NZIC Chemistry IN NEW ZEALAND

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Articles and Features

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Cover

Representation of the atomic model of an Al-Pd-Mn quasicrystal surface and the Nobel medal (see article by Brian Halton; artistry by Matt Walters, School of Biological Sciences, University of Canterbury).

Comment from the President

Welcome to the first issue of the 76th volume of Chemistry in New Zealand – we look forward to Peter Hodder's stewardship and wish his editorial and publishing team every success with the volumes to come. At the start of 2012, I look forward to my term as President and I would like to thank Gordon Rewcastle for his efforts on behalf of NZIC as President throughout 2011.

The New Zealand Oxford Dictionary defines chemistry as the branch of science dealing with the elements and the compounds they form and the reactions they undergo. This definition encompasses the central place of chemistry among the sciences underpinning, as it does, much of biology and spanning across to merge with physics. This breadth was clearly evident in the range of talks and posters presented at our 2011 Conference in Hamilton: congratulations to convenor Michèle Prinsep and her stellar team (Michael Mucalo (treasurer), Wendy Jackson (secretary), Annie Barker, Bill Henderson, Jo Lane, Brian Nicholson, Graham Saunders and ForumPoint2) for a very successful conference and a very fitting addition to our celebrations of 2011 as the International Year of Chemistry. All present at the meeting had no trouble recognising chemistry as the central science.

The vibrancy of our 2011 conference illustrated the depth of talent we have in our membership and this was reflected in the outstanding field of candidates for our 2011 prizes. This year the Maurice Wilkins Centre prize went to Professor David Williams, from the School of Chemical Sciences at Auckland University, and Dr Laurence Eyres, director of ECG Ltd, received the prize for Industrial and Applied Chemistry. Also this year, the 2011 ABA Books Denis Hogan award for Chemical Education went to Associate Professor Robert Maclagan from the University of Canterbury and Dr Bridget Stocker, from the Malaghan Institute of Medical Research in Wellington, was awarded the biennial Easterfield Medal from the Royal Society of Chemistry. Congratulations to all 2011 prize recipients.

Given the quality of the science presented at our 2011 conference, and demonstrated by our 2011 prizewinners, it is clear that *chemistry* in New Zealand is strong and healthy and it underpins much science and technology across schools, universities, Crown Research Institutes and industrial settings. The New Zealand Institute of Chemistry is the grassroots organisation for chemists throughout the country and provides a forum to support and foster chemists and chemistry to strengthen the economy and the well being of all New Zealanders. Therefore, I would like to end with a challenge for the branches in 2012. Surprisingly, given the central position of chemistry, our membership numbers have been declining from 1006 in 2006 to 905 in 2011. So this year at branch level, encourage your colleagues and students to join NZIC — make it a goal to increase your branch by 5 to 10 members in 2012. New Zealand needs chemists and chemists need NZIC.

Julian Eaton-Rye
NZIC President

About the President

Julian Eaton-Rye is in the Department of Biochemistry at the University of Otago. He completed a BSc Honours degree in Botany from the University of Manchester, UK in 1981 and obtained his PhD (Plant Physiology) in 1987 at the University of Illinois at Urbana-Champaign under the supervision of Govindjee. His PhD thesis research addressed the role of bicarbonate acting as a ligand to the non-heme iron of Photosystem II and participating in the protonation reactions associated with plastoquinone reduction on the acceptor side of the photosystem. He then obtained a Japan Society for the Promotion of Science postdoctoral fellowship (through the Royal Society, UK) and worked with Professor Norio Murata at the National Institute for Basic Biology in Okazaki, Japan (1987 – 1989). In Professor Murata's laboratory he studied the composition of the protein environment surrounding the manganese-calcium cluster of the oxygen-evolving complex. In 1989 he moved to the Center for Early Event in Photosynthesis at Arizona State University to take up a postdoctoral position in the laboratory of Professor Wim Vermaas where he began working with the cyanobacterial model organism *Synechocystis* sp. PCC 6803, and in 1993 he moved to Brookhaven National Laboratory, USA, as a Senior Research Fellow in the laboratory of Geoffrey Hind where he characterised a novel thylakoid-membrane protein kinase. Since his appointment at the University of Otago in 1994, his research group has studied the role of either the lumenal "extrinsic proteins" of Photosystem II or low-molecular-weight membrane-spanning "auxiliary" Photosystem II subunits found at the monomer-monomer interface of the Photosystem II supercomplex. His laboratory is also actively studying the role of three additional Photosystem II lipoproteins (Psb27, CyanoP and CyanoQ) that are present in isolated Photosystem II complexes from *Synechocystis* sp. PCC 6803 but are absent from the current atomic resolution structures from the thermophilic cyanobacteria *Thermosynechococcus elongatus* and *T. vulcanus*. This work has produced the first X-ray-derived crystal structure of CyanoQ and NMR solution structures of Psb27 and CyanoP. With respect to other professional activities Julian currently serves on the Executive Committee of the International Society of Photosynthesis and the International Scientific Committee of the Triennial International Symposium on Phototrophic Prokaryotes. He is also a consulting editor for the Advances in Photosynthesis and Respiration book series and an Associate Editor of the *New Zealand Journal of Botany*. He served as the President of the New Zealand Society for Plant Biologists (2006 – 2008). He recently coedited a comprehensive treatise on photosynthesis: Eaton-Rye, J.J., Tripathy, B.C. and Sharkey, T.D. (Eds.) (2012) Photosynthesis: Plastid Biology, Energy Conversion and Carbon Assimilation*, Advances in Photosynthesis and Respiration*, Vol 34, Springer, Dordrecht.

NZIC Conference 2011

The NZIC 2011 conference was held at the University of Waikato from 27 November–1 December. Over 250 delegates from both academia and industry attended, including 77 students. The wide-ranging programme included six plenary lectures, the Easterfield lecture, the student oral paper competition, 90 posters and 125 oral presentations. These were divided into concurrent Analytical and Environmental, Biological, Chemical Education, Industrial and Materials, Inorganic and Organometallic, Organic and Physical and Theoretical streams. The conference and accompanying trade exhibition was officially opened on Sunday 27 November by Professor Bruce Clarkson, the Dean of the Faculty of Science and Engineering at Waikato, followed by drinks and nibbles.

The excellent plenary talks began with Tom Rauchfuss' lecture *How Nature Makes and Uses Hydrogen: The Bioorganometallic Chemistry of Hydrogenases* which outlined synthesis and applications of enzyme models, and Bill Fenical's talk *Marine Microbial Anticancer Agents Select for Novel Intracellular Targets* which discussed the importance of determining the mechanism of action of novel microbial metabolites at an early stage of investigation. Neil Ward's lecture, *Analytical Rescue for Global Water Problems*, focused mainly on issues associated with arsenic levels in drinking water in Argentina, and Joe Schwarcz' talk, *Are Cows More Trustworthy than Chemists?*, discussed the mistrust of chemistry caused by a lack of understanding of basic chemical concepts by the general public. Duncan Bruce's lecture, *N-Heterocycles and their Complexes in Liquid Crystals: Non Covalency, Phosphorescence and Heterogeneous Catalysis*, outlined a wide range of structures and applications of liquid crystals, and Mike Bowers discussed investigation of the mechanism of peptide aggregation by mass spectrometry, particularly in relation to Alzheimer's disease in his talk, *Peptide Aggregation: What we know and why it is important*.

Dr Bridget Stocker presented the Easterfield award lecture, *Chemistry, Immunology and Sugars*, outlining the range of research carried out by her group at the Malaghan Institute of Medical Research. She had already been awarded her Easterfield medal by Gordon Rewcastle at a Royal Society dinner earlier in the year.

Richard Souness (Otago), Jonathan Puddick (Waikato), Jamie Withers (Manawatu), Janice Cheng (Wellington), Francine Smith (Canterbury) and Yiwen Pei (Auckland), all gave excellent talks in the student oral paper competition. The prize of $150.00 and a ticket to the conference dinner was awarded to Janice Cheng of the Malaghan Institute of Medical research for her talk, *The Synthesis of Dansyl α-Galactosyl Ceramide: a Fluorescent Probe for Monitoring Glycolipid Uptake During Cancer Immunotherapy.*

Ninety posters were presented during the two well attended poster sessions. One of the plenary speakers commented afterwards on the students' knowledge of and enthusiasm for their material. The Communicator of the Year award was presented to PhD student James Lewis of the University of Otago who won $150.00, a copy of the book *Letters to a Young Chemist* kindly donated by Brian Halton and a framed certificate for his poster, *Assembly, Dis-assembly and Re-assembly of an M_2L_4 Cage for Drug Delivery* reproduced on the inside back cover of this issue. Highly commended were master's student Maria Revell (University of Waikato) for her poster, *Investigation of the Stability of Fructooligosaccharides and Antioxidants in Prepackaged Yacon and Yyacon Products*, and PhD student Alasdair McKay (University of New South Wales) for his poster, *Bulky Triazenide Complexes of the Heavy Group 13 Metals*. Two secondary school students, Vincent Aw and Hao Jeng of Hillcrest High School who presented their poster, *Mathematical Formulations of the Titration Curve*, deserve special mention.

The scientific programme was accompanied by a busy social programme. On Tuesday evening, around 25 teams of three competed in a fun-filled Chemistry themed quiz, followed by pizza and drinks. Prizes were awarded as follows: First place: The Faculty of Huge Manatees and Social Sciences (Sarah Hoyte, Melanie Nelson, Theresa Vaughan) all from Victoria University of Wellington; Second Place: Nana Particles (Cleo Davie-Martin and Birthe Kortner, University of Otago and Kathryn Allan, Victoria University); Third Place: Cat in a Box (Simon Williams and John McDonald-Wharry, University of Waikato, Ben Deadman, University of Cambridge); Last Place: HFTP3000 (Sylvia Baars, Nicole Miller, Tony Davidson) all from Industrial Research Limited.

Wednesday afternoon was free time (and great weather). Many delegates took advantage of the tours offered: kayaking on Lake Karapiro, caving to Rotokauri Cave at Waitomo or wine-tasting and art-viewing at Vilagrads Winery and Inspirit Gallery. On Wednesday evening the conference dinner was held at the Academy of Performing Arts at Waikato, a great venue overlooking the campus lakes. Guests were entertained by local guitar duo Soundwave Acoustic during pre-dinner drinks and then moved through to the Playhouse to indulge in a three course dinner on tables decorated with Chemistry themed centrepieces and placemats featuring newspaper articles from an NZIC conference held in Hamilton in 1935 with 25 delegates! The NZIC President, Gordon Rewcastle presented the student oral paper prize to Janice Cheng, and Vyacheslav Filichev announced the results of the molecular anthology competition run by Manawatu branch. The winning molecule? It was carbon.

The NZIC AGM was held on Thursday lunchtime and the conference finished at afternoon tea. The knitted periodic table was on display throughout the conference and received much attention. Our thanks go to Sarah Wilcox and Wellington Branch for arranging this.

At Waikato we felt very fortunate to be hosting the conference in the International Year of Chemistry and to have the opportunity to showcase both the university and the Waikato region. Thank you to everyone for helping to make the conference successful: the organising committee, our sponsors, speakers, delegates and trade exhibitors, in addition to our conference managers ForumPoint2 who did a great job both off and on site.

See images of the conference on page 36.

New Zealand Institute of Chemistry

supporting chemical sciences

January News

NZIC NEWS

The Marie Curie Lecture Series continued to its IYC conclusion through October and November with *From the Bottom Up* by Prof *Alison* ***Downard***, in Napier, *The Light Fantastic* by Dr *Cather* ***Simpson*** in Christchurch and *The Wonderful World of Enzymes - insights into drug design, catalysis and molecular evolution* by Assoc Prof *Emily* ***Parker*** in Auckland.

Denis Hogan Award

The NZIC Council has awarded *Robert* ***Maclagan*** the 2011 Denis Hogan Award for Chemical Education, sponsored by ABA Books. This award is normally given to a secondary school teacher who has made an important contribution to chemical education in New Zealand. Robert was recognised for his role in initiating and organising the participation of New Zealand in the International Chemistry Olympiads from 1991. This involved both organising, fund-raising and training. He set up the New Zealand Chemistry Olympiad Trust and was a founding member of the Science Olympiad Association Council. The award honours *Denis* ***Hogan*** who was NZIC Registrar and worked at DSIR/ESR in Christchurch but played an important role promoting Chemical Education in New Zealand and was an Adjunct Senior Fellow in the department from November 1999 until his death in 2006.

AUCKLAND

Prof *Sally* ***Brooker*** from the University of Otago presented the October NZIC Seminar on the topic of *Spin Crossover Complexes and [M3LN] Macrocyclic Single-Molecule Magnets*. The annual NZIC Seminar was given at the AGM in November by Assoc Prof *Gordon* ***Rewcastle,*** with a presentation on *Development of the Phosphoinositide 3-kinase (pi3k) inhibitor PWT33597*. The talk outlined Gordon's research within the Auckland Cancer Society Research Centre, and the use of targeted anticancer therapy, and the successful medicinal chemistry development of a new drug treatment. As part of the International Year of Chemistry, Prof *Joe* ***Schwarcz*** gave a highly entertaining talk in November with the title *Are Cows More Trustworthy than Chemists?* Prof Schwarcz is director of the Office for Science and Society at McGill University, Canada, and was able to draw upon his extensive career in publicising chemistry and scientific developments through radio broadcasts and a number of popular book titles.

University of Auckland

A new addition to the academic staff is Assoc Prof *Christian* ***Hartinger***, an inorganic chemist with research interests in biological and medicinal inorganic chemistry, including metal complexes with anticancer activity. Also new to the staff is Dr *Nick* ***Lloyd***, recently graduated from the University of Waikato, with responsibilities for the high resolution mass spectrometer, and further MS equipment within the School of Chemical Sciences, such as a planned ICP-MS facility.

Four postgraduate Chemistry students were recognized for the quality of their presentations in the Faculty of Science Postgraduate Poster Competition. These included merit awards for *Jackie* ***Knobloch***, *Marsilea* ***Booth***, *Nor Fazhliyana* ***Mohtar***, and the third place prize to *Karthik* ***Kannappan***.

In October Prof *Margaret* ***Brimble*** was awarded the 2011 Adrien Albert Award for Medicinal Chemistry from the Royal Australian Chemical Institute (RACI). This followed Margaret's success in the Marsden round for 2011. In November Dr *Joanna* ***Wojnar*** won the Manhire Prize for Creative Writing by the Royal Society of New Zealand. Dr Wojnar is a post-doctoral research fellow working towards the synthesis of fish antifreeze glycopeptides under Prof Margaret Brimble. The title of her entry was *100% Chemical Free,* and discussed the use of the terms 'natural' and 'chemical', and the tendency to polarise these terms. Another winning entry was for Merck's recent Chemicals and Reagents 2011-13 catalogue promotion, and was made by Prof *Penny* ***Brothers***. Dr *Cather* ***Simpson*** presented her Royal Society Marie Curie Lecture on *The Light Fantastic* to a packed hall in Christchurch in November.

Seminars within the School of Chemical Sciences in recent months have included Dr *Sarah* ***Masters*** of the University of Canterbury, on *From Antiobiotics to a Jack-in-the-Box: Are Molecular Structures the Same in Different Phases?*; Dr *Chris* ***Hickey*** from the National Institute of Water and Atmospheric Research (NIWA) in Hamilton, who spoke on *Something in the Water? Ecotoxicity Investigations of Foam Toxicity to Marine Organisms*. A seminar was given on *Ocean Acidification – Integrating Chemistry and Marine Biology and What it Means for You* by Assoc Prof *Mary* ***Sewell*** from the School of Biological Sciences at the University of Auckland; while Prof *Andrew* ***Evans*** from Aberystwyth University in the UK spoke on the *Growth and Characterisation of Carbon-Based Semiconductors Using Real-Time Spectroscopy*. Prof *Juliet* ***Gerrard*** of the University of Canterbury gave a seminar on *Proteins as Supramolecular Building Blocks: From Enzymology and Drug Design to Nanotechnology*; Dr *Bridget* ***Stocker*** of the Malaghan Institute of Medical Research, Wellington, spoke on *Total Synthesis with and without Protecting Groups: Aza-Sugars*. To mark the 50th year of the invention of the laser, Dr *Cather* ***Simpson*** from the School of Chemical Sciences was joined by Dr *Tahei* ***Tahara***, Chief Scientist and Director of the Molecular Spectroscopy Laboratory at RIKEN, for a public lecture on the properties of ultrashort light pulses. Dr *Ali* ***Hosseini***, a University of Auckland graduate, spoke about his research as a postdoctoral research fellow at Stanford University, Cali-

fornia, on the topic of *Electrochemical Methods to Study O_2 Reduction: From Interdigitated Arrays to Hybrid Bilayer Membranes*; and Prof C S ***Pundir*** from the Department of Biochemistry, Rohtak, India, on *Polyaniline and Carboxylated Multiwalled Carbon Nanotube-Based Electrochemical Biosensors for Determination of Ascorbic Acid and Uric Acid*.

WAIKATO

University of Waikato

The annual ChemQuest competition, was recently held by the Department of Chemistry. A total of 60 teams from the greater Waikato region and Bay of Plenty participated. As usual, this was a fun-filled evening for students studying NCEA level 2 Chemistry. ChemQuest tests the students' knowledge of chemistry in a variety of ways. Alongside traditional general knowledge questions, there are also demonstrations to watch, smells to identify and music to listen to - all with a chemistry theme. The winning team was from Te Awamutu College and comprised Hayden Berkers, Liam Macintosh and Matt Harker.

The quiz was generously sponsored by James & Wells Intellectual Property and Hill Laboratories, as well as the Faculty of Science and Engineering, University of Waikato. Question master was *Bill* ***Henderson***, with *Brian* ***Nicholson*** the chief judge, assisted by numerous other staff and students from the Department.

Alan ***Langdon*** has received two grants through WaikatoLink and MSI; a Jumpstart grant to develop a proof of concept of the Perforated Electrode Flow Through (PEFT) cell applied to electro-pasteurisation of milk and juice and a Pre-Seed Accelerator Fund (PSAF) grant to develop a working prototype of the PEFT cell treating water for domestic drinking purposes, with the aim of securing a commercial licence of the technology at the end of the project. *Bill* ***Henderson*** been appointed to the editorial board of the *Journal of Coordination Chemistry*.

Oguejiofo Ujam (known to everyone as Ujams) has recently completed his PhD in the alkylation of platinum sulfide complexes and has now returned to his home country (Nigeria), where he is a lecturer at the University of Nigeria, Nsukka. *Hilary* ***Nath*** and Sheng Xu have both completed their doctorates with Alan Langdon. Hilary's PhD was entitled *The Development and Applications of a Micro-Gap Perforated Electrode Flow Through Cell*. By reducing the interelectrode gap to 40 microns, it has been possible to develop electrochemical processes for treating water and wastewater at naturally occurring electrolyte concentrations. Hilary will continue the work at Waikato on a post doctorate funded by WaikatoLink and MSI. Sheng's thesis topic was *Preparation of Mesoporous Solids Containing Encapsulated Metal Species of Technological Interest* and involved developing novel ways of loading the mesoporous silica MCM-41 with metal and mixed metal nano particles.

First Place From Te Awamutu College: Hayden Berkers, Liam Macintosh and Matt Harker, pictured with Dr Graham Corban (left) from Hill Laboratories.

Bill ***Henderson*** making a yellow precipitate of lead iodide, by mixing two colourless solutions.

Bill ***Henderson*** pouring liquid nitrogen into water.

The Chemistry Department was well represented at the recent 2011 Staff Excellence Awards, with *Joseph* ***Lane*** winning both an Emergent Teaching Excellence Award and an Early Career Research Excellence Award, and *Wendy* ***Jackson*** winning the university Health and Safety Excellence Award.

Recent seminars from visitors to the department included *Spin Crossover Complexes and [M_3Ln] Macrocyclic Single-molecule Magnets* from the Royal Society of Chemistry Australasian Lecturer, *Sally* ***Brooker***, University of Otago; and *The Future of Beekeeping in Thailand* from Panuwan Chantawannakul, Chiang Mai University, Chiang Mai, Thailand.

The NZIC conference was held at Waikato from 27 November-1 December and this is outlined in a separate report (see p. 3).

MANAWATU

Massey University, Institute of Fundamental Sciences

Paul ***Plieger*** has received funding for a two year postdoctoral position in inorganic synthetic chemistry, with the aim of synthesising new magnetic materials. Paul will also be supervising *Karla* ***Dunn***, who has received a Summer Scholarship and will continue the work started by *Amy* ***Willoughby*** on new manganese mixed-oxidation state materials.

Ross ***Davidson*** has successfully defended his PhD thesis, entitled *Cyclo- and Poly-phosphazenes Grafted with Tridentate Ligands, Coordinated to Iron(II) and Ruthenium(II)*. Ross was supervised by *Andrew* ***Brodie***, *Eric* ***Ainscough*** and *Mark* ***Waterland***.

James ***Stevens*** has recently completed his MSc degree under Paul Plieger's supervision. The topic of his thesis was on the solution and solid state analysis of xylylic di-copper complexes as receptors for encapsulating anions.

Congratulations to *Pat* ***Edwards***, *Shane* ***Telfer*** and *Dave* ***Harding***. Pat has been promoted to Senior Research Officer, Shane has been promoted to Associate Professor and Dave has been promoted to Professor.

Geoff ***Jameson*** was awarded the New Zealand Association of Scientists Marsden Medal for 2011 "in recognition of his sustained record of leadership and service to New Zealand science and his outstanding contribution to the chemical sciences".

Institute staff who attended the 2011 NZIC conference included Paul Plieger, Mark Waterland, *Gareth* ***Rowlands***, *Vyacheslav* ***Filichev***, *Simon* ***Hall***, *Shane* ***Telfer***, Geoff Jameson and *Peter* ***Derrick***. Students who attended included *Sebastian* ***Blackwood***, *Selvakumar* ***Sabapathi*** and *Jamie* ***Withers***.

The IFS hosted the 25th annual Massey – Victoria Symposium Day where students from both universities showcased their research. A large turnout from the Victoria contingent helped make the event a great success.

In a stunning display of both mental and physical prowess, the IFS staff have secured this year's institute trophy with victories over the student team in the annual quiz, netball and cricket matches; This marks the first time the trophy has left student possession since the competition began.

Mark Waterland and Vyacheslav Filichev hosted Felix Castellano (Bowling Green State University, Ohio, USA) and his wife *Lisa* at Massey University. Felix gave a seminar on *Upconversion Photochemistry: Sensitized Triplet Fusion* to the IFS and had several meetings with students and chemistry academic staff members in the following days. His visit was supported by the Massey University International Visitor Fund.

Trevor ***Kitson*** gave a talk as part of the IFS Public Lecture Series about ways to inspire students' chemical curiosity, drawing on experience gained from his time teaching in lectures and labs at Massey University. *Tim* ***Kemmitt*** (IRL) presented his work on ZnO transparent conducting films. *Allan* ***Ferguson*** (University of Canterbury) described his work involving single-molecule magnets and spin-crossover complexes. As part of the 2011 RSC Australasian lecture tour, *Sally* ***Brooker*** (University of Otago) presented her research into spin-crossover compounds and macrocyclic single-molecule magnets. *Simon* ***Loveday***, from the Riddet Institute at Massey University, talked about his work into the effect of calcium ions on the formation of whey protein nanofibrils. *Sarah* ***Masters*** (University of Canterbury) described the utility of gas electron diffraction in a variety of applications, including investigations into tetra(disyl)diphosphine and the benzyl radical. *Gordan* ***Rewcastle*** (University of Auckland) gave a lecture on his experiences developing phosphoinositide 3-kinase inhibitors, as part of his NZIC presidential tour. *Jonathan* ***Sperry*** (University of Auckland) gave a talk entitled *Synthetic Studies Towards Indole and Pyrazine Alkaloids*, describing the total synthesis of terreusinone from the marine fungus *Aspergillus terreu*. Joe Schwarz (McGill University) presented a lecture on the image problems facing chemistry and strategies for educating the public and counteracting widespread chemophobia.

WELLINGTON

The Branch congratulates Drs *Gary* ***Evans*** on being awarded the inaugural ***RSNZ Callaghan Medal***, *Bridget* ***Stocker*** who won the fiction section of the ***RSNZ Manhire Prize for Creative Science Writing***, and former VUW doctoral student *Joanna* ***Wojnar***, who collected the non-fiction section of this writing prize.

Congratulations from the Branch go to *Mark* ***Bartlett***, a PhD student working with Dr *Joanne* ***Harvey***, on becoming a runner up in the ***Elsevier Chemistry Challenge***. His proposal was in the top ten of those submitted in the challenge organised by the RACI and NZIC. He receives a subscription to NZIC. Congratulations also go to *Janice* ***Cheng*** who won the Student Paper competition at the NZIC conference; she was also the overall winner of the 2011 VUW PGSA Postgraduate Research Excellence Award; Janice works with Drs *Mattie* ***Timmer*** and *Bridget* ***Stocker*** in the Malaghan Institute/VUW.

The September Branch meeting was deferred in place of Victoria University's Inaugural Chancellor's Lecture ***A Prosperous 21st Century for New Zealand*** given by Prof Sir *Paul* ***Callaghan*** in the Wellington Town Hall on September 14. The lecture was an insightful discussion of Paul's concepts of a better New Zealand emerging from a science-based society and follows from his recent New Zealander of the Year addresses. October saw the Branch hold its AGM on the 12th when Dr *Peter* ***Hodder*** was re-elected to the Chairmanship for a further year. The Branch Secretary is Dr *Matthias* ***Lein*** and Treasurer Dr *Suzanne* ***Boniface***. Following the meeting, and continuing the Branch's IYC focus of presenting lectures of general appeal, Prof *Martin* ***Manning*** (NZ Climate Change Research Institute, VUW) spoke on *How far should we push growing demands on atmospheric chemistry?* (see *Chemistry in NZ,* **2011**, *75*, 78-84). He told us that climate change science has to understand how the CO_2 produced by fossil fuels is removed from the atmosphere and, because much of it is not, what an increasing greenhouse effect can mean for our climate system. This has already resulted in some surprises such as finding that CO_2 is not just dissolved into the oceans, and that warming is now causing a much faster loss of ice sheets than was expected ten years ago. But our climate and many other aspects of our global environment are also critically dependent on atmospheric chemistry, and that has already shown a major surprise: the Antarctic Ozone Hole. Furthermore, atmospheric oxidation is doing more to compensate for the increasing greenhouse effect than any other process and it is now in a state completely different from anything that has happened in the past. Ironically, by stopping the production of CFCs which damage the ozone layer, we have shifted to using gases that increase the need for oxidation in the

lower atmosphere, even though our understanding of that is still limited.

November saw three Branch activities. Firstly, Dulux New Zealand Ltd. hosted an introduction to paint that was followed by a site visit at its head office and factory in Gracefield. The Product Development Chemist, *Serena* ***Smalley*** (a recent addition to the Branch Committee) provided the introduction under the title *The Chemistry of Paint - What is it, how is it developed, and how is it manufactured?* This was followed by a site tour under the guidance of David Mortimer, the Operations Manager. The 22 members who attended had a very enjoyable evening and tour despite the wet conditions.

The Presidential address was given to the Branch on Wednesday November 16 by A/Prof *Gordon* ***Rewcastle*** of the *Auckland Cancer Society Research Centre* (ahead of the RSNZ awards ceremony) with the title *Development of the Phosphoinositide 3-Kinase (PI3K) Inhibitor PWT33597*. Gordon outlined the approaches to phosphoinositide-3-kinases (PI3Ks), which comprise a family of lipid kinases with three distinct classes that play key roles in cell physiology. He then showed how, starting with the known PI3K inhibitors PIK75 and ZSTK474, the lab identified a number of structural changes that enabled selection of novel analogues for advanced preclinical evaluation. This culminated in the discovery of PWT33597, a dual inhibitor of PI3K alpha and mTOR, with approximately 10-fold selectivity over PI3K gamma and PI3K delta.

On Nov 24 Prof *Joe* ***Schwarcz*** (Director, Office for Science and Society, McGill University, Montreal), one of the NZIC conference speakers, visited Wellington for the regional Chemistry Teachers' day at Victoria University and gave a public lecture entitled *Are cows more trustworthy than chemists?* His lecture attracted well in excess of 100 people, far more attendees than the teachers alone. Prof Schwarcz has received numerous awards for teaching chemistry and for interpreting science for the public. Among these are the Royal Society of Canada's McNeil Award and the American Chemical Society's prestigious Grady-Stack Award. He has appeared hundreds of times on the Canadian Discovery Channel, TV Ontario, Global Television, CBC-TV, CTV-TV and various radio stations and writes a weekly newspaper column in the *Montreal Gazette*.

Joe provided a delightful and fascinating discourse stating from the mid-1960s and the Du Pont pavilion at the World Fair, discussing the good and the bad of chemicals, the implications of modern analysis and the fact there is no good or bad chemical, rather there are safe and unsafe ways to handle and use them. He detailed a story in *Time* magazine about the relative merits of conventional and organic produce that featured a curious quote from a professor of nutrition education at Columbia University. When asked if she preferred butter or margarine, she replied, "I would rather trust a cow than a chemist." He then discussed and demystified why such negative comments about chemistry are common these days and the issues of toxic chemicals in our air, water, food and even in our blood. The International Year of Chemistry indeed has been an especially appropriate time to try to build a dike of scientific reality to stem the rising tide of chemophobia. His lecture is one that ought to be broadcast on our television screens.

The role that chemistry plays in our everyday lives is enormous, but generally goes unnoticed. At the close of 2011 and the International Year of Chemistry, The Royal Society of New Zealand's annual 'Talking Heads' series turns its attention to the way chemistry underpins our lives.

In three Sunday Feature programmes, *Kim* ***Hill*** talks to chemists to examine some of life's complex questions. What exactly are free radicals? How does UV light affect our skin? Is there a chemical difference between males and females? And is the saying "you are what you eat" correct? Later that day Joe was interviewed by Kim Hill in the Te Papa theatrette for the *Talking Heads* radio programme that aired on Dec. 4. It was the first of three broadcasts in the 2011 series held to mark the end of 2011 The International Year of Chemistry, and can be downloaded from: *http://www.radionz.co.nz/national/lecturesandforums/talkingheads*

The final event for the year was a Branch IYC dinner at the Southern Cross Hotel in early December – a more than fitting end to what has been an invigorating, although demanding, year for the Branch and its committee.

Victoria University – SCPS

The highlight of the spring period was the mid-October visit of 2005 Nobel Laureate Prof Bob Grubbs (Caltech) who renewed his acquaintance with staff, met our new members and gave an inspirational lecture entitled *Green Chemistry and Catalysis*. The very large gathering of staff, students and visitors heard Bob point out that the rules of the industry have been changed by the increased cost of petroleum carbon and energy sources, and the need to control emissions of carbon dioxide and other pollutants. As rules change new processes are required. He then showed how catalytic processes provide Green routes to many old and new chemicals and open new sources of carbon, by taking examples from his own metathesis work. Most important here was the knowledge that his new catalysts and procedures are now in use on an industrial scale in the conversion of biomass to needed petroleum and chemical intermediates products in Singapore and, soon, in Kentucky. A solution to the provision of *Z*-olefins stereoselectively has provided a major challenge to his group, but the final solutions is close. Success in generating the *E*-isomer is further away, while the ability to hydrate alkenes easily and effectively in a green catalytic and (ultimately) industrial procedure is well advanced.

In late September Dr *George* ***Britovseki*** (IC-London) visited the ***Spencer*** group, met staff for research discussions and gave his seminar *Towards Catalytic Alkane Oxidation via O_2 Insertion into Platinum Methyl Bonds*. He described his investigations into alkane C-H bond activation using metal hydroxo complexes, a reaction for which several examples have been reported, and surveyed the results and mechanistic implications. At the end of the month Prof *Sally* ***Brooker*** (Otago) visited to deliver the RSC-RACI-NZIC Australasian lec-

ture entitled: *Spin crossover complexes and [M_3Ln] macrocyclic single-molecule magnets*. She described her on-going interest in spin crossover in organometallic complexes and the recent results from the group in this and the single molecule magnet (SMM) arena focusing on self-assembling systems that feature transition metal complexes of triazole-based ligands, new pyrazine-based ligands, and a new class of macrocyclic SMMs.

Mid-October saw Dr *Sarah* ***Masters*** (Canterbury University) visit, meet staff and deliver an enthralling seminar entitled: *From a Jack-in-the-box to Cyclophanes – Gas Phase Structures and Chemistry*. The lecture covered the crystallographic technique of gas electron diffraction (GED) from which accurate gaseous molecular structures can be obtained, thus providing valuable structural information about molecules free from the interactions that can affect solid-state structures. This was illustrated by tetra(disyl)diphosphine, the benzyl radical and cyclophane decompositions. Much valuable information of reactive intermediates and reactive molecules can be expected to follow. Late November had Prof ***F. N.*** *Castellano* (Center for Photochemical Sciences, Bowling Green State University, Ohio) visit and deliver his lecture on *Upconversion Photochemistry: Sensitized Triplet Fusion*. This focused on the study of sensitized triplet-triplet annihilation (TTA) in solution using highly photostable metal-organic chromophores in conjunction with energetically appropriate organic molecules with large singlet-triplet gaps. Selective visible light excitation of the long-wavelength absorbing sensitizer efficiently generates long-lived triplet states that serve as energy transfer donors. In the presence of appropriate molecular acceptors, diffusion controlled triplet-triplet energy transfer takes place, producing the excited triplet state of the acceptor while regenerating the ground state of the sensitizer. When sufficient numbers of the sensitized triplets are produced, TTA takes place and results in either frequency up-converted light or the formation of desired chemical products. The group has examined various combinations of donor and acceptor that have been explored for light conversion that span the near-visible to the near-IR.

Dr *Martyn* ***Coles*** joined SCPS as an Assoc Prof (inorganic) on 26 September 2011. He is new to Wellington and the country, having only visited before. He comes to us from Sussex University where he has worked for the past 12 years. Before appointment to Sussex, Martyn researched at the UC-Berkeley and Iowa. He gained his university education at Durham University in the UK. His research interests are in synthetic inorganic and organometallic chemistry, with particular emphasis on the development of main group compounds as catalysts. Other on-going projects include the formation of materials containing extended hydrogen-bonded arrays and the synthesis of metal compounds as sources of novel materials. He is married to Robyn, a senior lecturer in chemistry at Sussex, and has a 2 ½ year old son.

Dr *Justin* ***Hodgkiss*** was one of the ten recipients of the 2011 Rutherford Discovery Fellowships announced by the RSNZ on September 8. Justin, formerly a lecturer in Physical Chemistry and PI in the MacDiarmid Institute, he has been promoted to Senior Lecturer effective from 1 Jan 2012. He gained his PhD from MIT as a Fulbright in 2006, did postdoctoral work in the Cavendish Laboratory at Cambridge, and then joined Victoria in 2009. Since his arrival he has built an advanced laser laboratory to study the photophysics and photochemistry of functional materials, recently gaining a detailed understanding of the physics of photocurrent generation in organic solar cells and elucidating how solar power conversion efficiencies can be markedly improved. His research programme is motivated by the promise of abundant clean energy organic solar cells at low-cost.

Late October saw Prof Ken MacKenzie mingle at Café Scientifique (Wholly Bagels, Lower Hutt) and speak on *More Environmentally-Friendly Cements: Do the Egyptian Pyramids Provide a Clue?* As Portland cement manufacture contributes the second-greatest greenhouse gas burden after thermal power generation, Ken pointed out that the hunt is on for more environmentally-friendly substitutes (green concretes), and outlined the inorganic geopolymers that could provide a solution.

In late October SCPS received their new Agilent 6530 Q-TOF mass spectrometer system, a replacement for the PE Biosystems Mariner TOF that was decommissioned some four years ago. The 6530 is capable of routine sub-2 ppm mass accuracy for MS and sub-5 ppm for MS/MS fragmentation analyses, and has enhanced sensitivity through proprietary technology. The Q-TOF will be used mainly for accurate mass chemical formula determinations within SCPS as well as analysis of natural products extracts for the Keyzers and Northcote groups. In addition to the LCMS, SCPS also took possession of a new Agilent 7920 compact GC to replace the ageing HP-5890. The new GC was a gift from Agilent, as was the 1120 HPLC given to the School last year.

ESR-Porirua

Dr *Wendy* ***Popplewell*** has returned to New Zealand to a post as a forensic toxicologist with ESR in Porirua. Since completing her PhD in Marine Natural Products at Victoria University (*Peter* ***Northcote*** supervisor) in 2008, she has had two postdoctorals, the first position at Rhodes University (Grahamstown, South Africa) and the second at the National Cancer Institute in Maryland, USA. Grahamstown saw Wendy carrying out further marine natural products work while the USA position provided a more biological focus to natural product research.

CANTERBURY

Trivia and Truffles

Despite aftershocks as regular as ocean waves, NZIC Canterbury still managed to have their annual Trivia and Truffles evening on Wednesday 26 October. Twelve teams participated in an evening of fun, wine and enough sugary treats to induce diabetes in a small township.

As usual the team names stretched the limits of chemistry and word-play with first, second and third prizes being taken by "Wolf Rams", "The Sugar Daddies" and "Generic Chemistry Pun" respectively, and "Brominium

Rhapsody" taking the best team name prize.

President's Lecture

On 9 November NZIC President, Associate Professor *Gordon W.* ***Rewcastle***, (Auckland Cancer Society Research Centre, Faculty of Medicine and Health Sciences, The University of Auckland), gave the Presidential lecture entitled *Development of the Phosphoinositide 3-Kinase (PI3K) Inhibitor PWT333597.*

In 2005 Prof Rewcastle became an associate investigator with the Maurice Wilkins Centre for Molecular Biodiversity, where he has been involved in an investigation of isoform-selective PI3K inhibitors as potential anticancer agents. The PI3Ks comprise a family of lipid kinases with three distinct classes that play key roles in cell physiology. Many tumours are characterised by hyperactivity in the PI3K pathway, so there is currently a great deal of interest in developing PI3K. The enzyme mTOR kinase similarly plays a critical role in cellular growth and metabolism, and the inhibitors of mTOR have demonstrated clinical benefits.

Starting with already known inhibitors, Prof Rewcastle's group identified a number of structural changes that enabled selection of novel analogues for advance preclinical evaluation. This work culminated in the discovery of PWT33597, a dual inhibitor of PI3K and mTOR. Following the successful medical chemistry development in Auckland 2010, scale-up chemistry and pre-clinical toxicology were performed China, US FDA Investigating New Drug (IND) approval was given in June 2011 and human clinical trials commenced on 1 July 2011.

International Year of Chemistry Royal Society - NZIC finale.

On 1 December, in what was an informative, entertaining and thought provoking event, Canadian Professor *Joe* ***Schwarcz***, director of McGill's Office for Science and Society, author, recipient of numerous national awards, columnist and radio show host gave a brilliant lecture to an audience of some 250 people entitled, *Are cows more trustworthy than chemists?*

Quoting Paracelsus, to the effect, "All things are poison, and nothing is without poison; only the dose permits something not to be poisonous" or more commonly rendered, "the dose makes the poison", Prof Schwarcz explained, with many amusing anecdotes, how many of our concerns about chemicals ranging from Bisphenol-A and trans fats in margarine to phosphorus and hydrogen peroxide are seriously inflated by the media and often predicated on studies that garner the media's attention thanks to potential sensational content rather than their scientific merit. Ranging in subject from the O.J. Simpson Trial to the prop intricacies of *I Dream of Genie*, Prof Schwarcz demonstrated that supposedly natural products can be as unhealthy as anything synthesised in a laboratory and how quack science might be discerned from the real thing which, unlike the former, is ideally self correcting. The take-home message from Prof Schwarcz was, chemically speaking, "life is a trade-off, and no matter how you look at it, it is better than the alternative".

If the frequency with which Prof Schwarcz had the audience in stitches is any indication at all, his recent book *Radar, Hula Hoops and Playful Pigs* will be a very entertaining read indeed. His lecture was followed by a panel discussion entitled, *Inside Out: the Chemistry of Food, Sex and Ageing* that "starred" *Kim* ***Hill***, Broadcaster, *Ian* ***Shaw*** , Professor of Toxicology at Canterbury University, Dr *Michael* ***Edmonds***, Science Manager at Christchurch Polytechnic and science blogger, and *Margreet* ***Vissers***, Deputy Director of the Free Radical Research Group at Otago University**.** The Talking Heads session can be heard as a podcast on the Radio New Zealand National website.

University of Canterbury

Coming and goings

It is with sadness the department announces the departure of *Sara* ***Syme*** on 14 October for "pastures anew" at CityCare. Sara was responsible for the Department's regular newsletters. An enthusiastic individual of great energy and vitality, she will be deeply missed. Dr *Petra* ***Huck*** who works for an atmospheric research company called Bodeker Scientific is visiting the Department (hosted by *Bryce* ***Williamson***) and will be co-supervising *Laura* ***Revell***'s PhD research project. The Department welcomes *Andrew* ***Watson*** who will be working as a postdoctoral in the AJF group for the next three years. Dr *Beatrice* ***Roy***, an academic from the University of Montpellier, also visited and was with the Department until December 2011. Dr *Yusuke* ***Tomabechi***, recent doctoral graduate from Tokai University, Japan is also visiting for a few months to do post doctoral work.

Nobel Prize winner (2005) Professor *Robert (Bob)* ***Grubbs*** from the California Institute of Technology and his wife Helen arrived back in the Department as Erskine visitors in October. Bob gave a series of lectures while visiting. His group focuses on the development of metal catalysts for the conversion of organic molecules. Catalysts developed at Caltech are being used in the discovery of new pharmaceuticals and for the production of plastic products. One example now being commercialized is the conversion of seed oils such as those used in cooking into fuels and other chemicals.

Awards

Dr *Sally* ***Gaw*** featured prominently in October, having been awarded a College of Science Early Career Research Grant which will support a PhD project for *Lauren* ***Raffensperger*** entitled *Investigating community waste water treatment plants as a source of emerging contaminants in Christchurch*. This project is a collaboration with Dr *Grant* ***Northcote*** (Plant and Food Research) and Dr *Louis* ***Tremblay*** (Cawthron). Sally was also nominated by her research group for the UCSA Supervisor of the Year 2011. *Sarah* ***Masters*** and Sally also ran a very successful workshop at the UC Community Open Day titled *Ironman*: a hands-on session in which participants extracted iron from cereal.

Laura Revell was also awarded two student presentation awards at conferences this year. The first was for her talk entitled *What is happening to ozone in the 21st century*? at the "Extreme Weather" conference held at Te Papa, Wellington on 9-11 February;

the second more recent prize was for her poster on *The chemical sensitivity of stratospheric ozone to nitrous oxide and methane* at the World Climate Research Programs Open Science Conference, held in Denver, Colorado on 24-28 October.

CPIT

On Wednesday 23 November, CPIT ran its Year 10 science competition which attracted teams from around the Christchurch area. The students all had a great time calibrating chemistry equipment and completing a quiz, which was then followed by an evening supper from Subway. The successful teams were: 1st, St Andrew's College (184/225); 2nd, Villa Maria College (178/225); 3rd equal, Burnside HS (157/225); 3rd equal, Villa Maria College (157/225).

Also on 23 November Dr Michael Edmonds from Christchurch Polytechnic Institute of Technology (CPIT) gave a talk entitled *Chemistry – Concepts, Context and Creating Stories* to the Head of Department day organised for secondary schools by the Canterbury Science Teachers Association.

OTAGO

The Branch again sponsored prizes for science fair projects at the Aurora Otago Science and Technology Fair, which was held in August. The recipients of the NZIC prizes were: Stuart van Turnhout and Max Freeman (Y7), *Water You Waiting For?*; Sam Howell (Y8), *Resistance*; Joshua Kim (Y9), *The Marathon of the Colours*; Joanne Rush (Y13), *What is the Concentration of Phosphate in the Kaikorai Stream*; Alliesha McMurray (Y13), *Phosphate Levels in the Upper Kaikorai Stream*; Catherine Ross (Y13), *Nitrates in the Kaikorai Valley*; and Ben Jones (Y13), *Chloride levels in the Kaikorai Estuary*.

The Branch held a student poster evening in September. The interdisciplinary event, hosted by the Otago Deparment of Pharmacy, was attended by students and academics from the Chemistry, Pharmacy and Biochemistry Departments, who discussed the finer points of their research over refreshments and nibbles. It is hoped the successful turnout (over 40 attendees and 20 posters) will become an annual event.

Finally, the Branch held its Annual General Meeting in November. The NZIC president, *Gordon* ***Rewcastle***, attended and presented a seminar.

University of Otago

The NZIC Conference, held in Hamilton in November/December, was very well attended by Otago academics and students, representing a variety of different fields of chemistry.

The Department was very successful in the latest Marsden funding round. *James* ***Crowley*** and *Carla* ***Meledandri*** received fast start funding for their respective proposals *Readily synthesised molecular actuator* and *Shape-controlled magnetic nanoparticles for biomedical applications*. *Sylvia* ***Sander*** and her Associate Investigators, *Claudine* ***Stirling***, *Keith* ***Hunter*** and *Philip* ***Boyd***, also received funding for their proposal *From soils to seas: how does the long-term fate of aerosol iron impact ocean productivity and global climate*.

BSc Honours student, *Christopher* ***Larsen***, was named winner of the grand prize in the ANZ Elsevier Chemistry Challenge 2011. The competition required the entrant to identify a research challenge and create a mini research proposal that would address it. Chris' research proposal was titled *A Rational Synthesis Towards Specific Size Single Wall Carbon Nanotubes*. The proposals were evaluated by the Elsevier Chemistry Challenge panel of local and regional academics and the grand prize was for US $1,000 cash. The Elsevier Chemistry Challenge was open to undergraduate and postgraduate students from Australian and New Zealand Universities, and so, as an undergraduate, Chris' win was a fantastic effort.

Keith ***Gordon*** was part of a team led by David Officer (Wollongong, Australia) that won an Australian Research Council Discovery grant to study artificial photosynthesis. Keith also spent a few weeks at Tokyo Institute of Technology in November as a recipient of a Japan Society for the Promotion of Science (JSPS) fellowship to provide advanced training to graduate students. Keith also visited Kookmin, Ulsan Institute of Technology and Pusan National University in Korea, and gave seminars at AIST, Waseda, Gakushuin and Ritsumeikan University in Kyoto. Keith also attended the 38th Annual Federation of Analytical Chemistry and Spectroscopy Societies (FACSS) meeting in Reno Nevada, October 3–5, 2011. He gave an invited lecture entitled *Designing New Electronic Materials for Solar Cell Applications Using Spectroscopy and Computational Chemistry*.

The Ninth Australasian Conference on Vibrational Spectroscopy (ACOVS9) was held in Wellington in November (22–24). This was a joint effort, with *Cather* ***Simpson*** (Auckland), *Justin* ***Hodgkiss*** (Victoria) and *Keith* ***Gordon*** (Otago) co-organising the event. About fifty participants heard talks on a wide range of topics from ultrafast spectroscopy as a probe of solvation structure to identifying counterfeit medicines with Raman spectroscopy. A large number of Otago students presented at the meeting. *Sara* ***Fraser***, *Anastasia* ***Elliott***, *Raphael* ***Horvath***, *Sam* ***Lind*** and *Matt* ***Reish*** gave talks, and Jacqui Kao, *Adamina* ***Craven*** and *Holly* ***van der Salm*** gave poster presentations.

Kimberly ***Hageman*** gave a presentation at the International Conference on Chemistry in the Environment in Zurich, Switzerland in September. She also gave a seminar at the "Risk management of chemical substances based on modeling and measurements" meeting held at Yokohama National University in Japan in October.

Chris Larsen receiving the grand prize in the ANZ Elsevier Chemistry Challenge 2011

The Pursuit of Atom Economy in Synthesis

Mark Bartlett[a]

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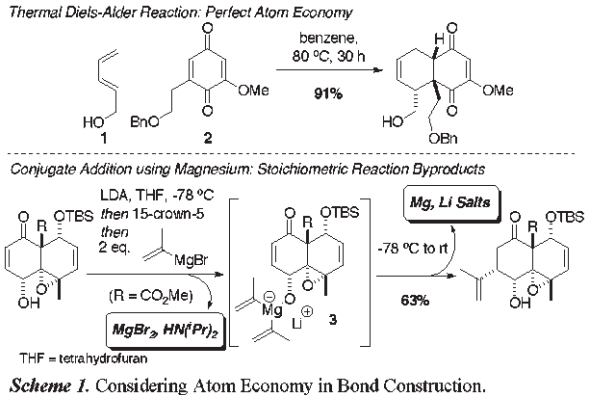
[a] Currently a visiting scholar in the Trost group at Stanford University

Dedicated to Professor Barry Trost, an inspiring chemist and mentor.

Introduction

Improving the efficiency of chemical synthesis has long been a fundamental goal for the chemical sciences. This goal has been pursued primarily through the development of new chemical transformations that generate molecular complexity in a facile and selective manner.[1] The efficiency of a chemical reaction has been measured using a variety of metrics, one of the most prominent being atom economy.[2] The Trost group has made a number of exemplary contributions to this area, developing powerful transition metal-catalyzed reactions with a wide range of synthetic applications. This article highlights recent applications of atom-economic reactions developed by the Trost group within the context of total synthesis. An emphasis has been placed on natural products connected to New Zealand through their isolation or research into their biological activity.

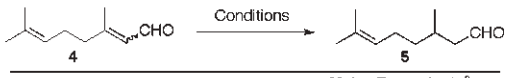
The goal of atom economy is to maximize the mass efficiency of a reaction – ideally, all the atoms of the starting materials are incorporated into the final product using only catalytic quantities of all other reagents. On a fundamental level, atom economy is enabled by the efficient activation of reagents, where control over the selectivity of bond-forming processes is paramount. In some cases the adjacent functional groups make bond forming inherently efficient, as is the case for the Diels-Alder reaction. This reaction can often occur in a stereoselective manner by simply heating the appropriate diene and dienophile, such as **1** and **2** respectively (Scheme 1).[3] The majority of cases are not as simple, and additional atoms are required to activate the reacting centres and direct reactivity. The conjugate addition shown in Scheme 1 highlights the necessity of additional atoms to activate the starting materials and direct the reaction to occur in a stereoselective manner.[4] In this case a nucleophilic carbon atom is created by the presence of an adjacent magnesium atom. Nucleophilic addition is then directed by the formation of the magnesium alkoxide ate complex **3**, which is formed by prior deprotonation of the hydroxyl group using lithium diisopropyl amide (LDA) and manipulation of the Schlenk equilibrium using a crown ether. Intramolecular delivery of the nucleophile ultimately provides a stereoselective conjugate addition, albeit with lithium and magnesium byproducts.

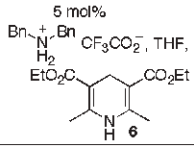
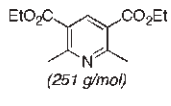


Scheme 1. Considering Atom Economy in Bond Construction.

Maximizing atom economy while maintaining high levels of selectivity remains challenging. The conjugate reduction of the α,β-unsaturated aldehyde, citral (**4**) serves to highlight the extensive efforts that are required to evolve an atom-economic solution (Table 1). This transformation posseses three major challenges: avoidance of 1,2-reduction of the aldehyde, the selectivity for the enone double bond in the presence of an electron-rich trisubstituted alkene and avoiding the generation of a reactive enolate capable of undergoing an aldol condensation. Table 1 shows a variety of conditions used to successfully perform this transformation while also considering the molecular weight of the reaction byproducts.

Table 1. Atom Economy in the Conjugate Reduction of Citral.



Conditions	Yield	Major Byproducts[a]
0.32 eq. $[(Ph_3P)CuH]_6$, 2.5 eq. TBSCl, benzene then TBAF, *p*H 7 buffer/THF	83%	$[(Ph_3P)CuCl]_4$, TBS-OH[b] *(1445, 132 g/mol)*
3 mol% $Pd(PPh_3)_4$, Bu_3SnH, THF, then H_2O/CH_2Cl_2	98%	Bu_3SnOH *(307 g/mol)*
5 mol%  $CF_3CO_2^-$, THF,	92%	 *(251 g/mol)*
10% Pd-C, NEt_3, HCO_2H, neat, 100 °C	91%	CO_2 *(44 g/mol)*
0.1 mol% $Rh(CO)_2acac$, (*R,R*)-chiraphos, H_2 (80 bar), toluene	99.8% (90% ee from *Z*-4)	none[c]

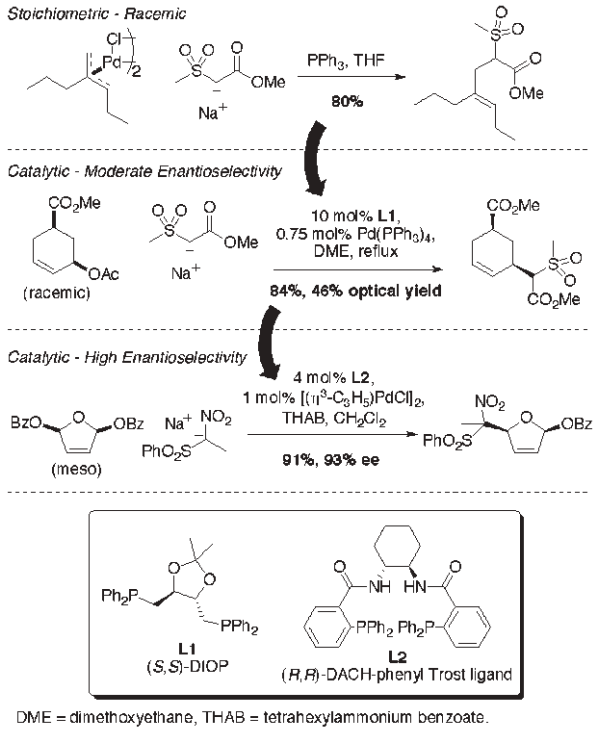
[a]Starting materials used in excess and solvents were not taken into account when considering atom economy as these can, in theory, be recycled. [b]While TBS-F is initially formed, under these conditions it is converted to TBS-OH and TBAF is regenerated. [c]While no byproducts are produced, a large excess of hydrogen gas is needed to facilitate this reaction. TBSCl = *tert*-butyldimethylsilyl chloride, TBAF = tetrabutylammonium fluoride, (*R,R*)-chiraphos = (*2R,3R*)-2,3-bis(diphenylphosphino)butane, ee = enantiomeric excess.

The use of Stryker's reagent, $[(Ph_3P)CuH]_6$, provides a very mild and selective hydride source for 1,4-reduction.[5] The resulting copper enolate is trapped as a silyl enol ether, which is subsequently hydrolyzed to produce the desired aldehyde **5**. This method does not use mass economically, producing the stoichiometric reaction byproducts $[(Ph_3P)CuCl]_4$ and TBS-OH with a combined molecular weight of 1577 g/mol. The remaining methods in Table 1 contain increasing levels of atom economy,

which include: Pd-catalyzed conjugate reduction using Bu_3SnH and hydrolysis of the resulting tin enolate,[6] organocatalytic transfer hydrogenation using the Hantzsch ester (**6**),[7] Pd-catalyzed transfer hydrogenation using formic acid and triethylamine,[8] and lastly, an enantioselective rhodium-catalyzed hydrogenation.[9] While excellent yield of the desired aldehyde **5** is obtained in all cases, the mass efficiency of most of these reactions is poor and therefore limits the broader application of this chemistry. The highly atom-economic rhodium-catalyzed hydrogenation is part of a patented process used by BASF for the industrial preparation of (-)-menthol. The rhodium catalyst used to facilitate this asymmetric transformation can be recovered after the reaction and reused multiple times.

Pd-Catalysed Asymmetric Allylic Alkylation: Total Synthesis of Hamigeran B

Palladium-catalyzed allylic alkylation, often referred to as the Tsuji-Trost reaction, has become a powerful synthetic tool and is capable of high levels of chemo-, regio-, and stereoselectivity.[10] The first report of this reaction was limited to the addition of enamine or malonate-based nucleophiles to stoichiometric π-allyl palladium chloride dimer.[11] Soon after this initial report, Trost and coworkers discovered that the addition of phosphine ligands dramatically enhanced the electrophilicity of π-allyl palladium complexes (Scheme 2).[12] This discovery greatly improved the reactivity of π-allyl palladium complexes, which significantly expanded the substrate scope of these reactions, and ultimately led to the development of chiral phosphine ligands for Pd-catalyzed asymmetric allylic alkylation (Pd-AAA).[13] Scheme 2 highlights the development of this methodology from the original stoichiometric racemic reaction to the modern catalytic enantioselective variant.

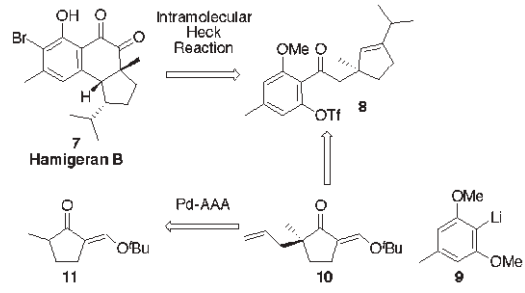


DME = dimethoxyethane, THAB = tetrahexylammonium benzoate.

Scheme 2. The Evolution of Pd-Catalyzed Allylic Alkylation.

Some of the earliest research in the Trost group on the alkylation of stoichiometric π-allyl palladium complexes was performed by Terry Fullerton, a New Zealand Fulbright Scholar conducting post-doctoral research at the University of Wisconsin - Madison.[14] Some of the most elegant applications of Pd-AAA reactions have been in the generation of chiral quaternary centres, a formidable task that often warrants special consideration in the planning of a synthesis.[15] The synthetic strategy for the total synthesis of Hamigeran B (**7**) was based on the use of a Pd-AAA reaction to form a challenging chiral quaternary center.

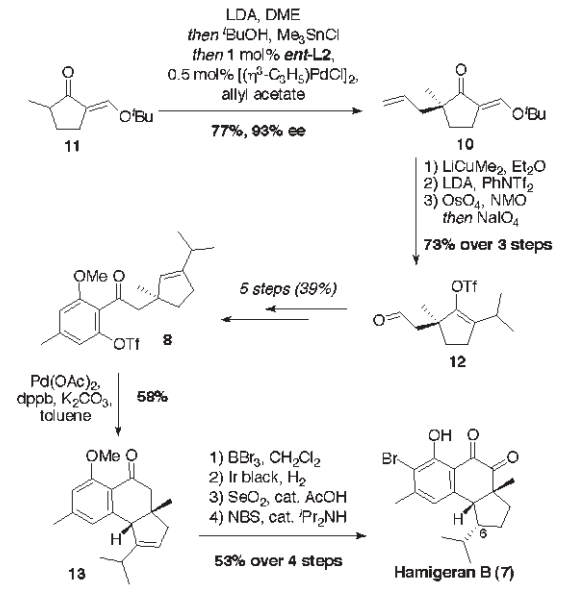
Hamigeran B is a secondary metabolite originally isolated from the poecilosclerid sponge *Hamigera tarangaensis* which Berquist and Fromont collected from the Hen and Chicken Islands in New Zealand.[16] This compound displays potent anti-viral activity against both polio and herpes viruses, with only slight cytotoxicity to host cells. Moderate anti-cancer activity against P-388 leukemia cells was also observed (IC_{50} = 13.5 μM). The principal disconnections in the retrosynthesis of hamigeran B are shown in Scheme 3. The carbocyclic core of **7** was envisioned to arise from the intramolecular Heck reaction of aryl triflate **8**. This intermediate can be traced back to the aryl lithium reagent **9** and the aldehyde produced from ozonolysis of the terminal alkene **10**. Alkene **10** could be generated using a Pd-AAA with a ketone enolate derived from **11**. This class of nucleophiles has proven to be much more challenging to employ in AAA reactions then stabilized enolates derived from β-dicarbonyl compounds.[17]



Scheme 3. Retrosynthetic Analysis of Hamigeran B.

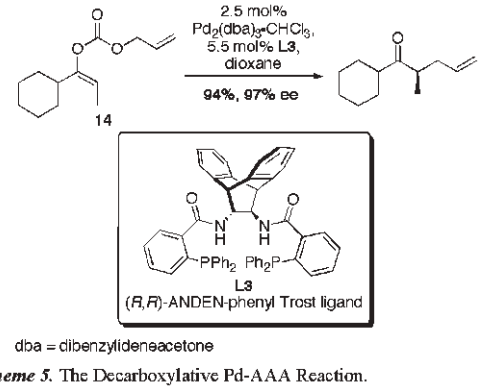
The synthesis begins with the formation of racemic ketone **11** from 2-methylcyclopentanone using a tandem formylation/vinylogous etherification sequence (Scheme 4). The prochiral tin enolate derived from **11** provides excellent yield and enantiomeric excess in the Pd-AAA reaction with only 1 mol% of the active palladium catalyst. It was discovered that when fresh *n*BuLi was used to generate LDA for this reaction the ee of the product, **10**, dropped dramatically. It was hypothesized that the presence of lithium alkoxides in older *n*BuLi sources aids the stereoselectivity of this process. It was ultimately discovered that the addition of 7 equivalents of *t*BuOH provides a reliable and scalable transformation. Lithium dimethylcuprate was then used to convert the *tert*-butyl enol ether into an isopropyl group. This was followed by formation of an enol triflate and a one-pot dihydroxylation–periodate cleavage to produce aldehyde **12**. In five steps this was converted to the aryl ketone **8** required for the intramolecular Heck reaction. The intramolecular Heck

reaction provided the desired product **13** in an optimized yield of 58%, along with two isomeric alkene side products in a combined yield of 29%. The use of a carbonate base rather than a tertiary amine base proved essential to avoid hydrogenolysis of the aryl triflate. Compound **13** was then deprotected using BBr_3, and the trisubstituted double bond reduced using an iridium-catalyzed hydrogenation to give the kinetically favoured product with the isopropyl group on the concave face of the molecule. The corresponding palladium-catalyzed hydrogenation gives the thermodynamically favoured *C6*-epimer, which is presumably a consequence of equilibration of a semi-hydrogenated intermediate. Lastly, oxidation using selenium dioxide and careful monobromination provides the natural product **7**. In total, hamigeran B (**7**) was prepared using a longest linear sequence of 16 steps.



Scheme 4. Total Synthesis of Hamigeran B.

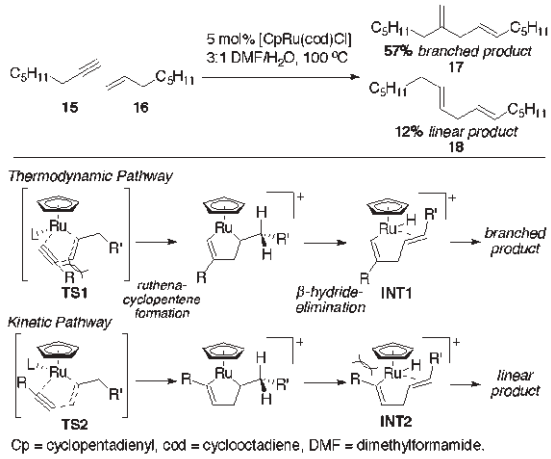
The decarboxylative Pd-AAA reaction has recently emerged as an attractive alternative to the traditional Pd-AAA with preformed metal enolates.[18] Allyl enol carbonates, such as **14**, can be used to prepare α-chiral ketones in excellent yield and enantiomeric excess, while also avoiding the use of stoichiometric tin additives (Scheme 5).[19] Ionization of the allyl carbonate and extrusion of carbon dioxide forms a cationic π-allyl palladium complex and an enolate anion. The formation of this tight ion pair is crucial in obtaining high enantioselectivity. This variant of the Pd-AAA reaction enables the use of milder reaction conditions and a wider variety of substrates.



Scheme 5. The Decarboxylative Pd-AAA Reaction.

Ruthenium-Catalyzed Alkene-Alkyne Coupling: Formal Synthesis of Mycalamide A

The formation of carbon-carbon bonds is fundamental to chemical synthesis, and yet many syntheses still depend on the use of activating groups or the presence of adjacent polarizing functionality to selectively construct these bonds. The ruthenium-catalyzed alkene-alkyne coupling provides a tool by which simple unsaturated carbons can be coupled in a highly atom-economic fashion (Scheme 6).[20] The coupling of 1-octyne (**15**) and 1-octene (**16**) produces a *ca.* 5:1 mixture of branched (**17**) and linear (**18**) products.[21] No homocoupling products of either alkyne or alkene are observed.

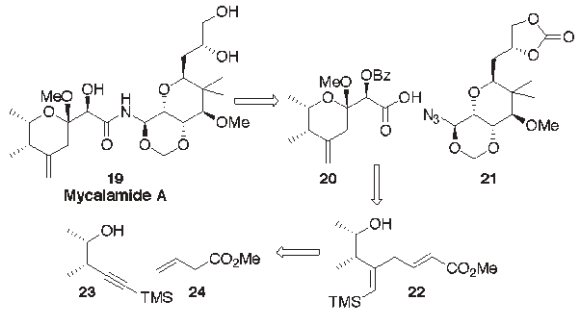


Scheme 6. Ruthenium-Catalyzed Alkene-Alkyne Coupling.

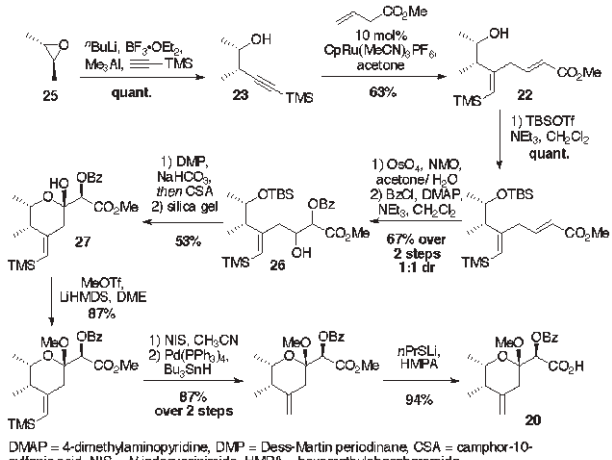
Two major mechanistic pathways have been proposed: one under kinetic control that leads to the linear product, the other under thermodynamic control that produces the branched product. The formation of the kinetic product is governed by the minimization of steric interactions in the transition state, and therefore **TS2**, where the alkynyl substituent points away from the alkene terminus, is favoured over **TS1**. In reactions where β-hydride elimination is slower than ruthenacyclopentane formation, the steric interaction between the alkynyl substituent and the $[CpRu]^+$ moiety becomes differential. Therefore, formation of the thermodynamic product is based on **INT1** being favoured over **INT2**. Utilizing certain alkyne substitution patterns and reaction conditions can lead to regioselective alkene-alkyne coupling, providing a powerful tool for chemical synthesis.

The Ru-catalyzed alkene-alkyne coupling was used to great effect in the synthesis of Mycalamide A (**19**),[22] a highly potent antitumor agent originally isolated from the New Zealand marine sponge *Mycale* sp.[23] Mycalamide A has been shown to inhibit protein synthesis and induce apoptosis in cancerous cells.[24] Retrosynthetic disconnection of the central amide bond provides (-)-7-benzoylpederic acid **20** and azide **21**, two fragments that have been utilized in a previous synthesis reported by Nakata and co-workers (Scheme 7).[25] Compound **20** was envisioned to arise from the 1,4-diene **22**, which in turn comes from the ruthenium-catalyzed alkene-alkyne coupling of **23** and the commercially available alkene **24**.

The homopropargylic alcohol **23** was prepared in a single step by the addition of TMS-acetylene to (*2S*,*3S*)-2,3-epoxybutane (**25**, Scheme 8). The steric bulk of the trimethylsilyl group serves to direct the subsequent Ru-catalyzed alkene-alkyne coupling, producing the branched product **22** regioselectively.



Scheme 7. Retrosynthetic Analysis of Mycalamide A.



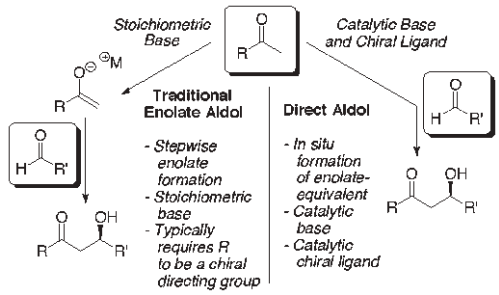
DMAP = 4-dimethylaminopyridine, DMP = Dess-Martin periodinane, CSA = camphor-10-sulfonic acid, NIS = *N*-iodosuccinimide, HMPA = hexamethylphosphoramide.

Scheme 8. Synthesis of (-)-7-Benzoylpederic Acid.

TBS-protection, dihydroxylation and selective monoesterification provided **26** as a 1:1 mixture of *syn* diasteromers. The absence of diastereoselectivity in this transformation proves to be inconsequential, as the oxidative cyclization of alcohol **26** produces a mixture of diastereomeric hemiketals that ultimately equilibrate to the desired compound **27** on silica gel. Methylation of **27** is followed by a two-step removal of the silyl group. Finally, palladium-catalyzed hydrogenolysis, followed by a dealkylative saponification provides (-)-7-benzoylpederic acid **20**. Azide **21** was prepared in 18 steps and together the two fragments constitute a formal total synthesis of mycalamide A.

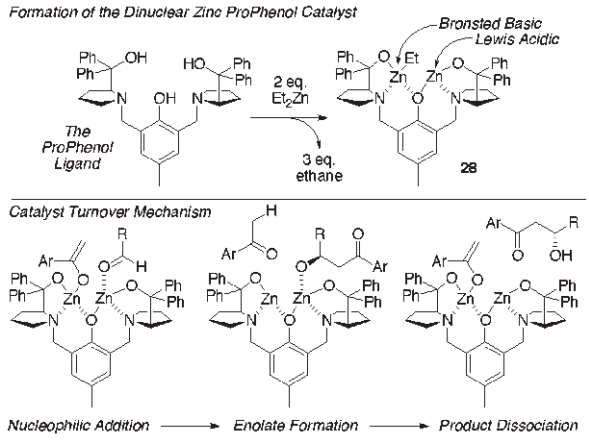
Dinuclear Zinc-Catalyzed Direct Asymmetric Aldol Reaction: Total Synthesis of Laulimalide

The aldol reaction has proven to be an incredibly powerful synthetic tool in the preparation of complex molecular targets.[26] The development of this reaction has enabled highly efficient transformations that produce β-hydroxy carbonyl compounds with excellent control of chemo-, regio- and stereoselectivity. The traditional aldol reaction involves the step-wise formation of an enolate by addition of a stoichiometric amount of base to a carbonyl donor, followed by addition of an aldehyde (Scheme 9). Control of enantioselectivity in this process has typically been achieved through the use of a chiral auxiliary on the donor, such as Evans' chiral oxazolidinone.[27] The direct aldol reaction provides an atom-economic variant of the traditional aldol reaction, avoiding the production of stoichiometric byproducts and the use of chiral auxiliaries.[28]



Scheme 9. Differentiating Traditional Enolate Aldol and Direct Aldol Reactions.

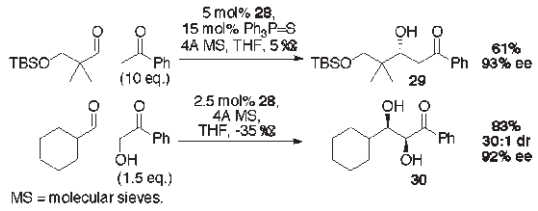
The major challenge of the catalytic direct aldol reaction with transition metal complexes is creating reaction conditions that enable catalyst turnover. The metal alkoxide that results from addition of an enolate to an aldehyde is often less basic then the starting enolate, which prevents catalyst dissociation and turnover. Chemoselectivity can also be a significant problem as the acceptor, an aldehyde, is often more acidic than the ketone or an ester equivalent used as the donor. Failure to address these issues results in low reactivity and the generation of a number of different aldehyde self-aldol side products. The dinuclear zinc ProPhenol catalyst **28** provides an elegant solution to these problems (Scheme 10).[29] This bifunctional Lewis acid/Brønsted base system serves to activate both reactants, create a chiral pocket for enantioselective addition, and acts as a proton shuttle to release the product from the catalyst.



Scheme 10. Zinc ProPhenol Catalyst and Proton Shuttle Turnover Mechanism.

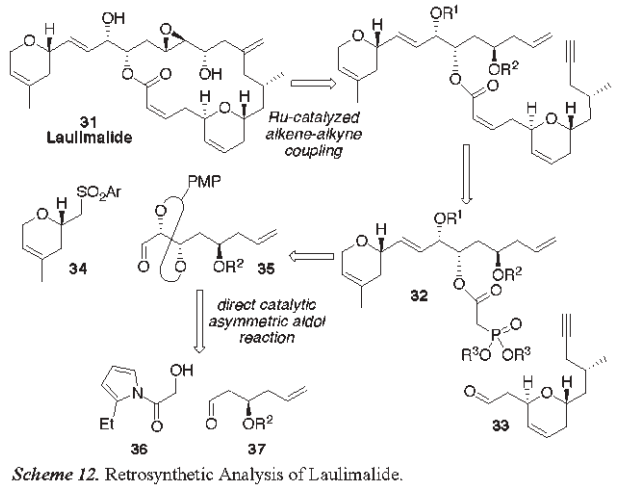
The acetophenone-based donors shown in Scheme 11 afford β-hydroxy ketone products **29** and **30** with excellent levels of enantioselectivity and good yields. Triphenylphosphine thiooxide was used as an additive to improve catalyst turnover; however, it was later discovered that the beneficial effects of this additive were limited to certain substrates.[30] A variety of α-hyxdroxy ketones have been shown to provide excellent yield, diastereoselectivity and enantiomeric excess with this methodology, creating two stereocentres in a single reaction. Interestingly, the aldehyde-derived stereocentre of **30** has the opposite

absolute configuration to the product obtained when acetophenone is used as the donor (**29**). This phenomenon is rationalized by a proposed bidentate co-ordination of the α-hyxdroxy ketone donor, bridging the two zinc atoms and altering the approach of the aldehyde to favour the opposite facial selectivity.



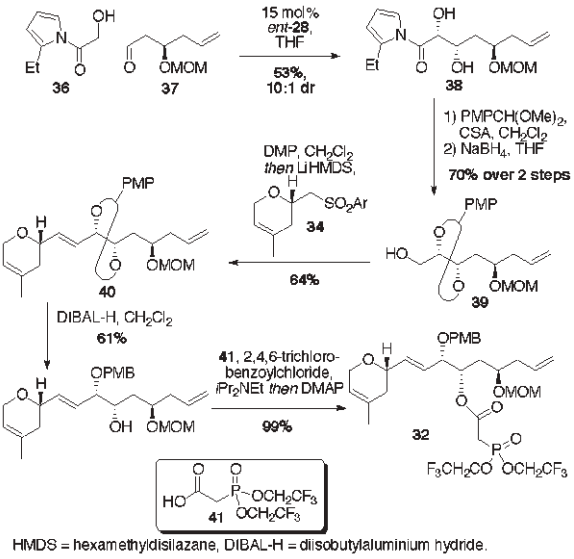
Scheme 11. Direct Asymmetric Aldol Reaction with the Zinc ProPhenol Catalyst.

The excellent atom economy and stereoselectivity of the Zn-ProPhenol aldol reaction was used to great effect in the total synthesis of the complex macrocyclic natural product, laulimalide (**31**).[31] Laulimalide displays microtubule stabilizing activity similar to that of Peloruside A, and, as a result, is highly cytotoxic towards a number of cancer cell lines.[32] The major retrosynthetic disconnections of this synthesis include macrocyclization via a ruthenium-catalyzed alkene-alkyne coupling and a *Z*-selective Still-Gennari olefination to tether the two major fragments **32** and **33** (Scheme 12). The Northern fragment **32** was envisioned to arise from Julia olefination to connect dihydropyran **34** and the protected polyol **35**, which in turn arises from the direct asymmetric aldol reaction of hydroxy 2-ethylacylpyrrole (**36**) and aldehyde **37**.



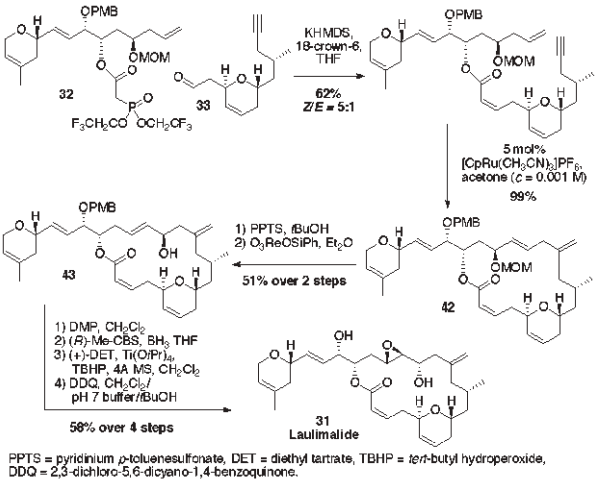
Scheme 12. Retrosynthetic Analysis of Laulimalide.

The forward synthesis commences with the preparation of the donor and acceptor for the direct asymmetric aldol reaction. Aldehyde **37** was prepared in four steps from (*S*)-glycidyl tosylate, via functional group interconversion and epoxide opening with a vinyl cuprate. The zinc ProPhenol catalyst *ent*-**28** facilitates the direct asymmetric aldol reaction of **36** and **37**, providing the desired product **38** in 53% yield and 10:1 diastereomeric ratio (dr) (Scheme 13). Formation of a *p*-methoxyphenyl (PMP) acetal followed by reduction of the *N*-acylpyrrole with $NaBH_4$ leads to alcohol **39**. Oxidation with Dess-Martin periodinane (DMP) and Julia-Kocienski olefination with phenyltetrazole sulfone **34** provided the desired *E*-alkene **40** selectively. The cyclic PMP-acetal is then selectively opened with DIBAL-H and the resulting alcohol is esterified with phosphonoacetic acid **41** under Yamaguchi conditions to complete the Northern fragment **32**.



Scheme 13. Synthesis of the Northern Fragment 32.

The Southern fragment **33** was prepared in 15 steps from *D*-aspartic acid and coupled to **32** using a Still-Genari olefination to produce a 62% yield of the desired product as a 5:1 mixture of *Z*/*E* geometric isomers (Scheme 14). Macrocylization was then achieved using an intramolecular ruthenium-catalyzed alkene-alkyne coupling. Under highly dilute reaction conditions this reaction provides near quantitative yield of the desired macrocycle **42**. MOM-deprotection under acidic conditions was then followed by allylic transposition, using a highly active perrhenate catalyst, $O_3ReOSiPh$. The desired rearranged product **43** was formed in 78% yield with complete retention of stereochemistry. The stereochemistry of the allylic alcohol was then inverted by oxidation with Dess-Martin periodinane (DMP) followed by Corey-Bakshi-Shibata (CBS) reduction. Subsequent Sharpless asymmetric epoxidation and PMB-deprotection furnished the natural product, laulimalide (**31**). The final step was performed in the presence of a pH 7 buffer to prevent the known acid-catalyzed rearrangement of laulimalide to isolaulimalide.[33]



Scheme 14. Total Synthesis of Laulimalide.

Concluding Remarks

The palladium-catalyzed asymmetric allylic alkylation, Ru-catalyzed alkene-alkyne coupling and the Zn-ProPhenol-catalyzed asymmetric aldol reaction all form carbon-carbon bonds in a highly atom-economic manner. The total synthesis of hamigeran B, mycalamide A and laulimalide clearly highlight the power and utility of these transition metal-catalyzed reactions. Although all of these syntheses rely on transformations with poor atom economy at some stage, the merit of each approach lies in the pursuit of atom-economic synthesis and the development of tools and synthetic strategies for this goal. Striving to adhere to the principles of atom economy necessitates an innovative and invention-based approach to synthesis and aids in expanding the frontiers of chemical synthesis.

Acknowledgements

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The Effect of Serendipity in Drug Discovery and Development

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Key words: *Sagacity, intuition, pharmaceuticals, anticancer and psychotropic drugs*

Introduction

It is well known that serendipity has played a pivotal role in the discovery of many drugs used today.[1-3] Indeed, two major classes of anticancer drugs were discovered with the aid of serendipity, i.e., Barnett Rosenberg's discovery of cisplatin and the breakthrough observation by Lieutenant Colonel Stewart F. Alexander that the chemical warfare agent nitrogen mustard depleted white blood cell numbers; aiding in the development of alkylation agents.[1-2] The question that therefore emerges is how important serendipity really is in drug discovery and development. The aim of this investigation is to compile a list of all marketed drugs and their derivatives used in the clinic today in which discovery was in some way based on or aided by a serendipitous event. The numbers obtained will be compared to the total number of marketed drugs, resulting in a quantitative measure of the impact of serendipity in the discovery of pharmaceuticals.

Methodology

Three books were analysed: *Laughing Gas, Viagra, and Lipitor*: *The Human Stories Behind the Drugs We Use*, [1] *Happy Accidents: Serendipity in Modern Medical Breakthroughs* [2] and *Drug Discovery, a History*.[3]In addition, one scientific paper was examined that contained a list of drugs discovered by the aid of serendipity.[4] These resources were studied and the stories containing serendipitous events were recorded. The nature of the serendipitous findings were categorised as ***laboratory based*** or ***clinical***. The drugs identified were reviewed in DrugBank [5-7] and only those that were approved, small molecule, and in clinical use were compiled. Furthermore, drugs with similar chemical structures and with the same notation (i.e., used to treat the same condition) as the parent drug were considered to be their derivatives, as identified by substructure and Tanimoto similarity searching in DrugBank.[5-7]

Serendipity in drug discovery and development

Serendipity refers to chance discoveries that have been exploited with sagacity.[3] This requires both a chance event and the mental ability to understand the occurrence and realize its potential. In this work, only stories that fit both requirements for serendipity were recorded. The serendipitous events were divided in to two categories; ***laboratory based*** and ***clinical***. A classic example of the former is Barnett Rosenberg's discovery of cisplatin, and an example of the latter is dimenhydrinate (Dramamine), which was developed as an antihistamine, but is now sold as a travel sickness medication owing to a chance observation/realisation by one of the participants in the clinical trials. The division of the drugs into these two categories is not always obvious but we believe that it helps in the analysis of the results. In his book *Serendipity* Royston M. Roberts coined the term "pseudoserendipity" to describe accidental discoveries of ways to achieve an end sought, in contrast to the meaning of 'true' serendipity, which describes accidental discoveries of things not sought. [8] Certainly, all of the drugs discovered in the clinic can be described as pseudoserendipitous according to this definition, as can many of the ones found in the laboratory.

To calculate the proportion of drugs with a serendipitous background, the total number of small molecule drugs on the market (FDA approved) is taken to be 1437, according to DrugBank.[5-7] Overington *et al.*[9] reported 1204 small molecule drugs in clinical use, which is a somewhat smaller number. It can be explained by noting that about 20 new drugs are released on the marked annually and the use of some is discontinued. Also, some drugs are allowed in Europe and elsewhere but not in the USA, which makes it difficult to define a precise number of drugs in worldwide clinical use.

In this analysis 84 drugs were identified to have serendipitous events aiding their discovery, which is 5.8% of all drugs currently in use. 31 drugs (2.2%) were found in the laboratory and 116 derivatives (8.1%) of these drugs were found, as shown in Table 1. 53 pharmaceuticals (3.7%) were discovered in clinical settings and 147 derivatives (10.2%) of those were identified (see Table 2). Therefore, in total there are 347 drugs currently on the market, in which discovery was aided by a serendipitous event, representing a staggering 24.1% of all drugs currently on the market. A graphical representation of the results is given in Fig. 1.

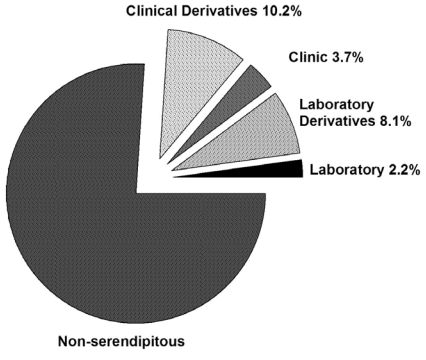

Fig. 1. The distribution of the serendipity types (***laboratory based*** and ***clinical***) and their chemical derivatives in clinical use (100% = 1437).

Serendipity in anticancer drug discovery and development

According to DrugBank[5-7] there are 88 anticancer drugs in clinical use today. Of the drugs identified with a ser-

Table 1 List of drugs discovered with the aid of serendipity in the laboratory, the number of identified derivatives and their therapeutic application.

Laboratory Drugs	Reference	Number of Derivatives	Application
Acetanilide	a(p.438) ,b	1	Antipyretic
Acetohexamide	a(p.393),b, c(p.184)	8	Diabetes II
Captopril	a(p.281), c (p.88)	8	Cardiovascular
Cisplatin	a(p.63), b, c(p.10), d(p.136)	2	Cancer
Diethylstilbestrol	a (p.196), b	1	Hormonal
Digoxin	a(p.39), c(p.84)	4	Cardiovascular
Ergotamine	a (p.341), c(p.159), d(p.296)	6	Cardiovascular
Ephedrine	a (p.100)	9	CNS
Griseofulvin	a (p.297), b	0	Antifungal
Heparin	a (p.269), b, d(p.234)	4	Cardiovascular
Isoniazid	a (p.396), b	0	Antibiotic
Lidocaine	a (p.434)	6	CNS
Lithium	a (p.62), b, c(p.140), d(p.261)	0	CNS
Marinol	a(p.111)	1	CNS
Mechlorethamine	a(p.440), b, c (p.8), d(p.122)	5	Cancer
Mecillinam	a (p.323)	1	Antibiotic
Methotrexate	a (p.249), c(p.18)	1	Cancer
Nalidixic Acid	a (p.394), c (p.69)	8	Antibiotic
Nitroglycerine	a (p.433), b, c (p.80)	2	Cardiovascular
Penicillin	a (p.289), b, c(p.54), d(p.59)	21	Antibiotic
Pentamidine	a (p.277)	0	Antiprotozoal
Physostigmine	a (p.96)	0	Ocular
Quinine	a (p.77)	1	Antiprotozoal
Sorafenib	d (p.163)	0	Cancer
Streptomycin	c (p.63), d (p.86)	7	Antibiotic
Sulfanilamide	a (p.384), c (p.50), d(p.54)	13	Antibiotic
Valproic acid	a (p.444),b	1	CNS
Vinblastine	a (p.102), c(p.12), d(p.133)	3	Cancer
Dicoumarol	a (p.111), b, d (p.236)	0	Cardiovascular
Warfarin	a (p.137), b, d (p.237)	3	Cardiovascular
Zinc Sulfate	a (p.62)	0	Wilson's disease

a=Ref.[3]; b=Ref. [4]; c=Ref.[1]; d=Ref.[2]; CNS = Central Nervous System.

endipitous origin, 13 are used to treat cancer and 18 are their chemical derivatives. This means that 35.2% of all anticancer drugs in clinical use had serendipity involvement of some kind. The statistical distribution is shown in Fig. 2. This is a larger portion of serendipitous effect than for pharmaceuticals in general, described in the previous section.

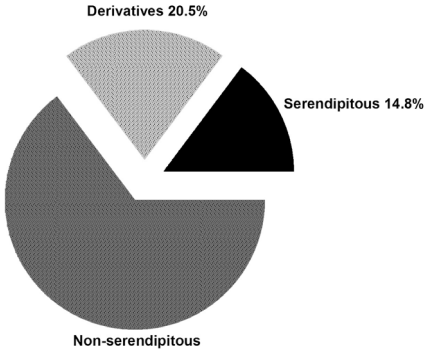

Fig. 2. The statistical distribution of anticancer drugs discovered with the aid of serendipity and their chemical derivatives in clinical use (100% = 88).

Of the primary serendipitous events anticancer drugs represent 15.5% (13/84), i.e., a sizeable portion. However, relatively few derivatives were found for anticancer drugs (6.8% of the derivatives). This highlights the difficulty in developing effective anticancer drugs.

The effect of serendipity in different therapeutic areas

When the primary serendipitous events are investigated it is clear that antibiotic, anticancer, cardiovascular and CNS drugs are the most common therapeutic application, with ~10 events for each (see Tables 1 and 2). Other therapeutic fields such as antiprotozoal and antifungal are also reported. Also, less common treatments for such conditions as gout and alcoholism occur. A high frequency of CNS discoveries is seen in the clinical settings in Table 2, i.e., 17 out of the total of 53. This reflects the difficulty in developing drugs that need to pass the Blood-Brain-Barrier[10] and the dearth of biochemical assays modelling the diseases of the mind and pain.

Discussion

Recently a new concept of Known Drug Space (KDS) has been developed to help drug designers to navigate chemical space based on the analysis of drugs in clinical use.[11-13] It is known that 10% of KDS are unaltered natural products and 29% are their derivatives (semi-synthetics).[14] Natural products are typically identified in screening pro-

Table 2 List of drugs found to be beneficial for other conditions than for which they were developed (clinical), the number of identified derivatives and their therapeutic notation.

Clinical Drugs	Reference	Number of Derivatives	Notation
Aminoglutethimide	a (p.367),b	0	Cancer
Alprostadil	a (p.186)	4	Cardiovascular
Amphetamine	a (p.130), b, c (p.160)	10	CNS
Aspirin	a (p.360), c(p.222), d (p.237)	0	Cardiovascular/Cancer
Auranofin	a (p.60) , d (p.137)	0	Anti-rheumatic
Carbamazepine	a (p.415)	1	CNS
Celecoxib	d (p.149)	0	Cancer
Chlordiazepoxide	a (p.411), b, c (p.135), d (p.282)	20	CNS
Chlorothiazide	a (p.391), b, c (p.86)	11	Diuretic
Clofibrate	a (p.274)	1	Cardiovascular
Dactinomycin	a (p.311)	0	Cancer
Diisopropyl fluorophosphate	a (p.435)	0	Ocular
Diltiazem	a (p.412)	0	Cardiovascular
Dimenhydrinate	a (p.405), b, d (p.2)	0	CNS
Diphenhydramine	a (p.405)	2	CNS
Diphenoxylate	a (p.124), b	1	Antidiarrheal
Dipyridamole	a (p.134)	0	Cardiovascular
Disulfiram	b, c (p.130), d (p.285)	0	Alcoholism treatment
Doxorubicin	a (p.313)	5	Cancer
Etomidate	a (p.335), b	0	CNS
Finasteride	d (p.311)	1	Baldness
Guanethidine	a (p.277), b	2	Cardiovascular
Haloperidol	a (p.123), b, c (p.154)	1	CNS
Imatinib	c (p.39)	0	Cancer
Imipramine	a (p.413) b, c (p.145), d (p.278)	10	CNS
Iproniazid	a (p.397), b, c (p.142), d(p.275)	1	CNS
Linezolid	c (p.144)	0	Antibiotic
LSD	a (p.350), b, c(p.159), d (p.288)	5	CNS
Meprobamate	b, d(p.271)	1	CNS
Mercaptopurine	a (p.253), c (p.19)	2	Immunosuppressive
Metronidazole	a (p.334)	1	Antiprotozoal
Mifepristone	a (p.203), b	0	Hormonal
Minoxidil	d (p.311)	0	Cardiovascular
Mycophenolic acid	a (p.289)	1	Immunosuppressive
Naloxone	a (p.120)	1	CNS
Norethindrone	a (p.200), b, c (p.118)	11	Hormonal
Pethidine	a (p.122), b	1	CNS
Phenobarbital	a (p.369)	6	CNS
Prednisone	a (p.208), b	6	Anti-inflammatory
Probenecid	d (p.78)	0	Gout
Procarbazine	a (p.397)	0	CNS
Promethazine	a(p.408), c (p.152), d (p.267)	20	Antihistamine
Quinacrine	a (p.382)	4	Antiprotozoal
Reserpine	a (p.102), c (p.138), d (p.274)	2	CNS
Salicyclic acid	a (p.358)	4	Anti-rheumatic
Sildenafil	a (p.136), c (p.111), d (p.222)	2	Erectile dysfunction
Sirolimus	a (p.306)	1	Immunosuppressive
Tamoxifen	a (p.199), b, c (p.23), d (p.139)	1	Cancer
Terfenadine	a (p.406)	1	Antihistamine
Thalidomide	c (p.20), d (p.151)	1	Cancer
Tolazoline	a (p.371)	0	Cardiovascular
Trimethadione	a (p.439)	1	CNS
Zidovudine	a (p.260), d (p.122)	5	Antiviral

a=Ref.[3]; b=Ref. [4]; c=Ref.[1]; d=Ref.[2]; CNS = Central Nervous System. LSD = Lysergische Säure Diäthylamid (lysergic acid diethylamide).

grams of soil bacteria and other biological sources, i.e., they are found but *not* designed. With this fact and the results presented in this paper it can be stated that KDS is to a large extent populated by chance rather than design. Using the drugs thus identified for analysis of their physicochemical properties reveals the right parameters for drug candidates and therefore allows for a designing element in drug discovery projects.

Serendipity in drug discovery has not been investigated to a great extent, but some papers were found in the literature. Opinions expressed vary greatly, which is not surprising

owing to the ambiguous nature of this phenomenon. For instance, Jeste *et al.* downplayed the importance of serendipity, arguing that few if any drug discoveries in their field of psychiatry were truly serendipitous. [15] Conversely, Lombardino and Lowe stated that "the role of serendipity, chemical intuition and creativity in thoughtfully selecting a chemical target to synthesize in order to discover the best-quality drug has not diminished" irrespective of the introduction of new technologies.[16] Furthermore, Klein strongly believed that a loss of chance observations and unexpected clinical benefits are due to recent changes in the process of drug discovery.[17] He criticises cost-control measures which remove a creative environment in hospitals that fosters serendipity.[17] Finally, Kubinyi suggested that researchers should not be manipulated by short-term business cycles: drug discoveries require good science, enlightened management, and freedom for researchers to act, challenge dogma and take risks.[4]

This investigation provides a limited scope of serendipitous drug discovery since only four sources were analysed. It is certain that not all serendipitous events are recorded; researchers may choose not to report them in favour of standard scientific methods of inquiry. It can therefore be argued that the impact of serendipity may be even larger than found in this investigation.

According to the results presented here ~24% of all drugs currently on the market were discovered with the aid of serendipity and, thus, may never have been discovered without the curiosity, observation, and sagacity of the researchers. This serves to highlight the unpredictability in drug research and the necessity to allow for and encourage freedom in research directions and ensure continuation of and promote the intellectual freedom of the scientists involved. Also a sound education in science is indispensable and the encouragement of critical thinking of our students is vital. The practice of teaching to the test where there are only *right* or *wrong* answers should be strongly discouraged (for further discussion see Lenox[18]).

Understanding the serendipity phenomenon is crucial so we can start to manipulate it to our advantage. We believe that quantifying serendipity's impact facilitates our understanding of it. Finally, Pasteur's comment on serendipity[19] certainly still holds true: "Dans les champs de l'observation, le hasard ne favorise que les esprits préparés" ["In the field of observation, chance favours only the prepared mind"]

Conclusions

This study found that 24% of all pharmaceuticals currently on the market were affected in a positive way during their development by serendipity, with CNS active drugs being very prominent for discoveries made in the clinic. Furthermore, 35.2% of all the anticancer drugs now in clinical use were discovered with the aid of serendipity. This leads to the conclusion that drug discovery is based on good science and intuition, critical thinking, sagacity and open-mindedness play crucial roles.

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Synthetic Cannabinoids

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Synthetic cannabinoids are a new phenomenon in the designer drug market worldwide. They are compounds that were developed over the last 40 years mainly as therapeutic agents for use in the management of pain. They are not structurally similar to any of the psychoactive cannabinoids, including tetrahydocannabinol THC (Fig. 1) found in cannabis.

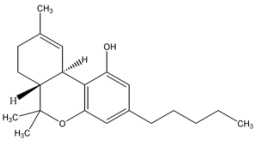

Fig. 1. THC

Synthetic cannabinoids have found a place in the drug market as they give the users a 'high' that mimics that obtained when smoking cannabis. This is because they bind to the cannabinoid receptors in the human brain and so are called cannabinoid receptor agonists. These receptors are responsible for many physiological processes including mood, pain sensation, memory and appetite.

The synthetic cannabinoids were first sold on the streets as synthetic cannabis blends. They were often marketed and sold as herbal blends or herbal smoking blends. The earlier brands on the market were "K2" and "Spice" (Fig. 2). The name "Spice" is now a generic trade name widely used in Europe to describe a herbal high product. In New Zealand and Australia the generic word "Kronic" was used when referring to the herbal blends, after one of the commercially available products being sold.

Fig. 2. Packaging and appearance of "Spice" herbal blend

The presence of synthetic cannabinoids in products being sold to the general public as herbal smoking blends first occurred in 2008.The European Monitoring Centre for Drugs and Drugs Addiction reported in *Understanding the "Spice" phenomenon* that at the end of 2008 German and Austrian authorities had both found the synthetic cannabinoid known as JWH-018 in "Spice" products.[1] In early 2009 two groups in German and Japan reported the detection of a second synthetic cannabinoid called the C8 homologue of CP 47,497.[2,3] In March 2009 the US Drugs Enforcement Administration (DEA) confirmed the presence of another synthetic cannabinoid called HU-210 in "Spice" products.[4] The synthetic cannabinoid JWH-073 was detected in powders seized in Europe.

These first three synthetic cannabinoids, reported in the scientific literature to be present in herbal smoking blends, have been synthesized along with many others, by different pharmaceutical companies and university research groups, for use as potential pharmaceutical compounds.

Since the 1990s Professor John W Huffman from the University of Clemson has led a research team developing compounds that could target the endocannabinoid receptors of the body. The team has synthesized over 450 compounds, which are commonly referred to as JWH compounds.

The structure of JWH-018, which was the first JWH compound detected in herbal blends, is given Fig. 3, and it can easily be seen that neither it nor JWH-073 (Fig. 4) are structurally similar to THC (Fig. 1)

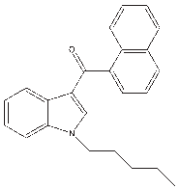

Fig. 3. JWH-018

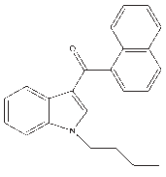

Fig. 4. JWH-073

HU-210, the synthetic cannabinoid detected in the "Spice" products analyzed in the US, (Fig. 5) is one of a series of compounds developed by Dr. Mechoulam's group at the Hebrew University in Israel and is named after the initials of the university.

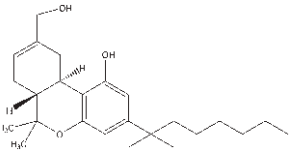

Fig. 5. HU-210

In the early 1980's a research group at the pharmaceutical company Pfizer investigated several synthetic cannabinoids for use as analgesics[5]. The compounds were known as the CP series. It was the C8 homologue of CP49,497

(Fig. 6) that was detected in the "Spice" products.

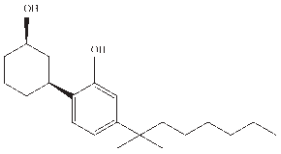

Fig. 6. C8 homologue of CP49,497

By June 2009 ESR had advised the Ministry of Health that in their opinion both HU-210 and CP47,497 and its homologues were structurally similar to THC and as such they would be defined as controlled drug analogues. In the case of JWH-018 and JWH-073, they were not structurally similar to THC and as such would not be controlled under the legislation of the time.

Over the next two years the number of herbal blends on the New Zealand and worldwide markets grew. The products could be easily bought on the internet or from "party shops". In most countries the synthetic cannabinoids found in these products, and there was often more than one per product, were not controlled. As the regulatory authorities of countries and states moved to control specific synthetic cannabinoids, initially JWH-018 and JWH-073, the composition of the products available for sale changed to replace those that became illegal. There was now a ready market for legal herbal blends and because there are large number of synthetic cannabinoids, many with known activity as cannbinoid receptors, so once one was banned, it was easy for the "industry" to use a replacement.

The synthetic cannabinoids can be grouped on the basis of their structures, as shown in Table 1.

Table 1. Synthetic cannabinoids

	Chemical name	Examples*
1	Naphthoylindoles	JWH-018, JWH-073
2	Naphthylmethylindoles	JWH-175, JWH-184
3	Naphthoylpyrroles	JWH-145, JWH-307
4	Naphthylmethylindenes	JWH-176
5	Phenylacetylindoles	JWH-250, RCS-08
6	Benzoylindoles	AM-694 (see Fig. 7)
7	Cyclohexylphenols	CP 47,497 and its homologues
8	Classical cannabinoids	HU-210

* The synthetic cannabinoids are usually referred to by their non-scientific names, and these have come about largely based on either by whom or where they were synthesized: JWH – John W. Huffman, CP – Charles Pfizer, WIN – Winthrop Pharmaceutical (Stirling-Winthrop), HU – Hebrew University, AM – Alexandros Makriyannis, RCS – believed to be "Research Chemical Supplier", an internet company selling chemicals

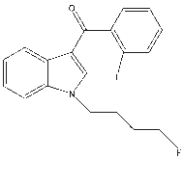

Fig. 7. AM-694

The herbal blends and smoking incenses are sold on the market as herbal mixtures in either a sealed pouch or a plastic bag held within a cardboard packet. The synthetic cannabinoids are either dissolved in a solvent and then sprayed onto the herbal mixture or the herbal mixture is soaked in the solvent which is then left to evaporate. The herbal mixtures used appear varied and are not usually specified on the packets, and have been reported to include some potentially psychoactive plants including: marshmallow, blue lotus and rosehip.[1] The wording on the packets to describe the contents often uses phrases like "natural organic extracts" and "100% legal herbs". Most of the packets are labeled "R18" and also inform the user to use in a well ventilated room. The packaging of herbal blends generally seems to be intentionally misleading and uninformative, but very eye-catching. Using ambiguous statements and labeling allows the manufacturers to avoid restrictions that would otherwise be imposed on their products. The use of imagery and wording relating to cannabis appears to be a method of indirectly informing the user of the effects of these products

In a survey carried out by the ESR Drugs laboratory in July 2011[6],43 legal herbal blend products were purchased from NZ websites and shops. (Figs 8 and 9) Eleven synthetic cannabinoids were detected in these products: JWH-018 was present in most herbal blends and there were often two or more synthetic cannabinoids in a single product. The survey also detected the presence of the prescription medicine phenazepam in two products, which were subsequently withdrawn from the market.

Fig. 8.

Fig. 9.

In August 2011, the New Zealand Government decided to list sixteen synthetic cannabinoids as Temporary Class Drugs. These sixteen synthetic cannabinoids had all been detected in the products analyzed as part of the ESR survey. In October 2011 three further synthetic cannabinoids were listed as Temporary Class Drugs.

The sixteen synthetic cannabinoids controlled in New Zealand in August 2011were JWH-018, JWH-022, JWH-073, JWH-081, JWH-122, JWH-201, JWH-203, JWH-210, JWH-250, JWH-302, AM-694, AM-2201, RCS-04, butyl analogue of RCS-04, 2-methoxy isomer of RCS-04 and the 2-methoxy isomer of butyl analogue of RCS-04. The three further synthetic cannabinoids listed as controlled were JWH-019, JWH-200 and AM-1220,

Being listed as Temporary Class Drugs means that it is currently illegal in New Zealand to import or sell these synthetic cannabinoids or products that contain them. As a result of this legislation the numerous herbal blend products that had been available to purchase from websites or in shops were withdrawn from the market.

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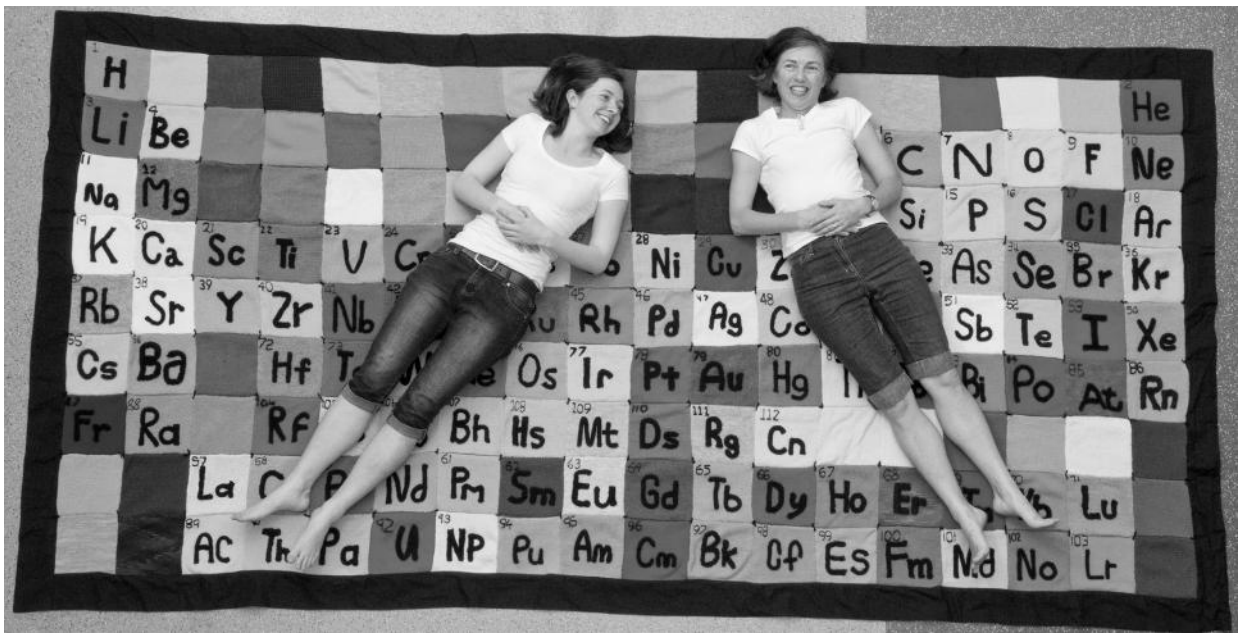
Chemistry in the News

The Periodic Table and knitting: What's the connection?

Anthea Lees



A woollen version of the Periodic table made its public debut at the NZIC conference at the University of Waikato in December 2011 and is now on permanent display in Victoria University's School of Chemical and Physical Sciences. The 'Knit the Periodic Table' project was sponsored by: the New Zealand Institute of Chemistry, Victoria University of Wellington and the Royal Society of New Zealand.

A call to knitters around New Zealand and the world, initiated by the Wellington branch of the New Zealand Institute of Chemistry, was made in August 2011 via the New Zealand International Year of Chemistry website. Knitters chose an element and were then emailed a pattern, which they followed to produce a 20 cm knitted square of this chosen element. It took over three months to complete the project and it has been estimated that over 8 km of wool was used. Some of the participants chose elements that meant something to them. Protactinium was chosen by an MSc student who had written about this element as part of her third year inorganic essay. Carbon was chosen by someone who used to work in the C-14 dating laboratories in New Zealand at a time when New Zealand had one of the few C-14 dating laboratories in the world. The element gold was knitted with wool, which had been coloured with gold nanoparticles, a process being developed in New Zealand.

Once all of the squares had been knitted and collected, they were stitched together to form a 3.5 m width Periodic table.

The project organisers Sarah and Rachel Wilcox think that the knitted version is a world first. "People have done all sorts of things with the Periodic Table – it's been sewn, baked, made into furniture and computer games. As far as we know, no one has knitted one this big before," says Sarah who is both a chemist and a knitter.

"It's also a chance to celebrate the cooperative nature of chemistry, as chemists typically work together to solve problems and make progress. Chemistry has applications in biology, physics, geology, engineering and medicine. It is part of our daily lives, though most of us are unaware of it."

Thanks go to Victoria University for use of the photograph.

Article

Chemistry of Aryl Trifluorovinyl Ethers

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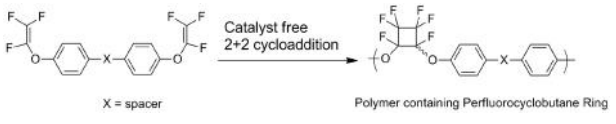
Introduction

Fluorine-containing polymers are one of the new and exciting research directions within the polymer science programme at the University of Auckland. In the plastics world, fluorine-containing polymers represent a rather specialised group of polymeric materials. Since the accidental invention of a bizarre white powder material (It was Teflon as we know today) by a DuPont scientist during his ongoing research on new refrigerant in 1938,[1] the production of fluoropolymers has grown to reach an estimated world demand of 235,000 metric ton in 2011.[2] Their many attributes include remarkable thermal and chemical attack inertness, solvent resistance and outstanding electrical properties. These properties offset their higher cost and greater difficulty in processing than is the case for most other non-fluorinated thermoplastics.

Table 1. Common fluorinated alkenes used in the production of fluoropolymers

Fluorinated Alkenes	Fluoropolymers
CF_2=CF_2	Poly(tetrafluoroethylene) PTFE
CF_2=CFCl	Poly(chlorotrifluoroethylene) PCTFE
CH_2=CF_2	Poly(vinylidene fluoride) PVDF
CF_3CF=CF_2 and CF_2=CF_2	Copolymer of hexafluoropropylene and tetrafluoroethylene (FEP)
$CF_3CF_2CF_2$-O-CF=CF_2 and CF_2=CF_2	Copolymer of perfluorovinylether and tetrafluoroehtylene (PFA)

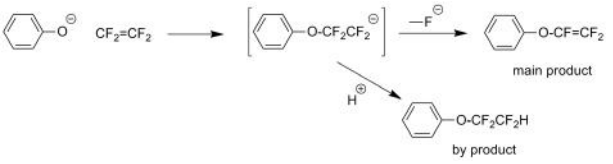
Fluoropolymers are typically made from the free radical polymerization of fluorinated alkenes.[3] Table 1 lists the most common monomers that are currently used in the manufacture of fluoropolymers. Unlike these polymers (prepared by free radical initiated polymerization), this article introduces a unique class of semi-fluorinated polymer containing perfluorocyclobutane (PFCB) ring structure (Scheme 1).[4] Linear thermoplastic PFCB polymers are prepared by [2+2] cycloaddition of a single molecule containing two aryl trifluorovinyl ether (Ar-O-CF=CF_2) groups following step growth kinetics. The synthesis and characterization of aryl trifluorovinyl ethers by different methods will be discussed.



Scheme 1. Synthesis of perfluorocyclobutane polymers via [2+2] cycloaddition of aryl trifluorovinyl ethers

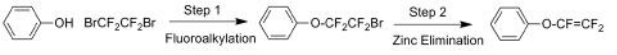
Synthesis of Aryl Trifluorovinyl Ether (Ar-O-CF=CF_2)

Aryl trifluorovinyl ethers can be prepared by several methods. In 1966 phenyl trifluorovinyl ether was obtained by the reaction of an alkali metal phenoxide (PhONa or PhOK) with tetrafluoroethylene in Parr bombs.[5] The yield of the reaction was mediocre because of the side reaction, where the reactive fluorocarbanions are trapped by the available proton donors in the reaction system to give saturated 1,1,2,2-tetrafluoroethyl phenyl ethers (Scheme 2).



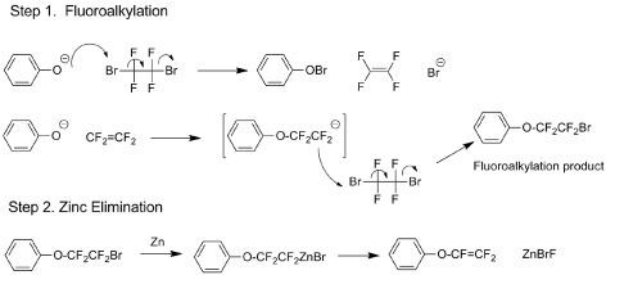
Scheme 2. Synthesis of phenyl trifluorovinyl ether using tetrafluoroethylene

A more efficient and mild way to prepare this compound in two step process (Scheme 3) was reported in 1993.[6] Starting from phenolic precursors, the first step is the fluoroalkylation with 1,2-dibromotetrafluoroethane ($BrCF_2CF_2Br$) to give 2-bromotetrafluoroethyl aryl ethers. In this reaction $BrCF_2CF_2Br$ (widely used as non-toxic fire extinguishing agent) served as a fluoroalkylation agent and as a trifluorovinyl precursor.



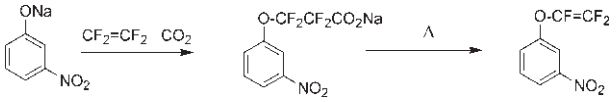
Scheme 3. Preparation of aryl trifluorovinyl ether using 1,2-dibromotetrafluoroethane

In contrast to the well-known alkylation paths, namely, S_N1 and S_N2, the fluoroalkylation reaction was rationalized by an unusual ionic chain mechanism.[7] As shown in Scheme 4, the reaction was initiated with the direct attack of electron-positive bromine (δ^+) on the $BrCF_2CF_2Br$ by phenoxide. Tetrafluoroethylene (CF_2=CF_2) was generated in-situ after loss of bromide anion. The phenoxides added to the CF_2=CF_2 to give the reactive fluorocarbanions, which were quickly terminated by bromide to form 2-bromo-tetrafluoroethyl aryl ethers. In the elimination step, zinc inserted into C-Br bond of 2-bromo-tetrafluorethyl aryl ethers in a similar way to the preparation of Grignard reagent. Finally, the aryl trilfuorovinyl ethers were obtained by the elimination of ZnBrF salt at elevated temperature.



Scheme 4. Postulated fluoroalkylation and zinc elimination mechanism.[7]

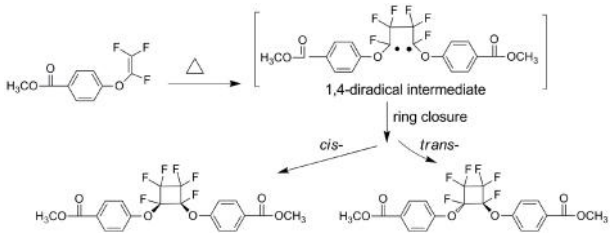
Although the above-mentioned 1,2-dibromotetrafluoroethane procedure was satisfactory for most phenolic compounds, for the deactivated phenols, such as those that are perfluorinated or that have strong electron-withdrawing groups, the reaction gave an extremely poor yield in the zinc elimination step, i.e., the zinc insertion product (Ar-O-CF_2CF_2-ZnBr) exhibited unusual stability. A new synthetic pathway to aryl trifluorovinyl ethers (Scheme 5)[8] involved the reaction of nitrophenoxide with tetrafluoroethylene and carbon dioxide to give 3-nitrophenoxy-2,2,3,3-tetrafluoropropionic acid salt. The salt was then heated up to decarboxylation temperature at 250 °C to afford the nitrophenyl trifluorovinyl ether in 46% decent yield.



Scheme 5. Nitrophenyl trifluorovinyl ether synthesized by Feiring *et al*.[8]

Cyclodimerization of Aryl Trifluorovinyl Ether

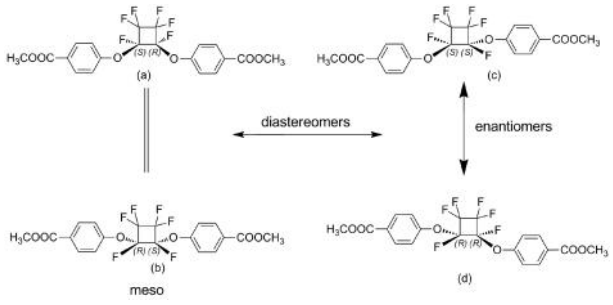
Cyclodimerization of fluorinated alkenes was observed as early as 1947 during the pyrolysis study of polytetrafluoroethylene (PTFE).[9] The ability of fluorinated alkenes to dimerize with themselves has been attributed to the energy relief of fluorinated double bond strain.[6] In the same fashion, the aryl trifluorovinyl ether groups (Ar-O-CF=CF_2) underwent thermally activated [2+2] cycloaddition to form bisaryloxy substituted perfluorocyclobutane (PFCB) rings. Scheme 6 depicts the model reaction of cycloaddition of aryl trifluorovinyl ethers. The thermal cyclodimerization of methyl 4-(trifluorovinyloxy)benzoate was carried out at 180 °C in the bulk for 12 hours under N_2. The dimer was crystallized from methanol to give a white solid in 75% yield.[10]



Scheme 6. Model reaction of [2+2] cyclodimerization of aryl trifluorovinyl ethers

According to the Woodward-Hoffman rule, thermally activated [2+2] cycloaddition took place in a non-concerted manner: the initial addition of one aryl trifluorovinyl ether to another with predominantly head-to-head regioselectivity gave a 1,4-diradical intermediate, followed by ring closure to form the 1,2-disubstituted perfluorocyclobutane (PFCB) ring. About equal amounts of the cis- and trans- stereoisomers were formed.

Further analysis of the products from cyclodimerization revealed that each cis- and trans- stereoisomer have two enantiomers. As can be seen in Scheme 7, the cis- product has two enantiomers (a) and (b), being (S, R) and (R, S) configuration respectively, according to the Cahn-Ingold-Prelog priority rules. Both the cis- enantiomers are meso compounds and optically inactive. The trans- product also has two enantiomers, being (S, S) and (R, R), which exist as non-superimposable mirror images of each other.



Scheme 7. Stereroisomerism of diester.[10]

Single crystals of cis- and trans- perfluorocyclobutane diester isomers were successfully isolated from the dimer mixture. Figure 1 illustrates the single crystal X-ray structures of cis- and trans- diesters, which provide the best evidence of perfluorocyclobutane ring structure and cis-/trans- isomerization. The cis- diester has a mirror plane of symmetry, with the PFCB ring being located perfectly in a same plane. For the trans- diester, on the other hand, the PFCB ring actually is not planar, having a dihedral angle of 162.86°.

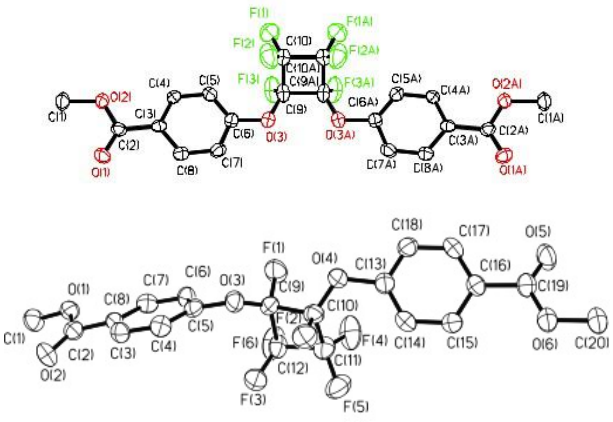


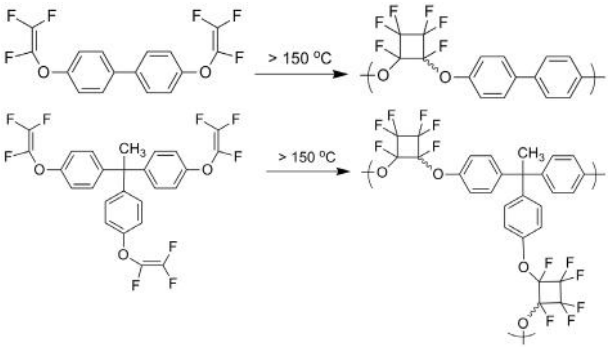
Fig. 1. Perspective drawing showing 50% thermal ellipsoids of diester single crystals, cis- (top) and trans- (bottom) stereoisomers.

Polymer Synthesis via [2+2] Cycloaddition of Aryl Trifluorvinyl Ethers

The model reaction above shows that aryl trifluorovinyl ethers have unique synthetic utilities in polymer formations. Perfluorocyclobutane (PFCB) ring-containing polymers with various macromolecular architectures (such as linear, branched and cross-linked) can be prepared by [2+2] cycloaddition of a single molecule containing multiple aryl trifluorovinyl ether groups. Typically, a PFCB polymer can be prepared by simply heating the aryl trifluorovinyl ether monomers in bulk or in solution above 150 °C. The PFCB backbone contains equal numbers of randomly distributed cis- and trans- 1,2-disubstituted hexafluorocyclobutanes. Therefore, most PFCB polymers are amorphous in nature with highly optical transparency

owing to catalyst-free polymerization processes. PFCB polymers have excellent solution processability in common organic solvents and glass transition temperatures of 120 – ~350 °C.

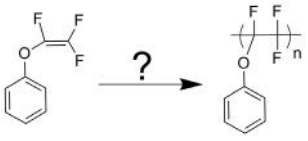
Since the phenolic compounds are accessible, PFCB polymers can easily incorporate a wide range of functional groups. Initially developed for aerospace and microelectronics applications at Dow Chemical,[6] PFCB polymers have received considerable attention as a versatile material for photonic applications,[11-12] quantum dot matrix,[13] hole transport materials for OLED[14-15] and as cross-linking groups in electro optic chromophores.[16] Scheme 8 shows two commercial examples of thermoplastic and thermosetting PFCB polymers.[6]



Scheme 8. Commercial examples of PFCB polymers

Other Attempts on Polymerization of Aryl Trifluorovinyl Ether

Besides the successful cyclopolymerization of aryl trifluorovinyl ethers, other polymerization techniques were attempted to polymerize the aryl trifluorovinyl ethers. For example, benzoyl peroxide (BPO) and azobisisobutylonitrile (AIBN) were used as free radical initiators to polymerize the aryl trifluorovinyl ether at the temperature below its cyclodimerization threshold (Scheme 9). However, they all appeared to be ineffective in producing polymers of high molecular weight. The results were unexpected when compared to the common fluorinated alkenes listed in Table 1, which are all polymerizable under free radical initiated polymerization conditions.



Scheme 9. Chain growth polymerization of aryl trifluorovinyl ether

Clearly, the free radical propagating species of aryl trifluorovinyl ethers are not stable. Aryl trifluorovinyl ethers also show no sign of photoreactivity under UV radiation.

Conclusions

In this review, various synthesis routes for aryl trifluorovinyl ether are discussed. Perfluorocyclobutane (PFCB) polymers are prepared via thermally activated [2+2] cycloaddition of aryl trifluorovinyl ether monomers. The cyclodimerizaton proceeds in a stereo-random fashion, giving roughly equal distribution of cis- and trans- stereoisomers. PFCB technology can serve as a versatile materials platform for many industrial applications. At present, free radical initiated polymerizations for aryl trifluorovinyl ethers are not successful. This is an area our laboratory has already initiated further work.

Acknowledgements

I started the aryl trilfluorovinyl ether synthesis and its polymerization when I joined Clemson University for PhD studies in 2001. I express my sincere gratitude to my research advisors and mentors at Clemson, including Dr. Dennis W. Smith Jr., Dr. Stephen H. Foulger, Dr. John Ballato, Dr. Earl Wagener and Dr. Darryl DesMarteau .

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The 2011 Nobel Prize in Chemistry

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2011 Nobel Laureate Daniel Shechtman; courtesy of the Technion – Israel Institute of Technology

The Royal Swedish Academy of Sciences has awarded the 2011 Nobel Prize in Chemistry to Dan Shechtman of Technion - Israel Institute of Technology, Haifa, Israel, for the discovery of quasicrystals. In 1982, Shechtman, a materials scientist, discovered crystals with structures that many believed to be impossible but he held his ground against fierce opposition, scorned even by luminaries including double-Nobel-prizewinner Linus Pauling. The crystals have the fascinating mosaics of the Arabic world reproduced at the level of atoms with regular patterns that never repeat themselves. This Nobel Prize in Chemistry is for work that has fundamentally altered the way in which chemists conceive of solid matter.

Dan Shechtman recorded an image counter to the laws of nature in electron microscope on the morning of 8 April 1982. He was working at the National Institute of Standards and Technology (NIST) in the US while on leave from the Technion. On entering the result into his notebook apparently he followed it with three question marks, saying to himself "There can be no such creature". The material he was studying was an unusual looking aluminium/manganese mix, which he hoped would yield useful information from electron microscopy at the atomic level. The microscope produced an image of concentric circles, each made of ten bright dots at the same distance from each other (Fig. 1) and contrary to all logic.

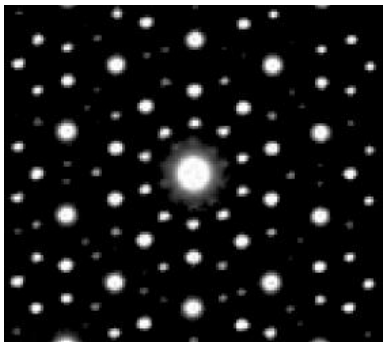

Fig. 1. Shechtman's ten-fold diffraction pattern; rotating the image through 36° results in the same pattern (adapted from *Scientific Background on the Nobel Prize in Chemistry 2011*, with permission from The Royal Swedish Academy of Sciences; www.nobelprize.org/nobel_prizes/chemistry/laureates/2011/info.htm).

Shechtman had rapidly chilled the glowing molten metal hoping for complete disorder among the atoms, but what he recorded was a pattern contrary to the laws of nature. There were ten dots in each circle - not the four or six accepted theory would generate. The crystal symmetry was not represented in the International Tables for Crystallography, and science plainly stipulated that a pattern with ten dots in a circle was impossible, and the proof for that was as simple as it was obvious. All solid matter consists of atoms symmetrically packed inside a crystal in a pattern that repeated periodically over and over again. Three-, four- and six-fold symmetries are common, but five-, seven- and higher-fold symmetries were regarded as impossible. Shechtman's image, with its ten concentric dots, showed that the atoms in his crystal were packed in a pattern that could not be repeated. In addition, having shown that he was not dealing with a twinned crystal, he rotated the crystal in the electron microscope in order to see how far he could turn it before the ten-fold diffraction pattern reappeared. That experiment showed that the crystal itself did not have ten-fold symmetry like the diffraction pattern, but instead was based on an equally impossible five-fold symmetry. If correct, the scientific community had to be mistaken in its assumptions.

When Shechtman advised colleagues of the discovery, he was faced with total opposition, even ridicule. Many claimed that he had a twin crystal, but he was sure this was not the case. Eventually, he was asked to leave his research group. However, he persisted with his study and, in 1983, he persuaded Ilan Blech, a colleague at the Technion, to look at his peculiar research findings. Together they attempted to interpret the diffraction pattern and translate it to the atomic pattern of a crystal. They submitted an article to the *Journal of Applied Physics* in the summer of 1984, but the article came back rapidly; seemingly the editor had decided it was inappropriate for publication. Shechtman then asked John Cahn, the renowned NIST physicist, to take a look at his data. Eventually Cahn did this, and then in turn, consulted with French crystallographer, Denis Gratias, in order to see if Shechtman could have missed something. According to Gratias, Shechtman's experiments were reliable and the data obtained in a manner he himself would have adopted had he conducted the experiments. Thus, it was that in November 1984 Shechtman finally published his data jointly with Cahn, Blech and Gratias in *Physical Review Letters*.[1]

The article had a dramatic impact on the crystallography community as it questioned the most fundamental truth of their science, namely, that all crystals consist of repeating, periodic patterns. Following the appearance of the paper, the wider audience subjected Daniel Shechtman to even more criticism, but, at the same time, other crystallogra-

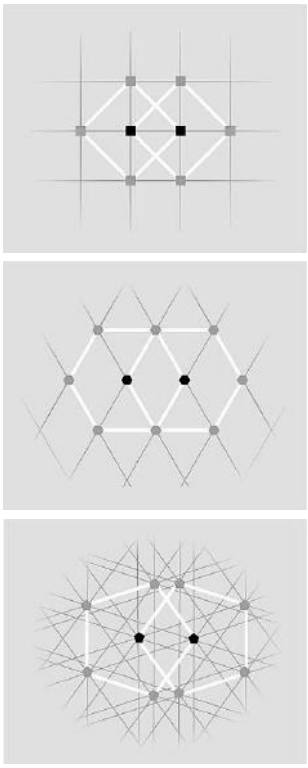

Fig. 2. Two 4-fold (upper) or 6-fold (centre) axes of rotation generate new rotational axes at the same distance of separation as in the original pair. Repeating the procedure yields periodicity. For the pair of 5-fold axes (lower), the procedure instead generates a new, shorter distance. An iterative procedure will thus fill the plane densely with 5-fold axes, and no periodicity will result (adapted from *Scientific Background on the Nobel Prize in Chemistry 2011*, with permission from The Royal Swedish Academy of Sciences; www.nobelprize.org/nobel_prizes/chemistry/laureates/2011/sci.html).

phers began to reassess results they had obtained, but presumed to be generated by a twinned crystal. Examples of quasicrystals flooded in from around the globe. Over the next while, other crystals began to appear with equally seemingly impossible patterns, such as eight- and twelve-fold symmetry.

At the time that Shechtman published his discovery, he still had no clear grasp of what the interior of the strange crystal looked like. Evidently its symmetry was five-fold, but how were the atoms packed? The answer to that question came from an unexpected quarter – that of mathematical games with mosaics.

During the 1960s, mathematicians began to explore whether a mosaic could be laid with a limited number of tiles so that the pattern never repeated itself, to create a so-called *aperiodic mosaic*. First successful in 1966, British professor Roger Penrose subsequently provided a more elegant solution by creating mosaics with just two different tiles, *e.g.* a fat and a thin rhombus.[2] His findings have since been used to analyze medieval Islamic Girih patterns, and it is now known that Arabic artists produced aperiodic mosaics out of five unique tiles as early as the 13th century. Such mosaics decorate the extraordinary Alhambra Palace in Spain and portals and vaults of the Darb-i Imam Shrine in Iran. Crystallographer Alan Mackay took to applying the Penrose mosaic to the atomic world to see whether atoms could form aperiodic patterns like the mosaics. An experiment in which circles (representing atoms) were substituted at intersections in the Penrose mosaic and then used as a diffraction grating actually provided ten-fold symmetry – ten bright dots in a circle.[3] The connection between Mackay's model and Shechtman's diffraction pattern was made by physicists Paul Steinhardt and Dov Levine.[4] During the review process of Shechtman's1984 article,[1] Steinhardt got the opportunity to read the manuscript and he realized that Mackay's theoretical tenfold symmetry really existed in Shechtman's laboratory. On Christmas Eve, 1984, only five weeks after Shechtman's article appeared in print, Steinhardt and Levine published an article where they described quasicrystals and their aperiodic mosaics.[4] The name "quasicrystals" was coined in this article and is a material that exhibits long-range order in a diffraction experiment and yet does not have translational periodicity.

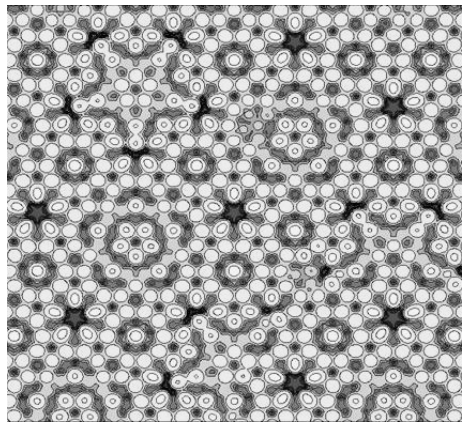

Fig. 3. Atomic model of an Al-Pd-Mn quasicrystal surface (*en.wikipedia.org/wiki/File:Quasicrystal1.jpg*).

In order to describe Shechtman's quasicrystals, a concept that comes from mathematics and art - *the golden ratio (τ)* – has to be invoked. In quasicrystals, the ratio of various distances between atoms is related to the golden mean. This mathematical constant occurs over and over again. Thus, the ratio between the numbers of fat and thin rhombi in Penrose's mosaic and the ratio of various distances between atoms in quasicrystals is always related to τ. In the mathematical number sequence 1, 1, 2, 3, 5, 8, 13, 21, 34, 55, 89, 144, 233, *etc*., each number is the sum of the two preceding numbers. Moreover, if a higher number in the sequence is divided by the preceding number, *e.g.* 233 by 144, the resulting number is close to the golden ratio. Both this *Fibonacci sequence* and the golden ratio are important in crystallography when a diffraction pattern is used to describe quasicrystals at the atomic level. Prior to the acceptance of Shechtman's results, chemists interpreted regularity in crystals as a periodic and repeating pattern, three-, four- and six-fold symmetries. The Fibonacci sequence too, is regular, despite never repeating itself, simply because it follows a mathematical rule. Thus, the golden ratio τ appears naturally in all manifestations of five-fold symmetry as the relation between the diagonal and the edge in a regular pentagon; it is inextricably linked to the Fibonacci sequence.

The interatomic distances in a quasicrystal are patterned in

an orderly manner, and the diffraction data allow one to see what a quasicrystal looks like on the inside. Importantly, however, this regularity is not the same as that for a periodic crystal. This realization led the International Union of Crystallography, in 1992, to alter its definition of a crystal. Previously, a crystal had been defined as *a substance in which the constituent atoms, molecules, or ions are packed in a regularly ordered, repeating three-dimensional pattern*, but now the definition is broader and is *any solid having an essentially discrete diffraction diagram.* This allows for possible future discoveries of other kinds of crystals.

The quasicrystals discovered by Shechtman in 1982 were synthetic intermetallics, and since then such systems have afforded very many quasicrystalline materials. The first quasicrystalline material in a different system came from dendrimer liquid crystals, but it was only in 2009 that the first report of naturally occurring quasicrystals appeared.[5] An alloy of aluminium, copper and iron, acquired by an Italian museum in 1990, but reported to have come from 200-million-year-old rocks in the Khatyrka River in Chukhotka, Eastern Russia, provided a diffraction pattern with ten-fold symmetry. The mineral was named icosahedrite, after the geometrical solid with sides consisting of twenty regular three-cornered polygons and with the golden ratio integrated into its geometry. Quasicrystals have also been found in very durable steel made by a Swedish company. They formulated a steel the analysis of which showed it to consist of two different phases - hard steel quasicrystals embedded in a softer kind of steel. Enhanced strength is seen because the quasicrystals function as armour; this product is now used in razor blades and thin needles for eye surgery. Despite being very hard, like glass, quasicrystals can easily fracture. Their unique atomic structure makes them poor conductors of heat and electricity. They have non-stick surfaces and are useful thermoelectric materials. Today, quasicrystals are being examined for use as in, amongst other things, surface coatings for frying pans, components for energy-saving light-emitting diodes (LEDs), and for heat insulation in engines.

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Additional information at *http//nobelprize.org*

Science Scene

Rutherford Medal

The 2011 Rutherford Medal, which is New Zealand's highest science and technology honour, was awarded to Professor Christine Winterbourn FRSNZ from the University of Otago. Professor Winterbourn was awarded the medal for her outstanding achievements and discoveries in free radical biology which have established her as a leading world authority in this field. She is the first woman to receive the award in its 20 year history. Prof Winterbourn did a Masters degree in Auckland in a class of thirty students of whom four were women. While she was honoured to get the medal, she did not think it was particularly significant that it had taken 20 years for a woman to win it. "I think it is more that the people who get these [Rutherford Medal] awards are at a certain time in their career, it is not a young person's award. It is more a randomness of coming from an era where women were very much in the minority. I know I will be the first of many," Winterbourn said.

Manhire prize for Creative Science Writing

Two chemists have been awarded the 2011 Royal Society of New Zealand Manhire prize for creative writing. As 2011 was the International Year of chemistry, the competition theme was 'Chemical world'.

Ten fiction entries were placed on the shortlist and Dr. Bridget Stocker of the Malaghan Institute of Medical Research in Wellington was the winner having written a piece entitled *Radium- a love story* which was told from the point of view of Marie Curie. Dr. Stocker was a participant in the Marie Curie series of lectures given throughout New Zealand during the International Year of Chemistry 2011.

In the non- fiction category eleven entries made the short list and the winning piece was entitled *100% Chemical Free*. Dr. Joanna Wojnor of the University of Auckland takes a look at the misuse of the term 'chemical free' and the negative connotations that go along with the term 'chemicals'. Other titles on the shortlist included: *The Nature of Weetabix* by Phillipa Werry and *Pectin, Radium & the Science of Making Gooseberry Jam* by Virginia Gow. The winners received $2,500 at a presentation function in Wellington.

All of the shortlist entries can be see on the website: *http://www.royalsociety.org.nz/programmes/competitions/manhire-prize/2011/*

New Zealand International Science Festival

Planning for the New Zealand International Science Festival is underway with the appointment of Chris Green as the new festival director for 2012. He states: "The great thing about being involved with such an event is the community spirit that exists to help bring it all together. The way in which community groups, Universities, Polytechnics, volunteers and businesses work together to make it all happen is exciting. There is a real creativity in our city, and the way in which people use their imaginations to create such an awesome experience for people of all ages makes the NZ International Science Festival something special to be a part of. The eighth New Zealand International Science Festival will take place in Dunedin, from 30 June to 8 July 2012. It will have more hands-on events based around the theme 'what makes us tick?' and will focus on presenting events that are inspirational as well as sheer fun, with the aim of raising public awareness of the role that science plays in all aspects of our everyday lives.

Dates of Note

Konrad ***Bloch*** was born on Jan 21, 100 years ago. He was a German-born American biochemist who shared the 1964 Nobel Prize for Physiology or Medicine with Lynen for discoveries concerning the natural synthesis of cholesterol and of fatty acids. It was Bloch who identified the chemical process by which the body turns acetic acid into cholesterol and discovered the point at which it is possible to regulate the amount of cholesterol the body produces. He also found that high blood levels of cholesterol cause fatty deposits on the inner walls of arteries. On the same day 222 years ago (1790), *Joseph-Ignace* ***Guillotin*** proposed the guillotine to the newly formed National Assembly of Paris as a humane method of execution. In comparison, on Jan 22, 15 years ago American *Lottie* ***Williams*** was reportedly the first human to be struck by a remnant of a space vehicle after re-entering the earth's atmosphere.

Morris William ***Travers*** was born on Jan 24, 1872. He was the English chemist who worked with Sir William Ramsay in London and discovered krypton on May 30, 1898. The name derives from the Greek word for *hidden* as it was from a fraction separated from liquid air that it was identified. *Ilya* ***Prigogine***, the Russian-born Belgian physical chemist who received the Nobel Prize for Chemistry in 1977 for his contributions to non-equilibrium thermodynamics, was born 95 years ago on Jan 25. On Jan 26, 1932, the US Patent Office received an application for the cyclotron by *Ernest Orlando* ***Lawrence*** as a *Method and Apparatus for the Acceleration of Ions*.

Feb 1 marks the 40th anniversary of the first commercial scientific hand-held calculator, the HP-35, while it was on the 2nd, 50 years ago that eight of the nine planets lined up for the first time in 400 years. Feb 7 marks the 5th anniversary of *Alan* ***MacDiarmid***'s death. He would have been 85 years old on Apr 14 this year. On Feb 8, 1672, *Isaac* ***Newton*** read his first optics paper before Royal Society in London. *Moses Gomberg*, the Russian-born American chemist who initiated the study of free radicals in chemistry when he first prepared the triphenylmethyl radical in 1900, died 65 years ago on Feb 12. This day also marks 100 years since *Robert* ***Millikan*** began collecting data from his famous oil drop experiment. *Étienne-François* ***Geoffroy***, who was the first to recognize the relative fixed affinities of reagents for one another, was born on Feb 13, 1672. It is 75 years on Feb 16 since *Wallace* ***Carothers*** received his patent for the synthetic fibre nylon. *Gottlieb* ***Kirchhof***, the German-Russian chemist who applied the first controlled catalytic reaction to produce glucose and developed a method for refining vegetable oil, was born on Feb 19, 1764. *Friedrich Konrad* ***Beilstein*** known for his famed *Handbuch* was born on Feb 17, 1838. *Herbert Henry* ***Dow***, founder of what is now the Dow Chemical Company, was born on Feb 26, 1866. Feb 27 marks 80 years since the discovery of the *neutron* by *James* ***Chadwick***. He was an English physicist who studied at Cambridge, and in Berlin under Geiger, then worked at the Cavendish Laboratory with Rutherford, where he investigated the structure of the atom. Feb 29, 1908 saw the first production solid helium by Dutch scientists.

Edward U. ***Condon***, the American physicist remembered for the Franck-Condon principle, was born on Mar 2, 1902 whilst on Mar 3, 1892, the first tuberculosis test on cattle in the US was made by Dr *Leonard* ***Pearson*** with tuberculin that he had brought from Europe. Mar 4, 1967, saw the first North Sea gas piped ashore to BP's Easington terminal on the east Yorkshire coast. The same day ten years later saw the first Freon-cooled Cray-1 supercomputer shipped to Los Alamos Laboratories in the US. Mar 5, 1808 saw the birth of *Petrus Jocobus* ***Kipp*** inventor of the Kipp's apparatus, while Mar 7, 1897 witnessed *John* ***Kellogg*** serve the world's first cornflakes to his patients at a mental hospital in Battle Creek, Michigan. *Charles* ***Friedel***, of Friedel-Crafts fame, was born on Mar 12, 1832. *Irène* ***Joliot-Curie*** died on Mar 17, 1956 while her husband *Frédéric* ***Joliot-Curie*** was born on Mar 19, 1900. Mar 18, 1987 was the day, 25 years ago, that the discovery of high-temperature superconductivity was announced at a packed meeting of the American Physical Society in New York City. Initially, the phenomenon (discovered in 1911) was known to occur only at 4° above absolute zero, when all electrical resistance in a metal sample disappeared. In 1986, researchers discovered a ceramic material that was a superconductor at a temperature of more than 30° above absolute zero.

The Sydney Harbour Bridge was opened on Mar. 19, 1932. Mar 23 is especially notable as, 50 years ago, in 1962, the first compound of any inert gas was made by *Neil* ***Barlett***. Platinum hexafluoride was reacted with xenon to form $XePtF_6$, a yellow-orange solid that was stable at room temperature. The previous autumn, he had prepared the remarkable compound $[O_2]^+[PtF_6]^-$ from oxygen and platinum hexafluoride. In that compound, the PtF_6 was such a strong oxidizer that the oxygen formed a positive cation. He recognized that the energy needed to remove an electron from oxygen (12.2 eV) was very close to that for xenon (12.13 eV) and this led to his remarkable product that ended the half-century belief that xenon was an inert gas; it is now known as a *noble* gas. On Mar 30, 1842, physician *Crawford W.* ***Long*** of Georgia, was the first to use ether as an anaesthetic during a minor operation.

Richard Wilhelm Heinrich ***Abegg*** was the German physical chemist who, in 1899 with Boländer, proposed a theory of valency to explain the capacity of an atom to combine with another atom in light of the newly discovered presence of electrons within the atom; he died on Apr 3, 1910. *Wilhelm* ***Ostwald***, the German chemist who almost single-handedly organized physical chemistry into a nearly independent branch of chemistry, died on Apr 4, 80 years ago, the same day that *C. Glen* ***King*** (University of Pittsburgh), isolated vitamin C, after five years of effort. On Apr 7, 1827, *John* ***Walker***, an English pharmacist, recorded his first sale of the friction matches he invented the previous year. *Robert Burns* ***Woodward*** was born on Apr 10, 95 years ago; additional to numerous complex natural

products syntheses, he evolved the concept of conservation of orbital symmetry with Hoffmann. The same day 350 years ago was the one, in 1662, that *Robert* ***Hooke*** read his first publication, a pamphlet on capillary action, to the Society for the Promoting of Physico-Mathematical Experimental Learning.

Apr 14, 1912, is the day 100 years ago that the *Titanic* sank. *David* ***Sarnoff*** picked up a message of distress call of the *Titanic* relayed from ships at sea: *S.S. Titanic ran into iceberg, sinking fast.* He was a 21 year old telegraph operator managing a powerful Marconi radio telegraph station on top of Wannamaker's department store in New York. He stayed at his post for 72 hours, receiving and transmitting the first authentic information on the disaster. On Apr 16, 1992, thalidomide was reported by Johns Hopkins medical researchers to improve the survival rate of patients who get bone-marrow transplants. *Glenn T.* ***Seaborg***, the American nuclear chemist who had the element he discovered named after him whilst still alive, was born 100 years ago on Apr 19. *Pierre* ***Curie*** died on Apr 19, 1906 as a result of an accident with a horse-drawn vehicle while Apr 20 is 100 years to the day that he and his wife, *Marie* ***Curie***, isolated 1 g of radium, the first sample of the radioactive element; it was refined from eight tons of pitchblende ore.

Brian Halton

School of Chemical & Physical Sciences

Victoria University

IP initiative takes aim at neglected diseases

Tim Stirrup and Katherine Hebditch

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The World Intellectual Property Organisation (WIPO) has announced a collaborative initiative between pharmaceutical companies and the global health research community to share intellectual property (IP) assets and expertise. The aim is to encourage the development of new drugs, vaccines and diagnostics to treat malaria, TB and neglected tropical diseases.[1]

The new initiative *WIPO Re:Search* will be managed by the non-profit organisation Bio-Ventures for Global Health (BVGH). Companies and research organisations will commit to making IP assets available under royalty-free licences to qualified researchers anywhere in the world. The assets are publicly available for view at *www.wipo.int/research/en/search/* and include patents, lead compounds and associated data, unpublished results, regulatory data and dossiers, screening technologies and expertise and know-how in pharmaceutical research and development. The programme states that it will offer the opportunity for researchers to work directly with scientists at pharmaceutical companies to advance R&D on these diseases.[2]

Just as important as the database is the establishment of the "Partnership Hub" to be run by BVGH. This hub will aim to foster collaboration between the organisations while BVGH will provide licensing support to the collaborators. As WIPO Re:Search moves forward, it is hoped that offerings from current partners will continue to grow while new providers join and contribute further to the information, compounds, and services available.

Pharma industry leaders back initiative

The impressive list of industry backers means that there exists real potential to open up the research vaults of some of the big players to allow access by stakeholders not solely driven by the bottom line. Alnylam Pharmaceuticals, AstraZeneca, Eisai, GlaxoSmithKline, Merck Sharp & Dohme, Novartis, Pfizer, and Sanofi have signed up to collaborate with a number of research organisations including the U.S. National Institutes of Health (NIH), California Institute of Technology, the Center for World Health & Medicine, the Drugs for Neglected Diseases initiative, Fundação Oswaldo Cruz (Fiocruz), Massachusetts Institute of Technology, Medicines for Malaria Venture, PATH, the South African Medical Research Council, the Swiss Tropical and Public Health Institute, the University of California, Berkeley, and the University of Dundee (UK). It is hoped that the initiative will facilitate new partnerships to develop treatments for the diseases that are often prevalent in very poor populations.

WIPO Re:Search is open to all organisations that agree to allow a selection of their IP relating to neglected tropical diseases to be licensed on a royalty-free basis for research and development in any country. The IP assets must also be offered on a royalty-free basis for sale of neglected tropical disease medicines in, or to, least developed countries.

Neglected tropical diseases

The development of treatments for malaria and tuberculosis is mentioned specifically but other diseases that are less well known are targeted under the banner of "neglected tropical diseases". This term is used by the World Health Organisation (WHO) to refer to less well known tropical diseases such as the parasite-borne diseases visceral leishmaniasis (VL), sleeping sickness (human African trypanosomiasis / HAT), and Chagas disease.

Although the collaborative effort to research and develop novel treatments for neglected tropical diseases is to be lauded, in many cases, high-tech solutions are not necessarily the answer. Many of the diseases already have effective treatments and the major problems are how to pay for and distribute the medicines, and how to educate the population about effective prophylactic measures. As stated in the First WHO Report on Neglected Tropical Disease[3]: *Control of*

neglected tropical diseases today relies on two pillars: access to treatment with safe and effective medicines available free of charge to affected populations, and judicious use of pesticides for vector control.

Interventions by the WHO that embody these two pillars have in many cases been phenomenally successful in reducing morbidity and mortality caused by neglected tropical diseases. For example systematic screening and treatment of at-risk populations have reduced cases of sleeping sickness to their lowest level in 50 years. In 2010, there were 7139 new cases, compared with 9878 cases in 2009, a decrease of 28% in just one year. This intervention was partially made possible by the donation of eflornithine, melarsoprol and pentamidine from Sanofi, which is also contributing US$25 million from 2011-2016 to support WHO's human African trypanosomiasis control programme. Similarly, Bayer, GSK, Johnson & Johnson, Novartis, Pfizer and Merck have made significant contributions of medicines and cash to support treatment programmes for a number of neglected tropical diseases.

A criticism that has been levelled at a number of big players in the Pharma industry is that the vast majority of their research dollars and expertise are used to develop high value treatments for diseases that afflict relatively rich populations. Whether true or not, the expensive, high quality research and trials that are carried out by big pharma are a vital part of validating products before they are brought to market. The high price of patented medicines means access by the world's poorer populations is often initially severely limited. Despite this, many tried and tested treatments are eventually made available to all but the poorest populations as a result of the indispensable competition provided by generic manufacturers.

This is not to say that pharmaceutical companies could not do more and Bio-Ventures for Global Health (BVGH) aims to persuade them to do so. BVGH was set up in 2004 with a start-up grant from the Bill & Melinda Gates Foundation, and the support of the Biotechnology Industry Association (BIO) of the USA and the Rockefeller Foundation. BVGH develops financial incentives to engage biopharmaceutical companies in global health research and development as well as delivering information on how they can apply their expertise and technologies to global health problems.

Evolution of the pharma industry

The provision of free medicines to poorer populations appears to be a growing facet of pharma company behaviour, possibly driven by the public pressure for positive corporate social responsibility strategies. The WIPO Re:Search programme fits well with these strategies as well as potentially providing a new perspective on shelved research programmes. There also exists the possibility of new IP being developed as a result of the programme that is not subject to the royalty-free agreements for use of existing IP.

A further aspect of the initiative that is suggestive of the future strategy of pharmaceutical companies is the collaborative approach sought with academic and governmental research institutions. The decline in success rates for new drugs[4] and the expiry of a number of patents on yesterday's blockbusters[5] is leading the industry away from the traditional "closed" model of big in-house R&D spend, towards a more open, collaborative model. As part of this transition, pharmaceutical companies are forming partnerships with biotech start-ups and academia to boost early-stage discoveries and secure IP rights to tomorrow's blockbusters. The collaborative approach to tackling global health issues and the open-sourcing of even a small portion of the knowledge held by pharma can only be a good thing and we look forward to the prospective treatments coming to fruition.

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

tim.stirrup@baldwins.com and *katherine.hebditch@baldwins.com* Patent Proze, Baldwins Intellectual Property, PO Box 5999, Wellesley Street, Auckland

References

1. Conditions covered by the WIPO Re:Search initiative include Buruli ulcer, Chagas disease (American trypanosomiasis), cysticercosis, dengue/dengue hemorrhagic fever, dracunculiasis (guinea-worm disease), echinococcosis, endemic treponematoses (yaws), foodborne trematode infections (clonorchiasis, opistorchiasis, fascioliasis, and paragonimiasis), human African trypanosomiasis (African sleeping sickness), leishmaniasis, leprosy, lymphatic filariasis, malaria, onchocerciasis, rabies, schistosomiasis, soil transmitted helminths, trachoma, tuberculosis, podoconiosis, and snakebite.
2. WIPO Re:Search Brochure/Flyer (October 2011) *http://www.wipo.int/export/sites/www/research/en/docs/flyer2011_10_20.pdf* Accessed 29 November 2011.
3. First WHO report on neglected tropical diseases *http://whqlibdoc.who.int/publications/2010/9789241564090_eng.pdf Accessed 29 November 2011*
4. Press Release on the 2010 Pharmaceutical R&D Factbook complied by CMR International. *http://thomsonreuters.com/content/press_room/science/RandD-roductivity-Declines* Accessed 29 November 2011.
5. Pharmaceuticals & Biotech Industry Global Report 2011. *http://www.imap.com/imap/media/resources/IMAP_PharmaReport_8_272B8752E0FB3.pdf* Accessed 29 November 2011.

Katherine Hebditch and Tim Stirrup of Baldwins Intellectual Property in Auckland specialise in chemistry and biotechnology patents. Katherine obtained her PhD in organic chemistry from the University of Manchester in the UK in 2004. She is currently working towards registration as a patent attorney. Tim obtained his PhD in molecular biology from the University of Southampton in the UK in 2007. He is also working towards registration as a patent attorney.

The Molecular Anthology competition

Vyacheslav Filichev

Institute of Fundamental Sciences, Massey University, (e-mail: *V.Filichev@massey.ac.nz*)

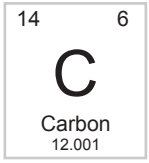
The *Molecular Anthology* competition was run by the Manawatu Branch of the NZ Institute of Chemistry as part of the activities of the 2011 International Year of Chemistry.

In the first stage of the competition, members of NZIC and the public were invited to nominate molecules or materials which, in their opinion, have changed New Zealand society. A brief description for each entry was placed on a web-site (*http://molecularanthology.massey.ac.nz*), which could help people to judge the impact of the molecule in our lives. The 39 entries received included molecules like caffeine, cholesterol, insulin, phosphate, Vitamin B-12 and water. Some less well known molecules were also nominated; examples included 2-isobutyl-3-methoxypyrazine, a compound with a very strong aroma; and Bi-2223, a semiconductor material.

In mid-July the second stage started and the web-site was opened for voting until late August. Overall, 395 votes were received. Carbon, with 87 votes, attained the first place. What a coincidence that carbon is a part of the IYC2011 logo! Caffeine was second, with 70 votes, while 1080 and keratin shared third place with 39 and 36 votes, respectively. While we thank everyone who made this project possible, our special gratitude goes to Ms Judith Edwards[1] who helped us to set up the Molecular Anthology web-site.

The descriptions of the winning molecules from the people who submitted them initially are given below.

First Place: Carbon



Carbon

I beg yo*ur pardon, Mrs Hawarden,*
But there's a problem in your garden.

It's about a kind of stuff called carbon.
Without it, all our lives would harden.

It's the very core of life, you see -
This essential building block called C.

There's lots of it down under ground.
And it helps the sea make that swishing sound.

It's in the soil, and every tree
And my dad says it makes me, me.

The air we breathe holds quite a bit
Of a relative Dad calls CO-shit.

Earthquakes make trouble with every jolt,
But it's no good to look for fault.

When the earth makes shakes,
It's very scary but carbon isn't airy-fairy!

It's a bigger problem anyhow:
The world's too warm, right here, right now.

The puzzle that we most need to play
Is getting some carbon out of the way.

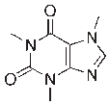
Spike and Frank O'Connor
12 May 2011

The nomination for carbon included a poem written by a dad (Frank) and a son (Spike). Here is the story that Frank told:

"The first line comes from a poem from my childhood, the second line is a twist on that poem's second line and we created our own entirely from there. So the credit should read Spike and Frank O'Connor… Spike turned nine this April, has an insatiable curiosity about the natural world (visible and otherwise), names David Attenborough as his favourite television personality and seems to have his grandfather's ability to piece things together to understand interrelationships from different fields of knowledge. This grandfather is a Massey Alumnus, from '49, and went on to a PhD from Cornell, time with DSIR then to a Chair at Lincoln.

"In Spike's second year, he often asked me to draw him a picture and make up a story. 'Fish' was Spike's first word, so they were included. Then he began to ask for drawings of taniwha and other animals doing particular things. A year passed and Spike began to draw his own pictures and to suggest words for my poems which began to grow alongside. In a book getting prepared for publication, Frank made the drawings and polished these poems; Spike tested rhythms, after suggesting rhymes and the antics of the taniwha. We did the same with this poem – he wanted the earthquakes included, for example, to add something from his own experience and feelings to the poem."

Second Place: Caffeine



On the far side of the river valley the road passed through a stark black burn. Charred and limbless trunks of trees stretching away on every side. Ash moving over the road and the sagging hands of blind wire strung from the blackened lightpoles whining thinly in the wind. A burned house in a clearing and beyond that a reach of

1. Involvement with this project was one of the last contributions Judith Edwards made to the chemists at the Institute of Fundamental Sciences at Massey University; she passed away on 4 December 2011.

meadowlands lay abandoned. Farther along were billboards advertising motels. Everything as it once had been save faded and weathered.

"One can only speculate on Cormac McCarthy's inspiration for the post-apocalyptic world that he envisioned in *The Road*. But it's a fair bet that he would have been in a better mood, had he started his day with a freshly brewed cup of coffee.

"Caffeine is an alkaloid synthesized from purine nucleotide precursors by a number of plant species. It is well known for its stimulatory effects on the human central nervous system, and it has been consumed for thousands of years. According to legend, sometime around 3,000 BCE a few leaves from a tea tree blew into a bowl of water that had just been boiled for the Chinese emperor, Shennong. He took a sip, and was pleasantly surprised by the flavour and restorative properties of the concoction.

"Here in New Zealand, tea has also been the caffeinated drink of choice for much of our recent history. From colonial times until the 1970s, the average Kiwi consumed around 3 kg of tea per year. Tea bags were introduced in 1969, but this advance in technology wasn't enough to stop the rise of coffee culture – first through the introduction of instant coffee (in the 1960s), and then through the proliferation of coffee roasters, espresso machines and trendy cafés with snobby baristas.

"As our most widely consumed psychoactive drug, it is difficult to conceive of a molecule that has had a bigger effect on the minds (and hearts, and tongues, and nostrils, and stomachs, and bladders) of New Zealanders. It is impossible to imagine our society functioning without it: from smoko in the shearing shed, to lattes in the boardroom, caffeine permeates our culture. Life without it would indeed be faded and weathered.

"But thankfully, caffeine-containing drinks remain legal! Though as chemists, it is worth remembering that caffeine is also considerably more soluble in ethanol (150 g L^{-1}) than it is in water (20 g L^{-1}). It's something to keep in mind, for your next departmental Christmas party…"

Wayne Patrick

Dr. Wayne Patrick is a Senior Lecturer in Biochemistry at the Institute of Natural Sciences, Albany Campus, Massey University and one of the recently announced recipients of the prestigious 2011 Rutherford Discovery Fellowships. In Patrick's laboratory, tools from functional genomics, directed evolution, microbiology and enzymology are used to address a fundamental question in molecular evolution, *viz*., "Where do new enzymes and metabolic pathways come from?" His web-site *http://patricklab.massey.ac.nz/* has more about his research interests.

Third Place: Keratin and 1080

Keratin

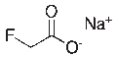
"New Zealand is globally known for its high-quality merino wool. Keratins are fibrous proteins which comprise the structure and large portions of the cell composition of living organisms. There are two primary keratins: the alpha-keratins and the beta-keratins. While both fulfil similar roles, they differ slightly in structure, composition and properties. The alpha-keratins are slightly basic or neutral and form a right-handed helical structure; the beta-keratins are slightly acidic and also form a right-handed helical structure. Keratins, as fibrous proteins, are elongated molecules in which the secondary structure forms the dominant structure. These proteins are the biological structural component of skin (soft keratins) and of nails, claws, hair, horn, feathers, and scales (hard keratins). Keratin from wool is a reactive, biocompatible, and biodegradable material. Pure keratin comprises up to 90% by weight of wool. Merino wool is typically 3-5 inches in length and is very fine.

"Man has used natural animal products, hides, furs and – eventually – wool throughout the ages for warmth and protection from the environment. Today wool continues to be popular for use in both apparel and textiles. This continued use and development of wool as a textile material over such a long period strongly suggests that this fibre has something special to offer. As long as there is grass for sheep to eat, they will produce wool. Like the South Island landscape where the Merino sheep thrive, the fibre itself results in garments ranging from practical and rugged, to the exquisitely beautiful. New Zealand Merino wool is used internationally in a variety of market segments: luxury suiting, fashion knitwear, active outdoor and lifestyle products. The finest Australian and New Zealand Merino wools are known as 1PP which is the industry benchmark of excellence for Merino wool that is 16.9 microns and finer."

Marianna Bulgarella

Marianna's interests in the natural world led her to pursue a career in Biological Sciences. As an undergraduate student at Patagonia National University in Argentina, she studied thermal physiology of guanacos, a camelid species. Later, she obtained a PhD degree at the University of Alaska Fairbanks, focusing on the population genetics and adaptation to high-altitude in the crested duck, a waterfowl species endemic to the Andes of South America. Her research interests include evolutional biology, population genetics, and physiological adaptation. Currently, she is a Postdoctoral Fellow at Massey University studying local adaptation in tree weta.

1080



"A controversial molecule with a very strong tie to New Zealand is a compound referred to as "1080" (read ten-eighty) after a catalogue number. The scientific name of the compound is sodium 2-fluoroacetate and it is a compound that is highly toxic to mammals.

"Before the arrival of humans to New Zealand there were no native mammals (bar some species of bats and cetaceans) and since the introduction of mammals by man the native fauna has been greatly threatened.

"Owing to threat from introduced mammals, the near absence of native mammals, the limited toxicity of 1080 to birds and its rapid decomposition, this compound is widely used in New Zealand, particularly in the South Island. However, in addition to wildlife-threatening rodents and possums the compound also kills dogs, cats and livestock: this issue combined with misunderstanding makes the use of fluoroacetate controversial among the farming community.

"This contention is manifest on road signs that bear the graffiti "ban 1080", which is enigmatic to tourists driving along New Zealand's beautiful tolkeinesque countryside: after all, "1080" is just a number to most people. In fact, this compound is unknown in the rest of the world, making it a compound with a strong link to New Zealand, which accounts for 80% of the global usage of 1080."

Matteo Ferla

Matteo is a PhD student in the biochemistry laboratory of Dr. Wayne Patrick doing enzyme evolution. He is half Italian and half English and has been in NZ for two years.

Conference Calendar

Asia Pacific Science Policy Studies (SPS) Research Conference

8-10 February 2012, Wellington

This conference, the first of its kind in New Zealand, explores how science policy is developed and implemented, and how scientific knowledge is used in the policy process and decision-making by governments and industry.

The conference will consider the broad sweep of social research on the relationships between science (including social science) and policy decision-making for national wellbeing through science, technology and innovation.

The programme offers a compelling line up of keynote addresses, contributed papers, events focused on indigenous contributions to science policy studies, and interactive opportunities. Contributed papers from across the Asia-Pacific region have been accepted from multiple disciplines and paper sessions will be guided by knowledgeable chairs and discussants. Early bird registration is open.

www.sps2012.org.nz/

Challenges in Organic Chemistry and Chemical Biology (ISAC S7)

12-15 June 2012, Edinburgh, UK

This will be the first event in the International Symposia on Advancing the Chemical Sciences (ISACS) series in 2012.

Organic chemistry is a core area of chemistry. Fundamental research in synthesis is leading to innovation through process improvement and invention of new types of transformations. Novel procedures can create the new substances which society needs to develop.

www.rsc.org/ConferencesAndEvents/ISACS/ISACS7/index.asp

ICOS 19- 19th International Conference on Organic Synthesis

1-6 July 2012, Melbourne, Australia

Conference Topics include: Total Synthesis of Natural Products; New Reagents and Reactions; Asymmetric Catalysis; Prospects in Bioorganic Chemistry and Chemical Biology; Synthesis of Organic Materials. Abstract deadline is 21 February 2012.

www.icos19.com/

Challenges in Inorganic and Materials Chemistry (ISACS8)

19-22 July 2012, Toronto Canada

This will be the second event in the International Symposium on Advancing the Chemical Sciences (ISACS) series in 2012

Themes: Catalysis; Total Synthesis; Methodology and Bioorganic Chemistry.

www.rsc.org/ConferencesAndEvents/ISACS/ISACS8/index.asp

21st IUPAC International Conference on Physical Organic Chemistry (ICPOC 21)

9-13 September 2012, Durham University, UK

ICPOC is the leading international conference on Physical Organic Chemistry and Chemical Reactivity. The conference will consist of plenary, invited and contributed lectures, as well as poster sessions.

www.rsc.org/ConferencesAndEvents/RSCConferences/icpoc21/index.asp

Grants and Awards

2012 Zonta Science Award Call for Applications

The Zonta Club of Wellington is calling for applications for the 2012 Zonta Science Award. The award has been established to further the status of women in scientific fields. The award is for an emerging woman scientist (i.e., a recent PhD graduate, not a woman well established in the science arena), not the top woman scientist in her field. Priority will be given to areas of science where funding is not readily available.

The aims of the award are to: encourage women to pursue a career in science; actively promote science as a career for women; encourage others already in the scientific field; and acknowledge the valuable contribution of women scientists.

The award recipient receives – $10,000 cash to fund travel expenses and/or research material and equipment; return air travel to Europe or the USA (to be used to attend professionally related conferences or places of further study); and a medal.

Applications must be received by 10 February 2012. For more information and the application form contact Wendy Saunders, Convenor, 2012 Zonta Science Award, Zonta Club of Wellington, PO Box 10274, Wellington.

Email: *saunderswendy77@gmail.com*

Management training award for women in science, engineering or architecture 2012

Applications are invited from women working in architecture, engineering or science who would benefit from a course in management training. The award is for $5,000 and may be used for fees, travel or other purposes relevant to undertaking the training such as child care. Applicants will have a graduate degree, be employed in an architecture, engineering or science company or institution.

Applicants will need to provide the selection panel with the following documents: brief C.V.; letter from their employer supporting the intended training (if self employed please justify the training requirement); details of the intended management course; budget for using the award.

The award will be granted on the merit of the application and is conditional on acceptance into a management course. Preference will be given to Wellington applicants or women attending a management course at a Wellington institution. Applicants who are already undertaking management training are also eligible to apply.

Applications to be sent to: The Scholarship Officer, N.Z. Federation of Graduate Women Inc. Wellington Branch, PO Box 2006, Wellington 6140.

Closing date: 20 February 2012.

Marsden Fund Preliminary proposal deadline 28 February 2012

www.royalsociety.org.nz/programmes/funds/marsden/application/timetable/

Charles Fleming Fund Publishing award

Up to $8,000 available annually to support the preparation of scientific books and relevant publications.

Deadline: 30 March 2012

www.royalsociety.org.nz/programmes/funds/fleming/publishing/

Charles Fleming Fund Senior Scientist Award

Up to $10,000 is available annually to support the research of a senior scientist at a university or Crown Research Institute in New Zealand, and that of their research group.

Deadline: 30 March 2012

www.royalsociety.org.nz/programmes/funds/fleming/senior-scientist/

James Cook Research Fellowships

Administered on behalf of Government, these are awarded to researchers who have the requisite qualifications and experience and are able to demonstrate that they have achieved national and international recognition in their area of scientific research. The Fellowships allow them to concentrate on their chosen research for two years without the additional burden of administrative and teaching duties.

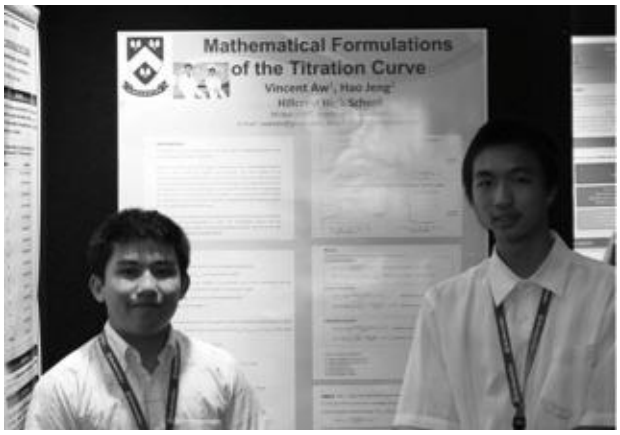
Categories for 2012:

- Biological sciences (including biotechnology)
- Physical sciences (including chemical sciences; geosciences, mathematical and information sciences)

Deadline: 29 June 2012

www.royalsociety.org.nz/programmes/funds/cook-fellowships

NZIC Conference Images



Top left: The quiz winners, The Faculty of Huge Manatees and Social Sciences (Melanie Nelson, Sarah Hoyte, Theresa Vaughan) from Victoria University of Wellington. ***Bottom left:*** Poster presenters Vincent Aw and Hao Jeng from Hillcrest High School. ***Top right:*** Communicator of the year James Lewis receiving his prize from NZIC President Gordon Rewcastle.