discover and understand new advanced materials and technologies to create new products, technologies and industries for New Zealand. Materials and technologies currently attracting world-wide attention that will be addressed by the Institute include: nano-engineered materials and devices, opto-electronics, superconductors, conducting polymers, functional materials and coatings, energy storage systems, soft materials, bio-materials and complex fluids.

The CoRE Fund Committee was impressed by the diversity of world-class research represented in the proposals and funded the maximum number of centres possible. Each centre will receive additional funding for expenditure on equipment.

All of the shortlisted proposals considered by the Committee had been selected by expert panels for their research excellence and their ability to train researchers. The Committee had to decide which proposals would bring the greatest benefits to New Zealand, in terms of economic, environmental and social development.

The five centres are hosted by particular institutions but all involve national collaborations of researchers. There has always been collaboration among researchers in different universities and other institutions, but the establishment of centres with dedicated long term funding (up to six years), will enhance this teamwork and stimulate greater research activity.

## University And CRI Combine Strength For Ground Breaking Research

The University of Auckland and the country's largest Crown Research Institute have signed an agreement to collaborate in life sciences research and education in a move that will strengthen national capability in the area.

Vice-Chancellor of The University of Auckland, Dr John Hood, and AgResearch CEO Dr Keith Steele said that the University of Auckland and AgResearch have complementary skills and resources in life sciences research, and that they intend to bring these together in a new partnership which will see enhanced research capability in a range of research areas of importance to New Zealand.

"Biotechnology will be pivotal to New Zealand's future economic and social success, with its wide-ranging opportunities in primary production, human health and environmental management. We believe the combined research strength will generate critical mass in specific biotech areas to open a range of new opportunities for building knowledge, and, ultimately, creating wealth," they said.

"New Zealand's resources for world-leading research are limited and the agreement formalises the opportunities to make the best of them. It makes sense for leading institutions to collaborate actively where there are real gains to be made from working together, combining the international networks of both.

"The research groups will build a stronger presence in New Zealand and internationally, and will be able to develop broader intellectual property portfolios.

"The agreement will also provide more opportunities for outstanding research students to work in a New Zealand research environment during and after their studies."

The University and AgResearch will also share investment in, and access to,research facilities and equipment.

The collaboration will focus initially on four selected areas of research:

- ***Structural bioinformatics*** - The collaboration brings together the active gene discovery programme at AgResearch with the Structural Biology programme at The University of Auckland. The University runs New Zealand's leading research facility for protein structure determination and the only group with integrated skills in bioinformatics, molecular biology and structural biology. The University's Molecular Biodiscovery group has just been granted funding as a New-Zealand wide Centre of Research Excellence.
- ***Plant genomics and flowering*** - The University of Auckland and AgResearch, together with other New Zealand researchers in the field of plant development and plant architecture have formed "Merinet". The aim of Merinet is to promote and coordinate research in New Zealand on the development and fate of meristems, the growing tips of plants, which control plant growth and form.
- ***Sustainability and wastewater management*** - AgResearch and The University of Auckland have identified common interests around the area of land use and impacts of farm practice on natural resource condition, particularly in relation to Maori.
- ***Growth and Development*** — The University of Auckland's first dedicated research institute, the Liggins Institute, and groups at AgResearch working in the areas of Muscle Genomics, Animal Health and Welfare, and Systems Biology, brings together leading researchers in fetal and postnatal growth that will significantly enhance growth and systems biology research in New Zealand.

## Marsden Fund Preliminary Proposals

The Marsden Fund has received 801 preliminary proposals, 671 Standard proposals and 130 Fast-Start proposals. This is a decrease compared with last year (706 Standard, 179 Fast-Start proposals) when the new Fast-Start programme caused a surge in the number of applications, but is still more than the previous year's total (756).

Panel meetings are scheduled for March and early April so invitations to submit full proposals will be sent to applicants in mid-April after the Marsden Fund Council has met.

This year we defined the panel subject areas in more detail and asked applicants to choose only one panel unless the research truly spans more than one panel area. (The Marsden Fund Council will check the proposals and may decide to refer a proposal to another panel.) This has approximately halved the percentage of each panel's proposals which go to a second panel as well. This has had a larger apparent effect on decreasing the number in each life science panel where there has usually been a large percentage of double panels chosen.

Data on preliminary proposals, by panel:
The numbers include proposals sent to more than one panel so adding up the number of proposals in each panel gives a total greater than the number of separate proposals given above. Last year's figures are given in brackets.

* Biomedical Sciences: Standard 106 (119), Fast-Start 9 (9)
* Cellular, Molecular & Physiological Biology: Standard 115 (147), Fast-Start 11 (13)
* Ecology, Evolution & Behaviour: Standard 123 (163), Fast-Start 20 (33)
* Earth Sciences and Astronomy: Standard 79 (75), Fast-Start 8 (16)
* Humanities: Standard 39 (39), Fast-Start 16 (16)
* Mathematical and Information Sciences: Standard 58 (54), Fast-Start 15 (20)
* Physical Sciences & Engineering: Standard 99 (120), Fast-Start 17 (22)
* Social Sciences: Standard 91 (78), Fast-Start 40 (56)

## Marsden Grant Explores Electronic Properties Of Zinc Oxide

Associate Professor Wei Gao of The University of Auckland's School of Engineering has won a prestigious Marsden Fund grant for exploring the electronic properties of zinc oxide. The three-year project has a budget of $400,000.

The grant is just one of three distinguished academic honours accorded to Dr Gao in the year 2001 - he was also elected a Fellow of the Royal Society of New Zealand, and awarded the RJ Scott Medal by the Royal Society for his outstanding contributions to engineering and science.

Dr Gao's Marsden project - "Unravelling the mysteries of zinc oxide" - is one of 82 new research projects which will receive $29 million support over the next three years from the Royal Society-administered Marsden Fund. The money is part of a government commitment to cutting edge research, and competition for a grant is intense. This year, just under 10 per cent of the 801 preliminary proposals were successful.

With his Marsden project, Dr Gao plans to conduct systematic research to establish the relationships between the composition, structure and electronic properties of Zinc oxide (ZnO) thin films.

Zinc oxide, he explains, is an old and inexpensive inorganic chemical, but it has unusual properties. "It can be made conducting and transparent - two properties you do not usually get together. Application is being pursued as transparent films for solar cells and coatings for electromagnetic wave screening.

"Recently, ZnO was found to have attractive photoemission properties - visible or ultraviolet light can emit upon excitation. Materials with these properties can be used to produce light diodes for display and lasers for telecommunication."

The behaviour of ZnO, however, remains a mystery, says Dr Gao. "Its properties are strongly affected by composition, microstructure, grain size and oxidation state. The impurities in ZnO also influence the electron structure and properties. These effects are not clearly understood. "We will use a set of special techniques - magnetron sputtering and ultra-low oxygen partial pressure reactor - to prepare ZnO and a selected group of oxide thin films, and to optimise the electronic properties described above. Attention will be given to the blue light emission and transparent-conducting properties related to electronic device technologies."

Dr Gao says the outcome of his Marsden Fund research will be a deeper understanding of the interrelations of processing parameters, microstructure and properties, and further development opportunities for ZnO and similar oxide semiconductor materials. Other members of his research group at The University of Auckland are Associate Professor Jim Metson, Dr Zhenquan Li and Dr Michael Hodgson.

Dr Gao is currently an associate professor in the Department of Chemical and Materials Engineering, and Co-ordinator of the Materials and Nano-Technology Research Cluster at The University of Auckland. He received his BE and ME from North-Eastern University and Beijing Central Research Institute, China, and DPhil from Oxford University, UK.

He also spent five years as a research associate, principal investigator and technical director of Rapid Solidification Lab at MIT, USA. At Auckland, he has taught 15 courses and parts of courses at both undergraduate and postgraduate levels, and supervised about 30 PhD and ME students. He actively conducts research in the areas of nano-materials and technology, advanced coating and surface engineering, high temperature corrosion and oxidation, superconductors, electronic materials, intermetallics, rapid solidification, amorphous alloys, electron microscopy and microanalysis, and computer modelling and applications of materials.

He has published 320 refereed research papers including 144 journal papers, a textbook, several chapters in books and encyclopaedia, holds five US and international patents and three MIT Disclosures, and has also been invited to give 15 keynote and invited lectures at international conferences. He is a fellow or member of many professional associations, and Honorary Professor for several overseas universities.

## Seeking A Fusion Energy Source

John Harrison, a lecturer at the Institute of Fundamental Sciences at the Massey University Albany campus, wants to create a miniature sun in order to undertake interplanetary travel.

Dr. Harrison is involved in an international project researching a way to harness nuclear fusion to produce endless, safe, clean energy. The 15-year project is headed by former Massey University lecturer Dr Francis Thio, now based at NASA's Marshall Space Flight Centre. It involves a team of researchers at NASA, the Los Alamos National Laboratory, the University of Nevada, the University of Alabama, the University of Zurich and, Massey University. And although the project's fruition

looks to be light years away, Dr Harrison is excited by the prospect of finding a non-polluting, renewable energy source.

"Achieving a controlled fusion energy source is one of the greatest scientific challenges of all time," he says. "The aim is to demonstrate the economic feasibility of this approach for energy generation on the one hand, and NASA's interest, which is to develop fusion energy as a source of propulsion for rapid interplanetary travel, on the other." Fusion energy would have many advantages, he says. "The fuel is cheap and abundant, it is clean because no greenhouse gases are produced and it is much safer than conventional nuclear power. "The idea is to create a 5 mm 'miniature sun' by rapidly compressing a target of ionized gas to high pressure and 20 million °C. Aiming an array of accelerators at the target produces jets of ionized gas that travel at 200 kmsec$^{-1}$. These merge and compress the target to a sun-like state."

The research of Dr Harrison and his doctoral student, Ian Shinton, a Bright Futures Scholarship recipient, is centred on developing fast acting valves that open and close in a few millionths of a second for injecting gas into the accelerators. Dr Harrison has a $100,000 translational spectrometer donated by a Zurich scientist to assist his research. The stainless steel spectrometer, the only one in the Southern Hemisphere, will allow the output of the valves to be precisely measured. "We are also developing specialised, ultra-hard, conducting, thin film coatings to protect the accelerator components against the extreme environment they have to work in and doing some mathematical modelling of the processes occurring inside the accelerators."

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## Hector Medalist 2001

The 2001 Hector Medal in chemical sciences was awarded to Professor Peter Schwerdtfeger (University of Auckland) for his outstanding research in theoretical chemistry. The Hector Memorial Fund was established in 1910 to support the award of the Hector Memorial Medal. It is now awarded biennially, in rotation, for mathematical and information sciences, chemical sciences, and physical sciences to the investigator who, working within New Zealand, has undertaken work of great scientific or technological merit and has made an outstanding contribution to the advancement of the particular branch of science. 2001 marked the turn of the chemical sciences.

Professor Peter Schwerdtfeger's research at the University of Auckland is concerned with fundamental aspects of interactions between atoms and molecules by using computational quantum methods. Computational quantum chemistry and physics is quantum theory applied to chemistry, condensed matter physics, fluid dynamics, particle physics and molecular biology. Early efforts in the late 1960s were concentrated on solving the so-called "Schrödinger equation" and its extension to solid systems by using either *ab initio* or density functional methods. The last 30 years has seen great progress in design of algorithms and increase in computer power; computational results now reach the level of experimental accuracy!

In molecular quantum chemistry (and condensed matter physics) one faces fundamental problems that the computer time scales exponentially with increasing number of interacting particles involved. Thus access to fast- and parallel processor machines with large memory and disk space requirements are essential for the computational treatment of such systems. The newly purchased IBM Regatta 32-processor supercomputer (with 166 Gflops/s, the fastest in this country) will help to fulfil this goal. This allows predictions to be made for properties of yet unknown atoms and molecules. For example, out of the four fundamental forces in nature the weak force leads to a breakdown of mirror image symmetry in molecules. Nature also reflects this as amino acids are left-handed and sugars are right-handed. Their mirror images (right-handed amino acids and left-handed sugars) are (with a few exceptions) not used in living organisms. Weak interactions could be responsible for this inherent asymmetry in nature. Despite many efforts, weak interactions in "handed" molecules have not been discovered yet. Peter's research group has made accurate predictions for such weak effects, and the laser group in Paris headed by Professor Christian Chardonnet is now preparing for experiments to detect such tiny differences between enantiomers.

New research is currently directed towards the study of structure and dynamics of large clusters. Answers to questions such as "when properties converge towards the solid state limit with increasing cluster size, why (in contrast to zinc and cadmium) is mercury a liquid at room temperature?" or "what is the mechanism of crystal growth?" are sought. When heavy elements are involved a relativistic formulation of quantum theory, known as the "Dirac equation", has to be applied. For a fully relativistic description of an atom quantum electrodynamic effects have to be included as well. It is currently a great challenge to describe even a simple molecule such as the mercury dimer by quantum chemical methods. Peter hopes to find an accurate relativistic description for the interaction between mercury atoms to tackle some of the problems mentioned above.

Peter says that he is very happy to live in such a beautiful country as New Zealand. He warns, however, of the continuing erosion of fundamental science in New Zealand: "We live in a time where the success of a scientist is measured by the k$ (kilo-dollars) brought into the system and not the quality of the research carried out. If New

Zealand wants to stay competitive in any research area, it must maintain and finance generously basic research. The Marsden Fund currently serves this purpose. Without it we would not have been able to carry out all these wonderful research programmes. However, a lot of top researchers are missing out and become very frustrated about the overall research opportunities in New Zealand. Under the current scheme it is very difficult to attract any good scientists from overseas."

*Since composing the above the Royal Society, on behalf of Government, has announced three new James Cook Research Fellowships. They have been ratified by The Governor General. The Physical Sciences Fellow is Peter Schwerdtfeger FRSNZ.* Ed.

## New FRST Board Members

Hon. Pete Hodgson has appointed three new Board members for the Foundation for Research, Science and Technology and reappointed three for a second term.

The new members are Professor Gary Hook and Associate Professor Pare Keiha, who will join the Board immediately. Dame Margaret Bazley will join the Board as Deputy Chair on 1 May 2002.

The three reappointed Board members are Neil Richardson (chair), Paula Rebstock and Dr Jim Watson. The other current members are Maxine Simmons, Neville Jordan and Andy Pearce.

## Bacteria May Become Inexpensive Pollution-Detectors

New Zealand scientists are using some of the world's smallest creatures to develop cheaper and easier ways to detect and measure toxic contaminants in water and soil. The technology, a new "biosensor", will help meet growing local and overseas demand for more cost-effective environmental monitoring, as governments and industry strive to minimise pollution and risk to public health.

Lincoln Ventures Ltd and Landcare Research are leading a $2M research project that will attempt to harness bacteria as the basis for a revolutionary biosensor kit, exhibiting capabilities previously unobtainable at the price envisaged. If the research is successful, the ultimate aim is to develop a new, export orientated, high technology industry for New Zealand around products that emerge from the research.

Current methods of measuring contaminants are mostly chemical and use very expensive instrumentation to measure individual toxic pollutants. The research programme will investigate the use of bacteria, which are very cheap to produce, to detect the toxins. The new biosensors will have the added advantages of detecting several contaminants in one analysis, thus further reducing costs.

Initial research is focussed on three common contaminants known to cause cancer: BTEX are a group of compounds found in the aromatic fraction of petrol and oil, while PAHs or polycyclic aromatic hydrocarbons are associated with fuel combustion and are a proposed priority target contaminant for New Zealand. PCBs or polychlorobenzenes are banned compounds that were manufactured as insulating products. They still exist in the environment and can accumulate in the food chain.

The research is led by Dr Neil Pasco of Lincoln Ventures Ltd and Landcare Research scientist Dr Gareth Lloyd-Jones who generated the ideas that underpin the research.

Dr Pasco explains that bacteria exhibit a multitude of reactions capable of signalling the presence of a particular contaminant and that this provides an opportunity for developing a bacterium-based biosensor. The problem is in assessing, from outside the bacterial cell, information produced by the many activities going on within the cell. Dr Lloyd-Jones points out that the rewards that will accompany a successful outcome are considerable.

The project is funded by the Foundation of Research, Science and Technology's New Economy Research Fund, which funds research capable of generating new wealth creating New Zealand enterprises. Lincoln Ventures Ltd and Landcare Research have put together a strong team to carry out the research with The Cawthron Institute, Lincoln University, University of Canterbury, University of Waikato, and the Christchurch Polytechnic Institute of Technology all providing specialist inputs to the project.

## Presentation Of The 2002 ZONTA Science Award

The seventh biennial Zonta Science Award will be presented to the winner by the Governor General, Dame Silvia Cartwright at Government House in Wellington on Tuesday 30 April at 6 pm. This award aims to promote the status of women in science. Judged by four leading scientists, and members of the wider community, the winner receives an around-the-world air ticket and $5000 cash to assist them pursue their science research, and a medallion designed by New Zealand artist, Tanya Ashken.

The presentation of the award will be followed by a dinner at Strawberry Fare. Tickets for both functions are now available. The cost of tickets to the presentation at Government House is $25 pp and the cost of the dinner afterwards is $28 pp (excluding alcohol).

## 2003 Royal Society Of Chemistry Australasian Lectureship

The New Zealand Institute of Chemistry calls for applications for the 2003 Royal Society of Chemistry Australasian Lectureship.

This lectureship, financed by an annual grant from the RSC to Australia and New Zealand, is held by a New Zealand resident every fourth year. The 1999 lecturer was Professor Bill Denny. The 2000-2002 lecturers were Professors Len Lindoy (University of Sydney), Paul Haddad (University of Tasmania) and Bill Kitching (University of Queensland).

The lectureship involves the recipient in lecture tours in Australia and New Zealand, coordinated by the respective RSC local representatives, Professors Graham Bowmaker (University of Auckland) and Alan Bond (Monash University).

The selection panel for the 2003 Lectureship will be Professor Graham Bowmaker (Auckland), Professor John Spencer (Wellington), Professor Leon Phillips (Christchurch) and Dr. Pat Holland (NZIC President).

Applications should include a CV, and an account of the work to be covered in the lectures. The major part of the work should have been carried out in New Zealand.

Nominations should be sent to:
Professor G.A. Bowmaker
Department of Chemistry, University of Auckland
Private Bag 92019 Auckland
The closing date is 31 July 2002.

## Gold Crest Wins Prize At Penang Young Scientists Congress

Linda Moore, one of the two New Zealand students selected to attend the SEAMEO 3rd Young Scientists Regional Congress in Penang, has won the prize for the "Best Impact on the quality of the environment or society" with her project "In The Zone". Eighteen exhibitors representing 10 Australasian countries attended this congress, the most prestigious event of its kind in South East Asia.

Linda, a student at Morrinsville College for the past 5 years, worked on her investigation for 2 years and was presented with her Gold CREST Award by the Hon. Pete Hodgson, Minister for Research Science and Technology, at the Genesis Energy National Science and Technology Fair last year. Linda's work also won her a place at the Genesis Energy National Science and Technology Fair in 2000 and 2001. She is enrolled this year for a science degree at the University of Otago. The Royal Society of New Zealand is grateful to support from Asia2000 to enable the New Zealand party of Linda and James Canny of Verdon College, Invercargill, to attend the Congress.

# *Guest Editorial* : Where to for the Institute?

Patrick Holland, NZIC President 2002

As incoming President it is part of my duties to take a look, with Council, at where we are heading as an Institute. At its most fundamental this question revolves around the services that we provide to our members who sustain the Institute through their subscriptions. The enrolment rate for new members is perhaps the key indicator of our attractiveness and current relevance to younger chemists but we must also be cognoscent of the needs of our existing members and suitably acknowledge our older members.

In reviewing our services we can take some pride as a profession in two current areas that reflect NZIC inputs and sponsorship. The revival of *Chemistry in New Zealand* over the past 6 months reflects not only the efforts of the new editor-in-chief but also the underlying enthusiasm of branch members in providing articles and news items. It is apparent that a readable, newsy journal is a key requirement of most of our members and I am sure the new system of diversified editorial responsibilities will ensure the continuing vitality of this service. The success of the "Molecules for Life" conference in Napier last December reflects credit principally on the good organization of the Manawatu conference committee. However, it was also very encouraging to see the enthusiastic participation of so many chemists young and old. The combined format of the conference (NZIC, NZSBMB, NZBA and BIOTENZ) was undoubtedly a strong success factor and this is a signal that needs to be heeded for future conferences and for the direction of NZIC.

One of the strongest inferences from the good response to the revived *Chemistry in New Zealand* and the recent conference is that we chemists are social animals. We need and enjoy outlets where personal interactions and information exchanges on chemistry related areas can take place in less formal ways than our perhaps high professional opinions or potentially 'geeky' research image might suggest. Not a startling insight but one that perhaps we need to take more account of in organizing our Institute 'business' both at national and branch level.

The changing nature of the chemistry profession and its contribution to the "Knowledge Society" are important drivers for changes in the way we interact and in our needs from the Institute. For many members chemistry is their base qualification whereas their profession may be leading to diverse fields of entrepreneurship or management. The career path may not involve much time at the laboratory bench. The drive to create more direct links from "innovation to wealth creation" is presenting challenges to teachers, research chemists, government and industry alike. The common thread for the Institute is the need for good means of communication at many levels and involving social, technical and professional components. Increasingly these interactions need to extend beyond both our immediate workplace and the realm of scientific publishing. Branch meetings, training courses, conferences and Web links can become key components of personal networking. Job-finding, job-training and facilitating some of the linkages necessary for development of high-tech companies and products are all areas where the Institute could be more active.

As part of our review of services to members, we include with this issue a survey form. We would appreciate your taking the time to complete and return the form so we can take account of your preferences.

# "Molecules for Life" 2001 NZIC Conference

*Andrew Brodie*
Chemistry – IFS, Massey University, Palmerston North

"Molecules for Life" has come and gone – was it a success? The organising committee knew it was taking a gamble in moving the conference from a university centre to a place that many people had never even been to! The other challenge the committee faced was to pull together a conference that would interest the members of the three participating societies (the New Zealand Institute of Chemistry, the New Zealand Society for Biochemistry and Molecular Biology and the New Zealand Biotechnology Association) sufficiently to come.

If you measure success by the total number of registrations – the conference definitely was! Over 400 people came, almost a quarter of whom were students who participated enthusiastically in all aspects of the meeting. If only our "political masters" could understand that there is an untapped reserve of young researchers who would be keen to contribute to New Zealand's "knowledge economy" given reasonable and realistic career prospects in science.

If you judge success by the quality of the scientific and social programme – the answer was yes! All plenary lectures were well attended, even those that had an 8.30 am start. And the fact that almost all of the social events were included in the registration fee meant you did not have to keep thinking about costs. You just enjoyed yourself.

If you judge success by the fine weather – it definitely was. There was a bit of rain to remind us we live in New Zealand but what else would you expect, even the sunny Hawkes Bay.

And if you judge success by the positive feedback from those of you that attended – the answer is a resounding yes! Several delegates said it was the best NZIC meeting they had ever attended. "I thought the conference went brilliantly, and that both the novel venue and the combination with other societies were excellent ideas," said **Leon Phillips**, 2001 President of the NZIC. "The plenary lectures were exciting and very valuable for someone like myself who has been out of touch with biology for a long time. The sponsored food was remarkably good (I know because a lot of people remarked on it), the poster sessions were interesting, the dinner was great, and the whole atmosphere was extremely pleasant. I wish more physical chemists had taken part, but you can't have everything!"

The meeting, held December 4-7, 2001, was based at the Napier War Memorial Conference Centre with lectures also being conveniently run across the road using the Century and Founders' Theatres in the Hawkes Bay Museum complex.

The conference opened on the evening of Tuesday 4 December with a session – "The Chemistry of Good Taste" aka a mixer – in the Ballroom of the Conference Centre. Crossroads Winery winemaker, **Malcolm Reeves** and NZDRI flavour chemist, **Justin Bendall** struggled to make themselves heard. Most participants appeared to be more interested in the practical side of the session rather than the theoretical, but those that listened to the speakers interludes did learn some interesting applied science.

The scientific sessions started the next morning with the opening plenary lecture by **Barbara Imperiali**, from the Department of Chemistry, MIT, speaking on her work on the *"Chemistry and Biology of Aspargine-Linked Protein Glycoslation"* (*see elsewhere in this issue*). She set a high standard for the other plenary speakers to match – which they did. For me the highlight was **Terry Collins** (Department of Chemistry, Carnegie Mellon University – see *Chemistry in New Zealand*, **2001**, *65(3)*, 15-17) with his lecture, *"Sustainability Science and the Economy of the Future"*. In this he challenged us all to think about the role of our profession in contributing to the sustainability of our modern civilisation. Each participant would have had a favourite lecture – for some it may have been **Ian Wilson** (The Scripps Research Institute, La Jolla) on *"The Molecular Basis of Combating Microbial Pathogens"* or **Chris Easton** (Research School of Chemistry, ANU- *see elsewhere in this issue*) on *"Cyclodextrans: Industrial Waste with Applications in Pharmacy, Catalysis and Microelectronics"* or **Ron Quinn** (Astra Zeneca, Griffith University) on *"Biotechnology: Natural Product Contributions to Drug Discovery"* or **Roy Tasker** (School of Science, Food and Horticulture, University of Western Sydney) on *"Research into Practice: Exploiting the Learning Potential of Interactive Multimedia for Visualisation"* or **Chris Sander** (Harvard Centre for Genomics Research, Boston) on *"Structural Genomics: The Protein Universe in 3D"* or **Arnold Demain** (Charles A Dana Research Institute, Drew University) on *"Antibiotics and Non-antibiotics: What's Old What's New?"*

I must agree with those of you who said there should have been some New Zealanders working in this country included in the plenary line-up. It would have given the young researchers present a chance to see that it is possible to do good science here, even though we do not have the resources available to us that all the overseas speakers have.

Each plenary lecture was followed by four concurrent sessions which covered many different themes, reflecting the interests of the three participating societies – Inorganic and Organometallic Chemistry, Biotechnology, Green Chemistry, Glycotechnology, Cellular and Molecular Biology, Physical Chemistry, Computational Biology, Structural Biology, Chemical Education, Electrochemistry, Bioactives, Fats and Oils, X-ray Crystallography, Molecular Design and Construction, and more. **Sally Brooker** (University of Otago) was presented with the NZIC Easterfield Medal, and talked about her metal-macrocycle research under the title, *"Running Rings Round Metal Ions."* A long standing tradition of NZIC conferences is the student paper competition and many of the winners have gone on to do very well in their subsequent careers. The winner at the 1988 conference, held at Massey University, was Canterbury PhD student, Sally Brooker! This conference's winner of the NZIC student oral paper competition was **Christopher Sumby** (University of Canterbury) with his lecture, *"Radiating New Directions in Molecular Architecture: The Synthesis and Coordination Chemistry of Ligands Containing a*

*[3]Radialene Core*" **Nick Lloyd** (University of Waikato) was awarded the prize for the best poster in the poster competition and **Richard Payne** (University of Canterbury) received second prize. A full report on the 2001 NZIC student oral and poster paper competitions and papers authored by the three prize winners appear elsewhere in this issue.

The NZIC specialist groups organised programmes – those from the organic and inorganic chemists being the most comprehensive. Three speakers in the Inorganic and Organometallic Chemistry sessions were from overseas: **Mike Ward** (Chemistry Department, Bristol University, UK) *"Self-Assembly in Coordination Chemistry: Anion-Templated Assembly of Supramolecular Cages,"* **Annie Powell** (Lehrstuhl für Anorganische Chemie II, Karlsruhe, Germany) *"Well Defined Polymetal-Oxo Cluster Aggregates as Building Blocks for Supramolecular Arrays"* and **Keith Murray** (Chemistry Department, Monash University, Australia) *"Molecular Magnetism: From Large Manganese Clusters to Extended Metal Dicyanamide Frameworks."*

The Chemical Education Specialist Group was revitalised at the conference as a result of an initiative led **Tony Wright** (Massey University) and interested members of the NZIC should be hearing more of its activities in the future.

The *Nanomaterials Symposium* was organised by **David Officer** (Massey University) to run in conjunction with the conference and this provided further choices for the less biologically inclined participants. It included physicists and chemists from Australia as well as local speakers all focussing on different aspects of nanomaterials. Keynote speakers in the symposium were **Gordon Wallace** (University of Wollongong) *"Nanocomponents: Enhancing the Performance of Electrofunctional Materials,"* **Burkhard Raguse** (CSIRO) *"Nanotechnology: From Molecules to Galaxies,"* **Paul Dastoor** (University of Newcastle) *"Polymers that Harvest Light,"* and **Leon Kane-Maguire** (University of Wollongong) *"Twists and Turns in Chiral Nanostructures."*

The success of any conference is dependent on the participant's satisfaction with the social programme and this meeting got the mix just right. The lunches were great with plenty for everyone, even the hungriest students. The Art Deco Walk led by Art Deco Trust volunteers was especially popular with the overseas delegates and gave them, and the rest of us that went on it, a real appreciation of the devastation caused by the 1931 Napier earthquake and the massive rebuilding programme that went on after it. The highlight was the conference dinner which had caused the committee a number of headaches as the number of registrants climbed past 300 and then 400. Where do you find a venue big enough to sit all these people? The answer was to hire a marquee which was erected on the foreshore adjacent to the conference centre. The food, again plenty, was served with precision and speed and satisfied us all. The singer, Erna Ferry, in an amazing non-stop performance, kept us entertained and got people up and dancing in the latter part of the evening. The "optional" dinner, held after the conference, at the Clearview Winery was popular and well attended.

The conference committee was fortunate to be able to attract some very generous sponsorship, including **Baldwin-Shelston Waters** (Gold Sponsor) and **Hort Research** (Silver Sponsor). This certainly helped to keep the costs down for the registrants and their financial assistance was much appreciated. The Trade Displays were held in the Ballroom where morning and afternoon teas were served as well as two of the evening functions. This pleased the participating companies as it meant delegates got plenty of opportunities to talk to the reps. The "Internet Café" set up by **Jeremy Dombroski** (Hort Research Ltd), was very popular.

All members of the conference committee worked hard to make sure this conference was the success it was but some people deserve special mention: **Mike Boland** (NZDRI) chaired the organising committee and kept us all on track as well as acting as treasurer. **Nick Robinson** (NZDRI) was the unflappable secretary, **Carol Taylor** (Massey University) did a great job on the abstracts and **Gill Norris** (Massey University) with her concern for detail, made sure many things of the things the rest of us would have forgotten about were attended to.

Mike Boland made the point that the conference was large for one that was not an international meeting. This was achieved by bringing together the members of three different scientific societies. Increasingly in modern science, important advances are not being made by groups in single disciplines working alone, but by multidisciplinary teams applying techniques and knowledge from several different areas. A nice example of this is provided by our own Nobel Prize winner, **Alan MacDiarmid** who, as an organometallic chemist, collaborated with a polymer chemist and a physicist. As he said[1] it was "an example of where 1 + 1 + 1 is more than 3!" This conference was an example of the same principle – the result was a much better meeting than anyone of the societies could have organised by themselves. An advantage of living in a small country is that is much easier to organise such events than in a large country where each discipline can readily get a critical mass by itself. I encourage future conference committees to build on the success of the Napier meeting and think beyond the traditional square. The next NZIC conference is to be organised by the Canterbury branch in 2003. The challenge is for them to make the meeting even better than Napier. It has been suggested Nelson would be a suitable venue!

**Reference**

1. MacDiarmid, A.G., *Chemistry in New Zealand*, **2001**, *65*, 8-17.

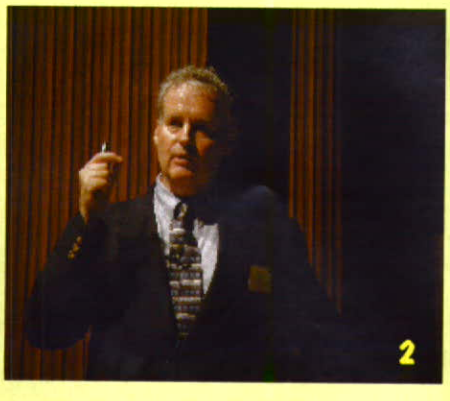
# "Molecules For Life"

## Conference Pictures










**Legend**

1. Andrew Brodie, Nick Robinson, Carol Taylor and Stan Moore on the Registration Desk. *(photo credit Trevor Loo)*
2. Terry Collins (Carnegie Melon University) delivering his plenary lecture. *(photo credit Trevor Loo)*
3. Sally Brooker with her Easterfield Medal. *(photo credit Andrew Brodie)*
4. Leon Phillips, 2001 NZIC President *(right)* hands over the chain-of-office to the incoming NZIC President, Pat Holland at the NZIC AGM. *(photo credit Andrew Brodie)*
5. Mark Patchett and Gill Norris decorating the marquee for the conference dinner. *(photo credit Andrew Brodie)*
6. Conference committee member, Barry Scott, at the conference dinner. *(photo credit Andrew Brodie)*
7. Graeme Gainsford (Industrial Research Limited), Catherine Dickson (Industrial Research Limited), Eric Ainscough (Massey University) and Derek Smith (University of Waikato) at the conference dinner. *(photo credit Andrew Brodie)*
8. Chris Sander (Harvard Centre for Genomics Research) and Ted Baker (The University of Auckland) at the dinner. *(photo credit Andrew Brodie)*
9. George Clark, Alison Clark, Warren Roper and Judy Roper (all from Auckland) at the dinner. *(photo credit Andrew Brodie)*
10. Conference Chairperson, Mike Boland relaxing at last at Clearview. *(photo credit Gill Norris)*

# Report on Attendance at 11th Annual Professors and Heads of Departments of Chemistry Conference (PHODS) Canberra, Australia 1-2 February 2002

At the invitation of Professor John White, President of the Royal Australian Chemical Institute (RACI), I attended the above meeting and presented a paper entitled "Chemistry in New Zealand". An invitation was also issued to the President of the NZIC to attend and have discussions with RACI representatives on matters of mutual interest, but it was decided that I should do this as well, and our President provided me with a list of matters to discuss.

The conference covered four main themes: new Government perspectives, University case studies, Australian Research Council matters, RACI matters. Government representatives were present to explain policy, and in some cases to defend policy against some fairly vigorous challenges from the meeting! Two of the RACI matters discussed were the accreditation of courses by the RACI, and RACI Corporate Membership. A recent survey highlights the considerable reduction in staff that has occurred in chemistry and other science departments in Australian universities over the last ten years. As a result, a number of chemistry departments in Australia have undergone (or are planning) a degree of integration or cooperation in order to continue to operate effectively in an environment of reduced resources, and a number of case studies (in Victoria, Perth and Tasmania) were discussed. The conference concluded with a panel discussion on "Maximising Opportunities for Australian Chemistry".

Some of the matters that I discussed with the President and other RACI officers are as follows with the questions having been provided by Dr. Pat Holland (NZIC President):

a) How successful are the benefits that RACI currently provide their members? *e.g.* loans, discount schemes for insurance, cell phones, professional indemnity.

   See RACI Website. We could try to organise some similar ones here - they might be of particular interest to our self-employed or small company members.

   They think it too early to say, but they still consider this an important part of their drive to increase membership from the current 8000 to a target of 12000. The fact that they have a National Director, Robert Barnes, with a strong background in business will no doubt be of great assistance in this.

b) Possibilities for some sort of joint membership to achieve a sub-set of mutual benefits *e.g.* receive each others journal, discounts for conferences.

   RACI is quite prepared to look at this. NZIC members get the same members' discount as RACI members at joint RACI/NZIC conferences, and I think that this might also extend to non-joint conferences, but this should be formalized.

c) More exposure for RACI in *Chemistry in New Zealand* and vice versa - articles, advertising for conferences and symposia.

   RACI is willing to cooperate in this way (see also point (d) below).

d) Other journal issues - viability; editorial work (comment positively on recent advances and the arrangement for Branches to take responsibility for particular issue numbers).

   *Chemistry In Australia* is also confronting the viability issue. John said that he thought that the corresponding Australian and New Zealand Physics Institutes journals had now combined, and saw this as a possible option for our chemistry Institutes. I left a copy of the latest issue of *Chemistry in New Zealand* with Professor Roy Jackson, Chair of their Journal Management Committee. I also presented copies of the two volumes of "Chemical Processes in New Zealand" to the RACI during the talk that I gave at the meeting. (I subsequently found that the New Zealand Institute of Physics and the Australian Institute of Physics had indeed combined their journals for about 5-6 years, the combined publication being called the *Australian and NZ Physicist*. However, this was unsuccessful and has now been discontinued. The content was predominantly Australian, and the cost was significantly greater for the NZIP members, many of whom are school teachers who found little of local interest or relevance, and who objected to the resulting higher membership subscription.)

e) Web site issues - ours is looking much better - how to deal with the 'coming soon' pages; how to keep updated regularly (theirs is currently <= mid-2001). Web publications (great that we have Chem NZ) and the need for 'members-only' access.

   RACI is very positive about web-based activities. The RACI Marketing Committee (contact: National Director, Robert Barnes) would be interested in cooperation. A project called "Outreach into Asia" involving electronic publications was mentioned, and they are wondering if the NZIC would like to be involved.

I was made to feel very welcome at the meeting, and I got the clear impression that RACI is keen to strengthen links with the NZIC. It was agreed that there should be a standing invitation for a New Zealand representative to attend the PHODS meetings in future to facilitate this.

*Graham Bowmaker*
Department of Chemistry, The University of Auckland
(e-mail: ga.bowmaker@auckland.ac.nz)

# CPC2002 – NZIC/ RACI Conference On Physical Chemistry

## Christchurch
## 3-7 February 2002

The conference was held at the University of Canterbury during a persistent spell of damp weather that helped to ensure full attendance at all the talks. There were just on 100 registrants, most from Australia and New Zealand but also including people from locations as remote as Hong Kong, Houston, and Newcastle-upon-Tyne. Partial support

for four of the plenary speakers was provided by the Royal Society of Chemistry, who was the conference's major sponsor. The event ran very smoothly with a remarkable absence of Powerpoint holdups. We (*i.e.* the organizing committee — see below) attribute this mainly to the expertise of graduate student **Mark Bart** who was in charge of the audiovisual system. The atmosphere of the conference was especially congenial, the programme unusually varied and interesting, and the plenary lectures outstanding. Many participants have since gone out of their way to say how much they enjoyed the meeting and, at the time of writing, it appears that it has resulted in a slight surplus of income over expenditure. Evidently we did something right!

The conference opened with the presentation of the 2001 Medal of the Division of Physical Chemistry of the Royal Australian Chemical Institute to **Professor Ken Ghiggino** of the University of Melbourne, who then gave his plenary lecture on photoinduced energy and electron transfer between the extremities of large molecules, with a lot of excellent basic science and obvious relevance to photosynthesis. The complete conference program is available from the author of this report. One thing, which will be apparent from the programme, is the unusually wide range of topics discussed, from Wigner intracules to the human genome, and this broad coverage was certainly an important factor in the success of the meeting. The challenging sessions of two-minute oral presentations by poster presenters, given just prior to their poster sessions, were greatly enjoyed by all except, possibly, the presenters themselves. A committee of Professors **Peter Gill, Jürgen Troe** and **Peter Geissinger** judged the student posters. First prize was awarded to **Duncan Wild** of the University of Melbourne, and "highly-commended" awards were made to **Rebecca Sampson** (Flinders University), **James Hutchison** (University of Melbourne), and **Nicola Gaston** (The University of Auckland).

The organising committee was **Leon Phillips** (chair), **Bryce Williamson** (secretary), **Colin Freeman** (treasurer), **Greg Russell, Peter Harland, Robert Maclagan, Rod Claridge** and **Murray McEwan**. The program committee was **Leon Phillips, Greg Russell, Henrik Kjaergaard, Murray McEwan** and **Douglas Russell**.

*Leon Phillips*
Department of Chemistry, University of Canterbury

# Protein Binding Studies Of Vitamin K Analogues For Use In An Immunological Assay

*Richard J. Payne* and Andrew D. Abell*

Department of Chemistry, University of Canterbury, Private Bag 4800, Christchurch

*Abstract*

An isotopically-labelled vitamin K analogue has been synthesised in six steps from commercially available menadione. Two coupling methods have been developed for the conjugation of this analogue to lysozyme. Novel detection methods of conjugates by electrospray mass spectrometry (ESMS) and liquid chromatography-mass spectrometry (LCMS) showed efficient coupling, with the binding of up to three analogues being observed.

## Introduction

The K vitamins are a family of essential lipid-soluble vitamins, comprising of several molecular forms. These compounds are widely distributed in nature and the major forms include the plant-derived phylloquinone (**1**) (also known as vitamin $K_1$ – Figure 1), and the menaquinones **2**, which are synthesised by bacteria.[1] These two forms of vitamin K differ in their substitution at the 3-position of the naphthoquinone ring.

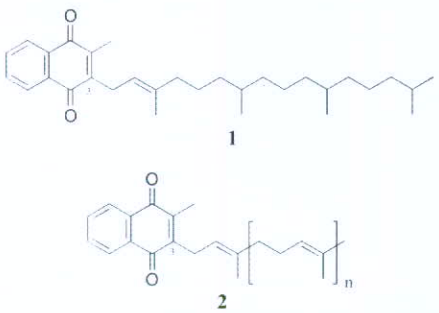


***Figure 1.*** Two major forms of vitamin K.

Methods for the measurement of vitamin K have been available since the 1980s with the development of physicochemical assays using high-performance liquid chromatography (HPLC).[2-5] However, problems exist with these assays in that they involve laborious sample preparation. Therefore, a more efficient method of measuring vitamin K in food and plasma samples is required. Here we present our initial studies on the development of an immunological assay for this purpose, known as an enzyme-linked immunosorbent assay (ELISA). This method offers the advantage of short sample preparation times and high-throughput screening, and is therefore considered an attractive alternative to HPLC.



### *Monoclonal Antibodies and ELISA Assays*

An ELISA assay requires the production of antibodies that recognise the antigen of interest, in this case vitamin K. In this method, a vitamin K-specific antibody is added to a sample of interest (plasma, breast milk, etc.) to bind the relevant antigen - in this case vitamin K. A second antibody labelled with an enzyme is then added. Formation of an enzyme-substrate complex produces a coloured product (yellow in Figure 2) which, when detected spectrophotometrically, gives a measure of the antigen (vitamin K) concentration in the sample (Figure 2).[6]

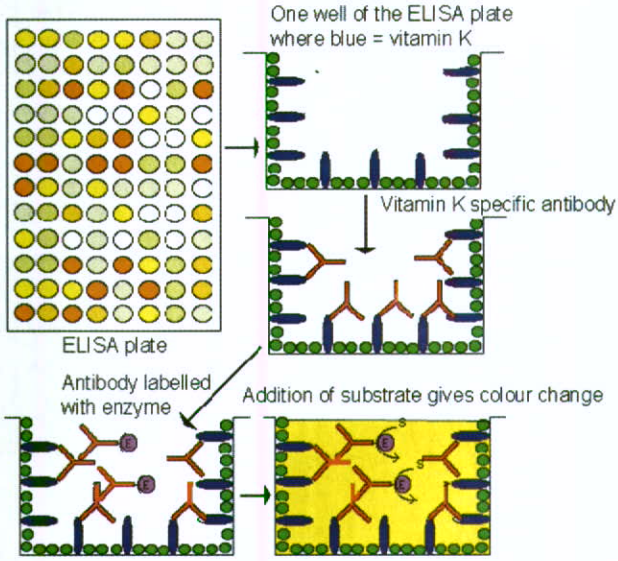



***Figure 2.*** Schematic of Enzyme-Linked Immunosorbent Assay (ELISA).

In order to develop an ELISA assay it is necessary, therefore, to produce monoclonal antibodies (MCAs) that recognise and bind vitamin K. This would involve the production of an immune response to vitamin K by an organism, *e.g.* a mouse, and then isolation of the associated MCAs. However, vitamin K itself cannot invoke an immune response in the organism, and as such cannot be used for this purpose. There are two main reasons for this. Firstly, it is non-polar and therefore not readily soluble in aqueous environments. Second and more importantly, the K vitamins are naturally occurring compounds and will not be recognised as foreign by the mouse. As a consequence, vitamin K must first be attached to a large molecule so that it is rendered water soluble and recognised as a foreign species by the mouse. In immunological terminology, vitamin K is known as a hapten, meaning that it is not itself immunogenic but can be rendered immunogenic if coupled to a larger carrier. Proteins are the molecular species often used to generate an immune response in this situation. Therefore, the ultimate aim of this project was to produce MCAs that specifically bind to the naphthoquinone core of vitamin K.

The process of MCA production involves innoculation of mice with a vitamin K-carrier protein conjugate, after which the β-lymphocytes produced are isolated from the spleen (Figure 3). As β-lymphocytes cannot be grown in culture they are fused with myeloma cells - a strain of rapidly dividing cells that may be grown profusely under specific culture conditions. The fused cells, called hybridomas, are separated by dilution to single cells and then grown in culture to give a series of cell lines each producing a single MCA. Each cell line is then screened for antibodies which recognise the naphthoquinone core of vitamin K. Those that specifically bind to the core are cultured further for the production of more antibodies.[7] It is proposed that these MCAs may then be utilised in an ELISA assay for the determination of vitamin K levels in plasma as described above. The initial step in the production of the required assay was, therefore, the synthesis of a vitamin K analogue with terminal functionality (X in Scheme 1), such as a carboxylic acid or amino group, which will allow conjugation to a carrier protein.[8]

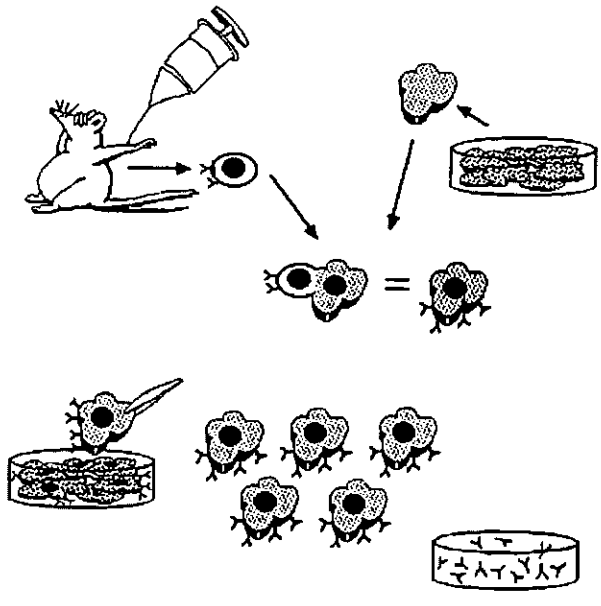
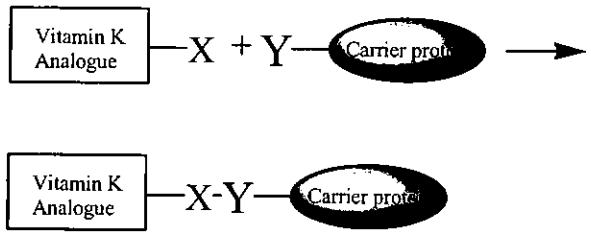


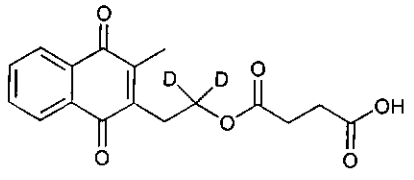
*Figure 3.* Schematic of monoclonal antibody production.




*Scheme 1.* Schematic of carrier protein conjugation to the vitamin K analogue.

## Results and Discussion

The initial phase of the research involved the design of a suitable vitamin K analogue that is capable of conjugation to a protein. Compound **3** was identified as the synthetic target as the carboxylic acid terminus could be attached to an amino group on the protein using standard chemical reactions. The analogue has the identical naphthoquinone core to natural vitamin K, but differs in substitution at the 3-position. It should be noted that a deuterium label was incorporated into the analogue to allow a future study of the protein-analogue conjugation by $^2H$ NMR spectroscopy.

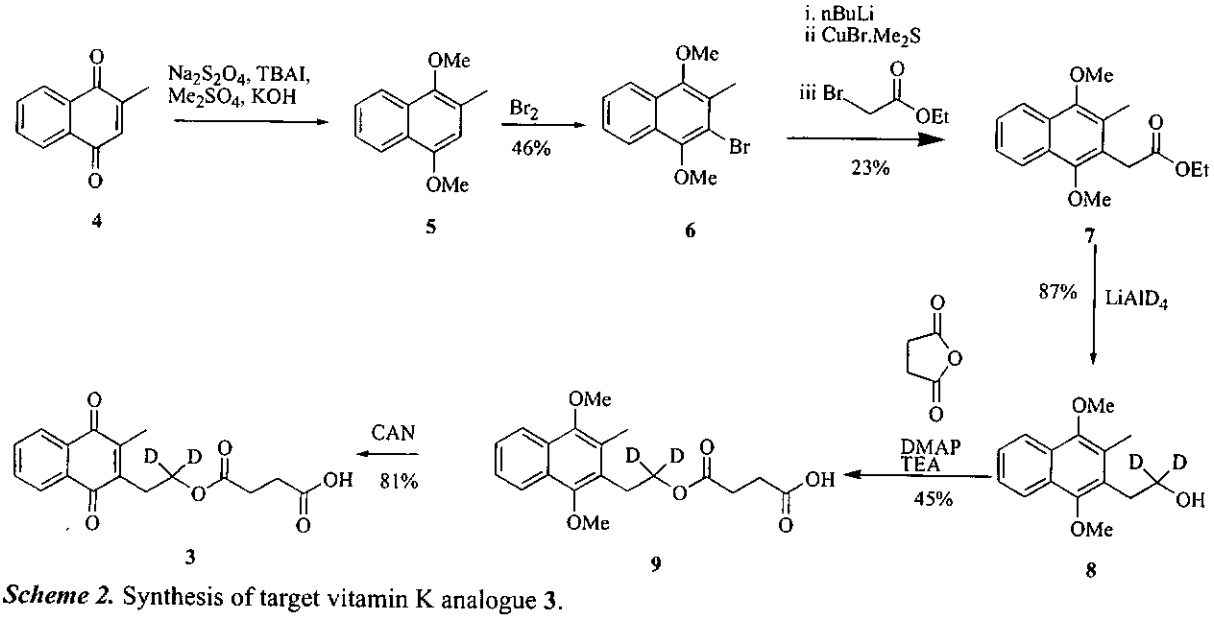



**3**

*Figure 4.* Target vitamin K analogue **3**.

### *Synthesis of a Vitamin K Analogue*

The vitamin K analogue **3** was prepared from commercially available menadione (**4**). The initial step in the synthesis required the preparation of a suitably protected naphthalene core. Quinone **4** was converted into the aryl bromide **6** via a novel two-step procedure. The first step involved reductive methylation using dimethyl sulfate and sodium dithionite with the use of the phase-transfer catalyst, tetrabutylammonium iodide (TBAI) to give the methoxy-




*Scheme 2.* Synthesis of target vitamin K analogue **3**.

protected quinone core **5** (Scheme 2). In the final step **5** was brominated to afford the desired aryl bromide **6** in 46% overall yield from **4**. The development of this method is significant in that the existing literature procedure for the preparation of **6** employs a 72 h bromination step.[9] The advantage of our method is that the bromination step is complete in 10 minutes and provides an improved overall yield.

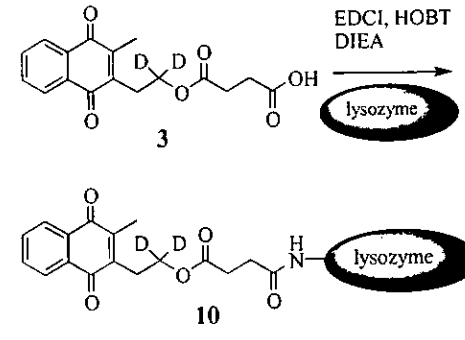
The next stage of the research involved the introduction of a suitable linker at the 3-position of **6**.[10] This was achieved by a cuprate-mediated coupling of ethyl bromoacetate to a lithiated equivalent of **6** via a copper dimethyl sulfide complex that gave **7** in 23% yield (Scheme 2). The literature method from which this reaction was adapted quoted a yield of 80% for an analogous reaction of **6** with geranyl bromide, however low yields were reported using methyl bromoacetate as the substrate.[11] In order to introduce a label into the vitamin K analogue to allow its subsequent detection in protein conjugates ester **7** was reduced with lithium aluminium deuteride. Alcohol **8**, labelled with deuterium at the 2-position of the hydroxyethyl group was obtained (Scheme 2).

The synthetic vitamin K analogue required the introduction of suitable functionality to allow conjugation to a protein. To achieve this **8** was reacted with succinic anhydride in the presence of dimethylaminopyridine (DMAP) to give the protected vitamin K analogue **9** in 45% yield (Scheme 2). Oxidative deprotection of **9** with cerium(IV) ammonium nitrate (CAN) afforded the desired vitamin K analogue **3** in 81% yield for use in the conjugation studies.

### *Coupling Studies*

The final phase of research concentrated on the coupling of analogues **3** and **9** to lysozyme (14.3 kDa). The coupling of the vitamin K hapten to a protein, in this case lysozyme, is crucial to the generation of monoclonal antibodies and hence the production of an ELISA assay. Lysozyme was used as a model in this situation as, although it is immunogenic, proteins such as bovine serum albumin (BSA) and keyhole limpet hemocyanin (KLH) are larger and produce greater immune responses in organisms. However, problems in detecting BSA-vitamin K conjugates in previous work[10] led to our preliminary studies on the smaller lysozyme protein. Two new methods were investigated for the coupling reactions.

In the first of these, termed the EDCI coupling method, lysozyme was dissolved in HCl/tris buffer (p*H*=8) and added to vitamin K analogue **3** (1.1 equiv.) in minimal DMF. To this was added dimethylaminopropyl ethylcarbodiimide (EDCI), hydroxybenzotriazole (HOBT) and diisopropylethylamine (Hunig's base) (Scheme 3). An electrospray mass spectrum (ESMS) and liquid chromatography-mass spectrometry (LCMS) analysis of the crude product indicated that a species corresponding to lysozyme plus one coupled vitamin K analogue had been produced (see Figure 5 where lysozyme conjugated to one molecule of **3** is apparent at 14,606 gmol$^{-1}$).




**Scheme 3.** EDCI coupling of **3** to lysozyme.

An alternative method for the formation of protein-vitamin K analogues was deemed necessary because of the low

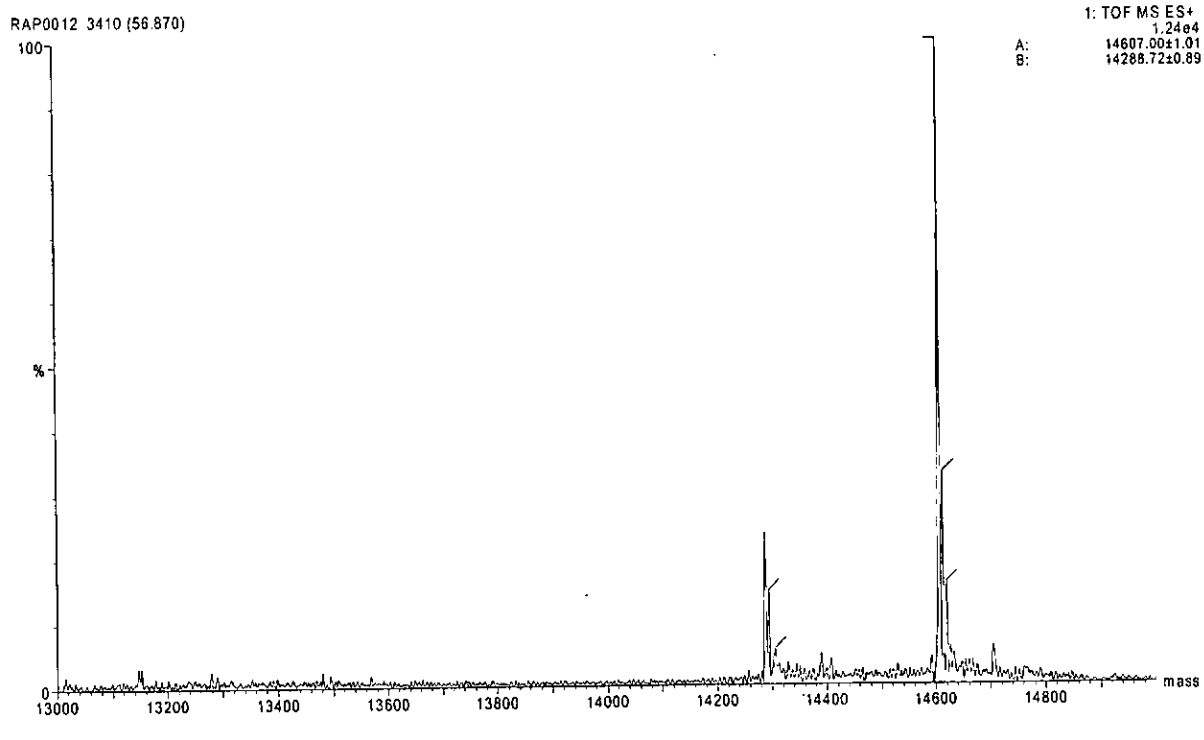
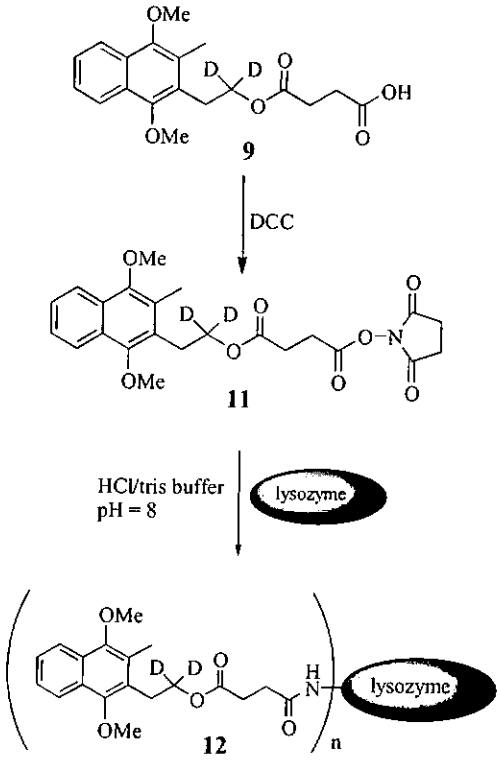



*Figure 5.* LCMS of lysozyme coupled to one vitamin K analogue.

yields obtained in the previous method. This was assessed from a relatively small conjugate peak compared to native lysozyme in the ESMS spectrum, as well as conjugation to only one analogue using the EDCI coupling methodology. Thus, the protected analogue **9** (1.1 equiv.) was coupled to *N*-hydroxysuccinimide in the presence of DCC to the activated ester **11** (Scheme 4). This was then coupled with lysozyme in HCl/tris buffer to give a conjugate that was analysed by ESMS and LCMS.




**Scheme 4.** Preparation of **11** and coupling to lysozyme.

The ESMS obtained showed species corresponding to lysozyme coupled to one, two and three vitamin K analogues (Figure 6a). Lysozyme coupled to one vitamin K analogue is apparent at 14,635 gmol$^{-1}$, two vitamin K analogues at 14,965 gmol$^{-1}$, and three analogues at 15,295 gmol$^{-1}$. The conjugates were then detected and separated by LCMS; Figure 6b shows native lysozyme with a peak at 14,305 gmol$^{-1}$. Figure 6c shows lysozyme conjugated to one vitamin K analogue with a peak at 14,636 gmol$^{-1}$ and Figure 6d that of lysozyme coupled to two vitamin K analogues with a large peak at 14,966 gmol$^{-1}$. Finally Figure 6d is that for lysozyme coupled to three vitamin K analogues with a peak at 15,299 gmol$^{-1}$. This succinimidyl ester method recently has been applied to the conjugation of **3** to the protein BSA. Preliminary LCMS results show BSA bound to three vitamin K analogues.

## Conclusions

We have developed an effective method for the synthesis of deuterium labelled vitamin K analogues suitably functionalised to allow for conjugation to a protein. Two methods were successfully developed for coupling to a protein (lysozyme); the formation of the conjugated species was quantified by ESMS and detected and separated by LCMS. The formation of protein-hapten conjugates have traditionally been studied using radioactive tracers and spectrophotomeric techniques.[12] The use of ESMS and LCMS techniques to detect conjugates is a much more efficient methodology to achieve this goal in the context of developing immunoassays and other related endeavours, in which formation of protein-molecule conjugates is desirable. The results obtained clearly show that the succinimidyl ester method is higher yielding than traditional EDCI coupling and will be used in future studies in this area.

## Future Work

Further work will be carried out on the coupling methods to the immunologically active BSA as it is commonly used for the development of ELISA assays. Protein-analogue conjugates are to be sent to the Canterbury Health Laboratories for immunological studies to be carried out. Moreover, the coupling methods developed are general and should be applied to various other systems in which an immunological assay may be desirable.


## Acknowledgements

The NZIC is thanked for their generous financial assistance in attending the Napier "Molecules for Life" Conference. We thank Mr Bruce Clark for his expertise with Mass Spectrometry and LCMS and the Marine Group in the Chemistry Department (University of Canterbury) for useful discussions on the coupling methods used in this research, and Dr Peter Elder for his help with the immunological studies.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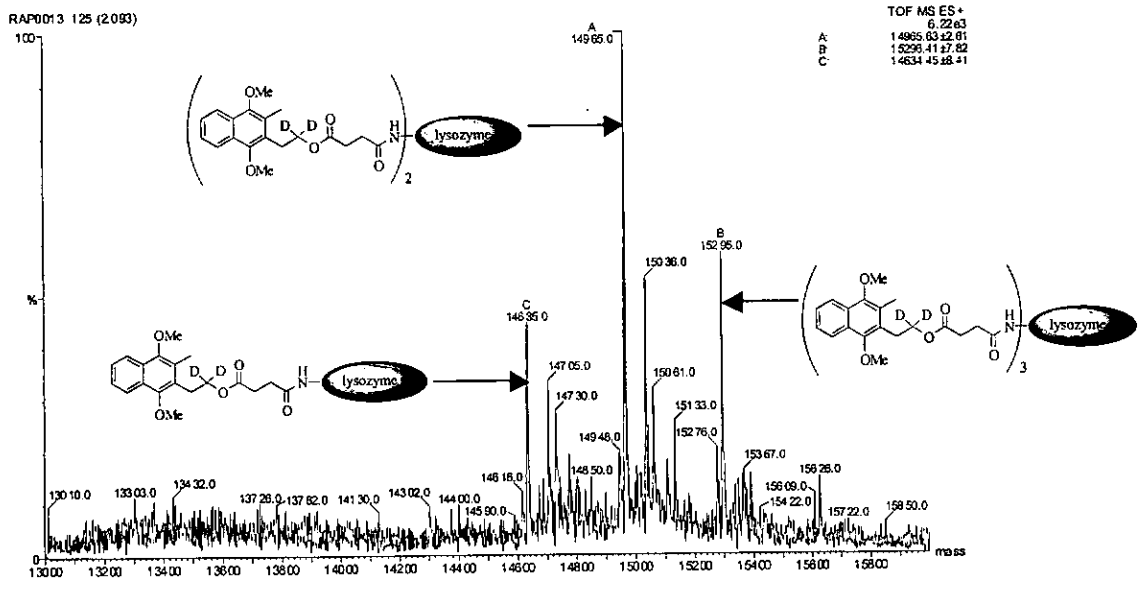


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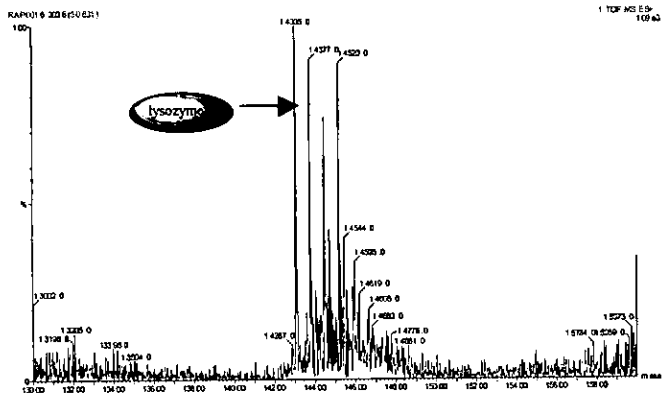


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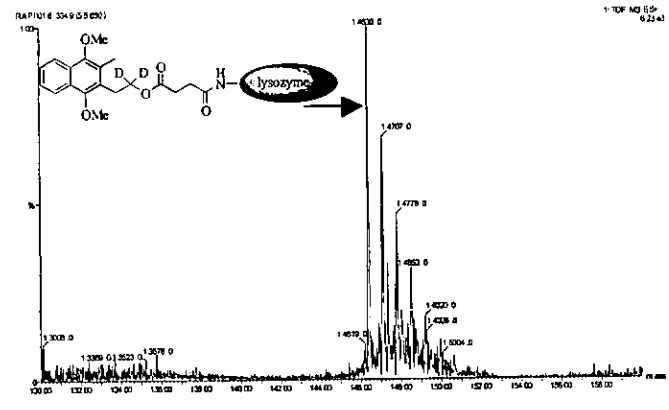


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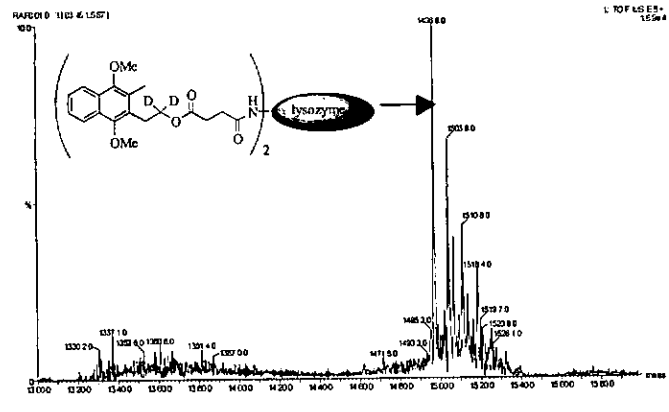


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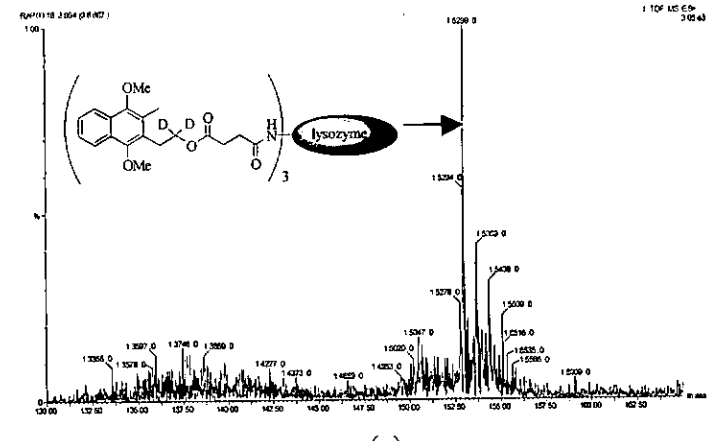



(e)

***Figure 6.*** Mass spectra of lysozyme-coupled products:
(a) Electrospray mass spectrum of crude product; (b) LCMS of native lysozyme; (c) LCMS of lysozyme coupled to one analogue; (d) LCMS of lysozyme coupled to two analogues; (e) LCMS of lysozyme coupled to three analogues.

# NZIC NEWS

## The 2002 NZIC Branch Chairpeople

### AUCKLAND

The 2002 Auckland Branch Chair is **Associate Professor Gordon Rewcastle** from the Auckland Cancer Society Research Centre (ACSRC) at the University of Auckland Medical School. This is Gordon's third year both as Branch Chair, and also as Auckland Branch Delegate to the NZIC Council, and follows an earlier appearance on the Branch Committee when he was Auckland Branch treasurer in 1984-85.

Gordon obtained his PhD in Organic Chemistry from the University of Auckland in 1978, and after postdoctoral study in the USA, he joined the Auckland Cancer Society's Research Laboratory in 1980. During the subsequent 22 years he has made a number of significant contributions to the anticancer drug development programme of the laboratory. These include having an active role in the development of the anti-tumour agents DMXAA (5,6-dimethylxanthanthenone-4-acetic acid) and CI-1033 (an irreversible inhibitor of the epidermal growth factor receptor), both of which are currently under clinical investigation.

The chemistry effort in the ACSRC involves a team approach; much of it in collaboration with Pfizer Global Research in the USA, and within this programme Gordon is the Group Leader of two projects in the separate areas of anticancer and antibacterial drug development. Previously, the design and synthesis of potent inhibitors of protein tyrosine kinases represented a major area of investigation, with this work culminating in the development of CI-1033, which first entered human clinical trials in 1999. Gordon made several important contributions to the design of this drug, and was responsible for performing the first chemical synthesis of it in 1997.

Gordon is the author or co-author of 72 scientific papers and 16 patent applications, and was the recipient of the NZIC/RSC Easterfield Medal in 1989.

### CANTERBURY

**Dr. Jan Waikaira** is the Chairperson for Canterbury this year. Jan grew up in Christchurch where she attended Cashmere High School for 4 years (all that her father felt he could afford). **Terry McCombs** was instrumental in getting her admitted to Teacher's College somewhat younger than the starting age and at age 18 her primary teaching career began at Christchurch South Intermediate. She was appointed Headmistress of Beckenham Primary school at age 22. While living in Palmerston (Otago) Jan was talked into taking over some classes at the local High School and her High School teaching career began. She subsequently taught maths, science and senior biology at Taumarunui High School for 11 years where she was 3rd Form Dean and Staff Representative on the Board of Governors.

Jan returned to Christchurch at a time when there was a huge teacher surplus (Mr Wellington managed to reverse that in 2 years) and could not get a full-time high school teaching job because she didn't have a degree. It was **Margaret Austin** who started Jan on her current career pathway by suggesting that she get a degree! Since the Education Department had declared that they were desperately short of teachers in maths, physics, chemistry, and economics Jan decide to try a part-time year taking the latter two. She was invited into the Economics Honours school but a decision to get "the 2nd year chemistry out of the way first" was to change her life for ever. She met up with a group of supportive and encouraging students who were so helpful that she stuck with them and went on in chemistry. She also has the highest praise for the staff of the University of Canterbury Chemistry Department who were really encouraging. A BSc seemed to be just a taste so Jan went on to do an MSc with **Graeme Wright**. This was followed by a PhD under the mentoring of **Vickie McKee** and **Ward Robinson**. As a graduate student she was part of the university Maori student mentoring scheme. After graduation Jan took up a postdoctoral fellowship at Brown University, Providence, Rhode Island, and in 1998 she returned to the University of Canterbury where she is a Senior Tutor, Stage One Mentor and manages the X-ray crystallography laboratory.

Jan has two daughters, a son and a grandson. Last year she married her long-time partner, **Don McNickle** who is New Zealand's only Queueing Theorist.

### MANAWATU

**Dr. Richard Haverkamp** is the Manawatu Branch Chairman for 2002. He is a Senior Lecturer in the Institute of Technology and Engineering at Massey University with responsibility for the BTech Chemical Technology programme. Before taking up his present position at Massey University in 1998, he worked at Colgate-Palmolive Ltd, Fletcher Challenge Ltd, DSIR, the University of Toronto, and was a lecturer in the Department of Chemical and Materials Engineering and Technical Director in the Research Centre for Surface and Materials Science at the University of Auckland. Dr Haverkamp has been on the Manawatu Branch committee of the NZIC for two years and this is his second term as Branch Chairman. He was elected to the Fellowship of the NZIC last year and is also a member of the Institute of Professional Engineers of New Zealand. If fact, he is Chairman of the local IPENZ branch committee and is on national IPENZ Board.

In 2000 he won a Futures Director's Award and was selected as the best teacher of undergraduate papers in his Institute. His present research interests cover the areas of process sensors, process improvement, and surface chemical and electrochemical reactions. The main techniques he uses in his research are atomic force/scanning tunnelling microscopy, X-ray photoelectron microscopy, electrochemistry and high temperature reactors. Companies extensively consult him and his comments, on topics ranging from "cattle gut racket strings" to "better roads" are often seen in the media.

## OTAGO

**Dr. Keith Gordon** is the Otago Branch Chairman for 2002. He is at present a senior lecturer in the Department of Chemistry at the University of Otago. He hails originally from Northern Ireland, and completed his BSc(Hons) and PhD at Queen's University, Belfast. He then spent two years at Los Alamos National Laboratory as a NATO postdoctoral fellow, and in 1993 came to Otago.

His research interests span Raman spectroscopy, electrochemistry and inorganic chemistry. He is pictured wearing the traditional Otago physical chemists' garb.

Keith's research interests cover the investigations of excited state structure using vibrational spectroscopy, drug polymorphs, and electroluminescent materials. The excited state structure of a compound, combined with the nature of the frontier molecular orbitals, is directly responsible for the photoreactivity of a compound. Using a combination of spectroscopic techniques and quantum calculations it is possible to probe and understand excited state properties. Such data may be used in the design of new smart materials. Keith's group uses vibrational spectroscopy to better understand how charge moves through thiophene-based conducting polymers, such as those used in plastic solar cells. An understanding of the molecular orbitals involved in these processes will assist in the design of better materials. This research is being carried out in collaboration with the Nanoscience Research Centre at Massey University.

His second area of research involves the polymorphic forms of drugs. These are of considerable interest because they can differ in their kinetics of adsorption and are patented as separate drugs. Keith's group, in collaboration with **Dr. Thomas Rades**, (Pharmacy Department at the University of Otago) uses Raman spectroscopy to quantify mixtures of polymorphs and they are developing experiments to observe polymorphic transformations in both crystalline and amorphous drug samples.

In contrast, electroluminescent materials are of considerable interest as they have the potential to take over from LCDs but utilise less electrical energy and can be made in full colour. The Gordon group is interested in using transition metal complexes in electroluminescent materials because of their high quantum yields for emission and chemical robustness. The utility of such complexes is studied by fabrication of bench test devices and their electrical and light emitting characterisation. The measurement of low concentrations of small molecules and ions may be accomplished by using highly emissive metal complexes. These may be designed to specifically interact with a target molecule or ion to radically change a property, such as emission. Under these conditions the emissive complex acts as a nanogauge for the environments being probed. Coupling the properties of the metal complex with a nanostructured substrate can also radically increase the sensitivity of the probe to the analyte of interest. (In collaboration with **Dr. Allan Blackman** (Chemistry Department at Otago) and the Nanophase Materials Group, Victoria University Wellington.)

## WAIKATO

**Dr. Richard Coll,** the Waikato Branch Chairman for 2002, completed his PhD in organometallic chemistry working with **Professor Jack Fergusson** at the University of Canterbury. After working as a lecturer in inorganic chemistry in the Pacific and Carribbean and a postdoctoral fellowship at Massey with **Professor Andrew Brodie** and his group, he joined the University of Waikato in 1995. Richard has recently completed a doctorate in science education from Curtin University of Technology working with **Professor David Treagust**. Richard's research interests are in the synthetic and structural chemistries of the platinum group metals. He joined the Center for Science & Technology Education Research at the University of Waikato and is presently Director of the Work-Based Learning Programme. His research interests in education are concerned with students' mental models of bonding and aspects of work-based learning. The US-based Co-operative Education Association recently awarded the Ralph W. Tyler Award to Richard for his research into work-based learning.

## WELLINGTON

**Professor Neil F. Curtis,** has taken the reigns of the Wellington Branch for a second time having been in the role during a part of the 1970s. Neil was born in Auckland in 1931 and was a student at Auckland University College of the University of New Zealand (as it used to be) from 1949 to 1955. He graduated BSc in 1952 (with a University Senior Scholarship, and a Duffus Lubecki Research Scholarship), MSc with First Class Honours in Chemistry in 1952 (with a University Research Scholarship and New Zealand University Postgraduate Scholarship in Science), and PhD in 1955. He then spent two years at University College, London, working with **Professor Sir Ronald Nyholm**, before being appointed to a lectureship in chemistry at the then Victoria University College in 1957. He remained at Victoria (which became Victoria University of Wellington) for the whole of his academic career, being progressively promoted to senior

lecturer, associate professor, and to a personal chair in chemistry in 1975. He served as Chairman of the Chemistry Department 1984-87 and retired in 1996. He is now an Emeritus Professor but still works a full day at the bench or writing papers.

In about 1970 Neil was elected to the Fellowship of the NZIC. He was an active member of the Branch Committee and served as Chairman. He was Chairman of the NZIC Conference Committee in 1979. In 1975 he was elected to the Fellowship of the Royal Society of New Zealand, and during 1981-1984 served as a Member Bodies representative on the Royal Society Council and Member Bodies Management Committee. He was elected Honorary Treasurer and Vice-President of the Royal Society 1987-1991. This was a time of major upheavals in the Royal Society and Neil was a member of the Ministerial Review of the Royal Society and was involved in negotiating the drafting of the new Act of the Society. He was Chairman of the Interim Council of the Society until this Act came into force in 1987. He was for many years the Royal Society representative on the National Science Fairs Board. He was awarded the Marsden Medal of the New Zealand Association of Scientists for his service to science in general and chemistry in particular.

Neil's research interests lie in coordination chemistry, particularly of amine compounds of the later transition elements. During research for his PhD he serendipitously discovered a reaction of simple components which produced a macrocyclic complex of nickel. This work, when published in 1961, initiated extensive studies that led to the discovery of many similar "template" reactions, in which amine and carbonyl compounds self-assemble around a metal-ion to form a ring with coordinated nitrogen atoms. Very many reactions of this type are now known, and there is an extensive literature on the subject. He has published some 140 papers on this, and related topics, including four reviews/book chapters.

# NZIC Branch News

## AUCKLAND

### The University Of Auckland

*Staff Achievements*

**Professor Peter Schwerdtfeger** has been awarded a James Cook Research Fellowship in the Physical Sciences. The two-year fellowship will allow Peter to work full-time on "The Search for Electroweak Effects in Molecules". The James Cook Research Fellowship is New Zealand's most prestigious award in science and technology. Peter was also the recipient of the 2001 Hector Medal in Chemical Sciences for his outstanding research in Theoretical Chemistry (*see elsewhere in this issue*).

**Professors Margaret Brimble** and **Graham Bowmaker** have been elected as Fellows of the Royal Society of New Zealand (*see page 8 in this issue*).

*Student Achievements*

**David Chen**, who completed his BSc(Hons) at the Department of Chemistry in 1997, has had his PhD work with **Ian Paterson** at Cambridge highlighted in *Angewandte Chemie International Edition* (November 2001). David had been working on the synthesis of the naturally occurring anti-tumour agent spongistatin 1, the most potent cytotoxic agent known. In the recent issue of *Chem@Cam* (Issue 13, Winter 2002), David's work was described as "one of the most remarkable total syntheses ever achieved in chemistry". David is now a post-doctoral fellow with **KC Nicolaou's** group at the Scripps Research Institute in San Diego. **Reuben Brown**, who has just completed his PhD with **Peter Schwerdtfeger**, has received an Alexander von Humboldt scholarship to undertake research in Theoretical Chemistry at the Technical University, Berlin.

Congratulations to **Daniel Furkert** and **Nicola Gaston** who were both awarded student prizes for presentations of their work at conferences. Daniel won a "best student oral presentation" prize at the RACI Annual Synthesis Symposium held in Melbourne on 7 December 2001 while Nicola won a highly commended prize for her poster "K-shell Ionisation Potentials" at the joint RACI/NZIC Conference on Physical Chemistry held in Canterbury on 3-7 February 2002. Nicola, who works with Professor Peter Schwerdtfeger, was the only student from a New Zealand university at this meeting to receive an award.

*Appointments and Promotions*

**Professor Douglas Russell's** 3 year term as Head of Department of Chemistry concluded at the end of 2001 and **Professor Graham Bowmaker** started his term on 1 January 2002.

Former NZIC Auckland Branch Secretary, **Dr. Jadranka Travas-Sejdic** has been appointed Research Assistant to the Pro Vice Chancellor of Tamaki, **Professor Ralph Cooney**. Jadranka is based in the Chemistry Department on the City Campus and will be assisting in the supervision of joint research projects with Professor Cooney. In addition, she will be involved in the establishment of the Centre in Molecular Electronics, along with teaching duties in Advanced Materials Chemistry. Jadranka graduated PhD from the Department in 1999 (under the supervision of **Associate Professor Allan Easteal**) and was previously employed as a Senior Project Manager at Pacific Lithium (NZ) Ltd. **Dr. Paul Kilmartin** has been promoted to Senior Lecturer and **Dr. Bob Anderson** has been promoted to Associate Professor from 1 February 2002.

*Three Births and a Wedding*

Congratulations to **Michelle Lai** and **David Appleton** who were married recently. Both Michelle and David are PhD students working with **Professor Margaret Brimble** and **Dr. Brent Copp**, respectively. Congratulations also to **Chi Zhang** (a PhD student working with **Associate Professor Allan Easteal**), whose wife gave birth to a daughter in October 2001; to **Marilyn Gabriel**, the Department's Purchasing Officer, who gave birth in December 2001 to a lovely bouncing boy, weighing in at 7 lb 9 oz and to **Dr. Adrian Blaser**, an Honorary Research Fellow, who is now the proud father of a daughter born on 31 December 2001.

*Bowls Away!*

The Department's inaugural indoor bowls pairs championship ended in a much anticipated and nailbiting final between the staff team "TBA2" (**Ron Bryant** and **Vern Rule**) and the student team "Wyatt-Angus" (**Cory Wyatt** and **Neil Angus**). Despite a shaky start, the very impressive TBA2 triumphed over Wyatt-Angus.

*Au Revoir!*

**Nicole van der Laak** has left for six months to begin her MSc work in France at Peugeot Citröen's research laboratories in Voujeaucourt.

## MANAWATU

The Manawatu Branch Committee for 2002 is as listed below:

| | |
|---|---|
| Chair | **Richard Haverkamp**, Massey University |
| Secretary | **Justin Bendall**, NZ Dairy Research Institute Ltd |
| Treasurer | **David Shillington**, UCOL |
| Council Delegate | **Carol Taylor**, Massey University |
| Branch Editor | **Andrew Brodie**, Massey University |
| Student Rep. | **Andrew Bent**, Massey University |
| Hawkes Bay Rep. | **Kath Fletcher**, retired chemistry teacher |
| Taranaki Rep. | **Lawrence Scott**, Contact Energy |
| Committee | **Barry Scott**, Merck NZ Ltd |
| | **Jeremy Dombroski**, Hort Research Ltd |
| | **Tony Wright**, Massey University |
| | **Geoff Jameson**, Massey University |
| | **David Harding**, Massey University |
| | **Stephen van Eyk**, NZ Pharmaceuticals Ltd |
| | **Grant Boston**, NZ Dairy Research Institute Ltd |

The first meeting of the year was a visit to the new Merck Ltd headquarters in Palmerston North, hosted by committee member **Barry Scott**, followed by a time of relaxation and socialising at the nearby 10 Pin Bowling Alley. The Branch Committee has planned an interesting year of events and branch members should have received their first newsletter by now detailing these; if anyone has not, then they should contact **Justin Bendall** at NZDRI (email justin.bendall@nzdri.org.nz). Branch members who were on the "*Molecules for Life*" organizing committee, chaired by **Mike Boland**, are now catching up with things after staging a very successful NZIC conference held in Napier in December 2001. The Branch sponsored students, **Aaron Marshall**, **Julian Adams**, **Rachel Anderson** and **Amy Watson**, to attend the conference with grants of $250 each.

**Landcare Research**

**Benny Theng** reports that he has been in Orleans for 4 months but is adjusting only slowly to the French way of life. That he says, in some respects, is reminiscent of New Zealand in the early 1980s. Remember those halcyon days before things got restructured, remodelled, and repositioned? With colleagues he is compiling the "*Handbook of Clay Science*." The majority of contributors that they have approached are positive and supportive and they are currently negotiating terms with a publisher, aiming to have the project substantially finished by mid-2003.

**Massey University**

Massey University opened its doors to the public on March 3 to celebrate its 75th anniversary. The College of Sciences had a great range of activities including a Chemical Magic Show performed by **Eric Ainscough** who is shown performing chemical magic! Fortunately the Marsden Lecture Theatre survived this but some of the audience may have suffered temporary hearing losses. Other activities put on by chemistry staff were testing home brew for its alcohol content, testing sunglasses for UV safety, weighing signatures and glass blowing demonstrations. Later in the year on July 5, as part of the anniversary celebrations, a reunion of all Massey University chemistry graduates will be held.

The *Annual Chemistry Research Symposium*, organised by **Carol Taylor**, was held on February 20. Postdoctoral fellows and graduate students all spoke about their research and then the day finished with dinner at a local Thai restaurant. The symposium gave an excellent overview of the wide-ranging research going on in chemistry at Massey University and served as an introduction and welcome to the 2002 Honours class. **Adrian Jull** has recently been appointed as a Senior Tutor in Chemistry and will be spending some of his time developing a programme for year 12 chemistry students to participate in on visits to Massey University. **Al Nielson** (Albany Campus) has recently returned from a very successful six months at Nottingham University working in the laboratories of **Martin Schröder**. Here he met up with former Massey staff member **Peter Gill**, who has the Chair in Theoretical Chemistry there. Recently, **Penny Brothers** (University of Auckland) visited and gave a very interesting lecture on her research titled "*Boron Porphyrin Complexes – More New and Unusual Structures*." **Wayne Campbell** has successfully defended his PhD in porphyrin chemistry and is now working as a research officer in the Nanomaterials Research Centre. New faces in the Centre are **Susan Habas**, a Fulbright Scholar from the University of California (Berkeley), and **Fiona Lynch** visiting (from Dublin City University, Ireland) as part of her PhD programme. Apologies to **Charlie Matthews**, who is working with **Emily Parker**, for getting his surname wrong in the last issue.

**Geoff Jameson** reports that the garden of biology, which is increasingly infested with chemists, is swarming with (g)nomes. At the 27th Lorne Conference on Protein Structure and Function and the preceding symposium on proteomics, both held not surprisingly at the seaside resort of Lorne, Victoria, Australia, the original gnome, genome, has spawned, somewhat truncated descendents, the prote-

ome, structure-ome, interact-ome, functio-nome, combi-nome, metabol-ome, and the list goes on. They are united by the eco-nome, the vast sums of money and economic restructuring needed to tend to their needs. More seriously, there is a widening gulf between the haves and have-nots of science. Clearly in New Zealand and to a lesser extent in Australia, we will have to think first and act second, rather than blast away indiscriminately. A structure-omics facility in Japan has six 800 MHz NMR machines, countless NMR machines in the 600-750 MHz range, and orders placed for 900 MHz and 920 MHz behemoths. A large group from Massey invaded Lorne, **Geoff Jameson** and **Emily Parker** from IFS along with PhD student **Julian Adams**, and **Gill Norris** and **Mark Patchett**, along with technician **Trevor Loo** from IMBS. The weather for much of the conference was more conducive to hot tea and coffee than to beer and wine, which flow liberally from the Trade Shows, held when the last lectures for the day finish at ~10:00 pm. Four posters were presented from the Massey contingent. Scientific notables were Nobel laureate, Robert Huber, and scientific knight, Sir Tom Blundell. Scientific highlights of a more chemical nature included Werner Kuehlbrandt (stunning electron microscopy images), Stan Opella (new NMR techniques for partially ordered systems), Richard Perham (molecular machines and a wonderful joke), John Moult (on CASP4, the on-going protein structure prediction project), Korda (on model-free force fields, so devoid of evolutionary bias that even a creationist in Arkansas could not object), Walsh (enzymatic assembly lines for polyketide and nonribosomal peptide - brilliant insights and chemistry), and Marilyn Anderson (plant cyclotides - circular polypeptides of novel biosynthesis and potent insecticides). By the end of the week, temperatures were rising into the 30s and for the first time in 27 years the conference dinner was held outside under the stars.

**Merck Ltd**

**Barry Scott** has just returned from a Merck Food and Environmental Sales and Marketing meeting in Bangkok. One product of interest was a new range of testing kits for in-process control for wine making. Merck also has strengths in testing for the drinking and waste water industries.

**New Zealand Pharmaceuticals Ltd**

Two new staff recently joined the Product Development Department at New Zealand Pharmaceuticals Ltd. **Janelle Carter** is a Massey University graduate who majored in biochemistry and physiological and molecular plant biology. **Jo-Anna Hislop** completed an MSc in the synthesis of flavour derivatives under the supervision of **Simon Fielder** of HortResearch and **David Harding** at Massey University. Jo-Anna also worked with David as a research assistant synthesising peptides. Their qualifications will complement the team's broad science skills base.

## OTAGO

The 2002 year started with a change of guard at the top. After two years as Branch Chair, **John Birch** has stepped aside and allowed **Keith Gordon** to make the step up from Branch Secretary. Paul Fawcett takes Keith's place as Secretary, and we welcome **Lyall Hanton** and **Steve Dickinson** (Student Representative) to the committee.

**Margaret Mills**, Head of Science at Queens' High School, and local NZIC committee member was recently awarded a New Zealand Science and Technology Medal. These medals are awarded by the Royal Society of New Zealand for "significant contributions to the advancement of science and technology". Margaret's contributions were made through the teaching of sciences and working to promote science.

**Paula Caradoc-Davies**, a former PhD student of Lyall Hanton, was recently awarded a three year FoRST Postdoctoral Fellowship for study in the Chemistry Department at Otago. Her research with Lyall will involve the development of methods for the design and synthesis of nanoscale "smart" boxes and cages. These materials will be designed to emit light when "empty" but quench their emission when they are filled on binding a guest molecule. Such materials may have applications in pollution sensing and control, and information storage.

**Sarah Webb** and **Professor Warren Tate** of the University of Otago Biochemistry Department recently published the paper "Heterosynaptic metaplasticity in the hippocampus *in vivo*: a BCM-like modifiable threshold for LTP" in the prestigious journal *Proceedings of the National Academy of Sciences of the USA*, along with co-authors from the Otago Psychology Department and the Howard Hughes Medical Institute at Brown University in Rhode Island. Their paper describes the role of protein synthesis in general and calcium-buffering proteins in particular in long-term potentiation (learning) in the rat brain.

The Otago Biochemistry Department played host to the triennial meeting of the ribosome research community at *The Dynamics of Ribosome Structure and Function* in Queenstown from January 27 - February 1. More than 160 scientists from Europe, North America, Asia and Australasia looked back on the recent elucidation of the atomic structure of the ribosome and looked ahead to the next challenges in understanding the biochemistry of protein synthesis.

**Henrik Kjaergaard** has just returned to the Chemistry Department following a sabbatical stint of seven months at the University of Colorado in Boulder. He spent this time investigating atmospheric water clusters. **Rex Weavers** is also a recent sabbatical returnee, in this case from six months in Melbourne.

**Barbara Duncan**, the senior teaching fellow in the Chemistry Department, announced her retirement at the end of 2001. Barbara arrived in the Department in 1990 as an experienced secondary school teacher and, over the past twelve years, has become an indispensable member of the academic staff. Her organisation of the first-year laboratory course and her tutoring of first-year students has been nothing less than extraordinary. During her time at Otago she has also instituted a "catch-up" course for students having a weak chemistry background, and over the past summer she organised and ran an inaugural bridging course in chemistry for the university summer school. I fear that we will only begin to truly appreciate Barbara's contribution to the Department after her departure, particularly when anxious first-year chemistry students seek assistance.

At the Inorganic and Organometallic Specialist Group (IOSG) AGM held at the recent NZIC conference in

Napier, **Associate Professor Sally Brooker** stepped down as Chairperson. **Dr. David Weatherburn** (Victoria University) has now taken up this role. **Dr. Graham Motson** (ex University of Bristol) has recently joined Dr. Brooker's research group, **Brookers Bunch**, as a Royal Society Postdoctoral Fellow. **Ian Hewitt**, currently a PhD student in **Professor Annie Powell**'s research group in Karlsruhe, is visiting Brookers Bunch for 5 months to further a collaborative project. **Dr. Udo Beckmann** (ex-MPI für Strahlenchemie) will be joining Brookers Bunch on 1 May as a Marsden Postdoctoral Fellow.

## WAIKATO

Waikato Branch has a host of activities planned for this year, a combination of regular and new events. The first planned event is the annual "start-of-year" BBQ for members and aspiring members. We also intend continuing our support for the Analytical Chemistry Competition and ChemQuest functions as well as supporting the Hamilton Science Fair.

University news centres, not surprisingly, on graduate completions and movements. **Michael Harvey** has just submitted his MSc on aminolysis reactions of thioesters carried out with **Lyndsay Main**, and is moving to ANU to do a PhD with **Professor Martin Banwell**. He will be the fourth Waikato graduate in the current Banwell group after **Dr. Brian Kelly** and PhD students **Gwion Harfoot** and **Rebecca Taylor**. Movements include **Nick Kim**, from Waikato University going to work at Environment Waikato where he is working as an analytical chemist. **Richard Coll** has just returned from four months sabbatical working in the area of chemical education. Richard worked with **Dr. Neil Taylor** at the School of Education at the University of Leicester and then spent two months in Thailand at Suranaree University of Technology (SUT) in Nakhon Ratchasima in the east of Thailand. SUT, like Waikato, runs a work-based learning degree in science and technology and Richard and his colleague **Dr. Dhirawit Pinyonatthagarn** looked at evaluation of work-based learning programs as well as aspects of internationalisation of work-based learning. Richard also moves on in June taking up a lecturing position in the Institute for the Advancement of University Learning at Oxford. **Jacinta Dalgety** (PhD, with Richard Coll) has secured a post at the University of North London. She took up the post in February and will complete her write up by the end of the year. The post builds on Jacinta's strengths in quantitative-based chemical education research that she developed during her PhD studies at Waikato.

Local CRI news has centred on travels, visitors and successes with external funding. **Bob Wilcock** (NIWA) has recently hosted **Professor Steve Chapra**, Tufts University, on a visiting scientist programme. They have utilised dissolved oxygen changes and productivity analysis to predict diurnal changes p*H* in streams, in which alkalinity is dominated by carbonate chemistry (most New Zealand streams in fact). Mesocosm experiments have been carried out with a number of different aquatic plants, enabling a closer examination of fundamental biochemical processes regulating the exchange of oxygen and carbon dioxide/bicarbonate in aquatic systems.

Last year **Robert Franich** (Forest Research) completed Phase 1 of a Master of Business Innovation and Entrepreneurship degree at Unitec, Auckland, and achieved the top average grade (A-) for assignments and projects for the year. For Phase 2, 3 and industry project, Robert Franich has been awarded a Bright Futures Enterprise Scholarship. The MBIE can be compared with an MBA, but with more emphasis on business creation from innovation, a pracademic degree course where science, technology, creativity, commercialisation, wealth creation and business meet. The Unitec MBIE is modelled on similar degrees from the Babson College, Boston MA, USA and Swinburne University of Technology, Victoria, Australia, and for a scientist, can be useful in cementing in the scholarship of entrepreneurship for application to the commercialisation of science.

**Michelle Goeth**, A science teacher at Rotorua Girls High School was awarded a Royal Society Teacher Fellowship for 2002, and is carrying out a study of the organic constituents of Lake Rotorua sediments, jointly with the University of Waikato, DOC, and Forest Research, Rotorua. This study was a direct outcome of a science symposium and public forum held in March 2001 in Rotorua and hosted by the Rotorua Branch of the Royal Society of New Zealand and the Lakes Water Quality Society, Rotorua.

During February 10-13, **Warren Grigsby, Jeremy Warnes, Michael Witt** and **Meeta Patel** of Forest Research attended the 25th Australasian Polymer Symposium, Armidale, Australia to further develop capabilities in polymer chemistry, particularly focused on adhesives chemistry at Forest Research, Rotorua.

**Rose Motion** from Papro, Forest Research, spent three months working at VTT Biotechnology in Helsinki, Finland, in 2001. This was part of an exchange of research staff working on a collaborative project on 'Antimicrobial biopolymer films'. Flexible films were formed from natural substances and a number of antimicrobial substances were incorporated into the films. The project was mutually beneficial and fitted within the packaging research frameworks of both participating institutes. Rose also gained an appreciation of the European packaging scene. It is anticipated that the collaboration will continue.

## WELLINGTON

November unexpectedly provided two Branch Meetings. **Professor Zvi Rappoport** (Hebrew University of Jerusalem), a sabbatical visitor to The University of Auckland, arranged to visit VUW and this encouraged us to persuade him to deliver his now famous lecture "*Chemistry on Stamps*". Despite relatively short notice a strong gathering welcomed him and were captivated by his superb discourse. It is hoped that the lecture may appear in a later issue of *Chemistry in New Zealand*. The more "regular" monthly meeting was held on the IRL Gracefield campus and **Dr. Marc Dalglish** of IRL spoke on "Ferroelectricity – a little chemistry and a lot of applications" at the Industrial Research Ltd Training Cottage on the Gracefield campus. Despite his title, Marc included quite a bit of solid state chemistry in his description of the fascinating and useful effects that follow from ferroelectricity. He illustrated the talk with specimens and demonstrations, including a shocking example of pyroelectricity. The IRL Fish Finder looked like a useful

application, but Marc could not be drawn on the details of its operation – presumably they are too commercially sensitive.

The Wellington Branch Committee for 2002 is:

**Chairman:** **Emeritus Professor Neil Curtis** (VUW)
**Secretary:** **Dr. Catherine Dickson** (IRL)
**Treasurer:** **Mr Alan Turner** (Consultant)
**Members:** **Dr. Suzanne Boniface** (Queen Margaret College), **Ms. Elizabeth Douch** (Tawa College), **Ms. Sue Freitag** (Opus International), **Dr. Graeme Gainsford** (IRL), **Dr. Vincent Gray** (Consultant), **Professor Brian Halton** (VUW), **Dr. W. E. (Ted) Harvey** (Consultant), **Mr. Rob Keyzers** (Student Rep.), **Dr. Peter Northcote** (VUW), and **Dr. Helen Palmer** (Baldwin Shelston Waters).

A select group of Branch members (limited to a total of 20) made a site visit on February 13 to the Schering-Plough animal vaccines production facility at Upper Hutt. After an overview of the company's operations by the manager (**Dr. Mark Baker**) the party was split into two groups, which were appropriately "suited up" before entering sterile areas. One group (led by **Paula Simmonds**) was shown through the fermentation area, and the other (led by **Ian Pawson**) through the ultrafiltration and packaging facility. At the close of the tours any malnourishment of the visiting party was sumptuously remedied.

**Dr. David Weatherburn** has taken over from **Associate Professor Sally Brooker** as Chairperson of the Inorganic and Organometallic Specialist Group (IOSG) of NZIC.

**BRANZ**

The first 12-month exposures of polymer materials have ended at four sites through the country, as a pilot to assess the feasibility of a polymer degradation map (akin to the atmospheric corrosion one produced by BRANZ). Accelerated weathering was also carried out on some of the materials using the BRANZ Atlas weatherometer, and the results from these accelerated tests will be compared to the naturally weathered samples. The NIWA climate database will be used to quantify the natural exposure conditions which the samples will have experienced. This work is funded by FRST. For more information, contact **Dr. Mark Jones**.

The BRANZ Atlas weatherometer is being de-commissioned after more than 20 years service, and is being replaced by a QSUN 3000 unit. This will mean BRANZ will still be able to provide a full set of accelerated weathering testing using the new unit and the existing QUV and salt spray units.

**Cawthron Institute, Nelson**

**Doug Mountfort** has been successful with Lincoln Ventures in the recent FRST tender for biosensor development. He currently has two young visiting scientists: **Marianne Matzke**, from Germany, and **Claire Debarnot** from France, researching biochemical aspects of biosensors.

**Jenny Smith** has received a L'Oreal/UNESCO fellowship and will visit France (Bernard Kloareg's group at Roskoff) to further her research on carbohydrate degrading enzymes. **Lincoln Mackenzie** has returned from six months sabbatical in Ireland. He assisted the Irish in investigations of marine biotoxins affecting their shellfish industry, particularly azaspiracids. Fortunately, these potent toxins have not been detected in New Zealand.

**Patrick Holland** and **Kirsten Todd** attended the 2nd International Conference on Hazardous Alga - Mitigation & Management in Qingdao, China, last November. The presentations on the new programme for biotoxin management in New Zealand based on LC-MS were received with great interest. The validation of a new multi-method for determination of 15 lipophylic toxins by LC-MS/MS has been completed and the method has been approved for regulatory use by MAF.

**Industrial Research Ltd**

There was good IRL representation at the most enjoyable NZIC Conference in Napier: **Drs. Mark Waterland, Catherine Dickson, Graeme Gainsford, Tony Davidson** and **Mr. Gabriel Ossenkamp** attended, the last gaining a high commendation for his conference poster in the student competition (see elsewhere in this issue).

**Ken MacKenzie** and **Jeff Tallon** have taken up joint appointments between IRL and Victoria University's School of Chemical and Physical Sciences, Ken as an Associate Professor and Jeff as a Professor of Physical Sciences.

The Applied Inorganic Chemistry, Ceramics & Materials Physics teams are being merged into one team, currently known as Advanced Materials and headed by **Dr. Bob Buckley**.

**Drs. Ian Brown** and **Glen Barris** attended the International Symposium on SiAlONs in Tomiura, Japan, last December. Ian was a member of the International Organising Committee and presented an invited paper; Glen also presented a paper. Ian took the opportunity to also visit ISEM (Institute of Structural and Engineering Materials) in Kyushu as well as Hitachi Metals Ltd and Krosaki Harima who are manufacturers of refractory ceramics. The CEO of ANSTO, Australia, **Professor Helen Garnett** visited the IRL Ceramics Team while on the campus.

**Dr. Neil Milestone** has been active in developing a new programme on potential utilization of $CO_2$ after separation, from industries such as cement and thermal electricity generation. In fact, activities in cementing systems have increased recently as both Fletchers and Carter Holt Harvey seek to develop new products. Input from the chemistry team lead by Neil provides vital input to these new ventures.

**Ulrike Wolf** has left AIC to return to Germany after 4 months with **Dr. Tim Kemmitt** as part of her degree training. Tim has been continuing to focus on commercial opportunities, visiting Australia, Auckland, and even the South Island, in search of the almighty dollar. Two other students have completed summer vacation projects: **Angela Gilmour** (Waikato) with **Dr. Cees Lensink** and **David Bones** (Canterbury) with **Dr. Najeh Al-Salim**.

**Victoria University**

The NZIC Wellington Branch Committee collaborated with the School of Chemical and Physical Sciences and presented a Secondary School Teachers' Day in November that attracted 46 participants from the southern North Island. The programme began with a talk by **Norman**

**Cates** of Weta Digital on the chemistry of the prostheses and make-up used in the production of the movie *The Lord of the Rings*. Norman illustrated his talk with several practical demonstrations and the audience had the opportunity to handle some of the prostheses and were able to compare the attributes of a pair of Hobbit feet made with two different elastomers.

The programme continued with lectures by John Hoberg (VUW) on strategies for teaching organic chemistry and Max Kennedy (IRL) on the biopharmaceutical and related industries in New Zealand. After lunch the teachers selected workshops from a range of topics including the determination of iron in food, the use of computer chemical drawing programs, and practical ways of making chemistry interesting to students.

The year began in earnest on February 7 when we saw the return to the campus of former pupil and Nobel Laureate **Professor Alan MacDiarmid ONZ FRS**. A joint function by the Science Faculty and Industrial Research Limited was held in the early evening at which the appointment of **Jeff Tallon** as Professor of Physical Sciences was announced. He and **Dr. Ken MacKenzie** have joint appointments with IRL and will be involved in the teaching and graduate programmes in Materials Science. The next day saw a VUW sponsored public forum "Science and Prosperity: Changing New Zealand Perceptions" taking the form of an open debate involving scientists in discussing the issues behind fostering and promoting New Zealand science and scientists to the world. In addition to **Professor MacDiarmid**, the panel included **Professors Paul Callaghan FRS, Gary Hook, Alex Malahoff,** and **Jeff Tallon FRSNZ** and **Dr. Val Orchard,** and **Ms. Jenny Morel**. **Professor Peter Englert**, Pro Vice-Chancellor and Dean of Science of the University chaired the forum. The lecture theatre at Old Government Buildings was filled to capacity with an audience that included not only the capital's scientists and policy makers, but also students from local secondary schools and from Victoria University. It was also encouraging to see the Governor of the Reserve Bank **Dr. Donald Brash** amongst the audience even if political representation was sparse. The panel responded to questions from the audience. These ranged over topics including the role of venture capital in the development of a high tech economy, the negative legacy of competitive research funding, the problems of attracting students into science, and encouraging young scientists to return to New Zealand after overseas training.

# NZIC Student Paper Competitions 2002

*Andrew Brodie*

Chemistry – IFS, Massey University, Palmerston North

The NZIC Student Paper Competition at the NZIC National Conference held in Napier last December once again showed that New Zealand has many enthusiastic young chemists carrying out exciting research. What's more, whether it be in an oral session or in a poster session, they are able to talk about it clearly and confidently. The judges of both the oral and poster competitions were most impressed with the high quality of the presentations which made their task very difficult. However, winners had to be chosen! These were announced at the conference dinner and the prizes, conference T-shirts and certificates, were presented to the student winners by the 2001 NZIC President, **Leon Phillips**.

*Papers by the winner of the Oral Paper Competition and the first two place-getters in the Poster Competition appear on pages 30-33, 52-53 and 16-20.*

Ed.

## *NZIC Oral Student Paper Competition*

The winner of the oral student paper competition was PhD student **Christopher Sumby** (University of Canterbury) with his paper, *"Radiating New Directions in Molecular Architecture: The Synthesis and Coordination Chemistry of Ligands Containing a [3]Radialene Core."* Christopher Sumby was born in Christchurch in 1977 and received his secondary education at Burnside High School before going on to complete a BSc(Hons) degree at the University of Canterbury in 1999. Since 2000 he has been working towards his PhD under the supervision of **Peter Steel** in the area of metallosupramolecular chemistry. He is a recipient of a New Zealand Vice-Chancellors' Committee Claude McCarthy Fellowship Award for 2002 and will use this to attend the 35th International Coordination Chemistry Conference in Heidelberg, Germany.

Since the conference, the research carried out by Sumby in collaboration with his supervisor has been published[1] and highlighted by David Bradley,[2] under the heading, "*Silver Platter in a Cage.*" Bradley writes,

*New Zealand chemists have used a new ligand to build a tiny cage around a silver platter. The platter carries a fluoride ion at its centre and is the first hexapodal prismatic metallosupramolecular assembly.*

*Silver cage compounds are not rare but only once before has a complex been synthesised in which the silver atoms were in a plane. However, the presence of a fluoride ion lying at the centre of the nanoscale silver salver surrounded by propellers of pyridine groups makes for an aesthetically pleasing and unique prismatic structure.*

*Peter Steel and Christopher Sumby of the University of Canterbury in Christchurch, New Zealand, point out that the programmed self-assembly of supramolecular compounds from bridging organic ligands and transition metal precursors has been a hot topic for at least a decade and all kinds of polygonal and polyhedral species have been produced. These various compounds are thought to have potential applications as functional materials, says Steel.*

*There is one particular polyhedron that had not until now been produced, in which a species of formula $M_nL_2$ comprised two ligands with several feet bridging n metal centres forms a hexagonal prism. Steel and Sumby set about adding this organometallic polyhedron to the chemists' shelf. They have developed an entirely new class of ligand based on a central radialene core with multiple heteroaryl substituents. These ligands, they believe will prove invaluable in the development of novel metallosupramolecular systems and have already demonstrated their worth in allowing them to create their caged silver platter system.*

The other students in the oral paper competition (with their lecture titles) were:
**Dan Furkert** (University of Auckland), *"Synthetic Studies Towards the Spirolides"*
**Aleksandra Muratovska** (University of Otago), *"Targeting Macromolecules to Mitochondria"*
**Cameron Evans** (University of Waikato), *"Analysis of Transition Metal Clusters by Electrospray Mass Spectroscopy"* and,
**Julian Adams** (Massey University) *"X-ray Structures of Bovine β-Lactoglobulin A Crystal Forms Grown at Low Ionic Strength."*

### *NZIC Poster Student Paper Competition*

There were 44 entries in the poster competition meaning the judges had a big job talking to each student and asking them questions. Presentation of the poster was important, but as most were done with PowerPoint or other software, the overall standard was very high. The winner of the first prize in this competition was first year MSc student, **Nick Lloyd** (University of Waikato) with his poster, *"New Stable Six-Coordinate Organotin Compounds."* Nick Lloyd was born in Tauranga and grew up there. He attended Tauranga Boys' College and was in the first cohort there to take the first-year University of Waikato Chemistry papers while still in the 7th form. He is currently studying for his masterate at Waikato and will complete his thesis at the end of 2002. His project, which involves novel higher coordination organotin compounds, is being supervised by **Brian Nicholson** and **Alistair Wilkins**. Nick also works part-time as a gopher for Landcare Research, Hamilton.

Second prize in this competition went to **Richard Payne** (University of Canterbury) with the poster, *"Protein Binding Studies and the Development of Immunological Assays for the Detection of Important Bio-Markers."* Richard Payne was born in Christchurch in 1980 and educated at Riccarton High School. In 2001 he completed a BSc(Hons) degree in chemistry at the University of Canterbury. The research for his honours project involved the synthesis of vitamin K analogues and conjugation of these species to proteins, with the overall goal to develop an ELISA assay for vitamin K. Liquid chromatography-mass spectrometry was used as a novel means of detecting these conjugates. His research interests are still in the area of biological chemistry and this year he has started a PhD at University of Canterbury with **Andrew Abell** in the area of enzyme inhibition but he hopes to spend some time at Cambridge University in the laboratory of **Chris Abell**. He has received a number of prizes including, University of Canterbury Senior Scholarship (2000), Haydon Prize in Chemistry (2000), C.E Fenwick Prize (2001), Charles Cook - Warwick House - Memorial Scholarship (2002), and a Canterbury Scholarship (2002).

The judges also awarded 4 Highly Commended Certificates to:
**Gabriel Ossenkamp** (Victoria University) *"Towards Functional Materials Through Surface-Esterification of Silica"*
**Meeta Patel** (University of Waikato) *"Polymer Chemistry Going Green"*
**Mary Gower** (University of Canterbury) *"Synthesis of Type II 3-Dehydroquinate Dehydratase Inhibitors"* and
**Yi Li** ((University of Waikato) *"Fructose-6-phosphate Phosphoketalase and the Detection of Bifidobacteria."*

Thanks must go to all the judges who made the hard decisions and to **Carol Taylor** for organising them and overseeing the competitions.

**References**


1. Steel, P. J. and Sumby, C. J., *Chem. Commun.*, **2002**, 322-323.
2. Bradley, D., *The Alchemist*, **2002**: http://www.chemweb.com/alchem/articles/1012295318709.html (accessed 14 February, 2002).


***Left:* Winners of the NZIC Student Paper Competitions.**
Back row standing left to right: Gabriel Ossenkamp (Victoria University), Yi Li (University of Waikato), Mary Gower (University of Canterbury), Meeta Patel (University of Waikato).
Front row kneeling left to right: Leon Phillips (2001 NZIC President), Christopher Sumby (University of Canterbury), Richard Payne (University of Canterbury), Nick Lloyd (University of Waikato).
(photograph credit Andrew Brodie).

# Radiating New Directions in Molecular Architecture; The Synthesis and Coordination Chemistry of Ligands Containing a [3]Radialene Core

*Christopher J. Sumby*

Department of Chemistry, University of Canterbury, Private Bag 4800, Christchurch, New Zealand

## Introduction

The controlled self-assembly of metallosupramolecular aggregates, constructed from multitopic organic ligands and transition metal components, is a rapidly expanding area of research.[1-7] In metallosupramolecular chemistry the metals act as a strong molecular 'glue' to bind together the organic ligands.[8] This methodology has resulted in a number of interesting topologies including molecular squares, ladders, cubes and helicates.[1] It is envisaged that these assemblies may be able to carry out a number of nanoscale processes allowing incorporation into potential molecular devices.[9-11] In this context we are engaged in the synthesis of a new class of bridging ligand that compose a central radialene core to which are attached multiple heteroaryl substituents.

Radialenes consist of cycloalkane cores to which are attached, to all ring carbon atoms, exocyclic methylene groups – thus they are per-substituted *exo*-methylenecycloalkanes.[12] The parent radialenes with the general formula $C_nH_n$ are shown in Figure 1. Radialenes have been of interest to both theorists and experimentalists because of their fascinating structures and their potential for novel electronic properties.[12] While radialenes have been known for 40 years,[13] the first hexa-aryl[13]radialenes were only synthesised relatively recently.[14-16]

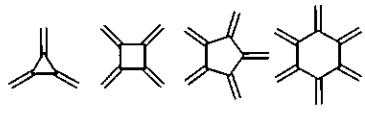
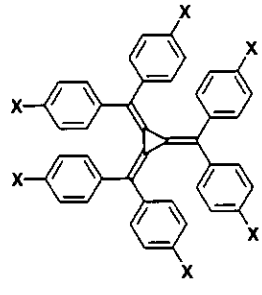


*Figure 1.* The parent radialenes.



X = H, I, Br, Cl, $NO_2$, CN, $CO_2Me$

*Figure 2.* Some of the recently synthesised hexa-aryl[3]radialenes.

We have recently undertaken the synthesis of a series of heterocyclic bridging ligands based around a [3]radialene core. This represents an extension of one of our research interests that involves the synthesis of multitopic bridging ligands based around arene cores.[17,18] A further attraction is that the [3]radialene based ligand, hexa(2-pyridyl)[3]radialene, is an example of the rare group of bridging heterocyclic ligands, shown in Figure 3, with a planar conjugated core capable of chelating to three metal atoms. The tritopic ligand hexa-azatriphenylene, is the most well known and commonly studied example of this group of ligand.[19,20] The only other example of this type of ligand is the triazine-based ligand, which because of its relative instability has received scant attention. We envisioned that trinuclear complexes of hexa(2-pyridyl)[3]radialene could show some novel metal-metal interactions through the highly unusual conjugated core.

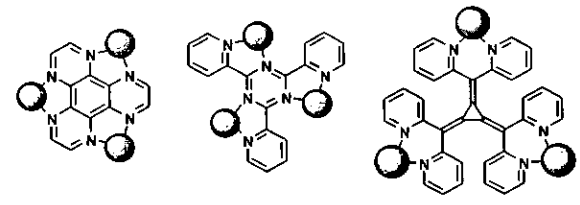


*Figure 3.* Complexes of trinucleating chelating ligands.

## Synthesis and Properties of Hexa-aryl[3]radialenes

There are two recently reported approaches to the synthesis of hexa-aryl[3]radialenes and the disconnections for these are shown in Figure 4. The first, and more generally applicable, method relies on the acidity of the methylene protons of diarylmethanes which can be deprotonated with n-butyllithium and the anions reacted with tetrachlorocyclopropene to give the hexa-aryl[3]radialene.[15] The second method is based on the cyclotrimerisation of copper carbenoids, which are generated from 1,1-dibromoalkenes, and has been used to prepare [3]- and [4]radialenes and dendralenes by varying the catalyst and temperature.[16]

We chose the first approach to synthesise hexa-aryl[3]radialenes because a key intermediate for the synthesis of one of the desired ligands, di-2-pyridylmethane, can easily be prepared from commercially available di-2-pyridylketone by a Wolff-Kishner reduction in high yield.[21] We have previously used di-2-pyridylmethane to synthesise tetrakis(2-pyridyl)ethane by an oxidative dimerisation with iodine and converted this compound to the novel ligand tetrakis(2-pyridyl)ethylene by treatment with DDQ in refluxing toluene.

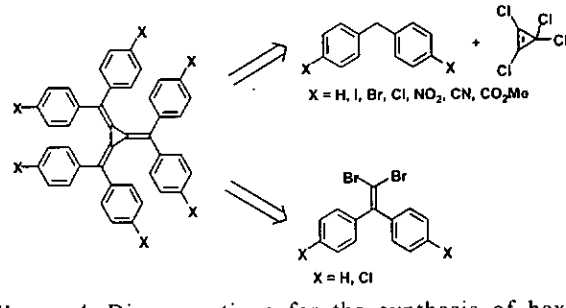
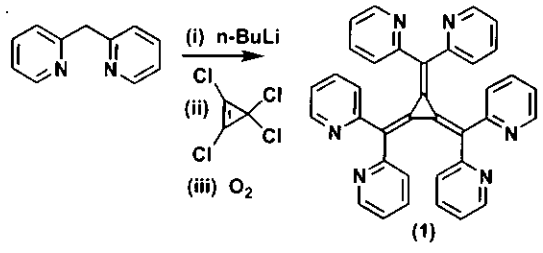



*Figure 4.* Disconnections for the synthesis of hexa-aryl[3]radialenes.

To synthesise hexa(2-pyridyl)[3]radialene (**1**) the anion of di-2-pyridylmethane was reacted with tetrachlorocyclopropene, as shown in Scheme 1 and then oxidised with molecular oxygen to give the [3]radialene in a good 72% yield. In a similar manner we have prepared hexa(3-pyridyl)[3]radialene (**2**).† We have also achieved the first synthesis of unsymmetrical hexa-aryl[3]radialenes and have prepared the unsymmetrical, **3**, and symmetrical, **4**, triphenyl-tri(2-pyridyl)[3]radialenes from 2-benzylpyridine and tetrachlorocyclopropene.




**Scheme 1**

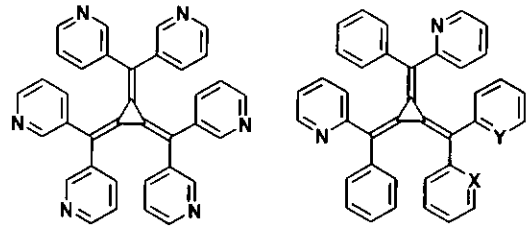



***Figure 5.*** The new [3]radialene ligands 2-4.

An X-ray crystal structure of **3** is shown in Figure 6. The bond lengths and bond angles are consistent with a cyclopropane structure and like other hexa-aryl[3]radialenes the molecule adopts a propeller-like conformation, in which the pyridyl and phenyl rings are twisted out of the plane of the [3]radialene core. In solution the hexa-aryl[3]radialene ligands also adopt a propeller conformation, similar to that shown in the solid state, as indicated by the unusually high-field shifts of the aromatic protons.

The electron withdrawing nature of the pyridine rings led us to believe that (**1**) would possess relatively low reduction potentials. There are two reversible reduction potentials to give the mono- and dianions respectively. The first process is cleanly reversible, while the second couple is less symmetrical and has associated with it a small oxidation peak at -0.7 V, the origin of which is not fully understood.‡ Table 1 shows that **1** and **2** have reduction potentials between that of the *p*-bromophenyl- and *p*-methoxyphenyl[3]radialenes. This result is somewhat surprising, because pyridine rings are much more electron withdrawing than *p*-bromophenyl and *p*-methoxyphenyl groups and should have reduction potentials akin to those of the *p*-nitrophenyl[3]radialenes.[15] However, as noted earlier, the pyridine rings are twisted out of the plane of the conjugated core and thus the strong resonance withdrawing effect of the pyridine rings has considerably less impact on the reduction potentials for the compounds.

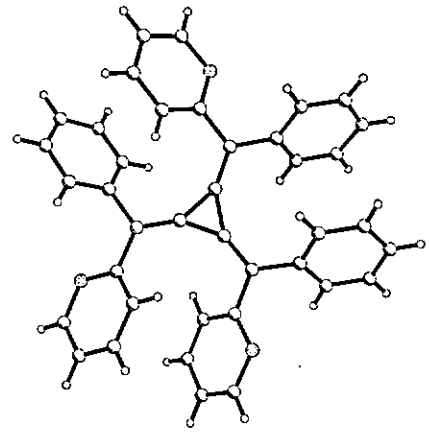


***Figure 6.*** A perspective view of **3**.

**Table 1.** The longest wavelength absorption maxima and reduction potentials of hexa-aryl[3]radialenes.[a]

| Compound | $\lambda_{max}$ (nm), log ε[b] | $^{1}E_{red}$ (V) | $^{2}E_{red}$ (V) |
|---|---|---|---|
| *p*-bromophenyl[c] | 485, 4.64 | -1.29 | -1.77 |
| **1** | 463, 4.40 | -1.20 | -1.55 |
| **2**[d] | 465, 4.48 | -1.17 | -1.64 |
| *p*-methoxyphenyl[c] | 488, 4.65 | -1.03 | -1.33 |

[a] Potentials measured relative to the $Fc/Fc^{+}$ couple (0.15 V) in dichloromethane with $(^{t}Bu)_4NPF_6$ as supporting electrolyte. [b] In dichloromethane. [c] Taken from ref. 15. [d] Taken from ref. 30.

**Complexes of Hexa(2-pyridyl)[3]radialene**

One can envisage a variety of modes of coordination for this ligand, which is isomeric with hexa(2-pyridyl)benzene but has a quite different spatial arrangement of the pyridine rings. Reaction of **1** with silver nitrate gave a complex **5**, the structure of which was determined using X-ray crystallography.[22] Two views of **5** are shown in Figure 7. The structure is a complicated coordination polymer with each ligand coordinating to four different silver atoms with a twisting arrangement along the coordination polymer. The silver atoms are in an approximately trigonal environment with silver-nitrogen distances of 2.206 Å and 2.209 Å. Two pyridine donors of the ligand are not involved in coordination. The ligands form a stack when viewed along the axis of the coordination polymer. Nitrate anions and solvent water molecules fill the voids between the stacked coordination polymers. The silver atom makes a weak contact with an oxygen atom of the nitrate anion, with a distance of 2.585 Å.

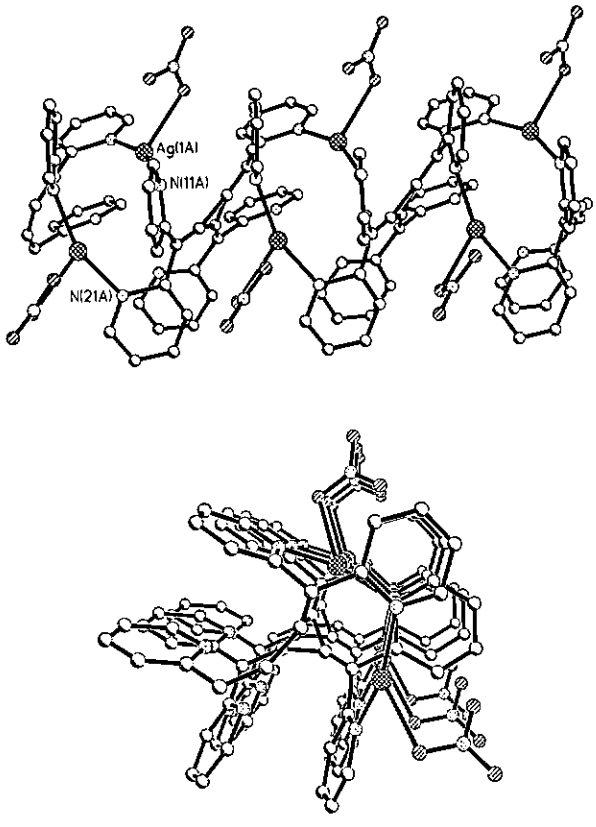



*Figure 7.* Two different perspective views of **5**.

By contrast when we reacted silver tetrafluoroborate with **1** the complex was found to have self-assembled into an $M_6L_2$ prismate cage **6** that encapsulates a templating fluoride anion.[23] This fascinating structure is a new example of the group of compounds shown in Figure 8 and called prismates. While there are a few reported examples of $M_3L_2$ and $M_4L_2$ prismates that have been prepared in the last few years,[24-27] the structure shown in Figure 9 is the first and only example of an $M_6L_2$ prismate cage.

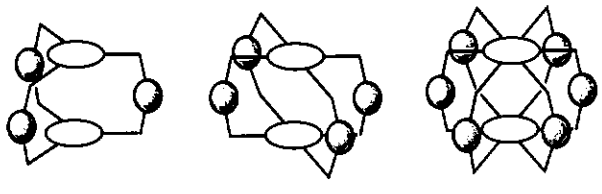


*Figure 8.* Representations of some examples of $M_nL_2$ prismates.

Figure 9 shows the $Ag_6(\mathbf{1})_2$ prismate, in which the ligand acts as a hexatopic donor to the silver platter in the middle of the ligand sandwich. The planar silver array surrounds the $m_3$-fluoride anion with three silver atoms coordinated with silver-fluoride bond distances of about 2.28 Å. The silver-silver internuclear distances vary from 3.30 Å to 3.64 Å in the structure, indicating very weak interactions between the silver atoms.[28] The complex is the first example of a planar silver-fluoride array and in addition there is an intriguing possibility of novel fluoride interaction with the [3]radialene core. The mean plane of the [3]radialene core is 2.70 Å from the fluoride anion suggesting a relatively strong interaction with the π-deficient [3]radialene core and the possibility of a three-centre-two-electron bond within the cage.[23,29]

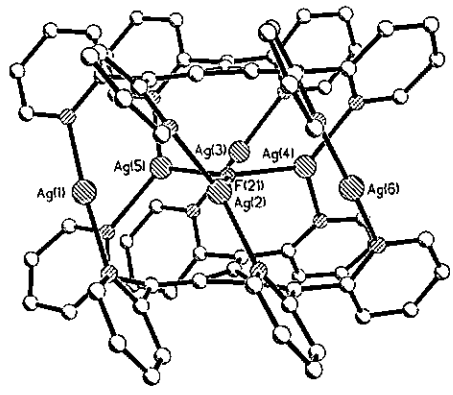



*Figure 9.* A perspective view of **6**.

X-ray crystallography on complex **7**, formed by reaction of **1** with silver hexafluorophosphate, revealed a coordination polymer of composition $M_4L_2$. Despite having the same stoichiometry as the silver nitrate complex, **7** has a different spatial arrangement of the atoms. The structure is shown in Figure 10 with $M_3L_2$ cages connected by bridging silver atoms. The outer silver atoms are trigonal planar coordinated by two chelating pyridine nitrogen atoms of one ligand and one pyridyl group of the other ligand, while the central silver atom is linear and coordinated by only one pyridyl group of each ligand. A fifth pyridine ring links the $M_3L_2$ cages together to form the polymer and the final pyridine ring of each ligand is uncoordinated. The silver-nitrogen distances within the cage structure range from 2.120 Å for the linear silver atom (Ag(2)) to between 2.180 Å and 2.321 Å for the trigonal planar silver atoms (Ag(1)) on the outer of the cage fragment. The linear silver atom (Ag(3)) is at a distance

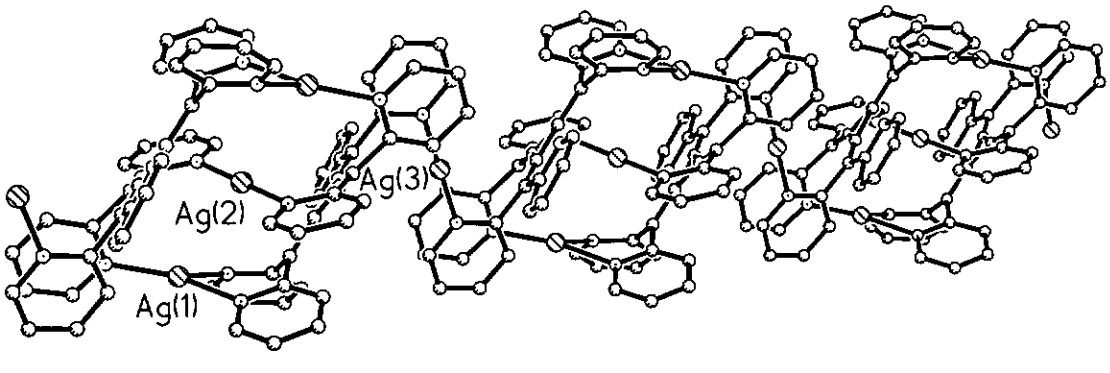



*Figure 10.* A perspective view of **7**.

of 2.140 Å from the nitrogen of the coordinated pyridine ring. The silver-silver distances are large (3.695 Å) indicating little or no interaction between the silver atoms within the cage.

### Conclusions and Future Prospects

The facile synthesis of some hexapyridyl[3]radialene ligands and their use in some fascinating coordination chemistry has been demonstrated. A variety of different structures were obtained by reacting **1** with silver salts and either coordinating or non-coordinating anions. Further work will revolve around extending the synthetic chemistry to allow for the incorporation of other heterocycles onto the [3]radialene core, and the synthesis of other ligands, like octa(2-pyridyl)[4]radialene, based around a [4]radialene core.


### Acknowledgements

I would like to acknowledge a few people for their help with this work, in particular my supervisor, Professor Peter Steel, for his guidance and Dr Alison Downard for her help with the electrochemistry. I also thank the University of Canterbury, the Royal Society of New Zealand Marsden Fund, and the Canterbury Branch of the NZIC for funding to attend the conference.


### References and Notes

† Recently, we have become aware that the group of Professor Oda at the University of Osaka has also synthesised both the hexa(2-pyridyl)- and hexa(3-pyridyl)[3]radialenes by a similar method.[30]

‡ In a personal communication Professor Oda has noted that he has made the same observation with both the 2-pyridyl and 3-pyridyl[3]radialenes.[30]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# Chemistry and Biology of Asparagine-Linked Glycosylation*

*Barbara Imperiali, Sarah E. O'Connor, Tamara Hendrickson and Christine Kellenberger*

Division of Chemistry and Chemical Engineering, California Institute of Technology
Pasadena, CA 91125, USA



***Abstract:***
*The biosynthesis of glycoprotein conjugates is a complex process that involves the collective action of numerous enzymes. Recent research on the chemistry and biology of asparagine-linked glycosylation in our group has been focused on two specific areas. These are the development of potent inhibitors of oligosaccharyl transferase and the investigation of the conformational consequences of the glycosylation process. Since asparagine-linked glycosylation is an essential eukaryotic process, an understanding of the details of this complex transformation is of utmost importance both to fundamental biochemistry and to a consideration of the mechanisms of homeostatic control.*

## Introduction

Protein glycosylation impacts both the functional capacity and structural framework of all glycoproteins.[1,2] The carbohydrate modifications of proteins fall into three general categories: *N*-linked modification of asparagine[3-5], *O*-linked modification of serine or threonine,[6] and glycosylphosphatidyl inositol derivatization of the *C*-terminus carboxyl group.[7] Each of these transformations is catalyzed by one or more enzymes which demonstrate different peptide sequence requirements and reaction specificities.

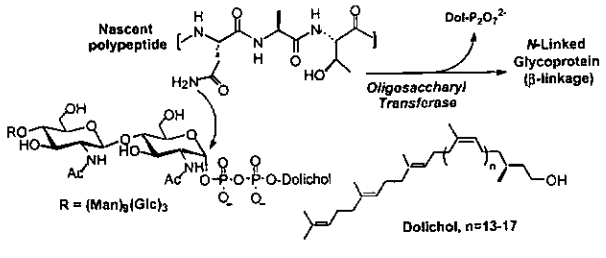


***Figure 1.*** Reaction catalyzed by oligosaccharyl transferase.

This paper will focus on *N*-linked glycosylation, which is the most common of the eukaryotic glycosylation reactions.[4] *N*-linked glycosylation is catalyzed by a single enzyme, oligosaccharyl transferase (OT), and involves the co-translational transfer of a lipid-linked tetradecasaccharide ($GlcNAc_2$-$Man_9$-$Glc_3$) to an asparagine side chain (in the consensus sequence Asn-Xaa-Ser/Thr) within a nascent polypeptide. The reaction is illustrated in Figure 1. This co-translational event occurs in the endoplasmic reticulum (ER) while the polypeptide is being biosynthesized on membrane-associated ribosomes. Approximately 14 residues of the nascent peptide must clear the luminal surface of the ER membrane before oligosaccharyl transferase-mediated glycosylation can occur, thereby implying that the active site of the enzyme resides in the soluble domain of the enzyme.[8] The subsequent diversification of these conjugates arises from enzyme catalyzed processing steps that occur in the ER and Golgi apparatus *after* the addition of the first triantennary oligosaccharide complex.

## The Role of Peptide Conformation in Asparagine-Linked Glycosylation

Oligosaccharyl transferase glycosylates at the tripeptide recognition sequence Asn-Xaa-Thr/Ser, where Xaa represents any of the encoded amino acids except proline.[9] Because *N*-linked glycosylation occurs before the nascent polypeptide has completely folded, the native protein structure presumably does not play a role in the recognition events that lead to this modification. However, since tripeptides can act as substrates for OT, the local secondary structure of the recognition sequence and adjacent peptide may well enable recognition by the enzyme and modulate the reactivity of the amide nitrogen that acts as a nucleophile to form the protein-carbohydrate linkage.

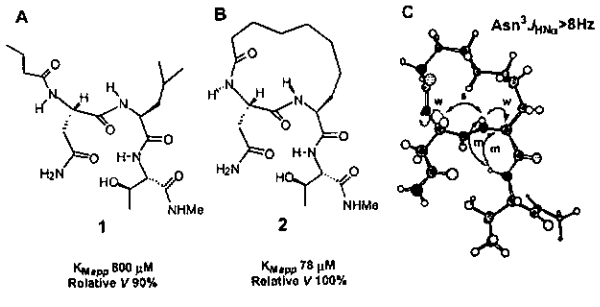


***Figure 2.*** Kinetic and structural analysis of oligosaccharyl transferase substrates. A. **1** - Linear Asn-Xaa-Thr tripeptide. B. **2** - Corresponding substrate constrained to an Asx-turn. C. Selected NMR data for solution state structural analysis of peptide **2** (strong (s), medium (m) and weak (w) ROEs as indicated were used in a simulated annealing protocol). The distinctive coupling constant for the asparagine NH-αCH was also used as a dihedral angle constraint in the structure determination.

The ability of oligosaccharyl transferase to recognize and glycosylate short peptidyl substrates has facilitated investigation of the structural requirements for glycosylation. Specifically, peptide analogs which contain the recognition elements of the consensus sequence, but which are constrained to specific conformations, such as β-turns or an Asx-turn, have been designed, synthesized, and analyzed for both solution state structure as well as proficiency in a standard glycosylation assay.[10,11] The parallel structural and kinetic analysis of these compounds has provided insight into the role of peptide conformation in asparagine-linked glycosylation. Figure 2 illustrates the kinetic and structural data for a flexible glycosylation

substrate **1** and the corresponding constrained analog **2**. These studies revealed that those peptides that were constrained specifically to an Asx-turn motif through a side chain to main chain macrolactamization as in compound **2** were more competent substrates for the enzyme than the corresponding linear analog **1**. It is noteworthy that the imposition of an Asx-turn constraint into the glycosyl acceptor peptide affords approximately a ten-fold improvement in the apparent $K_M$ for oligosaccharyl transferase. In contrast, peptides satisfying the Asn-Xaa-Thr/Ser tripeptide sequence, but constrained to various β-turn motifs through the cyclic hexapeptide architecture, failed to show glycosyl acceptor properties.[11] Thus, these studies with conformationally constrained peptides have led to the proposal that the recognition motif for *N*-linked glycosylation involves an Asx-turn.

The Asx-turn is characterized by a ten-membered ring hydrogen bonding network in which the hydrogen bond acceptor is the carbonyl oxygen of the asparagine side chain and the hydrogen bond donor is the backbone amide proton of the residue at (*i+2*) relative to asparagine (in this case the conserved hydroxy amino acid). This hydrogen-bonding motif is rather common in native proteins; approximately 18% of all asparagine and aspartic acid side chains appear to be involved in Asx-turns in proteins.[12] It should be noted that the homologous residue glutamine is never glycosylated and this apparent contradiction in reactivity may be explained by the distinct conformational preferences of this residue. Specifically, the carboxamide side chain of glutamine is seldom involved in short range hydrogen-bonding interactions.[12]

These conformational studies have formed a foundation for the development of a mechanistic model for the enzyme-catalyzed modification of the asparagine amide.[13] In this proposal, the unique hydrogen-bonding array provided by the Asx-turn is proposed to facilitate protonation of the carbonyl of the asparagine side chain while simultaneous, enzyme-mediated deprotonation at the nitrogen would effect the tautomerization of the carboxamide to an imidic acid or imidate species. Thus, tautomerization would afford a more nucleophilic species, which could in turn react with the electrophilic lipid-linked oligosaccharide (Figure 3). This mechanism incorporates both the issues of specificity and reactivity as well as the absolute requirement for a hydroxy amino acid by integrating substrate structural requirements with participation of enzyme active site residues. Thus, the likelihood of an Asn-Xaa-Thr/Ser sequence to undergo glycosylation would be governed by the ability of each potential substrate to adopt an Asx-turn conformation within the active site of the enzyme.

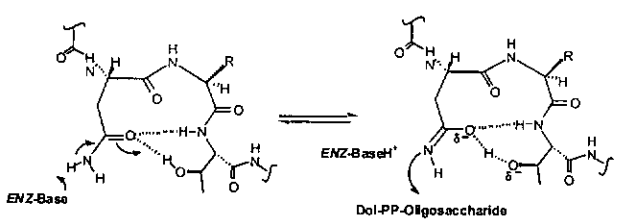


*Figure 3.* A proposal for the mechanism of action of oligosaccharyl transferase.

## Development of Potent and Specific Inhibitors of *N*-linked Glycosylation

The conformational and mechanistic studies with oligosaccharyl transferase have led to a number of related developments in our ability to understand the glycosylation reaction. An important observation in the tripeptide analog studies was that the replacement of the carboxamide functionality of asparagine with the corresponding reduced amine species (from the residue 1,4-diaminobutanoic acid - Dab) resulted in a peptide with weak inhibitory properties. For example, as illustrated in Figure 4, the linear tripeptide **3** shows inhibition of yeast oligosaccharyl transferase with a $K_i$ of approximately 1 mM. While the inhibitory properties of this peptide are rather weak, the kinetic analysis revealed that the mode of inhibition was clearly competitive. It was envisioned that improvement of the binding properties through further elaboration of the inhibitor structure could be achieved. The first critical feature of the inhibitor that was considered was the peptide backbone conformation. Since the Dab residue obviously lacks the critical carboxamide oxygen functionality that would promote formation of an Asx-turn, the Dab-Xaa-Thr motif was integrated into the constrained structure of inhibitor **4** (illustrated in Fig. 4).[10] This constraint was observed to improve the $K_i$ considerably to afford a tripeptide with a 100 μM $K_i$.

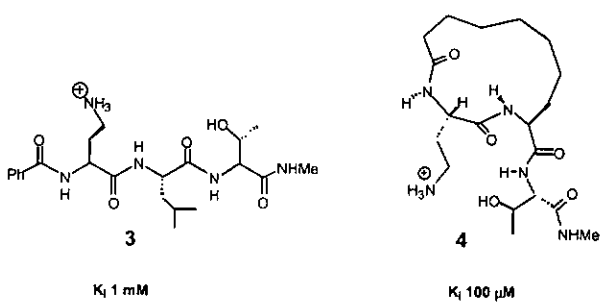


*Figure 4.* Competitive inhibitors of yeast oligosaccharyl transferase.

The further improvement of the peptide inhibitory properties was made possible by considering the fact that glycosylation substrates *in vivo* are not simple tripeptides, but rather, extended sequences with numerous residues flanking the tripeptide sequon in both *C*- and *N*-terminal directions. As the structure of oligosaccharyl transferase remains unknown it was not possible to use a rational approach to design the extended binding site. We therefore relied on the statistical studies of the sequences of *N*-linked glycoproteins as a guide for defining the ideal residues adjacent to the threonine of the tripeptide sequon.[14] Thus, the next phase of inhibitor development included elongating the peptidyl structures to provide extended binding determinants for interaction with oligosaccharyl transferase. Modification of compound **4** to include flanking *N*-terminal residues was not synthetically straightforward with the macrocyclic structure; however, extension in the *C*-terminal direction was quite feasible. In order to facilitate these studies, an efficient solid phase synthesis of this class of inhibitors was developed.

The synthetic approach to the family of extended binding inhibitors of oligosaccharyl transferase is outlined in Figure 5.[15] The key features of the synthesis of **4** that needed remediating before a comprehensive evaluation of the

utility of flanking residues could be carried out included a fairly challenging macrolactamization step and the use of the synthetic, non-natural amino acid α-aminodecanedioic acid (Add). Both of these features of the synthesis could be avoided if the critical cyclization was effected through the alkylation of a thiolate anion from the side chain of a central cysteine residue. The linear precursors to the constrained peptides could therefore be assembled by standard Fmoc-based solid phase synthesis protocols as illustrated in Figure 5. The final key steps in the assembly of the inhibitors include orthogonal deprotection of the cysteine thiol protecting group (tributylphosphine) of the resin bound peptide, followed by treatment with the mild base tetramethylguanidine to effect thiolate alklation by the 6-bromohexanoyl moiety. Using this chemistry, a family of sixteen pseudohexpeptides was prepared for evaluation as inhibitors of oligosaccharyl transferase.[16] All the inhibitors included a key, cyclic tripeptide core with the Dab amino acid as well as a nitrophenylalanine residue at the *C*-terminal position to allow facile and accurate quantification of inhibitor concentrations. The principal variation amongst the inhibitor structures was the identity of the flanking Xaa and Yaa residues. In this study we chose to assess placement of a basic (lysine), acidic (glutamic acid), neutral (valine), and polar, uncharged (threonine) residue at each of the Xaa and Yaa positions. Additionally, the peptides were all examined with both a fungal (yeast) and mammalian (porcine liver) oligosaccharyl transferase.

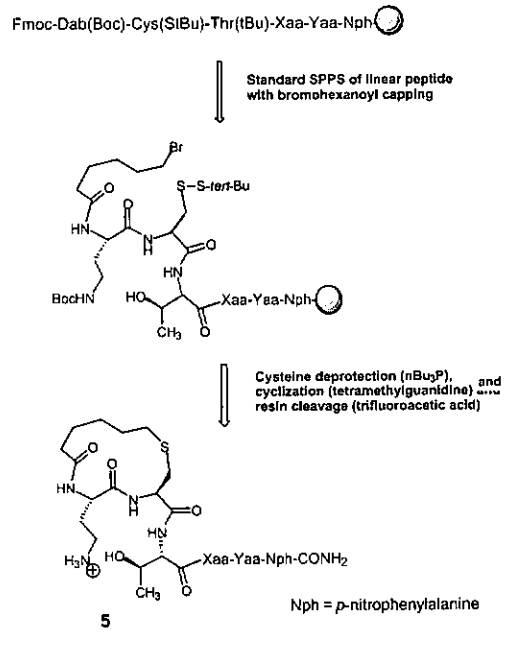


***Figure 5.*** Solid phase synthesis of extended binding inhibitors

The results of inhibition studies on the family of sixteen peptides that were prepared were quite dramatic. The estimated $K_i$ values for each of the inhibitors for oligosaccharyl transferase from both yeast and porcine liver are reported in Figure 6. $K_i$ values range from high μM to low nM, with optimum binding observed when the Xaa-Yaa residues are Val-Thr ($K_i$ 25 nM for yeast OT and 30 nM for porcine liver OT). In all cases, placement of the basic residue, lysine, at either position Xaa or Yaa, significantly deteriorates binding. The results from these studies are in remarkable agreement with the statistical analyses of Gavel and von Heijne[14] in their systematic study of peptide sequences of known glycoproteins in the protein literature. For example, at position Xaa, the most frequently observed residue is valine, and indeed the same residue was found as optimum in the inhibitor study. Similarly, the least frequently observed residue is lysine, and it is this residue that is found in this position in the poorest of the inhibitors.

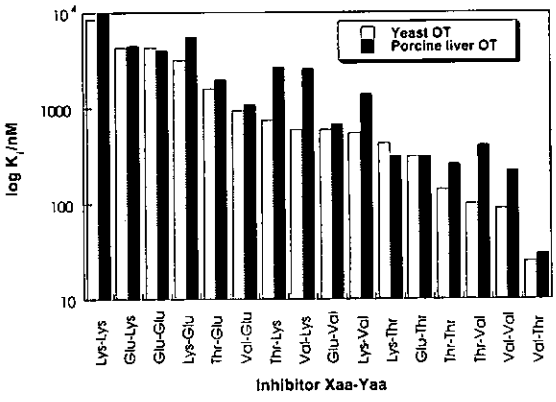


***Figure 6.*** Systematic evaluation of the inhibitory properties of the family of pseudohexapeptides related to peptide **5**. Residues Xaa and Yaa are varied as shown on the X axis.

An important feature of the studies concerns the efficacy of the inhibitors with the two different oligosaccharyl transferase preparations. The detailed genetic analysis of oligosaccharyl transferase from a number of different species reveals a complex oligomeric architecture that appears to be highly conserved throughout eukaryotic evolution.[5] It would therefore be anticipated that the cyclic tripeptide core would exhibit little species selectivity. However, this situation may not prevail with the extended binding determinants because there is less evolutionary pressure for the residues that interact with these determinants to be conserved. Indeed we observed that in some cases, *e.g.* Xaa-Yaa = Thr-Lys and Val-Lys, there was about a four-fold difference in the inhibition potency. These preliminary data suggest that it may be possible to design species specific inhibitors of *N*-linked glycosylation by exploiting the extended binding determinants.

While the peptidyl inhibitors that have been described are very potent for *in vitro* analyses of oligosaccharyl transferase activity, studies with these compounds in whole cell assays of *N*-linked glycosylation reveal the compounds to be ineffectual. This is presumably because the peptides are too polar and strongly solvated to be able to pass passively across the external cellular membrane and the ER membrane to gain access to the enzyme in its native cellular location in the lumen of the ER.

A current focus in our laboratories is the manipulation of the inhibitor structures to improve cellular permeability properties. These studies are timely because a specific cellular tool for inhibiting aspargine-linked glycosylation does not exist. Currently, the only inhibitor of *N*-linked protein glycosylation that demonstrates activity at a practical concentration is the microbial product tunicamycin.[17] However, the effect of tunicamycin on protein glycosylation is neither specific nor immediate because it functions by inhibiting the first step in the assembly of the oligosaccharide donor [Dol-P-P-$(GlcNAc)_2$-$(Man)_9$-$(Glc)_3$] essential in the formation of all asparagine-linked glycoproteins as illustrated in Figure 7. Furthermore, use of tunicamycin requires several cell

cycles before the supply of the donor is sufficiently depleted to arrest glycosylation. Catanospermine and members of the nojirimycin family of glycosylation inhibitors are also frequently used to probe the biological significance of cellular glycosylation.[18] However, like tunicamycin, these natural products do not function by inhibiting oligosaccharyl transferase directly; the molcular targets for these inhibitors are the processing enzymes that function to modify the structure of the triantennary tetradecasaccharide once it has been transferred to a nascent protein.

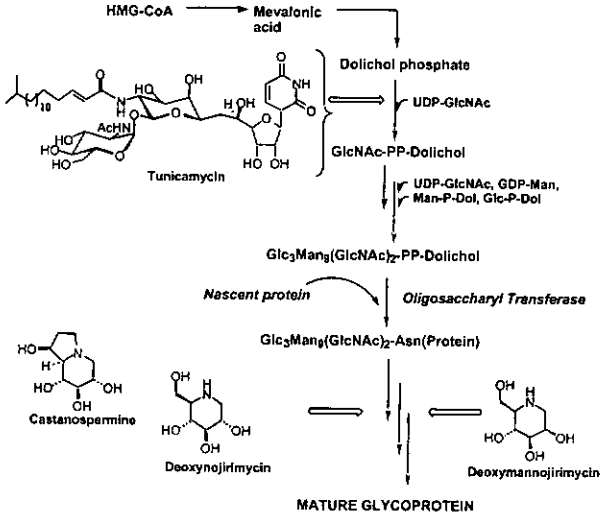


*Figure 7.* Survey of glycosylation inhibitors.

## Conformational Consequences of Asparagine-linked Glycosylation

An additional area of current interest concerns the study of the conformational consequences of asparagine-linked glycosylation. It is now evident that the co-translational timing of *N*-linked glycosylation can influence the conformational dynamics of the newly biosynthesized peptide proximal to the glycosylation site and that this structural modulation can potentially affect the subsequent folding of the glycoprotein product. The experimental evidence for this fact is derived from three types of experiments. First, the expression of glycosylated eukaryotic proteins in prokaryotic systems, which lack the glycosylation machinery, frequently results in the formation of aggregated or misfolded proteins. Second, the experiments involving deletion of glycosylation sites *via* site-directed mutagenesis have demonstrated the requirement of numerous *N*-linked glycosylation sites for proper protein folding. Finally, protein expression in the presence of the glycosylation inhibitor tunicamycin often results in misfolded proteins that fail to be secreted in a normal native conformation. It is not surprising that the large, hydrophilic carbohydrate moiety has a profound impact on the backbone structure of a polypeptide; numerous examples of glycosylation-mediated conformational change for both proteins and small peptides are available.[2] However, the structural details of the glycosylation-induced conformational changes have yet to be defined. The experiments carried out in this laboratory focus on the study of polypeptide segments that are patterned after glycosylation sites in native proteins. One peptide that has been studied in considerable detail by complementary spectroscopic methods is derived haemagglutinin from influenza A virus. These homotrimeric viral coat proteins are generally heavily glycosylated. For example, the 1968 Hong Kong X31 strain haemagglutinin has six glycosylated Asn-Xaa-Ser/Thr sites and it is estimated that 20% of the glycoprotein weight is carbohydrate.[19] A number of the glycosylation sites within each of the monomer units of haemagglutinin are strongly conserved and are found at β-turn motifs in the final folded protein structure.[19] We have carried out both fluorescence[20] and nuclear magnetic resonance (NMR) studies[21,22] on the segment of polypeptide that includes Asn-285. This glycosylated asparagine is found at the (*i+2*) position of a β-turn in the folded protein.

Initial experiments with this system included fluorescence resonance energy transfer (FRET) studies of appropriately derivatized peptides and glycopeptides representing the Asn-285 peptide sequence. Glycopeptides were prepared *in vitro* by oligosaccharyl transferase mediated glycosylation using the truncated glycosyl donor dolichylpyrophosphorylchitobiose.[20] These studies revealed that modification with the disaccharide had a significant impact on the polypeptide conformation in aqueous media. FRET studies suggested that the structure of the non-glycosylated peptide was fairly extended, as evidenced by the large interfluorophore distance. In contrast, the structure of the corresponding glycosylated peptide was significantly more compact with an interfluorophore distance of about 7 Å. The changes in the interfluorophore distances were consistent with a switch from an extended conformation to a compact turn conformation, strongly suggesting that glycosylation induced the adoption of a folded motif.

The results from the fluorescence studies encouraged us to pursue a detailed NMR analysis of similar systems with the goal of achieving greater insight into the molecular detail of the glycosylation induced conformational changes.[22] In this case the need for greater quantities of material necessitated the chemical synthesis of glycopeptides for study. Glycopeptide synthesis was effected using a modification of the methods developed previously.[23,24] Specifically, glycopeptides were prepared from the corresponding peptides in which an allyl-protected aspartic acid was substituted for the asparagine in the parent sequence. At the completion of peptide synthesis, the allyl group was deprotected using a palladium catalyst and then the glycosyl group was installed by coupling the resin-bound peptide with the appropriate unprotected glycosyl amine. The tendency for allyl esters of aspartic acid to undergo facile succinimide formation during the peptide synthesis necessitated the use of the 2-hydroxy-4-methoxybenzyl (Hmb) amide protecting group[25] on the glycine adjacent to the aspartic acid during the peptide synthesis.

**Ac-Orn-Ile-Thr-Pro-Asn$^{285}$-Gly-Thr-Trp-Ala-NH$_2$**
**6**

**Ac-Orn-Ile-Thr-Pro-Asn (GlcNAc)$_2$-Gly-Thr-Trp-Ala-NH$_2$**
**7**

The 2D NMR studies of peptide **6** and the corresponding glycopeptide **7** provided evidence that glycosylation with chitobiose, a disaccharide representing the first two β(1-4) linked *N*-acetylglucosamine residues of the native

tetradecasaccharide, induces the formation of a compact type I β-turn. The extended structure of the non-glycosylated peptide (**6** - Figure 8A) was found to resemble the Asx-turn which had been proposed to be important for oligosaccharyl transferase recognition. The more compact structure of **7** (Figure 8B), previously suggested by the FRET studies of the glycosylated derivative and supported by the NMR analysis, strongly resembled the type I β-turn found in the native protein. In the NMR analysis, NOE data were incorporated as distance restraints into a simulated annealing protocol to produce the illustrated structures (Figure 9A and B). The structure of the glycopeptide was remarkably similar to the structure found in the fully folded glycoprotein. Since approximately 30% of all glycosylation sites occur at sites which fold ultimately to β-turns,[26] this model peptide provides a relatively "general" context for the study of the conformational implications of *N*-linked glycosylation.

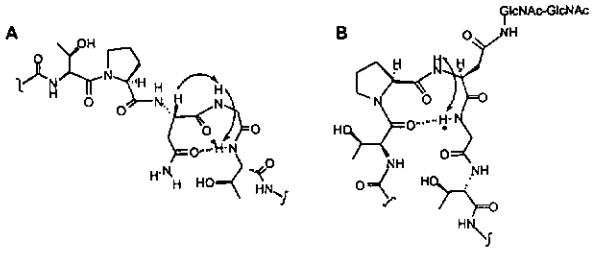


***Figure 8.*** Several strong key NOEs distinguish between an Asx and β-turn structure. Starred amide protons have a low variable temperature coefficient, suggesting the presence of intermolecular hydrogen bonds.

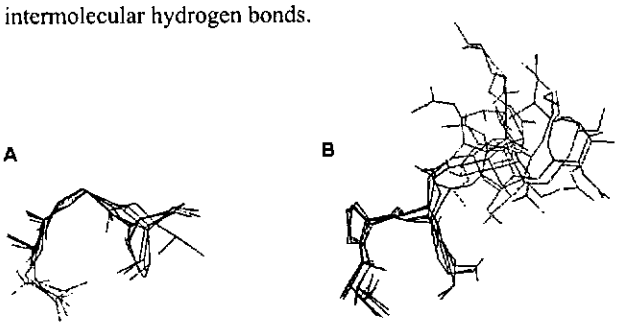


***Figure 9.*** Structures of **A** non-glycosylated and **B** glycosylated peptides derived from a simulated annealing procedure that incorporated all NOE data.

Despite the dramatic change in peptide conformation that was observed upon protein glycosylation, no obvious specific interactions between this peptide and the chitobiose moiety were observed in the NMR analysis. This suggests that the conformational changes observed after peptide glycosylation may be driven by either simple steric effects or by an alteration of the local water structure by the attached carbohydrate rather than by the formation of *specific* non-covalent interactions.

To further probe the nature of the interaction between carbohydrate and peptide, parallel NMR studies were performed on a family of glycopeptides in which key molecular elements of the sugar, specifically the C-2 *N*-acetamido groups, were modulated (Figure 10).[21]



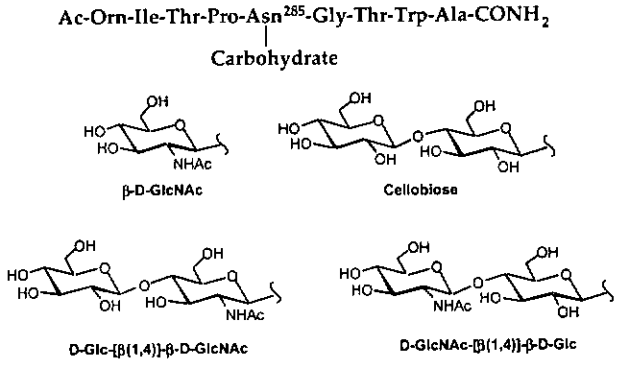


***Figure 10.*** Summary of glycopeptides studied by NMR.

The average structure of each glycopeptide in aqueous media was determined by examining NOE data and $^{3}J_{NH\alpha}$ values. To complement these structural studies, the conformational stability of the glycopeptides was assessed with $^{13}C$ $T_1$ relaxation values. These analyses revealed that chitobiose plays a unique role in modulating peptide conformation; no other saccharide appears to induce the native β-turn structure. Additionally, the chitobiose derivatized peptide appears to be more rigid at the glycosylation site than the other derivatives. The NMR derived structures of glycopeptides modified with cellobiose and D-Glc-[β(1,4)]-β-D-GlcNAc suggest that the *N*-acetyl group proximal to the peptide is critical for the induction of β-turn formation (Figure 11). Cellobiose, which lacks the proximal *N*-acetyl group, promotes a more extended peptide conformation (Figure 11A), while D-Glc-[β(1,4)]-β-D-GlcNAc (Figure 11B) promotes a β-turn structure. Since no evidence for a specific interaction between the carbohydrate and peptide was found, it would appear that the structural modulation is most likely effected through non-specific steric interactions. Surprisingly, the addition of an *N*-acetyl group may restrict rotation around the glycosidic bond, thereby promoting a more rigid carbohydrate conformation.

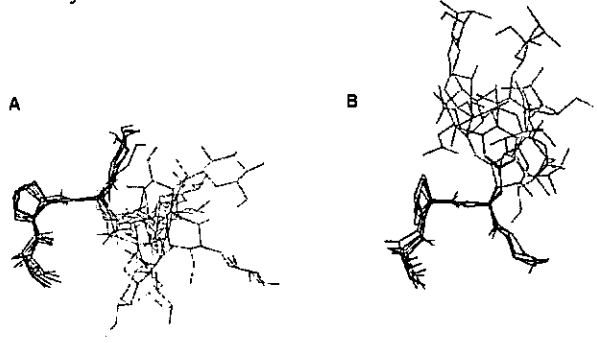


***Figure 11.*** Structures of **A**. Cellobiose modified glycopeptide and **B**. Peptide modified with Glc-[β(1,4)]-β-D-GlcNAc. Structures are derived from a simulated annealing procedure that incorporated all NOE data.

## Conclusions

Asparagine-linked glycosylation is one of the most complex enzyme-catalyzed protein modification reactions. Moreover, the co-translational timing of this transformation implies that glycosylation plays a unique role in the protein biosynthesis process. While remarkable progress has been made towards understanding the molecular players in the glycosylation reaction, there remain many obstacles to overcome before a clear mechanistic picture of the enzyme

emerges. In the next phase of research the complementary application of state-of-the-art bioorganic and biophysical methods, together with the tools of contemporary molecular biology will contribute to a more satisfactory description of this fascinating enzyme along with its many biological implications.

**Acknowledgment**

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# Patent Proze

*by Jane Calvert and Greg Lynch*

## Harmonisation of Patent Law

Those who seek patent protection for their research developments in a number of countries are frequently alarmed and sometimes frustrated with differences in patent law from country to country. The differences can range from minor procedural requirements through to important variations in substantive law. The need to file a variety of different forms signed by applicants and inventors is one example of differences in procedural requirements that have a compliance cost. Variations in substantive law can mean that the strength of a patent in one country may not match the strength of a corresponding patent in another country. An invention may even be patentable in one country but not in another.

The wide variety of legal regimes that make up the international landscape of patent law and practice leads to increased costs for inventors and applicants. Each jurisdiction has its own procedural rules. A multi-jurisdictional patent filing programme consequently has an assortment of actions which must be completed and a myriad of deadlines to be met to avoid the loss of patent rights altogether. In addition, there is considerable duplication of work for patent offices. Why is it that a patent application in one country can successfully pass rigorous examination and proceed to a granted patent only for the same process to be repeated in another country? It is complexities in the patent system such as these that are behind measures to harmonise both procedural and substantive patent law worldwide.

One difficulty with harmonisation is that each country (or region) considers that control over matters of economic importance, such as the grant of an exclusive right, is a fundamental principle (even a matter of preserving its own sovereignty). Nevertheless, there is a trend towards the harmonisation of patent law.

The Patent Cooperation Treaty (PCT) is already in place and has more than 100 member countries. The PCT provides a procedure for the filing of a single international patent application which, although must ultimately be scrutinised by each national or regional patent office, provides significant advantages for patent applicants. The PCT procedure provides applicants with additional valuable time before important and potentially costly decisions must be made. An automatic novelty search and an optional international examination provide an objective assessment of the patentability of the claimed invention and help smooth the path for examination in each of the elected countries or regions.

A second treaty known as the Patent Law Treaty (PLT) was concluded in 2000. The PLT harmonises and streamlines formal patent procedures relating to both national and regional patent applications and to the maintenance of patents. The PLT has not yet entered into force but will do so after 10 countries have ratified the treaty.

A third treaty currently being negotiated has the objective of harmonising substantive patent law internationally. The Substantive Patent Law Treaty (SPLT) is in draft form and a second round of talks took place at the World Intellectual Property Organisation (WIPO) in Geneva in November 2001.

The SPLT covers several basic legal principles that underpin the grant of patents in different countries, such as definitions for prior art, novelty, inventiveness and industrial applicability. The committee of WIPO that is responsible for the SPLT is due to meet again in May 2002. The committee will be operating in the context of the stated vision of the Director General of WIPO that "WIPO must continue to provide strong leadership in developing the patent system to facilitate the process of harnessing creative potential for economical benefit in all countries".

While we await with interest any developments with the SPLT, it is likely to be several years yet before such a treaty comes into force. Nevertheless, inventors and applicants worldwide will take considerable comfort from knowing that the harmonisation of international patent law is in progress. For all involved in the patent process, a simplified and less costly international patent procedure cannot come soon enough.

*Jane Calvert*

Jane Calvert and Greg Lynch are both patent attorneys and solicitors at Baldwin Shelston Waters, where they specialise in chemistry and biotechnology patents. Jane joined BSW after completing a PhD in chemistry at the University of Canterbury in 1994. Greg also joined BSW in 1994 after three years research at Industrial Research Limited in Wellington. Following completion of a PhD in chemistry at the University of Otago in 1989, he spent two years as a post-doctoral researcher at Oxford University.

*Greg Lynch*


Planning for Pacifichem 2005 has begun! On 13 December 2001 at a formal ceremony in Hawaii, the American Chemical Society (ACS) President (Atilla Pavlath), the Chemical Society of Japan (CSJ) President (Hiizu Iwamura) and a representative from the Canadian Society for Chemistry (CSC), the New Zealand Institute of Chemistry (NZIC), the Royal Australian Chemical Institute (RACI), and the Korean Chemical Society (KCS) signed a formal agreement to co-sponsor "The 2005 International Congress of Pacific Basin Societies" — Pacifichem '05. The congress is to be held in Honolulu from December 15-20, 2005. Pacifichem 2005 is the fourth meeting under the Pacifichem banner and the third in which the NZIC has participated as a co-sponsor.

New for 2005 is cosponsorship by the Korean Chemical Society. It had some 260 attendees at the last meeting and Professor Sang Chul Shim of KIAST will represent it on the committee. Representatives from Canada, Australia and New Zealand remain unchanged for the 2005 Congress but the USA and Japan have several new members. This will be the third congress in which NZIC and RACI are formal cosponsors. Members should not become alarmed at costs to NZIC as the agreement that was drawn up (and accepted by Council) places the financial responsibility for the congress on the three large societies. Our efforts in assisting with the congress planning are recognised through a financial incentive based upon our efforts and the number of New Zealanders that attend if the meeting is profitable.

***Agreement Signed for Pacifichem 2005***
*Standing from left to right: Professor Israel, Professor Murai and Professor Tatsumi.*
*Seated from left to right: Sang Chul Smim (KCS), Brian Halton (NZIC), Graham Johnston (RACI), Richard Oakley (CSC), Atilla Pavlath (ACS), and Hiizu Iwamura (CSJ).*

The four-day planning meeting reached agreement that despite the availability of an excellent Convention Centre in Honolulu, the 2005 Congress would be run in various hotel properties along the Waikiki beach front – a format that over the years has created a distinct Pacifichem flavour and ethos. Among a wide range of matters that were discussed, agreement was reached to retain organised symposia, run by members, as the basis of the scientific programme, and to update the subject areas for the congress by redefining some and creating one new one. There are to be **11** areas for 2005 as per:

01. **AGROCHEMISTRY** - including agriculture, carbohydrate, cellulose, food, pulp and paper chemistry.
02. **ANALYTICAL CHEMISTRY** - including clinical, electrochemical sensors, and trace analysis.
03. **BIOLOGICAL CHEMISTRY** - including biotechnology, genomics, microbial, and proteomics chemistry.
04. **CHEMISTRY AND THE COMMUNITY** - including chemical education, chemical economics and business, chemistry and the law, and public education and outreach.
05. **ENVIRONMENTAL AND GREEN CHEMISTRY**
06. **INORGANIC CHEMISTRY** - including geochemistry and nuclear chemistry.
07. **MACROMOLECULAR CHEMISTRY**
08 **MATERIALS CHEMISTRY AND NANOTECHNOLOGY**
09. **MEDICINAL CHEMISTRY** - including pharmaceutics.
10. **ORGANIC CHEMISTRY**
11. **PHYSICAL AND THEORETICAL CHEMISTRY**

Each subject area will have a number of area coordinators appointed to assist the scientific program planning committee. These volunteers will oversee, nurture and balance the symposia topics and operate under a convening coordinator. The NZIC will be in the process of selecting its area coordinators by the time this appears in print.

Much time was spent improving the procedures and protocols for the submission of symposia titles, the presentation of abstracts and the essential deadlines necessary. Thus anyone wishing to organise and RUN A SYMPOSIUM within any of the 11 areas must submit a proposal (on the requisite form available from the Pacifichem website). All proposals require three coorganisers to represent **ANY THREE** Pacific Basin countries (it is presumed that the majority by far will emanate from the countries of the six sponsoring societies).

The essential deadlines are:
February 15, 2003 for first round symposium proposals for decision by May 15, 2003.
September 15, 2003 for second round proposals with decision by January 15, 2004.
September 15, 2004 is the FINAL DEADLINE FOR PROPOSAL SUBMISSION with decision by January 15, 2005.

Contributed papers WILL be accepted for presentation in both SYMPOSIA and GENERAL SESSIONS – the deadline for Abstract submission will be in APRIL 2005.

Each of the 11 congress scientific areas will consist of thematic symposia and anyone interested in organising a symposium of their choice can submit a proposal to do so. The Congress requires that every symposium have at least THREE coorganisers, each one from a different Pacific Basin Country, with the main proponent acting as the coordinator for the arrangements. Anyone requesting approval to organise a symposium can obtain further information from the NZIC Pacifichem representative whose address appears below (the requisite proposal form will be available on the official Pacifichem website: http://www.pacifichem.org

The deadline for first round submissions is almost one year away but if Pacifichem 2000 is any guide almost 75% of the available space was requested in the first round. New Zealand has had a poor reputation for organising symposia though a good number of members acted as coorganisers. For 2005 we are hopeful that this number will be markedly higher. If a proposal is accepted for a given number of congress sessions the proposers will have ample time to set their programme to include invited speakers and to seek any additional sponsorship. Proposals received after the first deadline will be handled as indicated by the timetable above until all the congress sessions are filled.

The organizing committee has significantly increased the fund to sponsor scholars from developing countries of the Pacific Basin to the Congress. The New Zealand delegate has been appointed to refine the programme and convene the selection panel. In addition, the highly successful "Student Papers Competition" is retained and it is hoped that the additional sponsorship that is to be sought will enhance the prizes awarded.

Although four years away, Pacifichem 2005 is something for you to plan for – ask anyone who was at Pacifichem 2000 just how much they enjoyed the millennium meeting. You will be reminded of this and updated with information in future issues of *Chemistry in New Zealand* as it comes to hand.

*Brian Halton*
Pacifichem 2005 Representative
Phone: (04)-463 5954 (direct); Fax: (04)-463 5241
Email: brian.halton@vuw.ac.nz

# Report on the 1999 Easterfield Award Travel to the UK in 2001

*Sally Brooker*
Department of Chemistry, University of Otago, P O Box 56, Dunedin

I was very fortunate to be the first person to benefit from the recent addition to the Easterfield Award, namely a lecture tour in the UK courtesy of the NZIC and Royal Society of Chemistry (RSC). Being the first person to do this did however require flexibility as initially the NZIC stated that this was to involve delivering 'a lecture on the subject of his/her research at a meeting or meetings of the RSC'. But it eventually transpired that what the RSC actually wanted was a visit to the United Kingdom, for up to two weeks during their term-time, with lectures to be presented at a number of Departments as well as at an RSC mini-symposium.

It was a real pleasure to liaise with Stanley Langer of the RSC to set up this visit. He looked after me very well indeed, contacting hosts, coordinating the itinerary, booking train and air travel, etc. On arrival in London in October I visited him at Burlington House, a lovely old building on Piccadilly in central London, and he provided me with coffee, the final itinerary and tickets for all of the local travel. Wow! I then departed for Bristol, albeit on a train different to the one I was booked on as it was cancelled!

My day in Bristol was centred around discussions with the groups of Professors Mike Ward and Jon McCleverty and Dr John Jeffery, whom I had visited for six weeks on an RSC Journals Grant the previous year. In particular, it was very helpful to be able to discuss the draft of a collaborative paper with John, and to catch up with Graham Motson who is soon to join my group as a Royal Society Postdoctoral Fellow. Their new (ca. 2 years old) purpose-built synthetic chemistry building is gorgeous – I am yet to see anything better. I was also very keen to see their new diffractometer (Bruker SMART 6000 CCD) in action but unfortunately they were still sorting out some teething problems.

From Bristol I went to Sheffield, via London where I spent the weekend catching up with Dr Graham (Postdoctoral Fellow at UCL at the time) and Robyn and Paul Caygill. In getting to Sheffield I had another 'UK rail experience' as, despite merrily issuing a ticket from St Pancras for the Sunday concerned, they had closed the station for the day for repairs - apparently standard practice! This meant trekking (in the rain of course!) from St Pancras over to Kings Cross to catch the Thames Link to Luton where I could then get on the train to Sheffield... Thankfully we arrived in Sheffield only a little bit late as Professor David Fenton was kindly meeting me at the station. On Monday, after a full day of discussions, I presented my Easterfield Lecture "Running Rings Round Metal Ions" as a Departmental seminar. Sheffield is part way through a major refurbishment program so it was interesting to see the layout of some of the 'new' laboratories.

The next port of call was my first ever visit to Leeds where Dr Malcolm Halcrow was my host. There I was also able to catch up with a new collaborator, Dr Paddy McGowan, and his group. Having seen them in action, and had face-to-face discussions in front of their fume-hoods (at the coal face so to speak) proved very helpful with regard to bringing this new collaboration to fruition. It was also interesting to see familiar faces from downunder, in the form of Professor Colin Raston and Dr Michael Hardie (both ex-Monash). Leeds laboratories have already been refurbished and they appear to work well.

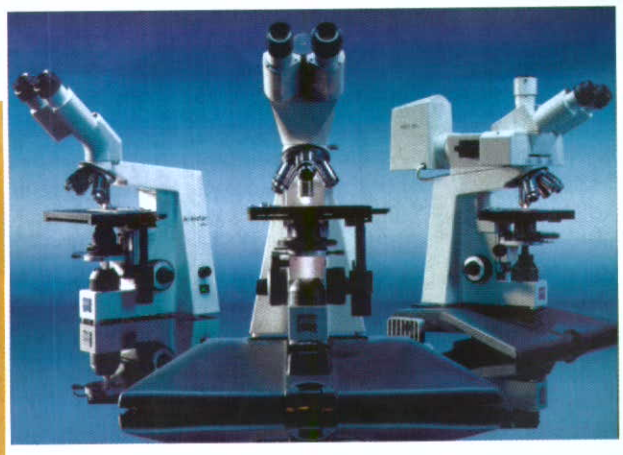
The Leeds visit concluded with an RSC mini-symposium "Ligand Design for the Control of Structure and Function" at which I was presented with the Easterfield Medal before giving the Easterfield Lecture. The next day I traveled down to Loughborough where I was met by Professor Vickie McKee (ex Canterbury). This wee kiwi felt very much at home in this department that sports nice big windows, making the most of the pleasant, open, rural views. Again laboratory refurbishments have been carried out. After a full day of interesting discussions with staff from all sections of the chemistry department I presented a Departmental seminar - at 5 pm on a Friday - to a full house, which to me captured the essence of the enthusiasm and energy within this Department.

Next stop was my first visit to Birmingham where Professors Ed Constable and Catherine Housecroft were my hosts. Their laboratories have also been refurbished and, thanks to having been teaching laboratories in their previous life, are pleasantly spacious. It was interesting to hear that they have been actively recruiting students. As a result they have, for the UK, a large class of around 95 first years, similar to Loughborough. Once again a full day was punctuated with presenting the Easterfield Lecture. A highlight of this visit was a discussion of various heterocyclic syntheses with Ed.

From Birmingham I flew to Dublin to visit, for the first time, Professor Han Vos at DCU. This is a relatively young University and at present the campus is in the midst of a massive building program. The chemistry department is part of a new three-storey building which captures the natural light in a large, attractive, central atrium. Han works with triazole-based ligands, an area in which we are also working. We discussed the possibility of him visiting Dunedin and we hope that he will be able to come out early in 2002 for a few weeks. I gave the Easterfield Lecture for the final time on this tour before moving on to Belfast to visit Professor Jane Nelson. Jane and I worked on two manuscripts on our collaborative studies, with one to be posted shortly. Hopefully Jane will be able to visit us in Dunedin again soon, perhaps in 2003.

I am very grateful to the NZIC and RSC for giving me this marvelous opportunity. Being awarded the Medal was a big buzz in itself, but this new exchange program is a fantastic bonus, and I am certainly looking forward to the reciprocal (RSC Corday Morgan Medal) visit by Professor Chris Hunter (Sheffield) in 2002.

## Axiostar plus - Starting Big



The Axiostar entry-level microscope from Carl Zeiss is now also available with high-quality fluorescence contrast and extensive ergonomic features - at a surprisingly low price! The Axiostar plus is ideal for doctor's offices, hospitals, laboratories, schools and universities, and even for open-air use thanks to its optional LED illumination.

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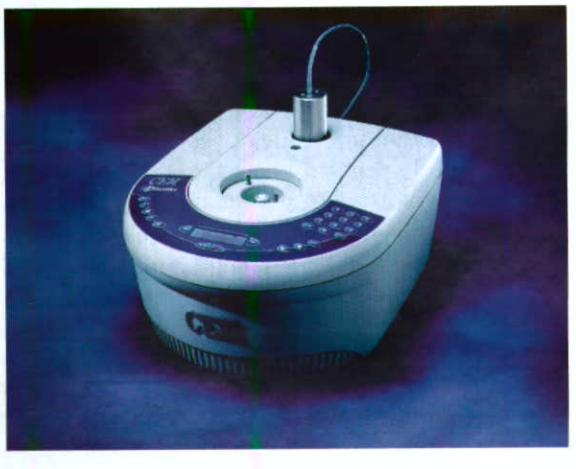

Ai Scientific announces the release of CEM's Discover focused synthesis instrument. The Discover optimises synthetic reactions while enhancing molecular diversity and productivity. Though ideally suited for use in the pharmaceutical industry where the generation of new compounds and their rapid optimization is essential, CEM's Discover is extremely beneficial wherever synthetic processes are employed. Due to the various configurations available, the Discover offers a clear option for converting traditional synthetic methods to rapid microwave methods. CEM's proprietary focused microwave technology allows chemists to perform synthesis reactions in minutes instead of hours, or even days, while simultaneously increasing yields as much as 50% and reducing side reactions. CEM's patented cavity provides instantaneous coupling to any sample load, while variable speed stirring assures complete mixing of reactants. Continuous microwave power delivery, as well as a temperature and pressure feedback, system provide unparalleled control of reaction conditions. In addition, a variety of vessel sizes and shapes (from 1 to 125 mL capacity) can be accommodated, including tubes for pressure-assisted reactions. The Discover provides the flexibility necessary to accommodate a variety of throughput needs.

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## PerkinElmer Announce The Newest Additions To The PYRIS Family Of Thermal Analyzers

Through our partnership with Seiko, PerkinElmer is able to complement its industry-leading power-compensation DSC and TGA with high performance materials characterization tools, including DMA, TMA and TG/DTA. This represents PerkinElmer's continued commitment to the thermal analysis business. These new instruments will be in the PerkinElmer colors with PerkinElmer standard nameplates and logo.

*PYRIS Diamond DMA*
The PYRIS Diamond DMA can determine characteristics such as glass transition, damping intensity, heat resistance, creep and stress relaxation of various materials, which allows the user to have a complete characterization of the processed materials. Furthermore this instrument can be used to evaluate the compatibility, anisotropy, vibration absorbency, molecular weight, degree of crystallinity and degree of orientation of polymeric and elastomeric materials. The DMA uses multiple pure deformation modes to measure time-dependent and temperature-dependent relaxation behaviours in materials.

The PYRIS Diamond DMA measures the dynamic mechanical properties (E′, E″, tan delta, stress, strain etc.) as a function of temperature or time. Typical materials tested are polymers, composites, soft solids, elastomers, films, fibres, etc. Testing is achieved by applying a variable sinusoidal synthetic oscillating stress to the sample that produces a dynamic strain in bending (single-, dual-cantilever and three-point bending), tension, compression and shear. All operating modes are pure deformation modes. Testing can be done with continuous frequencies from 0.01-100 Hz, with displacement amplitudes ranging from 0.5-100 microns. Temperature range is –150 °C to 600 °C (requires optional computer controlled sub-ambient liquid $N_2$ device). Maximum force is 18 N (Static Force is 10 N and Dynamic Force is 8 N) and tan delta resolution is 0.0001.

Key Features of DMA: Four deformation modes: tension, compression, bending, and shear; three bending modes: single-cantilever, dual-cantilever, and three-point bending; creep, stress relaxation, and static measurement (constant force); continuous selection of frequencies from 0.01 to 100 Hz with ability to superimpose up to 13 frequencies; synthesis oscillation frequency function (maximum 5 frequencies); dynamic stiffness range of 5.0 decades; temperatures from -150 °C to 600 °C; unique calibration procedure assures accurate sample temperatures; test and analysis parameters can be changed during a test; Fourier transformation method performs the noise free analysis; test measurement function for an evaluation before the actual measurement.

The PYRIS Diamond DMA Lab System includes: Standard DMA module with bending and tension measuring systems; accessory kit containing all communication cables and tools for basic instrument operation; operation manuals. Required Software (not included in Lab System): software for instrument control, data acquisition, basic and advanced data analysis. Optional Accessories: Air Cooling Unit with two switching flow meters; Auto Cooling Accessory with evaporating liquid $N_2$ cooling.

*PYRIS Diamond TMA*

The PYRIS Diamond TMA is an instrument for measuring the thermal mechanical properties of solid materials. Computerized control of both load and sample displacement amount has resulted in wider application fields. The TMA follows the long tradition of the technology, the first thermal mechanical analyzers to use constant load mode to measure temperature-dependent expansion behaviours in solid materials. Furthermore, the TMA modules flexible multi-purpose features facilitate various measurements including glass transition, softening, swelling, gel time, creep, stress-strain, stress-relaxation, Young's modulus measurements, and large volume TGA analysis.

The PYRIS Diamond TMA measures thermal mechanical properties (Expansion, CTE, creep and stress relaxation etc.) as a function of temperature or time. Typical materials tested are polymers, composites, elastomers, glass and metal etc. Testing is achieved by applying a load to the sample that produces a strain in tension, compression, penetration and bending. All operating modes are pure deformation modes. Testing can be done with a constant load up to 5.8 N. Temperature range is -150 °C to 1500 °C by using different heating furnaces. (Requires optional computer controlled sub-ambient liquid $N_2$ device). Maximum load is 5.8 N and TMA sensitivity is better than 0.02 micron metre.

Key Features of TMA: Five measurement modes: expansion, penetration, tension, bending and voluminal expansion; probe supporting method: cantilever and spring supporting; expansion, creep, stress relaxation; sample mountable vertically or horizontally; automated measurement of sample length; three kinds of different subtract probes are available (metal, quartz and alumina); wide measurement range (± 5 mm); temperatures from -150 °C to 1500 °C by exchanging furnace; unique design assures simple probe exchange; test and analysis parameters can be changed during a test; large volume TG measurement by replacing the probe with a suspended container; fusion protection feature prevents the sample melting to the sample stand.

PYRIS Diamond TMA Lab System Standard Version (-150 °C to 600 °C) includes: Standard TMA module with low temperature range furnace; standard accessory kit containing all the connect cables and the tools for basic instrument operation; operation manuals. Required Software (not included in Lab System): software for instrument control, data acquisition, basic and advanced data analysis. Optional Accessories: Air Cooling Unit with two switching flow meters; Auto Cooling Accessory with evaporating liquid $N_2$ cooling.

PYRIS Diamond TMA Lab System High Temp Version (Ambient to 1500 °C) includes: Standard TMA module with high temperature range furnace; standard accessory kit containing all the connect cables and the tools for basic instrument operation; operation manuals. Required Software (not included in Lab System): software for instrument control, data acquisition, basic and advanced data analysis. Optional Accessory: Air Cooling Unit with two switching flow meters.

*PYRIS Diamond TG/DTA*

The PYRIS Diamond TG/DTA is a uniquely capable instrument for measuring the gravimetry and thermal varieties in thermal process. Combining the high flexibility of the DTA feature with the proven capabilities of the TG measurement technology, the simultaneous TG/DTA measurement system can be used for such applications as oxidation, heat resistance, the amount of water, compositional analysis and the measurement of ash content in a sample. This system is also used to cover such needs as reaction rate and accelerated degradation tests. The TG/DTA measures gravimetry and thermal varieties in heating or cooling processes simultaneously as a function of temperature or time. All of the materials, solid or fluid, can be tested within the instrument's available temperature range. Typical applications are to measure inorganic salts decomposition, weight variety in chemical reactions and combustion processes. Testing is achieved by heating or cooling materials according to preset temperature programs. Test temperature range is from ambient to 1500 °C by exchanging the furnace only. Advanced software can simulate the measurement under any conditions. Autosampler system is an optional accessory. The maximum available sample number is 30.

Key Features of TG/DTA: Horizontal differential type balance; stable TG and DTA baseline; DSC heat flow conversion; high temperature precision (0.1 °C); high TG sensitivity (0.2 μg); high DTA sensitivity (0.06 μV); cooling time from 1000 °C to 50 °C (< 15 mins.); high gas flow control capability assures atmosphere control over a broad temperature range from ambient to 1500 °C; easy replacement of balance beam; unique simulation software can simulate any different measurement condition; test and analysis parameters can be changed during a test; Gas Transfer System enables the furnace to transfer the evolved gas to an analysis system such as FTIR or GC-MS.

PYRIS Diamond TG/DTA Lab System includes: TG/DTA module with high temperature range furnace; standard accessory kit containing all the communication cables and tools for basic instrument operation; sample vessels (Aluminum, Platinum and Alumina in different volumes); operation manuals; required software (not included in Lab System): software for instrument control, data acquisition, basic and advanced data analysis. Optional Accessories: Air Cooling Unit with two switching flow meters; Autosampler.

PYRIS Diamond TG/DTA Lab System Vacuum Version includes: TG/DTA module with high temperature range furnace; standard accessory kit containing all the communication cables and tools for basic instrument operation; Additional Vacuum Kit; sample vessels (Aluminum, Platinum and Alumina in different volumes); operation manuals. Required Software (not included in Lab System): software for instrument control, data acquisition, basic and advanced data analysis. Optional Accessories: Air Cooling Unit with two switching flow meters; Autosampler.

*EXSTAR Software, Version 6.2*
EXSTAR Thermal Analysis Software Package is designed for the measurement and analysis of thermal analysis parameters and control of thermal analysis instruments and is valid for all Seiko instrumentation PerkinElmer will be selling. It can control multiple instruments simultaneously. EXSTAR Software, Version 6.2 is provided on CD and may be customer installable.

EXSTAR Software includes the following calculations: DMA: DMA measurement software; DMA analysis software; Time-Temperature Superposition (TTS) master curve analysis; Activation energy analysis; Component analysis. TMA: Automated TMA Measurement software; TMA analysis software; TMA data subtraction; TMA viscoelasticity conversion; TMA expansion coefficient analysis. TG/DTA: TG/DTA measurement software; TG/DTA analysis software; Robotic TG/DTA measurement software (for optional Autosampler control); TG/DTA kinetics analysis; TG/DTA data subtraction; TG/DTA highway TA software.

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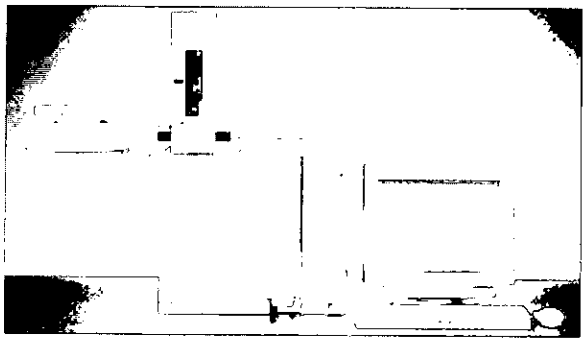

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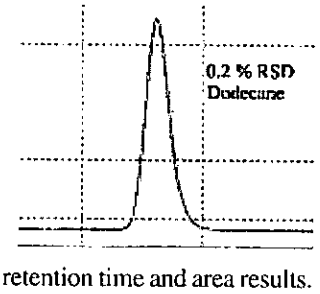


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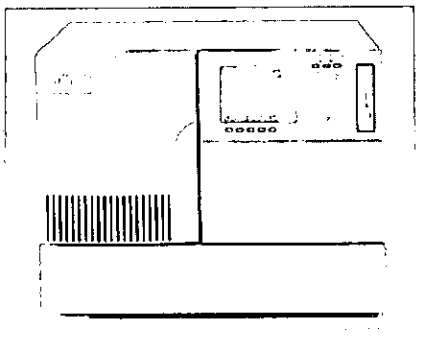

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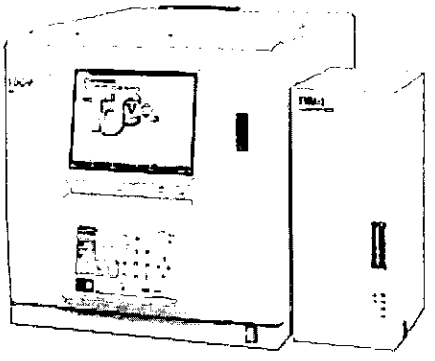

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# Cyclodextrins: Industrial Waste with Applications in Pharmacy, Catalysis and Microelectronics

*Christopher J. Easton*

Research School of Chemistry, Australian National University, Canberra ACT 0200, Australia
(e-mail: easton@rsc.anu.edu.au)

## Natural Cyclodextrins

Cyclodextrins[1] are naturally occurring cyclic sugars which are produced through the enzyme-catalysed degradation of starch. They have been known for more than a century, during which time they have been studied extensively by chemists, due to their ability to act as molecular hosts in the formation of host-guest or inclusion complexes with a wide range of guests (Figure 1). With hydrophobic guests, the solubility of cyclodextrins in aqueous solutions confers solubility on the guests in the host-guest complexes.

Despite sustained academic interest in cyclodextrins since their discovery, it is only recently that aspects of their commercial potential have been exploited. As little as twenty years ago, cyclodextrins were most commonly regarded by industry merely as waste by-products of the American corn starch industry. They crystallised from corn syrup and had to be removed to make the product acceptable to the consumer. Nevertheless, today they are used in many applications, and manufactured cheaply and efficiently on an industrial scale.[2]

### *Applications in the Food, Personal-Care and Pharmaceutical Industries*[3]

In many parts of the world the natural cyclodextrins are now used as food additives and in dietary supplements. They are incorporated in garlic flavouring, to limit the volatility and odour, while retaining the taste. They are exploited in fish oil preparations, in this case to mask the unpleasant taste as well as to reduce oxidative degradation of the oil. Examples of their applications in personal-care products include their use to formulate and stabilise peracid whiteners in toothpaste and their addition to deodorants to maintain sustained release of perfumes and absorb body odours. To achieve similar effects, cyclodextrins are also used in perfumes, and they are added to carpet and furniture cleaners to absorb stains and odours. These and most of the other commercial uses of cyclodextrins depend on the equilibrium shown in Figure 1.

It is easy to see many more applications of cyclodextrins, simply by noting the ingredients in products on supermarket shelves. The word cyclodextrin doesn't often appear because starch is frequently used instead. The latter is probably considered to be sufficiently informative but less likely to sound like a chemical!

Many potential applications of cyclodextrins in the pharmaceutical industry still await regulatory approval, but there is a great deal of interest in this area and a number of products have already been made available, particularly in Japan.

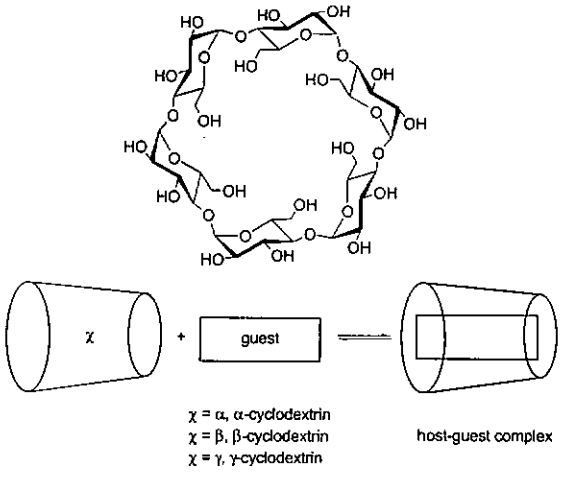



*Figure 1.* Structure of the cyclodextrins and the equilibrium for the formation of host-guest complexes. α-Cyclodextrin (shown) has six α-D-glucopyranose units, whereas β- and γ-cyclodextrin have seven and eight respectively. A truncated cone is often used to represent a cyclodextrin. A substituent drawn at the narrow end of the cone indictes that it replaces a primary hydroxy group in the cyclodextrin while a substituent drawn at the wide end of the cone indicates that it replaces a secondary hydroxy group.

Cyclodextrin host-guest complexes may be regarded as drug capsules, with the encapsulation occurring at the molecular level. One advantage of these complexes is that they can be used to prepare aqueous formulations of hydrophobic pharmaceuticals for oral, intravenous, ocular and other forms of administration. With oral administration, complexation of the drug may reduce its degradation in the acidic environment of the stomach, reduce irritation of the gastro-intestinal tract, and increase bioavailability of the drug by improving absorption in the small intestine.

The shelf-life of a drug may also be increased through complexation. Sustained release of drugs has also been accomplished using cyclodextrin formulations, according to the equilibrium shown in Figure 1 where the guest is a drug. The rate of drug absorption through the intestinal wall depends on the concentration of drug in the free state, which is determined by the position of equilibrium between the free drug and the cyclodextrin and the host-guest complex (the latter two components are not absorbed to any significant extent). This equilibrium is maintained while absorption proceeds, and makes the drug available in a controlled and sustained manner.

### *Chemical Applications*

There are also many chemical applications of cyclodextrin host-guest complexes. Often similar molecules will form quite distinct host-guest complexes which aid their separation. This is particularly the case with racemic guests, which form diastereomeric host-guest complexes,

since the cyclodextrins are homochiral.[4] Probably the most notable contributions in this area are those of Armstrong and co-workers, who have developed commercial cyclodextrin-based chromatography columns for the resolution of enantiomers. The enantioselectivity displayed by cyclodextrins in forming complexes with racemic guests is reflected in the stereoselectivity of reactions of included guest molecules, and the related use of cyclodextrins in asymmetric synthesis is another topical area.

In the broader context, cyclodextrins are capable of affecting the rate and regio- and stereo-selectivity of chemical reactions, by changing the microenvironment for those reactions through complexation and by preassembly of the reagents for multicomponent systems.[5] This ability of cyclodextrins to bind guest molecules and facilitate reactions of the bound species is akin to the catalytic activity displayed by enzymes and, for this reason, cyclodextrins have been studied extensively as enzyme mimics. The cyclodextrin hydroxy groups have been shown to participate in hydrolysis and esterification reactions which are similar to those catalysed by the serine esterases and proteases.

Alternatively, cyclodextrins can be used in conjunction with enzymes to improve the utility of enzymes in chemical processing.[6] In cases where enzymes are regulated biochemically through product or substrate inhibition, cyclodextrins can be added as complexing agents to prevent wasteful metabolism. The complexes act as substrate reservoirs or product traps, to increase the efficiency of the enzymes by reducing the concentrations of the products or substrates free in solution. When an enzyme catalyses an equilibration between two species, selective complexation of one of these can be used to drive the reaction in that direction, by altering the equilibrium position and the rate at which equilibration occurs. Cyclodextrins can also be used to increase the substrate selectivity displayed by enzymes, by preferentially complexing one or more substrates from a mixture that would normally be processed. They can also be used to remove enzyme inhibitors from solutions.

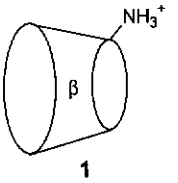
One particular application of cyclodextrins with enzymes and other proteins has arisen in protein synthesis. Overexpression of proteins often results in their misfolding when they are produced in high concentrations. To prevent this, surfactants such as SDS are added. Later the surfactants are removed through the use of cyclodextrins and the proteins then fold in the normal manner.

## Modified Cyclodextrins

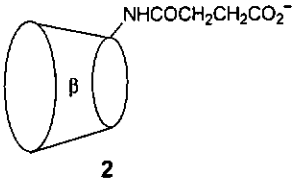
Most of the recent work of my research group, and that of our collaborators working in the group headed by Stephen Lincoln at the University of Adelaide, has involved modified cyclodextrins. The naturally occurring cyclodextrins are relatively inert molecular hosts, as they have only hydroxy functional groups. As a consequence, the range of host-guest interactions available to them is quite restricted. However, through modification, the natural cyclodextrins become effective scaffolds and templates for the generation of an extraordinary range of new molecular hosts, which opens up a vast range of chemistry not available with the natural forms.[5]

### *Enhanced Complexation*

By using modified cyclodextrins, it is possible to tailor a cyclodextrin host to a particular guest, to meet specific requirements in the host-guest complex. Possible modifications to a cyclodextrin include altering its cavity size, shape, charge and/or polarity. As an example, in aqueous solutions at near neutral p*H*, the β-cyclodextrin derivatives **1** and **2** form host-guest complexes with deprotonated carboxylic acids and protonated amines respectively. The extent of complex formation (or thermodynamic stability of the complex) is increased over that observed with natural β-cyclodextrin, due to the ionic host-guest interactions which are only made possible through the cyclodextrin modifications.[7] In addition, the cyclodextrin derivatives are each approximately forty times more soluble than β-cyclodextrin, so substantially more concentrated solutions of these compounds and their complexes can be prepared.

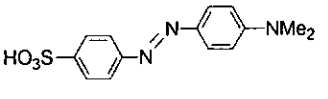



**1**




**2**

Covalently linked cyclodextrin dimers allow for the possibility of cooperative guest binding by the cyclodextrin cavities or annuli. This is illustrated by the thermodynamic stability of the complex of methyl orange (**3**) with the β-cyclodextrin dimer **4**, which is almost two orders of magnitude higher than that of the complex with the parent cyclodextrin. Recent work of Breslow and Zhang[8] on the particularly effective complexation of cholesterol by an alternative cyclodextrin dimer, indicates that compounds of this type may find application as dietary supplements to reduce cholesterol absorption. A similar use has already been proposed for the natural cyclodextrins.[9]

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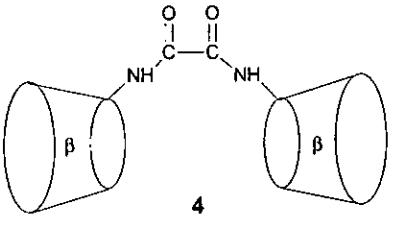
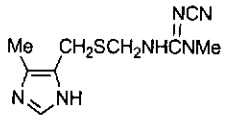



**4**

### *Pharmaceutical Applications*

The effects of cyclodextrin modifications can be useful in pharmaceutical applications.[7] For example, the modified cyclodextrins **1** and **2** have been used to prepare concentrated solutions of non-steroidal anti-inflammatory drugs such as Ibuprofen (**5**) and the anti-ulcer drug Cimetidine (**6**), respectively.[7] These exploit ionic interactions between the hosts and guests in their complexes. On oral administration, it is believed from studies with animal models that the drugs are released

rapidly in the stomach. This is due to the effect of dilution on the equilibrium shown in Figure 1 and also the loss of the ionic host-guest interactions in the acidic environment, on protonation of the guest in the former case, and the cyclodextrin **2** in the latter case. With these formulations, the non-steroidal anti-inflammatory drugs are released in microdispersed form, resulting in a decrease in the incidence of direct irritation of the gastrointestinal tract, while the unpleasant taste of Cimetidine (**6**) is masked.

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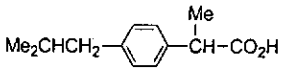
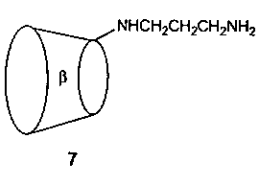



**5**

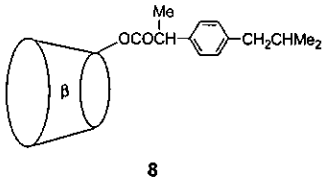
Covalently attaching drugs to cyclodextrins using amide and ester linkages is another form of cyclodextrin modification finding application in drug administration. The esters and amides are prodrugs and release the pharmaceutical agents through hydrolysis. With oral administration cyclodextrin esters are selectively broken down by enzyme-catalysed hydrolysis in the colon, and this methodology is therefore being using to develop treatments for colon cancer.[10]

### *Applications in Chemical Separation and Isomer Discrimination*

The ability to use modified cyclodextrins to tailor host-guest complexes to meet specific requirements and to increase the extent of host-guest interactions in the complexes provides improved procedures for chemical separation, including chiral discrimination.[4] The thermodynamic stabilities of the complexes formed between the enantiomers of tryptophan anion and the nickel(II) complex of the 6$^A$-aminopropylamino-6$^A$-deoxycyclodextrin **7** differ by an order of magnitude, whereas neither β-cyclodextrin nor the apometallocyclodextrin **7** displays enantioselectivity for complexation of that guest. The cyclodextrin ester **8** of Ibuprofen (**5**) is produced as a 5:1 mixture of the diastereomers through reaction of β-cyclodextrin with an excess of the acid chloride of Ibuprofen. A complementary selectivity of 10:1 occurs in the hydrolysis of the diastereomers, with the preferentially formed isomer hydrolysing the fastest. The marked stereoselectivity displayed by modified cyclodextrins, and illustrated by these examples, can be attributed to increased host-guest interactions resulting from metal complexation and covalent attachment of the host to the guest, respectively.




**7**




**8**

### Better Catalysts and Molecular Reactors

The option to introduce diverse functional groups with a controlled geometry and orientation, through modifications to the natural cyclodextrins, dramatically enhances the utility of cyclodextrins in chemical synthesis and catalysis. Now, no longer limited to hydroxy functional groups, modified cyclodextrins present a much greater range of possibilities to mimic the entire span of enzyme activity. This is exemplified by the bifunctional catalysis of the hydrolysis of 4-*t*-butylcatechol cyclic phosphate by a bisimidazole-substituted cyclodextrin (Figure 2),[11] and the 70,000-fold rate enhancement of the hydrolysis of a phosphate triester by the copper complex of the cyclodextrin **7** (Figure 3).[12]

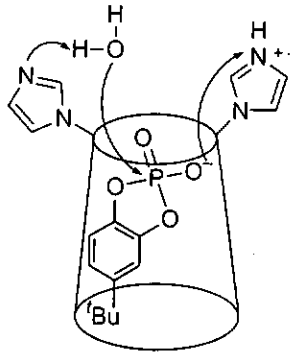



***Figure 2.*** Bifunctional catalysis by a modified cyclodextrin.

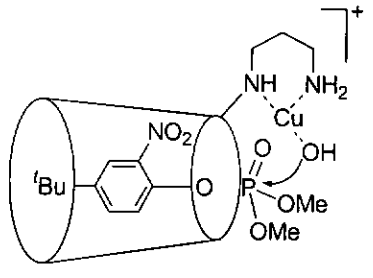



***Figure 3.*** Hydrolysis of a phosphate triester catalysed by a metallocyclodextrin.

Preassembly of reagents using modified cyclodextrins can also be used to alter the outcomes of chemical reactions. In this context, the cyclodextrins are behaving as molecular reaction vessels or molecular reactors. In our laboratories, attaching a dipolarophile to a cyclodextrin has been used to reverse the regioselectivity of nitrile oxide cycloadditions (Scheme 1),[13] while a linked cyclodextrin has been used as a template to prevent formation of indigo during the condensation of indoxyl with isatin-5-sulfonate to give the indirubin sulfonate (Scheme 2).[14]

### Molecular Switches and Applications in Microelectronics

Modifications to the cyclodextrins also lead to a wide range of photochemistry of cyclodextrin complexes, through which enhancement of guest reactivity occurs, and light harvesting devices and frequency switches may be constructed. A particularly interesting example in this area is shown in Figure 4.[15]

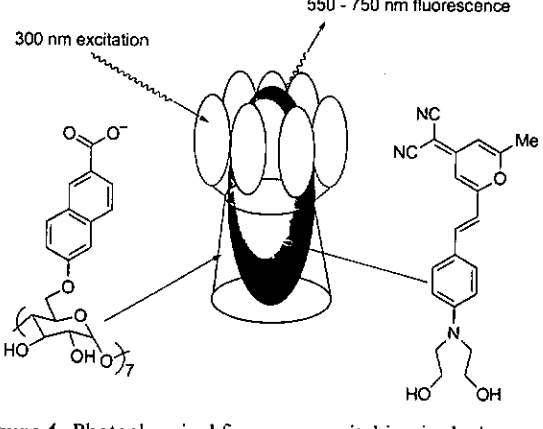
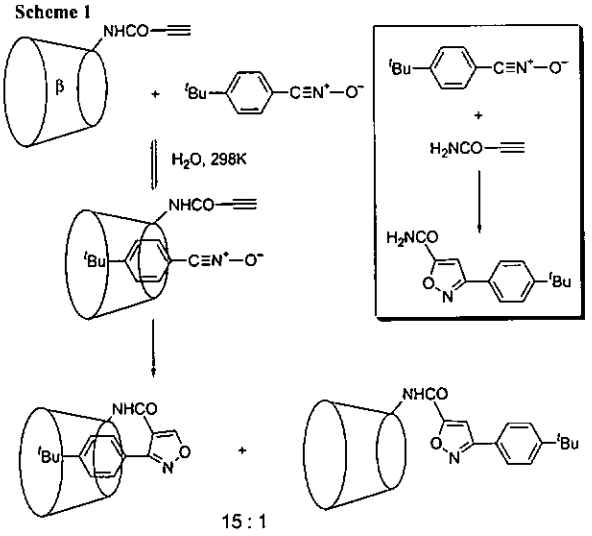
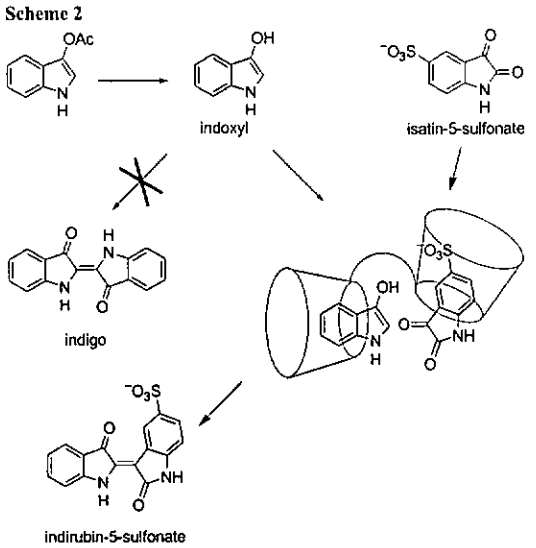



***Figure 4.*** Photochemical frequency switching in the host-guest complex of a modified cyclodextrin.

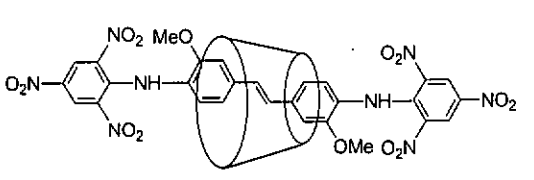
Scheme 1




Scheme 2




In the solid state, cyclodextrin host-guest complexes form regular arrays, which are particularly stable in the case of rotaxanes such as **9** and **10**.[16,17] Under these circumstances the guests interact to form molecular wires in one direction, but are insulated by the cyclodextrins from interaction with guests in other directions. This raises the possibility of using cyclodextrin complexes in microelectronics.

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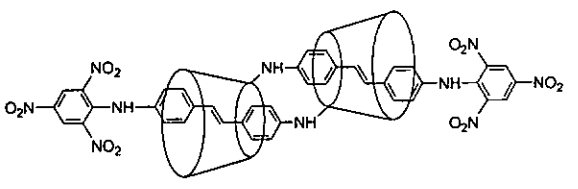


**10**

## Summary

In the space available it has only been possible to give a very brief overview of cyclodextrin chemistry and its applications. At this time, many more uses for natural and modified cyclodextrins can be envisaged. The current level of research and commercial activity in this area is enormous, as indicated by the frequency of journal articles and the level of patent activity in the field, and there is every reason to expect that this will lead to impressive new developments and applications.


## Acknowledgements

This is an abstract of a lecture that was presented at Molecules for Life 2001. I would like to take this opportunity to thank the conference organisers, and particularly Mike Boland and Carol Taylor, for giving me the opportunity to participate in a stimulating meeting at an excellent venue. Their attention to every detail was very much appreciated.


## References and Notes


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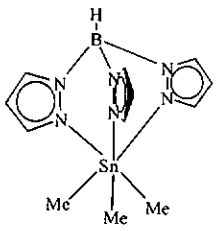
# Novel Six-coordinate Aryl- and Alkyltin Complexes

*Nicholas C. Lloyd*, Brian K Nicholson*, Alistair L Wilkins and Ralph Thomson*

Department of Chemistry, University of Waikato, Private Bag 3105, Hamilton.

## Introduction

Organo-tin compounds have wide applications as pesticides and as intermediates for organic synthesis.[1] They are invariably Sn(IV) derivatives and are generally four-coordinate.[2] The mixed organo/chloro compounds of the type $R_nSnCl_{4-n}$ do however have the ability to expand their coordination numbers to five or six. This depends critically on the substituents - with four organic groups, $R_4Sn$, there is no tendency at all to coordinate extra ligands, while at the other extreme $SnCl_4$ readily forms six-coordinate $[SnCl_4L_2]$ complexes since the electronegative halo groups increase the Lewis acidity of the tin centre.



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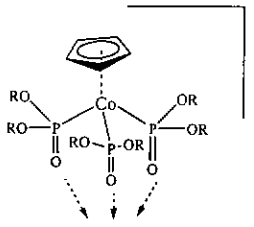

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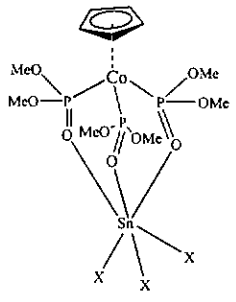
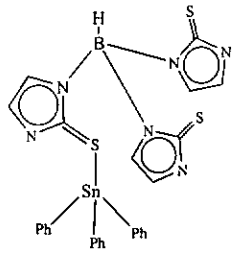


**3a** $X_3 = MeCl_2$
**3b** $X_3 = Me_2Cl$

**4a** $X_3 = Cl_3$
**4b** $X_3 = PhCl_2$
**4c** $X_3 = Ph_2Cl$
**4d** $X_3 = Ph_3$



5

In a previous study[3] it was shown that the complete series of six-coordinate methyl-tin-chloride complexes could be prepared using Trofimenko's tris(pyrazolyl)borate ligand,[4] including the first example of a six-coordinate trimethyltin centre in $Me_3Sn[(pz)_3BH]$, as in **1**.[3] The strong tendency of the tris(pyrazolyl)borate ligand to act as a tridentate chelating ligand overcomes the reluctance of the $Me_3Sn^+$ centre to form three extra bonds.

Recently Klaui[5] has introduced a new tridentate ligand, $[CpCo\{PO_3R_2\}_3]$-, **2**, (R = Me, Et) which is analogous to the Trofimenko one, but coordinates through three oxygen, rather than nitrogen, atoms. Although this ligand has been quite widely used in transition metal chemistry, there have been no previous reports in organo-tin chemistry, so we are currently investigating this aspect.

## Results

The reactions between the Klaui ligand (as the sodium salt) and the organotin chlorides $Me_nSnCl_{4-n}$ or $Ph_nSnCl_{4-n}$ (n = 0-3) generally proceeded smoothly in dichloromethane solution, with elimination of NaCl, to give the corresponding new complexes **3(a-b)**, **4(a-d)**. The only example for which no product has yet been isolated isolated is with $Me_3SnCl$.

To prove that the tin atom was six-coordinate the single-crystal X-ray structures of the $Ph_3Sn$ and the $Cl_3Sn$ derivatives were determined. The structures are illustrated in Figures 1 and 2 and show that the tin is indeed fully complexed - the first example to be established for a $Ph_3Sn^+$ centre, with a $C_3O_3$ coordination sphere. As expected the tridentate ligand is more tightly bound for the trichloro example (Sn-O 2.08 Å) than for the triphenyl one (Sn-O 2.21 Å), reflecting the more acidic centre in the former. Other differences are illustrated by the Cl-Sn-Cl and O-Sn-O angles of 87° and 95° respectively for **4a** and corresponding C-Sn-C and O-Sn-O angles of 104° and 79° for **4d**. While the X-ray structural data is for the solid state only, NMR studies (see below) confirm that the six-coordination is maintained in solution.

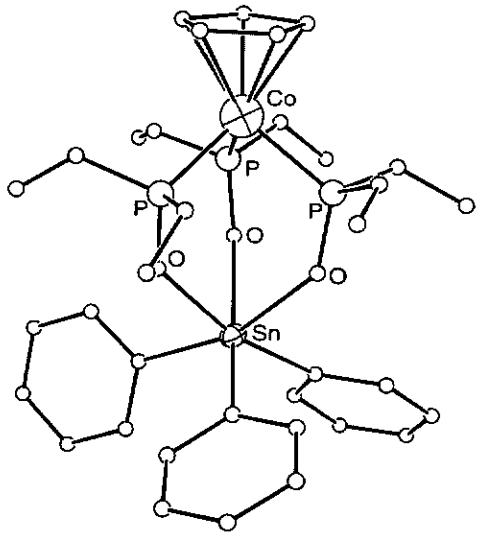


***Figure 1.*** The structure of $[CpCo\{PO_3Me_2\}_3]SnPh_3$

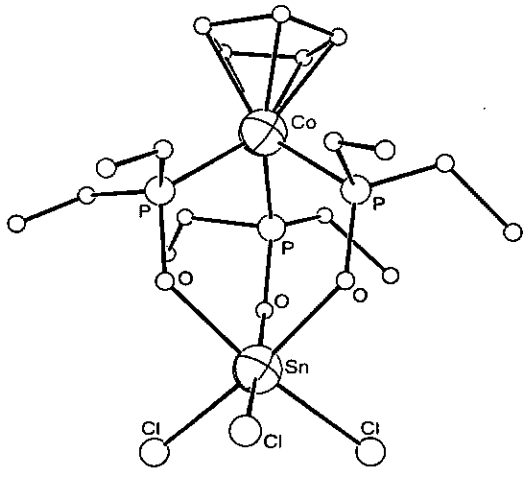


***Figure 2.*** The structure of $[CpCo\{PO_3Me_2\}_3]SnCl_3$

It is interesting that the $Ph_3Sn$ complex of the Klaui ligand formed straightforwardly, while the corresponding $Me_3Sn$ one did not, since for the tris(pyrazolyl)borate system the reverse was found - $Me_3Sn\{(pz)_3BH\}$ was readily isolated[3] whereas $Ph_3Sn\{(pz)_3BH\}$ has been reported to be unstable.[6] Reasons for this difference are not yet apparent.

### NMR Studies

The new complexes are rich in potential NMR information, with $^1H$, $^{13}C$, $^{31}P$ and $^{119}Sn$ nuclei amenable to study. The $^1H$ and $^{13}C$ spectra are complicated by virtual coupling arising from the high symmetry so that, for example, the signals for the Me groups in the $Ph_3Sn[CpCo\{PO_3Me_2\}_3]$ example show a complex splitting pattern to the three equivalent P nuclei.

The $^{119}Sn$ spectra are the most interesting, since the chemical shifts are characteristic of coordination number in solution, and provide information about the structural rigidity of the complexes. For the symmetrical $X_3Sn[CpCo\{PO_3Me_2\}_3]$ the $^{119}Sn$ signal is a quartet, arising from coupling to three equivalent phosphorus atoms, while for the unsymmetrical $RCl_2Sn^+$ or $R_2ClSn^+$ complexes the signals are more complicated, indicating some fluxionality. For all of the complexes the $^{119}Sn$ shifts lie in the -300 to -700 ppm region, where six-coordinate tin is expected, and furthermore they lie on a straight line when plotted against number of Cl groups on the tin (Figure 3). This shows the full series maintains in solution the six-coordination found crystallographically in the solid state.

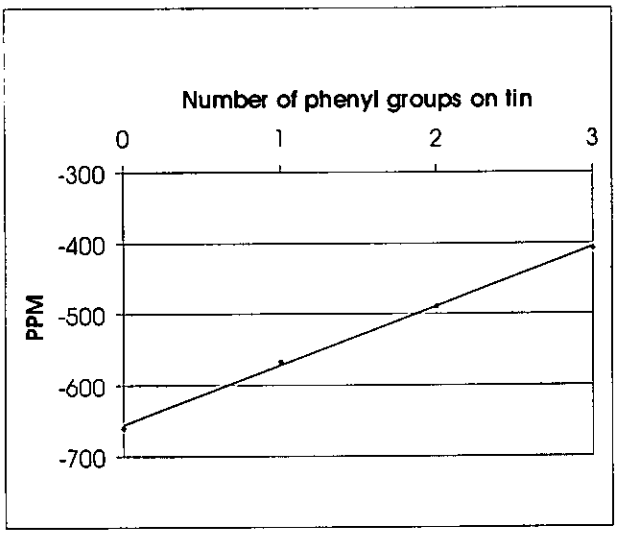



*Figure 3.* The $^{119}Sn$ chemical shift versus degree of phenyl subsitution for $[CpCo\{PO_3Me_2\}_3]SnX_3$

### Complexes With Tris(methimazolyl)borate Ligand

Another tridentate ligand related to the pyrazolyl-borate and Klaui ligands has been introduced very recently by Reglinski.[7] This is the tris(methimazolyl)borate anion **5** which coordinates through three sulfur atoms. This is therefore a softer Lewis base than the N- or O-donor analogues, so might be expected to form stable complexes with the relatively soft organotin centres. However our preliminary results show that with $Ph_3SnCl$, the complex that forms is four-coordinate with only one of the sulfur atoms attached to tin and the other two dangling. This is illustrated in Figure 4. $^{119}Sn$ NMR for this compound gives a signal at -58 ppm, which shows that four-coordination is maintained in solution. This is a unique example for this ligand since all other complexes reported so far involve tridentate coordination. Further work is needed to understand the reasons for this behaviour.

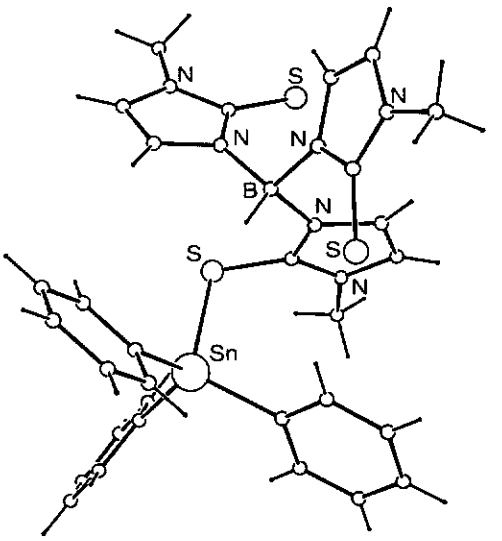



*Figure 4.* The structure of $[HB\{C_3N_2S\}_3]SnPh_3$

### Conclusions

The Klaui ligand is clearly useful for enforcing high coordination numbers on alkyl- and aryltin centres. It behaves differently from the pyrazolylborate ligands and so extends the range of compounds known. The related tris(methimazolyl)borate ligands however seem less powerful in encouraging higher coordination in tin chemistry. The three mono-negative tridentate ligands have complementary roles in their coordination chemistry of main group elements.

### Acknowledgements

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# CONFERENCES & SEMINARS

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**Format:** First day consists of a variety of invited speakers from science, media, education, art, and government, who demonstrate the range of activities that Antarctica New Zealand supports. The second day will be devoted to science activities.

*29-June - 7 July 2002*

**New Zealand International Science Festival**

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**Contact:** Graham Foster
Email: g.foster@zfree.co.nz

*9-12 July 2002*

**Western Pacific Geophysics Meeting 2002: Special Session On Southern Hemisphere Ozone**

**Venue:** Wellington, New Zealand
**Website:** http://www.agu.org/meetings/wp02top.html

*14-17 July 2002*

**ICOS-14 14th International Conference on Organic Synthesis**

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*25-30 August 2002*

**Gondwana 11 - Correlations And Connections**

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**Contact:** Professor Bryan Storey
Gateway Antarctica
**Website:** http://www.anta.canterbury.ac.nz/gondwana

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**Contact:** CME
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Email: alain.lecoroller@wanadoo.fr
**Website:** www.cme-emulsion.com

*20-25 October 2002*

**28th Meeting of the Federation of European Biochemical Societies; Jerusalem**

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28th International Conference
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**Website:** www.kenes.com/febs

# Chemists do more than dispense pills

## Bob Brockie's World of Science

Mention research chemists to Jo Blo and he'll think of those white-coated maniacs in television comedies and horror shows, or perhaps those wooden experts making five-second pronouncements on the news.

And, more than likely, Jo Blo will blame these guys for everything that's gone wrong with the modern world – thalidomide, Bhopal, Chernobyl, environmental poisons, GM food, faulty vaccines, Aids, and so on. He forgets that chemists invented all those drugs and the new materials with which we clothe, house, illuminate, transport, inform, entertain and wash ourselves. Research chemists have a serious image problem.

Chemists worldwide have long been unhappy with this situation and fill the correspondence columns of scientific journals with grievances about public incomprehension, getting the recognition they deserve and the money and kudos which go to exploitive entrepreneurs and businessmen.

They also complain that their profession has become publicly invisible. Astronomers are known as astronomers, biologists as biologists, but chemists are given other names – boffins, nerds, industrial or drug developers, molecular and materials scientists, and so on. Teenagers considering careers think chemistry is a pretty unsexy option, so it's becoming harder to attract new talent.

Research chemistry is big. Last year, 18,000 chemists attended the American Chemical Society's annual conference, and the New Zealand Institute of Chemistry has about 1000 members, about 200 from around Wellington.

New Zealand chemists have been busy over the years. They have invented new ways to extract salt from the sea, gold from ore, power from geothermal sources, steel from iron sands, ceramics from clay; they have extended the chemistry of natural gas and concrete; invented new wood, dairy, meat and fish products; stopped some diseases in their tracks and our wool from catching fire en route to Britain; turned wasteland into farmland, animal waste products into pharmaceuticals, developed synthetic fuels and new insights into medicine, forensics and environmental science.

At the moment they are following up promising leads with anti-cancer drugs from sponges and developing marine anti-fouling paint from toxic algae.

New Zealanders don't cut much ice in international commerce, economics, law, politics, peacemaking or the arts. Our metier is supposed to lie in sport and No. 8 fencing wire but, surprisingly, our real genius lies in chemistry. Our three Nobel Prize winners – the atom-splitting Ernest Rutherford, DNA's Maurice Wilkins and the man who will make paper computers, Alan MacDiarmid, are all chemists. Chemists, take a bow.

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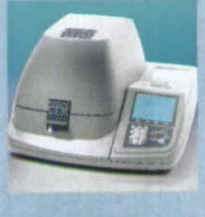

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