Chemistry IN NEW ZEALAND

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The fascinating chemistry of nudibranchs and their potential for new drug discovery

Covalent organic cages from symmetrical resorcin[4]arenes

Examining the structure and function of metal nanoparticles: a marriage of theory and experiment

Repurposing construction and demolition waste: a review of current recycling strategies

Methodologies for the determination of honey composition – an introduction to honey chemistry

The chemistry of Epichloë endophytes in New Zealand perennial ryegrass

Published on behalf of the New Zealand Institute of Chemistry in January, April, July and October.

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NZIC Chemistry IN NEW ZEALAND

Volume 85, No.3, July/October 2021

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Comment from the President

Greetings all! We find ourselves almost at the end of another year influenced by COVID and in the midst of another level 4 lockdown (August 2021). We still need to jump through hoops to get our international students across borders, research supplies ordered from overseas are delayed and businesses find it difficult to find skilled staff to fill job vacancies. However, our country is becoming increasingly vaccinated and this offers some hope for a freer 2022 in terms of people movements although obviously, the "Delta variant" of COVID is a "game changer".

There have been a number of happenings within the Institute and one which has had us collaborate with RACI in regard to relaying concerns. As you know, Pacifichem released its fee structure for virtual participation which unfortunately came as a shock to many here and in Australia who were planning to engage with the conference in an online capacity. Not only were the fees very high but the potential for participation in all "live" streamed events severely curtailed. We, along with RACI, issued a statement that was sent to the organising committee of Pacifichem to register our concern about this. A brief Twitter survey was also organised by Samantha Eason to gauge the feeling from chemists here and we got a reasonable level of response to that survey after a brief period of time of sending it out. The response from the organising committee to our concerns was that the expense of live streaming all face to face talks would have been prohibitive. They stated that the accessibility to preloaded talks is better than it would be if people were to participate as a face to face attendee. We thus have to accept this ruling and encourage people to maintain their participation where possible. At least the participation rate for students - for whom the experience of attending Pacifichem is the most valuable - is reasonable. Hence, it is hoped that despite the limitations you encourage your research students to participate if they already had plans to do so. It is still a lot cheaper than flying there and staying in a hotel and they would have access to a lot of reported research.

In other news, we have had a great number of applications/nominations for our NZIC prizes, especially the Easterfield Prize. We hope that by the time this issue comes out in print we will be able to announce the winners of these prizes.

The final piece of news to provide is that we have recently appointed a subcommittee to oversee and discuss the digitisation of our Chemistry in New Zealand journal. We wish to move right away from the print version of the journal and move to a wholly digital offering. This means being able to render the journal into a more exciting and interactive format and it will be the role of the committee to look more into these aspects.

I wish you all a safe and pleasant entry into spring as we move into the concluding months of 2021.

Michael Mucalo
NZIC President

In the April 2021 issue of *Chemistry in New Zealand*, two articles on Mātauranga Māori were reprinted from *New Zealand Science Review.* While permission to republish these articles was sought from and granted by the original publisher, the authors themselves were not contacted. Furthermore, it was discovered after their publication in *Chemistry in New Zealand* that it was unclear as to who owned copyright of the articles. As a result, the NZIC Executive has decided to remove these articles from the electronic version of the April 2021 issue. The editor apologises to the authors for any distress caused.

News

AUCKLAND

The University of Auckland

Events

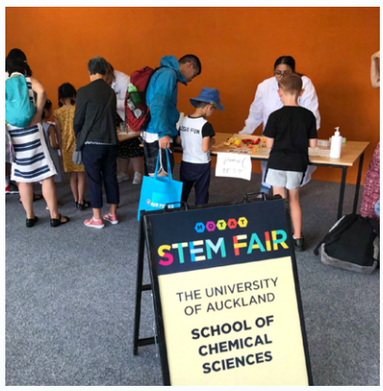
Our 2020 research highlights report has been published and includes introductions to new research academics who joined us in 2020, snapshots of recent grant successes and examples of research from our five research themes (Advanced Materials and Technologies, Chemical Sciences for Human Health, Innovations in Food and Beverages, Green Chemical Science for a Sustainable Future, and Pushing the Boundaries of Fundamental Chemistry). This was an initiative from the following SCS staff: **Erin Leitao, Davide Mercadante, Kirsty Anderson, Jadranka Travas-Sejdic, Victoria Louise Smith, Maya Breen, Izak Tait** and **Michael Groom.**

IUPAC Global Women's Breakfast

The IUPAC Global Women's Breakfast was held on the 9 February, sponsored by the NZIC Auckland Branch. This year's theme was Empowering diversity in science and all genders were invited to participate. The event was opened by **Distinguished Professor Dame Margaret Brimble** who shared her experience of working with IUPAC. Around 40 scientists from AUT and UoA working in chemistry and related fields at various career stages joined over the course of the breakfast and had a great time connecting with each other.

Creative Chemistry at the MOTAT STEM Fair

The School of Chemical Science had a booth at the MOTAT STEM Fair and it was a huge hit, with hundreds of eager primary students learning how to paint with acid/base chemistry and create their own colourful chromatography.



MOTAT STEM Fair

Farewells

Farewell to **Dr Wan-ting Chen**, who leaves SCS to take up a research scientist position at the National Synchrotron Radiation Research Center in Taiwan. Wan-ting completed a PhD in the Waterhouse Group in 2017 and since that time has been working as a research fellow in the SCS, with her research focused on the synthesis and synchrotron characterisation of new catalysts for the energy sector.

School of Chemical Sciences Seminars

Inaugural Lectures

Professor Duncan McGillivray gave his inaugural lecture in May entitled, *Wandering on the edge – making sense of (bio)material interfaces*. His talk highlighted that often scientific careers are not all carefully planned out, and that you should seize opportunities as they arise.

Professor David Barker gave his inaugural lecture entitled, *Molecule making – opportunity taking: a journey in synthetic chemistry.*

SCS Seminar Series

Dr Peter Swedlund (University of Auckland) presented *From molecules to systems: musings on using vibrational spectroscopy to gain insights into foods.*

Dr Sinisa Vidovic of Plant and Food gave a talk on *Adaptive stress physiology of non-typhoidal salmonella: microbiological linkages with food safety.*

Dr Juhong Chen of the Department of Biological Systems Engineering, Virginia Tech) presented on *Advanced and innovative biosensors for food safety.*

Dr Sophia Rodrigues of the University of Auckland talked about *Food oral processing: why the journey from food to bolus matters.*

NZIC Seminar Series

Dr Luija (Luke) Liu of Victoria University of Wellington presented on *Metal-organic framework-based 2D magnetic semiconductors*.

Dr Courtney Ennis of the University of Otago talked about *Laboratory simulations of Titan's cyanide aerosols.*

NZIC Chemistry Careers Evening

The Auckland Branch of NZIC hosted a Chemistry Careers Evening on 2 August. The event was attended by representatives from 10 companies that employ chemists; AsureQuality, ESR, Douglas Pharmaceuticals, Scion, Environmental Decontamination Ltd, Mint Innovation, Hill Laboratories, Ligar, Resene and Watercare. These representatives gave short presentations relating to the roles in their company they would look to chemistry graduates to fill, particular skills or attributes that they look for and upcoming opportunities. Attendees then had an opportunity to talk further with the representatives from each company during a networking breakout session. This event was well attended following on from the successful inaugural event last year with approximately 150 attendees from the University of Auckland, AUT and Massey University present.

Staff Successes

Davide Mercadante, in collaboration with the Selenko NMR group at the Weizmann Institute of Science in Israel, has just published a paper on the recognition of specific lipid signatures by α-Synuclein – the major protein player in Parkinson's disease. In this study, α-Synuclein has been related to specific lipid structures inside cells. This knowledge will help to understand both the physiological role of the protein (currently unknown) and its development towards assemblies that characterise fibril formation leading to severe neurodegenerative diseases, i.e. Parkinson's. The collaboration is now evolving towards the characterisation of the protein's supramolecular assemblies on lipidic cellular structures by looking at the protein directly inside cells.

Erin Leitao and **Kun Woo Park** had their article entitled, *The link to polysulfides and their applications featured on the cover of Chemistry Communications*.

Professor Penny Brothers was named an Honorary Fellow of the Royal Society of New Zealand for her many contributions to chemistry and to the study of porphyrins and their chemical cousins. Penny is currently the Director of the Research School of Chemistry at the Australian National University and she has a fractional appointment with UoA.

Dr Muhammad Hanif was awarded the Alan Sargeson Lectureship by the Inorganic Chemistry Division of the Royal Australian Chemical Institute (RACI). The Alan Sargeson Lectureship is a prestigious early career researcher award that acknowledges significant and innovative individual contributions to the field of inorganic chemistry by researchers within ten years of their PhD. The award is associated with a lecture tour of Australian and New Zealand Universities.

Distinguished Professor Bill Denny was made a Knight Companion of the

Order of New Zealand in the Queen's Birthday Honours for his services to medical research. Bill received his PhD from the then Department of Chemistry in 1969 and is an Honorary Professor in the School of Chemical Sciences. Bill recently retired as Co-Director of the Auckland Cancer Society Research Centre, which he had joined in 1972 and had been Director of since 1999. He still has a part-time role with the Centre. His research teams have taken 15 cancer drugs to clinical trials and have also developed an anti-tuberculosis drug. He co-founded the companies Proacta Inc, Pathway Therapeutics and Kea Therapeutics to commercialise the medicinal chemistry discoveries from his team. Amongst those activities, he also found time to lecture a module on drug discovery to our postgraduate students.

Bill has received much recognition for his research, including the Rutherford Medal for Science and Technology and the ACS Award in Medicinal Chemistry.

Matheus Vargas Orbis Diagnostics is one of the four finalists in the Breakthrough Innovator Award section of the Kiwinet Research Commercialisation Awards this year. Matheus is the Chief Scientific Officer of the start-up company Orbis Diagnostics, founded by **Cather Simpson** and **David Williams**, who have developed a "lab on a disk" to measure antibodies against SARS-CoV-2. Matheus based his PhD on developing the "lab on a disk" technology for milk analysis, and he and Orbis then pivoted to using this technology for the immunity assay.

Student Successes

Vice-Chancellor's Prize for Best Doctoral Thesis (2020)

Thuy Trang Pham won a Vice-Chancellor's Prize for Best Doctoral Thesis (2020). Trang's thesis entitled, Synthetic applications of the chitin-derived platform 3-acetamido-5-acetylfuran (3A5AF) was selected as one of five VC prize recipients out of the 471 doctoral degrees awarded in 2020. Trang was supervised by Jon Sperry during her PhD.

Nilushika Thambugala Athukoralalage, a PhD candidate in Food Science, won first prize for the NZIFST (New Zealand Institute of Food Science and Technology) annual poster competition held in Palmerston North in June.

The LH Briggs Prize for best PhD thesis from the SCS was awarded to **Thuy Trang Pham**. Trang studied the synthetic applications of a simple molecule derived from shellfish chitin. Her supervisor, **Jon Sperry**, says that Trang kick-started his sustainable synthesis programme. Trang is currently doing postdoctoral research with Professor Ning Yan at the University of Singapore.

PhD Defences

Essie Pearl successfully defended her PhD thesis, *Synthetic studies towards portimine A: the direct synthesis of 1,4-diketones in complex natural products*, supervised by **Dan Furkert** and **Margaret Brimble**.

Aakanksha Rani successfully defended her PhD thesis, S*ynthesis and self assembling properties of peptide-based hydrogels*. Aakanksha was supervised by **Margaret Brimble**, **Iman Kavianinia** and **Paul Harris** in the Brimble/Harris peptide lab in the School of Biological Sciences. Aakanksha's research was multidisciplinary and she was also supervised by **David Williams** and **Duncan McGillivray**.

Nicola Brant successfully defended her PhD thesis entitled, *Synthetic studies towards annotinolide C*, supervised by **Margaret Brimble** and **Dan Furkert**.

Professor Marie Wong (top panel) and Professor Siew-Young Quek (bottom panel) with the student prize winners at the NZIFST 2021 conference

Jakob Gaar successfully defended his PhD thesis entitled, *Synthesis of AGE-modified biologically relevant peptides for the generation and evaluation of antibodies*, supervised by **Paul Harris** and **Margaret Brimble**.

Vipin Kumar successfully defended his PhD thesis entitled, *Reinforcing silicon-silicon bonds using bridges*, supervised by **Erin Leitao**.

AUT

New Faces

A big welcome to **Taniela Lolohea**, our new lecturer in chemistry, who joined us in August. Taniela competed his PhD at the University of Auckland, under the supervision of Professor **Duncan McGillivray** and Professor **David Williams**. His research interests include plasma technologies to create functional surface coatings and activated surfaces. A recent focus includes building bespoke radio-frequency pulsed power supplies to produce densely energetic plasma which can deposit both organic and inorganic precursors.

We also welcome to **Ben Stackpole**, who will be doing a 3rd year research project with **Professor Nicola Brasch**.

Events

Dr Jack Chen gave an invited (virtual) seminar at the Australian National University as part of the ANU Seminar series. The talk was entitled, *Applying concepts from nature for the design of dynamic catalyst systems*.

Dr Jack Chen gave an invited talk at the Systems Chemistry Virtual Symposium (7-9 July) co-hosted by the University of Strasburg and the Technical University of Munich. The talk was entitled, *Exploiting the dynamic nature of self-assembled catalyst systems.* This symposium featured a virtual poster session on a platform called 'Gather.Town'. This allowed each delegate to assume a 64-bit avatar and virtually walk up to each poster, allowing everyone at the poster to interact with one another. A great platform for future events that need to be held virtually.

Congratulations

Jess Fredericksen was awarded a 1st class Honours degree and an AUT VC Scholarship for PhD studies. She began her PhD studies with Professor **Nicola Brasch** and Dr Brent Seale in May and will be working on developing vitamin B12 conjugates of antibiotics.

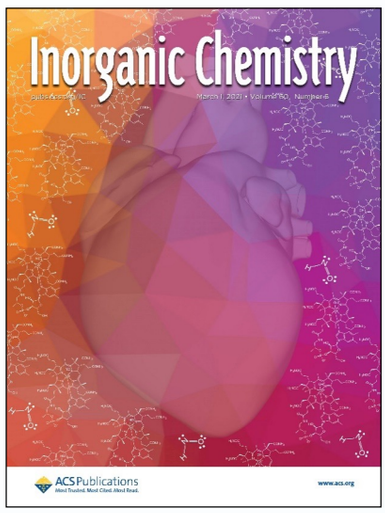
Dr Jack Chen and students **Pablo Solís Muñana**, **Joanne Salam**, **Chloe Zhijun Ren** and **Bronte Carr** published an article in Advanced Synthesis and Catalysis entitled, An amphiphilic (salen)co complex – utilizing hydrophobic interactions to enhance the efficiency of a cooperative catalyst. This work describes how the introduction of hydrophobic interactions can increase catalytic efficiency by enhancing cooperativity under homogeneous conditions and increasing interfacial area under biphasic conditions.

Professor Nicola Brasch and her former students **Dr Ruth Cink** and **Lynn Lisboa** published an article in Inorganic Chemistry entitled, Mechanistic studies on the reaction between aquacobalamin and the HNO donor Piloty's acid over a wide pH range in aqueous solution. PhD student **Rosie Mooney** created a stunning cover page artwork that was featured on the journal cover.

Dr Cassandra Fleming was awarded an HRC Emerging Researcher First Grant for the project *Light-responsive molecular tools to study tau-mediated neurodegeneration*. In collaboration with Associate Professor **Peter Crouch** (University of Melbourne) and Associate Professor **Chris Hall** (University of Auckland), Cassandra will be developing light-responsive inhibitors to study the role of key enzymes in the central nervous system of a zebrafish model system and their relationship to neurodegeneration.

PhD student **Jess Fredericksen** who works with **Professor Nicola Brasch** was awarded a prize for best poster presentation at the Dodd-Walls Symposium at the University of Auckland (4 prizes for ~60 posters).

Professor **Nicola Brasch**, her former student **Dr Ruth Cink**, Professor M. **Cather Simpson** and collaborators in the US and Hong Kong published an article in The Journal of Organic Chemistry entitled, *Mechanistic insights into rapid generation of nitroxyl from a photocaged N-hy-*



droxysulfonamide incorporating the (6-hydroxynaphthalen-2-yl)methyl chromophore. PhD student **Rosie Mooney** created another amazing artwork featured on the cover page which depicts the release of HNO from the photocaged HNO donor (PPG = photoprotecting group).

CANTERBURY

University of Canterbury

Congratulations to this year's Ferrier Public Lecturer, **Professor Antony Fairbanks**, from the School of Physical and Chemical Sciences (SPCS), University of Canterbury. His talk, *ProSugars and viruses; the roles that carbohydrates can play in both viral infection and immune evasion* was given in Wellington on 14 May and extremely well received.

Congratulations to these successful PhD candidates:

Ting Wu (supervised by **Alison Downard** and **Chris Fitchett**) - *Covalent carbon surface modification with iron porphyrin: application to oxygen reduction reaction.*

Shirley Celestine (supervised by **Richard Hartshorn**, **Jan Wikaira** and **Jolon Dyer**) - *New ion exchange materials from collagens*.

Carline Kleinjan (supervised by **Paul Kruger**) - *The supramolecular chemistry and magnetic properties of flexible tetrahedral cages and circular helicates*.

Mohammed S. Abdelbassit (supervised by **Owen Curnow**) - *Nonclassical polyhalides and chloride hydrate clusters stabilized by triaminocyclopropenium cations*.

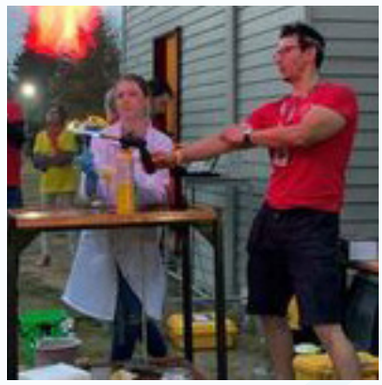
Siriluck Tesana (supervised by **Vladimir Golovko**) - *Synthesis of atomically precise metal clusters dispersed within the oxide supports for applications in green catalysis*.

Vladimir Golovko also co-supervised the following chemical and process engineering (CAPE) students:

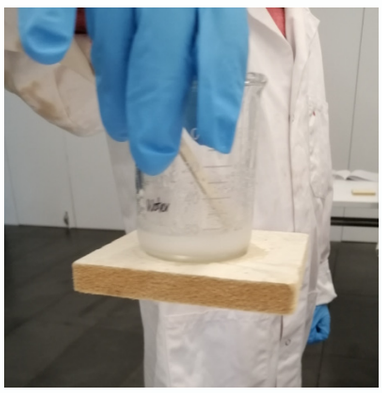
Maxime Savoie - *Development of photoelectrochemical anodes for solar redox flow batteries.*

Wasim Khan - *Nanostructured catalytic architectures for CO oxidation and reduction.*

The SPCS's Science Display at the Hororata Night Glow Festival was a complete success. The public enjoyed a mix of physics and chemistry demonstrations (including fire, atmospheric balloons, beds of nails, etc) throughout the evening, and the tent was never empty! Huge thanks go to **Graeme Plank**, **Sarah Lilley**, **Marie Squire**, **Chris Fitchett**, **Laura Revell**, **John Revell**, **Kylie Smith**, **Scott Smith**, **Lana Schiefer**, **Luke Whitehead**, **Yusuf Bhatti** and **Adrian McDonald** (and the assistant helpers **Henry**, **Greta**, **Everly**, **Mila**, **Elsie**, **Isla** and **Mason**).



Science Display at the Hororata Night Glow Festival.



SPCS at KidsFest

Congratulations to Sarah Masters

We are delighted to report that Sarah is the well-deserved recipient of a 2021 University of Canterbury Teaching Award. The award was accompanied by the following citation:

"Associate Professor **Sarah Masters** is leading innovation in chemistry teaching at the University of Canterbury, fostering strong links between students and staff across Colleges. She has developed an award-winning series of introductory videos for Stage 1 Chemistry laboratory classes and has a strong commitment to continuing professional development for postgraduate students.

Her overall aim is for her students to be inspired, not only by the material but also by the enthusiasm that she brings to the subject. "My approach to teaching can be summarised as 'kāore he mutunga o te ako' - there is no ending to learning," Associate Professor Masters says."

SPCS at KidsFest

This year was the 30th anniversary of the school holiday programme KidsFest, which has engaged thousands of Ōtautahi, Christchurch kids since the early 1990s, giving them hundreds of exciting and interactive activities to choose from during the winter school holidays. In 2020 the School of Physical and Chemical Sciences participated for the first time and the UC Science events had overwhelming popularity.

This year, under the organisation of **Dr Rodrigo Martinez Gazoni**, a UoC Postdoctoral Fellow, the School of Physical and Chemical Sciences delivered an even bigger showcase over two levels of Turanga in central Christchurch.

Rodrigo commented, "Allowing hands-on experimentation with physics and chemistry, while being able to chat with real scientists, or people working across the many different levels of science (from students to technical staff and academics), has proven particularly attractive for both kids and adults."

The positive response and access to even more space in the library inspired the school to gather more than 25 passionate undergraduate and postgraduate students, scientists, academics and technical staff, who shared their interest and expertise in science through a wide variety of UC-inspired activities for kids of all ages.

On the lower level the team's expanded event included scientific material including animations, augmented reality (AR) tools, virtual reality (VR) environments, real-life 3D models and more, for use across the various workshops held during the day. Chemistry played a big role with a hugely popular show delivered by **Sarah Lilley**, **Nathan Alexander** and **Sarah Masters**.

Upstairs, this was followed by a variety of hands-on workshops making slime, discovering thermodynamics and invisible ink writing/drawing. This included an amazing baby yoda picture!!!!

There were also interactive displays for everyone to try out. The different sessions, targeted at specific age groups, enabled a lot of children to take part in chemistry experiments that delighted both them and their carers

The day was a massive success, and we look forward to it again next year.

Thanks to everyone who took part:

Sarah Masters, Jan Wikaira, Chris Fitchett, Kylie Smith, Lana Schiefer, Rachael Hocking, Sarah Lilley, Ting Wu, Sagar Mothkuri, Nathan Alexander, Marie Squire, Benjamin Lowe, Anthony Turner, Rosemary Dorsey, Graeme Plank, Nicole Soriano, Rhia Hewett, Dona Banerjee, Daniel Craik, Alex McNeill, Rodrigo Martinez, and **Ro Reilly**.

2021 Ferrier Lecture

The 2021 Ferrier Lecture was given on 14 April 2021 by **Professor Antony Fairbanks**, University of Canterbury, Te Whare Wānanga o Waitaha, Christchurch. His lecture entitled, *Sugars and viruses: the roles that carbohydrates can play in both viral infection and immune evasion,* was extremely topical and looked at the role sugars play in influenza and SARS-CoV-2 and how anti-virals and RNA vaccines have and are being developed to combat these diseases. The Ferrier Lecture is named after Robin Ferrier whose particular belief was that young chemists could benefit greatly from mixing with leaders in their field. Therefore, invited Ferrier Lecturers, who are recognised internationally in chemistry or a related field, are brought to New Zealand to engage with postgraduate students as well as lecture. For more see: https://www.wgtn.ac.nz/ferrier/about/ferrier-lecture

New book publication

Plastic Legacies: Pollution, Persistence, and Politics is edited by **Trisia Farrelly**, **Sy Taffel** and **Professor Ian Shaw**. The synopsis reads:

"There is virtually nowhere on Earth today that remains untouched by plastic and ecosystems are evolving to adapt to this new context. While plastics have revolutionized our modern world, new and often unforeseen effects of plastic and its production are continually being discovered. Plastics are entangled in multiple ecological and social crises, from the plasticization of the oceans to the embeddedness of plastics in political hierarchies. The complexities surrounding the global plastic crisis require an interdisciplinary approach and the materialities of plastic demand new temporalities of thought and action. Plastic Legacies brings together scholars from the fields of marine biology, psychology, anthropology, environmental studies, Indigenous studies, and media studies to investigate and address the urgent socio-ecological challenges brought about by plastics. Contributors consider the unpredictable nature of plastics and weigh actionable solutions and mitigation processes against the ever-changing situation." For more see: https://www.aupress.ca/books/120302-plastic-legacies/

PhDs successfully defended

Rathiga Senthooran (supervised by Associate Professor Owen Curnow): *Synthesis and characterization of triaminocyclopropenium ionic liquids for selected applications*. The viva voce exam took place over Zoom with **Dr Cameron Weber** (Auckland) and **Associate Professor Jason Harper** (UNSW).

Michael Weusten (supervised by **Emily Parker** (principal now at Victoria University Wellington) and **Ren Dobson** (SBS)): *The role of the KDO8PS quaternary structure*. Examiners were **Associate Professor Chris Squire** (Auckland) and **Professor Jeffery Keillor** (University of Ottawa). Michael is Emily's last PhD student from UC.

Ben Howard (supervised by **Paul Kruger**): *Multi-functional ligands for metallosupramolecular assemblies: towards novel metal-organic frameworks*. The viva voce exam took place over Zoom with **Professor Lyall Hanton** (Otago).

Mohammad Firoozinia (from the **Emily Parker** group): completed under UC registration while working with Emily at VUW.

Hamilton Global Women's breakfast participants

NZIC

The Canterbury branch of NZIC sponsored the Tri-Sci (ChemSoc, PhysSoc and BioSoc) Quiz Night held on 14 May. Thanks to everyone who participated and helped organise the event. The questions were quite challenging. We are pleased to report that chemistry teams dominated with 1st place going to *Dr Lord Megatron and Amigos* (**Ting Wu**, **Nathan Harvey-Reid**, **Liam Carroll** and **Nicola Altenhuber**).

2nd place went to another chemistry team, *My group is smarter than me* (**Kim Fowler**, **Zach Stueven**, **Max Caplin**, **Hector Mancilla**) who pipped a mixed team, *Isodopes* (**Sarah Masters**, **Don McNickle**, **Mike Reid** and **Jan Wikaira**) in a playoff.

Winners of the Tri-Sci quiz night

Second place getters in the Tri-Sci quiz night

Third place getters in the Tri-Sci quiz night

MANAWATU

Jacob Scott has commenced his PhD working with **Professor Paul Plieger** and **Dr Octavio Perez-Garcia** (Zespri International) on a Callaghan funded project titled, *Molecular capsules for sensor applications*.

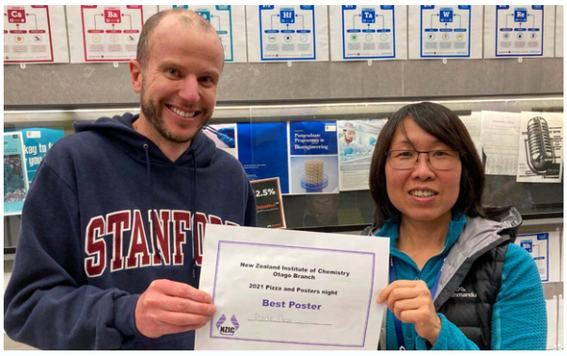
Seok Jun (Subo) Lee has successfully defended his PhD thesis titled, *Applications of multicomponent metal-organic frameworks*. Subo was supervised by **Professor Shane Telfer** and **Professor Geoff Jameson**.

Joel Cornelio has successfully defended his PhD thesis titled, *Photophysical and catalytic properties of multicomponent metal-organic frameworks*. Joel was supervised by **Professor Shane Telfer** and **Associate Professor Gareth Rowlands**.

Sidney Woodhouse and **Tyson Dais** had their paper titled, *The structural manipulation of a series of Ni4 defective dicubanes: synthesis, X-ray structures, magnetic and computational analyses*, accepted into the journal Dalton Transactions.

Professor Geoff Jones and **Professor Geoff Jameson** have both been awarded Professor Emeritus status.

Associate Professor Vyacheslav Filichev, Dr Elena Harjes and **Professor Emeritus Geoff Jameson**, with the support of **Dr Sean Mackay** from Massey Ventures Ltd., have been awarded $80,000 from Massey Ventures Ltd. and KiwiNet PreSeed Accelerator Fund for the project, *Improvement of APOBEC3 inhibitors*. Following on from HRC-BRC funding of $250,000 earlier this year, this funding will support further development on the road to potential commercialisation (patent pending) of inhibitors to the DNA mutator enzymes APOBEC3A and APOBEC3B. These enzymes of the innate immune system have a dark side where they are strongly implicated in evolution of resistance of many cancers to various therapies.



Otago NZIC branch president Allan Gamble presents the Posters and Pizza prizes to Denise Chen and Joe Mapley.

Marryllyn Donaldson has commenced her PhD working with **Professor Paul Plieger** and **Associate Professor Gareth Rowlands** on a project titled, *Synthesis of high-density magnetic materials*.

Suraj Patel has commenced his PhD working with **Associate Professor Gareth Rowlands** and **Professor Shane Telfer** on a project titled, *Two is better than one: catalysis through cooperativity*.

Yongdong Su successfully defended his PhD thesis titled, *Targeting DNA secondary structures using chemically modified oligonucleotides*. Yongdong was supervised by **Associate Professor Vyacheslav Filichev**, **Dr Tracy Hale** and **Dr Richard Winkworth**.

Hossein Etemadi successfully defended his PhD thesis titled, *Hydrothermal synthesis of iron oxide nanoparticles for potential technological applications*. Hossein was supervised by **Professor Paul Plieger** and **Associate Professor Catherine Whitby**.

OTAGO

The Otago branch of the NZIC hosted a Posters and Pizza night to celebrate the 400-level honours talks. **Denise Chen** (**Christina McGraw**'s lab) went home with the Best Poster award and a $50 Eureka voucher, while **Joe Mapley** (**Keith Gordon**'s lab) walked away with the People's Choice award and a $10 Dispensary voucher.

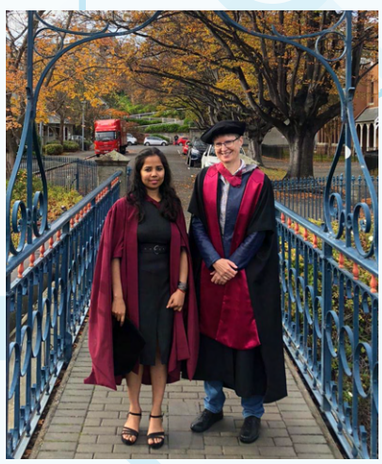
University of Otago, Department of Chemistry

Sally Brooker was interviewed about green hydrogen, resulting in the *Mindfood* article, *Clean energy gamechanger*, page 25, June issue.

There have been a number of PhD successes in the group of **Sally Brooker**. Congratulations to **Abdullah Abudayyeh** on having his PhD thesis, "*Catalysts for the hydrogen evolution reaction*", placed on the list of Exceptional PhD Theses in the Division of Sciences at the University of Otago, which means that "all three examiners of a candidate's thesis agree that the thesis is of an exceptional standard in every respect – research content, originality, quality of expression and accuracy of presentation – and is amongst the top 10% of theses examined." Congratulations to **Dr Sandhya Singh** on graduating with her PhD, *Spin crossover in iron(II) dinuclear helicates and tetranuclear cages*, from the University of Otago, in person, on a lovely autumn day in Dunedin (8 May 2021).

Congratulations to **Luca Bondí** on successfully defending his co-tutelle PhD (Universities of Otago and Florence), *Towards predictable tuning of spin crossover*, at the oral examination. The exam was held via Zoom with participants from 4 countries, specifically from the cities of Florence (Luca and **Professor Federico Totti**, co-supervisor), Rennes (**Professor Boris Le Guennic**, examiner),

Abdullah Abudayyeh, who has his PhD thesis placed on the Division of Science's Exceptional Theses list.



Sandhya Singh and Sally Brooker at Sandhya's PhD graduation.

Dublin (**Associate Professor Grace Morgan**, examiner) and Dunedin (**Professor Lyall Hanton**, examiner; **Associate Professor Nigel Lucas**, convenor; **Dr Anna Garden** and **Professor Sally Brooker**, supervisors). A truly international exam!

Congratulations to **Fola Akogun** on successfully defending his PhD thesis, *Carbazole complexes as catalysts for hydrogen evolution and CO_2 reduction* via Zoom on 20 May 2021.

Congratulations to **Kārlis Bērziņš**, **Sara Fraser-Miller** and **Keith Gordon** who recently published a paper entitled, *Recent advances in low-frequency Raman spectroscopy for pharmaceutical applications* in the International Journal of Pharmaceutics (https://doi.org/10.1016/j.ijpharm.2020.120034). This mini-review highlights the increasing use of low frequency Raman spectroscopy, a technique that allows the user to understand molecular ordering in systems with close to video-rate time resolution. An exemplar of this work was published by **Chima Robert**, **Kārlis Bērziņš**, **Sara Fraser-Miller** and **Keith Gordon** in *Molecular Pharmaceutics* (https://pubs.acs.org/doi/10.1021/acs.molpharmaceut.0c01126). This study entitled, *Monitoring the isothermal dehydration of crystalline hydrates usinglLow-frequency Raman spectroscopy* explored the simultaneous application of both low- and mid-frequency Raman regions to identify the dehydration changes as crystalline hydrates are transformed into their respective anhydrous forms. Early onset of dehydration was observed in the low-frequency region as compared to the mid-frequency Raman region.

Chima Robert, **Sara Fraser-Miller** and **Keith Gordon** also published a paper entitled, *Molecular monitoring of glioblastoma's immunogenicity using a combination of Raman spectroscopy and chemometrics in Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* (https://doi.org/10.1016/j.saa.2021.119534). This study investigated the molecular differences of immune cells after incubation with tumour condition media of glioblastoma stem cells upon ZEB1 inhibition, which are critical in cancer progression.

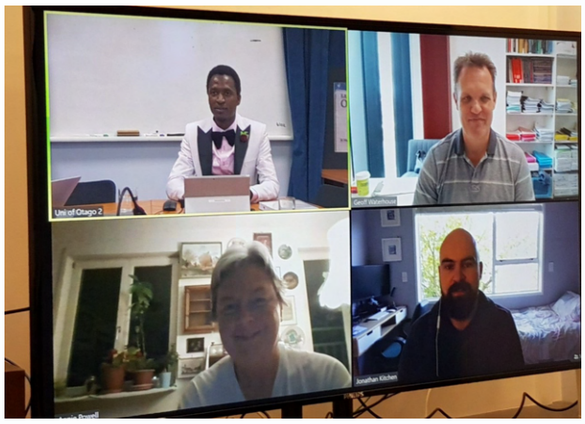
Jono Barnsley and **Keith Gordon** along with Australian researchers recently published a paper entitled, *Carbazole-substituted dialkoxybenzodithiophene dyes for efficient light harvesting and the effect of alkoxy tail length in Dyes and Pigments* (https://doi.org/10.1016/j.dyepig.2020.109002). This study examined how the tail length of dyes affects the performance of solar cells. **Jono** and **Keith** examined the spectroscopy of the dyes showing the nature of the excited state using resonance Raman spectroscopy and density functional theory calculations.

Sara Fraser-Miller has funding for a one year MSc thesis scholarship to work on a project developing a multi-spectroscopic probe for disease diagnosis. If you are interested please contact her (sara.miller@otago.ac.nz) or Keith (keith.gordon@otago.ac.nz) for more details.

The Otago branch of the NZIC co-sponsored the Department of Chemistry postgraduate symposium in July. It was a brilliant day with fantastic talks and **Matt Robb** and **Ciaran Ward** did a fantastic job of organising. Congratulations to all speakers, especially the prize winners, **Kaleb Winefield** (best talk), **Sam McIntyre** and **Charlie Ruffman** (runners up).

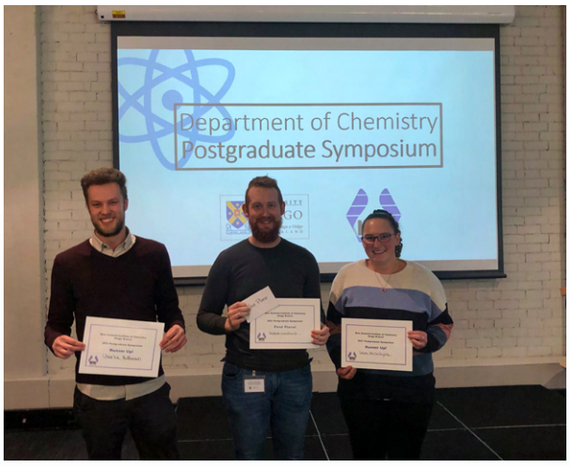
University of Otago, Department of Chemistry

Kārlis Bērziņš, **Sara Miller** and **Keith Gordon** along with European researchers recently published a paper



Fola after the oral examination, with the examiners, Professor Annie Powell (KIT, bottom left), Professor Geoff Waterhouse (Auckland, top right) and Dr Jonathan Kitchen (Massey Auckland, bottom right). Convenor Professor Claudine Stirling and supervisor Professor Sally Brooker were also present.

Luca after the oral examination, with the examiners and supervisors.



Prize winners at the Department of Chemistry Postgraduate Symposium: Charlie Ruffman, Kaleb Winefield and Sam McIntyre.

Speakers at the Department of Chemistry Postgraduate Symposium.

entitled, *Combined effect of preparation method and compression on the physical stability and dissolution behavior of melt-quenched amorphous celecoxib in Molecular Pharmaceutics* http://dx.doi.org/10.1021/acs.molpharmaceut.0c01208. The paper details the effects of compression (a key step in tablet making) on the dissolution properties of the active ingredient. Low frequency and UV vis spectroscopy are used to elucidate behaviour and develop an understanding of the interplay of differing forces on solubility enhancement.

Kārlis, **Sara** and **Keith** also published a paper entitled, *A new frontier for nondestructive spatial analysis of pharmaceutical solid dosage forms: spatially offset low frequency Raman spectroscopy (SOLFRS) in Analytical Chemistry* https://doi.org/10.1021/acs.analchem.0c04960. This new technique makes it possible to measure the spectra and thus the composition of materials underneath a surface. The low frequency Raman spectra allow deeper penetration so that chemical entities centimeters deep may be measured without any need to cut open the sample.

Joshua Sutton (who is now working at VUW) published a paper with **Paul Wagenknecht** and his team on *solvatochromism in Fe(II) Ti(IV) organometallic species with electron donor groups* (https://doi.org/10.1039/D0DT04282J). These materials are useful in non-linear optics and solar energy harvesting because of their optical properties. Using resonance Raman spectroscopy in concert with DFT calculations it was possible to show that the donor species were electron delocalised – this unusual phenomenon contributed to the solvatochromic nature.

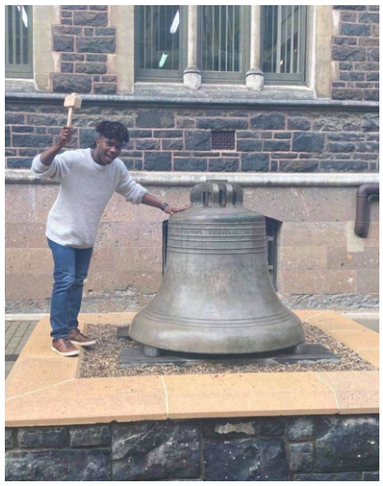
Fatema Ahmmed, **Ioan Fuller**, **Sara** and **Keith** published a paper in ACS Food Science and Technology entitled, *Raman and infrared spectroscopic data fusion strategies for rapid, multicomponent quantitation of krill oil compositions* https://doi.org/10.1021/acsfoodscitech.0c00139. The paper examines how data fusion at low, medium and high levels can improve the efficacy of Raman and IR spectroscopy in the quantification of omega-3 fatty acids in krill oil. The work is in collaboration with Otago alumnus **Daniel Killeen**, now at Plant and Food, Nelson.

Keith presented at the Pharmaceutical Solid State Research Cluster (PSSRC, https://www.pssrc.org/) at their virtual funding meeting on 20 May; the 1st funding workshop PSSRC 2021. **Keith** highlighted some of the new techniques developed at Otago in the last couple of years – notably spatially-offset low frequency Raman spectroscopy (SOLFRS) that allows one to interrogate the chemical composition of an object below its surface.

Sara Miller, **Jeremy Rooney** and **Keith Gordon**, along with their medical collaborators **Michael Lau** and **Michael Schultz**, published a paper entitled, *Can coupling multiple complementary methods improve spectroscopic based diagnosis of gastrointestinal illnesses? A proof of principle ex-vivo study using coeliac disease as the model illness in Analytical Chemistry* (https://doi.org/10.1021/acs.analchem.0c04963). This work demonstrated the potential to improve Raman spectroscopic based diagnostic methods by inclusion of additional, complementary spectroscopic methods using diagnosis of coeliac disease as the model illness.

Jeremy and **Keith** published a paper, in collaboration with the Department of Geology, entitled, *A common type of mineralogical banding in serpentine crack-seal veins*. In this paper published in Earth and Planetary Science Letters (https://doi.

Michael Schultz (Head of the Dunedin School of Medicine), Sara Miller and Keith Gordon.



Chima Robert ringing in his thesis submission

org/10.1016/j.epsl.2021.116930), Raman spectroscopy is able to detect the incredibly narrow bands of chrysotile within lizardite. Using a variety of samples from around the world it is shown that this Raman-based technology may be used for a host of samples. The geology suggests that recurrent small earthquakes led to the banding.

Fatema, Sara, Samanali Garagoda Arachchige and **Keith**, with researchers in Zoology and at Landcare, published a paper entitled, *Lake snow caused by the invasive diatom Lindavia intermedia can be discriminated from different sites and from other algae using vibrational spectroscopy in the Journal of Raman Spectroscopy* (http://doi.org/10.1002/jrs.6161). This study showed how Raman spectroscopy could be used to detect lindavia (lake snow) from other species and identify the lakes from which the lindavia had been sampled. This is part of a larger project looking at monitoring lakes with optical techniques.

Keith and Otago alumni **Cushla McGoverin** and **Fang Tian** published a paper entitled, *Potential of Raman spectroscopy in facilitating pharmaceutical formulations development – an AI perspective in the International Journal of Pharmaceutics* (https://doi.org/10.1016/j.ijpharm.2021.120334). This paper looks at the use of AI to augment the correlations between spectral data and therapeutic properties.

Sara, Jeremy and **Keith** were also involved in a paper looking at dog biscuits on Scott's ill-fated Antarctic expedition. The paper is reported in *Polar Record* https://www.cambridge.org/core/journals/polar-record/article/abs/feeding-the-team-analysis-of-a-spratts-dog-cake-from-antarctica/96E07502DFE77AA5D85F535C6B45D635.

Piumika Samanali Garagoda Arachchige (Samanali), **Peter Remoto** and **Keith Gordon** attended the Dodd Walls Symposium in Auckland (June 30 – July 2). **Samanali** and **Peter** presented posters on their work as well as presenting **Fatema Ahmmed**'s work as **Fatema** was unable to attend.

Keith gave a presentation on the Health and Environment Research Question – a key pillar of the CoRE's mission over the next eight years. Keith is the current question leader for this question. This Research Question seeks to use optical methods coupled with sophisticated multivariate analysis techniques (including AI) to non-invasively analyse materials and thus provide insight into their composition and other properties. There are a wide range of projects looking at food quality, water quality and diseased versus healthy tissue both ex vivo and in vivo.

There have been quite a few PhD submissions in the last few months including: **Kārlis Bērziņš**: *Low-frequency Raman spectroscopy in pharmaceutical applications*, **Jeremy Rooney**: *Analyses on low temperature curing waterborne coil coatings* and **Chima Robert**: *Vibrational spectroscopic analysis of complex systems*.

Keith Gordon was the winner of the University of Otago's Distinguished Research Medal for 2021.

WAIKATO

Waikato NZIC branch committee for 2021 is as follows:

Chairperson/Secretary:
Bill Henderson

Treasurer/Chemistry Education representative:
Martina Pietsch Brown

Council delegate/Branch editor:
Michèle Prinsep

Student representatives:
Amber Bell and Greer Tanner-Dempsey

Committee members:
Megan Grainger, Ingrid Lindeman, Lauren Gris

The annual recruitment evening was held recently at the University of Waikato, at which a small but enthusiastic group of existing and prospective branch members enjoyed pizza and drinks.

University of Waikato

Matthew Risi has started a PhD with **Bill Henderson** (second supervisor **Graham Saunders**), looking at thiourea coordination chemistry.

Three new MSc (research) students have recently started at Waikato. **Sinead Sanders** is working with **Bill Henderson** looking at applications of organophosphorus compounds in lanthanide separations, **Edie Thomas** is working with **Megan Grainger** to investigate the sensory profiles of native New Zealand honeys and **Tim Dyche** is working with **Michael Mucalo** investigating cleaner fertilisers.

Congratulations to PhD graduate **Haiming Tang** (supervised by **Bill Henderson**) who has recently been appointed to an academic position at Sichuan University of Science & Engineering in China. Congratulations also to MSc (research) graduates **Taylor Farr** and **Claire Voogt** (supervised by **Michèle Prinsep**) who were joint student speakers at the recent graduation ceremony at the Tauranga campus.

Dr Megan Grainger gave a presentation at the 2nd Bee Symposium, Rotorua, on her Marsden Fast-Start research on the effects of metals on honeybee health. She also spoke at the Apiculture Conference as a panel member in the science discussion on *The next NZ monofloral honey: how can science help us deliver better value?* **Amber Bell** (MSc) and **Megan Grainger** presented a poster titled, A sticky situation: low diastase activity in manuka honey at the Apiculture Conference held in Rotorua.

Hill Laboratories

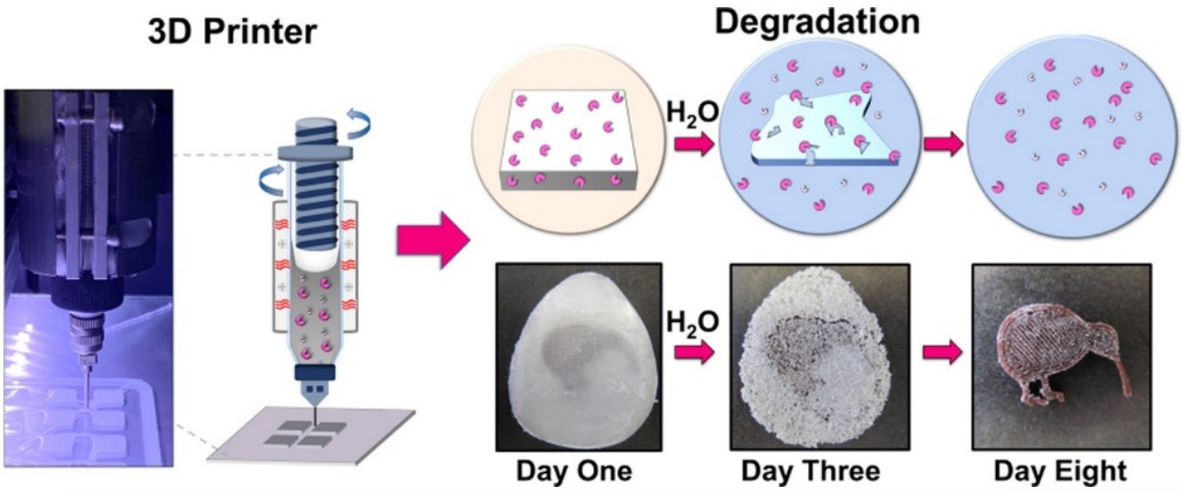
Riaan Botha has been appointed to the executive team in the role of General Manager – Sales & Marketing. Riaan joined Hill Laboratories about 18 months ago as the Market Sector Manager – Food and Bioanalytical, and so he will carry the learnings from this role forward into his new role, while also broadening his understanding of Hill Labs' Agriculture and Environmental sectors. Riaan is passionate about customer service and is most looking forward to working alongside an inspiring group of people, contributing to the culture at Hill Laboratories and playing his part in the continued growth and success of the company.

Scion

Polymer chemist, **Angelique Green** and colleagues at Scion have used 3D-printing techniques to produce rapidly degradable enzyme-embedded plastics. The research, which studies the degradability of polycaprolactone/amano lipase composite films, has recently been published (Biomacromolecules, 2021, 22(5), 1999–2009).

Taylor Farr (left) and Claire Voogt (right) with their supervisor Michèle Prinsep at the graduation ceremony.

Hill Laboratories' new General Manager - Sales & Marketing, Riaan Botha

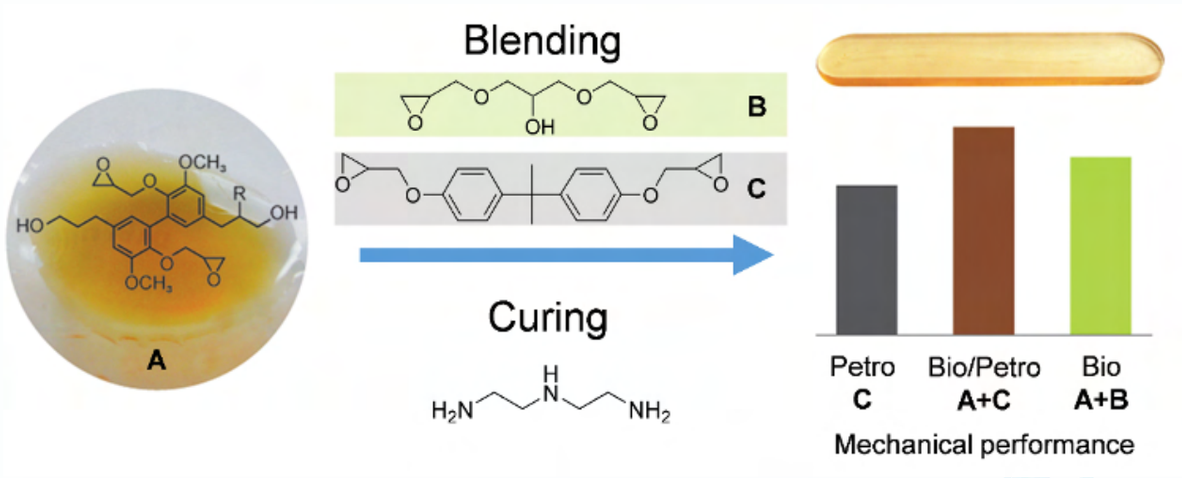


Thermal paste printing of PCL/AL composites (left); enzyme-mediated polymer degradation in water (right)

Biorefining chemists, **Kirk Torr** and **Daniel van de Pas** are exploring approaches to produce bio-oils from lignin for use in bio-based thermoset resin formulations. Native lignin is depolymerised to a bio-oil, reacted with epichlorohydrin and formulated to produce sustainable alternatives to bisphenol A-based epoxy resins (Biomacromolecules, **2020**, 21(4), 1548-1559; ACS Macro Letters, **2020**, 9, 1155-1160).

Bioenergy researchers, **Peter Hall** and **Bing Song** are optimising torrefaction and densification processes for converting woody biomass into solid biofuels that are durable, moisture resistant and have an energy density close to that of sub-bituminous coal. Torrefied wood briquettes or bio-coal (see image) can be shipped and handled like coal so they can be used in existing supply chains and boilers.

Torrefied, densified Pinus radiata wood briquettes prepared at Scion

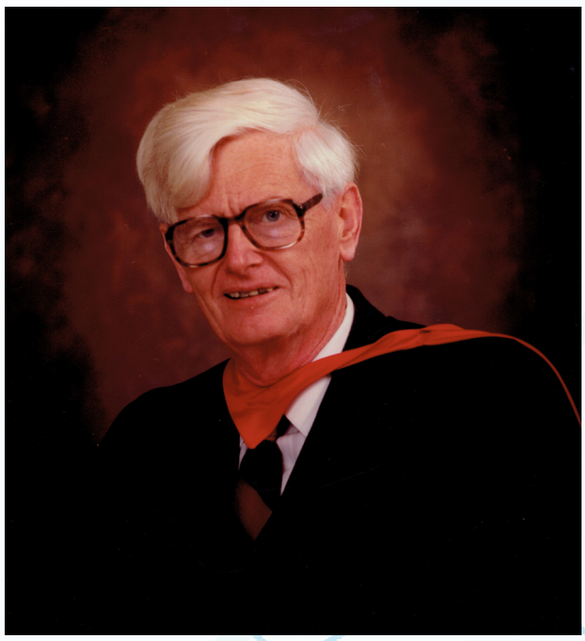


Glycidylated depolymerised lignin oil formulated and cured to produce bio-based epoxy polymers with enhanced mechanical properties

Arthur Derek Campbell

PhD (Otago), FNZIC, OBE, 1925-2020

Arthur Derek Campbell was born in Waimate in 1925, educated at Waimate High School and studied chemistry at the University of Otago. He graduated with an MSc (Hons) in 1948 and was appointed as an assistant lecturer in organic chemistry. He continued to study part-time for a PhD, undertaking aspects of organic synthesis and completing this degree in 1953.



At that time, one of the most common ways of identifying and confirming the structure of a chemical compound that you had synthesised was to calculate the exact ratio of the amounts of key elements such as carbon, hydrogen and nitrogen in a proposed chemical structure and then compare them with the ratios you analysed in an actual sample. Arthur realised there was no facility for such elemental analysis, at least in NZ, and so he developed the experimental techniques and apparatus to make such analytical measurements on literally a few milligrams of an organic compound. Word soon spread among other university chemistry departments both in NZ and offshore of this organic microanalysis facility at Otago University in Dunedin. Samples started to literally pour into the chemistry department for such analyses and so Arthur took on several scientific officers to assist him with this work. In the early 1970s, with the shift to the new Chem 1 building, he established an analytical laboratory to undertake this work. In recognition of Arthur's founding contribution this was subsequently called the Campbell Microanalytical Laboratory and it still exists today undertaking microanalyses.

Chemists are often adventurous souls in the course of their work and Arthur was no exception. A colleague, Ross Grimmett, for whom Arthur was his MSc supervisor, recalls one incident in the late 1950s when Arthur needed some trinitrotoluene (better known as TNT which of course is an explosive) for a synthesis. There were no supplies of it held in the chemistry department store and Arthur couldn't order it from overseas. So he phoned up the local army headquarters and a truck soon arrived from the Drill Hall with a jovial sergeant delivering an anti-tank mine (minus its detonator, we presume). Arthur proceeded to dissolve the TNT out of the mine by boiling it up in a large ceramic sink tub of benzene, decanting off the benzene and then carefully evaporating it to a concentrated solution from which the TNT crystallised on cooling. He only wanted a few grams of TNT, not several kilograms, so as the surplus would have been an ever-present hazard in the chemistry department store, Ross helped Arthur dispose of it safely, if not in an environmentally friendly manner, by "losing" 100 mL at a time over a week or so in the Leith river that runs through the university campus. The yellow colour soon dispersed in the running water and there was no obvious loss of wildlife.

Ross also recounts that Arthur had an old gas heater in his office in the old chemistry building. It used to have four ceramic towers but they had collapsed into a pile of ceramic chunks. So Arthur found the only way to light it without burning his fingers was to turn the gas on full, walk slowly to the door, then throw a lighted match at it. There'd be an initial loud explosion but once the ceramic bits had returned to rest it was safe for him to re-enter his room.

At the same time as he was undertaking organic microanalysis work and organic synthesis, Arthur became interested in teaching aspects of analytical chemistry and so, beginning with a half paper and then progressing to

a full paper, analytical chemistry became a mainstream paper along with others covering more traditional areas of organic, inorganic and physical chemistry. He soon realised he needed some academic assistance in mounting this paper and so he appointed the first lecturer in analytical chemistry in 1973 and then with that person's untimely death shortly later, another lecturer in 1976. That person was Dr Keith Grime and although he only stayed for 3 years before taking up a position in the US to be closer to his UK family, Keith has very fond memories of Arthur as he recounts:

'It's fair to say that Arthur's support and encouragement led to my very successful career at Otago University which in turn led to an international reputation through many publications in three years. This foundation formed the basis of my career that has led to me retiring as the Vice President of Corporate R&D for the mega company here in the US of Procter & Gamble. I have no doubts about Arthur's role in helping me achieve this lofty goal'.

On Keith's departure in 1979, Arthur appointed a young Auckland graduate (the late Professor Keith Hunter) who had undertaken a PhD in marine chemistry at the University of East Anglia. With Arthur's encouragement, Keith went on to establish additional papers in many aspects of environmental chemistry and built up a big research group.

At the same time as Arthur was undertaking his organic microanalysis work and teaching analytical chemistry, he was progressively promoted to lecturer, senior lecturer, associate professor and then a full professor in 1971. He undertook his share of departmental administration, being Chairman of the Chemistry Department from 1983 to 1988, Mellor Professor of Chemistry in 1983 and Dean of the Faculty of Science from 1980 to 1982. The title of Mellor Professor is reserved for just one senior academic at a time in the Otago chemistry department (usually the Head of Department) and recognises probably its most famous graduate viz. Joseph Mellor. Mellor had his initial chemical education in Dunedin and then went to England where he established an international reputation as a ceramic chemist and wrote a number of volumes of the text, *Treatise of Inorganic Chemistry*. The new chemical laboratories at the university fronting Cumberland Street are also named after him.

As a senior academic in the University, he was appointed to a number of committees including one involved in capital works that involved landscaping around the campus and in particular, deciding on what trees and where they should be planted. The university staff member responsible for such landscaping at that time (Robert Scott) fondly remembers Arthur and a lot of what you see today around the campus can be traced back to Arthur's contribution to careful horticultural planning many years ago.

Arthur retired from the university in 1988 and was conferred the title of Professor Emeritus.

During his illustrious academic career he was awarded a number of honours including a period as Chairman of the Chemical Testing Registration Advisory Committee of the Testing Laboratory Registration Council of New Zealand from 1973 to 1985. He was a bureau member from 1981 to 1989 of an IUPAC panel specifically covering microanalyses, and in 1979-80 he was NZIC President, for which he had previously been made a Fellow.

All of these achievements lead to Arthur being made an Officer of the Order of the British Empire (OBE) for services to science in 1989.

As Keith Grime indicated, Arthur was a very kind and supportive person and I experienced this as a very young lecturer when I joined the department in 1972. Other staff members feel the same way and to this end, one of our retired colleagues, David Fenby, has commented:

'In recalling Arthur as a colleague and as a Head of Department, one word leaps to mind – RESPECT! Respect for his scholarship, his many achievements, his administrative skills, and, above all, respect for the man that he was; he achieved, he guided, he advised with conviction, insight and gentleness. For me, he was a colleague and friend par excellence'.

Arthur was a great chemist, educator and a fine example to many others in all our lives. He will be missed by many people but he hasn't really died as a chemist, he has just 'ceased to react'!

Contributed by Barrie M. Peake
Chemistry Department, University of Otago, 1972 – 2015

George Bouet Petersen

DPhil, DSc (Oxon), HonDSc (Otago), FNZIC, FRSNZ, ONZM, 1933-2021

It is with great sadness that we acknowledge the passing of Emeritus Professor George B. Petersen ONZM FRSNZ in July 2021. George, a distinguished Fellow of the Royal Society of New Zealand since 1985, completed an undergraduate degree in 1954 at the University of Otago as the only student in Biochemistry. After completing an MSc in 1956, inspired by a single paragraph in a textbook about DNA, he left for Oxford to study for a Doctor of Philosophy working under the biochemist Ken Burton. George's research was developing novel chemistry to selectively degrade and analyse DNA – this was an important first step towards the goal of determining the sequence of the DNA nucleotides and eventually whole genomes.

He returned to New Zealand to work at the Plant Chemistry Division of the DSIR in Palmerston North before being appointed to the Chair of Biochemistry at the University of Otago in 1967 at age 34. George made key appointments in the Department of Biochemistry to focus research expertise that linked cellular information flow, coding, and catalysis via the biomolecules DNA, RNA, and protein. With this underpinning expertise, the department was equipped to study broad biological questions involving biochemistry, molecular biology, the genetics of bacteria, plants, animals, and molecular aspects of human health. When George's own research into chemical DNA sequencing methods was eclipsed by the inspired enzymic method developed by the Nobel Laureate Fred Sanger, George then worked with Sanger to help sequence the first large viral DNA genome and subsequently went on in New Zealand to facilitate the transfer of DNA sequencing and molecular biology expertise to the wider Australasian research community.

George Petersen's vision was well founded: this 'molecule of DNA' arguably has had more influence on science, on health, on genetics and society than any other in the last 70 years. George became widely known as 'the father of DNA' and fostered a new generation of students and scientists, many of whom themselves became passionate about the potential of DNA to transform our society and were trained to realise this potential. For over 30 years, George inspired his graduate students and others familiar with his work to have unselfish and high career goals to make a difference to society. Examples today are the work of Genomics Aotearoa, utilising cutting-edge DNA technologies making an impact on microbial, plant, animal and human genetics, and his former students either with highly successful award-winning careers of research and service to New Zealand science, or exhibiting the same inquisitive creative and pioneering spirit as George, one of which was the world's first commercially available nanopore technology. DNA technology is now being used to trace Covid-19 infections in New Zealand. Whole genome sequencing of each case of the virus, foreshadowed by George's work, allows us to link infections and respond faster and more accurately to outbreaks.

In 2003, George became the first Otago academic to be awarded the prestigious Rutherford Medal, in the same year as the 50th anniversary of understanding the structure of DNA. This followed many earlier awards: a Doctor of Science from Oxford University in 1993; the Marsden Medal of the New Zealand Association of Scientists in 1995; an ONZM for service to the community in 1997; and an Honorary Doctor of Science from Otago in 2000.

George Petersen also took many national leadership roles. He was Chairman of the Government Advisory Committee on Novel Genetic Techniques (ACGNT) 1978-1998, and he served many roles on the Medical and then Health Research Council between 1973-1990. He was National President of the New Zealand Institute of Chemistry 1985-1986. George was President of the Academy Council of the Royal Society

of New Zealand 1998-2000. A great contribution to New Zealand science was his establishing a desperately needed, and widely accepted, regulatory protocol for the introduction of genetic engineering into New Zealand, soon after the technology become possible. His leadership ensured a transparent and cautious approach to laboratory experiments involving genetically modified organisms (GMOs), including voluntary limitations initially imposed by DNA researchers themselves. The power of the new technologies to manipulate DNA, to form new organisms, from bacteria to plants and animals, raised huge ethical dilemmas. George was at the forefront of producing draft voluntary guidelines for New Zealand to regulate the use of these new genetic manipulation technologies. Critically, this prevented New Zealand becoming a 'wild west' for uncontrolled genetic experimentation by maverick scientists from abroad who wanted to use New Zealand for risky trials. Guidelines developed by George Petersen protected New Zealand and eventually led to the Hazardous Substances and New Organisms (HSNO) Act of Parliament passed in 1996.

George Petersen has left a rich legacy for New Zealand Science and New Zealand society.

Contributed by Stephen Sowerby, Peter Dearden, and Warren Tate CNZM FRSNZ

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Congratulations

Professor Penny Brothers elected Honorary Fellow of the Royal Society Te Apārangi

Earlier this year Professor Penny Brothers was elected to the Academy of the Royal Society Te Apārangi as an Honorary Fellow. Now the Director of the Research School of Chemistry at the Australian National University (ANU) in Canberra, Penny's many contributions to chemistry in New Zealand are briefly touched on here.

Penny graduated with a BSc and then MSc with First Class Honours in chemistry in 1979 from the University of Auckland (UoA), working with Professor Warren Roper. She then went to Stanford University for her PhD with Jim Collman, where she started working with porphyrins and met David Ware. She then returned to UoA as a postdoctoral fellow in 1986. She was hired as a lecturer in organic chemistry in 1988. Her publications during the 1980s almost all mention ruthenium and other heavy transition metals.

Many changes happened in Penny's career in the 1990s, and some of these show in her research papers. Collaborations, including with Peter Schwedtfeger, led to papers on heavy elements like thallium, while interactions with Philip Power and others started her interest in the lighter ele-

ments, especially boron. It is said that once you have had your fingers stained with porphyrins it never washes off, and Penny's interest in porphyrins has continued throughout her career. Penny's research has taken off in new directions over the last decade, showing true imagination. A major focus has been how light elements such as boron interact with porphyrins and their "chemical cousins", particularly compounds with smaller binding sites than porphyrins. Recently, she received a Marsden grant to investigate how her boron compounds might be used to identify where sugars are located in living cells. Another key part of Penny's research has been her collaborations with the Auckland Cancer Society Research Centre and in particular with David Ware. David is now within the School of Chemical Sciences at UoA and does much of the hands-on supervision of her research group now that Penny is based at ANU. Penny's collaborations extend overseas, with multiple visits to the US, especially Los Alamos, and more recently to the Arctic University of Norway in Tromso.

Penny has been a core member of the inorganic chemistry teaching group for her whole academic career, lecturing at all levels. In particular she has lectured main group chemistry. The main group elements are around the fringes of the periodic table in its traditional form. She was often describing the behaviour of elements that "break the rules" – or at least the simple rules we teach starting-out chemists. More recently she was involved in teaching green chemistry courses, where she developed sustainability linkages with other disciplines including psychology, using as a particular example the clothing industry.

Penny has also taken on advisory roles with leading international journals, and this has culminated in her being named as an Associate Editor for Chemical Communications, which is the flagship rapid communication journal of the Royal Society of Chemistry. She also has chaired a panel of the Marsden Fund and been on its Council.

Penny's service to the School, Faculty and University has been significant. When tasked with a new role, Penny will grab a piece of paper and start asking, "What do we need to do? What do we know? What do we need to find out?" Her service started very early in her academic career – being on the University Childcare Committee, Research Committee, and Academic Staffing Committee in the 1990s. She was also the Associate Deputy Vice Chancellor PBRF in 2010-2013 – a key role at the time. For the last two decades, most of her roles have involved academic and postgraduate activities. Of particular note was her serving on the Curriculum Commission and then as Assistant DVC (Academic) from 2004-2007. She has also led or been actively involved in changes to lecture timetabling, to foundation-level programmes and general education.

Penny has been very supportive of other staff, especially younger or female staff thorough both formal and informal roles. She has been a mentor with the University's Academic Leadership programme since 1999 and has also been actively involved with the New Zealand Federation of Graduate Women.

Penny has also been an active member of NZIC for many years, culminating in a term as national president in 2017. During her tenure she made a number of valuable contributions, including the modernisation of the Institute (development of a new website and online membership management system), enacting major constitutional change and reestablishing strong links with international member societies and governing bodies such as the Federation of Asian Chemical Societies and the Asian Chemical Editorial Society. The Institute is in a stronger position today due to her leadership.

Outside of chemistry, Penny's adventurous side is evident. As a student she did rock climbing, and even climbed El Capitan in Yosemite. She suspended that interest as she focussed on her career and her family, until a climb of Mount Rolleston got her restarted in climbing, to be followed by Mt Aspiring and Mt Cook amongst others. Talks with Penny in her office will often include glimpses of photographs of her or her companions in some remote valley, or on some peak. In 2017 Penny was President of both the NZ Alpine Club and NZIC!

NZIC congratulates Penny on being made an Honorary Fellow of the Royal Society Te Apārangi – it is certainly well deserved.

Contributed by Gordon Miskelly and Paul Plieger

Article

The University of Otago chemistry department bootcamp

Lynn Lisboa

Department of Chemistry, University of Otago, Dunedin (email: *lisly679@student.otago.ac.nz*)

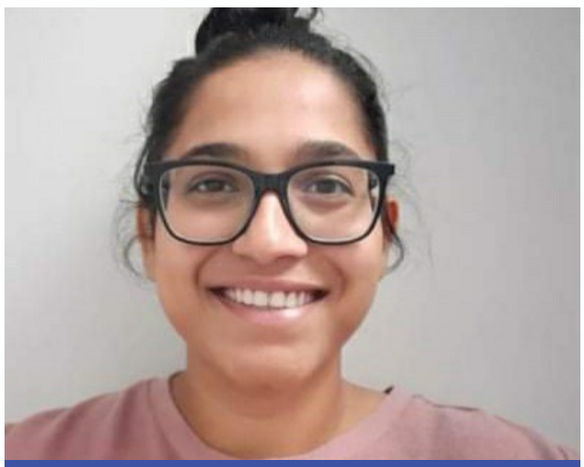
On Friday 9 April 2021, the chemistry department at the University of Otago held its first ever departmental bootcamp for postgraduate students. This was an off-campus event held at Portobello's Coronation Hall with beautiful views of the harbour. The theme for this bootcamp was molecular design which offered a wide range of student-based talks from synthetic to computational chemistry.

With no academics around, talks were relaxed and stress free and everyone who attended had a chance to present in a comfortable environment. It was great hearing about student research and the atmosphere to learn was apparent. I believe the opportunity to present was especially valued by our fourth years and new PhD students. This bootcamp could not have come at a better time, particularly with conferences and travel being extremely restricted. Of course, it was lovely to see each other outside the department.

As always, kai brings people together and it would not be a student-based event without some good grub. At the camp we were all kept happy with a warm bowl of nachos made by Samantha Jarvis, shown in the photo standing proud with her delicious work. We are very grateful to the department for providing us with ample food.

We did have some serious moments with a scenario-based discussion session towards the end of the camp. This allowed us to talk about how everyone handles the ups and downs of research, their work-life balance and a few different situations that most people go through in the span of their early research career. This was a wholesome session which helped us get to know each other a little better. And yes, there were also plenty of not-so-serious moments.

We ended our bootcamp with a small award ceremony. We were fortunate to be sponsored by the NZIC which allowed us to have six awards. The awards went to Matthew Robb (People's Choice), Nathan Bell (Best Talk), Nicholas Smith (Most Creative Talk), Ciaran Ward (Most Engaging Talk), Quinn van Hilst (Most Persistent Student) and Ian Liddle (Best Understanding of Project). We are extremely grateful to the NZIC for the sponsorship.



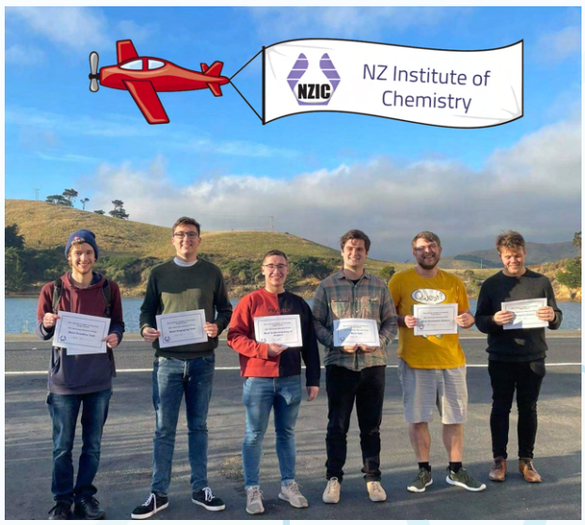
I am Lynn Lisboa, a third year PhD student working under the supervision of Professor James Crowley and Dr Dave McMorran. My PhD project is on the synthesis of switchable heterometallic Pt(II)/Pd(II) cages and their host-guest chemistry.

I was recently given the opportunity to organise the first ever chemistry department bootcamp for postgraduate students here at the University of Otago. This was really fun to do and the support I received was amazing. I hope the department continues to have events like this. On behalf of everyone at the bootcamp, I would like to thank the chemistry department and the NZIC for their support and sponsorship.

Lastly, I would like to thank the chemistry department at the University of Otago for trusting me with organising the event and giving our postgraduate community a chance to get to know each other outside the department. The event helped boost morale and brought us closer together. We are grateful to the NZIC for sponsoring our prizes and making this event that much more special. I thank Associate Professor Carla Meledandri for all the help with organising.

Happy faces at the end of a successful bootcamp

Samantha Jarvis and her big pot of chilli



Award winners (left to right): Nicholas Smith, Ciaran Ward, Ian Liddle, Nathan Bell, Quinn van Hilst and Matthew Robb

A not-so-serious moment

Prize winners' projects

Matthew Robb - People's Choice

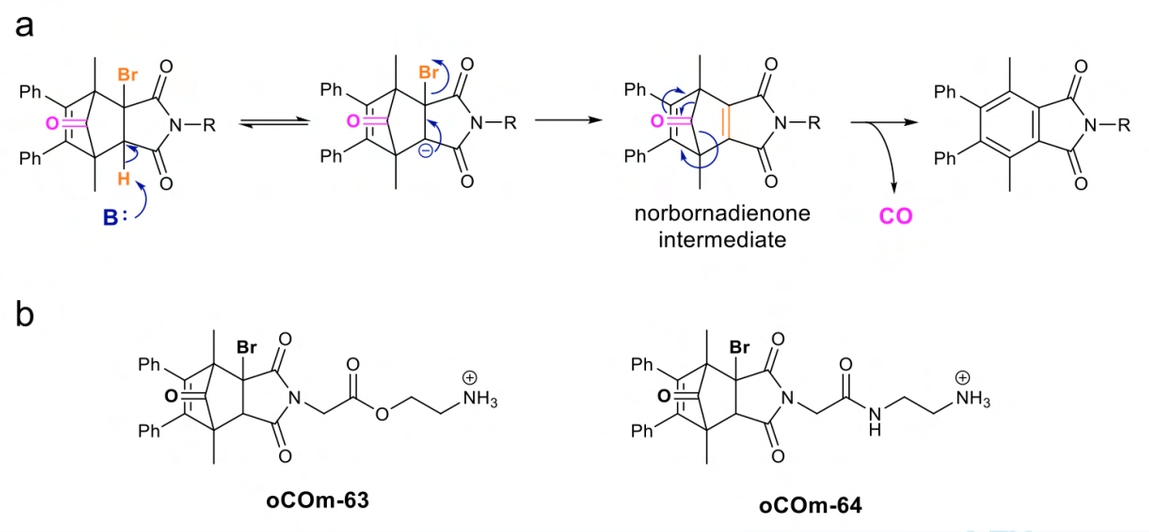
Metal centred redox potentials of complexes are well known to be dependent on ligand electronics – as established from extensive studies of the effect of systematic modification of the ligands. In this presentation I talked about the effect that coordinating different azine & diazine rings to the group 8 metal ions (Fe^{II}, Ru^{II} and Os^{II}) has on the electronic structures of the complexes. A combination of computational and experimental results was presented and discussed. The key finding was that through the use of DFT to determine the energy of the HOMO of the complexes, and cyclic voltammetry to determine the $E_{1/2}(M^{2+/3+})$ redox potential, a trendline can be set up for a family of compounds. It is then possible to use this trendline to predict the redox potentials of a new compound in the family.

Nathan Bell - Best Talk

Carbon monoxide releasing compounds have been described as useful therapeutic agents for ischaemic reperfusion injury. To date, these compounds are largely metal carbonyl complexes, which have issues with toxicity and aqueous solubility. In the Larsen group, an organic, pH-dependent CO-releasing prodrug system (called oCOm) has been developed. The CO release is believed to be by an $E1_{cb}$ elimination, then chelotropic decomposition (see Fig a.). It is hypothesised the rate-limiting step is the base-abstraction of the methine proton. By synthesising oCOms with electron-withdrawing groups on the imide nitrogen, which should increase the acidity of the methine proton, this project attempts to both determine the rate-limiting step of CO release and to provide oCOms that more rapidly release CO, with the initial goal of half-lives approximately one hour. To date, oCOms-63 and -64 (see Fig. b) have been synthesised, containing an ester and amide group respectively. As hypothesised, the acidity of the methine proton was greater in oCOm-63 than -64, and the rate of CO release from -63 was promising, with a half-life of approximately 77 minutes. However, both suffered from solubility issues is aqueous media, and work is ongoing to establish water soluble analogues, as well as to employ a broader range of electron-withdrawing groups and spacings from the imide nitrogen.

Nicholas Smith - Most Creative Talk

Metallic nanoparticles often exhibit useful properties such as for catalysis. These properties largely depend on the types of structures and surface features that a nanoparticle exhibits experimentally. These structures can be determined theoretically using global optimisation algorithms that explore the potential energy surface (PES) of nanoparticles in search of the most stable structure. Basin hopping algorithms explore the PES by taking an initial structure and perturbing it randomly, locating and moving to other stable structures in the process. Unfortunately, the algorithm can stagnate in deep energy wells, with high energy barriers, where the energy required to escape to structures in other wells is very high. This project aims to prevent stagnation and increase the computational efficiency of the algorithm by incorporating structural similarity into the decision making process. We hypothesise this will encourage the algorithm to



move to structurally distinct nanoparticles, even if they have high energies, allowing the algorithm to scale the walls of deep energy wells.

Ciaran Ward - Most Engaging Talk

My research focuses on modelling the hydrogen evolution reaction (HER) on MoS_2. By catalysing the electrochemical HER we have a clean method of producing an environmentally friendly fuel - hydrogen. Pt is currently the most active catalyst for the HER. However, the more earth abundant mineral - MoS_2 - has shown catalytic tuneability through the addition of support layers. I specifically look at Au and graphene supported systems.

To further understand and exploit this tuneability a complete understanding of the HER mechanism on supported MoS_2 is needed. This requires modelling the thermodynamic and kinetic contributions to the mechanism rigorously. Some findings point to the critical role that the solvent and potential play when modelling this system. I use state-of-the-art Vienna Ab initio Solvation Package with the solvent module (VASPsol) to correctly capture these factors.

Quinn van Hilst - Most Persistent Student

Metallosupramolecular assemblies (MSAs) such as cavitands, helicates, metallodendrimers and molecular metal knots have been shown to possess biological activity. Metallo-cages also show promise as potential vectors for drug delivery due to their inherent cavities and subsequent guest binding. Additionally, the cages themselves can also show cytotoxic acivity. Platinum complexes are well known for their cytotoxic activity, with certain platinum cages inheriting this activity as well. Interestingly, platinum complexes have also been shown to possess antibacterial activity, and little attention has been given to the possible antibacterial properties of platinum cages. Due to the relative inertness of platinum(II), platinum MSAs are not always readily accessible. Utilising a preformed platinum(II) tetraaldehyde complex as a capping unit, and a series of diamines as linkers, we have assembled a small family of platinum(II) cages using a dynamic covalent approach to the metallosupramolecular assembly. The cages will be tested for their bacterial and cytotoxic activity against a variety of cell lines and possible host-guest interactions will be explored.

Ian Liddle - Best Understanding of Project

Recently, a series of cannabinoid type 2 receptor (CB_2R) positive allosteric modulators has been discovered. These compounds share a common pharmacophore with several CB_2R agonists. Within the Vernall lab, we aim to explore the structure-activity relationship and binding mode for these CB_2R PAMs. Thorough molecular docking has positioned these compounds to bind in the CB2R orthosterics site. To support the docking model, several derivates containing hydrophilic or bulky groups that would reduce orthosteric binding are being synthesised. In collaboration with Professor Michelle Glass (Department of Pharmacology and Toxicology, UoO) the compounds will be tested for agonist and allosteric activity.

Book review

Book Review: *What is a chemical element?*

Scerri, E.; Ghibaudi, E. (Eds.), Oxford University Press, 2020

The opening words of the Introduction – "What is a chemical element?" – restates the book's apparently simple title. Rather more helpful is the title of Chapter 1 – "The many questions raised by the dual concept of 'element' ", because these words go to the heart of this collection of 14 essays, for which I found the editors' brief summaries in the Introduction (pp. 2-4) were helpful.

The overarching intent of the 14 essays is discussion of the dualism of the definition of chemical element. This is traced back to Dimitri Mendeleev[1] and persists to the present day in the Gold Book published by the International Union of Pure and Applied Chemistry (IUPAC).[2] The historic context of some essays stretch as far back as Aristotle, but most contributors confined their pre-Mendeleevian discourse to Antoine Lavoisier and John Dalton. Many essays also featured a discussion of the contribution of the philosopher Fritz Paneth[3] to their particular perspective.

Scerri's chapter ("The many questions….) sets the scene for the book well, gently taking the reader though the 'duality' of the IUPAC definition of 'element' that is central to the book. Along the way he makes "an appeal to authority" by reflecting on Mendeleev's recognition of duality, making "a clear distinction between the conception of an element as a separate homogeneous substance and as a material but invisible part of a compound", and Paneth's "abstract sense of 'element'". Although Scerri attributes Mendeleev's successful predictions of elements to his definition of element, he concedes that both Mendeleev and Paneth contributed to the continuing confusion. Unsurprisingly, therefore, references to Mendeleev, Paneth and the IUPAC Gold Book occur in many later chapters of this book. Scerri continues by considering the potential roles of the nucleus and of electrons in any definition of element, declaiming the former and somewhat supporting the latter. Somewhat distracting to the chapter's progress is his inclusion of the "Group 3" problem, which has been well rehearsed elsewhere.[4] The final part of his chapter discusses seven 'open questions' – "controversial issues … many of which are addressed in the present volume" (p. 22), leaving the reader to decide in which essays these issues are addressed. Making clear the link between these questions and the essays that follow could have been a fitting conclusion to the book – or, indeed, could be a suitable exercise for students perusing this book who are reading for a degree in the philosophy of science!

The next four chapters form a group examining the contributions to chemistry of "ancient theories", Antoine Lavioisier's "compositional definition of element" and "the positive attribute" provided by John Dalton's atomic weight, and – of course – Mendeleev. Chapter 4 – set in the eighteenth century, with the delightful subtitle "Colorless airs in late-eighteenth-century chemical practice" – might have been better placed as the first chapter in this group. In Chapters 2 and 4, the historic context of Lavoisier's and Dalton's work is clearly articulated, but the foreshadowed connection in Chapter 2 to Mendeleev's "conceptual framework" is less obvious. Chapter 3 describes Mendeleev's achievements, along the way making his contribution to chemical education (referred to, as expected, also in Chapter 14) clearer than do many accounts. Inevitably, there is some overlap between the history described in Chapters 2 through 5 as well as the highly readable scene-setting of "ambiguity" covered in Chapter 6. Perhaps refreshingly, in a book focused on ambiguity and dualism, Chapter 6 reaches a dogmatic conclusion: "The notion that all indecomposable constituents of substances are 'elements' – usually attributed to Boyle or Lavoisier, but definitely not endorsed by either of these authors – should now, finally, be abandoned."

Chapter 7 initially revisits Dalton's contribution, viewing it rather less charitably than in earlier chapters. It then turns to debate whether the superheavy elements that are synthesised rather than discovered in the traditional sense actually or only possibly exist, ultimately suggesting that "the existence of an SHE [superheavy element] is typically established when it exists long enough to be detected in a high-energy experiment in which nuclei of some kind are bombarded with particles of some other kind". Chapter 8 opens with the IUPAC dual definition of element and proceeds to discuss in detail the philosophies of Kant and Cassirer. Also dominated by philosophy associated with operational definitions, the aspect of Chapter 9 that piqued my

interest was its stance on "scientific revolutions", asserting that "all big revolutions concerned only very specific fields of science, with little or no impact on others, such as astronomy (Copernican revolution), mechanics (relativistic, quantum mechanics, biology (Darwinian revolution), geology (plate tectonics)…." Many scientists would counter this assertion by pointing out that the ideas of Darwin and the plate tectonicists, in particular, remain influential today in fields well beyond their initial application: fields as diverse as genomics and climate change, respectively. Moreover, the concept of scientific revolutions may itself be becoming passé,[5] and there are certainly recent critiques of its use in chemistry that counter Schummer's stance.[6]

Chapter 10 opens by noting that a multiplicity of meanings is not unique to the word "element". Initially appearing to advocate pragmatism, the writer concedes that "the multitude of different and often contradicting definitions leads to confusion among both students and professionals of chemistry" (p. 190). The distinctive feature of this chapter, however, is its recognition that, with the developments in nanochemistry, solid-state chemistry and materials science, "for the first time in their history, chemists have to hold the composition, the structure, the parts, the whole compound, the environment and the device together within the same explanation" (p. 198). This leads the chapter's author to ask whether "it would be useful to chemists to keep on referring to elements in the same way they previously did in order for them to address the increase in all those more and more individualized particulars?" (p. 200). He all but asks whether the application of 'dualism' to the definition of element is outmoded. A further consideration of Paneth's analysis of the concept of element in a subsequent chapter (Chapter 13) – leads to a similar thought: "The element might not be the only concept that lies at the crossroads of theory and experiment… other chemical concepts might exhibit a similar duality…" (p. 255).

Chapter 11 breaks into different ground in this book by exploring Putnam's twin earth ideas; Ostwald's assertion that "elements have to be made or prepared rather than only to be discovered" (p. 217), which recalls the debate about the existence of superheavy elements discussed in Chapter 7; and philosopher Bachelard's "unusual attempt … to come to terms with the peculiarities of chemistry" (p. 217). This delving leads to a concluding statement that "'Making of elements' can mean to invent abstract pictures derived from everyday experience, to search for the composition with or without the presuppositions of atoms and elements, or to run accelerators in order to form bigger atomic nuclei from smaller ones" (p. 222), and asserting: "This is enough to designate the real in chemistry as an achievement". Perhaps so, but the undeveloped relationship of this essay to others in the book may leave some readers dissatisfied.

For those less familiar with a mathematical approach, Chapter 12 opens with a reassuring title to its opening section, viz., "Concept-formation. How difficult is it?" Even if the mathematics appears difficult to some readers, the conclusion is understandable and seems reasonable.

The preliminary summary on p. 3 for Chapter 14 (the final chapter) indicated that, albeit with an educational focus, it would "take a stance for an abstract conception of the element, understood as a category identified by the atomic number." And so it does, but in a way that brings together many of the ideas of the previous twelve essays, and thereby becomes a satisfactory conclusion to the book.

As a final activity in undertaking this review, I looked at the end of each chapter for each contributor's conclusion or a summary of the essay's essential points. The length and format of these sections are highly variable, but I determined a 'sentiment score', a measure of marketability or the essay's potential interest to the reader, for either the whole concluding section, or – if it was long – excerpts that seemed to capture the essence of the chapter. The results of this endeavour are shown in Table 1, together with the sentiment scores of the editors' summaries in the book's introduction (pp. 2-4). The sentiment scores of the editors' summaries are generally lower than the sentiment scores of the contributors' conclusions (Fig. 1). Although some of the contributors' conclusions have high sentiment scores, which suggests that this book could be a useful addition to the chemist/philosopher's library, the negative sentiment of other chapters' conclusions and / or editorial summaries suggests that these particular contributions to the book may prove rather more challenging to some readers.[7]

Peter Hodder
School of Government,
Victoria University of Wellington, New Zealand
and
HodderBalog Social and Scientific Research,
Wellington, New Zealand

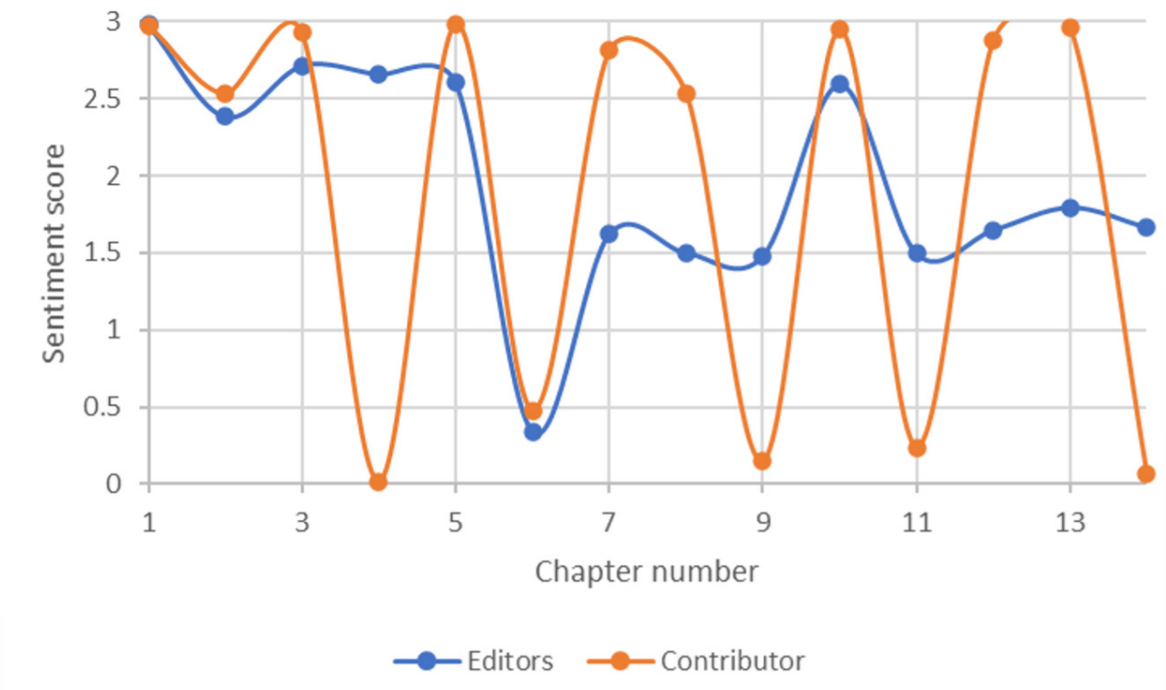


Fig. 1. Variation of sentiment scores of editors' summaries and sentiment scores of the essayists' conclusions, by chapter number (data in Table 1). Negative sentiment gives a 'sentiment score' between 0 and 1, neutral sentiment gives a 'sentiment score' between 1 and 2, and positive sentiment gives a 'sentiment score' between 2 and 3; see also footnotes to Table 1.

1. Mendeleev's work is often cited and discussed in the essays; see, for example: Mendeleev, D. I. Principles of Chemistry, vol. 1. Translated into English by G. Kamensky. Longmans, Green and Co.: London, 1891, p. 23; Mendeleev, D.I. Rev. Gen. Chm. Pur. Appl. 1899, 1: 211. Translated in Mendeleev on the Periodic Law, Selected Writings, edited by W.B. Jensen. Dover: Mineola, New York, 2002, p. 33.
2. McNaught, A.D.; Wilkinson, A. (compilers). IUPAC. Compendium of Chemical Terminology, 2nd ed. (the "Gold Book"). Blackwell Scientific Publications: Oxford, 1997. Online version (2019-) created by Chalk, S.J. S. J. ISBN 0-9678550-9-8. https://doi.org/10.1351/goldbook. (The definition of 'chemical element' in the "Gold Book" can be verified online at: https://goldbook.iupac.org/terms/view/C01022)
3. Often cited and discussed in the essays is: Paneth, F.A. The epistemological status of the chemical concept of element. British Journal for the Philosophy of Science 1962, 13: 1-14, 144-60. This paper was reprinted in Foundations of Chemistry 2003, 5: 113-145.
4. Scerri, E.; Parsons, W. What elements belong to Group 3 of the Periodic Table? In Scerri, E.; Restrepo G. (eds). Mendeleev to Oganesson. A Multidisciplinary Perspective on the Periodic Table. Oxford University Press: New York, 2018, pp. 140-151.
5. Schummer admits that much of his chapter draws on his mid-1990s publication: Schummer, J. Realismus und Chimie. Königshausen and Neumann: Würzburg, 1996. Doing so enables him to ignore more recent suggestions of an 'ecological ' rather than 'revolutionary' explanation for the progress of science, e.g., Scerri, E. 2016. A Tale of Seven Scientists and a New Philosophy of Science. Oxford University Press: New York, 2016, pp. 190-202.
6. Scerri, E.R. Reassessing the notion of a Kuhnian revolution: What happened in twentieth-century chemistry. In: Wray, K.B. (ed.). Interpreting Kuhn. Critical Essays. Cambridge University Press: Cambridge (United Kingdom), in press for 2021, pp. 125-144. Of Scerri's contribution to this book, the editor, Wray, writes, "Eric Scerri provides an analysis of the notion of a Kuhnian revolution, through a detailed examination of an episode in the history of chemistry, when chemists came to classify elements by their atomic number rather than by their atomic weight. Scerri considers the extent to which this change in chemistry constitutes a revolution in the sense articulated in SSR [i.e., Kuhn, T.S. The Structure of Scientific Revolutions. University of Chicago Press: Chicago, 1962.]
7. It is a little disappointing to observe that there are some places in the text where copy-editing and/or proof-reading have lapsed; examples include: occasional missing words from sentences, incomplete sentences, and incomplete in-text citations of references. Fortunately, these blemishes do not disrupt the flow of the chapters unduly, which justifies my relegation of this comment about them as the final footnote.

Table 1. Sentiment of chapters in Scerri & Ghibaudi (2020)*

Theme†	Chapter No.	Author and title of essay/chapter	Editors' preliminary summaries		Essayists' conclusions	
			Sentiment polarity and % ‡	Sentiment score ¶	Sentiment polarity and % ‡	Sentiment score ¶
[Summary]	1	Scerri, E.R. The many questions raised by the dual concept of 'element'	+98.1%	2.981	+97.8%	2.978
Elements as non-decompounded bodies	2	Bensaude-Vincent, B. From simple substance to chemical element	+38.4%	2.384	+53.4%	2.534
	3	Brooks, N.M. Dmitri Mendeleev's concept of the chemical bond prior to the periodic law	+71.6%	2.716	+92.6%	2.926
Pre-Lavoisieran chemistry	4	Blumenthal, G.; Ladyman, J.; Seifert, V. Referring to chemical elements and compounds: Colorless airs in late-eighteenth century chemical practice	+65.9%	2.659	-98.6%	0.014
A focus on Dalton	5	Banchetti-Robino, M.P. The changing relation between atomicity and elementarity: From Lavoisier to Dalton	+60.4%	2.604	+98.5%	2.985
The modern meaning of element	6	Earley, J.E., Origins of the ambiguity of the current definition of chemical element	-66.0%	0.340	-52.2%	0.478
	7	Hendry, R.F. The existence of elements, and the elements of existence	N62.3%	1.623	+81.3%	2.813
	8	Mahotiian, F. Kant Cassirer, and the idea of chemical element	N50.1%	1.501	+53.7%	2.537
	9	Schummer, J. The operational definition of the elements: A philosophical reappraisal	N48.0%	1.48	-85.4%	0.146
Epistemological concerns	10	Llored, J-P. Substance and formation: The case of chemical elements.	+59.3%	2.593	+99.0%	2.950
Reducible material character of chemistry	11	Ruthenberg, K. Making elements	N49.5%	1.495	-76.2%	0.238
Ontology of the chemical element	12	Restrepo, G. A formal approach to the conceptual development of chemical element	N64.9%	1.649	+88.2%	2.882
Reappraisal of connection between chemical operations and chemical theory	13	Hijmans, S.N. Chemical elements and chemical substances: rethinking Paneth's distinction	N79.6%	1.796	+96.7%	2.967
Educational problems caused by the dual definition of the elements	14	Ghibaudi, E.; Regis, A.; Roletto, E. The dual conception of the chemical element: Epistemic aspects and implications for chemical education	N66.6%	1.666	-93.8%	0.062

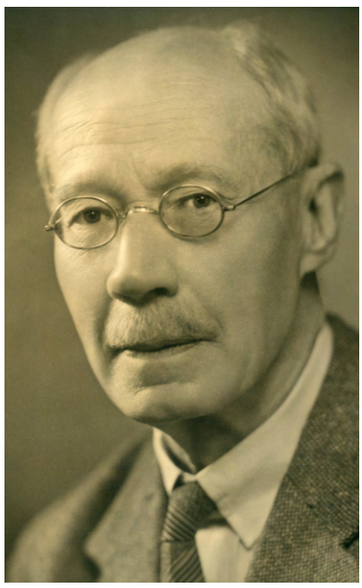
*The text used for sentiment analysis for each chapter is (i) the editors' preliminary summaries in the Foreword (pp. 2-4), and (ii) the contributors' conclusions: either the complete 'conclusion' section (as in Chapters 1, 4, 5, 9, 11, 12, and 14), excerpts if the section is very long (as in Chapters 2, 3, 6, 7, 8, and 13), or the introduction (as in Chapter 10).

† The theme of a cluster of contributions are indicated in the Foreword (pp. 2-4),

‡ Sentiment polarity (negative [-], neutral [N], or positive [+]) and percentage determined from: https://monkeylearn.com/sentiment-analysis/

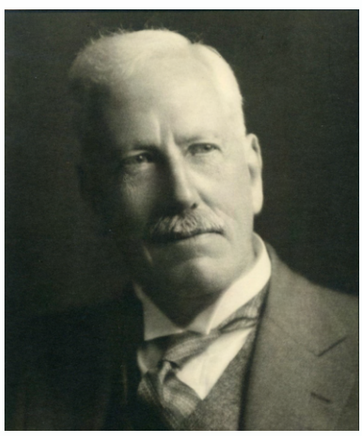
¶ Sentiment score is: 1-(negative %/100), giving a range of scores from 0-0.99; or 1+(neutral %/100), giving a range of scores from 0-1.99; or 2+(positive %/100), giving a range of scores from 2.00-3.00. On this basis sentiment scores will be between 0 and 3.

From the NZIC photo archives



Professor W P Evans,
1st NZIC President, 1931-1932

NZIC Conference 1951, Hamilton



Sir Thomas Easterfield,
2nd NZIC President, 1933

NZIC Conference 1948, Dunedin

NZIC Conference 1945, Palmerston North

Article

The fascinating chemistry of nudibranchs and their potential for new drug discovery

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Keywords: *drug*, *nudibranchs*, *natural products*, *secondary metabolites*

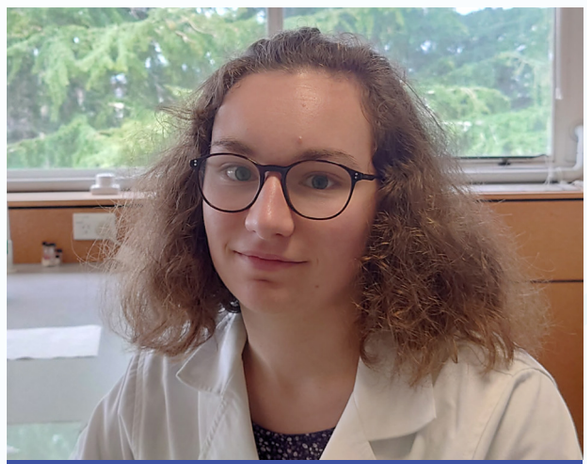
The marine environment and natural products

Due to its wide area (71% of the earth's surface), range of temperature (from -1.5°C in sea ice to 350°C in deep hydrothermal systems), pressure (1 to over 1,000 atmospheres) and light (complete darkness to photic zone), the ocean harbours a huge biodiversity of life fundamental to our planet.[1,2] More than 236,000 marine species are currently known according to the World Register of Marine Species (WoRMS)[3] and many more are yet to be discovered. Indeed, according to the international Census of Marine Life that recorded the diversity and abundance of life in the ocean from 2000 to 2010, at least 50% and potentially more than 90% of marine species remain currently undescribed by science.[2] Invertebrates account for approximately 60% of all marine animal diversity,[2] with most of them belonging to the phyla Bryozoa, Cnidaria, Porifera and Mollusca.[4]

This large degree of diversity favoured the production of a great variety of organic molecules, especially primary and secondary metabolites.[5] Unlike primary metabolites, secondary metabolites (also called natural products) are compounds that are not directly involved in the normal growth or reproduction of an organism but instead often provide selective advantage to the organism by increasing its survivability or fecundity.[6] Natural products in general are usually relatively small molecules with a molecular weight below 3,000 Daltons exhibiting considerable structural diversity.6 Approximately 28,500 marine natural products (MNPs) had been identified by the end of 2016. These secondary metabolites show diverse biological properties, with cytotoxicity and anticancer activity being the most common, useful for the development of new lead compounds for example.[5]

Marine natural products in medicinal chemistry

The importance of natural products (NPs) in drug discovery has been extensively documented,[5, 7-8] and is acknowledged by the World Health Organisation.[5,9] So far, six drugs from MNPs and derivatives have been approved by agencies such as the U.S. FDA (United States Food and Drug Administration), European Medicines Agency (EMEA), Japanese Ministry of Health and Australia's Therapeutic Goods Administration.[10] Fig. 1 highlights the approval year, the use and the origin of the six approved



Lauren Gris obtained her MSc degree from the Engineering Graduate School SIGMA Clermont, France, after completing two internships in New Zealand focused on natural products under the supervision of Brent Copp and Merilyn Manley-Harris. She is currently undertaking a PhD at Waikato University under the chief supervision of Michèle Prinsep, focusing on the chemistry of the relationship between nudibranchs and their marine invertebrate prey.

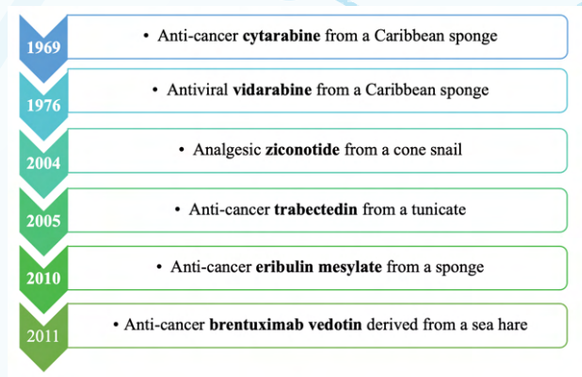


Fig. 1. The six MNPs and derivatives approved drugs

drugs of marine origin. Interestingly, four out of the eight approvals occurred in the 21st century.

The anticancer drug, cytarabine, was developed following the discovery of spongouridine from the Caribbean sponge *Tectytethya crypta*.[2] It is mostly used in the treatment of myeloid leukaemia and was the first drug derived from MNPs approved by the FDA. Vidarabine, isolated from the same sponge, was approved as an antiviral drug in 1976. While cytarabine is still in use today, vidarabine has been discontinued in the US and EU markets. The peptide ziconotide (Prialt), indicated for pain control, was the first FDA-approved drug (2004) directly isolated from a marine organism and corresponds to a toxin of the marine cone snail Conus magus. The snails produce a venom consisting of different peptide toxins, named conotoxins that they use for defence and prey capture. The anticancer FDA-approved drug (2015) trabectedin, (Fig. 2), was directly isolated from a marine source, the tunicate *Ecteinascidia turbinata*. Another anticancer agent, eribulin mesylate, is a synthetic derivative of the polyketide MNP halichondrin B. It was approved by the FDA in 2010 and by the EU in 2011 for patients with locally advanced or metastatic breast cancer.[2] The last approved anticancer drug related to a MNP is the antibody–drug conjugate (ADC), brentuximab vedotin. This drug was approved by the FDA in 2011 and in Europe in 2015. It consists of the cytotoxic compound auristatin, originally isolated from the mollusc *Dolabella auricularia*, and an antibody. Several other candidate compounds are present in the pipeline, and marine natural products are being evaluated in Phase I–III clinical trials in the United States and Europe for the treatment of various cancers.[11]

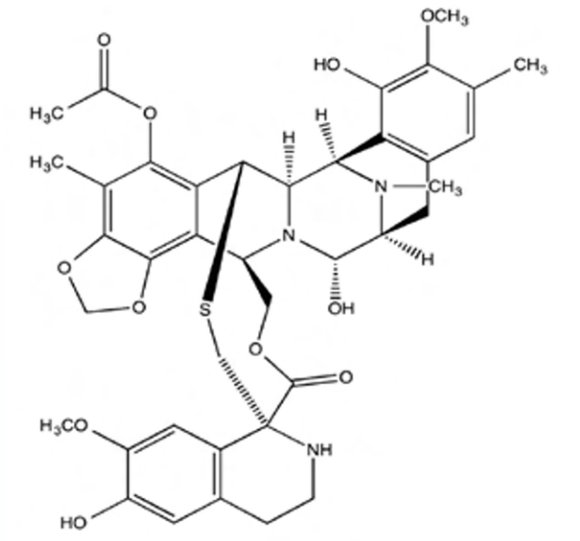


Fig. 2. Chemical structure of trabectedin

Nudibranchs

Nudibranchs (Fig. 3), are fascinating soft-bodied marine gastropod molluscs often referred as the “butterflies of the ocean”12 or more generally as sea-slugs. They bear some of the most fascinating shapes and colours found in the animal kingdom. The name *nudibranch*, coming from the Latin *nudus* for "naked," and the Greek *brankhia* for gills, refers to the exposed cerata on the backs of many species.[13] With more than 4,700 species known, nudibranchs are well represented within the Gastropoda class. They are found throughout the world's oceans, but are most abundant in shallow, tropical waters. Almost all nudibranchs live in the benthic zone, from shallow water to a depth of 30 metres, and their size rarely exceeds 5 cm.[14]

Nudibrachs are carnivorous and are most often found around their favourite sessile prey: sponges, bryozoans, cnidarians and even other nudibranchs.[14] They are essentially blind and perceive their environment, as well as their prey, through chemosensory interactions with their two highly sensitive tentacles, called rhinophores.[15] These

Fig. 3. A dorid nudibranch, Risbecia tryoni. Image used with permission of Yaroslav Trukhanov.

tentacles come in all shapes and are structured in favour of a great surface area so that chemical detection is maximised.[15]

Nudibranchs derive their colours from the food they eat, which aids in camouflage while they are feeding. Their lifespan varies widely, with some living less than a month, and with others living up to one year. They are hermaphrodites and can mate with any other mature member of their species.[16] Nudibranchs perform both the “male role” of donating sperm to a mating partner and the “female role” of receiving sperm from the partner simultaneously during copulation.[16]

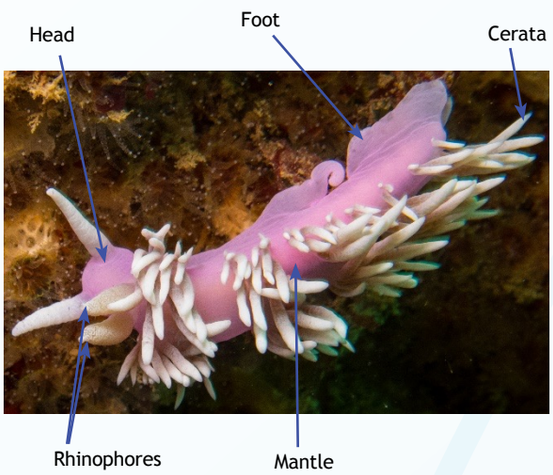
Chemical defence mechanism

Nudibranchs have few documented predators, despite their apparent lack of physical protection and slow moving capacities, suggesting that they have a particularly effective defence strategy.[17] After shedding their shells as larvae, nudibranchs thereafter remain shell-less.[13] To compensate for a lack of physical protection, they employ a unique chemical defence mechanism to protect themselves from predators.[14] The nudibranchs' defence mechanism relies on aposematism, meaning that their unpalatability is associated with a warning signal, such as vibrant colours which are intended for potential predators.[18] This strategy is beneficial both for the aposematic species and for its potential predators. Nudibranchs' unpalatability, causing a nauseating effect or even killing predators upon being consumed, comes from their toxic and distasteful secondary metabolites. They are obtained either directly from their prey by sequestration or by *de novo* biosynthesis.[19] The latter ability is regarded as an evolutionary step beyond the simple accumulation of dietary metabolites, since the *de novo* production of noxious substances allows the organism to become independent of specific food availability.[20] Nudibranchs are separated into Dorodina and Cladobranchia, two suborders (Fig. 4).3 Some aeolid nudibranchs, (Fig. 4A), (suborder Cladobranchia), possess a special defence mechanism: the ability to sequester nematocysts (stinging cells) from their cnidarian prey, such as hydroids, sea-anemones and soft corals.[21] Indeed, their mantle is extended into long projections called cerata, that contain branched digestive glands.[22] As the aeolids absorb oxygen through their skin, the cerata increase the surface area of the nudibranch, helping them absorb more oxygen.

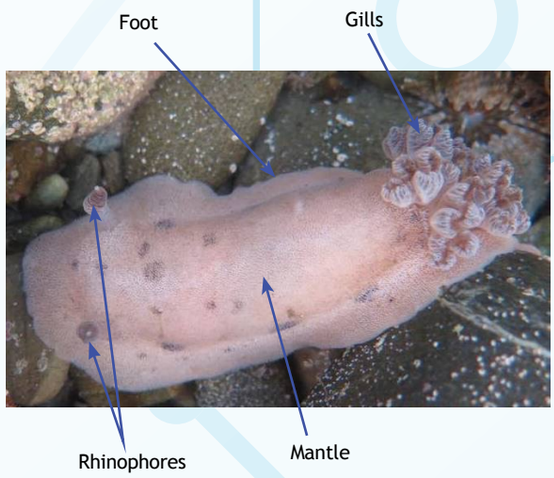
The tips of the cerata contain cnidosacs, the structure that houses the sequestered stinging cells, previously indicated as nematocysts.[22] The nematocysts are ingested and a portion of the stinging nematocysts remain undigested[23] and are passed through the digestive glands, migrated to the tips of the dorsal cerata and stored in cnidosacs within specialised cells termed cnidophages.[24] Once sequestered, these small capsules can be discharged by injecting venom into the tissues of other organisms for defensive purposes.[21] This specific ability is distributed across roughly 600 species within Cladobranchia.[21] The incorporation of stinging nematocysts into the cerata of nudibranchs is one of the truly unique methods of adaptation and survival in the animal kingdom.[23]

Aeolid nudibranchs can avoid nematocyst envenomation by their cnidarian prey while feeding because of several adaptations, including mostly behaviours that limit contact with their prey and by their mucus that specifically inhibits the discharge of nematocysts from Cnidarian tentacles.[25]

In contrast, dorid nudibranchs, (Fig. 4B), (suborder Doridina) have an intact digestive gland and are distinguished by the gills circling the anus, used for oxygen exchange.13 Dorid nudibranchs have a thick mantle that extends over the foot. Some dorid nudibranchs concentrate the toxic dietary metabolites in the more exposed parts of their body, in glands and/or spicules incorporated in the mantle skin, called mantle dermal formations (MDFs). The exact reason why dorid nudibranchs evolved in a way to develop these specific MDFs is still unknown. It has been proposed that their function is simply to concentrate and store the metabolites until they are released at an appropriate time.



(A) Aeolid nudibranch



(B) Dorid nudibranch

Fig. 4. (A)Anatomy of an aeolid nudibranch (Jason mirabilis) and (B) a dorid nudibranch (Alloiodoris lanuginata)

However, alternative reasons for the presence of MDFs in dorid nudibranchs have been proposed. In particular, it has been suggested that the defensive function of these structures is only secondary and that their primary function is to avoid autotoxicity.[26]

Glaucus atlanticus

Glaucus atlanticus, (Fig. 5), also referred to as the blue dragon, is an aeolid nudibranch that occurs in temperate and tropical oceans throughout the world.[27] It is characterised by a white dorsal surface and a dark blue ventral surface, can grow up to 3 cm and is flattened. Its cerata, (called papillae for this specific species), are characterised by a wing-like shape, and are extended on the left and right side of its body, which is quite unusual for nudibranchs. *G. atlanticus* drifts on the surface of the ocean, being carried by the currents and the winds[28] and unlike most of its congeners that move by crawling, it floats upside-down on the surface of the water by means of an air bubble that has been swallowed and stored in the gastric cavity.[27] In this way, it is able to move towards its prey, for example the Portuguese man-of-war, *Physalia physalis*, by using their cerata to make slow swimming movements and their rhinophores to sense chemicals indicating the prey's presence.[27]

When feeding, *G. atlanticus* use their jaws and radular teeth to grab and tear the soft tissues and tentacles of the man-of-war (Cnidaria) which contain stinging cells.[29]

It needs to sense the presence of the stinging cells to avoid inadvertently stinging itself upon any physical impact. *G. atlanticus* takes advantage of this chemical sensory perception to locate and eat the tentacles without the man-of-war detecting a chemically foreign body.

Having eaten the tentacles and the nematocysts they contain, the nudibranch selects the most potent nematocysts for its own use, discarding the others and concentrating the nematocysts in its cnidosacs, as previously explained. As a result, the tiny nudibranch is more venomous than the huge tentacles of the man-of-war.

Sequestration of secondary metabolites

As previously explained, the nudibranch's chemical defence mechanism relies on toxic and distasteful secondary metabolites that are obtained either directly from their prey or by *de novo* biosynthesis. These metabolites are especially interesting because of their pharmacological and biological properties and can become lead compounds for the development of new drugs.

Fig. 5. *Glaucus atlanticus* (left) eating *Physalia physalis* (right). Image used with permission of Doug Perrine.

Most of the metabolites sequestered are either terpenes, alkaloids or steroids, with some of them possessing antifeedant-properties. They are sequestered mostly from sponges, bryozoans or cnidarians.

Sequestration from sponges

The nudibranchs *Hypselodoris godeffroyana*, *H. maridadilus* and *H. infucata* are able to sequester two sesquiterpenoids, nakafuran-8 **(1)** and –9 **(2)**, from their common prey, the marine sponge *Dysidea fragili*, (Fig. 6).[30-31] Both compounds were isolated in the same ratio as found in the sponge prey and possess antifeedant properties against the common reef fish *Chaetodon* sp. but no antimicrobial activity was found.[31]

Sequestration from bryozoans

The three nudibranchs T*ambja abdere, T. eliora,* and *Tyrannodoris tigris*, and the bryozoan *Sessibugula translucens* live in a very close association. In particular, the nudibranchs *T. abdere* and *T. eliora* occur only in locations where *S. translucens* is common, and individuals are generally found on or near the bryozoan. According to field observations, *T. tigris*, which feeds on smaller nudibranchs, prefers to prey on *T. abdere* and *T. eliora* and is most found in areas where the *Tambja* nudibranchs are, and therefore the bryozoan *S. translucens* also occurs.

Chemical analysis of the nudibranchs *T. abdere, T. eliora,* and *T. tigris*, found in the Gulf of California, revealed the

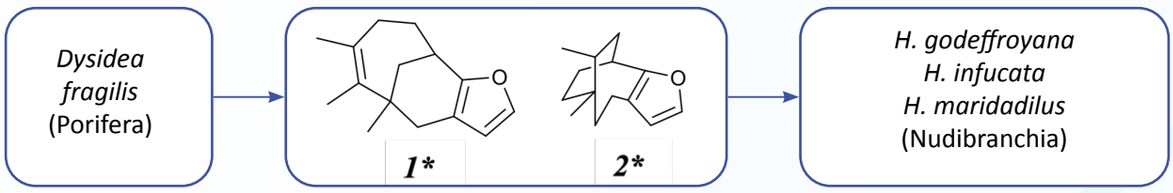


Fig. 6. Sequestration of sponge secondary metabolites by H. godeffroyana, H. maridadilus and H. infucata. Structures with a * symbol denote a sequestered metabolite.

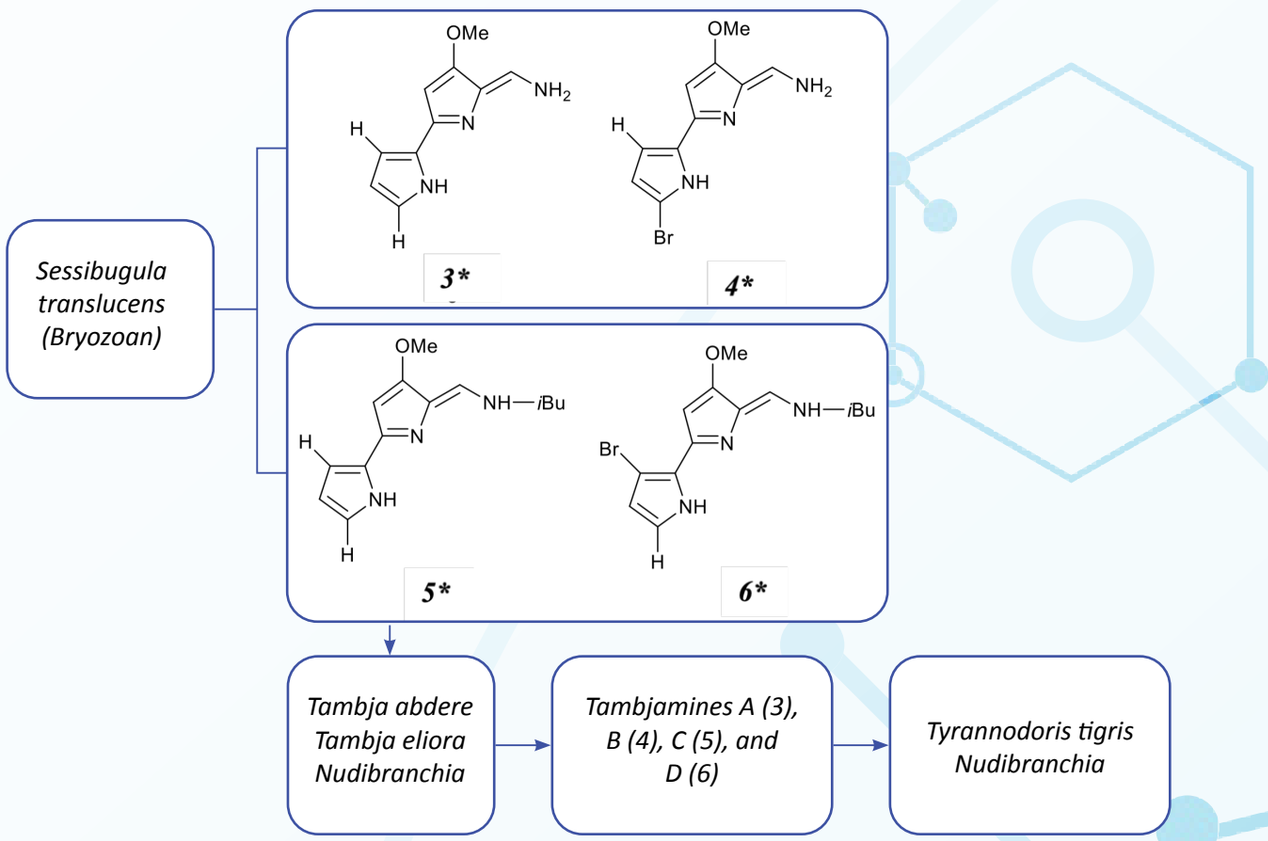


Fig. 7. Sequestration of bryozoan secondary metabolites by T. abdere, T. eliora and T. tigris. Structures with a * symbol denote a sequestered metabolite.

presence of the tambjamines A-D **(3-6)**.[32-33] The tambjamines are very likely sequestered from the bryozoan *Sessibugula translucens*, which contains the same four alkaloids (Fig. 7).[32-33] The compounds were screened for fish feeding inhibition, antimicrobial activity and as inhibitors of cell division in a sea urchin egg assay. All four compounds **(3-6)** showed feeding deterrence against spotted kelpfish *Gibbonsia elegans*,[33] compounds **3** and **4** inhibited cell division and showed moderate antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis* and *Vibrio anguillarum*.[32] Compounds **5** and **6** also showed moderate antimicrobial activity against *Candida albicans, S. aureus, B. subtilis* and *V. anguillarum* and mild activity against *E. coli*.[32] Additionally, compound **6** displays cytotoxicity against some human and murine cancer cell lines.[34]

In their attempts to avoid predation by *T. tigris*, the two species of *Tambja* employ very different escape responses: *T. abdere* produces a yellow mucus, containing large quantities of tambjamines that cause *T. tigris* to break off its attack. *T. eliora* does not seem to produce a defensive secretion but tries to escape from *T. tigris*' attack by a vigorous writhing motion. It was shown in laboratory experiments that *T. tigris* prefers to eat *T. eliora.* Field observations of *T. tigris* suggested that it could easily detect and follow fresh slime trails of *T. abdere, T. eliora* and several other nudibranchs,[33] showing that the tambjamines at low concentration act as a tracking pheromone but at higher concentration, as in the mucus, as an alarm/defensive pheromone.

Sequestration from cnidarian

Leminda millecra is a translucent pink nudibranch with a blue-edged mantle endemic to South Africa. This species, lacking external gills or cerata and possessing a distinct internal morphology, is the single representative of the Lemindidae family. *L. millecra* is particularly abundant at depths of 20-40 m, feeding on octocorals.[35] Its chemical analysis resulted in the isolation of four sesquiterpenes, millecrone A **(7)** and B **(8)**, as well as millecrol A **(9)** and B **(10)**.[35-36] Compound 7 inhibited the growth of the yeast *Candida albicans* whilst compound 8 was inactive against *C. albicans* but inhibited the growth of both the bacteria *S. aureus* and *B. subtilis*.[36] Gas chromatography-mass spectrometry (GC-MS) analysis identified the soft coral *Alcyonium faurias* as the source of compound 7 and the gorgonian *Leptogorgia palma* as the source of compound 8 (Fig. 8).[35] Three odorant terpene compounds (−)-atractylon **(11)**, (−)-isoatractylon **(12)** and isofuranodiene **(13)** were isolated from the Mediterranean octocoral *Maasella edwardsi* and its specialist predator, the nudibranch *Tritonia striata* (Fig. 9).[37] It was reported that food treated with the terpenes was rejected by the shrimp *Palaemon elegans.* The shrimp refused the food after repeatedly touching it with their mouths. It shows that although the compounds produce a characteristic smell when exposed to air, they are detected by direct contact in aquatic environments, by a "tactile" form of chemoreception. Thus, the mouthparts of the shrimp have been shown to act as "aquatic noses".[37] To conclude, the compounds studied act simultaneously

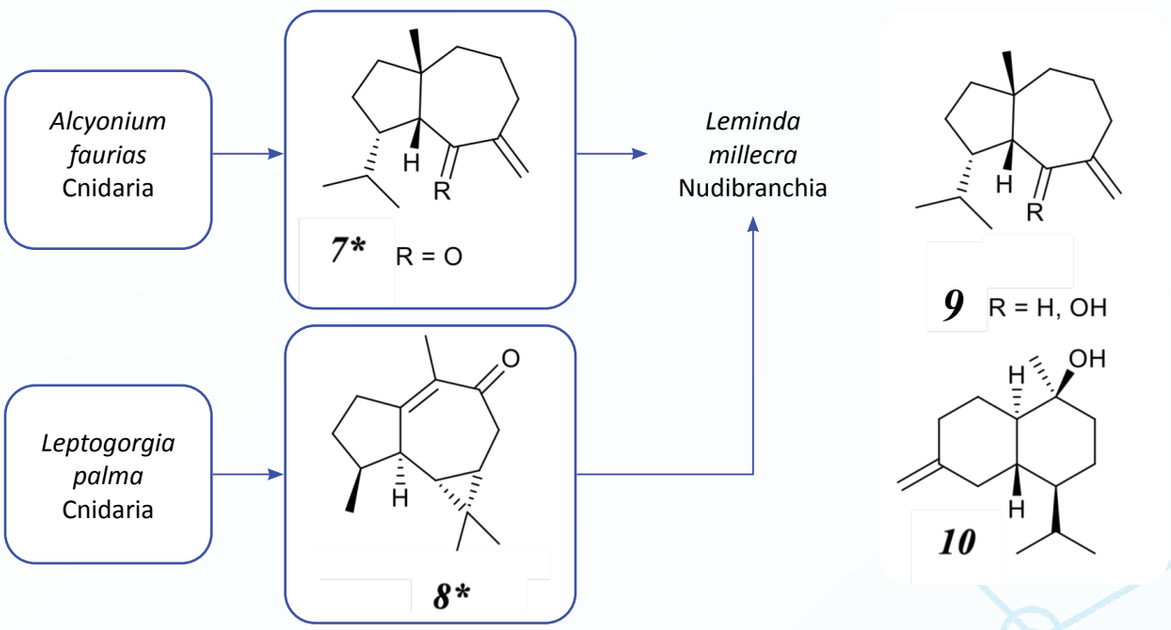


Fig. 8. Sequestration of coral and gorgonian secondary metabolites by L. millecra. Structures with a * symbol denote a sequestered metabolite.

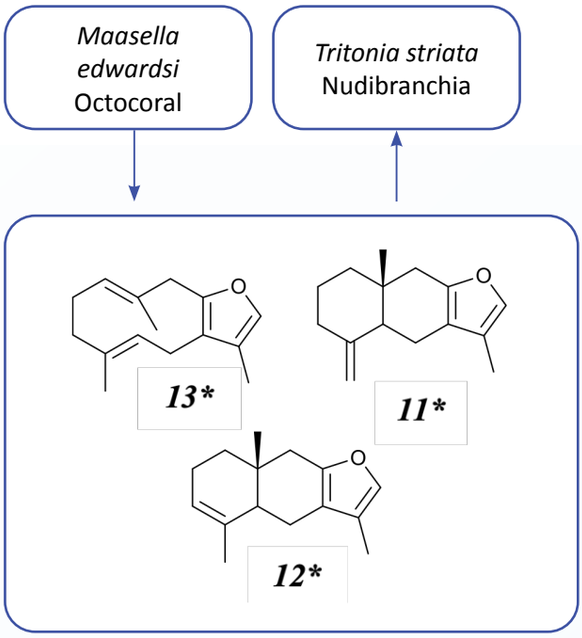


Fig. 9. Sequestration of octocoral secondary metabolites by T. striata. Structures with a * symbol denote a sequestered metabolite.

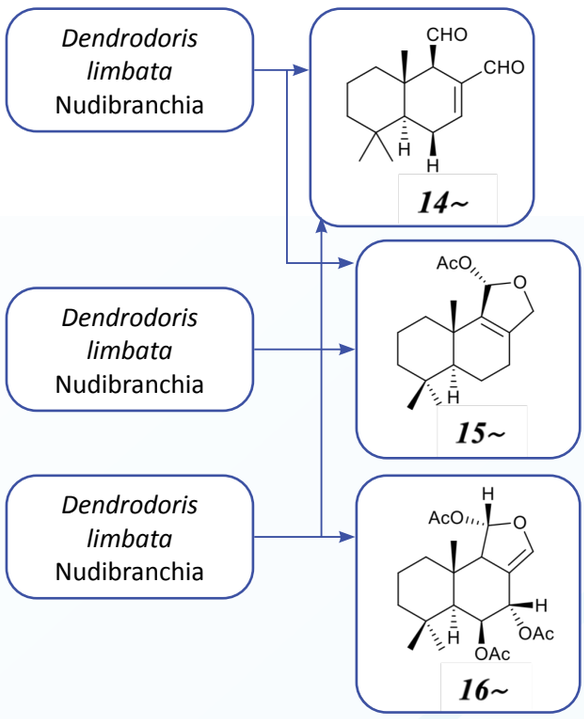


Fig.10. De novo biosynthesis by D. grandiflora, D. limbata and D. arborescens. Structures with a ~ symbol denote a biosynthesised metabolite.

as toxins, avoidance-learning inducers and aposematic odorant cues.

De novo biosynthesis

On top of sequestering metabolites from their prey, some nudibranchs can build up their defence mechanism by synthesising noxious secondary metabolites on their own through *de novo* biosynthesis.

A biosynthetic experiment with mevalonic acid labelled with carbon-14 showed that the nudibranch *Dendrodoris limbata* is able to biosynthesise *de novo* polygodial **(14)**, a sesquiterpenoid aldehyde stored in the mantle, which is a constituent of its chemical defence (Fig. 10).[38] This was the first proven example of *de novo* biosynthesis in a nudibranch.

Following this discovery, other feeding experiments with isotopically labelled precursors were set up and led to the discovery of new metabolites synthesised *de novo* by other nudibranch species. For instance, chemical investigation of the nudibranchs *Dendrodoris arborescens* and *D. limbata* showed that both nudibranchs, collected from geographically distinct areas (Italy and Japan), can biosynthesise *de novo* the drimane sesquiterpenoid 7-deacetoxyolepupuane **(15)** (Fig. 10).[39] Also, analysis of the mantle extract of the nudibranch *Dendrodoris grandiflora* showed that two drimane sesquiterpenes with antifeedant properties, polygodial **(14)** and 6β-acethoxyolepupuane **(16)**, are biosynthesised *de novo* by the nudibranch (Fig. 10).[40]

Conclusions

Marine ecosystems harbour high levels of animal biodiversity and are an important source of secondary metabolites with biological and pharmaceutical properties. Some of these molecules have been developed into pharmaceuticals, such as the anticancer drug trabectedin from a tunicate. Nudibranchs are shell-less and slow-moving gastropods and must protect themselves against various predators. Therefore, they possess a unique defence mechanism based on toxic and distasteful defensive metabolites, which are either sequestered from their prey such as sponges, cnidarians and bryozoans or *de novo* biosynthesised. Such metabolites with biological and pharmaceutical properties are of great interest for the discovery of new lead compounds.

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Article

Covalent organic cages from symmetrical resorcin[4]arenes

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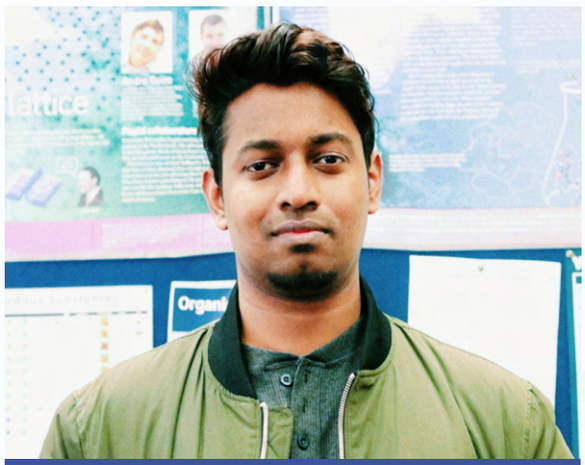
Keywords: *organic cages, resorcin[4]arenes, supramolecular chemistry, carbon-rich materials*

Introduction

Cage molecules have created a long-standing interest among supramolecular chemists. Work in this field began in the early 1980s when Nobel laureate Donald J. Cram, through his pioneering studies, introduced the first-of-its-kind authentic nanoscopic cage architecture by supramolecular assembly. This opened up new applications in host-guest chemistry, inner-shell catalysis, molecular recognition, crystal engineering and drug delivery.

Cram separated the cage molecules into two distinct categories: carcerand and hemicarcerand. The name carcerand was obtained from the Latin word 'carcer' meaning 'prison, jail; an enclosed place.' As the name suggests, during carcerand formation, some molecular components as guests remain inside the cage cavity permanently and form a carceplex. Even at elevated temperatures, incarcerated guests stay inside the cage. In contrast, hemicarcerand molecules can release incarcerated guests at high temperatures and can create a stable hemicarceplex with complimentary guests at room temperature. The property of encapsulating guests behind bars attracts researchers who wish to synthesise cage architecture using carbon-rich precursors as the basis of the cage, such as resorcin[4]arenes, calix[n]arenes, cyclotriveratrylene (CTV), etc.



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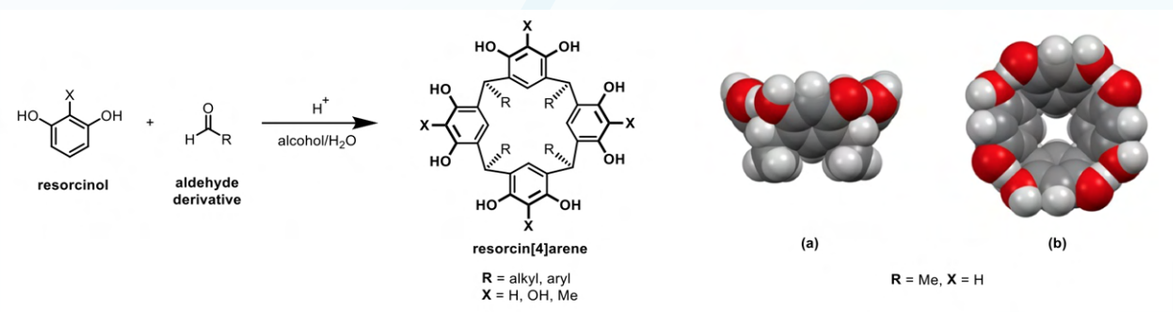
Resorcin[4]arenes

Resorcin[4]arenes are popular building blocks in the field of supramolecular chemistry.[1] They comprise four resorcinol moieties connected at the 4th and 6th positions by methylene bridges in a cyclic array. Synthesis of resorcin[4]arenes is readily accessible by single-step acid-catalysed condensation of resorcinol and various aldehyde precursors. Niederl and Vogel2 first described this (Scheme 1),



Scheme 1. Synthesis and space-filling molecular models of resorcin[4]arenes: (a) side view and (b) top view

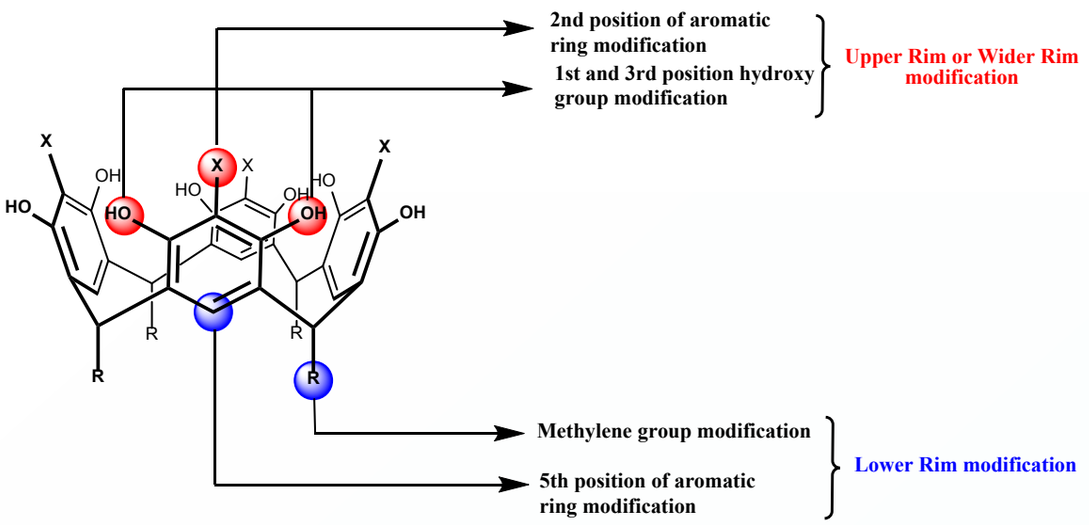


Fig. 1. Modification centres of resorcin[4]arene

following a similar approach for calix[n]arene synthesis. According to their published research, resorcin[4]arenes were synthesised by equimolar condensation between resorcinol and aldehyde in the presence of aqueous sulfuric acid.2

The readily available lowest energy configuration, the rccc isomer of resorcin[4]arene, possesses three centers of modification: (1) 2nd position of the aromatic ring (X, Fig. 1), (2) the hydroxyl of the aromatic ring (OH groups, Fig. 1) and (3) the lower rim (C5-Ar ring and R, Fig. 1), which can be functionalised by introducing convergent functional groups to obtain 3D host molecules that possess additional binding centres besides the cavity.

Conformation and configuration of resorcin[4]arenes

Resorcin[4]arene exhibits multiple isomeric conformations and configurations depending on the variation and combination of three main stereochemical elements:

The conformation exhibits five symmetrical arrangements of the macrocyclic core: Crown(C_{4v}), Chair(C_{2h}), Diamond(C_s), Saddle (D_{2d}), Boat (C_{2v}) (Fig. 2).[3]

The relative configuration of the stereochemical arrangement of the substituents at the methylene bridges derived from the aldehyde precursor gives rise to four distinct conformations: all-cis (rccc), cis-cis-trans (rcct), cis-trans-trans (rctt), and trans-cis-trans (rtct) (Fig. 3).

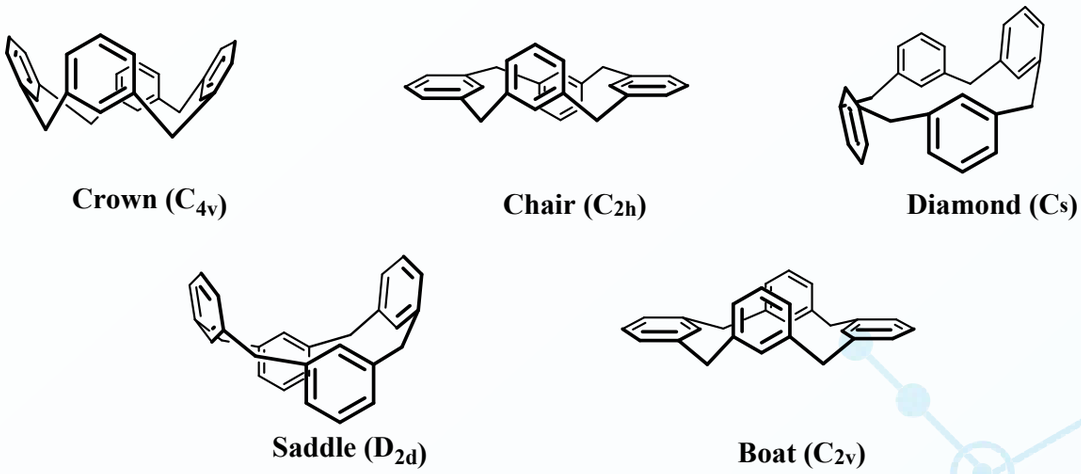


Fig. 2. Five symmetrical arrangements of resorcin[4]arene

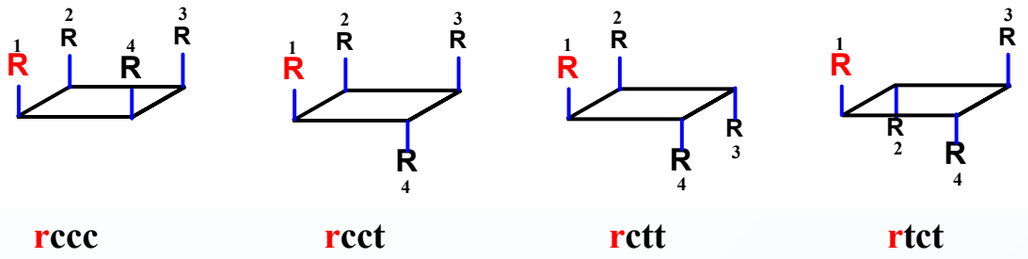


Fig. 3. The stereochemical arrangements of substituents at the methylene bridges

The individual configuration of the substituents at the methylene bridges. In conformations of the macrocycle with C symmetry, this may be either axial or equatorial.

When m-methoxy phenol as a precursor replaces resorcinol, the positional arrangement of the aromatic rings in the cyclic array gives rise to several regioisomers. The conformation with all cis substituents at the methylene bridges (rccc) has four distinct regioisomers based on the aromatic motif position in the array (Fig. 4).[4]

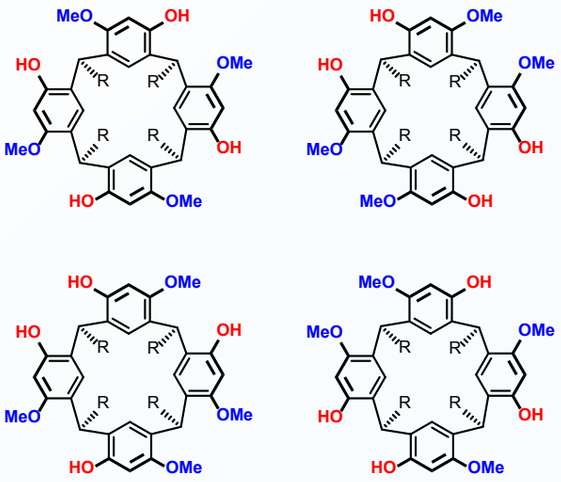


Fig. 4. Four possible regioisomers for the all cis (rccc) configuration

Cavitands

The term cavitand came into existence in 1982, when Donald J. Cram[5] first proposed "synthetic organic compounds that contain enforced cavities large enough to accommodate simple molecules or ions." Cavitands can embrace complementary electron-poor small organic guests by means of π–π interaction, CH–π interaction, CH–halogen interaction and halogen–π interaction with the aromatic concave array. According to Cram's proposed cavitand approach, two significant types of cavitand were synthesised from resorcin[4]arene by bridging two adjacent pairs of hydroxyl groups with alkyl linker (Fig. 5a)[5-6] and aromatic linker[5, 7-8] (Fig. 5b). Later, following the same line of research, Gibb *et al*.[9-10] in the early 2000s disclosed the synthesis of resorcin[4]arene-based cavitand by connecting two neighbouring hydroxyl pairs harnessing benzyl linker (Fig. 5c).

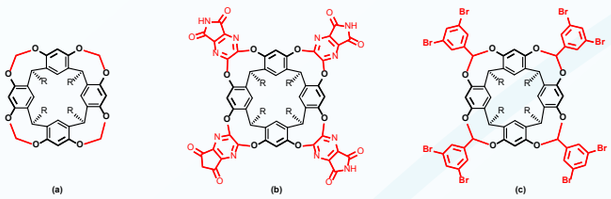
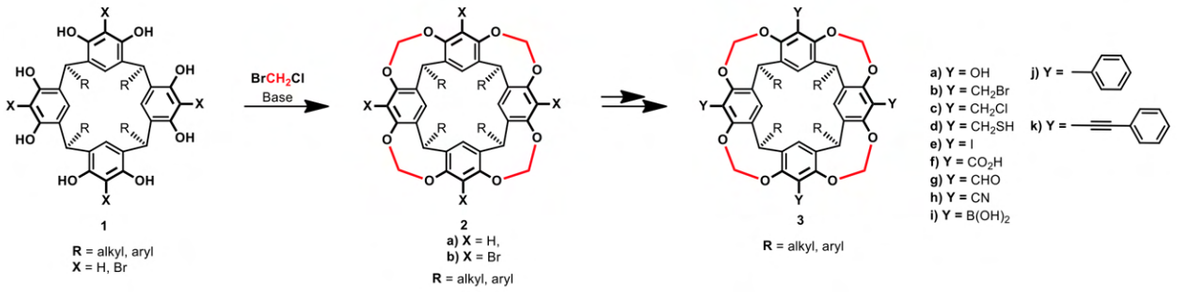


Fig. 5. Three common examples of cavitand: (a) alkyl linker, (b) aromatic linker, (c) benzyl linker

Methylene bridged linked cavitands provide extra stability due to their rigidity in a bowl structure. The synthesis of methylene bridged cavitand was demonstrated by Cram, by reacting bromochloromethane with a derivative of resorcin[4]arene in the presence of base using the SN_2 reaction mechanism (Scheme 2). Further experiments showed that bromine functionality at the 2nd position in the aromatic ring increases the yield significantly by hindering undesired polymerisation between two hydroxyl groups in the same aromatic ring. Tetrabromine cavitand **2b** can be further derivatised into tetrahydroxy cavitand **3a,**[11] tetra(bromomethyl)cavitand **3b,**[5] tetra(chloromethyl) cavitand **3c,**[12-13] tetra(sulfidemethyl)cavitand 3d,[12-13] tetraiodo cavitand **3e,**[5] tetracarboxy cavitand **3f,**[5] tetraformyl cavitand **3g,**[14] tetracyano cavitand **3h**[15] and tetrakis(dihydroxyboryl)cavitand **3i**[16] in subsequent reactions. Tetrabromo **2b** and tetraiodo cavitand **3e** are used to produce **3j** and **3k** by Suzuki–Miyaura cross-coupling and Sonogashira cross-coupling reactions respectively. The cavity depth, surface area and size is tunable by modifying the functional group and adjusting the bridging.



Scheme 2. Synthesis of methylene bridge cavitand and its derivative

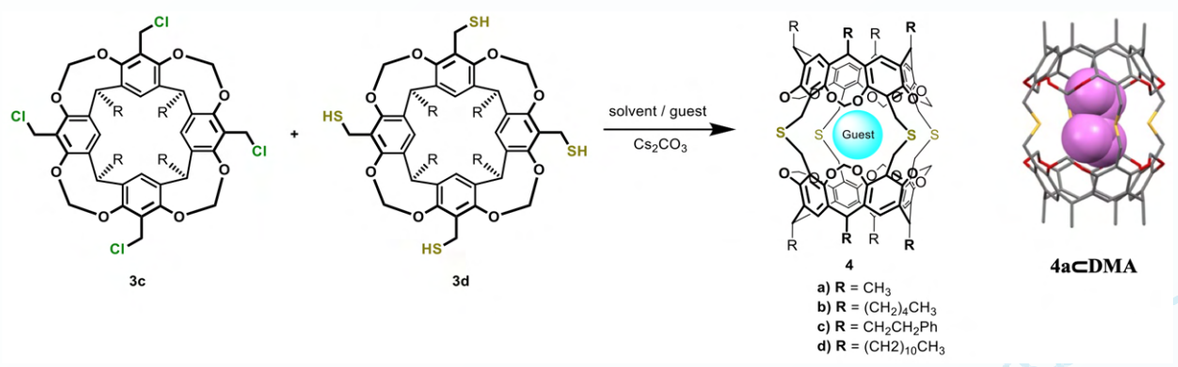
Covalent bond derived cages

Covalent bonds play a significant role in cage structure. Covalent bonds have stability advantages over all other types of bond including dynamic covalent bonds (i.e. C=N–, B–O) where, due to their reversible nature, they are prone to hydrolysis. The irreversible nature of covalent bonds leads to polymerisation reactions and often results in lower yield. However, this drawback can be minimised to some extent by using high solvent volume in the cage forming reaction. There are numerous examples of covalent bonds (i.e., thiol bond, acetal bond, amine bond, C–C bonds) that can be used to draw the connection between compatible hemispheric bowls and judiciously chosen linkers.

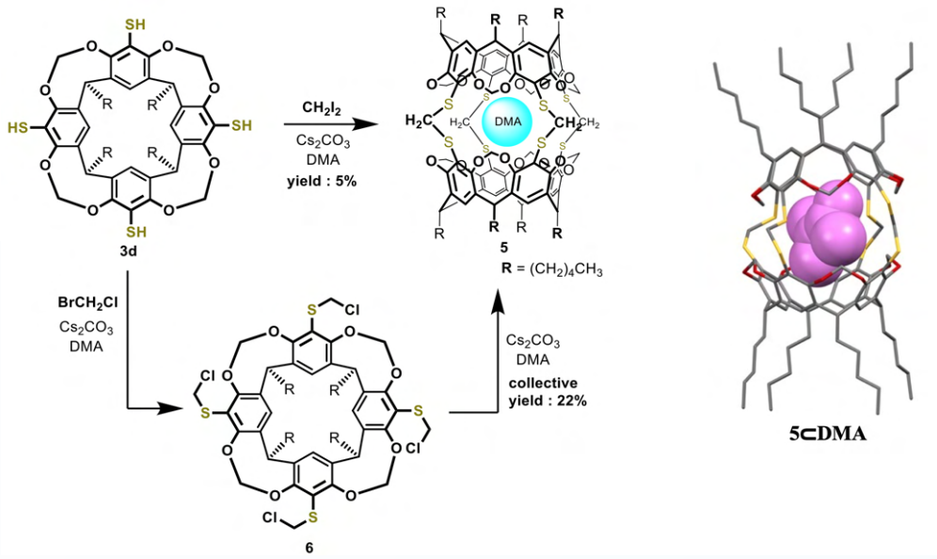
Thiol cages

Cram and co-workers[12-13] achieved the first synthetic breakthrough in the field of covalent cage architecture in 1985 when they demonstrated the proper cage molecule **4a** by the rim to rim joining of a hetero-cavitand, tetra(chloromethyl)cavitand **3c** bowl and tetra-(sulfidemethyl)cavitand **3d** bowl in the presence of Cs_2CO_3 in pseudo-diluted conditions (Scheme 3). The complete characterisation of this cage molecule was restricted due to lack of solubility. Using the same reaction scheme, a vast series of cage molecules **4b-d** were synthesised with different lower rim attachments and using a different solvent system including acetonitrile, DMF, *N,N*-dimethylacetamide (DMA), DMSO, methanol, ethanol, butanone and pentan-3-one.[17] The solvent molecules act as a template during synthesis and are permanently entrapped in the cage as a guest. ^{1}H NMR spectra provide conclusive evidence of this with an upfield shift of the solvent peak due to the shielding effect of the aromatic array.

In a similar line of research, Paek *et al.*[18] illustrated octathiol cage **5** obtained by "shell closure" reaction between two tetrathiol cavitand **3d** and four diiodomethane molecules in DMA with 5% yield (Scheme 4). After this, the Cram's group[19] synthesised the same octathiol cage **5** while mapping the reaction in a two-step conjugative reaction. Tetrachloromethyl sulfide cavitand **6** intermediate was synthesised by treating tetrathiol cavitand **3d** with excess bromochloromethane in the presence of base before proceeding to the final step. This two-step scheme increased the yield to as high as 22% by avoiding undesired polymerisation (Scheme 4).



Scheme 3. Synthesis of the tetrathiol cage 4 and molecular model 4a⊂DMA



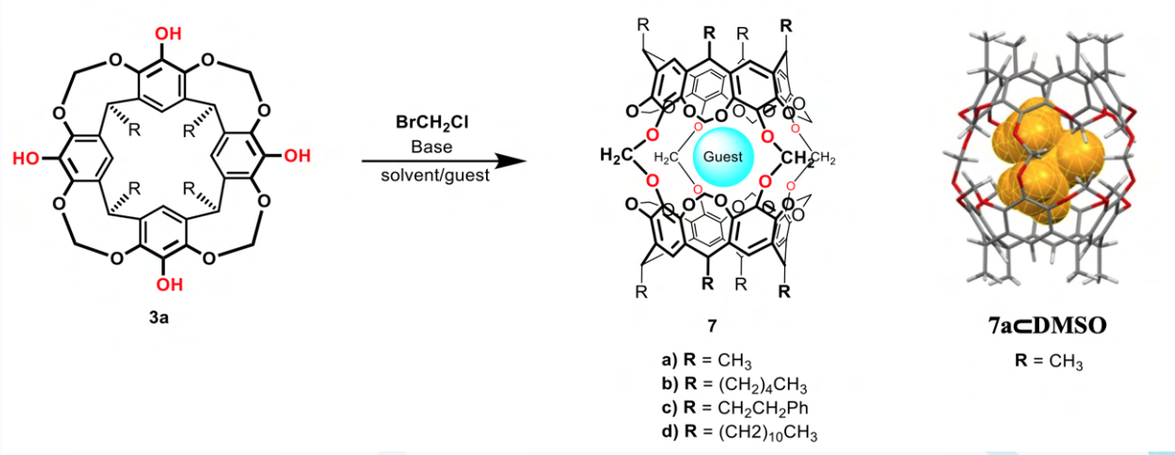
Scheme 4. Two-way approach for synthesising octathiol cage 5 with methylene linker and molecular model of 5⊂DMA

Acetal cages

After the breakthrough with thiol cages, the Cram group reported acetal cages **7a-d** where tetraol cavitand **3a** and bromochloromethane in 1:2 molar ratio were stapled together in a shell closure reaction in a polar aprotic solvent (Scheme 5). The reaction yielded a novel acetal cage with eight alkoxy covalent linkages.[11, 20-21] Further study of **7c** revealed that using the same process with different solvent systems led to varying yields: **7c⊂DMSO** (61%), **7c⊂DMA** (54%), **7c⊂DMF** (49%). While *N*-formylpiperidine was used as the solvent system, no carceplex was formed because the solvent molecule was too large to fit in the cage inner cavity during shell closure, demonstrating that the guest template inside the cavity of the intermediate is a definitive step for self-assembly. In a further experiment, when N-formylpiperidine was doped with 0.5 mol% DMA and used as a solvent system, **7c⊂DMA** was isolated in 10% yield. In a competitive templating situation, when DMA and DMF were used in equimolar amounts as a solvent, **7c⊂DMA** and **7c⊂DMF** formed in 5:1 ratio with 27% overall yield. It was concluded that a compatible template is a prerequisite for carceplex synthesis and there is a high degree of selectivity when it comes to competitive templating between two or more solvents. This templating effect was first proposed by the Cram group and was later studied in detail by Sherman and his research group.[20]

Template approach

Sherman *et al.*,[20] in their investigation of **7c**, chose NMP, a bulky polar solvent, as the poorest template reference to probe a wide range of non-solvent molecules as potential guests and tabulated the guests according to their



Scheme 5. Synthesis of acetal cage 7 with methylene linker and molecular model of 7a⊂DMSO

template ratio. To determine the template ratio, a shell closure experiment was carried out in NMP while doped with two competitive template molecules. From ^{1}H NMR of the hemicarceplex, a template ratio was calculated for two template molecules, which was normalised to NMP (the poorest template for the reaction). They found that the template ratios represent the relative rates of the guest-determining step. The guest-determining step rate increases exponentially by a factor of 106 while using a suitable template molecule. They came to five major conclusions:

(1) Seven or less non-hydrogen atoms favours optimisation of the template.

(2) The highest template ratio is shown by a moderate polarity guest (DMSO to benzene).

(3) Symmetry plays a major role in an incarcerated template, with 1,4-dioxane being 1400 times better than 1,3-dioxane.

(4) Secondary amines are not incarcerated.

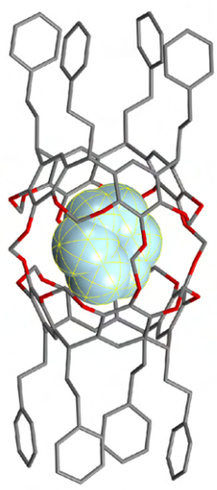
(5) Cyclic molecules are better templates than acyclic templates (Table 1).

In contrast to the template approach, Gibb and co-workers[22] reported the high yielding efficient synthesis of acetal cages with a deep cavity in the absence of a single template molecule. When 1 equiv. tetrakis(benzyl alcohol) cavitand **8** was treated with 2 equiv. bromochloromethane in the presence of potassium tert-butoxide in DMSO, the cage was obtained in an impressive 80% yield without any incarcerated template inside the inner cavity (Scheme 6). As a rational explanation, Gibbs *et al.* suggested that poorly acidic tetrakis(benzyl alcohol) cavitand **8** forms powerful charged hydrogen bonds (CHBs) with their conjugate bases in the presence of a base, which helps to self-assemble co-facially without a template.

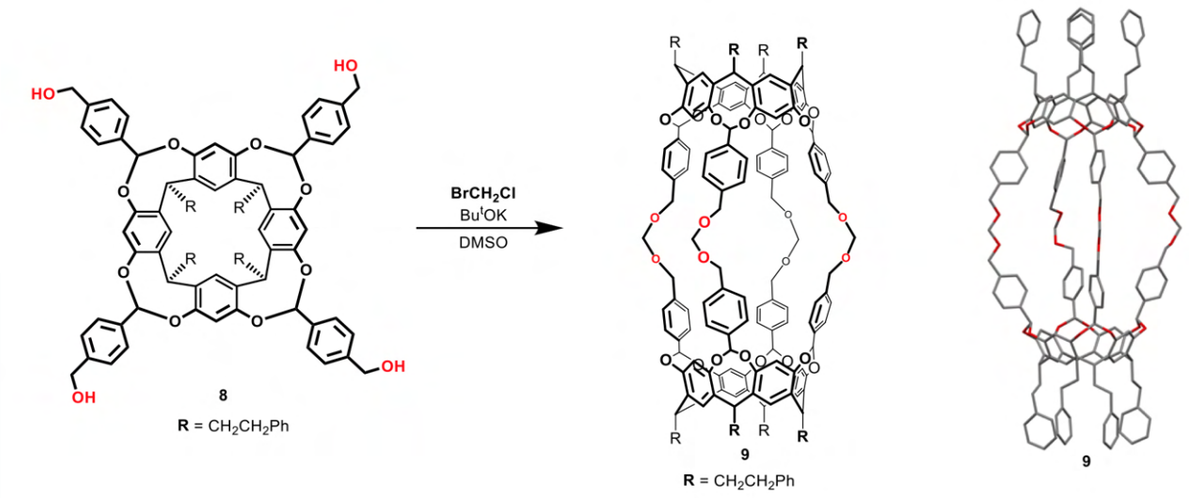
In studies that followed to access the acetal cage inner cavity, the Cram group used the longer equatorial linkers bridged between two tetraol bowl synthons **3a** by eight newly formed covalent bonds (Fig. 6). The inner space of the cage's internal cavity and the size of the equatorial window are also tunable, with different lengths of the linker between two cavitands. These cage motifs are known as hemicarcerands and the complexation product with guests as hemicarceplexes. These type of cages provide enough opening throughout the equatorial axis; using these portals, guest molecules can escape from the cavity at an elevated temperature or during workup of the crude

Table 1. Solvent template ratios for carceplex synthesis and molecular model of 7c⊂pyrazine, wherein yield represents the reaction when run with a single guest

Entry	Guest/Template	Yield	Template ratio
1.	pyrazine	87	1000000
2.	1,4-dioxane	68	290000
3.	dimethyl sulfide	52	180000
4.	dimethyl sulfoxide	63	70000
5.	1.3- dioxolane	64	38000
6.	pyridine	46	34000
7.	furan	54	12000
8.	tetrahydrofuran	50	12000
9.	benzene	43	2400
10.	pyrrole	73	1000
11.	tetrahydrothiophene	34	410
12.	1.3- dioxane	45	200
13.	acetamide	26	160
14.	trioxane	24	100
15.	acetonitrile	35	73
16.	dimethylacetamide	15	20
17.	dimethylformamide	4	7
18.	NMP	5	1



7c⊂pyrazine



Scheme 6. Synthesis of acetal cage 9 with methylene linker and molecular model of cage 9

reaction mixture. Cram and his research group explored this intriguing field by synthesising multiple host systems with various spanners between two tetraol cavitands **3a**. Cram and co-workers reported many hemicarceplex motifs with alkyl spanners, varying from ethane to hexane, diethyl ether.[23-28] Simultaneously, the Cram group made cages placing aromatic linkers such as substituted and non-substituted m-xylene, o-xylene and isophthalate between two tetraol bowls **3a**.[24-29] Along with the achiral enclosures, the Cram research group also synthesised chiral cages using chiral equatorial linkers, which are covalently stapled between two tetraol cavitands **3a**.[30]

Dynamic covalent bond derived cages

Simultaneous bond forming and bond breaking is key in dynamic covalent bond-derived cage formation. Cage architecture comprising multiple dynamic covalent bonds has proven to be more advantageous than pure covalent bonds in terms of error correction, proofreading capacity, self-sorting and controlled reversible bond formation. In dynamic covalent chemistry, the reacting synthon reaches dynamic equilibrium to minimise the kinetic side product and shift the reaction towards the thermodynamically stable cage molecule by self-recognition and error correction. Classic dynamic covalent bonding has the potential

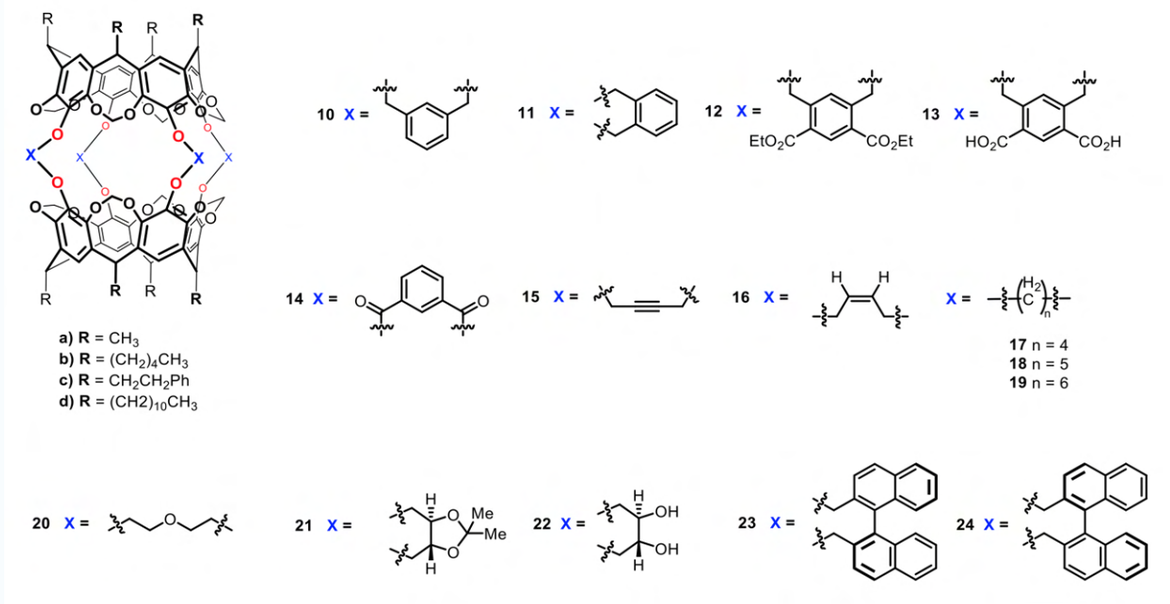


Fig. 6. Acetal bridge hemicarcerand derivative with different equatorial linkers

to assemble two complimentary bowls into a cage architecture by the implementation of reactions such as imine condensation, boronic ester or boroxame synthesis and alky metathesis.

Dynamic imine cages

The beginning of the imine cage era emerged when Quan and Cram[14] reported the very first imine cage **25** by constrictive binding, held together with eight newly formed imine bonds (Scheme 7). The reaction carried out between two tetra-formyl cavitands 3g and four 1,3-diaminobenzine linkers in dry pyridine at 65°C produced the cage in 45% yield. Kaifer *et al*.[31] proposed the synthesis of cage **25** at room temperature using $MgSO_4$, with the slightly acidic nature and water scavenging property of $MgSO_4$ serving as a catalyst and shifting the reaction rate in the forward direction. Later, Stoddart et al.[32] described the catalytic role in imine condensation by reporting cage **25** synthesis in the presence of triflic acid (TFA) as a catalyst in $CDCl_3$ at room temperature with over 90% yield (Scheme 7). Contributing to Schiff base chemistry derived hemicarcerands, Warmuth *et al*. synthesised imine cages by treating **3g** with a range of corresponding amine linker in 1:2 ratio in $CHCl_3$ with TFA as a catalyst.

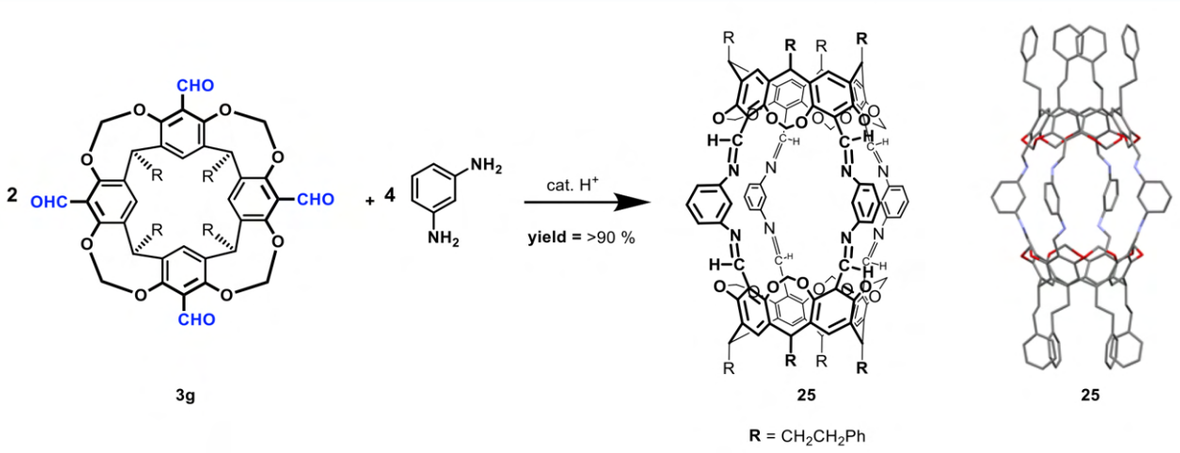
In contrast to the co-facial dimeric imine cage, Warmuth and co-workers[33] produced octahedral imine cage **26** while investigating the reaction between tetra-formyl cavitand **3g** and 1,2-ethylenediamine in $CHCl_3$ in the presence of TFA (Scheme 8). The octahedral imine cage has six tetra-formyl cavitands and twelve 1,2-ethylenediamine linkers held together through 24 newly formed dynamic imine bonds. The Warmuth group further reduced all of the cage imine bonds to stable amine bonds with $NaBH_4$ before isolation by reversed-phase HPLC in 63% yield. Furthermore, the group[34] established the relationship between the solvent templating effect and cage structure, keeping the solvent variable. Warmuth *et al*. reported tetrahedral imine cage **27** was produced by reacting four **3g** molecules and eight 1,2 ethylenediamine molecules when THF was used as the solvent. A square antiprism imine cage **28** was observed when the same reaction was performed in DCM (Scheme 8). Following the same dynamic covalent approach, Warmuth and the research group[35] reported a rhombicuboctahedron polyamine cage made up of six cavitand molecules and eight 1,3,5-tris(p-aminophenyl)benzene molecules as the amine precursor in 60 - 70% yield.

Dynamic boronic ester cages

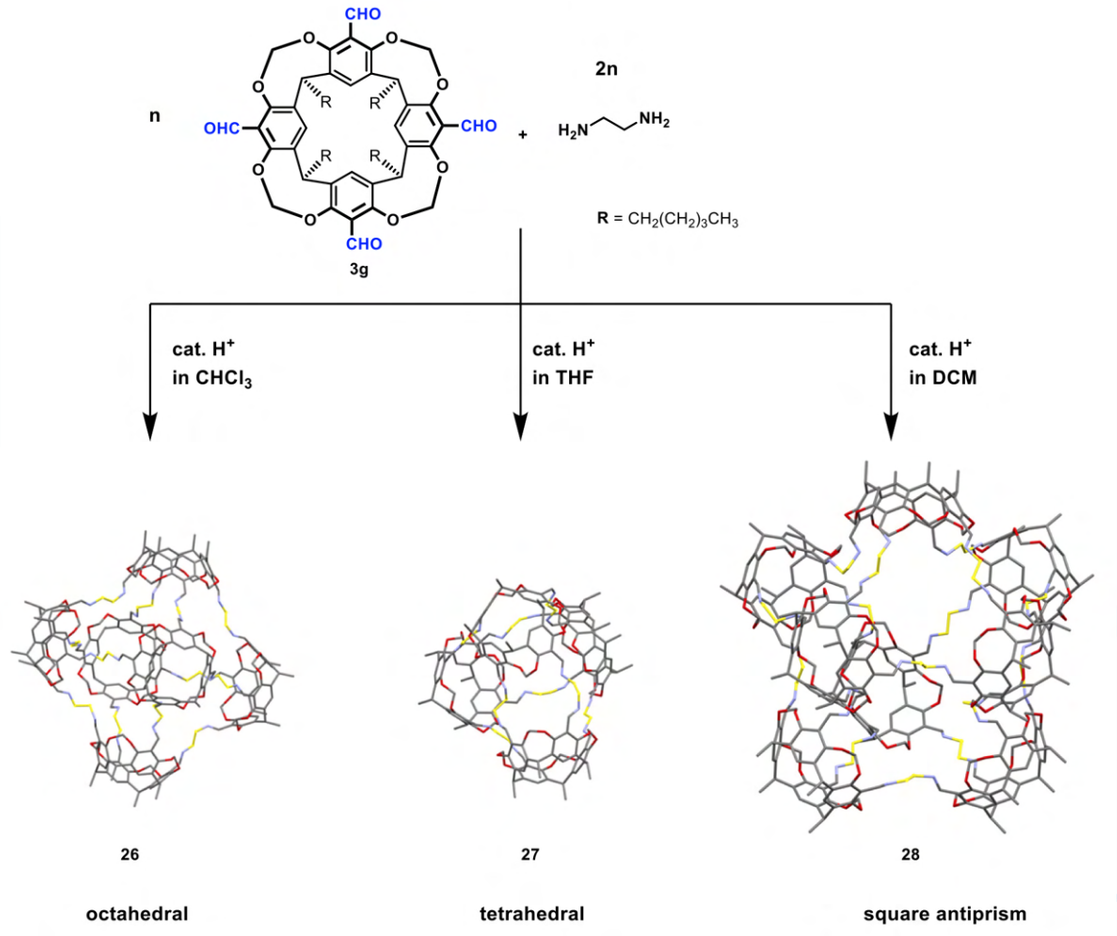
The boronic ester bond is another example of a reliable dynamic covalent bond for construction of cage architecture by self-assembly. In pioneering work, Kobayashi *et al*.36 reported the first of their kind, with boronic ester bond derived cage **29** created by treating tetraboronic acid cavitand **3i** and compatible 1,2-bis(3,4-dihyroxyphenyl)ethane as equatorial linkers in 1:2 molar ratio in $CDCl_3$ or C_6D_6 at 50°C (Scheme 9). After a detailed investigation, the group commented on the complementary guest encapsulation properties of the cage, guest orientation inside the cage cavity and the solvent effect in encapsulation.

Conclusions

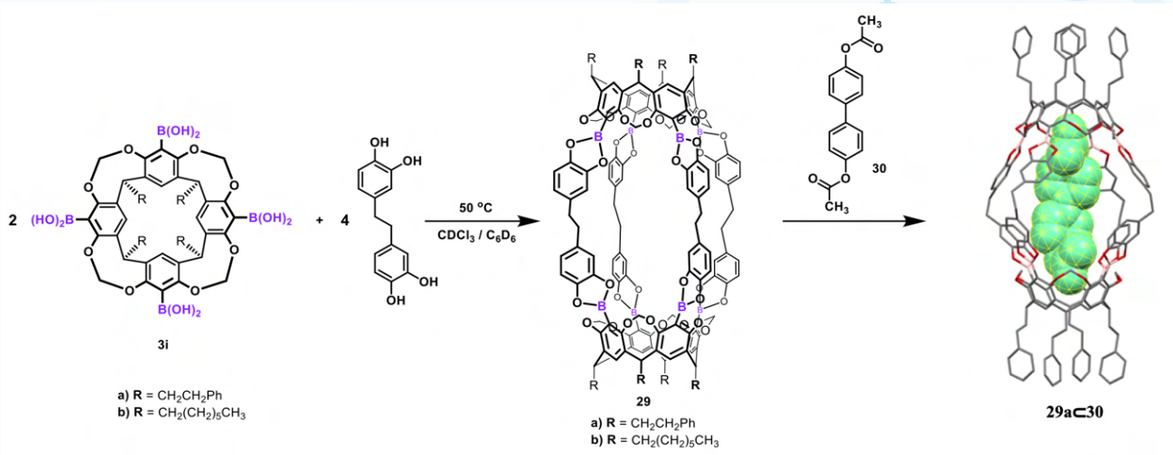
The theory of robust bond formation (both covalent and dynamic covalent) has successfully been adopted for the genesis of organic cage skeletons. Bonds used to connect two or more hemispheric bowls are the cornerstone for shell closure reactions. Cages from covalent and dynamic covalent bonds are particularly robust and able to withstand harsh conditions compared to cages derived from



Scheme 7. Synthesis of co-facial imine cage 25 and its molecular model



Scheme 8. Syntheses of octahedral 26(18-components), tetrahedral 27(12-components) and square antiprismatic 28 (24-components) imine cages by imine condensation reaction in various solvents. Products of the reactions are shown as capped stick representations, wherein the appended groups R of 26, 27 and 28 are replaced by methyl groups for clarity.



Scheme 9. Synthesis of co-facial dynamic boronic ester cage 29 and its hemicarceplex 29a⊂30 with suitable guest 30 in the molecular model

hydrogen or coordination bonds. Although resorcin[4]arene-based cages occupy a tiny portion of supramolecular assembly, they are well established through their extensive modification and applicability as potential hosts. The cage-forming approach could furnish more opportunities for application in many supramolecular fields, including host-guest chemistry.

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Article

Examining the structure and function of metal nanoparticles: a marriage of theory and experiment

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Introduction

Metallic nanoparticles have captivated the interest of the scientific community and public due to their highly attractive and unusual properties relative to their bulk properties. For example, while gold is inert in the bulk,[1] gold nanoparticles display interesting catalytic properties such as high activity for CO oxidation[2] and selective oxidation of hydrocarbons.[3] Nanoparticle applications are also being developed in the fields of human and animal based medical procedures,[4] energy storage devices[5] and the catalysis of reactions,[6,7] including in industrial processes.[8] However, nanoparticles have been used unwittingly in art for thousands of years, including in Egyptian gold-plated ivory,[9] Mesopotamia pottery,[10] European stain-glass windows[11] and the Roman Lycurgus cup (Fig. 1).[12-13]

Fig. 1. The Roman Lycurgus cup appears green when illuminated from the outside (a). However, when illuminated from the inside (b), the cup appears purple-red in colour as a result of the gold nanoparticles in the cup that absorb and scatter the green and blue wavelengths of light, allowing only red light to pass through the cup. Image reproduced courtesy of The Trustees of the British Museum under Creative Commons license CC BY-NC-SA 4.0.

The atomic-scale structure of nanoparticles can be investigated experimentally and computationally. Experimental techniques allow researchers to gain insight into nanoparticle structure but imaging techniques often use electron beams that can deform nanoparticles due to heating and atom loss.[14–16] Furthermore, the resolution of these images can be limited and often lacks a view of the 3D structure of nanoparticles. Computational techniques bypass these issues that cause deformations, and allow researchers to view high resolution 3D models of nanoparticle structure.

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However, computational methods are also limited by the simplifications that are required to perform calculations. The inclusion of time, temperature and solvent effects can also add challenges in these models. Due to the various difficulties present in sampling nanoparticle structure, computational and experimental techniques are often used to complement each other and give a wider perspective on the natural structures of nanoparticles. The combination of experimental and computational techniques is useful for elucidating the underlying reasons for the existence of various structures and features, as well as to predict how nanoparticles can be tuned to take advantage of particular properties that can be used in practical applications.

This article discusses how the structures and properties of various small noble metal nanoparticles containing <1,000 atoms are studied computationally and experimentally. To begin, the common types of structures that small nanoparticles exhibit, called motifs, are discussed. Then follows how the structures of nanoparticles are elucidated com-

putationally using global optimisation algorithms and how these structures are compared with experimental results to gain insight of the features that dominate nanoparticle structure. Finally, how the properties of small nanoparticles are investigated computationally are explained, focusing on how computational catalytic studies are performed on small metallic nanoparticles.

The structural motifs commonly observed in small nanoparticles

The common types of structures that are observed in nanoparticles containing <1,000 atoms fall into three types of motifs (Fig. 2).[17] The first is the octahedral motif which is based on the face-centred cubic (FCC) crystal structure. For this reason, the octahedral motif is often referred to as the FCC motif. The second is the icosahedral motif (Ih) which is made up of 20 symmetrical FCC segments that are cut into trigonal pyramids. The third is the decahedral motif (Dh) that is based on five FCC elongated tetrahedrons that all share a common edge along the fivefold axis.

There are two (often competing) features of nanoparticles that determine their structural preference. These are the stabilising effects of the interior (bulk) of the nanoparticle and the surface energy of the nanoparticle. Small nanoparticles often have a high surface area to volume ratio and therefore surface effects are more important than bulk effects. Icosahedral nanoparticles are often expected to be favourable at small sizes because they contain energetically favourable surface features and offer the greatest surface area to volume ratio.[17,18] At larger nanoparticle sizes, bulk effects become more important. Icosahedral nanoparticles have a strained core which makes them unfavourable at larger sizes.[17,18] In contrast, octahedral nanoparticles maintain preferred equilibrium distances between atoms which minimises the strain of the core; therefore, the octahedral motif is often expected amongst larger nanoparticles.[17] Decahedral nanoparticles are considered a mixture of the icosahedral and octahedral motifs and therefore are considered to be observed at intermediate sizes.[17,18] Many computational studies support the notion of a crossover from icosahedral to decahedral to octahedral as the nanoparticle size increases.[19–21] However, this trend is not always observed as the structural preference of nanoparticles can alternate between several motifs over the nanoparticle size range. The structural preference has been found to oscillate between the decahedral and octahedral motifs for Cu, Pd, and Au nanoparticles up 10,000 atoms in size,[18,20,22] and can dramatically change with the addition or loss of a single atom. For this reason, generalisations of nanoparticle structure across sizes are not always reliable and computational studies generally have to focus on investigating nanoparticle structure across selected size ranges.

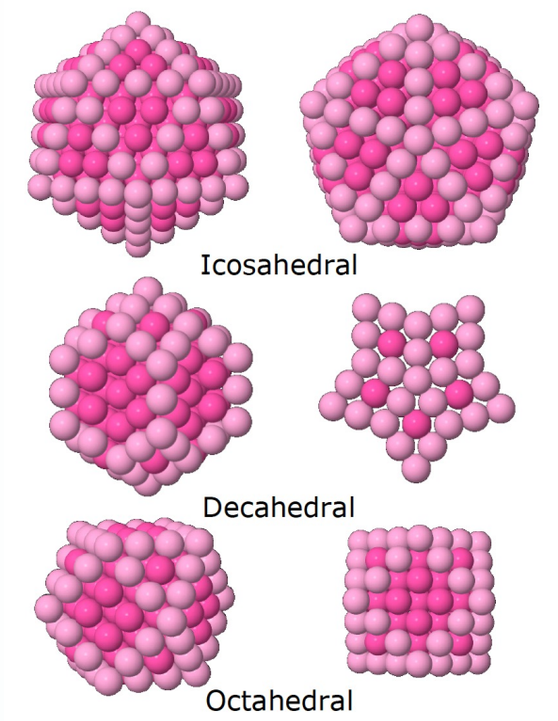


Fig. 2. A side view (left) and top view (right) of the three common types of motifs that are observed in small nanoparticles

How low energy nanoparticles are obtained computationally

Determining the types of low energy structures that a nanoparticle may exhibit is an inherently trickly problem to solve as a nanoparticle containing N atoms can be arranged in a plethora of different ways. Each atom can be moved in 3 directions in space, meaning that a nanoparticle can be rearranged across at least 3N degrees of freedom. For example, estimates indicate that nanoparticles containing 55 and 100 atoms could have more than 10^{21} and 10^{40} stable structures respectively.[23–25] Only the lowest energy of these stable structures will likely represent the types of nanoparticles observed experimentally. Therefore, efficient computational techniques are required to obtain the most stable nanoparticle structures.

Global optimisation algorithms are designed to create a number of structurally diverse nanoparticles in order to locate low energy stable structures as efficiently as possible. These algorithms first generate a single structure or a set of structures before proceeding via a generalised three step process; first, a structure or a number of structures

from the set are modified in some way as to create new structures. Second, these modified structures are "locally minimised" such that any meta-stable or unstable structures are transformed into stable structures. This local minimisation step is often essential for efficiently globally optimising nanoparticles.[26–28] Third, the energies of these modified structures are compared to the original structures to determine whether to keep them or not for future iterations. This three-step process is repeated numerous times until the researcher is confident that the majority of low energy stable structures have been obtained.

There exist many types of global optimisation algorithms, all differing on how they create new structures during the first step. One commonly used global optimisation algorithm is the genetic algorithm. The genetic algorithm is based on Darwin's theory of evolution in biology (Fig. 3), where individuals within a population (i.e. a set) of nanoparticle structures are mated together and mutated to create new offspring nanoparticles. Mating involves cutting two nanoparticles in half and splicing them together, while mutation often means structurally perturbing a single nanoparticle. These new offspring structures obtained via mating or mutation are all locally minimised. This creates a number of new stable offspring from the original population of nanoparticles. A natural selection method is then used to remove those original nanoparticles and offspring that are least fit. Fitness is usually based on the relative energy of a nanoparticle compared to the other nanoparticles in the population; the lower the energy of a nanoparticle, the fitter it is and the more likely it will survive into future generations; the higher the energy of a nanoparticle, the less fit it is and the more likely it will be removed from the population. This process, called a generation, repeats numerous times. As the genetic algorithm proceeds, some of the offspring from each generation will be fitter than their parents, driving the genetic algorithm to locate the lowest energy structures that a nanoparticle may form experimentally. This continues until the researcher is confident the majority of the lowest energy nanoparticle structures have been obtained. Other examples of global optimisation algorithms used in nanoparticle research can be found in the literature.[17, 29-30]

Comparisons of computational results with experimental studies

As mentioned previously, computational chemists often focus their attention on the structural elucidation of nanoparticles at selected sizes. This is often performed by running a global optimisation algorithm multiple times upon a metallic nanoparticle (containing a set number of atoms). The structures that are obtained from these multiple global optimisations are then collated and the lowest energy structures assessed for their structure and motif type, as well as for their relative energy compared to the other structures and motifs obtained.

In general, the types of structures that are observed are very dependent on the metal that the nanoparticle consists of. Computationally, Cu nanoparticles often express an icosahedral structure up to a few hundred of atoms in size,[22, 31–34] while Au and Pt nanoparticles can be energetically competitive between several motifs at sizes containing only a few tens of atoms.[35] Au nanoparticles are also interesting because they maintain this energetically competitiveness between motifs even at larger sizes, as well as because they can display unusual types of motifs. For example, Au20 has been shown (computationally and experimentally) to prefer a pyramidal tetrahedral structure,[36-40] while many other small Au nanoparticles containing less than 100 atoms are often disordered.[41] Many computational and experimental studies have found that the Au55 nanoparticle typically forms a distorted icosahedral structure which contains three diamond-shape surfaces (Fig. 4).[35, 42–46] This type of structure forms because of the desire of Au to maintain its equilib-

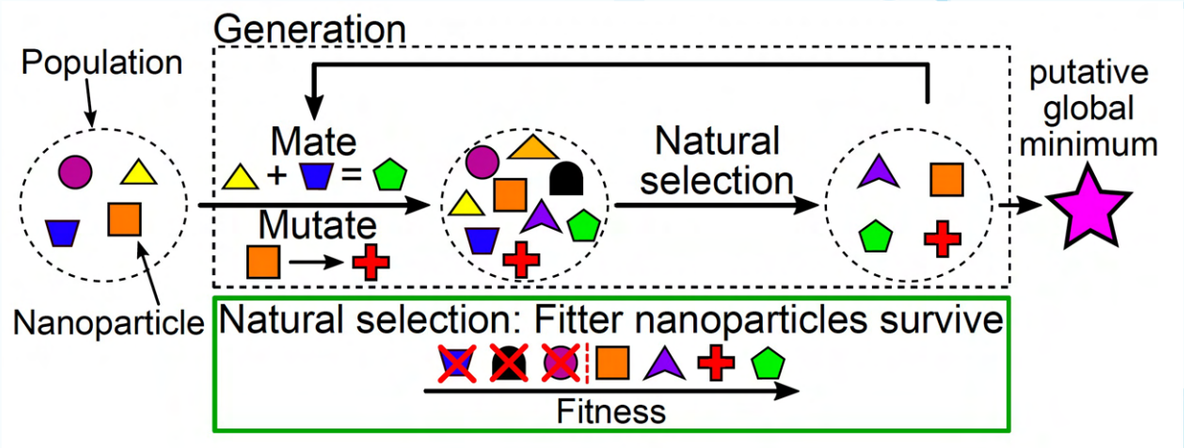


Fig. 3. Schematic of the genetic algorithm

rium bond distances between atoms, which are generally compressed in icosahedral nanoparticles.[47] This causes the usual 13 atom icosahedral core to expand and contain 15 atoms instead.[48,49]

Larger Au nanoparticles containing several hundred atoms tend to form distinct structures.[50–53] Computationally, all three motifs have all been found to be energetically competitive at larger sizes, especially between the octahedral and decahedral motifs.[18,35] This agreed with Li et al. who experimentally studied the structural preferences of Au nanoparticles with 309 ± 6 atoms.[52] Li et al. found that no single motif dominated the distribution of these Au nanoparticles. The decahedral motif was energetically preferred (32%), followed by the octahedral motif (25%), while icosahedral nanoparticles were rarely observed (8%). The remaining nanoparticles could not be confidently assigned. Foster and Palmer also sampled 309 ± 6 atom Au nanoparticles, synthesised with the same procedure as Li *et al*., but further annealed these Au nanoparticles under the electron beam during imaging with scanning transmission electron microscopy (STEM).[54] This led to a change in the ordering of motifs, where the octahedral motif was preferred (56%), followed by decahedral (37%) and icosahedral motifs (7%). This was an interesting result because it showed that these Au nanoparticles became kinetically locked during their synthesis. This was also interesting because it conflicted with computational studies of nanoparticles of these sizes, although the competitiveness of these two motifs was captured computationally.[18,35]

Wells *et al.* investigated the structures of 561 ± 13 atoms, 742 ± 17 atoms, and 923 ± 23 atoms using the cluster beam deposition method.[53] Here, the proportion of nanoparticles that were obtained across all these size ranges maintained a ratio of 40 - 45% decahedral, 30 - 40% octahedral and 0 - 5% icosahedral, while the other 15 - 25% could not be identified. This consistent ratio of motifs indicated that these Au nanoparticles were likely kinetically trapped at a certain size. Molecular dynamic simulations supported the notion that these nanoparticles would maintain their original motif even at temperatures of 600 K. Foster et al. also observed that the population of decahedral and octahedral Au561 nanoparticles could be described by Boltzmann's distribution at high temperatures (between 400 K - 800 K), and measured the energy difference between these two motifs as 0.040 ± 0.020 eV, where the FCC motif was the energetically lower energy motif.14 This further highlighted how kinetic trapping can play a major role in nanoparticle structure at larger sizes, as the FCC motif was the energetically favourable motif for Au561.

While the motifs of Au nanoparticles were often energetically competitive, Pt nanoparticles showed different behaviour. Recently, a combined computational and experimental study of Pt nanoparticles containing between 10 - 600 atoms was performed. This study gave a unique insight of the types of motifs that Pt nanoparticles exhibit.[35] Here, a computa-

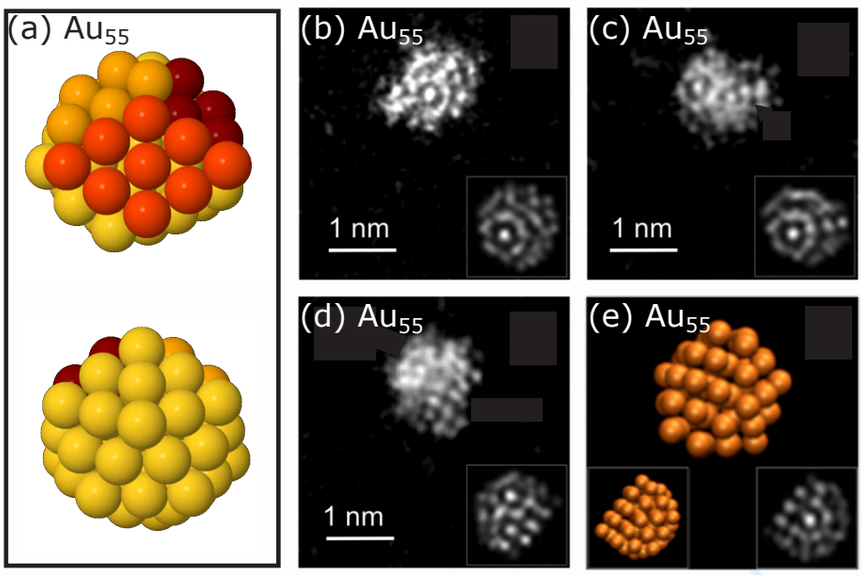


Fig. 4. A model of the distorted icosahedral Au55 nanoparticle from the view of the diamond-shape surfaces (a: top) and from the icosahedral side of the nanoparticle (a: bottom). Experimentally obtained Au55 nanoparticles imaged from scanning transmission electron microscopy (STEM) along with simulated STEM images of computational models in the bottom right-hand corners (b - d). A model of the distorted icosahedral structure with its simulated STEM image in the bottom right-hand corner (e). The diamond-shape surfaces in (a) are coloured shades of red and orange for ease of viewing. Figure reproduced with permission of reference 42.

tional study was performed on Pt nanoparticles between 55 ± 1, 101 ± 2, 147 ± 3, 228 ± 4, and 309 ± 6 atoms (Fig. 5a). Like Au nanoparticles, small Pt nanoparticles between 55 ±1 and 101 ± 2 atoms in size were also energetically competitive between the icosahedral and octahedral motifs, but with a pronounced preference towards the octahedral motif. This preference was unusual as octahedral nanoparticles are often unstable at smaller sizes due to their high surface energy compared to icosahedral nanoparticles. However, this was in agreement with previous theoretical work by Kumar and Kawazoe, who postulated that the stability of the octahedral motif was due to the high stability of the smaller, flat triangular Pt6 and square planar Pt9 segments that make up octahedral structures. However, the energetics of larger Pt nanoparticles between 147 ± 3, 228 ± 4 and 309 ± 6 atoms in size diverged, such that there was a clear energetic preference for the octahedral motif, followed by the decahedral motif. The icosahedral motif was very unfavourable at larger sizes.

Experimentally, the majority of Pt nanoparticles below 250 atoms could not be identified, either because these smaller nanoparticles were amorphous or because no defining features of these motifs could be identified in STEM images (Fig. 5b).[35] However, Pt nanoparticles above 250 atoms tended to prefer the octahedral motif, which was consistent with the previously mentioned computational results. This agreement between experimental and computational work showed that larger Pt nanoparticles were energetically controlled, such that larger Pt nanoparticles were influenced most by the energies of the structures they formed rather than other thermodynamic or kinetic controls (such as observed in larger Au nanoparticles). This result highlights what further understanding can be gained when computational and experimental studies are used together to complement each other.

Case study: Metal nanoparticles as catalysts

Metals are commonly used as catalysts in nature and in commercial applications, such as Pt in the production of H2,[55] Fe and Ru in the Haber-Bosch process[56] and Cu in the reduction of CO_2 to methanol and other hydrocarbons.[57] New catalysts are always sought after to improve the efficiency and rates of various reactions. Nanoparticles are often seen as a way to improve the performance of metal catalysts because they contain large surface area to volume ratios compared to bulk metals, thereby increasing the total surface area available for the amount of material used and thus getting more "bang for buck".[58] Surfaces are important in catalysis as these are the interfaces where reactions are catalysed; therefore, increasing the surface area of a material often leads to increased catalysis. Furthermore, nanoparticles can have a variety of different surface features compared to the bulk, some of which may enhance catalytic activity further.[6]

Commonly, the catalytic properties of metal nanoparticles are computationally examined by first understanding the types of surface features that nanoparticles of interest contain. These surface features are then modelled in extended surface in order to understand their catalytic properties (for example, Fig. 6).[59,60] While this is a good first approach for understanding the catalytic behaviour of nanoparticles, nanoparticles often are not perfectly structured and can contain surface defects and other strains that cannot be easily modelled with extended surfaces.

Currently, the Garden group at the University of Otago is investigating the electrochemical CO_2 reduction reaction (CO2RR) upon Cu nanoparticles by using models of Cu nanoparticles instead of extended surfaces. This was performed by first globally optimising a series of small Cu nanoparticles using the genetic algorithm. In this study, the lowest energy Cu_{55},

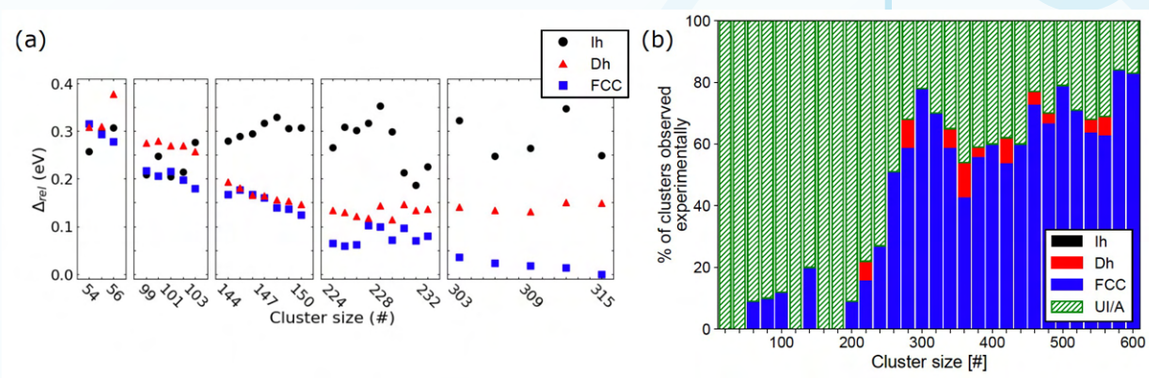


Fig. 5. (a) Overview of the computationally low energy icosahedral (Ih, black), decahedral (Dh, red), and octahedral (FCC, blue) Pt nanoparticles obtained across various size ranges (the lower the energy, the more stable the motif). (b) The types of structural motifs observed experimentally from STEM images of Pt nanoparticles between 10 and 600 atoms. Δrel represents the energy of the nanoparticle per approximately the number of surface atoms that nanoparticle contained and UI/A indicates unidentified/amorphous structures (green). Figure reproduced with permission of reference 35.

Cu_{78}, Cu_{101}, Cu_{124} and Cu_{147} nanoparticles were obtained. A selection of these low energy nanoparticles is shown in Fig. 7. The majority of Cu nanoparticles obtained in this study were icosahedral in nature, either with full or partial shells. However, some of these lowest energy nanoparticles were deformed versions of the icosahedral motif. An example in Fig. 7c shows an elongated icosahedral Cu_{78} nanoparticle that contains a small island of Cu on top of its surface.

The CO2RR was then modelled upon the Cu nanoparticles shown in Fig. 7 and compared to the CO2RR upon a flat surface of Cu atoms. The main results from this study are shown in Table 1, which shows the calculated external potential that would need to be applied to these nanoparticles in order to catalyse the reduction of CO_2 to methanol. The more negative the potential, the greater the external potential that has to be applied to the nanoparticle.

Table 1. Limiting potentials for the electrochemical reduction of CO2 to methanol upon an extended Cu surface as well as for the low energy Cu nanoparticles given in Fig. 7

Surface/nanoparticle	Limiting potential / V
Cu(111)	-0.76
Cu55 (a)	-0.81
Cu78 (b)	-0.72
Cu78 (c)	-0.39
Cu147 (d)	-0.66

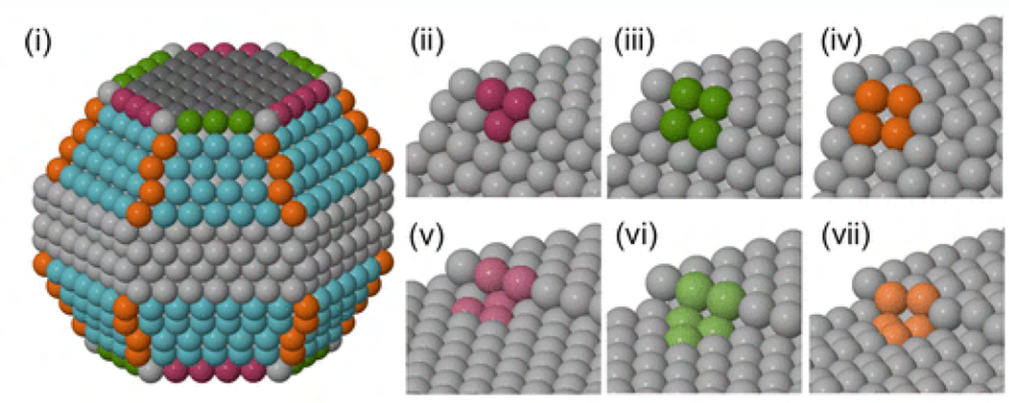
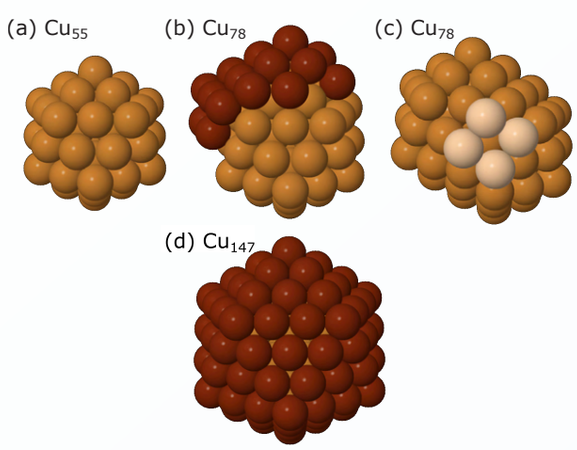


Fig. 6. Representation of the different active sites within an extended surface (ii - vii) and their relative position on a generalized nanoparticle (i). Figure reproduced with permission of reference 59.



The majority of the Cu nanoparticles that were studied required an applied potential that was equivalent to that of a flat surface of Cu atoms. The exception to this was the elongated Cu78 nanoparticles given in Fig. 7c, where the applied potential required to catalyse this reaction was half that required by the extended Cu surface and for the other Cu nanoparticles examined in this study. Here, the intermediates of the CO2RR preferred to bind to the Cu island on top of this nanoparticle. Furthermore, the Cu island was able to minimise the energy required to perform the energetically largest step in the CO2RR. This suggests that Cu nanoparticles that contain defects such as Cu islands may provide an avenue for improving the catalytic properties of Cu nanoparticles towards the CO2RR. Efforts are ongoing to understand more about how these defects modify the energetics of the CO2RR in Cu nanoparticles. Watch this space!

Fig. 7. A selection of low energy Cu nanoparticles, including (a) a Cu_{55} nanoparticle, (b) and (c) two Cu78 nanoparticles and (d) a Cu_{147} nanoparticle. All the nanoparticles shown here have an icosahedral motif. Atoms coloured red signify the developing outer shell of larger icosahedral structures, while the four atoms highlighted cream in (c) show an island of Cu atoms on top of the main icosahedral structure.

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Article

Repurposing construction and demolition waste: a review of current recycling strategies

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Increased construction activities throughout the world have led to the generation of construction and demolition waste (CDW) in massive volumes each year. Proper management of this waste has become a global challenge. This article is divided into two sections. The first section provides an overview of CDW generation around the world, specifically in New Zealand. The drawbacks of landfill disposal of CDW and the importance of recycling are briefly discussed. The second section discusses the current recycling strategies of CDW and the challenges associated with these methods.

Construction and demolition waste (CDW)

Construction waste can be defined as waste from the construction, repair, and remodelling of commercial buildings, individual residences and other structures. Demolition waste can be defined as the waste from razed buildings and other structures.[1]

There are two main sources for CDW generation; anthropogenic sources and natural sources. Anthropogenic sources contribute to the generation of both construction waste and demolition waste. Unnecessary waste can be generated during construction processes of buildings due to excessively ordered supplies or mishandling of materials by unskilled labourers, and during renovation and maintenance processes. Demolition waste is generated during the complete or selective removal of existing structures.[2] Natural events that generate waste include unpredicted disasters such as earthquakes or extreme weather-type events like floods, hurricanes, etc., which lead to unavoidable demolition waste through damage.[3]

Even though the construction sector plays an important role in significantly contributing to the effectiveness and prosperity of the overall economy, it has also become the dominant contributor to total waste generation in many countries.4 China, India and the USA are the largest contributors to global CDW generation.[2] Table 1 summarises the CDW generation in a selection of countries.

Even though landfill disposal is the most common CDW management method in many countries (the global average of landfill CDW is about 35%),[11] it is not considered to be an effective waste management strategy due to several factors.[11] The construction and demolition sector is one of the main consumers of natural resources and energy. The current practice of dumping waste at landfills effectively represents a disposal of still utilisable resources and a waste of energy.[12] Moreover, CDW disposal in landfills can cause environmental pollution as some percentage of these waste materials might contain hazardous substances from chemical and industrial treatments that could leach out. With the majority of this waste being disposed of at landfills, most developed countries are now facing issues with landfill capacity which further highlights the importance of investigating more sustainable solutions to address this problem.[13]

Table 1. Construction and demolition wate generation in several countries

Country	Year	Total mass (millions of tonnes)	% Contribution to total waste generation	Reference
China	2014	1130	30-40	5
India	2016	112-419	50-80	6
United States	2014	583	N/A	7
Australia	2017-18	20.4	43	8
South Korea	2011	68	50	9
Spain	2009	35	25-30	10
Canada	2011	9	27	2

CDW generation in New Zealand and landfill disposal

It has been reported that half of the total waste generated in New Zealand consists of CDW.14 Fig. 1, compiled from information sourced from the Ministry for the Environment,[15] illustrates the composition of the CDW disposal to landfills. Based on average composition, timber and rubble (i.e. fragments of stone, bricks or concrete) are the main contributors to CDW in New Zealand.

Landfill disposal is the most common waste disposal method in New Zealand and almost all waste from construction and demolition, which is estimated to be over 4 million tonnes, is sent to cleanfills and landfills.[2,15] A landfill is defined as a waste disposal site used for the controlled deposit of non-hazardous, solid and degradable waste into or onto land. Landfill material will degrade, producing landfill gas (CO2, CH4) and leachate over time.16 In contrast, cleanfill sites accept materials that will not undergo any physical, chemical or biological transformations that will cause adverse health effects or environmental effects. Cleanfill materials are represented by virgin, naturally sourced matter such as clay, soil, rock and inert materials.[16]

The New Zealand government has identified pressure on landfills as a huge burden and has introduced acts such as the "Waste Minimization Act 2008" to encourage recycling and reuse of materials so reducing disposal at landfills.[17] The government has also planned to progressively increase the national waste disposal levy over the next four-year period with the revenue earned from the waste disposal levy being targeted toward initiatives that bring about waste minimisation and resource recovery.[18]

Circular economy concept

In the field of waste minimisation and recycling, it is very relevant to talk of the concept of a circular economy. This is defined as an economic system which reduces, reuses, recycles and recovers materials from production, distribution and consumption processes.[19] Even though recycling 100% of waste materials to create an entirely circular economy is not yet feasible, it is important to make strident efforts to reach this goal for achieving a sustainable future. New Zealand has taken several actions in order to achieve a "Zero Waste Economy", such as creating the "Zero Waste New Zealand Trust", a non-profit organisation which has a focus on providing support to organisations and individuals involved in waste management.[20]

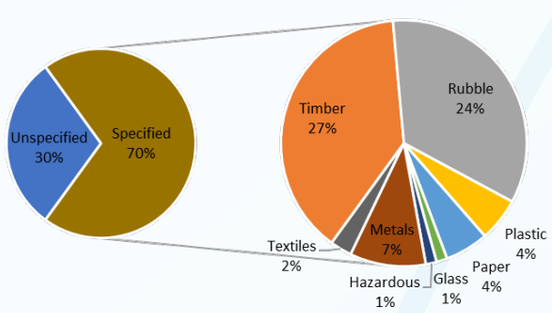


Fig. 1. Construction and demolition waste distribution of New Zealand in landfills

Recycling of CDW

Recycling and reuse of CDW is a way to save valuable, still usable natural resources and energy, allowing more utilitarian value to be extracted from these materials. Investigation of possible recycling techniques and reuse options for the components of CDW has become an emerging research area recently. The recycling method of a waste material is dependent on several factors such as the chemical composition, presence of impurities and the presence of hazardous substances.

Concrete

Concrete is one of the most widely used materials globally, and therefore a huge amount of concrete waste is generated each year (e.g as in "rubble"). The main components of concrete include silicon dioxide (SiO_2), calcium carbonate ($CaCO_3$), calcium oxide (CaO) and aluminum oxide (Al_2O_3).[21]

Recycled concrete aggregates have been applied in the production of concrete for pavements, sidewalks, curbs and gutters, as well as in building and bridge foundations.[22] Concrete waste has also been used to synthesise new materials such as geopolymeric binders.[23] Geopolymer is an inorganic material that forms polymeric Si-O-Al bonds (Fig. 2) and is synthesised from the chemical reaction between aluminosilicate oxides in an alkaline solution.[24-25] Geopolymers have attracted attention as these materials are resistant to heat and can replace conventional cement.[26]

Treatment of wastewater contaminated with pollutants such as phosphate and heavy metals has been investigated using waste concrete as a low-cost adsorbent.[27-28] The adsorption mechanism is dependent upon the adsorbate. For instance, phosphate in the wastewater reacts with the Ca^{2+} leached from concrete to precipitate hydroxyapatite (Eq. 1), and heavy metal ions are removed through co-precipitation of metal hydroxides ($M\text{-}(OH)_x$).[28-29] Concrete waste has also been applied as an alternative desulfurisation agent. Several studies have investigated concrete waste as an adsorbent for SO_2 in flue gas desulfurisation systems.[26]

$$10Ca^{2+} + 6PO_4^{3-} + 2OH^- \rightarrow Ca_{10}(PO_4)_6(OH)_2 \quad \text{(Eq. 1)}$$

Even though improper disposal of concrete waste negatively impacts soil, some studies suggest that recycled concrete can be used to amend and stabilise the soil.[30] CaO from concrete reacts with the water in the soil (Eq. 2), increasing the electrolyte concentration and pH of the soil which improves the dissolution of SiO_2 and Al_2O_3. The dissolved SiO_2 and Al_2O_3 react with dissolved Ca^{2+} ions via pozzolanic reactions to give calcium-silicate-hydrate (C-S-H) gel and calcium-aluminate-hydrate (C-A-H) gel that will improve the soil.26

$$CaO + H_2O \rightarrow Ca(OH)_2 + Heat \quad \text{(Eq. 2)}$$

Wood waste

Wood waste comprises treated and untreated wood, sawdust from wood processing, off-cuts, shavings and virgin wood mixed with waste wood.[31] The composition of wood waste varies depending on the source and is essentially composed of cellulose, hemicellulose, lignin and extractives.[32] Wood waste can also contain hazardous substances like heavy metals (Cu, Cr, As) due to prior preservation treatments.[33] Wood waste has been used as a raw material for other products, land application and as a low-cost adsorbent for water treatment.

Waste timber from construction sites has been investigated as fibre to manufacture wood-magnesium oxychloride cement (MOC) board.[34] The solid wood recovered from construction has been recycled into glued laminated timber products, and wood chips recovered from particleboard production have been applied as a raw material for the production of gypsum-based materials (gypsum-wood cylindrical products and solid bricks).[35-36]

Wood waste has also been used to produce biochar from untreated wood waste which is used as a soil amendment. Biochar is produced when organic biomass is pyrolysed with limited oxygen or no oxygen.[37] Biochar improves soil quality enhancing water retention capacity, cation exchange capacity and pH of the soil.[38] Biochar also has the potential to take up nutrients, pesticides and minerals in the soil, inhibiting the movement of these chemicals to groundwater and surface water.[39]

Some studies report untreated wood waste as an effective adsorbent for treatment of water contaminated with pollutants such as heavy metals and organic dyes. Wood waste possesses functional groups such as phenolic OH, C=O, C=C, and C-O groups and utilises adsorption mechanisms such as chemisorption (formation of chemical bonds by sharing electrons between the pollutants and functional groups on the adsorbents) and physisorption (formation of electrostatic interactions or Van der Waals forces between pollutants and adsorbents) for adsorptive removal of pollutants.[40-41] Biochar prepared from wood waste has also been used as an adsorbent for water treatment.[42-43] Biochar preparation increases the surface area of the adsorbents due to the decomposition of organic matter and the formation of micropores. The destruction of ester and aliphatic alkyl groups and exposure of the aromatic lignin core under higher pyrolysis temperatures facilitate the surface area increment.[44]

Masonry

Masonry waste consists of mixed waste comprising bricks, ceramics and tiles along with any other masonry rubble.31 The chemical composition of masonry waste is quite heterogeneous and contains CaO, SiO_2, Al_2O_3, and ferric oxide (Fe_2O_3) as major components.[45] The literature reports several recycling methods for masonry waste such as construction materials production and water treatment.

Aggregates derived from masonry waste are used for the manufacture of construction materials such as roof elements, mortars, concrete blocks, concrete titles, etc.[45] It has been reported that recycled brick masonry aggregate can be successfully applied as a 100% replacement for coarse aggregate in concrete for use in pavement and structural elements.[46]

Several studies report the potential of crushed brick powder, clay tiles and powdered silica ceramics for the treatment of water pollutants such as heavy metals and organic dyes.[47-49] According to characterisation studies, these materials possess high surface area and porous structures and therefore have the potential to be used as adsorbents.

Gypsum board

Gypsum board constitutes a considerable amount of CDW in some countries.[7] It contains $CaSO_4.2H_2O$ as the main component. Recycled gypsum board is used in new gypsum board and cement production and in land applications.

Reuse of recycled gypsum board for new gypsum board production is the main recycling method of gypsum board. Recycled gypsum board has also been successfully used in cement production as a substitute for virgin gypsum.[50]

Recycled gypsum board is applicable as a soil amendment material for general agriculture, mushroom growing, forestry and mine reclamation, compost amendments and residential lawns. Dissolving gypsum in soil water results in release of calcium and sulfate ions and therefore, it is applied to soil as calcium and sulfate fertiliser (Eq. 3).[50]

$$CaSO_4.2H_2O \rightarrow Ca^{2+} + SO_4^{2-} + 2H_2O \quad \text{(Eq. 3)}$$

It is also applied to reduce soil erosion, to remediate sodic soil (soil with excessive Na, as a Ca source and to aid in the alleviation of subsoil Al phytotoxicity.[51]

Glass

Waste glass is a small percentage of current demolition material as it was only used in mirrors, windows and insulation products in older buildings. Sodium oxide (Na_2O), magnesium oxide (MgO), SiO_2, CaO, and Al_2O_3 are major components of glass.

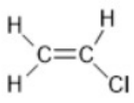
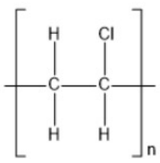
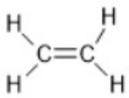
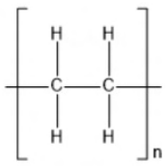
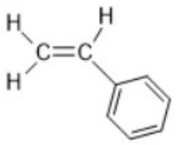
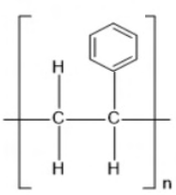
Waste glass has also been investigated as a raw material. Recycled glass is used as a replacement for sand in cement production and as a substitute for gravel in hot-mix asphalt. Waste glass has also been researched as an aluminosilicate precursor material in geopolymer concrete preparation.[52]

Some studies have investigated the potential of waste glass for water treatment. Crushed recycled glass has been tested as an alternative filter medium for silica sand.[53] A novel adsorbent has been prepared by hydrothermal treatment of waste glass followed by acidic activation of the surface of the adsorbent with HCl for treatment of heavy metals (Cd, Cu, Fe, Pb, and Zn). Based on the results, high removal efficiencies of 99-100% have been observed for all the studied heavy metals.[54]

Plastic waste

Plastic also makes a small contribution to CDW in most countries. However, plastic can cause a significant environmental impact once disposed of as it can take centuries to biodegrade and lead to microplastics. When landfilled or incinerated, the chemicals contained within plastics (furans, dioxins, bisphenols, heavy metals, phthalates, etc.) can cause serious water and air pollution.[55] Polyvinyl chloride (PVC) is the most commonly used plastic in the construction sector, being commonly used for manufacturing door and window frames, pipes and ducts. Polyethylene and polystyrene also make a significant contribution to the construction sector's plastic consumption. The chemical structures of these materials are summarised in Table 2.

Table 2. Chemical structures of PVC, polyethylene and polystyrene

Polymer	Monomer structure	Polymer structure
Polyvinyl chloride		
Polyethylene		
Polystyrene		

Plastic is recycled via two primary processes; mechanical recycling and chemical recycling. During the mechanical recycling process, plastic is mechanically crushed and melted before extrusion into pellets which can be used in new plastic materials production. The chemical recycling method involves the depolymerisation of plastics into monomers using heat and pressure.[56] The recycled plastic is used for many purposes including using monomers for new plastic production, as naphtha for new chemicals and plastics and as a transportation fuel for automobiles and aviation.[57-58] Recycling of PVC is challenging due to the release of HCl, which leads to equipment corrosion. This problem is circumvented by pretreating the mixtures to reduce chlorine content or by employment of HCl scavengers. However, research outcomes arising out of this area are still sparse.[59]

Challenges for CDW management

In short, the most challenging barriers to overcome in CDW management and its effective use are the high availability and relatively low cost of virgin materials as well as the cost and time associated with sorting and recycling CDW. Moreover, initiatives to use CDW are also negatively impacted by the lack of standards as applied to recycled materials, illegal landfill disposal of CDW and lack of community awareness of the negative effects of CDW. Therefore, further research is required to develop novel recycling and reutilisation strategies for proper management of CDW.[60]

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Article

Methodologies for the determination of honey composition – an introduction to honey chemistry

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Keywords: *honey, carbohydrates, sugars*

Introduction

For centuries, honey has been a highly sought-after commodity due to its natural sweetness. Known as "liquid gold",[1] honey is extremely diverse in its constituents. As a result of this, honey chemistry is an ever-growing field, with an immense number of varieties of honey available in the market today. With 1.85 million tonnes of honey produced in 2019 alone,[2] valued at US$7 billion,[3] such a successful worldwide industry is full of "fake" honeys that have been adulterated by additives. Using an array of analytical techniques, honeys must be authenticated as pure before they reach the supermarket shelf. This article will discuss constituents of honey, methods to analyse the composition and how these can be used for the detection of fraudulent honey within the global market.

Composition of honey

Typically, honey is a supersaturated mixture of sugars and water, often interspersed with a variety of organic compounds such as amino acids, vitamins, antioxidants and organic acids that contribute to its taste, aroma and texture. This is the result of the natural honey producing process, the work of the humble honeybee. A forager bee will leave the hive to collect nectar from nearby flowers and plants. Each plant has a unique nectar composition that contributes many substances to the honey blend. The honey is classified as floral or honeydew depending on the nectar source. Floral honeys are derived from flowering plants and nectar collection is often limited by seasonal and environmental changes. Honeydew is a secreted nectar from small insects such as aphids and as such, honeydew honeys have slightly different compositions.

Upon returning to the hive, worker bees pass the nectar between each other using the body temperature of their mouths to reduce the moisture content, saturating the solution, and producing what we know as honey. It is then sealed in a cell and stored for later consumption by the colony or collection by apiarists. To prevent bacterial and fungal growth in the honey, the mouth-to-mouth method incorporates peptides and enzymes from the salivary glands, which results in many chemical reactions within the honey.[4] Some of these anti-microbial substances remain in the honey we consume and contribute to its antibacterial properties.

I am in my third year of a BSc at the University of Waikato, majoring in chemistry, minoring in biochemistry and Japanese. I aim to begin a research MSc next year in the field of honey chemistry, with a long-term goal of developing more effective pharmaceuticals through further study in medicinal chemistry.

Carbohydrates

Carbohydrates in honey are categorised as monosaccharides and oligosaccharides, from two to six sugar units; occasionally polysaccharides longer than this may be found.

The most commonly occurring monosaccharides are D-glucose and D-fructose. It is known that each of these sugars exists in a constant five-way equilibrium involving the two chair forms of the alpha and beta pyranose rings, the alpha and beta furanose rings and the acyclic form. As glucose is an aldose, it prefers a pyranose configuration, whereas fructose, while still preferring a pyranose arrangement, occurs in large proportions in a furanose arrangement because it is a ketose. One of the pyranose forms of glucose and one of the furanose forms of fructose are shown in Fig. 1.

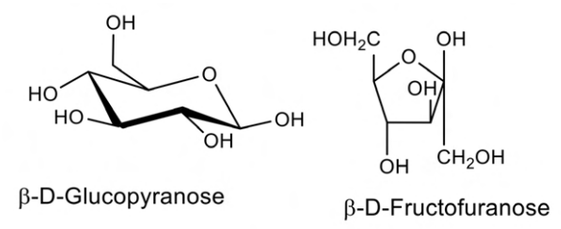

Fig. 1. Common structures of glucose (left) and fructose (right)

Oligosaccharides are comprised of combinations of the alpha and beta pyranose conformations of glucose and furanose conformations of fructose with a variety of glycosidic linkages between them. The most common oligosaccharides are sucrose, comprised of α-D-glucopyranose and β-D-fructofuranose, and maltose, comprised of two α-D-glucopyranoses. D-galactose is occasionally found in oligosaccharides but as a monosaccharide, it is toxic to bees so its presence in melibiose and raffinose can be indicative of a hive's health.

As of 2009, 37 oligosaccharides have been isolated from honey.[5] Carbohydrates are transported around most plants as sucrose. Enzymes in the bee or insect will break down this sucrose into fructose and glucose, hence a high proportion of monosaccharides are present in honeys. However, as enzymes catalyse reactions in an equilibrium state, occasionally they run backwards and stitch random monosaccharides together into oligosaccharides, thus producing the wide variety of oligosaccharides found in honeys. As the nectar used for honeydew honeys goes through both other insects and the bees, the more diverse range of enzymes yields a more complex carbohydrate profile. Sugars found in floral honey are given in Table 1 whilst the sugars found in honeydew honey are given in Table 2.

While there is significant variation in honeys depending on the origin of the honey, the basic carbohydrate composition is known to be noticeably different in floral honeys compared to honeydew honeys. For example, the fructose, glucose and sucrose levels in a selection of Spanish and French floral honeys[6-7] averaged around 40%, 30% and 0.1% compared to around 30%, 23% and 0.67% respectively in several New Zealand honeydew honeys.[8-9]

The fructose/glucose ratios (F/G ratio) of floral and honeydew honeys are about the same at 1.3:1,[6-9] but honeydew honeys have significantly higher levels of oligosaccharides.[6-9] Of particular interest are tri and tetrasaccharides present in honeydew honeys but not in floral honeys.

Table 1. Sugars found in floral honeys with nomenclature[6,7]

Length of sugar	Name	Nomenclature
Monosaccharide	Glucose	Glc
	Fructose	Fru
Disaccharide	Sucrose	α-D-Glc*p*-(1↔2)-β-D-Fru*f*
	Maltose	α-D-Glc*p*-(1→4)-D-Glc*p*
	Maltulose	α-D-Glc*p*-(1→6)-D-Glc*p*
	Turanose	α-D-Glc*p*-(1→3)-D-Fru*p*
	α,β-Trehalose	α-D-Glc*p*-(1↔1)-β-D-Glc*p*
	Palatinose	α-D-Glc*p*-(1→3)-D-Fru*p*
	Laminaribiose	α-D-Glc*p*-(1→2)-D-Glc*p*
	Melibiose	α-D-Gal*p*-(1→6)-D-Glc*p*
	Isomaltose	α-D-Glc*p*-(1→6)-D-Glc*p*
	Gentiobiose	α-D-Glc*p*-(1→6)-D-Glc*p*
Trisaccharide	Raffinose	α-D-Gal*p*-(1→6)-α-D-Glcp-(1↔2)-β-D-Fru*f*
	Neo-kestose	β-D- Fru*f*-(2→6)-α-D-Glcp-α-D-Fru*f*
	1-Kestose	β-D-Fru*f*-(2↔1)-β-D- Fruf-α-D-Glc*p*
	Erlose	α-D-Glc*p*-(1→4-α-D-Glc*p*-(1↔2-β-D-Fru*f*
	Melezitose	α-D-Glc*p*-(1→3-β-D-Fru*f*-(2↔1-α-D-Glc*p*
	Maltotriose	α-D-Glc*p*-(1→4-α-D-Glcp-(1→4-α-D-Glc*p*
	Panose	α-D-Glc*p*-(1→6-α-D-Glcp-(1→4)-D-Glc*p*

Table 2. Sugars found in honeydew honeys with nomenclature[8,9]

Length of sugar	Name	Nomenclature
Monosaccharide	Glucose	Glc
	Fructose	Fru
Disaccharide	Sucrose	α-D-Glc*p*-(1↔2)-β-D-Fru*f*
	α,β-Trehalose	α-D-Glc*p*-(1↔1)-β-D-Glc*p*
	Cellobiose	β-D-Glc*p*-(1→4)-D-Glc*p*
	Turanose	α-D-Glc*p*-(1→3)-D-Fru*p*
	Nigerose	α-D-Glc*p*-(1↔1)-α-D-Glc*p*
	Maltose	α-D-Glc*p*-(1→4)-D-Glc*p*
	Gentiobiose	β-D-Glc*p*-(1→6)-D-Glc*p*
	Palatinose	α-D-Glc*p*-(1→3)-D-Fru*p*
	Isomaltose	α-D-Glcp-(1→6)-D-Glc*p*
Trisaccharide	Erlose	α-D-Glc*p*-(1→4)-α-D-Glc*p*- (1↔2)-β-D-Fru*f*
	Melezitose	α-D-Glc*p*-(1→3)-β-D-Fru*f*-(2↔1)-α-D-Glc*p*
	Maltotriose	α-D-Glc*p*-(1→4)-α-D-Glc*p*-(1→4)-α-D-Glc*p*
	Panose	α-D-Glc*p*-(1→6)-α-D-Glc*p*-(1→4)-D-Glc*p*
Tetrasaccharide	Maltotetraose	α-D-Glc*p*-(1→4)-α-D-Glc*p*-(1→4)-α-D-Glc*p*-(1→4)-α-D-Glc*p*

Vitamins

Honey provides significant nutritional value from its high carbohydrate content and as such has historically been a staple food for many civilisations. Furthermore, it is a natural source of essential vitamins, adding to its nutritional importance. Those most commonly found in honey include thiamine (B1), riboflavin (B2), niacin (B3), pantothenic acid (B5), pyridoxine (B6), folic acid (B9), ascorbic acid (C) and phylloquinone (K1).[10]

Amino acids

It has been found that all amino acids are present in trace amounts in honey. One such study showed that proline was the most prevalent amino acid and was derived from the bee's haemolymph, an insect's equivalent of blood. Proline is important for bee health as it is metabolised into the intermediates of the citric acid cycle and provides the additional energy required for flight.[11]

Organic acids

Honey is considered somewhat acidic, with a pH of about 4, due to an average 0.6% composition of organic acids such as acetic, citric, formic and lactic acids. The most notable of these organic acids is gluconic acid, which is produced by the oxidation of glucose in honey. The acidity of the honey creates an environment in which many bacteria and fungi cannot survive. The presence of organic acids contributes to honey's antibacterial properties and long shelf-life.[12]

Antioxidants

To prevent tissue decomposition by free radicals, it is important to consume foods rich in antioxidants such as honey. These antioxidants include flavonoids, carotenoids and phenols. The concentration of antioxidants can be linked to the colour of the honey. Darker honeys are known to contain more compounds with antioxidant properties and are thus of particular interest to apiarists.[10]

Enzymes

Often remnants of the mouth-to-mouth transfer during honey production, enzymes make up a significant portion of the composition of honey, aside from sugar and water. There are a variety of enzymes that are used to help convert nectar into honey. Such enzymes include amylase that catalyses the condensation reaction which results in the formation of the glycosidic bond between monosaccharides to form oligosaccharides.

Subclasses of amylase include amylo-1,6-glucosidase which specifically caters for the creation of a 1-6 glycosidic linkage. Glucose oxidase is another enzyme found in honey, which is responsible for the conversion of glucose into gluconic acid and hydrogen peroxide. Both gluconic acid and hydrogen peroxide help deter bacterial growth in the honey. Invertase catalyses the hydrolysis of sucrose into individual fructose and glucose units.[13] This allows the bees to convert the high sucrose content of nectar into fructose and glucose, which are more readily metabolised.

Therefore, monosaccharides are most prevalent in honey and sucrose is only present in small amounts. In the case of honeydew honeys, the additional pathway through another insect provides an opportunity for additional enzymes to be present in the honey. The extent of these is an ever-growing collection of biological catalysts.

Anti-microbial activity

Iron found in the microbial cell wall catalyses the decomposition of hydrogen peroxide, producing free radicals which attack the cell wall and degrade any microbes in the honey. These radicals are strong oxidants so the presence of hydrogen peroxide in honey deters microbial growth, keeping the honey fresh when stored in the hive.[14]

The acidic nature of honey means that the proteins in the cell wall, comprised of pH-sensitive amino acid peptide chains, are denatured, causing the cell to collapse and thus inhibiting further growth. This also prevents microbes from growing in the honey during storage.[15]

Honey displays the osmotic effect, where water flows towards a saturated solution. The saturated nature of honey makes it a difficult environment for microbial cells, which require water to survive, as they become dehydrated in the honey environment.[14]

Non-peroxide activity

Mānuka honey is world-renowned for its health benefits and unusually high antibacterial properties. Researchers have linked these unique properties to a compound called methylglyoxal (MGO) and its precursor, dihydroxyacetone (DHA), shown in Fig. 2.

In 2006, German scientists investigated "non-peroxide activity" in mānuka and found there was a positive correlation with the concentration of MGO in the honey. This was confirmed by researchers at the University of Waikato,[16-17] who isolated the active fraction of this honey, and later investigated the origin of the MGO. It was found that the mānuka flower's nectar contained high levels of DHA and no MGO.

Freshly made honey was comprised of high levels of DHA and a small amount of MGO. This indicated that MGO was the product of one of the many reactions involved in the conversion from nectar to honey. When stored at 37°C, to simulate the conditions in a cell in the beehive, it was found that the DHA levels decreased over time while the MGO levels increased in a related manner.[16-17] The mechanism for the conversion of DHA to MGO is complex and is known to involve catalysis by natural proteins and amino acids in the honey.[18]

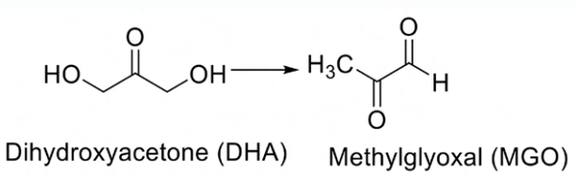

Fig 2. Formation of methylglyoxal from dihydroxyacetone

Analysis methods

Due to the diverse range of carbohydrates found in honeys, many apiary businesses need to be able to qualitatively and quantitatively analyse these substances to assign a value to their unique product. Each honey's sugar profile can also provide an idea of which plants the nectar may have been sourced from and the enzymes involved in the formation of the honey. More importantly, the analysis of carbohydrates in honey can reveal whether the honey has been adulterated. There are many methods to analyse the sugar constituents of honey. Techniques such as high-performance liquid chromatography (HPLC), gas chromatography-mass spectrometry (GC-MS) and UV-visible spectroscopy (UV-Vis) are used to ascertain honey carbohydrate compositions, as well as the presence of any other compounds, particularly those involved in biological activity.

HPLC

HPLC can be used to separate honey samples into their fundamental sugars. One such method separates the carbohydrates by size through size exclusion chromatography (SEC) and distinguishes similarly sized monosaccharides through ligand exchange chromatography (LEC). Using SEC, larger oligosaccharides will elute first. If the sample contains any trisaccharides, these elute very early, followed by disaccharides. The monosaccharides elute last but are separated by LEC. Glucose and fructose coordinate to a metal ion as ligands.

These coordinate differently and as such, fructose will have a longer retention time than glucose. Furthermore, sugar standards of known concentration can be used to quantify the amount of sugars in honey. The use of detectors following elution also allows for the detection of biologically active compounds. On account of its qualitative and quantitative value, HPLC is an effective method for the creation of a sugar profile for a given honey sample.

GC-MS

Additionally, GC-MS can be used to confirm the basic constituents of honey. GC requires samples to be volatile. Honey is not naturally volatile so must be derivatised to run on a GC column. One such derivative uses N-trimethylsilylimidazole (N-TMSI). This reacts with the hydroxyl groups in the sugars and replaces them with per-

O-trimethylsilyl. The benefit of silylated sugar derivatives is thermal stability and volatility.[19] These allow the sugar to be analysed using a gas chromatography column. The resulting chromatogram has the monosaccharides eluting first, separated into alpha and beta configurations of the pyranose and furanose rings of fructose and glucose. Oligosaccharides will then elute from smallest to largest.

The order of elution for these monosaccharides can be determined using mass spectrometry with silylated samples. It is known that hexoses and hexuloses fragment differently and will display a unique combination of peaks, allowing for the identification of the pyranose and furanose conformers of fructose and glucose.[20]

UV-Vis spectroscopy

The presence of antioxidant phenolics in honey can be detected and quantitated using UV-Vis absorbance spectroscopy. Most commonly found are phenols and flavonoids which, when reduced by certain reagents, produce electronic transitions in the ultraviolet and visible range of electromagnetic radiation. A variety of standards and reagents are used to detect the antioxidants.

Gallic acid, as shown in Fig. 3, is similar in structure to most naturally occurring phenols and when combined with Folins-Ciocalteu phenol reagent, is used as a standard for measuring phenolics in honey samples.[21]

Catechin, as shown in Fig. 4, is similar in structure to most naturally occurring flavonoids and when combined with aluminium trichloride reagent, is used as a standard for measuring flavonoid content in honey samples.[21]

Adulteration of honey

To produce cheaper honey, there have been many instances of adulteration of honey with artificial syrups such as high fructose corn syrup and cane sugar. Additionally, in larger scale apiary operations, during harsher winter months, bees can be fed with artificial feed comprised of high concentrations of one sugar over the other. The honey produced from bees fed with syrups is considered adulterated with a different composition to naturally produced honey. The resulting adulterated honeys reduce the market value of honey. These additives can be detected using various analytical methods. Sugars derived from sugar cane and corn are formed via the C4 pathway, whereas nectar is formed via the C3 pathway. The C4 and C3 pathways are photosynthetic routes where CO_2 is converted to a storable carbohydrate via four carbon intermediates and three carbon intermediates, respectively. There is a noticeable difference between the amount of ^{13}C isotope found in each pathway, and this is measured to detect if a pure honey sample has been adulterated with C4 sugars.[22] Additionally, the ratio of fructose to glucose is an indication of potential adulteration.

A study showed that a sample of Jarrah, an Australian floral honey, had an F:G ratio of 1.3:1.[23] When high glucose rice syrup was artificially added, it was found that the F:G ratio decreased to 0.8:1, indicating an increase in glucose. A lower F:G ratio is indicative of the addition of glucose to a honey. Similarly, a higher F:G ratio implies added fructose. The F:G ratio can be quantified using methods such as HPLC and GC. As it is often expensive and not worth the effort to produce a replica honey mixture that perfectly matches the natural food source of the bees, these low-cost adulteration methods are becoming more common in honey production.

Conclusions

Honey chemistry has many opportunities for the discovery of new medicinal and nutritional sources derived from natural products. Its complex composition provides a

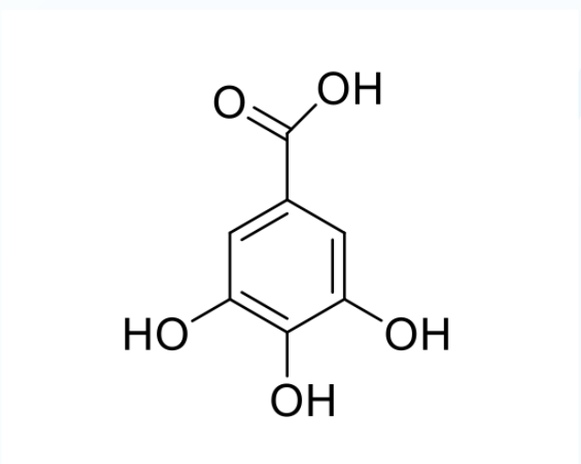

Fig 3. Structure of gallic acid, a standard for phenolics

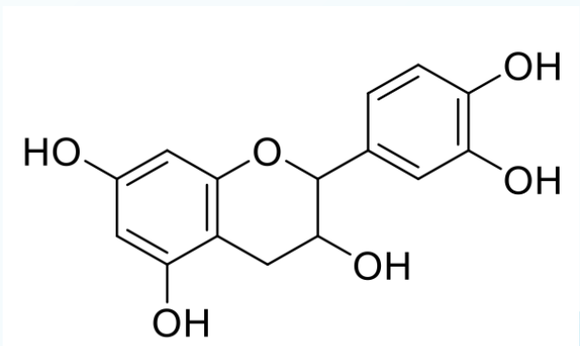

Fig 4. Structure of catechin, a standard for flavonoids

range of properties for potential use across a wide variety of industries. The numerous methods of analysis allow us to investigate the contents of the diverse array of honey available on the market today. Similarly, it allows us to maintain a high level of honey purity by identifying adulterated samples.

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Article

The chemistry of *Epichloë* endophytes in New Zealand perennial ryegrass

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Keywords: *Epichloë endophytes*, *alkaloids*, *perennial ryegrass*, *bioactives*

Introduction

Nature has a wonderful way of adapting to and protecting itself from the pressures of environmental change. The combination of perennial ryegrass (*Lolium perenne*), *Epichloë* fungal endophytes and the alkaloids they produce is an example of this in New Zealand's pastoral agriculture.

New Zealand has a unique farming environment, dominated by one grass species - perennial ryegrass (*Lolium perenne*). This is a temperate climate grass that prospers in New Zealand due to its ability to compete against other grass species, tolerate the pressures of grazing and treading from animals, its ease of establishment and high nutritional value.[1-2] However, with the introduction of pest insects into the country and endemic pests, fungal endophytes are essential to avoid perennial ryegrass from being decimated by predation (Fig. 1).[1] There are six main ryegrass pest insects in New Zealand: the African black beetle, grass grub, root aphid, porina, pasture mealybug and the Argentine stem weevil (Fig. 2). These are destructive both above and below ground, attacking both root and herbage structures.[3-4] The changing climate has caused these insects to become more prevalent and therefore more destructive to the perennial ryegrass. The solution to this is the alkaloids of *Epichloë* endophyte infected grasses.

In the late 19th to early 20th centuries when New Zealand's agricultural industry was increasing, it was unknowingly introduced to a wild-type fungal endophyte, known as the common toxic or standard fungal endophyte, *Epichloë festucae* var. *lolii* (previously known as *Neotyphodium lolii* and *Acremonium lolii*).[1,5-6] The fungal endophyte produced secondary metabolites to protect itself against not only pest insects but grazing animals. These alkaloids significantly harmed grazing animals causing diseases such as ryegrass staggers and heat stress, putting serious productivity pressures on farmers. It wasn't until 1980 when the cause of these detrimental effects was determined, leading to the discovery of *Epichloë* endophytes and their bioactive alkaloids.[1,6]

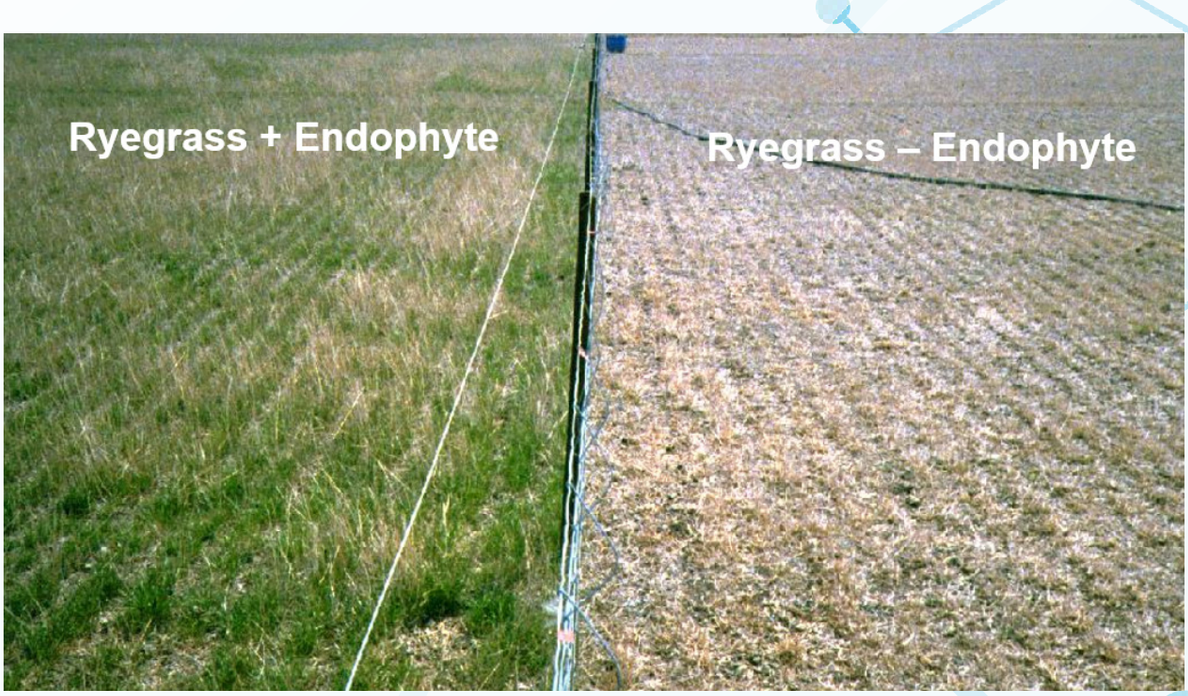


Fig. 1. Left: endophyte-infected pasture resistant to damage. Right: endophyte-free pasture susceptible to damage. Image credit: AgResearch Ltd.

African black beetle

Grass grub

Pasture mealybug

Root aphid

Porina

Argentine stem weevil

Fig. 2. The six main pest insects of New Zealand. Image credit: AgResearch Ltd.

But what is an endophyte? This is a general term for something living within a plant, in this instance *Epichloë* endophytes are fungi growing intercellularly amongst grass cell walls (Fig. 3). This is a symbiotic relationship between the plant and fungi. The plant benefits with an increase in reproduction and growth rate and most importantly a means to defend itself, utilising secondary metabolite alkaloids produced by the *Epichloë* endophyte. In return, benefits to the *Epichloë* endophyte include a protective environment, sugars and nutrients and a way to transmit/grow to the next generation.[7] The secondary metabolites produced are not essential for the primary functions of the fungi or the plants but help to defend the plants, enhancing their survival and life.

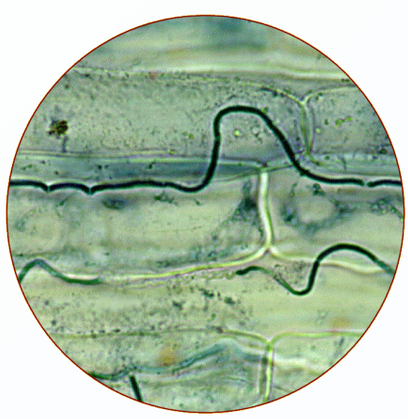


Fig. 3. Endophyte hyphae growing intercellularly alongside the plant cells. Image credit: AgResearch Ltd.

To improve agricultural production, scientists and plant breeders have researched and utilised fungal endophytes that produce protective alkaloids against pest insects but minimise the negative impacts to grazing animals. The two main success stories are the AR1 and AR37 *Epichloë* endophytes. AR1 was first released in 2001 and is still broadly used today. Its bioactive alkaloid is peramine which gives protection against Argentine stem weevil and some bioactivity against black beetle. Although this does not provide protection against a lot of pest insects it is considered animal safe.[1,8] AR37 was released in 2007 and gives stronger insect protection to a range of pests, although the bioactive alkaloids, epoxyjanthitrems, cause ryegrass staggers in sheep.[3,9] However, the staggers produced are less severe than those seen on common toxic endophyte and can be managed with stock rotation and companion planting. Bioactive alkaloids produced by *Epichloë* endophytes are often novel/new compounds and hard to identify, so research continues to fully understand these interactions and discover novel alkaloids.

The alkaloids

There are three main classes of *Epichloë* endophyte alkaloids in perennial ryegrass: indole diterpenes, peramine and the ergot alkaloids.[10] While they vary significantly in structure, they are all derived from amino acids such as tryptophan and are nitrogenous heterocyclic compounds. *Epichloë* strains that occur naturally can produce one or more of these alkaloids.[11] Each class has a complex biosynthetic pathway with multiple related precursors and

analogues. The slight changes in structure can completely change their bioactivity, making it difficult to predict their effectiveness on structure alone.

Indole diterpenes – lolitrems, paxilline and epoxyjanthitrems

Indole diterpenes such as the lolitrems, paxilline and epoxyjanthitrems are characterised by having the same core indole group (Fig. 4) that connects to different diterpene units.

Fig. 4. Structure of indole group

Lolitrems

Lolitrems A-D were first described in the early 1980s by Gallagher *et al*.[12] The most predominant of these compounds is lolitrem B. The structure of lolitrem B (Fig. 5) was elucidated in 1984 and is unique to *Epichloë* endophytes.[13-16] Due to its fluorescence, high molecular weight and low volatility, lolitrem B is relatively easily detected at low concentrations in seed and herbage extracts using mass spectrometry and HPLC.15 Lolitrem B is a lipophilic tremorgenic neurotoxin that causes muscle tremors and loss of coordination in grazing animals. It is widely accepted to be the causative agent of ryegrass staggers in animals grazing common toxic (also known as wild-type) endophyte-infected grasses.[11] Although it has shown bioactivity against Argentine stem weevil larvae and porina, levels as low as 2 ppm *in planta* are enough to cause tremors so it is undesirable in *Epichloë* cultivars.[17, 18] Lolitrem B and other related compounds concentrate either in the base of the plant leaf sheath or in seed heads, so staggers tend to occur in warmer months when there is a shortage of feed, meaning animals graze closer to the ground.[14]

Epoxyjanthitrems

Five epoxyjanthitrem compounds have been isolated and are unique to the AR37 and NEA12 *Epichloë* endophytes. These are referred to as epoxyjanthitrems I-IV and triol. In pure form they are unstable, making them difficult to work with and it is only recently that these instability issues have been resolved and structural elucidation confirmed via NMR assignment.[19] They are structurally

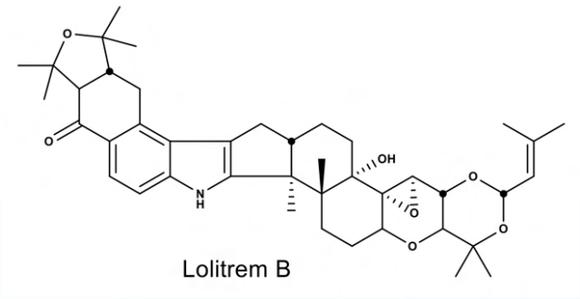


Fig. 5. Structure of lolitrem B

similar to lolitrem B and other known janthitrems (janthitrems A-D (Fig. 6) produced by *Penicillium* ¬which are also tremorgenic) and therefore they are thought to be the cause of the ryegrass staggers seen with AR37.[18-19] Comparative tremorgenicity studies using small animal models between the epoxyjanthitrems and janthitrems B and D indicate that the [11,12-] epoxy group (Fig. 5) is significant in producing tremors.[20] However, this structure is also hypothesised to be responsible for the novel bioactivity against pest insects induced by these compounds.[1,18] Most recently, a study has shown pure epoxyjanthitrem I, (Fig. 7) reduces the weight and feeding of porina in a dose dependent manner.[19] Work continues on these compounds to fully understand their impacts.

Paxilline

Paxilline (Fig. 8) was first isolated from the fungus *Penicillium paxilli* in 1974 and since then has been found in a range of fungi including *Epichloë*. It is thought to be a precursor in the biosynthetic pathway of lolitrem B and was subsequently shown to be tremorgenic to mice and cockerels, producing a sustained tremor that lasted for several hours. [16,21] However, in comparison to lolitrem B, this tremor is shorter in duration and less potent, making it unlikely that paxilline causes tremors in the field. The structure of paxilline was reported a year later by Springer *et al*.[22] Paxilline produces bioactivity against Argentine stem weevil larvae, impacting both their growth rates and survival, and reduces the food consumption and weight gain of porina larvae but only at high concentrations. It shows slight bioactivity against several other insects, but not against black beetle.[18,23]

Ergot alkaloids – ergovaline

The ergot alkaloids can be found in a wide range of fungi and other plants. Ergovaline (Fig. 9) is the main ergopeptide alkaloid produced by endophyte-infected perennial ryegrass and thus is the most understood. Ergopeptide alkaloids are recognised by their tricyclic peptide moiety joined to an ergoline ring or lysergic acid structure.[24] Ergovaline is the cause of an animal disease, fescue toxicosis, in

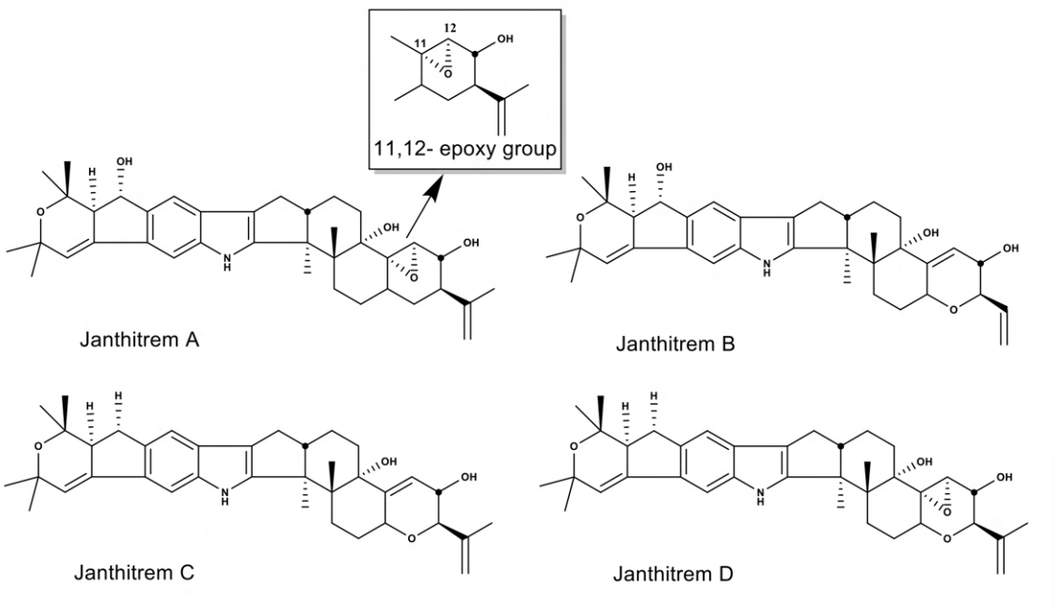


Fig. 6. Structures of janthitrem A with highlighted 11,12-epoxy group, janthitrem B, janthitrem C and janthitrem D.

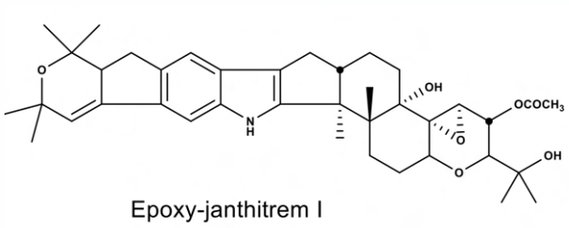


Fig. 7: Structure of epoxyjanthitrem I

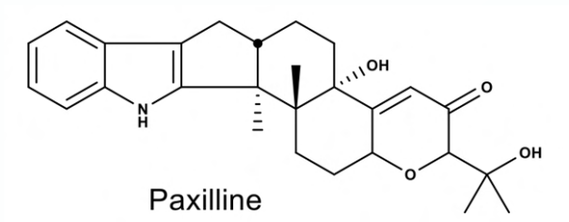


Fig. 8. Structure of paxilline

the United States, which is characterised by heat stress, reduced weight gains and lameness in grazing animals. It acts as a vasoconstrictor, increasing an animal's core temperature and restricting their ability to regulate heat.[25] Higher temperatures can increase the levels of ergovaline as well as affect how the toxin interacts with the animals, leading to heat stress.[26] Ergovaline is expressed by the common toxic endophyte in perennial ryegrass and an increased level of ergovaline was produced by the novel endophyte Endosafe, ultimately leading to its withdrawal from the market.[14] While ergovaline has shown bioactivity against a wide variety of pest insects such as black beetle and Argentine stem weevil adults, its risk to the health of grazing animals makes it an undesirable alkaloid for endophytes in New Zealand, although some seed companies have commercialised endophytic products with low ergovaline concentrations.[6]

Peramine

Peramine (Fig. 10) is a pyrrolopyrazine metabolite that is unique to the *Epichloë* endophytes. It was identified by Rowan and Gaynor (1986) after it was noted that endophyte-free pasture was decimated by Argentine stem weevil whereas endophyte-infected ryegrass remained resistant to their effects.[27] Stem weevil adults feed on the leaf blade and lay their eggs in the stem, but once hatched, larvae mine the centre of the tiller, severely damaging the plant. Peramine deters adult stem weevil from feeding on the tiller and thus reduces egg laying.[28] Larval feeding is also deterred by peramine which negatively impacts growth and development.[8] Unlike other secondary metabolites, peramine is uniformly distributed throughout the herbage. Although the bioactivity of peramine against

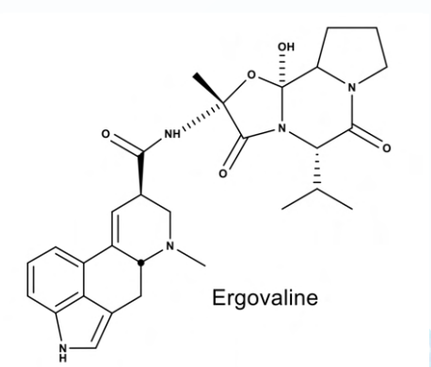
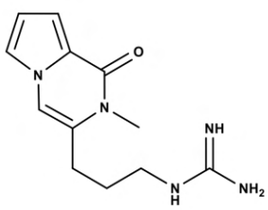


Fig. 9. Structure of ergovaline



Peramine

Fig. 10. Structure of peramine

insect pests is limited, it is considered animal safe and thus is a highly desirable alkaloid in endophytes and is a target in the endophyte discovery process.[29]

Conclusions

Although alkaloids such as lolitrem B, ergovaline and peramine have been widely studied and are understood, there is still a lot that is unknown about *Epichloë* endophyte alkaloids and their effects on pest insects and grazing animals. Plant breeders and scientists continue to research *Epichloë* endophytes in an attempt to develop the perfect endophyte for New Zealand's environment, one that shows strong bioactivity against all six pest insects without causing any harmful effects to grazing animals. This research includes investigating the precursors and analogues of the major alkaloids mentioned above, as well as collecting *Epichloë* endophytes from around the world looking for favourable chemistry profiles.

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