



The Institute
of
Chemistry of Ireland

IrishChemicalNews

JOURNAL OF THE INSTITUTE OF CHEMISTRY OF IRELAND

FEATURE:

Control and Exploitation of Phosphine Oxidation: The Taming of a Chemical *Enfant Terrible*



ALSO FEATURED IN THIS ISSUE:

- Industrial News
- Company member profile
- REACH – what it means for Ireland
- Elemental Su Doku
- Wesley Cocker – An Appreciation
- Literature Focus
- The ICN Crossword



Speciality Chemicals.....



.....our Speciality



With the increasing importance of quality in the analytical laboratory and with trace level determinations now regarded as part of the routine, it takes a special reagent manufacturer just to keep up. A manufacturer like ROMIL, that has been dedicated to achieving the highest standards of chemical purity for more than two decades.

ROMIL-SpS™ Super Purity Solvents are high purity solvents suitable for a wide range of applications. Since one grade only need be stocked for a variety of methods, ROMIL-SpS™ products also have the benefit of assisting laboratories, not only in their compliance with health, safety and environmental legislation, but also in their quality system accreditation to international standards such as ISO 9000 and ISO 17025.



USP's official Reference Standards are highly characterised specimens of drug substances, excipients, impurities, degradation products, dietary supplements, compendial reagents and performance calibrators. They are required for use in conducting official USP-NF tests and assays. In addition to USP-NF-based standards, USP provides Reference Standards specified in the Food Chemicals Codex as well as authentic substances - high-quality chemical samples - as a service to analytical, clinical, pharmaceutical, and research laboratories.

When you purchase USP's official Reference Standards from Lennox we do all the hard work! by looking after the licence and other formalities.

Speciality Chemicals are only a part of our extensive chemical portfolio available from leading names like; Alfa Aesar, BDH Prolabo, Fluka, Merck, Molekula, Riedel-de Haën and many more.

For further details please contact our chemicals sales team on 01-455 2201, email. sales@lennox.ie or visit www.lennox.ie

Editorial

First of all on behalf of the ICI council I would like to wish all our readers the very best for 2008. In addition to the regular items, this expanded issue incorporates a contribution from Prof. Michael Hynes on the new REACH legislation which will have repercussions for all those involved in the handling and usage of chemicals in one form or another. We have also included a profile of the Chemistry Dept. at UCG from **Dr. Niall Geraghty**. Our feature article this month comes from UCD, from where **Prof. Declan Gilheany** has recently published two landmark papers on the control of phosphine oxidation, we are delighted that he has been able to summarise these potentially very important developments in the field of asymmetric catalysis (*inter alia*) for our readers. The ICN is also pleased to be able to publish an appreciation of **Prof. Wesley Cocker** – a longtime servant of Irish chemistry and researcher of international renown. Personally speaking, Prof. Cocker made a strong impression on me when he spoke at my graduation 10 years ago (mentioned in Prof. McMurray's appreciation) when he was a young, vibrant octogenarian. The crossword and su doku are retained; be warned however - we act on feedback and these are now more difficult!

We welcome comments and suggestions on the balance and direction of the ICN - members are also strongly encouraged to submit essays, articles and correspondence on any issues /developments affecting chemistry, either globally or in Ireland. This is your institute and magazine after all – we need to hear from you!

Dr. Stephen Connon

School of Chemistry, TCD
connonst@tcd.ie

Contents

Editorial	1
REACH	2
SciFest	8
Conference Report	10
Department Profile	11
Feature Article	16
Literature Focus	19
Industrial News	28
Prof. Wesley Cocker- An Appreciation	29
Schools Chemistry Essay Competition 2007	31
Company Member Profile	32
Congress 2008	33
The ICN Crossword	34
Elemental Su Doku	35

REACH – what it means for Ireland

Prof. Michael J. Hynes¹

School of Chemistry, National University of Ireland, Galway

What is REACH?

- REACH stands for Registration, Evaluation, Authorisation and Restriction of Chemicals. It is the new EU chemicals legislation and came into force on 1st June 2007.
- REACH has one key central aim: to protect human health and the environment from the risks arising from the use of chemicals.
- REACH aims to simplify the control of chemicals on the EU market and will replace a number of European Directives with a single piece of legislation. It will also result in changes in national legislation.
- REACH aims to make the people who place chemicals on the market - either by manufacturing or importing them - responsible for understanding and managing the risks associated with their use.
- REACH switches responsibility for the control and safety of chemicals from regulatory authorities to those who manufacture, import and use them.
- Every single company using chemicals anywhere in the EU will be affected by REACH.
- REACH will require a registration, over a period of 11 years, of some 30,000 chemical substances. The registration process requires the manufacturers and importers to generate data for all chemical substances produced or imported into the EU above one tonne per year. The registrants must also identify appropriate risk management measures and communicate them to the downstream users.

Overview of REACH

The REACH Regulations, officially known as REGULATION (EC) No. 1907/2006 of the EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 December 2006, became law on 1st June 2007. The Regulation concerns the Registration, Evaluation, Authorisation and Restriction of Chemicals, establishes a European Chemicals Agency, amends Directive 1999/45/EC, repeals Council Regulation (EEC) No. 793/93 and Commission Regulation (EC) No. 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC. A number of other Directives as well as the Irish legislation implementing them will be repealed on a phased basis. The REACH regulation contains 141 articles (subdivided into titles), 10 appendices and 17 annexes. While the original version ran to over 800 pages, the current version has been reduced to 278 pages by the simple expedient of reducing the font size. Despite what may be argued by the EU and other proponents, it is an extremely complex piece of legislation. The evidence for this is clear, one only has to look at the massive volume of REACH documentation now available. The Reach Implementation Projects (RIPs) which are intended to guide users are themselves weighty and indeed complex documents. Perhaps the one of most interest to industry, 'REACH Implementation Project 3 - Development of REACH Guidance for Industry' contains ten separate chapters covering areas such as the registration dossier (3.1), the chemical safety report (3.2), information

requirements on intrinsic properties of substances (3.3), data sharing (3.4), down-stream user requirements (3.5), Global Harmonised Systems on classification and labelling (3.6), authorisations (3.7), substances in articles (3.8), socio-economic analysis (3.9), and substance identity (3.10).

REACH – a new paradigm for the regulation of chemicals – 'no data, no market'

REACH represents a new paradigm in the regulation of chemicals. Specifically, it reverses the responsibility for assessing chemical risks onto manufacturers and importers rather than the regulators and regulatory authorities. This also means a transfer of the costs. It introduces a 'no data, no market' provision that will prohibit the manufacture or placing of substances on the EU market unless they have been registered under REACH. For this registration the necessary risk assessment dossiers will have to be produced. Owners of data are entitled to compensation for a period of 12 years from anyone referring to their data. Data must be derived under Good Laboratory Practice standards (see Directive 2004/10/EC). REACH requires specific authorisations for sale or use of substances that meet criteria identifying them as 'substances of very high concern'. These will be listed in Annex XIV of the REACH regulation and the initial list is due by 1st June 2008. This will be publicly available. It mandates data sharing under the 'one substance, one registration' rule.



TopChem Laboratories is an independent contract research company specialising in organic synthesis services to the pharmaceutical and fine chemical industries.

PRODUCTS & SERVICES

Custom Synthesis: APIs, intermediates, impurities, metabolites

Process Development: Optimisation, Troubleshooting, Cost reduction

Consultancy: Literature searches, technical training, MSDS service

Scale-up: GMP, non-GMP

CONTACT DETAILS

David Hopkins, Commercial Manager
TopChem Laboratories Limited,
70 Western Parkway Business Park,
Ballymount Drive, Dublin 12.
Tel. 01 4608818. Fax 01 4504833
www.topchem.ie



Replace messy oil baths and heating mantles

Radleys Heat-On:

- Fits on to most leading brands of stirring hotplate including IKA and Heidolph
- A sleek design which reduces the mass of the block to be heated, improving heat-up times
- Deep wells which maximise heated surface area to improve heat-up time and minimise the difference between the block and solution temperature
- Optional quick release safety lifting handles allow movement of the block while still hot
- A fluoropolymer coating which protects the block from chemical attack and actually improves heating efficiency compared with uncoated aluminium
- Fast Heating - a 250ml flask of water can be boiled in under 9 minutes
- Two probe holes for use with a separate temperature probe
- Can be used up to +200°C, and to +260°C for short periods
- A unique well design prevents cracking of glassware
- Safe, clean, low cost alternative to oil baths

**For round
bottom flasks from
10ml to 5 litres**



RR61040	Heat-On 250ml Block	€ 300
RR61045	Heat-On 500ml Block	€ 325
RR61050	Heat-On 1 Litre Block	€ 350
RR61055	Heat-On 2 Litre Block	€ 475
RR61060	Heat-On 3 Litre Block	€ 500
RR61063	Heat-On 5 Litre Block	€ 750
RR61080	Safety lifting handles (pair)	€ 100

 **LABPLAN**
Science Support Solutions

Allenwood Business Park,
Naas, Co Kildare.
Ph: 045-870560
Fax: 045-870811
Web: www.labplan.ie

REACH deals with substances

REACH applies primarily to substances. It is very broad in its scope and applies to all chemical substances that are manufactured, imported, placed on the market or used within the European Community, either on their own, in a preparation or in an article in quantities greater than 1 tonne *per annum*. In the main, there are few exemptions for substances that are covered by other Directives and Regulations. It is largely aimed at 'Existing Substances' *i.e.* those that were on the market before 18 September 1981. In REACH, these are termed 'phase-in' substances. There are estimated to be approximately 100,000 of such substances of which about 30,000 are used in quantities of greater than 1 tonne *per annum*. Approximately 1,500 of these are thought likely to meet the criteria required to make them 'substances of very high concern'. Of these, 900 are already identified and another 600 or so are predicted to be identified as the data for them are generated to meet the requirements of REACH. These substances will require authorisation and may be restricted.

REACH will affect everyone who uses chemicals

Everyone who uses chemicals will be affected by REACH in some way or other. Included are chemical suppliers including manufacturers and importers, preparation suppliers of paints, oils, adhesives, detergents etc and down-stream users which includes anyone who uses substances.

Reach will be implemented over an 11 year period according to the following timeline:

- 1st June 2007 - REACH came into force
- 1st June 2007 - European Chemicals Agency (ECHA) in Helsinki in operation.
- 1st June 2008 - Non-phase in substance registration (*i.e.* 'new' substances)
- 1st June 2008 - 1st December 2008 - Pre-registration for phase-in substances

During this time, potential registrants must submit certain information to the ECHA (*via* REACH IT), including information on the identity of the substance, the potential registrant, the envisaged deadline for registration and the tonnage band within which he/she manufactures or imports the substance. Failure to pre-register substances will require them to meet the requirements of REACH with immediate effect.

- November 2010 - 1st phase-in substance deadline which will include:

Substances manufactured/imported at $\geq 1,000$ tonnes *per annum*

Carcinogens, mutagens, substances toxic to reproduction (CMRs) categories 1 and

Substances toxic to the environment (symbolised by N) and those having risk phrases R50-53 at ≥ 100 tonnes *per annum*

- June 2013 - 2nd phase-in substance deadline for substances manufacturer/imported at ≥ 100 tonnes *per annum*
- June 2018 - 3rd phase-in substance deadline for substances manufactured/imported at ≥ 1 tonne *per annum*.

The EU hopes that the 'one substance, one registration' dictat will apply and pre-registration will assist in this. Once pre-registration is completed on 30th November 2008, the ECHA shall, by 1st January 2009, publish on its web site a list of pre-registered substances. This will include only the names of the substances including their EINECS and CAS numbers if available, other identity codes, the first envisaged registration deadline and the tonnage band (which will influence the registration deadline). The identity and contact details of potential pre-registrants will also be available. This will enable companies to ascertain if they are eligible to participate in a Substance Information Exchange Forum (SIEF), *i.e.* if other organisations have also pre-registered the substance. Communication within the SIEF will enable a determination of the information already available. Depending on the tonnages involved, additional information may be required and this will have to be obtained from accredited laboratories. Only one study shall be conducted per information requirement within each SIEF by one of the participants acting on behalf of the others.

The REACH actors

The responsibilities of the various actors involved in the process are outlined in Table 1. In Ireland the Health and Safety Authority (HSA) has been named as the competent authority and they have a designated web site to assist individuals and organizations affected by REACH.²

The impact of REACH on Irish industry

The ultimate impact of REACH on Irish industry and indeed on European industry is difficult to predict. There will be legal challenges to REACH which may affect the current implementation. For example an application for judicial review by four companies (SPCM of France, C H Erbslöh of

Germany, Lake Chemicals & Minerals of England and Hercules of Delaware, USA) is currently before the UK High Court and may eventually end up in the European Court of Justice (ECJ). The UK government is understood to have responded that at least one of the three claims meets the criteria for referral to the ECJ and stands a 'reasonable prospect of success'. Perhaps the best analysis of the impact of REACH on Irish industry is the Regulatory Impact Assessment (RIA) carried out by ERM Environmental Resources Management Ireland Ltd (ERM Ireland) on behalf of Forfás and published in April 2005. The concluded that:

- REACH will generate significant financial costs for chemical manufacturers (upstream industries) in Ireland.
- The costs to downstream chemical users will be significantly higher than those estimated for the upstream manufacturing industry.
- The impact on the pharmaceutical industry will be lessened because substances used only in human and veterinary medicinal products are exempt from most requirements of REACH. Exactly how this will operate is still not fully clear.
- The ICT hardware industry and SMEs, as predominantly downstream users, are likely to feel the greatest impact.

Central Statistics Office data for Irish external trade for Jan-Dec 2006 shows that total exports were ?88.7 billion of which ?41.7 billion or 47% was chemicals and related products. The chemical and related products sector is of extreme importance to the Irish economy and anything that impacts adversely on it must be viewed with considerable concern. The costs of REACH will be proportionately higher in Ireland than in other EU countries. It is estimated that in Europe, 85% of chemicals will be reported via consortia, while in Ireland this will be only 50%. This is because Ireland's chemical industry is focused on pharmaceutical and speciality chemicals and the formation of consortia will not be an option. In 2003, Ireland's chemical industry output as a proportion of total EU output was 2.9%. However, the proportion of notifications under existing EU chemicals legislation (93/793/EU) was 4%. As such the proportion of total REACH costs applicable to Ireland will be between 2.9 and 4% of total EU costs.

REACH will involve significant administration costs

While much has been made of the costs of registering substances with the European Chemicals Agency in Helsinki, my experience of REACH to date leads me to believe that the

major costs will be incurred in indirect costs such as administration. Estimates of these vary from 2-6 times the direct costs of testing and regulation. Highly qualified people will be required to deal with REACH resulting in considerable administrative and technical resource costs and this will mean that their talents can not be fully employed in other areas of the organisation. My opinions on this are reinforced by a statement in the August 2007 issue of the Magazine of the Institute of Environmental Management and Assessment which states *"The commercial winners from REACH are likely to be those businesses that make the most of strategic opportunities, which will almost certainly require them to engage their top executives in the issues posed by the Regulation from the beginning"*.

Some chemicals may be discontinued?

Undoubtedly, some chemicals essential to the production and profits of downstream users will risk being removed from the market because it is not worth paying the costs of testing and registration. The argument here goes that if this is the case then the substance is under-priced and if there are no substitutes then it will be profitable for the users to pay more. A bigger risk is that a chemical essential to users may be removed from the market because it is found to be hazardous. There are however some safeguards in REACH against this in that socio economic aspects (SEA) may be considered. Confidentiality and intellectual property issues have also been raised as a area of concern to Irish industry, however we are assured by the ECHA that this will not be an issue and that REACH contains strong protection against such disclosures.

The Globally Harmonised System (GHS) for labeling of chemicals

Another potential problem lies in the introduction of the Globally Harmonised System (GHS) for the labeling of chemicals. On 27th June 2007, the European Commission adopted the *"Proposal for a Regulation of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures, and amending Directive 67/548/EEC and Regulation (EC) No 1907/2006"* (COM (2007) 355 final).³ The proposal aligns the EU system of classification, labelling and packaging of substances and mixtures to the United Nations GHS. GHS will mainly affect chemical manufacturers, suppliers and users. Under the proposed regulation, these groups have the general obligation to self-classify and label their substances and

mixtures. It will also affect workers and consumers involved in hazard communication through labels and SDS's. 'Hazard Statements' and 'Precautionary Statements' will replace the now familiar 'Risk Phrases' and 'Safety Phrases' respectively. The familiar hazard symbols will be replaced by 'Pictograms'. These will take the form of a square set at 45° and will have a white background and red border. There are 16 GHS 'Hazard Classes' each of which contains one or more 'Hazard Categories'. The GHS pictograms are quite different to the existing hazard symbols. It is clear that much of the current training will need to be updated in order to deal with the GHS system. The UK Government has stated that the European Commission's proposed Regulation on classification and labelling of chemicals has the potential to "very considerably" increase compliance costs for businesses, signalling its intention to oppose any such extension of scope when negotiations resume. It concludes that the draft GHS Regulation offers no significant additional health, safety and environmental benefits to the UK above those offered by the current system. One can only assume that similar considerations apply to Ireland.

Life under REACH

REACH comes with a hefty price tag and aims to provide many benefits. It should provide a high level of protection for human health and the environment because more detailed information on a large number of chemicals will become available as part of the registration process. For some of these there are information shortfalls that prevent an acceptable risk assessment. It will also offer greater access to everyone to chemical, health and environmental information. Hopefully, this will enable everyone to handle chemicals in a safer manner. However, this will only be achieved following a concerted educational process.

Some incentives for research have been built into REACH with the goal of enhancing innovation in the EU and these are to be warmly welcomed. REACH seeks to achieve this by raising the threshold for registration from the current 10 kg to 1 tonne. This will allow research and development on substances to be carried out below this volume without registration. In addition there are various exemptions from the general obligation to register for product and process orientated research and development, PPORD. (See Article 9 for details). Arising from the implementation of REACH, the coming years will however be challenging ones for producers, importers and users of chemical substances. There will be further challenges as NGOs continue to target

the chemical industry and the substances they use and produce. Chemophobia is alive and well and the media have convinced people that the word 'chemical' means something that is toxic, polluting and unnatural. To a certain extent distorted science and disinformation about chemicals resulted in REACH. Is the tide turning? A recent survey showed that 43% of respondents were worried about the potential closure of European manufacturing, 38% were worried about added bureaucracy, 14% were worried about extra animal testing while 5% were worried about talking to your competitors

Useful REACH sites for further information

Irish Health and Safety Authority REACH help:

<http://www.reachright.ie>

IBEC REACHAID website: <http://www.reachaid.ie>

European Chemicals Agency in Helsinki:

http://ec.europa.eu/echa/home_en.html

EU Commission REACH website:

http://ec.europa.eu/enterprise/reach/index_en.htm

European Chemical Industry Council (Cefic):

<http://www.reachcentrum.org/>

ESIS: European chemical Substances Information System:

<http://ecb.jrc.it/esis/>

	Registration	Evaluation	Authorisation	Restriction
Industry	Collects and submits data (includes supply chain data). Assesses risks and identifies risk management measures. Keeps registrations updated. Proposes testing schemes.	Provides further information if requested to do so.	Submits application dossier to ECHA. Provides substitution plans where required. Demonstrates that CMR's can be "adequately controlled". Creates R&D plans for future substitution.	Removes product from market. May appeal against restriction order.
Chemicals Agency	Receives registration dossiers and checks them for completeness. Maintains the database and provides information to the public (mostly through its web site)	Co-ordinates the work of the Member State authorities, develops evaluation criteria, takes decisions on requesting more information from industry if all Member States agree.	Publishes applications on its website. Recommends priorities; drafts opinions. Supports Commission in decision-making	Provides opinions and comments. Publishes Member State restriction proposals and its Committee's draft opinions on the Internet.
Member State Authorities (HSA in Ireland)	Enforcement	Reviews individual dossiers. Prepares rolling plans for substance evaluations and implements. Prepares draft decisions on further information requirements.	Submits proposals for authorisation of substances that are considered to pose serious and irreversible effects equivalent to CMRs, PBTs and vPvBs.	Proposes restrictions.
Commission		Takes decision on requesting more information from industry if Member States do not all agree.	Takes decisions on setting priorities and on granting authorisations.	Takes decisions on restrictions of production, marketing and use.

References

1. M. J. Hynes is owner and MD of REACH for hynes (reachforhynes@eircom.net)
2. www.reachright.ie
3. See http://ec.europa.eu/enterprise/reach/ghs_en.htm
4. Estimates of the costs and benefits vary enormously depending on the source.
5. www.thereachblog.com

SciFest: Irish Investigative Ingenuity at ITT Dublin

Dr. Brian Murray

Dept. of Science, IT Tallaght, Tallaght, Dublin 24

SciFest, a one-day secondary schools science competition for the Dublin region, was first run in April 2006 in the Institute of Technology Tallaght (ITT Dublin), and again in May this year, with support from the Institute of Chemistry of Ireland on both occasions. This article describes the background and philosophy of the competition, and exciting new developments for 2008.

The annual Young Scientist and Technology Exhibition (YSTE), sponsored by BT, is one of the most successful science competitions in Europe, with winners regularly going on to win prizes at international competitions. Entrance to the YSTE has however become very competitive and all projects are pre-screened by a panel of judges.

An issue at third level and in industry

Despite the popularity of science projects in many schools, the numbers of those going on to study Science in college have declined in recent years, despite the related industrial sectors being key drivers of economic success. Increasingly, third-level colleges and their industrial stakeholders need to identify and target niche groups of students with an established interest in the sciences.

Towards a solution at ITT Dublin

One of the teachers anxious to provide an outlet for students doing science projects is Sheila Porter of Loreto College, St. Stephen's Green. She regularly mentors large numbers of students for YSTE, and has a long string of award winners to her credit, but nevertheless was actively seeking an outlet for those whose projects were not accepted for the YSTE finals. She identified similar needs in many other schools in Dublin, and approached me to facilitate a local competition.

We wanted a smaller, less formal event, but with serious science still as the main criterion for a good project. We hoped that students could present their projects, get feedback, win prizes and be encouraged to perhaps develop their projects further with a view to submitting them for acceptance at the YSTE the following year. For our part, we

had run many open days in science for schools, and especially transition year students, and had found that one of the most common challenges to be that a significant proportion of any class are not interested to start with, and can quickly get bored.

SciFest

What was really attractive about Sheila's proposal was that our guests would all have "put their hands up" for Science, and were likely to have an above-average interest in science/technology beyond school. Thus was born "SciFest", a one-day event for second-level students of all ages, predominantly aimed at the Dublin area. We decided on scheduling the exhibition/competition in a morning (the "serious" stuff), followed by the inevitable free lunch plus afternoon fun in the form of Lectures and Laboratory Demonstrations.

A wide range of projects

In 2006 and again in 2007, we received ca. 70 entries involving approximately 200 students from 15 schools. Topics investigated were as varied as you can get, for example: *"How Altruistic are you?"*, *"Pardon? - The effects of MP3 Players on Ears"*, *"If We Put all the Air in the Classroom into the Waste Paper Bin, Could we Lift It?"*, *"Is Red Cabbage An Effective Indicator?"*, *"Crutchinator"* (a crutch that adapts to your gait), *"An Evaluation of Attitudes and Knowledge of Female Transition Year Students in Dublin to Breastfeeding"*, *"Assisting Good Environmental and Agricultural Conditions By Enhancing Nitrate Uptake using Electromagnetic Stimulated Water"*, *"The Sleeping Habits of Dublin Teenagers"*, and *"Chlorine Content of a*

Variety of Packaged and Unpackaged Lettuce". The MP3 project, one of the 2006 entries, won a prize, and was further developed and accepted for entry into the YSTE in 2007 where it took first prize in its category.

Invasion of the staff common room (is nothing sacred?)

On the day, our staff common room buzzed with 200 brains trying to catch a judge's ear, and a large crew of lecturers from science, engineering, and humanities augmented the judging panel of external academics and industrialists. The most enjoyable part of the day for the contestants was the many people who dropped in and asked questions and made suggestions, most of whom *were not* judges. Eanna Ní Lamhna, of An Taisce and *"Mooney Goes Wild"* RTE Radio 1 fame, opened the event, and the Mooney programme also interviewed participants at their stands.

This year's event had Wyeth as major sponsors, and we also received support from a number of companies, and from several professional bodies, including the ICI. Thanks to the very generous support, 30 groups or individuals won prizes, with the overall prize going to Katie Maher, of Lucan Community College (taught by Audrey Byrne), with her senior individual physics project *"Monitoring the rotation of the sun from the movement of the sunspots"*. As well as a perpetual glass trophy, a robotic kit, and a cash prize, Katie also won a bus-trip to the W5 Science Museum in Belfast for herself, her teacher, and 50 schoolmates. Good science clearly pays! The chemistry entries, though small in number, were high in quality, and the judges awarded the highest number of prizes (proportionately) in this discipline.

Junior SciFest

Primary school science is developing rapidly, with many class groups doing projects, but they have limited outlets to exhibit their work. As a small step to address this, we ran a trial *"Junior SciFest"* this year, featuring two local schools. With the emphasis very much on participation rather than competition, we asked each school to submit a group project carried out by interested pupils of the 6th classes. The two entries were highly topical: *"The Carbon Footprint in St Columcille's National School, Knocklyon"* (taught by Vivian Ruddy) and *"Energising Environment"* (Michelle Thornton, Holy Rosary, Firhouse).

SciFest to go National in 2008

The development of the SciFest concept has been followed closely by colleagues at Intel, who have now decided to back a national rollout, hosted by the Institutes of Technology, with the support of Discover Science and Engineering (DSE). Fittingly, Sheila Porter of Loreto College – who got the whole idea started – has been seconded from her school for 2007-08 to get ball rolling across the country.

And finally, a word of thanks to the other members of the organising committee, Adrienne Fleming, Bernie Creaven, Miriam O'Donoghue, and Philippa Murray, and to Dawn Carty, our liaison in Wyeth.



(Left to right) - Eanna Ní Lamhna, President of An Taisce and panellist on "Mooney Goes Wild on One", opening SciFest 2007. The overall winner, Katie Maher, of Lucan Community College, being presented with her prizes by Brian Corrigan, head of regulatory affairs at Wyeth.

Conference report: ESOR Congress

Neil Maguire

This year the 11th European Symposium on Organic Reactivity (ESOR XI) took place at the University of Algarve, Portugal. In spite of being one of the youngest state universities in Portugal, the University of Algarve can claim recognition from the international scientific community. The University boasts an academic community of just under 10,000 people distributed across fifty first cycle courses as well as approximately thirty master courses and a large number of areas within which the University of Algarve delivers Ph.D. degrees.

The scientific focus of the ESOR Symposia is organic reactivity. ESOR XI aimed to highlight recent achievements in this highly interdisciplinary field of research and to further expand its frontiers. The symposium comprised of state of the art lectures and communications under three major topics: (i) structure *versus* chemical reactivity and biochemical functions, (ii) new sustainable processes and (iii) new materials and molecular machines, emphasising the key role of physical organic chemistry as a core subject in the development of science.

Each day the conference began with two plenary lectures. One of which was given by Prof. Herbert Mayr who gave an interesting talk on nucleophilicity scales - further extending a concept first developed by Ritchie, Swain and Scott. Also in attendance from NUI Galway were Prof. William J. Spillane and Jean-Baptiste Malaubier. Prof. Spillane gave an oral presentation on the second day of the conference. Jean-Baptiste and I presented posters on the wednesday evening of the conference, which were two engaging hours with plenty of interest in our posters. Debates and discussions on the posters continued into the following day and correspondences have been continued with a number of interested parties since our arrival home. Also present were Prof. Rory More O'Ferrall and Prof. Frank Hegarty from UCD and Dr. Ann Marie O'Donoghue formally of UCD now at Durham University.

The symposium was organised by Prof. Maria de Lurdes Cristiano from the University of Algarve. The organising committee left nothing to chance and included in the program a number of social events. On the Tuesday of the conference we left the campus by bus to Silves, the Moorish capital of the Algarve to visit its castle and museum. Then, we proceeded to Porta da Piedade, famous for its rock formations. On the way back we stopped in Lagos, one of the most picturesque towns of the Algarve, where we taken to an ancient slave market, the statute of Prince Henry the Navigator and the Golden Chapel of St. Anthony. After the poster session on the Wednesday of the conference we were treated to a concert delivered by the Algarve Philharmonic Orchestra. The conference dinner was held on the Thursday night (the final night) of the conference, on the charming surroundings of Quinta de Nossa Senhora Menina.

It was commented at the conference by many seasoned attendees that this was the best structured in terms of the quality of presentations and the social program. I would like to thank the Institute of Chemistry of Ireland for their kind sponsorship of my stay in Faro, without which I would have missed the opportunity to be in the company of such experts in the field and to receive their first hand advice and ideas.

Department Profile: The School of Chemistry, National University of Ireland Galway

Dr. Niall Geraghty,
School of Chemistry, National University of Ireland, Galway

Galway's association with chemistry began with the remarkable Richard Kirwan (1733-1812) who lived in Cregg Castle which is situated near Corrandulla, about 10km from Galway city. This was a period which saw chemistry emerge as an independent discipline, and Kirwan was in correspondence with many of the great chemists of the time, including Lavoisier, Priestly and Cavendish. His international reputation was such that he was invited by Catherine the Great to lead the chemistry section of the Russian Academy of Sciences. He is principally remembered today as one of the last proponents of the phlogiston theory.

However in 1791 he recognised that the available experimental evidence made the theory untenable and abandoned it. When the Queen's College Galway opened in 1849, chemistry was one of its principal subjects, although as there was no Science Faculty its study was undertaken in the Arts Faculty. The first Professor of Chemistry (1849-1856) was Edmond Ronalds who had worked in Liebig's famous *Schule für praktische Chemie* at Giessen, and subsequently with Liebig's student, A.W. von Hofmann, who was Professor at the Royal College of Chemistry in London. Ronalds was Secretary of the London Chemical Society from 1848 to 1850 and the first editor of the Journal of the Chemical Society (1848 to 1849). One of the School's most remarkable Professors was Tom Dillon (1919-1954) who from the foundation of the National University of Ireland in 1908 worked with UCD's first Professor of Chemistry, the prolific Hugh Ryan. In the course of this work he met a young chemistry student, Geraldine Plunkett, who was the sister of Joseph Plunkett, one of signatories of the Easter Proclamation in 1916.

Dillon and Geraldine Plunkett were married on Easter Sunday of that year and began their life together in the Imperial Hotel which was situated above Clery's, directly opposite the General Post Office. They had thus a grandstand view through open second-story windows of the momentous events of the following day. Dillon was involved in the War of Independence and was interned in Gloucester Prison from May 1918 to January 1919. Remarkably, on release he went directly to Galway and secured the position of Professor of Chemistry which he took up the following October. Dillon's immediate concerns in Galway were not entirely centred on chemistry as the family felt unable to sleep in the house they had purchased in College Road due

to the activities of the Black and Tans. He was succeeded by Proinsias Ó Colla in 1954 who reinforced the School's reputation for carbohydrate chemistry that was substantially based on the seaweed research initiated by Dillon. Dick Butler took over in 1981 and successfully guided the School through the enormous challenges of the last twenty-six years while maintaining a very active research group whose main focus was heterocyclic chemistry.

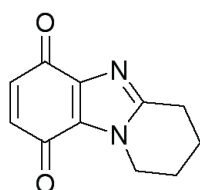
The School of Chemistry of NUI Galway has now, one hundred and fifty years after the appointment of its first professor, built up a distinguished international reputation and is a central and vibrant part of the University. The School's teaching objectives as outlined in its mission statement are *to train and educate students to the highest professional, scientific and internationally recognised standards and to produce scientifically literate graduates with a broad and deep knowledge of fundamental chemical principles, who can function independently and have the confidence to tackle any problems in chemistry.*

In terms of research it seeks *to carry out and publish scientific research of international standing at a fundamental level and in response to the economic needs of the region and the country.* Over the years in NUI Galway several thousand students have obtained B.Sc. degrees in chemistry and many hundreds have obtained Ph.D. degrees by research. The vast majority of these graduates occupy senior positions throughout the Irish economy.

In keeping with its mission statement the School provides a wide range of courses which reflect all the key areas of modern analytical, inorganic, organic and physical chemistry, with approximately 800 students across three Faculties taking chemistry in their first year. It seeks to be innovative and responsive in terms of the courses it provides and thus for example was the first third level institution to provide a substantive course in validation at undergraduate level. This area is of enormous importance in industry and the course has, as a result, attracted a lot of favourable comment. A postgraduate course in analytical chemistry and biochemistry, which produces graduates at Higher Diploma and MSc level, has also been very well received as it targets an important interface area in Irish industry. The School has on a continuing basis integrated important developments and new techniques into its undergraduate programmes and has sought to do this as early as possible: thus the use of molecular modelling and cheminformatics is introduced in the second year of the BSc programme.

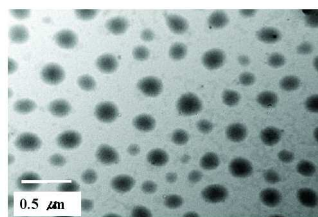
The research infrastructure within the School provides access to high-field NMR (400MHz), mass spectrometry and X-ray crystallography as well as standard spectroscopic (IR, UV, and fluorescence) and chromatographic (HPLC, GC, GPC, *etc.*) techniques. More specialised instrumentation is available within the School's individual research groups and clusters, almost all of which has been acquired as a result of successful applications to a wide range of agencies in Ireland and abroad. Overall this infrastructure supports a high level of research activity with many of the projects currently under way, in keeping with the strategic plans of the School and University, involving biomedical chemistry, energy and environment compatible processes.

Dr. Fawaz Aldabbagh and his research team are carrying out research in two broad areas, the first of which is the preparation of new, highly potent, bioreductive anti-tumour agents that selectively target hypoxic cells of solid tumours.¹ Hypoxic cells lack oxygen, are slow to divide and are associated with cancer relapse and spread. Benzimidazolequinone, which has been prepared by this group is more than 300 times more cytotoxic than the clinically used drug, mitomycin C. Work in this area is being funded by Science Foundation Ireland (SFI) and the Environmental Protection Agency (EPA)



Benzimidazolequinone

The preparation of new polymeric materials using controlled radical polymerizations is also being investigated by this group.² These processes involve a stable free radical, termed a nitroxide, which prevents the irreversible termination reactions associated with other radicals. This facilitates the control of molecular weight and allows sophisticated well-defined polymer architectures to be prepared. These nitroxide-mediated polymerizations have also been carried out in supercritical carbon dioxide giving materials with controlled particle size and microstructure. Further advantages include the positive use of a greenhouse gas, and the isolation of dry polymers after carbon dioxide venting.

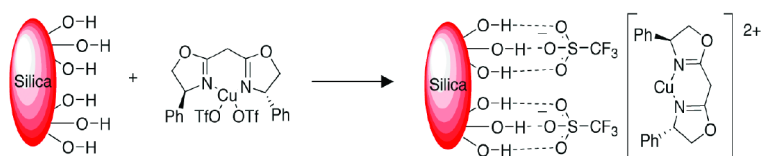


Colloidal polystyrene prepared in supercritical carbon dioxide

The School of Chemistry in NUI Galway, acquired an international reputation in the middle years of the last century due to classical synthetic and structural work in carbohydrate chemistry. This tradition has been revitalised in the work of **Prof. Angela Savage**. Currently research in biopharmaceutical chemistry in the School is focused on the needs of the biopharmaceutical industry with a major project in this area being funded by Bristol-Myers Squibb and the Industrial Development Authority. The aim of this project is to develop rapid methods for glycosylation analysis of recombinant glycoproteins, in particular for the structure determination of both O- and N-linked oligosaccharides obtained from recombinant glycoproteins of interest to the biopharmaceutical industry. This work is being carried out in collaboration with research groups in Dublin City University which together comprise the **Centre for Bioanalytical Sciences (CBAS)**. The advanced analytical methods being employed include both liquid and gas chromatography, together with mass spectrometry (ion-trap, Ciphergen, and GC-MS), lectin affinity microarrays, and NMR spectroscopy. This group is also working on the structure determination using NMR spectroscopy of prebiotic oligosaccharides of interest to the food industry, and of polysaccharides of microbial origin. In addition to Prof. Savage, the group consists of one senior scientist, three postdoctoral fellows and three PhD students.

Enantiomers are forms of a substance which are mirror images of each other and are thus related in the same way as a person's left and right hands. As the biological activity of the two forms can be quite different – for example one form of ibuprofen is completely inactive – it is vital for the

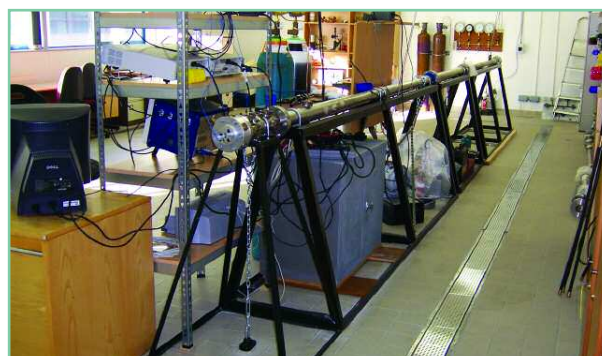
pharmaceutical industry that methods are available for the production of a single enantiomer. This is difficult to achieve and requires precise reaction control. Dr. Pat O'Leary and his group are engaged in an SFI funded project directed towards the preparation of new types of catalysts which selectively deliver the required enantiomer in a variety of key reactions. In addition they are endeavouring to make these new catalysts more environmentally friendly through the use of 'greener' reagents and the development of techniques that allow the catalysts to be recovered and reused. They have recently developed a catalyst which is immobilised on a solid (silica) and can thus be filtered from a reaction mixture and reused.³



The Combustion Chemistry Centre, C³, is directed by **Dr. Henry Curran** and is concerned with the application of combustion research to the design of energy-efficient engine and gas turbine combustion systems, and the impact of their use on toxic and greenhouse gas emissions. C³ is helping to deliver an integrated approach to the sustainable development of biofuels by joining with the University's Microbial Bioenergy and Molecular GlycoBiotechnology Groups. The Centre has a number of active research projects. Three of these are funded under the Irish National Development Plan by research awards from SFI, the EPA, and the Irish Research Council for Science, Engineering, and Technology (IRCSET). Two other projects are large-scale EU FP6 Marie Curie grants (BurnQuest and CleanBurn programmes), and there is also a collaborative project which involves US universities and is funded by the US Air Force Office of Strategic Research. The Centre has one industry-linked project which involves Rolls-Royce Canada. The high profile of the Centre is in part due to the experimental facilities which it has assembled. These include a twin-opposed piston rapid compression machine, a low-pressure shock tube with a high level of instrumentation and a high-pressure shock tube. These facilities which are unrivalled anywhere in the world, together with access to supercomputer facilities, allow the Group to study in detail the events that occur when a fuel burns in an internal combustion engine, a gas turbine, or an incinerator.

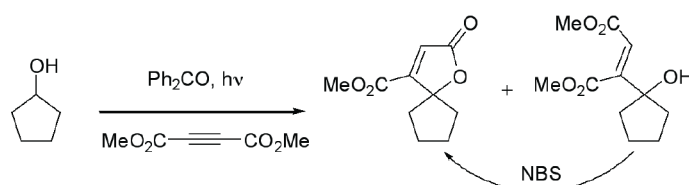


Rapid compression machine

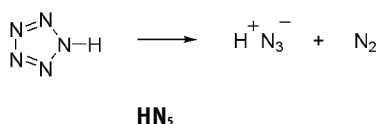


High-pressure shock tube

The photochemical generation of radicals for synthetic purposes - effectively using a photon of light as a chemical reagent - avoids many of the safety and sustainability issues associated with the generation of these important reaction intermediates. The research group of **Dr. Niall Geraghty** is using this approach in the context of an important synthetic problem - the generation of carbon-carbon bonds in unactivated systems such as cycloalkanes, cyclic ethers and secondary alcohols. The approach involves the absorption of light by a photomediator molecule that then abstracts a hydrogen atom from the substrate generating a nucleophilic carbon radical. This in turn reacts with an electron-deficient alkyne, forming a new C-C bond. The group has shown that the reaction can proceed via a chain reaction⁴ and that in addition a recyclable photomediator and solar radiation can be used,⁵ thus adding to the attraction of the method from the sustainable, green chemistry perspective. On two occasions funding has been secured under the EU IHP Programme to allow members of the group to carry out work at the Plataforma Solar de Almeria in Spain.



The research group led by **Professor R.N. Butler** has an established international reputation in the area of heterocyclic chemistry. It has also recently been studying the use of water as a medium for organic synthesis, as well as the “on-water” phenomenon where water-insoluble reactants can give high yields of products under mild conditions.⁶ The importance of the balance between hydrogen bonding and hydrophobic effects on reaction transition states has been highlighted in this work.^{6a,b} Butler's group is also working on new high-energy high nitrogen compounds and recently produced the long-sought unstable molecule HN_5 in solution for the first time.⁷ This remarkable molecule, although short-lived at -40°C , is the nitrogen analogue of nitric acid, HNO_3 , and its anion, N_5^- , is a new form of the element nitrogen which was hitherto known only as gaseous N_2 , cationic N_5^+ and anionic N_3^- .

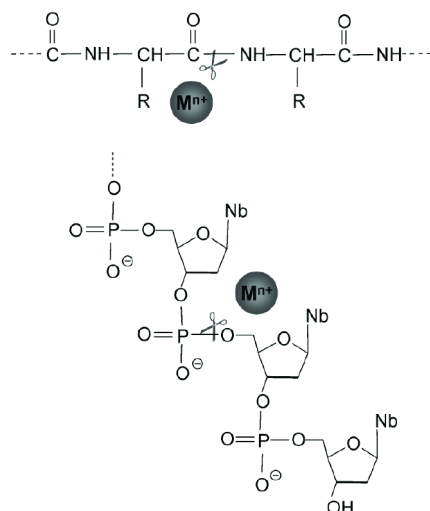


This work has added to the semantic debate as to whether charged forms of elements should be described as allotropes.

Dr. Alan G. Ryder leads the **Nanoscale Biophotonics Laboratory (NBL)** which was established in 2003 with an SFI Investigator award. The group focuses on developing novel measurement methodologies for applications in the physical and life sciences. The research being undertaken is interdisciplinary in nature and involves integrating aspects of biology, chemistry, materials science, and physics. The Group's core fluorescence research involves the use of both fluorescence and Raman spectroscopies. Some specific projects include the development of a non-contact method for measuring the polarity in-situ of biomedical polymers,⁸ the preparation of novel nanostructured substrates for metal enhanced fluorescence (MEF) based ultra-sensitive sensors and assays, the development of analytical methods on the micron-scale using fluorescence correlation spectroscopy (FCS) and fluorescence lifetime imaging microscopy (FLIM),⁹ a study of the interaction of proteins with surfaces using fluorescence methods,¹⁰ and an analysis of crude petroleum oil, again using fluorescence.¹¹ In the area of Process Analytical Technologies (PAT) they are developing quantitative analytical methods for forensic applications and the biopharmaceutical industry using optical spectroscopy and chemometrics.¹² The latter project is part of the CBAS project which also involves Bristol-Myers Squibb and DCU.

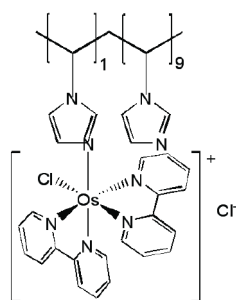
Cyclamate (sulfamate) sweeteners, RNHSO_3Na , have been the focus of the research group led by **Prof. Liam Spillane** for over two decades. The main thrust of its work has been on structure-activity (taste) relationships (SARs) probed by altering the R and sulfamate portions of the molecule.^{13,14} Development of SARs deepens the understanding of how sweeteners work and can lead to the design of better tastants. Cyclamates are used throughout the EU and in about 120 other countries worldwide as tabletop, beverage and food sweeteners. Although cyclamates, in common with other non-nutritive sweeteners, cannot replicate the texture, mouthfeel and bulk effects of sucrose, they are very good in admixtures with other sweeteners both nutritive and non-nutritive, and good synergistic effects are frequently found. Despite the development of numerous new sweeteners over the last 25 years cyclamates hold a high market share and are among the top five sweeteners sold. The group is also interested in sulfamate esters RNHSO_3R for another unrelated reason: certain sulfamates have been shown over the last eighteen years to have strong therapeutic potential in areas as diverse as the prevention of breast cancer and glaucoma. Although as a result many new sulfamate esters have been made and tested, virtually nothing is known regarding their mechanism(s) of action in the body. Mechanistic studies¹⁵ using simple models, and more recently the actual active esters, are being pursued in support of efforts to design and produce more efficacious sulfamate esters for medicinal use.

Dr. Andrea Erxleben is the most recent addition to the academic staff of the School and was recently awarded a prestigious Stokes Lectureship by SFI. She works in the field of bioinorganic and coordination chemistry, focusing on the interactions of metal ions with peptides and nucleic acids. She is particularly concerned with the reactions of the antitumour active organometallic compound molybdocene dichloride (Cp_2MoCl_2) with peptides and nucleic acid constituents. Currently active projects in this area are aimed at gaining insight into the reaction behaviour of the bioactive Cp_2MoCl_2 in biological systems and at using it as a cleaving agent for peptide bonds.^{16,17} She has recently shown that coordination of Cp_2MoCl_2 to the thiolate group of short cysteine-containing oligopeptides leads to hydrolytic cleavage of the neighbouring peptide bond. She is also interested in metal-mediated phosphate diester hydrolysis and the synthesis of structural and functional mimics of hydrolytically active, dimetallic enzymes. Thus homo- and heterodinuclear metal complexes are being developed that are models for the active sites of peptidases, phosphatases and nucleases.¹⁸ The synthesis of coordination polymers and the importance of hydrogen bonding in 2D and 3D networks¹⁹ are also areas of interest.



Metal-mediated cleavage of peptides and nucleic acids

Dr. Dónal Leech and his group focus their research on the preparation and characterisation of electron-transfer catalysts and modified electrode surfaces which will eventually find application in biomolecular electrochemical technologies and devices. The group was the first to demonstrate the bioelectrocatalytic reduction of oxygen by a laccase enzyme which is catalysed by inorganic redox complexes, and have utilised these systems in such diverse areas as the bleaching of paper pulp, the sensing of enzyme inhibitors, the production of electricity in biocatalytic fuel cells and as labels for the amplification of DNA hybridisation events yielding highly sensitive assays for DNA sequences. Present research in this area is focused on building libraries of biomolecules, structured electrode surfaces, chemical immobilisation methodologies, and electron transfer catalysts, as part of a rational approach to integrating these materials to provide improved sensors and fuel cells.



Structure of one of the redox polymers used as a catalyst in the laccase reduction of oxygen

The **Crystallography Group** in NUI Galway was set up by **Prof. Patrick McArdle**, the late Prof. Des Cunningham, and **Dr. Tim Higgins**. The first single crystal 4-circle diffractometer in Ireland was installed in Galway in 1981 and this was followed by a second 4-circle diffractometer and the first area detector system in the country. The Group solved

its first protein crystal structure in 1991 and overall hundreds of crystal structures have been solved for researchers in Galway and in most other Irish research centres. Polymorph analysis using powder diffraction is carried out on a regular basis for many of the pharmaceutical companies which have facilities in Ireland. The Crystallography Group is constantly striving to maintain its position at the forefront of European crystallography and currently new single crystal and fast transmission powder diffraction equipment is being purchased. The Group is a partner in the recently announced SFI funded **Solid State Pharmaceuticals Cluster** involving five universities and nine pharmaceutical companies. The Galway group will develop projects involving amorphous content analysis, polymorph analysis and crystal morphology prediction. The Group makes free modelling and crystallography software available at <http://www.nuigalway.ie/cryst/>.

References

1. F. Aldabbagh, M. P. Carty, S. Hehir, P. Kavanagh, D. Leech, M. Lynch and J. O'Shaughnessy, *Chem. Eur. J.* **2007**, *13*, 3218.
2. F. Aldabbagh, R. McHale, M. Okubo and P. B. Zetterlund, *Macromol. Chem. Phys.* **2007**, *208*, 1813.
3. C. McDonagh, P. O'Conghaile, R. J. M. Klein Gebbink and P. O'Leary, *Tetrahedron Lett.* **2007**, *48*, 4387.
4. N. W. A. Geraghty and A. Lally, *Chem. Commun.* **2006**, 4300.
5. N. W. A. Geraghty and R. A. Doohan, *Green Chemistry* **2005**, *7*, 91.
6. (a) R. N. Butler, W. J. Cunningham, A. G. Coyne and L. A. Burke, *J. Am. Chem. Soc.* **2004**, *126*, 11925; (b) R. N. Butler, A. G. Coyne, W. J. Cunningham, E. M. Moloney and L. A. Burke, *Helv. Chim. Acta* **2005**, *88*, 1611; (c) R. N. Butler, A. G. Coyne and E. M. Moloney, *Tetrahedron Lett.* **2007**, *48*, 3501.
7. (a) R. N. Butler, J. C. Stephens and L. A. Burke, *Chem. Commun.* **2003**, 1016; (b) R. N. Butler, J. M. Hanniffy, J. C. Stephens and L. A. Burke, unpublished work; (c) R. N. Butler, J. C. Stephens and J. M. Hanniffy, *Tetrahedron Lett.* **2004**, *45*, 1977.
8. A. G. Ryder, B. Szczupak, Y. A. Rotchev, A. S. Klymchenko, A. Gorelov, T. J. Glynn, *Proc. SPIE – Int. Soc. Opt. Eng.* **2005**, *5826*, 1.
9. C. Braet, H. Stephan, I. Dobbie, D. Togashi, A. G. Ryder, Z. Földes-Papp, N. Lowndes, and H. P. Nasheuer, *Exp. Mol. Pathol.* **2007**, *82*, 56.
10. D. M. Togashi and A. G. Ryder, *Exp. Mol. Pathol.* **2007**, *82*, 135.
11. A. G. Ryder, *Applied Spectroscopy* **2004**, *58*, 613.
12. A. G. Ryder, *J. Forensic Sci.* **2002**, *47*, 275.
13. W. J. Spillane, D. P. Kelly, P. J. Curran and B. G. Feeney, *J. Agric. & Food Chem.* **2006**, *54*, 5996.
14. W. J. Spillane and Jean-Baptiste Malaubier, *Tetrahedron Lett.* **2007**, *48*, 7574.
15. C. J. A. McCaw and W. J. Spillane, *J. Phys. Org. Chem.* **2006**, *19*, 512.
16. A. Erxleben, *Inorg. Chem.* **2005**, *44*, 1082.
17. A. Erxleben, L. Yovkova, *Inorg. Chim. Acta* **2006**, *359*, 2350.
18. A. Erxleben, J. Hermann, *J. Chem. Soc. Dalton Trans.* **2000**, 569.
19. A. Erxleben, *Inorg. Chem.* **2001**, *40*, 2928.

Feature Article

Control and Exploitation of Phosphine Oxidation: The Taming of a Chemical Enfant Terrible

Prof. Declan Gilheany

School of Chemistry and Chemical Biology,
University College Dublin, Belfield, Dublin 4, and

Celtic Catalysts, Nova UCD, Belfield, Dublin 4

Prof. Declan Gilheany and his team at UCD have made two landmark discoveries in the field of phosphine chemistry.

Their research is a fine example of how one can exploit the fruits of basic science research to the benefit of the Irish economy in a relatively short time frame.



Abstract. Recent work at UCD has shown that phosphine oxidation can be slowed down sufficiently to render it controllable. Primary phosphines have been designed that are air-stable and tertiary phosphines can be oxidised in such a way that the oxygen atom can be delivered to a chosen side of the molecule at will. The latter process has been exploited to synthesise commercially viable tuned catalysts for asymmetric hydrogenation reactions.

Primary phosphines (RPH_2) have a notorious reputation for being easily oxidised, sometimes catching fire in air. Add this to their bad smell and suspected toxicity and it is no wonder that many chemists shy away from their routine use. This is a pity because they have an impressive range of potential applications in diverse areas such as asymmetric ligand precursors,¹ biomedicinals,² polymers,³ carbohydrates⁴ and macrocycles.⁵ In contrast, **tertiary** phosphines (R_3P) are routinely used in preparative chemistry: for example, in the Wittig and Mitsunobu reactions. Ironically the synthetic utility of phosphines in these processes derives from the same property which causes the spontaneous combustion of the primary phosphines – the high strength of the $\text{P}=\text{O}$ double bond.⁶

For a number of years, our laboratory in UCD has worked to find ways to control the formation of the $\text{P}=\text{O}$ bond. In the primary phosphines, this took the form, simply, of slowing the reaction down so that the compounds became air stable. For the tertiary analogues, a more ambitious goal was to control the stereochemistry of the oxidation process. In the former case, the result was pure serendipity while in the latter it was the result of sustained and determined effort. Both projects had their origin in our interest in asymmetric catalysis – the ideal way to make chiral drugs, which account for more than two thirds of present drug candidates. We wanted to make transition metal catalysts based on **P**-stereogenic phosphines. The idea is that this places the stereochemical information on phosphorus and therefore as close as possible to the metal centre – to quote W. S. Knowles in his 2001 Nobel Lecture: "that is where the action is". However, to date, **P**-stereogenic phosphines have been inaccessible because they were extremely difficult to synthesise.

Non flammable primary phosphines⁷

We wanted to make a *P*-stereogenic version of the well-known MOP ligand. **Dr. Lee Higham** had joined the group as an EU Marie Curie Fellow and, based on his own experience, he suggested an approach via the primary phosphine MOPH_2 (**1**). Normally this would not have been a favoured route because of the pyrophoric reputation of these materials, but we were confident we could contain the problem because we had suitable laboratory set-up (Schlenk lines, glove box, *etc.*). Lee carried out the bench work in collaboration with **Rachel Hiney**, then a PhD student supported under an Embark scholarship from IRCSET. One day, when Rachel took some of the compound out of the Schlenk flask, it did not catch fire and indeed, it emerged that we did not need any precautions - MOPH_2 was air stable - even in solution! Subsequent work showed that it just takes one extra fused benzene ring to bring about air stability, the simplest stable case being 2-naphthylphosphine (**2**). The photo shows a side-by-side comparison of the latter with phenylphosphine. It is clear which compound is stable.

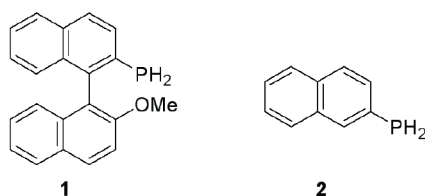
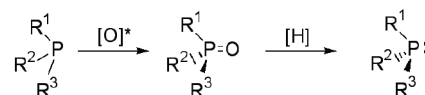


Figure 1. Non-flammable primary phosphines

Why should such a simple change have such a profound effect? It is obviously not a steric effect and a number of lines of evidence lead us to think that it is also not due to conjugation of the phosphine lone pair with the aromatic system; for example, the 1- and 2-naphthyl cases have similar stabilities. We believe it is more likely to be inhibition of a step in the oxidation mechanism after the initial addition of oxygen. Whatever the reason, the useful fact remains: conjugated primary phosphines are as stable as moderately reactive aldehydes. Phenylphosphine can be replaced in applications by 2-naphthylphosphine resulting in a substantial chemical safety improvement. It is ironic that the stability of these compounds was probably not discovered earlier because no one was prepared to take them out of an inert atmosphere!

P-Stereogenic Tertiary Phosphines⁸

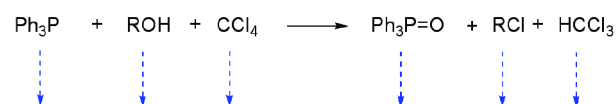
We have been working on this previously intractable problem for ten years. Our general approach is shown below.



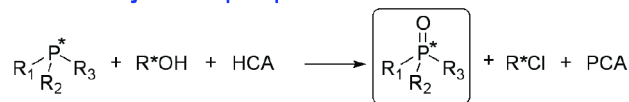
Scheme 1. General approach to *P*-stereogenic tertiary phosphines

It is based on the idea of kinetic resolution in the chiral oxidation of phosphines to selectively produce one enantiomer of the oxide. Once achieved, the oxide would be converted back to phosphine by reduction with silanes. The problem with this nice Scheme is, of course, that oxidation of phosphines is very fast, so selectivity is hard to achieve. So we began with a search of very weak oxidants. One early promising lead, found by **Valerie Wall**, was to use half an equivalent of a chiral epoxide. However, we could not get satisfactory selectivity and, in addition, there was still the problem of the 50% maximum yield of this type of classical kinetic resolution. We then did a systematic search for ANY reaction where phosphine oxide was one of the products and where one of the reagents could be rendered chiral. We looked at Wittig, Horner-Wadsworth-Emmons, Arbusov, Perkow, Mitsunobu and many other obscure organophosphorus reactions. **Shane Robinson** did much of this leg-work and he was rewarded when he hit upon the redox dehydration known as the Appel conditions,⁹ Scheme 2.

Appel reaction



Modified asymmetric phosphine oxidation



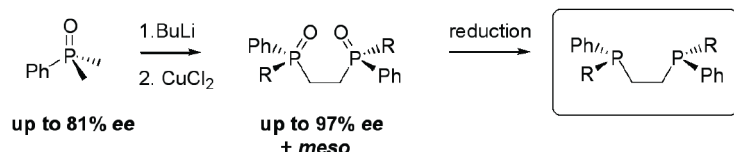
HCA = hexachloroacetone, PCA = pentachloroacetone

Scheme 2. Approach to *P*-stereogenic tertiary phosphines based on a modified Appel reaction

Ordinarily the Appel conditions are used to convert alcohols to alkyl chlorides. The process is useful because the conditions are mild and reaction occurs with complete inversion of configuration of the alcohol. The only (fairly minor) problem is separation of the alkyl chloride from the unwanted triphenyl phosphine oxide. From our perspective however the phosphine oxide is the desired product. Shane found that when he ran the reaction using racemic tertiary phosphine (*e.g.* phenylanisylmethylphosphine, PAMP)

in combination with (-)-menthol (Scheme 2) the product (PAMPO) was enriched in one enantiomer. Also significant was that the process could be run to 95% yield with no loss of the enrichment, which means that it is a *dynamic* resolution. Subsequent work by **Colm O'Mahony**, **Cormac O'Connor** and **Enda Bergin** raised the selectivity to over 80% *ee* and showed that it was applicable to a wide range of tertiary phosphines. They also replaced carbon tetrachloride with (the less poisonous) hexachloroacetone (Scheme 2).

We have recently been awarded a grant by SFI to purchase an IR reaction monitoring system to study the mechanism of this intriguing process with a view to raising the selectivity to \rightarrow 90% *ee*. However, even at 80% *ee*, it is commercially viable. This is because, in a subtle chemical trick suggested by **Eoghan McGarrigle** in the laboratory, the oxide products can be dimerised and reduced (Scheme 3) to give analogues of the famous DiPAMP ligand (for which Knowles received the Nobel Prize). The dimerisation gives both the *dl*- and *meso*-isomers and, statistically, a proportion of the minor enantiomer is tied up in the *meso*. Therefore the *dl*-isomer becomes further enriched in the major, so that an 80% *ee* in the monoxide becomes \rightarrow 96% *ee* in the dioxide. This meant that we could guarantee to be able to make, in bulk, almost any variant of DiPAMP, including many not previously available.



Scheme 3. Phosphine dimerisation leads to enhanced optical purity

Enterprise Ireland had supported Shane's early exploratory work through a Basic Research grant, and now that the commercial potential was clear, an EI Strategic Research grant supported **Dr. Brian Kelly** to take the process forward. Brian had already determined that he wanted to start a catalyst exploration company and this provided the ideal environment for commercialisation of the technology. With further help from EI and venture capital funding, we spun out "Celtic Catalysts" from UCD (www.celticcatalysts.com). Subsequently the **Celtic Catalysts** research team explored the usefulness of the set of DiPAMP analogues for asymmetric hydrogenation to make amino-acids. Results from benchmark tests show that these catalysts are among the best available. In particular, the case wherein the *o*-anisyl group of DiPAMP is replaced by an *o*-tolyl moiety provides \rightarrow 99% *ee* at catalyst loadings as low as 0.0001%. In summary we have found a way to control phosphine oxidation stereochemically. This was a very significant scientific achievement. At the same time, it also

represented a substantial commercial opportunity and it is a great example of the interplay between basic science and industry/job creation/benefit to the Irish economy. On a final biographical note: I am very pleased that I was a member of the 1998 Forfas *Technology Foresight* Exercise (Chemical and Pharmaceutical Panel). Our remit was to predict Ireland's technology needs in 2016 and it was the forerunner of SFI. I believe that our success in commercialising our basic science breakthrough provides a good example of what was envisaged by *Foresight* 10 years ago.

References

1. A. Grabulosa, J. Granell, G. Muller, *Coord. Chem. Rev.* **2007**, *251*, 25.
2. K. V. Katti, H. Gali, C. J. Smith, D. E. Berning, *Acc. Chem. Res.* **1999**, *32*, 9.
3. H. Dorn, R. A. Singh, J. A. Massey, A. J. Lough, I. Manners, *Angew. Chem. Int. Ed.* **1999**, *38*, 3321.
4. T. Hanaya, H. Yamamoto, *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2320.
5. E. P. Kyba, S-T. Liu, *Inorg. Chem.* **1985**, *24*, 1613.
6. D. G. Gilheany, *Chemical Reviews*, **1994**, *94*, 1339.
7. L. Higham, R. Hiney, H. Muller-Bunz, D. G. Gilheany, *Angew. Chem. Int. Ed.* **2006**, *45*, 7248.
8. E. Bergin, C. T. O' Connor, S. B. Robinson, E. M. McGarrigle, C. P. O'Mahony and D. G. Gilheany, *J. Am. Chem. Soc.* **2007**, *129*, 9566.
9. R. Appel, M. Halstenberg in *Organophosphorus Reagents in Organic Synthesis*, J.I.G. Cadogan (Ed.), Academic Press, London, **1979**, Ch. 9.

Literature Focus

David O. Scanlon, Gemma-Louise Davies, Giuseppe La Spina, Padraic Nagle, Paraic Keane, Manuel Natali, Aldo Peschiulli and Isabel M. Unwin.

School of Chemistry, The University of Dublin, Trinity College, Dublin 2, Ireland.

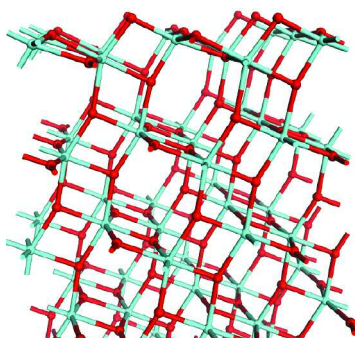
Literature focus is a feature consisting of short abstracts highlighting recent developments of interest in the literature selected by postgraduate researchers.

Edited by Isabel M. Unwin

Photocatalysed de-NO_x

Photocatalytic Reduction of NO by CO on Titanium Dioxide under Visible Light Irradiation

A. A. Lisachenko, R. V. Mikhailov, L. L. Basov, B. N. Shelimov and M. Che, *J. Phys. Chem. C* 2007, 111, 14440

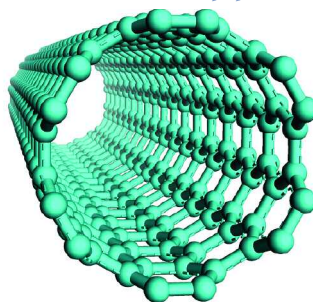


Lisachenko and co-workers have reported for the first time how the photoassisted reduction of NO by CO into N₂ and N₂O can occur upon TiO₂ catalysts upon visible light irradiation ($\lambda > 380$ nm) at room temperature. The selectivity of photoreduction of NO into N₂ reaches 90-95%.

Nanotube Absorption

Triplet State Absorption in Carbon Nanotubes: A TD-DFT Study

S. Tretiak, *Nano Lett.* 2007, 7, 2201

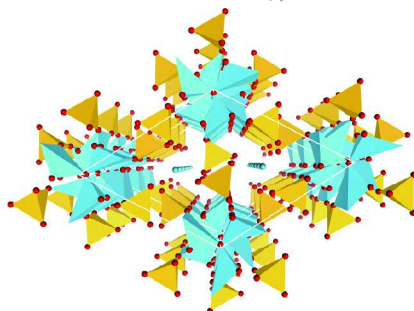


Time-dependent density functional theory (TD-DFT) is used to predict properties of triplet excited states in single walled carbon nanotubes (CNTs). The results demonstrate striking similarities of the electronic features between CNTs and π -conjugated polymers.

Novel SOFC Materials

Developing apatites for solid oxide fuel cells: insight into structural, transport and doping properties

E. Kendrick, M. S. Islam and P. R. Slater, *J. Mater. Chem.* 2007, 17, 3104

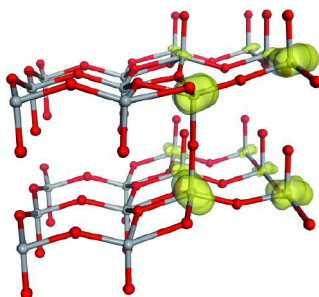


Kendrick *et al.* have modelled new oxide-ion conductors based on interstitial oxide ions, as an alternative to the more conventional perovskite- and fluorite- based oxide ion conductors, in which conduction proceeds *via* oxygen vacancies.

Oxide Vacancies

Oxygen vacancies in transition metal and rare earth oxides: Current state of understanding and remaining challenges

M. V. Ganduglia-Pirovano, A. Hofmann and J. Sauer, *Surf. Sci. Rep.* 2007, 62, 219

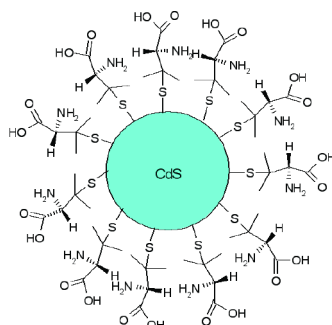


Ganduglia-Pirovano and co-workers have reviewed the chemistry of one of the most important defects associated with catalysis on oxide surfaces: the neutral oxygen vacancy. Comparison of experimental and theoretical results show the ability of state-of-the-art quantum mechanical methods to provide important insights into these vital systems.

Mirror Image Luminescent Nanoparticles

Chiral highly luminescent CdS quantum dots

M. P. Moloney, Y. Gun'ko and J. M. Kelly, *Chem. Commun.* 2007, 38, 3900

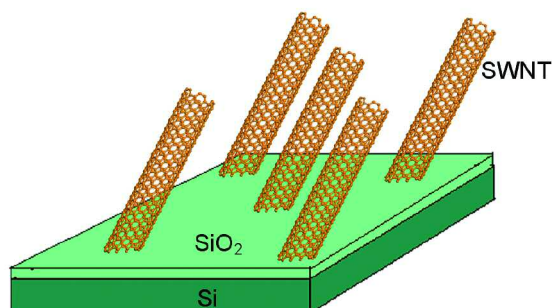


Strongly white-emitting ($\lambda_{\text{max}} = 496 \pm 10\text{nm}$) D- and L- penicillamine-capped CdS nanoparticles, which show strong circular dichroism in the range 200-390nm, have been prepared for potential use as fluorescent chemical and biochemical chirality sensors, molecular recognition nanodevices or biomedical uses.

Nanotube Arrays

Oriented assembly of single-walled carbon nanotubes and applications

L. Huang, Z. Jian and S. O'Brien, *J. Mater. Chem.* 2007, 17, 3863

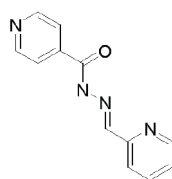


O'Brien *et al.* have reported the assembly of single-walled carbon nanotubes in a horizontal and vertical aligned orientation via solution deposition and direct chemical vapour deposition as well as other growth mechanisms for use in nanotube-based device fabrication and applications.

Fe^{II} Chelators

Hydrazone chelators for the treatment of iron overload disorders: iron coordination chemistry and biological activity

P. V. Bernhardt, P. Chin, P. C. Sharpe and D. R. Richardson, *J. Chem. Soc., Dalton Trans.* 2007, 30, 3232

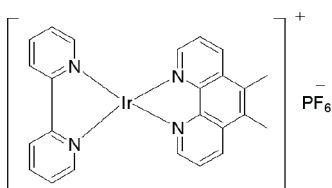


Richardson *et al.* report the first schematic study of the Fe^{II} coordination chemistry of chelates of the potentially tridentate ligand 2-pyridinecarbaldehyde isonicotinoyl hydrazone (HPCIH) and its analogues, which have shown to be orally-active drugs for the effective treatment of Fe overload disease.

Lanthanides and Photochemistry

The role of substituents on functionalized 1,10-phenanthroline in controlling the emission properties of cationic iridium(III) complexes of interest for electroluminescent devices

C. Dragonetti, L. Flaciola, P. Mussini, S. Righetto, D. Roberto, R. Ugo and A. Valore, *Inorg. Chem.* 2007, 46, 8533

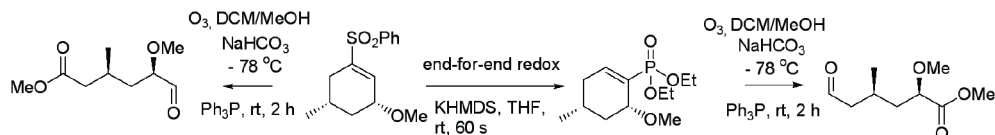


Dragonetti *et al.* report on how photochemical properties (including tuning of the colour of emission, quantum yield, emission lifetimes and especially the role of the nonradiative pathway of decay) are dependent on the nature and number of substituents of phenanthroline on a class of cationic Ir(III) complexes which are promising for use as electroluminescent devices.

Enantiopure Polypropionates

Conversion of Cyclic Vinyl Sulfones to Transposed Vinyl Phosphonates

M. N. Noshi, A. El-awa, E. Torres, and P. L. Fuchs, *J. Am. Chem. Soc.* 2007, 129, 11242

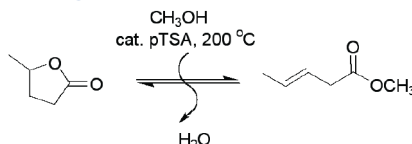


The Fuchs group report on a new, high yielding one-pot vinyl sulfone to vinyl phosphonate transposition at ambient temperature. **17 examples: Yield 60-95%.**

'Bio-based' Nylon

Towards 'bio-based' Nylon: Conversion of Δ -valerolactone to methyl pentenoate under catalytic distillation conditions

J. P. Lange, J. Z. Vestering and R. J. Haan, *Chem. Commun.* 2007, 3488

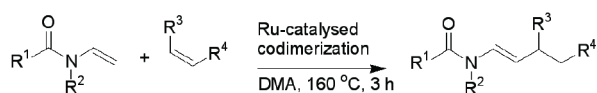


An efficient route for producing nylon polymers from renewable feedstock has been achieved by the conversion of Δ -valerolactone and methanol to methyl pentenoate under mild conditions using strong acid catalysts under catalytic distillation. **Yield 98%.**

C-C Coupling Reactions

Heterodimerization of Olefins: A Highly Promising Strategy for the Selective Synthesis of Functionalised Alkenes

L.J. Gooßen and N. Rodríguez, *Angew. Chem. Int. Ed.* 2007, 46, 7544



The selective codimerisation of enamides with other alkenes to give alkylated enamides has been achieved with ruthenium catalysts. This could open up atom-economic access to functionalised alkenes.

Chromic Behaviour

Thermo-to-Photo-Switching of the Chromic Behaviour of Salicylideneanilines by Inclusion in a Porous Coordination Network

T. Haneda, M. Kawano, T. Kojima and M. Fujita, *Angew. Chem. Int. Ed.* 2007, 46, 6643

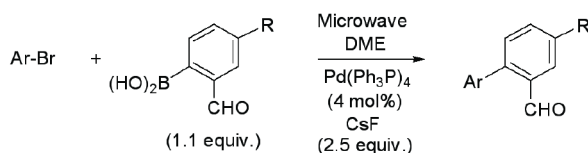


Haneda and co-workers have reported an approach to control the physical properties of salicylideneanilines by inclusion in a coordination network of nitrobenzene clathrate complex and to study, by single-crystal X-ray analysis, the relationship between the dihedral angle and the chromic behaviour of these labile compounds without any chemical modification.

Suzuki Coupling

Microwave-Assisted Suzuki Cross Coupling Reaction, a Key Step in the Synthesis of Polycyclic Aromatic Hydrocarbons and their Metabolites

A. K. Sharma, K. Gowdahalli, J. Krzeminski and S. Amin, *J. Org. Chem.* 2007, 72, 8987

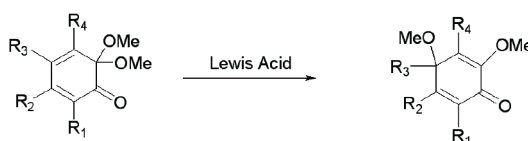


Sharma and co-workers report on a highly efficient method of the Suzuki coupling for precursors of polycyclic aromatic hydrocarbons through microwave irradiation. **12 examples: Yield 76%-93%**

p-Quinol Ethers

1,3-Methoxy Rearrangement of Masked O-Benzoquinones: A Novel Synthesis of p-Quinol Ethers

C. Yang and C. Liao, *Org. Lett.* 2007, 9, 4809

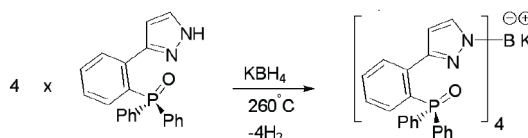


Yang *et al.* reported the conditions for this reaction and also on a one-pot preparation of p-quinol ethers.

Novel Ligand

A novel tetrakis(pyrazolyl)borate ligand bearing triphenylphosphine oxide substituents

S. Kealey, N. J. Long, A. J. P. White and A. D. Gee, *J. Chem. Soc., Dalton Trans.* 2007, 42, 4763

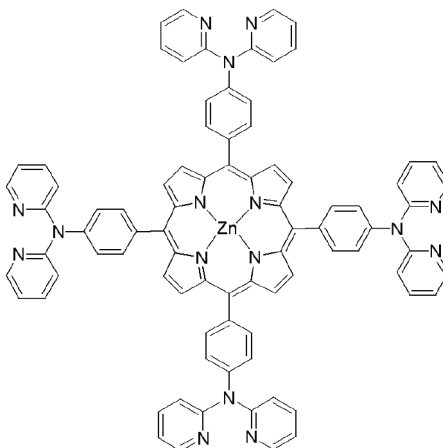


A new poly(pyrazolyl)borate ligand containing a phosphine oxide has been reported. It forms a mixed N, O donor ligand and an unexpected $\eta^3\text{-N}_2\text{O}$ species was isolated in coordination to thallium while complete η^6 chelation could be achieved by coordination to europium. **Yield: 56%**

Fluorescent Sensor

A Copper(II) Ion-Selective On-Off-Type Fluoroionophore Based on Zinc Porphyrin-Dipyridylamino

Y.-Q. Weng, F. Yue, Y.-R. Zhong and B.-H. Ye, *Inorg. Chem.* 2007, 46, 7749

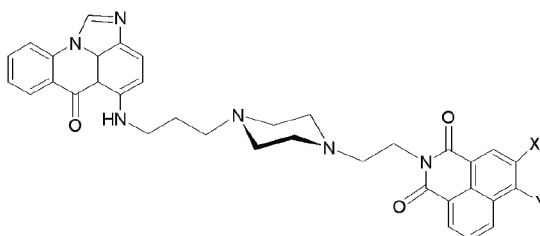


Weng and co-workers have synthesized a new fluorescent sensor which shows a high sensitivity for Cu^{2+} ions and exhibits fluorescence quenching upon the binding of the Cu^{2+} ion with an “on-off”-type fluoroinophoric switching property.

Bifunctional Antitumour Agents

Optimization of Naphthalimide-imidazoacridine with Potent Antitumour Activity Leading Clinical Candidate

H .K. Hariprakasha, T. Kosakowska-Cholody, C. Meyer, W. M. Cholody, S. F. Stinson, N. I. Tarasova and C. J. Michejda,

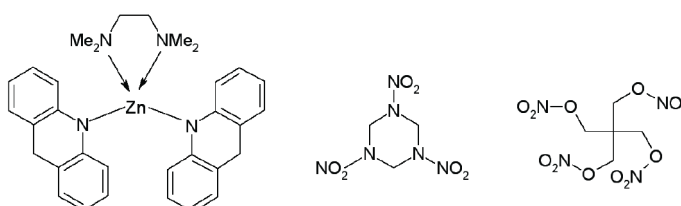


Hariprakasha and co-workers have reported on a series of unsymmetrical bifunctional antitumour agents, which inhibit the growth of many tumour cell lines and cause rapid apoptosis.

Fluorescence Sensor

A Fluorescence Turn-On Mechanism to Detect High Explosives RDX and PETN

T. L. Andrew and T. M. Swager, *J. Am. Chem. Soc.* 2007, 129, 7254

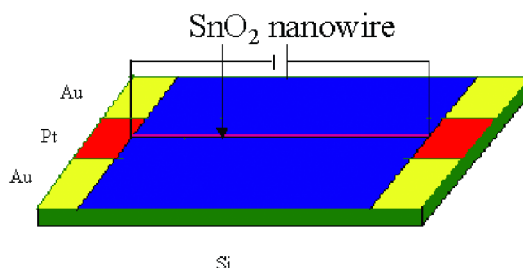


A zinc-acridine complex (1) shows enhanced fluorescence at 480 nm in the presence of two common explosives. In the presence of RDX the fluorescence enhancement is 80-fold, and is attributed to photoreduction of acridine.

Humidity-sensing Nanowire

High-Sensitivity Humidity Sensor Based on a Single SnO₂ Nanowire

Q. Kuang, C. Lao, Z. L. Wang, Z. Xie and L. Zheng, *J. Am. Chem. Soc.* 2007, 129, 6070

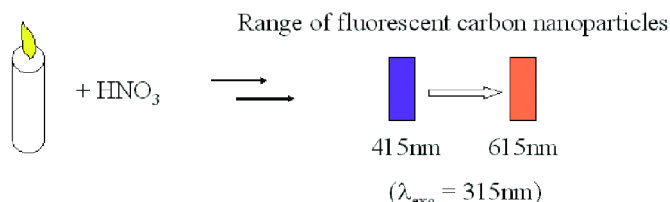


A single SnO₂ nanowire is an effective sensor for relative humidity over a large range (5%-85%). The sensing mechanism is based on the higher conductivity of the wire in the presence of water vapour.

Fluorescent Carbon Nanoparticles

Fluorescent Carbon Nanoparticles Derived from Candle Soot

H. Liu, T. Ye and C. Mao, *Angew. Chem. Int. Ed.* 2007, 46, 6473

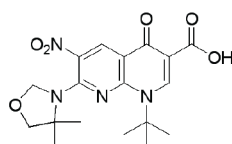


Carbon nanoparticles with a range of fluorescence colours (violet-orange) were prepared from candle soot. The fluorescence colour may depend on either the charge or the size of the particle, although the exact chemical identity of the particles is unknown.

Antimycobacterial Activities

Antimycobacterial Activities of Novel 1-(Cyclopropyl/tert-butyl/4-fluorophenyl)-1,4-dihydro-6-nitro-4-oxo-7-(substituted secondary amino)-1,8-naphthyridine-3-carboxylic Acid.

D. Sriram, P. Senthilkumar, M. Dinakaran, P. Yogeeswari, A. China, and V. Nagaraja, *J. Med. Chem.*, 2007, ASAP article.

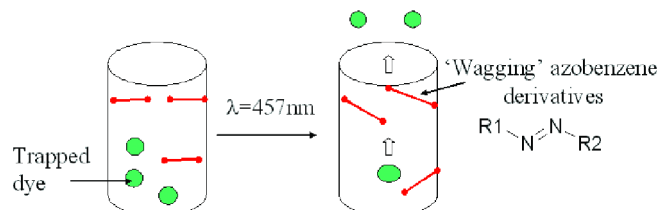


The authors have reported the synthesis of a new compound which displays in vitro and in vivo antimycobacterial activities higher than those of *Isoniazid*.

Mesoporous Materials

Photo-Driven Expulsion of Molecules from Mesostructured Silica Nanoparticles

S. Angelos, E. Choi, F. Vogtle, L. de Cola and J. L. Zink, *J. Phys. Chem. C* 2007, 111, 6589

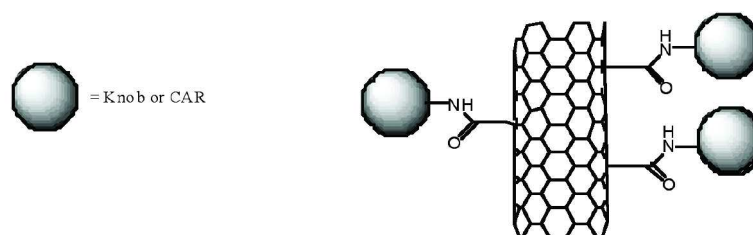


The photoinduced cis-trans isomerisation of azobenzene derivatives is used for the controlled release of dye from mesoporous silica nanoparticles. The 'wagging' of the azobenzene molecule under 457 nm irradiation allows the dye to diffuse out of the silica, where it can then be detected by fluorescence spectroscopy.

Single walled Nanotubes

Functionalized Carbon Nanotubes for Detecting Viral Protein

Y.-B. Zhang, M. Kanungo, A. J. Ho, P. Freimuth, D. Lelie, M. Chen, S. M. Khamis, S. S. Datta, A. T. C. Johnson, J. A. Misewich, and S. S. Wong, *Nano Lett.* 2007, 7, 3086

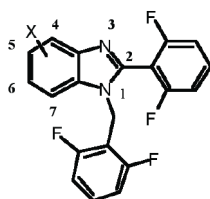


Zhang and co-workers have reported SWNT functionalised *via* amide bond with either Knob protein domain for *Adenovirus* or its human receptor CAR. Both functionalised carbon nanotubes and proteins retain their electronic properties and biological activities as an application for potential biosensors.

Inhibitors of HIV-1 Reverse Transcriptase

Synthesis, Biological Activity, and Crystal Structure of Potent Nonnucleoside Inhibitors of HIV-1 Reverse Transcriptase That Retain Activity against Mutant Forms of the Enzyme

M. L. Morningstar, T. Roth, D. W. Farnsworth, M. Kroeger Smith, K. Watson, R. W. Buckheit, Jr., K. Das, W. Zhang, E. Arnold, J. G. Julias, S. H. Hughes and C. J. Michejda, *J. Med. Chem.* 2007, 50, 4003



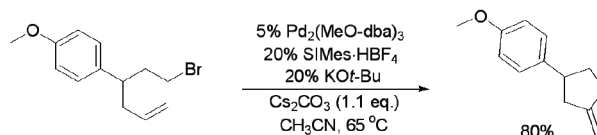
X substituent position	substituent	% inhibition (1μM)
4	CH ₃	71
5	CH ₃	42
7	CH ₃	1
4	Br	78
4	NO ₂	51

In the new compounds synthesised by Morningstar and co-workers the substitution in position 4 plays a fundamental role in activity against the wild type and the mutant forms of the HIV-1 RT, regardless of the type of substituent. The level of inhibitory activity drops dramatically as the substitution changes from the 4 to 7 position.

Heck Reaction

An Expansion in the Scope of Palladium-Catalyzed Heck Couplings to Include Alkylations

L. Firmansjah and G. C. Fu, *J. Am. Chem. Soc.* 2007, 129, 11340

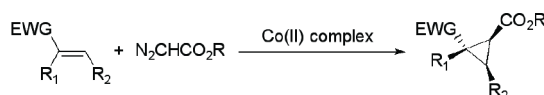


A method for achieving palladium-catalysed intramolecular Heck reactions of unactivated and β -hydrogen-containing alkyl bromides and chlorides is reported. These reactions appear to proceed via a pathway distinct from related but radical-mediated transformations catalysed by other metals. **13 examples: yield 66-85%.**

Asymmetric Cyclopropanation

Cobalt Based Asymmetric Cyclopropanation of Electron-Deficient Olefins

Y. Chen, J. V. Ruppel and X. P. Zhang, *J. Am. Chem. Soc.* 2007, 129, 12074

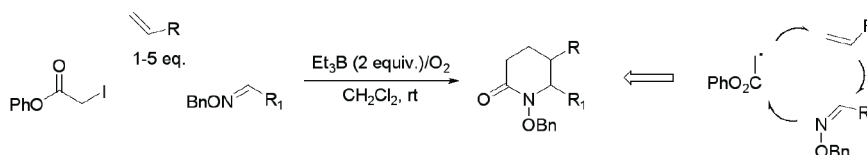


A general and efficient catalytic system, based on a Co(II) complex, for asymmetric cyclopropanation of various electron-deficient olefins is described. Synthetically precious cyclopropane derivatives were obtained in high yields and high stereoselectivity under convenient conditions. **20 examples: yield 73-96%.**

Multicomponent Reactions

Synthesis of Multi-Substituted Piperidinones via a Multicomponent Radical Process

E. Godineau and Y. Landais, *J. Am. Chem. Soc.* 2007, 129, 12662

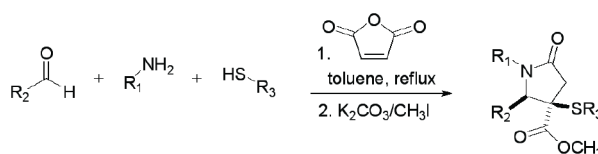


A new and straightforward method for accessing the piperidine skeleton based on a combination of radical and ionic processes has been developed. This is a one-pot synthesis of highly functionalised substrates starting from readily available building blocks. **10 examples: up to 92% yield.**

γ -Lactams

A One-Pot Four-Component Reaction to Form Tetra- and Pentasubstituted γ -Lactams with High Diastereoselection

J. Wei and J. T. Shaw, *Org. Lett.* 2007, 9, 4077



A new one-pot MCR between amines, maleic anhydrides, and thiols has been discovered to form tetrasubstituted γ -lactams. 3-Substituted maleic anhydrides lead to pentasubstituted lactams. Radical reductive desulfurisation of the product yields the corresponding syn-disubstituted lactam. The anti-diastereoisomer is accessed by desulfurisation with Raney nickel and treatment with potassium tert-butoxide. **18 examples: up to 94% yield.**

Industry News

Dr. Donal Coveney,

TopChem Laboratories Limited, 70 Western Parkway Business Park,
Ballymount Drive, Dublin 12, Ireland.

Merck announced a €200m investment to set up a new facility in Carlow. The IDA backed investment will create 170 new jobs in a human vaccine facility. This new facility will add to the 460 people employed by Merck in Tipperary and Dublin.

Unfortunately the bad news very much outweighs the good news in this issue starting with **Abbott** which unexpectedly announced the closure of the Galway stent facility. It appears that questions on the efficacy of drug eluting stents have led to a significant reduction in the uptake of these devices in general. Some recent studies have shown that statins, blood pressure pills and aspirin can be as effective. My Galway contacts were not surprised as other stent manufacturers have also been negatively impacted by this trend.

Amgen announced a complete cessation of all activities at the construction of the new facility in Cork. This follows on from the previous announcement of a postponement (ICN, Issue 1, 2007). Alas it was hardly a surprise given the ongoing negative news coming from Amgen in general culminating in an announcement of 12,000 job cuts worldwide.

Bristol Myers Squibb recently outlined an intention to reduce the number of manufacturing sites by 50% by 2010 and to trim headcount by 10%. No indication as yet as to how these changes will impact the Irish facilities.

Outsourcing

Several of the big Pharma players have flagged an intention to substantially increase outsourcing. While this might provide a boom for outsourcing partners, the likelihood is that this will be in India and China rather than closer to home. Clearly some of this outsourcing will impact negatively on multinational facilities in Ireland.

Pfizer have already indicated that two Irish facilities will be offloaded, but recently indicated an intention to increase outsourcing to up to 30% of its manufacturing from the current level of 15%.

AstraZeneca stunned observers by initially indicating that it was going to outsource all of its manufacturing! There was some noticeable backpedalling however as public sentiment was not so enthusiastic about such ambitions. Not as uncomfortable as those AZ employees working in manufacturing I suspect. It now appears that the outsourcing will be confined to older products and advanced intermediates.

In 2000 **GSK** owned 108 manufacturing sites, but by 2006 this number had fallen to 80 and the firm is anticipating further cuts. In 2001 only 9 per cent of the **GSKs** primary active pharmaceutical ingredient (API) costs were outsourced, now that figure has jumped to 41 per cent and continues to climb. However the production of newer products will remain in-house. Preserving such “crown jewels” seems to make a lot of sense (AstraZeneca please note!).

Product Withdrawal

Pfizer voluntarily withdrew Exubera – an inhaled insulin product, not for safety reasons, but for commercial reasons. Despite promising Wall Street sales of \$2bn per annum, Pfizer accepted defeat after a number of years of poor market performance with sales of only \$7m so far this year. There were high hopes for this product as it offered patients a non-injectable option. However the drug delivery device was cumbersome and not as convenient to use as anticipated. The device apparently bore a marked resemblance to a “bong”. Maybe I have led a sheltered life – but I had to look this up (Google of course) and I apologise to readers who know this already – it’s a smoking device used to smoke cannabis and other illicit drugs. This comparison, while amusing did little to endear the drug delivery device to the public and the medical community.

Seriously though this was a massive blow for Pfizer with a \$2.8bn charge and this presents a big setback for the prospects for other inhaled insulin products.

All in all a mixed bag this time round and some clear negative trends emerging for the Pharmaceutical sector. Readers are encouraged to inform us of industry news and developments – especially positive news please!

Prof. Wesley Cocker- An Appreciation

Prof. Brian McMurray FICI

School of Chemistry, The University of Dublin,

Trinity College, Dublin 2, Ireland.

Wesley Cocker, who died on 30th January this year, was a key figure in the development of academic chemistry not only in Trinity College but in the island as a whole. A native of Lancashire, and a graduate of Manchester University where he finished up as personal assistant to Lapworth, who was one of the pioneers in the study of organic reaction mechanisms.



(Left to right) - Wesley Cocker in his Newcastle days, and later as a Professor at TCD

After a career in ICI, where he studied methods for the making of methyl methacrylate - the precursor of Perspex - and diazonium salts used in dyestuff manufacture (recently he told me that his greatest contribution to the firm was the recognition that a precipitate, formed in one particular process and that they had been throwing out, was in fact the diazonium salt intermediate that they wanted) he joined up with his cousin William (later Sir William) in Cocker Chemicals. They started off manufacturing mercaptobenzthiazole, a rubber accelerator used in tyre manufacture, a Goodyear product that the firm had overlooked patenting in the United Kingdom. Later, Cocker Chemicals built up a relationship with Reckitts, and made the component chemicals of the antiseptic Dettol. He hankered after an academic career and moved to Exeter, then awarding external University of London degrees. There he carried out research on amino acid chemistry.

From Exeter he moved to Newcastle-on-Tyne where he lived during the Second World War. He had married Eleanor, a fellow Lancastrian, while in Exeter, and his daughter Katharyn was born in Newcastle. He was appointed to be head of one of the fire-watching teams in the University. He recorded that the Vice-Chancellor served under him in the team. On most occasions that he was on duty, there were no air raids, and he always claimed that this enabled him to pursue his research interests. He came under the influence of Professor Clemo there. Clemo had realised – in the middle of a lecture – that a key reaction in santonin chemistry (santonin to desmotroposantonin) could be explained by a methyl migration. This meant that a structure which fitted

the isoprene rule to be assigned to santonin. T&H Smiths, the extractor of santonin, obtained one batch of *Artemesia* which contained no santonin, but rather another sesquiterpene lactone, which was called pseudosantonin (ψ -santonin). Clemo was invited to determine its structure. He handed the problem to Wesley who brought it with him when he moved to Trinity in January 1947.

The department that he inherited in Trinity was physically in bad shape and the chemistry course out of date. He easily could deal with the latter by introducing a course involving new concepts. The former problem took longer. It was not a problem that was confined to Trinity. Wesley set to work on the receptive College Officers and between them they sought funds to knock down the worst (Victorian) parts of the department and replace them with more modern structures. This happened in two stages, but the final result was a much more satisfactory department. He had built up a very good relationship with AIN Roberts, the College architect and he never went home in the evening without visiting the sites when they were under construction. In this respect his time in Cocker Chemicals in charge of a chemical factory stood him in good stead.

As soon as he arrived, he initiated a vigorous research programme. Apart from ψ -santonin, he investigated alkyl group loss in dehydrogenation reactions of perhydronaphthalenes, a spin-off from the ψ -santonin work, and the structure of the diterpenoid, marrubiin, a constituent of Horehound which was used in cough remedies. He was quick to show that the latter contained a furan ring. He was able to persuade T&H Smiths to fund a project into santonin chemistry and this developed into a prolonged study. The stereochemistry which he assigned to the methyl group in the lactone ring depended on an explanation of the santonin-desmotroposantonin rearrangement. Eventually this turned out to be incorrect. He was consoled by the knowledge that the incorrect structure had been accepted as correct by no less a world authority than RB Woodward who himself earlier had contributed to santonin chemistry.

He has recorded that one of the most satisfactory projects was carried out in the Easter vacation, then seven weeks long. We in the department had realised that we could prove the absolute stereochemistry of ψ -santonin by converting it to an intermediate which could also be obtained from alantolactone, whose absolute stereochemistry had just been proved. He, starting from ψ -santonin, and I, starting from alantolactone, completed the job just at the end of the seven weeks!

Wesley later embarked on a study on the chemistry of the monoterpene (+)-3-carene and its double bond isomers, and in a series of papers with Patrick Shannon he elucidated their hydrogenation products, their hydroboration products, and some oxidation products. His collaboration with Patrick continued after he retired. Indeed until he fell and broke his hip, he continued to come into the laboratory. His last project was to synthesise a number of amides derived from toluene as potential enzyme inactivators.

He recognised the value that spectroscopy could play in determining the structures of molecules, and apart from the monies raised for building purposes, he obtained funding to purchase of the first UV spectrometer, the first IR spectrometer, the first NMR spectrometer, and the first mass spectrometer in the Republic of Ireland. I remember that, on one occasion when he was in his 80s, I carried out some NMR measurements for him using a technique new to us. On showing the results to him, I remarked that I had learnt something that day. His response was instant and emphatic: 'And so have I'.

He was an excellent and considerate supervisor of graduate students, encouraging them when experiments were not working out as planned and always coming up with fresh suggestions. He took pride in the successes of his students in their careers, though he said rather ruefully that so many of his early graduate students went into the brewing industry. This was a strain on his teetotal Methodist principles. His background also helped in that when he arrived in Dublin, he became firm friends with his fellow Methodist, Ernest Walton, head of the Physics Department. It certainly made for the smooth running of the old Experimental Science course. But he was a chemical ecumenist, and he built up a very close relationship with Professor Tom Wheeler in UCD, and there was a lot of coming and going between the two departments. Indeed at one stage a series of joint undergraduate lectures were planned and started, but they fell foul of an Archbishop's ban. In the late 40's, Wheeler and Professor Tom Dillon (UCG) had organised a one day meeting where graduate students from both places gave talks about their research. Trinity College joined in the next year and the meetings grew into what became the Irish Research Students Colloquium.

While he was able, Wesley was a regular attendee, and frequently was a favoured speaker at the Colloquium dinner.

Elected a Member of the Royal Irish Academy shortly after he arrived in Dublin, he served on its Council, as a Vice-President, as Senior Vice-President and as Science Secretary. One of his last outings from the Nursing Home was to attend a lunch in the Academy given for long standing Members. As the oldest Member present, he was made much of, and at the end made a short speech. Another honour that he received gave him particular satisfaction was the honorary PhD from Dublin City University. Those present on that occasion still remember the address that he gave to the new graduates.

He played a prominent part in the chemical societies in Dublin. At various times he was a member of the local committees of the Society of Chemical Industry, the Royal Institute of Chemistry, and the Chemical Society. He served on the Council of the Chemical Society in London, and became a Vice-President of both the Royal Institute of Chemistry and the Society of Chemical Industry. A founding signatory in the revived Institute of Chemistry of Ireland, he was elected Vice-President with the supposition that he would become President in due course. However during his Vice-Presidency, his Methodist principles asserted themselves. He realised that, if President, he would have to preside over dinners and receptions where alcohol would be consumed. His commitment to his teetotal beliefs would not allow him to do so, and he tendered his resignation. His action was misunderstood at the time, and led to a cooling of relations with the Institute for a period. All that was forgotten later on when he was made an Honorary Member of the Institute. He was very pleased with the honour.

Wesley Cocker; born January 31st, 1908; died January 30th, 2007.

Schools Chemistry Essay Competition 2007

James P. Ryan, FICI

Following the decision of the RIA to withdraw as host of the Schools Chemistry Essay Competition in 2005, the Institute of Chemistry of Ireland had agreed to become the new host. The Irish Times is also associated with the competition. Essays were invited from secondary schools all over Ireland, North and South. The rules stated that the essay should be 1,500 words long, explaining clearly and accurately the significance of any aspect of chemistry in an engaging, informative and easily intelligible manner. A list of sources was also requested and the use of graphics was encouraged.

The 1st prize of €600 and bronze sculpture by John Coen was sponsored by AGB Scientific Ltd, The Irish Times and the Institute of Chemistry of Ireland. The winning essay was 'Biopolymers' by Sean O'Callaghan, Patrician Academy, Mallow, Co. Cork.

Sean's essay dealt with synthetic and natural polymers in equal measure. The diverse uses of plastic in all forms were outlined. The problems of disposal *versus* recycling were compared. So-called biodegradable plastics are not always completely degraded. Regarding biopolymers, the uses of starch polyhydroxybutyrate (PHB) and polylactides (PLA) were considered. PLA can decompose harmlessly in the human body. But when the cost of producing these substances is taken into account, they may not be quite so eco-friendly after all.

The 2nd prize of €300 was sponsored by The Royal Society of Chemistry, Republic of Ireland Section. This was won for the essay '*Star Trek – The next generation*' by Andrea Mullins, Ardee Community School, Ardee, Co. Louth.

Andrea's essay focused on the theory of teleportation. The experiments of Professor Eugene Polzik were described. Methods using light, quantum mechanics, magnetism and what's called 'entanglement' have been examined. In one experiment an atom was transported incompletely over a distance of fifty-five millimetres. Quantum measuring and quantum feedback are integral parts of the process, as is the Heisenberg Uncertainty Principle. She also considered the complexities of transporting larger objects such as molecules, but human transport may have to wait until the 22nd century.

The 3rd prize of €300 was sponsored by The Society of Chemical Industry, Republic of Ireland Section. This was won for the essay '*A little radiation can be good for you*' by

Hannah Cagney, Mount Anville Secondary School, Mount Anville Road, Goatstown, Dublin 14.

Hannah's essay pointed to the good and the bad effects of radiation. The different types of radiation were described, including radioactive sources and mobile phones. The effects of ionising radiation on biological material such as cells and DNA can produce damage and mutations. She concluded that radiation is not something to be afraid of; rather, the appropriate handling of radioactive substances is the major issue.

Six further essays were highly commended.

These were (in alphabetical order):

'Ozone depletion by CFCs', Reem Al Sabah, Loreto Secondary School, Balbriggan, Co. Dublin.

'Alcohol and the genius behind it', Jonathan Carr, St. David's Christian Brother School, Malahide Road, Artane, Dublin 5.

'Organic Chemistry', Patrick Farnan, St. Colman's College, Newry, Co. Down, Northern Ireland.

'What makes glow-worms glow?', Imogen McBean, Rathdown School, Glenageary, Co. Dublin.

'Why do onions make you cry?', Jennifer Smith, Rathdown School, Glenageary, Co. Dublin.

The judging committee consisted of: James P. Ryan (ICI), Chairman, John Daly (RSC), David Birkett (SCI) and Dick Ahlstrom (Irish Times). The prizegiving took place in September 2007.

Company Member Profile

JVA Analytical Ltd

As part of the ongoing development of JVA Analytical, in December 2008 we have become part of United Drug plc a diversified company involved in laboratory & healthcare supply and services.

www.jva.ie
Ph 01-4569822
gerry.grady@jva.ie

JVA Analytical Ltd is responsible for the Sales, Service & Support of several leading Instrumentation manufacturers companies in Ireland. Varian (www.varianinc.com) are known as manufacturers of the highest quality Instrumentation. CEM (www.cem.com) are the world's leading provider of innovative microwave systems. CTC (www.ctc.ch) is the leader in GC & LC automation.

From the date the company was founded in 1992, we had a clear aim: to provide excellent support and service to our customers. This has always been the core value of our company, and is reflected in the company logo **"Supporting & Servicing Excellence"**. As an example of this commitment, we were the first company to have locally trained GC-MS engineers, not relying on external engineering support; this was in 1992, when GC MS was not routine. Now we routinely install, train and support LC & GC Triple Quad systems for highly sophisticated applications. JVA Analytical consists of 19 people, of those the vast majority are in the field providing the practical support our customers require. There are 10 highly trained field service engineers, 2 involved in training and 1 managing vital IQ/OQ/PQ documentation.

It's only possible to mention a few product highlights.

- **Varian Spectroscopy** products: market leaders in Ireland for many years for Atomic Absorption & ICP-OES providing unrivalled productivity and reliability. Varian Cary UV-Vis all the way from routine Cary 50 to the Super-Research grade Varian Cary 6000 UV-Vis-NIR.
- **Varian GC / Mass Spectrometry**; a major part of our business, from entry level Saturn 2100 to the Varian 320 GC Triple Quad which delivers limits of detection not possible on benchtop MS. The Varian LC Triple Quad has been the choice of several monitoring agencies in Ireland. The Varian 500 LC-MS Ion Trap and the ICP-MS 820 are outstanding devices with numerous patents guaranteeing class leading performance.
- **Varian Dissolution products** (previously VanKel) continue to be market leaders in Ireland, with innovative products such as the 9030 Dissolution Apparatus and the 400-DS App. VII, the first small-volume apparatus for testing medical devices such as drug-eluting stents.
- Varian is market leader in **semi prep & production scale HPLC**. Whether you want to purify 20mg or 20kg of product we can provide the HPLC, all the way to industrial SKID systems.
- **CEM** are suppliers of the Microwave Acid Digestion system used for AA & ICP sample preparation, and measurement of Moisture and Fat with the "Smartrac" NMR

instrumentation, but increasingly CEM is known for **Rapid Organic Synthesis** and **Peptide Synthesis**. The **CEM Liberty** allows the lab to make higher purity peptides faster; it's capable of synthesising 12 peptides a day unattended.

- Microwave synthesis using the **CEM Discover** has become the method of choice for many chemists, biochemists and Proteomics laboratories for a multitude of reactions for one reason: it simply works better!
- **CTC Analytics** are acknowledged leaders in GC & HPLC sample automation. The **CombiPal** is well known, a highly efficient, productive and reliable combination of Liquid & Headspace autosampling for GC & MS systems. The **ITEX** accessory offers Purge & Trap sensitivity in a compact, headspace system.

Service & Application support

We have a Chemistry background so we have keen understanding of the pressures our customers work under. We are application and solution orientated, that's key to how we view our business. We have a position of **Application Chemist** whose job is solely to work with customers to get applications running on their site. In our service department the emphasis is not just to fix the instrument, it's also to support the application. Only by this approach do we ensure total customer satisfaction. **Training** is also vitally important. In recent years there is much more staff mobility. While this is great for staff, it's not so good for the Lab Manager running complex analysis to a deadline. Thus the committed support of a professional vendor is vital to ensure that productivity and quality is maintained. We have the people to provide this level of assistance.

As well as looking at the equipment, we would encourage companies to evaluate what commitments the supplier has to providing the long term local support and service that make for satisfactory ownership. JVA Analytical has a 15 year proven commitment to our customers, and this has been rewarded with significant growth every year since our foundation. This ongoing vote of confidence from our customers is sincerely appreciated and we look forward to many years of cooperation.

Insitute of Chemistry of Ireland: Congress 2008: Theme: Nanotechnology

Margaret Franklin

Nanotechnology is a popular buzzword these days. However, there is sometimes confusion as to what the term actually means. The original concept, first envisioned in the late 1950s by Richard Feynman and popularised by K. Eric Drexler in the 1980s, arose from the idea that functional systems, in effect, 'molecular machines', might be built by the manipulation of matter on the atomic scale. Later however, the term was applied to any structures smaller than about 100 nanometres, even if produced by merely grinding bulk matter down to nano-sized particles. (A 'top-down', rather than the original 'bottom-up', approach.)

Nanotechnology is now a rapidly developing interdisciplinary field, involving, for example, supramolecular chemistry, engineering, applied physics, materials science and colloidal science. It may have the potential to provide enormous benefits in a huge variety of applications, such as the further miniaturisation of computer chips, the manipulation of so-called quantum 'dots', drug formulation, cosmetics manufacture, medical devices, food technology, recycling and detoxification of waste. But much of the technology is at an early stage of development and there are concerns that it may not live up to its promise. Matter on the nanoscale has different properties to matter in bulk. Some of these properties can be exploited to useful purpose, but others give rise to

concern, particularly in such areas as food safety, environmental protection and the use of nanotechnology in health care.

This year's annual congress brings together a number of leading researchers, who are developing different applications of nanotechnology, in fields as diverse as microelectronics, biosensors, ecology, drug delivery, medical devices and in the recycling of plastics. The various presentations may remove some of the confusion that surrounds this emerging field and should spark a lively discussion on what is sometimes a rather controversial subject.



*School of Chemistry, TCD
School of Chemistry and Chemical Biology, UCD*

Carry out cutting-edge research leading to a Ph.D. under the supervision of one of more than 40 leading researchers. There is wide range of research projects on offer from synthesis and medicinal chemistry to computational and materials chemistry. In Dublin Chemistry we have excellent resources and currently more than 180 postgraduate research students.

In Dublin Chemistry your research is supported by a structured taught programme which ensures you receive up-to-date education in areas such as advanced synthesis, nanochemistry, molecular modelling, chemical biology, structure elucidation and spectroscopy. The programme also provides Master Classes from invited international scientists.

An Enhanced PhD Experience!

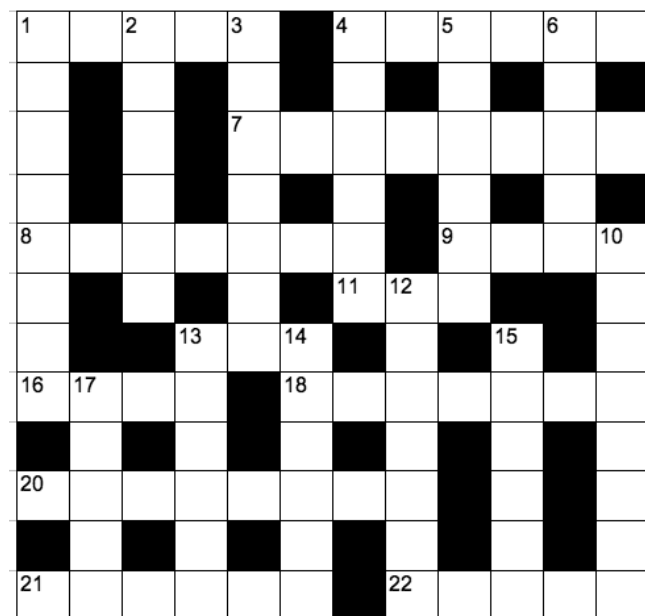
www.dublinchemistry.ie



The ICN Crossword

Dr. Donal Coveney FICI

TopChem Laboratories Limited, 70 Western Parkway Business Park,
Ballymount Drive, Dublin 12, Ireland.



Down

- 1 Distinctive atomic cloud (8)
- 2 Maternal remnant of crystallisation? (6)
- 3 Lawless brute escapes from the funfair (7)
- 4 Carry it off with coolness, confidence (6)
- 5 Magical potion (6)
- 6 Chunk of precious metal (5)
- 10 Of the east - Asian (8)
- 12 Adds on to (7)
- 13 Three strung together - chemically of course (6)
- 14 Phenolic antiseptic from a bunch of (6)
- 15 Salt solution - sounds medical (6)
- 17 Forest tree with smooth bark sounds coastal? (5)

Across

- 1 Measure of solution strength - not to put a tooth in it! (5)
- 4 Vinegar acid (6)
- 7 Dental cavity repairs (7)
- 8 Precious metal (7)
- 9 On it shuffled (4)
- 11 Unit of pressure and piece of soap (3)
- 13 Abbreviated common explosive (3)
- 16 One thousandth of 11 across - briefly! (4)
- 18 Seven carbons - straight up (6)
- 20 Gentleman steering the vessel (8)
- 21 Asymmetric (6)
- 22 Odour (5)

Last Issue Solution

Across.

1. Cuprate 6. Savour 7. Prism 8. Engage
9. Integer 12. Data 13. Frit 14. Aground
17. Bodice 18. Bliss 19. Cicero 20. Placebo

Down.

1. Capri 2. Print 3. Ester 4. Avogadro 5. Tungsten
10. Narcotic 11. Entwined 14. Aesop 15. Urine 16. Disco

Elemental Su Doku

Dr. David Birkett

Henkel Ireland Ltd., Tallaght Business Park, Whitestown, Dublin 24, Ireland

	F				N		O	
He		C						Be
		Li	Be			F	He	
N			O		F	Li		
				H				
		F	Li		B			He
	C	N			Be	He		
F						C		B
	Be		C				H	

Notes



Varian GC 320 Triple Quad Mass Spec



VARIAN



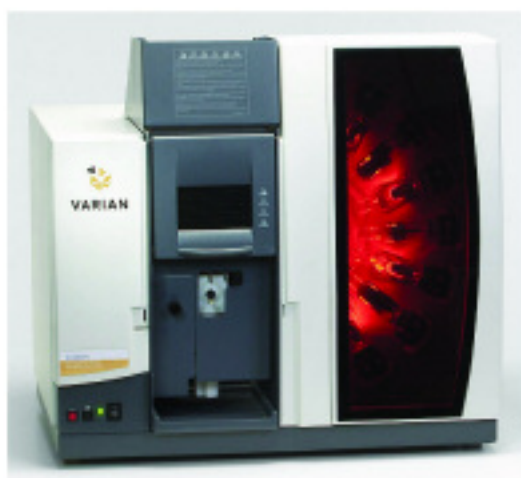
Varian ICP-MS with CRI



Varian Prep Scale HPLC



Varian Dissolution Systems



Varian SpectraAA Fast Sequential AA



Supporting & Servicing Excellence



Varian Cary UV-Vis Spectrometers

CEM Explorer 48



CEM

JVA Analytical Ltd

Supporting & Servicing Excellence...

Ph 01-4569822 Email sales@jva.ie
www.jva.ie