NZIC Chemistry IN NEW ZEALAND
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Comment from the President

I would like to begin this by dedicating it to our colleagues in Christchurch who have had to endure so much as a result of the February 22nd earthquake. The NZIC Council was in session that day, at the University of Canterbury Staff Club, so we all experienced the shake, but having to stay an extra night because the airport was closed is nothing compared to the continuing difficulties experienced by those who live and work there. Just to let you know that we are all thinking of you.

The earthquake and its aftermath have also had an effect on NZIC publication activities, since these are all based in Christchurch. We had been planning to produce a second volume of *New Zealand is Different* to coincide with the 2011 International Year of Chemistry, but owing to the Department of Chemistry at the University of Canterbury being effectively closed for two months, publication of this may now slip to early 2012. However, other IYC events outside Christchurch continue as planned, with the National Secondary School Quiz having been held in Wellington early in July. Details of a number of other activities can be found elsewhere in this issue of the Journal.

Finally I would like to mention the ending of one of the biggest chemistry displays that was available world-wide. The US Space Shuttle might have been a product of aerospace engineering, but it was chemistry that got it in to orbit. Each of its two solid rocket boosters contained 500 tonnes of chemical propellant (aluminium powder and ammonium perchlorate bound together by a polybutadiene acrylic acid acrylonitrile terpolymer) which was all burned up in just 124 seconds (at 2300 °C), producing 13.8 million Newtons of thrust. In addition, the large fuel tank that fed the shuttles three main engines contained 735 tonnes of liquid hydrogen and liquid oxygen (all consumed in just eight minutes), adding up to an impressive display of chemical combustion.

Gordon Rewcastle

President

New Zealand Institute of Chemistry

supporting chemical sciences

July News

We were saddened to hear of the death of Dr. *Jack* ***Fergusson*** in a road accident at the end of May. Jack (77) had been retired for some time after many years as an inorganic chemist in the Chemistry Department at the University of Canterbury.

Associate Professor *Allan* ***Easteal*** passed away on the 6th June 2011.

The Institute congratulates Prof *Warren* ***Tait*** (Otago – Biochemistry) on becoming a Companion of the New Zealand Order of Merit in the Queen's Birthday Honours.

The RSNZ (NZIC) ***2011 Marie Curie Lecture Series*** has continued with lectures in New Plymouth (March 22) by Dr *Bridget* ***Stocker*** on *Chemistry, immunology and the sweet stuff*, Dunedin (April 19) by A/Prof *Kate* ***McGrath*** from *Materials to miracles*, Nelson in May by Prof *Penny* ***Brothers***, and June in Palmerston North by Prof *Christine* ***Winterbourne*** *Living with oxygen*. The 2011 RSNZ Distinguished Speaker, Prof *Robin* ***Clark*** CNZM, FRS, Hon. FRSNZ undertook his lecture tour over a two week period from March 23. His lecture *Science meets art: investigating pigments in art and archaeology* followed the article we published in *Chemistry in New Zealand* in the January issue (**2011**, *75*, 13-20).

Kate McGrath, from Victoria University's School of Chemical and Physical Sciences, was appointed Director of the MacDiarmid Institute for Advanced Materials and Nanotechnology in mid-May and took up her appointment on July 1, from when she was also appointed full professor at VUW. Kate has been a Principal Investigator with the Institute since 2002, and is a member of the Institute's Science Executive Committee; she will remain at Victoria University.

MEMBERSHIP MATTERS

MNZIC

Mrs *Rashida* ***Longley***, Mrs *Priyanka* ***Parikh***, Mr *Jonathan* ***Riddell***, (Auckland).

Ms *Wendy* ***Jackson*** (Waikato).

Mr *Carrol* ***Walkley*** (Manawatu).

Dr *Paul* ***Teesdale-Spittle*** (Wellington)

Mr *Aidan* ***Haig***, Mrs *Carolyn* ***McLellan*** (Otago).

Prof *Anthony* ***Hill*** (Overseas)

STUDENT MEMBERS

Mr *Ashveen* ***Nand***, Mr *Xiao* ***Wang*** (Auckland).

Miss *Meenakshi* ***Batra***, Miss *Anna* ***Carter***, Mr *Neville* ***Coughlan***, Mr *Kyle* ***Devey***, Mr *Dominic* ***Fitzpatrick***, Mr *Hamish* ***Galt***, Ms *Alexandra* ***Keyte Beattie***, Miss *Jessica* ***MacAskill***, Miss *Samantha* ***Muir***, Miss *Adelle* ***Nancekivell***, Miss *Nicola* ***Noort***, Mr *Sam* ***Pachal***, Miss *Maria* ***Revell***, Mr *Prakash* ***Srinivasan***, Ms *Keri* ***Thomas***, Mr *Stephan* ***Turner***, Mr *Yuan* ***Wang***, Ms *Wenjuan* ***Yang*** (Waikato).

Mr *Sebastian* ***Blackwood***, Miss *Rachael* ***Knapp***, Miss *Ashley* ***Way***, Miss *Amy* ***Willoughby*** (Manawatu).

Mr *Cullum* ***Boston***, Miss *Hilary* ***Corkran***, Dr *Peter* ***Ferguson***, Mr *Gerard* ***Moggre***, Mr *Chenlong* ***Yu*** (Wellington).

Mr *Solomon* ***Wasseyehun*** (Canterbury).

Mr *Alistair* ***Lee***, Mr *James* ***Lewis***, Mr *Samuel* ***Walsh***, Miss *Cleo* ***Davie Martin*** (Otago).

BRANCH NEWS

AUCKLAND

On Monday 23rd May, the NZIC Auckland Branch held a competition at St Cuthbert's College to select the secondary school team of *four* students to represent the Auckland region at the National NZIC Quiz final. This Secondary School Chemistry Quiz was held in Wellington on Tuesday 5 July 2011 with the NZIC Auckland Branch providing funding for the team and a mentor to travel to this event. The format for the Auckland competition was a nine-round quiz consisting of chemistry theory and trivia questions. There were 34 teams of 4 students, from 22 schools, with the team from Whangarei Girls High School travelling the furthest. After answering almost 100 questions, the final results gave the top 5 schools in order as:

1st ***Macleans College***; 2nd ***Auckland Grammar***; 3rd ***St Cuthbert's College***; 4th: ***Alfriston College***; 5th ***Onehunga High School***

Congratulations to all the students involved and to the winning team. The afternoon proved to be highly competitive as well as entertaining.

The April NZIC Branch seminar featured Prof *Antonio* ***Ricco*** (NASA Ames Research Centre, California and Biomedical Diagnostics Institute, Dublin City University) who spoke on *Life Science Research in Outer Space: New Platform Technologies for Low-Cost, Autonomous Small Satellite Missions*, and the approaches he uses to develop miniaturised integrated instruments and platforms for economical, frequent space access for autonomous life sciences experiments in outer space. Dr Ricco described three of NASA's recent custom-developed *nanosatellite* missions – GeneSat, PharamaSat, and O/OREOS - showing the implementation of miniaturized analytical payload systems.

Massey -Albany

Prof *Peter* ***Schwerdtfeger*** is currently Deputy Head of the *New Zealand Institute for Advanced Study* and for the *Institute of Natural Sciences* at Massey-Albany. He gave the 2011 ceremonial address (Festvortrag) on the occasion of the young achievers prize (Mez-Starck MSc Prize) for the top MSc chemistry students at the University of Ulm (Ulm is the birthplace of Albert Einstein). His talk showed how Einstein's relativity influences the chemistry and physics of gold. He also delivered an NZIC talk on *Beyond the Periodic Table–Going for the Superheavy elements* and a chemistry seminar lecture on *Left or Right in Nature–The Origin of Biomolecular Homochirality* at Victoria University in Wellington. Peter is currently on a two and a half months leave to participate at international conferences in Spain, Germany and Austria, and to give lectures at universities throughout Germany. *Tim* ***Hangele*** (Cologne University) and *Anna-Lena* ***Deppenmeier*** (Göttingen University) joined the Centre for Theoretical Chemistry (CPCT) for postgraduate studies. Four current members of CTCP (Dr *Elke* ***Pahl***, Dr *Anastasia* ***Borschevsky***, Tim and Peter) are invited to present talks or posters at the WATOC congress in Santiago de Compostela in Spain. Anastasia will also visit the GSI in Darmstadt to collaborate on superheavy element research, and will give an invited lecture at the TAN11 conference in Sochi (Russia) to talk about her research on transactinides. Dr *Kyle* ***Beloy*** (currently working at CTCP on the variation of fundamental constants in space-time) has accepted a fellowship at NIST-Boulder (Colorado). Dr *Susan* ***Biering*** joined CTCP as a postdoctoral fellow to work on high-pressure materials.

University of Auckland

The Chemistry Department has recently had a name change, and from 1 May 2011 is known as the School of Chemical Sciences. Continuing on from his role as Head of Department, Prof *Jim* ***Metson*** has been appointed as Head-of-School for a five year term. As Jim commented recently, *although this builds on a very long and distinguished history, the name change is far more than symbolic as it does reflect the increasing diversity and reach of chemistry*.

A recent addition to the School academic staff has been Dr *Donald* ***Wlodkowic*** as a Senior Lecturer. Donald has established the BioMEMS Research Group, with interests in constructing laboratories-on-a-chip, and has a joint appointment with the School of Biological Sciences. Also expected to join the School in July is Dr *Jianyong* ***Jin*** as a Senior Lecturer in Polymer Chemistry.

A sad note has been the passing of two staff members from the Departmental scene. In March *Linda* ***Wright***, a highly valued member of the undergraduate technical staff, suddenly passed away. Many members of the Department, past and present, attended her funeral in support of Linda's family, who have strong connections to the Department also through Linda's father, A/Prof *Graham* ***Wright***. More recently, news came through of *Alan* ***Grout***'s passing. Alan worked in the Department for many years, including the transition from Old Choral Hall to the current building in the late 60s and later became Chief Technical Officer.

In June, the School held its third annual research showcase with the winners of the PhD research showcase abstract competition, *Jin* ***Akagi***, *Orla* ***Finch***, *Cosmin* ***Laslau***, *Gerard* ***Logan***, *Anna* ***Matuszek***, *Najimah* ***Hassan***, giving oral presentations. The winner of the L.H. Briggs prize for the top Chemistry PhD submitted in 2010 was announced at the May Chemistry graduation reception. From some 20 PhD theses submitted last year, the award went to Tanja Kjällman, for a thesis entitled *Surface-Immobilized Hairpin DNA Sensors for Direct and Specific Detection of Target DNA*. Under the supervision of A/Prof *Jadranka* ***Travas-Sejdic***, Tanja demonstrated sensor sensitivity down to 4.7 fM of target and was capable of detecting single-base mismatches, fulfilling the requirements for a high-quality DNA sensor.

On the media front, the 14th April episode of *Our Changing World* on National Radio featured the new research in the Microfabrication, including Lab-on-a-chip. The episode included an exercise in gowning-up the radio presenter for entry into the Clean Room, hosted by Prof *David* ***Williams***, *Jin* ***Akagi***, Dr *Bryon* ***Wright*** and Dr *Donald* ***Wlodkowic***. The laser micromachining undertaken in the nanometer range and femtosecond time scale in the Photon Factory was explained by Dr *Cather* ***Simpson***, Dr *Charles* ***Rohde*** and Joshua Bradfield. On a slightly larger scale, Dr *Gordon* ***Miskelly***, completed the Oxfam 100 km trail walk with wife *Denise* ***Albert*** and team members in *The Sequel* who were well within time, completing the event in 20 hours and 32 minutes; they raised over $4000 for Oxfam.

In March, Prof *Margaret* ***Brimble*** received a Dean's award for Teaching Excellence for her contribution in Postgraduate Research Supervision. Recently, Margaret was re-elected as a Titular Member of the Organic and Biomolecular Division of IUPAC (Division III) and appointed as Division Secretary. She is attending the IUPAC IYC General Assembly in Puerto Rico in July in her role and also delivering the Medicinal Chemistry Symposium plenary lecture. Margaret also gave an invited lecture at the ACS meeting in Anaheim in a special symposium to celebrate IYC.

Seminars within the School in recent months have included Prof *Kevin* ***Smith*** (Boston University) talking on *Observation of Intrinsic Electron Quantum Well States in Solids*; Prof *Annie* ***Powell*** (Karlsruhe Institute of Technology) on *The Apotheosis of Coordination Chemistry*; Prof *Santi* ***Nonell*** (Universitat Ramon Llull, Barcelona) outlined research on biomedical applications of light, photofunctional materials and molecules, sunscreens for photo-protection in two talks in April entitled *Why Blood is Red and Grass Green: on the Colours of Life, Count Dracula and the Photodynamic Therapy of Cancer,* and *Porphycenes for photodynamic therapy applications*. In addition to his NZIC address, Prof *Antonio* ***Riccо*** spoke on *Microfluidics for Biomedical Research and Point-of-Care Diagnostics* and the development and biomedical applications of polymer microfluidic array platforms. May was a busy month for visiting speakers that included Prof *Lloyd* ***Davis*** (University of Tennessee Space Institute): *Femtosecond Laser Fabrication of Devices for Single-Molecule Spectroscopy and Applications in Biotechnology*; Prof *Steven* ***Ley*** CBE FRS FMedSci (Cambridge): New *Tools for Molecule Makers*, that included the use of solid-supported reagents and advanced scavenging agents for organic synthesis as a 2011 Maurice Wilkins Centre Lecture. He also presented the 2011 de le Mare Memorial Lecture on *Adventures in Natural Product Synthesis* that looked at more efficient methods of synthesis with less waste and lower energy consumption. Prof *Martin* ***Albrecht*** (University College Dublin) spoke on *Synthetic and Catalytic Application of (Abnormal) Carbene Ligands*; Dr *Boniface* ***Fokwa*** (RWTH Aachen University) on *Rational Design of New Itinerant Magnets looking at transition metal-rich borides containing a m*agnetically active element; and Prof *Lisa* ***McElwee-White*** (NSF-CCI Center for Nanostructured Electronic Materials, University of Florida) on *Mechanism-Based Design of Precursors for the Deposition of Inorganic Materials*.

CANTERBURY

The Canterbury launch of IYC was to occur at *Science Alive!* on March 4 but these plans were rudely interrupted by the February 22nd earthquake. Several events planned for March and April including a fireworks demonstration/lecture will now occur later in the year. Having spent several months dealing with the results of the earthquake and thousands of aftershocks (an outline of how it affected different institutions is provided below) the Branch committee is now determined to get IYC celebrations underway.

Prof *Ian* ***Shaw*** (Toxicology, Canterbury and Food Safety, Lincoln) gave a public lecture at Christchurch Polytechnic Institute of Technology (CPIT) on Tuesday May 17 entitled *Poisonous Chemistry*. The lecture was well attended with an audience of over 60 members. In his lecture, Ian narrated a trip through the human body's response to the cornucopia of chemistry it is exposed to, every second of every day. He discussed the science of toxicology, and why some toxic chemicals have emerged as some of the most useful medicines of our time.

CPIT

With CPIT occupying the south east corner of the Red Zone for several weeks post-earthquake some challenges resulted. However, thanks to the collegial assistance of our colleagues at Lincoln University and the hard work of CPIT staff our science programmes were up and running within three weeks at Lincoln University. Thanks to Lincoln, theory and computer-based work was achieved during April-May before the students, now back at CPIT's city site, completing intensive practical components of their coursework.

With the city site now designated as safe, CPIT is providing a useful venue for NZIC events as the demand on Canterbury University space largely precludes external events. In addition to being the Chair of the Canterbury Branch and 2nd Vice-President of the NZIC, *Michael* ***Edmonds*** is Programme Manager for the School of Applied Sciences and Allied Health at CPIT as well as teaching analytical chemistry.

University - Chemistry

The majority of buildings on the University campus stood up well to the February earthquake, but it took time to fully assess the safety of so many of the buildings. While this was being done, a tent city was created on campus to house lectures. The reduction in teaching space meant an expansion to the teaching day and week to include early morning, evening, and Saturday classes!

The Rutherford building, which houses Chemistry and Physics, took a lot of time to both assess and reoccupy. When first occupied, limits were placed on the number of people allowed in the building at any one time and the lift and toilets were placed

off limits. One can only marvel at the dedication of anyone working on the upper floors under these conditions.

Some of our PhD students have found temporary alternative research space in other laboratories around the country and further afield. The generosity of those offering such place, including IRL, is greatly appreciated.

Dr Michael Edmonds and Prof *Richard* ***Keene*** have both had their adjunct appointments renewed. Richard (Nevitt Professor of Chemistry, School of Pharmacy & Molecular Sciences, James Cook University, Townsville) has had a close association with the UC since visiting as an Erskine Fellow in 2000, returning on sabbatical leave in 2003. He became an Adjunct Professor in 2004 and has returned a number of times since then, collaborating with *Peter* ***Steel***, with whom he has held a number of RC and Marsden grants. Richard anticipates another visit in August this year.

Dr *Sarah* ***Masters*** took up her position as a lecturer in Physical Chemistry on January 6. She completed her PhD at the University of Edinburgh in 2000 where her thesis concerned the static and dynamic effects of sterically demanding ligands on gas phase molecular structure, in particular *jack-in-the-box* molecules. Sarah was awarded the Edinburgh Royal Society/BP Personal Research Fellowship in 2005 to develop new methods for the structure determination of short-lived species, an area she will continue to research in her current position. Dr *Nabyl* ***Merbouh***, originally from Morocco, arrived in Christchurch in January. He studied chemistry at the University of Tours (France) and received his PhD at the University of Connecticut before accepting a lectureship in organic chemistry and spectroscopy at Simon Fraser University (Canada) in 2005. He has been involved heavily in undergraduate training and research but in while here he will be working with Prof Fairbank on polysaccharide synthesis. *Patrick* ***Dronk*** also arrived in January (from Breda, Netherlands) and completed an internship with the Curnow group characterizing different ionic liquids in order to complete his degree. He has returned home.

As noted in the April issue, husband and wife academics A/Profs *Robert* and *Margaret* ***Maclagan*** retired from University in January having clocked up 80 years of service between them. The Maclagan's now have assumed adjunct professor status. Margaret was the driving force behind the 1989 establishment of the Bachelor of Speech and Language Therapy degree at UC, while Robert's primary research interest has been computational chemistry. He witnessed some dramatic changes in computing since his 1972 arrival at UC and commented recently *my laptop now is more powerful than the sole University computer was when I arrived. While I have dinner it could do all the computing I did for my entire PhD*. Robert has also been involved intimately as coach, mentor and organizer with NZ's participation in the International Chemistry Olympiad even before the first national team competed in Pittsburgh, US in 1992.

ESR

ESR's facility adjoining the University of Canterbury, thankfully, is built like a brick privy and despite a few cracks here and there weathered both the September and February earthquakes fairly well; it was up and running approximately a week after each event. The main chemistry laboratory situated on the top, *i.e.* third, floor bore the brunt of the shaking both times, resulting in large quantities of broken glassware. Thanks to prescient building and safety officers, worse damage was avoided for the most part and the laboratories new LC/MS/MS/MS was up and running again in short order.

ESR management responded promptly after the February quake by organizing a staff gathering that provided not only the opportunity to touch base with co-workers but also that most important of food groups, pizza! While the ESR building survived, the homes of many staff members were not spared and ESR has been very flexible and understanding as staff juggle work with insurance, EQC claims, and stress. Thus, it is with regret that we note the resignation of ESR's CEO, *John* ***Hay***; *Fiona* ***Thomson-Carter*** accepted the role of CEO until *Graham* ***Smith*** (CEO of ITEK - the technology transfer arm - University of South Australia) arrives in early August.

MANAWATU

Dr *Ken* ***Whittle*** FNZIC, Dean of Science and Technology at the Eastern Institute of Technology, retired in June after a career of over 38 years service in the Polytechnic sector. Prior to this appointment Ken spent 27 years at UCOL as the Chemistry Lecturer and then as the Head of Faculty. He also held positions within the Manawatu Branch as the Treasurer, Chairman and Council Delegate. We wish him well in his future years.

Massey University

New postgraduates in Chemistry include *Katie* ***Aitkenhead***, studying chiral cyclophanes and *Shane* ***Chapman***, studying chiral monophosphines, both are supervised by Gareth Rowlands. *Paul* ***Pleiger***'s new students are *Nick* ***Bent***, studying anion binding, and *Nishani* ***Mudiyanselage***, studying quinoquinoline dyes, while *Amy* ***Willoughby*** and *Nirosha* ***de Silva*** are studying single molecule magnets. *Megan* ***Fowler*** is studying NMR metabolomics under the supervision of *Pat* ***Edwards***. *Mark* ***Waterland***'s new students are *Robert* ***Mc Ewan***, studying photonic crystals, and *Ashley* ***Weigh***, studying ionic liquids. *Pania* ***Te Whaiti*** is developing hydrogels for metal recovery under the supervision of *Dave* ***Harding***. *Shane* ***Telfer*** is now supervising *Sebastian* ***Blackwood*** and *Rachael* ***Knapp***, who have started projects on dipyrrin synthesis while *Sanjay* ***Gupta*** and ***Selvakumar*** have begun work on a Marsden-funded project developing metal-organic frameworks.

Shane Telfer contributed a chapter towards the recently published *Plain's Science*. The chapter details scientific discoveries made in the Manawatu, focusing on the key contributions made by Massey University scientists to understanding the bioinorganic chemistry and structural biology of lactoferrin. Shane was also programme co-chair at Crystal 27, the conference of the Society of Crystallographers in Australia and NZ, which is held every second year.

At the conference *Rajesh* ***Deshpande*** presented a poster on his research into photolabile protecting groups in metal-organic frameworks, and *Geoff* ***Jameson*** gave a keynote talk on the transformational nature of Massey's Spider X-ray diffractometer.

Before returning to Germany in April, *Janina* ***Fischer*** (MPI-P, Mainz) presented a lecture on the subject of her PhD research—the preparation of novel crescent-dimer structures by colloidal lithography. She has since been awarded her PhD. In May, *Andreas* ***Stasch*** (Monash University) shared his work on the synthesis of stable molecular magnesium(I) compounds containing Mg-Mg single bonds as part of the Alan Sargeson Lectureship tour.

OTAGO

In early March, the Branch helped fund the *Chemistry for Christchurch* Magic Show, an event organized by the Chemistry Department's Outreach Team to raise funds for the Red Cross Christchurch Earthquake Fund. This event, held on a Saturday afternoon, was so popular that in addition to the reserved 600-person lecture hall, four additional rooms had to be opened for remote *via* video link presentation; around 700 people attended. The show featured exploding balloons, hands-on fire and liquid nitrogen fountains, all to the delighted gasps of the children in the audience and the general consensus was *it should be held more often*! Through gold coin entry donations and a barbeque that followed, more than $3100 was raised. A television interview about the event can be seen at: *www.ch9.co.nz/content/chemistry-christchurch-goes-bang-0*

This year's Interschool Chemistry Quiz was held on Thursday May 19, earlier than normal so as to fit with the National Quiz in Wellington in early July. Some 49 teams of Year 12 and 13 students represented 15 schools from Otago and Southland. The quiz for the *Bunsen Burner of Wisdom* was held in the Hutton Theatre of Otago Museum and consisted of six rounds of questions on both chemistry and general knowledge. The annual Chemical Haiku competition was also a highlight of the evening. When the dust and pizza crusts settled, the ***cbf*** team from James Hargest High School was declared winner. This is the first time that a team from a non-Dunedin school has won. The ***milliVolts*** (St Hilda's Collegiate) came second and ***Premature Extrapolation*** (Otago Boys High) came third. The event was supported by Poppas Pizzas, the University Book Shop, the Otago Museum, the Otago NZIC Branch, and Otago University. It was run by many students and staff from the Chemistry Department. The Otago NZIC Branch donated $500 to help the winning team travel to Wellington for the July National Quiz.

The two Best Chemical Haiku were:

I pity the fool
Who thinks chemistry ain't cool
It makes the nerds drool.

'A' Team – Taieri College

Name: Elephantus
Carbon, oxygen and stuff
He ate my peanut.

Ba-Radius – Otago Girls High School

2011 Winners of the Otago-Southland Interschool Chemistry Quiz, holding the Bunsen Burner of Wisdom

Chemistry Department

A ground-breaking gel for healing wounds after sinus surgery has been successfully commercialized in a collaborative deal for the University. Potentially, the gel could lead to a reduction in the number of post-operative complications, which frequently occur following sinus surgery. Leading US-based medical technology company Medtronic have purchased the patent to a medical gel application developed by the OU chemists in partnership with the Adelaide University and Robinson Squidgel, a Wellington-based company. The sale was brokered by a team comprising *Brian* ***Robinson***, *Jim* ***Simpson***, *Stephen* ***Moratti*** and *Lyall* ***Hanton***. Peter-John Wormald (Adelaide) and ENT surgeon, Simon Robinson of Robinson Squidgel Ltd., performed the clinical trials. More information can be found at: *www.otago.ac.nz/news/news/otago016627.html*

Two of the PGSF programs involving Plant & Food Research staff have had their funding extended by the Ministry of Science and Innovation (ex FRST). Nutrigenomics NZ, a collaboration with AgResearch and Auckland University, has a further 4-year contract for its work on nutritional genomics applied to Inflammatory Bowel Disease. *Nigel* ***Perry*** leads the Biomolecular Discovery objective, using *in vitro* assays to direct the isolation of bioactive compounds from NZ foods, beverages and herbs.

Flavours of New Zealand, a collaboration with the Federation of Māori Authorities, is developing new flavours from native plants to add value to NZ food exports. The current lead is an extract from manuka foliage using a particular regional chemical type. A bulk concentrated extract has been prepared by supercritical fluid extraction at IRL, and is now being incorporated into foods to present to potential commercial partners.

In May, the Department's 13 Honours and PGDipSci students gave 15-minute talks about their research in a symposium held at the Otago Museum. The successful event showcased the talent of these young researchers.

Three of *Kimberly* ***Hageman***'s PhD students attended the Society of Environmental Toxicology and Chemistry meeting in Milan (Italy) last May. *Karen* ***Lavin*** gave a talk about the atmospheric transport of contaminants to Arthur's Pass National Park and the determination of their geographical sources. *Ruma* ***Ghosh*** spoke on the toxicological effects of brominated flame retardants on fish from McMurdo Sound. *Pourya* ***Shahpoury*** presented a poster describing concentrations and trends of current and historic pesticide in NZ pastoral streams. Karen received a travel award from the NZ Federation of Graduate Women and Pourya one from the Otago Ecology Research Group.

WAIKATO

Prof *Robin* ***Clark*** (UC-London) gave his RSNZ lecture *Science Meets Art: Investigating Pigments in Art and Archaeology* to an enthusiastic Waikato audience in Hamilton in March.

Waikato University

Alistair ***Wilkins*** is spending three months in Oslo as part of his collaboration with the Norwegian Veterinary Institute, while *Merilyn* ***Manley-Harris*** has departed for a short sabbatical at the University of Montana.

Nick ***Lloyd*** has completed his PhD (supervisor: *Brian* ***Nicholson***) and is looking for new opportunities, whilst *Julia* ***Lin*** completed her BSc(Hons) (with *Bill* ***Henderson***) on the chemistry of cycloaurated complexes. New PhD students in the Department include *Megan* ***Grainger*** working on aspects of honey chemistry (with Merilyn Manley-Harris), *Kyle* ***Devey*** investigating methods of non-destructive soil testing methods (with Hill Laboratories, Brian Nicholson and *Michael* ***Mucalo***) and ***Jacob Jaine*** (with Michael Mucalo and *Graham* ***Saunders***) studying the immobilisation of metal nanoparticles on novel supports for use as heterogeneous catalysts.

Steven ***Wu*** has begun his MSc with Bill Henderson and is looking at luminescent complexes containing thiourea ligands, while *Neville* ***Coughlan*** is a BSc(Hons) candidate working with Bill on water-solubilising metal complexes. The Department has enjoyed hosting one of *Owen* ***Curnow***'s PhD students, *Ruhamah* ***Yunis*** for a few weeks so she could continue her laboratory work while the Canterbury labs were being restored for use after the February earthquake.

In collaboration with colleagues from Otago and Canterbury Universities, Michael Mucalo helped run the 21st Australasian Society of Biomaterials and Tissue Engineering Conference (ASBTE 2011) held 27-29 April in Queenstown. The extremely successful meeting attracted around 130 delegates, predominantly from the Australian and NZ biomaterials community, but with representatives from the USA, UK, Europe, Singapore, China, Taiwan, Korea, and Iran. Plans were laid for the establishment of NZ's own Biomaterials and Bioengineering Society in which Michael and colleagues from Otago and Canterbury will be playing a founding role. Graham Saunders and Brian Nicholson attended the Crystal27 Conference in Rotorua.

WELLINGTON

The Branch meeting on Wednesday March 9 was preceded by drinks, a barbeque and ice-cream as a part of the student membership drive. The meeting itself took the form of an eloquent discourse by Dr *Justin* ***Bendall*** (Fonterra) on *Bad Taste: The Chemistry of Food & Beverage Taint Compounds* – he even provided a sample of 'corked' wine! The taint in a food or beverage, whether produced by chemical means or by microbiological means, is regarded by consumers as an indication that the food is unfit for consumption. Although relatively few customers complain about a food taint, many more lose confidence in the product and its brand and avoid it. More importantly, a taint can be associated with a food safety hazard from microbiological spoilage or gross chemical contamination. Thus, the causes of food taints need to be quickly identified and remedied. Justin outlined some of the procedures and the chemistry behind taint problems that Fonterra has encountered, and discussed the lessons that can be learnt by other NZ food manufacturers.

April saw us addressed by Prof *Peter* ***Schwerdtfeger*** (Massey-Albany) on the topic of a part his April *Chemistry in New Zealand* (2011, 75, 91-95) article under the title *Beyond the Periodic Table – Going for the Superheavy Elements*. Peter alerted us to the Goeppert-Mayer's 1948 prediction that nuclear shell closure effects will increase the nuclear stability substantially, and that Meldner demonstrated in 1967 that the next proton/neutron shell closure (nuclear island of nuclear stability) would occur at the nuclear charge Z=114 and neutron number N=184, the next island of nuclear stability. He took us through the past decade that has seen the production of new elements for the Periodic Table up to nuclear charge 118, and asked: *How far can we go? Where does the Period Table end? Can we do chemistry with such exotic elements? What is the chemical and physical behaviour of these exotic elements?* A thoroughly enjoyable lecture and good food for thought!

The May meeting was held on the VUW campus on May 11th when *Joel* ***Baker*** (Professor of Geochemistry and Cosmochemistry, VUW) addressed the gathering on *A geochemist's window into Earth's origins, past and future*. He described how the measurement of the elemental and isotopic composition of meteorites, rocks and fossils can be made with increasingly greater sensitivity and precision to give unique quantitative insights into the processes and timescales of the formation of the Solar System, the evolution of our planet, how volcanoes work, and past and future climate change. He explained the analytical tools that geochemists use to study the natural world, and illustrated them with three recent examples from his research work. These were: i) how measurement of the mass-independent abundance of magnesium isotopes in meteorites provides unprecedented insights as to how quickly and what happened on small planets that formed in the young Solar System some. 4567 million years ago; ii) just how big some volcanic eruptions have been in Earth's past and the effect they may have had on Earth's climate and biosphere; and iii) how the elemental composition of tiny microfossils from deep sea sediments can provide quantitative constraints of past changes in ocean temperature and chemistry that have direct relevance to predicting the scale and rapidity with which current anthropogenically-forced climate change may affect us.

Ian ***Miller*** now has an e-book in print entitled *Aristotelian Methodology in the Physical Sciences (Elements of Theory)* (Kindle Edition; Amazon Digital Services). Ian poses the questions: How do you form a theory? How can you be more creative? How do you analyse data and theories?, and then provides his answers. Underlying his discourse is that fre-

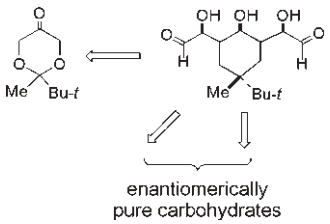
quently there is more than one way of viewing a particular problem, and if you look at a given problem a different way, you may see something fresh. He offers an update on Aristotle's methodology and applies it to problems from both chemistry and physics.

Victoria University – SCPS

As noted earlier in this news section Kate McGrath was appointed Professor on 1 July. Prof Jan Reedijk (Leiden University, Netherlands) visited on Mar 21, met with staff and students and gave a seminar on *Multifunctional Metal-DNA Interaction: Inspiration for new Antitumor Drugs*. Dr *James* ***Crowley*** (Otago University), a VUW graduate from the mid-1990s, visited the School on March 29 and gave a seminar on his way to Massey University. He spoke about his productive and elegant work involving *supramolecular synthesis – macrocycles, cages and materials* in the metallosupramolecular arena that is establishing him as a driving force in chemistry at Otago. Dr *Bridget* ***Stocker*** (Malaghan Institute) gave her lecture *Chemistry, Immunology and the Sweet Stuff* in the Marie Curie series in New Plymouth on Mar 22 while the new MacDiarmid Director Prof Kate McGrath's *From Minerals to Miracles* was in Dunedin on April 19 prior to her MacDiarmid appointment; they attracted some 40 and 100 people, respectively.

On Apr 7, Prof Abhik Ghosh (Tromsø, Norway) revisited the School, discussed his new book *Letters to a Young Chemist* that outlines the real benefits of chemistry to society (see book review elsewhere), met with colleagues and addressed us on *From Corroles to Chirality*, outlining the benefit of these ligands in high-valent transition metal complexes. A week later Prof. *Peter* ***Schwerdtfeger*** (Massey–Albany) spoke to the School on *Left or Right in Nature - Biomolecular Homochirality and Chemical Evolution* before his evening Branch address (see above). Just before the Easter recess, Prof *Martin* ***Banwell*** (ANU) revisited us and gave a particularly lucid and elegant seminar on *New, Enabling Methodologies for Natural Products Synthesis* that attracted some 40 members of the School. His work started with the fermentation-induced dihydroxylation of simple benzene derivatives and provided a range of fascinating and potentially useful *ent*-natural products.

Dr *David* ***Jefferson*** (Chemistry Department, Cambridge University) spent two months working with Dr *Richard* ***Tilley***'s nanomaterials group from mid-February while Prof *Marek* ***Majewski*** (Saskatchewan, Canada) spent a month with the VUW biochemists and gave the chemists a delightful lecture *Playing symmetry games on the dioxanone scaffold* in mid-May, in which he provided his group's work with 2-methyl-2-*t*-butyl 1,3-dioxan-5-one that has provided a clean entry into chiral carbohydrates as illustrated below:



The 2011 Alan Sargeson Lecture *The Chemistry of Molecular Magnesium(I) Compounds* was presented in the School by Dr *Andreas* ***Stasch*** in mid-May as part of his NZ lecture tour.

Peter ***Clark*** and *Matthias* ***Herzhog*** have completed their MSc (Hons.) programmes and are expected to return for PhD research, Peter in Oxford and Matthias at VUW.

ChemEd 2011 will be held 17-20 July in Palmerston North. It will be a great way ***for educators to join together to celebrate the*** **International Year of Chemistry**. ***Be inspired by*** leading international and national speakers including ***Jonathan Hare*** (UK) who did his PhD working with Sir Harry Kroto and is well known for his television work on series such as *Rough Science* and ***Tony Wright*** (Australia) who has a passion for chemistry education using digital technology.

For further information see *www.chemed2011.co.nz*

What's New in Olefin Metathesis Catalyzed by Molybdenum and Tungsten Complexes?

Richard R. Schrock

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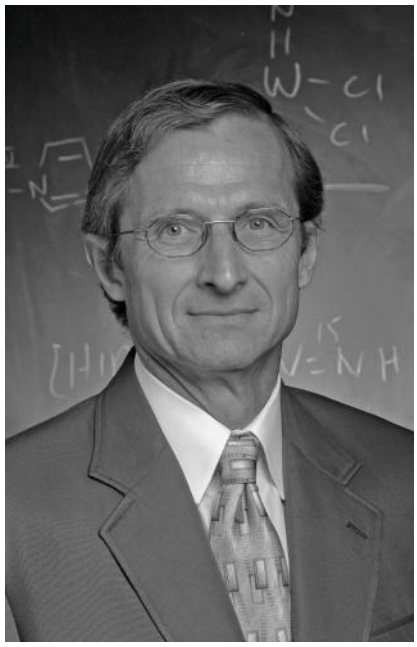
(e-mail: *rrs@mit.edu*)

About the Author

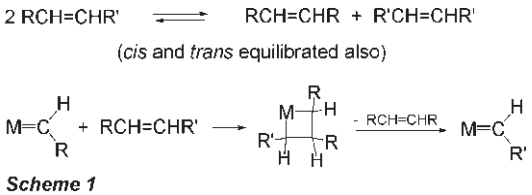


Richard Royce Schrock was born on January 4, 1945, in Berne, Indiana. He is recognized for his contributions to olefin metathesis for which he received the 2005 Nobel Prize in chemistry (with Grubbs and Chauvin). He attended Mission Bay High School in San Diego, holds a BA from the UC-Riverside and a PhD from Harvard University. His postdoctoral period was spent with Lord Jack Lewis at Cambridge. After a spell in industry with DuPont at the Wilmington Experimental Station, he joined the faculty of the Massachusetts Institute of Technology in 1975, became full professor in 1980 and (since 1989) holds the Frederick G. Keyes Professorship in Chemistry there. Schrock is a member of the American Academy of Arts and Sciences, the National Academy of Sciences and was elected to the Board of Overseers of Harvard University in 2007. He is married, has two sons and lives in Winchester, Massachusetts.

On his 8th birthday, Richard's elder brother Theodore presented him with the proverbial chemistry set to help satisfy his love of building things. Thus, began his interest in chemistry. He created a small laboratory at the end of a storage area for canned goods with shelves for the ever expanding collection of test tubes, beakers, and flasks (obtained by mail order with money earned from an early morning paper round). At 13 years, Harry Dailey, the then high school chemistry teacher, stoked his interest in chemistry with more textbooks and discarded equipment and this has continued unabated.

Schrock was the first to elucidate the structure and mechanism of so called 'black box' olefin metathesis catalysts. Initial work at DuPont involved the synthesis of tantalum alkylidenes, alkylidenes being a crucial resting state in the catalytic cycle of olefin metathesis. His work at MIT has led to a detailed understanding of a group of molybdenum alkylidenes and alkylidynes, which are active olefin and alkyne metathesis catalysts, respectively. Schrock has done much work to demonstrate that metallacyclobutanes are the key intermediate in olefin metathesis, with metallacyclobutadienes being the key intermediate in alkyne methathesis. Schrock carbenes are named after him. Richard Schrock's work is ongoing with goals of furthering the understanding of metathesis selectivity and developing new catalyst architectures. His work outside of metathesis includes elucidation of the mechanism of dinitrogen fixation and developing single molecule catalysts which form ammonia from dinitrogen, mimicking the activity of nitrogenase enzymes in biology.

We are now well past the 50th anniversary of an observation by H. Eleuterio (in 1956) of a reaction that ultimately came to be known as *olefin metathesis*, a metal-catalyzed reaction that cleaves and rearranges carbon-carbon double bonds.[1] The generic version and the accepted mechanism, which was first proposed by Hérrison and Chauvin,[2] are both shown in Scheme 1. Over the last forty years much research has been directed toward the synthesis and study of metathesis catalysts that are *well-defined*, *i.e.* that are not altered substantially during the reaction and that have been isolated, structurally characterized, and studied in detail. Most of these are either *high oxidation state* catalysts that contain Mo or W, which will be discussed here, or ruthenium-based catalysts.[3]



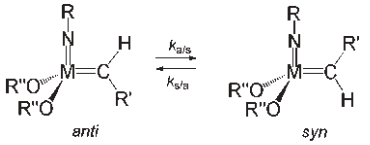
Scheme 1

What could be called first generation Mo and W catalysts have the formula $M(NR)(CHR')(OR'')_2$.[4] The first examples were prepared 1986.[5] They are electron deficient (14 electron count) complexes, sensitive to air and water, and thermally unstable when the composite steric crowding (provided by the four ligands) is insufficient to slow bimolecular coupling of alkylidenes. Methylidene

species are especially unstable toward bimolecular decomposition. The challenge has been to design M(NR)(CHR')(OR")$_2$ species or, less commonly, M(NR)(CHR')(OR")$_2$(L) species, in which the donor ligand L is labile but the complex is still capable of isolation and employed as the initial alkylidene species in an alkene metathesis reaction.

The metallacyclobutane intermediate in a metathesis reaction often can be observed and in some cases isolated. Metallacyclobutanes have been found to have either a trigonal bipyramidal structure in which imido and alkoxide groups are in axial positions, or a square pyramidal structure in which the imido ligand is in the apical position.[4d] It is not known whether one of these, or some other metallacyclobutane, is formed initially. In any case, five-coordinate metallacyclobutane species readily interconvert on the NMR time scale, so observed structures may be located in relatively shallow minima on the energy surface.

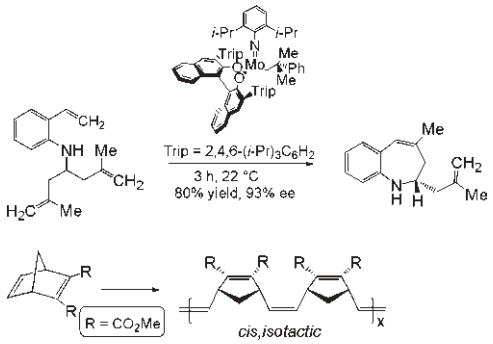
An important feature of M(NR)(CHR')(OR")$_2$ species is the possibility of forming isomers, a *syn*-alkylidene, in which the alkylidene substituent points toward the imido ligand, and an *anti*-alkylidene, in which the alkylidene substituent points away from the imido nitrogen (Scheme 2).[6] The rates of interconversion of these two isomers depend dramatically on the nature of OR" and can vary by as many as six orders of magnitude. The interconversion of *syn* and *anti* isomers is by rotation about the M=C bond in the four-coordinate species. They also interconvert during a metathesis reaction if all possible metallacyclobutanes can form. At first sight, an olefin metathesis reaction is more complicated as a consequence of interconversion of *syn* and *anti* isomers, but since the M=C bond resists rotating in the process of forming a metallacyclobutane intermediate, *Z* (*cis*) selective metathesis reactions become possible.



Scheme 2

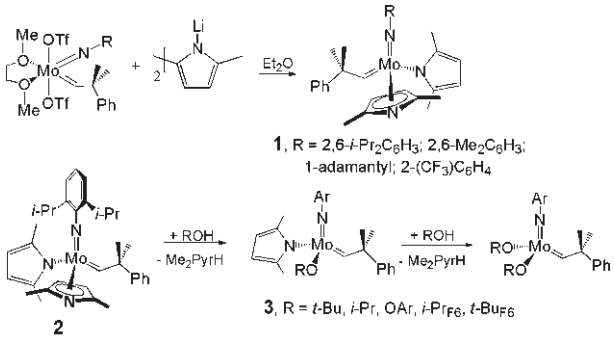
Second generation catalysts were reported in 1993 in the context of controlling the structure of ROMP (Ring-Opening Metathesis Polymerization) polymers[7a] and, in 1998, in the context of enantioselective organic reactions[4a,7b] Second generation catalysts contain a bidentate biphenolate or binaphtholate ligand as shown for an asymmetric ring-closing reaction shown in Scheme 3 (upper).[8] An example of stereoselective ROMP is the synthesis of *cis,isotactic*-poly(dicarbomethoxynorbornadiene) shown in the lower part of Scheme 3. An account of the use of Mo and W catalysts to prepare ROMP polymers stereoselectively has appeared recently.[9]

The dramatic increase in the number of possible catalysts and the extreme sensitivity of the outcome of a given metathesis reaction to subtle changes in the catalyst requires that catalysts be generated *in situ*, at least for screening purposes. A convenient method would be through addition of an alcohol or diol to an M(NR)(CHCMe$_2$R')X$_2$



Scheme 3

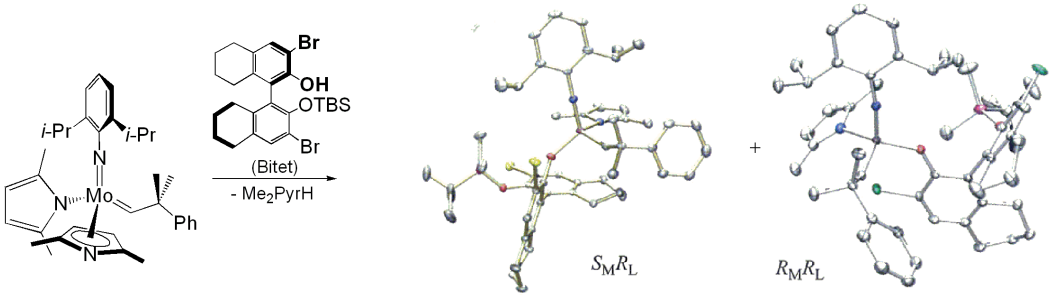
species. The search for M(NR)(CHCMe$_2$R')X$_2$ precursors to catalysts led to the discovery of M(NR)(CHCMe$_2$R')(pyrrolide)$_2$ complexes, *e.g.* **1** shown in Scheme 4. Bispyrrolide species are often found as 18 electron M(NR)(CHCMe$_2$R')(η^1-pyrrolide)(η^5-pyrrolide) species, *e.g.* **2** (Scheme 4), but these are in ready equilibrium with 14 electron M(NR)(CHCMe$_2$R')(η^1-pyrrolide)$_2$ species **3** that can react easily with alcohols or diols (biphenols or binaphthols) to give known catalysts *in situ*. These *in situ* catalysts behave in metathesis reactions as they do when they have been isolated and purified since the pyrrole is relatively innocuous.



Scheme 4

A reaction between the bispyrrolide and a monoalcohol takes place through a monoalkoxide monopyrrolide (MAP) intermediate. In many cases this intermediate forms in good yield and can be isolated and characterized. Crystal structures (see *e.g.* Fig. 1) confirm that the pyrrolide is bound in an η^1 fashion and that the alkylidene is the *syn* isomer. Two of the most important features of MAP species are i) they are highly efficient in olefin metathesis reactions, in fact, much *more* efficient than their bisalkoxide relatives, and ii) the metal itself is a stereogenic centre. There is some indication that the first is a consequence (in part) of the second, according to theoretical studies.[10] The chirality at the metal centre has major implications for reactions with an olefin, since the olefin is likely to approach the tetrahedral metal centre in only one of four ways *for electronic reasons*. Brunner recognized that the metal itself, perhaps, should be the strongest determinant of which of the four approaches to the metal is the lowest energy.[11]

In order to probe the efficiency of the metal's chirality in a metathesis reaction, an enantiomerically pure auxiliary was added (BitetOH = ROH), as shown in Scheme 5. The result is formation of a 7:1 mixture of diastereomers S_MR_L and R_MR_L where L is OBitet. These diastereomers have



Scheme 5

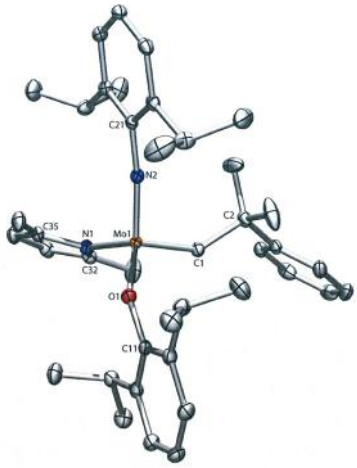


Fig. 1. The structure of Mo(NAr)(CHCMe$_2$Ph)(Me$_2$Pyr)(OAr)..

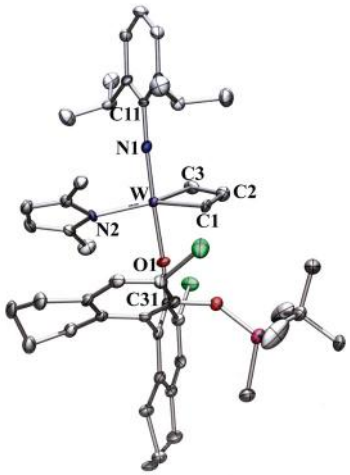
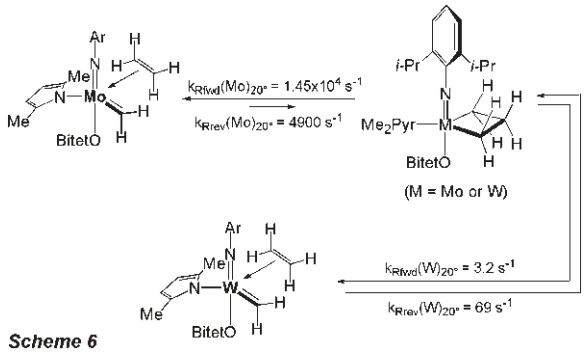


Fig. 2. The structure of W(NAr)(CH$_2$CH$_2$CH$_2$)(Me$_2$Pyr)(OBitet).

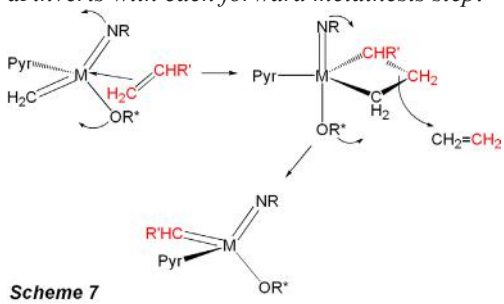
been isolated and characterized. They are configurationally stable in the absence of an olefin. However, in the presence of an olefin, such as ethylene, they interconvert rapidly (~100 s^{-1}) to form a 2:1 equilibrium mixture of methylene complexes that are themselves in equilibrium with unsubstituted TBP metallacyclobutane species, several of which have been structurally characterized; an example is shown in Fig. 2.

In the process of studying the interconversion of metallacyclobutane species of the type shown in Fig. 2, where the metal is Mo or W, it was found that they are in equilibrium with ethylene/methylidene species of unknown geometry, that the rate of *opening* the metallacyclobutane to the ethylene/methylidene species when M = Mo is ~4500 times faster than when M = W, and that the equilibrium toward the metallacyclobutane is much larger when M = W than when M = Mo (Scheme 6). These studies help explain what had been observed qualitatively, namely that Mo systems turn over much more rapidly under ethylene than analogous W systems.



Scheme 6

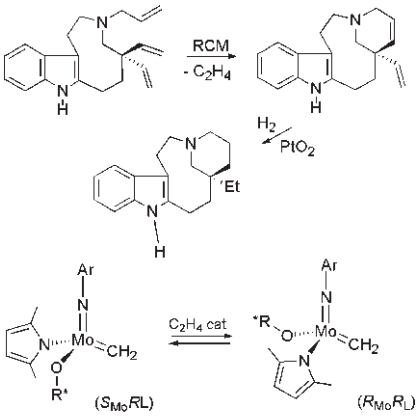
Detailed studies have led to several key proposals as to how MAP species react with olefins. As shown in Scheme 7, it is proposed that i) metallacyclobutanes that contain *axial imido and alkoxide* ligands (as in Fig. 2) are the crucial metathesis intermediates in MAP catalyst systems, ii) an olefin arrives on the CNO face (and therefore leaves) *trans* to the pyrrolide, and iii) the configuration at the metal *inverts with each forward metathesis step*.



Scheme 7

Two dramatic results led to a focus on MAP species since *ca*. 2007. The first is a synthesis of (+)-quebrachamine that involves the desymmetrization ring-closing reaction shown in Scheme 8. This reaction was found to be catalyzed by Mo(NAr)(CHCMe$_2$Ph)[OCMe(CF$_3$)$_2$]$_2$ (15 mol%, 12 h, 98% conversion; 71% yield), but by *no* second generation asymmetric Mo catalyst that was tried. Yet the *7:1 mixture* of Mo(NAr)(CHCMe$_2$Ph)(OBitet)(Me$_2$Pyr) diastereomers (see Scheme 5) was found to give rise to an efficient ring-closing reaction (2 mol%, 1 h, 98% conversion; 75% yield, 95%ee)[12,13] This finding was explained in terms of the unusually high reactivity of MAP species in general, a rapid equilibrium between diastereomers in the presence of ethylene, and the low reactivity of *one* of the two diastereomers.[14] It is proposed that the reaction proceeds *via* the ($S_{Mo}R_L$) methylidene diastereomer (Scheme 8) in a two-step ring-closing process that

leads to overall retention of configuration at the Mo center. Any ($R_{Mo}R_L$) methylidene diastereomer that is present is a much poorer catalyst for this particular ring-closing reaction. Therefore, the reaction proceeds efficiently to give product in high ee.



Scheme 8

The second finding is that shown in Scheme 9. The ring-opening cross-metathesis reaction proceeds rapidly and efficiently to give the expected product in high % ee. Most importantly, the phenyl substituted double bond is >98% *Z*. This finding gave rise to the proposal that the *large* aryloxide in combination with the *small* imido substituent allows only the *all cis* metallacyclobutane and, therefore, only the *Z* product, to form (Scheme 10). Achiral phenoxides were also efficient for *Z* selective reactions, especially the O-2,6-(2,4,6-*i*-$Pr_3C_6H_2)_2C_6H_3$ (OHIPT) ligand. A space-filling model of the TBP structure of W(NAr)($CH_2CH_2CH_2$)(Pyr)(OHIPT) (Fig. 3) reveals that the three *anti* protons (those opposite the imido ligand) of the metallacyclobutane are in contact with the methyl protons in the *ortho*-isopropyl groups of the OHIPT ligand. Therefore, no substituent is likely to be found in an *anti* position in a metallacyclobutane intermediate of this type. If secondary isomerization of the *Z* product into the *E* product can be avoided, then *Z* selective processes should prevail.

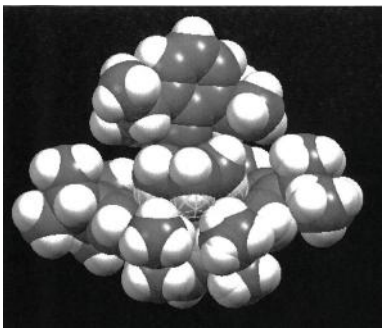
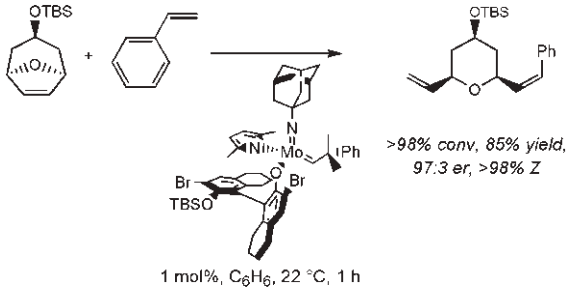
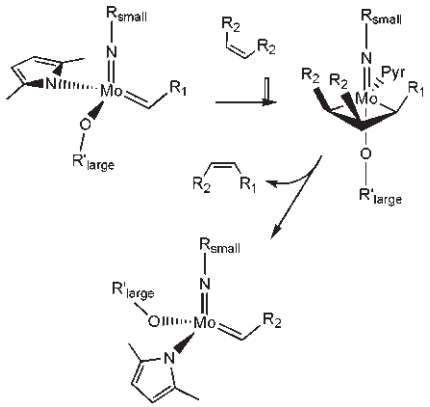


Fig. 3. A space filling model of the TBP structure of W(NAr)($CH_2CH_2CH_2$)(Pyr)(OHIPT).

Z-selective metathesis homocoupling of terminal olefins has been a long-sought goal of olefin metathesis. It should proceed as shown in Scheme 11, especially with complexes that have a *large*/*small* combination of aryloxide and imido substituent, respectively. *Z*-selective metathesis homocoupling of terminal olefins was found to proceed with high efficiency with the appropriately designed *tungsten* catalysts, either at elevated temperatures (80-120 °C)[15]

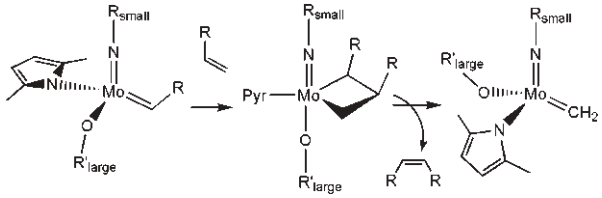


Scheme 9



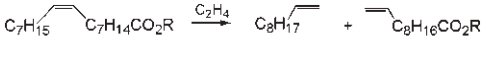
Scheme 10

or room temperature.[16] Most molybdenum-based catalysts that have been tried appear to be less efficient that tungsten-based catalysts, possibly because of secondary rapid isomerization of the initial *Z* product. The relatively high molecular weight of the product allows the starting material to be removed readily and the desired product to be isolated in relatively pure form. It is preferable to remove ethylene from the reaction as efficiently as possible in order to minimize secondary reactions of methylidene species, including decomposition.



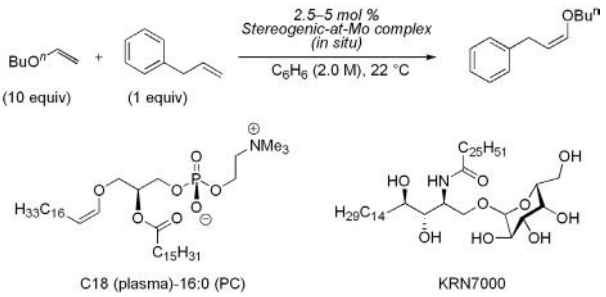
Scheme 11

Ethenolysis is a reaction in which ethylene is added to an internal olefin to yield (ideally) a mixture of the two terminal olefin products. Clearly ethenolysis catalysts must be stable to ethylene, and unsubstituted metallacyclobutane species cannot be too stable toward loss of ethylene. Ethenolysis is especially important in terms of obtaining useful chemicals from renewable feedstocks such as oleic acid esters (Scheme 12). Mo(NAr)($CHCMe_2Ph$)(Me_2pyr)(OBitet) has been shown to catalyze ethenolysis of methyl oleate at room temperature and 10 atm of ethylene with a high selectivity (>99%) to 1-decene and methyl-9-decenoate in high yield (95%).[17] Turnover numbers currently are in the range of 5000-10000, a number that is likely to depend critically upon the purity of the oleate. Tungsten catalysts are not as efficient as molybdenum catalysts for ethenolysis as a consequence of the stability of the unsubstituted metallacyclobutane, as noted earlier.



Scheme 12

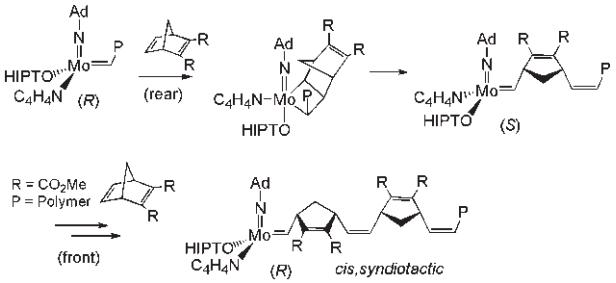
It has been demonstrated that MAP catalysts are efficient for the stereoselective synthesis of *Z*-olefins through catalytic *cross*-metathesis reactions. One of many potentially important classes of desirable cross-metatheses is one that employs an enol ether, as shown in Scheme 13.[18] This type of reaction has allowed a dramatically improved diastereoselective and enantioselective synthesis of the antioxidant plasmologen C18 (plasm)-16:0 (PC), a phospholipid derivative that is found in electronically active brain and heart tissues and which has been implicated in Alzheimer's disease.[19,20] A second example is the anti-tumor agent KRN7000 (Scheme 13).[21] Ethylene is detrimental to the rate cross-metathesis and also diminishes *Z*-selectivity by increasing methylidene concentration and consequent isomerization of *Z*-product to *E*-product.



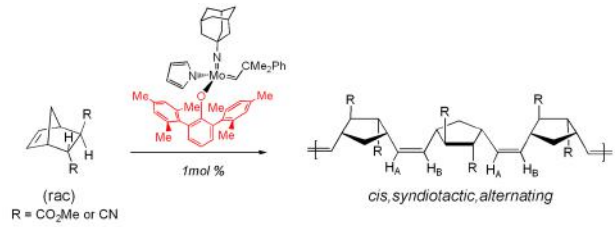
Scheme 13

MAP catalysts have also had an impact on ROMP chemistry. As mentioned earlier, the *cis,isotactic*-poly(2,3-dicarbomethoxynorbornadiene) is obtained through enantiomorphic site control employing biphenolate and binaphtholate catalysts (see Scheme 3). In the case of MAP initiators, the required approach of an olefin *trans* to the pyrrolide in a *Z*-selective manner followed by inversion of the configuration at the metal automatically forms a *cis,syndiotactic* polymer from the same monomer, as shown in Scheme 14.[22] Effectively, the monomer is forced to add sequentially to *opposite* sides of the M=C bond. This *stereogenic metal control* appears to be a new method of controlling polymer structure. New structures become possible. For example, racemic 2,3-dicarbomethoxynorbornene is polymerized by the hexamethylterphenoxide catalyst shown in Scheme 15. Since the metal inverts with each insertion, the enantiomers assemble in a perfectly alternating manner to give a *cis,syndiotactic* polymer in terms of the basic structure, or *cis,syndiotactic,alternating*. The only other polymer of this type is prepared through polymerization of *rac*-1-methylnorbornene by $ReCl_5$, a catalyst whose detailed mode of reaction has not been elucidated.[23]

Stereogenic-at-metal (SAM) MAP species are opening up many new possibilities in the area of olefin metathesis. It is not yet known to what degree the pyrrolide ligand is necessary for the high reactivity and efficiency of MAP species; MAP species could be only a subset of a larger class of SAM species that are as efficient or even more efficient than MAP catalysts. Although more time will be required and methods devised to prepare new SAM species, we can look forward to an increasingly bright future for olefin metathesis with Mo and W catalysts in organic and polymer chemistry.



Scheme 14



Scheme 15

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Article

The Palladium-Catalysed Ullmann Cross-Coupling Reaction

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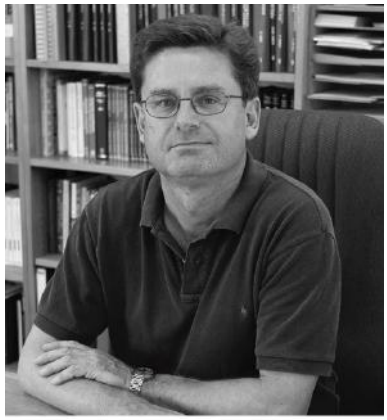
About the Senior Author



Martin Gerhardt Banwell was born in Lower Hutt on the 24th of November in 1954 of a German mother, Margot, and New Zealand father, John, who was a senior geophysicist principally involved with the exploration and development of geothermal resources in the central North Island (RSNZ Cooper medallist, 1964). The old DSIR Geophysics Division Building at Wairakei, now under GNS and refurbished, was named the Banwell Building after him on May 17 last.

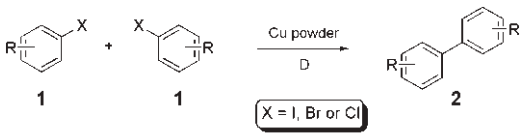
Martin attended schools in Taupo, Stokes Valley, and Wellington prior to secondary education at Scots College in Wellington, for a while in Mexico City (1967-68) and then at Wellington College (1969-72) before entering Victoria University and gaining his BSc and Honours degrees (1975 and 1976). He spent a couple of months at the Australian National University as a Vacation Scholar working under the supervision of Lew Mander.

Despite the excellent (and tempting) facilities of the ANU, Martin returned to Wellington and commenced his doctoral studies that were completed in 1979 under the supervision of Brian Halton. His postdoctoral was with Prof. Leo Paquette at Ohio State University. The sojourn at Ohio lasted about a year after which time Banwell accepted appointment as a Senior Teaching Fellow at the University of Adelaide. There he met his wife of some thirty years, Cathy Beckwith. In 1982 he took up a lectureship in organic chemistry at the University of Auckland, left for the University of Melbourne in 1986 and moved through the ranks becoming Associate Professor–Reader in 1993. He accepted appointment as a Senior Fellow at the Australian National University and settled in Canberra in 1994. He was appointed Professor in 1999.

In the year 2000, Martin was elected an Honorary Fellow of NZ's Royal Society and has continued to distinguish himself in his chosen field. He has held numerous fellowships and lectureships and continues to hold editorial board responsibilities for publications of high esteem. He has supervised in excess of 100 doctoral, masters and honours candidates and has employed 25 postdoctoral fellows; his publications number some 276 including some 15 book chapters and nine patents.

Introduction

Carbon-carbon (C–C) bond-forming processes are pivotal in synthetic organic chemistry because they allow for the assembly of more complex molecular systems from simpler ones.[1] Accordingly, an extraordinarily diverse range of methods for creating C–C bonds has been established over the last one hundred years or so and this provides the capacity to construct a remarkable array of chemical structures.[2] Amongst the most venerable of these methods is the Ullmann reaction that has a number of forms,[3] the first of which was reported in 1901[4] and involves the homo-coupling of an aryl halide **1** in the presence of an excess of copper *powder* to give the corresponding symmetrical biaryl **2** (Scheme 1).[5,6]



Scheme 1. The original Ullmann reaction.

Since its discovery, the extensive applications of the Ullmann reaction have resulted in a clear delineation of its scope and limitations.[4-6] Thus:

(i) Both halogenated aromatic and heteroaromatic compounds can participate in the reaction.

(ii) Iodinated aryls are more reactive than their brominated counterparts that are, in turn, much more reactive than the corresponding chlorinated systems. Fluorinated compounds do not react.

(iii) Intramolecular variants of the reaction have been exploited to create from 4- to 24-membered ring systems.

(iv) Substituents play an important part in determining the efficiency of the reaction with electron-withdrawing groups (especially $–NO_2$, $–CO_2R$ and –CHO) located adjacent to the halogen having particularly beneficial effects, while analogously located bulky ones have a deleterious effect. Electron-donating groups located anywhere on either ring generally diminish the yields of the coupling product.

(v) Substrates incorporating functional groups with active hydrogens, *e.g.* OH, CO_2H, NH_2, SO_2NH_2, can

participate in competing reactions including those involving C–O and C–N bond formation.[3]

(vi) While active forms of copper with freshly cleaned metal surfaces are normally used (and sonication often facilitates these reactions), various copper (I) salts (especially Cu_2O and Cu_2S) can also be employed although not normally with the same levels of efficiency.

(vii) DMF is the most commonly employed solvent, although the use of pyridine, quinoline, nitrobenzene, DMSO and *p*-nitrotoluene has also been reported.

(viii) Temperatures in excess of 200 °C and long reaction times are often required.

(ix) In reactions leading to unsymmetrical biaryls, products arising from competing homo-coupling processes are often observed.

Various studies have been undertaken in attempts to understand the precise pathway by which the Ullmann coupling products are formed and both aryl radical- and aryl copper-mediated processes have been considered.[6] The latter is now the more widely accepted, not least because various aryl copper species can be isolated and have been shown to react with aryl halides so as to give biaryls.

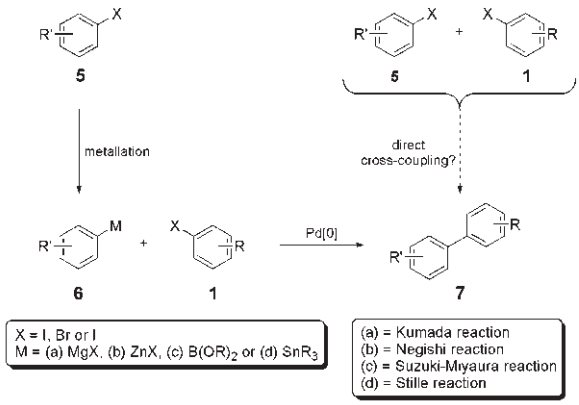
In efforts to overcome the significant drawbacks associated with the Ullmann reaction, as recorded in entries (viii) and (ix) above, several modifications to it have been introduced. Perhaps the most notable of these involve the use of Ni[0] complexes (in place of copper metal),[6,7] preformed aryl copper species,[8] CuTC in NMP (Scheme 2)[9] (for abbreviations see above the list of references), or catalytic Pd[0].[10] While each of these modifications allows for the reaction to be carried out under much milder conditions, *i.e.* at lower temperatures, and/or the construction of highly substituted biaryls, they remain largely confined to the synthesis of symmetrical systems.[6]

3 4

Scheme 2. A modified Ullmann reaction that proceeds at room temperature.

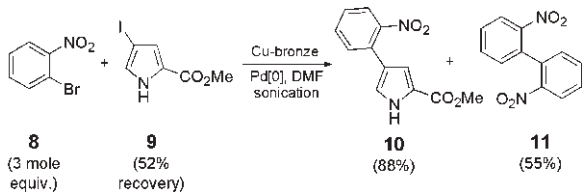
Pd[0]-Cross-Coupling Chemistries

The application of the Ullmann reaction to the synthesis of unsymmetrical biaryls and related products has received only modest attention. In part, this is because of the advent and demonstrated utility of various Pd[0]-catalysed cross-coupling processes, most notably the Kumada,[11] Negishi,[12] Suzuki–Miyaura,[13] and Stille[14] reactions (Scheme 3). However, when one considers that the metal- or metalloid-containing coupling partner **6** used in these processes is often generated from the corresponding halide **5**, the capacity to affect the direct cross-coupling of halogenated systems, *i.e.* **5** + **1**→ **7**, in an efficient manner would be advantageous. Shimizu and co-workers of the Kowa Company in Japan[15] appear to have been the first to employ the Ullmann-type version of this approach in a useful fashion (and as part of a program concerned with the development of new antiarrhythmic active agents). Remarkably, however, there have been few additional applications of this Pd[0]-catalysed Ullmann cross-coupling process since it was reported in 1993.



Scheme 3. Comparison of the Pd[0]-catalysed cross-coupling and direct cross-coupling approaches to unsymmetrical biaryls of the general form 7.

As part of a programme directed towards synthesis of the alkaloid rhazinilam,[16] we had occasion to carry out the cross-coupling of *o*-nitrobromobenzene (**8**) with the iodinated pyrrole **9** (Scheme 4) as a means of obtaining compound **10** which embodies key elements of the target natural product. In the event, and following the protocols defined by Shimizu,[15] but using ultrasonication to promote the reaction and DMF (rather than DMSO) as the solvent, we found that product **10** could be obtained in 88% yield based on recovered pyrrole **9**; 2,2'-dintrobiphenyl (**11**) (55%) represented a major by-product.



8 (3 mole equiv.) **9** (52% recovery) **10** (88%) **11** (55%)

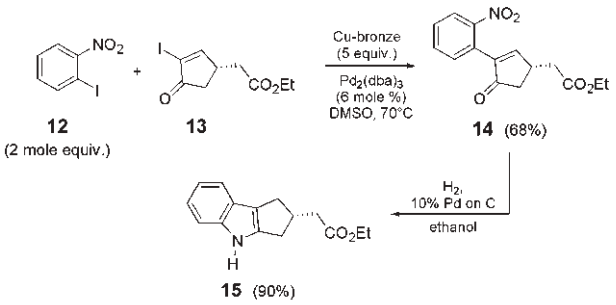
Scheme 4. The Pd[0]-catalysed Ullmann cross-coupling route to pyrrole 10.

Our view of the mechanism for the conversion **8** + **9** → **10** is based on the proposals of Shimizu.[15] Thus, we believe that substrate **8** reacts with copper metal to form a Cu(I) aryl species that engages in a substitution reaction, at palladium, with the product of oxidative addition of Pd[0] to pyrrole **9**. The ensuing arylpyrollopalladium(II) complex then undergoes 1,1-reductive elimination to give product **10** with concomitant regeneration of Pd[0].

The Pd[0]-Catalysed Ullmann Cross-Coupling Approach to Indoles

There were several aspects of the reaction shown in Scheme 4 that attracted our attention. In particular, it was operationally very simple, the coupling partners were readily available, the conversion **8** + **9** → **10** proceeded under mild conditions and the yield of the desired product was reasonably high despite the seeming electronic incompatibility of the coupling partners (pyrroles are very electron-rich aromatics). Encouraged by these features, we have since used the title reaction as a key step in the synthesis of a number of heterocyclic systems. So,

for example, we were able to show[17] (Scheme 5) that the Pd[0]-catalysed cross-coupling of the iodo-analogue **12** (of nitroarene **8**) with the α-iodocyclopentenone **13** gave the expected product **14** in 68% yield, and that upon subjecting the last compound to reaction with dihydrogen in the presence of 10% Pd on C the annulated indole **15** could be obtained in 90% yield.



Scheme 5. Example of the application of the Pd[0]-catalysed Ullmann cross-coupling reaction to the synthesis of indoles.

This type of procedure has proved sufficiently reliable that we have been able to use it in the synthesis of some relatively complex target natural products. So, for example, cross-coupling of the α-iodinated enone **16** with aryl iodide **12**[18] (Scheme 6) afforded compound **17** (75%) that was subjected to a simple sequence leading to the azide **18** (87%). Thermolysis of this last compound provided, *via* an intramolecular 1,3-dipolar cycloaddition reaction and subsequent loss of dinitrogen, the ring-fused aziridine **19** (72%) that underwent cleavage of the three-membered ring on treatment with HCl, thus giving the α-chlorocyclohexanone **20**. Reductive dechlorination and cyclization of this last compound could be accomplished using $TiCl_3$, thereby affording the tetracyclic species **21** in 46% overall yield from precursor **19**. Subjection of compound **21** to a ring-annulation protocol developed by Heathcock[19] involved its initial treatment with α-chloroacetyl chloride. The resulting amide was then engaged in a Finkelstein reaction using sodium iodide in acetone and this gave the corresponding α-iodoacetamide **22** that cyclised upon exposure to silver triflate thereby affording the lactam/indolenine **23** (35% from **21**). Finally, treatment of compound **23** with lithium aluminium hydride gave the racemic modification the target natural product aspidospermidine **24** in 77% yield.

Since compound **24** bears some resemblance to the eastern hemisphere of the clinically important binary indole-indoline alkaloid vinblastine (see Fig. 1), we are currently attempting to adapt this chemistry to its synthesis.[20]

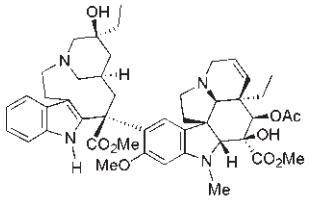
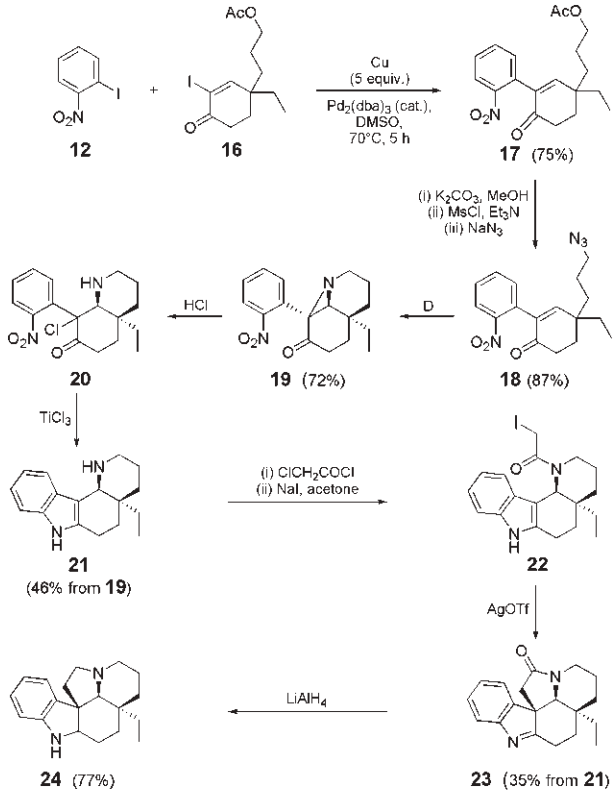


Fig. 1. The clinically significant binary indole-indoline alkaloid vinblastine.

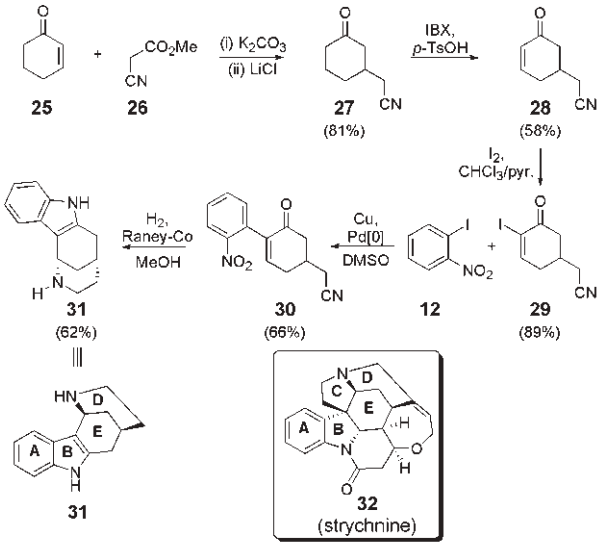
In related and ongoing studies, we are also using this indole-forming process to assemble a key substructure associated with the alkaloid strychnine (**32**) (Scheme 7), a structurally fascinating compound that was an important



Scheme 6. Application of the Pd[0]-catalysed Ullmann cross-coupling reaction route to the synthesis of the alkaloid aspidospermidine.

part of the doctor's medicine chest in Victorian times, but which is now more well known for its toxic effects.[21] The reaction sequence starts[22] with the conjugate addition of the methyl α-cyanoacetate (**26**) to cyclohex-2-en-1-one (**25**) and this leads, after ester hydrolysis and decarboxylation, to nitrile **27** in 81% yield. Regioselective dehydrogenation of this last compound could be achieved using IBX in the presence of *p*-TsOH and the enone **28** (58%) so-formed was subjected to a Johnson iodination reaction, thereby affording the corresponding α-iodoenone **29** in 89% yield. Compound **29** served as the substrate for the pivotal Pd[0]-catalysed cross-coupling reaction with aryl iodide **12** and the α-arylenone **30** was thereby obtained in 66% yield. Treatment of this last compound with dihydrogen in the presence of Raney-cobalt then afforded the tetracyclic compound **31** in 62% yield. While the sequence of events associated with the conversion **30** → **31** has not been firmly established, it is presumed that the first step involves reduction of the nitrile residue in compound **30** to the corresponding amine, which then adds in an intramolecular hetero-Michael addition reaction to the tethered enone. Reduction of the nitro group then follows and the aniline thus formed engages in an intramolecular Schiff-base condensation reaction to give an indolenine that then undergoes a prototropic shift, thus generating the observed indole **31**. A comparison of the structure of **31** with that of strychnine (**32**) reveals that the former embodies the ABDE-substructure of the latter.

The prospects for exploiting this reaction sequence so as to prepare compounds more closely related to strychnine seem reasonable. For example, the Heathcock annulation process[19] that was successfully employed in the closing stages of our synthesis of aspidospermidine (see Scheme 6) could be used to annulate the C-ring of strychnine to



Scheme 7. Application of the Pd[0]-catalysed Ullmann cross-coupling reaction route to the synthesis of ABDE-substructure associated with the alkaloid strychnine.

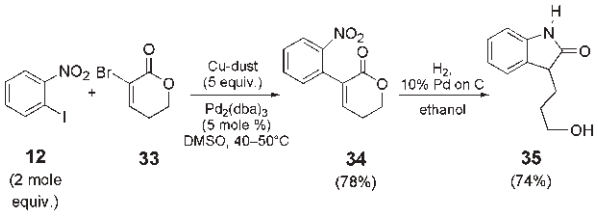
compound **31**. Furthermore, the initial conjugate addition reaction **25** + **26** → **27** likely could be carried out in an asymmetric fashion[23] and so allow for the construction of compounds such as **31** in enantiomerically enriched form. These sorts of possibilities are currently being pursued in our laboratories, although the challenges are great and all the more so because of the extraordinarily concise and elegant syntheses of natural product **32** that Reissig[24] and Vanderwal[25] have reported recently.

Improving the Cross-Coupling Reaction

As we have endeavored to exploit the Pd[0]-catalysed Ullmann cross-coupling reaction in increasingly complex situations, the deficiencies of our originally defined protocols[16,17] have become more apparent. In particular, the relatively high temperatures (≥ 70 °C) required, the continued formation of homo-coupling products, *e.g.* compound **11**, Scheme 4, and the relatively modest yields of the desired products continue to hamper our work. Accordingly, we have recently paid some attention to trying to improve the basic reaction. In that connection, we have found[26] that by using either freshly cleaned dendritic copper or freshly prepared copper nanoparticles we can run the cross-coupling reactions at close to room temperature, thereby reducing the formation of homo-coupling products to negligible levels. As a result, yields of the desired product in excess of 90% can now be realised. Interestingly, we have observed that DMSO is uniquely effective as the solvent for these reactions – DMF and NMP, solvents that have frequently been used in the more conventional Ullmann reactions, give poor yields of the desired cross-coupling products.

The Pd[0]-Catalysed Ullmann Cross-Coupling Approach to Oxindoles, Quinolines, 2-Quinolones and Phenanthridines

Given the utility of the indole-forming sequences shown above, we have sought to extend such cross-coupling/reductive cyclization protocols to the preparation of other heterocyclic systems of biological significance. The oxindole or indolone motif represents a privileged structure in medicinal chemistry and is embodied in a number of intriguing natural products. Consequently, we sought to prepare it using the title reaction. A representative example of process we have developed as a result is shown in Scheme 8.[27] Thus, cross-coupling of substrate **12** with two molar equivalents of bromolactone **33** using freshly activated copper *dust* (3 micron dendritic material, the surface of which had been cleaned with EDTA under ultrasonication) in the presence of 5 mole % $Pd_2(dba)_3$ gave the desired product **34** in 78% yield. Exposure of this to dihydrogen in the presence of 10% Pd on C then afforded the mono-alkylated oxindole **35** in 74% yield. This second step of the reaction sequence necessarily involves reduction of the double bond within the lactone ring of the substrate as well as the nitro group. Presumably, it is the resulting amino-lactone that undergoes an intramolecular *trans*-acylation reaction resulting in cleavage of the lactone ring and formation of the lactam ring associated with the observed oxindole.



Scheme 8. Example of the application of the Pd[0]-catalysed Ullmann cross-coupling reaction to the synthesis of mono-alkylated oxindoles.

Extensions of such cross-coupling/reductive cyclization protocols to the preparation of quinolines proved straightforward, as highlighted by the reaction sequence shown in Scheme 9.[28] Thus, the ring-fused β-bromo-α,β-unsaturated aldehyde **37** (readily prepared from α-tetralone **36** in good yield[29]) engages in cross-coupling with the bromoarene **38** and the cinnamaldehyde **39** so-formed (in 89% yield) readily undergoes reductive cyclization under the usual conditions, thus affording the ring-fused quinoline **40** in 91% yield. We have used this same sort of reaction sequence to establish a two-step synthesis from 6-bromopiperonal and *o*-nitrobromobenzene **8** of the phenanthridine-containing and biologically active natural product trisphaeridine (Fig. 2).[30] Given the now ready availability of the relevant substrates,[31] non-ring-fused quinolines are also accessible using the same type of chemistry. Furthermore, the synthesis of 2-quinolones is readily achieved[28] by engaging β-bromo-α,β-unsaturated esters in the same type of reaction sequence as shown in Scheme 9.

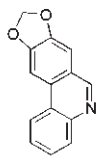
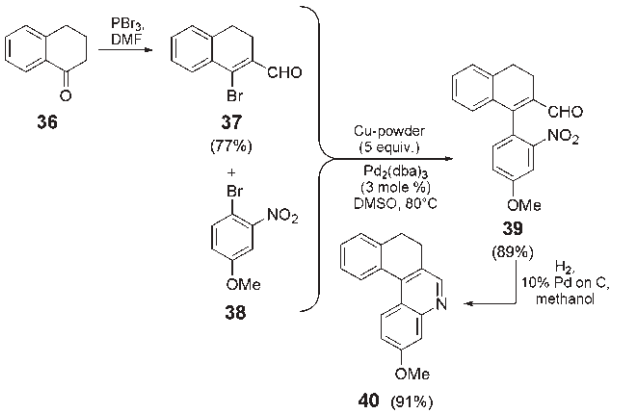


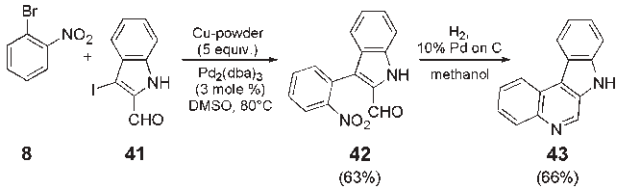
Fig. 2. The phenanthridine-containing natural product trisphaeridine.

A variation on the above mentioned reaction sequence is shown in Scheme 10. It involves cross-coupling of the readily available 3-iodoindole **41** with *o*-nitrobromobenzene (**8**) to give the 3-arylindole **42** (63%) that undergoes the usual reductive cyclization reaction on exposure



Scheme 9. Example of the application of the Pd[0]-catalysed Ullmann cross-coupling reaction to the synthesis of a fused quinoline.

to dihydrogen in the presence of Pd on C to afford 7*H*-indolo[2,3-*c*]quinoline **43** (66%), a scaffold that has been sought after for the development of new antiplasmodial drugs.[32]



Scheme 10. Application of the Pd[0]-catalysed Ullmann cross-coupling reaction to the synthesis of 7H-indolo[2,3-c]quinoline (43), a platform for the development of new antiplasmodial drugs.

Future Prospects

The Pd[0]-catalysed Ullmann cross-coupling reactions described above should continue to provide an effective means for the ready preparation of a useful range of heterocyclic compounds of medicinal and structural interest. Indeed, in an extension of the chemistry outlined in Scheme 10, we are now endeavouring to prepare members of the recently described marinoquinoline class of natural product (Fig. 3), some of which show useful levels of activity against *Palsmodium falciparum* K1 (IC_{50} values between 1.7 and 15 μM).[33]

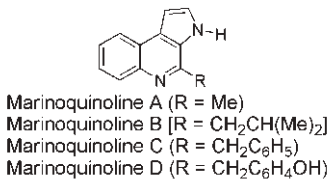
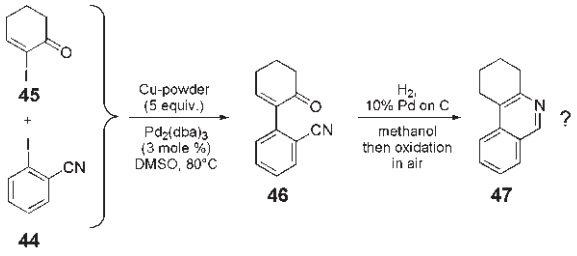


Fig. 3. The structures of some recently isolated marinoquinolines.

Another area of interest concerns the identification of cross-coupling partners that can be used in place of the *o*-nitrohaloarenes featured in all of the studies described above. In keeping with observations made regarding the original Ullmann reaction (see Introduction), it seems clear that a strongly electron-withdrawing and *ortho*-related substituent needs to be associated with one of the coupling partners participating in the Pd[0]-catalysed process. Some preliminary experiments (Scheme 11) suggest that *o*-iodobenzonitrile **44**, for example, does participate in the same types of coupling processes. Thus, this compound reacts with α-iodocyclohex-2-en-1-one **45** to give α-arylcyclohex-2-en-1-one **46**. This, in turn, undergoes reductive cyclization to give, after aerial oxidation of what is presumed to be an intermediate dihydroisoquinoline, the annulated isoquinoline **47**.[26]



Scheme 11. Application of the Pd[0]-catalysed Ullmann cross-coupling reaction to the synthesis of isoquinolines?

A third aspect of the Pd[0]-catalysed Ullmann cross-coupling reaction that continues to fascinate us concerns the α-arylcyclohex-2-en-1-ones such as **18** and **30** formed in these processes. In particular, the double bond embedded within such cross-coupling products has – by virtue of the attachment of the strongly electron-withdrawing carbonyl and *o*-nitrophenyl groups at the same end of it – some potentially very useful electrophilic properties that should be capable of exploitation in various settings.

On the basis of the foregoing, we see the title reaction as providing a very effective method for the construction of a wide-range of medicinally relevant compounds, most particularly heterocyclic ones. As such, the reaction warrants further attention and development.

Acknowledgements

We thank the Institute of Advanced Studies and the Australian Research Council for their generous support of this research. MTJ and TAR are the grateful recipients of Australian Postgraduate Awards that have supported them during their PhD studies.

Abbreviations Used

CuTC	copper(I) thiophene-2-carboxylate
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
IBX	2-iodoxybenzoic acid
MsCl	methanesulfonyl chloride
NMP	*N*-methyl-2-pyrrolidinone
Raney-Co	Raney cobalt
p-TsOH	*p*-toluenesulfonic acid

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2011 International Year of Chemistry

Calendar of Events

International Year of CHEMISTRY 2011

July

ChemEd conference in Palmerston North (July 17-20)

Nature of Science Series begins (with the RSNZ)

Molecular Anthology Project Completed – Presentation at ChemEd Conference

August

RadioNZ lecture series

September/October

Prof Bob Grubbs, 2003 Nobel Laureate, Erskine Fellow in residence at University of Canterbury

November

2011 Research Honours Dinner

Elemental Project concludes

December

NZIC Conference in Hamilton

Exhibition of Elemental Project at NZIC Conference

Up-to-date information will be posted on the NZ website: **www.yearofchemistry.org.nz**

Article

Fraud in Organic Chemistry*

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Dedicated to the Memory of Athel Beckwith

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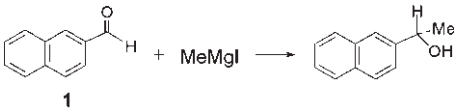
Under the general heading of scientific misconduct there is a classification into fabrication, falsification, and plagiarism (FFP). Fabrication is making up scientific publications out of whole cloth whereas falsification is changing results that already exist so that those reported do not actually represent the research record. The distinction is often unclear and the more general term *fraud* is used here for both kinds of behaviour. Misconduct is also used for lesser evils such as failing to cite the work of others or delaying the return of refereed papers. Plagiarism, using another's intellectual property without giving credit, is a very different phenomenon and is discussed separately.

The prevalence of fraud in the field of organic chemistry has been a topic of long interest. Investigations of fraud by the author include the literature, word of mouth and discussions following a much-presented lecture entitled *Sin in Chemistry*: *Mistakes and Fraud in the Chemical Literature*, as well as some 60 years as a practicing organic chemist.

Blatant Fraud

Participants in the May 1994 Bürgenstock Stereochemistry Conference (including this author) had the unusual opportunity of witnessing fraud in real time. On arrival, each participant received a reprint of a paper entitled *Enantioselective Reactions in a Static Magnetic Field*.[1] One of the free afternoons of the conference was sacrificed to a presentation of this work by G. Zadel, the doctoral student, advanced to PhD, from the University of Bonn who was mainly responsible for the work. The senior author, Professor Breitmaier, declined the conference invitation on the grounds that his teaching duties made it impossible for him to attend.

The remarkable results included 98% enantioselectivity (either + or -) in the reaction of 2-naphthaldehyde (**1**) with methyl magnesium bromide in a magnetic field of 1 tesla and a number of similarly startling results of Grignard and metal hydride reactions! The speaker gave a good presentation and handled himself well in a vociferous discussion period after his presentation.



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It was revealed in the discussion that at least two other laboratories had tried to reproduce these results and failed to observe any enantioselectivity whatsoever. Workers from one of these had journeyed to Bonn, bringing their own glassware and chemicals and the enantioselectivity was reproduced under Zadel's direction. It was successful with Zadel in Bonn but not elsewhere without him; something was very fishy.

The problem was resolved just a few weeks later when *Angewandte Chemie* published a short paper by Breitmaier entitled *No Enantioselective Reactions in a Static Magnetic Field*.[2] Zadel had admitted that optically active product had been added surreptitiously to the tubes before exposure to magnetic fields and the Grignard reaction. There was no enantioselective reaction at all; the optically active material had been there from the beginning. I felt cheated.

The above example is a clear-cut case of fraud, outstanding in the rapidity of its exposure. The true description of the experiments was not given, the presentation was a lie, and the perpetrator confessed to his actions. The maximum punishment available to universities for serious misconduct such as this is usually revocation of the culprit's degree or loss of his position. The University of Bonn did, in fact, revoke Zadel's DPhil degree. He appealed and his appeal was denied by a lower court in Köln. Ten years after the original paper appeared, a higher court in Münster refused to consider his appeal, effectively terminating the legal struggle to avoid the consequences of his actions.

What could have been the motivation for Zadel's actions? This is a puzzle. Working in an area of considerable current interest[3] where similar experiments of others had given minimal results, he could be certain that his work would be checked and shown to be fraudulent. How could he expect to avoid being shown a charlatan and suffer penalties for his actions?

A considerable number of books on the subject of scientific misconduct have appeared over the years.[4-9] With the exception of the Grayson books that are largely intended to be bibliographic in nature, they recount in more or less detail the story of frauds that have been exposed and comment on the factors involved. There is a good deal of repetition among them and much bemoaning of the present state of science.

Historic Fraud

The chemical literature in its enormity is the repository of our knowledge of chemistry. Millions of papers combine to provide the information on which chemistry is based. There is an unwritten agreement amongst all chemists that what appears in our published papers is as nearly as possible the whole truth. Deviation from this agreement is a sin against chemistry and the culprit is a sinner who

deserves severe punishment. M. Polanyi wrote :[10]

> *If each scientist set to work every morning with the intention of doing the best bit of safe charlatanry which would just help him into a good post, there would soon exist no effective standards by which such deception could be detected. A community of scientists in which each would act only with an eye to please scientific opinion would find no scientific opinion to please.*

The idea of fraud by scientists has become widespread as evidenced by the publication of novels[11,12] and plays[13] in which scientific fraud is a significant element. There is even a blog on retraction of scientific papers.[14]

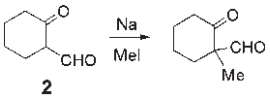
Fraudulent Papers in Organic Chemistry

Listings of all the cases of fraud detected in organic chemical and related literature by the author over the passing decades appears chronologically below.

1940: Goldwasser and Taylor's[15] analysis of hexene mixtures by fractional distillation was checked by Whitmore *et al*.[16] who obtained very different results using identical equipment.

1943: Stockstrom's results concerning approaches to the synthesis of Vitamin D were retracted by Dimroth, his supervisor.[17] They were imaginary results existing only on paper and are referred to as *thought* or *Gedanken* experiments.

1944: Paranjape and coworkers[18] reported a total synthesis of racemic santonin in 1943 but one year later[18] reported that, upon checking the optical rotation of their synthetic product, they found that it was optically active with an optical rotation close to that of natural santonin. They claimed that the optical activity was introduced in the initial step, the base catalyzed methylation of 2-formylcyclohexanone (**2**). The subsequent steps were reported to lead to total synthesis of the natural, optically active santonin. Cornforth, Cornforth, and Dewar[19] obtained only a racemic (liquid) methylation product when they repeated the base catalyzed step, as would be expected.



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1957: Hammond and Ravve[20] reported the reaction of the triphenylmethyl radical with aromatic compounds. The result was corrected by Benkeser, Gosnell, and Schroeder[21] and a subsequent examination by Hammond[22] led to the conclusion that the incorrect results had been fabricated; he blamed himself in part for rushing into print.

1963: Benkeser, Grossman, and Stanton reported[23] syntheses of interesting silacyclopentadiene and related compounds over 1961-62. However, a retraction by Benkeser and Stanton appeared within two years[23] as Grossman had fabricated results. Among other things, he took advantage of the fact that the C and H compositions of $C_mH_nSi_p$ are nearly identical to those from $C_mH_nN_{2p}$. The C,H analyses Grossman obtained came from nitrogen compounds that fit the requirement. When Benkeser received the results from the analytical laboratory, they were in agreement with the values calculated for the silicon compound as silicon had not been analysed. The fraud was exposed when other researchers in the laboratory could not repeat Grossman's results. His doctorate degree was revoked by Purdue University.

1979: Chatterjee reported work related to the synthesis of aconitine.[24] Cornforth and Pengelly[25] were unable to repeat the first three steps of this work.

1986: Breslow and Mehta published three papers[26] reporting turnover rates of catalysis by small molecules that approached the values for enzymes. These were retracted when it was not possible to repeat the results.

1994: Zadel's doctoral work[2] in Breitmaier's laboratory has been discussed.

2006: A number of papers in synthetic organic chemistry from the Sames group[27] were withdrawn and one paper was corrected[28] with statements that included *the laboratory of the corresponding author (D. Sames) has been unable to reproduce some of the key results*. B. Sezen was found guilty both by the Federal Agency and by Columbia University[29] of fabricating her results.

2009: A paper by Gilbert, Fischer and Chen[30] in 2000 on the allyl radical was shown to be a fraud after workers in other laboratories encountered difficulties in reproducing the results. A retraction and a new paper appeared in 2009.[31]

2009: Krishna Murthy at the University of Alabama fabricated ten protein structures.[32]

2010: An editorial in *Acta Crystallographica* by Harrison, Simpson and Weil[33] reported at least 70 fabricated X-ray crystallographic structures by T. Liu and H. Zhong from Jinggangshan University, China. The Chinese took *bona fide* sets of published X-ray data, replaced one or more of the atoms, made minor adjustments to the structure, and submitted the results to *Acta* as a set of original data for the accompanying *new* structure. They have admitted to 70 such fabrications and more are expected.

Finally, a curious affair in the 1930s in the laboratory of Prof. F. Kögl at the University of Utrecht involved fraud but how and by who has never been clarified. It was examined in detail by Prelog when he was sorting Ruzicka's papers posthumously for the ETH files. He found reports concerning Kögl, Ruzicka's successor at Utrecht, one of which stated that tumour cells contained higher than normal concentrations of D-amino acids;[34] the experimental result could not be repeated. Prelog's summary (in German and available from the author) was concluded by him, stating that *there is good material for a detective novel here!*

Frequency of Fraud

Fraudulent papers do not advertise themselves. If work appearing in the literature is significant and relevant to the work of others, likely it will be repeated; otherwise it may rest quietly in its fraudulence as if it did not exist

at all. Even if it seems problematic, few would wish to spend the time and effort to examine its probity - it may just be ignored. Not much credit is given for uncovering fraud. There are also small frauds, such as data smoothing to give a better fit to a desired curve, combustion analyses being doctored a bit so that the values for carbon and hydrogen will fall within the acceptable range, a variety of cosmetic changes introduced into papers, *etc*. These are almost impossible to check.

There only appears to be one attempt to estimate the number of frauds in science and this is due to Broad and Wade.[5] In all probability it would have been better left unwritten. Thus, they say that *most of the cases described (here) involve major fraud by which we mean the reporting of an experiment that did not take place. Minor fraud occurs when the experimenter selects or distorts the data from real experiments so as to make them appear smoother or more convincing. We would expect that for every case of major fraud that comes to light a hundred or so go undetected. For each major fraud, perhaps a thousand minor fakeries are perpetrated. The reader can supply his own multiplication factors; ours would indicate that every major case of fraud that becomes public is the representative of some 100,000 others, major and minor combined, that lie concealed in the marshy wastes of the scientific literature*. The authors gave no basis for their numbers but the fraudulent papers in organic chemistry are merely fourteen cases in seventy years! Remarkable! Are there more? Undoubtedly. How many? We have no idea - but almost certainly far fewer than the 1.4 million predicted by Broad and Wade.

One can state with reasonable confidence, therefore, that fraud is not a major problem in organic chemistry. A reason for this, at least in part, is the nature of research in organic chemistry. Experiments are generally well defined and the results easy to characterize by a variety of standard techniques. The chances of fraud being detected are high and the risk is too great a gamble. The results presented here certainly support the idea that fraud is not a major factor in organic chemistry.

Another approach to evaluating fraud has come from Swazey, Anderson and Lewis.[35] They polled 2000 doctoral students and 2000 faculty members in departments of chemistry, civil engineering, microbiology and sociology at the 99 largest graduate departments in the USA. The participants were asked questions principally concerned with exposure to falsification and plagiarism. Some 6- 9% of students and faculty reported direct knowledge of falsification or plagiarism by student or faculty, but it is not known how many of these are in common.

There are far more instances of fraud in the biomedical area. Research grants are considerable, large groups of researchers common, and pressure is applied to gain results that justify funding renewal. Junior staff are often isolated from the real functions of the laboratory and intermediate staff not involved scientifically in productive ways.

Factors Reducing Public Disclosure

A significant factor comes into play in reducing the publicity attending fraud. It is much less troublesome to expel the culprit quietly from his position and sweep the whole affair under the carpet rather than go through the pain and inconvenience of a procedure against an individual (who may shout loud and long that he is being discriminated against and is innocent of any sin). It is easier for non-tenured staff such as graduate students and postdoctoral fellows to lose their financial support, be told to go elsewhere, and the whole affair forgotten. Moreover, the person exposing a fraud may be subject to considerable criticism by colleagues.[36]

The accepted criterion for fraud is inability of other workers to repeat a given procedure after due diligence. At the very least, one must be careful before making accusations that may affect an individual's life and career. An example given by Prelog[37] describes the banishment of a student from Votocek's laboratory because the glutamic acid that he had synthesized was optically active; he had been instructed to prepare synthetic glutamic acid and it was expected to be racemic. His product was optically active and, therefore, not synthetic. Later, it was shown that racemic glutamic acid has a considerable tendency to undergo spontaneous resolution upon crystallization, but it was too late to reinstate the banished student whose subsequent fate remains unknown. In all probability he had not cheated.

Legal Treatment of Misconduct in the USA

Much of the scientific and medical research performed in the USA (and increasingly elsewhere) is funded[38] by Federal grants in the form of contracts between the government agency and the institution where the work is to be performed. Misconduct may be a breach of contract and the government may be entitled to recover all or part of the funds allotted. The US Federal government began to take an active interest in how its science money was being spent with regard to questions of fraudulent events in 1981. There were several hearings of cases of scientific misconduct, mainly in the area of biomedical research and, subsequently, laws and procedures were set in place for the legal treatment of scientific misconduct. A detailed guide for ethical scientific behaviour now has been published.[39]

Plagiarism

Plagiarism, the third of the FFP trio, is very different from the fraud discussed thus far. It has been defined in federal law as *the appropriation of another person's ideas, processes, results or words without giving appropriate credit*. It is usually considered in the context of appropriating someone else's words as if they were one's own. Plagiarism is a special kind of sin, a violation of intellectual property; the expression *intellectual violence* has been used to describe it. One finds the fruits of one's hard-won scientific achievement appearing, perhaps slightly modified, under someone else's name, and often in an obscure journal so as to minimize the possibility of detection - it is never a pleasant experience. The damage to science is minimal since the plagiarist does not introduce anything

new; he simply clutters up the literature with useless material and, presumably, benefits by increasing his list of publications.

Sometimes fate takes a hand in plagiarism, as in the case of S. F. Martin and L. Paquette.[40] A grant application by Martin was rejected by a committee headed by Paquette. Sometime later, Martin received a grant proposal by Paquette for evaluation. Whole sections of the text were identical with parts of Martin's rejected application. A variety of excuses were proffered, including graduate student and postdoctoral interference, but Paquette was found guilty of misconduct and banned from participation in granting committees for ten years. Also, he supposedly agreed with his university to reduce his research group from 40 co-workers to a more modest 20 who he had time to properly supervise.

Chemical and Engineering News, among others, periodically carries reports of such cases. One, in 2008, reported[41] more than seventy plagiarized papers over the 2004-2007 period from an Indian professor. What he had hoped to gain from such a number, other than increased probability of detection, is unclear.

At the University of Bremen, a Chinese guest employed his time copying the doctoral theses of his host's group members. He published a series of papers in Chinese, all plagiarized from the doctoral theses.[42] The plagiarism was detected as soon as a paper appeared in an international journal but it was withdrawn only after vigorous protests; it is being expunged from the chemical literature as was Zadel's paper[1] from the on-line issue of *Angewandte Chemie*.

The availability of most of the published literature in chemistry on the Internet and the ability to modify computer files on personal computers has made it technically easy to plagiarize papers. Thus, a paper can be downloaded, appropriate changes made to the title, authors, abstract and first paragraph, and drawings modified at will so that there is a *new* paper ready for submission. However, computer programs are now available that can detect plagiarism. *CrossCheck*, a commercial program developed by iParadigm (Oakland, CA), applies text matching to a large database of published papers. Reportedly, *Nature* is using CrossCheck for screening submitted manuscripts. The same company also has programs (Turnitin) for screening student papers such as essays in English. Machine examination for plagiarism will undoubtedly be improved with time and the scientific journals can be expected increasingly to examine papers for plagiarism upon submission.

Peer Review – The Defence Mechanism

The peer review system, using anonymous referee(s) to evaluate the suitability of articles submitted for publication, was begun in the 19th century or earlier by *Nature* and the *British Medical Journal*;[43] it is standard practice today.[44] Undoubtedly, it has contributed enormously to maintaining standards in published papers. Occasionally, referees hide behind their anonymity to make things excessively difficult. J. D Dunitz reportedly found an unsigned referee's report on Mendeleev's paper in a deserted laboratory at the ETH. It stated:

> *This paper is just a rehash of a lot of known facts and contains nothing new. In the unlikely event that it should be published, the table should be omitted since it takes up a lot of space.*

An entertaining example of a referee carrying things to an extreme!

Chemists and scientists in general do not think in terms of fraud when reading a paper. They assume that, while authors may make mistakes, they don't cheat. Considering the small number of fraudulent papers in organic chemistry, this is a pretty good assumption.

Peter Golitz, the talented editor of *Angewandte Chemie*, published a report[45]in 1994 on the sequence of events in the publication of the Zadel paper that opened this article. The paper was sent to three referees. Ref. *A* said it was not worth publishing and should be rejected immediately, *B* said it described a very significant breakthrough and should be published at once, while *C* recommended that further work be done before it was considered for publication. An editor's dilemmas - publish garbage or not publish a breakthrough paper! Further work was done, *A* and *B* did not change their opinions but *C* did, and the paper appeared in *Angewandte Chemie*. Fortunately, only a few weeks passed before the fraud was exposed but two papers describing unsuccessful efforts to repeat the published work had already appeared in the journal.[46]

A classic example of not publishing a breakthrough paper is Beluzov's work on oscillating reactions[47] where a reacting solution oscillates between two different colours as the reaction proceeds. The work was rejected twice because it was *theoretically impossible*. Impossible or not, a Gordon Conference is now held on the subject every summer!

We cannot know how many fraudulent papers have been caught by the refereeing system, since such papers would not be published and nothing would be known about the attempts to have them accepted for publication. We cannot expect referees to spot every blemish of a submitted article, particularly if it is fraudulent.

Conclusions

The research supervisor can do a great deal to minimize the possibility of fraud. Firstly, research groups should be maintained at a size such that the 'boss' has sufficient time available to give some attention to every co-worker. Secondly, co-workers should understand the objectives of their work without ever feeling that it is incumbent upon them to get a certain result. Pressure of this sort is asking for trouble, especially with a weak personality. One of the invariable excuses of someone caught in fraud is that he was under extreme pressure to get results – and fabrication (or falsification) provided a quick solution.

The best strategy to reduce fraud to the absolute minimum has to be the education of future generations of chemists on the subject, both from the idealistic and practical points of view. The US National Science Foundation and

National Institutes of Health have mandated a course in scientific ethics as a condition of their awards of training grants for graduate students.[48] Such a course has to be a valuable tool in having students think about the general aspects of their chosen career and how they should, and would, behave in a variety of situations including their conduct in research.

Finally, for those interested, an E-mail address is now available to exchange information on scientific fraud: SCIFRAUD@UACSC2.ALBANY.ED

Acknowledgments

Our thanks are due to the following for helpful discussions: Profs. R. West (Madison), J. Berson (Yale), A. Eschenmoser (Zurich), S. Braslavsky (Mulheim/Ruhr), J. D. Dunitz (Zurich), J. Wolinsky (West Lafayette), A. E. Halevi (Haifa), M. Haley (Eugene); Drs. P. Golitz (Weinheim) and H. Bernstein (Haifa – deceased). Mss. H. Ilovich and E. Yaskin (Chemistry and Biology Library of Technion), and A. Zeidman-Karpinski (Science Library, University of Oregon) were most helpful.

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Development of NNZ-2566 as a Drug Candidate for Traumatic Brain Injury: The Neuren Story

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About Margaret Brimble

Margaret Brimble MNZM, FRSNZ, FRSC, FNZIC, FRACI holds the Chair of Organic and Medicinal Chemistry at the University of Auckland. She graduated with an MSc (Hons) in Chemistry in 1982 from that university and gained her PhD in organic chemistry as a Commonwealth scholar under the direction of Prof. Ray Baker at the University of Southampton in 1986. Margaret then took up a lectureship at Massey University where she began her independent bioactive natural products work. She was a visiting professor at the UC-Berkeley in 1992, moved to Sydney University in 1994, and returned to NZ as Professor of Organic Chemistry at the University of Auckland in 1999. She was instrumental in establishing the first new interdisciplinary degree in medicinal chemistry in NZ and is now Chairperson of Organic and Medicinal Chemistry and was Director of Medicinal Chemistry, Neuren Pharmaceuticals Ltd.

Margaret was appointed Titular Member of IUPAC Organic and Biomolecular Chemistry Division (Division III), is Co-Chair Organising Committee – Zing European Gordon Conference on Synthesis and Biosynthesis of Natural Products to be held in Egypt in February 2012 and was co-Chair of the IUPAC 14th International Conference on Organic Synthesis held in Christchurch in 2002. She is a Trustee and Chairperson of RSNZ's Rutherford Foundation, past-President of the International Society of Heterocyclic Chemistry and a past member of the Marsden Fund Council (Chairperson of the PCB panel). Her editorial board responsibilities include Organic and Biomolecular Chemistry and Natural Product Reports, Synthesis and Synlett, Scientific Reports, the Wiley-Blackwell Postgraduate Chemistry Series, the Journal of Heterocyclic Chemistry, Marine Drugs, Chemistry Insights, Perspectives in Medicinal Chemistry.

Margaret has received numerous national and international accolades, not least those of her MNZM and the L'Oreal-UNESCO Laureate and the RSC Natural Products awards that have been recorded in these pages. Most recently she opened the 2011 Marie Curie *Women in Science* lecture series in Wellington in February.

Neuren Pharmaceuticals, Neuroprotection and NNZ-2566

Neuren Pharmaceuticals Ltd.[1] is a NZ based biopharmaceutical company whose principal business activities are the discovery, development and commercialization of pharmaceuticals for the treatment of brain injury and neurodegeneration. The company's focus is the preservation, treatment and monitoring of neuronal function in neurodegenerative disease in chronic conditions such as Parkinson's and Alzheimer's disease and following acute ischemic and traumatic brain injury. Herein, we outline the medicinal chemistry effort that led to the discovery of NNZ-2566, currently in phase II human clinical trials as a potential therapeutic agent to treat traumatic brain injury (TBI) with $US18 million funding from the US Army Medical Research and Material Command.

The ability to reduce the damage and consequences of brain injury is referred to as neuroprotection and NNZ-2566 is the most promising neuroprotective drug currently in development for TBI. This is a considerable achievement as there is currently no neuroprotective drug approved for TBI on the market. The fact that the US Army is prepared to fund the trial to the extent of over $US18 million speaks for itself and validates NNZ-2566 as a valuable drug candidate establishing Neuren Pharmaceuticals Ltd. as a major player at the forefront of clinical research into TBI. Few biotech companies find themselves in such a position with the real possibility of dramatically improving shareholder value and making a major contribution to public health. NNZ-2566 is Neuren's lead clinical stage asset. The discovery and development of NNZ-2566 was undertaken through a contractual arrangement with Neuren Pharmaceuticals Ltd. administered by Auckland Uniservices Ltd. All of the medicinal chemistry was conducted in the Brimble laboratory in Auckland University's Chemistry Department.

Drugs for Traumatic Brain Injury (TBI): An Unmet Medical Need with Significant Market Opportunity

In the US, traumatic brain injury (TBI) is the primary cause of death and disability in persons under 45 years old, occurring more frequently than breast cancer, HIV-AIDS, multiple sclerosis, and spinal cord injury combined.[2,3] In the US alone, approximately 1 million TBI patients are either treated and released from the emergency department or admitted to the hospital each year. Of the approximately 300,000 hospital admissions, nearly half have mild or moderate TBI. This trauma affects up to 90 New Zealanders every day and can result in lifelong disability. The cost of medical care for these individuals exceeds $NZ1 billion dollars p.a. and places considerable financial burden on the limited resources of our small country. Moreover, the societal and personal impact is equally severe.

Overall, the leading causes of TBI are falls and motor vehicle accidents; however, penetrating ballistic-like brain injury (PBBI) represents one of the most severe categories and is the leading cause of TBI-related death in the US in both civilian and military populations.[4,5] With no drugs approved for this indication, TBI represents a large unmet medical need as well as a significant market opportunity. Neuren Pharmaceuticals Ltd. has estimated total sales of NNZ-2566 in the first 10 years following approval to exceed $US2 billion in the US alone, with peak gross revenues of $US341 million. Assuming drug registration success, this would result in a net present value exceeding $US250 million.

In addition to the damage caused by the initial brain injury, secondary injury takes place in the minutes and days following the injury (Fig. 1). These processes, which include alterations in cerebral blood flow and the pressure within the skull, contribute substantially to the damage from the initial injury. NNZ-2566 provides a unique opportunity for neuronal rescue therapy designed to ameliorate the effects of secondary injury caused by brain trauma.

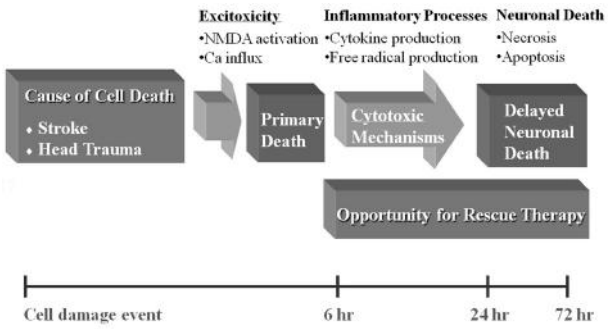


Fig. 1. The brain injury cascade.

Besides the direct cellular and molecular effects of TBI, up to one-third or more of patients experience non-clinical or non-convulsive seizures in the acute, post-injury period. Non-convulsive seizures (NCSs) are associated with increased brain injury and long-lasting cognitive and neurological deficits. Generalized convulsive seizures are readily recognizable, but NCSs occur without motor manifestation and, therefore, are often undiagnosed. Even though NCSs are difficult to detect and treat, prompt medical intervention should be provided to prevent synergistic brain damage and worsening of the prognosis.[6] The unanswered medical need to control and treat NCSs effectively in brain-injured patients underscores the importance to develop novel therapeutic drugs with both neuroprotective and antiepileptic properties.

Independent animal studies conducted by the Walter Reed Army Institute of Research (WRAIR) indicated that NNZ-2566 significantly reduced the number and duration of non-convulsive seizures following brain injury.[7] The compound possesses a unique therapeutic potential as a safe prophylactic agent that synergistically provides neuroprotection and reduces injury-induced seizures. The WRAIR suggest that neuroprotective effects of NNZ-2566 may, in part, be functionally attributed to the compound's ability to modulate expression of multiple neuroinflammatory mediators in the injured brain.[8]

Presently, there are no drugs approved for TBI. This and the serious and life-threatening nature of the condition supported the approval of NNZ-2566 for Fast Track designation by the US FDA.

The Initial Lead: Discovery of GPE

Studies have shown that NNZ-2566 prevents secondary damage to brain cells in patients with TBI by interfering with the inflammatory and apoptotic phenomena that are up-regulated following an acute brain injury, thereby reducing the number of brain cells impacted upon by the initial injury. NNZ-2566 is a synthetic analogue of a naturally occurring molecule produced by the brain in response to injury. The natural molecule is a small part of the endogenous insulin-like growth factor-1 (IGF-1) protein that can be truncated in the brain by an acid protease to form the des(1-3)IGF-1 fragment and the N-terminal tripeptide, glycine–proline–glutamate (GPE) (Fig. 2).[9]

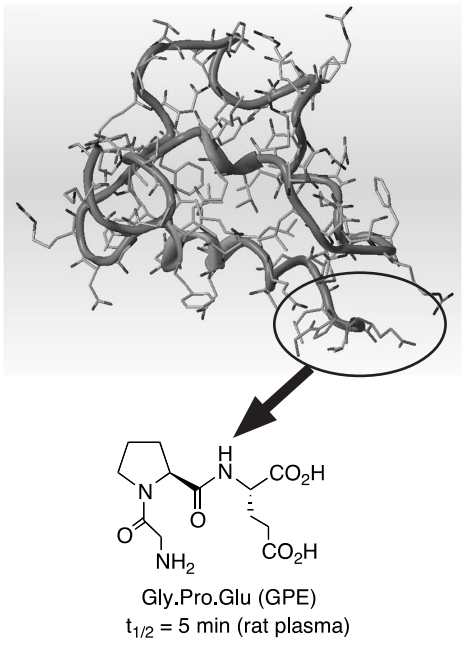


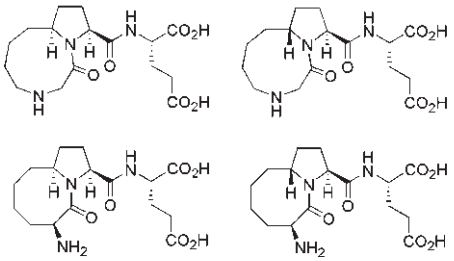
Fig. 2. Cleavage of tripeptide Gyl.Pro.Glu. (GPE) from the N-terminus of insulin-like growth factor 1 (IGF-1).

IGF-1 is neuroprotective and improves long-term function after brain injury. However, its clinical application to neurological disorders is limited by its large molecular size, poor central uptake and mitogenic potential. The endogenous tripeptide GPE also exhibits neuroprotective properties in animal models for ischemic injury. GPE thus provided a novel lead molecule for the development of new drugs to treat neurological disorders. However, it is not enzymatically stable and has a plasma half-life of less than 5 min. in rats;[10] hence, intravenous infusion of GPE becomes necessary for stable and potent neuroprotection. Our goal, therefore, was to find a synthetic analogue of GPE that was a more potent neuroprotection agent, had a longer half-life, and was able to penetrate the blood-brain barrier.

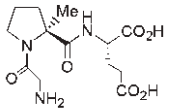
The Development of NNZ-2566

For the invention of NNZ-2566, the challenge was that the initial neuropeptide lead GPE did not target a single, highly specific component in a well-known biological pathway. We had to design and develop synthetic analogues of the naturally occurring neuropeptide to modulate expression of multiple inflammatory mediators in the injured brain. Over 120 such compounds were synthesized.[11] The process to optimize GPE into therapeutic leads involved investigation into areas such as improving proteolytic stability, improving bioavailability (transport across the gastrointestinal tract and blood-brain barrier), and formulation development. Synthetic approaches to achieve these parameters included increasing the lipophilicity of the analogues,[12] removal of amino acid characteristics such as the α- and γ-carboxylic acid groups in the glutamic acid residue,[13-15] using D amino acids, introducing bulky α,α-dialkyl amino acids and *N*-methyl amino acids that are not recognized by proteases. Further structural changes included introducing appropriate functionality to alter the *cis-trans* conformation of the proline *N*-carbonyl to the side chain amido carbonyl attached to C2,[16] modification of the peptide linkages, and reduction in the degrees of freedom of the peptidomimetic by linking the side chains using Grubbs' ring-closing metathesis.[17] Examples of compounds from this latter stratagem are summarized in Chart 1. Formulation development included the selection of suitable protease inhibitors and permeation enhancers for optimal oral delivery.

Chart 1. Examples of synthesized macrocyclic analogues of GPE.



To overcome the instability of tripeptide GPE in plasma, one of the GPE analogues resulted from α-methylation of the proline ring to give GPE G-2MePE (now known as NNZ-2566). Its half-life[18] in the blood and in the brain was significantly prolonged compared with that of GPE, and oral bioavailability improved considerably compared to the parent peptide. *In vivo*, NNZ-2566 reduced injury size in rats subjected to acute focal stroke.[18] An intravenous infusion of NNZ-2566 of 4 h duration (3–10 mg/kg/h), initiated 3 h after endothelin-induced middle-cerebral artery constriction (MCAO), significantly reduced infarct area as assessed on day five. Neuroprotective efficacy in the MCAO model was also observed following oral administration of the drug (30–60 mg/kg) (Fig. 3).



$t_{1/2}$ (rat brain) = 74 min

NNZ2566

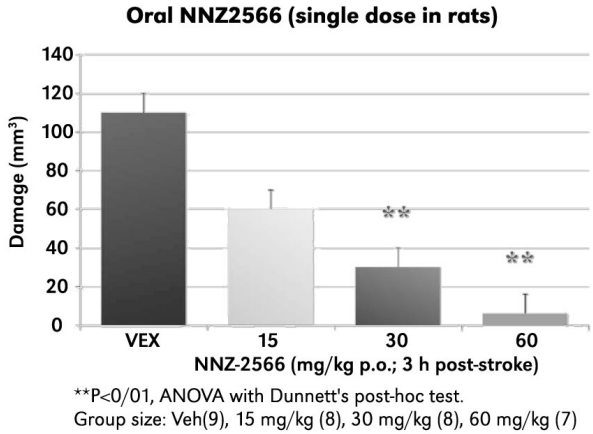


Fig. 3. MCAO-induced ischemic brain damage: effect of oral NNZ2566 – see ref. 18.

In vitro, NNZ-2566 significantly attenuates apoptotic cell death in primary striatal cultures, suggesting that attenuation of apoptosis is one mechanism of action underlying its neuroprotective effects. Independent experiments carried out by the WRAIR demonstrated that in animal models NNZ-2566 reduced the level of expression of genes associated with inflammation, necrosis and apoptosis – key elements of the brain injury cascade – and reduction in the functional deficits induced by these phenomena.[7,8] These data further supported the development of NNZ-2566 as a neuroprotective agent for acute brain injury, and it was shown to have a good safety profile in preclinical and phase I studies. It is currently in phase II clinical trials for the treatment of cognitive deficits following traumatic brain injury.

After the discovery of NNZ-2566 we provided on-going analytical and preparative support for the scale-up and current Good Manufacturing Practice (cGMP) production of the newly developed active pharmaceutical ingredient (API). We also went on to develop two new classes of compounds for Neuren Pharmaceuticals Ltd. called diketopiperazines (DKPs) and macrocyclics that have been rationally designed as candidates for both acute and chronic neurological conditions. Our second drug candidate NNZ-2591 is also under serious consideration by Neuren Pharmaceuticals Ltd. for entry to human clinical trials for TBI.

The Future of Peptide Chemistry at The University of Auckland

The discovery of NNZ-2566 as a pre-eminent drug candidate for TBI not only has obvious potential health benefits in NZ but also for the world population. The global market for novel therapies in areas of significant unmet medical need such as TBI is large and the downstream economic benefits to NZ from the development of the world's first drug for TBI also would be significant.

Importantly for our medicinal chemistry team, the work carried out for Neuren Pharmaceuticals Ltd. was a catalyst for the development of a larger peptide and peptidomimetic synthesis laboratory for NZ biopharma that is now located in the Institute for Innovation in Biotechnology (IIB) in our university. The purpose-built peptide synthesis laboratory is also equipped to undertake the synthesis of peptides under cGMP. In partnership with the Malaghan Institute of Medical Research, and with funding from the Health Research Council, this state-of-the-art peptide chemistry laboratory is set to produce long peptides as components for melanoma vaccines to be used in human clinical trials.

Acknowledgements

We thank Dr Mike Bickerdike (Neuren Pharmaceuticals Ltd.) for helpful advice and The Maurice Wilkins Centre for Molecular Biodiscovery for on-going support of the peptide synthesis platform.

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CHEMICAL EDUCATION TRUST

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Applications are invited from secondary school teachers (via Head of Chemistry and Head of Science) for grants from the ***NZIC Chemical Education Trust*** to promote the teaching of chemistry in their school. For the 2011 distribution, grants of around $500 are envisaged, but greater or lesser amounts can be applied for.

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Institute of Fundamental Sciences
Massey University
Private Bag 11-222
Palmerston North 4442

Fax: 06 350 5682

Email: A.Brodie@massey.ac.nz

Applications that arrive after the closing date or do not include full details, as listed above, will not be considered.

From Pesticides to Paint *via* Pharmaceuticals - the Evolution of New Zealand's Applied Carbohydrate Chemistry R&D

Richard H. Furneaux and Gary B. Evans

Carbohydrate Chemistry Group. Industrial Research Ltd., PO Box 31-310, Lower Hutt
(e-mail: *g.evans@irl.cri.nz*)

About the Senior Author

Richard H. Furneaux BSc(Hons), PhD, FNZIC, FRSNZ, founded, and leads a world-renowned team of chemists at Industrial Research Ltd. (IRL) whose focus is on the discovery and commercialization of *Glycotherapeutics*—drugs and dietary supplements based upon knowledge of the role of complex carbohydrates in biological processes. They partner nationally and internationally for biology and biochemistry. He has been involved with (and for a year managed) the GlycoSyn business unit at IRL, which undertakes process development and cGMP manufacturing by organic chemical synthesis of small molecule drugs for use in proof-of-concept human clinical trials. Together these units total 55 technical and support staff.

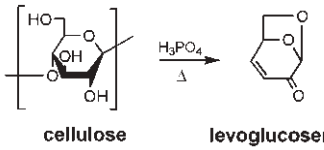
Richard was born in Wellington and educated at Scots College. He gained an Honours degree in physical chemistry before turning to the art of organic synthesis and a PhD under Prof. Robin Ferrier's supervision. He had post-doctoral positions with Prof. Fred Shafizadeh at the University of Montana and then back at VUW, before joining DSIR Chemistry in 1980; it became IRL in 1992. Richard, a Fellow of the Royal Society of New Zealand, was awarded its Hector Medal in 2006. He has authored 186 original papers and 25 reviews or book chapters. He is the NZ representative on the International Carbohydrate Organization. His research team has grown from 3 to 32 members since its inception in 1985, and since 1995 has produced 281 publications, 27 reviews, 29 published patent series and 57 other reports.

The team is focused on the rational design and synthesis of drug candidates based on knowledge of the role of carbohydrates in biology, in partnership with World Class Biologists. The flagship project is the collaboration with the biochemistry/biology team of Prof. Vern Schramm at Albert Einstein College of Medicine in New York, which is focused on inhibitors of carbohydrate and nucleoside processing enzymes for use as pharmaceuticals.

Carbohydrates are ubiquitous in nature and highly varied in their structures. From crystalline cellulose to the sweetest of sugars and even DNA itself, they pervade life on Earth. New Zealand is rich in carbohydrate resources with its diverse forest botany, virtual mountains of lactose as it comprises 2 – 8% of milk by weight, and a vast coastline draped with seaweeds.

The Carbohydrate Chemistry Group, based at Industrial Research Limited (IRL) in Lower Hutt, has seen these resources as an opportunity upon which to build arguably the largest and most productive carbohydrate chemistry team in the world. This is the story of how the now Group Manager, Dr. Richard Furneaux led the team to become the 32-strong international group that it is today.

Richard began work as a Research Chemist in the Applied Chemistry Group of the Chemistry Division of the Department of Science and Industrial Research (DSIR) under Dr Ian Miller.[1] Chemistry Division was the perfect place for the applied research that he had a passion to do, with a supportive management and freedom to pursue ideas to enhance NZ's economic well-being. Early adventures were in the carbohydrate chemistry of seaweed polysaccharides and the transformation of cellulose to a class of cyclic ether herbicides *via* levoglucosenone using Michael or conjugate addition chemistry (Scheme 1).[2]



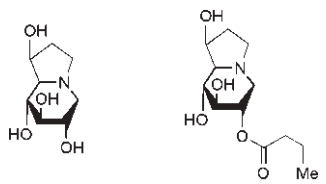
cellulose **levoglucosenone**

Scheme 1. Acid catalysed pyrolytic conversion of cellulose to levoglucosenone

The lead compound, named PT-9 from Dr. Peter Tyler, was sent to Jealot's Hill Research Station, part of ICI Agrochemicals, for testing and was found to be active at concentrations as low as 1–10 g/ha. In a significant collaboration, a plethora of analogues were synthesized and tested, but PT-9 was hard to beat. However, it was active but not very selective, and was a little too volatile and water soluble. Although PT-9 was only four synthetic steps from waste paper, up against Roundup® (non-selective) and Treflan™ (selective, less potent, but very cheap) it could not compete on cost-of-goods. Subsequently, at a review meeting at ICI in 1988, it was agreed to cease work on the project.

New collaborations with the National Institutes of Health (NIH) in the US led to their testing of compounds for biological activity that ranged from NZ seaweed-derived polysaccharides to iminosugars. Later, other plant-based extracts were included and so began a fifteen year relationship with the NIH/NCI (National Cancer Institute) to screen natural products and IRL's own drug candidates. As part of this relationship, the Carbohydrate Chemistry Group also re-synthesized lead compounds for the NCI under two consecutive five-year contracts. Of particular interest was a range of iminosugar enzyme inhibitors – sugar-shaped alkaloids where the ring oxygen is replaced by a nitrogen atom. These molecules, primarily made by plants, are used to fool the enzymes of potential predators that metabolise sugars, and interfere with their normal function.

The head of the ICI Corporate Carbohydrate Chemistry Group expressed an interest in the biological activities of castanospermine derivatives, especially the anti-HIV lead 6-*O*-butanoylcastanospermine (Celgosivir).[3] A collaborative research programme was established utilising pharmaceutical screens at ICI to test the castanospermine-based targets synthesized by the Carbohydrate Chemistry group. This work led to an interest in iminosugars[4] in general, together with their associated biological activity. Nearly 200 castanospermine analogues[5] were made and tested in both agrochemical (herbicides and fungicides) and pharmaceutical (cancer and glycosidase) screens. Other compounds that were part of the ICI collaboration included allosamidin—a potent chitinase inhibitor, tagetotoxin—a potential herbicide, and the insecticide dyshomoerythrine.[6]



castanospermine Celgosivir

Group numbers had grown to thirteen by the time the team became part of the newly established CRI, Industrial Research Limited, in 1992. A conscious decision was made then to increase the group's commercial revenue in the event that government funding priorities changed. So began the creative tension between commercial work and discovery science that continues to this day.

In 1993, Richard Furneaux met the Head of MAF's Wallaceville Animal Research Centre, Dr. Paul Atkinson who had returned to NZ in 1991 after twenty three years at the Albert Einstein College of Medicine (AECOM). Atkinson mentioned that a former colleague, Professor Vern Schramm,[7] was having difficulty finding a chemistry group to synthesize a target molecule he had designed. Under a US/NZ Co-operative Science Program Grant, Drs. Furneaux and Tyler met Schramm at a New York Yacht Club to discuss the blueprint design that he had for an inhibitor of nucleoside hydrolases. Nucleoside hydrolases and phosphorylases are salvage enzymes and in humans are implicated in a variety of immune disorders.[8]

Schramm's hypothesis was that the *virtual* molecule in question was potentially the perfect inhibitor of such enzymes. Tyler recognized that the enzyme purine nucleoside phosphorylase (PNP) would be the best and most commercially relevant target, and inhibitors could be used to treat a variety of human ailments from rheumatoid arthritis to T-cell cancers. Rate enhancements of 10^{15} are common in enzymology, and such inhibitors could, therefore, provide unprecedented utility in drug design. Armed with a bar napkin bearing the structure of the proposed enzyme inhibitor (coincidentally containing an iminosugar at its core) and an agreement with AECOM to share all royalties from their collaboration 50:50 (with the proviso that AECOM would take the lead in commercialising the attendant IP), then Furneaux and Tyler returned home and set to work.

Realising Schramm's blueprint design took considerably longer than was first envisaged but, in 1997, immucillin-H (ImmH; immucillin: penicillin for the immune system)[9] eventually was synthesized and sent to be assayed in his biochemistry group's enzyme screens, particularly against the now preferred target, PNP. Screening revealed that against bovine PNP, ImmH afforded inhibition constants at concentrations far lower than previously reported for other compounds and bore out the predictions of transition state theory.[10,11] With a lead compound identified, work began on turning the synthetic process from a *twenty one* step linear synthesis into a practical *twelve* step convergent synthesis.[12]

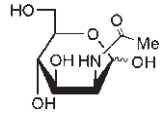
A thirty month-long process then began to find an investor to license the patented technology. One company, BioCryst Pharmaceuticals, already had a drug in Phase III clinical trials targeting PNP. In 1997, this compound (BCX-34) failed a Phase III clinical trial against psoriasis but management still believed that PNP was a good biological target for the treatment of T-cell mediated diseases. Consequently, BioCryst showed considerable interest in licensing the IRL collaborative IP in the area of PNP inhibitors, and more specifically Immucillin-H, in order to plug the gap left by the failure of BCX-34. So, in June 2000, BioCryst signed an agreement with IRL and AECOM to license all PNP inhibitors generated as a result of the collaboration. Since that time compounds from an additional three generations of inhibitors have fallen under this license.

Inextricably linked with the license agreement was the supply of kilogram quantities of ImmH to BioCryst in order for animal toxicology and human clinical trials to progress. Furneaux had recognized that although the intellectual property package had value for IRL, real value for NZ could only be gained if scalable processes to synthesize the immucillins could be developed by IRL, and the technology then transferred to a local chemical manufacturer. To realise this step-change in manufacturing, IRL first required the facilities to safely take chemical processes from a gram to a kilogram scale. In August 2000, Furneaux presented a proposal to the IRL Board to build a fit-for-purpose facility, which would house equipment to synthesize kilogram quantities of new chemical entities (NCEs) as well as assure the quality of the prod-

uct and the safety of processes.

A small process development team under Dr. Paul Benjes was seceded from the Carbohydrate Chemistry group in 2005. Its purpose was to specialize in laboratory scale development work, intermediate scale synthesis of good laboratory practice (GLP) material, and kilogram scale current good manufacturing process (cGMP) synthesis. The IRL GlycoSyn group is based now in the facilities Furneaux proposed in 2000 and officially opened by the Prime Minister, Helen Clark, in 2003.

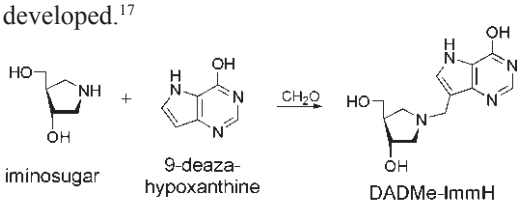
In an innovative marketing approach, a chemical sales website (now GlycoFineChem) was begun in the late 1980s offering for sale small quantities of 10–20 iminosugars. Acting as an internet *shop window* for the Carbohydrate Chemistry group, the business has enabled the initial sale of compounds such as *N*-acetylmannosamine, worth only a hundred dollars, to grow into multi-million dollar sales. Following some further work on the production process from glucosamine, both at IRL and New Zealand Pharmaceuticals (NZP), the technology package was licensed to NZP and is now worth more than $NZ10 million.



***N*-acetylmannosamine**

ImmH moved through animal toxicity trials and into BioCryst's first human patient in July 2002. Science progress was significant also, with the biological activity of a selection of immucillins featured on the cover of the ACS journal *Biochemistry*.[13] In 2004, ImmH was granted orphan drug status by the US FDA for the treatment of T-cell cancers. This enabled BioCryst to receive prefiling regulatory guidance as well as reduced filing fees, and meant potential market exclusivity in the US for a period of seven years, should ImmH receive approval by the FDA.

A second generation family of inhibitors was based on work by Schramm's group to clone and express the human form of PNP and generate a blueprint for an inhibitor of this enzyme. Dr. Gary Evans completed the twenty-two step linear synthesis of DADMe-ImmH in early 2001 and screening against the human enzyme showed it was four times as potent as ImmH.[14] Soon, a convergent process was patented[15] using the Mannich Reaction[16] and a scalable chemoenzymatic synthesis of the iminosugar was developed.[17]



Scheme 2. Scalable synthesis of DADMe-ImmH.

Other compounds were made to target methylthioadenosine phosphorylase (MTAP), an enzyme implicated in the control of polyamine synthesis which is upregulated in proliferating cells such as cancer cells.[18] The compounds were exquisite inhibitors of the human MTAP enzyme and, when assayed against tumour cell lines, showed strong activity against head and neck tumours that are notoriously difficult to treat.[19] Ultimately, it was shown that the mode of action was probably the inhibition of whole body MTAP, the consequent alteration of methylthioadenosine levels in the body and the subsequent effect this has on DNA methylation.[20]

Schramm had also identified a biological target that would potentially disrupt quorum sensing in bacteria – the way bacteria communicate that ultimately results in an infection. Methylthioadenosine nucleosidase (MTAN) was the target and modified immucillins were designed and synthesized in order to inhibit this enzyme. These compounds were more potent than any inhibitor that had been synthesized to-date and had some of the lowest inhibition constants ever reported for any enzyme, in the femtomolar (10^{-15} molar) range. The work was so significant that the prestigious international journal, *Journal of Biological Chemistry* featured an excerpt of this work on its cover.[21]

Another class of compounds that were a focus for the group were the phosphatidylinositol manno-oligosaccharides (PIMs) from the cell walls of bovine tuberculosis.[22] When isolated, these natural PIMs were shown to be potent immunomodulators and Carbohydrate Chemistry group members set about the challenging task of synthesizing and characterising them. The PIMs have proven to be valuable tools in probing immune responses and ultimately may have commercial worth as adjuvants.[23]

In late 2005, Roche and BioCryst announced an exclusive sub-licence to develop and commercialize DADMe-ImmH for the prevention of acute rejection in transplantation and for the treatment of autoimmune diseases. The deal, the fifth largest Biotech/Pharma one of 2005, meant that Roche would obtain worldwide rights to DADMe-ImmH in exchange for a $US25 million up-front payment, a $US5 million payment for the supply of material during the first two years of the collaboration, and future event payments potentially reaching $US530 million in addition to royalties on product sales. Following this, early in 2006, a sub-license agreement was announced between BioCryst and Mundipharma to develop ImmH for markets outside North America. The agreement involved an initial $US10 million payment and future event payments of as much as $US155 million. But the big reward and big risk nature of the *pharmaceutical game* was clearly bought home in May 2008 when Roche returned the rights to DADMe-ImmH to BioCryst following an inconclusive Phase II trial. Subsequently, in 2010, BioCryst announced positive results for a Phase II trial of DADMe-ImmH in gout.

Other applications for the immucillins have included the treatment of malaria through the inhibition of malarial PNP. Initial work looked at inhibiting the isolated enzyme and generated some beautiful crystal structures of the inhibitor in the active site of the enzyme, which were

featured on the cover of the *Journal of Biological Chemistry*.[24] This work was supported by the NZ and US governments and the Medicines for Malaria Venture, financed through the Bill and Melinda Gates Foundation.

In 2009, when Resene approached Furneaux to help prepare their entry for the IRL-run competition *What's Your Problem New Zealand?* he jumped at the chance to help. Their vision was to develop new waterborne paint, based on resins made from up to 80% sustainable ingredients, and so break a long-term reliance on gas and oil for the product. The Resene bid won the $NZ1 million prize on offer and this work has now attracted additional FRST funding to support the research over the next four years.

Richard Furneaux is forever chasing opportunities that only he sees, and at times, only his team can realise. He is justly proud of what his group has accomplished, just as the group members themselves are proud of his achievements. He is also the first to acknowledge the assistance of support and business development staff and senior managers, without whom none of this would have been possible.

Acknowledgement

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The IRL Carbohydrate Chemistry Group

The Last 25 Years of Chemistry in Otago and Southland

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Chemistry in Otago and Southland involves on one hand the large scale industrial chemical processes of aluminium smelting at Tiwai, milk processing at Edendale, gold extraction at the Macraes mine and fertilizer manufacture at Awarua and Dunedin. On the other hand, fundamental chemical research and the teaching of chemistry is dominated by the activities of the Chemistry Department at Otago University (OU) and the science departments of the polytechnics and high schools in the area.

Otago University

OU Chemistry moved in to a new undergraduate laboratory building in 1971 and a new research/administration building in 1972. It has remained there since, although internal refurbishment to laboratories and office space has occurred in both buildings over the years, particularly to meet new occupational safety and health requirements and to optimize space utilization among university departments. The past 25 years has seen major changes to both departmental management and the funding regime. There has been a positive move to a committee management structure. A period of tight budgets in the late 80s was relieved when chemistry became one of the first departments in the university to be given budget flexibility and control within defined parameters. By 1996, this flexibility had provided for ten new academic staff appointments and support for their research. The period 1995 onwards saw an emphasis on quality teaching and research. The past decade has seen this quality research being recognised in the award of many Marsden and FRST grants, individual prizes for excellence, and a high ranking in the national PBRF exercise. External research funding now plays a pivotal role in the financial health of the Department and has led to a big increase in the number of research fellows and assistants appointed.

Research

Physical Chemistry

The Department had a long tradition in undertaking what might now be considered as classical physical chemistry beginning in the 1950s with Hugh Parton (electrochemistry) and Max Pankhurst (aqueous solution chemistry). This tradition was continued by Arch Matheson (1969-1990) and Bob Smith (1965-1991) undertaking classical electrochemical analysis of aqueous solutions, and Dave Fenby (1967-1996) examining aspects of the thermodynamics of the mixing of organic liquids. Research in zeolite and surface chemistry was initiated by Chris Pope (1961-1997), and William Ducker (1994-1997) introduced the technique of atomic force microscopy to study surfactant behavior. Kate McGrath (1997-2003) extended surface chemistry research by studying aspects of biomineralisation. Such biophysical research continues with Guy Jameson (2006-) who is studying physicochemical aspects of metal-containing enzymes and, most recently, Carla Meledandri (2009-) researching the design and synthesis of nanoscale materials for combined bioanalysis and targeted drug delivery. Extensive research into the kinetic behavior of aqueous inorganic systems, particularly cobalt coordination and porphyrin compounds, was undertaken by Dave Buckingham (1978-1995) and his scientific officer Charles Clark (1978-2000).

Keith Gordon (1993-) focuses on understanding the properties of conducting polymers, nanostructured electromaterials, dairy products and pharmaceuticals using spectroscopy and computational chemistry. Keith was

University of Otago Chemistry Building

NZIC President in 2006 and is a founding Principal Investigator in the Wellington based MacDiarmid Institute. Henrik Kjaergaard (1996- 2009) introduced acoustic spectroscopy to the Department and developed theoretical calculations to study fundamental aspects of molecular vibrations in small molecules of interest in atmospheric chemistry. Jim McQuillan (1975-) began his research on UV-vis and IR spectroelectrochemistry but, more recently, has developed internal reflection IR spectroscopy to study adsorption reactions on metal oxide particles and adhesion of biomolecules. He is the current President of IUPAC Division I - Physical and Biophysical Chemistry.

Organic Chemistry

Organic chemistry in 1985 was ably lead by Peter Grant (1962-1991) with assistance from Ross Grimmett (1967-1996), Rob Smith (1971-) and Rex Weavers (1975-2011). Primary research activities involved natural products and synthetic transformation of readily available NZ materials (Grant, Weavers) together with synthetic organic and organometallic chemistry (Smith) and heterocyclic reactivity (Grimmett). In addition, Ross Grimmett produced a series of well-cited comprehensive reviews in azole chemistry. The Department was well equipped for this work – particularly with NMR spectrometers. The following decade saw appointment of Dave Larsen (1990-) and Chris Hunter (1989-1990; he subsequently returned to the UK and developed a high profile career at Sheffield) and emphasis on natural products chemistry was diluted somewhat with wider research scaffolds such as carbohydrates and other bioactives examined. The move towards more biologically oriented study was enhanced by the appointment of Eng Tan (1992-) and Alan Hayman (1992-) with research interests in enzyme reactions and bio-organic chemistry, respectively.

From about 1995 onwards the organic research moved more towards biology and medicine, with many staff becoming involved in projects with colleagues in biological and biomedical departments. Facilities were maintained at useful levels and, while routine NMR had always been well resourced and supported, the changed emphasis required more HPLC equipment and better mass spectroscopic facilities than in the previous years.

In 1991, a joint venture was initiated between Chemistry and MAF Technology (now the Plant & Food Research CRI) and a plant extracts research unit (PERU) was created. Its objective was to discover and develop biologically-active natural products from NZ native plants and introduced crops. This successful entity is housed within the Department and is led by Nigel Perry (1996-) and employs four permanent researchers. Linkages with biological researchers in OU, nationally and internationally are strong, and some 120 multidisciplinary papers and reviews have been published and three patents filed to date.

In the twenty year period from 1985, over 180 publications were authored by organic chemists from Otago University. However, the last five years has seen more changes to the organic chemistry profile with Rob Smith commencing a staged retirement and Rex Weavers' departure this year. Recent new staff members with interests in chemical synthesis are James Crowley (2008-) and Nigel Lucas (2008-) and they are expected to take organic chemistry in new and exciting directions in the future. Organic chemistry originated from efforts to understand the natural biological processes at the molecular level, while its future at OU seems secure with continuing research in this area along with the synthesis of new biomolecules and materials being actively pursued.

Inorganic Chemistry

Inorganic chemistry has for many years been intertwined with physical chemistry as the application of physical methods strongly supported the synthetic research programme. An early staff appointment was that of Melville Carr (1959-1996) with specialist research interests in geothermal reactions, NZ clays such as montmorillonite, the properties of coal and the gasification of coal to manufacture liquid fuels. In 1985, the organometallic chemistry of Brian Robinson (1967-2010) and Jim Simpson (1969-), and the transition metal studies of Lyall Hanton (1981-) and Bob Cunninghame (1970-1995) were complemented by Dave Buckingham's (1978-1995) and Charles Clark's (1978-2000) appointments and the cobalt(III) mechanistic work has been continued by Allan Blackman (1991-). Electrochemistry, EPR, photochemistry, and single crystal structure determinations were essential techniques for the Robinson/Simpson research on electroactive clusters and then aryl ring ferrocenyl fluorophores. In recent years, this work was reinforced by the theoretical calculations of Henrik Kjaergaard (1996-2009).

The fluorophore work spawned studies in polymer clays and, ultimately, the foray into polymer gels by Lyall Hanton and Steve Moratti (2006-). Lyall Hanton's interest in arsenic ligands moved to nitrogen- and sulfur-based systems and into metallosupramolecular chemistry thanks to the brief appointment of Chris Hunter in 1989. Macrocyclic chemistry became a successful research area when Sally Brooker joined the staff in 1991. David McMorran's appointment as a senior teaching fellow in 2003 contributed to the metallo-supramolecular interests. Again, coordination chemistry has retained a strong physical bias through Sally Brooker's interest in magnetic materials and Allan Blackman and Keith Gordon's work on photoactive metal complexes. In 2008 appointments of James Crowley and Nigel Lucas were made, with both having strong organic/inorganic research interests. James' research is centred on metallo-supramolecular systems and molecular machines, while Nigel has interests in the organometallic chemistry of graphene systems.

Environmental and Analytical Chemistry

Research into Environmental Chemistry and the associated teaching courses at OU grew out of analytical chemistry courses developed in the 1970.by microanalyst Arthur Campbell (1948-1987). Keith Hunter (1980-) joined the department as a lecturer in Analytical Chemistry and he initiated aspects of trace metal research in marine chemistry with the establishment of clean room facilities and associated instrumentation. He also worked successfully with marine biologists to establish an interdisciplinary postgraduate teaching and research programme in marine

science that included use of expanded facilities at the university's Marine Biological Laboratory at Portobello on the Otago Peninsula.

In 1990, Barrie Peake (1972-) moved his research interests from spectroscopic studies of free radicals and joined Keith Hunter, assisting him in the teaching of new courses in aquatic chemistry, marine chemistry and marine pollution. He has also established research on aspects of trace metals in aquatic environments, natural aquatic photochemistry and dissolved organic matter and, most recently, is investigating the environmental fate of pharmaceutical compounds. Russell Frew (1996-) has established research on the application of natural isotopes in the environment as well as a commercial isotope-measurement laboratory (see below).

The Department and the National Institute of Water & Atmospheric Research (NIWA) established a joint National Centre of Excellence for chemical and physical oceanography in 1996. Phillip Boyd (1996-) and Kim Currie (1996-), assisted by a number of postgraduate postdoctoral students, have developed significant research activities in the areas of climate change that include iron-limitation of marine productivity, and long term trends in oceanic CO_2 chemistry.

Kim Hageman (2006-) has developed research involving organic pollutants, particularly airborne material in remote environments, using GC-MS. The Community Trust of Otago Centre for Trace Element Analysis was established in 2005 with Claudine Stirling as the Scientific Director. This centre is involved in inductively-coupled plasma mass spectrometry measurements of ultra-low levels of a range of trace metals using both quadrupole and multi-collector instrumentation. Sylvia Sander joined the Department in 2001 as a research fellow and has developed research in trace metal techniques in aquatic environments.

Applied Chemistry and Chemical Process Technology

Research and teaching of applied chemistry began in the early 1940s and was continued during the review period with the appointment of Don Brasch (1967–1996), Derek Whyman (1970-1990) and Vivian Alexander (1971-1989) with respective research interests in carbohydrate and pulp and paper chemistry, plasma chemistry, and automatic control theory.

With the then impending retirement of Don Brasch, a chemical engineer Paul Addison (1994-2004) was appointed with research interests in the commercial extraction of chitin from shellfish and he was assisted by Graham Caygill (1994-1999). In the late 1990s a decision was made to reduce the applied chemistry component of at least the Chemistry Honours courses and instead, just offer papers in the new Bachelor of Applied Science degree in conjunction with other subjects such as applied microbiology, biochemistry and food science. By 2004, there was only one remaining applied chemistry staff member, Paul Addison; and his departure that year marked the end of our teaching and research in this area.

Teaching Activities in Chemistry at OU

Lectures

The Chemistry Department has always prided itself on the quality of its undergraduate and graduate teaching. At first year, a large proportion of the students are required to study chemistry as a prerequisite for highly competitive entry to Medical School. So the introductory chemistry syllabus has always been guided largely by the needs of the Medical School and those of associated departments such as physiology, structural biology, biochemistry, microbiology, pharmacology, human nutrition, dentistry, pharmacy and physiotherapy, many of whom also require their students to pass a first year chemistry course.

Up until 1996, first year Chemistry consisted of a single course (Intermediate CHEM 112) of two papers covering lectures and a weekly laboratory extending over the academic year. In 1995, the Medical School reduced its entry requirements for chemistry and this also corresponded with the widespread introduction of a two-semester in place of the three-term academic year. Accordingly, in 1996, CHEM 112 was divided to provide single semester papers (CHEM 111: Molecular Reactivity required for entry to Medical School; CHEM 111 Molecular Architecture to cater for other non-health related disciplines). Students majoring in Chemistry were strongly encouraged to take both these papers. The CHEM 112 content was further rearranged in 2003 to give the present CHEM 191 Chemical Basis of Biology and Human Health paper.

Until 1988, second and third year chemistry teaching consisted of three full-year papers with the classical titles of Advanced 1 (or 2) Physical Chemistry, Organic Chemistry and Inorganic Chemistry, and a half paper at second year in Analytical Chemistry. In 1989, the programme was rearranged into a number of smaller, one semester with more specific titles such as Chemical Reactivity, Chemical Synthesis, Coordination Compounds, Electrochemistry and Surface Reactions, *etc*., along with the introduction of new papers such as Biological Chemistry and Environmental Chemistry to reflect the changing interests of the students and trends in chemical research within the Department. This wide selection of papers continues in various forms although, beginning in 1999, the titles of many of the papers reverted back to the more classical Physical Chemistry, Organic Chemistry, and Inorganic and Main Group Chemistry, *etc*. New 3rd-year chemistry papers introduced in 2010 include Instrumental Methods of Analysis (CHEM 306) and Marine Biogeochemistry (CHEM 365). A new programme in Forensic Science is also being developed across the university with a 2nd-year Analytical and Forensic Science paper (FORS 202) that has a significant Chemistry component to it.

Postgraduate teaching has always involved a series of lectures to the 4th year Chemistry Honours, first year MSc and the Postgraduate Diploma in Science (PGDipSci) students. As with undergraduate chemistry, the postgraduate offerings were originally grouped under the traditional chemistry subject areas. However, since the early 1990s, staff have been given much more freedom, with each lecturer able to give a 10 lecture module of their choice but

typically related to their research interests. The modules are collected together and examined in blocks at the end of Semester 2.

Up until the mid-1980s, assessment of the chemistry lecture courses was based entirely on end-of-year, closed book written examinations. However, with the increasing student demand for more internal assessment, a significant component of the assessment of undergraduate chemistry papers is now derived from student performance in laboratory and assignment work during the semester. The style of teaching Chemistry has also changed significantly over the last 25 years. Up until 1985 it was very much based on *chalk and blackboard* illustrated with 35 mm slides but, with advances in computer technology, the use of overlays, overhead projectors, white boards and, most recently, PowerPoint presentations are common. Ready student access to spreadsheet software and electronic databases and periodicals has also led to an expectation by teaching staff of more sophisticated calculations, data analysis and interpretation by the student.

Chemistry Outreach Activities

As in most NZ universities, the Department has had an increasing involvement with science teachers and students of all ages in local schools since the early 1990s. These activities were started by Barbara Duncan (1990-2003) and developed further by David McMorran (2004-) and David Warren (2006-). The current focus is the delivery of *hands on* chemistry activities for schools across Otago and Southland, as well as developing a support network for teachers in the region. Activities are delivered by a team of PhD and senior undergraduate chemistry students, who at the same time develop a range of skills that enhance their potential to be future ambassadors for chemistry. These activities include teaching chemistry lessons in intermediate and primary schools, providing access to university laboratories and resources for NCEA students who are carrying out internal achievement standards, the development of teaching resources for local school teachers, the development and delivery of experiments for the new OU Advanced Sciences Academy and the delivery of lessons to high school students as part of Marae-based Wananga on the North Island East Coast and Invercargill.

Other notable activities have included a *Chemistry for Christchurch* fund-raising magic show in February to an audience of *ca.* 800 people that was organised and delivered by outreach students, the Otago regional chemistry quiz which has run since 2004 and attracts up to 200 participants, and the Healthy Harbour Watchers programme (also established in 2004) by a local science teacher in conjunction with the departmental staff (see *Chemistry in New Zealand* **2010**, *74,* 141-145).

Alan Blackman regularly contributes articles on topical aspects of chemistry to the Otago Daily Times and he has been doing so since 2001.

Long-standing Chemistry Support Staff

There have been many non-academic Departmental staff with us over part or the whole review period and who have played an invaluable role assisting in all aspects of research and teaching. Able research assistance has been provided by John McAdam (1992-) (Inorganic), Abdul Rahman Manas (2002-) (Organic), Malcolm Reid (1996-) the research laboratory manager for marine chemistry research, and technical help from Pauline Bandeen (1990-) (Organic). Mervyn Thomas (1974-) has ably maintained the NMR facilities, assisted by Ian Stewart (2004-) who has also managed the X-ray diffraction, HPLC and LC-MS instrumentation. John Wells (1981-) has assisted many research staff and students as the glassblower, while Garth Tyrell (1971-) and his fellow technicians have designed, constructed and helped maintain much of the mechanical research equipment in the department. Steven Gray (1975-2006), Jimmy Kerr (1982-2006), Nigel Alefosio (2005-), and Sean Bray (2006-) have all managed the departmental store efficiently. Cathy Bennett (1985-) has been the departmental administration manager during this review period.

Commercial Activities within the Department

Special mention must be made of the role of staff assisting in the running of the Campbell Microanalytical Centre based in the Department. They have undertaken mainly elemental analysis of miniscule amounts of compounds submitted by clients from throughout NZ and overseas. This work was undertaken under the direction of Prof. Arthur Campbell until he retired in 1987 and then Marianne Dick (1982-2009) and Bob McAllister (1976-).

In 1997, OU acquired the analytical facilities of the private Dunedin Company Zentech, and established a small commercial environmental and analytical chemical consulting company (Chem Search) within Chemistry. This group led by John Watson (1997-2008) and assisted by David Barr (1997-) and Dianne Campbell (2001-) undertook a wide range of analyses, mainly of environmental samples for external organizations such as the Macraes gold mine operation, several Central Otago wineries and the Ministry of Fisheries. They also assisted researchers in related aspects of their work until the Chem Search operation was closed at the end of 2008.

In 2004, Russell Frew established fully commercial facilities within the university under the name Isotrace NZ Ltd. This is for accurate measurement of stable isotopes and isotopic ratios such as $^{2}H/^{1}H$, $^{13}C/^{12}C$, $^{18}O/^{16}O$, and $^{34}S/^{32}S$. In 2008, the company was incorporated into the Department as a research unit that continues to provide commercial services, but its main role now is to support research activities across the university that involve isotopic measurements. The unit is currently managed by Robert van Hale (2008-) and assisted by Dianne Campbell.

Influence of Advances in Computer Technology

The advent of microprocessors and associated microcomputers in the later 1970s has had a profound effect on all aspects of research, teaching and administration. Up until 1985, there was only one central mainframe computer in the university and the Chemistry staff used this mainly for refining X-ray crystallographic data collected with the assistance of Ward Robinson and his group in Canterbury, and for simulation of EPR spectra (Peake). Once micro-

processors became routinely available in the early 1980s, Peake interfaced them to a range of analytical instruments as a research exercise and, subsequently, they progressively became integral to every aspect of chemical instrumentation.

As the computational speed and memory capacity of stand-alone microcomputers evolved, students taught before 1985 to program the single central mainframe computer using punched cards, were progressively introduced to programming in languages such as BASIC, Pascal, C++ and MatLab on departmental microcomputers with keyboard and visual display screen. The advent of commercial word processing and spreadsheets packages such as the Microsoft Office suite of programs has made such facilities essential tools in any chemistry department. By the mid-1990s, research and teaching presentations evolved to computer projection of graphical and textual material prepared using graphical packages such as Microsoft PowerPoint.

The appointment of Keith Gordon (1993-) and Henrik Kjaergaard (1996-2009) as physical chemists saw the development and use of increasingly sophisticated computer programs to undertake molecular orbital calculations for research purposes. Our own X-ray diffractometer facilities, acquired in 2006, have also led to extensive in-house crystallographic data analysis. In keeping with the global community, chemistry communication via the World Wide Web is fundamental to our operation. The Department is fortunate in having its own computer support personnel, Richard Coulbeck (1982-1995), the late Andrew McCallum (1992-2001), Simon Money (2001-2006) and Matt Rooney (2006) to maintain and develop its computer facilities.

Chemistry Teaching at the Otago Polytechnic (Dunedin) and the Southern Institute of Technology (Invercargill)

The Science Department at Otago Polytechnic taught chemistry until 2003. Its staff, John Waddick and the late Tony Herd, provided courses for the NZ Certificate in Science and, after 1997, the National Diploma in Science (Level 6). The OU Chemistry Department used this course for technician training but after 2004 the viability of the three year national diploma declined and resulted in the Otago Polytechnic management closing the entire programme at the end of 2006.

Chemistry has been taught at the Southern Institute of Technology only as part of a paper in Years 1 and 2 of the Bachelor of Nursing in the School of Nursing, and as part of the Environmental Science paper in Years 1 and 2 of the Bachelor of Environmental Management programme in the School of Social and Environmental Studies.

Industrial Chemistry

Although chemical-based industries in Otago-Southland are relatively small in number compared to some other areas of New Zealand, they all make a significant and unique contribution to NZ's overall manufactured output.

In 1971, New Zealand Aluminium Smelters Limited (NZAS) commenced production of the world's highest purity (99.98%) grade aluminium at NZ's only aluminium smelter at Tiwai Point, near Bluff. Current annual output is *ca.* 360,000 tonnes of which over 90 % is exported to Japan. The electrolytic Hall-Heroult process is used to reduce alumina (Al_2O_3), sourced as bauxite from Australia and dissolved in a bath of molten sodium aluminium fluoride (Na_3AlF_6) at 960 °C. The smelter has an extensive on-site and off-site monitoring programme to assess the effects of discharges to land, air and water mainly arising from the gases such as hydrofluoric acid emitted in free and particle-bound forms during the electrolytic reduction. NZAS has well equipped (NZS/ISO/IEC 17025:2005) quality accredited laboratories for the analysis of raw and process materials, environmental samples and cast aluminium. Analytical techniques include the routine use of modern X-ray diffraction, X-ray fluorescence and optical emission spectrometers to assess product quality and fluoride ion specific electrochemistry to ascertain fluoride impact upon environmental samples.

Milk processing at Edendale in Central Southland has a long history beginning in 1881, but it has significantly expanded since 1985 with the spectacular growth in dairying in Southland. Fonterra took over Southland Dairy Cooperative Ltd. in 2001; prior to this, in 1998, the Co-op had merged with Alpine Dairy Products. Fonterra has since increased annual production at Edendale, particularly of milk powder from none in 1985 to 250,000 tonnes in 2010 (estimated value ~ $NZ 2 billion). This is made up of whole and skim milk powder, buttermilk powder and milk protein concentrate powder. Other milk products currently manufactured at the plant include cheese, anhydrous milk fat and mineral casein. Organic chemistry plays a significant part in the production of many milk products, *e.g.* manipulation of pH to separate proteins. Some chemical analyses are undertaken in factory laboratories utilising near infrared technology, as well as titrations for determining product composition and quality. Comprehensive chemical testing of finished products is now carried out at centralised Fonterra laboratories. On-site testing of the potable water supply (for residual chlorine) and pH, and environmental monitoring of the chemical oxygen demand arising from waste water treatment is made.

Superphosphate is one of the most important fertilisers used in NZ due to its cost and nutrient content. Some 160,000–250,000 tonnes per year are manufactured in Southland at the Ballance Agri-Nutrients plant at Awarua (between Invercargill and Bluff). The manufacturing process involves reacting sulfuric acid with phosphate rock, which converts the insoluble unavailable phosphate in the rock into a water-soluble and plant available form. Various additives such as serpentine rock, potash, sulfur and trace elements such as molybdenum, cobalt, copper, selenium and boron can be mixed or blended with superphosphate to make it a versatile fertiliser for NZ farmers. These manufacturing processes involve a large number of chemical reactions that are monitored by laboratory staff on a daily, sometimes-hourly, basis to ensure the super-

phosphate meets Fertmark registered levels. In the early 1990s, the laboratory at Awarua was restructured owing to cost, and staffing was reduced from fourteen to four. Core manufacturing analysis is completed in-house but specialist and sales-related testing is outsourced. Environmental outputs from the plant are subject to Resource Management consents and on-going Regional Council monitoring of discharges. This is additional to monitoring carried out by the on-site laboratory staff.

OceanaGold (NZ) Ltd. has been involved since 1990 in the mining of quartz rock and extraction of gold at Macraes Flat in the East Otago Region. Production has increased from about 75,000 oz of gold in 1990 to 260,000 oz in 2010, grossing $NZ 423 million. The extraction process involves crushing and grinding the ore followed by a flotation process to make a gold concentrate. The concentrate is then subject to pressure oxidation followed by leaching and desorption, then electrowinning to produce gold of about 88-92% purity. The cyanide used during the processing is neutralized prior to the by-product tailings being deposited in the Tailings Dams. The company conducts extensive environmental monitoring that includes chemical analysis of surface and ground water, waste rock geochemistry, and dust and other airborne emission analyses.

Other Otago-Southland industries that use chemical processes in their production include the Dunedin companies: Ravensdown Fertiliser Cooperative Ltd., Cadbury Confectionery Ltd., Cerebos Gregg's Ltd. (manufacturer of coffee, deserts and condiments), and Speight's and a number of smaller boutique breweries scattered around the two provinces.

NZIC Branch Activities

This Branch has its origins in the Otago Chemical Society which was formed in 1929 as a local section of the Institute of Chemistry of Great Britain and Ireland. This society, along with others elsewhere in NZ, was wound up and replaced in 1935 as the component Branches of the New Zealand Institute of Chemistry. The past 25 years has seen the Otago Branch maintain a small but steady membership and meeting schedule. There are relatively few chemists employed in chemistry-related industry in the Dunedin and greater Otago/Southland area, meaning that Branch membership has consisted mainly of academic staff and research students from OU Chemistry with some interest from the Biochemistry, Pharmacy, Pharmacology, Physiology and the Food Science Departments, as well as the Invermay Agriculture Centre in Mosgiel. A notable exception was Stan Winter from the Southland Co-Op Fertiliser Ltd. in Awarua who participated in Branch activities in the 1980s including being Branch Chairman in 1989 and NZIC President in 1991.

NZIC conferences have been organized by the Branch in Dunedin in 1985, 1997 and 2008 and members have made regular contributions in various ways to the NZIC journal. Organized site visits have been to the NZ Aluminium smelter in Bluff, the dairy processing facility at Edendale, the Ravensdown Fertiliser works in Dunedin, as well as to several local breweries and some Southland lignite mines. Over this time, Branch meetings typically have involved talks from academic chemists on the staff or visiting appropriate departments at OU, and national NZIC touring lecturers. In recent years, student participation has been fostered through quiz and poster evenings (supplemented by free alcohol and food!) and the provision of financial support for student attendance at conferences in NZ and overseas.

The Future

The present large-scale chemical processing industries in the area such as the aluminium smelter at Tiwai, gold mining at Macraes, milk processing at Edendale and fertiliser manufacture at Awarua and in Dunedin are likely to continue and even expand their operations in the foreseeable future. There is potential for new large scale chemical industry involved in the conversion of the extensive lignite deposits in Southland into more usable forms of energy such as briquettes and liquid fuel. Similarly, Holcim Cement is currently investigating establishing a large cement manufacturing facility at Weston, inland of Oamaru. There is also potential for more involvement of chemistry in any expansion of the Central Otago wine industry that has come to the fore in the past 25 years, and in any petrochemical industry that might be established should economic amounts of petroleum be discovered from exploration about to be undertaken off shore from Otago. Although a few new OU chemistry graduates and Polytechnic science graduates have been employed by these industries during the review period, if the various developments come to fruition, opportunity will exist for increased contact and/or the involvement of chemists in these industries.

Other future chemical activities in the area will continue to be centred on the chemistry and associated departments of OU. The current areas of research being undertaken by the academic staff of OU promise to lead to significant new knowledge as well as providing excellent training for research students. OU on its various campuses has a long established international reputation for excellence in the both teaching and research, particularly in biological and health disciplines. We envisage that new exciting areas of co-operative chemical research will include smart drug design and delivery, synthesis of new materials, and food science research, and that they will have significant biological and medical as well as chemical importance. The present marine chemistry research group at OU also has a significant international reputation for its research into the oceanic effects of increased atmospheric CO_2 levels and resulting global climate change. It is envisaged that this research will continue to develop in conjunction with the present NIWA Joint Centre of Excellence in Chemical and Physical Oceanography

Chemistry in Otago is in good heart!

Acknowledgement

I acknowledge the help of my long-standing colleagues Jim McQuillan, Brian Robinson and Rob Smith in helping me recollect these past events in the OU Chemistry Department, the contributions of other Departmental staff, and the help of senior management in various chemical-based industries in Otago-Southland.

Chemistry in the Manawatu: Reflecting on the Last 25 Years

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Introduction

The NZIC's Manawatu Branch covers the rich dairy country and natural gas fields of Taranaki in the west, through to the educational and scientific centres of Palmerston North and across to the important wine growing areas of Hawkes Bay and Gisborne in the east.

The character of the active local Branch, based in Palmerston North, has changed over the years. Chemists from the Applied Biochemistry and Grassland Divisions in the old DSIR, the NZDRI and Massey University all regularly attended meetings and in turn, took on the Branch Chairmanship with a chemist from industry taking on the role from time to time. The NZDRI played host to the local Branch meetings for many years. However, more recently and with employment environments changing, the more active members now mainly come from Massey University, although the present long-serving secretary, Justin Bendall is employed by Fonterra; the treasurer, David Shillington by the polytechnic, UCOL; the president, Ghislaine Cousins by NZ Pharmaceuticals Ltd.; and the immediate Past-President, Barry Scott by Shimadzu Scientific Instruments Ltd. The Branch has always supported the national body, *e.g.* Grant Boston (formerly from Fonterra) was the Honorary General Secretary for 7 years, Lawrie Creamer edited *Chemistry in NZ* and Andrew Brodie *ChemEd NZ*. The Branch became the first to hold the NZIC conference outside a university city - Napier, 2001 ably organised by Mike Boland and his hard working team, and well attended and rated.

Taranaki

Natural Gas

Almost all of NZ's natural gas has been found in Taranaki and it provides the feedstock for the ammonia/urea/methanol plants in the region. The first large find, made in 1959 near Kapuni by the Shell BP Todd consortium, led to the first production of natural gas from this field in 1971for distribution around the North Island. In 1969, the consortium drilled NZ's first offshore well, discovering the Maui field some 30 km off the coast of Taranaki; production began in 1979. Natural gas is now one of NZ's primary energy resources and Maui alone supplies about 80% of our total gas requirements. Taranaki's five offshore fields (Tui and Maari: crude oil, Maui, Pohokura and Kupe gas-condensate (light oil) developments) return billions of dollars in foreign exchange or import substitution measures annually.

Methanex NZ Ltd.

The methanol plants at Motunui and Waitara Valley began as part of the *think big* projects of the National government in the late 1970s. The Motunui plant opened in 1986, converting natural gas to methanol and the methanol to synthetic petrol using the Mobil methanol-to-gasoline (MTG) process. Operation of the plant demonstrated the first-of-a-kind application of the zeolite catalyst ZSM-5 but the process became uneconomic in the late 1990s owing to falling oil prices; the plant switched to producing methanol for export. In 1993 the plants became known as *Methanex NZ Ltd*., when the Canadian company, Methanex, acquired them from Fletcher Challenge Ltd. Since 2004, the plants have been operated in a flexible manner to match gas availability and methanol market requirements. For example, in October 2008 Methanex restarted one of its two plants at Motunui and shut down its Waitara Valley one to give a capacity of 950,00 tonnes of methanol p.a. Currently, the company contributes more than $220 million per year to the country's economy.

Fig. 1. The Methanex plant (courtesy Methanex NZ Ltd).

Dow AgroSciences (NZ) Ltd.

A major New Plymouth industrial company is Dow AgroSciences (NZ) Ltd., which began as the agricultural chemicals company, Ivon Watkins Ltd. in 1944. The Dow Chemical Company of Michigan purchased shares in Ivon Watkins over several years completing this in 1988. Ten years later, the company took on its present name when Dow acquired the shares held by Eli Lilly. The plant received bad publicity from its manufacture of the herbicide, 2,4,5-T (2,4,5-trichlorophenoxyacetic acid) because of the dangers associated with the carcinogenic contaminant, *dioxin*; production ceased in 1987. Today Dow AgroSciences (NZ) is a formulation and packaging plant supplying over 70 agricultural products to farmers, horticulturists and forestry customers here and in Australian.

Envirofur

This company, located just outside Stratford, occupies a niche spot in manufacturing possum fur products. Unlike most commercial tanning companies, Envirofur uses only sodium chloride and other non-toxic substances gaining

a Taranaki Regional Council Environmental Award for *creating a fashion product from a pest and increasing awareness of the negative environmental impact of possums*.

Ballance Agri-Nutrients (Kapuni) Ltd.

The Kapuni ammonia/urea manufacturing plant in Taranaki, is a *think big* project from the Muldoon years. Initially run by Petrochem, it was sold to the Bay of Plenty Fertiliser Co-operative (now Ballance Agri-Nutrients) in 1992. Using some 7 petajoules (7 x 10^{15} joules) of natural gas the plant produces ammonia, most of which is converted to over 260,000 tonnes of premium grade granular urea a year – one half NZ's requirement. The urea is used as a nitrogen-rich fertilizer in the agricultural, horticultural and forestry sectors and as a component in the manufacture of other products.

Fonterra Kapuni

The Kapuni plant, first opened in 1947, is home to one of Fonterra's four lactose plants and is the only site with a refinery. It produces refined-grade lactose for Fonterra's ingredients business by extracting whey, a by-product of the cheese manufacture at their Whareroa factory, near Hawera. The Kapuni plant also produces pharmaceutical grade lactose for use in the manufacture of tablets, capsules and vaccines. A small quantity of the site's dry lactose is further processed into inhalation grade lactose used in asthma inhalers. The plant received the Lactose and Derivatives Quality Award from the NZ Institute of Food Science and Technology two years running (2005 and 2006).

Fonterra Whareroa

The Fonterra Whareroa factory near Hawera is one of the world's largest dairy factories and a significant employer in Taranaki. Cellulose resins, invented by John Ayers (a Massey chemist), are used for the recovery of whey protein for human consumption. The international demand for it is high as nutritional supplements in *e.g.* protein-fortified sports drinks, foaming agents (for whipped products) and jelling agents (in yoghurts). The new process is ten times more effective than those previously employed, and is now used in the UK and US.

Wanganui – Manawatu

Tasman Tanning Ltd.

This Company began as a family business in 1953 and now employs over 200 staff in the sourcing, processing and selling a broad range of leathers for upholstery, footwear, accessories, and the aviation and marine industries worldwide. They supply leather for furnishings hides, for Air New Zealand's lie-flat Premium Business Class seats throughout its Boeing 747s and 777s, and for the seats for Jetstar Australia and Asia. The main mineral tanning material is chromium(II) sulfate since it is used in the preparation of shoe upper leathers and clothing leathers, in fact, in all leathers where softness, stretch and suppleness are required. A key step is believed to be the formation of a chromium-collagen complex.

NZP Ltd.

New Zealand Pharmaceuticals Ltd., established in 1971, is located just out of Palmerston North. It was as a joint venture between the meat industry and Tasman Vaccine Laboratories Ltd. to extract products from meat industry waste materials. Since 1985, the core business has remained in the extractives arena primarily around bile acids, which continues to grow both in terms of volume and new products. While cholic acid remains the core, a number of new derivatives have expanded the bile acid offerings. These include compounds such as methyl cholate, sodium taurocholate and glycocholic acid shown in Fig. 2.

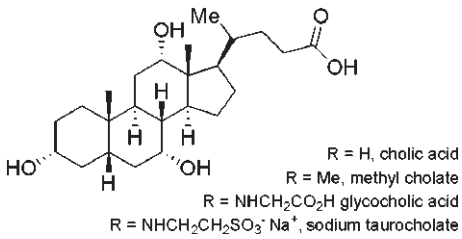

Fig. 2. Cholic acid and derivatives (courtesy NZP).

The bile acid derivatives shown in Fig. 2 are synthesized from NZP's naturally derived cholic acid using newly developed techniques and capabilities. In 2004, NZP was awarded a FRST TechNZ contract to develop a platform technology enabling chemical synthesis. This also allowed NZP to work with David Harding (a Massey chemist) to develop technology in the chemoenzymatic area, and the IRL carbohydrate team to develop conventional small molecule chemical synthesis capability. One project within the *enabling* contract was the synthesis of bile acid derivatives.

There are several new commercial applications for bile acid derivatives which coincided with NZP's expansion into the synthetic arena. Some of these include: vaccine production; excipients (inactive substances that serve as a vehicle or medium for a drug or other active substance) in drug delivery; and as components of *fasted* and *fed* state simulated stomach and intestine fluid which are used in pharmaceutical diagnostics. In this application, studies are undertaken to determine the dissolution abilities of various tablet formulations and drug substances and the *survivability* of drug candidates in a testing biological environment. Despite the growth of cholic acid derivatives, the compound itself continues to surprise with its commercial durability. A new application of cholic acid is NZP's recent use in the treatment of a rare intestinal disease. After many years as a pharmaceutical intermediate, cholic acid is now an Active Pharmaceutical Ingredient (API) and NZP is proud to be the supplier. The application required a Drug Master File (DMF), which has added to the growing NZP *GMP API* DMF portfolio.

Alongside the expanding bile acid range and other animal-derived products like heparin, NZP has also moved into small molecule carbohydrate chemistry using knowledge developed alongside IRLs carbohydrate team. From 1998, NZP began producing pinitol from extraction of plant tissue and in 2003 their first synthetic carbohydrate, N-acetyl-D-mannosamine was added to the product list.

This carbohydrate is an interesting monosaccharide, rare in nature, but is an essential sugar required for the *in vivo* synthesis of sialic acid and many important glycoproteins. It is also a prospective starting material for several antiviral drugs including Zanamivir.

The steady growth in synthetic products gave the opportunity to build a new Good Manufacturing Process (GMP) compliant factory and this was opened in 2007 by the then Prime Minister, Helen Clark (Fig. 3). Growth in the carbohydrate area continued and in 2009 Dextra Laboratories (a UK-based carbohydrate and custom synthesis company with GMP facilities and capabilities) was acquired. It strengthens NZP's global offerings and the UK and NZ and scientists make valuable exchange visits.

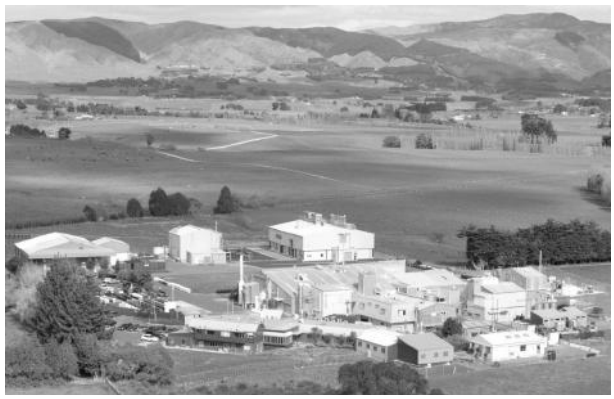

Fig. 3. New Zealand Pharmaceuticals showing (upper right) the Special Products Facility (courtesy NZP).

Glaxo Pharmaceuticals Ltd.

The multinational company, GlaxoSmithKline began in the small Manawatu settlement of Bunnythorpe where dried milk was processed for 70 years. In 1951 a new plant for the manufacture of pharmaceutical products was built in Palmerston North and, in 1994, when opening the new $11 million *dry powder inhalations facility* on the site, the Prime Minister, Jim Bolger said, *Glaxo was a great success story by any standards*, with the company being the second largest pharmaceutical company in the world. However, the plant was closed in 1996 with Glaxo retaining only a marketing division based in Auckland.

Crown Research Institutes

25 years ago, an important employer of chemists and biochemists in Palmerston North on sites adjacent to Massey University, was the DSIR. The scientists worked in various Divisions –Applied Biochemistry (renamed Biotechnology in 1988), Crop Research or Horticulture and Processing. In 1990, when the Divisions were reorganised across the country, DSIR Grasslands and Fruit and Trees came into being, but not long after, in 1992, a major change came to government science with the creations of Crown Research Institutes (CRIs). Most staff was reassigned to one of the new AgResearch, HortResearch or Crop and Food Institutes. A result of the change was that teams who had worked together for many years were split up. A range of DSIR researchers from the mid-1980s will be remembered and some can be found in one of the CRIs today (see below). Others moved to a CRI but have since retired or are employed elsewhere, *e.g.* Mike Boland, John Shaw, Laurie Kennedy, Julian Lee, Graeme Russell, Ces Johnson, Denis Body, Peter Reay and Simon Fielder. The Director of the Biotechnology Division, John Robertson, took redundancy and became a lawyer. In 1994, a new CRI for the area - Landcare Research - was established in purpose-built premises on the Massey Campus with many of its staff relocating there from the DSIR Land Resources headquarters at Taita. The most recent change to the CRIs was in 2008 when Plant & Food Research formed following the merger of HortResearch and Crop & Food Research.

AgResearch

Research in the *Grasslands* section of this CRI focuses on plant breeding and plant molecular biology (particularly functional genomics), ruminant nutrition and land management. Chemists there include Mike Tavendale, Wade Mace and Don Otter, together with semi-retired staff such as Brian Tapper and Geoff Lane. A major effort has been made to take exploratory research discoveries into commercial products. Concurrently, the major advances in molecular biology over this period coupled with improved tools of analytical chemistry have opened up new opportunities for elucidating and manipulating biosynthetic pathways.

The outstanding example of commercialization of discoveries based on chemical research is the introduction to the market of grass cultivars with selected strains of endophytic fungi to enhance the performance of pasture grasses and the livestock grazing them. These were based on 1980s MAFTech Ruakura and DSIR Palmerston North discoveries, when fungi of *Epichloë* and related species growing as endophytes in grasses were found to produce an array of metabolites, both mammalian toxins and the insect feeding deterrent peramine. Subsequent developments led to a grass cultivar providing improved grass and livestock performance.

Fig. 4. Dr. Geoff Lane measuring concentrations of flavour compounds (courtesy AgResearch).

The context for chemical research into biological questions has been transformed by developments in molecular biology, and this has been matched by much improved chemical analytical capabilities. Sensitive and selective LC-MS of fungal endophyte metabolites and biosynthetic intermediates in gene deletion and complementation stud-

ies have played an important part in progress towards elucidating their biosynthesis. Chemical analyses have also been important in the manipulations of proanthocyandin (PA) synthesis. PAs (condensed tannins) in forage plants have been of interest since research in DSIR demonstrated they can confer desirable attributes to ruminant forage diets. However, plants that naturally produce them at appreciable levels in the leaf do not perform well in grazed pasture. The productive forage legume white clover (*Trifolium repens)* biosynthesises PAs in flowers and leaf trichomes, but not in other tissues; they comprise only a very minor component of the diet of livestock grazing white clover-containing pastures. Recently, AgResearch chemists demonstrated by LC-MS analyses that the introduction into white clover of a transcription factor controlling PA synthesis resulted in the formation of PA oligomers at significant levels in leaf tissue.

Advances in genomics, in particular high through-put gene sequencing technology, have also generated opportunities and posed challenges for chemists. AgResearch chemists have undertaken a number of metabolomics studies both independently, and in collaboration with former Plant and Food chemists, applying GC-MS and untargeted LC-MS analyses to discover key metabolites differentiating biological systems under different treatments.

Plant & Food Research

Science at Plant and Food Research on the Palmerston North site covers a range of activities from the development of sustainable production systems and bioprotection technologies to the breeding of elite cultivars. Previously, chemistry in HortResearch focused on flavour volatiles and their biosynthesis especially in apple and kiwifruit using GCMS and deuterium labelled precursors (Daryl Rowan, Adam Matich and Martin Hunt), pigments, phenolics and antioxidants in fruit (Peter Reay and Tony McGhie) and lipid oxidation processes determining food quality (Cecil Johnson, Peter Reay, Daryl Rowan, Simon Fielder). This research was supported by GCMS and HPLC (Martin Hunt) and synthetic chemistry (Simon Fielder and Barry Bunn). Within the constraints of horticultural research, some excellent chemistry has been published including an early paper on the complications of solid phase microextraction for volatile analysis and the first synthesis of the dendralene hydrocarbons. The transition into Plant & Food Research has provided little change in daily activities of the chemists. The benefit of merger is increased interaction with former Crop & Food CRI colleagues and the opportunity to move into new areas of research, *e.g.* selenium metabolism of brassicas and the use of biomarkers as a proxy for health status in trials to validate functional foods. Daryl Rowan, Adam Matich, Tony McGhie, Harry Martin, Rona Lunken and Martin Hunt are now the Phytochemistry Team as part of PFR's Biological Chemistry and Bioactives Group. A recently installed high resolution Time of flight LCMS offers exciting new opportunities for further explorations in plant chemistry.

Landcare Research

Since its establishment on the Massey Palmerston North Campus, Landcare Research has had no more than ten staff engaged in chemical research, often in collaboration with scientists in NZ and overseas. As expected, the research is largely concerned with agricultural, land, and soil issues, *e.g.* interactions of clay and soil minerals with small and polymeric organic molecules, soil organic matter stability and transformation, inorganic soil nanoparticles for pollution control, role of nanoclays in carbon stabilization and enzyme immobilization. The chemistry and biochemistry of carbon, nitrogen and phosphorus in soils under pasture and in waters flowing from farms to rivers is also important. The CRI also houses the accredited Environmental Chemistry Laboratory (NZS/ISO

Fig 5. The pilot plant at Fonterra (courtesy FRC).

17025), which provides analytical services on soil, plant and water samples.

The Fonterra Research Centre

A major employer of chemists in NZ in the 1980s was the dairy industry, in particular the NZ Dairy Research Institute (NZDRI) which employed nearly 300. Until 1988, it even published its own scientific journal *The New Zealand Journal of Dairy Science and Technology*. This journal had a high international recognition and prestige, but the overhead cost of its production proved too high and it was incorporated into the *International Dairy Journal*. With the advent of the Fonterra Co-operative Group in 2001, NZDRI was initially retained within the company, but in 2002 it was renamed the Fonterra Research Centre (FRC) – thus a small piece of history and a national entity of considerable international repute became a subsidiary in a much larger organisation. Mike Boland says: *One of my strongest memories from my time as Section Head of Protein Chemistry at the DRI is that of a young Jeremy Hill, now Director of Innovation for Fonterra, but then a newly recruited scientist, attempting to dissolve material that had cooked onto a plate heat exchanger, in order to try to analyse it. We knew it was protein based – but which proteins? Jeremy's idea was to heat it in the fume hood in concentrated nitric acid. Needless to say, there was quite a loud bang and the sample was never seen again!*

With annual exports in excess of $11 billion, the dairy industry is NZ's biggest export earner. The Fonterra Co-operative Group, which includes the FRC, is the largest company in this country. The FRC is the world's largest dairy research centre with 110 scientists and 130 support staff and has one of the world's largest registered dairy pilot plants. In addition, they have research and development centres in Australia, the Netherlands and the USA.

The culture in the FRC changed when it became a core part of Fonterra's Marketing and Innovation group, with emphasis on a more rapid commercialization of new ideas. Projects were allocated with both staff and capital resources based in accordance with their rankings that were determined by more robust commercial analysis and the likelihood of profitable return. Initially, there was a move away from long-term fundamental research, but its need is now better recognised and to some extent *blue skies* research has started to re-emerge.

Chemists at the FRC span a range of sub-disciplines. There has long been a core of physical chemists (although many are now approaching retirement age), but also analytical chemists, organic chemists, chromatographers, functional chemists, spectroscopists, and even the occasional inorganic chemist. An ability to adapt and grow skills into new areas of expertise is almost an unwritten job requirement, and this can take chemists quite far from their original discipline. In addition to the research chemists, the Analytical Services Group (ASG) contains skilled analytical chemists. Dairy products are a challenging matrix to analyze, and the ASG is tasked with making the non-routine become routine, so that test methodology can fit dairy products. This requires a comprehensive understanding of dairy products' composition, thinking about how the techniques work, possible interferants, and the nature of the answer being sought and whether the techniques applied are appropriate to the question.

Leather and Shoe Research Association (LASRA) of NZ

Leather chemistry encompasses almost all aspects of applied chemistry in a single discipline since leather results from the chemical alteration of natural skins and hides to give a stable material suitable for a wide range of applications from shoes to clothing and furniture. LASRA is situated close to the CRIs and Fonterra, but has been actively involved in supporting the leather and footwear industries since 1928. Their laboratories produce research and technical services specializing in developing practical opportunities for companies and making sense of analytical and testing work for clients. Advances in chemistry are reducing chemical wastage, especially in the challenging early stages of processing, and developing new properties in leather, such as thermal heat resistance, water resistance, chemical resistance and improved comfort and health properties. LASRA is actively engaged in an Innovation funded three- year research project in these areas, specifically using nano- and micro-sized particles to provide leather with gain-shift improvements in all these properties.

The Education Sector

Chemistry has been an important part of the educational scene in Palmerston North for many years with the secondary schools, the polytechnic, UCOL (Universal College of Learning) and Massey University all contributing.

Secondary Schools: The Manawatu secondary schools have long benefitted from the support of the NZIC Manawatu Branch and the university chemistry academics. For many years the Manawatu Branch ran a quiz with a range of questions to challenge school students. The small entry fee charged was deposited in a trust run by the Branch that still grants funds to schools in the region. Since the days when Geoff Malcolm was Head of Chemistry, there have been well-supported evenings for chemistry teachers from throughout the Branch region. Eric Ainscough was legendary for his Chemical Magic shows, needing a water trough to cool the singes on his arm on one occasion following a demonstration of the oxidation of sucrose by potassium chlorate. Andrew Brodie continued the support and it was Tony Wright in his time at Massey who added to the evenings with a series of fascinating demonstrations. More recently, chemistry tutor, Adrian Jull's organisation of the Year-12 Chemistry Field Trips to the university have specifically focussed on topics in the school curriculum. These have succeeded in giving students from Taranaki to Hawkes Bay (and places in between) a chance to experience a modern chemistry laboratory but the numbers of schools involved has had to be limited. In January 2009 an inaugural NanoCamp, supported by the MacDiarmid Institute, was held on the Massey campus. School students spent a week delving into nanoscience carrying out hands-on investigations into topics ranging from solar cells to AFM and carbon nanotubes. One of the organisers, chemistry lecturer

Shane Telfer, said the camp aimed to stimulate students' interest in science: *We're hoping to spark an interest and they end up doing science or engineering at university. It doesn't matter which science, as long as they're enthused*.

Alan Furness, a long time NZIC member and Branch Chairman, made an impact on many secondary school students. Having attended Freyberg High, he completed a PhD in chemistry at Massey and then taught for some years at Palmerston North Boys' High before moving on to UCOL. His charismatic style and enthusiasm was missed by many after leukaemia sadly cut his career short, but his name is remembered with the establishment of the *UCOL Excellence and Innovation in Teaching Award*.

UCOL: The polytechnic's history spans more than 35 years, producing many of NZ's finest technically trained scientific laboratory staff. Its name changed from the Manawatu Polytechnic in 1998, two years after the government provided a $22 million capital injection to rebuild and consolidate the campus on one central Palmerston North city site. Since 1997, David Shillington (Head, School of Applied Sciences) has been responsible for the teaching of chemistry at UCOL. During the 1970s and 1980s, employees were given time off work to complete their studies in the New Zealand Certificate in Science (NZCS) as part-time students, but in the early 1990s the NZCS was extended to full-time students. In 1997, National Diplomas in Science (NDS levels 5 & 6 registered on the NZ Qualifications Framework) replaced the NZCS and graduates had to master fundamental laboratory skills and unit operations to within commercially acceptable time frames and standards. A new standard, including industry placements for students, has been introduced as part of the programme.

Massey University: Chemistry has always played an important part at Massey. Over 80 years ago, a lecturer in soil chemistry and an assistant lecturer in chemistry were appointed to the staff of the Massey Agricultural College and all students had to enrol in the second year paper, *Advanced Chemistry,* as a requirement for the BAgrSc degree. The Department of Chemistry and Biochemistry was formed 1963 with third year chemistry papers for the BSc being introduced in 1967, thus allowing students to then graduate with a full chemistry major. By the 1980s, after a period of rapid expansion, the chemistry group was well established under the leadership of the Professor Geoff Malcolm (Physical Chemistry). Right from the early days, the Head and Professor of Biochemistry, Dick Batt, expected all academic staff to be actively involved in research especially that of a biological orientation. One of the advantages of being in a combined chemistry-biochemistry department was the relative ease for chemists to get involved in biochemical research, and biochemists such as Graeme Midwinter were especially generous in sharing their knowledge. Protein crystallography at Massey went from strength to strength, being built on the work of Ted Baker who had determined the structure of the enzyme actinidin from Kiwi fruit – the first protein structure to be determined in the Southern Hemisphere. In 1983 when Auckland chemist, Neil Waters, was appointed Vice-Chancellor of Massey University, his wife Joyce Waters joined the crystallography group. Paul Buckley, Len Blackwell and Trevor Kitson were working in the field of enzyme kinetics, Bill Hancock was interested in peptide synthesis and inorganic chemists, Eric Ainscough and Andrew Brodie, with the encouragement of Sylvia Rumball, carried out studies on the metal binding properties of lactoferrin, a protein found in human milk. Subsequently, through the 1980s lactoferrin, from both human and bovine sources, became a major focus of Ted Baker's protein crystallography group, culminating in the publication of detailed structural studies on these important biological molecules. John Ayers' interest in applied chemistry led to the successful development and commercialisation of cellulose resins with the generation of over $2.5 million in royalties. The most successful outcome of his work has been the use of his cellulose resins for the recovery of whey protein *e.g.* at Fonterra Whareroa (see above). The biological orientation of analytical chemists, Robert Brooks and Roger Reeves focused on metal uptake by plants – sometimes called biogeochemistry. Physical chemist, Gavin Hedwig researched the physical properties of peptides.

The late 1980s and early 1990s saw a number of staff changes as people started to retire or move on to other positions, but fortunately replacements were always approved. Bill Hancock left for Genetech in the US and David Harding and David Officer (now at Wollongong) were appointed as lecturers in organic chemistry; Margaret Brimble was initially appointed to replace Len Blackwell while he was on leave without pay but after five years she moved to Auckland University. Ian Watson departed to become the foundation principal of Massey's Albany campus and Sylvia Rumball was promoted to Dean of Science. Over the next decade a number of new appointments were made but many of these talented young chemists were headhunted by NZ or overseas universities as the push for improved research ratings increased. Canterbury graduate, Geoff Jameson returned to NZ in 1994 to become more involved in structural biology and Auckland graduate, Simon Hall (who was the Department's third attempt to replace Robert Brooks – the first appointee stayed four hours!) came in 1997 to take responsibility for analytical chemistry; Pat Edwards, who started as a post-doctoral fellow with Ken Jolley, is now the NMR laboratory manager. Staff appointed since 2000 have opened up new research areas – inorganic chemists Shane Telfer and Paul Plieger, organic chemists Vyacheslav Filichev and Gareth Rowlands, spectroscopists Mark Waterland and XianZhen Zhao (shared with physics) and tutors Adrian Jull and Karen Lyons (part time). Ashton Partridge, also appointed in this period, has moved on. Three technical staff deserve special mention – Vern Sixtus (now retired), Andy Trow and Graham Freeman – for their dedication to chemistry over many years.

Dick Batt retired in 1988 after 24 years heading the Department of Chemistry and Biochemistry and it took some time to find a permanent replacement. The University advertised the post as Head of Department and Professor of Biochemistry and, after advertising twice, failed to make an appointment; the academic staff, unused to the

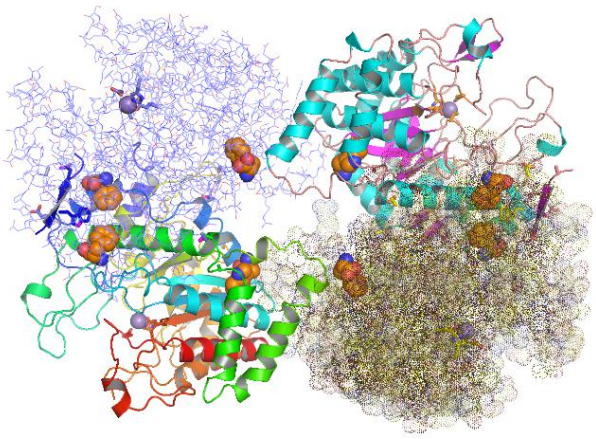

Fig 6. 3-Deoxy-D-arabinoheptulosonate-7-phosphate synthase from Mycobacterium tuberculosis showing active site with metal centre and synergistic feedback inhibitors, phenylalanine and tryptophan (courtesy Prof. Geoff Jameson).

democratic decision process, found it difficult to reach a consensus view on the candidates. Eventually, a chair in chemistry was advertised to be combined with headship and Andrew Brodie was appointed.

Over the next few years, a number of other changes occurred in the life of the Department. Physical chemist John Harrison moved north, in 1995, from his temporary position to start teaching first year chemistry at the Albany campus. Initially with no laboratories, he ran evening classes at the nearby Kristin School. Recently, the University has offered the BFoodTech(Hons) degree in collaboration with Singapore Polytechnic, which has meant an annual intensive period teaching a chemistry paper in Singapore by Geoff Jameson and David Harding.

In 1996, the Department was split and Chemistry became a separate entity but it did not survive as the new Vice-Chancellor, James McWha, who arrived that year, decided faculties had to be merged into much larger colleges under Pro-Vice-Chancellors. Small departments had to go and so, in 1998, Chemistry was incorporated in an Institute of Fundamental Sciences along with physics and mathematics (joined by statistics several years later). Since none of the existing departmental heads were keen on heading the new budget centre, biophysicist David Parry bravely took on the job. The Centre for Structural Biology, led by Geoff Jameson, spans this Institute and the neighbouring Molecular BioSciences, thus helping to maintain chemistry's important links with biochemistry (Fig. 6). In 2007, mass spectrometrist Peter Derrick arrived as Head of the Institute. This year, the separate disciplines within the Institute have been reorganised and chemistry with biophysics now form a multidisciplinary group.

Hawkes Bay - Gisborne

Ravensdown Fertiliser Co-operative Ltd.

This Company was formed after a series of takeovers during 1977-78 of the five fertiliser works formerly owned by Kempthorne Prosser and Co Ltd. and the Dominion Fertiliser Company. In 1987, Ravensdown merged with East Coast Fertiliser Co., a co-operative that owned and operated a single works at Awatoto, Napier, and in 1997 the New Plymouth operation of Farmers Fertiliser was purchased by Ravensdown. At the Awatoto plant, superphosphate is manufactured by reacting finely ground rock phosphate with sulfuric acid (made at the plant) to convert the insoluble mineral phosphate into a soluble form available to plants. The resultant product contains 9.1% total phosphorus, 10.8% sulfur (present in the sulfate form), and 20% calcium. As phosphate rock contains traces of other elements, these are also found in the final product. They include beneficial elements such as magnesium, iron, copper, zinc and manganese. The Ravensdown co-operative is now the largest NZ supplier of fertiliser, directly supplying more than half of that used in agriculture. Less than a decade ago they were mainly a solid NPKS fertiliser supplier but today they offer a comprehensive range of services and products from soil testing to agrochemicals.

The Wine Industry

Finally, chemistry over the last 25 years in the Manawatu Branch region would not be complete without the inclusion of the famed Hawkes Bay/Gisborne region wine industry. The Hawkes Bay is home to over 70 wineries and Gisborne around 40. The analytical laboratory is involved throughout the wine making process, particularly at the harvesting, fermentation and purification steps, which all need to be monitored closely. Winemakers require knowledge of chemistry and some, such as Dr. Alan Limmer, original owner and winemaker of Stonecroft Wines, are fully trained chemists; Alan was elected to Fellowship of the NZIC in 2005. After a series of *undrinkable fermentation experiments* at school and graduating with a PhD in Earth Sciences and Chemistry, Alan found himself in Hawkes Bay managing an analytical chemistry facility with links to the fledgling wine industry. Eventually, he founded Stonecroft and he continues to be actively involved in the vineyard and winery as a consultant.

Concluding Comments

This overview has provided a selection of chemically based activities important to NZ's economy within the Institute's Manawatu Branch. The activities are varied and reflect the natural and human resources of the region. If one word could be used to describe the last 25 years for us, it would be *change* – especially in management structures of most organisations rather than in job profiles. Takeovers have resulted in larger companies, sometimes with international ownership. It is certain change will continue as only recently Science and Innovation Minister, Wayne Mapp, announced that he was considering another restructure of the CRIs!

Acknowledgements

My thanks to a number of people who supplied information for this article: Dr Geoff Lane (AgResearch), Dr Benny Theng (Landcare Research), Carol Walkley, Dr Shane Telfer, Associate Professors Eric Ainscough and David Harding (Massey University), Dr Daryl Rowan (Plant & Food Research), Dr David Shillington (UCOL), Dr Justin Bendall (Fonterra Research Centre), Laurie Sands (Envirofur), Dr Ghislaine Cousins (New Zealand Pharmaceuticals Ltd), Dr Mike Boland (Consultant, formerly Fonterra), Dr Gregor Yeates (formerly Landcare Research), Andrew Syme (Dow AgroSciences) and Dr Warren Bryson (LASRA). Information on companies has come mainly come from their web sites.

The NZIC Conference 2011: Hamilton

Preparations for the NZIC Conference to be held from 27th November to 1st December this year on the University of Waikato campus are well in hand. The Waikato University organising committee comprises Michèle Prinsep (Convener), Michael Mucalo (Treasurer), Wendy Jackson (Secretary), Bill Henderson, Colin Milne, Brian Nicholson, Jo Lane, Graham Saunders and Annie Barker and they *look forward to welcoming many members of NZIC and affiliated societies to Hamilton in this International Year of Chemistry. The committee is* pleased to announce the following Plenary Speakers:

Professor Omar Yaghi (UCLA)

After receiving his BS degree from the State University of New York at Albany and his PhD from the University of Illinois-Urbana (1990) with Prof. Walter Klemperer, he was an NSF Postdoctoral Fellow at Harvard University (1990-92) with Prof. Richard Holm. He is currently the Jean Stone Chair Professor in Physical Sciences and Professor of Chemistry and Biochemistry at UCLA. Omar Yaghi's early accomplishments in the design and synthesis of new materials were honoured by the Solid State Chemistry Award of the ACS and Exxon Co. (1998) and the Sacconi Medal of the Italian Chemical Society (1999). He is the recipient of the ACS Chemistry of Materials Award (2009). Professor Yaghi's research interests all revolve around *reticular chemistry* - the linking of a wide range of molecular building blocks (including organic molecules, inorganic clusters, dendrimers, peptides and proteins) into extended structures held together by strong bonds.

Professor Duncan Bruce (University of York)

After graduating from the University of Liverpool with his PhD in 1981 under the supervision of David Cole-Hamilton, he took up a temporary lectureship in Inorganic Chemistry at the University of Sheffield. In 1986 he was awarded a Royal Society (London) Warren Research Fellowship, which he held at Sheffield until 1991, was appointed as a lecturer and became co-director of the Sheffield Centre for Molecular Materials. In 1995, he was appointed Professor of Inorganic Chemistry at the University of Exeter. Following the closure of chemistry at Exeter in 2005, Duncan Bruce took up his present position of Professor of Materials Chemistry at the University of York. He has a range of research interests, all of which involve liquid crystals.

Professor Neil Ward (University of Surrey)

Neil Ward has research interests centred on environmental, food and biomedical analysis, with a special focus on the development of instrumental methods for analysing samples for total multi-element and metal speciation, using inductively coupled plasma-mass spectrometry. He has studied the involvement of trace and ultra-trace elements in human fluids and tissues in relation to many human disorders for more than 30 years.

Professor Michael Bowers (UC-Santa Barbara)

After receiving his BS degree in Chemistry from Gonzaga University and PhD in Physical Chemistry from the University of Illinois (Champaign/Urbana) under W. H. Flygare, he spent two years in the army as a 1st Lt. trained as an armour officer primarily detailed to the Jet Propulsion Laboratory. Professor Bowers' research involves determination of the structure, reaction dynamics and mechanism of exotic species in the gas phase *via* state-of-the-art ion beam technologies and methodologies.

Professor Bill Fenical (Scripps Institute, UC-San Diego)

Bill Fenical received his BS degree in biochemistry from California State Polytechnic University in 1964. His noted career has been recognised with a number of honours including the Paul Scheuer Award in Marine Natural Products Chemistry (1996), the Silver Medal Award from the International Society of Chemical Ecology (1997), the Lifetime Achievement Award and designation as ASP Fellow from the American Society of Pharmacognosy (2006), and the Ernest Guenther Award in the Chemistry of Natural Products from the ACS (2006). His research focuses on the discovery of medicinally valuable compounds derived from marine microorganisms.

Invited Lecturers and Conference Structure

Outside of the plenary lectures, the conference will break into a minimum of five independent streams. These will have academic and industrial speakers from NZ, Australia, and further afield presenting their work at the conference and include the following:

Analytical and Environmental Chemistry

Profs ***Peter Derrick*** (Massey), ***Alison Downard*** (Canterbury), ***Keith Gordon*** (Otago), ***Ian Shaw*** (Canterbury), and ***David Williams*** (Auckland), Drs ***Craig Depree*** (NIWA), ***Sally Gaw*** (Canterbury), ***Roger Hill*** (RJ Hills Laboratories Ltd.), ***Pat Holland*** (Cawthron Institute), ***Kim Hageman*** (Otago), ***Travis Horton*** (Canterbury), ***Gordon Miskelly*** (Auckland), ***Grant Northcott*** (Plant & Food Research), ***Chris Oze*** (Canterbury), ***Masayuki Satake*** (Tokyo) and ***Peter Swedlund*** (Auckland).

Industrial and Materials Chemistry

Profs ***Ralph Cooney*** (Auckland), ***Simon Hall*** (Massey), and ***Kenneth McKenzie*** (Victoria), Drs ***Skelte Anema*** (Fonterra), ***Ian Brown*** (IRL) ***Robert Franich*** (SCION), ***Joe Gamman*** (Mighty River Power), ***Stefan Hill*** (SCION), ***Harvey Indyk*** (Fonterra), ***Max Kennedy*** (Ministry of Science and Innovation), ***Peter Maxwell*** (Innovation Park Waikato), and ***Terry Smith*** (Ballance), and Messrs. ***David Addison*** (Thermal Chemistry Limited) and ***Kevin Palfreyman*** (Fonterra).

Inorganic and Organometallic Chemistry

Profs ***Tony Hill*** (ANU) and ***John Spencer*** (Victoria), Drs ***Phil Andrews*** (University of Sydney), ***Peter Boyd*** (Auckland), ***Marcus Cole*** (New South Wales), ***James Crowley*** (Otago), ***Tim Kemmitt*** (IRL), ***Lou Rendina*** (University of Sydney), ***Shane Telfer*** (Massey) and ***James Wright*** (Auckland).

Organic Chemistry

Prof ***Bill Denny*** (Auckland Cancer Centre) and Drs ***David Barker*** (Auckland), ***Brent Copp*** (Auckland), ***Rob Keyzers*** (Victoria), ***Dave Larsen*** (Otago), ***Joanne Harvey*** (Victoria), ***Gareth Rowlands*** (Massey) and ***Moana Tercel*** (Auckland Cancer Centre).

Physical and Theoretical Chemistry

Profs ***Julian Gale*** (Curtin), ***Henrik Kjaergaard*** (Copenhagen), ***Kathryn McGrath*** (Victoria) and ***Douglas Russell*** (Auckland), and Drs ***Deborah Crittenden*** (Canterbury), ***Justin Hodgkiss*** (Victoria), ***David Huang*** (Adelaide), ***Matthias Lein*** (Victoria), ***Shih-Chun Lo*** (Queensland), ***Carla Meledandri*** (Otago), ***Jóhannes Reynisson*** (Auckland), ***Cather Simpson*** (Auckland), ***Christopher Thompson*** (Monash) and ***Bayden Wood*** (Monash).

General Matters

Bed and breakfast accommodation is available on site for $70 per night. Social events include a welcome function on the Sunday evening and a fun chemistry-themed quiz on the Tuesday evening. The afternoon of Wednesday Nov 30 will be set aside for delegates to take one of the arranged excursions or to explore Hamilton and its surrounds independently. The conference dinner is to be held that evening in the beautiful setting of the WEL Academy of Performing Arts on campus.

For further details see: ***www.nzic2011.co.nz*** or contact any member of the organizing committee.

Patent Proze: From the bench to the boardroom

Tim Stirrup and Katherine Hebditch

Baldwins Intellectual Property, PO Box 5999, Wellesley St, Auckland

The idea of using your organisation's Intellectual Property (IP) as a means to achieve commercial success is often bandied around with little or no explanation about exactly how this can be done. We provide below a brief outline of an IP strategy that can lead you from the bench to the boardroom.

Understanding your current and potential IP assets

The first step in developing a successful IP strategy is finding out exactly what IP you currently have by conducting an IP audit. This systematic review of the IP assets owned, used or acquired by an organisation should include all staff and should provide an element of education in what constitutes existing and potential IP.

Existing IP assets can include patents, trademarks, registered designs, plant variety rights, trade secrets or copyright owned by the organisation, and any IP licensed to or from third parties. Less obvious IP assets include work manuals, databases, methods, publications and product/process know-how.

The IP assets of most relevance to chemists will often be patents that protect inventions. Patents can provide protection for new compounds, compositions, apparatus, methods of production, methods of treatment of diseases, isolated or recombinant nucleic acids/proteins or non-naturally occurring microorganisms and other subject matter. However, an effective IP strategy will also assess and consider using other forms of IP such as registered designs, trade secrets, copyright and trade marks.

Once the IP assets have been identified, the ownership of those assets should be assessed. There will often be IP clauses in funding, collaboration, consultancy or employment contracts that determine who owns any IP developed and attaches conditions to the use of that IP. If it is unclear which party owns a particular asset this should be cleared up as soon as possible to avoid lengthy and costly disputes down the line. As a general rule of thumb, if IP is generated by an employee in the normal course of their employment, then the IP will belong to the employer. This is especially true if the employee is employed as a researcher/innovator whose role is primarily to generate knowledge and IP.

The next step is to determine the extent of use of the asset and to evaluate the importance and value of the IP assets identified. Most organisations are able to evaluate the relative importance of the asset in comparison to other assets held by the organisation. This relative evaluation is likely to take into account factors such as how closely the asset is aligned with the organisation's core goals, the expected longevity of the IP asset, *i.e.* is the patent/trade mark about to expire? and how exclusive/unique the asset is, *i.e.* is it a minor improvement to standard laboratory practice or a ground-breaking new technology?

Dollar valuation of IP assets is an extremely tricky proposition owing to the array of factors that can affect the value, such as market demand, competitor activity, rate of technological change, logistical capability, *etc*. A good place to start is to ask how much it would cost to replace the IP asset if it were lost or how much income the asset is expected to generate in the next few years.

The value of some IP assets relies on external factors over which the organisation may have little or no control. An IP audit should identify where and how these factors could present risks to the organisation's IP position and the value of its assets. For example there may be a risk if the main IP asset of an organisation is a person or team with knowledge of techniques or processes. If the person/team leaves, the IP position/value may be compromised. Similarly, there is a risk if the IP assets of the organisation rely entirely on the provision of a licence by a third party or rely on a single supplier for an essential product. If the licence is not renewed or the supplier ceases trading, it could have a catastrophic effect on the organisation.

Using your IP assets

Once an IP audit has been completed, you should consider how these IP assets align to your organisation's goals and therefore how they can best be used. Businesses generally want to see a financial return for their investment, but increasingly this can also be said for universities, Crown Research Institutes (CRIs) and many university-based institutes. As this transition to a more commercially focused academic sector continues, recognising and understanding IP is becoming a more important part of a researcher's intellectual arsenal.

The commercial use of IP assets can be broadly broken down into three categories – direct use of the IP, licensing and sale. For example, an organisation discovers a new polymer and a method of producing the polymer and obtains patent protection. Direct use of the product would involve the organisation producing and selling the polymer to customers in New Zealand and other countries in which the patent has been granted. Patent rights are territorial therefore the patent is only valid where applications have been made and patents granted. This means that the organisation could not prevent other parties from making and selling the polymer in countries where a patent has not been granted.

Licensing of IP assets can provide revenue to the licensor where manufacture or sale of the product by the licensor alone would have been difficult or expensive. It can also enable smaller players to expand into new markets that would otherwise not have been logistically or economically feasible. Universities have traditionally seen the patent right as an endpoint in itself. The core business will be to licence to sell the patent right.

Licensing can also be used in more complex arrangements to suit the business purpose and marry different parties' capabilities and expertise. Among these arrangements are cross-licensing (you license technology X to me and I license technology Y to you) and strategic alliances (I license technology X to you and you market/produce technology X for me). Licensing of IP assets is a common outcome with New Zealand based organisations because of the logistical and financial hurdles encountered with commercialising technology in major overseas markets.

Sale of the IP asset is a good way to quickly raise funds and profit from an unused or under-used resource. In contrast, royalties from licensing can take time to accrue and are dependent on the competency of the licensee in utilising the asset.

Freedom to operate

Even if the generation of IP assets for commercial gain is not the goal, an understanding of IP is advantageous so that steps can be taken to avoid infringing the IP of other parties. This is generally termed *freedom to operate* (FTO) and requires an awareness of the rights of other parties and ensuring that your activities do not infringe those rights.

If you do not want to patent an invention it can be advantageous to publish your work. Since a patent is only granted for novel inventions, the invention cannot have been previously published or be otherwise known. Therefore *defensive publication* of your research can block other parties from being granted a valid patent which could block your research.

Using IP analysis to direct your organisation

An understanding of how your organisation's IP assets fit into the IP landscape can guide your future research direction and help understand risks and opportunities for commercialising technologies. A patent landscape analysis identifies patent rights that already exist around a specific concept. The scope and density of patents around particular technologies or disciplines is analysed and compared to an organisation's IP assets and capabilities. Areas of technology or particular disciplines that have sparse IP *vegetation* are identified as opportunities for development. Such an analysis also helps to determine obstacles that may hinder an organisation's commercialisation goals or freedom to operate.

A sustainable IP strategy for tomorrow's world

An integral part of a successful and sustainable IP strategy is the continual re-assessment of IP assets and the promotion of a culture that fosters and rewards the awareness and creation of IP. Promotion of these factors enables organisations to recognise, assess and potentially capitalise on commercial opportunities in a timely and efficient way.

If you have any queries regarding intellectual property related matters (including patents, trademarks, copyright or licensing), please contact:

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Chemistry in the News

Molecules Impacting on New Zealand Society… Vote for your favourite.

As part of the International Year of Chemistry celebrations in New Zealand, the NZIC Manawatu Branch launched its Molecular Anthology competition. The aim is to find the molecule or material that has most changed New Zealand society.

Submissions were displayed on their website which closed on 10 June. A short-list of molecules was compiled by a committee and voting will take place (deadline 31 July 2011) on the website to rank the top ten molecules or materials. Results will be announced at the NZIC conference in December of this year. Molecules already submitted include caffeine, cholestorol, cyanide, insulin, ethanol, polypropylene, vitamin B-12 and water.

Have your say by casting your vote: *http://molecularanthology.massey.ac.nz/*

New Zealand Students Shortlisted for Google Science Fair

Two New Zealand students, Jun Bing and Alec Wang from Albany Senior High School, had their project *A working model of a device capable of filtering out carbon dioxide from car exhausts* shortlisted as semi-finalists in the Google Science fair. Google launched the Science Fair this year in partnership with CERN, the LEGO Group, National Geographic and Scientific American. Students world-wide between the ages of 13 and 18 are eligible to enter this competition and compete for prizes including once-in-a-lifetime experiences, internships and scholarships.

The students worked on this project as part of their Gold CREST award, a New Zealand science and technology scheme run by the Royal Society of New Zealand. Voting closed on 20 May and the winners were announced shortly after. The total number of entries reached 7,500 from 10,000 budding scientists from over 90 different countries. Ju and Alec were among the top 60 semi-finalists. Their project summary can be seen on the website at: *www.google.com/events/sciencefair/projects/working_model_of_a_device_capable_of_filtering_out_carbon_dioxide_from_car_exhausts.html*

PeriodicTable Welcomes Elements 114 and 116

Two new elements with the atomic numbers 114 and 116 have been added to the Periodic Table following a three-year review process involving a joint working party between the International Union of Pure and Applied Chemistry (IUPAC) and the International Union of Pure and Applied Physics (IUPAP). The working party examined all the evidence and published a paper in the *Journal of Pure and Applied Chemistry http://iupac.org/publications/pac/asap/PAC-REP-10-05-01/*

The elements were discovered following atom-smasher experiments called cross bombardments. Calcium was smashed together with the heavy element plutonium to create 114 and with curium to create 116. The collaborative research work was jointly performed between Russian researchers at the Joint Institute for Nuclear Research in Dubna and American researchers from the Laurence Livermore Laboratory in California. These researchers published their preliminary evidence for these elements in 2004.

Over the past 250 years, there have been basically 100 new elements discovered, said Paul Karol, a chemistry professor at Carnegie Mellon University and chair of the committee that recommended the additions. *But it is becoming more and more difficult to do this so when a new element is discovered, it's actually pretty exciting.*

The elements will eventually be named and given chemical symbols. Before this discovery, Copernicium (Cn), recognised in 2009, was the newest element in the periodic table.

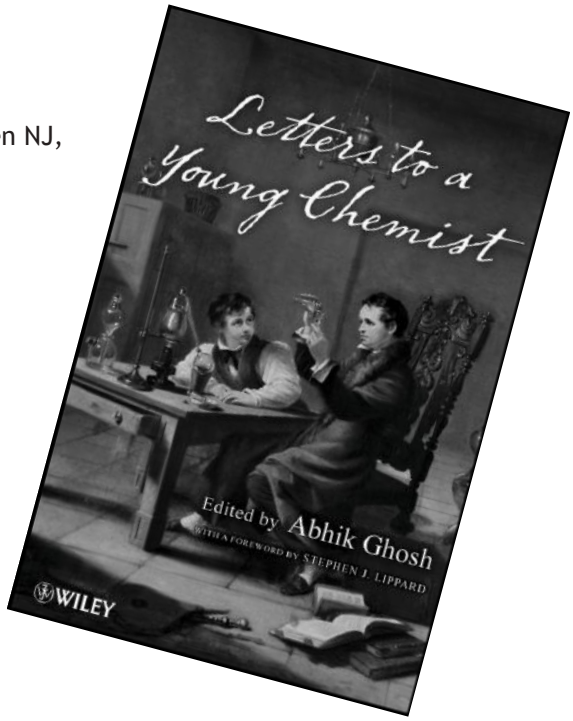
You can see Prof. Martyn Poliakoff of Nottingham University talk about the new discovery on You Tube: *www.youtube.com/watch?v=24-pj9uG_8g*

Book Review

Letters to a Young Chemist

Edited by Abhik Ghosh: John Wiley & Son Inc., Hoboken NJ, 2011, pp. 298. ISBN 98-0-470-39043-6 (paper).

$US 39.95, NZ 57.99.



There have been a good number of books written as *Letters to a Young ...,* the earliest of which I am aware being the 1803, 3rd edition of the Rev. John Bennett's *Letters to a Young Lady* 'to improve the heart, to form the manners and to enlighten the understanding'. Since then the noted book … *to a young poet* appeared in 1902 with the genre expanding rapidly in the past fifteen years from the appearance of Letters to a Young Doctor (1997), … Lawyer (2005), … Mathematician (2006), … Teacher (2007), and ... Architect (2009). The appearance of this book … *to a Young Chemist* in 2011, the International Year of Chemistry, is more than appropriate. IYC looks back at *the achievements of chemistry and its contribution to the wellbeing of humankind* while the book with its seventeen letters looks forward to what we can expect in the future. It is a book that every undergraduate student of chemistry should cherish; every teacher of the subject at the high school level should read (and ensure that there is a copy in the school library!); and every academic should own. It describes the excitement of the forefronts of our discipline in simple terms so that the fictitious Angela can make a sensible choice for her future career in science, ideally in chemistry.

The range of books on popular science has, until now, had little on chemistry. This title deserves to be held by every public library as the interested layperson will quickly come to see just why it is that our discipline is so exciting and vibrant, and what it is that makes it so essential for the future of humankind. How better could one start to explain nanotechnology than by beginning with *The Cat in the Hat Comes Back* (as does Michael Sailor), or recalling Angela's appendectomy as a child to unravel the intricacies of anaesthesiology (as do the Sessler brothers)?

Abhik Ghosh has drawn a good gender mix of seventeen academic research chemists at various stages in their careers, and asked them to write a letter to the fictitious student, Angela, who is just entering second year studies at the University of California–San Diego (UCSD). Angela has taken first-year chemistry courses and is recently returned from the summer working as an undergraduate student in Ghosh's lab in Tromsø (Norway). Each author writes to Angela, some adopting a fictitious persona (Carl Wamser becomes *Uncle Carl*, Elizabeth Nolan a presumed cousin, Cynthia Burrows someone well known), describing their research area, what it is that fascinates them with it, where it is heading and why it is of significance, all with a view to encourage Angela into chemistry research. The editor has chosen four fundamentally important areas of Chemistry, providing five letters covering concepts *From Fundamentals to Applications*, six on *Chemistry and the Life Sciences*, three letters on *Fundamental Materials*, and three on *Chemistry and Energy*.

The book is aimed at a general audience and, although it carries a number of chemical diagrams, formulae, figures and equations, none are essential to gaining a good understanding of the topic under discussion.

With such a wide range of authors, it is inevitable that the style, the assumed background and the level of coverage varies, but this is not such a bad thing as each letter has its own way of drawing the reader into its subject matter and offering advice [Marye Anne Fox: *choose your mentor (and your spouse) carefully*]. Again, there is some overlap between the chapters and inevitable with the all encompassing absorption of UV light and fluorescence as it appears in *Let's Get Physical* (Marye Anne Fox), *Let's Visualize Biology: Chemistry and Cellular Imaging* (Elizabeth M. Nolan), *Bioinorganic Chemistry: Show Your Mettle by Meddling with Metals* (Kara L. Bren), *The Advantage of Being Small: Nanotechnology* (Michael J. Sailor), *Happy Campers: Chemist's Solutions to Energy Problems* (Penelope J. Brothers), and *Clean Electrons will Save the World* (Carl C. Wamser). The most notable overlap occurs in the section on Energy and Chemistry as each of the three authors discusses hydrogen storage, though under different guises. Overall, the overlaps are incidental as the explanations in one chapter enhance the descriptions in another.

The book is well presented and contains relatively few typographical errors. However, the decision not to use colour has diminished the impact (and clarity) of many of the figures (dominantly in the biological area) and that of the nanoflask (Fig. 12.4: Supramolecules to the Rescue - Cohen) has the guest molecule appear behind and not inside its host. Hopefully these issues can be addressed for future editions, which I presume to be guaranteed and look forward to.

Brian Halton
Emeritus Professor
Victoria University of Wellington

Dates of Note

Sir *William* ***Ramsay*** died 195 years ago on July 23. He is the Scottish chemist who discovered the inert gases, neon, krypton and xenon, and co-discovered argon, radon, calcium and barium. He was the 1904 Chemistry Nobel laureate in recognition of his services in the discovery of the inert gaseous elements in air, and his determination of their place in the periodic system. *Stephanie* ***Kwolek***, the American chemist who invented Kevlar, has her 88th birthday on July 31, the day that *Friedrich* ***Wöhler*** was born in 1800. He is best known for the synthesis of urea from ammonium cyanate (1828), but he found a method (1827) for the production of metallic aluminium in the form of a grey powder (by heating $AlCl_3$ with K) and he succeeded in the isolation of beryllium (as a black-grey powder), as well as of yttrium and crystalline silicon. In 1862, he produced acetylene from calcium carbide.

Richard ***Kuhn***, the Austrian biochemist who was awarded the 1938 Nobel Prize for Chemistry for work on carotenoids and vitamins, died 44 years ago on Aug 1. Sir *Alexander* ***Fleming***, the Scottish bacteriologist who discovered penicillin, was born 130 years ago on Aug 6 and shared the Nobel Prize for Physiology or Medicine in 1945. *William Hyde* ***Wollaston*** was the English scientist who discovered palladium (1803) and rhodium (1804), during his investigation of platinum ore. He developed a method of forming platinum known as *powder-metallurgy* and was the first to produce malleable and ductile platinum on a commercial scale. He was born 245 years ago on Aug 6. Count *Amedeo* ***Avogadro*** was the Italian chemist and physicist who found that at the same temperature and pressure equal volumes of all perfect gases contain the same number of particles (Avogadro's Law) in 1811 – 200 years ago; he was born on Aug 9, 235 years ago. *Aaron* ***Klug***, the British biochemist who received the 1982 Nobel Prize for Chemistry for his development of crystallographic electron microscopy and his structural elucidation of biologically important nucleic acid-protein complexes, celebrates his 85th birthday on Aug 11. *Paul* ***Sabatier*** shared the 1912 Nobel with Victor Grignard. His research was on catalytic organic synthesis, and he discovered the use of finely divided nickel as a catalyst in hydrogenation; he died 70 years ago on Aug 14, 1941.

100 years ago on Aug 15, Procter & Gamble Co. introduced *Crisco* the first solidified shortening product made entirely of vegetable oil and produced by hydrogenation, then a new process. *Aleksandr* ***Butlerov***, the Russian chemist whose 1861 theory of organic chemistry structure was an important step towards the modern understanding the discipline, died 125 years ago on Aug 17, 1886. Application by ***W. H.Perkin*** for his aniline dye patent was made on August 26, 1856 titled *Dyeing Fabrics* to *producing a new colouring matter for dyeing with a lilac or purple colour stuffs of silk, cotton, wool or other materials.* It was sealed on 20 Feb 1857. Sir *Ernest* ***Rutherford*** was born on Aug 30, 1871 and died on Oct 19, 1937. *Michel-Eugène* ***Chevreul*** was the French chemist who began the study of the chemistry of fats and discovered fatty acids, which led to a great improvement in the quality of stearine candles and in the fats used to make soaps. He was born 225 years ago on Aug 31, 1786.

Karl August ***Folkers***, the US chemist who isolated vitamin B_{12} for the first time, was born on Sept 1, 105 years ago, while *Ludwig Eduard* ***Boltzmann***, the physicist who founded statistical mechanics, died 4 days later on Sep 5 that same year. *William* ***Henry*** died on Sep 2, 1836 (175 years ago). He was the English physician and chemist, who proposed in 1803 what is now known as Henry's law. It states that the amount of a gas absorbed by a liquid is in proportion to the pressure of the gas above the liquid, provided that no chemical action occurs. Sir *Robert* ***Robinson****,* the British chemist who received the 1947 Nobel Prize for his research on a wide range of organic compounds, notably alkaloids, was born 125 years ago on Sept 13, 1886. *Ferid* ***Murad*** celebrates his 75th birthday on Sept 14; he is the American co-winner of the 1998 Nobel Prize for Physiology or Medicine for discovering that nitric oxide acts as a signalling molecule in the cardiovascular system. *Gabriel* ***Fahrenheit***, the German physicist of temperature scale fame and who lived most of his life in Holland, died 275 years ago on Sep 16, 1736. *Frederick* ***Soddy***, the English chemist and physicist who received the 1921 Nobel Prize for his work investigating radioactive substances, died 55 years ago on Sept 22. Sir *Geoffrey* ***Wilkinson***, joint recipient with Fischer of the 1973 Nobel Prize for their work, performed independently, on the chemistry of the organometallic, so called *sandwich compounds*, died 15 years ago on Sept 26.

Charles ***Darwin*** returned from his voyage on the *HMS Beagle* to the Pacific 175 years ago on Oct 2, 1836. On the same day in 1956, the Atomicron, the first atomic clock in the US, was unveiled in New York City; its basis of timing was the constant frequency of the oscillations of the caesium atom, namely, 9,192,631,830 MHz. In 1956, Dr. *Albert* ***Sabin*** developed the oral Polio vaccine as advised on Oct 6, 1956. In 1876, on Oct 9, the first two-way telephone conversation occurred over outdoor wires – Alexander Graham Bell had a conversation with Watson over the telegraph line linking Boston and East Cambridge. On Oct 12, 75 years ago, the success in making of X-ray moving pictures of internal organs of the human body was reported at the 37th annual meeting of the American Roentgen Ray Society by Drs Stewart, Hoffman and Ghiselin.

King Charles II granted a Charter to the ***Royal Society*** on October 16, 350 years ago as on that day Moray and Neile had "*... kissed the hand of the King in the Company's name*". The King indicated that he would grant the petition and he also indicated that he wished to become a Fellow of the new Society. The Charter of Incorporation passed the Great Seal on 15 July 1662 and the Royal Society of London officially existed from that date with the name of *The Royal Society*. *Henry* ***Cavendish***, the Nice-born English physicist and chemist, who conducted experiments in diverse fields, discovering such phenomena as the composition of air and the nature and properties of hydrogen, was born on Oct 10, 280 years ago. The creation of the heaviest man-made element, ***Ununoctium (Uuo 118)***, was announced on Oct 16, 5 years ago. *William A.* ***Mitchell***, the American food scientist who worked as a chemist for General Foods Corp, and held more than 70 patents (Pop Rocks candy, Cool Whip, quick-set Jell-O Gelatin), was born 100 years ago on Oct 21.

Conferences

New Zealand Institute of Chemistry Conference (NZIC) 2011

27 Nov - 1 Dec 2011, University of Waikato, Hamilton, NZ

Five eminent international chemists, Professor's Omar Yaghi, Duncan Bruce, Neil Ward, Michael Bowers and Bill Fenical are the keynote speakers for the conference. In addition, there will be a variety of local and international presentations, covering a wide range of topics from all areas of chemistry and related scientific pursuits.

Registrations open: **15 June 2011**

Call for abstracts open: **1 July 2011**

Abstract submissions close: **1 September 2011**

Standard registration deadline: **26 October 2011**

http://www.nzic2011.co.nz/

RACI Biomolecular Division Conference

4-8 December 2011, Peppers Sands Resort, Torquay, Victoria, Australia

The RACI Division of Biomolecular Chemistry invites you to attend our biennial conference Biomolecular at the Beach. The conference will be held at the superb Peppers The Sands Resort at the beginning of Victoria's world famous Surf Coast in the beautiful seaside town of Torquay. The conference themes of Medicinal Chemistry, Chemical Biology and Drug Discovery and the stellar line-up of invited speakers from Australasia and around the world, promise to make the science as spectacular as the location

Deadline for abstract submission: 23 September 2011

http://www.raci-bio-conf.org/

RACI Inorganic Division Conference

2011 Inorganic Conference of the Royal Australian Chemical Institute and the New Zealand Institute of Chemistry

4-8 Dec 2011, University of Western Australia, Perth.

Confirmed Plenary Speakers include:

Professor Munetaka Akita, Tokyo Institute of Technology

Professor Matthias Beller, Leibniz Institute for Catalysis

Professor Neil Champness, The University of Nottingham

Professor Luisa De Cola, Westfälische Wilhelms Universität Münster

Professor William B Tolman, University of Minnesota

Abstract deadline: 1 October 2011

http://www.ic11.org.au/

14th International Union of Pure and Applied Chemistry Conference on Polymers and Organic Chemistry (POC 2012)

6-9 January 2012, Doha, Qatar

The POC 2012 is officially soliciting papers on all aspects of polymers and organic chemistry including, advances in polymer synthesis, macromolecular engineering with biomolecules, organic and polymer synthesis or orthogonal chemistry, polymers as therapeutics, polymers from renewable resources, polymers in energy, polyolefins, and responsive and smart materials.

Deadline for paper submission: 30 September 2011

http://www.poc2012.com/news

33rd Australasian Polymer Symposium (33APS)

12 – 15 February 2012, Wrest Point Convention Centre, Hobart, Tasmania.

This exciting programme covers all areas of polymer science and engineering, including synthesis, characterisation, processing, modelling and materials. Topics will range from the latest techniques in polymer synthesis to applications in materials science, medicine, energy and environment.

Deadline for abstracts: 2 September 2011

http://www.33aps.org.au/2012/index.php

2nd International Conference on Agrochemicals Protecting Crops, Health and Natural Environment - The Role of Chemistry for Sustainable Agriculture

15-18 February 2012, Delhi, India

Topics include: New generation synthetic and natural agrochemicals, agrochemicals delivery systems towards occupational and environmental safety, pesticide resistance management, biotechnology and crop protection-current and future approaches, organic approaches to pest management, pesticide management for human safety and food security, pesticide industry: prospects and constraints, agrochemical detection, analysis and quantification.

Abstract deadline: 30 November 2011

Website: http://www.apchne.com/home

4th Congress of the European Association for Chemical and Molecular Sciences (EuCheMS) Chemistry Congress

26-30 August 2012, Prague, the Czech Republic

Congress topics include: Analytic Chemistry, Electrochemistry, Education and History, Professional Chemists, Food Chemistry, Environment, Energy and Green Chemistry, Inorganic Chemistry, Life Sciences, Nanochemistry, Nanotechnology, Organic Chemistry, Polymers, Physical, Theoretical and Computational Chemistry and Solid State Chemistry

Abstract submission deadline: 5 May 2012

http://euchems-prague2012.cz/

19th International Conference on Organic Synthesis in conjunction with The 24th Royal Australian Chemical Institute Organic Conference

1-6 July 2012, Melbourne, Australia

Along with an outstanding group of plenary lecturers, invited speakers and the Thieme-IUPAC Award Lecture, there will be parallel sessions from students, postdoctoral fellows and early career academics. There will also be Thieme-IUPAC poster prizes especially aimed at students. As part of the RACIOrganic24 programme, there will be prizes for student talks and posters as well as the presentation of the 2012 A. J. Birch Medal, the premier award of the RACI Organic Division.

Register you interest to attend at the website.

http://www.icos-19.com/