Editorial

The first issue of *Green Chemistry* follows 18 months of market research, consultation and discussion with the academic, industrial and public chemistry communities, and detailed planning with the RSC and a very supportive editorial board. The primary decision to go ahead with a new journal was not taken lightly: only after long and frank discussions over questions such as journal proliferation, academic credibility and industrial relevance did chemists from a wide variety of backgrounds reach consensus on the importance and timeliness of the project. The supportive evidence for this is overwhelming and includes the number of recent relevant publications, the emphasis placed on relevant research by national and transnational funding agencies, an increasing awareness in industry of the importance of concepts such as waste minimisation and atom utilisation, and greater involvement by governments in controlling the use of resources and the production and disposal of waste. The emergence of these, and other, underpinning concepts as general principles which can be used in the conception and execution of synthetic chemistry, and in the usage of the chemicals produced, has been critical in the evolution of Green Chemistry.[1]

The title *Green Chemistry* was itself the subject of considerable discussion and debate. We considered many alternatives, but none carried the same combination of widespread use and appreciation, as well as simplicity and impact. We are particularly indebted to colleagues in the United States who have been largely responsible for getting the terminology into common practice as well as for giving it credibility and value through initiatives such as the Presidential Green Chemistry Challenge Scheme. The definition of Green Chemistry given by the individual who has done most to promote it, Paul Anastas, and his co-author John Warner serves nicely to define the main objectives of this journal:

> *Green Chemistry is the utilisation of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products.*[2]

Green Chemistry is to be an information resource as well as a high quality international journal. It will report on research activities and interests in chemical aspects of clean technology from academic, industrial and public sectors. Each issue will have two sections. The back section will contain primary research papers, communications and reviews. The style and format of these articles will be very flexible, to allow the widest possible range of formats. The front section of the journal will contain news and views on research, industrial highlights, and legislative issues, grants and other promotional initiatives, conferences, and educational items. We seek to inform those working in relevant areas, but also to promote and encourage relevant research and teaching, and the application of the principles of green chemistry.

The research articles in the first few issues of Green Chemistry should help to set the tone of the journal. These will cover:

- clean synthesis (*e.g.* new routes to important chemical intermediates including heterocycles)
- enhanced atom utilisation (*e.g.* more efficient methods of bromination)
- the replacement of stoichiometric reagents (e.g. catalytic oxidations using air as the only consumable source of oxygen)
- new solvents and reaction media (*e.g.* use of supercritical fluids and reactions in ionic liquids)
- water-based processes and products (*e.g.* organic reactions in high-temperature water)
- replacements for hazardous reagents (*e.g.* the use of solid acids as replacements for traditional corrosive acids)
- intensive processing (*e.g.* the use of spinning disc reactors)
- novel separation technologies (*e.g.* the use of novel biphasic systems such as those involving a fluorous phase)
- alternative feedstocks (*e.g.* the use of plant-derived products as raw materials for the chemical industry)
- new safer chemicals and materials (*e.g.* new natural product-derived pesticides)
- waste minimisation and reduction (*e.g.* applying the principles of atom utilisation and the use of selective catalysts).

In the front section of Green Chemistry we will be carrying highlights from research and industry, news items on recent public consultation documents and new funding initiatives, networks and award schemes, reports from recent conferences and a conference diary as well as letters, comments and opinions on relevant issues. In addition we will have non-research articles designed to inform the reader of various important topics such as the effectiveness of environmental legislation as applied in different regions of the world, the development of green chemistry teaching courses and educational packages, status checks on current research programmes and introductions to specialist and emerging subjects such as new chemical reactor designs.

We look forward to receiving a wide range of article types and news items with coverage reflecting the development and application of the principles of green chemistry in education, industry and research. We would also like to hear your views on any educational, governmental, industrial, public or research issue relevant to green chemistry. We intend the journal to act as a forum for the discussion of the many emergent and controversial issues surrounding green chemistry.

The 20th century has been highly successful for chemistry and society has come to depend on the products of the chemical industry to maintain our current standard of living and improve our quality of life. On the eve of the 21st century, however, the public are more aware of the hazardous substances that many chemical processes use and generate than the benefits of the products. Chemistry and the chemical industry have tarnished images. With your help we can use this journal to convey the means and motivation for chemists to make a difference.

James Clark, York, January 1999

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1 For further background reading, see J. Clark, *Chem. Br.*, 1998, **34**(10), 43.

2 Green Chemistry: Theory and Practice, P. T. Anastas and J. C. Warner, Oxford University Press, Oxford, 1998.

New glue for plywood

Soya bean glue –

a new high-performance adhesive from a renewable resource

The preparation of plywood involves the spraying of several sheets of wood with a glue, followed by compressing the layers together to form a lamellar composite. Traditionally, the glues utilised in this process have been petroleum based, and thus have problems associated with control of volatile organic components, as well as being derived from non-renewable resources.

Glues derived from soya bean protein, a cheap and renewable resource, have been known for some time, and can be used for a few light applications such as labelling and packaging. Unfortunately, their poor performance in humid environments has precluded their use in many areas. Early attempts to rectify this problem used phenol–formaldehyde resins as modifiers to cross-link the proteins and render them more water-stable. This has not proved a viable solution, since formaldehyde is slowly released, leading to toxicity problems, and for many years the use of soya bean protein in adhesion has not been an attractive proposition.

Now this situation has changed. A research team at Kansas State University, led by Xiuzhi Susan Sun, has managed to dramatically improve the performance of soya bean protein as a glue, without the need for treatment with cross-linkers. Their approach centres on the modification of the protein structure. Native material is globular, with hydrophilic regions on the outside of the structure, leading to low resistance to water, and poor performance of glues in humid environments. The interior of the protein contains hydrophobic regions, which should improve the water-resistance of the material. Sun's approach has been to effect structural changes to the protein, converting it from a globular to a partial random coil form, resulting in the exposure of the hydrophobic regions of the protein. These changes enhance the performance of the protein dramatically, and make it into a very promising candidate in a variety of applications.

Plywood can now be successfully fabricated from a variety of woods using the new glue. These materials can survive severe water treatment without any sign of delamination; furthermore little reduction in adhesive strength is observed. The unmodified protein, by comparison, shows no adhesive properties under these testing conditions. Other important benefits include the ability to spray the aqueous protein solution evenly – a consequence of good viscosity properties – allowing much better coverage and improved sticking.

For further information visit http://www.oznet.ksu.edu/dp_grsi/faculty/sun.htm

Biotechnology helps UK engineers win top environment award

The top UK environment award in 1998 for engineers was won for work on reducing harmful emissions. The Engineering Council's *1998 Environment Award for Engineers* was won by a team from BIP Ltd., Oldbury, West Midlands, UK. The award, which comprised a £5000 prize and the Lloyd's Register Trophy, was for developing a process that brings together biotechnology and engineering. The company has developed a roof-mounted bio-reactor for installation in plastics and resins plants which emit formaldehyde and methanol. The bio-reactor contains micro-organisms which feed on these compounds and hence reduce the environmental impact of the emissions.

US MTBE controversy

The US government is fighting efforts in the Californian legislature to ban methyl *tert*-butyl ether (MTBE), the oxygenated fuel additive, which has been linked to ground water contamination in various parts of the US (*Chemical Market Reporter*, 28 November 1998). The argument used by the National Government is that the use of MTBE as an additive improves air quality. They are concerned that if California manages to halt the use of MTBE, air quality throughout the country will be adversely affected. Officials in one Californian town, however, claim that the problem is so bad that more than one in three drinking water wells have had to be closed down due to contamination.

It has also been reported that, in connection with worries about MTBE, US Filter and Envirogen have agreed to develop a fluidised bed biological treatment system for the compound. (*The Chemical Engineer*, 1998, **666**, 8).

Atom efficiency in Antwerp

BASF have announced that the amount of waste produced at their Antwerp site (*ChemPress*, 1998, **32**(17), 5) was 9926 tonnes in 1997, the first time that the company has achieved less than 1 kg of waste per tonne of product. Emissions to the atmosphere were up by 3%, and waste to water increased by 13%, on top of an increase in production of 17%. Landfill waste was down by around a third, and waste to incinerators reduced by about a quarter; 76% of solid waste was recycled.

New investments in the Czech Republic in refinery

Ceska rafinerska (CRA) of Litvinov has announced an investment programme of CEK 10bn to the year 2002. The major thrust of this initiative is the construction of deep crude oil processing facilities. These new units will allow the company to convert heavier, sulfur-rich, fractions of crude oil into cleaner, lighter fuels, and thereby reduce the amount of polluting heavier fuel oils (*Hospodarske Noviny*, 1998, **42**(189), s6).

Steel works are seeking to reduce mercury emissions

Mercury under pressure

The Tianjin Bohai Chemical Co (China) has announced that it is building an 85,000 tonnes per annum membrane caustic soda plant. This will replace its existing 58,000 tonnes per annum mercury process caustic soda plant, which has been the cause of serious pollution problems (*China Chemical Reporter,* 1998, **9**(30), 13).

Three US Steel works in the Great Lakes area have signed a voluntary agreement with the Lake Michigan Forum, which will lead to a reduction in mercury consumption at their steel mills. This will contribute to the implementation of the Toxics Reduction Strategy with Canada, an agreement that aims to achieve a 50% reduction in the use of mercury by 2006.

On a similar theme, the Dutch company Begemann Milieutechniek BV has taken delivery of a cryogenic waste gas purification unit from Aga Gas BV. This will be used in Begemann's processing of mercury containing wastes (*Nederlandse Chemische Industrie,* 1998, **40**(16), 9).

New products and processes

Adipic acid

A new process for adipic acid that eliminates the production of nitrous oxide and gives only water as a byproduct has been announced by scientists at Nagoya University in Japan (*Chemistry and Industry,* 1998, 717). The process is based on the use of hydrogen peroxide to oxidise cyclohexene, and gives a yield of about 93% adipic acid.

Polymers

At the University of Twente in Holland, polymers that degrade to carbon dioxide, water and biomass are being developed. These include poly(ester)amides and poly(ester)urethanes. Several degradable polymers are also being marketed by industry. These include an aliphatic polyester from Showa High Polymer (Japan), and random aliphatic-aromatic copolymers based on terephthalic acid, adipic acid and 1,4-butanediol from both BASF (Germany) and Eastman (USA) (*Chemisch Weekblad,* 1998, **94**, 1).

Oxidation with supercritical water

Nittetsu Semiconductor (Japan) have brought into operation what is claimed to be the first supercritical water-applied oxidation system for the destruction of waste, including developer, stripping liquid and ammonia liquid (*Japan Chemical Week,* 1994, **39**, 10).

Concrete removes nitrous oxide

Mitsubishi Materials (Japan) has developed and tested a new type of concrete paving block which purifies the air around it by removing nitrous oxide from the atmosphere. The blocks contain titanium dioxide that can act as a photocatalyst and is activated by sunlight and rain, promoting the oxidation of nitrous oxide to nitric acid which is washed away or neutralised by the alkalinity of the concrete (*Chemical News,* 1998, **69**, 28).

Solvent replacement in metal cleaning

Avon Ames, part of Avon Rubber, has successfully implemented an 80% reduction in solvent use in its metal cleaning operations. This has been achieved by phasing out the use of 1,1,1-trichloroethane, and replacing it with the ICI system Cleanfast DLS and the solvent Triklone LE (*Rubber Trends,* 1998, 3rd quarter, 104).

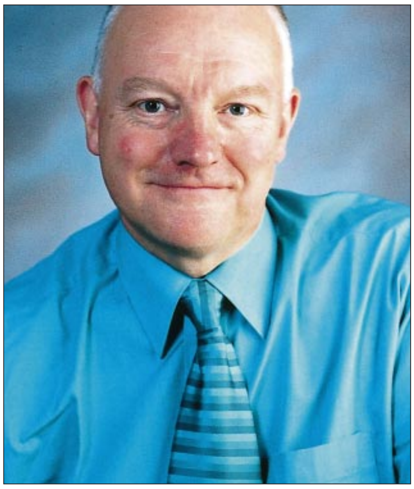
Trouble brewing for brominated flame retardants

Following publication last autumn of research showing the presence of brominated flame retardants in fish and birds in the Baltic, the Swedish environment minister has contacted the US Environmental Protection agency and Japanese Environment Agency to encourage co-operation with the European Union on tackling the problems caused by these compounds (*European Chemical News,* 1998, **69**(1829), 60). In response to Sweden's criticism of the UK over slow action on the release of these substances, the UK environment minister said that any action must await the outcome of a Europe-wide assessment programme, the findings of which will be made public this year (*The Chemical Engineer,* 1998, **666**, 11).

The market – legal and illegal

The US market for environmental consultancy has been worth about $7bn per annum since 1993, and remains steady. The market for remediation consultancy and remediation construction was worth a total of $8bn in 1997– an increase of 3% over 1996. It is generally considered that the environmental services market is stagnant and will decrease in the future.

A thriving illegal market has developed for banned chemicals with an estimated 30,000 tonnes per annum of chemicals, including CFCs and carbon tetrachloride, being smuggled into industrialised countries from developing countries and the former USSR. The official consumption of CFCs in industrialised countries has decreased to less than 15,000 tonnes per annum, from 1 M tonnes per annum in the mid 1980s.



John Emsley, the 1998-1999 John Jeyes lecturer

John Jeyes lectureship

The 1998-99 John Jeyes lecturer is Dr John Emsley (University of Cambridge). He was given the award for his contributions to the perception of humans and their pivotal role in the environment with good sound common sense descriptions on the beneficial aspects of modern chemistry to humankind. His lecture is entitled ‘False alarms: a closer look at some environmental scares’. It is based on items of the type covered during his period writing the ‘Molecule of the Month’ column for *The Independent* newspaper when he responded to exaggerated scares about various chemicals that were being blamed for causing environmental pollution. He showed that while many of these alarms appeared to be based on sound scientific evidence, most were eventually found to be false alarms when exposed to rigorous testing. He examines why certain chemicals find themselves in the glare of the media spotlight, what effect adverse publicity has, how eventually the fears are shown to be groundless, and why this rarely gets reported.

The ‘false alarms’ that Emsley considers include those relating to PVC, phthalate plasticisers and dioxins, chlorination of water supplies, dichloromethane as a solvent, aluminium and Alzheimer’s disease, nitrate fertilisers and drinking water, phosphates in detergents, antimony fire-retardants, food additives and E-numbers.

Emsley also discusses the ways that chemists and the chemical industry might work to generate a better climate of public opinion in the coming millennium, which will be needed if we want young people to study chemistry.

The methyl bromide saga

According to the Montreal Protocol, the European Union as a developed area is not due to terminate the use of methyl bromide as a soil fumigant until 2005. However, the European Commission has been seriously considering a proposal banning the use and production of the chemical by 2001, bringing Europe into line with the USA, Australia and Japan. The earlier ban is not popular with producers, farmers and lawmakers, who have been pushing for a deferral. In the US, Environmental Protection Agency officials have expressed a willingness to defer the ban while alternatives are developed. Some of the suggested alternatives, such as methyl iodide and phosphine, present their own problems. Other possible replacements include carbon dioxide and heat treatment.

Methyl bromide, used as a soil fumigant in the production of many crops, e.g. *strawberries, is being replaced because of its ozone-depleting properties*

Companies announce improved environmental performance

Schering (Germany) has committed its businesses to sustainable development, and, within the framework of the international responsible care programme, to continuous improvement in safety, environmental protection and health care conditions. In 1997, Schering invested DM 28M in environmental protection facilities, mainly in improving existing plants and equipping new plant. The recycling of 13 M tonnes of solvents saved the company DM 19M of the cost of the raw material. Company targets for the year 2000 include a 12% reduction in the amount of non-recoverable waste, a 15% reduction in the level of waste consumption, and a 5% reduction in electric energy consumption, compared to 1996 figures. They are also aiming for a reduction in their carbon dioxide emissions by the year 2005.

Reckitt and Colman aims to operate an environmental policy that is globally responsible and also meets or exceeds local environmental standards. Their Hull site in the UK recycled almost half of its total waste in 1997. In their Belle Mead site in New Jersey, USA, a thermal oxidiser is used to destroy 98% of volatile organic waste.

UPM-Kymmene (Finland) has an environmental policy based on the environment management principles laid out by the International Chamber of Commerce. Capital expenditure on environmental protection was FM 66M in 1997. Total emissions of gaseous sulfur compounds were down by 22%, and by over 30% when the increase in production is taken into account.

Outokumpu (Finland) have announced a fall in sulfur dioxide emissions from their Harjavalta smelter to 2700 tonnes (16 kg per tonne of metal produced) in 1997.

A ‘growth’ industry: renewable raw materials

Ian Bartle and Nigel Oliver report on an independent UK agency set up to promote the development of nonfood crops

Plants are natural, clean and sustainable ‘biorefineries’– non-toxic, biodegradable and CO_2-neutral – with the potential to deliver an array of raw materials for industry in place of mainly petrochemical sources. With world-wide interest in such crop-derived products, UK industry (British Sugar, Cargill, Dalgety, DuPont (UK), HGCA, ICI, NFU, PBI-Cambridge, Pira International, Sustainable Industries Ltd and Zeneca, together with BBSRC, DTI and MAFF) has been proactive in the establishment of an independent national agency, ACTIN, to address market opportunities, supply chain issues and barriers to progress, and to promote networking in this industrial, *i.e.* non-food, crops arena.

Potential issues for those in industry are: re-evaluation of the manufacturing process, the establishment of new supply chains (where appropriate extending upstream into the research community), technical hurdles, and environmental and regulatory issues. These are all major considerations towards achieving the desired end result – a novel and competitive product from a renewable feedstock. The disciplines of plant biochemistry and biotechnology; biochemical and process engineering; chemistry; materials science and processing; and life cycle analysis or processing modelling all play an important role.

ACTIN (Alternative Crops Technology Interaction Network) was established in 1995 to promote crop-derived oils, fibres, starches and speciality chemicals as renewable raw materials for industry. Dedicated ACTIN staff and the vertically-integrated group of sponsors with a diversity of viewpoints (representing the science base, producers, processors and end users) provide a coherent central resource supplemented by ACTIN’s extensive Database, its Special Interest Group members (ACTIN^{2020}) and links into related initiatives at the European level.

There is a close association with a £4M UK Government LINK Programme (‘*Competitive Industrial Materials from Non-Food Crops’*) which intends to manage approximately 15 projects in this area (see below).

ACTIN provides objective help, to industry or the research community, to facilitate and add value to particular interests in this area. A useful starting point is the Web site (http://www.actin.co.uk) or Help Desk (Tel. +44 (0)1372 802054; email: info@actin.co.uk).

Plant-derived indigo for industrial use

The earliest known source of indigo was *Isatis tinctoria* (woad), a biennial or perennial herb, indigenous to northern Europe. Woad produces two indoxyl-forming substances in its leaves, indican and isatan B, which, when exposed to the air, form the blue compound, indigo.

> ‘ACTIN promotes crop-derived renewable raw materials for industry’

Since the 17th century, it has not been grown in Western Europe as a source of indigo. As a consequence, there has been no recent attempt to breed woad to improve indigo precursor content or crop architecture.

Changes in legislation and a growing demand from consumers and manufacturers for naturally-derived products from renewable resources, have led to a revived interest in woad as a source of indigo for industry, leading to the need for new systematic research on this crop.

This LINK project, funded by MAFF, addresses the recognised need for a greater commitment towards bio-based materials and chemicals and will develop varieties of *Isatis* that give improved yields of indigo, by a rapid programme of marker-assisted plant breeding from existing lines. Also, an experimental extraction process will be scaled-up to produce quantities of indigo for industrial purposes.

L. FUCH'S *Flora*, 1545

There is renewed interest in woad as a source of indigo for industry

The research will be carried out by a group from IACR-Long Ashton and University of Bristol, along with Silsoe Research Institute (SRI), which will provide the appropriate engineering skills. Harvesting equipment and the extraction process will be developed by SRI in association with a seeds company and Express Separations. The end-product will be used in the manufacture of natural dyes and pigments.

Semiochemicals for aphid control

Aphids are the most important group of agricultural and horticultural pests in the UK and most of Europe, causing direct damage to a wide variety of crops but also transmitting virus diseases. The recent identification of the attractant pheromones produced by sexual female aphids has opened up new possibilities for the development of novel pest management strategies, either avoiding use of broad-spectrum pesticides or retaining their use for 'fire-fighting' when aphid problems are extreme.

This project seeks to provide products for the control of pest aphid species in the field, using the chemicals which occur naturally in their environment and which act by non-toxic mechanisms. It also aims to improve the method of production so as to use clean technologies rather than chemical synthesis.

Aphids are attacked by a wide range of natural enemies including parasitic wasps, more correctly termed parasitoids, and studies, particularly at Rothamsted, have demonstrated the importance of these parasitoids as natural biological control agents. However, to be effective, early season synchrony of parasitoids and aphids must be achieved. Recent laboratory and field studies at Rothamsted and Imperial College, Silwood Park, have shown that some parasitic wasps are strongly attracted to the pheromones produced by sexual female aphids to attract mates. This innate response is being used to develop a sustainable aphid control strategy, based on the use of synthetic aphid sex pheromones, to achieve early season synchrony between natural populations of parasitoids and aphid pests and to conserve and enhance field margin parasitoid populations in autumn.


Aphids, a serious agricultural pest, could be controlled with sex pheromones

The aphid sex pheromones possess a number of chiral centres, and are thus difficult synthetic targets. Two important aphid sex pheromone components are isomers of the monoterpenoids nepetalactone and nepetalactol, designated as having the (4a*S*,7*S*,7a*R*)-configuration. A synthetic route to the (4a*S*,7*S*,7a*R*)-nepetalactone and the corresponding nepetalactol has been developed from commercially available starting materials, which must be of a high enantiomeric purity to yield materials which exhibit biological efficacy. The high cost of the starting materials, resulting in a cost exceeding £1000/g of pheromone, combined with the toxic nature of some of the required reagents, means that production of the pheromone from this route is not practical.

The (4a*S*,7*S*,7a*R*)-nepetalactone is produced by the catmint *Nepeta cataria* and another valuable isomer (4a*R*,7*S*,7a*S*)-nepetalactone by *Nepeta racemosa*. High yields of these compounds, of the order of 1g/kg of fresh plant material, can be obtained by conventional steam distillation methods. However, use of novel and more environmentally benign extraction protocols with reduced usage of organic solvents, including microwave extraction, are also being investigated. A high extraction efficiency, combined with a yield potential of up to 10 tonne/ha of fresh plant material, demonstrates that the production of aphid sex pheromones from commercial production of *Nepeta* species is economically viable. The lactol components of the aphid sex pheromones can be derived by a simple one-step reduction of the corresponding lactone. Although this synthetic route is amenable to large scale production, a cleaner approach to reduction, based on the use of enzyme chemistry, will be investigated for the production of high enantiomeric purity nepetalactols.

The pheromone is most attractive when released into a crop area at physiological levels which involve very low concentrations. To achieve this, a formulation will be developed which impregnates the pheromones into a resin.

The project, funded by MAFF, will involve IACR-Rothamsted and three industrial partners: English Hop Products, which has expertise and facilities for the extraction and purification of essential oils, Richard Wood Partnerships, who will propagate and grow several *Nepeta* species cultivars to determine which give products with high enantiomeric purity and good overall yield, and AgriSense-BCS, which has considerable experience with pheromone formulation and currently markets several pheromone-based products.

Plant fibres as ion-exchange media

Ion-exchange materials based on pure cellulose have been used for the past two decades. They are characteristically available in very pure forms, have high


A copper adsorbent derived form sugar beet pulp produced at the BioComposites Centre, Bangor, UK

exchange capacities and are the main alternative to synthetic (petroleum-based) ion-exchange resins. Lignocellulose is also highly reactive and lends itself readily to ‘graft modification’. This principle has been investigated since the early 1970s and the range of substrates is a testament to the imagination of workers in this field. Thus, to date, ion-exchangers have been derived from such diverse materials as wood flour, coconut coir, sugar beet pulp and even empty corn cobs.

The main obstacle to full exploitation has been the lack of facilities to produce these materials in quantities greater than a few kilograms. Recently, through a Foresight Challenge initiative, BP Chemicals has made its pilot-scale plant at Hull available to the BioComposites Centre.

In the 'IONEX' project scientists at the Centre are making use of this facility to transfer their expertise in lab-scale chemical modification of plant fibres to produce low cost ion-exchangers. Hickson and Welsh, in its role as end user, provides guidance as to the desired properties of these materials to ensure they can be a commercially viable complement to existing ion-exchange systems. The environmental impact and fate of the new materials will be assessed by Imperial College London.

The IONEX project, which is funded by MAFF and EPSRC, will run parallel to the wider Foresight initiative and enable the potential of chemically modified agricultural materials such as flax and hemp fibres and sugar beet pulp to be realised in true industrial applications. The project is co-ordinated by The Biocomposites Centre at Bangor who also provide the scientific input to the project.

Starch for packaging materials

The objective of this project is to develop technology for the conversion of starch into mouldable packaging materials. The result would be a new range of environmentally friendly materials made by clean, solvent-free processing routes and which, although tailored for recyclability, have attractive properties for ultimate disposal by, for example, composting. Use of such materials would help meet future legislation and reduce the use of non-renewable oil-based components.

The Centre for Biomimetics at Reading University is currently evaluating the properties of materials produced from wheat starch compared with expanded polystyrene.

Sustainable surfactants

The Central Science Laboratory of the UK Ministry for Agriculture, Food and Fisheries (MAFF) was the venue for a one-day seminar in York last November, organised by LINK in association with ACTIN (Alternative Crops Technology Interaction Network), BACS (British Association for Chemical Specialities), and the Royal Society of Chemistry (Speciality Chemicals Sector). This event, entitled *Sustainable Surfactants: Renewable Feedstocks for the 21st Century*, was designed to help establish industry/education partnerships appropriate for the collaborative LINK programme on *Competitive Industrial Materials from Non-Food Crops.*

The programme opened with an introduction by the Chairman, Dr David Karsa (Akcros Chemicals and BACS), who briefly considered the goals of developing new products from non-food crops, market trends and relevant chemical processes. This was followed by a presentation from Dr Guido Bognolo of ICI Surfactants on *The Needs of the Surfactants Industry*. Dr Bognolo started by comparing natural and synthetic products, noting that 70 – 75% of the surfactant consumption in industrialised countries is of petrochemical origin whereas natural products dominate in developing countries. In the industrialised countries, there is a trend towards converting from synthetic to natural based products. This is driven by increasing demands for mildness (due to more frequent washing), for finding and using replacements for environmentally unacceptable products (such as those based on linear alkylbenzenes), and for increasing product specificity. In contrast, the emergence of new manufacturing technologies in developing countries is causing a trend in the opposite direction: from natural to synthetic products. It is believed that raw materials availability will not be a driving factor at the macro level but may influence the choice of specific alkyl chain lengths in the surfactant products.

Dr Karl-Heinz Hill from Henkel gave a talk entitled *Fats and Oils as Oleochemical Raw Materials: Recent Developments and Perspectives.* He began by reviewing statistics on world production and consumption of oils and fats and the basic oleochemical processes. This showed a clear trend away from the use of synthetic surfactants, towards those based on natural products. For example,

Natural versus man-made surfactants

NATURAL/RENEWABLE
Alkyl polyglucosides
Biosurfactants,
  ***e.g.* Surfactin and Emulsan**
Fatty amides
Fatty amines
Glucamides
Glycerol and polyglycerol esters
Lecithins
Ligoin sulfonates
Phosphoric acid esters from
  derived fatty alcohols
Protein derivtives
Saponins
Soaps
Sorbitol and sorbitan esters
Sugroglycerides
Sucrose esters
Sulfates from naturally
  derived fatty alcohols

MAN-MADE
Alkanolamides
Alkyl and alkyl aryl ether
  carboxyates
Alkyl aryl sulfates
Alkyl aryl sulfates
Alkyl aryl ether sulfates
Alkyl capped ethoxylates
Alkyl ether sulfates
Alkyl isethionates
Alkyl phenol ethoxylates
Alkyl phenol/formaldehyde
  condenstes and their
  alkoxylated derivatives
Alkyl sulfates from synthetic
  fatty alcohols
Alkyl sulfonates
Amino oxides
Betaines and amidobetaines
Ester quats
Ethylene oxide/Propylene oxide
  copolymers
Fatty acid esters ethoxylates and
  polysorbates
Fatty acid ethoxylates

The strengths and weaknesses of renewable products

STRENGTHS
low environmental impact
new opportunities
new functionality

WEAKNESSES/CHALLENGES
natural variability
cost
complexity
unknown technology

alkyl benzenesulfonate production has recently decreased, whereas the manufacture of fatty alcohol ether sulfates is increasing. A new manufacturing process based on a solid catalyst is now available for manufacturing natural product-based fatty acid ester ethoxylates. Among the new natural products, alkyl polyglycerides offer many useful properties for application in personal care products, and are also attracting interest for agricultural applications.

> ‘the potential for renewable feedstocks needs to be more widely recognised’

Dr Peter Carruthers from the University of Reading talked on *LCA: Environmental Benefits of Vegetable Oil-based Surfactants*, in which he described results from a recent research project combining life-cycle assessment (LCA) and cost-benefit analysis (CBA). Oleochemical alcohol ethoxylates use 30 – 40% fewer non-renewable raw materials than the petrochemical-based products. The environmental costs of manufacturing petroleum-based surfactants are consistently higher than those of the vegetable oil-based products, with the rapeseed derived product showing the best figures.

The Political Influences on the Supply Chain (Agenda 2000) was the subject of a talk given by David Clayton from MAFF. Agenda 2000 is an EU initiative paper (published in 1997), aimed at enhancing the European Community’s competitiveness, opportunities for individuals and environmental performance as it grows in size. Renewable raw materials are seen as providing opportunities for agriculture and forestry, and for contributing to job creation in rural areas. However, the EU Commission is at an early stage of thinking on this and a report early in 1999 on any post Agenda 2000 industrial crops regime should set out its proposals.

Dr Ingegard Johansson of Akzo Nobel talked on *Recent Successes: Industrial Applications*. By using a technique known as Principal Component Analyses, it is possible to screen a large number of potential new alkyl glycoside products in terms of a wide range of relevant properties. Structural variants including the chain length and the degree of branching of the hydrophobic part of the molecules have been considered and shown to be highly influential on product properties. These qualitative structure/property relationships can be used to help apply the best products to different applications such as detergency and agrochemicals.

Ian Bartle outlined the collaborative programme on *Competitive Industrial Materials from Non-Food Crops* (See box below).

Link Programme on Competitive Industrial Materials from Non-Food Crops

The objectives of the programme are to overcome technical barriers to the wider use of crop-derived raw materials by industry, with an emphasis on crops of medium to high value that are economically viable. The programme priorities are technologies which:

- improve the value of existing crops
- improve the quality and reliability of crop-derived materials
- address the need for changes in process strategies
- produce new products from plants

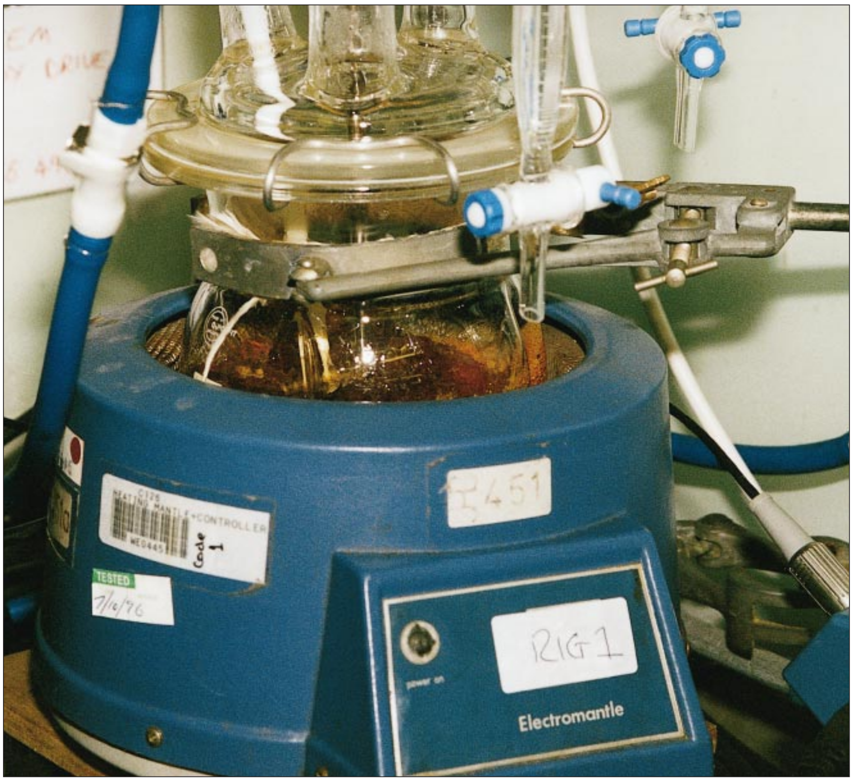
The Role of Renewables in Crop Protection was the title of the talk given by Dr Susan Critchley, from Zeneca Agrochemicals. In a typical herbicide formulation, while the active ingredient is commonly synthetic, most of the other components including the solvent and emulsifiers can be natural product-derived. There are thousands of candidates as emulsifiers. They can be ionic, non-ionic or blends. Similarly, there are a good variety of possible solvents. Under renewable products, there are several likely emulsifiers, including sucrose esters and sorbitan ester ethoxylates while alkylated vegetable oils are among the very few possible solvents.

While there are many drives to encourage the increased use of renewables, the reality is that the range of components currently meeting the criteria for industrial usage is relatively narrow. This provides real opportunities for the development of new natural product-derived substances and for the suppliers of raw materials.

In his talk on *Design Criteria for Sustainable Surfactants*, Dr Paul Reynolds, from the Bristol Colloid Centre considered the essential properties of a surfactant from first principles enabling the optimum product to be designed for individual applications. The ideal cement surfactant, for example, needs to be a good stabiliser, have high pH tolerance and have good mobility. This could well be a polymer possessing carboxylate units, which can co-ordinate surface Ca^{2+} ions of a cement grain. Such functionality could be provided by a synthetic-natural co-polymer.

W J Mulder of ATO-DLO gave a presentation entitled *Surfactants from Plant Proteins*. Proteins have many useful properties including biodegradability, intrinsic surface activity, and a large number of functional groups suitable for chemical modification. They are readily available, of reasonable cost, and are from a renewable source. Protein surfactants are currently used in several food and non-food applications. Useful chemical modifications include the esterification of amino acids with long chain aliphatic alcohols. These modifications can lead to dramatic increases in emulsifying activity, and future uses are likely in both food manufacture (*e.g.* as emulsifiers) and in non-food application (*e.g.* as detergents, wetting agents and in cosmetics).

In his concluding remarks, the Chairman noted the positive attitude of this sector of the industry towards making environmental improvements in its products and processes. The area of renewable feedstocks is ripe for new research and for academic-industrial collaboration, as well as commercial innovation and exploitation, but it is essential that this potential is more widely recognised.



Chemical synthesis in progress at the Centre for Clean Technology, University of York, UK

The RSC Green Chemistry Network

The Green Chemistry Network, recently launched by the Royal Society of Chemistry, will promote the practice and progress of green chemistry, and publicise the benefits of sustainable development for chemists and the general public.

The Green Chemistry Network will provide:

- educational materials for universities and schools to support the teaching of green chemistry concepts and practice
- a newsletter and books on aspects of green chemistry
- training courses for teachers, university and industry researchers and managers
- a national database on green chemistry linked to other overseas networks via the RSC web site
- conferences and seminars for industry and academia
- technology transfer brokerage
- links to other key organisations (learned societies, trade associations, government departments, research councils, educational groups and other green chemistry networks.

The hub of the Green Chemistry Network is located at the University of York, within the new University Centre for Clean Technology, and alongside the Science Education Group (who specialise in the development of educational material for schools and colleges), the Chemical Industry Education Centre and the award-winning Green Chemistry Research Group. The day-to-day running of the network is organised by the network manager, who reports directly to the network director. The director is, in turn, responsible to a management board appointed by the RSC. A technical advisory board ensures representation from other key organisations and provides a valuable source of expertise for the Network.

(A larger article on the Green Chemistry Network appeared recently in *Chemistry in Britain*, October 1998, 43. Interest in the GCN can be registered by email to greennet@york.ac.uk)

1998 Presidential Green Chemistry Challenge Award Winners

The Presidential Green Chemistry Challenge has been running since 1995 to promote pollution prevention and industrial ecology in the chemical industry through ‘cheaper, cleaner, smarter chemistry’. Awards are made for three focus areas (use of alternative pathways, use of alternative reaction conditions, and the design of chemicals for green chemistry) and for a small business and an academic. The 1998 winners are:

Pyrocool Technologies Inc.– for the development and commercial introduction of an environmentally responsible fire extinguishment and cooling agent

Pyrocool Technologies were rewarded for their development of a new fire-fighting formulation of highly biodegradable surfactants designed for use in very small quantities as a universal fire extinguishment and cooling agent. The product does not contain halon gases (ozone depleters), glycol ethers or fluorosurfactants (which can release hydrofluoric acid on use). It is a mixture of non-ionic surfactants, anionic surfactants and amphoteric surfactants with a mixing ratio (with water) of only 0.4%. It has already been employed successfully against numerous fires both in America and elsewhere, notably stopping a major oil tanker fire at sea in just 12.5 minutes thus saving 80% of the ship's cargo.

Argonne National Laboratory – for novel membrane-based process for producing lactate esters: non-toxic replacements for halogenated and toxic solvents

The award-winning ANL process is based on selective membranes that permits the low-cost synthesis of high-purity ethyl lactate and other lactate esters from carbohydrate feedstocks. The process requires little energy input, is highly efficient, and eliminates the large volumes of salt waste produced by conventional processes. In the new process ammonium lactate is converted to the acid which is then converted to the ester. The innovation will eliminate the need for toxic substances, expand the use of renewable carbohydrate feedstocks, and reduce pollution and emissions.

Rohm and Haas Company – for the invention and commercialisation of a new chemical family of insecticides exemplified by CONFIRM™ selective caterpillar control agent

Rohm and Haas have been given their second award for a discovering a new class of chemistry, the diacylhydrazines, that offers farmers, consumers and society a safer, effective technology for insect control in turf and a variety of agronomic crops. One member of the family CONFIRM™ is a breakthrough in caterpillar control. It is chemically, biologically and mechanistically novel. It does not pose any significant risk to the applicator, the consumer and the ecosystem. It will replace older, less effective, more hazardous insecticides.

Caterpillars can be controlled by diacylhydrazines – a new class of insecticides

Flexsys America L.P. – for elimination of chlorine in the synthesis of 4-aminodiphenylamine, a new process which utilises nucleophilic aromatic substitution for hydrogen

Flexsys' award originated from their decision to explore new routes to a variety of aromatic amines, which would not rely on the use of halogenated intermediates. Of particular interest was the identification of novel synthetic strategies to 4-aminodiphenylamine (4-ADPA), a key intermediate in the rubber chemicals family of antidegradants (total world market ca. 150,000 tonnes per annum). The new chemistry is based on nucleophilic substitution for hydrogen (NASH). The new process for 4-ADPA generates 74% less organic waste, 99% less inorganic waste, and 97% less waste water. If just 30% of the world's capacity to produce 4-ADPA and related materials were converted to the new Flexsys process, some 35,000 tonnes per annum less chemical waste and 0.7M tonnes per annum less waste water would be generated.

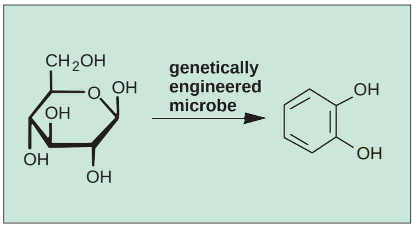
(For a more thorough account of this fascinating new chemistry, see the next issue of *Green Chemistry*)

Professor Barry Trost, Stanford University (academic award) – for the development of the concept of atom economy

Professor Trost's award is in recognition of his enunciation of a new set of criteria by which chemical processes should be evaluated. They fall into the two categories of selectivity and atom economy. The importance of the concept of atom economy is now explicitly acknowledged throughout the chemical industry. Professor Trost has set the challenge for those involved in basic research to create new chemical processes that meet the objectives. A major application will be in the synthesis of fine chemicals and pharmaceuticals, which, in general, are not very atom efficient.

Professors Karen Draths and John Frost, Michigan State University – for the use of microbes as environmentally benign synthetic catalysts

The award-winning Draths-Frost syntheses of adipic acid and catechol use biocatalysis and renewable feedstocks to create alternative synthetic routes to chemicals of major industrial importance. The syntheses rely on the use of genetically manipulated microbes as synthetic catalysts. In excess of 1.9 M tonnes of adipic acid is produced annually and used in the manufacture of nylon 66. Most commercial syntheses of adipic acid use petroleum-derived benzene and involve a last step which employs nitric acid resulting in the formation of nitrous oxide by-product. This leads to some 10% of the annual increase in atmospheric nitrous oxide levels. Benzene is also the starting material for most of the catechol currently produced whereas the Draths-Frost synthesis uses a single, genetically engineered microbe to catalyse the conversion of glucose to catechol.



The Draths-Frost synthesis of catechol

For further information on The Presidential Green Chemistry Challenge Awards Program see http://www.acs.org/govt/whatshot/gcaward.htm and http://www.acs.org/govt/whatshot/gcaward.htm

The Green Chemistry Institute

The Green Chemistry Institute (GCI) was established in 1997 by a group of people from US academia, industry, national laboratories and government. It is a not-for-profit organisation dedicated to environmentally benign chemical synthesis and processing research and education. The GCI organising committee comprises Sid Chao (Hughes Environmental) and Jack Solomon (Praxai) from industry, Dennis Hjeresen and Bill Tumas (both Los Alamos) from the national laboratories, and Joe DeSimone and Bill Glaze (both North Carolina) from academia. Joe Breen is the executive director and can be contacted by email at breenj@westat.com. A GCI Newsletter helps to keep interested parties up-to-date with information on green chemistry awards, conferences and other news.

Opportunities for Research Funding

A number of funding bodies offer grants for research into areas related to chemical clean technology: this list is by no means comprehensive, but describes some of the opportunities available.

United Kingdom Engineering and Physical Science Research Council

The *Chemical Engineering College* covers the transformation of raw materials to final products by substantial physical or chemical changes of state, rather than by mechanical manipulation, fabrication or machining. It is also concerned with such aspects of process design as have an important impact on process technology. Key areas include waste minimisation, clean processes and highly selective separations.

The *Synthetic and Biological Chemistry College* will consider proposals in the area of clean synthesis including the development of new processes characterised by low energy consumption, non-toxic reagents, recyclable solvents, clean effluent and minimum wastage. Other relevant areas include novel synthetic methodology, novel reagents, regioslective and stereoselective synthesis and biological chemistry.

The *Combustion Research Programme* is aimed at enhancing the research on generic and fundamental combustion issues leading to innovation, greater efficiency, lower emissions, greater control and enhanced safety of combustion. Calls for proposals are announced annually. The programme includes within its remit research in areas including waste incineration, catalytic combustion and post-combustion clean-up.

The first call for proposals for *Collaborative Research involving Chemists and Chemical Engineers* was announced in 1998 with a deadline for outlines last November. The scope of the call covered catalysis, clean processes, combustion, electrochemistry and electrochemical engineering.
(Web site: http://www.epsrc.ac.uk)

United Kingdom Biotechnology and Biological Sciences Research Council
The BBSRC Engineering and Biological Systems programme includes applied biocatalysis and encourages collaboration between chemists and biologists in areas such as the control of selectivity and activity in catalysis and the integration of catalysis into synthetic processes. Under ‘environmental technology’ the two priority areas are: availability of pollutants in soils to organisms, and novel liquid effluent technologies.
(Web site: http://www.bbsrc.ac.uk)

European Community Fifth Framework Programme
The European Community’s Fifth Framework Programme for research, technological development and demonstration activities (1998-2002) has competitive and sustainable growth as one of its thematic programmes. Within this, the first key action area is innovative products, processes and organisation which covers the development of new and improved methods of design, advanced equipment and process technologies for production that increase the quality and reduce the costs of processes for services and products. Under ‘eco-efficient processes’, one of four sub-topics, the goal is to minimise ‘full life-cycle impact’ on the environment. This takes account of all essential elements of the industrial system, ranging from extraction, through production, to waste management, with emphasis on resource intensive processes. The priorities are as follows:

- clean and eco-efficient processing technologies
- research aimed at mastering basic phenomena, such as synthesis, catalysis, separation and reaction mechanisms, process modelling and simulation
- impact monitoring and assessment of risks
- *in situ* and on-line recovery of waste: novel processes for treatment, reuse and safe disposal of waste and for upgrading, reusing or dismantling products and production systems

The other sub-topics are: efficient design and manufacturing (including manufacturing technologies and equipment for optimal use of resources and for product miniaturisation), intelligent production, and organisation of production and work. (Web site: http://cordis.lu/fifth/home.html)

USA Environmental Protection Agency
The US Environment Protection Agency's Office of Research and Development awards research grants and fellowships to develop the sound environmental research necessary to ensure policy and regulatory decisions.
(Web site: http://www.epa.gov/ORD/)

USA National Science Foundation
The Chemical and Transport Systems Division of the National Science Foundation supports research that involves the development of fundamental engineering principles, process control and optimisation strategies, mathematical models, and experimental techniques. Special emphasis is on environmentally benign chemical and material processing, and its programmes include chemical reaction processes. The Division of Chemistry's Organic Synthesis programme includes the development of new reagents and methods for organic synthesis and new organic materials. Applications of catalysis are considered under engineering, and under inorganic, bioinorganic and organometallic chemistry.
(Web site: http://www.nsf.gov).

Green Chemistry in UK Parliament

The take-home message from the 1998 RSC Parliamentary Links Day in the UK on ‘Good news from chemistry’ was clear: the solutions to many environmental problems will be found through chemistry. In a series of talks to a large audience, made up of members of the Houses of Commons and Lords, as well as RSC members and distinguished guests, it was made clear that professional chemists are cleaning up existing products and processes, and in many cases replacing these with more environmentally friendly alternatives.

After an introduction on Meeting the Environmental Challenge given by the then President of the RSC, Professor Eddie Abel, Stephen Falder of H Marcel Guest Ltd described the ingenious role of the chemists in effectively helping to preserve the tropical hardwood forests. Were it not for paints and coatings that

Fuel cells are the most promising power source for the electric cars of the future

permitted the use of softwoods in the industrial revolution, the forests would have suffered the same fate as the medieval hardwoods of Europe.

Kirsty Clode of BP Chemicals described the *Cativa* process for the production of acetic acid. This is based on a new catalyst and promoter system involving iridium, which improves energy efficiency and reduces waste and emissions. The process took 3 years to progress from early laboratory trials to installation on a 290 kilotonne per annum plant in the USA.

Fuel cells are widely considered to be the keys to the cars of the future. This was the subject of the talk given by Robert Evans of Johnson Matthey plc. While we cannot completely stop or control emissions from combustion engines, electric vehicles offer zero emission, with the fuel cell considered to be the most promising power source for them. The subject illustrates the importance and value of an interdisciplinary approach by bringing together the areas of environmental chemistry, electrochemistry and catalysis.

More and more we are looking to develop products in a sustainable way. One interesting example of this is the replacement of finite petroleum-based feedstocks by sustainable crop-based feedstocks in areas such as paints. Phil Taylor from ICI Paints described work going on in this area, notably the use of the carbohydrate family and especially starch in the polymer systems used in commercial paints.

Margaret Mills from Zeneca Agrochemicals gave a talk on how the agrochemicals industry is meeting the environmental challenge. This included discussion on chemical ways of reducing the amount of pesticide entering the environment through increased activity (leading to reduced dosage) and the selective use of one isomer.

Finally James Clark described some clay-based and other environmentally benign catalysts that can be used as replacements for hazardous reagents and catalysts that are widely used in the manufacture of fine and speciality chemicals. He also announced the formation of the *RSC Green Chemistry Network.*

A fuller account of the RSC 1998 Parliamentary Links Day including detailed summaries of the talks along with articles on related subjects can be found in Science in Parliament, *July/August 1998.*
Further information on the establishment of the RSC Green Chemistry Network can be found in Chemistry in Britain, *1998,* 43.

UK Government consultation paper: sustainable production and use of chemicals

The UK Government's 1998 consultation paper on sustainable production and use of chemicals sought views on ways in which we might take a much more precautionary approach to chemicals in the environment. While recognising that chemicals underpin the quality of modern life and that the chemicals industries make a significant contribution to the UK economy, the paper addressed the need for the chemicals industry to respond to the challenges of sustainable development and improving eco-efficiency. It also considered the importance of policy making and regulation being more transparent.

With regard to sustainable development it is recognised that important current challenges are the adoption of more eco-efficient practices in the chemical industry and encouraging innovation in resource usage. The government wants to encourage voluntary action (adopting public performance indicators, environmental management systems and engaging in increased dialogue with stakeholders), but it is also considering suitable targets and indicators of progress towards better eco-efficiency. Generally, the Government wants to seek ways to increase the speed of innovation, reduce toxic impact, and develop eco-efficient products.

The consultation paper also recognises the burdens imposed by the new Chemicals Notification Scheme, and the possible need for improving progress under existing legislation. It also addresses the question of possible framework legislation on chemicals at the EU or UN level.

Other issues raised by the paper include options for reducing risks from chemicals, such as self-assessment, replacement and action against chemicals based on persistence, bio-accumulation or toxicity. The paper also invited comments on proposals for facilitating informed public participation in policy making on chemicals in the environment.

Further reading

Sustainable production and the use of chemicals, Department of the Environment, Transport and the Regions, 1998. Document reference 98EP0058

Opportunities for Change: Consultation Paper on a revised UK strategy for sustainable development. Department of the Environment, Transport and the Regions, 1998. Document reference 97EP0277.

The first UK strategy on sustainable development can be found in *Sustainable Development – The UK Strategy*, Department of the Environment, CM2426 HMSO 1994, ISBN 0-10-124262-X.

Royal Commission on Environmental Pollution

In its 21st Report, *Setting Environmental Standards*, the Royal Commission on Environmental Pollution calls for a new approach to deciding environmental policies. The key feature of this new approach is that, as well as drawing on rigorous and dispassionate analysis, there must be greater sensitivity to people's values. The study was led by Sir John Houghton, who stepped down as Chairman in the summer of 1998.

The report emphasises that protecting the environment has become much more complex. Increasingly, the task is to prevent damage which may be global in scale and occur some way into the future. Moreover, the commitment to sustainable development means that pursuing material well-being and enhancing social equity have to be reconciled with protection of the environment. Other points covered in the report include recognising the limits of scientific assessment of environmental issues, the need for independent investigation on research programmes, and the care required to ensure that life cycle analysis approaches encourage, rather than hinder, improvements in stages of the cycle.

> ‘the task is to prevent damage which may be global in scale and occur some way into the future’

Some of the key conclusions from the Royal Commission's 21st Report are listed below:

- Decisions about environmental policies must be based on the scientific evidence and an analysis of technological options, but they must also take into account risks and costs.
- Any body involved in setting standards should, in all its pronouncements, draw an explicit distinction between scientific statements and recommendations it wishes to make after considering a scientific assessment in conjunction with other factors; and should identify clearly what those other factors are.
- When environmental policies or standards are adopted, it should always be made clear in an explicit statement whether they are designed to protect the natural environment, human health, or both, and the degree and nature of protection they are intended to afford.
- In a scientific assessment of an environmental issue there are bound to be limitations and uncertainties associated with the data at each stage. Standard setting and other decision-making procedures should recognise that. The requirement for sound science as the basis for environmental policy is not a requirement for absolute knowledge or certainty and should not be interpreted as such.
- To prevent development of new understanding being restricted by established regulatory procedures, vested interests or small closed communities of experts, publicly funded programmes of environmental research should include provision for independent investigation and enquiry.
- To ensure that the full range of options and repercussions are considered, assessments of technological options carried out as inputs to decisions on environmental policies or standards should be on a life cycle basis.
- Broadly based assessments of options on a life cycle basis must not be allowed to become an excuse for avoiding or delaying significant improvements available at particular stages in the cycle.
- Environmental standards should be set for the smallest area for which it is sensible and effective to do so.
- Use of a combination of direct regulation, economic instruments and self-regulation is the best way to further general adoption of clean technology, whilst not putting at risk compliance with numerical standards set to protect humans and the natural environment against specific hazards.

(Based on a news release from the Royal Commission on Environmental Protection, October 1998)

The Royal Commission on Environmental Pollution (Steel House, 11 Tothill Street, London,UK SW1H 9RE) has a web site at http://www.rcep.org.uk

Royal Society of Chemistry Millennium Conference

Green chemistry and aspects of sustainability will be among the major themes for the Royal Society of Chemistry’s Annual Conference in the year 2000. The conference will be the second in a new style, which is hoped will become the premier event in the RSC calendar. It will be held between 16-20 April 2000 in Manchester, a key geographical centre for the UK chemical industry.

There will be four half-day sessions devoted to aspects of sustainability. The first two sessions will present some of the work funded by the UK’s Engineering and Physical Sciences Research Council (EPSRC) cleaner synthesis programme. During the 1990s this programme has supported university research into a number of key areas including catalysis, novel solvent systems, electrochemistry and reactor design. These sessions will describe the outcome of several of these projects, and include examples of industrial applications. Papers on broader aspects of green chemistry, such as renewable feedstocks and substitution of cleaner products are also planned.

A third session will deal with educational and promotional aspects of sustainability, and will cover national and international efforts to co-ordinate relevant research and training, and the development of new educational materials. Awards for innovation and best practice will be presented. The fourth will deal with general concepts of sustainability. This session should be informative, provocative and sometimes controversial, and will address political and socio-economic issues.

A poster session is also planned and anyone interested should contact Stanley Langer at the Royal Society of Chemistry, Burlington House, London, UK W1V 0BN (langers@rsc.org).

The obtrusive towers of today's chemical complexes should be replaced with more compact and inconspicuous equipment

Process Intensification and Green Chemistry

Colin Ramshaw from the Centre for Process Intensification and Innovation at the University of Newcastle upon Tyne in the UK advocates a step change in the philosophy of plant and process design

When the concept of process intensification was developed within ICI in the late 1970s, the main intention was to make big reductions in the cost of processing systems, without impairing their production rate. The term 'Process Intensification' describes the strategy of making dramatic (100-1000 fold) reductions in plant volume in order to meet a given production objective. It is well known that the cost of the main plant items (*e.g.* reactor, separators *etc.*) only represents around 20% of the cost of a production system, with the remainder being incurred by pipework, structural support, installation and so on. A major reduction in equipment size, with hopefully a high degree of telescoping of plant function, could lead to large cost savings by eliminating support structure, column foundations and long pipe runs.

Advantages

The degree of miniaturisation involved is that needed to generate the cash savings required. Thus volume reductions of the order of 100 times must be our target in order to secure the desired impact on costs. While an individual intensified unit may cost a little more than the conventional equivalent, (although hopefully it will not) it must generate substantial overall savings in the cost of the process system. In addition, the process intensification philosophy should be applied across the whole spectrum of unit operations used in the plant. Bearing in mind the dramatic size reduction which is sought, process intensification will probably involve novel and unusual approaches to equipment design. It is not a strategy for the faint-hearted. Herein lies one of its main disadvantages, namely the lack of new design codes to engender confidence in those who specify new equipment. Radical and unconventional approaches will be the order of the day. Many searching questions will be posed, such as the need for turbulent flow in pipes, the use of batch rather than continuous operation and the application of merely terrestrial acceleration to multi-phase systems, to name but a few. It is a sobering thought that if chemical engineers were given a free hand to

> 'major reductions in equipment size could lead to large cost savings'

design the human digestive and metabolic system, our bodies would be much larger and require many kilowatts to operate them. On the other hand, nature operates unobtrusively with laminar flow in high density matrices (kidneys and lungs) on a semi-continuous basis, and copes with fouling problems by coughing. As scientists and engineers we should not be too arrogant to learn a few lessons from the natural world.

While cost reduction was the original target for process intensification, it quickly became apparent that there were other important benefits, particularly in respect of improved intrinsic safety, reduced environmental impact and energy consumption. Given the anticipated plant volume reductions, the toxic and flammable inventories of intensified plant are correspondingly reduced, thereby making a major contribution to intrinsic safety. This point has been well made by Trevor Kletz, who has commented that 'what you don't have cannot leak'.[1]

With regard to the environment, the intensified plant of the future will be much less obtrusive, with the distillation and absorption towers of our present chemical complexes being replaced by more compact and inconspicuous equipment, which may be hidden by the boundary tree line. In addition, the cost of effluent treatment systems will be less, allowing tighter emission standards to be reached economically. However, the most telling environmental influence of process intensification could well be in the development of new reactor design for truly clean technology. Rather than accept mere 'end of pipe' solution, we must create fluid dynamic environments which allow the intrinsic chemical kinetics free rein. We then have a far better prospect of designing reactors which operate intensively and which give high selectivity. This would facilitate the delivery of a high quality product without an expensive downstream purification sequence.

The high heat and mass transfer coefficients which can be generated in intensified equipment can be exploited to reduce the concentration/temperature driving forces needed to operate energy transformers such as heat pumps, furnaces, electrochemical cells *etc*. This enhances the equipment's thermodynamic reversibility and hence its energy efficiency. For example we have shown at Newcastle that the application of elevated acceleration fields to a simple chlorine cell can reduce its voltage by over 0.4 V.[2] Similarly the Rotex absorption air conditioner[3] which will soon be entering field trials, demonstrates a very high performance while avoiding the arcton/chlorofluorocarbon working fluids used in vapour compression air conditioners. Instead a water solution of mixed alkali metal hydroxides is employed. Therefore innovative applications of process intensification thinking can improve our capacity to meet the energy and global warming targets which were recently agreed at Kyoto.

Spinning disc reactor technology

The nuclear reprocessing industry is likely to be a major beneficiary of process intensification on several counts. Much of the life cycle cost associated with any nuclear operation is involved in the final decommissioning of the equipment. Intensified plant, with its dramatically reduced size and shielding requirement, allows the overall life costs to be significantly reduced. In addition, reprocessing operations must take into account the permitted inventories in each of the process units, in view of criticality considerations. This can result in operation at lower concentrations than those preferred from an economic point of view. Intensified reprocessing avoids this limitation and facilitates the use of higher, more economic concentrations.

The envisaged size reductions inevitably mean that process residence times will be much less than those we are currently used to and our control philosophy must be amended accordingly. Indeed we must ask whether we need control at all in the conventional sense of requiring ultra-rapid feedback from novel fast-response process sensors. The parallel between the slow-response Aga cooker and a fast-response gas flame is relevant here and it is common knowledge that food can be effectively prepared using either! Fast-response reactors open up the possibility of switching to more severe process conditions that would be prohibited in conventional units in view of the tendency to degrade the product. It may be possible to exploit a virtuous circle:- short residence time – higher temperature – faster kinetics – smaller reactor – shorter residence time. In a more general business sense there will be an improved ability to change the process output in response to market demand. Therefore, rather than transport hazardous chemicals on the railways and public highways, it may be feasible to operate a distributed production strategy, with economic manufacture on a customer's site as is currently done for oxygen and nitrogen. This has obvious environmental and safety advantages. However the R & D community must generate appropriate cost-effective process engineering equipment and most importantly, this must be marketed effectively so that it is widely used.

Example

The manufacture of fine chemicals is conventionally performed in stirred vessels operated batchwise to produce typically 50-5000 tonnes per annum. The drug industry operates on a similar basis but with a lower output (5-100 tonnes per annum) having a very high value. In both cases there is a very strong incentive to improve intrinsic safety by minimising process inventories and avoid reaction 'run-away'. As far as the drug industry is concerned there is also strong pressure to reduce the time needed to bring new molecules to market in order to maximise the profitable manufacturing period available within the 20-year life of the patent. Therefore regulatory authority approval for a new process will be achieved much more quickly when continuous production at the laboratory scale can be achieved for the desired rates, using proven equipment, because the need for approval at larger scale has been eliminated, *i.e.* the laboratory scale is the full scale.

Finally, in the context of reducing process labour costs, there is a strong business interest in eliminating inter-batch cleaning by operating the process continuously (on a 'desktop') while being controlled by its dedicated computer. Recent research at Newcastle University[4] has shown that spinning disc reactors (SDRs) are eminently suitable for helping to meet these business objectives for several important processes. Their key characteristic is an ability to stimulate intense heat/mass transfer between a highly sheared liquid film and the rotating disc over which it moves, or the adjacent gas phase. This allows rapid reactions which involve viscous liquids or large exotherms to be precisely controlled.

Following extensive discussions with potential industrial partners in the pharmaceuticals/fine chemicals area, it has become evident that there is considerable interest in the opportunities presented by spinning disc reactor technology. The target reactions are those which are intrinsically fast and exothermic, but which are currently limited by poor heat and mass transfer when performed in conventional stirred vessels. This can result in large inventories of hazardous material, possible reactor run-away and poor quality product. A reactor design based on spinning discs provides an excellent heat and mass transfer environment for the reacting liquid and promises to overcome these disadvantages.

SDR technology offers the possibility of a step change in manufacturing operations, particularly with respect to the following attributes:

- Ability to cope with very fast exothermic reactions (corresponding to heat fluxes of up to 100 kW/m^2 .
- Low inventory/intrinsic safety (liquid film thickness are 50-200 (μm).
- Rapid response (liquid residence times are 1 – 5 seconds).
- Easy cleaning.
- Close control (due to short residence times).

However in general it is perceived that the biggest obstacle to the adoption of SDR technology will be business process issues rather than technology. In particular, chemists involved in process development have both a lack of awareness of SDRs and a fear of 'mechanical' innovations.

At Newcastle we are tackling this problem by manufacturing prototype SDRs in our workshops and then arranging to have them operated in the laboratories of our industrial collaborators. Initial results are very promising and it is anticipated that several joint projects will emerge in order to perfect the technology for each client's application. Ultimately it is the intention to have simple proven versions of SDRs available when the process route is being developed by the chemist. Hopefully this will encourage the adoption of a continuous processing strategy from the outset, because once beakers or flasks are used in the initial process development it is very difficult thereafter to gain support for a continuous option.

It is recognised that a typical fine chemical/drug process involves many operations in addition to the reaction stage. These may be extraction, precipitation, solids removal, drying, distillation etc. In order to bring the desk top plant to reality, intensified versions of the relevant conventional equipment must be made readily available to the process research chemist, otherwise we will end up with the same old pots and pans as before. Although this is a challenging target, the business benefits justify its enthusiastic acceptance.

Conclusions

- A strategy of process intensification requires a step change in the philosophy of plant and process design.
- If effectively implemented, it will lead to major improvements in environmental acceptability, energy efficiency, intrinsic safety and capital cost.
- A major cultural change is required on behalf of chemists, engineers and managers and it is this, rather than technical difficulty, which represents the main obstacle to progress.

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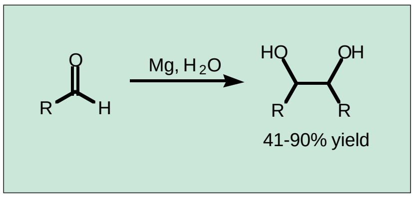
3 'An intensified absorption heat pump,' C. Ramshaw and T. L. Winnington, *Proc Int. Refrigeration*, 1998, vol. 85, p. 26.
4 'The spinning disc reactor for styrene polymerisation,' K. V. K Boodhoo, R. J. J. Jachuck and C. Ramshaw, *Proc. Conf. on Process Innovation and Intensification,* October 21-22, 1998, Manchester, UK (Inst. Chem. Eng.).

Pinacol coupling

Researchers at Tulane University in New Orleans have recently described a simple and clean method for performing pinacol coupling reactions (W.-C. Zhang and C.-J. Li, *J. Chem Soc., Perkin Trans 1*, 1998, 3131). Previously reported methods for this important organic reaction, which leads to the formation of a carbon-carbon bond, have included the use of strong reducing agents such as sodium metal, chromium, vanadium, or $TiCl_3$, under anhydrous conditions in organic solvents. The new method simply involves reacting the aldehyde or ketone with magnesium metal in water. The reaction rate and yield are enhanced by addition of a catalytic quantity of ammonium chloride, giving isolated yields of 41 to 90%, for a large range of substrates. The reaction is most efficient for aromatic aldehydes, and can be performed successfully on alkyl, alkoxy, and halo-substituted benzaldehydes.



Ultrasonic activation

The activation of reactions using non-conventional heating methods such as microwaves or ultrasound is currently the subject of considerable research effort *(see Raj Varma's review article in this issue)*. Takahide Kimura and co-workers at the Shiga University of Medical Science, Japan, have recently demonstrated the existence of an intrinsic difference in reactivity between radicals formed by photolysis and those formed on treatment with ultrasound (*J. Org. Chem.*, 1998, **63**, 6719). Both forms of irradiation caused fragmentation of bromotrichloromethane ($BrCCl_3$) into bromine and trichloromethyl radicals, but only the ultrasonic method produced the dimeric product Cl_3CCCl_3. Also, when irradiating mixtures of oct-1-ene and $BrCCl_3$, they found that 1,2-dibromooctane was formed in a much higher proportion (compared to the $BrCCl_3$ adduct) under sonolysis than photolysis, indicating a preference for Br_2 formation under the former conditions. The authors concluded that, under sonolysis, the radicals are formed in high concentrations in heterogeneous, localised 'hotspots', making them prone to dimerisation. In contrast, photolysis forms radicals in a dispersed state, and will either recombine, or take part in chain reactions.

Sol-gel encapsulated biological material–

efficient, stable catalysts

For several years, researchers have tried, with some success, to immobilise biological catalysts (*e.g.* enzymes, catalytic antibodies, whole cells) on or in robust matrices in order to enhance their lifetimes. Similar approaches have also been investigated for other applications such as biosensors. One commonly utilised approach is the encapsulation of the catalytic species inside a silica sol-gel polymer.

Such polymers are robust and should be good host materials for the biocatalysts, being stable and allowing the preparation of a variety of final forms such as films powders and fibres. Further fine-tuning is also possible through the use of organically modified silanes, leading to a silica with enhanced organophilicity. Such materials are particularly good hosts for lipases, which are much more active in more hydrophobic silica hosts (*Reetz et al., Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 301). Other notable successes include trypsin immobilised in silica, which remains active long after solution phase trypsin has autodigested (Shtelzer *et al., Biotech, Appl. Biochem.*, 1992, **15**, 227). Acid phosphatase has also been reported to have a half-life of 720 seconds in silica at 70 ^{o}C and pH = 5.6, but only 6 seconds in solution under the same conditions. (Braun *et al.* in *Biotechnology: Bridging Research and Application*, ed. D Kamely *et al.*, Kluwer, Boston, 1991).

Difficulties in this approach are many – the formation of a sol-gel polymer involves the hydrolysis of SiOR groups, generating alcohols, which often irreversibly damage the catalyst. Similarly the silica precursors can react with the catalyst directly, rendering it inactive. Other difficulties include shrinkage of the gel upon drying, leading to localised pressure and a reduction in enzyme activity and poor diffusion characteristics causing slow reaction.

Recent research published by Gill and Ballesteros (*J. Am. Chem. Soc.*, 1998, **120**, 8587), and carried out in Madrid and the UK has highlighted a general approach to the problem, which has been shown to give excellent results in a variety of areas. The key to their approach was to move away from the standard silica precursors such as $(MeO)_4Si$ and $(EtO)_4Si$, both of which liberate damaging low molecular weight alcohols, replacing them with glycerol silicates. The glycerol liberated during the preparation of the materials is biocompatible, and helps the gel to dry in a controlled fashion, leading to stable matrices for the enzyme.

The activity of the encapsulated materials is high, between 83 and 98% of the native material for a range of enzymes and whole cells (yeast, *R. miehei*, and *P. oleovorans* were all successfully J6 encapsulated). The amounts of biomaterial encapsulated can also be much higher than with traditional methods, with 20-30 wt% biomaterial being achieved in many cases.

A striking example of the importance of the glycerol-based route over the traditional route is given by the hydrolysis of the nerve agent diethyl 4-nitrophenyl phosphate by a phosphatase enzyme. >95% hydrolysis was achieved under continuous conditions over a period of 700 hours, compared with a steady 35-40% hydrolysis with conventional material. Under the same conditions polyurethane encapsulated material, initially very active, had lost ca. 30% of its original activity.

A series of synthetically useful transformations are also possible, including the synthesis of a pentapeptide *N*-Cbz-L-[Leu^5]-YGGFLNH$_2$, resolution of *(R,S)*-ibuprofen methyl ester to *(S)*-ibuprofen, selective hydrocyanation of hexadienal, and reduction of a ketoester. In all cases, initial activity was higher (2-50%) than that of the non-immobilised material, and loss in activity after prolonged use was much less.

The authors suggest that the excellent results obtained in a wide range of reactions are an interplay of the lower toxicity of the synthesis procedure, the better mixing of the host and the biomaterial, and the excellent porosity characteristics of the host.

Teaching green chemistry

After a career as a synthetic chemist and polymer chemist in industry, Albert Matlack from the University of Delaware in the USA has developed a course in green chemistry. He had been inspired by reading a report in Chemical and Engineering News *(April 4, 1994, p34)* **on a symposium on Environmental Chemistry Education, which put forward the idea of teaching green chemistry.**

Choosing the material for the course involved making a list of every environmental problem that I could think of that involved chemistry. The next step was to attend the symposium on Green Chemistry at the Washington meeting of the American Chemical Society in August 1994. Putting these two together, along with a lot of journal reading, resulted in the following course[1] outline:

1 The need for Green Chemistry
2 Doing without toxic chemicals (illustrated by phosgene)
3 The chlorine controversy
4 Toxic heavy metal ions
5 Solid catalysts and reagents for ease of work-up
6 Solid acids and bases
7 Separations
8 Working without organic solvents
9 Biocatalysis and biodiversity
10 Stereochemistry
11 Agrochemicals
12 Materials for a sustainable economy
13 Chemistry of longer wear
14 Chemistry of recycling
15 Energy and the environment
16 Population and the environment
17 Environmental economics
18 Greening

Some of the impetus for 16 and 17 came from attending meetings of the Ecological Society of America and the American Association for the Advancement of Science.

Green chemistry is the chemistry of a sustainable future. A sustainable future is one that allows future generations as many options as we have today. The industrial ecology being studied by engineers and green chemistry are both parts of one approach to a sustainable future. On the other hand, environmental chemistry, as taught today, is largely the study of what man has put into the environment and its effect, as well as how to remediate contaminated sites.

Green chemistry is interdisciplinary. When I lecture on waste minimisation, ion exchange resins and zeolites, I sound like a chemical engineer. When I talk about population and the environment, I sound like a physician, When I go into renewable energy, I act like a physicist. The social impact of scientific discoveries is included: two common criticisms of scientists are that their training is too narrow and that they do not consider the social impact of their work. I now read at a lot of journals that I barely looked at before, such as *Progress in Organic Coatings*, *Waste Age's Recycling Times*, *Rubber World*, *TAPPI Journal*, *etc.*, and I look at the catalysis and chemical engineering journals more carefully that I used to. Review articles in the Encyclopaedia of Chemical Technology and Ullmann's Encyclopaedia of Industrial Chemistry have also been very useful. Gordon Research Conferences on biocatalysis, membranes and zeoloites have also helped.

'green chemistry is the chemistry of a sustainable future'

The course was first given in the spring of 1995, and was taught for the fourth time in the fall of 1998. Since there was no text, I have written one with about 3000 references. There are several messages which I would like students to take home from the course:

- If you don't use a chemical, you don't have to buy it and you can't lose it.
- Green chemistry need not be expensive. If the whole chemical process is rethought and modified, the result may be cheaper.
- It may be not be possible to green every step of the process at once. For example, a recent synthesis of ibuprofen reduces the number of steps from six to three, but still caries out an acylation step with acetic acid and hydrogen fluoride.
  It may be possible to substitute a solid acid, such as a zeolite, for the hydrogen fluoride.
- Each of us is part of the problem, in that we buy cars painted with solvents, have a bathroom in the house, use electricity, use single-use disposable items etc.
- The problems are social and political as well as technological, and are not just economic.
- There is often a hierarchy of approaches to a problem. To illustrate, trichloroethene is often used to clean metal parts and has become a common contaminant of groundwater and the atmosphere. Putting a lid on the degreasing tank will reduce losses to the air. If the tank is sealed whilst in use, the solvent drained and then vacuumed out, and the vacuum released before opening, very little trichloroethene is lost. If the cleaning is done with an aqueous

detergent, then there is no chlorinated solvent to lose. The biggest change comes from altering the manufacturing process for the metal part so that there is no grease to be removed.

The course is taught for three hours one evening a week, to seniors, graduate students, and to people working outside the university who want to keep up with developments. Some of the most interested students are those from industry, who can relate to the subject matter better. One chemical engineer from DuPont would bring in photocopies of papers that he felt would be useful for the rest of the class. Each section has required outside reading and student exercises, which are designed to be more than just plugging numbers into a formula. Students may be asked to give an opinion on a question such as: Is nuclear energy the solution to global warming, or does it have too many problems? I have them go to the local farm and garden supply store to see what is being sold to put on lawns and crops. Then they look up the toxicities of the chemicals and decide what might happen if these substances washed off into the nearest stream. The next step is to consider friendlier alternatives. The course is designed to take them to the frontiers of research in green chemistry, and they are expected to apply what they learn, not just memorise a list for a quiz. A frequent exam question involves a procedure from organic syntheses that uses a lot of different solvents and toxic chemicals. They are asked what might be done to make it greener.

The challenge of a three-hour class is to use enough interactive class exercises to keep the students awake and alert. If done properly, these can help the students learn to speak in public and to lead group discussions. One exercise involves the selection of two discussion leaders by lot to lead a discussion of a paper assigned for outside reading. I have had the class help me list the toxic heavy metal ions on the blackboard, then completed the list as needed. Then each student gets to pick one to report on at the next class. Every student is required to know the material on all the metal ions for future exams. If reports are longer and cover an applications area, then a dry run may be required. About half an hour before the end of the class I often divide the students into groups to work on a real life problem. After about fifteen minutes, or whenever they seem to have stopped working constructively, we put their suggestions on the board, rotating among the group spokespersons. I then add or delete from their list as needed. A modification of this approach seems to be a good way to revise for exams. They are split into two groups, and each student in group 1 gets to ask one question of group 2. I keep score on the board, but if the same person answers two questions in a row, I only award half a point. When group 1 finishes, the questioning and answering is reversed. After alternating a few times, we decide which team has won.

Field trips are possible. These might include visits to a solar house, a farm using sustainable agriculture, a tannery, a plant manufacturing solar cells *etc.* Term papers are also possible. These might take the form of investigative reporting, where the students check companies to see how green their processes are. For both field trips and term papers, the reports should identify what chemicals are being used and make proposals for reducing the use of energy and toxic chemicals etc. The present course does not have a laboratory, but students could profit by having one that introduces them to techniques that they might not encounter in their regular courses. Experiments might include:

> 'the biggest challenge of green chemistry is to get people to adopt it'

- The synthesis, characterisation and evaluation of a zeolite.
- Running a reaction in an extruder
- Using a catalytic membrane reactor
- Adding ultrasound or microwaves to a reaction
- Making a chemical by plant cell culture
- Performing biocatalysis
- Making a compound by organic electrosynthesis
- Running a reaction in supercritical carbon dioxide
- Using a heterogeneous catalyst

Ideally, the students would use a known reaction first, then do one which hasn't been done before. This may help them to write research proposals.

Some of the other faculty are very sympathetic to the course in green chemistry. Others, however, would prefer that their students take 'core' courses such as advanced organic chemistry and organometallic chemistry. My goal is to stop teaching green chemistry as a separate course and instead insert portions of it into all the other chemistry and chemical engineering courses. However, the chance of getting these faculties to take my course so that they can do this is virtually nil. Some faculty members are happy with what they are doing now and couldn't care less about how things are done in industry. Some schools don't even teach polymer chemistry! There is still the perception that the chemistry of industrial processes and of applications is simpler and less elegant than that done in schools. The artificial delineation of disciplines works against interdisciplinary research, although this is where much new knowledge is found. With chemistry, biology and chemical engineering departments in separate buildings, it is not too surprising that cross fertilisation is low.

The biggest challenge of green chemistry is to get people to adopt it. We would like to see it incorporated into every course from high school onwards. We would like to see all of industry embrace it. The reasons that business has been slow to adopt it are not just economic (see, for example, J. Johnson, *Chemical and Engineering News,* August 17, 1998, p. 34). They may involve a perception of risk in unfamiliar methods or a corporate culture that does not reward risk taking or a change so large that the company is reluctant to start. While my course attracts a few students from industry, I need a lot more.

[1] For an alternative description of a course in Green Chemistry, see Terrence Collins, *Journal of Chemical Education*, 1995, **72**, 965.

Green Chemistry Books

Green Chemistry: Theory and Practice

P T Anastas and J C Warner
Oxford University Press, Oxford, 1998
160 pp.
ISBN 0-19-850234-6
Price £45

Green Chemistry: Frontiers in Benign Chemical Synthesis and Processes

P T Anastas and T C. Williamson
Oxford University Press, Oxford, 1998
448 pp
ISBN 0-19-850 170-6
Price £65

It is both fortuitous and appropriate that the first issue of this journal should be shortly preceded by the publication of two very interesting books by Paul Anastas, founder and promoter of Green Chemistry. The two are very different. The first *Green Chemistry Theory and Practice* is a real book written by Anastas, who is based at the US Environmental Protection Agency, and John Warner, recently appointed professor at the University of Massachusetts at Boston. By contrast, the second, *Green Chemistry: Frontiers in Benign Chemical Synthesis and Processes* is a collection of single and multi-authored chapters, edited by Anastas and his EPA colleague, Tracy Williamson. The books are intended to be complementary and successfully avoid any but the most trivial overlap.

Green Chemistry: Theory and Practice is intended to be a student text and it tells a story. It begins by briefly summarizing some of the more shameful episodes of chemical manufacture: Times Beach, where dioxins in waste oil contaminated the road-side and forced the US federal government to buy up and demolish the whole town; the Love Canal (Niagara Falls) where a school and housing were imprudently built on a chemical waste dump; the Cuyahoga river, which caught fire in 1969; and finally the tragedy at Bhopal, where the unintended release of methyl isocyanate killed perhaps thousands of those living in shanties near the plant. The authors are careful to put these relatively rare incidents into context and to stress the more general problems of chemical emission and waste. Quite early on, they introduce the 'equation'

Risk = function [Hazard, Exposure]

and define Green Chemistry as *'the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products'*. This is a usefully succinct definition, which I have used successfully with my own students. The main part of the book centers on the twelve principles of Green Chemistry, which it is perhaps appropriate to quote here in our first issue.

1 It is better to prevent waste than to treat or clean up waste after it is formed.
2 Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
3 Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
4 Chemical products should be designed to preserve efficacy of function while reducing toxicity.
5 The use of auxiliary substances (*e.g.* solvents, separation agents, *etc.*) should be made unnecessary wherever possible and, innocuous when used.
6 Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.
7 A raw material or feedstock should be renewable rather than depleting wherever technically and economically practicable.
8 Unnecessary derivatization (blocking group,protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible.
9 Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
10 Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products.
11 Analytical methodologies need to be developed further to allow for real-time in-process monitoring and control prior to the formation of hazardous substances.
12 Substances and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires.

These principles are explained briefly and are then expanded into whole chapters (or large parts thereof). As the summary of a vision, the book is brilliant. One can feel the enthusiasm of the authors throughout. As a student text, it probably fails, albeit gallantly. There are really too few chemical examples to justify its use as a course text. It would be very difficult to set an examination based on the book; one could hardly ask the students to memorize the 'Twelve Principles' like the Catechism. Nevertheless, the book is potentially very valuable. I see it as a vehicle for initiating a fruitful dialogue between chemical producers and regulatory enforcers without the confrontation, which often characterizes such interactions.

Green Chemistry Frontiers in Benign Synthesis and Processes is quite different; it contains serious chemistry and is targeted on practicing chemists. It consists of 20 chapters, by a total of 68 authors, all but three of whom are US-based. It begins with an overview by Anastas and Williamson, which is a broad précis of 'Green Chemistry: Theory and Practice' without the Twelve Principles. The remaining chapters are grouped under six headings; Alternative feedstocks and

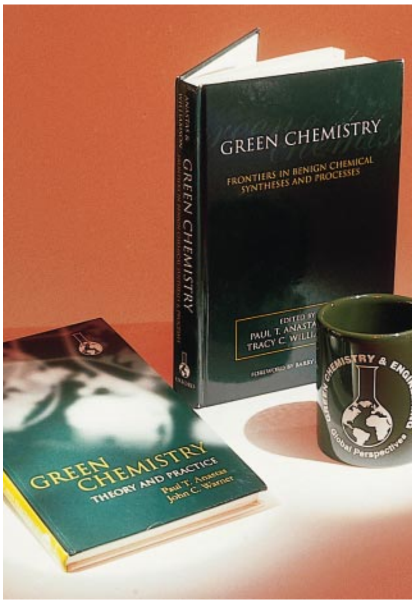


Photo: B. Case

reagents, Catalysis, Biocatalysis and bioprocessing, Alternative solvents, Uses of carbon dioxide and lastly, Alternative synthesis and processing.

Multi-authored books have problems and this one is no exception. The most serious is the disparity in the level of the chapters. Some chapters begin at a high level with no concessions to the non-specialist reader as, for example, in the chapter on Palladium-catalyzed Allylic Alkylation by Barry Trost, who also wrote the Foreword to the book. Others, like the chapter on pollution prevention via molecular recognition by John Warner (co-author of *Green Chemistry: Theory and Practice*), begin at a level which is almost too elementary and risks hiding the elegance of the chemistry. Undoubtedly each reader will pick out different chapters but I particularly enjoyed two, co-incidentally the two with the most authors. The chapter on the design of green oxidants by Terry Collins and his 11 co-workers gives an excellent account of the long development of stable transition metal complexes for catalyzing oxidation by H_2O_2. It is one of the few chapters, which attempt to explain why the chemistry worked and not merely how (it contains the only molecular orbital diagram in the book). The other chapter, which I enjoyed, was from Steve Buelow and his 10 co-authors, summarizing their recent research in homogeneous catalysis in supercritical CO_2. This chapter is particularly welcome because the group at Los Alamos has been quite slow in publishing their results, presumably for reasons of intellectual property.

Overall, the book gives a useful snap-shot of the current state of Green Chemistry. Admittedly, it is heavily biased towards the USA but, after all, Green Chemistry was born in Washington. The major Italian Green Chemistry Consortium is represented in the chapter by its founder, Pietro Tundo, and Maurizio Selva. As far as I can judge, most authors have given due credit to non-US groups in their field but it is a pity that there are no contributions from UK or Japan, both of which have active Green Chemistry Groups. More seriously, there is only one chapter from industry, the last one in the book. It is a lively account of environmental improvements in the commercial synthesis of progesterone by Bradley Hewitt of Pharmacia and Upjohn. The absence of industrial contributions is particularly sad, in view of the excellent industrial examples which have been highlighted by the US Presidential Green Chemistry Challenge initiated by Anastas and his colleagues four years ago.

In summary, these are excellent books but they are for libraries, for regulators or serious practitioners of Green Chemistry. Nevertheless, the message is clear. Green Chemistry is hard, it is intellectually challenging but most of all, it is fundamental to the future of chemical production.

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Organic Reactions in Aqueous Media

Chao-Jun Li and Tak-Hang Chan
John Wiley & Sons Inc., New York, 1997
214 pp
ISBN 0-471-16395-3
Price $59.95

Many approaches for minimising the environmental impact of a chemical process involve reducing the quantities of chemicals consumed in that process. This may be by replacing stoichiometric reagents with catalytic ones, or running the reaction without any solvent at all. In many organic reactions, the second option may not be possible, as the solvent is involved in the reaction either directly, or indirectly by stabilising transition states or acting as a heat transfer medium. On too may occasions, sadly, little consideration is given to the choice of solvent: it is chosen because it worked in the last reaction, or because it is readily available.

Where a solvent must be used, water is, without doubt, the most acceptable in terms of cost and environmental impact. However, despite its large liquid range and extremely high specific heat capacity, it is frequently overlooked as a solvent for organic reactions, perhaps because of a misplaced belief that organic reactions must require an organic solvent. Written by leading researchers in the field, Organic Reactions in Aqueous Media endeavours to show that this belief is far from true, citing hundreds of examples of common, more obscure reactions which can be performed in water, aqueous salt solutions, and mixed water-organic co-solvent systems.

An illustrative example given in the book is the Barbier-Grignard reaction, which is of great synthetic importance due to the formation of a carbon-carbon bond. Undergraduate practical classes teach students to perform this type of reaction under scrupulously anhydrous conditions using magnesium or zinc metal, and the reaction is followed by an aqueous work-up step. Recent research has, however, produced a startlingly different procedure, which exploits the relatively low first ionisation energy of indium, along with its resistance to boiling water and reluctance to form oxides. Using indium metal in place of magnesium allows Barbier-Grignard reactions to be performed in water, and the reaction conditions are mild enough to allow the use of functional groups, such as acetals and carboxylic acids, which would not survive the conventional system.

Covering numerous other examples, there are chapters on nucleophilic additions and substitutions, oxidations, reductions and hydrogenations, and metal catalysed organic reactions including Heck reactions and hydroformylations. There is also a short, but vital, chapter on industrial applications of some of these reaction systems.

There is a strong overall bias towards synthetic organic chemistry, ranging from small, relatively simple molecules, right up to natural products and multi-ring compounds, with a greater emphasis on what can be done than why the reactions proceed. However, the introduction to the book does discuss the factors which may influence reactivity in aqueous systems, reactions and solubilities in supercritical water, and the ‘hydrophobic effect’. The use of aqueous salt solutions is considered too: the ability to alter the internal pressure of an aqueous solution by changing the concentration or nature of the solute may be exploited in reactions which are strongly influenced by pressure. For example, the rate of the Diels–Alder reaction between cyclopentadiene and butenone in water is doubled on the addition of lithium chloride.

This volume is an excellent and enlightening attempt to bring together current knowledge on the surprisingly wide range of organic reactions which may be performed in aqueous systems. Water as a solvent may not be the solution to every problem, but it should certainly be high on the list of solvents to try. If a new edition of this book were to be published in ten years time, I would be very surprised if the chapter on industrial applications had not grown enormously.

SJT

Massachusetts Toxics Use Reduction Act

By the end of the 1980s significant shifts had occurred in attitudes towards pollution. Particularly in the United States, phrases such as pollution control were being replaced by pollution prevention or source reduction. In one US state, this ethos was enshrined in law. Becky Allen examines the impact of the Massachusetts Toxics Use Reduction Act on chemical users in the state and whether it could have an effect on green chemistry.

As Green Chemistry goes to press, the latest data on the use of toxic chemicals and generation of toxic waste in Massachusetts during 1997 are being analysed by the Massachusetts Toxics Use Reduction Institute and the Department of Environmental Protection. The analysis – due for release in Spring 1999 – is significant because enshrined in the Toxics Use Reduction Act 1989 (TURA) is the target to cut toxic waste generation in the state by 50% by 1997. However, between 1990 and 1996, Massachusetts firms had already reduced hazardous waste generation by 34%, and cut their use of toxic chemicals by 24%.

According to the Massachusetts Toxic Reduction Programme*: ‘A central goal of TURA is to cut in half by 1997 the quantity or toxic and hazardous wastes generated by Massachusetts industries – using toxic use reduction techniques – while enhancing the capacity of Massachusetts businesses to grow and prosper.’

The Act itself defines toxics use reduction as ‘in-plant changes in production processes or raw materials that avoid, or eliminate the use of toxic or hazardous substances or generation of hazardous by-products per unit of product, so as to reduce risk to the health of workers, consumers or the environment, without shifting risks between workers, consumers, or parts of the environment.’

TURA only applies to certain industries in the state, including mining and manufacturing, to companies with over ten full-time employees, and firms that manufacture, process or use specified volumes of chemicals on various US Environmental Protection Agency lists. Where it does apply, companies are required to file annual reports giving quantities of each listed chemical used or generated, and to submit a toxics use reduction plan every two years. Fees are charged by the state for filing the forms and for help in preparing plans.

A cost-benefit analysis between 1990 and 1997 estimates total savings to businesses under TURA of $14 million, excluding any net benefit due to reduced occupational and environmental exposures. Costs totalling $76.6 million include compliance costs of $49.4 million as well as capital investment by

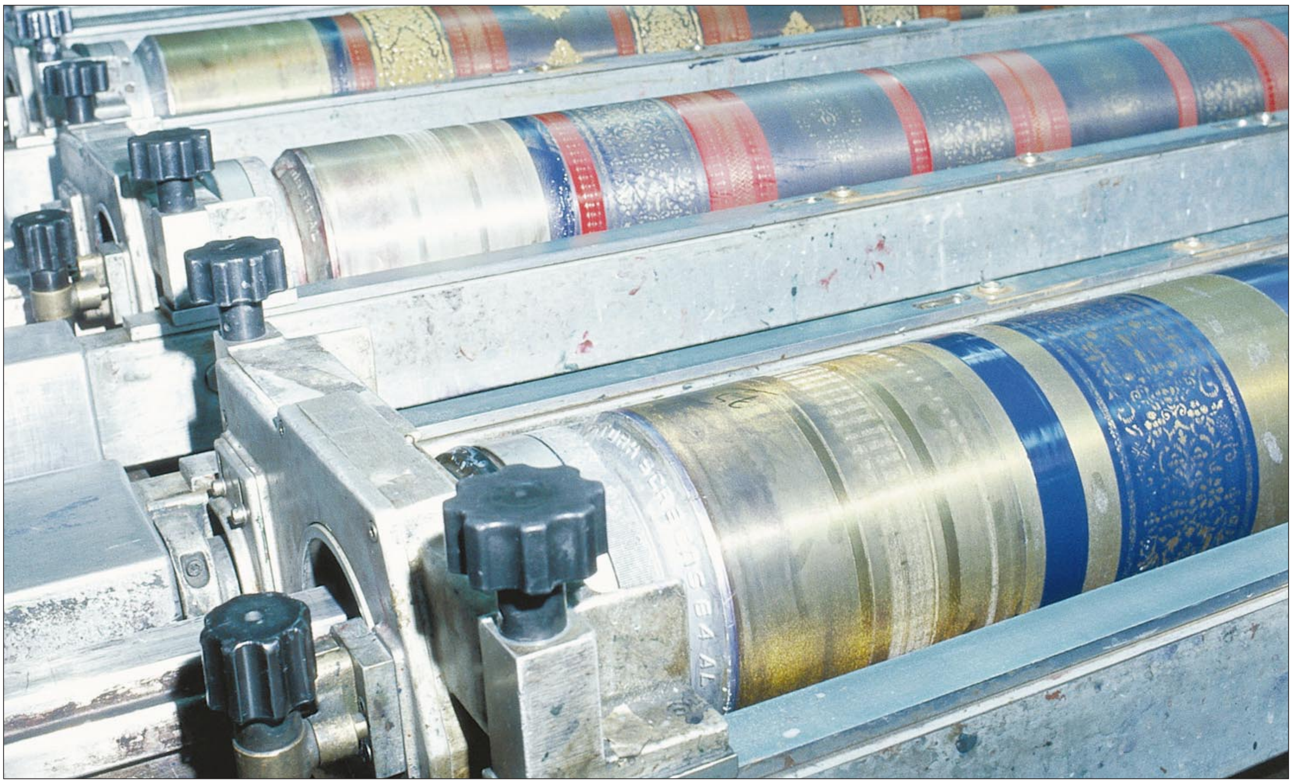
The goal of TURA is to cut toxic and hazardous wastes generated by Massachusetts industries, while enhancing the capacity of businesses to grow and prosper

TURA establishes six toxics use reduction techniques:

- **chemical input substitution**
- **product reformulation**
- **production unit redesign or modification**
- **production unit modernisation**
- **improvement in operations and maintenance**
- **closed-loop recycling**

Planning toxics use reduction in a business involves a step-by-step process:

- **setting goals and priorities**
- **analysing the process**
- **identifying TUR options**
- **evaluating TUR options**
- **implementing TUR changes**
- **measuring progress**



Textile printing is one area where companies are participating in TURA programmes

businesses. Benefits largely accrued from savings in firms' operating costs ($88.2 million).

Among the 600 companies participating in the TURA programme is the Cranston Print Works Company of Webster, MA. Cranston prints and finishes cotton and blended fabrics, and the printing process involves acid treatment of dyes. Process changes included in-process acid recycling and carbon dioxide treatment of wastewater. The acid stream in-line recovery unit has reduced the company's annual acetic acid use by over 130,000 kilos, and the substitution of carbon dioxide for sulfuric acid to treat the alkaline wastewater has eliminated an annual use of sulfuric acid of around 1.2 million kilos.

According to Cranston, the capital expenditure on the acid recycling system was $235,000, and $93,000 on the carbon dioxide wastewater system. Annual savings include $84,000 previously spent on acetic acid, and $200,000 in wastewater treatment costs.

Despite its impact on chemical use and waste generation, TURA has been a less important catalyst for green chemistry in Massachusetts (a state which does not have a large chemical manufacturing sector) than consumer pressure. Feedback from industry in Massachusetts supports the business theory that customer needs drive new products and innovation, says Liz Harriman of the Massachusetts Toxics Use Reduction Institute. According to Harriman: 'I do not think that the chemical industry in Massachusetts has felt strongly motivated to go to green chemistry by TURA . . . However, some progressive chemical companies and formulators of chemistries have made a lot of progress in going to safer formulations.'

Instead, Harriman thinks that the impetus will come from further down the supply chain. 'It makes sense that the users of toxic chemicals have nothing to lose and everything to gain by going to less hazardous, cost-effective materials. On the other hand, it is risky and expensive for chemical manufacturers to develop new materials, when the existing ones are working and selling . . . We are counting on the users of those chemicals and formulations, who are more motivated to use safer chemistries, to convince their suppliers that "that's what the customer wants." This is, of course, a much more convincing argument for the chemical company,' she says.

Top five toxic chemicals used in Massachusetts (by volume):

1 Styrene monomer
2 Copper
3 Sodium hydroxide
4 Hydrochloric acid
5 Sulfuric acid

Top five toxic chemicals generated as by-product in Massachusetts (by volume)

1 Sodium hydroxide
2 Toluene
3 Sulfuric acid
4 Methyl ethyl ketone
5 Ethyl acetate

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*Massachusetts is Cleaner & Safer: Report on the Toxics Use Reduction Program, Massachusetts Toxics Use Reduction Programme, 1997. Evaluating Progress: a Report on the Findings of the Massachusetts Toxics Use Reduction Program Evaluation, Massachusetts Toxics Use Reduction Programme, 1997.

First Postgraduate Summer School on Green Chemistry, Venice, Italy

August 29 – September 6, 1998

Venice – the venue for the first Green Chemistry Summer School

The First Postgraduate Summer School on Green Chemistry was held in Venice, Italy (August 29 – September 6, 1998) at the new campus of Venice International University (VIU – http://www.unive.it/–viu), on the island of San Servolo.

Its aim was to teach young graduate and postgraduate chemists from different European countries how to approach pollution prevention from a chemical standpoint. It was the first of a series of three Summer Schools: the second will be held from September 6 to 12, 1999; and the third in the year 2000. The deadline to apply for this years' School is 15 June (see http://www.unive.it/inca).

Each Summer School is organized by the Italian National Interuniversity Consortium 'Chemistry for the Environment' (INCA). Its director, Professor Pietro Tundo, chair of Organic Chemistry of the Department of Environmental Sciences of Ca' Foscari University in Venice, is an active researcher in Green Chemistry. He was among the first European scientists to indicate Green Chemistry as a fundamental tool to approach pollutant source reduction for the chemical industry.

Funding is provided through activity no. 4 of the 'Training and Mobility of Researchers' (TMR) program of the European Commission, entitled 'Euroconferences, Summer Schools and Practical Training Courses' (http://www.cordis.lu/tmr/home.html). It covers travel and lodging scholarships for European students who are accepted at the School, while funds to cover instructors' expenses come in part from INCA itself.

To reduce costs, and to accelerate and simplify application procedures, all contacts are maintained through a web page (http://www.unive.it/inca) and the authors' e-mail alvise@unive.it.

The intended participants are young researchers in chemistry (the age limit is 35) from the European Union, either from academia or industry, interested in understanding the issues of pollution prevention, and to address them through the innovation of chemical processes, and also in view of the need to anticipate the evolution of environmental regulations, for the chemical industry. Instructors are selected based on their internationally recognized contribution to research and promotion of Green Chemistry. Lessons are at the level of state-of-the-art research contributions, but also cover background material extensively. Existing clean chemical processes, case histories, and topics related to current research in Green Chemistry are explained, in order to familiarize students with the strategies behind designing 'greener' synthetic routes.

For the first year, emphasis was given to the description of chemical technologies for new catalytic processes, and to the use of alternative solvents and reagents; a total of 12 lessons were held. Policy issues, which steer the development of Green Chemistry at the industrial, academic and governmental levels, were also widely discussed, prompted by the interest shown by students.

Forty-five students attended, from thirteen different countries. A poster session gave them the opportunity to establish new contacts, and to exchange information about their research in Green Chemistry. Posters of high scientific level were presented by most of the students attending; three were judged outstanding, and were presented with a book award and a certificate by the instructors. Marcella Bonchio (in Professor Scorrano's group at the University of Padova) was recognized for her work on 'Ti(IV) and Zr(IV)/chiral trialkanolamine peroxo complexes: a new class of catalytic enantio selective oxidants'; William Gray (in Professor Poliakoff's group at the University of Nottingham, UK) won with a poster on 'Organic reactions in supercritical fluids'; and Annegret Stark (in Professor Seddon's group at The Queen's University of Belfast, UK) for a poster on the 'Manufacture of two important ionic liquids'.

The following is a short summary of the lectures, divided into the three focus areas of last year's Summer School. Each session often evolved into an interactive discussion, rather than a traditional lecture, which followed the pattern laid out by the speaker.

Catalytic processes

The development of new catalytic systems proved to be one of the most commonly used approaches towards cleaner chemical processes. In fact, seven of the twelve lectures had catalysis as the main focus. In particular, solid catalysts were treated extensively, since they have the advantage of being non-toxic, easy to handle and recoverable; they can be made polyfunctional; and they may afford shape selectivity, and minimize waste. Bernard Witholt (ETH – Zürich, Switzerland) described the use of biocatalysis in the production of a variety of compounds, both in aqueous media and in organic solvents. An overview of the advantages of enzyme catalysis was given, *i.e.* stereo- and regio-specificity, limited use of toxic reagents, limited generation of harmful side products, technical advantages, not to mention the psychological advantage of being able to label the products as 'biological'. Future trends to expand the scope of biocatalysis were finally outlined. Mieczyslaw Makosza (Polish Academy of Sciences, Poland) was among the first scientist, in the early 1960s, to develop phase transfer catalysis and to explain the mechanism of the reaction at the interface. His lecture described a number of applications of this technique (*e.g.* in carbene chemistry), and it highlighted the environmental advantages of this technique over traditional processes, and its applicability even at the industrial level.

James Clark (University of York, UK) showed the applications of heterogenised catalysts (*e.g.* zeolite and clay supported peracids, fluorides, hydroxides, metals, alkoxides, *etc.*), for a variety of reactions. These catalysts have the advantage of being non-toxic, easy to handle and recoverable and minimize waste.

Michel Guisnet (Universite de Poitiers, France) described zeolites, their chemical characteristics, and their applications as catalysts for reactions such as oxidations, reductions, alkylations, and in the refining industry (*e.g.* for hydrocracking and isomerization). Other reactions, which occur selectively in the presence of zeolites, were also addressed.

Jose M. Lopez Nieto (Universidad Politecnica de Valencia, Spain) talked about supported acid and superacid solid materials and their use as alternative catalysts for reactions of the petrochemical industry. In addition, the alkylation reaction of isobutane catalyzed by solid acids was discussed.

Ferruccio Trifirò (Università di Bologna, Italy) compared the traditional processes for the production of methyl methacrylate and cyclohexanone oxime, with alternative industrial processes of low environmental impact. The use of *n*-butane in place of benzene for the production of maleic anhidride, was also covered. The second part of this lesson was devoted to heterogeneous oxidation catalysts for the production of fine chemicals, en route to more sustainable chemical processes.

Wolfgang Hölderich (RWTH Aachen, Germany) focused on the characterization by spectroscopic methods of solid catalysts, used for industrial ammoximation, and isomerization reactions.

Alternative solvents and reagents

The use of new harmless, inexpensive, and recoverable solvent systems in place of traditional toxic organic solvents is another area of widespread interest.

Joe DeSimone (University of North Carolina at Chapel Hill, USA) was among the first to recognize the applicability of fluid CO_2 as a solvent for extractions, separations and chemical reactions. The development of perfluorinated surfactants for these purposes, using CO_2 as the non-polar solvent, was described. The industrial application of such systems to the dry-cleaning industry in the US gave a clear indication of the industrial applicability of research in the field of Green Chemistry.

Jan Engberts (University of Groningen, The Netherlands) showed that Diels–Alder reactions, are accelerated in water relative to organic solvents; an effect that can be explained by hydrophobic destabilization of the initial state, and by the stabilization of the transition state. In some case water showed also a favorable effect on selectivity. Lewis-acid catalysis in water was also addressed, showing that, in some cases, extremely efficient catalysis can be obtained.

Kenneth Seddon (The Queen's University of Belfast, UK) gave a captivating lecture on the preparation and use of ionic liquids as clean solvents. Among the advantages of such solvent systems are their high polarity, large liquid range, low vapor pressure, easy recovery, and stability to water. Ionic liquids can be designed to optimize a reaction, and are promising for two-phase catalysis.

In addition a promising area for the development of cleaner processes is to replace harmful reagents with Green reagents. Pietro Tundo (Università Ca' Foscari di Venezia, Italy) developed a lecture on the use of dimethyl carbonate (DMC) as a green reagent. DMC is now produced by oxidative carbonylation of methanol rather than from phosgene. It was shown that it can be successfully employed in methoxycarbonylation reactions and methylation reactions, in place of traditional toxic and dangerous reagents such as dimethyl sulfate and methyl iodide.

Green Chemistry Research Policies

A lecture was devoted to the factors that stimulated the birth of the concepts behind Green Chemistry. Joe Breen (The Green Chemistry Institute, USA) and Paul Anastas (Environmental Protection Agency, USA) described the approach taken in the U.S. to encourage industry and academia to pursue the development of cleaner chemical technologies. Many examples were given of successful greener processes, which are currently being developed by industry and academia. The need for efficient dissemination of information on Green Chemistry, at all levels of society, industry, government, and academia, was stressed.

A round-table discussion was also held, attended, not only by the instructors and students of the Summer School, but also by Robert Visser (OECD Head of the Environmental Health and Safety Division) and Canice Nolan (European Commission Directorate General XII). Discussion led to further understanding of the policy issues and funding matters, particularly in the EU, regarding Green Chemistry. Not surprisingly, all students found this session particularly interesting, a fact that indicated a concern, not only for fundamental aspects of research, but also for its political aspects.

Finally, also thanks to the relaxed and interactive atmosphere established between attendees and instructors, a number of comments and suggestions were collected, to improve the Summer School on Green Chemistry in 1999 and 2000.

Students wrote a document (see following article), which indicates that they often learned for the first time at this Summer School about the concept of ‘Green Chemistry’, and about the novel idea that chemical technologies and processes can and should be sustainable and environmentally compatible. In this respect the students recognized the importance of the principles laid out during the School. Among other ideas, the creation of a mailing list and web server was proposed, in order to establish a network of researchers and institutions, dedicated to the international exchange of information on Green Chemistry. It is currently being prepared within INCA’s web site, and it will hopefully contribute to consolidate the network of young ‘green’ chemists started at the Summer School.

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Young Chemists establish first European Network on Green Chemistry

The students who attended the first Green Chemistry Summer School have established the first European Network on Green Chemistry for students and other young scientists with strong commitments to the principles and practice of green chemistry. A Web page has already been set up and it is hoped that once the network has been established projects can be undertaken in association with related bodies both in industry and academia. Close links have already been established with the Royal Society of Chemistry's Green Chemistry Network (*via* Professor J. Clark, University of York, UK), the Green Chemistry Institute and INCA. The website also includes links to other related sites and information about Green Chemistry literature.

Our major concern

Our driving force is the promotion of Green Chemistry. We consider this to be the implementation of environmentally benign processes in industry, private enterprises and academia. We hope to bring the ideas of Green Chemistry closer to chemists of all fields, who should act responsibly and in the interests of global sustainability.

Our strategy

We plan on a rapid and efficient exchange of ideas between chemists, both in Europe and throughout the world:

- the ENGC will provide expertise in Green Chemistry;
- we will work on an efficient communication between people from industry, academia and politics;
- we will participate at meetings involving Green Chemistry;
- we plan to organise workshops and meetings;
- we will work on improving the reputation of chemistry as a whole.

The ENGC is organised by the following individuals:
Marcella Bonchio, University of Padova, Italy (marcella@chor.unipd.it)
Emanuelle Fromentin, University of Poitiers, France (fromentin@hotmail.com)
Keith Gray, University of Nottingham, UK (pczwkg@unix.ccc.nottingham.ac.uk)
Markus Haider, MIT., USA. (mmhaider@mit.edu)
Michael Valkenberg, RWTH Aachen, Germany (Valkenberg@rwth-aachen.de)

The ENGC can also be contacted at http://www.engc.org.

Statement by participants at the Summer School

Introduction

We as chemists understand the damage caused to the environment by many chemical processes. We recognize our responsibility to work towards a chemistry that will sustain and improve the quality of life for future generations. We think this can be achieved through a process governed by the principles of Green Chemistry as were laid down during lectures and discussions at this summer school. A revolutionary change like this can only be attained by close cooperation of the chemical industry and academia with responsible politicians, economists, non-governmental organizations and the general public.

To further this cause we have outlined the major objectives that should be addressed by the chemical community:

- Education – emphasis on environmental issues.
- Solvents in chemical processes – reduction or even replacement by environmentally benign systems.
- Atom efficiency of chemical reactions – reduction of chemical waste by increasing yields and selectivities of the processes.
- Avoidance of hazardous substances as far as possible.
- Energy efficiency of chemical processes.
- Remediation – water, air and soil

Final goal: overall sustainability

Conclusions

We, the participants of this Summer School on Green Chemistry, very much appreciate this meeting in Venice. It stimulated intense discussions on all aspects of Green Chemistry. We believe our objectives could be advanced through further meetings of this kind that may lead to the establishment of a European network of young chemists. We anticipate the possibility of exchange and co-operation on these issues with related groups worldwide. In this respect we would greatly appreciate continued funding.

Acknowledgments

We thank all those involved in organizing this event, particularly Professor Pietro Tundo, Dr. Alvise Perosa, their co-workers and all the lecturers. We also would like to express our gratitude to the European Union for funding.

Conference Diary

March 1999

Green Chemistry Symposium and 217th American Chemical Society National Meeting — **March 21–25**
Anaheim, USA
(natlmtgs@acs.org)

5th European Symposium on Electrochemical Engineering — **March 24–26**
University of Exeter, UK
(http://sci.mond.org)

RSC Carbohydrate Group Spring Meeting: Carbohydrates as a base for therapeutic agents — **March 25–26**
University of York, UK
(robert.field@st-and.ac.uk)

Engineering Solutions to Formulation Problems — **March 25**
UMIST, Manchester, UK
(carl.formstone@ukag.zeneca.com)

5th International Conference on Solar Energy Storage and Applied Photochemistry (SOLAR'99), and 2nd International Training Workshop on Environmental Photochemistry (ENPHO'99) — **March 30–April 4**
Sonesta Hotel, Heliopolis, Cairo, Egypt
(http://www.photoenergy.org/solar99.html)

Biotechnology for Chemists Symposium — **March 31**
London, UK
(conference@rsc.org

April 1999

6th Meeting on Supercritical Fluids: Chemistry and Materials — **April 10–13**
University of Nottingham, UK
(http://www.nottingham.ac.uk/supercritical/conf2.htm)

2nd International Conference on Organic Process Research and Development — **April 20–23**
New Orleans, USA
(scientificupdate@dial.pipex.com)

May 1999

195th Meeting of the Electrochemical Society — **May 2–7**
Seattle, WA, USA
(http://www.electrochem.org/meetings/195/meet.html)

16th North American Catalysis Society Meeting: Catalysis and the Environment — **May 30–June 4**
Boston, MA, USA
(http://www.dupont.com/nacs/Boston99/)

July 1999

Gordon Conference on Green Chemistry — **July 11–16**
Oxford, UK
(jhc1@york.ac.uk)

Advances in Polymerisation Methods: Controlled Synthesis of Functional Polymers — **July 12–15**
Prague, Czech Republic
(sympo@imc.cas.cz)

Pre-OMCOS Symposium on Organometallics and Catalysis — **July 14–16**
Rennes, France
(http://www.univ-rennes1.fr/umr6509/pre-OMCOS)

10th IUPAC Symposium on Organometallic Chemistry Directed towards Organic Synthesis — **July 18–22**
Versailles, France
(genet@ext.jussieu.fr)

7th International Symposium: The Activation of Dioxygen and Homogeneous Catalytic Oxidation–ADHOC99 — **July 19–23**
University of York, UK
(http://www.rsc.org/lap/confs/adhoc-99.htm)

August 1999

218th American Chemical Society National Meeting, with symposium on Green Chemistry — **August 22–26**
New Orleans, USA
(natlmtgs@acs.org)

September 1999

4th European Congress on Catalysis (Europacat 4): Catalysis and Chemical Technologies for a Sustainable Future — **September 5–10**
Rimini, Italy
(http://www.fci.unibo.it/ec4)

Euromembrane 99 — **September 19–22**
Leuven, Belgium
(http://www.vito.be/euromembrane99/)

Biotrans '99 — **September 26–October 1**
Sicily, Italy
(http://dept.chem.polimi.it/biotrans)

Green chemistry: challenges and opportunities

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Summary

The green chemistry revolution is providing an enormous number of challenges to those who practice chemistry in industry, education and research. With these challenges however, there are an equal number of opportunities to discover and apply new chemistry, to improve the economics of chemical manufacturing and to enhance the much-tarnished image of chemistry. In this article which is based on his Inaugural Lecture at the University of York in 1998, Professor Clark reviews some of the challenges, considers some of the new and successful "greener" chemistry in practice and uses two areas of chemistry to examine the scale and diversity of current problems and the exciting opportunities for innovative chemistry research and application.

James Clark obtained his BSc and PhD degrees from Kings College, London. After postdoctoral positions in Canada and Exeter he moved to York in 1979. He is currently Professor of Industrial and Applied Chemistry and the Royal Academy of Engineering–EPSRC Clean Technology Fellow in Heterogeneous Catalysis. His research interests cover various aspects of Green Chemistry including clean synthesis and new materials. He was recently appointed as the first director of the RSC Green Chemistry Network.

The challenges to chemists[1]

Sustainable development is now accepted by governments, industry and the public as a necessary goal for achieving societal, economic and environmental objectives. Within this, chemistry has a key role to play in maintaining and improving our quality of life, the competitiveness of the chemical industry and the natural environment. This role for chemistry is not generally recognized by government or the public. In fact chemicals, chemistry and chemists are actually seen by many as causes of the problems.

The European Chemical Industry Council (CEFIC) survey in 1994 showed that 60% of the general public had an unfavourable view of the chemical industry and in the USA, a survey carried out for the Chemical Manufacturers Association (CMA) in 1993 showed that only 26% were favourably disposed towards the industry. The pharmaceutical and plastics sectors scored better than the chemical industry as a whole, possibly because the general public are more aware of their products and their benefits. The chemical industry is consistently regarded less favourably than the petroleum, gas, electricity, lumber and paper industries. The main reasons given for unfavourable opinions of the chemical industry are concerns over adverse environmental impact, transport, safety and waste. Less than one third of those interviewed believed that the chemical industry is concerned about protecting the environment and less than one half believed that the chemical industry is working hard to develop techniques to solve environmental problems.

The negative public opinions of the chemical industry can in some ways be contrasted with the tremendous economic success of the industry. It is one of the most successful and diverse sectors of manufacturing industry in many regions of the world. The range of chemical products is enormous and these products make

Green Context

This review of Green Chemistry has been written by James Clark whose contribution to the development of the subject in the UK has been recognised in numerous ways; for example he was awarded the SCI Environment Medal and holds a Royal Academy of Engineering/Engineering and Physical Sciences Research Council Clean Technology Fellowship. It is an authoritative paper reviewing the challenges facing the chemical industry, providing examples of significant advances in manufacturing routes to a number of products as well as drawing attention to the importance of education. In short it explains what green chemistry is all about.

Timothy Lester, Deft Technology and Design.

an invaluable contribution to the quality of our lives with manufacturing plants having capacities ranging from a few tonnes per year in the fine chemicals area to 500,000 tonnes per year in the petrochemicals area. However, these manufacturing processes also lead to millions of tonnes of waste, and the reduction or elimination of this waste is now a central issue for the industry, the authorities, and the general public. There is a danger that if the economic success of the industry is not matched by a clearly perceived improvement in environmental performance then, at best, the industry will be regarded by the general public as a necessary evil.

The challenge for chemists and others is to develop new products, processes and services that achieve the societal, economic and environmental benefits that are now required. This requires a new approach which sets out to reduce the materials and energy intensity of chemical processes and products, minimise or eliminate the dispersion of harmful chemicals in the environment, maximise the use of renewable resources and extend the durability and recyclability of products—in a way which increases industrial competitiveness.

Some of the challenges for chemists include the discovery and development of new synthetic pathways using alternative feedstocks or more selective chemistry, identifying alternative reaction conditions and solvents for improved selectivity and energy minimisation and designing less toxic and inherently safer chemicals. In chemical synthesis, the ideal will be a combination of a number of environmental, health and safety, and economic targets (Fig. 1).

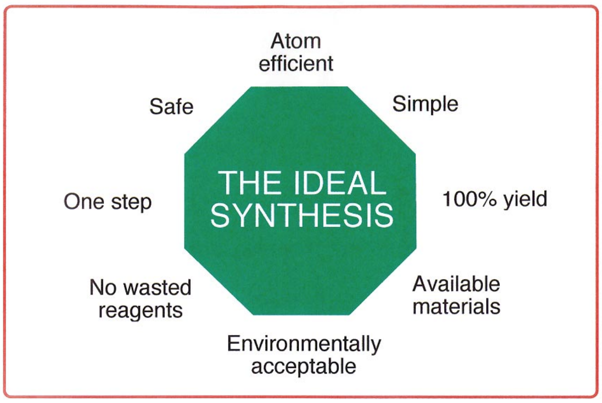

Fig. 1 The ideal synthesis.

Although many chemists, and some large and smaller companies, are actively pursuing ‘green chemistry’ there are still many barriers to progress. These include a general lack of awareness and training in schools, universities and industry and a management perception that green chemistry is a cost without benefits.

The drive towards clean technology in the chemical industry with an increasing emphasis on the reduction of waste at source will require a level of innovation and new technology that the chemical industry has not seen in many years. Mature chemical processes, that are often based on technology developed in the first half of the 20th century, may no longer be acceptable in these environmentally conscious days. ‘Enviro-economics’ will become the driving force for new products and processes. This can be seen by considering the ever-escalating and various ‘costs of waste’ (Fig. 2).

The costs of waste can truly be enormous. It has been estimated that compliance with existing environmental laws will cost new EU member states \$130 billion. In the US, \$115 billion was spent in 1992 on waste treatment and disposal. New European legislation and tighter national laws will make matters worse.

Industry and academe are now reacting to these challenges and many are seeing the opportunities—be they in winning research funding, unprecedented opportunities for translating new, greener chemistries from the research bench to the production plant or in gaining commercial advantage from the application of new low-waste processes or the marketing of new environmentally friendly products or technologies. The rapidly growing interest in green chemistry is partly witnessed by the growth in relevant conferences with regular events now being held in the USA, Europe and Asia. The Gordon Green Chemistry conferences (held alternately in the USA and Europe since 1995) along with other recent international meetings are good examples of effective meetings of industrial, academic and governmental chemists and engineers with a variety of backgrounds, interests and areas of expertise but with the common goal of seeing the application of green chemistry throughout the chemical and allied industries.[2]

Additionally, the emergence of Green Chemistry organisations in the USA, Italy and the UK are indications of the growing interest in the concept and the recognition of the value of networking such diverse activities. It is particularly significant to note that many of these organisations place education as high on their agenda as research—the long term future of the subject and indeed of the industry will depend on future generations. In the US, a particularly important and strategic development was the emergence of the Presidential Green Chemistry Challenge awards. These have had numerous benefits, not least the open disclosure of many new and exciting products and processes that will be of real benefit to the environment and to the image of chemistry.

Green chemistry in practice

Through the US Presidential Green Chemistry Challenge awards, other promotional initiatives and a general increase in public awareness, an increasing number of headlines have drawn attention to scientific and commercial breakthroughs in reducing the environmental impact of chemical products and processes. These include: new marine antifoulant to replace tributyltin oxide (Rohm and Haas); environmentally friendly high solid coating reduces VOCs (Bayer); new route to a steroidal intermediate involving catalytic oxidation with no heavy metal waste (Pharmacia and Upjohn); new microemulsion based solvent for industrial cleaning (Dow); full plant trials for a new polymerisation catalyst that gives a 90% reduction in waste (GE Plastics); new commercial hydrogenation process based on supercritical fluid technology promises to be greener and safer than existing processes (Thomas Swan); new environmentally friendly route to herbicide intermediate (Monsanto); envirocats launched as environmentally friendly replacements for hazardous reagents and catalysts (Contract Chemicals).

Some individual case studies can be used to illustrate the environmental advantages that are being achieved in some chemical processes.[1]

Disodium aminodiacetate (DSIDA) is a key intermediate in the manufacture of Roundup$^{\text{TM}}$, the environmentally friendly herbicide. The traditional manufacturing route to DSIDA was based on old Strecker chemistry and suffered from numerous serious environmental and health and safety problems: the use of the highly toxic hydrogen cyanide which requires special handling and gives rise to operator, environmental and local community risks; the exothermic generation of unstable intermediates requires special care to avoid runaway reactions; the process gen-

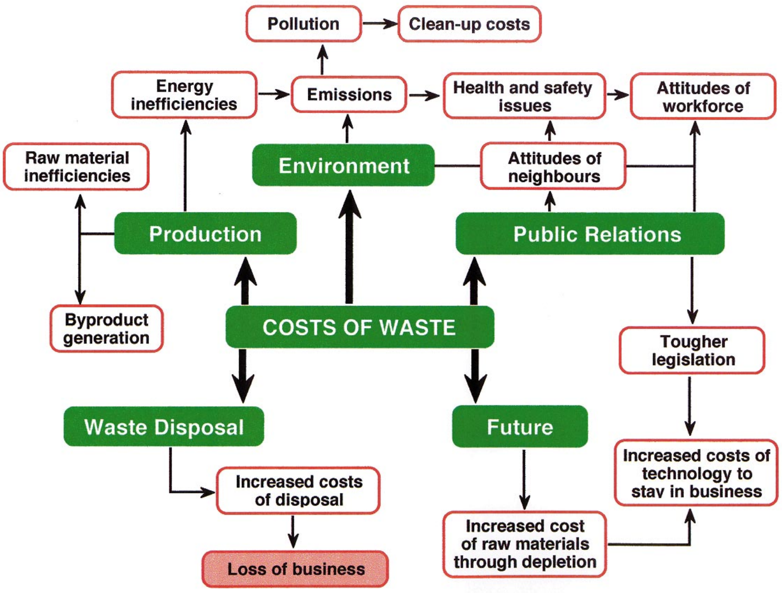

Fig. 2 The costs of waste.

erates at least 1 kg of waste per 7 kg of product; the waste contains cyanide and formaldehyde and needs treatment prior to disposal.

The new DSIDA manufacturing process is cleaner and safer. It is based on the catalytic dehydrogenation of diethanolamine and involves: less toxic and less volatile starting materials; endothermic and inherently safer chemistry; a ‘zero waste’ route: after removal of the catalyst, no further purification is required before the intermediate is used in the next stage of the herbicide manufacture; a new active and reusable solid catalyst which has applications wider than in this process.

Overall the new catalytic process gives higher product yields and involves fewer process steps.

The classical route to hydroquinone, a very useful intermediate in the manufacture of polymeric materials, suffers from very poor atom utilisation (*i.e.* a small fraction of the atoms consumed in the process end up in the final product) and leads to the production of enormous volumes of waste. The manufacturing method is shown in Fig. 3.

As can be seen, the production of one mole of hydroquinone leads to the production of mole equivalents of ammonium sulfate and iron(II) oxide and more alarmingly 4 mole equivalents of manganese sulfate. This is an example of a process with a poor environmental acceptability factor (high waste to product ratio)[3] made worse by the hazardous nature of the waste.[4] The poor atom efficiency of the process is best illustrated by some simple atom economy calculations (Table 1).

The new Upjohn route is a great improvement (Fig. 4). Overall only 3 kg of acetone waste are produced per 10 kg of hydroquinone product, and there are no significant amounts of salt waste.

4-Isobutylacetophenone is a key intermediate in the manufacture of the bulk active pharmaceutical ibuprofen. The conventional method of preparation is based on a Friedel–Crafts acylation, which uses greater than stoichiometric quantities of $AlCl_3$. To produce 1000 tonnes of 4-isobutylacetophenone, 760 tonnes of $AlCl_3$ are required and a corresponding amount of aluminium waste in the form of aluminous water is generated when the product–catalyst (Lewis base–Lewis acid) complex is broken down by quenching with a large volume of water. In addition, large amounts of acidic gaseous emissions have to be scrubbed from the off-gas stream. Later stages in the process involve cyanide and elemental phosphorus (which does not end up in the final product) making the whole manufacturing process extremely hazardous and wasteful (Fig. 5).

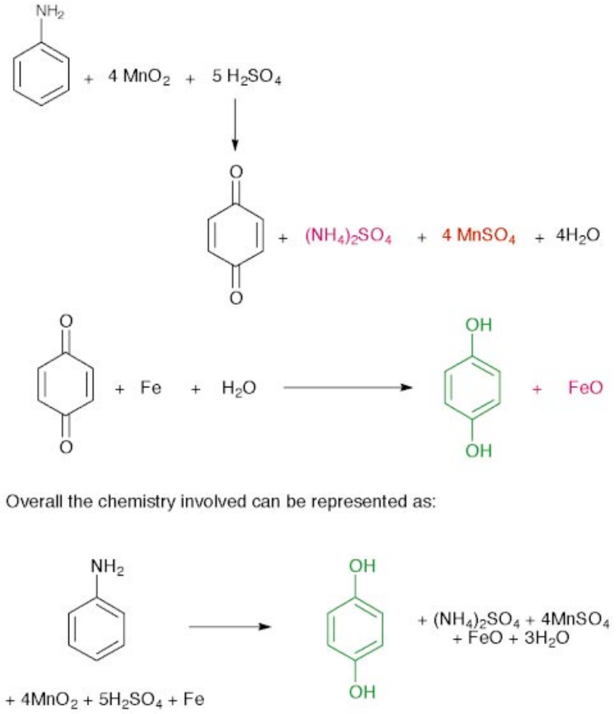

Fig. 3 The classical route to hydroquinone.

Increasing pressure from generic competition (as the product came off patent) and to reduce the environmental impact led to Boots, in collaboration with Hoechst Celanese, developing a new cleaner process based on the use of HF as the Friedel–Crafts catalyst. Hydrogen fluoride is extremely corrosive and requires quite expensive plants for safe handling. The dangers resulting from any escape into the environment are also considerable. However, while the use of HF presents serious difficulties, unlike $AlCl_3$ it can be separated and recycled and the process is run continuously with complete containment. The total removal of cata-

Table 1 Atom accounts for the classical route to hydroquinone

Element	Fate	Atom utilisation
Carbon	Product(s)	Up to 100%
Hydrogen	Product and waste	Up to 33%
Oxygen	Product and waste	Up to 13%
Manganese	Waste	0%
Sulfur	Waste	0%
Iron	Waste	0%

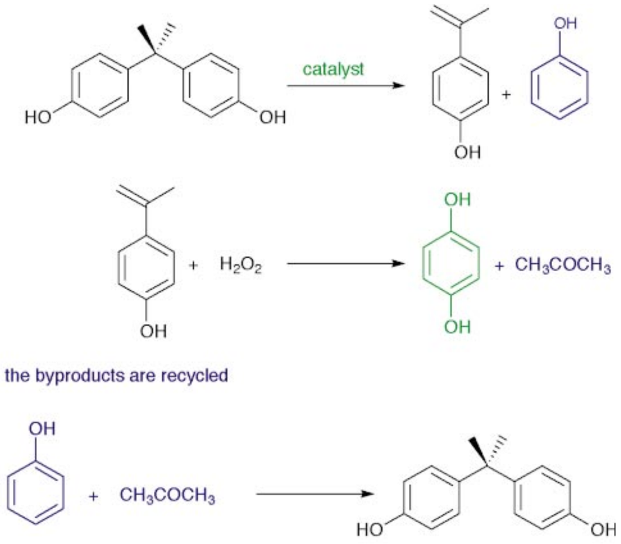

Fig. 4 The new Upjohn route to hydroquinone.

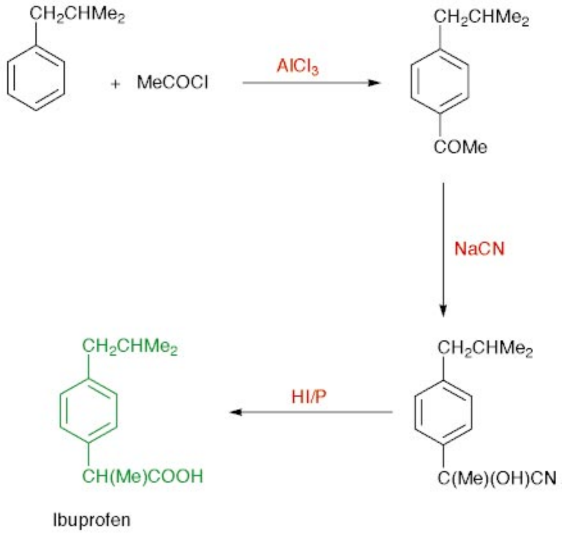

Fig. 5 The traditional manufacturing route to 4-isobutylacetophenone.

lyst waste in this step is an important development in the pursuit and application of green chemistry. In the overall process 6 stoichiometric steps with <40% atom utilisation have been replaced by 3 catalytic steps with *ca.* 80% atom utilisation.

Important generic areas of chemistry

To help illustrate the many challenges ahead and the opportunities for new greener chemistry, two very broadly based generic areas of chemistry can be at least superficially examined in terms of their scope, the environmental unacceptability and poor atom economics of typical processes, and the goals and possible approaches of green chemistry. The emphasis will be on batch-type processes involving liquid phase reactions as practiced by fine, speciality chemical and chemical intermediate manufacturers around the world.

Acid catalysed reactions

Acid catalysis is the most widely used type of catalysis with applications in all sectors of the chemical, pharmaceutical and allied industries, although the largest scale use is in the petrochemical industries where the processes are largely quite efficient and the use of solid acids is well established.[5]

Traditionally most liquid phase organic reactions have been catalysed by strong Brønsted acids such as H_2SO_4 and HF and by soluble Lewis acids such as $AlCl_3$ and BF_3. Their chemistry is extremely diverse with just a few examples shown in Fig. 6.

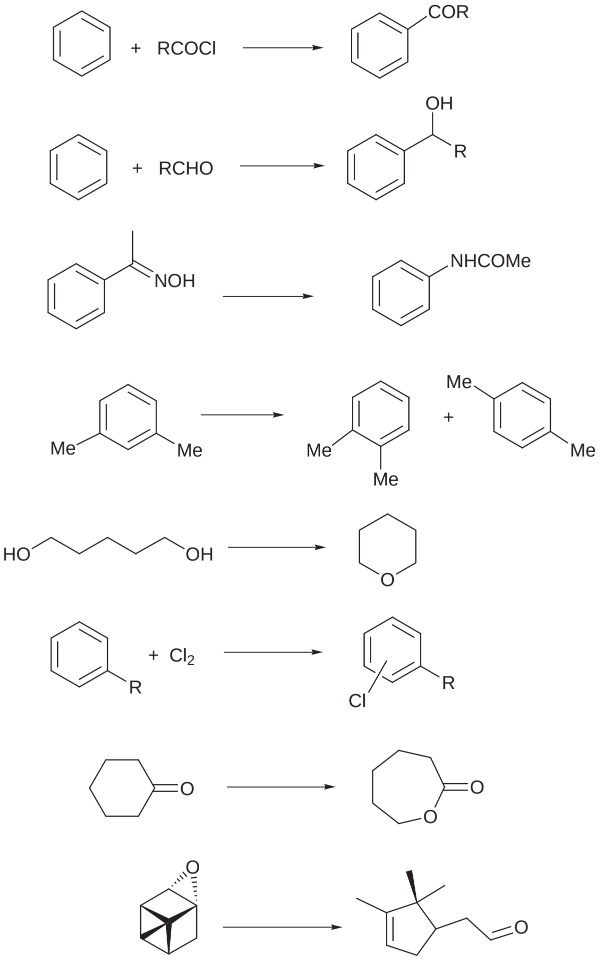

Fig. 6 Some examples of acid-catalysed organic reactions carried out in industry.

These acids have many important advantages—they are cheap, readily available and very active. Unfortunately, they also suffer from some serious disadvantages, which are becoming increasingly prominent in these environmentally conscious days—they are difficult to separate from the organic products and their use leads to large volumes of hazardous waste. In the petrochemical industry, where acid catalysis is vital to many of the business areas, solid acids including zeolites have become established in the large-scale vapour phase processes. Continuous processes operating in contained plants can involve solid catalysts running for greater than a year before being removed and replaced. The efficiency of such processes is very high and the relative quantities of waste can be impressively low. Solid acids are only beginning to impact non-petrochemical process chemistry.[6]

Friedel–Crafts acylations (including benzoylations and sulfonylations) are real and alarming examples of very widely used acid-catalysed reactions which are based on 100 year old chemistry and are extremely wasteful. The reaction of an acid chloride with an aromatic substrate requires a greater than stoichiometric quantity of aluminium chloride as the 'catalyst' (>2 mole equivalents in sulfonylations). Every molecule of the ketone product forms a complex with one molecule of the catalyst, effectively removing it from the reaction. The organic product is released by using a water quench with the resulting emission of about 3 equivalents of HCl which need to be scrubbed from the off gases leading to the production of 3 equivalents of salt waste. Once the organic product has been recovered, aluminous water remains, which must be disposed of. The overall process generates considerably more waste than product (Fig. 7).

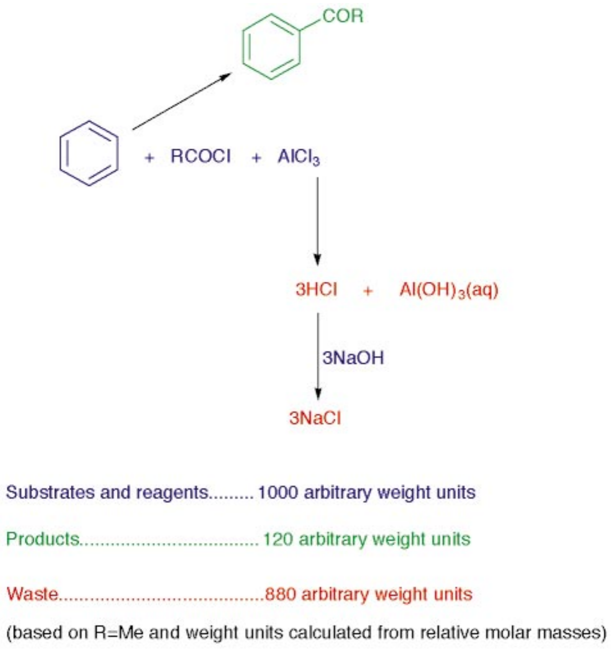

Fig. 7 Friedel–Crafts acylation showing a typical starting materials/products/waste balance.

Many other industrial processes are catalysed by $AlCl_3$. These include alkylations and the production of resins *via* cationic polymerisation. While these reactions do not require the use of stoichiometric quantities of the Lewis acid, none of the catalyst is recovered and all such processes show the same atom accounts (Table 2).

The green chemistry goal for such reactions should be to remove all elements from the accounts other than those involved in the organic chemistry and, of course, to push the organic chemistry towards 100% selectivity to the desired product.

A number of new, more environmentally friendly acids for liquid phase organic reactions, notably solid acids (which are generally easier and less energy and resource consuming to recover than soluble acids), have been discussed and are beginning to find their way into industrial usage. These include zeolites,[7] clays and other mixed metal oxides, inorganic–organic composite materials, functionalised polymers and supported reagents[8,9] as well as lanthanide triflates.[10] Other interesting 'green' solutions to the problem include the use of ionic liquids.[11]

Table 2 Atom accounts in a typical $AlCl_3$-catalysed Friedel–Crafts acylation

Element	Fate	Atom utilisation
Carbon	Products and by-products	Up to 100%
Hydrogen	Products, by-products and waste (from quench)	<<100%
Aluminium	Aluminous water/aluminium salts	0%
Chlorine	Waste water (from quench) and salt (from HCl scrubbing)	0%
Oxygen	Waste water	Down to 0%

Bromination chemistry is a relatively small area of organic chemistry but one with many useful applications (including photographic chemicals, pharmaceutical and agrochemical intermediates) and an international speciality chemical industry based on it. The chemistry is largely based on the use of elemental bromine and the problems associated with the use of traditional acid catalysts are compounded by the low atom utilisation of the bromine. The most important bromination reactions include aromatic bromination, bromodehydroxylation and the α-bromination of carboxylic acids (Fig. 8).

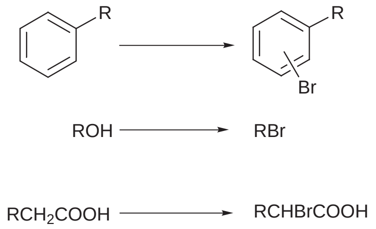

Fig. 8 Important bromination processes.

Aromatic bromination reactions are typically catalysed by Lewis acids such as $FeCl_3$ and $AlCl_3$ which present the familiar environmental problems of separation difficulties usually leading to HCl emissions and the production of large volumes of aqueous and salt waste. In the case of the aliphatic brominations phosphorus and sulfur reagents are commonly used. The α-bromination of carboxylic acids is carried out using red phosphorus, in some cases in near stoichiometric quantities. The phosphorus ends up as a cake of phosphates and other phosphorus species containing bromine and organic contaminants. It can only be disposed of after treatment. Additionally, all of the above reactions usefully employ no more than 50% of the bromine with an equivalent amount being converted to HBr which needs to be scrubbed from the off gases and removed as NaBr. The atom accountability in such reactions again tells a story of inefficiency and waste (Table 3).

In reactions using stoichiometric levels of phosphorus and with a substrate molecular weight of 100, even 100% efficient organic chemistry only gives 40% of the final mass as product, with 60% being waste. At a more likely level of 80% efficient organic chemistry, the figures change to 31% product and 69% waste.

A clean synthesis approach to bromination reactions should be able to greatly improve their environmental performance and atom efficiency. It is now known for example, that aromatic

Table 3 Atom accounts in a typical phosphorus-catalysed α-bromination

Atom	Fate	Atom utilisation
Carbon	Products (including side products)	Up to 100%
Hydrogen	Products plus HBr	<100%
Bromine	Products plus HBr	Up to 50%
Phosphorus	Phosphorus residues	0%
Sodium	Salt	0%

brominations, at least for other than strongly deactivated substrates, can be effectively catalysed by solid acids (including supported mild Lewis acids that are easily recovered and can be reused many times).[12] It should also prove possible to replace the phosphorus in aliphatic brominations. Furthermore, it should be possible to devise economical methods for oxidatively regenerating the bromide side-product to bromine ideally using oxygen, which will lead to water only as a side product. The effect of these improvements on the atom accounts would be dramatic (Table 4).

Table 4 Atom accounts in a clean bromination using a reusable catalyst and aerial regeneration of the bromide

Element	Fate	Atom utilisation
Carbon	Products (including side-products)	Up to 100%
Hydrogen	Products	Up to 100%
Bromine	Products	Up to 100%
Oxygen	Water/steam	0%

The effect on the mass efficiency is equally impressive with 100% efficient organic chemistry leading to 94% of the final mass as product and only 6% as waste. Even at 80% efficient organic chemistry, the figures are 75% product and only 25% waste respectively.

Partial oxidations

The partial oxidation of organic molecules (typically hydrocarbons) is a diverse and widely used area of chemistry with applications in almost all of the important fine and speciality chemicals industries including the manufacture of pharmaceuticals, agrochemicals and monomers (some of the most important transformations are shown in Fig. 9). Established manufacturing methods include those based on cobalt–acetic acid–bromide systems (*e.g.* for the side chain oxidation of alkylaromatics). While these are catalytic in cobalt the corrosive nature of the systems and the large reaction volumes are drawbacks. These coupled with the high temperatures and pressures that are often required give rise to problems for the operator and the plant, and improved catalytic reaction systems need to be developed.[1]

Peroxide reagents are useful in many partial oxidation reactions including epoxidations, Baeyer–Villiger reactions and hydroxylations. Peroxides can be hazardous however, and the more reactive organic peroxides such as percarboxylic acids do present serious difficulties to the operator especially in large-scale processes.

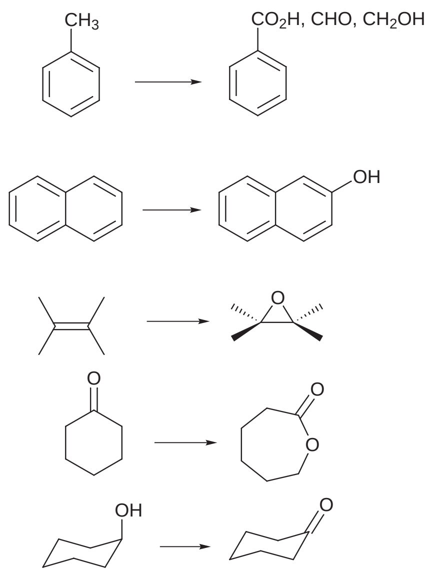

Fig. 9 Some important partial oxidation reactions.

Stoichiometric metal oxidants such as chromium(VI) and manganese(VII) are perhaps the best known oxidising agents in chemistry. While they are commonly associated with volumetric analysis and bench scale reactions, their use on a large scale leads to large volumes of toxic metal waste.[1,13] Rather surprisingly, such reagents continue to be used in some industrial processes such as the conversion of secondary alcohol functions to ketones. In a typical reaction, the feedstocks are a source of chromium(VI), acid and an organic solvent as well as the organic substrate (Fig. 10). The wasteful nature of such processes is evident when the work-up of the final reaction mixture is considered (Fig. 11). Typically, the mixture will undergo a water quench to

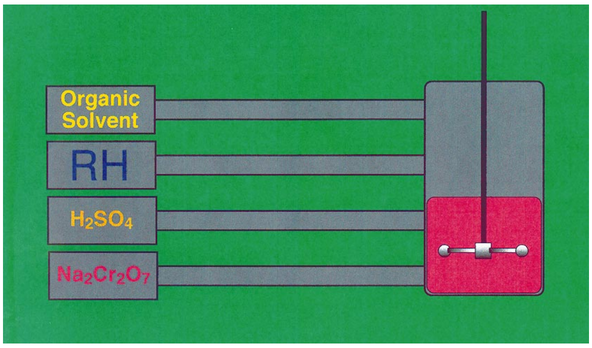

Fig. 10 The feedstocks for a typical partial oxidation process based on stoichiometric chromium(VI).

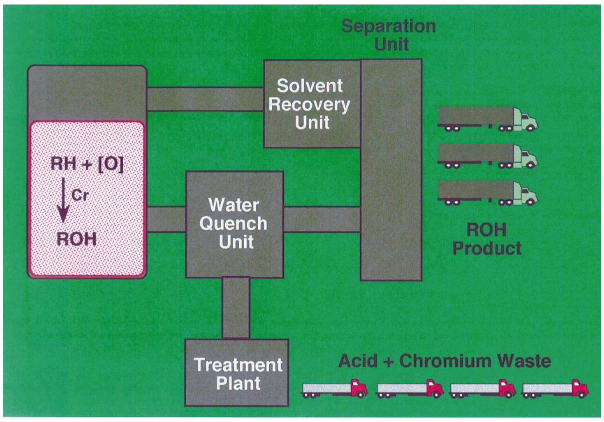

Fig. 11 The work-up and product recovery from a process based on stoichiometric chromium(VI).

liberate the product and considerably larger quantities of acid and chromium waste. The combination of toxic metal, acid and organic residues represents a particularly difficult form of waste, which must be treated before disposal. Even with 100% efficient solvent recovery, these processes will generate considerably larger volumes of waste than product. The high added value of partially oxidised products may continue to make the chemistry economically viable but it cannot be considered environmentally acceptable.

A simple exercise in atom accountability in the partial oxidation of an organic substrate with a stoichiometric chromium reagent system can also be used to highlight the problems (Table 5).

Table 5 Atom accounts in a typical organic partial oxidation using a stoichiometric chromium reagent system

Element	Fate	Atom utilisation
Carbon	Product(s)	Up to 100%
Hydrogen	Product(s) and waste acid	<<100%
Chromium	Chromium salts	0%
Sodium	Waste salts	0%
Sulfur	Waste acid	0%
Oxygen	Product(s) and waste salts	<<100%

Of the input atoms in the case of a simple hydrocarbon oxidation, only carbon, hydrogen and oxygen are required in the final product. Chromium, sodium and sulfur are used yet do not appear in the final product.

Table 6 Atom accounts for a partial organic oxidation using air/oxygen and a catalyst (excludes any catalyst waste)

Element	Fate	Atom utilisation
Carbon	Product(s)	Up to 100%
Hydrogen	Product(s) (may include water)	Up to 100%
Oxygen	Product(s) (may include water)	Up to 100%

In the ideal synthesis, the only atoms that leave a process should leave in the form of useful product (Table 6). The most environmentally acceptable source of oxygen is air, directly leading to only nitrogen as waste (of course, oxygen itself or oxygen-enriched air can also be used in the actual process). For most organic oxidations using air, a catalyst will be required to enable the reaction to occur at moderate temperatures and pressures (even with a catalyst many important partial oxidations currently require very forcing conditions suggesting the need for improved catalysis). Thus, in the ideal partial oxidation process, only the organic substrate, air and (a small amount of) catalyst should be introduced into the reactor (Fig. 12). If the catalyst can be retained in the reactor in some way (and subsequently reused either *via* a continuous mode of operation, or *via* fresh charge of substrate), then the work up of the reaction mixture should only involve product recovery and unreacted substrate recycling (Fig. 13). In some partial oxidations (*e.g.* the side chain oxidation of alkylaromatics), water will also be produced in the reaction but water is just about the most environmentally acceptable side product, at least when pure, and can be used as a source of energy if vented off as steam. This, of course, ignores any organic side products which commonly occur in many partial oxidations but these are also prevalent in the older and more wasteful processes, indeed the use of some newer forms of catalysis (*e.g.* those based on shape selective microporous solids) can improve reaction selectivity.[14]

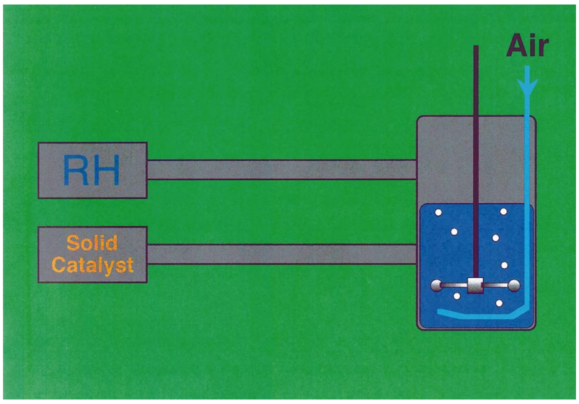

Fig. 12 Feedstocks for an ideal partial oxidation using air and a catalyst.

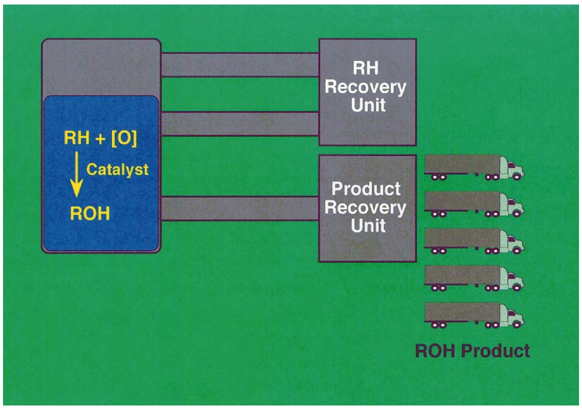

Fig. 13 The work-up and product recovery from an ideal catalytic partial oxidation process using air.

To keep such an ideal process as simple, efficient and clean as possible, an active and selective catalyst is required. Furthermore, to avoid any potentially difficult catalyst separation stages, it should remain in a separate phase from the organics (and, of course, not leach any of its component parts into the organic phase). In the case of a simple stirred reactor, a particulate solid catalyst could be used although the ultimate separation of such a material from a liquid (decantation, filtration, *etc.*) may not be a trivial exercise. For continuous flow reactions, catalyst pellets may be more appropriate. Fortunately, useful progress is being made in the discovery and application of solid catalysts for partial oxidation reactions. These include mixed metal oxides such as the titanium silicate 'TS1' (*e.g.* for the hydroxylation of small aromatic compounds) and supported reagent type catalysts (*e.g.* for alkene epoxidations).[9,14,15]

Concluding remarks

The drive towards clean technology in the chemical industry and the emergence of green chemistry related issues in chemical research and education are unlikely to be short term 'fashions'. In the future, the synthetic chemist will need to be as concerned about atom efficiency as the synthetic route and the process chemist will need to be as concerned about the waste produced as the product to be made. It is already becoming evident that the more successful chemical manufacturing companies of the future will be those that can exploit the economic, legislative and public image advantages that a clean technology approach to chemical manufacturing can provide. Also, the more successful chemistry researchers and educationalists will be those that can appreciate the value of green chemistry in innovation, application and teaching (as well as recognising the important role that green chemistry can play in enhancing the attractiveness of chemistry as a discipline).

While many exciting new greener chemical processes are being developed it is clear that a far greater number of challenges lie ahead. In two of the largest generic areas of chemistry, acid catalysis and partial oxidations, there are countless processes operated by almost every type of chemical manufacturing company, producing products of incalculable value yet also producing almost immeasurable volumes of hazardous waste. New greener chemistry is needed. One of more important development areas in this context will be the more widespread use of heterogeneous catalysis in liquid phase organic reactions. The enormous range of reactions and the rapidly growing number of new catalysts will require the use of rapid screening methods and the use of innovative engineering to fully exploit the new chemistry. Synthetic chemists must be more prepared to work with catalyst chemists who must in turn work more closely with chemical and process engineers. For every challenge offered by the green chemistry revolution there is also an exciting opportunity.

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Paper 8/07961G

Halogen exchange reactions for CFC alternatives

The behaviour of fluorine-18 labelled hydrogen fluoride towards prefluorinated chromia containing nickel(II) or zinc(II)

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Summary

Highly active catalysts are required for the conversion of CF_3CH_2Cl to the CFC-alternative refrigerant, CF_3CH_2F, by HF vapour under heterogeneous conditions. Chromia impregnated with a very low level of zinc(II) is a superior catalyst precursor to chromia alone. The behaviour of prefluorinated chromia and prefluorinated chromia containing zinc(II) or nickel(II) towards fluorine-18 labelled HF indicates that two types of labile surface fluoride are present, only one of which is catalytically active. Proposals are made to account for the role of Zn^{II} and Ni^{II}.

Introduction

The necessity to develop syntheses suitable for the large scale production of CFC-alternative refrigerants such as 1,1,1,2-tetrafluoroethane (HFC-134a) following the Montreal Protocol has led to renewed interest in the fundamental aspects of heterogeneous catalytic fluorination. The vapour phase halogen exchange reaction, $CF_3CH_2Cl + HF \rightarrow CF_3CH_2F + HCl$, presents a particular challenge because of its thermodynamically limited nature, hence the catalyst used must be highly active. Various metal oxides and fluorides have been evaluated, most obviously chromia,[1,2] since it was the catalyst of choice for CFC production under heterogeneous conditions. Pretreatment with HF[1] or a fluorine-containing alkane[2] is required, suggesting that the catalyst is a fluoride or oxofluoride phase rather than an oxide. Other active catalysts include those derived from hydrated CrF_3 or Cr^{III} hydrofluorides, in each case promoted by MgF_2,[3] CrF_3 supported on γ-AlF_3,[4] and Co^{II}, Mg^{II} or Cr^{III} supported on γ-AlF_3.[5] Prefluorinated Co^{II} on alumina is a catalyst for the related reaction in which CF_3CHClF is converted to CF_3CHF_2.[6] Despite this activity, in no case is definitive evidence available concerning the nature of the catalytically active sites, although for fluorinated chromia there is circumstantial evidence that catalytic activity is related to the extent to which reversible oxidation of Cr^{III} sites in the precursors can be achieved.[1b,7]

In none of the previous studies has consideration been given to the nature and extent of the interactions between anhydrous HF and the surface of an, often highly fluorinated, catalyst. This important aspect of an overall mechanism is now addressed using the results of experiments in which the behaviour of HF labelled with the radioactive isotope fluorine-18 (β^+ emitter, $t_{1/2}$ = 110 min) towards a range of highly fluorinated catalysts of varying activities has been examined. The catalysts are derived from chromia or chromia containing nickel(II) or zinc(II) precursors and the behaviour of representative examples with respect to catalytic activity in the reaction $CF_3CH_2Cl + HF$, and to the individual reagents HF and CF_3CH_2Cl, is compared in Table 1.

Results and discussion

The key step in the formation of an active catalyst is an extensive prefluorination (623 K, 18 h) of the precursor by flow of anhydrous HF. Conversion of Cr^{III}–O to Cr^{III}–F is slow, however XPS measurements on fluorinated chromia catalysts containing Ni^{II} or Zn^{II} provide strong evidence for the presence of NiF_2 and ZnF_2. In contrast, although the Cr $2p_{3/2}$ binding energies in these samples approach that of α-CrF_3, there is no evidence for Cr^{III} in a completely fluorinated environment in agreement with previous observations.[1,2] Supporting evidence for the complete fluorination of Ni^{II} and Zn^{II} is provided by TEM examination of two fluorinated catalysts containing Ni^{II} or Zn^{II} in which lattice spacings attributable to MF_2, M = Ni or Zn, were observed. Neither α-CrF_3 nor α-Cr_2O_3 appeared to be present.

The most active catalyst of those in Table 1 is derived from a precursor containing a small Zn^{II} loading ($\equiv$0.25% w/w) on chromia. This catalyst is significantly more active than the corre-

Green Context

The hydrocarbon CF_3CH_2F is the current drop-in replacement for the CFC CCl_2F_2, which is banned under the Montreal protocol.

One of the large scale preparative routes to this replacement involves the catalytic fluorination of trichloroethene with HF. The last step, the conversion of CF_3CH_2Cl to CF_3CH_2F, is limited thermodynamically. In order to carry out this process efficiently and cleanly, the catalysts used must be extremely active and very selective. This article presents results relating to such a catalyst, chromia doped with either Ni(II) or Zn(II). These model catalytic systems display markedly better performance compared to the undoped material. The role of the dopants is discussed. ***DJM***

sponding undoped material. Increasing the Zn^{II} content (for example to 4% w/w) however leads to decreased catalytic activity, even though the apparent activation energy for the reaction is lowered. The Ni^{II} study, using higher doping levels obtained by co-precipitation, shows a similar pattern, increasing Ni^{II} content resulting in decreased activity and apparent activation energy.

Interactions between the fluorinated catalysts and [^{18}F]-labelled HF under flow conditions at 573 K are substantial (Table 1). These experiments were carried out using $H^{18}F$ whose specific count rate (count min^{-1} $mmol^{-1}$) was independently determined, enabling the interaction between HF and a fluorinated catalyst to be quantified as equivalent to mmol of HF uptake per g catalyst (Table 1). Small variations in the uptakes of [^{18}F] are observed but no simple relationship exists between the extent of the interaction with $H^{18}F$ and the identity and extent of the M^{II} dopant. However, subjecting all prefluorinated [^{18}F]-labelled catalysts to HF flow leads to significant reductions (40–75%) in [^{18}F] activity, Table 1. A similar situation is encountered when CF_3CH_2Cl is flowed over prefluorinated catalysts that have been labelled by subsequent $H^{18}F$ treatment but the fractions of [^{18}F] removed (25–45%) are smaller. It appears that on these highly fluorinated surfaces, two types of labile surface fluorine are present but only that which is labile both to HF and to CF_3CH_2Cl treatments is catalytically active.

In contrast to HF, CF_3CH_2Cl interacts weakly with the fluorinated catalysts. Exposure of samples of working Zn^{II}-containing catalysts to chlorine-36 labelled CF_3CH_2Cl did not result in any measurable [^{36}Cl] radioactivity being detected from the surface. However, after prolonged thermal treatment to desorb HF, the interaction of [^{36}Cl]-CF_3CH_2Cl with the surface could be detected using a direct Geiger–Müller monitoring technique.[8] In these experiments a substantial [^{36}Cl] count from the surface (>1000 count min^{-1}) was obtained only when more highly Zn^{II}-doped catalysts were exposed to [^{36}Cl]-CF_3CH_2Cl at, or above, 423 K. The [^{36}Cl] species deposited on the surface was strongly bound, for example [^{36}Cl] surface count rates were unaffected by removal of CF_3CH_2Cl vapour and by prolonged pumping at room temperature. These observations suggest that in the absence of HF, a non-catalytic halogen exchange process occurs that is similar to the Halex type and which involves Zn^{II}–F bonds rather than Cr–F as the source of the active fluoride.

The results obtained here enable several points of general relevance to the catalytic fluorination of CF_3CH_2Cl by HF to be made. The presence of a large quantity of labile surface fluoride as a result of the pre-fluorination of the catalyst precursors is an important factor in determining the subsequent catalytic behaviour. In this respect catalytic fluorination of CF_3CH_2Cl resembles catalytic fluorination of chlorofluoroethanes over fluorinated chromia.[9] The presence of a large quantity of labile fluoride derived from adsorbed HF will be beneficial also in suppressing the dehydrofluorination of CF_3CH_2F and CF_3CH_2Cl, processes which in other circumstances, using unfluorinated or lightly fluorinated catalysts,[2] are competitive with the conversion of CF_3CH_2Cl to CF_3CH_2F. Under the conditions used here, dehydrofluorination is not observed above trace levels. Similar considerations should apply to catalysts derived from mixed metal fluorides[3–5] or fluorinated alumina.[6]

However, an inescapable consequence, which is illustrated by the [^{36}Cl] study, is that the interaction of CF_3CH_2Cl with a catalyst surface will be inhibited and that blocking of active sites by HF will occur. Fluorinated chromia (Table 1) is likely therefore to have a relatively small number of catalytically active sites; they are possibly surface Cr atoms whose Lewis acidity has been promoted by a disordered oxygen/fluorine environment and which are highly active.

Finally, an explanation for the behaviour of the MF_2, M = Zn or Ni, doped fluorinated chromia catalysts (Table 1) is proposed. The presence of an M^{II} species directly adjacent to the Cr active site will result in a perturbation of the adsorption behaviour of HF and we speculate that this is the origin of the lower apparent activation energies observed for Zn^{II} and Ni^{II} doped catalysts (Table 1). The dopant provides an additional pathway for the transfer of catalytically active fluoride to replenish the active site and to remove surface chloride, the effect being apparent most obviously from a comparison of the first two catalysts in Table 1. At higher levels of Zn^{II} doping and at all levels examined for Ni^{II}, it appears that the number of active Cr sites is reduced, hence the catalysts are less active.

We thank EPSRC and ICI Klea for support of this work.

Table 1 Catalytic fluorination of CF_3CH_2Cl to CF_3CH_2F by anhydrous HF over fluorinated chromia containing zinc(II) or nickel(II)

Catalyst precursors[a]		Microreactor experiments[b]		[^{18}F] experiments at 573 K, flow conditions[c]		
Metal(II)	Precursor stoichiometry[d]/ mol (100 g Cr_2O_3)$^{-1}$	Conversion at 573 K[e]/ % m^{-2} g	Apparent activation energy[f]/kJ mol^{-1}	Uptake of [^{18}F] by catalyst/mmol g^{-1}	[^{18}F] remaining after HF flow (%)	[^{18}F] remaining after CF_3CH_2Cl flow (%)
None	—	0.18	179	0.29–0.33	31	54
Zn	0.004	0.27	113	0.32–0.33	28	60
Zn	0.067	0.11	92	0.55–0.63	60	75
Ni	0.066	0.14	152	0.61–0.96	47	66
Ni	0.658	0.055	130	0.29–0.89	25	61

[a] Zn^{II}-containing precursors prepared by aqueous $ZnCl_2$ impregnation of commercial amorphous chromia followed by calcination under N_2 flow at 873 K (12 h). Ni^{II}-containing precursors prepared by coprecipitation from Cr^{III} and Ni^{II} aqueous nitrates (mole ratios 20:1 or 2:1) followed by calcination under N_2 flow (18 h) at 723 or 923 K. [b] Monel metal rig, HF:CF_3CH_2Cl = 4:1, feed rates 20 cm^3 min^{-1} (HF) and 5 cm^3 min^{-1} (CF_3CH_2Cl); catalysts were prefluorinated at 623 K (18 h) before use; catalytic runs were performed under temperature ramping (623–523 K) conditions. [c] Monel metal rig, $H^{18}F$ flow at 573 K (0.5 h) then cooled under N_2 flow then HF or CF_3CH_2Cl flow at 573 K (0.5 h). [d] Units chosen to facilitate comparisons between Zn^{II} and Ni^{II} catalysts. [e] Based on GC data and BET areas of working catalysts. CF_3CH_2F was the only product detected, although trace quantities (<1%) of olefinic products were observed >623 K. [f] Temperature range 523–573 K.

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Paper 8/08021F

Preventing termite attack

Environmentally friendly chemical combinations of cashew nut shell liquid, sulfited wattle tannin and copper(II) chloride

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Summary

In this study, a combination of three chemicals (cashew nut shell liquid, sulfited wattle tannin and copper(II) chloride) has been used to develop an environmentally friendly termite preservative. Cashew nut shell liquid (CNSL) is a by-product of cashew nut kernel processing factories and its use in the preservative formulations minimises the wastes from the factory as well as the amount of conventional hazardous preservatives from entering the environment. The formulated preservatives were tested for their ability to preserve wood blocks from a soft wood, ponderosa pine (*Pinus ponderosa*) and a hard wood, trembling aspen (*Populus tremuloide*). Sulfonated wattle tannins alone or combined with copper chloride at different concentrations, and cashew nut shell liquid (CNSL) without or with copper chloride were used in treating the 14 × 14 × 14 mm wooden blocks from the two wood species. The samples were exposed to termite attack in the surveyed fields in Arusha and Moshi, Tanzania. After 108 days exposure, evaluation of termite attack by measuring the weight losses and damage showed that the test wood treated with the combinations 40% CNSL + 1% CuCl$_2$ and 40% CNSL + 2% CuCl$_2$ were among the least damaged.

Introduction

Termites are destructive insects which attack both field and harvested produce. Wood products are also subject to termite and other bio-hazard attack if preventative measures are not taken. These bio-hazard attacks reduce the service life of wood products. In Tanzania for instance, the average service life of a non-durable wood species is about three years although it can be extended by the use of wood preservatives.[1] The extended durability period depends on, among other things, the species of wood, the type of preservative used and the place at which the wood is stored or used. In Tanzania, a survey reports[1] that wood preservation is carried out using creosote (60%), pentachlorophenol (20%), and copper chromium arsenate (20%). The common wood preservatives documented elsewhere to be effective against termites include chlorinated products, boric acid and arsenic compounds.[2–5] Apart from creosote, which is moderately toxic when heated to decomposition, pentachlorophenol, arsenic and chromium compounds are rated as highly toxic industrial materials.[6,7] Chromate salts are associated with cancer of the lungs while arsenic compounds can cause a variety of skin abnormalities including itching, pigmentation and even cancerous changes.[6] Work on preventing termite attack by adding insecticides to wood adhesives used on fabricated building materials has been done and showed good anti-termite properties.[4]

The resistance of wood treated with copper(II) compounds derived from tri- and di-alkylamine–boric acid complexes to termite attack is also found to be good, and is environmentally more acceptable than the use of conventional wood preservatives.[8] Copper complexed with condensed tannin is observed to be an efficacious wood preservative although the combination of the sulfited bark extract (tannin) and copper chloride is reported to be a more effective wood preservative.[9] A notable advantage of using a combination of copper compounds instead of conventional wood preservatives is that termites readily acquire toxic doses by consuming small amounts of the treated wood and thus the nearby untreated wood is protected from termite attack. Moreover, copper compounds are active against fungal attack and hence can also protect the wood in this way.

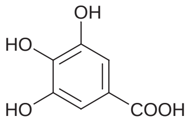
Despite their environmental acceptability over conventional wood preservatives, large doses of copper complexes are environmentally less friendly than chemicals mainly derived from natural sources. The wood preservatives commonly used in Tanzania exert a negative environmental impact as their effluent streams contain particularly persistent toxic compounds such as pentachlorophenol, arsenic and chromium compounds, this calls for the development of alternative wood preservatives from local natural materials. The latter entails finding more environmentally acceptable substances from natural sources like wattle tannins and cashew nut shell liquid (CNSL) that are less toxic than the

Green Context

The discovery and application of environmentally benign new products and product mixtures which can effectively replace hazardous chemicals are important areas of green chemistry. Traditional wood preservatives used in developing countries are often based on a potent mixture of toxic species such as chlorinated phenols, arsenic and chromium compounds. Copper-based preservatives are promising alternatives but can involve unacceptably large quantities of combinations of compounds. In this article the novel combination of cashew nut shell liquid, sulfited wattle tanin and small amounts of copper are shown to be effective mixtures for the prevention of termite attack. ***DJM***

conventional wood preservatives used in Tanzania.[6] The possible effluents from either pilot or full scale processes using this new technology will comprise the less toxic cashew nut shell liquid, tannin and small concentrations of copper chloride.

As might be expected from its biological origin, wattle bark extract contains, as well as tannins, a number of chemically distinct constituents. The common hydrolysis product of tannin is gallic acid shown in structure I. In the tree bark, tannin is said to be involved in the protection of the tree from insect and fungal attack.[10] The wattle tannin based adhesive from Tanzania has been extensively characterised and was useful in the formulation of anti-termite compounds.[11] On the other hand, CNSL is an extensively studied,[12–14] naturally occurring phenol obtained as a by-product during the processing of cashew kernels, and contains several phenolic compounds. A major monophenol component of the technical CNSL distillate is cardanol which has a C_{15} side chain in the *meta* position, as shown in structure **II**. The other two chief constituents of the CNSL are anarcadic acid and cardol, shown in structures **III** and **IV** respectively. Minor components include 2-methylcardol (**V**) and a small percentage of polymeric materials. The degree of saturation of the C_{15} alkyl side chain varies from complete saturation to partial unsaturation as shown in structure **VI**.



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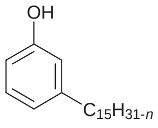

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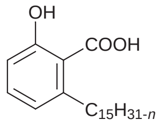

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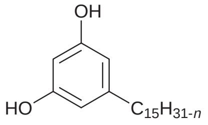

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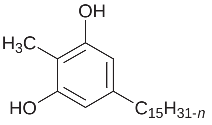

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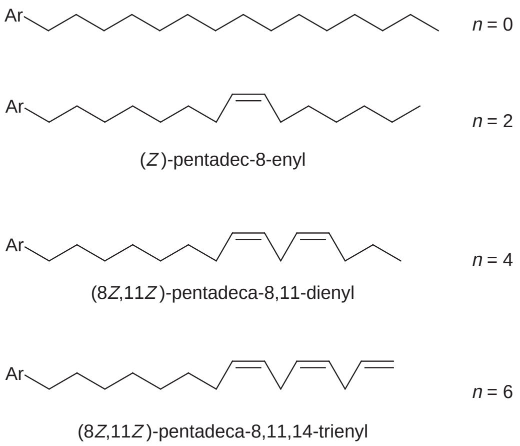

VI (structures of C_{15} chains in **II**–**V**)

The phenolic character and the unsaturation in the alkyl side chain make CNSL constituents important reactive materials in the preparation of binders for coatings and anti-corrosive paints and resins.[13] Cashew nut shell liquid is also reported to be used in protecting wood against termites and is especially used in making insecticidal formulations.[15] Since some of these plant natural products have good insecticidal activity and low toxicity to humans, interest in using them as wood preservatives is inevitable.

The above reported use of these natural products against termites has stimulated our interest in developing an anti-termite wood preservative from combinations of cashew nut shell liquid (CNSL), copper(II) chloride, and sulfited wattle tannins. The study objective was to develop a wood preservative using Tanzanian natural products with insecticidal and biocidal activities. Screening of the ability of CNSL and sulfited wattle tannins from Tanzania in combination with commercial wood preservatives to protect against termite attack was done. The wood preservative formulations included the combination of CNSL and $CuCl_2$ at different concentrations, wattle tannins and copper chloride, CNSL alone, wattle tannin alone, copper chloride alone and the control was copper chromium arsenate (CCA).

The uptake and commercialisation of this technology on a large scale is technically feasible by on site recycling of these by-products. This can be achieved by proper engineering design and innovation so as to incorporate the technology into the existing processing factories. On a pilot scale however, off-site recycling is a necessity in order to establish technical and economic viability towards large scale technology. Success in the recycling of cashew nut shell liquid and wattle tannins will be a step towards a cleaner technology which is about minimising the environmental impact of the by-products from the processes. The cost of designing and re-designing the process seems to be one of the probable barriers against commercialisation of the technology. Other likely barriers are the standard of the end-use material and the availability of markets for these preservatives and their products.

This paper reports and discusses the termite preservatives formulated from various combinations of compounds. The amount of CNSL in the combinations was large as cashew nut shell liquid is a by-product of the process and its use in preservative formulations will reduce process releases to the environment. The call for the latter aims at replacing the conventional environmentally hazardous compounds. The results of field tests against termite attack of wood blocks on the formulated preservatives are also reported and discussed.

Materials and methods

Test wood sample preparation and treatment

The test wood blocks were prepared from sapwood of two species; a soft wood ponderosa pine (*Pinus ponderosa*) and a hard wood, trembling aspen (*Populus tremuloide*). Seven hundred and seventy sapwood blocks, each of 14 × 14 × 14 mm size, were cut from air-dried sapwood of the two wood species. The test wood blocks were labelled and conditioned to 50% relative humidity and constant temperature (70 °F) to a constant weight. The blocks were randomly assigned to various treatments as per American Wood Preserver Association (AWPA) standard E10-91.[16] The weight of each block was recorded after treatment with the formulated preservative compounds.

Formulation of preservatives and wooden block treatment

The preservatives were formulated from sulfited wattle tannins, CNSL and copper salts in different concentrations. The control treatments included CCA, copper chloride, dimethyl sulfoxide (DMSO) and distilled water. The treatments were recorded in two categories coded as AS and PP for trembling aspen and ponderosa pine wood species respectively. The original weights of the treated test wood blocks were recorded and thereafter screened against harvesting termites of *Kalotermes spp.* for 108 days field exposure in Arusha and Moshi, Northern Tanzania. The test cubes were spread on top of the pre-cleaned experimental grounds before covering them with the dry plant materials.

Water at an amount of 1000 $cm^3\ m^{-2}$ was sprinkled on the plant materials to provide an appropriate environment for termite activity underneath.

Damage assessment of wood blocks

Damage and weight loss were recorded at an interval of two weeks, with a few exceptions. Damage on the block surfaces was observed visually whereas the block weight losses were determined by collecting the samples from the field and exposing to the laboratory atmosphere for moisture stabilisation before weighing them using a Sartorios analytical balance.

Results and discussion

Field surveys

The fields for exposure of the test wood blocks were surveyed and a large number of termite mounds, measuring up to three metres, on the open plains of Babati, West Kilimanjaro, Sanya plains and along the wheat growing belt of Mbulu Tanzania, were recorded. Damage on big trees, fallen timber, and in seedbeds was also recorded in West Kilimanjaro, Karatu and in Sanya plains. The damage incidence in field crops including beans, maize and wheat was at a peak during the harvesting period (July/August–October) in this part of Northern Tanzania. Considerable damage was also recorded on storage structures in some homesteads visited.

Termite screening responses

The results of different termite screening responses on the remaining percentage weight of the wood blocks after 108 days of field exposure are shown in Fig. 1 and 2. Some of these damage responses showed better results than the commercially used CCA. From the results in the figures, three distinct groups of treatment responses have been identified although they were not all consistent.

The first group is that of the least damaged treated test wood with their mean percentage weight losses after 108 days of field exposure: 3% CCA (2.2%), 1.5% CCA (3.3%), 0.5% CCA (4.8%), 2% $CuCl_2$ (5.5%), 40% CNSL + 2% $CuCl_2$ (10.0%), 2.5% $CuCl_2$ (10.5%), 40% CNSL + 1% $CuCl_2$ (10.8%). The fact that there were no dead termites recorded on the test ground surfaces suggests that the observations can be explained by the possibility that the blocks were not, or only slightly, damaged because either the impregnated chemicals acted as termite repellants or the chemicals made the blocks unpalatable to termites. The repellency effect by some of the plant materials to some insects, including aphid species, is well reported elsewhere.[17]

The second group consists of susceptible impregnated wood blocks. This group includes the following treatments with their percentage loss at 108 days of exposure: water (49.2%), DMSO (30.7), 5% tannin (20.5) and 2% tannin (15.6). These observations may be explained as being due to the effect of the impregnated chemicals in that either the test blocks were still palatable to termites or the chemicals acted as termite attractants. The latter possibility is supported by the well documented literature in that the choice of plant materials for consumption by insects is influenced by a complicated processes involving physical and/or chemical responses.[18]

The third group was evaluated as that of moderate damage. It should be noted however, that there was no consistency in weight losses in all the identified groups. This may have been due to uptake of either moisture or soil particles from the test grounds and a study is underway to identify the cause of this inconsistency.

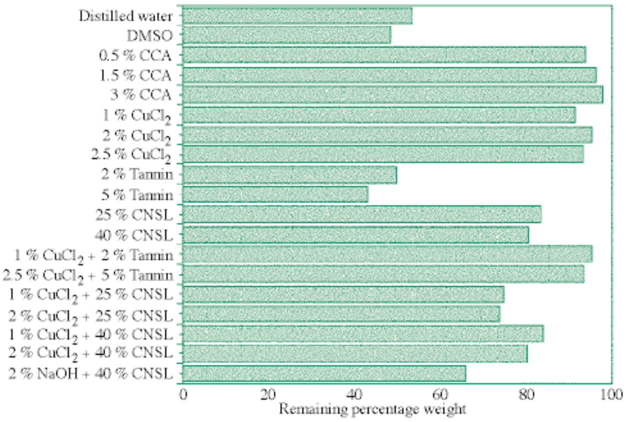

Fig. 1 Remaining percentage weight of wooden blocks after 108 days of field exposure of sample (AS).

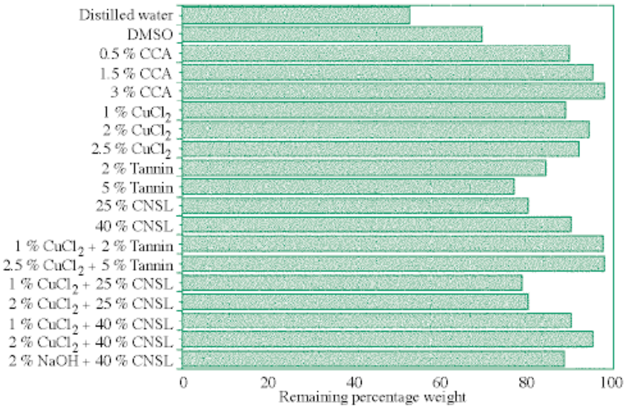

Fig. 2 Remaining percentage weight of wooden blocks after 108 days of field exposure of sample (PP).

Conclusion

Sharp differences between preservative effectiveness on test wood damage have been noticed in terms of the test wood damage response and weight loss. The survival of the termites in the test wood blocks shows that the formulated preservative does not act by killing the termites but is rather linked to the possibility that the compounds made the wood blocks unpalatable to termites or were termite repellents. The least damaged blocks are suggested for a screen against other termite species so as to establish the suitability as anti-termite compounds. If the formulated preservatives are active against other termite species, there is a necessity to try the preservative on a large scale, for it may turn out to replace the environmentally unfriendly wood preservatives currently used in the country.

Cleaner technology is about minimising the adverse environmental impact of releases from industrial processes, and the success in recycling cashew nut shell liquid and wattle tannin will reduce wastes from these processing factories.

Acknowledgements

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Sulfated metal oxide catalysts

Superactivity through superacidity?

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Summary

Sulfated metal oxides are a useful group of strong acid catalysts. The nature of their acidity, the identities of the active sites and their use in hydrocarbon transformation reactions are discussed.

Introduction

Acid catalysis is of fundamental industrial importance. It plays a vital role in the petroleum industry where acid catalysts are employed in the various isomerisation, cracking and alkylation reactions used to upgrade oil. Acids are also employed as catalysts for large scale polymerisation processes and display activity for hydration/dehydration reactions such as the interconversion of ethanol and ethylene. In the following, we briefly describe the interest which one particular class of solid catalyst has attracted because of its extremely high efficacy for some such reactions.

Supported metal oxides and their preparation

Some metal oxides, when sulfated, develop the ability to catalyse reactions characteristic of very strong acid catalysts at low temperatures, although with limited lifetimes. This not only presents the opportunity of saving energy but also generates a thermodynamic advantage. Isomerisation of straight chain alkanes to more highly branched isomers, which not only have higher octane numbers but are more useful as intermediates for further synthesis, is more favourable at lower temperature. Arata has identified a range of active sulfated oxides including those based on SO_4^{2-}/ZrO_2, SO_4^{2-}/Fe_2O_3, SO_4^{2-}/SnO_2, SO_4^{2-}/TiO_2, SO_4^{2-}/SiO_2, SO_4^{2-}/Al_2O_3 and SO_4^{2-}/HfO_2.[1,2] With the exception of Al_2O_3, sulfation must be performed on the amorphous precursors of the oxides such as hydroxides or oxyhydroxides in order to result in high activity. Although a variety of sulfation reagents can be used, most researchers have employed either dilute sulfuric acid (usually 0.5 mol dm^{-3}) or an aqueous solution of ammonium sulfate. The oxide precursor is generally immersed in the sulfating solution, left for a period of time, filtered, dried and calcined (heated in air or oxygen). Variation of any of these parameters can markedly affect the resultant catalytic activity. The temperature of calcination required to generate maximum performance depends upon both the oxide and the sulfation reagent. For example, in the case of sulfated iron oxide, maximum activity for *n*-butane isomerisation develops after calcination at 500–550 °C and for sulfated zirconia after 600–650 °C. Only a small uptake of sulfate is required, with optimum sulfur content being in the region of 1–2 wt%.

As well as promoting a variety of acid catalysed reactions, sulfation is also observed to affect physical properties, for example, it lowers crystallinity and increases surface area. The latter effect is always an important consideration in heterogeneously catalysed processes where reactions occur on surfaces. In the oxides where polymorphism (*i.e.* two or more crystal forms of the same chemical composition) occurs, sulfation has been observed to preferentially stabilise one form. Zirconia is an example of such a material. It can exist in the monoclinic, tetragonal, cubic and orthorhombic crystal forms depending upon the method of preparation and conditions. Sulfate is one of a range of dopants observed to favour the formation of the tetragonal phase over the more commonly encountered monoclinic form.[3]

The nature of their activity

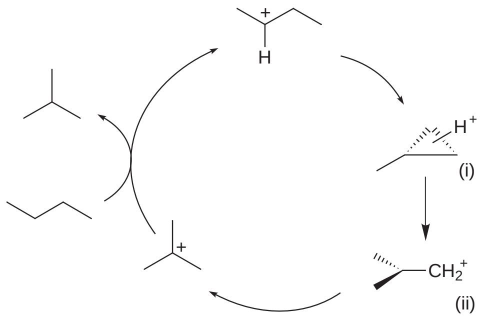
It is always of interest to understand the mechanism of operation of a catalyst, since in some cases this can allow one to improve existing catalysts or develop new ones. *n*-Butane isomerisation to produce isobutane is probably the most well studied reaction catalysed by sulfated metal oxides. One mechanism of this reaction involves the generation of an intermediate substituted protonated cyclopropane cation (i) and primary carbenium ion (ii) which undergoes C–C and C–H bond fission and rearrangement (the unimolecular or intramolecular route—adapted from ref. 4); see Scheme 1.

This process is characteristic of strong acid catalysis—the intermediate carbenium ion can be produced by either a Lowry–Brønsted acid route (1) or a Lewis acid route (2) (Scheme 2). The observation that sulfated systems exhibit greater activity than concentrated sulfuric acid indicates that the oxides do not simply function as supports for H_2SO_4, although this is a point of debate.[5]

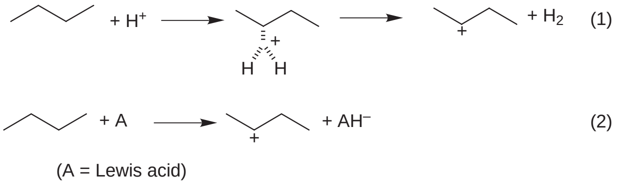
Many researchers have therefore concluded that these systems are 'superacidic'. Following Gillespie, a superacid is defined as a

Green Context

Of all the classes of industrial transformations, the conversion of hydrocarbon feedstocks into useful functional building blocks is arguably the most fundamental, since it provides all other processes with their raw materials. These reactions are typically catalysed by strong acids. It is therefore no surprise that there has been a great deal of work on solid acids, although the exact nature of their mode of action is not always clear. One particularly good example of this is given by the sulfated metal oxides. This review, intended for the non-specialist, provides an accessible description of the nature of these materials. While their activity is greater than that of sulfuric acid, their acidity is less clearly defined, with opinion moving away from the original position that these materials were superacids. This is based on the accumulation of reaction evidence as well as refinements in the physical techniques used to characterise the materials. ***DJM***



Scheme 1 Intramolecular butane isomerisation mechanism.

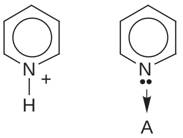


Scheme 2 Acidic activation routes of butane.

material which exhibits an acid strength greater than 100% H_2SO_4 (*i.e.* has a Hammett acidity function $\leqslant -12$).[6] This is, of course, a Lowry–Brønsted based definition. A definition of superacidity exists for Lewis acidity in that any material exhibiting an acid strength greater than anhydrous $AlCl_3$ is termed superacidic.[6] Initially attempts to measure the acid strengths of sulfated oxides centred around the use of Hammett acidity indicators. In this method, the acid strength of the material is determined by its ability to change an organic base adsorbed onto the solid into its conjugate acid form which is associated with a colour change. Therefore, if an indicator changes colour it is indicative that the material possesses a Hammett acidity value equal to or lower than its pK_a. A wide range of such indicators are available with different pK_a values. Samples of the material are suspended in an inert solvent (*e.g.* sulfuryl chloride) and tested with indicators of varying strength. Although application of this method indicates that the materials are strong acids, it is not without limitations: (i) equilibrium between the base and solid sample must be established which can take very long times; (ii) interaction with the solvent molecules or the adsorbate can generate misleading results, for example it has been reported that red shifts can occur which generate erroneous conclusions;[7] (iii) a colour change must be observed which can be difficult when the sample is coloured, *e.g.* SO_4^{2-}/Fe_2O_3; (iv) with most indicators it is not possible to distinguish between Lowry–Brønsted and Lewis acidity.

More favoured approaches to determining the acid site strengths and densities of solids involve studies of the adsorption of base probe molecules such as ammonia and pyridine, and also the use of test reactions such as the dehydration of isopropanol to produce propylene.[8] Microcalorimetry in conjunction with uptake measurements allows one to determine the heat of adsorption of a probe molecule which can be related to site strength and density. An example of the application of this method is provided in a study of sulfated zirconia by Dumesic and co-workers[9] who have studied the heat of adsorption of ammonia at 150 °C as a function of uptake—in this way, they determined a *differential* heat of adsorption which relates to the population of sites of various acid strength. By selective poisoning of the sets of these sites, it may be possible to determine the strength of sites responsible for a particular catalytic reaction. Thermal desorption methods determine site strength and density by measuring the loss of adsorbed probe molecules as a function of sample temperature. However, these approaches have been limited in their application due to adsorbate decomposition (*e.g.* ref. 10) which means that the true interaction of the probe molecule with the acid site is not being examined. Consequently, thermal desorption studies of adsorbed substituted benzenes (which are weaker bases than those generally used) was suggested as suitable. Subsequently, in some systems this method itself was shown to suffer the limitation of oxidation of benzene and even the evolution of SO_2 during heating.[11] So, in summary, many of the adsorption/desorption measurements have been limited by the intrinsic high reactivity of these materials. Therefore, spectroscopic studies of adsorbed molecules, which can also provide valuable information on acidic properties of solids, have been quite widely adopted in this field.

Following work by Parry in the 1960s, infra-red spectroscopic studies of the adsorption of pyridine have become routine for the discrimination of Lowry–Brønsted and Lewis acid sites on heterogeneous catalysts.[12] Pyridine interacts with the two types of site respectively in the manner shown in Scheme 3.



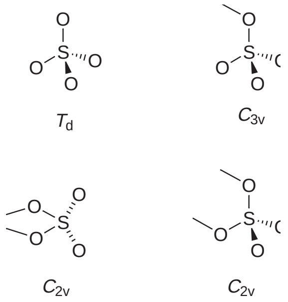
Scheme 3 Interaction of pyridine with Lowry–Brønsted (H^+) and Lewis acid (A) sites.

Infra-red bands unique to each form can be distinguished in the 1400 to 1700 cm^{-1} region of the spectrum. Furthermore, a knowledge of the absorption coefficient for each species makes quantification possible and acid site strength can be determined from the loss of band intensity as a function of temperature. However, it has been shown that application of some these methods to determine the acidic properties to sulfated metal oxides is severely limited due to oxidation and/or decomposition reactions which occur between adsorbent and adsorbate, *e.g.* ref. 13. Consequently, techniques such as FTIR studies of carbon monoxide adsorption have been applied. When CO interacts with Lewis acidic sites, the C=O stretching frequency increases *via* σ-bond donation. The shift in frequency can be directly related to Lewis acid strength.[14] Low temperature studies of the influence of CO adsorption on the OH groups of the oxides can be used to determine Lowry–Brønsted strength. As mentioned below, many of the studies currently published employing these techniques indicate that although sulfated metal oxides may be strong acids, they are not superacidic. Here we have only briefly touched on some of the measurements of acid site strength which have been reported, however, a more detailed description of various methods of acid site strength determination on solids along with their associated limitations is available elsewhere.[15]

The nature of the active site

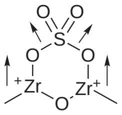
Many different proposals describing the nature of the active catalytic site have been made. Generally, these have been based around the symmetry of the co-ordinated sulfate ion. In principle a number of symmetries for SO_4^{2-} are possible (Scheme 4). It is possible to distinguish these forms by examination of the sample infra-red spectra in the 1200 to 900 cm^{-1} S=O stretching region.[16] As a consequence of the gross selection rule that a change in dipole moment must occur for a transition to be infra-red active, the different forms of sulfate give different numbers of bands. The T_d form of SO_4^{2-} (*i.e.* tetrahedral symmetry like the

CH_4 molecule) gives two infra-red active transitions in this region, the C_{3v} form (*i.e.* pyramidal symmetry like the NH_3 molecule) three and the C_{2v} form (*i.e.* symmetry like the H_2O molecule) four. An additional consideration is that the C_{2v} form of sulfate can occur in bridging or chelating configuration. Both C_{2v} and C_{3v} forms have been commonly reported by different researchers in the literature and therefore different models of the active site have been made.[17]



Scheme 4 Different SO_4^{2-} symmetries.

One such proposal from Arata for SO_4^{2-}/ZrO_2 is shown in Scheme 5, in which sulfate adopts a bridging C_{2v} symmetry. It is argued that the sulfate group enhances the Lewis acidity of the Zr cations by an inductive effect (Lowry–Brønsted acidity can be generated from this form as described below).



Scheme 5 Proposed active site in SO_4^{2-}/ZrO_2.

Alternative proposals for catalytic activity

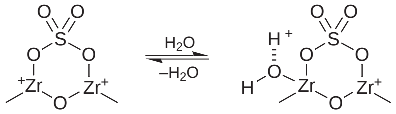
Increasingly, based on spectroscopic and calorimetric studies, the consensus is emerging that sulfated metal oxides do not possess the superacidity originally postulated. A number of recent studies have demonstrated that the acid strength is similar to that encountered for transitional aluminas or protonic zeolites. An example of this is provided in a study by Drago and Kob[18] in which they have applied the 'cal-ad' method to the determination of acidity of sulfated zirconia and related systems. In this method a calorimetric titration of a basic probe is carried out in a hydrocarbon solvent of similar molecular mass. It is claimed that this technique allows the determination of the number, equilibrium constant and site strengths of different acid sites on solids. The results for the highest enthalpies of pyridine adsorption in cyclohexane for various SO_4^{2-}/ZrO_2 samples along with silica and the zeolites HZSM-5 and HY are given in Table 1.

Table 1 Results of 'cal-ad' measurements of pyridine adsorption on various solids—adapted from ref. 18

Material	$-\Delta H_{ads}$(pyridine)/ kJ mol^{-1}
SiO_2	50 ± 4
H-ZSM-5	171 ± 4
HY	142 ± 4
SO_4^{2-}/ZrO_2 calcined at 600 °C	130 ± 8
SO_4^{2-}/ZrO_2 calcined at 300 °C	63 ± 4
$Pt/SO_4^{2-}/ZrO_2$	125 ± 4
$Fe/Mn/SO_4^{2-}/ZrO_2$	109 ± 4

Along with many other studies, the data in Table 1 certainly suggest that SO_4^{2-}/ZrO_2 based systems are not superacidic. However, this view is still contentious. Amongst those who believe that superacidic sites are present, there continues to be disagreement as to whether these are Lowry–Brønsted or Lewis in nature. A possible explanation for the division of opinion on all these matters relates to the observation that the catalytic activity of these materials is strongly dependent upon storage/pre-treatment conditions.

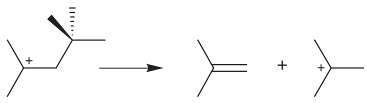
Inter-conversion of Lewis and Lowry–Brønsted sites can occur by hydration/dehydration processes—



Scheme 6 Proposed interconversion of Lewis and Lowry–Brønsted acidic sites in SO_4^{2-}/ZrO_2.

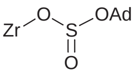
see Scheme 6. An important question, therefore, is if not superacidity, what is the origin of the exceptional behaviour of these catalysts?

Sachtler and coworkers have performed experiments which aim to address this problem.[19] They noted that although $Fe/Mn/SO_4^{2-}/ZrO_2$ (reputedly the strongest 'superacidic' sulfated metal oxide known to date) had acid sites of similar strength to SO_4^{2-}/ZrO_2 in their measurements, its butane isomerisation activity was much greater. Furthermore, they pointed out that the occurrence of the unimolecular isomerisation mechanism described above is not expected at the low temperatures of activity for these catalysts because of the primary carbenium ion intermediate. By analysing the product distributions in reactions using doubly isotopically labelled butane, $^{13}CH_3CH_2CH_2{}^{13}CH_3$, they have shown that the reaction occurs by formation of a bimolecular (intermolecular) intermediate which isomerises to give the 2,4,4-trimethylpentyl carbenium ion, followed by β-fission to yield an isobutene molecule and the isobutyl carbenium ion (Scheme 7). The catalytic cycle then progresses by the loss of a hydride species from the *n*-butane reactant to the isobutyl carbenium ion to generate the isobutane product and the C_8 intermediate *via* reaction with the isobutene. Unlike the intramolecular process, this pathway does not involve the intermediacy of the unfavourable primary carbenium ion.



Scheme 7 Decomposition route of C_8 intermediate.

They proposed that the activity of sulfated metal oxides arises from their ability to stabilise reaction intermediates possibly by the formation of C–O–S bonds such as sulfate esters. Farcasiu and colleagues have made a comprehensive study of the pathways involved in the reaction of adamantane over SO_4^{2-}/ZrO_2.[20] They have proposed that rather than behaving as a superacid, this system operates *via* a one electron oxidation mechanism in which an electron is transferred between the substrate and the sulfate group. A sulfite ester is proposed to be an intermediate in the reaction, as shown in Scheme 8.



Scheme 8 Adamantyl sulfite ester. Ad = adamantyl radical.

Limitations to application

Despite the current controversy over the mechanism of operation of sulfated metal oxides, it is obvious that they possess extraordinary catalytic behaviour. However, to our knowledge, they have not yet found commercial application. They deactivate quickly on use due to poisoning of active sites by the deposition of coke (carbonaceous residues). This can be overcome to some extent by including hydrogen in the feed, which hydrogenates the coke as it is formed, or by the inclusion of additional catalyst components, *e.g.* Pt, which retard coke deposition. Such deactivation is not necessarily a limitation to industrial application. Fluidised catalytic cracking is a large scale catalytic process in which zeolites are used to convert long chain hydrocarbons into more useful shorter chain forms. In operation the catalyst becomes rapidly deactivated by coking, its lifetime is usually about 3 seconds! However, the process has been engineered such that regeneration, which involves the exothermic combustion of coke by air, supplies the heat necessary to conduct the reaction. A major limitation for the application of sulfated metal oxides relates to preparation. It is difficult to prepare separate batches of catalyst which exhibit reproducible catalytic performance. This problem, which may relate to inhomogeneous sulfation, needs to be addressed and has already been the subject of some research attention.[21]

Summary

In this short article, we have attempted to briefly describe some of the current interest in sulfated metal oxide catalysts. Due to limitations of space, we have not been able to fully describe some of the emerging areas of interest. We have only briefly mentioned the inclusion of additional metallic components. In some cases these may have proved beneficial by suppressing deactivation (*e.g.* $Pt/SO_4^{2-}/ZrO_2$) whereas in others they enhance the intrinsic catalytic activity (*e.g.* $Fe/Mn/SO_4^{2-}/ZrO_2$).[22] The range of reactions to which these materials are being applied is also broadening. In our own work, we are investigating the effect of combining the unique activity of sulfated systems with the underlying catalytic activity of the base oxides for methane oxidation (see for example refs. 23, 24). In experiments performed at elevated pressure using iron oxide based catalysts, we have observed that the sulfation procedure suppresses the low temperature (*i.e.* <400 °C) total oxidation activity of these materials, (presumably by a site blocking mechanism) whilst enhancing activity at higher temperature (*i.e.* >500 °C) leading to some production of selective oxidation products (methanol and higher hydrocarbons) probably as a consequence of the stabilisation of higher surface areas and the formation of new types of active site. In the case of iron oxide systems prepared from goethite, the sulfation procedure also generates interesting structural effects which are currently the subject of further study.

Although much remains to be explained about sulfated metal oxides in general, their remarkable catalytic activity is clear.

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Paper 8/07963C

Organic reactions without an organic medium

Utilization of perfluorotriethylamine as a reaction medium

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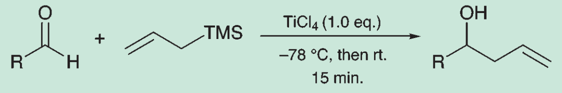
Summary

Perfluorotriethylamine is a good alternative reaction medium for Lewis acid catalyzed reactions and it can be easily recycled by simple extractive workup.

Introduction

One of the most important issues in scientific society is the environmental problem. Thus far, there have been increasing demands for substitutes for toxic and/or harmful solvents like CH_2Cl_2.[1] Recently, inert and less toxic fluorous (perfluorinated) fluids have been recognized and are attracting attention as new alternative solvents.[2] However, it is still not clear what kind of reactions to run in these solvents and how to run them. This fact allowed us to survey the scope and limitations of the utility of fluorous liquids as alternative reaction media for Lewis acid catalyzed reactions, which are of great current interest due to their unique reactivities and selectivities. We examined the Hosomi–Sakurai reaction[3] as a model reaction, and the results are summarized in Table 1.

Table 1 Results of the Hosomi–Sakurai allylation in various solvents



Entry	R	Solvent	Yield (%)[a]
1	*n*-C_5H_{11}	Perfluorohexane	67
2		Perfluoro-2-butyltetrahydrofuran	57
3		Perfluorotributylamine	78
4		Perfluorotriethylamine	90
5		CH_2Cl_2	92
6		Hexanes	63
7		Neat	67
8	CH_2CH_2Ph	Perfluorotriethylamine	98
9	*c*-C_6H_{11}		Quantitative

[a] Isolated yield.

Results and discussion

As shown in Table 1, perfluorotrialkylamines were better reaction media than perfluorohexane[4] and perfluoro-2-butyltetrahydrofuran (entries 1–4). In addition, perfluorotriethylamine was superior to perfluorotri-*n*-butylamine (entry 3 *vs*. 4) presumably due to higher lipid solubility derived from the shorter perfluoroalkyl chains, and turned out to be as appropriate a solvent as CH_2Cl_2 which is commonly used in this reaction (entry 4 *vs*. 5). Only modest yields were obtained when the reaction was carried out in nonpolar hexanes (entry 6) or without solvent (entry 7). These results clearly show that some solvent effects of perfluorotriethylamine promoted the reaction. Some comments are worth noting, *e.g.* (1) the basicity of perfluorotrialkylamine is so low that the amine does not interact with a strong Lewis acid like $TiCl_4$,[5] (2) however, the amine's polarity might be retained to some extent,[6] which might be as important a factor in the promotion of reaction as lipophilicity. Althogh the lipid solubility of perfluorotri-*n*-butylamine is lower than that of perfluorohexane, perfluoro-2-butyltetrahydrofuran (critical solution temperatures in mixtures with *n*-hexane are 59 °C for perfluorotributylamine, 20 °C for perfluorohexane and 29 °C for perfluoro-2-butyltetrahydrofuran)[7] and hexanes, it was found to be a better reaction medium. Among fluorous amines, perfluorotriethylamine, which exhibits relatively high lipophilicity due to its short perfluoroalkyl chains and suitable boiling point, could be an ideal alternative solvent. To the best of our knowledge, this is the first application of perfluorotriethylamine as a reaction medium.

The catalytic version of this reaction[8] using acetal in place of aldehyde also proceeded smoothly (Fig. 1). Furthermore, recycling of the solvents is under investigation from both environmental and economical points of view. While perfluorotriethyl-

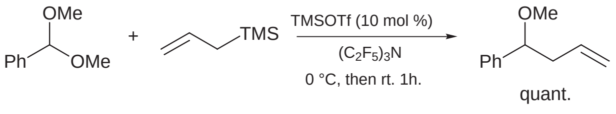


Fig. 1 Catalytic allylation in perfluorotriethylamine.

Green Context

The search for replacements for halogenated solvents is a key area for investigation, with many of these solvents due to be phased out or banned completely. This report describes the use of perfluorinated amines as an alternative medium for reactions involving Lewis acid catalysts. The solvent may be readily recovered and reused. ***SJT***

amine shows some miscibility with organic materials, extractive workup with ethyl acetate/water resulted in high recovery of the reaction medium (90%). Successive reuse of the recovered solvent in the same reaction without further purification yielded amounts of product as high as in the first cycle (Fig. 2). This result clearly shows that the highly hydrophobic character of the perfluorinated material allows us to recycle directly the reaction medium for highly moisture-sensitive reactions. This is another merit of fluorous reaction media.

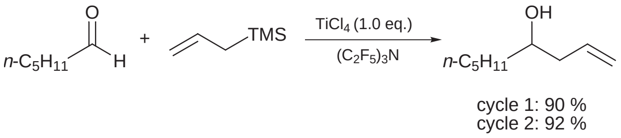


Fig. 2 Recycling perfluorotriethylamine without purification.

In conclusion, we have shown that perfluorotriethylamine is a promising alternative reaction medium. Further studies to clarify the scope and limitation of fluorous reaction media are actively in progress in our group.

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9 Typical procedure is as follows. Under a nitrogen atmosphere, titanium tetrachloride (0.220 ml, 2 mmol) was added dropwise to aldehyde (2 mmol) and allyltrimethylsilane (0.333 ml, 2.1 ml) in perfluorotriethylamine (4 ml) at −78 °C. After completion of the addition, the dry ice–acetone bath was removed and the reaction mixture was stirred for 15 min at rt. The reaction was quenched with 4 ml of water, and stirred for a few minutes. Then, 3.6 ml of fluorous solvent was recovered by three phase extraction (organic layer: 4 ml of ethyl acetate). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by silica gel chromatography afforded the homoallyl alcohol.

Paper 8/08193J

Diels–Alder reactions in ionic liquids

A safe recyclable alternative to lithium perchlorate–diethyl ether mixtures

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Summary

Diels–Alder reactions in neutral ionic liquids (such as 1-butyl-3-methylimidazolium trifluoromethanesulfonate, 1-butyl-3-methylimidazolium hexafluorophosphate, 1-butyl-3-methylimidazolium tetrafluoroborate, and 1-butyl-3-methylimidazolium lactate) are reported. Rate enhancements and selectivities similar to those of reactions performed in lithium perchlorate–diethyl ether mixtures have been observed. As the ionic liquids used have no measurable vapour pressure, are thermally robust, will tolerate impurities such as water, and are recyclable, it is envisaged that these systems could be used on an industrial scale.

Introduction

The Diels–Alder reaction is an important and widely used reaction in organic synthesis,[1] and in the chemical industry.[2] Rate enhancement of this reaction has been achieved by the use of solvents such as water,[3] surfactants,[4] very high pressure,[5] lithium amides,[6] alkylammonium nitrate salts,[7] and macrocyclic hosts.[8,9] In the past decade, lithium perchlorate–diethyl ether mixtures (LPDE) have received a great deal of attention,[10] due to their significant rate acceleration and the improved selectivities obtained. The improved reactivity in these media is thought to be due to high internal pressure,[11] and the Lewis acidic nature of the lithium ion.[12] Room temperature ionic liquids have been found to be excellent solvents for a number of reactions, such as the Friedel–Crafts reaction,[13] isomerisations,[14] and hydrogenation.[15] The execution of Diels–Alder reactions in ionic liquids has several distinct advantages, in that the ionic liquids have no measurable vapour pressure, can be recycled, are non-explosive, are thermally robust, and are more convenient to use.

Here, we have performed a number of Diels–Alder reactions in neutral ionic liquids such as 1-butyl-3-methylimidazolium trifluoromethanesulfonate ([bmim][OTf]),[16] [bmim][PF$_6$],[17] [bmim][BF$_4$],[18] and [bmim][lactate]. ¶ Rate enhancements and selectivities similar to those of reactions performed in LPDE[10] have been observed. The initial results in this study of a number of simple Diels–Alder reactions in several ionic liquids are given in Table 1.

Results and discussion

The reaction of cyclopentadiene with three dienophiles in [bmim][OTf] was studied by gas chromatographic analysis (see entries 1–7). The reactions all proceed smoothly at ambient temperatures, giving almost quantitative yields of the Diels–Alder adduct after 24 h. It can be seen that the *endo–exo* selectivity depends on the dienophile and reaction temperature. For example, the selectivity improves from 1.6 : 1 to 2.4 : 1 in going from 20 °C to −15 °C (see entries 4 and 6). The selectivity also appears to be slightly higher in the initial stages of the reaction (see entries 3, 4, 5, 6, 8 and 9). It was decided to investigate whether the rate of the reaction is affected by the ionic liquid chosen. For example, the amount of product after 2 h is greater for the [bmim][lactate] ionic liquid (entry 8) than for a similar reaction carried out in [bmim][OTf] (67% after 2 h at 20 °C). No

Green Context

This article on Diels–Alder reactions in ionic solvents highlights the potential opportunities which ionic solvents could offer. Significant rate enhancement and high yield/selectivity are some of the key requirements for a 'green' process. These appear to have been achieved. Use of ionic solvents could replace the best alternative, lithium perchlorate–diethyl ether, avoiding the generation of lithium perchlorate based wastes and avoiding significant safety issues associated with diethyl ether and pressure reactions. However, the product isolation protocol, as stated in the paper, does require the use of organic solvent and distillation, both of which significantly reduce the overall 'greenness' of the process, and this requires further development. It will also be essential to demonstrate efficient recycling of the ionic solvent. It is early days, and the green gauntlet has been thrown down. The promise of such novel reaction procedures now needs to be realised and demonstrated by an holistic comparison with current technologies. ***DJM***

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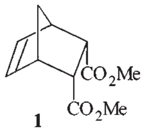
¶ The [bmim][lactate] ionic liquid was synthesised by the reaction of sodium (*S*)-2-hydroxypropionate and [bmim]Cl in acetone. The resultant precipitate of sodium chloride was filtered off and the acetone evaporated.

Table 1 The reaction of dienes with dienophiles in various solvents. Unless otherwise stated, the reactions were performed with a 1.5:1.0:1.0 molar ratio mixture of diene:dienophile:solvent.

Entry	Solvent	Dienophile	Diene	Product	Temp./ °C	Time/h	Yield (%)	*endo* : *exo* ratio
1	[bmim][OTf]	dimethyl maleate	cyclopentadiene	**1**	20	18	98	4.2 : 1
2	[bmim][OTf]	ethyl acrylate	cyclopentadiene	**2**	20	18	96	6.0 : 1
3	[bmim][OTf]	acrylonitrile	cyclopentadiene	**3**	20	2	80	1.7 : 1
4	[bmim][OTf]	acrylonitrile	cyclopentadiene	**3**	20	24	98	1.6 : 1
5	[bmim][OTf]	acrylonitrile	cyclopentadiene	**3**	–15	3	5	3.0 : 1
6	[bmim][OTf]	acrylonitrile	cyclopentadiene	**3**	–15	24	96	2.4 : 1
7	[bmim][OTf]	acrylonitrile	cyclopentadiene	**3**	–15	72	99	2.4 : 1
8	[bmim][lactate]	ethyl acrylate	cyclopentadiene	**2**	20	2	87	4.4 : 1
9	[bmim][lactate]	ethyl acrylate	cyclopentadiene	**2**	20	24	99	3.7 : 1
10	[bmim][BF_4]	ethyl acrylate	cyclopentadiene	**2**	–15	24	99	5.0 : 1
11[a]	water	ethyl acrylate	cyclopentadiene	**2**	20	1	30	3.5 : 1
12[a]	5 M LPDE	ethyl acrylate	cyclopentadiene	**2**	20	1	61	8.0 : 1
13[a]	[bmim][PF_6]	ethyl acrylate	cyclopentadiene	**2**	20	1	36	8.0 : 1
14	[bmim][PF_6]	DMAD[b]	isoprene	**4**	20	15	45	
15	[bmim][PF_6]	DMAD	isoprene	**4**	80	2	98	
16	[bmim][OTf]	ethyl acrylate	isoprene	**5**	70	24	97	2.5 : 1[c]
17	[bmim [PF_6]	but-2-en-3-one	isoprene	**6**	20	18	11	4.0 : 1[c]
18	[bmim][PF_6][d]	but-2-en-3-one	isoprene	**6**	20	6	98	20.0 : 1[c]
19	[bmim][BF_4][e]	ethyl acrylate	isoprene	**5**	20	2	90	40 : 1[c]

[a] 1.0 molar in diene and 0.2 molar in dienophile, dissolved or suspended in solvent. [b] DMAD = dimethyl acetylene dicarboxylate. [c] This ratio represents a 4- to 3-isomer ratio, not an *endo* : *exo* ratio. [d] 5 mol% ZnI_2 added. [e] 10 mol% $BF_3{\cdot}OEt_2$ added.



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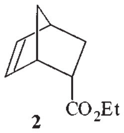

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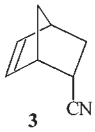

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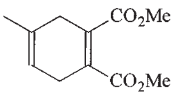

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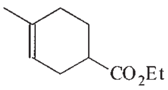

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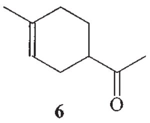

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enantioselectivity was observed in the [bmim][lactate] reactions. It should be noted that [bmim][lactate] is considered to have a greater degree of hydrogen-bonding interactions than [bmim][OTf]. Also, the reaction in [bmim][lactate] is heterogeneous and the products and starting materials are isolated by decanting off the upper organic layer, whereas the [bmim][OTf] reaction is homogeneous. In this case the products can be extracted from the [bmim][OTf] ionic liquid by solvent extraction with either diethyl ether or hexane. The ionic liquid can then be used straight away for further reactions without loss of reactivity.

In order to directly compare the performance of a Diels–Alder reaction in an ionic liquid with similar reactions in lithium perchlorate–diethyl ether mixtures (5 M LPDE) and water (the same conditions used by Grieco *et al.*[10]), the conversion after a given period of time was determined for similar amounts of solvent. The reaction of ethyl acrylate with 5 mol eq. of cyclopentadiene (0.2 M and 1.0 M respectively) in equal volumes of water, 5 M LPDE or [bmim][PF_6] was performed (entries 11–13). As can be seen, the conversion after 1 h in the ionic liquid is intermediate between that of water and that of 5 M LPDE. The selectivity in the ionic liquid reaction (entry 13) is the same as for the LPDE reaction (entry 12). However, it should be noted that the reaction rate in an ionic liquid is dependent upon the ionic liquid chosen and in this case, [bmim][PF_6] gives lower rate enhancement than the [bmim][lactate] ionic liquid. Also, the preferred reaction conditions in the ionic liquids use higher concentrations of reactants (*i.e.* 1.5 : 1.0 : 1.0 molar ratio of diene to dienophile to ionic liquid). The conversion rates are higher (typically 40–60% conversion after 1 h) and less of the cyclopentadiene dimer by-product is formed.

One of the main advantages of ionic liquids is the large thermal operating range that is possible (typically −40 °C to 200 °C), which enables excellent kinetic control. Reactions can be effected by heating the bottom part of a sealed tube containing ionic liquid. Since the ionic liquid has virtually no vapour pressure, the pressure created from volatile compounds (such as isoprene) is modest and specially designed high pressure apparatus is not necessary.

The reaction of isoprene with dienophiles such as ethyl acrylate or but-3-en-2-one in ionic liquids (see entries 16–18) is slow at room temperature, but proceeds smoothly at 70–80 °C. For these reactions, the products differ in their regiochemistry, in contrast to the previous reactions in which the products differ in their stereochemistry. In order to see if Lewis acids could be used to promote Diels–Alder reactions in ionic liquids, the reaction of but-3-en-2-one with isoprene was investigated (see entry 17). The uncatalysed reaction is slow and gives moderate selectivity for the 4-isomer. The addition of 5 mol% of zinc(II) iodide dramatically increases the rate of the reaction and improves the selectivity to 20 : 1 for the 4-isomer (see entry 18). It was found that the ionic liquid remained catalytically active after the products were extracted from the ionic liquid with diethyl ether and fresh starting materials were added. This implies that the zinc(II) iodide catalyst remains in the ionic liquid during solvent extraction. Even better selectivities and reaction rates are observed when $BF_3{\cdot}OEt_2$ is used as a catalyst in the [bmim][BF_4] ionic liquid (see entry 19). Note: the reaction rates and selectivities in the [bmim][BF_4] ionic liquid without a Lewis acid present are similar to those in the [bmim][PF_6] ionic liquid.

Conclusion

Ionic liquids are excellent solvents for the Diels–Alder reaction. In terms of conversion after a given time period, they are similar to those of lithium perchlorate–diethyl ether mixtures. All of the ionic liquids investigated so far promote the Diels–Alder reaction to varying extents, but the factors that affect this are at present not fully understood. Ionic liquids have several advantages over lithium perchlorate–diethyl ether systems, in that they can be used over a wide temperature range (−40 °C to 200 °C), can be used under pressure, are not oxidising or explosive, are easily recycled and can be used in conjunction with Lewis acids. More general advantages are that ionic liquids have no measurable vapour pressure, are thermally robust, will tolerate impurities such as water, and if the extraction solvent is recycled, generate almost no waste products. It is envisaged that these systems could be used on an industrial scale.

Acknowledgments

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Paper 8/08052F

Epoxidation and oxidation of alcohols

A new procedure using the methylalumoxane/*tert*-butyl hydroperoxide system

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Summary

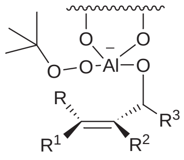
Here reported are the first applications of methylalumoxane, an oligomeric compound of formula $(MeAlO)_n$, as a catalyst for the epoxidation of allylic alcohols and the oxidation of benzylic, aliphatic (cyclic and linear) alcohols into the corresponding carbonyl compounds.

Introduction

Epoxidation of allylic alcohols to carbonyl compounds represent two fundamental preparative processes: in fact the appropriate exploitation of the reactivity of the epoxy alcohol or carbonyl functionalities often represents the key step of synthetic sequences leading to more complex molecules. Both the processes are achievable through a wide variety of procedures, which, especially as regards the conversion of alcohols to carbonyl compounds, are often based on the employment of transition metal reagents such as Cr(VI), Mn(VII), Mn(IV), Pb(IV), *etc.* However, these procedures are frequently affected by serious disadvantages (strong toxicity to humans and the environment, frequent requirement of high oxidant/substrate ratios to complete the reaction with consequent formation of noticeable amount of polluting waste, variable selectivity deriving from the occurrence of secondary reactions, *etc.*). In recent years these problems have been partially circumvented by supporting or incorporating the oxidative reagents into an inorganic matrix.

Our interest has been recently attracted by the unusual catalytic properties showed by aluminosilicates in oxidative processes.[1] In particular we found that commercially available aluminosilicates (3 Å and 4 Å molecular sieves), without any previous metal impregnation can be conveniently employed as heterogeneous catalysts in the stereoselective epoxidation of allylic alcohols with *tert*-butyl hydroperoxide (TBHP).[2,3] The observed regio- and stereoselectivity have been reasonably explained through the previous formation of tetracoordinate Al centres of type **A** on the external surface of the catalyst and the subsequent evolution to epoxy an alcohol by a Sharpless-type process.

Alumoxanes are aluminium- and oxygen-containing materials, characterized by the presence of at least one oxygen bridge between two aluminium centres.[4] In particular, alkylalumoxanes, easily available by carefully controlled hydrolysis of aluminium alkyls, belong to an industrially important class of oligomeric compounds of formula $(RAlO)_n$.[5,6] For example, methylalumoxane (MAO) (R = Me, n = 5–12) was found to be an efficient cocatalyst for group 4 metallocene catalyzed ethylene and propylene polymerization,[7,8] and for the synthesis of highly syndiotactic polystyrene in the presence of tetrabenzyltitanium.[9]



A

Here we report that MAO has been shown to be a more convenient catalyst for the epoxidation of allylic alcohols with TBHP: in fact, because of the presence of a much greater number of active catalytic Al sites in these oligomeric species, in comparison with the ones situated on the outer surface of the molecular sieves, the fast formation of epoxy alcohols **2** was found to occur in a satisfactory way and under milder conditions (Scheme 1).

Results and discussion

Methylalumoxane can be considered an effective catalyst: in fact comparable results have been observed by the employment of solid MAO, obtained as a white powder after careful removal under reduced pressure of both the solvent and Me_3Al,[10] a com-

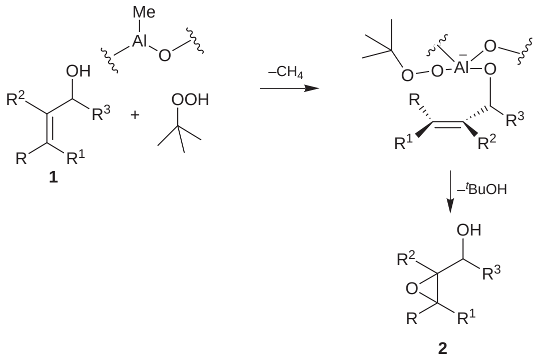
Green Context

Oxidations including epoxidations are of fundamental importance to synthetic organic chemistry—the products are used as intermediates and final products in numerous sectors of the chemical industry including pharmaceuticals and polymers. Unfortunately oxidation chemistry is commonly associated with the employment of toxic reagents and catalysts such as those based on high oxidation state heavy metals. In this article, a non-toxic catalyst is effectively used in a range of oxidation reactions; its ability to function in a hydrocarbon (as opposed to halogenated) solvent is a bonus and adds to the credibility of the chemistry as an environmentally acceptable oxidation methodology. ***JHC***

Table 1 Epoxidation of allylic alcohols with MAO/TBHP system

Run	Alcohol	Catalyst	Time/h	T/°C	Yield (%)[a] d.r. (T/E)
a	*trans*-2-Hexen-1-ol	MAO	16	r.t.	68
		3A Molecular sieves	96	45	63
b	Geraniol	MAO	2	4	70
		MAO	2	r.t.	82
		3A Molecular sieves	48	60	67
c	*trans*-2-Nonen-4-ol	MAO	20	4	70 (65/35)[b]
		3A Molecular sieves	20	40	70 (37/63)
d	*trans*-3-Tridecen-5-ol	MAO	2	r.t.	78 (64/36)[b]
		3A Molecular sieves	48	45	81 (34/66)
e	3-Methyl-2-nonen-4-ol	MAO	2	r.t.	75 (58/42)[b]
		3A Molecular sieves	18	40	71 (14/86)
f	4-Methyl-3-nonen-5-ol	MAO	3	4	84 (65/35)
		3A Molecular sieves	72	45	89 (12/88)
g	2-Methyl-2-nonen-4-ol	MAO	2	4	80 (>95/5)
		3A Molecular sieves	18	45	65 (82/18)

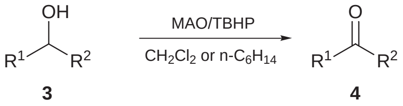
[a] Experimental details for the reactions catalyzed by 3A molecular sieves are reported in ref. 8. All the yields refer to chromatographically pure compounds. Values in parentheses refer to the *threo/erythro* (T/E) diastereoisomeric ratio (d.r.). [b] ^{1}H NMR yields.



Scheme 1

mon contaminant present in 5–10% amounts in the commercial product. With respect to molecular sieves, a lower degree of stereoselectivity was observed in the case of secondary allylic alcohols (with the exception showed in Table 1, entry g) but, rather surprisingly, *threo* diastereoisomers proved to be invariably the predominant products. It seems reasonable that this stereochemical outcome may be originated by the structural and conformational features of MAO, with the involvement of both linear and cyclic oligomers characterized by different degrees of flexibility. As regards the preparative aspects, it should be noted that no loss of efficiency was observed by performing geraniol epoxidation on a 10 mmol scale or in hydrocarbon solvent (83% yield).

The synthetic potential of the MAO/TBHP system has been further confirmed by its employment in a new, highly efficient procedure for the conversion of alcohols into the corresponding carbonyl compounds (Scheme 2). As reported in Table 2, very satisfactory results have been obtained with a variety of secondary benzylic and aliphatic (linear and cyclic) alcohols. Note the high efficiency and selectivity of the process: in fact, final products are usually obtained in very high yields and contaminated only by very low amounts of the starting materials.



Scheme 2

Table 2 MAO-catalyzed oxidation of alcohols to ketones with TBHP

Run	Alcohol	t/h	Yield (%)[a]
a	1-Phenylethanol	2	92
b	1-(1-Phenyl-2-methyl)propanol	4	>95[b]
c	α-Tetralol	6	84 (16)[b]
d	1-(2-Naphthyl)ethanol	16	>95[b]
e	1-(4-Bromophenyl)ethanol	3	95
f	1-(4-Methoxyphenyl)ethanol	7	94
g	4-*tert*-Butylcyclohexanol	6	45 (55)[b]
h	4-*tert*-Butylcyclohexanol	12	95
i	Dihydrocholesterol	14	85
j	Octan-2-ol	16	90
k	3-Methylcyclopentanol	12	93

[a] Yields refer to isolated, chromatographically pure, compounds. Values in parentheses refer to starting materials. [b] ^{1}H NMR yields.

As regards the stereochemical aspects, rather poor diastereoselectivity was observed in the case of 4-*tert*-butylcyclohexanol, employed as a 80/20 *trans*/*cis* mixture; in fact, the interruption of the oxidation after 6 h (Table 2, entry g) afforded the carbonyl compound in 45% yield, resulting the recovered starting material as a 70/30 *trans*/*cis* mixture.

The possibility of the employment of very mild conditions can be highly appreciated in the oxidation of sensitive alcohols, such as, for example, 1-(4-methoxyphenyl)ethanol which is rapidly changed into the corresponding mixed *tert*-butyl peroxide in 67% yield by treatment with the zeolite/TBHP system. On the grounds of these initial results, the exploitation of the catalytic properties of oligomeric alumoxanes seems to disclose a route to new procedures for the oxidation of organic functionalities characterized by high simplicity (as regards both set-up and work-up), efficiency and selectivity.

Experimental

Preparation of solid MAO

A 10% toluene solution of MAO (10 ml) is submitted to distillation under a slow flow of Ar at 80 °C under reduced pressure (2.0 mmHg). After the complete removal of the solvent and of trimethylaluminium, a white powder (800 mg) is obtained, which can be stored without any appreciable loss of activity in a dry-box for 8–10 days.

Experimental procedure for oxidation reactions

Reactions were performed by stirring, in an ice bath and under an argon atmosphere, MAO (1.8 ml, 10% toluene solution), dry CH_2Cl_2 (12 ml) and the substrate (2 mmol). After 10 min, TBHP (1.5 eq) was added and the reaction, monitored by TLC and/or GLC, was continued at room temperature for the times reported in Tables 1 and 2. Then H_2O (2 ml) was added and the filtered solution was directly poured onto the top of a silica gel chromatographic column. Elution with *n*-pentane/diethyl ether mixtures afforded the pure epoxy alcohols and ketones.

Alternatively, the substrate (2 mmol) was added to a solution of solid MAO (100 mg) in *n*-hexane (6 ml); after addition of TBHP (1.5 eq) the reaction was continued as reported above.

Acknowledgement

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Paper 8/09768B

Homogeneous dehydrosulfurisation under ambient conditions

Harnessing the facile polyhedral rearrangement in the ruthenium carbonyl cluster $Ru_5C(CO)_{15}$

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Summary

Reaction of the square pyramidal cluster $Ru_5C(CO)_{15}$ with H_2S affords the bridged butterfly species $(\mu\text{-H})Ru_5C(CO)_{14}(\mu\text{-SH})$ in which H and SH coordinate with simultaneous cleavage of one Ru–Ru bond and displacement of one CO. Subsequent reaction with CO regenerates the starting cluster and eliminates elemental sulfur (S_8) and dihydrogen. These reactions take place at ambient temperatures and pressures.

Introduction

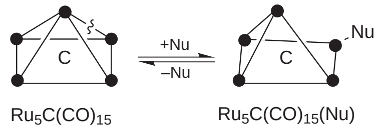
Hydrogen sulfide is generated in vast quantities from the hydrodesulfurisation of sulfur compounds prevalent in petroleum and natural gas.[1,2] With increasingly stringent environmental legislation the need to remove sulfur from fuels is becoming increasingly important due to the problems associated with their emission into the environment.[3,4] The environmental problem does not end with the generation of H_2S, but the H_2S then must be disposed of in some way. Industry achieves this by the dehydrosulfurisation of H_2S to elemental sulfur using the Claus process[5] that operates according to the equation below:

$$2\ H_2S + SO_2 \rightarrow 3/8\ S_8 + 2\ H_2O$$

The Claus process is comprised of a very efficient heterogeneous alumina catalyst that operates at temperatures in excess of 300 °C. Homogeneous catalysts are also known but offer no significant advantage as they also require relatively harsh conditions[6] and bacteria have also been used.[7] In this paper we describe some preliminary results concerning a homogeneous system employing $Ru_5C(CO)_{15}$ which has certain differences and therefore possible advantages over the existing systems. Firstly, SO_2 is not required and as such the limitations imposed in the equation above are no longer present, and secondly, the process operates under ambient conditions which could potentially reduce energy expenditure.

Results and discussion

The square pyramidal cluster $Ru_5C(CO)_{15}$, initially prepared[8] and studied[9,10] by the Johnson–Lewis group, is known to undergo a facile polyhedral rearrangement to a bridged butterfly (pseudo-trigonal bipyramidal) geometry on reaction with small nucleophiles (see Scheme 1). For example, the reaction of $Ru_5C(CO)_{15}$ with acetonitrile affords the addition product, $Ru_5C(CO)_{15}(NCMe)$, and redissolving this cluster in a non-coordinating solvent such as dichloromethane results in regeneration of the starting compound.[10] Poë *et al.* have established that this polyhedral rearrangement mechanism is important in certain substitution reactions involving 2-electron donor ligands.[11] In addition, the framework of $Ru_5C(CO)_{15}$ has also been found to act as a support on which certain organic transformations take place and the chemistry of this cluster has been reviewed recently.[12]



Scheme 1

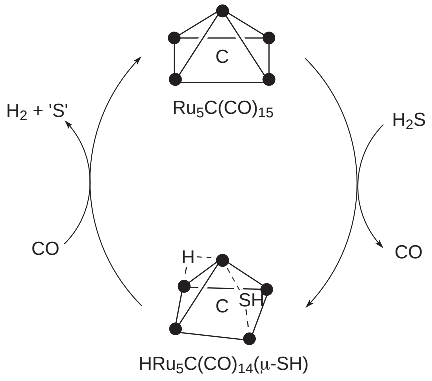
$Ru_5C(CO)_{15}$ reacts rapidly with H_2S, H_2Se and HSR (R = Me, Et) at room temperature to afford $HRu_5C(CO)_{14}(\mu\text{-SH})$, $HRu_5C(CO)_{14}(\mu\text{-SeH})$ and $HRu_5C(CO)_{14}(\mu\text{-SR})$ (R = Me, Et), respectively.[13] These derivatives are structural analogues and definitive characterisation of $HRu_5C(CO)_{14}(\mu\text{-SEt})$ has been obtained by a single crystal X-ray diffraction analysis.[13] In accordance with a cluster with a total electron count of 76 the Ru atom skeleton adopts a bridged butterfly topology. The SEt group coordinates to one of the hinge Ru atoms and the bridging Ru

Green Context

The splitting of hydrogen sulfide into its elements represents a useful reaction, turning a waste product into two valuable feedstocks. The system under study here allows this reaction to proceed under extremely mild conditions under an atmosphere of CO. The CO is not used up in the reaction, but is shuttled on and off the metal cluster, and can be recovered for reuse. At this stage in the work, the system is not catalytic. Further developments towards a genuinely useful system would require a catalytic version of the system to be developed. *DJM*

atom. The hydride ligand apparently bridges the Ru–Ru hinge bond. Closure of the cluster skeleton to the square pyramid found in the precursor can be achieved by thermal elimination of one carbonyl ligand.

In our experiments, instead of heating $HRu_5C(CO)_{14}(\mu\text{-}SH)$ to eliminate carbon monoxide, we treated it with CO at atmospheric pressure in a solution of refluxing dichloromethane, *ca*. 42 °C (Scheme 2).[14] Regeneration of $Ru_5C(CO)_{15}$ was complete within 25 minutes. After removal of the solvent the residue was found to contain $Ru_5C(CO)_{15}$ (as indicated by the characteristic IR ν_{CO} stretching frequencies) and elemental sulfur which was detected by mass spectrometry. The mass spectrum confirmed the presence of sulfur showing a typical sequential regression from S_8 to S_1 and a qualitative test for H_2 gas proved positive. The entire process (*i.e.* H_2S followed by CO) was repeated several times using the same batch of cluster and slight decomposition was observed with wet solvents. While this process is not catalytic it represents a simple homogeneous method for dehydrosulfurisation under ambient conditions based on the facile structural rearrangement common to $Ru_5C(CO)_{15}$. It is quite remarkable that rupture of the Ru–S–Ru bond is quite so facile and this could be due to the fact that the sulfur ligand bridges an unsupported Ru–Ru vertex rendering it somewhat unstable. While the process operates under very mild conditions that could, in principle, save energy expenditure, it is complicated by the need for CO. However, the CO is not actually consumed and as long as none is lost from the system it could be reused indefinitely.



Scheme 2

This work compliments earlier desulfurisation studies carried out by Deeming and co-workers using the triruthenium cluster $Ru_3(CO)_{12}$. $Ru_3(CO)_{12}$ was found to react with benzo[*b*]thiophene under relatively mild conditions to form $Ru_3(CO)_8(C_8H_6)$ in which one Ru–Ru bond has been cleaved. However, this process was not found to be reversible.[15] We also intend to study other clusters for related activity such as $Os_6(CO)_{18}$ [16–18] which also undergo facile polyhedral rearrangements.

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Paper 8/08023B

Selective monoacylation of ferrocene

An eco-friendly procedure on the solid phase of alumina

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Summary

A simple, efficient and environment-friendly procedure has been developed for acylation of ferrocene with direct use of carboxylic acid in the presence of trifluoroacetic anhydride on the solid phase of alumina. A wide range of structurally varied carboxylic acids have been found to provide selectively the monoacylated products in high yields.

Introduction

Ferrocene and its derivatives have been the subject of current interest because of their potential uses as chiral ligands in organic synthesis[1] and as important materials in various fields.[2] Thus, derivatization of ferrocene has received special attention.[3] Acylation of ferrocene is a very important reaction as it introduces a carbonyl functionality which is highly manipulable. Although a number of methods are available in the literature[4] for acylation of ferrocenes they have serious disadvantages of producing a mixture of products containing mono- and di-acylated derivatives together with unreacted starting material which requires separation at a subsequent stage. More seriously, the use of toxic chemicals like $AlCl_3$, BF_3, PCl_3 and acid chlorides entails environment pollution. Thus, an efficient and eco-friendly procedure for this important transformation is needed. Recently, we have introduced a simple procedure for regioselective acylation of aromatic ethers with carboxylic acids on the solid phase of alumina in the presence of trifluoroacetic anhydride[5] and we have discovered that this procedure also works very well for acylation of ferrocene.

Results and discussion

In a typical general procedure, a mixture of carboxylic acid and trifluoroacetic anhydride was added to ferrocene adsorbed on the surface of activated acidic alumina and mixed uniformly with shaking. The mixture was kept at room temperature with occasional shaking for a certain period of time until the reaction was complete. The product was isolated by simple extraction of the solid mass by ether followed by usual workup.

Several structurally varied carboxylic acids were used in this acylation reaction to provide the corresponding monoacylated ferrocenes in excellent yields. The results are summarised in Table 1. The reactions with aromatic acids are rather slow and conversions are not complete even after 8 hours. However, no side product is isolated in these reactions; only the unreacted ferrocene and carboxylic acids were recovered. In general, all the reactions are very clean and monoacylated products are obtained as the sole isolable compounds. Presumably, alumina acts here as a Lewis acid in effecting the Friedel–Crafts acylation of ferrocene with the mixed anhydride of the carboxylic acid and trifluoroacetic anhydride.

Conclusion

This method on the solid surface of alumina provides a very convenient and efficient procedure for acylation of ferrocene. The notable advantages of this methodology are direct use of carboxylic acids, mild conditions (room temperature), operational simplicity, generality, excellent selectivity (only monoacylation occurs), high yields (85–98%) and no environmental pollution, and thus it offers significant improvements over other procedures involving Friedel–Crafts acylation of ferrocenes.[4] We believe this will find significant applications in the synthesis of ferrocene derivatives.

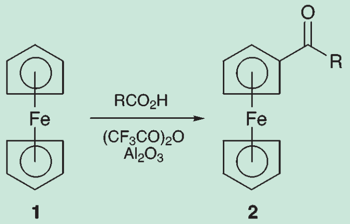
Representative experimental procedure

A solution of ferrocene (186 mg, 1 mmol) in dry CH_2Cl_2 (2 ml) was adsorbed on the surface of activated (heated at 150 °C for 3 h under reduced pressure and then cooled under nitrogen) alu-

Green Context

Functionalised ferrocenes are currently of great interest due to their potential as planar-chiral ligands for, *e.g.*, hydrogenation catalysts. One of the most important methods of functionalisation of these materials is Friedel–Crafts acylation, a process which typically uses substantial quantities of strong Lewis acids such as aluminium chloride. The development of alternative, green procedures is therefore of interest. The use of alumina and trifluoroacetic anhydride as an activating system for carboxylic acids has been shown to allow the highly selective monoacylation of ferrocene. It is thought that the reaction proceeds *via* a mixed carboxylic/trifluoroacetic anhydride. Yields are excellent in most cases, in others the unreacted carboxylic acid can be easily recovered. Work up procedures are simple and convenient on a small scale, but would need further optimisation to provide a genuinely green overall process. ***DJM***

Table 1 Acylation of ferrocene with carboxylic acid/ TFAA on the surface of alumina



Entry	RCO_2H, R =	Time/h	Yield of **2** (%)[a]
1	CH_3	0.5	98
2	CH_3CH_2	0.5	90
3	$PhCH_2$	1.5	96
4	$CH_3(CH_2)_6$	1.0	93
5	$CH_3(CH_2)_{16}$	1.0	94
6	$CH_3CH(NO_2)(CH_2)_2$	1.0	85
7	$PhS(CH_2)_3$	1.5	88
8	$(CH_3)_2CH$	0.5	95
9	$(Ph)_2CH$	1.5	93
10	$PhSCH_2CH(CH_3)$	1.5	89
11	C_6H_{11}	1.0	92
12	Ph	8.0	55[b]
13	*p*-OMe–Ph	8.0	58[b]

[a] Yields refer to pure isolated products, fully characterized by spectral and analytical data. [b] The rest is recovered starting material.

mina (acidic, 3 g) and then the solvent was evaporated off completely under vacuum. To this was added a mixture of acetic acid (120 mg, 2 mmol[6]) and trifluoroacetic anhydride (525 mg, 2.5 mmol[6]) with shaking. The mixture was then kept at room temperature with occasional shaking under a moisture guard for a certain period of time as required to complete the reaction. [In all the reactions, a colour developed (usually pink, but in a few cases green and blue) and darkened with progress of reaction.] The solid mass was then eluted with Et_2O, and the ether extract was then washed with an aqueous solution of sodium hydrogen carbonate and brine and dried over anhydrous sodium sulfate. Evaporation of solvent furnished practically pure (by ^1H NMR) monoacetyl ferrocene (223.5 mg, 98%). This was further purified by filtering it through a short column of silica gel to afford the analytically pure product, mp 85–86 °C. The other acylated products are also obtained following the same procedure and identified by spectral (IR, ^1H and ^{13}C NMR) and analytical data.

The unreacted carboxylic acids (Table 1, entries 12, 13) were recovered from the hydrogen carbonate extract by acidification and extraction with ether. However, trifluoroacetic acid, possibly being too water soluble and not being a high boiling liquid (bp 72 °C), was not isolated in this work-up process.

Acknowledgements

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6 With 1 equivalent of carboxylic acid and 1 equivalent of trifluoroacetic anhydride the reaction is considerably slow and the conversion is also not complete even after 12 h. However, use of 2 equivalents of carboxylic acid and 2.5 equivalents of TFAA accelerated the reaction to a great extent producing only the monoacylated product. But, interestingly, use of 4 equivalents of carboxylic acid and 8 equivalents of TFAA leads to diacylation quantitatively (2 examples) although the condition is yet to be generalised.

Paper 8/08890J

Selective *para*-bromination of phenyl acetate

under the control of zeolites, bases, acetic anhydride or metal acetates in the liquid phase

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Summary

HBr formed during the bromination of phenyl acetate has a major influence on the selectivity of the reaction. Sodium forms of zeolites X and Y increase the selectivity markedly by a process of cation exchange that removes this HBr. Removal of the HBr prevents formation of phenol and allows the bromination of PA to give almost exclusively the *para* isomer in quantitative yield. Bases, acetic anhydride and some metal acetates also improve the selectivity. These findings offer a variety of strategies for clean synthesis of *para*-bromophenyl acetate.

Introduction

The chemicals industry is increasingly required to minimise its environmental impact.[1] The needs are particularly acute in the field of electrophilic aromatic substitution[2] where reactions can be poorly regioselective, may produce polysubstituted as well as monosubstituted products, and often use large quantities of Lewis acids, which are destroyed during the work-up process and then require disposal. Because of their special crystalline structures, zeolites can influence the selectivity of aromatic substitution.[3] The *para* isomer is favoured because steric factors favour the transition state within the zeolitic cages. We have previously shown, for example, how the use of zeolites or other solids can help to gain selectivity over nitration,[4] chlorination,[5] bromination,[6] methanesulfonylation[7] and allylation[8] reactions of simple aromatic compounds.

Despite the many applications of zeolites in catalytic processes, relatively little attention has been paid to the use of zeolites in the field of aromatic bromination. Several studies have shown that various ion-exchanged zeolites enhance the rates and *para*-selectivities of brominations of alkyl- or halogeno-arenes,[9–14] but in the case of toluene, for example, the selectivities were still not ideal. Sasson *et al.* reported that sodium exchanged Y zeolite improved the *para*-selectivity in the bromination of toluene, but that the selectivity and rate of reaction diminished as the reaction proceeded.[15,16] We were able to show that there is a highly selective stoichiometric reaction with the zeolite followed by a slower and less selective catalytic reaction and have developed a generally useful method for *para*-bromination of alkyl- and halogeno-benzenes.[6] It was of interest to know if this approach would be useful in providing a cleaner approach to the industrially important production of *para*-bromophenyl acetate. It was not obvious what would happen during bromination of phenyl acetate, which is not only reactive (more reactive than halogenobenzenes but less than toluene),[17] but also capable of cleavage by HBr to give phenol, an even more highly activated compound. In fact, certain zeolites turned out to provide highly selective reactions, primarily by removing HBr in an efficient manner rather than through any reliance on shape selectivity. Therefore, we investigated alternative approaches for the removal of HBr and now report several possible ways for conducting the reaction in a cleaner manner.

Results and discussion

1. Bromination of phenyl acetate over zeolites

Preliminary studies on the bromination of phenyl acetate **1** in the presence of a sodium-form mordenite zeolite in dichloromethane showed that the initial reaction rate was much lower than in its absence, but that the selectivity was enhanced.[18] After some time, however, the reaction rate suddenly increased dramatically and simultaneously the selectivity declined. A possible explanation was that the HBr generated by the reaction was absorbed by the zeolite, either through direct absorption into the narrow channels

Green Context

The selective bromination of aromatics represents a major challenge in the preparation of many important intermediates. This contribution investigates the factors influencing selectivity in the bromination of a reasonably activated system, phenyl acetate. The results indicate that the major contribution of zeolites in this reaction is not, as might be expected, due to shape selectivity, but is rather a consequence of their ability to scavenge HBr, which causes a non-selective competitive reaction. The paper goes on to evaluate alternative methods for the effective removal of HBr. The importance of this paper is that it provides a series of highly selective routes to the desired products, with minimal side reactions, and that it demonstrates that a careful study of a reaction can lead to a much improved understanding of the real factors at play. ***DJM***

or *via* ion-exchange, until the capacity was exceeded, whereupon an unselective HBr-catalysed process took over. Indeed, when HBr was added to a reaction mixture over mordenite, similar results to those without mordenite were obtained.

It seems likely that HBr reacts under these conditions with **1** to produce phenol, which reacts more rapidly and less selectively with bromine. The zeolite serves to remove the HBr. In view of these findings, an extensive study on bromination of **1** over various zeolite catalysts was carried out and the results are presented in Table 1.

Table 1 Bromination of **1** in the presence of various catalysts[a]

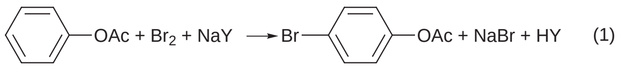
Catalyst	**1** (%)[c]	**3**[b] (%)[c]	**2** (%)[c]	Others[b] (%)[c]
None	100	—	—	—
None[d]	67	—	7	26
HY	99	—	1	—
NaY	32	—	68	—
NaX	42	—	58	—
Naβ	96	—	3	—
NaMord	97	—	2	—
NaZSM-5	100	—	—	—
$AlCl_3$	3	5	52	33

[a] Bromination of **1** (10 mmol) with bromine (10 mmol) over catalyst (3 g) in CH_2Cl_2 (30 ml) at room temp. for 2.5 h. [b] Compound **3** is 2-bromophenyl acetate; others are phenol, 2-bromophenol, 4-bromophenol, 2,4-dibromophenol and 2,4-dibromophenyl acetate. [c] Absolute yields were determined by quantitative GC. [d] 20 mmol of **1** and 20 mmol of bromine were used in otherwise identical conditions.

As the results in Table 1 show, use of NaY zeolite as catalyst gave a much better rate enhancement than use of HY, indicating that strong acidity is not preferred for the selective *para*-bromination of **1**.[19] Use of NaY and NaX zeolites exhibited excellent *para*-selectivity and gave high yields under very mild conditions. Indeed, even when the phenyl acetate was completely converted, the only product obtained in the presence of NaY was 4-bromophenyl acetate **2**. Sodium forms of other zeolites also gave good *para*-selectivity but the yields were much lower than with NaY under comparable conditions. These results are consistent with a lower rate of diffusion into the more restricted pores of the other zeolites.

A range of different cation-exchanged Y zeolites were next compared (Table 2). The results showed that all the zeolites produced **2** selectively, but the fastest reactions and best yields were obtained with the Na and K forms.

We conclude that a highly selective stoichiometric reaction involving the NaY or KY zeolite takes place [eqn. (1)], as found



1 **2**

with toluene.[6] There appears to be no advantage from the stronger acidity associated with some of the multivalent cations[20] nor from the lesser or greater geometrical constraints brought about by other alkali metal cations.[21,22]

The yield of **2** could be improved further by increasing the reaction temperature, the reaction time, the amount of bromine or the amount of zeolite. The reaction of **1** (10 mmol) with bromine (20 mmol) in the presence of NaY (4 g) for 5 h at 25 °C led to a quantitative yield of **2**.

Table 2 Effect of compensating cation on the zeolite Y catalysed bromination of **1**[a]

Catalyst	**1** (%)[b]	**2** (%)[b]
La-Y	97	3
Mg-Y	91	9
Al-Y	91	9
Li-Y	56	43
Na-Y	32	68
K-Y	43	56
Cs-Y	78	21

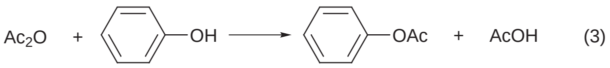
[a] See footnote *a* to Table 1. [b] Absolute quantities, determined by GC. No other products were observed.

Although it should be possible to recover the HY zeolite–NaBr solid mixture and heat it to give back the NaY zeolite,[6] or to reconvert the HY into NaY by a standard ion-exchange process, such processes would render the overall synthesis more expensive than simple reaction of bromine with **1**. Therefore, the effects of alternative additives capable of removing HBr were investigated. An additional benefit from such additives might be the avoidance of the need for solvent.

2. Effect of acetic anhydride (Ac_2O)

Addition of Ac_2O to the reaction medium might limit phenol formation by trapping HBr formed and by converting any incipient phenol back into its acetate [eqn. (2) and (3)].

$$Ac_2O + HBr \longrightarrow AcBr + AcOH \qquad (2)$$



The effect of Ac_2O on the selectivity was therefore investigated. The results showed that with zinc chloride or aluminium bromide as catalyst the reaction produced negligible amounts (<1%) of 2-bromophenyl acetate (**3**) in the presence of an equimolar amount of acetic anhydride, even at high conversions (>90%) of the substrate. The process could be optimised to produce a final mixture containing *ca.* 99% of **2** by use of a small excess of bromine, no solvent and a reaction time of 5 h at −4 °C. Without catalyst the reactions were very slow.

3. Influence of bases

An alternative method for removal of HBr would be to add a base to the reaction medium. Therefore, reactions were carried out in the presence of solid $NaHCO_3$, Na_2CO_3 and NaOAc together with dichloromethane as solvent (Table 3). As shown in Table 3, all these bases resulted in high selectivity, though the reactions were slow, being *ca.* 80% complete after 24 h at 0 °C.

4. Influence of certain metal acetates

Electrophilic aromatic bromination over thallium(III) acetate is highly regioselective.[23,24] It is possible in the present case that certain metal acetates could act both as catalysts and as scavengers of HBr, thereby providing another possible way of gain-

Table 3 Effect of bases on the selectivity of bromination of **1**[a]

Base	Amount of base (mmol)	Time/h	**1**(%)[c]	**3**(%)[c]	**2**(%)[c]	Others[b] (%)[c]
—	0	1.5	12	5	76	7
$NaHCO_3$	38	24	21	3	76	—
$NaHCO_3$	50	24	19	1	80	—
NaOAc	50	24	26	1	73	—
Na_2CO_3	25	24	22	1	77	—

[a] Bromination of **1** (50 mmol) with bromine (50 mmol) in the presence of base and CH_2Cl_2 (10 ml) at 0 °C. [b,c] See corresponding footnotes to Table 1.

ing selectivity. Several metal acetates were therefore tried either in the presence or absence of acetic anhydride (Table 4). Excellent selectivity was obtained, particularly with zinc acetate, even when Ac_2O was not used in the reaction. It is likely that the selectivity results because HBr generated in the reaction is trapped by the zinc acetate to give acetic acid and zinc bromide, thereby avoiding the formation of phenol. The reaction occurred much more rapidly than in the absence of the salt. Either the zinc acetate itself or the product zinc bromide could have been responsible for catalysing the reaction, which was complete within 5 h at 0 °C. Although this method is highly selective, however, it will be unattractive for commercial use on grounds of potential environmental impact.

Table 4 Effect of some metal acetates on the bromination[a]

Metal acetate (mass/g)	Ac_2O/mmol	Time/h	**1** (%)[b]	**3** (%)[b]	**2** (%)[b]
$Cu(OAc)_2$ (3)	40	3	28	—	71
$Co(OAc)_2$ (5)	40	4	41	1	58
$Hg(OAc)_2$ (5)	40	5	2	1	96
$Zn(OAc)_2$ (5)	40	5	—	1	99
$Zn(OAc)_2$ (5)	—	5	—	1	99

[a] Reaction conditions: **1** (40 mmol), bromine (60 mmol), metal acetate and acetic anhydride, at 0 °C. [b] See footnote *b* to Table 2.

Conclusions

HBr formed during the bromination of **1** is a main factor influencing the regioselectivity. The HBr reacts with **1** to produce phenol, which then reacts rapidly and indiscriminately. Zeolites NaY and NaX can accelerate the bromination of **1** and significantly increase the selectivity by a process that incorporates cation exchange to remove the HBr formed. Heating the recovered zeolite–NaBr mixture or ion-exchanging the recovered zeolite with aqueous NaCl should regenerate its activity. Simple bases can also improve the selectivity by neutralising the HBr formed, while acetic anhydride increases the selectivity because it can react with both HBr and phenol to prevent the unwanted side reactions. However, these reactions are then slow unless additional catalysts are added. Finally, the bromination of **1** with bromine is also improved by certain metal acetates, notably zinc acetate, which acts both to remove HBr and to catalyse the reaction. These studies reveal a variety of strategies that might have benefit for the clean bromination of phenyl acetate or related substrates.

Experimental

Reagents

Samples of NaY and NaX zeolites were provided by Union Carbide, while ZSM-5, β and mordenite zeolites were supplied by PQ Zeolites (now Zeolyst International). Other cation forms of zeolites were prepared by a literature procedure.[16] All zeolites were heated overnight at 140 °C before use. All bases and metal acetates were dried overnight at 100 °C. Solvents were used without additional purification.

Standard procedure used during method development

Procedure for zeolite-catalysed bromination of PA.

Phenyl acetate (10 mmol), the zeolite (3 g) and dichloromethane (30 ml) were mixed in a three-necked round-bottomed flask fitted with a calcium chloride guard tube and a magnetic stirrer and protected from light. The mixture was stirred at room temperature for 15 min, after which bromine (10 mmol) was added. After a suitable time (typically 2.5 h), the reaction mixture was filtered through a sintered funnel and the solid was rapidly washed with acetone. An aqueous sodium hydrogen sulfite solution (10%, 30 ml) was quickly added to the filtrate to remove bromine and hydrogen bromide. The organic layer was washed with distilled water (3×30 ml), dried over anhydrous magnesium sulfate, and filtered. Dodecane (60 ml, 0.045 g) was added as internal standard and the solution was subjected to quantitative GC analysis.

The residual solid was stirred with acetone (15 ml) for 30 min in order to desorb any materials in the channels of the zeolite, then filtered. An aqueous sodium hydrogen sulfite solution (10%, 30 ml) was quickly added to the filtrate and the aqueous phase was then extracted with dichloromethane (3×10 ml). The organic layer was treated and analysed according to the method described above.

Bromination of 1 in the presence of bases.

The procedure was similar to the procedure for zeolite-catalysed bromination of **1**, but with a base present instead of a zeolite and with the following components and conditions: **1** (50 mmol), bromine (50 mmol), base (50 mmol) and dichloromethane (10 ml), at 0 °C for 24 h.

Bromination of 1 in the presence of metal acetates.

The procedure was similar to the procedure for zeolite-catalysed bromination of **1**, but with a metal acetate present instead of a zeolite and with the following components and conditions: **1** (40 mmol), bromine (60 mmol), Ac_2O (40 mmol) and metal acetate (3–5 g), at 0 °C for 3–5 h (see Table 4 for details). No other solvent was used.

Bromination of 1 in the presence of acetic anhydride.

The procedure was similar to the procedure for zeolite-catalysed bromination of **1**, but with acetic anhydride present instead of a zeolite and with the following components and conditions: **1** (40 mmol), bromine (40 mmol), Ac_2O (60 mmol), at 0 °C for 5 h. No other solvent was used.

Acknowledgements

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Paper 8/08242A

Asymmetric epoxidation of olefins

The first enantioselective epoxidation of unfunctionalised olefins catalysed by a chiral ruthenium complex with H_2O_2 as oxidant

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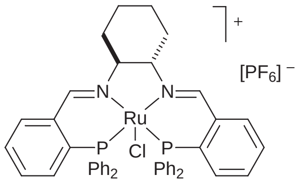
Summary

Up to 40% ee was obtained in the asymmetric epoxidation of styrene and other unfunctionalised olefins catalysed by the ruthenium(II) complex $[\mathrm{RuCl(PNNP)}]\mathrm{PF}_6$ (PNNP = *N*,*N′*-{bis(*o*-diphenylphosphino)benzylidene}-(1*S*,2*S*)-diiminocyclohexane) using hydrogen peroxide as the primary oxidant.

Introduction

Catalytic epoxidation of olefins is both a major industrial technology and an essential synthetic method.[1] However, several problems are still unresolved, in particular the nature of the oxidant and the product selectivity, including enantioselectivity in the case of asymmetric epoxidation.[2,3] Although hydrogen peroxide is a cheap and environmentally friendly oxidant, as required for large-scale applications, its use in homogeneous catalysis is generally hampered by the decomposition reaction which is catalysed by most transition metals.[4] Accordingly, the use of H_2O_2 in ruthenium-catalysed oxidation reactions is scarcely documented.[5–7] In the field of asymmetric catalysis, the Mn(III) salen-based methodology[2,3] has successfully extended the scope of the epoxidation reaction to unfunctionalised olefins, but a general protocol suitable for *trans*-substituted and terminal olefins is still lacking. Thus, there is considerable interest in the development of alternative catalytic systems. Lately, ruthenium complexes with chiral N,O- and N,N-donor ligands have been tested as asymmetric epoxidation catalysts.[8–10]

Since metal complexes with either achiral[4,11] or chiral[4] phosphines are scarcely used in catalytic epoxidation, we have started an investigation of Ru(II) complexes containing chiral tetradentate P,N-ligands. We find now that the novel cationic complex $[\mathrm{RuCl(PNNP)}]\mathrm{PF}_6$ **1** [PNNP = (*N*,*N′*-bis{*o*-diphenylphosphino)benzylidene}-(1*S*,2*S*)-diiminocyclohexane)], and its aquo derivative $[\mathrm{RuCl(H_2O)(PNNP)}]\mathrm{PF}_6$ **2**, catalyse the asymmetric epoxidation of unfunctionalised olefins with hydrogen peroxide as the primary oxidant under mild conditions (1 mol% catalyst, 20 °C, 2–6 h) (Scheme 1). Most interestingly, only a small excess of H_2O_2 is used. The selectivity to epoxide is high (52–80%) with both **1** and **2**. The ee values are up to 41%. To the best of our knowledge, this is the first asymmetric epoxidation catalysed by a ruthenium complex that exploits hydrogen peroxide as the primary oxidant.



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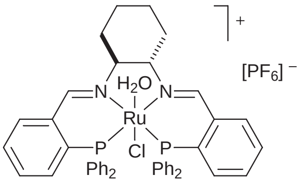

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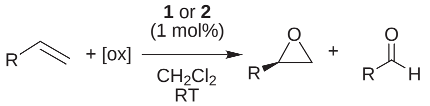


Scheme 1

Results and discussion

The reaction of $[\mathrm{RuCl_2(PNNP)}]$[12,13] (see Experimental section) with $\mathrm{TlPF_6}$ in dry CH_2Cl_2 gives a highly reactive species which

Green Context

Epoxidation is a vital chemical transformation, which allows the transformation of alkenes into highly reactive and versatile synthetic intermediates, which can be further converted into a wide range of important products. Many epoxidations require reagents such as NaOCl, periodates, or other high oxidation state iodine compounds. These oxidants are used in conjunction with catalysts, and are typically very efficient, but inevitably lead to a great deal of waste. Comparatively little has been done on epoxidations using cleaner reagents such as air or hydrogen peroxide. This article describes an efficient and selective catalyst which allows epoxidation with hydrogen peroxide to occur under mild conditions. Some success has also been achieved with chiral versions of the catalyst.

The use of dichloromethane as solvent is not ideal, and a greener solvent would be preferable, but the ability to use one of the most ideal oxidants is a very significant move in the right direction. ***DJM***

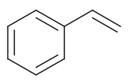
Table 1 Asymmetric epoxidation of alkenes with H_2O_2 as oxidant

					Selectivity (%)[a]			
Run	Substrate	Catalyst	*t*/h	Conv. (%)	Epoxide	RCHO	Configuration[b]	ee[c](%)
1	**3**	**1**	6	35	81	9	*S*	37
2[d]	**3**	**1**	6	24	50	40	*S*	40
3	**4**	**1**	2	100	55	[e]	1*S*,2*R* [f]	41
4	**5**	**1**	4	26	62	17	1*R*,2*R*	4
5	**6**	**1**	6	22	72	0	n.d.	25
6	**3**	**2**	6	39	68	9	*S*	30
7	**4**	**2**	2	84	50	[e]	1*S*,2*R* [f]	25
8	**5**	**2**	3	14	52	4	1*R*,2*R*	10
9	**6**	**2**	6	6	70	0	n.d.	22

[a] By GC analysis (SE 54) with decane as internal standard. [b] By comparison with an authentic sample (chiral GC analysis). [c] Determined by chiral GC (Supelco a-DEX 120). [d] Solvent is 1,2-dichlorobenzene. [e] Small amounts of overoxidation products have been detected by GC MS (see text). [f] By the sign of the optical rotation.

we formulate as $[RuCl(PNNP)]PF_6$ **1**. Complex **1** behaves as a 1:1 electrolyte in dry CH_2Cl_2, and is extremely reactive toward most O- and N-donors. Thus, **1** gives adducts with H_2O, THF, CH_3OH, acetone, diethyl ether, and acetonitrile. In solvents containing traces of water, the aquo complex $[RuCl(OH_2)(PNNP)]PF_6$ **2** is formed along with **1**. Pure **1** can be observed (by ^{31}P NMR spectroscopy) only under rigorously water-free conditions. At this stage, we cannot exclude that **1** is a labile dichloromethane solvate. The reaction of **1** with an excess of H_2O gives **2**, which is isolated and characterised as a mixture of diastereomers.

Addition of 30% aqueous H_2O_2 (7 equivalents) to a CH_2Cl_2 solution of styrene and (*S*,*S*)-**1** (1 mol%) yields (*S*)-styrene oxide with 81% epoxide selectivity and 37% ee (Table 1, run 1). The oxidative cleavage of the C=C double bond is a minor side reaction. Only 9% of **3** is converted to benzaldehyde after the reaction time, whereas other ruthenium–phosphine epoxidation systems afford substantial amounts of cleavage products.[14] Addition of methanol to the reaction solution allows the recovery of polystyrene according to the mass balance. Although the conversion of **3** is only moderate (35%), the system activity (TOF = 5.8 h^{-1}) is an order of magnitude larger than for ruthenium systems containing N- or N,O-donor ligands.[15,16] The dichloro species $[RuCl_2(PNNP)]$ is catalytically inactive.



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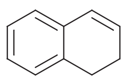

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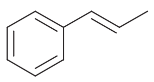

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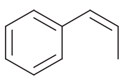

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Next, we investigated the epoxidation of alkenes **4**–**6** with precatalyst **1** (runs 3–5): 1,2-dihydronaphthalene **4** is converted quantitatively within 2 h giving the (−)-(1*S*,2*R*)-epoxide with 55% epoxide selectivity and 41% ee. Minor amounts of 1,2-dihydroxy-3,4-dihydronaphthalene and 1-oxo-2,3,4-trihydronaphthalene are detected by GC MS among the reaction products. Quantitative conversion of **4** is obtained also with a substrate to catalyst ratio of 200:1. The epoxidation of the *cis*-disubstituted olefin **6** is highly stereospecific, giving nearly exclusively the *cis*-epoxide (99:1 *cis*-to-*trans* ratio) with 25% ee (the ee of the *trans* epoxide is 38%). This selectivity is much higher than observed in Mn-catalysed epoxidations,[3,17] and suggests a concerted, non-radical addition to the double bond. Substrate **5**, a model for *trans*-olefins, gives nearly racemic epoxide (4% ee) with conversion comparable to that of styrene. Precatalyst **2** gives similar results as **1** (runs 6–9), but is less active and affords lower chemo- and enantio-selectivity. We are investigating the co-ordination chemistry of **1** and **2** in order to rationalise this behaviour.

The effect of a series of parameters has been investigated using **1** as precatalyst and **3** as substrate. Lowering the reaction temperature (0 °C) or buffering the aqueous phase at different pH values (3.4, 8.0) does not improve either conversion or epoxide selectivity. No reaction is observed in co-ordinating solvents such as pyridine and acetonitrile, due to the formation of relatively inert solvates.[18] When THF is used, benzaldehyde is the major product. The use of an aromatic solvent improves very slightly the enantioselectivity:[8] 1,2-dichlorobenzene gives the highest ee (40%), but lower epoxide selectivity (50%) (run 2).

Finally, oxidants other than H_2O_2 can be used in the epoxidation of styrene in the presence of **1** (1 mol%) under analogous experimental conditions. Iodosylbenzene gives nearly quantitative conversion (95%) to the (*S*)-epoxide (60% selectivity, 30% ee, 24 h). The O_2/heptaldehyde system gives (*S*)-styrene oxide with 50% selectivity and 27% ee, albeit with low conversion (15% after 4 h). Good conversion (75%) but low chemoselectivity (16% (*R*)-epoxide with 10% ee) is obtained with $NaIO_4$, which mainly affords oxidative cleavage (57% benzaldehyde). No reaction occurs with aqueous NaOCl, whereas *tert*-butyl hydroperoxide and $[NBu_4][HSO_5]$ give oxidation products other than the epoxide.

Conclusion

We have shown that a new class of ruthenium complexes with a tetradentate chiral phosphinoimino ligand catalyses the asymmetric epoxidation of alkenes with a variety of oxidants. In particular, H_2O_2 is activated with high efficiency, which is probably related to the oxophilicity of **1**. The stereospecifity of the epoxidation reaction with H_2O_2 suggests that the intermediates involved have little radical character. Our present efforts are directed to improving the activity and enantioselectivity of this system.

Experimental

Preparation of $[RuCl_2(PNNP)]$

Prepared in 91% yield as a 1:4 mixture of the *cis*- and *trans* isomers by stirring $[RuCl_2(PPh_3)_3]$ (282 mg, 0.294 mmol) and PNNP (194 mg, 0.294 mmol) in CH_2Cl_2 (30 ml) for 4 h at room temperature, followed by addition of hexane and partial evaporation of the solvent. Calc. for $C_{44}H_{40}Cl_2N_2P_2Ru$: C, 63.62; H, 4.85; N, 3.37. Found: C, 63.46; H, 4.90; N, 3.13. *cis*-Isomer: δ_P (101 MHz, $CDCl_3$, 85% H_3PO_4) 36.1 (d, J = 31.8 Hz, 1 P), 88.3 (d, J = 31.8 Hz, 1 P). Data for the *trans*-isomer are as in ref. 13.

Preparation of complex 1

A CH_2Cl_2 solution (30 ml) of [$RuCl_2$(PNNP)] (244 mg, 0.294 mmol) and $TlPF_6$ (124 mg, 0.352 mmol) was stirred for 3 h at room temperature under argon. After filtering over Celite and adding hexane, evaporation of CH_2Cl_2 yielded red-brown **1** in 74% yield. Besides reacting with most oxygen donors, **1** tenaciously retained variable amounts of non co-ordinating solvents, such as hexane. Therefore, no reasonable elemental analysis could be obtained. MS (FAB$^+$) *m/z*: 796 ($[M]^+$ + H, 100), 760 ($[M]^+$ − Cl, 17). δ_P (101 MHz, CD_2Cl_2, over molecular sieves, 85% H_3PO_4) 49.7 (d, $J_{P,P'}$ = 28.2 Hz, 1 P), 59.0 (d, $J_{P,P'}$ = 28.2 Hz, 1 P), −144.4 (septet, $J_{P,F}$ = 714 Hz, 1 P, PF_6). δ_H (250 MHz, CD_2Cl_2, over molecular sieves, Me_4Si) 8.85 (d, $J_{P,H}$ = 10.0 Hz, 1 H, H–C=N), 8.6 (br s, 1 H, H–C=N). $\Lambda_M = 40\ \Omega^{-1}\ cm^2\ mol^{-1}$ (10^{-3} mol dm^{-3} CH_2Cl_2 solution).

Preparation of complex 2

Pr^iOH–H_2O (1:1, 10 ml) was added to a filtered (Celite) CH_2Cl_2 (40 ml) solution of **1**, prepared *in situ* from [$RuCl_2$(PNNP)] (302 mg, 0.363 mmol) and $TlPF_6$ (165 mg, 0.471 mmol). Evaporation of CH_2Cl_2 yielded orange-yellow **2** in 83% yield. Calc. for $C_{44}H_{42}ClF_6N_2OP_3Ru$: C, 55.15; H, 4.42; N, 2.92. Found: C, 55.83; H, 4.94; N, 2.37%. δ_P (101 MHz, $CDCl_3$, 85% H_3PO_4), isomer **2a**: 45.5 (d, $J_{P,P'}$ = 31.8 Hz, 1 P), 65.0 (d, $J_{P,P'}$ = 31.8 Hz, 1 P); isomer **2b**: 42.9 (d, $J_{P,P'}$ = 26.9 Hz, 1 P), 50.9 (d, $J_{P,P'}$ = 26.9 Hz, 1 P), −144.4 (septet, $J_{P,F}$ = 714 Hz, 1 P, PF_6). δ_H (250 MHz, $CDCl_3$, Me_4Si), isomer **2a**: 8.80 (d, $J_{P,H}$ = 10.2 Hz, 1 H, H–C=N), 8.68 (br s, 1 H, H–C=N); isomer **2b**: 9.21 (d, $J_{P,H}$ = 9.0 Hz, 1 H, H–C=N), 8.88 (d, $J_{P,H}$ = 9.0 Hz, 1 H, H–C=N). MS (FAB$^+$): *m/z* 813 ($[M]^+$, 10), 795 ($[M]^+$ − H_2O, 100), 759 ($[M]^+$ − Cl − H_2O, 24). ν_{max}($CHCl_3$)/cm^{-1}: 3685 (m), 3604 (m), 3485 (m, br) (Ru–OH_2); 1630 (m, Ru–N=C), 1602 (m, Ru–OH_2). $\Lambda_M = 39\ \Omega^{-1}\ cm^2\ mol^{-1}$ (10^{-3} mol dm^{-3} CD_2Cl_2 solution).

Epoxidation studies

In a typical catalytic run, the olefin (0.96 mmol), decane (internal standard, 0.17 mmol) and precatalyst **1** or **2** (9.6 μmol, 1 mol%) were dissolved in dry, distilled CH_2Cl_2 (5 ml) under argon. Aqueous hydrogen peroxide (0.7 ml 30%, Perhydrol (Merck), 9.8 M solution, 6.86 mmol) was added in one shot to the brown solution under vigorous stirring. The solution darkened immediately, and gas was evolved. The GC traces of the reaction solutions indicated that there was no induction time, the formation of epoxide being observed just after adding H_2O_2. Continuous addition of H_2O_2 over 4 h has a negligible effect on the outcome of the reaction.

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Solvent-free organic syntheses

using supported reagents and microwave irradiation

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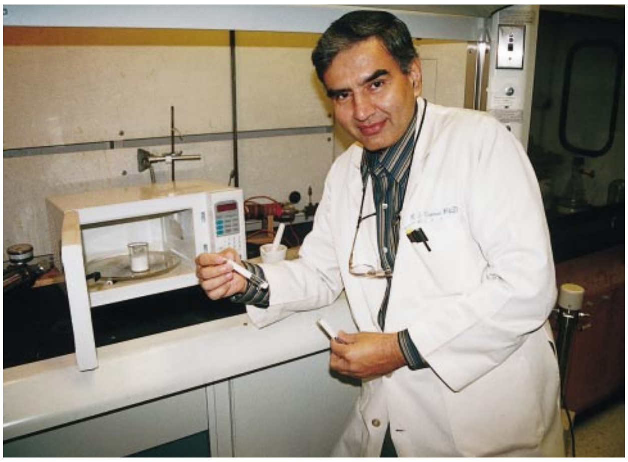
Summary

Recent developments in microwave-accelerated solventless organic syntheses are summarised. This expeditious and solvent-free approach involves the exposure of neat reactants to microwave (MW) irradiation in conjunction with the use of supported reagents or catalysts which are primarily of mineral origin. The salient features of these high yield protocols are the enhanced reaction rates, greater selectivity and the experimental ease of manipulation. Among other reagents recently described in the literature on this eco-friendly green approach, the use of recyclable mineral oxides or supported reagents from our laboratory such as $Fe(NO_3)_3$–clay (clayfen), $Cu(NO_3)_2$–clay (claycop), NH_4NO_3–clay (clayan), NH_2OH–clay, $PhI(OAc)_2$–alumina, $NaIO_4$–silica, CrO_3–alumina, MnO_2–silica, $NaBH_4$–clay, *etc*. are highlighted in MW-promoted deprotection, condensation, cyclization, rearrangement, oxidation and reduction reactions including the rapid one-pot assembly of heterocyclic compounds from *in situ* generated intermediates.



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1. Introduction

Heterogeneous organic reactions have proven useful to chemists in the laboratory as well as in the industrial context. These reactions are effected by the reagents immobilized on the porous solid supports and have advantages over the conventional solution phase reactions because of the good dispersion of active reagent sites, associated selectivity and easier work-up. The recyclability of some of these solid supports renders these processes into truly eco-friendly green protocols. Although the first description of surface-mediated chemistry dates back to 1924,[1] it was not until the late 1970s that the technique received genuine attention with the appearance of two reviews,[2] followed by a series of books and account articles.[3]

A related development that had a profound impact on these heterogeneous reaction is the use of microwave (MW) irradiation techniques for the acceleration of organic reactions. Since the appearance of the first article on the application of microwaves for chemical synthesis in polar solvents,[4] the approach has blossomed into a useful technique for a variety of applications in organic synthesis and functional group transformations.[5–34] The focus has lately shifted to less cumbersome solvent-free methods[7–35] wherein the neat reactants, often in the presence of mineral oxides or supported catalysts, undergo facile reactions to provide high yields of pure products thus eliminating or minimizing the use of organic solvents.

Microwave reactions involve selective absorption of MW energy by polar molecules, non-polar molecules being inert to MW dielectric loss. The initial experiments with microwave techniques centered around the use of high dielectric solvents

Green Context

The combination of supported reagents and microwave irradiation can be used to carry out a wide range of reactions in short times and with high conversions and selectivity, without the need for solvents. This approach can prove beneficial since the recovery of solvents from conventional reaction systems always results in some losses. Recovery of both products and inorganic support/catalyst is generally possible, leading to an efficient and low waste route to a range of products. ***SJT***

such as dimethyl sulfoxide (DMSO) and dimethylformamide (DMF). The rate enhancements in such reactions are now believed to be due to rapid superheating of the polar solvents. However, in these solution-phase reactions, the development of high pressures and the use of specialized Teflon vessels and sealed containers are some of the limitations. During recent years, a practical dimension to the microwave heating protocols has been added by accomplishing reactions on solid supports under solvent-free conditions. In these reactions, the organic compounds adsorbed on the surface of inorganic oxides, such as alumina, silica and clay, or 'doped' supports absorb microwaves whereas the solid support does not absorb or restrict their transmission. The bulk temperature is relatively low in such solvent-free reactions although higher localized temperatures may be reached during microwave irradiation. These solvent-free MW-assisted reactions provide an opportunity to work with open vessels thus avoiding the risk of high pressure development and increasing the potential of such reactions to upscale.

2. Microwave accelerated solvent-free organic reactions

The practical feasibility of microwave assisted solvent-free protocols has been demonstrated in useful transformations involving protection/deprotection, condensation, oxidation, reduction, rearrangement reactions and in the synthesis of various heterocyclic systems on inorganic solid supports. Herein, we describe our results on this environmentally benign microwave approach for the synthesis of a wide variety of industrially important compounds and intermediates, namely enones, imines, enamines, nitroalkenes, oxidized sulfur species and heterocycles which, obtained otherwise by conventional procedures, contribute to the burden of chemical pollution. Recent work in this area by other research groups is also included. Most of the reactions described herein are performed in open glass containers (test tubes, beakers and round-bottomed flasks) using neat reactants under solvent-free conditions in an unmodified household MW oven or a focused MW oven operating at 2450 MHz. In many cases, the comparisons of the MW-accelerated reactions have been made by conducting the same reaction in an oil bath at the same bulk temperature. The problems associated with waste disposal of solvents (used many-fold in chemical reactions) and excess chemicals are avoided or minimized. Some of the supported reagents, namely clay-supported iron(III) nitrate (clayfen), and copper(II) nitrate (claycop), are prepared according to the literature procedure.[36]

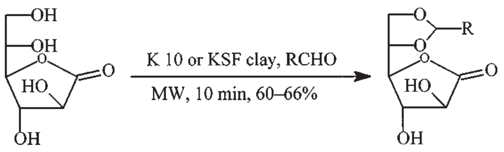
The general procedure involves simple mixing of neat reactants with the catalyst/promoter or their adsorption on mineral or 'doped' supports.

2.1. Protection/deprotection reactions

The protection/deprotection reaction sequences form an integral part of organic manipulations such as the preparation of monomer building blocks, fine chemicals and precursors for pharmaceuticals and these reactions often involve the use of acidic, basic or hazardous and corrosive reagents and toxic metal salts. In this section, the MW-accelerated protection/deprotection of functional groups that have been carried out under solvent-free conditions are highlighted.

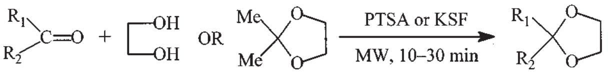
2.1.1. Formation of acetals and dioxolane.

Loupy and coworkers have efficiently prepared acetals of 1-galactono-1,4-lactone in excellent yields by adsorbing the lactone and the aldehyde on montmorillonite K 10 or KSF clay followed by exposing the reaction mixture to microwave irradiation (Scheme 1).[34e]



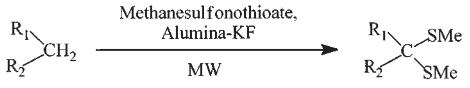
Scheme 1

Hamelin *et al.* have successfully protected aldehydes and ketones as acetals and dioxolanes using orthoformates, 1,2-ethanedithiol or 2,2-dimethyl-1,3-dioxolane.[37] This acid-catalysed reaction proceeds in the presence of *p*-toluenesulfonic acid (PTSA) or KSF clay under solvent-free conditions (Scheme 2). The yields obtained with the microwave method are better than those obtained using the conventional heating mode (oil bath).



Scheme 2

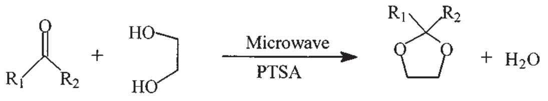
Villemin *et al.* have prepared thioacetals using an essentially similar technique.[34f] The active methylene compounds are adsorbed on alumina–KF, mixed with methanesulfonothioate and are irradiated in a microwave oven to generate thioacetals in good yields (Scheme 3).



$R_1 = R_2 = CO_2R$, CN, Ph, $PO(OEt)_2$

Scheme 3

In the presence of ethylene glycol and *p*-toluenesulfonic acid, a mixture of ketone and aldehyde leads to the formation of dioxolane upon exposure to microwaves (Scheme 4).[37]

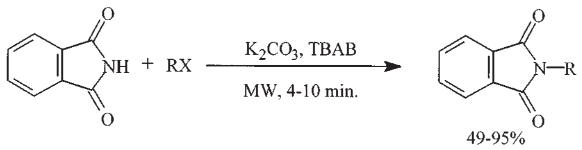


$R_1 = H$; $R_2 = Ph$

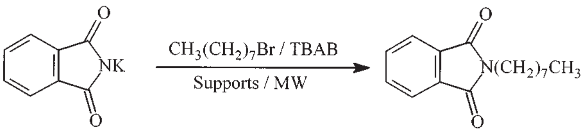
Scheme 4

2.1.2. N-Alkylation reactions.

A variety of solvent-free N-alkylation reactions have been reported which entail the use of phase transfer agents such as tetrabutylammonium bromide (TBAB) under microwave irradiation conditions. The important recent examples are N-alkylation of phthalimides (Scheme 5)[38] or its potassium salt (Scheme 6)[39] in the presence of potassium carbonate and TBAB.

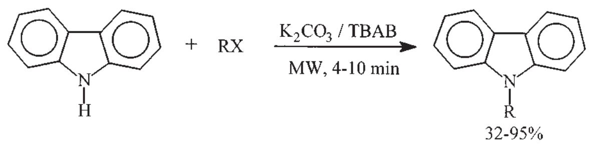


Scheme 5

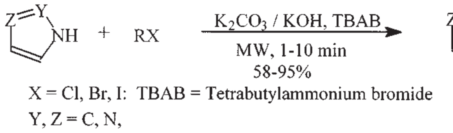


Scheme 6

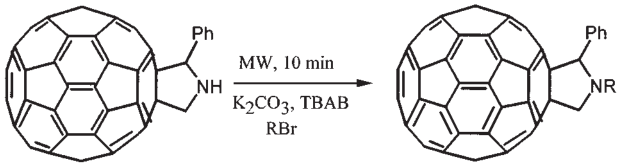
The approach has been extended to a variety of heterocyclic systems, namely carbazole (Scheme 7),[40] other azaheterocycles using K_2CO_3/KOH and TBAB (Scheme 8)[41] including pyrrolidino[60]fullerenes (Scheme 9).[42]



Scheme 7



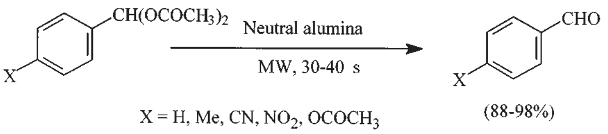
Scheme 8



Scheme 9

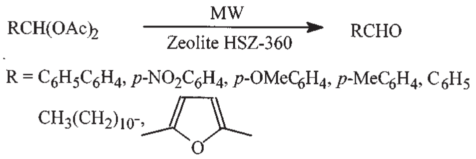
2.1.3. Cleavage of aldehyde diacetates.

The diacetate derivatives of aromatic aldehydes are rapidly cleaved on a neutral alumina surface upon brief exposure to MW irradiation (Scheme 10).[11] The selectivity in these deprotection reactions is achievable by simply adjusting the time of irradiation. As an example for molecules bearing an acetoxy functionality (R = $OCOCH_3$), the aldehyde diacetate is selectively removed in 30 s, whereas an extended period of 2 min is required to cleave both the diacetate and ester groups. The yields obtained are better than those possible by conventional methods and the protocol is applicable to compounds encompassing olefinic moieties such as cinnamaldehyde diacetate.



Scheme 10

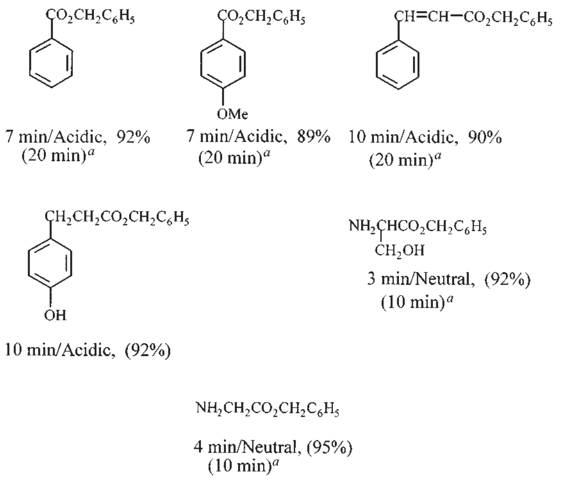
Essentially, a similar reaction has been reported using zeolites wherein 1,1-diacetates undergo deprotection under microwave irradiation in solvent-free conditions (Scheme 11).[43] However, it was not reported whether the reaction occurs on the surface or inside the zeolite pore structures.



Scheme 11

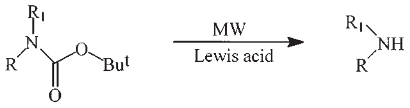
2.1.4. Debenzylation of carboxylic esters.

The promising solvent-free debenzylation of esters (Scheme 12)[13] paves the way for the cleavage of the 9-fluorenylmethoxycarbonyl (Fmoc) group that can be extended to protected amines by changing the surface characteristics of the solid support. The optimum conditions for cleavage of N-protected moieties require the use of basic alumina and irradiation time of 12–13 min at ≈130–140 °C.



Scheme 12 [a] Times in parentheses refer to deprotection in an oil bath at the same temperature.

This approach may find application in peptide bond formation that would eliminate the use of irritating and corrosive chemicals such as trifluoroacetic acid and piperidine, as has been demonstrated recently for the deprotection of N-boc groups (see Scheme 13).



Scheme 13

2.1.5. Selective cleavage of N-*tert*-butoxycarbonyl group.

The solventless cleavage of the *N*-*tert*-butoxycarbonyl (Nboc) group is achieved readily in the presence of aluminium chloride 'doped' neutral alumina upon exposure to microwave irradiation (Scheme 13).[44]

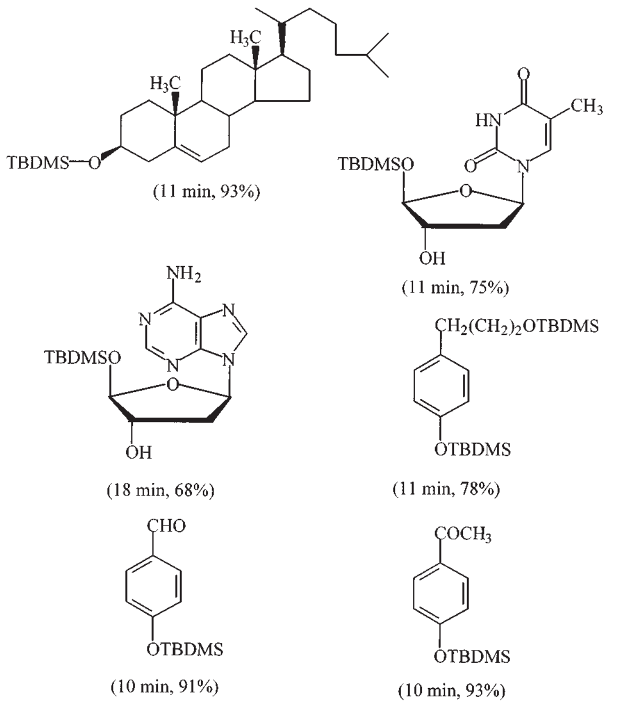
2.1.6. Desilylation reactions.

tert-Butyldimethylsilyl (TBDMS) ether derivatives of a variety of alcohols are rapidly deprotected to regenerate the corresponding hydroxy compounds on alumina surface under MW irradiation conditions (Scheme 14).[12] This approach circumvents the use of corrosive fluoride ions which are conventionally employed for cleaving the silyl protecting groups.[12]

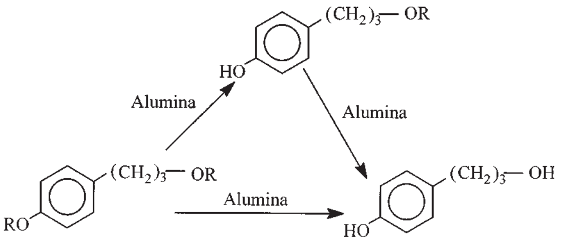
2.1.7. Deacylation reactions.

The orthogonal deprotection of alcohols is possible on a neutral alumina surface using microwave irradiation (Scheme 15). Interestingly, chemoselectivity between alcoholic and phenolic groups in the same molecule can be achieved simply by varying the reaction time; the phenolic acetates are deacetylated faster than alcoholic analogues.[10]

The optimization of relevant parameters with an unmodified household microwave oven such as the power level of microwaves employed and pulsed techniques (multistage, discontinuous irradiation to avoid the generation of higher tempera tures) has been used to obtain good results.[10]



Scheme 14

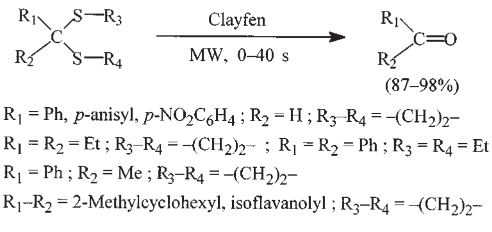


Where R = $COCH_3$

Scheme 15

2.1.8. *Dethioacetalization reaction.*

Among the processes for the regeneration of carbonyl compounds, the cleavage of acid and base stable thioacetals and thioketals is quite challenging; the deprotection of thioacetals invariably requires the use of toxic heavy metals such as Hg^{2+}, Ag^{2+}, Ti^{4+}, Cd^{2+}, Tl^{3+}, or reagents such as benzeneseleninic anhydride.[9] We have accomplished the dethioacetalization reaction in high yield and in solid state using clayfen (Scheme 16).[9]



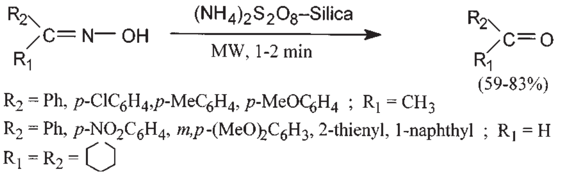
R_1 = Ph, *p*-anisyl, *p*-$NO_2C_6H_4$; R_2 = H ; R_3–R_4 = –$(CH_2)_2$–
R_1 = R_2 = Et ; R_3–R_4 = –$(CH_2)_2$– ; R_1 = R_2 = Ph ; R_3 = R_4 = Et
R_1 = Ph ; R_2 = Me ; R_3–R_4 = –$(CH_2)_2$–
R_1–R_2 = 2-Methylcyclohexyl, isoflavanolyl ; R_3–R_4 = –$(CH_2)_2$–

Scheme 16

2.1.9. *Deoximation reactions.*

The important role of oximes as protecting groups owing to their hydrolytic stability has provided motivation for the development of newer deoximation reagents such as Raney nickel, pyridinium chlorochromate, pyridinium chlorochromate–H_2O_2, triethylammonium chlorochromate, dinitrogen tetroxide, trimethylsilyl chlorochromate, Dowex-50, dimethyl dioxirane, H_2O_2 over titanium silicalite-1, zirconium sulfophenyl phosphonate, *N*-haloamides, and bismuth chloride.[8]

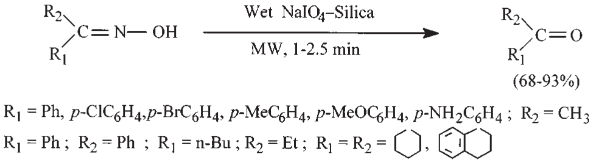
The solvent-free deprotection of protected carbonyl compounds has been successfully demonstrated using relatively benign ammonium persulfate on silica (Scheme 17).[8] Neat oximes are admixed with a solid supported reagent and the contents are irradiated at full power in a MW oven to regenerate free aldehydes or ketones in a process that is applicable to both aldoximes and ketoximes. The role of the surface is critical since the same reagent supported on a clay surface delivers predominantly the Beckmann rearrangement products, the amides.[34k]



R_2 = Ph, *p*-ClC_6H_4,*p*-MeC_6H_4, *p*-$MeOC_6H_4$; R_1 = CH_3
R_2 = Ph, *p*-$NO_2C_6H_4$, *m,p*-$(MeO)_2C_6H_3$, 2-thienyl, 1-naphthyl ; R_1 = H
R_1 = R_2 =

Scheme 17

A facile deoximation protocol with sodium periodate impregnated moist silica (Scheme 18) has been introduced that is applicable exclusively to ketoximes[14]

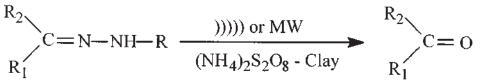


R_1 = Ph, *p*-ClC_6H_4,*p*-BrC_6H_4, *p*-MeC_6H_4, *p*-$MeOC_6H_4$, *p*-$NH_2C_6H_4$; R_2 = CH_3
R_1 = Ph ; R_2 = Ph ; R_1 = n-Bu ; R_2 = Et ; R_1 = R_2 =

Scheme 18

2.1.10. *Cleavage of semicarbazones and phenylhydrazones.*

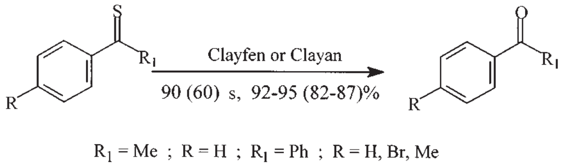
Aldehydes and ketones are also rapidly regenerated from the corresponding semicarbazones and phenylhydrazones using ammonium persulfate impregnated on montmorillonite K 10 clay (Scheme 19) under either microwave or ultrasound irradiation conditions.[15] However, in these solventless procedures microwave exposure achieves results in minutes whereas ultrasound-promoted reactions require 1–3 h for completion of the deprotection reaction.



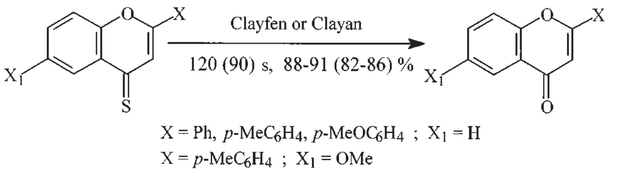
Scheme 19

2.1.11. *Dethiocarbonylation.*

Several reagents such as trifluoroacetic anhydride, CuCl/MeOH/NaOH, tetrabutylammonium hydrogen sulfate/NaOH, clay/ferric nitrate, $NOBF_4$, bromate and iodide solutions, alkaline hydrogen peroxide, sodium peroxide, bases *e.g.* KOBu, thiophosgene, DMSO, trimethyloxonium fluoroborate, tellurium based oxidants, photochemical transformations, dimethyl selenoxide, benzeneseleninic anhydride, benzoyl peroxide, halogen-catalyzed alkoxides under phase transfer conditions, $NaNO_2$/HCl, $Hg(OAc)_2$, $SOCl_2/CaCO_3$, and singlet oxygen have been used for dethiocarbonylation.[16] However, these methods have certain limitations such as the use of the stoichiometric amounts of the oxidants which are often inherently toxic or require longer reaction time or involve tedious procedures. In a process that is accelerated by microwave irradiation, we have accomplished efficient dethiocarbonylation wherein a variety of thioketones are readily converted into the corresponding ketones under solvent-free conditions using clayfen or clayan (Schemes 20, 21).[16]



Scheme 20



Scheme 21

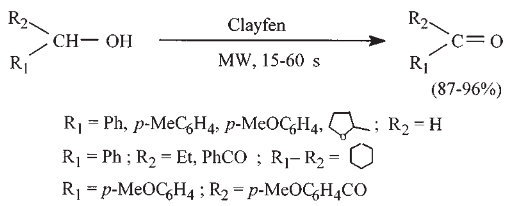
2.2. Oxidation reactions: oxidation of alcohols and sulfides

The conventional oxidizing reagents employed for organic functionalities are peracids, peroxides, manganese dioxide (MnO_2), potassium permanganate ($KMnO_4$), chromium trioxide (CrO_3), potassium chromate (K_2CrO_4) and potassium dichromate ($K_2Cr_2O_7$),[45a] though these reagents have their own limitations in terms of toxicity, work-up and associated waste disposal problems.

Metal-based reagents have been extensively used in organic synthesis. The utility of such reagents in the oxidative transformation is compromised due to their inherent toxicity, cumbersome preparation, potential danger (ignition or explosion) in handling of their complexes, difficulties in terms of product isolation and waste disposal. Introduction of metallic reagents on solid supports has circumvented some of these problems and provided an attractive alternative in organic synthesis because of the selectivity and associated ease of manipulation. Further, the immobilization of metals on the surface avoids their leaching into the environment.

2.2.1. Selective and solvent-free oxidation with clayfen.

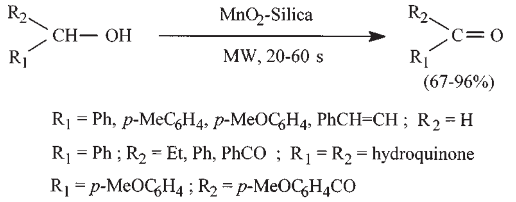
We have developed a facile method for the oxidation of alcohols to carbonyl compounds wherein montmorillonite K 10 clay-supported iron(III) nitrate (clayfen) is used under solvent-free conditions. The process is accelerated tremendously by exposure to MW irradiation[17] and the reaction presumably proceeds *via* the intermediacy of nitrosonium ions. Remarkably, no carboxylic acids are formed in the oxidation of primary alcohols. The experimental procedure simply involves mixing of neat alcohols with clayfen and a brief irradiation of the reaction mixtures in a MW oven for 15–60 s in the absence of solvent. This extremely rapid, manipulatively simple, inexpensive and selective protocol avoids the use of excess solvents and toxic oxidants. Using clayfen [iron(III) nitrate] in the solid state and in amounts that are half that of used by Balogh and Laszlo[36] we have achieved a rapid synthesis of carbonyl compounds in high yields (Scheme 22).[17]



Scheme 22

2.2.2. Activated manganese dioxide–silica.

Using manganese dioxide–silica, an expeditious and high yield route to carbonyl compounds is developed. Benzyl alcohols are selectively oxidized to carbonyl compounds using 35% MnO_2 ‘doped’ silica under MW irradiation conditions (Scheme 23).[18]



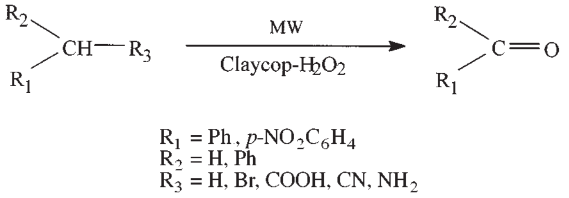
Scheme 23

2.2.3. Claycop–hydrogen peroxide.

Metal ions play a significant role in many of these oxidative reactions as well as in biological dioxygen metabolism. Copper(II) acetate and hydrogen peroxide have been used to produce a stable oxidizing agent, a hydroperoxy copper(II) compound, which is also obtainable from copper(II) nitrate and hydrogen peroxide [eqn. (1)]. The resulting nitric acid, however, requires neutralization by potassium bicarbonate to maintain a pH ≈5.

$$2Cu(NO_3)_2 + 2H_2O + H_2O_2 \longrightarrow 2CuO_2H + 4HNO_3 \qquad (1)$$

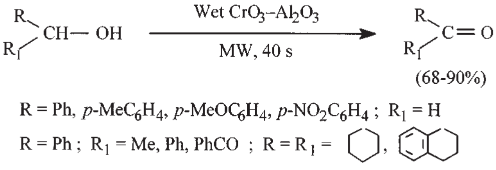
Copper(II) nitrate impregnated on K 10 clay (claycop)–hydrogen peroxide is an effective reagent for the oxidation of a variety of substrates and provides excellent yields (Scheme 24)[19] wherein the maintenance of pH of the reaction mixture is not required.



Scheme 24

2.2.4. Chromium trioxide impregnated wet alumina.

The utility of chromium(VI) reagents in the oxidative transformation is compromised due to toxicity, involved preparation of its various complexes and cumbersome work-up and disposal problems. Chromium trioxide (CrO_3) impregnated pre-moistened alumina is an efficient oxidising system which converts benzyl alcohols to carbonyl compounds by simply admixing the substrates with the reagent at room temperature (Scheme 25). The reactions



Scheme 25

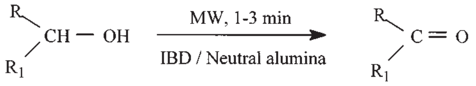
are relatively clean with no tar formation, typical of many CrO_3 oxidations. Interestingly, no overoxidation to carboxylic acids is observed.[20]

Acyclic α-nitro ketones are obtained in one-pot operation *via* a solvent-free approach that utilizes *in situ* oxidation of the nitroalkanols with premoistened alumina supported chromium trioxide.[43b]

2.2.5. Nonmetallic oxidants—iodobenzene diacetate (IBD) 'doped' alumina.

Iodoxybenzene, *o*-iodoxybenzoic acid (IBX), bis(trifluoroacetoxy)iodobenzene (BTI), and Dess–Martin periodinane are some of the common organohypervalent iodine reagents which have been used for the oxidation of alcohols and phenols, but the use of iodobenzene diacetate (IBD) in this area, in spite of its low cost, has not been fully exploited. Most of these reactions, however, are conducted in high boiling DMSO and toxic acetonitrile media that result in an environmental pollution load. Also, IBX has been reported to be explosive under heavy impact and heating over 200 °C.

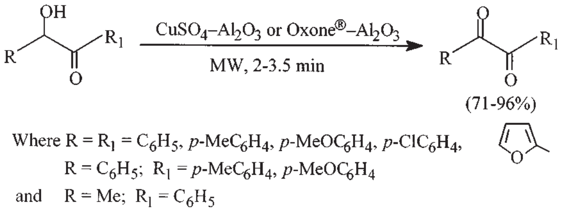
A facile oxidation of alcohols to carbonyl compounds occurs rapidly with alumina-supported IBD under solvent-free conditions and MW irradiation, in quantitative yields.[21] The advantage of using alumina as a support is apparent in marked improvements in yields obtained with the alumina–IBD system as compared to neat IBD (Scheme 26). Interestingly, 1,2-benzenedimethanol undergoes cyclization to afford 1(3*H*)-isobenzofuranone.



Scheme 26

2.2.6. Copper sulfate–alumina or oxone®–wet alumina.

The oxidative transformation of α-hydroxyketones to 1,2-diketones has been accomplished by a variety of reagents namely nitric acid, Fehling's solution, thallium(III) nitrate (TTN), ytterbium(III) nitrate, clayfen, and ammonium chlorochromate–alumina.[22] In addition to the extended reaction time, most of these processes suffer from drawbacks such as the use of corrosive acids and toxic metallic compounds that generate undesirable waste materials. Consequently, there is room for the development of an eco-friendly solvent-free protocol for the oxidation of benzoins. Recently, we have found that both symmetrical and unsymmetrical benzoins can be rapidly oxidized to benzils in high yields using solid reagent systems, copper(II) sulfate–alumina[22] or Oxone®–wet alumina[23] under the influence of microwaves (Scheme 27).

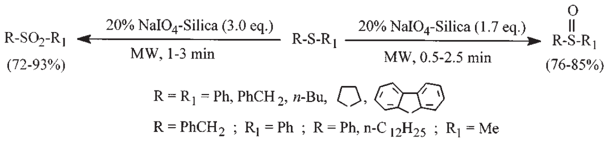


Scheme 27

Interestingly, under these solvent-free conditions, primary alcohols *e.g.* benzyl alcohol and secondary alcohols *e.g.* 1-phenylpropan-1-ol undergo only limited oxidative conversion which is of little practical utility. Apparently, the process is applicable only to α-hydroxyketones as exemplified by various substrates including a mixed benzylic/aliphatic α-hydroxyketone, 2-hydroxypropiophenone, that affords the corresponding vicinal diketone.[23]

2.2.7. Sodium periodate on silica—oxidation of sulfides to sulfoxides and sulfones.

Sulfides are usually oxidized to sulfoxides under strenuous conditions using strong oxidants like nitric acid, hydrogen peroxide, chromic acid, peracids, and periodate.[24] Using MW irradiation this oxidation is achievable with the desired selectivity, to either sulfoxides or sulfones, using silica 'doped' with 10% sodium periodate under reduced power and reaction time (pulsed techniques).[24] Consequently, a much reduced amount of the active oxidizing agent is employed which is safer and easier to handle (Scheme 28).

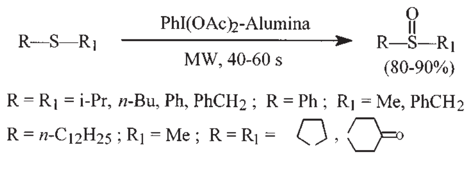


Scheme 28

Importantly, various refractory thiophenes that are often not reductively removed by conventional refining processes can be oxidized under these conditions, *e.g.* benzothiophenes are oxidized to the corresponding sulfoxides and sulfones using ultrasonic and microwave irradiation, respectively, in the presence of $NaIO_4$–silica.[24] A noteworthy feature of the protocol is its applicability to long chain fatty sulfides which are insoluble in most solvents and are consequently difficult to oxidize.

2.2.8. Iodobenzene diacetate–alumina.

As described earlier (section 2.2.5), the solid reagent system IBD–alumina is a useful oxidizing agent and its use is extendable to the expeditious, high yield and selective oxidation of alkyl, aryl and cyclic sulfides to the corresponding sulfoxides upon microwave activation (Scheme 29).[25a]



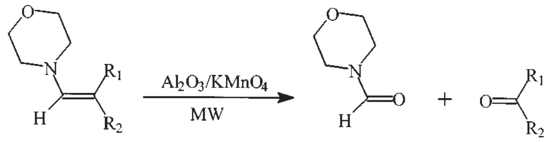
Scheme 29

In a solid state reaction with clayfen, a variety of alkyl, aryl and cyclic sulfides are rapidly oxidised to the corresponding sulfoxides in high yield upon microwave thermolysis.[25b]

2.3 Other oxidation reactions

2.3.1. Oxidation of enamines.

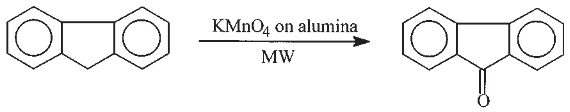
Under solvent-free conditions, Hamelin's group[34g] has successfully oxidized β,β-disubstituted enamines into carbonyl compounds with $KMnO_4$–Al_2O_3 in domestic (255 W, 82 °C) as well as in focused (330 W, 140 °C) microwave ovens. The yields are better in the latter case whereas no ketone formation is observed when the same reactions are conducted in an oil bath at 140 °C (Scheme 30).



Scheme 30

2.3.2. *Oxidation of arenes with permanganate ($KMnO_4$)–alumina.*

$KMnO_4$ impregnated alumina oxidises arenes to ketones within 10–30 minutes in solvent-free conditions using focused microwaves (Scheme 31).[45b]



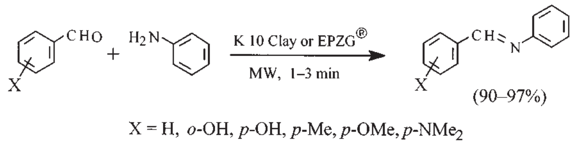
Scheme 31

2.4. Condensation reactions

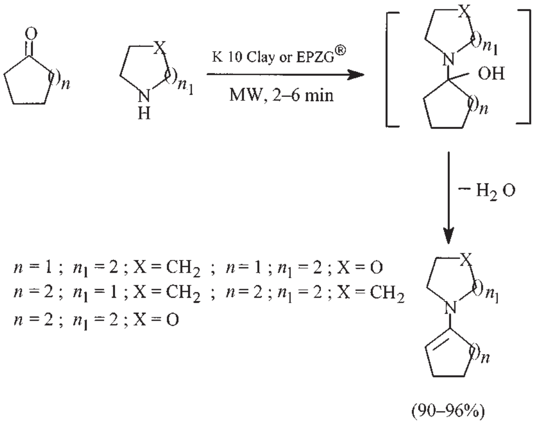
2.4.1. *Synthesis of imines, enamines and nitroalkenes.*

The driving force in the preparation of imines, enamines and nitroalkenes is the azeotropic removal of water from the intermediate, which is normally catalyzed by *p*-toluenesulfonic acid, titanium(IV) chloride, and montmorillonite K 10 clay. Conventionally, a Dean–Stark apparatus is used which requires a large excess of aromatic hydrocarbons such as benzene or toluene for azeotropic water elimination.

MW-induced acceleration of such dehydration reactions using montmorillonite K 10 clay[26] (Schemes 32, 33) or Envirocat reagent,[27] EPZG® (Schemes 32, 33) has been demonstrated in a facile preparation of imines and enamines *via* the reactions of primary and secondary amines with aldehydes and ketones, respectively.



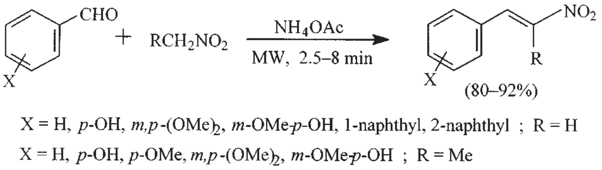
Scheme 32



Scheme 33

Microwaves, generated at the usual frequency of 2450 MHz, are ideally suited to remove water in imine or enamine forming reactions. For low boiling starting materials, reduced power intensities of microwaves coupled with pulsed techniques have been used.[26,27]

The Henry reaction, condensation of carbonyl compounds with nitroalkanes to afford nitroalkenes, also proceeds rapidly *via* this MW approach and requires only catalytic amounts of ammonium acetate involving neat reactants thus avoiding the use of a large excess of polluting nitrohydrocarbons normally employed (Scheme 34).[28]

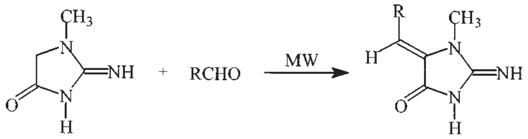


Scheme 34

The reduction, oxidation and cycloaddition reactions emanating from α,β-unsaturated nitroalkenes provide easy access to a vast array of functionalities that include nitroalkanes, N-substituted hydroxylamines, amines, ketones, oximes, and α-substituted oximes and ketones.[46] Consequently, there are numerous possibilities of using these *in situ* generated nitroalkenes for the preparation of valuable building blocks and synthetic precursors.

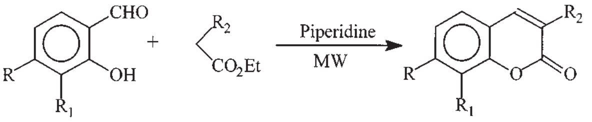
2.4.2. *Knoevenagel condensation reactions—Coumarin synthesis.*

An expeditious Knoevenagel condensation of creatinine with aldehydes has been achieved using focused microwave irradiation (40–60 W) under solvent-free reaction conditions at 160–170 °C (Scheme 35).[47]



Scheme 35

Villemin and Martin[34l] have synthesized 5-nitrofurfurylidine by the condensation of 5-nitrofurfuraldehyde with active methylene compounds under microwave irradiation using K 10 and $ZnCl_2$ as a catalyst. The useful synthesis of coumarins *via* the microwave promoted Pechmann reaction[48a] has been extended to solventless systems wherein salicylaldehydes undergo Knoevenagel condensation with a variety of ethyl acetate derivatives under basic conditions (piperidine) to afford coumarins (Scheme 36).[48b]



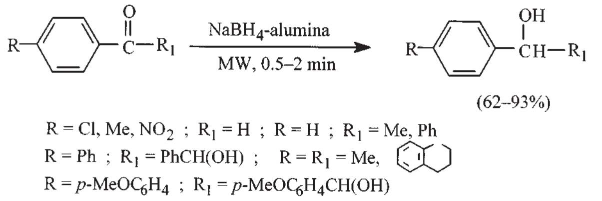
Scheme 36

2.5 Reduction reactions

2.5.1. *Borohydride reduction of carbonyl compounds to alcohols.*

Relatively inexpensive sodium borohydride ($NaBH_4$) has been extensively used as a reducing agent in view of its compatibility with protic solvents and safer nature. The solid state reduction of ketones has also been achieved by mixing them with $NaBH_4$ and storing the mixture in a dry box for five days. The major disadvantage in the heterogeneous reaction with $NaBH_4$ is that the use of solvent slows down the reaction rate while in the solid state reactions the time required is too long (5 days) for it to be of any practical utility.[32]

We have developed a rapid method for the reduction of aldehydes and ketones that uses alumina supported $NaBH_4$ and proceeds in the solid state using microwaves.[32] The process in its entirety involves a simple mixing of carbonyl compound with (10%) $NaBH_4$–alumina in the solid state and irradiating the mixture in a MW oven for 0.5–2 min (Scheme 37).



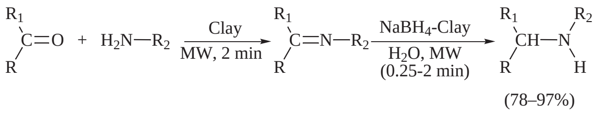
Scheme 37

The useful chemoselective feature of the reaction is apparent from the reduction of *trans*-cinnamaldehyde (cinnamaldehyde/$NaBH_4$-alumina, 1:1 mol equivalent); the olefinic moiety remains intact and only the aldehyde functionality is reduced in a facile reaction that occurs at room temperature.

No side product formation is observed in any of the reactions investigated and reaction does not take place in the absence of alumina. Further, the reaction rate improves in the presence of moisture. Alumina absorbs enough moisture during the recovery of the product that it can be recycled again by mixing with fresh borohydride and reused for subsequent reductions without any loss of activity. The air used for cooling the magnetron ventilates the microwave cavity thus preventing any ensuing hydrogen from reaching explosive concentrations.

2.5.2. Reductive alkylation of amines.

Reductive amination of carbonyl compounds has been well documented using sodium cyanoborohydride, sodium triacetoxyborohydride or $NaBH_4$ coupled with sulfuric acid. These reagents either produce waste stream or involve the use of corrosive acids. The environmentally benign methods developed in our laboratory have now been extended to a solvent-free reductive amination procedure for carbonyl compounds using wet montmorillonite K 10 clay supported sodium borohydride that is facilitated by microwave irradiation (Scheme 38).[33]



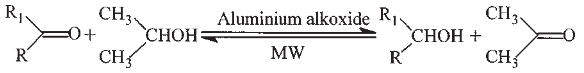
R = i-Pr,Ph, o-HOC_6H_4, p-$MeOC_6H_4$, p-$NO_2C_6H_4$; R_1 = H; R_2 = Ph
R and R_1 = -$(CH_2)_5$-; R_2 = Ph; R and R_1 = -$(CH_2)_6$-; R_2 = n-Pr
R = p-ClC_6H_4; R_1 = H; R_2 = o-HOC_6H_4; R = R_1 = Et; R_2 = Ph
R = n-C_5H_{11}; R_1 = Me; R_2 = morpholine, piperidine
R = i-Pr; R_1 = H; R_2 = n-$C_{10}H_{21}$

Scheme 38

These practical applications of $NaBH_4$ reductions on mineral surfaces for *in situ* generated Schiff bases have been successful.[33] The studies pertaining to the solid state reductive amination of carbonyl compounds on various inorganic solid supports such as alumina, clay, silica, *etc*., and especially on K 10 clay surface deliver secondary and tertiary amines rapidly.[33] Clay not only behaves as a Lewis acid but provides water from its interlayers that enhances the reducing ability of $NaBH_4$.

2.5.3. Reduction of carbonyl compounds with aluminium alkoxides.

The efficient reduction of carbonyl compounds using isopropyl alcohol and alumina, as demonstrated in a series of papers by Posner,[49a] has now been translated to a solventless and expeditious reduction scheme that utilises aluminium alkoxides under microwave irradiation conditions (Scheme 39).[49b]

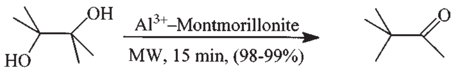


Scheme 39

2.6. Rearrangement reactions

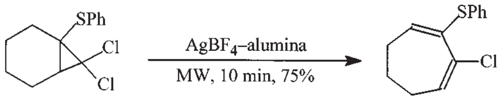
2.6.1. Pinacol–pinacolone rearrangement.

Loupy and colleagues have reported a solventless pinacol–pinacolone rearrangement using microwave irradiation.[34i] The process involves the irradiation of the *gem*-diols with Al^{3+}-montmorillonite K 10 clay for 15 min to afford the rearrangement product in excellent yields (Scheme 40). These results are compared to conventional heating in an oil bath where the reaction times are too long (15 h).



Scheme 40

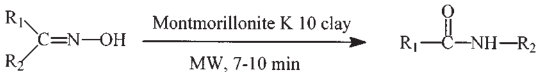
An efficient ring expansion transformation is described by Villemin and Labiad under solventless conditions (Scheme 41).[34j] This solvent-free microwave protocol is superior than the reactions conducted in conventional methanolic solution.



Scheme 41

2.6.2. Beckmann rearrangement.

Bosch *et al.* have achieved the Beckmann rearrangement of ketoximes with montmorillonite K 10 clay in ‘dry’ media in good yields (Scheme 42).[34k]

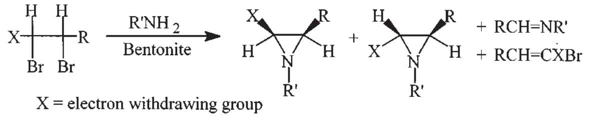


Scheme 42

2.7. Synthesis of heterocylic compounds

2.7.1. Aziridines.

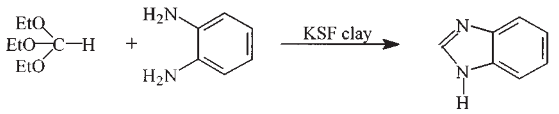
Among the various protocols known for the synthesis of the title compounds, the focused microwave approach under ‘dry’ conditions is especially notable in view of the observation that elimination predominates over the Michael addition under MW irradiation when compared to the classical heating under the same conditions (Scheme 43).[50]



Scheme 43

2.7.2. Benzimidazoles.

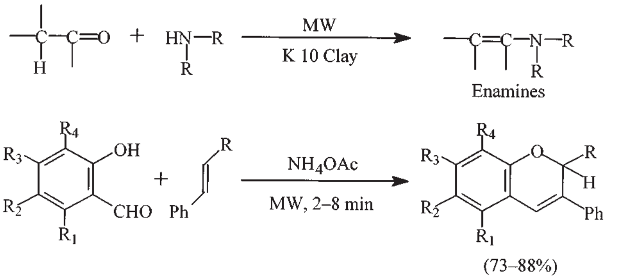
Benzimidazoles are prepared rapidly by condensation reaction of *ortho*-esters with *o*-phenylenediamines in the presence of KSF clay under either refluxing conditions in toluene or solvent-free conditions using focused microwave irradiation (Scheme 44).[51]



Scheme 44

2.7.3. Isoflav-3-enes.

Isoflav-3-enes, possessing the chromene nucleus, are well known oestrogens and several derivatives of these oxygen heterocycles have attracted the attention of medicinal chemists. Despite the availability of several methods for the synthesis of chromene derivatives, there is demand for the development of eco-friendly synthetic methods for these derivatives. We have discovered a facile and general method for the synthesis of isoflav-3-enes substituted with basic moieties at the 2 position (Scheme 45).[29] The results are especially promising in view of the convergent one-pot approach to the heterocyclic systems such as 2-substituted isoflavenes wherein the generation of the enamine derivatives *in situ* and inducing subsequent reactions with *o*-hydroxyaldehydes in the same pot is the key feature (Scheme 45).

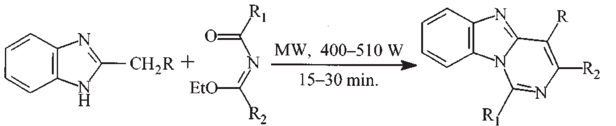


R = morpholinyl or piperidinyl or pyrrolidinyl
$R_1, R_3, R_4 = H; R_2 = H, Cl, NO_2$

Scheme 45

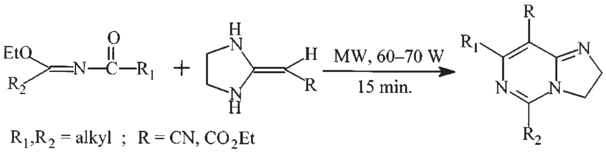
2.7.4. Bridgehead nitrogen heterocycles.

Microwave energy has found application in the rapid synthesis of bridgehead nitrogen heterocycles under solvent-free conditions. Rahmouni *et al.* have synthesised pyrimidino[1,6-*a*]benzimidazoles (Scheme 46) and 2,3-dihydroimidazo[1,2-*c*]pyrimidines (Scheme 47) under focused microwave irradiation in moderate yields from *N*-acylimidates and activated 2-benzimidazoles and imidazoline ketene aminals, respectively.[34h]



$R = CN, CO_2Me, CO_2Et$

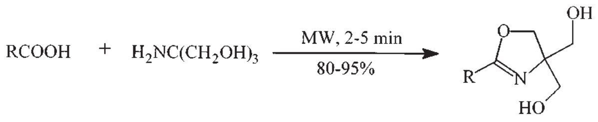
Scheme 46



Scheme 47

2.7.5. Synthesis of 2-oxazolines.

Oxazolines are readily prepared from carboxylic acids and α,α,α-tris(hydroxymethyl)methylamine under microwave irradiation conditions (Scheme 48).[52]



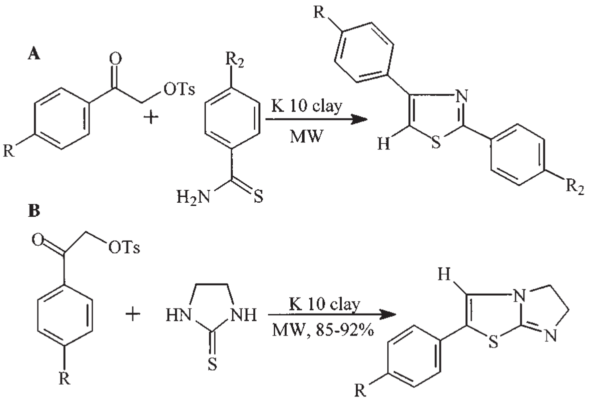
where R = 2-furyl, phenyl, heptadecenyl

Scheme 48

2.7.6. Substituted thiazoles.

Thiazole and its derivatives are simply obtained by the reaction of α-tosyloxyketones, which are generated *in situ* from arylmethyl ketones and [hydroxy(tosyloxy)iodo]benzene (HTIB) with thioamides in the presence of K 10 clay using microwave irradiation (Scheme 49A) in a process that is solvent-free in both steps.[53]

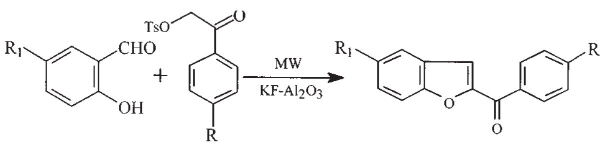
The case of corresponding bridgehead heterocycles, however, is a special one where microwave effects really become apparent since the reactions of α-tosyloxyketones with ethylenethioureas remain incomplete in an oil bath whereas in a microwave oven they are completed in a short time (Scheme 49B).[53]



Scheme 49

2.7.7. Synthesis of 2-aroylbenzofurans.

Naturally occurring and pharmacologically important 2-aroylbenzofurans are easily obtainable in the solid state from α-tosyloxyketones and salicylaldehydes in the presence of a base such as potassium fluoride doped alumina using microwave irradiation (Scheme 50).[53]

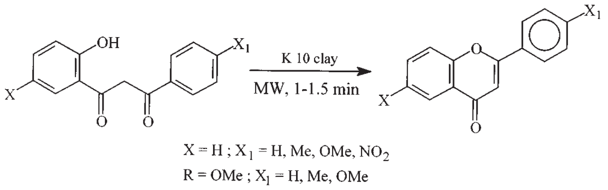


Scheme 50

2.7.8. *Flavones.*

Flavonoids are a class of naturally occurring phenolic compounds widely distributed in the plant kingdom, the most abundant being the flavones. Members of this class display a wide variety of biological activities and have been useful in the treatment of various diseases. Flavones have been prepared by a variety of methods such as Allan–Robinson synthesis and synthesis from chalcones *via* an intramolecular Wittig strategy.[30] The most prevalent approach, however, involves the Baker–Venkataraman rearrangement, wherein *o*-hydroxyacetophenone is benzoylated to form the benzoyl ester followed by treatment with base (pyridine/KOH) to effect an acyl group migration, forming a 1,3-diketone.[30] The diketone formed is then cyclized under strongly acidic conditions using sulfuric acid and acetic acid to deliver the flavone. Therefore, opportunities exist for the development of an expedient approach using benign and readily available starting materials.

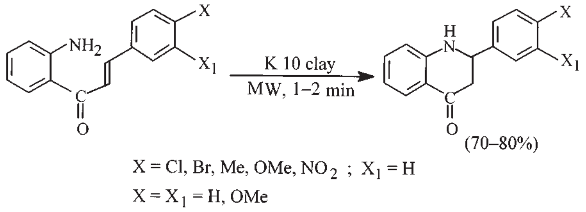
We have achieved a solvent-free synthesis of flavones which simply involves the microwave irradiation of *o*-hydroxydibenzoylmethanes adsorbed on montmorillonite K 10 clay for 1–1.5 min. Rapid and exclusive formation of cyclized flavones occurs in good yields (Scheme 51).[30]



Scheme 51

2.7.9. *Synthesis of 2-aryl-1,2,3,4-tetrahydro-4-quinolones.*

In yet another solventless cyclization reaction using montmorillonite K 10 clay under microwave irradiation conditions, readily available 2′-aminochalcones provide easy access to 2-aryl-1,2,3,4-tetrahydro-4-quinolones[31] which are valuable precursors for the medicinally important quinolones (Scheme 52).



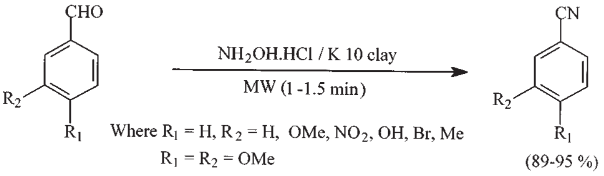
Scheme 52

2.8. Miscellaneous reactions

2.8.1. *Transformation of aromatic aldehydes to nitriles.*

The preparation of nitriles from aldehydes is an important chemical transformation.[54] However, in most cases the aldoxime is first prepared and subsequently dehydrated using a wide variety of reagents such as *O,N*-bis(trifluoroacetyl) hydroxylamine or trifluoroacetohydroximic acid,[55a] chloramine/base,[55b] (H_2SO_4/SiO_2),[55c] *p*-chlorophenyl chlorothionoformate/pyridine,[55d] triethylamine/dialkyl hydrogen phosphinates,[55e] $TiCl_4$/pyridine,[55f] triethylamine/phosphonitrilic chloride[55g] and 1,1′-dicarbonylbiimidazole.[55h] These conventional methods entail the dehydration of aldoxime which is a time demanding process even for one-pot reactions.[55i] We envisaged the application of hydroxylamine 'doped' on K10 clay to effect the above conversion in a one-pot synthesis using microwaves.

Arylaldehydes are rapidly converted into nitriles in good yields (89–95%) with hydroxylamine hydrochloride supported on montmorillonite K 10 clay in the absence of solvent.[55j,k] The reaction is a general one as exemplified by a variety of aldehydes (Scheme 53) that undergo this facile conversion to afford high yields of the corresponding nitriles (89–95%) within a short MW irradiation time (1–1.5 min).[55j,k] In the case of aliphatic aldehydes, however, only poor yields of nitriles (10–15%) are obtained with complex byproduct formation.



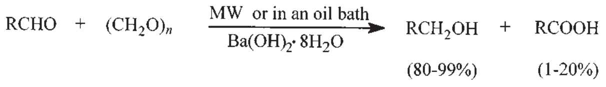
Scheme 53

2.8.2. *Conversion of aldehydes to alcohols—Solid state Cannizzaro reaction.*

The title reaction is the disproportionation of an aldehyde to an equimolar mixture of primary alcohol and carboxylic salt[56] and is restricted to aldehydes that lack α-hydrogens and therefore can not undergo aldol condensation. Several investigations[57] have been made on this oxidation–reduction reaction, which is usually carried out in homogeneous and strongly basic conditions. The relative importance of the Cannizzaro reaction in synthetic organic chemistry decreased considerably after the discovery of lithium aluminium hydride, $LiAlH_4$, in 1946. The lower yields of the desired products has been another limitation of this reaction. However, the crossed Cannizzaro reaction,[57a] using a scavenger and inexpensive paraformaldehyde to produce alcohol in higher yields, had been another choice prior to the introduction of hydride reducing agents.

Normally conducted in solution, we explored this reaction on a variety of mineral oxide surfaces.[58a] The reaction under microwave irradiation conditions failed completely with calcium hydroxide and in the presence of a strong base such as sodium hydroxide, the reaction remains incomplete with concomitant formation of several unidentified products reminiscent of our earlier observations on basic alumina surface.[58b] Interestingly, we discovered that the reaction proceeds rapidly on a barium hydroxide, $Ba(OH)_2{\cdot}8H_2O$, surface which demonstrates the first application of this reagent in a solvent-free crossed Cannizzaro reaction.[58a] Barium hydroxide has been previously used as a catalyst in a variety of organic syntheses[59] including the Wittig–Horner reaction,[60] the reaction of chalcones with hydroxylamine[61] and the synthesis of isooxazolines and pyrazolines.[62] In a typical experiment, a mixture of benzaldehyde (1 mmol) and paraformaldehyde (2 mmol) is mixed with barium hydroxide octahydrate (2 mmol) and then irradiated in a microwave oven (100–110 °C) or heated in an oil bath (100–110 °C) (Scheme 54).

In general, aldehydes bearing an electron withdrawing substituent undergo reaction at a much faster rate than aldehydes with electron releasing groups appended.

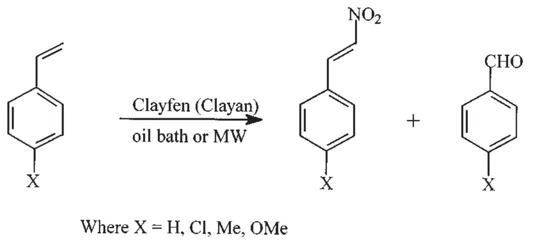


$$\mathrm{RCHO} + (\mathrm{CH_2O})_n \xrightarrow[\mathrm{Ba(OH)_2\cdot 8H_2O}]{\text{MW or in an oil bath}} \underset{(80\text{-}99\%)}{\mathrm{RCH_2OH}} + \underset{(1\text{-}20\%)}{\mathrm{RCOOH}}$$

Scheme 54

2.8.3. Side chain nitration of styrenes—preparation of β-nitrostyrenes.

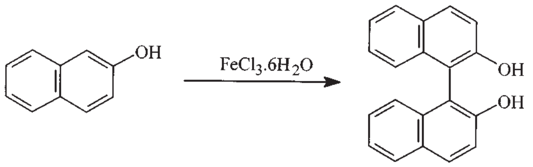
We have recently described a facile solid state synthesis of β-nitrostyrenes from readily available feedstock, styrene and its substituted derivatives using inexpensive 'doped' clay reagents, clayfen and clayan (Scheme 55).[63] In a typical experiment, the neat reagent, styrene and clayfen or clayan are mixed in a glass container and the solid mixture is heated in an oil bath (≈100–110 °C, 15 min) or irradiated in a microwave oven (≈100–110 °C, 3 min). In the case of clayan, intermittent warming is recommended at 30 s intervals to maintain the temperature below 60–70 °C. Interestingly, we observed the reaction proceeds only in the solid state and leads to the formation of polymeric products in solution phase reactions.



Scheme 55

2.8.4 Oxidative coupling of β-naphthols.

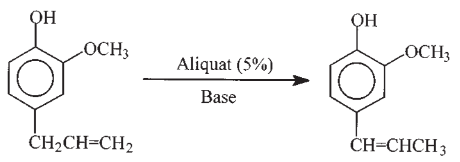
β-Naphthols undergo a quick and efficient self coupling reaction in the presence of iron(III) chloride, $FeCl_3\cdot 6H_2O$, under focused microwave irradiation in solvent-free conditions when compared to classical heating mode (Scheme 56).[64]



Scheme 56

2.8.5. Eugenol isomerization.

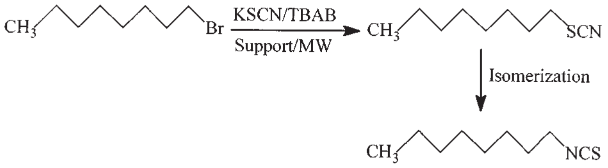
Isoeugenol, an important feedstock for the flavor industry to manufacture vanillin, is normally prepared by base-catalysed isomerization of naturally occurring eugenol. In the presence of potassium *tert*-butoxide, *t*-BuOK, and a catalytic amount of phase transfer reagent, eugenol undergoes isomerization to isoeugenol under solvent-free conditions (Scheme 57).[65]



Scheme 57

2.8.6. Synthesis and isomerization of octylthiocyanate.

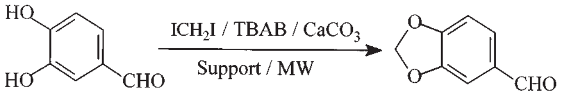
Vass and coworkers have examined various non-traditional supports which, although they are chemically inactive and couple poorly with microwaves, produce some useful chemistry. As an example, octylbromide undergoes thiocyanation reaction with potassium thiocyanide, KSCN, in the presence of a phase transfer catalyst, tetrabutylammonium bromide (TBAB) on sodium chloride surfaces and it further isomerizes to isothiocyanate (Scheme 58).[39]



Scheme 58

2.8.7. Methylenation of 3,4-dihydroxybenzaldehyde.

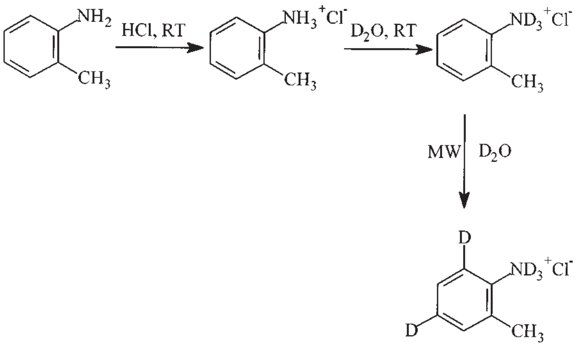
3,4-Dihydroxybenzaldehyde undergoes methylenation rapidly in the presence of a phase transfer catalyst on a benign calcium carbonate surface; presumably the bonding of the vicinal hydroxyl groups is low thereby enhancing the reaction with the alkylating agent under solvent-free microwave irradiation (Scheme 59).[39]



Scheme 59

2.8.8. Synthesis of radiolabelled compounds—exchange reactions.

Jones and coworkers[66b–d] have added a new dimension to the classical tritiation efforts of Wilzbach[66a] using microwave irradiation and solid hydrogen/deuterium/tritium donors with minimal radioactive waste generation. The group has nicely circumvented the traditional disadvantages associated with tritium labeling techniques as exemplified with deuteriated and tritiated borohydride reductions,[66b] based on similar MW-expedited reduction accomplished on alumina surfaces.[32] The hydrogen exchange reactions that require elevated temperatures and extended reaction time (24 h)[66c] are the real beneficiaries of this microwave approach.[66d] The high purity of labeled materials, efficient insertion and excellent regio-selectivity are some of the salient features of this emerging technology (Scheme 60).



Scheme 60

In an elegant application of the microwave-accelerated reactions, Stone–Elander and co-workers have synthesised radiolabelled organic compounds *via* nucleophilic aromatic and aliphatic substitution reactions, esterifications, condensations, hydrolysis and complexation reactions using microwaves.[67] The use of monomodal cavities on microscale organic reactions are real success stories of MW-expedited reactions.

3. Conclusion

This article summarizes the recent activity and eco-friendly features of the solvent-free reactions that are activated by exposure to microwave irradiation. The solventless approach opens up numerous possibilities for conducting selective organic functional group transformations more efficiently and expeditiously using a variety of supported reagents on mineral oxides. The author's own work, performed using an unmodified household microwave oven (multimode applicator), demonstrates the immediate practical applications in laboratory scale experiments. Some of the more recent work does point out the advantages of using monomode systems with focused electromagnetic waves (Prolabo) wherein not only improved temperature/power control is possible but also relatively large scale reactions (1 litre capacity) can be conducted[68] with additional options available for continuous operation. The engineering and scale-up aspects for the chemical process development have already been discussed.[69] The major industrial applications of MW-enhanced clean chemistry include the preparation of hydrogen cyanide, a chlorination plant, drying of pharmaceutical powders and pasteurization of food products.

There are distinct advantages of these solvent-free protocols since they provide reduction or elimination of solvents thereby preventing pollution in organic synthesis 'at source'. Although not delineated completely, the reaction rate enhancements achieved in these methods may be ascribable to non-thermal effects. The chemo-, regio- or stereo-selective synthesis of high value chemical entities may see the translation of these laboratory 'curious' experiments to large-scale operations pending the design of bigger microwave reactors and the participation of equally enthusiastic teams of chemical and electrical engineers to harness the true potential of this clean technology.

4. Acknowledgments

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