Editorial

The number of applicants this year to read chemistry in UK Universities fell to 19257—representing a decrease of some 9.2% on the previous year. In my experience there are similar trends in many countries in Europe and elsewhere. Should we be concerned, and can green chemistry affect this trend? I have heard it said that this is not a problem since the industrial demand for chemists in many parts of the world is also falling. Germany, for example, went out of equilibrium in the early 1990s when its previously buoyant chemical industry cut right back on its high recruitment levels for graduate chemists. This created a ripple effect as large numbers of German chemistry graduates sought employment in other countries. I have spoken to company managers in the UK who report high proportions of job applicants from France and Italy, for example, and I am aware of the increasing numbers of students from mainland Europe now seeking PhD places in the UK. Of course an increase in graduate mobility is to be applauded and if the number of qualified chemists on the market reduces then salaries may well be driven upwards, which in turn might encourage more students to read chemistry and related subjects. However, if instead of simply considering the changing market requirements for graduate chemists we consider the reasons for the reduction in student application numbers then I believe that there is a real and immediate cause for concern.

The choice of university subject is certainly influenced by career opportunities and financial reward (although we must remember that we want chemistry graduates in more walks of life than the chemicals and related industries and academia!), but it is also heavily influenced by interest and perceived reputation and status. Over many years chemistry has attracted many able young minds because it was seen as a challenging and interesting subject of real value to society. Unfortunately chemistry seems mostly to grab the headlines these days as a result of a disaster rather than an invention or benefit to society. If we are to continue to attract bright young people into chemistry and to encourage a wider participation in chemical subjects, then we must address the fundamental issue of subject image.

So how can green chemistry help? Young people are instinctively interested in environmental issues. If the apparent environmental aspects of chemistry are negative, *i.e.* chemistry is considered to be damaging to the environment, then many young people will be antagonistic towards the subject. On the other hand, we can attract students if we emphasise the vital role chemistry has to play in understanding our environment, and how the principles of green chemistry are being used to better manage the environment and to provide the lifestyle we want at minimum cost to the environment. How can we do this?

We must first realise that you cannot start too early! Even before students are taught chemistry as a distinct subject, they can learn about green chemistry aspects of environmental issues. It is important that our children are brought up believing that chemistry is for the environment not against it! Once students start studying chemistry and start carrying out chemical experiments then we have a growing number of examples, case studies and experiments that can be used to teach good practice. We have been able to publish a lot of relevant material in *Green Chemistry*, but we need more good examples. Practical classes are excellent vehicles for teaching green chemistry. Most of us will have gone through an undergraduate practical course with synthetic experiments that were based on the principle that the end justifies the means—obtaining a pure product was the essential goal. We should expect our students to calculate not only the product yield but also the atom efficiency, the solvent usage and the waste, as well as at a later stage in their course the economic and environmental feasibility of the method. If you know of such examples of green chemistry experiments then please let us know so that we can share them with the chemistry community. We should aim to make our students aware at an early stage of an educational version of the triple bottom line: better chemistry, better education and better environment!

James Clark, York, September 1999

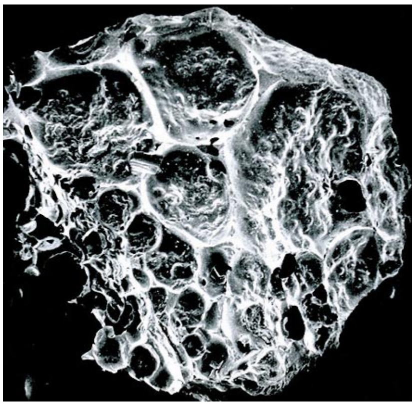
Raw macadamia nut shells being placed in a special oven where they will be carbonised and activated at temperatures above 800 °C. USDA-ARS photo by Scott Bauer

Activated carbon from nuts

A team of scientists led by Wayne Marshall at the USDA-ARS Commodity Utilization Research Unit located at the Southern Regional Research Center, outside New Orleans, USA, are recycling nut shells into activated carbon. Christopher Toles, formerly with ARS but now with Northeastern University in Boston, Massachusetts, is also involved in the research. The shells are ground and exposed to temperatures of up to 900 °C in combination with steam, certain gases, or acids. Such treatment activates, or opens, millions of microscopic pores in the carbonised shells, enabling them to hold on to chemical molecules. Oxidation confers a negative charge to the shells, helping them to capture metal ions in solution. Various nut shells have been tried, including pecan and almond, but so far the activated carbon from macadamia nut shells has been found to adsorb the broadest range of organic molecules. It is estimated that 14,600 tons of macadamia shells could yield about 3000 tons of activated carbon material.

In one comparative study with 6 commercial adsorbents, use of activated macadamia shells led to a 3- to 4-fold increase in the ability of a standard Environmental Protection Agency air sampling procedure to detect benzene at concentrations of 100 parts per billion. The nut shell carbon also performed well in small-scale studies to remove copper from industrial waste water. The potential of the carbon as an adsorbent material for gas chromatographic analysis of air is particularly encouraging. To foster commercial collaboration, the team has applied for patent protection on its activation procedures. Other nut shells are being investigated, such as hazelnuts, black walnuts and Brazil nuts, as sources of activated carbons.

Today's usual activated carbons are made from coal, peat, coconut shells and wood. The nut shells represent a renewable low-value agricultural waste source of activated carbons, widely used to adsorb many organic compounds from air or water.



Scanning electron micrograph showing the effect activation has on the gross structure of nut shell carbon granules. While it is impossible to see active micro- and meso-pores, the large pits are significant evidence of gasification. USDA-ARS photo by Chris Toles.

MTBE

A report by a Federal 'Blue Ribbon Panel on Oxygenates in Gasoline' which took six months to complete has concluded that there should be a substantial reduction in the use of MTBE as a fuel additive. The panel was appointed by the US EPA in November 1998. Although air quality has been improved by the use of MTBE, it has led to polluted water supplies through leakages from underground storage tanks. In the 1990 Clean Air Act, a 2% oxygen content by weight is required in reformulated gasoline. This legislation would have to be repealed before use of MTBE could be reduced. MTBE consumption in the US is around 300,000 bbl/day, with most of this being in California and the north east. MTBE is added as an oxygenate to more than 85% of reformulated gasoline. Oxygenates must be used to reduce vehicle emissions in cities failing to meet clean air standards. Ethanol is used in around 8% of reformulated gasoline. The use of MTBE has already been banned in Maine and by the end of 2002 it is to be phased out in California. For more information on the Blue Ribbon Panel report see the article on page G142 of this issue of *Green Chemistry*.

Thermal polyaspartate enhances pesticide activity

Speaking at the 3rd Annual Green Chemistry and Engineering Conference in Washington DC, USA, at the end of June, Ramon Georgis of the Donlar Corporation of Bedford Park, IL, USA (the first recipient of the Presidential Green Chemistry Award) reported that polyaspartic acid prepared by the thermal polymerisation of aspartic acid (thermal polyaspartate) can enhance the effectiveness of herbicides and insecticides, affording kills at lower concentrations of active ingredient. In combination with polyaspartate, kill effectiveness was enhanced by up to 3 times for several classes of herbicides in the control of broadleaf weeds, while experiments with red fire ants and tobacco budworm demonstrated that kill effectiveness was enhanced by up to 4 times with certain organophosphate and carbamate insecticides. Website: http://www.donlar.com

Spherilene polyethylene technology

Montell is pleased to announce that another Spherilene process polyethylene plant has successfully started up. The 260,000 tonnes/y plant, which is also the world's largest Spherilene process plant to date, is operated by OPP Petroquimica in Brazil under license from Montell. Montell's polyethylene gas-phase reactor 'swing' technology is capable of producing a wide range of resin types from conventional High Density Polyethylene (HDPE) and Linear Low Density Polyethylene (LLDPE) grades to high-value specialities, including the recently developed HP Quattropolymer grades. Spherilene process plants are designed for minimal environmental impact, avoiding emissions by recycling through the process itself or recovery in the nearby steam-cracker. The Spherilene technology also facilitates smooth start-ups and re-starts after shutdowns. Montell is a global leader in the production, marketing and sale of polyolefins, advanced materials and related products and is the world's largest producer of polypropylene. Montell is also the recognised leader in the development of polypropylene catalysts and process technologies.
Website: http://www.montell.com

Ultrapure water

Ion exchange resins remain the dominant method to achieve ultrapure water, but membrane-based continuous (electric) deionisation (CEDI) is emerging as a powerful alternative technology. The power generation industry is the largest consumer of ultrapure water and, in terms of the volume of ultrapure water produced and used, industrial boiler applications dwarf the electronics industry. But the electronics industry is where the growth is, and is where innovation in water treatment technologies is taking place. The electronics sector of the ultrapure water market is expected to take an upturn in 1999 as semiconductor manufacturers invest again in new facilities and plant expansions. CEDI is an attractive clean option because it uses electricity and not chemicals to regenerate ultrapure water and its other advantages include quick and easy installation and continuous operation. But CEDI still requires reverse osmosis pre-treatment and sometimes even an ion exchange resin polishing stage. Nevertheless the growing number of companies moving into CEDI technology suggests that this may well become the dominant technology. In response suppliers of ion exchange resins are innovating to improve resin regeneration efficiency and reducing operating costs to compete. One approach is the development of uniform particle resins which take advantage of advanced production technology to produce specific particle sizes for cations and ions in resins used in ion exchange resin systems.

Gas-to-liquid technology

...the Lubrizol Corp., a Cleveland, Ohio, speciality chemical company, together with Syntroleum Corp., a Tulsa, Oklahoma, energy technology company, on 3 Aug 1999 announced an agreement to develop and test additives for use in clean fuels manufactured using Syntroleum's proprietary gas-to-liquids (GTL) process. Under the agreement, initial programmes will focus on the development of additives to enhance the performance of the 'designer fuels' being developed under Syntroleum's previously announced programme with DaimlerChrysler. Websites: http://www.lubrizol.com and http://www.syntroleum.com.

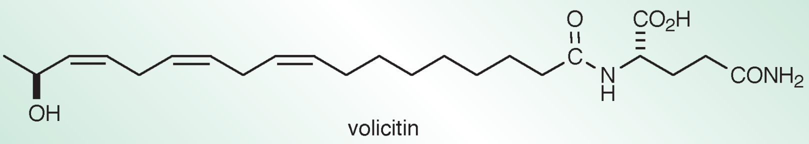
...ARCO and Syntroleum Corp. have announced the completion and the successful start-up of their Natural Gas-to-Liquids pilot plant. Located at ARCO's Cherry Point refinery near Bellingham, Washington, USA, the 70 bbl/day pilot plant has achieved initial operating targets and is proceeding with the evaluation programme. The pilot plant is testing new reactor designs and high-performance Fischer–Tropsch catalysts for the Syntroleum Process, a proprietary process for converting natural gas into synthetic fuels and hydrocarbon-based speciality chemicals.
Website: http://www.arco.com

...Early Entrance Co Production Plant (EECP)
Rentech Inc. of Denver, Colorado, will be part of a project team of companies, led by Texaco, that have been selected by the US Department of Energy (DOE) to develop the engineering design for a new type of energy facility called: 'the Early Entrance Co Production Plant' (EECP). The design will combine Texaco's gasification technology with Rentech's Fisher–Tropsch technology to provide high quality transportation fuels and electricity from coal and petroleum coke. The DOE will contribute \$8 to \$8.7 M to the 3 to 5 year project with a total cost of \$14.4 M.
Website: http://www.gastoliquids.com

...Induction-Coupled Plasma Reforming Process
Rentech Inc. of Denver, Colorado, on 3 August 1999 announced that Thermal Conversion Corp. of Kent, Washington, had successfully demonstrated the use of its Induction-Coupled Plasma (ICP) Reforming Process for the controlled production of synthesis gas from natural gas at its 1 MW pilot scale test facility in Kent. Synthesis gas, or syngas (a mixture of hydrogen and carbon monoxide), is the feedstock for the production of clean liquid fuels *via* the Fischer–Tropsch process.
Website: http://www.gastoliquids.com

Natural defence compound synthesised

With support from Bayer and BASF, Georg Pohnert and his colleagues at the Max Planck Institute in Jena, Germany, have devised a short stereoselective route to the specific component (17-hydroxylinolenoyl)-L-glutamine (commonly called volicitin) (*Chemical Communications*, 1999, 1087). Volicitin is the component in beet armyworm caterpillar saliva which triggers plants attacked to give off a cocktail of terpenoids attracting parasitic wasps that kill the caterpillars (*Chemistry in Britain*, August 1997, 15).



volicitin

Stannic oxide sol provides excellent antistatic efficacy

EPS-6 is a new amorphous stannic oxide solution developed by Yamanaka Chemical for the production of coating films that provide a semi-permanent anti-static layer. The new material is environmentally friendly because it does not require the use of a doping agent and it is water-based. Plastic films, electronic materials and various moulded products are all suitable applications for EPS-6. New technology for the prevention of crystallisation of stannic oxide during production has also been developed by the company.

Enzymic production of L-aspartic acid

By 2000, a new 2000–3000 tonnes/y facility for production of L-aspartic acid is planned to be brought onstream by Nippon Shokubai, using its own novel technology. Global demand for L-aspartic acid is estimated at 10,000 tonnes/y, with the major end-use being artificial sweeteners. Potential new applications include biodegradable materials, including chelating agents, polyaspartic acid and water absorbent resin. These areas are to be expanded by the company. Genetically modified *E. coli* is used to produce an enzymatic catalyst for use in the new process. No sulfuric acid is used in the process, thus making it more environmentally friendly. Website: http://www.shokubai.co.jp

Clean fuels

...the potential of dimethyl ether (DME) as an alternative fuel is being assessed in several countries. For example, the Indian Institute of Petroleum, Gas Authority of India Ltd. and Indian Oil Corp. have signed a Memorandum of Understanding with BP Amoco of the US for the development of DME as a clean alternative transport and power plant fuel in India, while the Shaanxi New Fuels & Burning Equipment Co. of China and Jiuyun International Resources Co. of the US are to jointly develop a project to make super-clean dimethyl ether fuel from coal.

...BP announced recently its plans to introduce a range of cleaner fuels for motorists in the Paris region, which will lead to significant reductions of automobile and road transport emissions. The range includes a new Ultra Low Sulfur Diesel (ULSD), launched in Paris in September 1999; it will reduce sulfur emission by 90% on all diesel vehicles, without any detrimental impact on performance and will be offered at no extra cost to motorists. ULSD also reduces other emissions substantially and enables new particulate reduction technology to be fitted on buses and other transport vehicles. BP will be the first oil company in France to offer *en masse* the new diesel which already anticipates the 2005 EU sulfur specifications. Website: http://www.bpamoco.com.

...US companies Johnson Matthey and Clean Diesel Technologies have agreed to do joint research into platinum-based catalysts, with the aim of developing diesel fuel additives able to increase the performances of the particle filters of diesel motors, in order to reduce the emission of particles into the atmosphere. Website: http://www.matthey.com.

...on 22 July 1999 BP Amoco designated Atlanta as its first ‘Clean City’ in the US by introducing new, 30 ppm lower sulfur premium gasolines at both BP and Amoco service stations in the greater Atlanta metropolitan area. Earlier in 1999, BP Amoco announced its Clean Cities programme, in which it will voluntarily bring cleaner fuels to 40 cities around the world by the end of the year 2000. BP and Amoco service stations in the 25-county Atlanta area are now offering new, lower sulfur premium gasoline year round. Since April 1999, BP Amoco has made cleaner fuels announcements in London, Paris and Istanbul.
Website: http://www.bpamoco.com

Inorganic ‘glass paint’

ThermaCell Technologies Inc. has filed for a patent covering a new kind of environmentally friendly paint that uses inorganic glass to replace organic resins, creating a longer lasting finish for the same price as regular paint. Because it does not contain any volatile organic compounds, ThermaCell’s ‘glass paint’ meets the new, highly restrictive regulations regarding the elimination of environmentally harmful paint ingredients in states like California. Inorganic Hybrid Silicate is the technical name for the product. The company plans to use its ‘glass paint’ to aggressively expand into California, one of the largest paint and coatings markets in the US. The company plans to launch a licensing programme to enable other manufacturers to market their own brands of ‘glass paint.’ Inorganic Hybrid Silicate is resistant to weathering, ultraviolet rays, acid rain, fading, solvents, water, and mildew. It does not chalk, has no odor, does not create harmful vapour barriers; contains no solvents, organic binders, biocides, or mildewcides; and is available in clear and pigmented. ThermaCell Technologies Inc. is a technologically enhanced manufacturer and marketer of paints, coatings and building materials. The company manufactures conventional paints, coatings and building materials through traditional trade and retail venues. The company also manufactures VaxCell microspheres, which provide greater insulation, protection, strength, longevity and value in paints, coatings and building materials. Website: http://www.thermacell.com

Biochemie to quadruple 7-ACA capacity

Biochemie is to build a new production plant for 7-aminocephalosporanic acid (7-ACA) in Frankfurt at a cost of DM 85 M ($45 M). It will use an enzyme catalytic process and will have a capacity of over 400 tonnes/y. Startup is due in 2000. The company, which is the antibiotics subsidiary of Novartis, already has a 100 tonnes/y 7-ACA plant at the site which uses the same process. It bought the site from Hoechst in 1998. The new unit will take its total 7-ACA output to 700–800 tonnes/y, making it the world’s leading producer. 7-ACA is an important antibiotic intermediate. The enzyme process is cheaper and cleaner than conventional production methods.

Synetix wins environmental award

Synetix, ICI’s recently established business, has been awarded the Queen’s Award for Environmental Achievement for Hydecat, a process that treats sodium hypochlorite produced from waste chlorine streams. Effluent is passed through the catalyst bed using gravitational feed and has no moving parts of pumps. Sodium hypochlorite (bleach) is converted by the process from a potentially harmful mixture to a benign common salt solution and oxygen. Over

20 companies in 9 countries have successfully applied the Hydecat technology, with cost savings. Website: http://www.synetix.com

Environmentally friendly credit cards

Visa International, one of the world's largest credit card companies, has recommended that credit cards can now be produced with a more environmentally friendly material, glycol-modified PET (PETg), as a substitute for PVC. Visa issued over 580 M cards worldwide in 1998. Manufactured by Eastman Chemical in the US, 75% of PETg's sales are in Europe and there is growing demand in Japan and the US. Website: http://www.visa.com

Fuel cells

DaimlerChrysler
DaimlerChrysler (DC) is leading the race to market fuel cell cars, and is developing methanol as its preferred fuel. DC's experimental car, the Necar 3, is based on the A-Class Mercedes which has its engine under the body of the car, but the power unit is in the rear. It is claimed that the Necar 3 has a range of 400 km on the 40-litre tank of methanol fitted to the car. Hydrogen is the simplest fuel for fuel cells but its storage is difficult, and hence the interest in methanol. The American Methanol Institute estimates that 2 M methanol fuel cell vehicles in 2010 will require 2.64 M tonnes methanol and in 2020 35 M vehicles would need 46 M tonnes together with a capacity increase of 35% to produce it.
Websites:
http://www3.daimlerchrysler.com/ and
http://methanol.org/fuelcell/

Please note, in relation to the News item on page G91 of the last issue of *Green Chemistry* (August 1999), that the Zevco Emission Vehicle Company Ltd. no longer have any involvement with the fuel cell-powered Millennium Taxi.

Ford
On 16 August 1999 The Ford Motor Co. opened the first filling station in North America that can refuel vehicles with either liquid or gaseous hydrogen. It is the second such filling station in the world and bolsters Ford's commitment to clean hydrogen vehicles. Ford intends to be the leader in the production of fuel cell vehicles. This refuelling station, right on the site of the North American Research and Engineering campus, gives Ford an edge by allowing them to easily refuel and conduct tests on the company's vehicles and in the labs. The station officially opened with the refuelling of Ford's P2000 HFC (hydrogen fuel cell) sedan, which is powered by gaseous hydrogen. The station will help Ford researchers analyze the benefits of liquid *vs.* gaseous hydrogen refuelling, different types of nozzles for refuelling and different pressures for optimal refuelling with hydrogen. While primarily used for fuel cell development, Ford also is conducting significant research on hydrogen powered internal combustion engines. Website: http://www.ford.com

New refrigerant as CFC replacement

Solpower Corp. has announced projected benefits resulting from chlorofluorocarbon (CFC) global banning initiatives. Europe, Canada and Japan have recently introduced more effective usage bans on CFCs that have significantly increased the market opportunities for Solpower Corp's SP34E, a direct drop-in replacement gas for R12 and R134A refrigerants. SP34E has captured almost 15% of the Australian refrigeration market in less than a year. Solpower Corp. reports that its refrigerant gas SP34E is the solution to the Montreal Protocol initiatives for implementation of CFC bans. In addition to being a direct drop-in replacement for R12 and R134A, Solpower's SP34E also will not damage the ozone layer, requires minor system modification, requires no special system handling equipment, is compatible with mineral oils and PAG/POE oils, outperforms both R12 and R134A in most cases and is more efficient than R134A with more capacity and lower head pressures. Website: http://www.solpower.com

Biomass ethanol plant

Many in the USA are convinced that ethanol from biomass is the fuel for the future, especially with the proposed phaseout of MTBE. For example, Massachusetts-based BC International Corp. are planning to construct a 'biorefinery' next year south of Oroville in California. It will convert about 75,000 tons of rice straw, 125,000 tons of orchard slash and 40,000 tons of other agricultural waste into 22 million gallons of ethanol each year. BC International already have a similar plant in operation in Jennings, Louisiana.

Adhesives for US postage stamps

The USA's first self-adhesive postage stamp was issued by the US Postal Service (USPS) in 1974. Self-adhesive stamps were reissued in 1987 and sales have grown rapidly to reach a projected 93% of stamps sold in 1999. Their use is adversely affecting the efficient recycling of paper, however, since the pressure-sensitive adhesive (PSA) on the stamp breaks down in the repulping process to clog equipment and to appear as dirt or imperfections in the recycled paper. The USPS contracted Specialized Technology Resources Inc. in 1995 to develop environmentally benign PSAs and Franklin International and Spinnaker were also employed. A new PSA, Covinax 2000, has been developed and is currently under extended testing. Website: http://www.duracet.com

Catalysts

...Low-temperature hydrogenation
French chemists have developed a highly efficient catalyst system for hydrogenating aromatic compounds to make cleaner diesel fuels. The fully recyclable catalyst operates at room temperature and atmospheric pressure. ENSC de Rennes has developed a new liquid–liquid system based on rhodium metal particles just a few nanometres in diameter suspended in water to form a colloid. The second phase is the aromatic reactant and its products, and therefore no solvent is needed. The system efficiently hydrogenates benzene and its derivatives to their cyclohexane equivalents. This system appears to be the most efficient for converting benzene to cyclohexane, and toluene, cumene, anisole and phenol to their hydrogenated forms in very mild conditions. Website: http://ensc-rennes.fr

...a computer programme which can assist in the production of catalysts has been announced by Dewi Lewis of University College London. He developed the programme alongside David Willock of the University of Wales, using patterns found in nature to invent improved types of catalyst which can speed up chemical reactions. Called Zebedde (zeolites by evolutionary de novo design), the compter program, which duplicates the biased randomness found in evolution, selects molecular fragments from a library to be used in a catalyst.A series of potential combinations is produced, which a researcher then selects from, based on an understanding of chemical properties. Zebedde has the potential to speed up and simplify the use of catalysts in synthesising lead substitutes for petrol or for producing gasoline.

...Magic catalysts. In a recent issue of *Chemistry in Britain* (August 1999, **35**(8), 25–27) there was an article on the development of catalysts using tungsten and molybdenum, in consequence of shrinking reserves of platinum and other Group VIII transition metals. The article describes the work by Malcolm Green's laboratory in the Wolfson Catalysis Centre at the University of Oxford (http://www.chem.ox.ac.uk/icl/catcentre/carbides.jpg), Marc Ledoux's group at the Université Louis Pasteur in Strasbourg and others in the application of molybdenum and tungsten carbides to a range of industrial and environmental reactions. Examples of the use of the carbides include Fischer–Tropsch synthesis of hydrocarbons, benzene hydrogenation, hydrodesulfurisation of thiophenes and isomerisation of hexane, heptane and octane. Examples of the use of the nitrides include ammonia synthesis from its elements and hydrodenitrogenation.

Biodegradable plastic from GM plants

The biotechnology giant Monsanto claims to have created genetically modified (GM) plants that can 'grow plastic'. The plants, principally oilseed rape, contain four added genes from bacteria that naturally produce a biodegradable plastic called PHBV, according to a recent article in *Nature Biotechnology*. Biodegradable plastics have been produced before using bacteria alone but the process has been too expensive and the end-product has been too brittle for most applications. The new GM process produces a biodegradable product which is suitable for commercial use. Ken Gruys, who leads this research at Monsanto, says that this a really only a first step since the current yield of plastic is only 3%. He says that the next step is to refine the GM process to make it suitable for high-yield production; this may take up to 10 years.

Metallocene catalysts

According to Univation Technologies, the global market for metallocene catalysed polyethylene (PE) will grow at a rate of 45% per year up to 2010. The regions experiencing greatest growth are forecast to be North America, Asia and Western Europe. Univation Technologies is a licensing joint venture established by Union Carbide and Exxon Chemical to sell Unipol technology. Competing technology is supplied by Dow Chemical/BP Chemical by their Insite/Innovene technologies. The technology has been installed in PT Peni's PE plant in Indonesia, which is producing commercial quantities of product. The key to metallocene catalysis growth will be consistent production of LLDPE using the technology, according to the Catalyst Group, consultants based in Houston, Texas. The market leaders in metallocene catalysis are Exxon and Dow. New research is being carried out into styrene/ethylene interpolymers (Index) by Dow. Another company using metallocene technology is Phillips Petroleum at Bartlesville, Oklahoma, which produces PE which it sells under the mPACT brand name.

Ethane-to-ethylene

A novel approach to the production of ethylene is being developed by a team from the University of Minnesota and the Polytechnic University in Milan. They flow a mixture of ethane, hydrogen and oxygen over a catalyst made by depositing platinum and tin on alumina. The gaseous mixture would be expected to explode, but apparently the presence of the ethane prevents this. The hydrogen in the product balances that needed in the feed. Conversions of 60% with a selectivity of 85% have been achieved. The mechanism of the reaction is obscure.

The colonnade at St.Peter's in Rome is being cleaned with Hydro Facade.

Hydro Facade cleaning up Rome

Rome's city fathers are paying to clean the faces of nearly 7000 buildings as the eternal city prepares to celebrate the new millennium in style. Hydro Facade, a cleaning compound made from pure calcium carbonate, will be used to clean and polish some very important buildings in Rome. The list includes Italy's national assembly, known as Montecitorio, the government building Palazzo Chigi, and Villa Farnesina, which houses the country's foreign affairs department. The Hydro product will also be used to clean the colonnade at St. Peter's. In Rome, Hydro Chemicals works together with a local company, Agep Srl. The companies have carried out a large number of jobs over the past three years, not only in cleaning the surfaces of major buildings, but in removing graffiti from subways and trains. Website: http://www.hydro.com

More 1999 Presidential Green Chemistry Awards

Paul Anastas, Mary Kirchchoff and Tracy Williamson of the US EPA present the second in a series of short profiles on this year's Presidential Green Chemistry Awards.

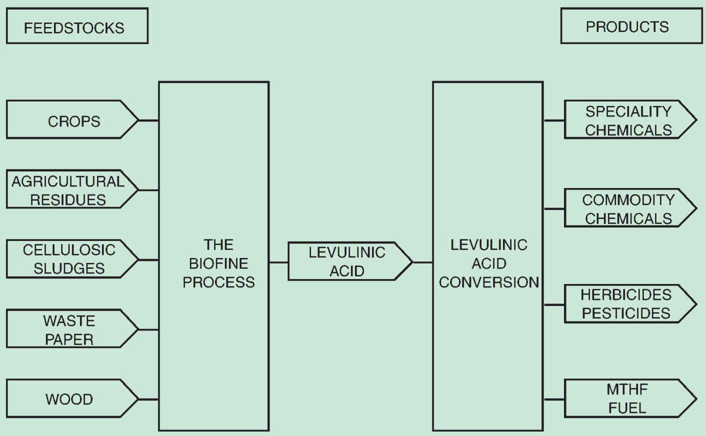
To Biofine[1] for their economic conversion of cellulosic biomass to chemicals

Replacing petroleum-based feedstocks with renewable ones is a crucial step toward achieving sustainability. When considering alternatives to traditional feedstocks, attention often focuses on plant-based materials. Renewable biomass conserves our dwindling supplies of fossil fuels and contributes no net CO_2 to the atmosphere. Biofine has developed a high-temperature, dilute-acid hydrolysis process that converts cellulosic biomass to levulinic acid (LA) and derivatives. Cellulose is initially converted to soluble sugars, which are then transformed to levulinic acid. By-products in the process include furfural, formic acid, and condensed tar, all of which have commercial value as commodities or fuel. Feedstocks used include paper mill sludge, municipal solid waste, unrecyclable waste paper, waste wood, and agricultural residues.

Plant at South Glen Falls, NY, in which levulinic acid is produced from cellulosic biomass.

Levulinic acid serves as a building block in the synthesis of useful chemical products. Markets already exist for tetrahydrofuran, succinic acid, and diphenolic acid, all of which are levulinic acid derivatives. The use of diphenolic acid (DPA) as a monomer for polycarbonates and epoxy resins is currently under investigation. An industry/government consortium has conducted research on two additional derivatives with commercial value: methyltetrahydrofuran (MTHF), a fuel additive, and δ-amino levulinic acid (DALA), a pesticide.

The conversion of levulinic acid to MTHF is accomplished at elevated temperature and pressure using a catalytic hydrogenation process. MTHF is a fuel additive that is miscible with gasoline and hydrophobic, allowing it to be blended at the refinery rather than later in the distribution process. Using MTHF as a fuel additive increases the oxygenate level in gasoline without adversely affecting engine performance. MTHF also boasts a high octane rating (87) and a low vapor pressure, thereby reducing fuel evaporation and improving air quality. MTHF represents the first practical example of the direct incorporation of hydrogen in liquid fuels.



The Biofine process

DALA can be obtained from levulinic acid in high yield using a three-step process. DALA is a broad-spectrum pesticide that is non-toxic and biodegradable. Its activity is triggered by light, selectively killing weeds while leaving most major crops unaffected. DALA

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[1] Biofine is a 'virtual' company formed for the purpose of owning the levulinic acid process patents and other related intellectual property. BioMetics Inc. is a (bio)chemical engineering consultancy and engineering company which designed, built and operated the Biofine large-scale demonstration plant at South Glen Falls, New York.

also shows potential as an insecticide.

Diphenolic acid is synthesized by reacting levulinic acid with phenol. DPA has the potential to displace bisphenol-A, a possible endocrine disruptor, in polymer applications. Brominated DPA shows promise as an environmentally-acceptable marine coating, while dibrominated DPA may find use as a fire retardant.

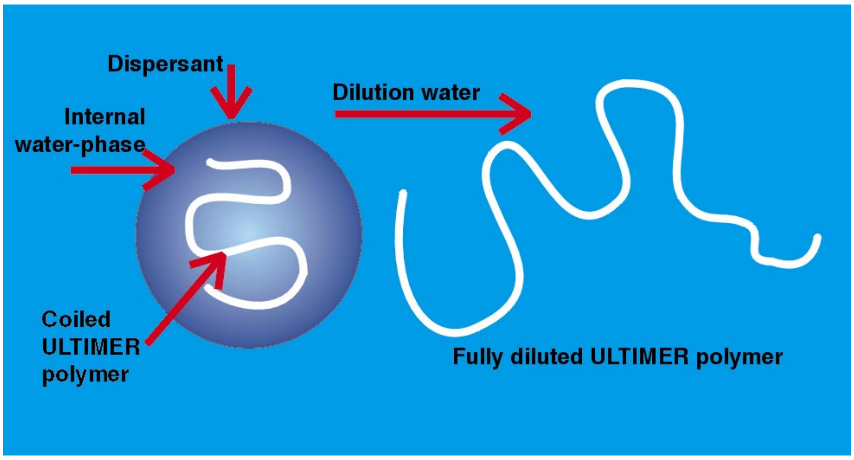
Currently, levulinic acid has a world-wide market of about one million pounds per year at a price of \$4–6/lb. Large-scale commercialization of the Biofine process could produce levulinic acid for as little as \$0.32/lb, spurring increased demand for LA and its derivatives. Using the Biofine process, waste biomass can be transformed into valuable chemical products. The ability to produce levulinic acid economically from waste biomass and renewable feedstocks is key to increased commercialization of LA and its derivatives.

For more information on the Biofine process contact Dr. Steve Fitzpatrick on sfitzp@biometicsma.com

To Nalco Chemical Company for ULTIMER®—the first of a new family of water soluble polymer dispersions

High molecular weight polyacrylamides are commonly used as process aids and water treatment agents in various industrial and municipal operations. Annually, at least 200 million pounds of water soluble, acrylamide-based polymers are used to condition and purify water. These water soluble polymers assist in removing suspended solids and contaminants and effecting separations. Traditionally, these polymers are produced as water-in-oil emulsions. Emulsions are prepared by combining the monomer, water, and a hydrocarbon oil/surfactant mixture in approximately equal parts. Although the oil and surfactant are required for processing, they do not contribute to the performance of the polymer. Consequently, approximately 90 million pounds of oil and surfactant are released to the environment each year. Nalco has developed a new technology that permits production of the polymers as stable colloids in water, eliminating the introduction of oil and surfactants into the environment.

The Nalco process uses a homogeneous dispersion polymerization technique. The water soluble monomers are dissolved in an aqueous salt solution of ammonium sulfate then polymerized using a water soluble free radical initiator. A low-molecular-weight dispersant polymer is added to prevent aggregation of the growing polymer chains. For end use applications, the dispersion is simply added to water, thereby diluting the salt and allowing the polymer to dissolve into a clear, homogeneous polymer solution. This technology has been successfully demonstrated with cationic copolymers of acrylamide, anionic copolymers of acrylamide, and non-ionic polymers.



ULTIMER® polymers are totally water-based. Therefore activation for use is as simple as diluting the product prior to feeding.

Development of water based dispersion polymers provides three important environmental benefits. First, the new process eliminates the use of hydrocarbon solvents and surfactants required in the manufacture of emulsion polymers. Dispersion polymers produce no VOCs, and exhibit lower biological oxygen demand (BOD) and chemical oxygen demand (COD) than emulsion polymers. Second, the salt used, ammonium sulfate, is a waste by-product from another industrial process, the production of caprolactam. Caprolactam is the precursor in the manufacture of nylon; 2.5—4.5 tons of ammonium sulfate are produced for every ton of caprolactam, providing a ready supply of feedstock. Finally, dispersion polymers eliminate the need for costly equipment and inverter surfactants needed for mixing emulsion polymers. This technological advantage will make waste water treatment more affordable for small- and medium-sized operations.

Nalco's dispersion polymers contain the same active polymer component as traditional emulsion polymers without employing oil and surfactant carrier systems. The polymers are produced as stable colloids in water, retaining ease and safety of handling while eliminating the release of oil and surfactants into the environment. By adopting this new technology, Nalco has conserved over one million pounds of hydrocarbon solvent and surfactants since 1997 on two polymers alone. In 1998, the water based dispersions utilized 3.2 million pounds of ammonium sulfate, a by-product from caprolactam synthesis that would otherwise be treated as waste. Additional environmental benefits will be realized as the dispersion polymerization process is extended to the manufacture of other polymers.

For more information on Nalco Chemical Company and ULTIMER® polymers see the web site: http://www.nalco.com

Green chemistry in an industrial ecology context

Thomas Graedel discusses extending green chemistry from merely green synthesis to greening of entire life cycles

Industrial ecology, like green chemistry, is less than a decade old. Nonetheless, its importance has become widely recognized, as has its perspective—to view the entire modern technological system, and the products of that system, much as biological ecologists view natural ecosystems and individual organisms.[1] In systems of both types, flows of resources and energy are studied in order to assess the use of materials and energy, sources of loss, loss mechanisms and techniques for amelioration. Industrial and biological ecology analyses can be performed on scales as large as that on the entire global society or natural system, or as small as a single product, creature or physical process.

A characteristic that distinguishes industrial ecology from many other environmentally related topics is its breadth in space and time. In the case of a product, for example, it looks not just at the manufacturing stage, but at all life stages—from birth to death or, ideally, from birth to reincarnation. Such breadth has not typically been a characteristic thus far of green chemistry approaches, which focus on minimizing or avoiding residues of all kinds, especially hazardous ones, arising from the manufacturing process.[2] This approach is laudable but unnecessarily narrow, failing to capture many environmental aspects of chemical manufacture, use and disposition. Hence, it is appropriate to expand the concept of green chemistry so as to place its approach squarely within the industrial ecology context. As shown below, adding a life-cycle perspective to green chemistry enlarges its scope and enhances its environmental benefits.

The product life cycle

The concept of life-cycle assessment (LCA) was originally developed to aid in assessing the environmentally related attributes of manufactured products. It considers five life stages: Pre-manufacture, Manufacture, Product delivery, Product use and End of life.[3] The stages are characterized in part by the ways in which resources are used. Energy is consumed at each stage, process chemicals or consumables in most, and water in some. Each stage has the potential to generate residues. When the product becomes obsolete, it may have the potential to be refurbished, remanufactured or recycled.

> ‘adding a life-cycle perspective to green chemistry enlarges its scope and enhances its environmental benefits’

It is worth noting that this approach has evolved from that of a decade or two ago, when the sole interest of manufacturers, government regulators, and other interested parties was on residues from the manufacturing stage. That focus has since been broadened considerably to include energy, water, and natural resources, and to recognize that a product’s environmental impacts during manufacture may not be the most important. Indeed, sometimes (as with the automobile) the impacts at life stages other than manufacturing are dominant.

The product designer has many opportunities to influence resource flows and associated environmental impacts. In the conceptual tool generally employed as part of an industrial ecology design activity, termed Design for Environment (DFE), environmental considerations are added to other design considerations

Thomas E. Graedel is Professor of Industrial Ecology in the School of Forestry and Environmental Studies, Yale University, a position he assumed in 1997 after 27 years at AT&T Bell Laboratories. He was the first atmospheric chemist to study the atmospheric reactions of sulfur and the concentration trends in methane and carbon monoxide. One of the founders of the newly emerging field of industrial ecology, he co-authored the first textbook in that specialty and has lectured widely on its implementation and implications. His matrix assessment tool, developed while at AT&T, is a widely-used standard for the environmental assessment of products and services.

(safety, performance, cost, *etc*.). The ideal result is a product that is environmentally superior while it simultaneously meets or exceeds its other design targets.

How might such a life-cycle concept be applied to chemical products? Consider any firm that buys a chemical from a supplier and manufactures a final product, especially a product that may eventually be recycled. Examples include a company that purchases ABS (acrylonitrile–butadiene–styrene) thermoplastic resin and uses injection molding to form it into desk telephones, or a company that buys cyanides to plate one metal on another. In either case, the life stage sequence is shown in Figure 1.

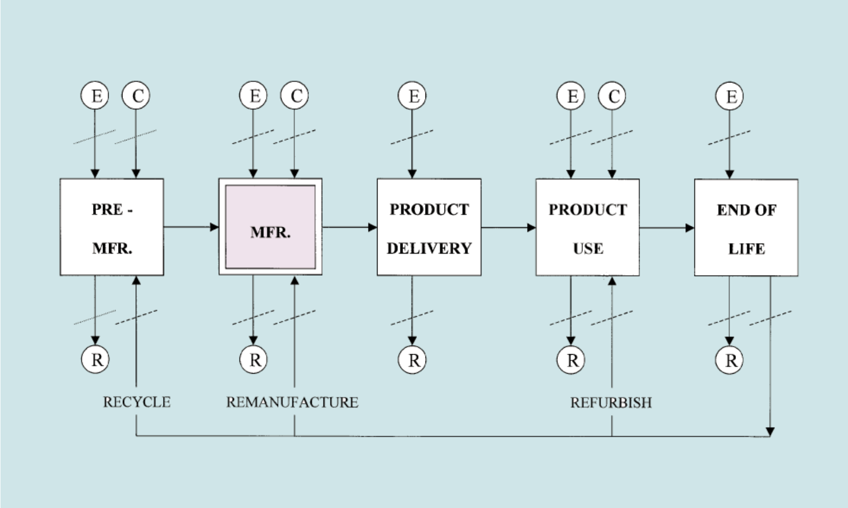


*Figure 1. The life cycle of a recyclable chemical product.**

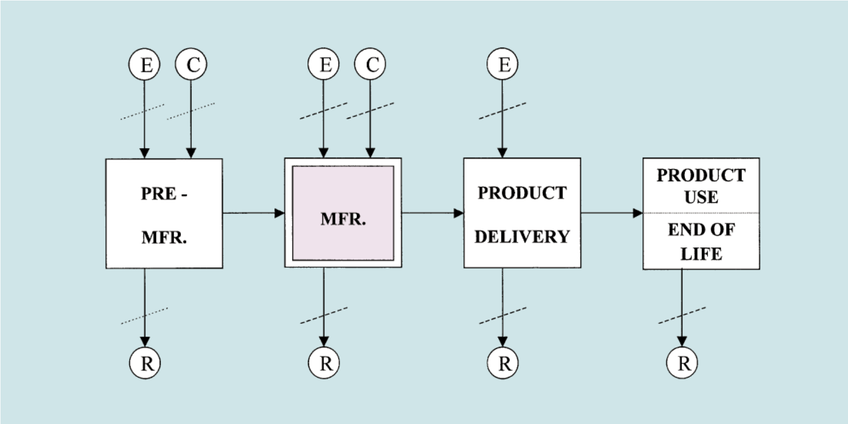


*Figure 2. The life cycle of a dissipative chemical product.**

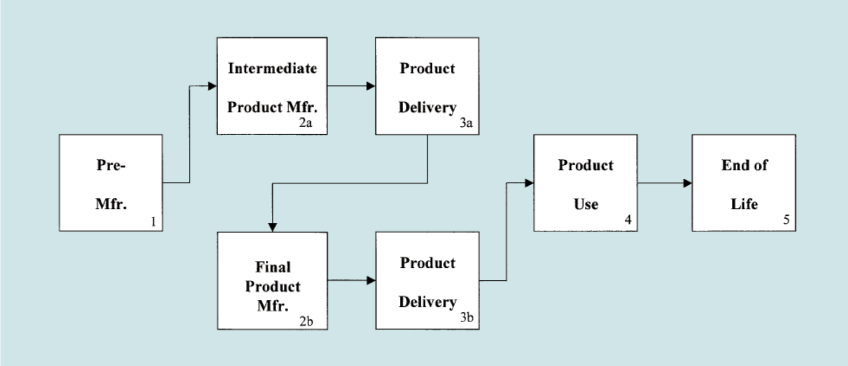


*Figure 3. The life cycle of a chemical intermediate (possible reuse routes are omitted for clarity).**

The designer of the product that uses ABS or nickel plating clearly influences the environmental aspects of more than the manufacturing stage; in actuality, she or he has the potential to affect all life stages implicitly or explicitly, for good or ill. An environmentally sensitive chemical product designer can, for example, optimize supplier manufacturing processes, determine the use of consumables while the product is in service, and help to define eventual product recyclability.

A common variation on this theme is for the chemical product to be one that is dissipated in use, such as a pharmaceutical preparation, a hair spray, or a herbicide. The life stage sequence in this case is shown in Figure 2. In this case, the manufacturer directly controls all life stages but Premanufacture, and can influence that stage through its interactions with suppliers. Products designed to be dissipated in use have, of course, no End of life stage and thus no prospect for recycling. Nevertheless, the life cycle approach, as modified, retains its ability to focus attention to the use of resources other than raw materials, as well as to consider the environmental implications of the product or its constituents prior to the manufacturing stage, during packaging and shipping, and during product use.

Finally, consider the manufacture not of a final product, or a chemical product designed to be dissipated in use, but of a chemical intermediate such as ABS resin. The customer for that product views the life cycle from the perspective of Figure 1, where both the resin manufacture and those steps that produced the ABS feedstocks are in the Pre-manufacturing life stage. From the perspective of the ABS resin manufacturer, however, only the feedstock processing is Premanufacture, and the Manufacture and Product Delivery life stages must be considered twice, once for manufacture of the chemical intermediate, once for the final product (Figure 3). At first glance, the chemical company that manufactures the resin might be thought to influence only life stages 2a, 3a, and perhaps 1. In fact, the resin designer directly influences stages 2b and 5 as well, because the type and concentration of fillers, plasticizers, flame retardants, and other additives define much of the final product processing and potential recyclability. A green chemistry life-cycle approach thus involves not only in-plant actions, but also working with the final product

* On these diagrams, the double-lined box indicates the life stage within which the principal activity of the designer's corporation resides. A circled E indicates energy input, a circled C the input of process chemicals or consumables, a circled R the generation of residues. Reuse of the product or its components or materials is an option in the last life stage. The dashed lines indicate resource or residue flows that can potentially be directly influenced by the product designer. The dotted lines indicate flows that may be influenced as a result of negotiations with suppliers.

manufacturer in a joint effort to improve environmental performance.

Industrial ecology goals for green chemists

To build on the already substantial green chemistry accomplishments described in this journal and elsewhere, green chemists should place their activities within an industrial ecology context.[4] Many of the guidelines and tools developed for the evaluation of assembled products and of industrial processes can be adapted for use in green chemistry as supplements to the manufacturing-oriented guidelines that already exist.[3] In this connection, a few goals that merge green chemistry and industrial ecology are as follows:

- Adopt a life-cycle perspective regarding chemical products and processes
- Realize that the environmentally-related activities of your suppliers and your customers determine, in part, the greenness of your product
- In the case of non-dissipative products, consider recyclability as well as manufacture
- In the case of dissipative products, consider the environmental aspects of product delivery and use as well as manufacture
- Perform green process design as well as green product design

‘green chemistry is more than green synthesis’

How might directing efforts toward these goals redefine the practice of green chemistry? A first demonstration of that redefinition is that consideration of the earliest life stage will lead naturally to the use of sustainable feedstocks.[5] A second is that consideration of potential environmental impacts in product delivery and customer use will lead to such innovations as reusable containers for liquid chemicals, as well as agreements to lease, recover, purify, and reuse processing chemicals. A third is that considerations of the End of life stage will encourage product formulations that avoid non-recyclable additives or coatings.[6] A particularly commendable example of the latter is a photosensitive epoxy covercoat recently developed by IBM scientists; it is very rugged during normal service, but can readily be stripped away photochemically to enable recovery of the underlying electronic components and materials.[7]

‘entire life cycles need to be greened’

Green chemistry has accomplished much with its emphasis on decreased toxics, diminished byproduct flows, solvent substitutions, and other activities within the factory walls. It is now time to look beyond these walls and recognize that green chemistry is more than green synthesis. It is the minimization of the environmental impacts of not only an industrially utilized molecule, but also of its feedstocks and its products. As green chemists green the activities within their facilities, they should also green entire life cycles, because that is how the environmental benefits will be greatest.

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Focus on—Professor John Hay

Mike Lancaster of the Green Chemistry Network continues his series on leading Green Chemistry/Clean Technology groups, reporting on the work of John Hay and his colleagues at the University of Surrey in Guildford, UK

After completing his Ph.D. at Edinburgh University, John Hay spent his early career at the BP Amoco Research Centre in Sunbury-on-Thames working in the field of polymer science, especially advanced materials. His association with Surrey began in 1989 when he joined Kobe Steel Europe Ltd., based on the University Research Park. Professor Hay joined the academic staff full time in 1994 as Reader in Organic Chemistry and became Professor of Materials Chemistry in early 1999.

Supercritical fluids

John Hay's interest in clean technology really started in 1992 when he saw the now classic DeSimone paper in *Science* on the ‘Synthesis of Fluoropolymers in Supercritical Carbon Dioxide’. Although the 'inert' properties of fluoropolymers have enabled their use in applications such as lubricants for computer disks and sealants for aircraft fuel systems, they have posed problems for their synthesis. They are conventionally made by homogeneous free radical polymerisation but the only suitable solvents have been CFCs—the main cause of damage to the ozone layer. The use of $scCO_2$ improved the 'greenness' of the manufacturing process at a stroke.

The search was now on to clean up other polymer syntheses; use of $scCO_2$ offers the possibility of using an inexpensive, recyclable, environmentally sound alternative to organic solvents. Early on Professor Hay began to collaborate with Steve Howdle at Nottingham, combining the Nottingham group’s expertise in supercritical fluid technology with the polymer expertise at Surrey. Through an EPSRC (Engineering & Physical Sciences Research Council) grant the teams started to look at polymerisation of acrylate systems. In terms of its solvent power $scCO_2$ has many similarities to fluorocarbons—being a good solvent for siloxanes and fluoropolymers but a non-solvent for both hydrophilic and lipophilic polymers. One of the problems with polymerisation of acrylate systems in $scCO_2$ is the difficulty in building up molecular weight due to lack of solubility. The Surrey group has been concentrating on synthesis of dispersion stabilisers, in particular siloxanes, to overcome this problem. The approach has been successful, with a number of stabilisers such as poly(dimethylsiloxane)monomethacrylates proving useful at enabling reasonable molecular weight polymers to be obtained. During the course of this work valuable information on the nature of polymerisation in supercritical fluids was noted by the Nottingham collaborators. For instance wall effects were observed in stirred solutions which were inhibiting polymer growth. Although there is some industrial evidence that metal ions inhibit acrylate polymer growth this is not usually a cause for concern, but owing to the very high diffusion rates in $scCO_2$ it is thought that this factor is now coming into play. The effect is, however, minimal in unstirred reactions.

Apart from polymer synthesis John Hay sees supercritical fluids playing a key role in polymer coatings technology. The setting up of a new Centre for Supercritical Coatings Technologies (S-COAT) has recently been announced. Through his time in industry he realises how vital it is to get both industry and engineers involved at an early stage in the development of new technology. In setting up the new Centre he is working closely with Professor Mojtaba Ghadiri, an expert in particle technology in the University’s School of Engineering in the Environment.

The Centre currently has support from EPSRC (*e.g.* a recent grant worth £240,000) together with money from the Joint Research Equipment Initiative (JREI); industrial partners include Chemical and Polymer, Messer UK and Lafarge Braas. The core technology in use at the centre will be the UniCarb™ process, developed by Union Carbide and Nordson, for spray coating substrates from supercritical carbon dioxide. The process uses decompressive atomisation technology to produce droplets, the rapid decompression and evaporation of the two within the coating material producing high internal forces, which overcome surface tension and cohesive forces and produce a highly uniform spray. Professor Hay will be the Centre Manager whilst Chemical and Polymer will carry out marketing activities both for the centre and any technology developed. The Centre’s resources (50%) will be available for hire by industry whilst the remaining time will be used for

R&D programmes. Surrey will be the only university outside the US with a licence to use the UniCarb™ process.

The main focus of the early work will be around developing an understanding of how dispersion coatings are formed from supercritical fluids, techniques used to study behaviour at the spray nozzle including rheology and high-speed photography. By optimising parameters such as temperature, pressure, dispersant and solids loading, the team hopes to be able to gain a detailed knowledge of the underlying science and engineering, which should aid the development of industrially acceptable coatings from dispersion systems.

Advantages of the UniCarb™ Process Compared to Conventional Coating Processes

- **Reduced operating and capital costs**
- **Significant reduction in VOC emissions**
- **Reduced worker exposure to organic solvents**
- **Improved coating appearance and performance**
- **Lower maintenance costs**

Although not with dispersion polymers, the UniCarb™ process is having some commercial success as an environmentally friendly method of spray coating with polymers. Uses include painting of warships at a US Navy base to avoid nearby residents being exposed to solvent vapours and painting of agricultural machinery by the Italian company Salchi. Several car-manufacturing companies are also assessing the technology.

Polymer curing

Another of John Hay's Clean Technology research areas is in the field of polymer curing. He has recently been awarded an EPSRC grant with chemistry and physics colleagues to work on polymer and composite processing using electron and proton beams; partners in this research include British Aerospace, Akcros and DERA.

Electron beam processing uses high-energy electrons to initiate polymerisation and crosslinking in suitable composite matrices. Since the particle beam is operated at low temperature, the technique allows the elimination of most of the drawbacks associated with conventional thermal cure. Advantages of this technique include:

- Reduced energy use, estimates suggesting that operating costs will be at least 25% lower than with autoclave curing techniques.
- Reduced volatile production, this low temperature technique greatly reduces the formation of volatile degradation products.
- Reduced curing times enabling greater throughput.

Although details of this work are confidential at present there are high hopes that industrial uses for this technology will be realised.

Radioactive waste reduction

In association with Professor John R Jones and others at the University, John Hay is looking at ways of reducing the volume of radioactive waste produced as a result of the large number of ^{14}C and ^{3}H samples that are detected using liquid scintillation counting. The Surrey team has been working on an EPSRC / ROPA funded programme in which sol–gel technology plays an important part. The primary solute of the scintillation system can be incorporated in the sol–gel glass, thereby greatly reducing the amount of aromatic solvent, usually toluene, which is normally required. This is done without any loss in the counting efficiency.

In a separate venture, Professor Jones is looking at cleaner ways to produce tritium labelled pharmaceuticals. These are being increasingly used to study metabolic pathways but conventional methods are often not very efficient at incorporating the tritium. Professor Jones has found that by using microwave technology the efficiency of the radiolabelling synthesis step can often be significantly improved. Dr Tim Danks is also researching the use of microwaves in high efficiency, solvent-free organic synthesis.

The Green Chemistry Movement

The University of Surrey is undoubtedly at the forefront of UK universities in terms of teaching Green Chemistry. As an example, John Hay along with Drs Cunningham and Faulkner has introduced a 20-hour lecture course entitled ‘Clean Organic Chemistry’. This final year option course aims to make the student aware of the environmental challenges facing the organic chemicals industry as well as presenting approaches to cleaner and more selective syntheses. Most aspects of Green Chemistry are covered in the course including:

- Alternative solvents
- Supported catalysis
- Selective asymmetric synthesis
- Use of non-thermal energy sources

John Hay's time in industry has helped him achieve a good understanding of what industry wants from clean technology and he has had little difficulty in finding industrial partners. He does, however, believe that finding interested parties can be a difficult and time consuming task for academics and there is a definite role to play for an organisation such as the Green Chemistry Network in facilitating the process of technology transfer and introducing potential partners. Workshops on particular technology themes would be an ideal way. Hay believes that the EPSRC clean technology initiative was most valuable in encouraging academics to think about the area. This, coupled with an ever-increasing requirement for industrial partners, should enable a greater and faster uptake by industry. With all new technology a product champion is required to drive it forward, one major problem in the UK at the moment being that industry reorganisation is moving at such a pace that the 'champion' is rarely in the job long enough to be able to see the project through. As a consequence industry often loses interest in a project before completion—there is no real answer to this until industry becomes more stable.

The Unicarb ™ process uses carbon dioxide to replace organic solvents in spray coating systems.

Membrane science in the next decade

V. V. Volkov, V. V. Teplyakov, I. S. Kalashnikova, L. Valuev and N. A. Platé from the A. V. Topchiev Institute of Petrochemical Synthesis in Moscow maintain that membranes will make an increasing contribution to many areas of clean technology including the exploitation of renewable feedstocks and the analytical monitoring of wastestreams

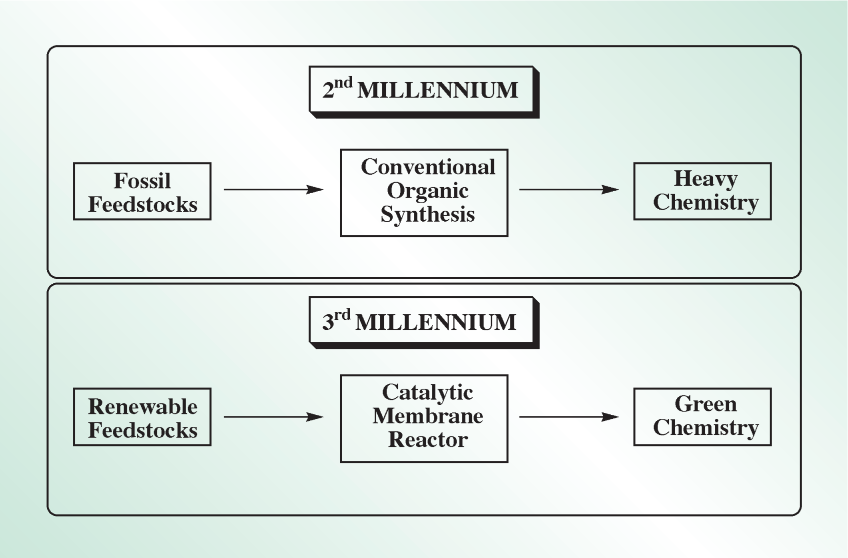
As we enter a new millennium we reflect upon the concept of membrane science and technology. This is impossible without making a critical analysis of the state-of-the-art in this field. Our speculations are evoked in part by, and agree to a large extent with, an ideology which is currently in progress, the so-called clean technology, green chemistry, or benign chemistry.

Intense scientific and technical progress has resulted in the average life expectancy rising from 47 in 1900 to 75 years in the 1990s. These almost unbelievable achievements have come at a price. The manufacture, use, and disposal of synthetic chemicals have had many negative side-effects on human health and the environment. This is primarily due to the fact that synthetic chemists are at the beginning of the process—designing synthetic pathways to produce a target product at the lowest cost with the higher yield—while the problems have traditionally been identified with the end of the process—the waste stream. Therefore, the comparatively young membrane technology was traditionally considered as a part of separation technologies aimed at solving the present-day problems.

In our opinion, such a passive position with today's membranology does not allow one to completely reveal its potential in realization of chemical and biochemical processes. This potential is evident from the determining role which membranes (especially in combination with catalysis) play in the vital activity of living organisms and plants. The membrane technology of the next generation must, first of all, do no harm. Therefore, a membranologist should switch to a new ideology and start to play an active role in designing novel synthetic methodologies that use renewable rather than depleting feedstocks (fossil fuel), maximize the incorporation of all materials used in the process into the final product, apply catalytic rather than stoichiometric reactions, prevent waste, *etc*. The active position of a membranologist in the design of chemical and biochemical processes should primarily manifest itself in such conceptual approaches as the membrane reactor, the membrane bioreactor, the catalytic membrane reactor, catalysis in membrane reactor, and membrane contactor. In these systems a chemical reaction and a membrane separation are coupled in one unit operating in a continuous mode. This provides a considerable advantage due to the shift of an equilibrium to the desired side, a decrease in the inhibiting action of the products, or creating a driving force for membrane separation.

As for the coming decade, this period should become a turning point in the passage to the new membrane ideology. From the point of view of particular technical problems, we can consider the role of membranes in the processes of more efficient processing of fossil fuels upon transition from depleting to renewable feedstocks. Recently, great attention has been paid to the development of inexpensive and effective technologies that can be used for methane conversion to easily transportable fuel. The creation of membrane reactors, in which air is used as a source of oxygen, is one of the promising directions in this field. An oxygen selective membrane, which can separate oxygen from air and supply oxygen of 100% purity into a reactor, is a key element of such reactors, which are currently under development at various research centers. The concept, which is based on a complex approach to the problems of developing inorganic materials for catalytic membrane reactors, is very attractive. At the first stage, a starting material is used to form a reactor on the whole (reactor shell, membranes, joints, *etc*.). Then, the necessary separation and catalytic functions are given to the membrane *in situ*, strongly depending on conditions of a specific oxidation process and hydrocarbon feed.

` During the process of conversion to useful organic chemicals, crude oil undergoes oxidation. This oxidation step has historically been one of the most environmentally polluting steps in all heavy organic syntheses. In general, agricultural and biological feedstocks can be used as excellent alternative feedstocks, which are highly oxygenated by nature. Furthermore, syntheses can be accomplished that are significantly less hazardous than those involving petroleum



products. Therefore, many organizations are interested in developing technologies for the production of chemicals and fuels from renewable sources, and replacing the use of non-renewable petroleum feedstocks. The ethanol and ABE (acetone–butanol–ethanol) fermentation processes are very attractive as means of chemical and fuel production from biomass. In either case, the final product must be recovered and isolated in a useful form, preferably using a low-energy process. On this basis, several integrated product removal membrane techniques have been investigated for solvent removal. Organophilic pervaporation has been considered as a promising membrane technique. In addition, the membrane bioreactor concept (continuous removal of inhibitory product) allows the fermenter to be run at low steady-state solvent concentrations and improves the productivity of the fermentation. However, the low membrane flux characteristic of common membrane materials limits the commercial potential of pervaporation technology. Thus, high membrane flux is a key performance criterion that determines the cost of a membrane system.

Poly(1-trimethylsilyl-1-propyne) (PTMSP) is a polymer exhibiting extremely high permeability for gases and vapors of organic compounds and high mechanical and film-forming properties. Application areas of PTMSP include gas and vapor separation and pervaporation. Catalytic processes of PTMSP, preparation with controlled characteristics, ensuring preparation of flat-sheet and hollow-fiber membranes with significantly improved stability, have been developed in Russia. As for the membrane bioreactor application, the high flux PTMSP organophilic membranes have been developed and the pervaporation technique has been integrated into the 0fermentation processes for solvent removal during both batch and continuous ethanol and ABE fermentations (Figure 1). Pervaporative removal of inhibitory/target product promotes cell mass growth and, as a consequence, higher sugar consumption.

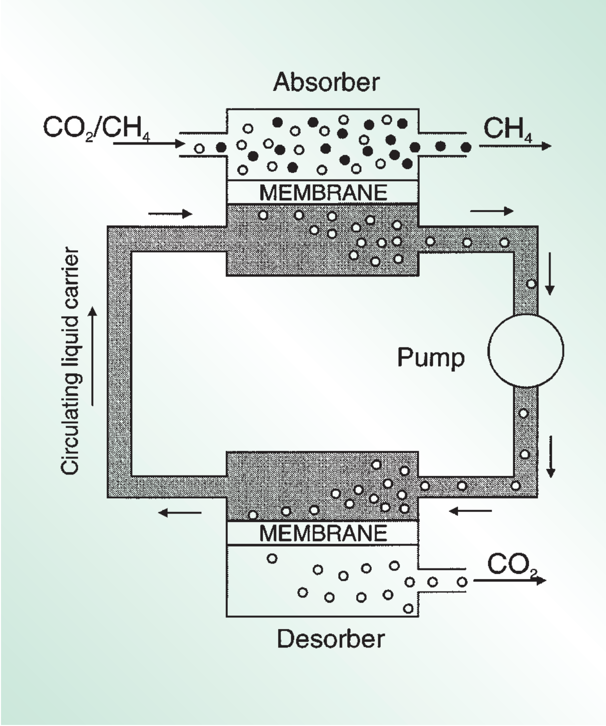
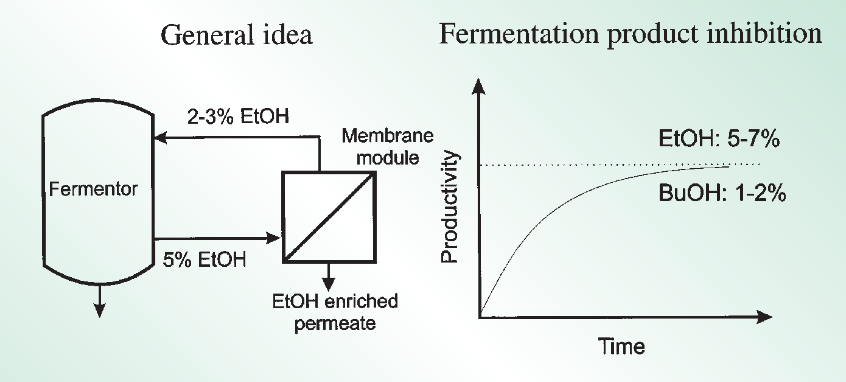


Figure 2

New effective membrane processes can be created based on membrane contractors (Figure 2). For example, membrane systems with microbiological carriers (another type of membrane bioreactor) can offer not only the selective transport of the components of gas mixtures but also their transformation into useful products. For example, it is expedient to use a closed biomembrane system for the processing of organic wastes and regulating the composition of a gas phase with extraction of valuable gas components. The systems (three blocks) includes several main components: a suspension of microorganisms and a set of nonporous polymer membranes. The first block accumulates a biomass by blue-green algae with absorption of carbon dioxide and evolution of oxygen upon the action of light. *Spirulina platensis* as a microorganism culture can be used. In the second block, the community of anaerobes, methanogens, and acetogens absorb the algae biomass from the first block and process it to soluble organic compounds, as well as to methane and carbon dioxide. The third block is intended for processing of simple organic compounds using non-sulfuric purple bacterium (*Rhodobacter capsulata*) or heterotrophic bacterium (*Terhydrogenium kirishi*) with conversion to a mixture of hydrogen and carbon dioxide. This system will produce hydrogen, oxygen, methane, and other useful gases of high-purity grade. The resulting biomass can be returned to the second part of the system and partially used as an additional feed or fertilizer.



Pervaporation properties of PTMSP organophilic membrane

Feed	Feed concentration	Separation factor	Permeate
EtOH/H_2O	6% EtOH	18	54% EtOH
BuOH/H_2O	1% BuOH	91	48% BuOH

Figure 1

At present, a considerable amount of research is being done in the field of analytical chemistry. In order to effect changes of processes during their operation, one need to have accurate and reliable sensors, monitors, and analytical techniques to assess the hazards that are present in the process stream. For this purpose, the analytical techniques that are being developed can be used both in-process and in real-time. If the sensors are coupled directly with the process control, this hazard minimization may

Portable gas-analyzer for air pollution control: detection limit, 1–10 ppm.

very well be automated. Nowdays, various types of sensors: electrochemical, semiconducting, calorimetric, biological, optical, piezosorption, *etc*. are developed and manufactured. Among them, the most simple and cheap are sensors of mass-metric type, or quartz microbalance, whose operation quality is mainly determined by a coating applied on electrodes of a piezoresonator (piezocrystal), the so-called sensitive layer. The possibility for using various polymers as sensitive membrane layers for chemical sensors–gas analysers can be proposed: Si-containing polymers with good membrane properties that can be used to determine the concentration of hazardous vapors in the range 0.05–1 g m^{-3}; transition-metal complexes with N- and O-containing polymers useful for the determination of a concentration of 1,1-dimethylhydrazine with a detection limit of 1 mg m^{-3}; modified polycarboxylic acids for the determination of NH_3 with a detection limit of 5 mg m^{-3}. There are many medical-related problems that can be solved only by employing membranes. Success of the modern membrane technology in the field of artificial organs, for example artificial kidneys, provides the most appreciable sale capacity in the world. This triggers an idea about the further development of membranes in medicine. The systems for targeted drug delivery are also promising and we are close now to solving the problem of insulin oral administration using hydrogel matrices. In creating a new peroral insulin preparation (Figure 3) we took into account all the experience gained in this field and the achievements of biospecific chromatography. In order to protect the useful hormone against proteolytic enzymes, we used a water-swelled polymeric hydrogel containing chemically bound (and, hence, not washed-out to the environment) inhibitors of these enzymes and insulin in the free state. The polymeric hydrogel was additionally modified by polysaccharide. Upon peroral administration, the hydrogel species travel in the digestive tract and pass the esophagus and stomach to reach the small intestine. During this passage, insulin is reliably protected against the action of penetrating proteolytic enzymes, because these are bound with an immobilized inhibitor. On reaching the intestine, the hydrogel species are accumulated on the walls as a result of the biospecific interaction of polysaccharides contained in the hydrogel with lectins of the mucous membrane. In what follows, the hormone diffuses from the volume of hydrogel immediately toward the blood capillaries and enters the circulatory system. Note that insulin enters, like the hormone produced by natural secretion, into the portal vein; that is, the liver directly takes part in the control of the insulin dose delivered to the circulatory system.

It might be expected that in future ‘smart’ polymers, which are sensitive to a variation in temperature, pH, electromagnetic field, *etc.*, will be involved more extensively into the membrane field. Moreover, systems controlled by neuromediators or hormones will be elaborated. No doubt, these inventions will allow us to approach living systems developed during prolonged evolution in nature.

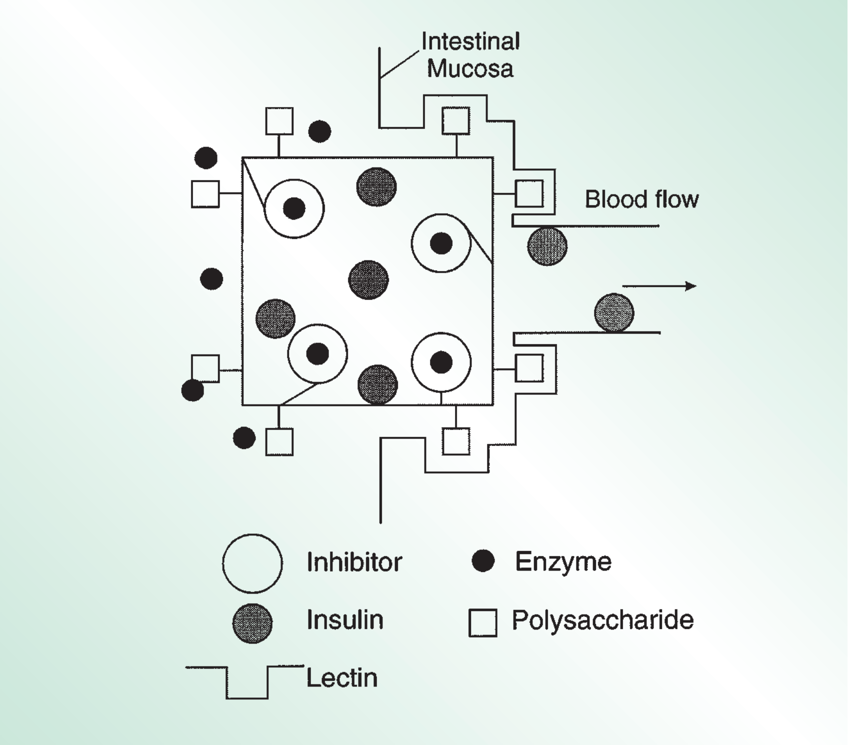


Figure 3

At the GCN launch in Sheffield, left to right: Professor Tony Ledwith (RSC President), Dr. The Hon. A. H. Todd (Master of the Salters' Company); Professor James Clark (GCN Director).

Royal Society of Chemistry launches the Green Chemistry Network

The British Association Festival of Science in Sheffield was the venue for the official launch of the Green Chemistry Network on Thursday 16th September. Over 80 guests from education, research, industry and the press, together with a few members of the general public, attended the lunchtime event. Professor Tony Ledwith, President of the Royal Society of Chemistry (RSC), gave the welcome speech during which he emphasised the need for all associated with the teaching, development and commercial exploitation of chemical technology to work together to create a more eco-friendly industry. He said the network had a key role to play in this facilitating process.

Professor James Clark, Director of the Green Chemistry Network, described the Network's activities and gave an overview of what Green Chemistry is all about, highlighting the multi-disciplinary approach (involving engineers and biologists) required to make the Green Chemistry movement a success. During lunch guests were able to discuss posters describing Green Chemistry in action provided by BP Amoco, Hickson & Welch, Johnson Matthey, ACTIN, Bio-Wise and the Clean Technology Groups at Nottingham and York.

One of the highlights of the event was the announcement by Dr. The Hon. A H Todd, Master of Salters' Company, of the establishment of the UK Green Chemistry Awards. These awards, sponsored by the RSC, Salters' Company, The Jerwood Charitable Foundation, DTI and DETR, are aimed at encouraging more research in Green Chemistry, sharing of best practice by industry and publicly acknowledging advances being made by UK industry and research base. Full details of these Awards, which will be administered by the GCN, and how to apply appear on page G136 of this issue of *Green Chemistry*.

Lord Sainsbury, UK Minister for Science, commenting on the GCN launch, said: 'The need for environmental good practice in industry is already changing the way we work. Our increasing understanding of the science of our environment will continue to drive this change. I am therefore delighted that this week the Royal Society of Chemistry will launch the Green Chemistry Network and associated journal entitled *Green Chemistry*. This UK network will promote the principles and practice of Green Chemistry. It will also provide a very welcome UK focus and the means for those involved in industry, research and teaching of chemistry to work together to ensure that chemistry based industries of the future are more eco-friendly and sustainable.'

The Green Chemistry Network aims to promote awareness and facilitate education, training and practice of Green Chemistry in industry, academia and schools. The GCN is based within the Centre for Clean Technology at the University of York Department of Chemistry under the directorship of Professor James Clark. For further information, contact: Mike Lancaster, Green Chemistry Network, Department of Chemistry, University of York, York YO10 5DD, Tel. 01904 434549.

President Clinton's Executive Order on Biobased Products and Bioenergy

On August 12, 1999, President Clinton issued Executive Order 13134, 'Developing and Promoting Biobased Products and Bioenergy'. The goal of the directive is to further the development of a comprehensive national strategy that includes research, development, and private sector incentives to stimulate the creation and early adoption of technologies needed to make biobased products and bioenergy cost-competitive in national and international markets. The targeted goal is to triple U.S. use of biobased products and bioenergy by 2010.

The focus of green chemistry is the design of chemical products and processes that reduce and/or eliminate the use and/or generation of hazardous substances. A number of contributors to the field of green chemistry have made important contributions toward the goals of the executive order. In fact, the discovery, development, and commercialization of biobased products and processes has consistently been an active area of research and development in green chemistry as evidenced by work presented at Gordon Research Conferences on Green Chemistry and the annual Green Chemistry and Engineering conferences and published in the *Green Chemistry* Journal. Several of the U.S. Environmental Protection Agency's Presidential Green Chemistry Challenge Awards have gone to individuals whose research and development efforts facilitate the use of renewable feedstocks and the synthesis or production of biobased products.

Definitions in the Executive Order

Biomass is any organic material that is produced by the process of photosynthesis. It can be found in crops and crop wastes and residues, wood and wood wastes and residues, animal wastes, municipal wastes and aquatic plants.

Bioenergy is any power, fuel and process for the development of chemical products derived from biomass.

DOE Support Bioenergy Executive Order

Following President Clinton's Executive Order on Bioenergy unveiled on 12 August, U.S. Secretary of Energy Bill Richardson announced the following day more than $13 million in financial assistance to promote the growth of the biomass industry (http://home.doe.gov/news/releases99/augpr/pr99216.htm).

According to the executive order, current technology for biobased products and bioenergy has the potential to provide affordable electricity, fuel, chemicals, pharmaceuticals, and other materials from renewable farm and forestry resources. Investing in these technologies should create new markets for farm and forest waste products and economic opportunities for underused land, creating new value-added business and employment opportunities for farmers, foresters, ranchers, and other businesses in rural America. Through the development of biobased products, there is also the potential to reduce dependence on foreign oil, improve air quality, water quality, and flood control, decrease erosion, and help minimize net production of greenhouse gases.

Findings and recommendations

The findings and recommendations of the following reports and publications are relevant to the executive order:

- **the recently released National Academy of Sciences report 'Biobased Industrial Products';**
- **'Technology Vision 2020: The U.S. Chemical Industry' by the American Chemical Society, American Institute of Chemical Engineers, Chemical Manufacturers Association, Council for Chemical Research, and the Synthetic Organic Chemical Manufacturers Association (http://membership.acs.org/I/IEC/docs/chemvision 2020.pdf)**
- **'Plant/Crop-based Renewable Resources 2020: A Vision to Enhance U.S. Economic Security Through Renewable Plant/Crop-Based Resource Use;' (a consortium of contributors from U.S. agricultural, forestry, and chemical communities, available through the Department of Energy)**
- **'Agenda 2020' by the U.S. Forest Products Industry.**

The full text of the Executive Order can be obtained from http://www.pub.whitehouse.gov/urires/I2R?urn:pdi://oma.eop.gov.us/1999/8/13/4.text.1

National Sustainable Fuels and Chemicals Act of 1999

U.S. Senate Agriculture, Nutrition and Forestry Committee Chairman Dick Lugar introduced legislation creating a novel research initiative focused on producing fuels and chemicals from a wide variety of plants, trees, grasses and agricultural residues. The bill was written to amend the National Agricultural Research, Extension, and Teaching Policy Act of 1977 to authorize research to promote the conversion of biomass into biobased industrial products. It passed the Committee on Agriculture, Nutrition, and Forestry unanimously and is now being prepared as a report to Congress. The bill is supported by 15 Senators of both parties.

This Act is known as the 'National Sustainable Fuels and Chemicals Act of 1999'. In the proposed legislation, `biomass' is defined as any organic matter that is available on a renewable or recurring basis, including plants, trees, grasses, agricultural crops and residues, wood and wood residues, municipal waste, animal waste and residues, and aquatic plants. The term 'biobased industrial product' means any power, fuel, feed, chemical product, or other consumer good derived from biomass. According to Lugar, the conversion of biomass into biobased industrial products offers outstanding potential for improved strategic national security and balance of payments, healthier rural economies, improved environmental quality, near-zero net greenhouse gas emissions, technology export, and sustainable resource supply. It is expected that biobased chemicals could provide functional replacements for essentially all organic chemicals that are currently derived from petroleum; and have clear potential for environmentally benign product life cycles.

Lugar's research initiative would be jointly administered by the Secretary of Agriculture and Secretary of Energy and gives priority in funding to consortia composed of technical experts from academia, national laboratories, Federal research agencies and industry. The purpose of the cooperation and coordination is to promote research and development related to understanding the key mechanisms underlying the recalcitrance of biomass and advancing technologies that will result in large-scale commercial production of low cost biobased industrial products. Innovative in both purpose and structure, the initiative will promote integrated research partnerships as the best means of overcoming technical challenges that span multiple academic disciplines while leveraging scarce Federal discretionary spending. The bill would authorize $48 million a year for six years.

Green Chemistry Teaching at York

The Clean Technology Centre at the University of York has recently received funding from the RSC and the University of York teaching innovation fund to develop an undergraduate Green Chemistry practical course. The aim of this is to teach the basic principles of Green Chemistry, and to emphasise the increasing importance of environmental considerations to the chemical industry. The mini-projects will be designed to follow a common structure including:

- introduction and planning
- practical
- interim workshop and literature search
- practical
- review workshop and write-up

The first stage of the mini-project will involve a workshop in which the students are taught the basic principles of Green Chemistry, including waste minimisation, atom efficiency and life cycle analysis. They will then choose from a broad selection of existing chemical reactions (including the option to suggest a reaction of their own preference), and, with assistance, plan a practical based on previously reported procedures. In stage 2, students will carry out the chemical synthesis using traditional methods but, in addition to the familiar tasks of isolating the product and measuring its yield and purity, they will be expected to record data on the waste produced (spent reagents, unrecovered solvents, by-products). Stage 3 will involve improvement of the process, using a hierarchical template for analysis of the chemical reaction. This will start with questioning whether another, less environmentally demanding, chemical might be able to perform the same function as the target function; *i.e.* is a polluting chemical actually necessary at all? Consideration will then be given to the impact of the starting materials and the conditions of the chemical transformation itself, including the solvent, temperature, catalyst and other reagents. The assessment will also cover other considerations such as the economics of the process, transport considerations, and whether any of the reagents might be from renewable sources. This will probably be the most demanding part of the project and so, as well as receiving advice from tutors, the students will be guided through the process by a series of questions and calculations. They should now be in a position to design a new set of reaction conditions, and test them experimentally (after approval by a member of staff). In this second practical the student will again record product yields, selectivities, waste quantities and consider the potential for recovery of any of the waste components. Finally, the students will compare the two processes and review the improvements that have been made, and how these might be translated to an industrial scale.

If any readers wish to know more about these projects, or have suggestions for reactions which might be suitable for study, they can contact Stewart Tavener at the Department of Chemistry, University of York, or by e-mail (sjt4@york.ac.uk)

Kenneth G Hancock Memorial Student Award in Green Chemistry

The Hancock Memorial Award provides an opportunity for undergraduate and graduate students in the United States to compete for a prestigious memorial scholarship in recognition of their studies and/or research in green chemistry. The award provides a monetary sum and national recognition for outstanding student contributions to furthering the goals of green chemistry. Applications must address one or more of the following three green chemistry focus areas:

- The use of alternative synthetic pathways for green chemistry
- The use of alternative reaction conditions for green chemistry
- The design of inherently safer or less toxic chemical products.

The application, which must take the form of a report of no longer than 6 pages, should be sent to the Office of Pollution Prevention and Toxics, US EPA, Washington DC 20460 and marked for the attention of Tracy Williamson (room 338, East Tower). Further information can be obtained by calling 202 260-2659.

This annual award is in honour of Kenneth Hancock, the late Director of the Division of Chemistry at the National Science Foundation, who was one of the architects of the 'Environmentally Benign Chemical Synthesis and Processing' approach to the manufacture of chemicals. The next deadline for the awards is February 1, with the awards being at the 2000 Presidential Green Chemistry Awards Ceremony in Spring 2000 in Washington DC.

Green Chemistry Network to administer UK Green Chemistry Awards

UK Awards for Green Chemistry have been established supported by the RSC, Salters' Company, the Jerwood Foundation, DTI and DETR. The announcement and first call for nominations was made by Dr. The Hon. Sandy Todd, Master of Salters' Company, at the Green Chemistry Network Launch meeting in Sheffield on 16th September.

The awards are designed to encourage more people to engage in Green Chemistry research, promote recent developments by industry and encourage sharing of best practice. A similar scheme run in the US (US Green Chemistry Presidential Awards) has met with considerable success and has led to greater openness by industry of progress being made. Awards will be made both for academic research and commercial development by industry of Green Chemical Technology.

Full details of the awards and how to enter are given below. Administration will be carried out by the GCN at the University of York with an expert panel appointed by the RSC and Salters' judging the nominations. The first of these annual awards will be made next year with nominations closing 31 March 2000.

There are three Awards, namely:

- An Annual Academic Prize of £10,000 to a young academic, preferably working in collaboration with industry. This Prize is known as the Jerwood Salters' Prize and is sponsored by the Salters' Company with the generous financial support of the Jerwood Foundation .
- Two Annual Awards to UK companies for technology, products or services,one company at least being a Small or Medium Enterprise (SME as defined by DTI guidelines). These awards consist of a trophy and certificate.

Selection Criteria

1. The nominated Green Chemistry technology should offer significant improvements in chemical processes, products and services through research and commercial exploitation of novel chemistry; so to achieve a more sustainable, cleaner and healthier environment as well as creating competitive advantage.

Examples include:

- Innovative chemistry to reduce environmental impact of products and processes.
- Waste reduction at source during manufacture or processing of chemical roducts.
- Reduction in the toxicity, flammability or explosion potential of substances entering the environment.
- Improving the use of natural resources such as renewable feedstocks.
- Improving the efficiency of energy or other utility utilisation during manufacture or processing of chemicals.

2. The technology must have reached a significant milestone during the last 5 years, within the UK (for example, for Industry Awards the technology should be in development or commercial use, for the Academic Prize the key technology steps should have been researched and demonstrated or patents applied for).

3. The technology should be generally applicable to a broad-based segment of chemical manufacturers, users or society and key features of the technology should be readily transferable.

4. The technology should be original and of high scientific merit.

5. For the Academic Prize the nominee should normally be a UK resident under 35 years of age and have developed the technology in co-operation with a company with operations in the UK.

6. For the Industry Awards, the company should have significant manufacturing and/or research facilities in the UK.

How To Enter

Self-nominations are allowed and encouraged. There is no standard entry form or entrance fee. Entrants must submit a report (maximum 8 sides).

The report should include the following:

1 A front page containing the project title, the person (to whom all correspondence will be addressed), the organisation's address (if applicable) and other contributors (organisations or individuals who have contributed financial or technical support towards the project).

2 A second page containing:

- **Statement indicating whether the nomination is for the academic or industrial awards. If the nomination is for the industrial awards a statement indicating whether the organisation is eligible for inclusion in the SME award category**
- **Project title**
- **Statement confirming that the nominated Green Chemistry technology has been demonstrated, implemented or researched during the last 5 years, within the UK as appropriate**
- **An abstract of not more than 400 words briefly describing the nominated project, highlighting the Green Chemistry concepts and environmental benefits involved**

The remaining 6 pages may be used to describe the Green Chemistry technology involved together with how the nomination meets the selection criteria. Please note that all entries received will be considered public information. Nominees are encouraged to be as open as possible when describing the chemical technology and environmental benefits. It is important to give enough information to enable the selection panel to make an informed judgement both on the scientific merit of the technology, the more general applicability of the technology and of the potential environmental benefits involved.

Three copies of all entries must be submitted to:-
Mike Lancaster
Manager—
RSC Green Chemistry Network
Department of Chemistry
University of York
Heslington
York YO10 5DD

To be received no later than 31st March 2000.

All qualifying entries will be judged by an expert panel, appointed by the RSC and Salters' Company, with winners being informed by the end of September 2000. All winners will be expected to give a presentation of their work at an appropriate RSC conference and to submit a paper to *Green Chemistry*.

Green Chemistry—evolution or revolution?

Stuart Cook of Hickson and Welch describes how an elderly multistage production process has been made more green by an innovative evolutionary strategy applied to existing technology

The manufacture of optical brighteners used in today's washing powders, is a good example of green chemistry evolution.

There is a perception of a need for revolutionary change in technology to introduce commercial 'green' chemistry. Industrial experience is, however, that whilst a revolution is sometimes necessary to find 'green' as opposed to 'end of pipe' solutions, often there is much that can be achieved by an innovative evolutionary strategy applied to existing technology.

A good illustration of this mixed approach is illustrated by a review of the last decade of progress in the manufacture of stilbene-based fluorescent brightening agents. These are produced on a *ca.* 100,000 tpa scale world-wide, with Ciba-Geigy (EU and USA), Sigma (Italy) and Hickson & Welch Ltd. (UK) as some of the major producers. Waste and emission problems figured in many of the processing stages since production began in the 1950s. As one of the few fully integrated producers, working until recently from basic toluene to finished fluorescent brightener, over a 7-stage sequence (see scheme opposite), Hickson & Welch's processing perspective contains some interesting lessons, showing evolution to be as important and effective as revolution in side-stepping 'green' challenges at minimum additional cost. Such additional costs can, of course, be either from additive 'end-of-pipe' processing equipment and costs, or from major reinvestment in entirely new 'green' technology.

Each step shown in the scheme is described below in numbered sequence, and the 'green' revolutionary and evolutionary options described.

Step 1

Toluene is conventionally mononitrated with mixed sulfuric/nitric acids, adjusted to 80% sulfuric acid strength with water. The spent mixed acid was separated and discharged to waste, and the mixed mononitrotoluene isomers washed with sodium hydroxide solution to remove *ca.* 0.5% phenolic and oxidation products. The alkaline washings are discharged to waste. The washed mononitrotoluenes are fractionally vacuum-distilled at high temperature to isolate pure *p*-nitrotoluene. Unwanted by-products from the still base are incinerated.

Problems

- There is heavy output of 'spent' contaminated 70% sulfuric acid wastes to low grade acid users such as the coking and steel industries.
- The high output of dilute nitrophenol sodium salt washings is toxic to biotreatment systems.
- There is high energy consumption in sulfuric acid production and high-temperature vacuum distillation.

The 'Green' chemistry solution

The vision over many years has been the direct nitration of toluene with nitric acid using catalysts such as modified clays, which are known to be capable of producing high proportions of the higher value *p*-nitrotoluene isomer (conventional mixed acid gives 65% of the saleable but lower value *o*-nitrotoluene isomer).

The problem is that the water of reaction released from direct nitric acid nitration tends to degrade the catalyst.

Hickson piloted such technology using reduced pressure distillation to strip reaction water from the heterogeneous catalyst continuously.

Rapid evolutionary progress on the conventional technology made the planned reinvestment and switch uneconomic, however.

The evolutionary approach

The disappearance of the demand for 'used' sulfuric acid in the coke and steel industries threatened to undermine process economies. Installation of an acid recovery unit enabled a closed cycle to be established, the sulfuric acid becoming effectively a reusable catalyst. As the reaction starts at 80% H_2SO_4 and discharges at 70% H_2SO_4, only a proportion of the acid needs be recovered to 99% strength, and mixed with 99% nitric acid and 70% spent acid to achieve the necessary 80% starting strength. This 'spent acid' recycle improves recovery economics.

The need for thorough wastewater biotreatment threatened to demand reacidification and solvent backwashing of all alkaline wash liquors, to remove nitrophenols for separate incineration. For manufacturers pursuing this route it can cost almost as much in capital and operations to acidify and backwash the waste as making the mixed mononitrotoluene itself (and the extracts still need incineration). Hickson demonstrated and ran for 10 years a process which entirely omitted the alkaline wash and consequent activity. This omission gives wash waters so low in nitrophenols as to be readily biodegradable. The mononitrotoluene preferentially holds phenols unless alkali is added, and the phenols then exit in the still-base oils. Less saleable mononitrotoluenes in fact need to be left in still-base oils for burning, an added economic advantage.

The strong 'folklore' that the phenols cause instability in stills was shown by detailed investigations to be totally unfounded.

One of the major hazards in nitrotoluene manufacture is, in fact, the entry of sodium phenolates into the high temperature (*ca.* 190 °C) nitrotoluene stills because of poor washing. Explosions have been thus caused. The new system eliminated this hazard. The phenols, as opposed to their sodium salts, are stable.

The effect of these changes eliminated the prospect of waste acids and nitrophenol wastes undermining the process economics and improved rather than added to process costs overall. Evolution rather than revolution both eliminated environmental threats and improved process waste/energy/yield economies.

Step 2

p-Nitrotoluene is sulfonated by adding 25% oleum to the liquid mononitrotoluene, then adding the mixture to water to give the optimum 50% sulfuric acid strength for filtration of the solid sulfonated product which precipitates. The wet cake is redissolved in water for subsequent use.

Problems

Large volumes of waste acid filtrate are generated.

The reaction mixture is thermally unstable and this limits reaction rates and temperatures when large batch processing inventories are involved. Large volumes of relatively dilute oleum are necessary to provide both heat-sink and sufficient drowned out 50% acid to give a stirrable product slurry for filtration. Higher strength oleum gives not only over-viscous slurries upon precipitation, but also undesirable highly coloured by-products unless excellent mixing is achieved during sulfonation.

The 'Green' chemistry solution

p-Nitrotoluene can be sulfonated with gaseous SO_3 rather than oleum, eliminating all waste acid generation. This is achieved by conducting the reaction in a suitable refluxing solvent, then simply extracting the product from the recycle solvent with water to give a solution suitable for the next step. The technology is proven on significant scale.

The evolutionary approach

Rather than entirely reinvesting in the gaseous SO_3 technology, it was in fact found possible to all but eliminate waste acid problems and simultaneously reduce process costs.

If a continuous low inventory tube reactor is adapted, much higher strength oleums can give pure product safely. The problem of producing a mobile final slurry is avoided at these higher strengths by recycling spent acid to dilute the slurries for filtration.

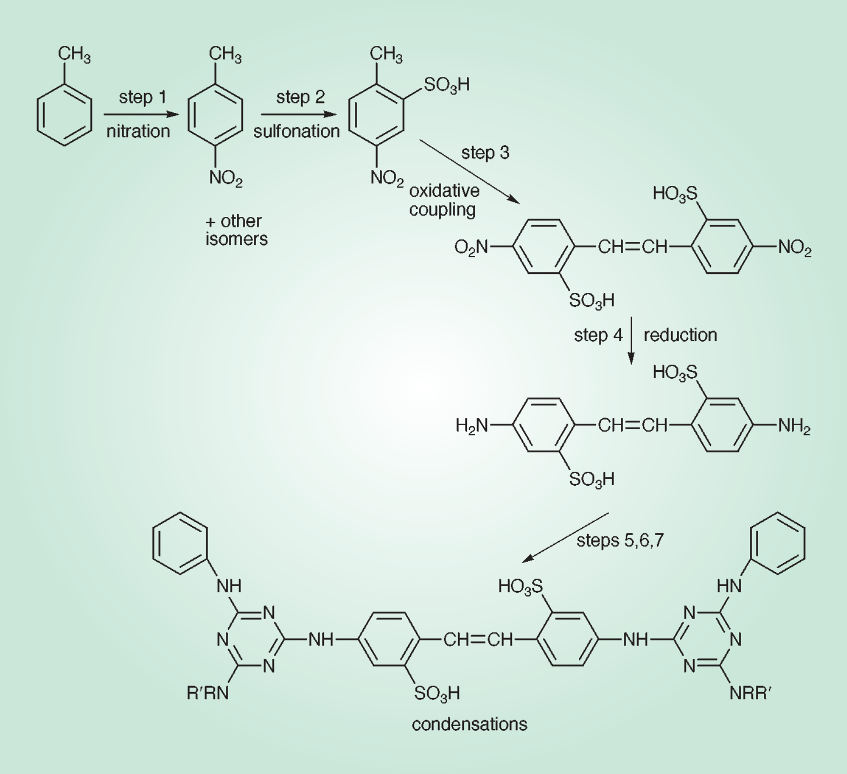
In addition, although 50% acid traditionally gives optimum product recovery, at 70% the shape of the solubility curve and reduced volumes mean that only *ca.* 1% yield is unprecipitated. This is insignificant compared with savings in energy, filtration times, output and intensity gains, so 70% not 50% acid can be adopted economically once the real cost of waste acid is in the equation.

The 'traditional' process can thus be transformed to give a small acid recycle/recovery problem, and improved economics, by evolution.

Step 3

A *ca.* 4% *p*-nitrotoluene sulfonic acid solution is heated slowly to 70 °C in the presence of *ca.* 4% caustic soda solution and manganese catalysts with vigorous aeration.

Over *ca.* 20 hours there is an 80% conversion to 2,2′-dinitrostilbene 2,2′-disulfonic acid (DNS), and the solution can be neutralised, cooled and the 80% yield of 'DNS' filtered from the cold aqueous salt solution.



Problems

A low intensity and slow process.

Very vigorous continuous aeration with excellent agitation is essential to prevent highly coloured polymeric by-products. High-energy usage is incurred for mixing and aeration and holding high temperatures during aeration (which causes evaporative cooling).

The major historic issue is that filtrates are high in salt and rich in the 20% of raw materials converted to non-biodegradable and often highly coloured benzoic acids, aldehydes and azo linked polymers. Disposal is a colour and COD (chemical oxygen demand) issue even where salts are tolerated.

The 'Green' chemistry solution

The best solution would be to raise the yield, the reaction rate and avoid air and water!

Some manufacturers adopt sodium hypochlorite oxidation. This is faster, gives identical optimum yields and uses less direct energy, but only avoids the liquor and waste organics problem if yield is sacrificed and even higher salts levels are acceptable in wastes. Potential organochlorine generation is difficult to disprove, although Hickson & Welch production demonstrated no evidence of detectable organochlorines from the use of sodium hypochlorite bleach.

The extra cost of hypochlorite *versus* air is nicely negated by the much faster and more intense process achievable.

Some commercial production at enhanced yields is claimed with pure gaseous oxygen in liquid ammonia or alkylamine solvents. The technology has not been widely adopted. Flammability must be one restricting concern.

Most western producers resorted to expensive and energy intensive wet air oxidation to treat the aqueous wastes at end-of-pipe.

The evolutionary approach

Extensive reoptimisation of process conditions using pure oxygen not air and controlling oxidation potentials in appropriate narrow band widths with optimised manganese catalysts enable reactor dilution, energy consumption and waste output to be reduced by *ca.* 50%, and reaction times to be substantially cut.

The remaining but reduced salty waste load can be biotreated 'as is' with specially selected bacteria for river discharge, but the optimum is a relatively low pressure/temperature oxygenation with catalysed acid, and then more full and rapid biotreatment with conventional biomass.

The evolved effect is a major capital, energy and waste treatment saving, and a process which is not only more green but more economic.

Step 4

'DNS' sodium salt is redissolved in water and fed slowly into a refluxing bed of iron borings and water. The resulting diamine solution is blown from the iron borings bed, filtered to remove iron oxide sludge, and acidified to precipitate the diamine, which is filtered off for use. The iron sludge filter cakes are disposed of to the steel and coke industry.

The 'Green' chemistry solution

Hydrogenation instead of iron reduction is cleaner and generates neither the need for iron borings nor disposal routes for contaminated iron oxide sludges.

The evolutionary approach

Although great strides were made to improve ultimate quality by iron reduction, without resorting to expensive custom made iron powders instead of scrap metals, the revolution of hydrogenation is irresistible.

Platinum type catalysts are essential, and the fact that the diamine product reacts with the dinitro starting material to produce highly coloured and damaging azoxys and aldehydes poses significant challenges.

Both Hickson and others have developed successful hydrogenation technologies, with major economies and sufficiently clean reactions to use the hydrogenated solutions directly without acidification/filtration.

Steps 5, 6 and 7

Diaminostilbene sulfonic acid (DAS) sodium salt solution is traditionally fed slowly into a chilled solution of cyanuric chloride in acetone or methyl ethyl ketone. A base is added as the reaction proceeds to hold an appropriate pH value. Sufficient excess cyanuric chloride is used to compensate for the inevitable water hydrolysis during the slow diamine addition. Over-rapid amine addition leads to polymers with poor mixing, and accelerated hydrolysis with rising temperatures. The former is the prime risk if crushed ice is used to fix temperatures at 0 °C, the latter if external cooling is used to maximise agitation and mixing.

The resulting slurry is then treated sequentially with a further amine and alkali at 50–60 °C, then a third amine whilst distilling out the solvent and precipitating the product and raising the temperature to 90–100 °C. Optimum conditions give 98% yield on DAS, of 99% pure brightener!

Problems

- Large volumes of flammable solvents require distillation, drying and recycle.
- Neutralisation by strong bases of the hydrochloric acid released as the cyanuric chloride reacts is difficult to control for optimum quality. Self-buffering bases such as bicarbonate are convenient but give CO_2 evolution and consequent VOC containment issues.
- Up to 10% excess cyanuric chloride can be necessary to balance consumption in hydrolysis side reactions. If allowed to react, the part hydrolysed cyanuric chlorides give undesirable 'off' colours to the fluorescent products whitening effects.

The 'Green' chemistry solution

Reacting entirely in water is an obvious dream, by simply not having solvent containment or flammability issues to address. Cyanuric chloride is, however, insoluble in water and reacts with water if it does dissolve without being able to react immediately with diamine.

The diamine component reacts further with the desired product if ever allowed to be in excess itself, and the desired product precipitates in pure water, tending to occlude other components. We surely cannot obtain 98% yield at 99% purity in just water with these constraints?

The evolutionary approach

Different fluorescent brighteners were found to pose different challenges. Those for paper and textile industries tend to be water soluble, and often sold in fact as water based solutions. By careful temperature regulation and addition of diamine to cyanuric chloride slurried in water, it is in fact possible to react the slowly dissolving cyanuric chloride before it hydrolyses in solution, but without accumulating unreacted diamine which would quickly 'polymerise' with the product.

For over 10 years the water-soluble textile and paper brighteners have been made 'aqueous' by several manufacturers. Their solubility helps in terms of occlusion of raw materials inside precipitating products. It is even possible to sell the entire unisolated reaction mixture as product, sometimes removing salts by membrane technology to eliminate precipitation risks in stored solutions.

Detergent destined brighteners do, however, pose greater challenges, as they are water insoluble and have high purity and impurity constraints. Low molecular weight cyanuric chloride by-products ('melamines') can, for example, generate serious odour problems in washing powders and cannot be tolerated at more than 0.1% w/w levels. The particle size and crystal form of the precipitated brightener is also crucial to achieve good wash behaviour in detergents over a wide washing machine temperature range, and to produce a good appearance to the formulated washing powder. The absence of 'solvent' introduces new challenges in achieving desirable particle size behaviour.

In 1998 Hickson & Welch overcame these problems and successfully introduced entirely new production technology which avoided major investments in essential solvent containment improvements, and eliminated all the fire risks inevitable with high volume solvent distillation recycle. Despite substantial progressive yield and raw material gains over recent years in solvent technology, the understandings necessary to make the entirely new water based process work also enabled even higher yields to be obtained by, for example, cutting cyanuric chloride consumption by 3–5%.

Overall summary

Although a revolutionary technology change was necessary in some processing stages to avoid end-of-pipe cost additions, in several other stages the evolutionary approach proved as effective, even where alternative 'green' technology was available in principle.

The feared and anticipated additional 'green' costs were largely side-stepped by Hickson & Welch and the economic savings achieved did, in fact, free more resources for investment in 'green' infrastructures, such as a more efficient combined heat and power gas turbine system and a more modern and thorough biotreatment plant.

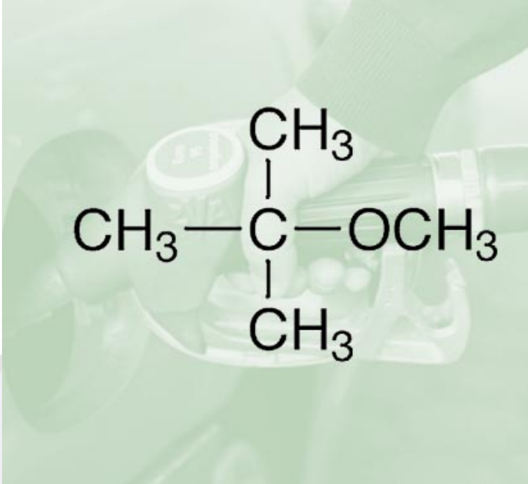
An open mind to innovative R&D work is the secret, and the avoidance of long-term company researchers constraining new workers with an 'it cannot be done, we tried it years ago' attitude.

Which of your processes have been worked on for years and years—and have no further development potential left in them for chemists and engineers? We were surprised what our Production and R&D teams gradually did to 'green' elderly processes in elegant ways.

Hickson & Welch can Trace back its roots on the present Yorkshire site to 1915, and for 40 years it has been basic in the manufacture of nitrotoluenes and products based upon them. Nowadays the company employs 500 people and is increasingly specialising in the process development and manufacture of complex life science products under contract to major multinationals. The company's successful work in reducing waste emissions has recently led to a Cremer and Warner prize, the National Crystal Award from the Green Organisation and commendation from the Yorkshire Wildlife Trust.

The author graduated in chemistry from Leeds University in 1967. During a 32 year career in fine chemical process development and manufacturing he has for 10 years the R&D director of Hickson & Welch. He can be contacted on +44 (0)1977 712231 or stuart.cook@hickson.co.uk/

MTBE–friend or foe?



$$CH_3-\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}}-OCH_3$$

A panel of experts has called on the US Government and the Environmental Protection Agency (EPA) to 'substantially reduce' the use of methyl tertiary-butyl ether (MTBE) as a fuel additive in gasoline. Becky Allen reports

The Blue Ribbon Panel and its recommendations

The Blue Ribbon Panel on Oxygenates in Gasoline was set up by the EPA in November 1998. The 13-member panel—including representatives from the petrochemical industry as well as health experts and academics—met six times before producing its report in July 1999.[1] Although it found that reformulated gasoline provides 'considerable' air quality improvements, the panel said that 'MTBE in drinking water supplies can and should be substantially reduced,' and highlighted MTBE's persistence and mobility in water. The panel stressed that its recommendations should be implemented rapidly and as a single package, but stressed that: 'MTBE is currently an integral component of the US gasoline supply. As such, changes in its use must be implemented with sufficient time, certainty and flexibility to maintain stability of US fuel supply and gasoline prices.'

> 'MTBE in drinking water supplies can and should be substantially reduced'

Among the panel's recommendations are a raft of measures to prevent leaks from underground storage tanks (USTs), thought to be the major cause of ground water contamination by MTBE. The panel also recommended further research on the field performance of USTs, and the introduction of requirements to improve leak detection, monitoring and siting of tanks. The panel said that more research is also needed on modelling the behaviour of gasoline and oxygenates in groundwater, and on levels of MTBE, ethanol, benzene and other gasoline compounds in drinking water supplies. According to the EPA, MTBE has been detected in 5–10% of drinking water supplies in areas of high oxygenate, although the vast majority are below 20 parts per billion.

The panel's report drew on a $500,000 study of MTBE by the University of California (UC) in 1998.[2] The UC report recommended a gradual

Blue ribbon panel on oxygenates in gasoline recommendations[1]

- **improvements to US water protection programmes, including over 20 specific recommendations to reduce leaks from underground storage tanks'**
- **'substantial' reductions in MTBE and other fuel additives**
- **changes to the US Clean Air Act to remove the current requirement for fuels to contain 2% by weight of oxygen**
- **EPA to seek mechanisms to ensure no loss of current air quality benefits**

What is MTBE?

MTBE was introduced in 1979 as a fuel additive to increase octane rating, but is now used in much higher concentrations as a fuel oxygenate to improve air quality. In the USA, oxygenated fuels are used in federal reformulated gasoline in certain areas, and in the EPA's winter oxygenated fuels programme. Over 85% of reformulated gasoline contains MTBE, while 8% contains ethanol. There has been growing concern about its use following detection of MTBE in water supplies in California, Maine and other states. MTBE readily dissolves in water, can move rapidly through soils and aquifers, is resistant to microbial decomposition and is difficult to remove in water treatment. The EPA has not established drinking water standards for MTBE, but issued a Drinking water advisory in December 1997 of 20–40 micrograms per litre (μg/L), primarily for taste and odour considerations.

Source: US Geological Survey, water.wr.usgs.gov/mtbe/

phase-out of MTBE in California, which has tougher air quality standards than the rest of the USA. According the UC report: 'Technical advances in new automobile emission controls and combustion systems, and in new gasoline formulations, have dramatically decreased the air quality benefits associated with adding oxygenates to gasoline, making the potential for water contamination by MTBE a cost that is not offset by a corresponding benefit.'

Dissenting voices

A majority of the panel agreed that improvements in leak prevention, treatment and remediation would not adequately protect drinking water supplies from MTBE contamination, and so recommended that MTBE use be reduced. Two members of the panel, however—Todd Sneller of the Nebraska Ethanol Board and Debbie Starnes of Lyondell Chemical—disagreed with the recommendation to limit use of MTBE. According to Starnes, the recommendations would cost $1–3 billion a year to implement. 'The panel did not identify any increased public health risk associated with MTBE use in gasoline. No quantifiable evidence was provided to show the environmental risk to drinking water from leaking underground storage tanks (LUST) will not be reduced to manageable levels once the 1998 LUST regulations are fully implemented and enforced . . . Unfortunately, there appears to be an emotional rush to judgement to limit the use of MTBE,' she said.

> 'the panel recommendations do not accurately reflect the benefits provided by the use of oxygenates in reformulated gasoline'
> (Sneller)

Sneller's objections centred around the panel's assessment of the air quality benefits of oxygenates. 'The panel's report concludes that oxygenates fail to provide overwhelming air quality benefits associated with their required use in gasoline. The panel recommendations, in my opinion, do not accurately reflect the benefits provided by the use of oxygenates in reformulated gasoline,' Sneller said. The panel found that reformulated gasoline substantially reduced vehicle emissions of volatile organic compounds, carbon monoxide, benzene and 1,3-butadiene. However, an earlier report from the White House Office of Science and Technology Policy found that MTBE use can result in increased emissions of formaldehyde and nitrogen dioxide, and attributes falling carbon monoxide levels in US cities over the past 20 years to better vehicle emission control technology and tougher standards.[3]

Mixed reception for the report

Some organisations like the Clean Fuels Group, the renewable Fuels Association and the American Water Works Association have welcomed the report, while others, like the Oxygenated Fuels Association and the National Petrochemical and Refiners Association, have expressed reservations and concerns over its recommendations.

> 'there is a complex decision-making process involved in substituting one chemical for another'

Conclusion

The Blue Ribbon Panel's conclusion highlights the complex decision-making process involved in substituting one chemical for another, if gains to one part of the ecosystem are not be made at the expense of another. 'The introduction of reformulated gasoline has had substantial air quality benefits, but at the same time raised significant issues about the questions that should be asked before widespread introduction of a new, broadly-used product. The unanticipated effects of reformulated gasoline on ground water highlight the importance of exploring the potential for adverse effects in all media and on human and ecosystem health, before widespread introduction of any new, broadly-used, product,' the panel says.

Members of the Blue Ribbon Panel

Dan Greenbaum,
Health Effects Institute (Chair)
Mark Buehler,
Metropolitan Water District,
South California
Robert Campbell,
Sun Oil
Patrick Ellis,
Delaware Department of Natural Resources and Environmental Conservation
Linda Greer,
Natural Resources Defense Council
Jason Grumet,
NESCAUM
Anne Happel,
Lawrence Livermore National Laboratory
Carol Henry,
American Petroleum Institute
Michael Kenny,
California Air Resources Board
Robert Sawyer,
University of California, Berkeley
Todd Sneller,
Nebraska Ethanol Board
Debbie Starnes,
Lyondell Chemical
Ron White,
American Lung Association

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Inherently Safer Design—a course for science and engineering students*

J. P. Gupta (email jpg@iitk.ac.in) from the Indian Institute of Technology in Kanpur in India outlines the value of a one-semester training course in applying the principles of inherently safer design to chemical process safety

Introduction

Until the Bhopal Gas Tragedy in 1984, there were few courses and few researchers in chemical process safety around the world. That tragedy shook everyone out of complacency: the public, media, legislators, judiciary, academics, NGOs (non-governmental organisations) and the process industry. Now there are more courses, more researchers, more research journals, more conferences and more legislation on process safety and loss prevention. The result, to quote Trevor Kletz,[1] is that 'the loss prevention movement has prevented many hundreds of deaths'. Considering that for each fatality, there are 2–3 serious or permanent injuries, many more minor injuries, together with trauma and economic loss, the value of loss prevention can be appreciated.

With interest in the field of loss prevention aroused, should chemical process industry (CPI) be content with minor improvements? No! Although most of the public accept that chemicals are essential to their way of life, they are at the same time looking to the CPI to get its safety act together—*fast*. Fortunately for the CPI, Trevor Kletz propounded the concept of Inherently Safer Design (ISD) over 2 decades ago—a concept which has been accepted very gradually by the CPI and other stakeholders. There have been several research papers, books and conferences on the topic.[2–7]

ISD has been defined as 'Any improvement in a layer of protection which is permanent and inseparable and not easily weakened or removed from the system'.[5] It has been divided into the following five categories:

- Intensification or minimization of the amount of hazardous material present at any given time, be it in a reactor, pipeline, transport vehicle or storage tank. For example, use of continuous tubular reactors instead of a large batch reactor.
- Substitution of a hazardous material by a less-hazardous or non-hazardous one. Replacement of flammable organic solvents by water is an example.
- Attenuation or toning down of the operating conditions of pressure, temperature, concentration, *etc*. For example, over several decades, the pressure in ammonia synthesis has come down from several hundred bar to about one hundred bar.
- Limitation of the effects of any hazard materializing by bunds, fence wall, judicious layout, siting away from habitation, *etc*.
- Simplification of the plant. Simpler plants are easier to design, fabricate, erect, operate, control and maintain.

Such inherent safety aspects do not require periodic testing, maintenance or replacement, as is the case with the

Currently Professor of Chemical Engineering at the Indian Institute of Technology (IIT) Kanpur, India, Dr. Gupta worked as a research engineer with UOP Des Plaines, USA (1967–68) in petroleum refining operations and taught at the University of Pennsylvania, Philadelphia, USA (1971–72) before joining IIT Kanpur in 1972. He has been a consultant to companies in India and USA. His teachings and research have been in the areas of transport phenomena, unit operations, design of process equipment, chemical plant safety, hazard analysis and disaster management. He teaches courses on these topics to students as well as to practising engineers from Industry and has helped start such courses in India and abroad.

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* Adapted with permission from a talk on 'Teaching Inherently Safer Design to meet the Safety Needs of CPI in the Next Millennium', Keynote lecture delivered at the National Safety Council Seminar on 'Safety and Health-Challenges in the next Millennium', Taj Mahal Hotel, Lucknow, India, July 16, 1999.

add-on or engineered safety items. There will, however, be a continued need for engineered (or add-on) safety, since some activities are better done that way, and some activities will not be made as safe as is reasonably possible by ISD alone. The proportion of (and hence the cost and probability of failure of) add-on safety will nevertheless reduce as more people start to practise ISD.

Basically, ISD requires questioning in an unbiased and thorough manner all the steps from choosing a product, process to produce it, design and layout of equipment and control systems, operating conditions, transporting product to the market and its use by consumers. Inventories at each step must also be carefully considered since so much money is tied up in them, and they can cause significant damage and casualties due to fire, explosion and toxic release. The cases of Bhopal and Mexico City are still fresh in the memory.

The present author firmly believes that if ISD principles are followed along with process miniaturization as forcibly argued by Benson and Ponton[9] the CPI in 2020 will look a lot different and friendlier. Equipment sizes will be smaller due to higher efficiency and distributed production at the customer site. Operating conditions will be less severe due to the development of better catalysts and friendlier process routes, and inventories will be significantly smaller following the ‘just-in-time’ principle, to the extent the infrastructure can support it. All of this will reduce the capital cost and costs related to operation (less energy, personnel requirements), inventory size, maintenance, process upgrading, transport of raw material and products, environment protection and decommissioning of the plant at the end of its useful life.

The key to achieving all the above is spreading the word about ISD, practising it vigorously—one may even say ruthlessly—and publicizing the gains obtained (keeping in mind the inventor company’s desire to maintain confidentiality to recover its expenditure and more). For any idea to spread, it has to be taught at the earliest, appropriate stage. In the case of ISD, the appropriate time is the first-degree course in science and engineering. I describe a one-semester course on ISD. For engineers and scientists to apply ISD principles, support from the organisation bosses is essential,[10] because ISD challenges the *status quo* in design and operation, and management need to be persuaded to consider doing things differently.

The concepts of ISD, as stated by Kletz and further elaborated by others, are so simple and common sense that they can be understood by anyone with a basic scientific knowledge. Hence our course will benefit those in the construction, automobile, metallurgical, aviation industries, *etc.*, until more focussed courses are developed in these areas.[8]

The ISD Course

The one-semester course consists of 3 lecture-hours per week for 12–14 weeks; the lectures can consist of three 1-hour lectures per week, or, as the present author prefers, two 1½-hour lectures per week.

The ‘highly recommended book’ for the course is that by Trevor Kletz.[2] Since there are no other ISD courses (this being the first course as far as is known) and the book was not really written as a standard textbook, it needs to be supplemented by other publications.[3–7]

Students need to be encouraged to study the various topics in advance of the lecture, since ISD attempts to change fundamental attitudes towards safety and current ideas on how process plants should be designed and run. Hence, reading in advance will better prepare students to understand the lectures and hopefully modify their thinking. Therefore, the instructor needs to give advance reading assignments on at least a weekly basis.

The students should already know the techniques of hazard identification, risk analysis, calculation of consequences, *etc.* †—topics covered in a normal Loss Prevention or Chemical Process Safety courses[11–14]. This will help them in determining the situation both before and after the ISD principles are applied.

For each topic mentioned below, it is necessary for the lecturer to give examples utilizing the related ISD methodology; such examples are quoted in the literature cited at the end of this article.

Topics covered in the ISD Course

Hazards in CPI

Knowing these is the first step to think of ways to avoid, minimize or contain them.

Selected major accidents

Discussion on these brings out the potential major plants have to cause disaster. It is preferable that students examine the case studies given by Lees[11] and present them in class. The instructor may supplement these with photographs and videos, as available. It is vital to point out how these accidents could have been avoided or effects minimized by using ISD principles. For example, at Bhopal there was no need to:

- use the process route that produced MIC (methyl isocyanate) as an intermediate
- store so much MIC when, even with the existing process, a different reactor design would have cut the inventory of MIC to a few kilograms in the reactor with no intermediate storage of many tonnes required[2]

Review of ISD methodologies

This should give an overview of ISD techniques and at what stage in the evolution of a plant these should be applied—actually, the earlier the better, starting at the lab process development stage, but these can be applied with advantage at just about any stage and even on the installed and operating plants. It has been well said about ISD techniques: ‘Start early and never stop’.[5]

Attention should then be turned to specific ISD methods with available examples provided in each case. The hazard potential of pre- and post-ISD application should be analyzed in each case to justify the application and cost of ISD.

Intensification or minimization of hazardous substances

This should be done at every stage possible: in storage or warehouse; in process equipment such as reactors, distillation towers, heat exchangers, mixers, *etc.* and in transportation. Reduced amounts of hazardous substances reduce the possible consequences of any hazard such as fire, explosion, or toxic release.

Substitution of a more hazardous material by a less- or non-hazardous one

The consequences of any hazard materializing would be proportionately less. This requires serious thought at the process development stage as it becomes very expensive to substitute a hazardous substance by a less hazardous one at a later stage, when add-on safety features are the only way left. According to Trevor Kletz, the life-long cost of an add-on feature is twice its capital cost

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† If the students do not know these techniques, they need to be taught in 8–10 one-hour lectures before starting on ISD.

due to the need for testing, repairing and maintenance all through its life.

Attenuation or moderation of operating conditions

The pressure, temperature, concentration, *etc.* should be reduced as much as possible at every stage to reduce the consequences of any failures. At times, attenuation may run counter to intensification since reduced temperature or concentration lowers the reaction rate resulting in larger inventory in the reactor. Such situations should also be pointed out, so that ISD is used sensibly, not blindly as a panacea.

Limitation of the effects of failures

Siting plants away from habitation should be considered, as well as plant design and plant layout to minimise the effects of failures both on-site and off-site. Control of habitation or maintenance of a 'green corridor' around hazardous plants can limit the off-site effects.

Simplification of plants

Simpler plants are obviously easier to operate and so one should not attempt to do too many different operations in the same equipment—it involves too much piping, valves, bypass lines, *etc*. Wrong setting of valves, less than thorough cleaning after earlier usage, *etc.*, can result in problems. Simpler plants also cost less to fabricate, operate, maintain and control.

Other ISD techniques[2]

- design plants to be error-tolerant
- avoiding the domino effect
- making incorrect assembly difficult
- provide easy control of a process

Software safety

Computers have just about taken over the control of all major CPI, with software generally written by non-chemical engineers. Software errors can be significant, especially in new or one-of-a-kind software, and these must be thoroughly tested. Examples of disasters caused by software errors are available.[15,16]

Use of indices to rate ISD

DOW, Mond and PIIS (Prototype Index of Process Safety, Loughborough University) can be used to rate the effects of ISD techniques. Other indexing techniques may also be developed in due course as more experience is gained in ISD.

Life cycle approach

Consider all aspects from R&D, process development and design, plant erection and commissioning, operation, modifications, attention to upset conditions, maintenance and decommissioning after the plant has run its useful life, applying ISD principles at each stage.

R&D needs

The R&D in process safety has not kept pace with the need.[17] It is very important to emphasize this and point out areas in need of R&D. Depending upon availability of laboratory facilities and background of the students, some of these could be given as a semester project, under close supervision since students will not have much experience in laboratory safety.

Decision making regarding ISD usage

Why is ISD taking so long to be accepted? Answers to this might include: conflicts of ISD with environmental regulations, trade-offs between ISD and other techniques, etc. Also, warn the students that the applicability of ISD techniques should be thoroughly investigated lest they should create a different set of hazards.

Maintenance of Records[2,10]

Many decisions on process safety and application of ISD are taken based on sound principles, knowledge and experience, but the people making the decisions eventually move on. New hands might be tempted to alter the system by tinkering here and there, or in one big push. Accidents are likely to happen if reasons for decisions made years ago are not known. Hence, it is most important to record the reasons and calculations done for each decision and design. Before making any change, reasons for the existing design, operating conditions, *etc.*, must be known. This will avoid accidents and much grief later on. Students should therefore be asked to write in simple and understandable terms the changes they propose in any class exercise design using ISD concepts.

Since ISD is a relatively new field, it is not easy to offer a full course in it, and it is still less easy to examine student performance in it. The teacher will have to devise innovative ways to test a student's grasp of the topics. Experts from nearby industries can be helpful in testing by proposing real problems to which the students may be asked to apply ISD techniques. Since there will not be one correct answer in most cases, grading of students' responses will also have to be innovative. It should not mar a student's interest in ISD for the rest of his/her life. That would arrest the progress of ISD more than the teaching of the course would advance it!

It is strongly recommended that the students should be taken on a tour of at least one safety-conscious large CPI about two-thirds of the way through the course. The chosen industry's reactants, products, processes, operating conditions, annual production, customer location, *etc.*, should be discussed beforehand to the extent that the company's commercial and technological confidentiality considerations allow. This would prepare the students to apply ISD principles after viewing the plant personally. Company personnel should be on hand to discuss the students' recommendations on the use of ISD in their plant; both the company and the students will gain.

If students have not had a process safety or loss prevention course, then they first need to learn the following topics for hazard analysis. This will help them analyze the benefits and costs of applying ISD methodologies:

- HAZOP
- Dow and Mond Indices
- Fault-tree Analysis and Event-tree Analysis
- Pool Fire, Fire Ball and Explosions
- Gas Dispersion

Students need only simple models and examples since their aim is to compare the pre- and post- ISD systems.

Conclusions

Teaching of ISD will spread the message and give new insights to future designers. While this article has dealt with a one-semester course, the same has also been

Recommended journals on chemical process safety

The Chemical Engineer, IChemE (UK)
Journal of Hazardous Materials, Elsevier
Journal of Loss Prevention in the Process Industry, Elsevier
Loss Prevention Bulletin, IChemE (UK)
Loss Prevention News, Loss Prevention Association of India
Process Safety and Environmental Protection, Trans IChemE, Part B
Process Safety Progress, AIChE

repackaged for practising engineers as a 3-day short course. The vast experience of these practising engineers will produce intense interaction and will be extremely helpful in further refinements of the full-semester course as well as in more committed practice of ISD.

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CONFERENCE

ADHOC - 99

The Seventh International Symposium on Dioxygen Activation and Homogeneous Catalytic Oxidation (ADHOC-99) was held at York, UK, from 19–23 July 1999. At the meeting, attended by both chemists and biochemists, progress was reported towards the ideal homogeneous oxidation catalyst—one with high selectivity, high stability, and low environmental cost.

Biochemists gave several presentations on the mode of action of soluble and membrane-bound methane monooxygenase, which catalyses the dioxygen oxidation of methane to methanol. Such biological oxidases, or microorganisms containing them, show excellent selectivity and are being used to produce a variety of chiral organic compounds of commercial values in the pharmaceutical and other industries. Chemists reported on the production of several new homogeneous oxidation catalysts, e.g. soluble manganese complexes for olefin epoxidations; chelating diamine–palladium complexes for oxidation of olefins to ketones (a green version of the Wacker reaction); and soluble titanium-containing silicate cage compounds as analogues of the titanium-containing zeolite TS-1, already widely used for 'green' peroxide oxidation.

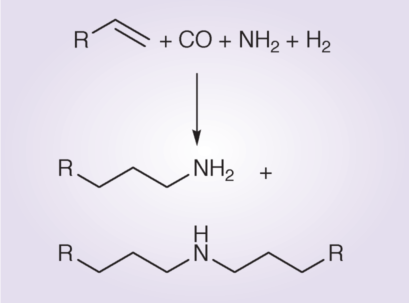
'Green' oxidation (minimum environmental cost) requires the use of hydrogen peroxide or air (or its reactive component dioxygen) as oxidant. The meeting demonstrated that highly selective catalysts for such 'green' homogeneous oxidation are being developed, but catalyst stability remains a problem.

Hydroformylations

Hydroformylation and related reactions have been the subject of intense activity recently. Three papers have been published, using different techniques, all of which contribute to highly active and selective routes to functional molecules from simple starting materials.

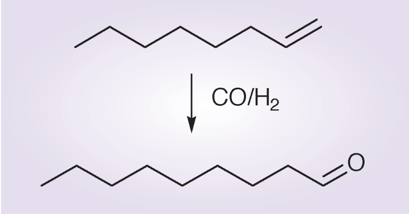
Amines from alkenes, CO and hydrogen

A new, highly atom economic and selective route to primary and secondary amines has been developed by researchers form Celanese in Oberhausen and the University of Rostock. Burkhard Zimmerman, Jürgen Herwig and Matthias Beller (*Angew Chem., Int. Ed.*, 1999, **38,** 2372) have shown that a combination of Rh and Ir can selectively convert alkenes to amines *via* hydroformylation, imine formation and reduction of the imine. The reaction is carried out using water soluble phosphine ligands, allowing a two-phase reaction to take place, with excellent catalyst separation after completion of the reaction. Selectivity problems to be overcome include *n* : iso hydroformylation, aldol condensation and reduction of aldehyde, and primary : secondary amine formation. The choice of ligand allows control over *n* : iso selectivity; sulfonylated triphenylphosphine gives reasonably high proportions of the *n*-isomer (76–87%). Primary : secondary amine ratios can be influenced by the ratio of ammonia : alkene, with 9 : 1 being the best achieved. Additionally, the relative polarities of the aqueous and organic phases can be adjusted such that the initially formed primary amine can be more rapidly transferred to the organic phase (and thus away from the catalyst), avoiding the formation of secondary amine. In this way a 96% selectivity to primary amine can be achieved. The use of sulfonated binaphthyl-phosphine ligands allows a much higher degree of control, with *n* : iso ratios of 99 : 1 being achieved, and selectivities of 99 : 1 secondary amine being achievable at a 2 : 1 ratio of alkene to ammonia.



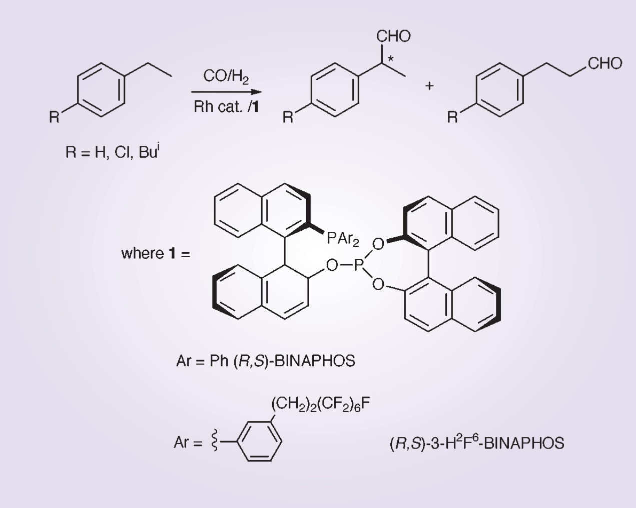
Water-soluble phosphine ligands

A further example of the use of water-soluble phosphine ligands in hydro-formylations has been described by the group of Piet van Leeuwen (*Chem. Commun.*, 1999, 1633). Their approach is based on the supported aqueous phase concept first described by Mark Davis (*Nature*, 1989, **339**, 454). A rhodium complex, based on the sulfoxantphos ligand, was shown to be active in the hydroformylation of alkenes with high *n* : iso ratios. Using pure alkene as substrate and solvent increased rates, which were significantly slower with *e.g.* toluene as solvent, and good rates of conversion could be achieved, with relatively high *n* : iso ratios. No loss of Rh into the liquid phase was detected, and catalysts could be reused several times with no loss in performance.



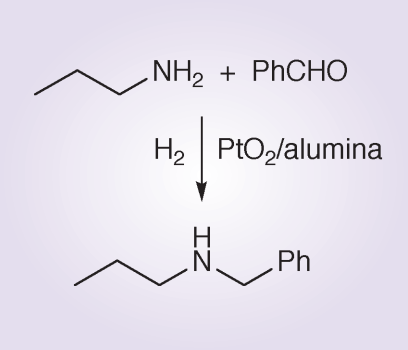
Hydroformylation in compressed carbon dioxide

The use of supercritical and near-supercritical carbon dioxide as an environmentally benign solvent is the subject of an increasing number of articles. Walter Leitner and Giancarlo Francio of the Max Planck Institut für Kohlenforschung in Mülheim an der Ruhr have recently published details of a hydroformylation using perfluoro-substituted BINAPHOS-Rh as a catalyst in liquid or supercritical carbon dioxide (*Chem. Commun.*, 1999, 1663). The synthesis of the complex ligand is described, as is use of its Rh complex as an active catalyst in the hydroformylation of styrene. Good enantioselectivities were achieved, and high regioselectivities (in favour of the iso product—compare with the earlier methods which favour the *n*-isomer) were found.



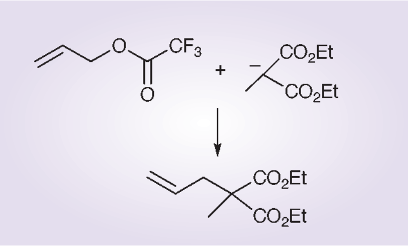
New, water-soluble form of Adam's catalyst

Manfred Reetz and Michael Koch of the Max Planck Institut für Kohlenforshung, Ruhr, Germany, have reported the preparation of a new, water soluble, form of Adams Catalyst, which is made simply by stirring an aqueous solution of $PtCl_4$ in the presence of a carbobetaine $[C_{12}H_{25}(CH_3)_2N^+(CH_2)_3CO_2^-]$ and excess NaOH (*J. Am. Chem. Soc.*, 1999, **121,** 7933). Adams Catalyst is a high surface area form of PtO_2, which is normally prepared by reaction of H_2PtCl_6 with $NaNO_3$ at 450 °C, and is an excellent hydrogenation catalyst. The new form of the catalyst is colloidal, with particle sizes of 1.8 ± 0.3 nm. This colloidal PtO_2 could be easily immobilised onto alumina supports, forming catalysts which are highly active in the reductive amination of benzaldehyde by *n*-propylamine. A similar procedure was used to prepare a water soluble bimetallic platinum–ruthenium oxide colloid. Although these new materials are water soluble, no attempt to use them as catalysts in aqueous solution was reported.



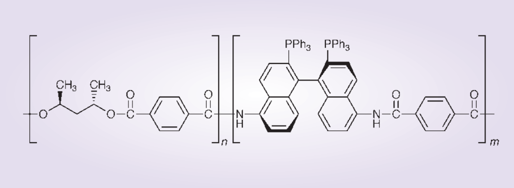
Dendrimeric catalysts in flow reactors

A group from the Netherlands led by Piet van Leeuwen has developed a novel dendrimeric Pd catalyst which can be used in a continuous flow membrane reactor (*Chem. Commun.*, 1999, 1623). These catalysts are derived from carbosilanes with terminal phosphines. The dendrimers are large enough to be recovered by nanofiltration, and contain Pd-phosphine complexes on their outer surface. These catalysts are active in the allylic alkylation reaction, where *e.g.* allyl trifluoroacetate was reacted with sodium diethyl methylmalonate, with the displacement of the trifluoroacetate. Batch reactions resulted in excellent activity under mild conditions, and continuous reaction using a molecular weight cut-off membrane led to initially excellent results, but reduced activity after a few cycles. Retention of catalyst in the reactor was excellent, and the reasons for the reduction in activity are currently being examined. Nonetheless, this approach does hold promise for immobilised and active Pd catalysts.



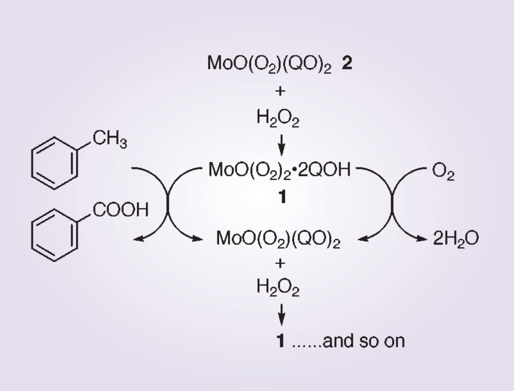
Soluble polymer support for 'one-phase catalysis and two-phase separation'

The combination of the advantages of heterogeneous and homogeneous catalysis is an important goal for green chemists, and several approaches, including the use of fluorous biphase catalysis and ionic liquid biphases, have achieved considerable success. Albert Chan and co-workers at the Hong Kong Polytechnic University, China, have tackled the problem from a different angle, by attaching their catalyst to a polymer backbone which is soluble under reaction conditions, but which precipitates on workup (*J. Am. Chem. Soc.*, 1999, **121**, 7407). A chiral phosphine was incorporated into a polyester and used to coordinate a ruthenium complex, to form an asymmetric hydrogenation catalyst which was active in the reaction of 2-(6′-methoxynaphthyl)acrylic acid, giving quantitative conversions and enantiomeric excesses as high as 93.6%. Upon completion of the reaction (which was performed in 3:1 toluene–methanol), methanol was added, and the catalyst was precipitated, filtered and reused, retaining its activity for more than ten cycles.



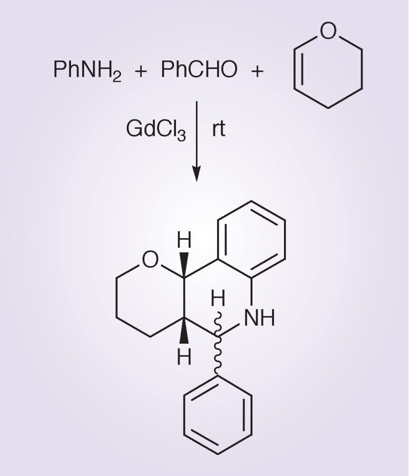
Oxidation of alkylaromatics using air and hydrogen peroxide

The search for simple and efficient systems for the conversion of alkylaromatics into oxygenated derivatives is an important theme, with many approaches being investigated. Particularly valuable would be a system which could use clean, cheap oxidants such as air or hydrogen peroxide as primary oxidant, but which avoids the need for high temperatures and pressures, and corrosive solvent/promotor mixtures. Ramgopal Bhattacharyya and co-workers from Jadavpur University in Calcutta have discovered a distorted molybdenum species which can oxidise compounds such as toluene and *o*-xylene to the corresponding acids under mild conditions (*Chem. Commun.*, 1999, 1627).Their catalyst is based on a molybdenum–quinoline complex which contains a 2-peroxo ligand and an oxo ligand. In the presence of oxygen and hydrogen peroxide, the complex functions as an effective catalyst for the oxidation of toluene to benzoic acid, *o*-xylene to phthalic acid and *p*-xylene to *p*-toluic acid. Conditions are mild, with reactions proceeding to high yield in refluxing acetonitrile in only a few hours. Turnover numbers are typically 1000 +. Running the reactions with only one of the two oxidants results in significantly reduced performance.



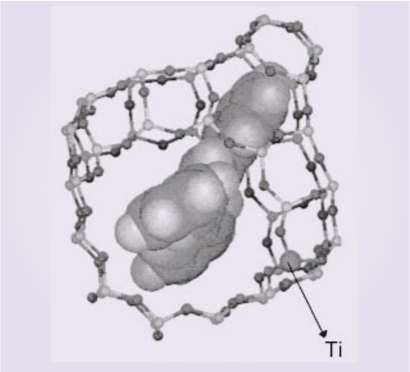
One-pot preparation of quinolines catalysed by lanthanide chloride

The aza-Diels–Alder reaction of *N*-arylimines with olefins is an important method for the preparation of tetrahydroquinoline derivatives, a class of compounds which exhibit anti-inflammatory and other biological activities. Meihua Xie and colleagues from the Chinese Academy of Sciences, Shanghai, have reported a simple one-pot reaction between an amine, benzaldehyde and dihydropyran or dihydrofuran, which offers advantages over existing methods (*J. Org. Chem.*, 1999, **64,** 6462). The new method avoids having to prepare and purify the arylimine beforehand, which may be tricky because imines are prone to hydrolysis. The reaction requires a lanthanide chloride catalyst ($GdCl_3$ worked best)—previous methods have used BF_3, $Co_2(CO)_8$ or $Ni(CO)_4$—and proceeds in a variety of solvents, including THF, DCM, diethyl ether and acetonitrile. The highest reported yield was 86%.

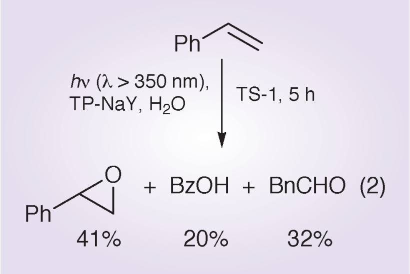


Photocatalysis within zeolite cages

The use of photocatalysis is potentially a very clean methodology. Avelino Corma, Hermeegildo Garcia and co-workers from the University of Valencia have developed the concept using photosensitisers encapsulated in zeolites as a system for the epoxidation of alkenes using just water and light (*Chem. Commun.*,



1999, 1641). This remarkable system relies on the generation of hydroxyl radicals from water using the excited state of the photosensitiser 2,4,6-triphenylpyrylium cation inside a Ti containing zeolite. Remarkably, the sensitiser is not destroyed by the water or the hydroxyl radicals formed, as is the case in bulk water where it is rapidly hydrolysed, but allows the effective conversion of alkenes to epoxide to occur.

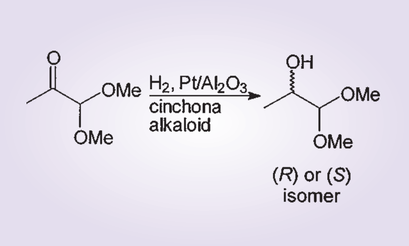


Catalyst life extended in ionic liquids

Concerns have been raised that since homogeneous catalysts only have limited life spans, the widespread interest in developing catalytic protocols using aqueous and ionic liquid solvents is unnecessary. Peter Wasserscheid and his team at the Institut für Technische Chemie und Makromolekulare Chemie in Aachen, Germany, have been investigating the hydroformylation of methyl 3-pentenoate, a precursor to adipinic acid and many other products, using rhodium based catalysts (*J. Catal.*, 1999, **186,** 481). They have compared the activity of the catalysts under homogeneous conditions in toluene and dichloromethane and using the ionic liquid [BMIM][PF_6] (1-butyl-3-methylimidazolium hexafluorophosphate). In the reactions carried out in organic solvents deactivation of the catalysts takes place rapidly whereas in the reactions conducted in the ionic liquid the catalyst remains active for considerably longer periods with turnover numbers typically 600% greater.

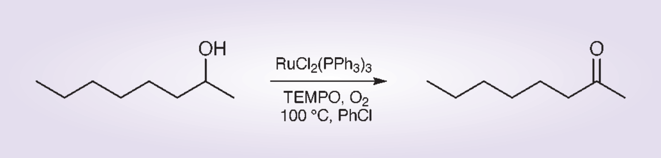
Enantioselective hydrogenations using cinchona-modified catalysts

Two groups have independently reported identical results relating to the selective reduction of α-hydroxy acetals using cinchona-modified Pt/Al_2O_3 catalysts. M. Bartok *et al. (Chem. Commun.,* 1999, 1725) and M. Studer *et al* (*Chem. Commun.*, 1999, 1727) have extended the use of this method to the reduction of dimethyl acetals. The products are valuable synthetic equivalents to α-hydroxy-aldehydes. The method in the best cases produces high enantioselectivities (up to 97%) and good rates of reaction, and is reported to be simpler and more cost-effective than other methods. The conversion of the products to other valuable synthons was also demonstrated.



Aerobic oxidation

In a recent communication (*Chem. Commun.*, 1999, 1591) Roger Sheldon and colleagues at the Delft University of Technology in The Netherlands describe $RuCl_2(PPh_3)_3$–TEMPO as an effective catalyst for the aerobic oxidation of non-activated aliphatic alcohols and a broad range of other alcohols to aldehydes and ketones. $RuCl_2(PPh_3)_3$ on its own was a poor catalyst for these reactions, but the addition of TEMPO, itself not active as a catalyst, led to a substantial increase in activity. This is one of the most reactive catalysts reported to date for the aerobic oxidation of (aliphatic) alcohols.



IPTS Cleaner Pathways Workshop

The Institute for Prospective Technological Studies (IPTS), which is part of the European Commission's Joint Research Centre, recently held a workshop on June 24–25 in Seville, Spain, on 'Strategies to facilitate the use of cleaner pathways for the production of substances and materials'. The IPTS is one of the eight institutes of the Joint Research Centre. Its role is the observation and follow-up of technological change; in order to get a better understanding of the links between technology, economy and society and to provide techno-economic intelligence to the European Commission. Under its environment work programme IPTS is assessing the socio-economic impact that development of clean processes, products and services will have.

Towards the end of 1998, IPTS carried out an 'expert inquiry' survey into sustainable technologies for the chemical industry with the aim of identifying innovation options which would both provide the European chemical industry with competitive advantage and provide environmental benefits. The findings from this survey are still being analysed and currently remain confidential. In addition to this survey this workshop aimed to improve IPTS' understanding of how clean technology can be developed and taken up by the chemical industry, with particular focus on how future EU policies could help. The workshop was arranged around particular themes, which are briefly summarised.

Efficiency of carbon use and clean production examples

The next two papers concentrated on improving the efficiency or carbon use. Martin Patel from the Fraunhofer Institute for systems and innovation research presented a flow model for the manufacture, use and waste management of synthetic carbon products within Germany. The study indicated that the total primary energy related to the life-cycle of synthetic organic materials in Germany is approximately 1700 PJ with CO_2 emissions around 57 million tonnes, however relative to the economy this is equivalent to 12% of the energy used and only 6% of CO_2 emissions. The share of carbon based materials produced by recycling is less than 10% of the total domestic consumption, indicating grounds for significant improvement. The study also indicated that potential savings achievable by 2005 amounted to 15% of energy used and 28% of the CO_2 emitted, most of these savings could be made by using waste as a resource.

Michele Aresta from the METEA Research Centre stressed the importance of life cycle analysis in determining how sustainable a product or process actually is. He then went on to demonstrate the potential role of carbon dioxide in chemical synthesis. Use of carbon dioxide as a raw material would not only help preserve fossil fuel carbon, it can be the source of many cleaner synthetic routes than currently employed. Amongst the examples quoted was the potential for replacing phosgene in the synthesis of carbonates and carbamates (Figure 1). Should these processes become economically viable it will be a significant improvement on the current preferred commercial routes involving reaction of phosgene with alcohols or amines, not only due to the problems associated with use of phosgene but also due to the production of HCl.

Examples of how commercial organic synthesis pathways had been 'greened' were given by Bjorn Akermark from the Swedish Royal Institute of Technology. An interesting example is the case of acetic acid, originally made by fermentation of ethanol. This is one of several biotechnology processes which may be considered green because of their use of renewable resources but which in fact produce copious amounts of waste. This process was later replaced by conventional organic processes which did not offer any real environmental advantages; these included production of acetic acid *via* acetylene made from calcium carbide and the Wacker process using ethene as starting material. It was not until the Monsanto methanol carbonylation process came on stream that acetic acid production could be considered to be clean.

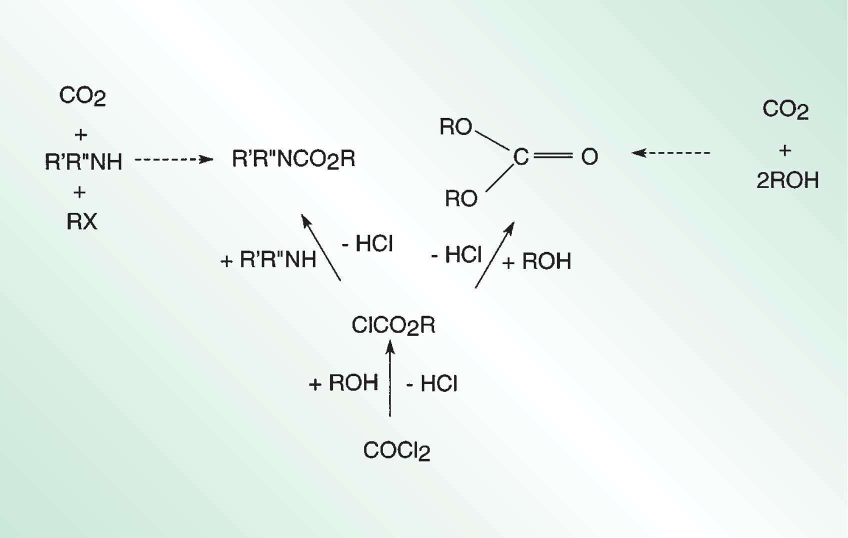


Figure 1

Green Chemistry programmes

The next session discussed some of the green chemistry movements within Europe. Kurt Wagermann from Dechema, whose organisation is sponsored by the German Federal Ministry, the chemical industry, Allcheme and universities, is pulling together the sustainable chemistry movement in Germany. There is a current working party discussing how best to incorporate the ideas of sustainability into the education curriculum, school and university education being seen as key to the future of clean chemical production. Dechema are also coordinating a R&D programme on inherently safer chemical products, solvent free processes and chemicals from renewable feedstocks. One of the debates currently going on is whether government funded programmes should be under one 'sustainable manufacturing' umbrella or whether the ideas on sustainability should be included in all programmes.

Pietro Tundo representing INCA described the origins of the green chemistry movement in the US and the various definitions and principles of Green Chemistry. Recommendations from the 1998 OECD workshop on sustainable chemistry were discussed, these included proposals for sustainable chemistry awards, the call for member countries to undertake R&D programmes into sustainable chemistry and for OECD to promote the incorporation of sustainable chemistry concepts in education. INCA itself is a consortium of Italian universities with a common interest in Green Chemistry, which is supported by government. The consortium is currently looking at several thematic areas including clean chemical processes transformation within the environment and advanced analytical methodologies. The consortium also run an annual EU sponsored summer school on Green Chemistry for young graduates, this year's was held in Venice in September.

Mike Lancaster from the Royal Society of Chemistry's Green Chemistry Network explained the networks activities in promoting Green Chemistry in education and industry in the UK. The drivers enabling industry to adopt cleaner technologies were discussed and case studies presented. As chemists become more skilled in financial workings of companies and accounting procedures become more focused on individual processes it is becoming easier for companies to appreciate the effect clean technology can have on the bottom line. An excellent example of this is the recent conversion of Hickson & Welch's optical brighteners process to use water in place of volatile organic solvents. The Hickson's process was becoming uncompetitive due to high raw materials cost and increasing cost of waste disposal and regulation compliance. This is a classic case of a company turning to clean technology to save money—in this case £300,000 p.a. Although many of the tools Green Chemists require are available they are not readily accessible and the philosophy and culture of Green Chemistry has not yet percolated through industry and educational establishments. Networks such as the GCN have significant roles to play facilitating the 'greening' of both education and industry.

Jacques Calzia from CEFIC described the Sustech programme under which the European chemical industry is undertaking collaborative research into sustainable technologies. Through Sustech the industry is demonstrating its willingness to respond to public concern, and to be a willing partner with government on moving towards cleaner technologies. The R&D projects being undertaken are all designed to produce cost savings and include areas such as bioprocess engineering, contaminated land remediation, separation technology and design. Through these programmes CEFIC aim to influence EU policy, enhance the public reputation of the chemical industry and have a greater influence on university research.

Gerard Riviere presented the role of COST in encouraging a multidisciplinary approach to research and sharing of best practice. The 28 members of cost are working on 20 scientific areas, the chemistry section of which is a fairly recent development. The programmes are funded by individual countries' research councils but endorsement by COST helps to ensure that grants are available.

History of Clean Technology Development and the Role of Government

Luitgard Marschall from Münchner Zentrum für Wissenschafts und Technikgeschichte provided a fascinating account of the development of the German chemical and biotechnology industries in the 20th century. At the beginning of the century both industries were of comparable importance but due to the shortage of agricultural crops and government policy after the First World War the chemical industry began to grow at the expense of the biotechnology companies. This situation continued for the next 50 years, Germany losing most of its biotechnology expertise along the way. From the seventies onwards Government policy has tried to resurrect the biotechnology industry but this has been difficult in light of competition from Sweden, Japan and the US who never lost expertise in this area. The lesson for the Clean Technology movement is that all disciplines, including chemistry, biotechnology and engineering, have an important role to play and EU policy should reflect this need and encourage interdisciplinary research.

Mahshid Sotoudeh from the Austrian Academy of Science discussed the demand for cleaner technologies, highlighting some of the problem areas and barriers. One of the areas of concern was the focusing of R&D on the production process with little attention being paid to the end use, waste generation and recycling. There is a need for greater understanding of eco-efficiency concepts in product life cycle. She concluded that one of the main barriers to adoption of cleaner processes was lack of communication between and inertia of interested parties (industry, customers, universities, policy makers and environmental activists) and called for structural changes and more discussion.

Klaus Jacob (Free University of Berlin) presented a study on the link between legislation and the decline in production of chemicals. The main conclusion were that the major drop in production of hazardous chemicals came before any regulation, indicating industry does respond to environmental pressure. He advocated government setting targets to develop clean technology but not rigorous legislation.

Gerald Petit (EU Commission DGIII) addressed issues of the global competitiveness of the chemical industry and how the EU wishes to integrate internal market, environmental, health & safety and employment issues with sustainable development. Any EU industry regulation would need to take these factors into account. DGIII is hoping to work more closely with organisations such as CEFIC to develop industry co-operation through benchmarking and initiatives to improve training and education.

The workshop concluded with groups presenting their views on the problems and solutions to industry becoming more sustainable with ideas on how policy should be developed to encourage this process. Examples include:

- Development of a readily accessible clean technology toolkit
- Encouragement for education establishment to incorporate sustainable concepts
- Tax incentives for development of clean products and processes
- Awards to encourage clean production and R&D
- Greater company openness in environmental accounting
- Development of methodologies which will define what a sustainable product is
- Easier access to risk capital for eco-friendly developments

The workshop demonstrated the wide interest in clean, green, sustainable chemistry in Europe and by pulling all the various strings together hopefully IPTS will be able to propose a policy approach which encourages both industry and educationalists to become more green whilst maintaining industry competitiveness.

Mike Lancaster,
Green Chemistry Network

Ionic liquids at the RSC Congress

The use of ionic liquids as solvents for organic reactions was a major theme of the 1999 summer meeting of the Molten Salts Discussion Group, held as part of the RSC Annual Congress at Heriot-Watt University in Edinburgh, Scotland (6–7 September). Ionic liquids are seen as potentially green replacements for conventional organic solvents and are currently the subject of a great deal of interest from both industry and academia.

Dr Tom Welton from Imperial College, London, gave the opening talk of the meeting, entitled ‘Molten Salts as Reaction Media for Organic Solvents’. This gave a general introduction to those physical properties of molten salts which make them attractive for organic synthesis. He explained that, at normal working temperatures, ionic liquids have no vapour pressure and so do not evaporate: this is an important property from a clean technology point of view as solvent evaporation is a major source of VOC emissions. It also gives the additional advantages that the solvent may be handled in a vacuum, and that volatile solutes are readily removed by distillation. Ionic liquids are highly polar, but poorly nucleophilic, making them good solvents for polar and ionic compounds, without coordinating strongly to metal centres. The combination of these two properties makes ionic liquids particularly suitable for reactions involving transition metal catalysts.

Dr Welton explained how the use of large anions and bulky organic cations reduces the coulombic interactions and so reduces the melting point; for example, $[EtNH_3]^+NO_3^-$ has a melting point of only 12 ºC. Many of the most recently developed ionic liquids are based on the 1,3-dialkylimidazolium cation. Several of the physical properties of the ionic liquid, including the melting point, miscibility, viscosity, and even the selectivity of the chemical reaction may be controlled simply by altering the length of the alkyl groups and the nature of the anion. For example, in Diels–Alder reactions, the ratio of *endo* to *exo* product is sensitive to the structure of the ionic liquid used. Some other examples of successful reactions performed in ionic liquids were given, including alkene dimerisation, and rhodium-catalysed hydrogenations. In the latter case, the turnover frequencies and product yields were higher those seen for polar solvents such as acetone or acetonitrile.

Dr Paul Dyson from the University of York, UK, who is involved in a collaborative project with Dr Welton, talked about the applications of ionic liquids for hydrogenation catalysis using a liquid biphase approach. At low temperatures, ionic liquids are immiscible with water but, on warming past a critical temperature, form a single phase in which the reaction occurs. Upon completion, the reaction is cooled and phase separation occurs; the water soluble products are now in the aqueous phase and can easily be recovered, whilst the catalyst remains in the ionic liquid ready for reuse. This combines the reactivity advantages of homogeneous catalysis with the separation advantages of a heterogeneous system. In principle, this is similar to fluorous biphase catalysis, but has the advantage of not requiring any special fluorinated ligands: many ‘off-the-shelf’ catalysts may be used. 1-Octyl-3-methylimidazolium tetrafluoroborate was found to be a particularly useful ionic liquid for these applications, as phase mixing occurs at a convenient 58 ºC. This liquid biphase approach has been used successfully for the hydrogenation of butynediol using a rhodium phosphine complex catalyst. This biphasic approach also works with mixtures of ionic liquids and organic solvents, and a ruthenium complex catalysed hydrogenation of benzene to cyclohexane was found to proceed in a molten salt–neat substrate system at a rate of 500 turnovers per hour.

Dr Rob Thied of BNFL, UK, introduced QUILL, the Queen’s University Ionic Liquids Laboratories, which is a collaboration between academia and industry, and includes 17 industrial members. QUILL is based at Queen’s University in Belfast, Ireland, and will be the first international research centre to focus on ionic liquids (see *Green Chemistry*, 1999, **1**(3), G58). QUILL’s objectives were described as: pooling of resources and the ‘gearing’ of funding; collection and sharing of fundamental data; advancing the understanding of ionic liquids; development of applications of ionic liquids technology; solving engineering challenges whilst minimising risk; gathering of IPR (intellectual property rights) where appropriate; and development of industry–industry and industry–academic liaisons. The research conducted at QUILL will be industrially relevant, pre-competitive and interdisciplinary, and will address the measurement of physical parameters critical to the use of ionic liquids on an industrial scale, including specific heat capacities, corrosiveness, recyclability, long term chemical stability, and disposal after its useful lifetime. Dr Thied’s talk was followed by a lively discussion after it was revealed that QUILL will not be sharing the results of their measurements of fundamental properties with non-consortium members, until they are sure that IPR will not be compromised. Dr Thied said that this was to protect the investment of the consortium companies, and could not estimate when the data might become available. This was met with disappointment by at least one member of the audience, who pointed out that public money was involved, and felt that such important information should not be kept secret.

Stewart Tavener,
University of York

Conference Diary

November 1999

Clean Products and Processes II **November 14–19**
Lake Arrowhead, California, USA
(http://www.engfnd.org/9br.html)

International Congress of Chemistry and Environment **November 27–30**
Indore, India
(http://www.chemenviron.com)

December 1999

Clean Processes and Environment: The Catalytic Solution **December 6–8**
ESCPE-Lyon Campus de la Doua, Villeurbanne, France
(http://www.cpe.fr/lcoms/cartier)

January 2000

2nd Asia-Pacific Congress on Catalysis **January 31 –February 2**
Sydney, Australia
(http://www.chemsoc.org/events/_events/00001018.htm)

February 2000

AAAS Annual Meeting and Science Innovation Exposition including a workshop on Sustainability through Science **February 17–22**
Washington DC, USA
(http://www.aaas.org/meetings/2000/index.htm)

March 2000

ACS National Meeting: Celebrate Chemistry in the 21st Century **March 26–31**
San Francisco, California, USA
(http://www.acs.org/meetings/future/newsanfran.htm)

April 2000

Green-Tech® 2000 **April 3–5**
Royal Dutch Jaarbeurs, Utrecht, Netherlands
(http://www.europoint-bv,com)

5th International Symposium on Supercritical Fluids: ‘Supercritical Fluids for Sustainable Technology’ **April 8–12**
Westin Atlanta North Hotel, Atlanta, Georgia, USA
(http://www.issf2000.org)

CAPoC5—5th International Congress on Catalysis and Automotive Pollution Control **April 12–14**
Université Libre de Bruxelles, Belgium
(http://www.ulb.ac.be/sciences/surfcat/CAPoC5/)

9th International (and 4th European) Symposium on Supercritical Fluid Chromatography and Extraction. **April 13–14**
In cooperation with Analytica Conference 2000
Munich, Germany
(sfc2000@mx.uni-saarland.de)

RSC Annual Conference including Symposium ‘Towards Sustainability’ **April 16–20**
UMIST, Manchester, UK
(http://www.rsc.org/lap/confs/sciprog.htm)

May 2000

Synthetic Methodology and Total Synthesis: New Horizons in Natural Product Chemistry **May 16**
University of Glasgow, UK
(http://www.rsc.org/lap/rsccom/dab/perkidiv.htm)

InBio Europe 2000. Biocatalysis—New Science and Applications **May 23–24**
Crown Plaza Hotel, Amsterdam, The Netherlands
(http://www.scientificupdate.co.uk)

16th Canadian Symposium on Catalysis **May 23–26**
Banff, Alberta, Canada
(http://www.gch.ulaval.ca/~sayari/16csc/)

June 2000

R'2000 Recovery, Recycling, Re-integration. 5th World Congress with Trade Show **June 5–9**
Toronto, Ontario, Canada
(barrage@peak.ch)

4th Annual Green Chemistry and Engineering Conference **June 27–29**
National Academy of Sciences,
Washington DC, USA

July 2000

4th International Symposium—Supported Reagents and Catalysts in Chemistry **July 2–7**
St Andrews University, UK
(http://ch-www.st-andrews.ac.uk/conferences/)

12th International Congress on Catalysis Granada, Spain **July 9–14**
(http://lcpb00.lc.ehu.es/12icc/index.html)

5th Gordon Conference on Green Chemistry **July 16–21**
Connecticut College, New London, CT
(http://www.grc.uri.edu/00sched.htm)

IEX 2000: Ion exchange at the Millennium Organised by the SCI **July 16–21**
Churchill College, University of Cambridge, UK
(http://sci.mond.org/conference/meetings/IEX.HTM)

August 2000

ACS 220th National Meeting including Green Chemistry—Applications in Academia and Industry Symposium **August 20–24**
Washington DC, USA
(http://www.acs.org/meetings/future/washdcacp.htm)

Selected highlights in the application of ion-exchangers

as supports for reagents in organic synthesis

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Summary

The development of cleaner and more efficient synthetic routes to minimise environmental damage has been approached in many ways. Amongst these are: improved catalytic methods, solvent free reactions, reactions employing water as the solvent, the application of supercritical fluids, new asymmetric methods to minimise the production of unwanted isomers and atom-efficient synthesis. In all of these cases, the focus is to reduce the amount of materials required to perform the desired synthetic step, to obtain products requiring the minimum amount of expensive and/or complex purification steps, and therefore to reduce waste. The use of supported reagents to achieve a variety of useful organic transformations, whilst achieving at least some of these objectives, is the object of this review.

1 Introduction

The rapid expansion in the field of combinatorial chemistry has, to a great extent, been dominated by Solid Phase Organic Synthesis (SPOS)[1] and, consequently, a great deal of effort has been directed towards the adaptation of classical solution phase reactions to solid phase. An alternative strategy is to perform conventional solution phase chemical transformations, and remove either the product, or unwanted by-products, by the application of a suitable resin. In both of these cases, ion-exchange resins have often been employed as a simple method of achieving the desired purification step.[2] Simultaneously, there has been extensive growth in the application of modified polymers, and polymers incorporating reactive functional groups as reagents in organic synthesis,[3] and the use of ion-exchange resins as catalysts.[4]

The vast majority of ion-exchange resins are macroporous materials, predominantly based on relatively inert, divinylbenzene cross-linked polystyrenes. There are four main groups of resin, each with a different functional group; strong cationic (sulfonic acid), strong anionic (quaternary amine), weak cationic (carboxylic acid) and weak anionic (tertiary amine). In addition to these differences, the counter ion, where present, can vary in each individual resin and can be altered by washing. The resins themselves have a nominal load, or exchange capacity, of between 2 and 5 mmol g^{-1} depending upon the exact nature of the resin, *i.e.* degree of cross-linking, moisture content and their mode of preparation.

The use of commercially available ion-exchange resins to prepare supported reactants, thus providing a third method for performing solution phase chemistry without the need for specialist polymers, has grown rapidly in line with new solid phase methods. This continued expansion implies that it is set to become an important tool for clean organic synthesis in the future. The aim of this review is to demonstrate some of the areas in which such reagents have been employed, and their benefits over conventional solution phase reagents in those cases highlighted.

Antony Chesney was born in Manchester, England, and obtained his BSc (1989), MPhil (1990) and PhD (1993) from the Department of Chemistry at the University of Sheffield. The later two were under the supervision of Dr. Istvan Markó, with theses on approaches to the Manzamine family of alkaloids, and novel amine ligands for asymmetric catalysis respectively. In 1993, he joined the group of Professor Martin Bryce at the University of Durham, where he worked on sulfur–nitrogen and selenium–nitrogen heterocycles, new electron donors and donor–acceptor systems, novel ferrocene derivatives, asymmetric catalysis and selective metal-ion sensors. In 1998, he moved to Bioprocessing Ltd., which became a Division of Millipore in 1999, where his research focuses on solid phase chemistry targeted at resins for solid-phase synthesis, scavenger resins for reaction purification, natural polymers and chromatographic media for high-throughput affinity applications. He is a co-author on more than 20 research publications.

Green Context

The use of supported reagents in chemistry offers many potential environmental advantages compared to traditional reagents. This article describes some of the highlights from the recent literature on the use of ion-exchangers as supports for reagents in organic synthesis. Commercially available ion-exchange resins can be modified so as to make them active for various organic reactions including oxidations, reductions, and halogenations. These are very important areas of chemistry where current methods can lead to major environmental problems due to the use of highly toxic reagents or serious separation difficulties. ***JHC***

The advantages of reagents supported on ion-exchangers are potentially manifold, and briefly comprise the following:

(i) They can be employed in excess in order to drive the desired reaction to completion. This is especially straightforward, since each resin can be tailored to achieve an ideal loading of reagent, most often greater than 1 mmol g^{-1}, and in some cases higher than 2.5 mmol g^{-1}.

(ii) Contamination of the final product with reagent or reagent by-products is minimised, leading to a cleaner product which can be used directly in the next synthetic step with the minimum of purification.

(iii) Removal of the resin is easily achieved by filtration, thus greatly simplifying the reaction workup.

(iv) Standard analytical techniques such as TLC, HPLC or GC can easily be employed to monitor the progress of the reaction.

(v) The possibility of recycling the supported reagent or regenerating it for future use arises, thus minimising waste solids.

(vi) The exposure of workers to toxic and/or noxious materials can be minimised once the resin has been prepared.

(vii) Many ion exchange resins and, indeed, reagents supported on them, are commercially available and are relatively inexpensive, if they can be recovered and re-used.

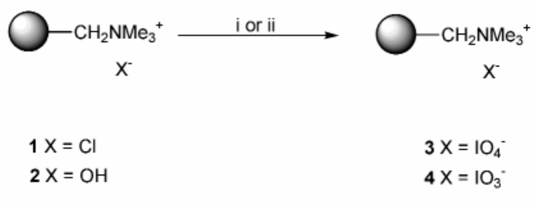
There are a few obvious disadvantages associated with using these materials which are mainly concerned with the scale of applications, although in areas where the reagent can be packed into a bed or column this should not prove problematic. A second potential problem is with temperature stability of the resins, although routinely they are stable up to 70 °C, and in some cases higher temperatures although often for shorter time periods. One final possible limitation is that the reactions are often slower than the corresponding solution phase analogues, due to the requirements of reagent/product diffusion to and from the active site. These minor problems may however be overcome by employing specially designed polymers, or by careful analysis of the exact reaction requirements prior to the use of these reagents.

These reasons clearly demonstrate the usefulness of such reagents; they are clean, potentially re-usable and create less waste than conventional materials and, as such, represent reagents for 'green chemistry.'

2 Supported oxidants

2.1 Periodate and iodate

The preparations of the periodate forms **3** of the macroporous ion-exchange resins Amberlyst 26 and Amberlite IRA 904[5] from their corresponding chloride forms **1** and of the iodate analogues **4** from the hydroxide version of those matrices **2**, as shown in Scheme 1, were first described by Harrison and Hodge.[6] Typical loadings of the oxidants on the supports ranged from 1.3 to 2.0 mmol g^{-1}, as determined by iodometry.



Scheme 1 *Reagents and conditions*: i $NaIO_4$ (aq); ii HIO_3 (aq).

Their application as supported oxidants in a variety of reactions carried out in both protic and aprotic environments was established. The oxidation of quinol to benzoquinone was found to be highly solvent dependent, with the best results being achieved when the oxidants were supported on Amberlyst A26, and with the reaction being performed in methanol. In the case of both **3** and **4**, such conditions led to the formation of benzoquinone in 89% isolated yield. A number of oxidative conversions of quinols to *p*-quinones and of catechols to *o*-quinones were subsequently described, with high isolated yields of the desired materials being obtained in the overwhelming majority of cases.

Reagent **3** was also successfully employed in the cleavage of 1,2-diols to the corresponding carbonyl species. The reactions were carried out in refluxing dichloromethane, with product yields ranging from 86% for the conversion of 2-phenylpropane-1,2-diol to acetophenone, rising to 97% for the analogous transformation of 1-phenylethane-1,2-diol to benzaldehyde. Interestingly, the authors reported that no oxidation occurred when α-hydroxy ketones were subjected to the reagent, a fact that they suggest may allow selective oxidations to be performed, although no evidence to support this was documented.

The conversion of several sulfides to their corresponding sulfoxides utilising reagent **3** under a variety of conditions was also demonstrated. The most successful reactions employed methanol as the reaction solvent, and were extremely mild. Finally, the oxidations outlined in Scheme 2 were performed. These indicate that **3** can act on a broader group of reactions, thus demonstrating the material's potential as a versatile and clean oxidant.

$$\mathrm{PhNHNHPh} \xrightarrow[89\%]{\text{i}} \mathrm{PhN{=}NPh}$$

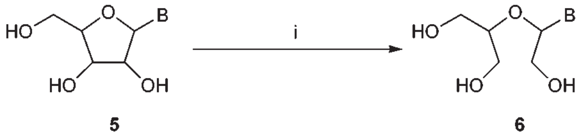
$$\mathrm{Ph_3P} \xrightarrow[100\%]{\text{i}} \mathrm{Ph_3P{=}O}$$

$$\mathrm{PhC(O)NHOH} \xrightarrow[65\%]{\text{ii}} \mathrm{PhC(O)NO}$$

Scheme 2 *Reagents and conditions*: i **3**, $CHCl_3$, 20 °C, 2 h; ii **3**, $CHCl_3$, 20 °C, 18 h.

A potential problem with **3** lies in benzylic oxidations, where the possibility of polymer-backbone oxidation may occur. This was not investigated in the original paper, and may need further research. At no point in this research was the residual iodine functionality on the resin identified, and no attempts to re-oxidise the material were performed. Presumably, if the periodate was simply reduced to iodate, then the spent reagent could easily be regenerated by application of an external oxidant.

An interesting application of periodate resin **3**, in conjunction with resin-bound borohydride, was the conversion of nucleosides **5** to the corresponding trihydroxynucleosides **6** as described by Bessodes and Antonakis.[7] Simply filtering a solution of the nucleoside through a column containing a well-mixed bed of a 1:1 mixture of the two resins facilitated the reaction (Scheme 3).



B	% Yield
Adenine	70
Cytosine	79
Guanine	40
Uracil	73

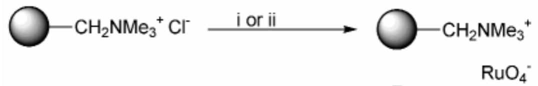
Scheme 3 *Reagents and conditions*: i Mixture of **3** and BH_4^- resin.

The process described was therefore extremely clean, and has the advantage that due to the fact that no reaction takes place between the resin bound materials, the intermediate dialdehyde need not be isolated. This renders such a procedure especially useful when the reaction intermediate is potentially unstable, or when it may be lost during a work-up procedure.

Periodate-containing resins have also been successfully employed in the high-yielding and remarkably clean oxidations of α-haloketones[8] into carboxylic acids, and in the rapid conversion of a range of sulfides to sulfoxides.[9] These examples demonstrate still more transformations which can be readily accomplished using this versatile and easily prepared oxidant.

2.1 Perruthenate

In 1997, Hinzen and Ley[10] described the preparation of polymer supported perruthenate **7**, on Amberlyst IR27.[11] Their initial preparation (Scheme 4) involved the use of ultrasound to effect the reaction between the resin and potassium perruthenate, and afforded a resin with a nominal load of the oxidant of approximately 1 mmol g^{-1}.



7

Scheme 4 *Reagents and conditions*: i KRuO$_4$))), 10 min.

The application of **7** to the oxidation of alcohols to their corresponding carbonyl species in a manner analogous to that using tetrapropylammonium perruthenate (TPAP) was investigated. Selected results of these initial experiments are contained in Table 1. In all cases, the oxidations were carried out in dichloromethane at room temperature, with 20 mol% of **7** and, initially, in the presence of co-oxidants. The reactions were simply monitored by TLC, and filtration followed by removal of the solvent afforded the crude products, which were analysed by GC. In cases where the reaction was found to be incomplete (Table 1, entries 1–3), the only by-product detectable was the initial alcohol, with no products of over oxidation being detected. The addition of 4Å molecular sieves was found to greatly increase the rate of the reactions (*cf.* entries 5a and 5b), presumably by the removal of water. When a solitary equivalent of co-oxidant was employed (entry 3) no nitrogenous by-products from the excess *N*-methylmorpholine *N*-oxide (NMO) were present in the sample after solvent removal, since the free amine is relatively volatile. The use of stoichiometric or greater amounts of **7** (entries 4b,c and 5c) led to the formation of the desired aldehydes in excellent yields, without the need for a co-oxidant, thus rendering the process highly atom-efficient and clean.

In order to demonstrate that the process was 'green', the spent resin was shown to be re-usable in combination with a co-oxidant. As an example, the oxidation of benzyl alcohol using NMO as the re-oxidant was attempted, and gave, as expected, benzaldehyde, although in decreasing yields: >95% (1st cycle), 88% (2nd cycle) and 72% (3rd cycle). Alternatively, the used resin can be regenerated externally, by re-oxidation with a solution of NMO, and then re-used as normal in the oxidative sequence.

An improvement to the effectiveness of this reagent was later demonstrated, in which molecular oxygen was employed to effect the *in situ* re-oxidation of **7**.[12] The optimum results were found to be when an oxygen atmosphere was employed, and the reaction was performed using 10 mol% of **7** in hot toluene. Representative results of this useful synthetic modification are contained in Table 2, with the yields quoted being based on GC analysis of the residue obtained after filtration of the mixture and solvent removal. In the cases of incomplete conversion, the only detectable by-products were once again the starting alcohols. Indeed, even under the relatively forceful conditions employed, no over-oxidation to the corresponding carboxylic acids was observed for any of the substrates, and no decomposition products were detected.

The selectivity of the **7**/O$_2$ system was also studied, and a remarkable difference between the activity of primary and sec-

Table 1 The oxidation of alcohols to carbonyl compounds with **7**

Entry	Alcohol	Product	*t*/h	Yield (%)	Co-oxidant	Sieves
1	cyclohexanol	cyclohexanone	48	64	TMAO[a] (1.5 eq.)	yes
2	1-phenylethanol	acetophenone	18	60	TMAO (1.5 eq.)	yes
3	$C_8H_{17}OH$	$C_7H_{15}CHO$	16	54	NMO (1 eq.)	yes
4a	benzyl alcohol	benzaldehyde	16	>95	NMO[b] (1.5 eq.)	yes
b			26	85	none[c]	no
c			48	>95	none[c]	no
5a	cinnamyl alcohol	cinnamaldehyde	16	>95	NMO (1.5 eq.)	yes
b			36	>95	NMO (1.5 eq.)	no
c			48	85	none[c]	no

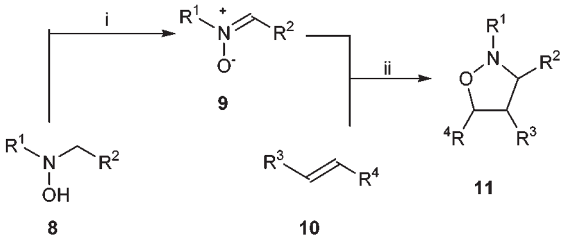
[a] TMAO = trimethylamine *N*-oxide. [b] NMO = *N*-methylmorpholine *N*-oxide. [c] Equimolar or greater amounts of PSP were employed in these cases.

Table 2 The oxidation of alcohols with **7**, using molecular oxygen as the co-oxidant

Entry	Alcohol	Product	*t*/h	*T*/°C	Yield (%)
1	cinnamyl alcohol	cinnamaldehyde	1	75	>95
2	benzyl alcohol	benzaldehyde	0.5	75	>95
3	3-pyridinemethanol	3-pyridine carbaldehyde	1	75	>95
4	$C_8H_{17}OH$	$C_7H_{15}CHO$	8	85	91
5	$Me_2N(CH_2)_3OH$	$Me_2N(CH_2)_2CHO$	8	85	>95

ondary alcohols was noted. The oxidation of a 1:1 mixture of benzyl alcohol and 1-phenylethanol in toluene at 75 °C for 3 h afforded only benzaldehyde, and no acetophenone. A similar experiment with octan-1-ol and octan-2-ol afforded an 83% conversion of the primary alcohol and only a 13% uptake of the secondary material. This slightly lower selectivity was attributed to the longer reaction time of 6 h, and to the higher temperature of 85 °C employed to achieve this conversion. These conditions are required as both substrates are non-activated.

An extension of the usefulness of **7** as a mild and clean oxidant was later demonstrated by the conversion of hydroxyamines **8** into nitrones **9**.[13] These were subsequently trapped *in situ* with a 1,2-dipolarophile, **10**, to form isoxazolidines **11** (Scheme 5). A variety of hydroxyamines were subjected to this procedure, and owing to the mild nature and hence chemoselectivity of **7** other amino functions present were not oxidised.



Scheme 5 *Reagents and conditions* i **7**, $CHCl_3$; ii $CHCl_3$, 60 °C.

The application of **7**, or the more powerful permanganate oxidant (prepared in an identical fashion to **7**),[14] as the primary step in multi-step procedures to prepare a range of organic molecules typified by **12**–**21** have been described (Fig. 1).[15] In many cases, several reagents supported on ion-exchange resins, and a number of simple resins themselves, were employed to achieve the desired conversions. In some cases, Ley has developed new routes to existing resins such as polymer supported cyanoborohydride,[16] whilst in others he has described modifications to the application of previously well-documented reagents in novel circumstances. Overall, the application of **7** and later the stronger permanganate derivative, demonstrates that oxidation reactions can be carried out cleanly and efficiently with these reagents supported on ion-exchange resins. Such reactions can often be carried out with a catalytic amount of oxidant, and with efficient recycling of the spent resin upon completion of the oxidative procedure, and avoid the often tedious workup procedures associated with potassium permanganate in particular.

3 Supported reducing agents

3.1 Borohydride and cyanoborohydride

Borohydride supported on a suitable ion-exchange resin, **22**, was first described by Gibson and Bailey in 1977 (Fig. 2).[17] They prepared the reagent from the chloride forms of Amberlyst A26, Amberlite IRA-400, Amberlite IRA-401S and the free base of Amberlite IRA-938.[18] The activities of these materials in the reduction of benzaldehyde were investigated, and the authors concluded that Amberlyst A26 was the resin of choice for supporting the reagent, if a rapid conversion of the carbonyl to the alcohol was desired.

The application of a borohydride reagent prepared on the anion exchange resin AG1-X8[19] in the chemoselective reduction of aldehydes and ketones serves to illustrate the potential usefulness of such reagents in selective organic synthesis (Table 3).[20] These results demonstrate that the resin employed was remarkably selective between aldehydes and ketones (entries 1–3), and that the rate of reduction was faster in methanol than in ethanol (*cf.* entries 1 and 3). Interestingly, the reagent is also selective between different types of aldehyde, with aromatic substrates being reduced much more rapidly than aliphatic materials (entry 3). A distinct selectivity can also be seen between aromatic aldehydes possessing electron donating groups, and those with electron withdrawing moieties attached, the latter being reduced more rapidly (entry 4). Lastly, the reagent is also selective between cyclic and acyclic ketones (entry 5), with the cyclic material being reduced preferentially, a fact which is opposite to that normally observed with selective reducing agents.[21] Colorimetric studies on the reaction residues after solvent removal confirmed that no boron was present, thus demonstrating the stability of the resin towards reagent and by-product leaching.

The report[22] of a selective reduction of α,β-unsaturated carbonyl compounds to the corresponding unsaturated derivatives, employing resin **22** prepared on Amberlite-400, demonstrates yet another potentially interesting selectivity of these materials. In this study, the rate of reaction was found to be dependent upon three factors: the polarity of the solvent, the amount of resin added, and the steric hindrance around the carbonyl site. The overall yield of the reaction was however found to be independent of the amount of resin added, and the prolonged reaction times found to be requisite in non-polar solvents did not compromise the purity of the product. Amberlyst A26 was also investigated in this study, and under identical reaction conditions it was found to facilitate the reductions in approximately one third of

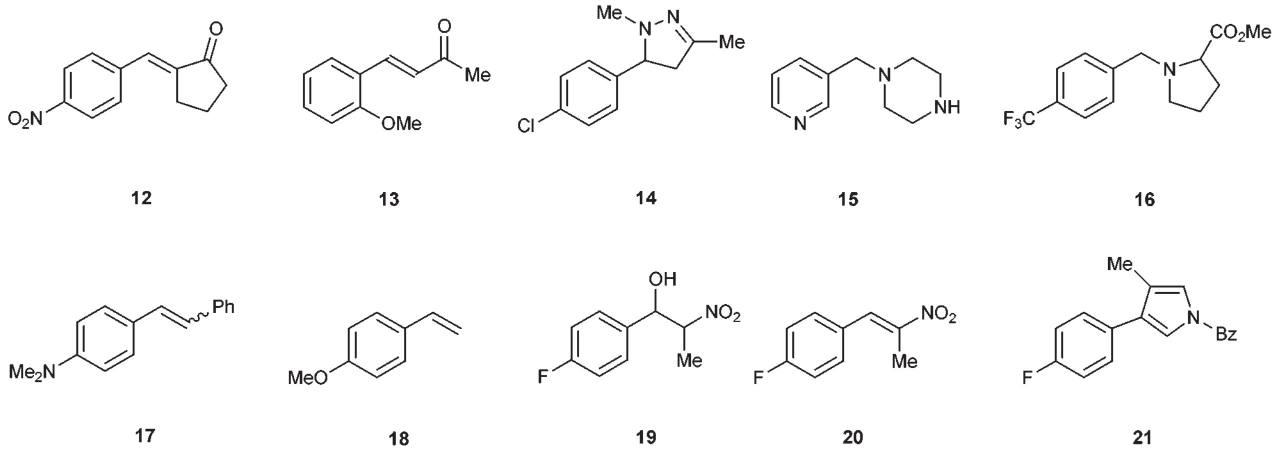
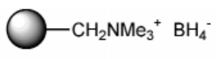


Fig. 1 Examples of molecules synthesised by routes employing **7**.

Table 3 Representative examples of the selective reduction of carbonyl compounds with borohydride resin **22**

Entry	Carbonyl mix	Solvent	*t*/h	*T*/°C	Reduction (%)^a
1	benzaldehyde	EtOH	5	−25	99
	acetophenone				1
2	benzaldehyde	EtOH	5	−25	100
	heptan-2-one				0
3	benzaldehyde	MeOH	1	−10	98.5
	hexanal				6.5
4	*p*-nitrobenzaldehyde	MeOH	1	−10	92.3
	p-methoxybenzaldehyde				5.2
5	cyclohexanone	MeOH	9	0	95.1
	heptan-4-one				3.9

^{a} Determined by GLC with reference to an internal standard.

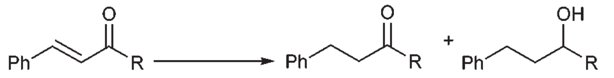


22

Fig. 2 Generalised formula of borohydride resin.

the time previously required, thus confirming the original rate experiments conducted by Gibson.[17] Table 4 contains examples of the reactions accomplished in this manner.

A similar study, employing borohydride prepared on Seralite SRA-400,[23] was described by Nag *et al.*[24] They reported that **22** prepared on this base matrix was effective in reducing the ethylenic linkage in α,β-unsaturated cyanoacetates, mono- and diacetates and ketones. When α,β-unsaturated aldehydes were subjected to the reagent however, total reduction to the saturated alcohols was observed. For example, the reduction of ethyl cinnamate **23** afforded an 80% yield of the unsaturated alcohol **24**, and none of the fully saturated material **25**, whereas cinnamaldehyde **26** gave none of the target alcohol **27**, instead giving solely 3-phenylpropan-1-ol **28** (Scheme 6). These results contrast sharply with those in Table 4, where both α,β-unsaturated aldehydes and ketones were reduced to their corresponding alcohols without concomitant reduction of the double bond.



23 R = Et
26 R = H

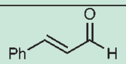
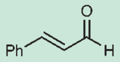
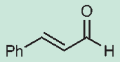
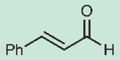
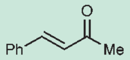
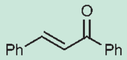
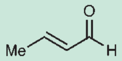
24, 25 R = Et 80 : 0
27, 28 R = H 0 : 95

Scheme 6 *Reagents and conditions*: **22**, dioxane or EtOH, 60 °C, 2 h.

From the results obtained using these resins, it is apparent that judicious choice of the polymeric support is required when dealing with unsaturated carbonyl compounds, since two polystyrene resins with different properties give opposing results. These differences may be due to the physical nature of the resins (macroreticular or gel-type), active surface area, porosity, initial pH, method of preparation of the reagent and total exchange capacity of the resin.

The reduction of conjugated double bonds in α,β-unsaturated nitroalkanes **29** with **22** on Amberlite IRA-400 to furnish nitroalkanes **30** has also been reported (Scheme 7).[25] Examples of the generality of this reaction are contained within Table 5. The relatively high yields for this process were reported as unoptimised in this study, but no reduction of the nitro functionality was noted. The fact that no boron was present in the reaction

Table 4 The selective reduction of α,β-unsaturated carbonyl compounds with **22**

Entry^a (%)	Substrate	Solvent	*t*/h	Yield
1		MeOH	1.5	99
2		MeOH	0.25	99
3		benzene	60	99
4		EtOH	3	99
5		MeOH	4	90
6		MeOH	28	89
7		MeOH/H$_2$O	0.25	85

^{a} Entries 1,3,7 employed 0.5 g of resin per mmol of substrate, entries 2,4–6 1 g mmol^{-1}.

29 **30**

Scheme 7 *Reagents and conditions*: **22**, MeOH, 20 °C, 1 h.

Table 5 Reductions of a,b-unsaturated nitroalkanes **29** to nitroalkanes **30** with **22**

Entry	R	R^1	R^2	Yield (%)
1	-(CH$_2$)$_4$-		H	80
2	C$_6$H$_5$	H	CH$_3$	81
3	*p*-BrC$_6$H$_4$	H	CH$_3$	80
4	*o,m*-(C$_2$H$_5$O)$_2$C$_6$H$_3$	H	CH$_3$	83
5	C$_{10}$H$_7$	H	H	79
6	2-thienyl	H	CH$_3$	78
7	5-bromo-2-thienyl	H	CH$_3$	82

products was confirmed by NMR spectroscopy, demonstrating that no reagent leakage from the support was occurring.

Kabalka *et al* have reported the clean conversion of aryl azides **31** into aryl amines **32** and of aryl sulfonyl azides, **33** into aryl sulfonamides **34** by employing borohydride resin (Fig. 3).[26] In the twenty-three examples cited, the molar ratio of reagent loaded on the resin to azide was fixed at 1.25 : 1, and yields of >93% were achieved in all cases where a reaction occurred. The following points can be ascertained from the reactivity of a number of substrates:

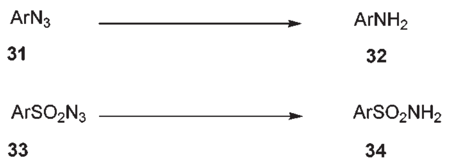


Fig. 3 The reduction of azides utilising resin **22**.

(i) Electron withdrawing groups on the aryl ring facilitate the reaction at room temperature, whilst electron rich substrates required the use of elevated temperatures, and longer reaction times.

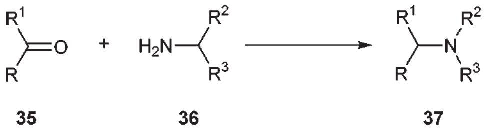
(ii) The rate of reactivity of the three isomeric nitroaryl azides decreased in the order *p*-nitrophenyl azide > *o*- > *m*-. The former requires 2 hours in methanol at room temperature, the latter takes 11 hours under the same conditions.

(iii) Polar solvents were vital for the success of the reaction. The reduction of *p*-toluenesulfonyl azide was complete in 30 minutes in methanol at room temperature, but took 2 hours in ethanol, and gave no reaction whatsoever in either benzene or hexane.

(iv) The reagent did not reduce alkyl azides, even in refluxing methanol.

These results are in direct agreement with those previously discussed for the reduction of carbonyl and α,β-unsaturated carbonyl compounds, indicating that certain reaction conditions, *i.e.* a polar solvent and electron-deficient substrates, are desirable in order to achieve rapid conversions.

Borohydride exchange resin has been shown to be significantly more stable in acidic media than sodium borohydride itself, and this property has been exploited to allow it to be employed in the reductive amination of aldehydes and ketones, conversions which are normally achieved using sodium cyanoborohydride (Scheme 8).[27] The authors cite twenty-six examples of the reaction outlined in Scheme 8, employing an array of six carbonyl compounds **35** and seven amines **36**, to prepare products **37**. In all cases, GC analysis confirmed the presence of the desired adducts, although these were not always isolated. Table 6 contains selected examples of the reaction to indicate the scope and limitations of the system. Generally, under identical reaction conditions, the aldehydes studied were found to react faster than the ketones, and gave higher product yields. The majority of amines which were tested reacted well, but both aniline (entry 2) and diethylamine (entries 3 and 6) afforded lower product yields, presumably due to electronic and steric reasons respectively. Ammonium acetate was found to be effective as a source of ammonia, although in all cases, the secondary, and not the primary amines were isolated from the mixture (entry 4).



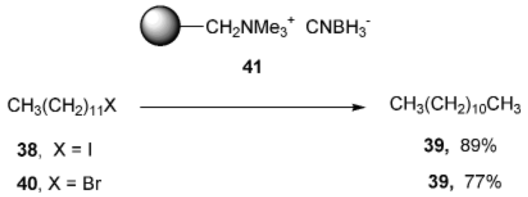
Scheme 8 *Reagents and conditions*: i Et_3NHCl, **22**, EtOH, RT; ii NaOH.

Table 6 Reductive aminations of carbonyl compounds utilising borohydride resin **22**

Entry	R	R^1	R^2	R^3	*t*/h	Yield^{a} (%)
1	C_5H_{11}	H	C_6H_{11}	H	1	98 (89)
2	C_5H_{11}	H	C_6H_5	H	1	53 (—)
3	C_5H_{11}	H	C_2H_5	C_2H_5	1	93 (86)
4^{b}	C_5H_{11}	H	H	H	0.5	99 (90)
5	C_6H_{11}	H	C_2H_5	H	1	94 (85)
6	C_6H_5	H	C_2H_5	C_2H_5	1	65 (58)
7	$–(CH_2)_6–$		$–(CH_2)_4–$		1	96 (89)
8	C_5H_{11}	CH_3	CH_3	CH_3	3	78 (68)
9	C_6H_5	CH_3	$–(CH_2)_4–$		6	53 (—)

[a] % Analytical yield, isolated yield in parentheses.
[b] Ammonium acetate (10 eq.) added, yields quoted are those of the secondary amine.

These results compare favourably with those obtained by Hutchins *et. al.* when using supported cyanoborohydride **41**.[16] The material, which was prepared on Amberlyst A26, was also employed to effect the conversion of pyridinium bromides into tetrahydropyridine derivatives, dimethylation of amines, the reduction of ketones, and the dehalogenations of **38** and **40** to alkane **39** in good yields (Scheme 9). The time taken to achieve the desired conversions was reported to be greater than that required with standard solution phase cyanoborohydride, presumably due to less efficient substrate/polymer contact, but the reactions were extremely clean. The authors' report that the toxic cyanide residues associated with free sodium cyanoborohydride are retained on the Amberlyst resin, and not extracted into either aqueous or organic media. They also demonstrate that the resin can be regenerated by a simple washing procedure, as in the case of borohydride resin **22**.



Scheme 9 *Reagents and conditions*: **41**, HMPA, 90 °C, 8 h.

The application of borohydride resin to reactions analogous to those in Scheme 9 has been reported,[28] as have the transformations of aliphatic acid chlorides into aldehydes.[29] These latter examples demonstrate still more potential uses for the resin, which have not been fully capitalised on.

The application of resin **22** in conjunction with a variety of nickel,[30] copper[31] and palladium[32] salts, to achieve selective functional group interconversions, is a rapidly expanding area within the field of supported reagents. The actual reactive species in the majority of these cases are the metal borates, which are formed on the surface of the resin, which also provides hydride to drive the reaction. Representative examples of the application of these systems can be found in Table 7.

In many of the cases listed in Table 7, there is no mention of the presence of, or indeed lack of, the metal salt in the final product. Indeed, in some cases an aqueous workup is performed to clean up the reactions prior to product identification. These factors, coupled with the fact that in none of the examples listed is

Table 7 The use of **22** in conjunction with metal salts

Entry	Metal	Reaction			Yields (%)	Ref.
1	Ni	RNO_2	→	RNH_2	91–98	28(*a*)
2	Ni	RX	→	RH	70–100	28(*b*)
3	Ni	ArCH=NOH	→	$ArCH_2OH$	65–90	28(*c*)
4	Ni	$RC{\equiv}CR^1$	→	(Z)-RC(H)=(H)R^1	98–100	28(*d*)
5	Ni	ArCHO	→	$ArCH_3$	80–98	28(*e*)
6	Cu	$RCH{=}CHCO_2R$	→	$RCH_2CH_2CO_2R$	90–99	29(*a*)
7	Cu	$R_3N{-}O$	→	R_3N	61–98	29(*b*)
8	Pd	RSAc	→	RSH	90–96	30

there any reference to the resin either being re-cycled or re-used, make these applications of less interest than many of those previously discussed. The fact that a variety of reactions can be approached in this manner with excellent yields does however demonstrate further potential uses for more complicated reagents supported on ion exchange resins.

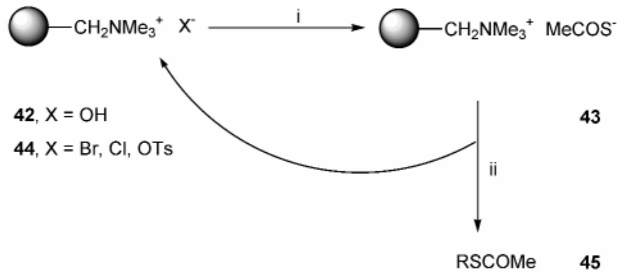
3.2 Miscellaneous reducing agents

The preparation of dithionite anions on a variety of Amberlyst cationic exchangers has been described.[33] The materials were employed to accomplish the reduction of a variety of aldehydes and ketones to the corresponding alcohols, using benzene as the reaction solvent. The results of the study were however disappointing, with yields lower than those observed for **22** for identical transformations with, for example, benzaldehyde only being reduced in 53% yield (*cf.* Table 1 entry 1, 99%).

There have also been isolated reports of the use of hydridocarbonylferrate anions,[34] phosphine–copper(I) cyanoborohydride,[35] and aluminium hydride[36] supported on suitable polymeric ion-exchange resins to perform functional group reductions, but these materials do not appear to have found widespread applications at the present time.

4 Sulfur and selenium

The immobilisation of thioacetic acid **46** on Amberlyst A26 (hydroxy form) **42** has proved useful for the clean conversion of alkyl halides **47** into thioacetates **45** (Scheme 10).[37] The reactions were performed under a variety of conditions dependent upon the nature of the substrate, but always with a slight excess of resin **43**; examples of these are outlined in Table 8.



Scheme 10 *Reagents and conditions*: i MeCOSH (**46**), H_2O; ii RX (**47**).

As can be observed from Table 8, the reaction conditions are relatively mild, with alkyl bromides reacting readily at room temperature, whilst chlorides and tosylates require slightly morevigorous treatment (compare entries 1–3). Secondary alkyl bromides (entry 5) require the application of elevated temperatures, but the reaction is clean, with no elimination products being observed. The spent resin **44**, containing halide or tosylate groups, can be efficiently recycled simply by washing with dilute sodium hydroxide solution and treatment with thioacetic acid.

Table 8 The synthesis of thioacetates **45** from alkyl halides **47** with resin **43**

Entry	RX	Conditions[a]	Yield (%)
1	n-$C_8H_{17}Br$	hexane, 20 °C, 2 h	90
2	n-$C_8H_{17}Cl$	hexane, Δ, 2 h	92
3	n-$C_8H_{17}OTs$	benzene, Δ, 2 h	95
4	$C_6H_5CH_2Br$	hexane, 20 °C, 2 h	87
5	n-$C_6H_{13}CH(CH_3)Br$	hexane, Δ, 2 h	90
6	$H_2C{=}CHCH_2Br$	diethyl ether, 20 °C, 2 h	100

[a] Δ refers to the reflux temperature of the chosen solvent

Tamami and Kiasat have recently reported the synthesis of acyl disulfides **50**, using sulfur supported on Amberlyst A26.[38] Reagent **49** was readily prepared from elemental sulfur and the ion-exchanger, and is postulated to contain sulfur as S_2^{2-} units. This material rapidly, and cleanly, converts acid chlorides **48** to the corresponding diacyl disulfides, with no trace of the acyl sulfides being found (Fig. 4). Examples of its scope are contained in Table 9. Since the reactions are performed in non-aqueous media, no hydrolysis of the acyl chlorides occurs, and the products are therefore uncontaminated by carboxylic acids. Sulfur leaching was found to be non-existent, and the resin could be regenerated after use, with the regenerated material being re-used with no decrease in the measured yields.

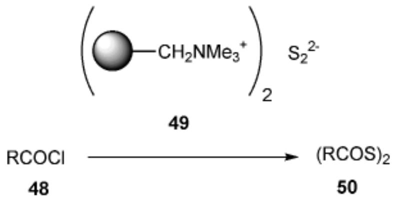
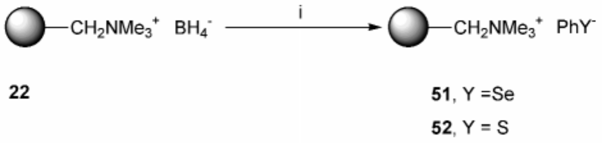


Fig. 4 The conversion of acyl chlorides to diacyl disulfides with **49**.

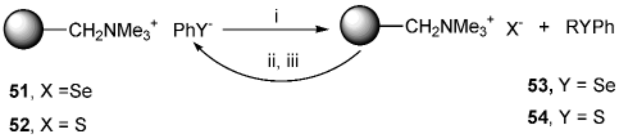
Table 9 The formation of diacyl disulfides **50** with reagent **49**

Entry	**48**, **50**, R =	*t*/min	Yield (%)
1	C_6H_5	20	98
2	p-$CH_3C_6H_4$	30	94
3	p-$NO_2C_6H_4$	50	90
4	o-Cl-C_6H_4	50	94
5	$C_6H_5CH{=}CH$	20	92
6	$C_6H_5CH_2$	20	96
7	CH_3	15	83

The preparation of immobilised phenyl selenide **51**[39] and phenyl sulfide **52**[40] ions on Amberlyst A26 have also been reported, with the materials easily being prepared by reduction of diphenyldiselenide **53** or diphenyldisulfide **54**, with borohydride resin **22**, and gave materials with reagent loads approaching 2 mmol g^{-1} (Scheme 11). The benzoselenolate and benzothiolate ions formed by this procedure are reportedly stable once attached to the resin, although in the case of the latter, the actual structure may not be as simple as that shown in Scheme 11, and is in fact postulated to be a complex mixture of the general formula: $\mathrm{BH}_x(\mathrm{OMe})_y(\mathrm{PhS}^-)_{4-x+y}$. In any event, both resins effectively transfer the chalcogen species to alkyl halides **47**, to afford the corresponding phenylselenides **53** or phenyl sulfides **54** as shown in Scheme 12. Collected representative results for both reagents are outlined in Table 10. As expected, alkyl iodides react more rapidly than the corresponding bromides (compare entries 1 and 2), although isolated product yields are almost identical. Sulfur reagent **52** appears to be less reactive than the analogous selenium derivative under similar conditions (*cf*. entries 5 and 6), although the yields with the former reagent are appreciably higher. The selectivity of bromides over chlorides is also noteworthy, and can readily be seen in entry 7, where an excellent yield of 4-chlorobutyl phenyl disulfide was obtained, due to the higher reactivity of reagent **52** with the bromide terminus of the substrate. Interestingly, although α-bromo esters react cleanly with **51** (entry 8), the authors reported that α-halo ketones only afforded diphenyl diselenide and/or alkyl aryl ketones.

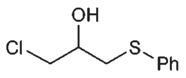


Scheme 11 *Reagents and conditions*: i $(\mathrm{PhX})_2$, EtOH, 0–5 °C, 1 h.



Scheme 12 *Reagents and conditions*: i RX, solvent, 20 °C; ii NaOH; iii $(\mathrm{PhX})_2$, EtOH, 0–5 °C, 1 h.

Reagent **52** was also reacted with epoxides, to furnish β-hydroxy-substituted products. In the case of epichlorohydrin, a 95% yield of 1-chloro-3-(phenylthio)propan-2-ol **55** was obtained, whilst with epibromohydrin, both epoxide ring-opening and bromo-substitution occurred, to yield 1,3-bis(phenylthio)propan-2-ol **56** almost exclusively. These results again indicate the dramatic reactivity difference between alkyl chlorides and bromides in this reaction. As with the majority of the resins so far discussed, the materials can be regenerated after use, simply by following the initial procedure, and employing a stoichiometric amount of either diphenyl diselenide or diphenyl disulfide.



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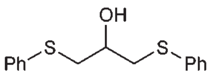

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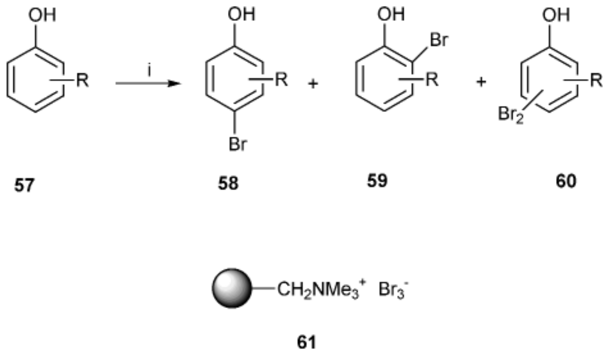
5 Halogens

Tribromide on Amberlyst A26 **61**[41] has successfully been employed in the selective *para*-bromination of substituted phenols **57**.[42] When phenols are brominated using standard reagents, the potential exists not only for the formation of the desired *para*-bromo product **58**, but also to form the *ortho*-substituted material **59** and poly-brominated adducts **60**, with the later two being unwanted and often difficult to remove.

The desired conversion was easily performed, simply by stirring a mixture of the resin with the starting phenol, in dichloromethane in the dark, and monitoring the mixture by GC (Scheme 13). The reaction was applied to a number of phenols, and the results are summarised in Table 11. The yields of the *para*-brominated materials **58** are more than favourable when compared with those obtained by other, often more complex methods. Indeed, the very low levels of poly-brominated compounds **60** measured are greatly superior to other routes tested by the authors. The spent resin can be re-converted to the active tribromide by simply washing with a solution of bromine in a suitable solvent, and no decrease in either yield or reaction selectivity was reported with such regenerated material, indicating that no resin degradation had taken place.



Scheme 13 *Reagents and conditions*: i **61**, $\mathrm{CH_2Cl_2}$, 20 °C, dark.

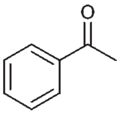
Resin **61** was also employed by Parlow[43] to synthesise α-bromoacetophenone **63** from acetophenone **62**. This material was

Table 10 The reaction of alkyl halides **47** with phenyl selenide and phenyl sulfide resins

Entry	Reagent	RX (**47**)	Product	Solvent (*t*/h)	Yield (%)
1	**51**	n-$\mathrm{C_{10}H_{21}I}$	n-$\mathrm{C_{10}H_{21}SeC_6H_5}$	EtOH (1)	76
2	**51**	n-$\mathrm{C_{10}H_{21}Br}$	n-$\mathrm{C_{10}H_{21}SeC_6H_5}$	EtOH (4)	80
3	**52**	n-$\mathrm{C_8H_{17}I}$	n-$\mathrm{C_8H_{17}SC_6H_5}$	MeOH (6)	96
4	**52**	n-$\mathrm{C_8H_{17}I}$	n-$\mathrm{C_8H_{17}SC_6H_5}$	MeOH (6)	10
5	**51**	$\mathrm{C_6H_5CH_2Cl}$	$\mathrm{C_6H_5CH_2SeC_6H_5}$	EtOH (1)	80
6	**52**	$\mathrm{C_6H_5CH_2Cl}$	$\mathrm{C_6H_5CH_2SC_6H_5}$	MeOH (3)	95
7	**52**	$\mathrm{Br(CH_2)_4Cl}$	$\mathrm{Cl(CH_2)_4SC_6H_5}$	MeOH (3)	96
8	**51**	$\mathrm{C_2H_5O_2CCH_2Br}$	$\mathrm{C_2H_5O_2CCH_2SeC_6H_5}$	$\mathrm{Et_2O}$ (1)	80
9	**51**	$\mathrm{CH_3I}$	$\mathrm{CH_3SeC_6H_5}$	$\mathrm{Et_2O}$ (1)	100

Table 11 The bromination of substituted phenols with **61**

			Yield (%)		
Entry	R	*t*/h	**58**	**59**	**60**
1	H	24	86	7	trace
2	*p*-CH_3O	4	90	7	trace
3	*o*-Cl	24	76	20	trace
4	*o*-CH_3	5	85	trace	trace
5	*m*-CH_3	3	60	trace	8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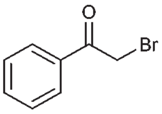

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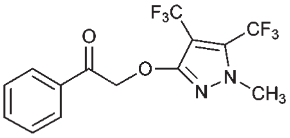

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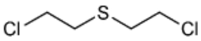

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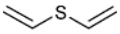

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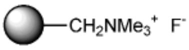

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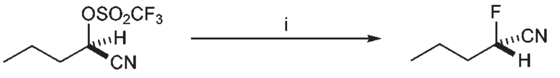
employed in the synthesis of pyrazole **64**, in which all of the synthetic steps were performed using polymer-supported reagents either in sequence, or simultaneously in one pot.

The fluoride form of Amberlyst A26 **67** has also been employed to great effect in the clean removal of silicon protecting groups in carbohydrate chemistry,[44] and in the conversion of gaseous sulfur mustard **65** to divinyl sulfide **66**.[45]

More interestingly, **67** has been employed to transform protected uridines **68** into either 2,3′-anhydro-2′-deoxyuridines **69**, or 2′,3′-didehydro-2′,3′-dideoxyuridines **70** (Scheme 14).[46] The authors report that either **69** or **70** can be selectively formed, simply by judicious choice of reaction conditions, and that they can be isolated in yields of up to 90% for the most favourable substrates. The reactions were also reported to be extremely clean, with little or no side-product contamination, and with the materials being released from the resin by the simple addition of methanol. There is however no report of the resin being re-cycled after use.

In 1993, Stelzer and Effenburger reported that **67** could be employed to fluorinate 2-(sulfonyloxy)pentanitriles.[47] The conversion of the trifluoromethyl derivative **71** to fluoropentanitrile **72** demonstrates the salient feature of this reaction (Scheme 15).



71 **72**

Scheme 15 *Reagents and conditions*: i **67**, CH_2Cl_2, 0 °C, 18 h.

The reaction proceeds smoothly, with absolute inversion of the stereochemistry at the reactive site, affording **72** in 62% yield and with 92% enantiomeric excess, starting from enantiopure **71**. The use of *p*-tolylsulfonates in this reaction was investigated, but despite prolonged reaction times (156 h) and elevated temperatures (45 °C) **72** was only isolated in 5% yield.

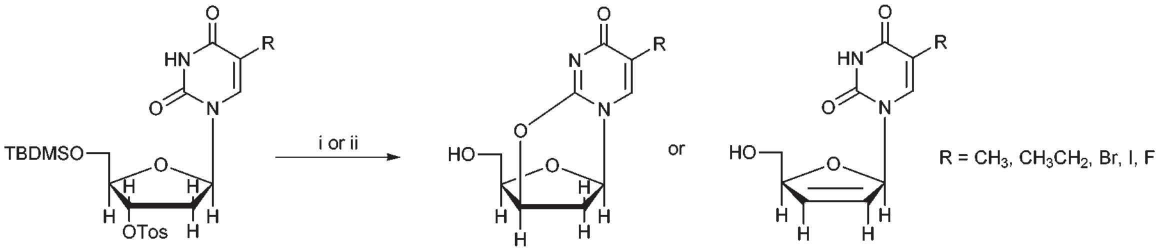
A similar stereochemical inversion had previously been observed for the conversion of the methanesulfonate of (−)-(*R*)-octan-2-ol into (+)-(*S*)-2-fluorooctane.[48] In that study, an identical trend was observed in the fluorination of steroidal alcohols, methanesulfonates and tosylates, with both high yields and enantiomeric excesses being observed when **67** was employed as the source of fluoride.

A caveat with **67** is that in none of the examples in which it was used, was it regenerated. Such a step is however feasible, by treatment of the spent resin with a source of F^-, although workers will presumably wish to avoid the use of toxic materials such as HF.

6 Conclusions

There are many reactions in which the application of reagents supported on ion-exchangers has been shown to be as efficient as or, in some cases, more efficient that the corresponding solution phase chemistries. Areas such as the oxidation and reduction of functional groups have received a great deal of attention, and many interesting and useful applications have been reported in these areas. Elsewhere, there is continued growth in the use of suitably functionalised resins in complex organic synthesis, with multi-step procedures in which no work-up is involved prior to product isolation being reported.

The advantages of ion-exchange resins chiefly lie in the fact that they require no specialised polymer synthesis and purification techniques, thus rendering them simple to use. This, coupled with their physical stability, compatibility with a wide range of solvents including, in some cases, water and their toleration of a great num-



68 **69** **70**

Scheme 14 *Reagents and conditions*: i **67,** THF, 0 °C, 3 h; ii **67,** THF, 70 °C, 36 h.

ber of reaction conditions and reagents, makes them ideal as platforms on which to build reagents to perform synthesis. Where problems may arise due to interference of the polymer backbone, new polymers must be sought with a view to increasing the scope of the reagents previously described, and with a view to the preparation of even more reagents.

Overall, the fact that the resins can often be recycled, and that they are readily removed by filtration, thus leading to lower amounts of waste associated with complicated and often tedious work-up and purification procedures, means that they potentially have a much wider rôle to play in the future of green chemistry.

7 Acknowledgements

The author is grateful to the members of staff at the Bioprocess Division of Millipore (Consett, UK) and to Dr Patrick Steel (University of Durham, UK) for help and advice.

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5 Amberlyst and Amberlite are both trademarks of Rohm and Haas Co. Amberlyst A26 is a macroreticular resin, with a nominal exchange capacity of 1.0 mmol ml^{-1} wet, whilst Amberlite IRA 904 is a gel-type polystyrene resin with an exchange capacity of 0.6 mmol ml^{-1} wet. They are both available from Fluka.

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Paper 9/05804D

A low waste route to large scale enzymatic resolution

of a chiral dopant of ferroelectric liquid crystals

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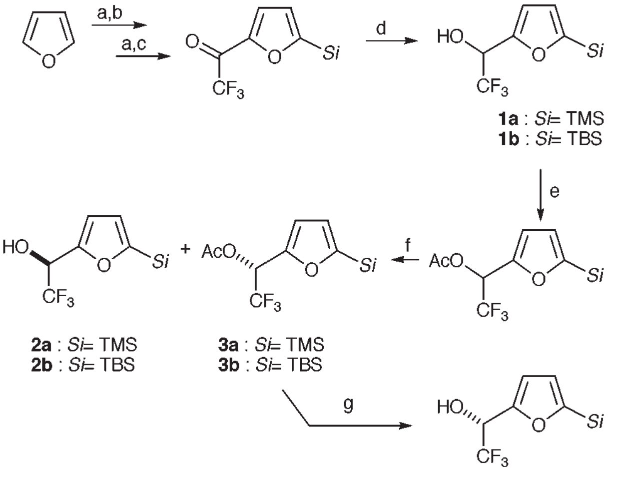
Summary

A new large scale route to enzymatic resolution of a chiral dopant of ferroelectric liquid crystals, in the absence of any organic medium or water, is described. After removal of the catalyst in this low waste process, no further operation is required before direct distillation.

Introduction

The challenge in chemistry to develop practical processes, reaction media, conditions and/or uses of materials based on the idea of green chemistry is one of the most important issues in scientific society.[1] In particular, studies of zero waste routes and/or reusable catalysts for improved selectivity and energy minimisation have brought us closer to achieving the societal, economic and environmental goals that are required now and in the future. While optically active fluorine-containing molecules have been recognized as an important class of materials because of their interesting characteristics and potential applicability in optical devices such as ferroelectric (FLCs) or antiferroelectric liquid crystals (AFLCs),[2] a practical synthetic route to a furanol leading to fluorinated 6-deoxy sugars, key chiral dopants, has been found based on enzymatic resolution in organic or aqueous media. These processes generate waste containing solvent media and enzyme. For example, in the *aqueous medium* shown in Scheme 1, excellent resolution of both esters **1a** and **1b** was realized by lipase PS (*Pseudomonas cepacia*, Amano Pharmaceutical Co., Japan) to give chiral alcohols **2a** and **2b** in 98 and >99% ee at 49 and 48% conversion, respectively. The corresponding enantiomers both with 94% ee were also obtained after hydrolysis of the recovered chiral acetates **3a** and **3b**, the optical purity of which would be readily improved by subjecting them to further enzymatic hydrolysis. However, in this process, the reaction mixture must be maintained at about pH 7 by titration with 1 M NaOH (aq).[3] Further, when the conversion was found to reach about 50%, flocculant (P-713, Daiichi Kogyo Seiyaku, Japan) was added and the whole mixture was filtered through Celite-545 to remove the enzyme. Based on the above operations, the separation of enzyme and products is not easy on the large scale, and the enzyme is not reusable. Moreover, this process, as shown in Table 1, generates at least 20–30 l of waste containing water and organic solvents (for extraction) per 1 kg of product.

In contrast, as shown in Table 2 and Scheme 2, enzymatic esterification of **1a** in *organic solvent* was realized by using Novozym 435 (*Candida antarctica*, Novo Nordisk Co., Ltd.) to give chiral ester **3c** in 93 (in $CHCl_3$) and 97% ee (in CCl_4) at 48 and 49% conversion, respectively. In both cases the corresponding enantiomer (93 and 92% ee respectively) was also obtained. However, in systems with organic solvents other than CCl_4 and



Scheme 1 (a) *n*-BuLi, THF; (b) *Si*-Cl; (c) CF_3CO_2Et; (d) $NaBH_4$; (e) AcCl, pyridine; (f) lipase PS (*Pseudomonas cepacia*, Amano Pharmaceutical Co., Japan), H_2O; (g) K_2CO_3, MeOH. (TMS = trimethylsilyl, TBS = *tert*-butyldimethylsilyl).

Green Context

The enzymatic resolution of racemates requires excellent selectivity, and the ability to recover and reuse the enzyme. Typically, enzymic systems are run in water, but many are also carried out in organic solvents. This contribution describes a resolution which takes place with excellent enantioselectivity, without the need for either aqueous or organic media. This no-solvent approach allows easy separation of the enzyme, which can be used without loss of activity or selectivity, and simple isolation of product by distillation. It is thus superior to routes based on aqueous systems or organic solvents, both of which are briefly compared in the paper. *DJM*

Table 1 Enzymatic resolution of the racemic acetate of furanol (**1a**) in water

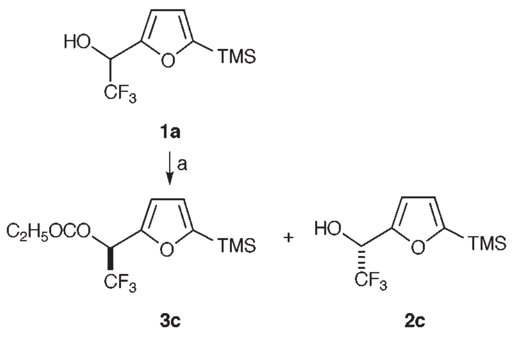
Racemic acetate[a]/g (mmol)	Lipase PS/g	Chiral alcohol **2a**[c]/g (mmol)	Chiral acetate **3a**[d]/g (mmol)	Recovered material balance (%)
62.4 (218)	30	21.6 (90.5)	26.0 (93)	83
67.2 (240)	25	25.3 (106)	27.7 (94)	85
73.6 (263)	26	27.5 (114)	31.5 (111)	87
90.4 (323)	32	31.4 (131)	40.7 (143)	85
199 (711)[b]	36	77.8 (327)	84.5 (302)	88

[a] Water (1800 ml) was used in the above system. All reactions were stopped at 50% hydrolysis ratio at 40 °C. [b] Water (3000 ml) was used in this case. [c] Optical purity >96% ee. [d] Optical purity >94% ee.

Table 2 Enzymatic esterification in organic solvent[a]

			Optical purity (% ee)	
Organic solvent	Time/h	Conversion (%)	Ester **3c**	Alcohol **2c**
CH_2ClCH_2Cl	18	44	98	79
CCl_4	26	49	97	92
CH_3Cl	41	48	93	93
$CHCl_3$	168	42	>99	72
CH_3CN	168	42	>99	72
$PhCH_3$	168	33	96	46

[a] Alcohol (1 g, 4.2 mmol), vinyl propionate (6.3 mmol), organic solvent (5 ml), enzyme (0.1 g, *Candida antarctica*), reaction temperature 35 °C.



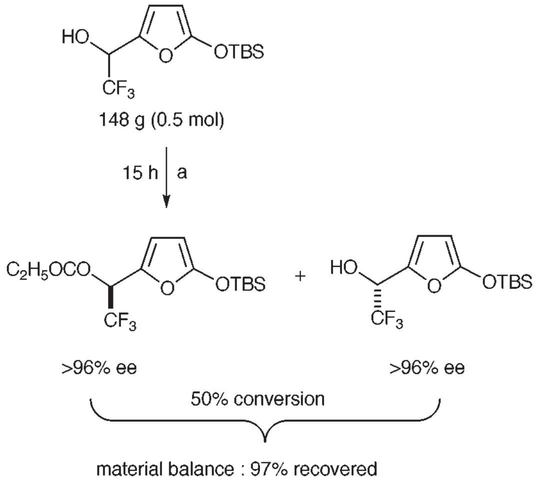
Scheme 2 (a) Vinyl propionate, Novozym 435 (*Candida antarctica*, Novo Nordisk Co., Ltd), organic solvent.

$CHCl_3$, the recovered alcohol is not obtained in good optical purity. In the next stage, we examined a large scale process containing substrate (**1a**, 910 g, 3.82 mol), vinyl propionate (573 g, 5.73 mol), enzyme (*Candida antarctica*, 191 g) and CCl_4 (2500 ml) for 10 h at 50 °C, giving the corresponding ester (1.81 mol, >94% ee) and recovered furanol (1.70 mol, >95% ee) after 52% conversion with 92% recovered material balance. This large scale process was also found to generate at least 5–10 l of waste which contains CCl_4, water and organic solvents (for extraction) per 1 kg of product. Moreover, chloromethane and carbon tetrachloride are not inherently safer chemicals.[4]

Results and discussion

We have thus developed a third version of this system which can be carried out on a large scale.

The new large scale process is simpler and safer. It is based on the enzymatic esterification of furanol without an organic medium or water and involves: a 'zero waste' route: a reusable catalyst: after removal of the catalyst, no further operation is required before direct distillation of the products. This process, involving furanol (148 g, 0.5 mol), vinyl propionate (75 g, 0.75 mol) and Novozym 435 (*Candida antarctica*, 30 g), was carried out for 15 h at room temperature, giving the corresponding ester (>96% ee) and recovered furanol (>96% ee) after 50% conversion with 97% recovered material balance (Scheme 3). Further, recycling of the enzyme and vinyl propionate (21.5 g, 0.215 mol) were investigated from both environmental and economic points of view. Successive reuse of the recovered enzyme upon filtration and excess vinyl propionate in the same reaction without further purification resulted in product yields as high as those obtained in the first cycle.



Scheme 3 (a) *Candida antarctica* (30 g, Novo Nordisk Co., Ltd.), vinyl propionate (75 g).

The preparation of 6-deoxy-6,6,6-trifluorosugars was achieved by ring-opening and recyclization of butenolides which were constructed by oxidative transformation of the corresponding furanol, after derivatization into their lactol forms,[5] and then ferroelectric liquid crystals were synthesized *via* the six-membered ring lactols as the chiral intermediate.[6]

Thus it is now possible to achieve excellent enantioselectivity without organic or aqueous media, with a simple work-up procedure and using a recyclable catalyst.

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Paper 9/05805B

Heterogeneously catalysed hydrolytic decomposition of CFCs

How to deal with CFCs still deposited in refrigerators and foams

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Summary

The hydrolytic decomposition of dichlorodifluoromethane (CFC-12) on modified zirconium oxide surfaces and on charcoal has been studied. The reaction was carried out under flow conditions at 450 °C. Complete CFC-12 conversion was obtained by employing a molar excess of water in the gas phase which depresses the formation of poisoning zirconium oxofluoride phases. These phases are responsible for the formation of unwanted monochlorodifluoromethane (CFC-13). The long-term stability of the catalysts was found to depend strongly on the CFC concentration in the gas phase. The lower the CFC concentration, the better the catalyst stability and catalytic activity. Pure charcoal can also be used as a catalyst for CFC hydrolysis. However, charcoal, owing to its reductive nature, may result in the formation of unwanted by-products and, thus, cannot be considered either as a serious catalyst nor as a suitable support.

Introduction

Chlorofluorocarbons (CFCs) have been used as refrigerants in freezers, refrigerators, and in air-conditioning units in automobiles and buildings. As blowing agents, they were used in making both rigid foam in items such as foam ice chests and fast-food boxes, and flexible foam in furniture cushions and foam pillows. Because of this, CCl_2F_2 (CFC-12) and CCl_3F (CFC-11) are the most widely produced CFCs and are still present in many foams and refrigerants. Because they are very stable, volatile and chemically inert, once released into the atmosphere they are very long-lived. For example, the atmospheric lifetime of CCl_2F_2 is estimated to be 116 years. CFCs are sources of stratospheric chlorine and as such perturb the O_3/O_2 equilibrium.

The need to replace environmentally damaging chlorofluorocarbons (CFCs) led to establishing a production of non-ozone depleting hydrofluorocarbons (HFCs). According to the Montreal and London protocols, the production and usage of CFCs has been stopped in industrial countries and will be stopped by 2010 in developing countries. Therefore, it is required that the supply of CFCs still held in industrial and developing countries be destroyed or, even better, converted to useful, environmentally-friendly chemical feedstocks.

Converting CFCs to useful chemical reagents or feedstock is without any doubt the best approach. By hydrodechlorination, a CFC can be converted to a useful HFC as shown for CFC-12 which can be converted to HFC-32 [see eqn. (1)]

$$CCl_2F_2 + 2H_2 \rightarrow CH_2F_2 + 2HCl \qquad (1)$$

However, this reaction requires a suitable metal catalyst, like palladium or platinum.[1–6] Although excellent laboratory methods have been developed which could be feasible for CFC removal from gas streams after condensation, scale-up is likely to present economic and technical difficulties.

Several alternative approaches have been proposed such as incineration,[7] UV or ultrasound treatment,[8,9] use of chemical reagents,[10] or supercritical water and high temperature plasma. However, incineration of CFCs is the only industrial method used to destroy CFCs. Unfortunately, this process is energy intensive and, if not properly performed, can result in the release of toxic products. An alternative approach to incineration is the catalytic oxygenation of C_1 and C_2 CFCs by means of O_2 and/or H_2O to give CO_2 over acidic oxide catalysts.[11–20] A variety of catalysts, zeolites, TiO_2, ZrO_2 and V_2O_5, have been reported. $ZrO_2(PO_4)$ and V_2O_5, for example, are particularly active. Temperatures above 500 °C are required, and catalyst deactivation due to metal fluoride formation is a disadvantage. Therefore,

Green Context

The subject matter of this article is the development of a new chemical process which leads to the reduction in the environmental impact resulting from the use of chlorofluorocarbons (CFCs) in refrigerant and other systems. CFCs are still widely used. In sealed systems (*e.g.* refrigeration), they present little hazard. It is only when the equipment has reached the end of its working life that a risk assessment must be undertaken. Any process for CFC removal must take into account the realities of the situation, *e.g.* the quantity of material (small in a single refrigeration unit, but large if many units are to be destroyed), skill of those undertaking the operation, economic factors, *etc.* Catalytic destruction is one of the viable methods providing the process does not result in the emission of other ozone-depleting chemicals. This process provides a method which fulfils that objective. Other methods involve the high temperature incineration of CFCs (with a very high energy usage—in itself generating carbon dioxide), and hydrolytic decomposition at *ca.* 450 °C, requiring a catalyst and low CFC concentrations in the reactor. Hydrodechlorination, which could lead to useful hydrofluorocarbons, is possible on a laboratory scale but is not yet ready for scale-up. ***DJM***

oxide catalysts are more suitable for the removal of CFCs from dilute gas streams, rather than for large quantities of CFCs. It should also be noted that such processes are not entirely benign from an environmental standpoint. However, hydrolytic decomposition of CFC-12 and CFC-11 [*cf*. eqn. (2)], both contained in gas streams from refrigerant recovery in concentrations of about 0.5 vol%, presents an interesting alternative to the high temperature incineration. The advantage of such a process would be prevention of cost and energy intensive condensation steps.

$$CCl_2F_2 + 2H_2O \rightarrow CO_2 + 2HCl + 2HF \qquad (2)$$

The reaction is exothermic, but kinetically hindered. Therefore, a suitable catalyst and elevated temperatures are needed.

On the basis of former mechanistic investigations,[19] it was proved that Lewis acidic sites dominant on the surface of the catalyst are important sources of competitive dismutation reactions which result in the formation of higher fluorinated derivatives [eqn. (3)].

$$2CCl_2F_2 \rightarrow CCl_3F + CClF_3 \qquad (3)$$

On the other hand, it is well known that the stability of a CFC increases with the amount of fluorine atoms in the molecule. $CClF_3$ formed *via* dismutation is more stable than CFC-12 itself. Hence, $CClF_3$ can not completely be destroyed under the reaction conditions. Lewis acid centres are generally produced when an oxidic catalyst becomes fluorinated.[21] Therefore, oxides of metals which form non-volatile fluorides, easily hydrolysed in the presence of water, are potential candidates as *hydrolysis catalysts*. Under such circumstances, the formation of Lewis acid metal fluorides can be suppressed by a water reach gas phase (a gas phase containing a critical concentration of gaseous water). Based on this finding, sulfated zirconia was found to be an excellent heterogeneous catalyst for the hydrolysis reaction [eqn. (2)].[20] Here, we report on the dependence of the hydrolysis reaction on the reaction conditions, such as the water to CFC ratio, the CFC partial pressure, and the long term stability of the catalysts.

Experimental

Catalyst preparation

The catalyst precursor zirconium dioxide hydrate was prepared as described in detail previously[20] by hydrolysing $ZrOCl_2 \cdot xH_2O$ with aqueous ammonia until pH 8 was achieved. The precipitate was washed with water and calcined overnight at 110 °C. Characteristic data for the solid zirconia catalyst used are described in detail elsewhere.[20]

Catalytic hydrolysis

The heterogeneously catalyzed hydrolysis of CFC-12 was performed under normal pressure using a gas flow reaction apparatus as described elsewhere.[19] The flow reactor (nickel, length 400 mm, inner diameter 5 mm) was heated with a controllable electric furnace. The catalyst powder was pressed into pellets, subsequently crushed, and sieved to obtain particle diameters of 250–500 μm. For each reaction, a charge of 750 mg of the catalyst was placed in the reactor on a nickel sieve. First, the catalyst was calcined at 500 °C in a pre-dried nitrogen gas flow (flow rate: 19.8 ml min^{-1}) for 1 hour. After calcination, the reaction temperature was adjusted and a constant gas flow containing CFC-12, water vapour, and nitrogen was allowed to pass through the catalyst. The nitrogen and CFC-12 gas flow were kept constant by a gas flow controller (MKS Instruments). The constant nitrogen stream was passed through a thermostated saturator with distilled water. Then, CFC-12 and nitrogen/water were mixed and introduced into the reactor.

The residence time t_r was estimated by subdividing the free volume of the catalyst bed by the gas flow of all components. The analysis of gaseous products (CFCs and CO_2) was performed by GC as described previously.[19] Hydrogen fluoride and chloride were determined by absorption in 1 M NaOH for 2.5 min and were titrated using 0.5 M H_2SO_4. Their concentrations were measured with ion-sensitive electrodes.

Characterization of the catalysts

The catalysts were characterized before and after reaction by the following methods. XRD was performed using a XRD 7 Seiffert-FPM (Cu-Kα). The specific surface areas of the samples were determined by the standard BET method of nitrogen adsorption using an ASAP 2000 system (Micromeritics, maximum experimental error ±1%). The chlorine and sulfur contents were obtained from elemental analysis.

Results and discussion

For a stoichiometric hydrolysis reaction according to eqn. (2), two molecules of water are necessary to destroy one molecule of CFC-12. In Fig. 1, the dependence of the conversion degree of

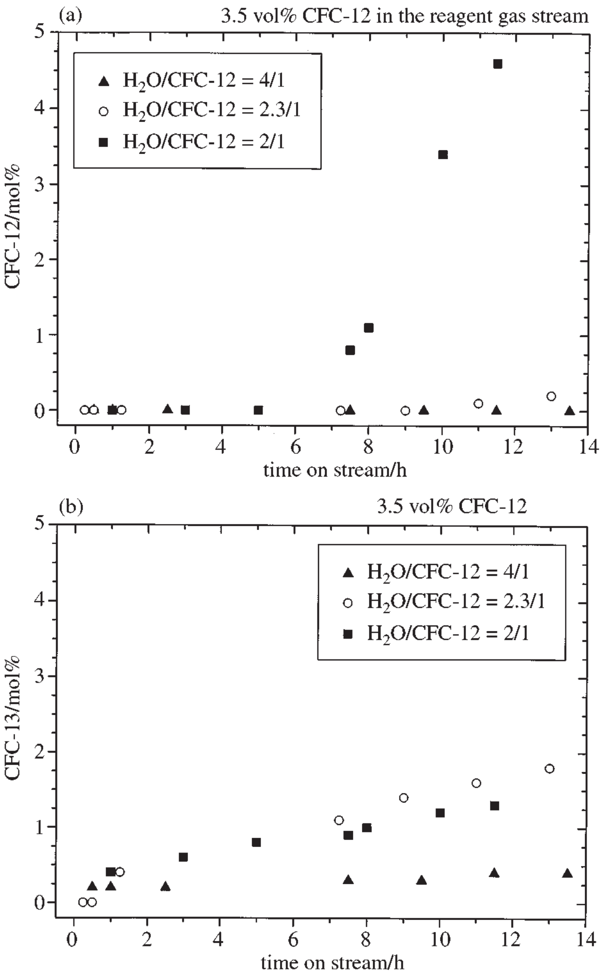

Fig. 1 Relative CFC-12 contents in the product gas after hydrolysis on zirconia as a function of the time on stream for varying water vapour concentrations (reaction temperature: 450 °C, residence time: 2 s): (a) concentration of unconverted CFC-12 (relative to the original amount of CFC-12), (b) concentration of CFC-13 formed (relative to the original amount of CFC-12).

CFC-12 on the molar ratio H_2O/CFC is shown. As can be seen in Fig. 1(a), in the case of a H_2O/CFC molar ratio of 2:1, complete conversion of CFC-12 can only be obtained during the first few hours of time on stream. After about 7 hours, increasing amounts of undestroyed CFC-12 are detectable. Even a slight excess of water in the gas phase (H_2O/CFC = 2.3/1) results in a drastically different situation: as can be seen, a higher molar ratio in the gas phase guarantees almost complete conversion of CFC-12. Under these conditions, the catalyst is still active even after a long time on stream (*cf.* Fig. 2). By employing stoichiometric amounts of water, all of the water is consumed in the CFC hydrolysis reaction [eqn. (2)]. Four molecules of hydrogen halides are formed (2HCl and 2HF) from one molecule of CFC-12. Thus, a product gas phase is formed with a comparatively high concentration of hydrogen halides. As has been shown, HF reacts with the oxide catalyst, particularly Al_2O_3,[19] forming the corresponding fluoride. Thus, a strong deviation due to the uptake of fluoride by γ-Al_2O_3 was observed between the theoretical and actual concentrations of HF in the product gas. Less intensely but similarly, zirconia becomes partially fluorinated forming several oxofluoride phases[20] which are (i) less active in the hydrolysis reaction and (ii) the source of a competitive dismutation reaction under these conditions. In Fig. 1(b), the formation of CFC-13 at H_2O/CFC ratios equal to or near the stoichiometric composition can be seen. Traces of CFC-13 are formed only when employing an excess of water. All zirconia catalysts were found to be slightly fluorinated (XRD showed $ZrOF_2$ phases) after use when incomplete destruction was detected. Thus, excess water in the reaction gas can suppress the formation of metal fluoride phases, which are the reason for the incomplete conversions and unwanted side products. Simultaneously, a slight loss of sulfur in the catalyst was found from elemental analysis of the solid. The decreased sulfur content causes decreased acidity and activity of zirconia and is a further reason for the observed slight decrease in conversion.

Since the chemical stability of the catalyst is strongly attacked by the very corrosive hydrolysis products HCl and HF, the dependence of the conversion on the partial pressure of the CFC was investigated. Fig. 2 displays the results for three representative CFC concentrations. In accordance with expectation, the long term hydrolysis activity decreases as the CFC concentration in the gas phase increases. For instance, with 14.2 vol% CFC-12 in the reagent, a product gas phase will be obtained according to eqn. (2) that contains about 45% hydrogen halides. This is in fact a highly corrosive chemical system. Hence, the same explanation for the loss of catalytic activity can be used as given above, namely the formation of metal oxofluoride phases.

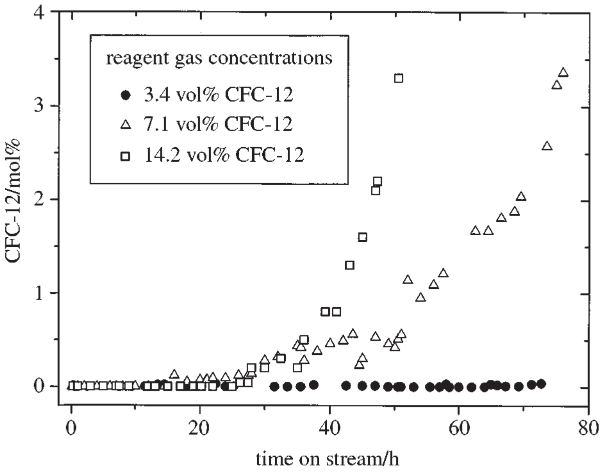

Fig. 2 Relative CFC-12 contents in the product gas after hydrolysis on zirconia for varying CFC-12 concentrations in the reagent gas phase (reaction temperature: 450 °C, residence time: 2 s, n_{water}/n_{CFC-12} = 2.3/1).

However, the most important point for possible technical applications is the long term stability of the catalyst. Since the fluorination of the catalyst seems to be the most poisoning effect, the CFC concentration in the gas phase should be as low as possible. As can be seen from Fig. 3, complete conversion of CFC-12 was still obtained after a time on stream of 120 hours with only 3.5% CFC-12 in the reagent. Unfortunately, with increasing reaction time a slow but permanently increasing amount of CFC-13 can be detected. Even after 120 hours time on stream, complete CFC-12 conversion was found without any CFC-13 formation with CFC-12 concentrations of only 0.5%. This means that, owing to a further reduction of the CFC concentration in the educt gas phase, the HX concentration in the product gas phase has also been reduced resulting in better suppression of any catalyst fluorination. This experiment involved a CFC concentration 7 times lower than that in the experiment described in Fig. 3; therefore one should check the catalytic activity after a time that much longer because the same amount of CFC could have been destroyed. This was however not possible under our conditions. However, it is believed that the effect of a significantly lower concentration of HF in the gas phase strongly influences the catalytic activity, and that under these conditions the catalyst will be even more active than was calculated.

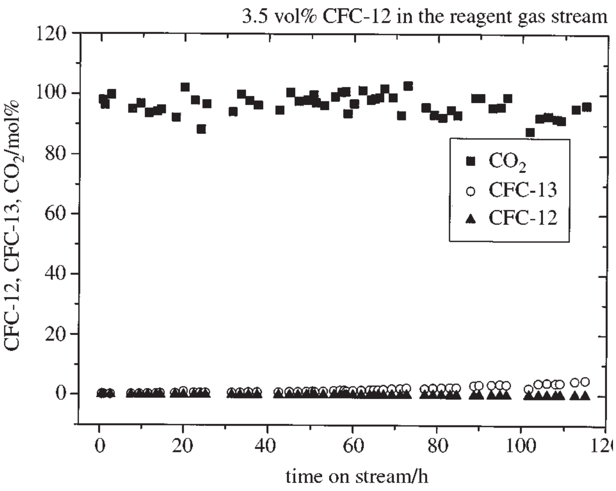

Fig. 3 Long term activity of zirconia in the hydrolysis reaction of CFC-12 (reaction temperature: 450 °C, residence time: 2 s, n_{water}/n_{CFC-12} = 4/1).

In order to reduce the amount of sulfated zirconia necessary, the possibility of suitable and cheap catalyst supports was examined. Owing to the highly corrosive gas phase after catalytic destruction, very few supports are 'suitable'. All γ-aluminas tested in this regard reveal the expected behaviour; namely the formation of AlF_3 phases resulting in remarkable amounts of unwanted CFC-13. The formation of $AlCl_3$ was even observed, which is a very powerful dismutation catalyst and causes additional problems due to sublimation leading to deposits at the outlet of the reactor. Calcined α-Al_2O_3 is better, as expected, but it becomes slowly fluorinated leading to similar problems with ongoing time on stream. Charcoal is known as a suitable support for fluorination catalysts and has been widely used in technical processes for the production of CFCs and HFCs. Owing to the extraordinarily high surface area and several different types of active sites, charcoal itself is also known as a good catalyst. Therefore, pure charcoal was tested first. In pre-investigations, it was found that temperatures of at least 500 °C had to be employed in order to reach complete conversion degrees for CFC-12. Fig. 4 displays the characteristic behaviour of the most active type of charcoal used here. At 500 °C, complete conversion of CFC-12 was achieved up to 400 minutes time on stream. After this period, steadily increasing amounts of unconverted CFC-12 were detected. Moreover, about 3% CFC-13 was always formed, which may be explained by the presence of a few tenths of a percent of metal salts (mainly zinc and iron) on the charcoal which come from the synthesis procedure. Here too, hydrogen fluoride from the product gas reacts with the metal oxides. The fluorides formed act as dismutation catalysts which cause the formation of stable CFC-13 [*cf.* eqn. (3)]. However, there are some differences in comparison to sulfated zirconia. With charcoal, the formation of small amounts of $CHClF_2$ (HCFC-22), traces of ethanol, and remarkable amounts of carbon monoxide were detected. These products are formed by side reactions including a partial reduction and hydrogenation of CFC reagents. The charcoal catalyst lost weight steadily. Carbon is constantly consumed by competitive reactions which may involve some of the following reactions:

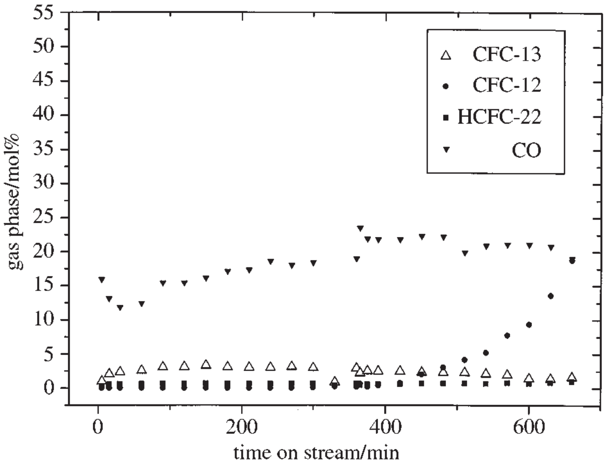

Fig. 4 Catalytic activity of charcoal as a catalyst in the hydrolysis reaction of CFC-12 (reaction temperature: 500 °C, residence time: 2.8 s; $n_{\text{water}}/n_{\text{CFC-12}} = 2.3/1$; CFC-12 concentration in the reagent gas: 20 vol%).

Excess water of the reaction gas may react with carbon under these conditions ($T = 500$ °C):

$$H_2O + C \rightarrow CO + H_2 \qquad (4)$$

CO_2 formed could react with coal according the Boudouard equilibrium:

$$CO_2 + C \rightarrow 2CO \qquad (5)$$

As mentioned in the introduction, hydrodechlorination reactions occur with a CFC in the presence of a suitable catalyst [*cf.* eqn. (1)]. Hydrogen was not detected because it was used in the GC as a carrier gas. Yet the formation of $CHClF_2$ could be understood as a result of a partial hydrodechlorination reaction of CFC-12.

$$CCl_2F_2 + H_2 \rightarrow CHClF_2 + HCl \qquad (6)$$

Traces of metallic zinc or iron possibly formed under these reductive conditions can act as hydrogenolysis catalyst. Similar behaviour was observed when charcoal was used as a support. In all cases, non-negligible amounts of CO were detected which is, unfortunately, a great disadvantage to this application.

Conclusion

Sulfated zirconia is a very suitable catalyst for hydrolytic destruction of CFCs. For the most widely distributed CFC, CCl_2F_2, complete hydrolytic conversion into CO_2, HCl, and HF can be achieved at temperatures as low as 450 °C. Even pure charcoal can be used as a catalyst at temperatures equal to or above 500 °C. Unfortunately, under these conditions the formation of carbon monoxide occurs. Alumina is not useful as a support for zirconia owing to the formation of fluorinated alumina which itself is a good dismutation catalyst. Dismutation reactions result in the formation of very stable CFC-13 which, unfortunately, can not completely be destroyed under these conditions.

Taking into account the highly corrosive atmosphere (especially HF), it seems less feasible to use catalysts like zeolites or even aluminium phosphates which were found to be unstable in a gas phase containing HF. Even the zirconia catalyst, which is believed to be one of the very few suitable catalysts for an industrial application, only exhibits acceptable long term stability at very low CFC concentrations in the gas phase. Only at very low CFC concentrations, such as are present in original waste gases from the refrigerant, can recovery of the possible formation of poisoning oxofluorides as well as the loss of sulfur, somehow be suppressed. However, reactivation of a partially fluorinated zirconia catalyst can be achieved by treating the used catalyst with sulfuric acid. Thus, a comparatively simple recovery cycle can be established.

As for the hydrogen halides formed, there are several technical processes in use to remove them from the product gas phase. Therefore, this problem was not treated here.

Generally it can be stated that this kind of CFC disposal is restricted to waste gas treatment where condensation procedures due to low CFC concentration are too expensive and do not represent a general solution for the necessary CFC recovery.

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New Ca-sequestering materials

based on the oxidation of the hydrolysis products of lactose

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Summary

The Ca-sequestering capacity of the equimolar mixture of aldonic acids or aldaric acids obtained by selective catalytic oxidation of the hydrolysis products of lactose (D-glucose and D-galactose) was determined using a Ca ion selective electrode. Also, the Ca-sequestering capacity of each component of these mixtures was quantified. The addition of boric acid at pH = 10 enhanced the Ca-sequestering capacity substantially, especially for D-gluconic acid and D-glucaric acid. Apparently the configuration of the vicinal diol moiety at the 3,4-position is of major importance in defining the Ca-sequestering capacity of aldonic and aldaric acids in the presence of borate. The effect of the concentration of NaOH on the Ca-sequestering capacity was evaluated in the range of 1–5 wt.% by titration with 0.1 M calcium acetate. The polyhydroxycarboxylic acids exhibit an optimum Ca-sequestering capacity up to one mol Ca ions per mol carboxylate group at these high pHs.

Introduction

Lactose or milk sugar is among the most abundant carbohydrates. Its principal source is (sweet) whey, the main by-product of cheese and casein production in the dairy industry.[1,2] The EU production of lactose is estimated at 250 000 tons per year. Lactose is used in the manufacture of various food and infant nutrition products. One third of the lactose produced finds application in the pharmaceutical industry as a filler, sweetener and binder in tablets, and other oral and inhalation products. Owing to the large dairy industry in the EU, only part of the whey is processed for the production of lactose.

Much effort was made to develop new processes and products based on lactose, to enlarge its total market. We mention the heterogeneous catalytic hydrogenation of lactose to lactitol,[3] a promising sugar substitute in dietetic products with low caloric values and non-cariogenic effects. The commercial production of lactulose, which is obtained by isomerization of lactose by means of the Lobry de Bruin–Alberda van Ekenstein reaction,[4] is executed by several companies of which Solvay Pharmaceuticals is the major producer. Lactulose is applied as additive in baby food, in the reduction of the serum cholesterol and as nutritional supplement improving and protecting intestinal flora. Heterogeneous catalytic oxidation[5] and the microbiological oxidation[6] of lactose to lactobionic acid have also been developed. The facile dehydrogenation of lactose at high pH over a noble metal catalyst to provide lactobionic acid[7] is nowadays applied commercially. Lactobionic acid may be used as an acidulent or complexing agent for metal ions in the food and pharmaceutical industry.[8] Reaction of lactobiono-lactone with fatty alcohols or amines leads to the formation of new surfactants.[9,10] Hendriks *et al.*[11] have studied the alkaline oxidative degradation of lactose to *O*-β-D-galactopyranosyl-(1,3)-D-arabinonate. Anthraquinone-2-sulfonate was used as the catalyst and the desired product was formed with selectivity up to 95%. The degradation of lactose towards galarose (*O*-β-D-galactopyranosyl-(1,3)-D-arabinose) was accomplished by hydrogen peroxide using borate as the catalyst and protecting agent.[12] In a previous study, we have reported on the selective oxidation of lactobionic acid to 1-carboxylactulose (2-ketolactobionic acid).[13]

The present work deals with the selective catalytic oxidation of an equimolar mixture of D-glucose and D-galactose which may be obtained by hydrolysis of lactose. An equimolar mixture of aldonic acids or aldaric acids may be obtained depending on the oxidation procedure (see Fig. 1).

Here we report on the Ca-sequestering capacity of these mixtures using a Ca ion selective electrode, aiming at the development of a new group of alkaline sequestering agents. Such sequestering agents are biodegradable/biocompatible. Their sodium salts may find application in de-rusting and paint-stripping of metals, in mineral tanning of hides, and as a concrete additive for extending setting time and enhancing compressive strength. The ammonium salts of aldonic acids are used as latent acid catalysts in textile printing. Their chelating properties under highly alkaline conditions make these sequestering agents suitable for the prevention of the formation of insoluble soap films in alkaline cleaning of glassware and food processing equipment.

Green Context

The development of alternative processes and products based on sustainable, non-petrochemical resources is a growing area of interest (see *Green Chemistry*, 1999, 1, 107). Lactose is produced in great quantities, and can be converted to several useful products, using benign chemical and biochemical transformations. This paper deals with the preparation and empirical testing of certain derivatives of lactose for use in Ca-binding applications, many of which use substantial amounts of petrochemical-derived materials at the moment. *DJM*

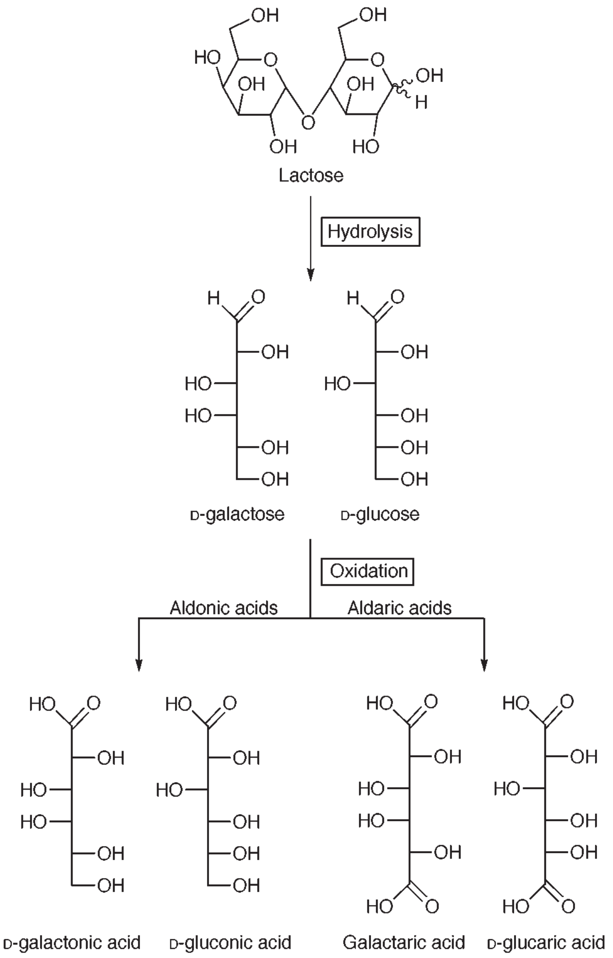

Fig. 1 Structures of the aldonic and aldaric acids obtained by oxidation of the hydrolysis products of lactose.

We have also quantified the Ca-sequestering capacity of each component of these mixtures of aldonic acids and aldaric acids. Moreover the influence of the addition of boric acid on the Ca-sequestering capacities was investigated. The effect of the NaOH concentration on the Ca-sequestering capacity was also evaluated.

Results and discussion

1 Ca-sequestering capacity of the polyhydroxycarboxylic acids

The Ca-sequestering capacity of the aldonic and aldaric acids was measured using a Ca ion selective electrode. A solution of known concentration of a given sequestering agent was titrated with 10^{-3} M $CaCl_2$ at 25 °C, pH = 10 (NH_3 buffer) and ionic strength $\mu = 0.045$ while the activity of unbound Ca ion in solution was determined. The titration curve of sodium D-gluconate is presented in Fig. 2 as an illustrative example.

We have applied the same method to sodium D-galactonate, disodium D-glucarate, disodium galactarate, and equimolar mixtures of sodium D-gluconate/sodium D-galactonate and of disodium D-glucarate/disodium galactarate. The results are summarized in Table 1.

Sodium D-gluconate, sodium D-galactonate and the equimolar mixture thereof exhibit the same Ca-sequestering capacity. Disodium D-glucarate and disodium galactarate have a higher Ca-sequestering value due to the presence of the second carboxylate group at the 6-position. The Ca-sequestering capacity of disodium D-glucarate is 30% higher than that of disodium galactarate. The basis of this difference is not clear yet, disodium galactarate is an isomer at the 4-position of disodium D-glucarate. The Ca-sequestering capacity of the equimolar mixture of these two aldaric acids seemed to be equal to the contribution of each acid taken separately. Nevertheless, the Ca-sequestering capacities of the polyhydroxycarboxylic acids studied remain very low when compared to other sequestering agents such as dicarboxy starch (0.3–1 mmol Ca g^{-1} sequestering agent depending on the oxidation degree.[14]

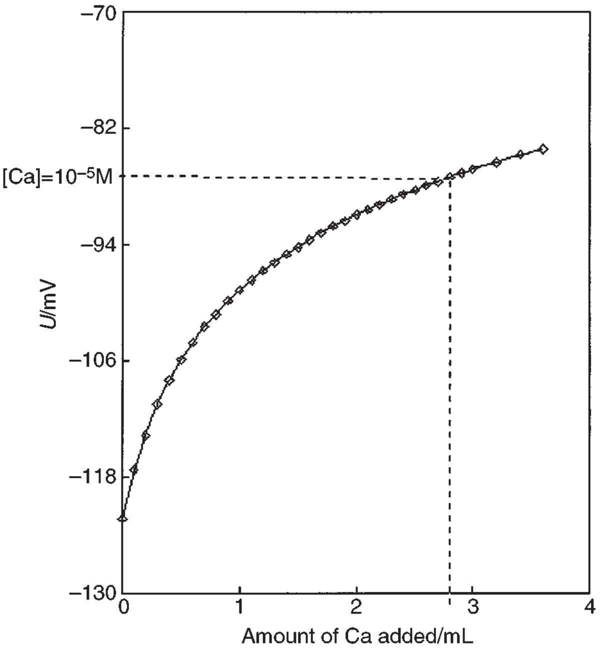

Fig. 2 Titration of a solution of sodium D-gluconate (0.1 g in 100 mL H_2O = 5.5 mM) with 10^{-3} M $CaCl_2$.

Table 1 Measurement of the Ca-sequestering capacities (Ca ion selective electrode, $T = 25$ °C, pH = 10 (NH_3 buffer), $\mu = 0.045$)

	Ca-sequestering capacity	
Sequestering agent	$\times 10^{-2}$ mmol Ca g^{-1}	mg Ca g^{-1}
Sodium D-gluconate	2.8	1.12
Sodium D-galactonate	2.8	1.12
1 : 1 mixture sodium D-gluconate/sodium D-galactonate	2.8	1.12
Disodium D-glucarate	4.2	1.68
Disodium galactarate	3.2	1.28
1 : 1 mixture disodium D-glucarate/disodium galactarate	3.8	1.52

2 Effect of the addition of boric acid on the Ca-sequestering capacity

The effect of the addition of boric acid on the Ca-sequestering capacity of polyhydroxycarboxylic acids was reported in the literature.[15] The structure and the stability of borate esters of polyhydroxycarboxylic acids in aqueous media have been studied with ^{11}B and ^{13}C NMR.[16,17] Some rules are:

- at pH < 9 borate esters in which the carboxyl group and the α-hydroxy group are involved predominate in solution;

- when the pH is increased the stability of these esters decreases. The carboxylate group becomes free and borate mono- and diesters in which two hydroxy groups are involved are formed preferentially.
- borate esters of *threo*-diol moieties are more stable than borate esters of *erythro*-diols.[18,19]

We have examined the effect of the addition of boric acid on the Ca-sequestering capacity of the polyhydroxycarboxylic acids studied. Boric acid was applied in two molar ratios to the sequestering agent. The Ca-sequestering capacity was measured using the Ca ion selective electrode under the conditions described above (25 °C, pH = 10, NH_3 buffer, $\mu = 0.045$). The results are presented in Table 2.

Table 2 Effect of the addition of boric acid on the Ca-sequestering capacities (Ca ion selective electrode, $T = 25$ °C, pH = 10 (NH_3 buffer), $\mu = 0.045$)

	Ca-sequestering capacity/ mg Ca g^{-1}		
	Molar ratio H_3BO_3 : sequestering agent		
Sequestering agent	0.00	0.50	1.00
Sodium D-gluconate	1.12	5.20	6.80
Sodium D-galactonate	1.12	1.68	2.24
1 : 1 mixture sodium D-gluconate/sodium-D-galactonate	1.12	3.20	4.00
Disodium D-glucarate	1.68	12.64	17.32
Disodium galactarate	1.28	2.00	3.60
1 : 1 mixture disodium D-glucarate/disodium galactarate	1.52	7.6	9.56

Clearly the Ca-sequestering capacity of the aldonates and aldarates studied increases upon the addition of boric acid. The D-glucose derived compounds (sodium D-gluconate and disodium D-glucarate) exhibit a better Ca-sequestering capacity upon the addition of boric acid than the oxidation products obtained from D-galactose (sodium D-galactonate and disodium galactarate). This difference is certainly due to the configuration of the vicinal diol moiety at the 3,4-position. In the case of sodium D-gluconate and disodium D-glucarate, the hydroxy groups at the 3- and 4-positions of two molecules are esterified with boric acid (Fig. 3). The diester formed predominates in solution and its structure was elucidated in previous ^{11}B and ^{13}C NMR studies.[16,17,20] This diester with the *threo*-diol configuration is more stable than a diester of *erythro*-diol configuration[18,19] and generates a strong calcium coordination site formed by the spatial proximity of two carboxylate groups which belong to two molecules of the sequestering agent involved in the formation of the diester. The high Ca-sequestering value of disodium D-glucarate upon the addition of boric acid compared to the Ca-sequestering value of sodium D-gluconate is due the presence of the additional carboxy group at the 6-position forming a second Ca binding site (see Fig. 4 for a modelled di-(calcium borate)–D-glucarate complex). Each Ca is surrounded by six ligand atoms of the borate–glucarate ester (two carboxylate oxygens, two hydroxy and two borate oxygens). Two water ligands will complete the Ca coordination sphere.

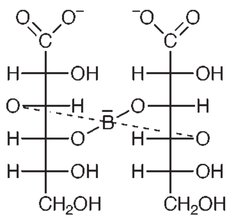

Fig. 3 Projected structure of borate diester of sodium D-gluconate.

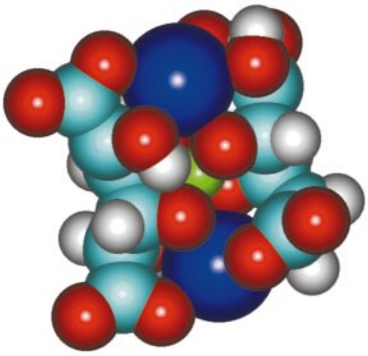

Fig. 4 Modelled di(calcium borate)–D-glucarate complex (green = B, dark blue = Ca, grey = H, red = O, light blue = C).

The Ca-sequestering capacities of sodium D-galactonate and disodium galactarate, the oxidation products of D-galactose, do not increase (Table 2) to the same extent as the oxidation products of D-glucose. The formation of borate diester with the oxidation products of D-galactose with a *threo*-diol configuration is only possible with the vicinal hydroxy groups at the 2,3- or the 4,5-positions. In the case of disodium galactarate, the stability of such a borate diester will be influenced by the proximity of the negatively charged carboxylate group. The resulting calcium coordination site is probably weaker than that formed by the borate diester of disodium D-glucarate.

As for sodium D-galactonate, the stability of the borate diester with the *threo*-diol configuration at the 2,3-position will suffer again from the proximity of the negatively charged carboxylate group, while the borate diester with the *threo*-diol configuration at the 4,5-position will provide a more flexible diester, and hence a weaker calcium coordination site.

Further increase of the molar ratio boric acid/sequestering agent from 0.5 to 1.0 led to an increase of the Ca-sequestering capacity. In the case of sodium D-gluconate, the dimerization might be enhanced by a second borate ester formed at the 5,6-position.

The Ca-sequestering capacities of the equimolar mixtures of sodium D-gluconate/sodium D-galactonate and disodium D-glucarate/disodium galactarate also increase upon the addition of boric acid. The resulting Ca-sequestering capacity seems to be equal to the sum of the sequestering value of each component. This would suggest that no formation of mixed borate diester takes place in solution, which seems improbable.

3 Effect of the concentration of NaOH on the Ca-sequestering capacity

The profound effect of the NaOH concentration on the Ca-sequestering capacity of the aldonates, as measured by titration of a 1 wt.% solution of a given sequestering agent with 0.1 M calcium acetate, is shown in Fig. 5. It should be noted that here the turbidity method was applied and crystallization inhibition might contribute to the macroscopic effect observed.

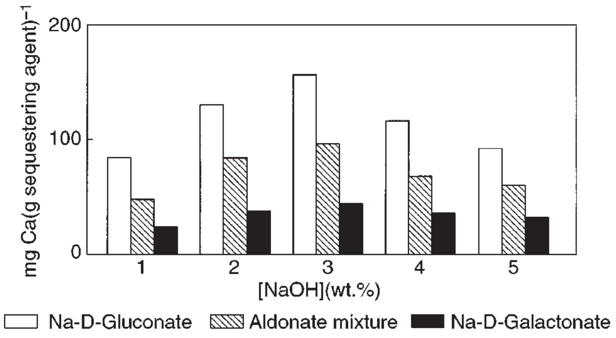

Fig. 5 Effect of the concentration of NaOH on the Ca-sequestering capacity of sodium D-gluconate, sodium D-galactonate and the equimolar mixture thereof.

Sodium D-gluconate displays high Ca-sequestering capacity at these high pHs and exhibits an optimum value at a NaOH concentration of about 3 wt.% (pH = 13, molar ratio NaOH: D-gluconate is 16.4). The molar ratio of sodium D-gluconate/Ca ions added was slightly over 1 (1.18). This means that essentially each Ca ion is coordinated to a molecule of sodium D-gluconate. The carboxylate group and the ionized α-hydroxy group of sodium D-gluconate probably serve as coordination sites for the hydrated Ca ion. The theoretical Ca-sequestering capacity of sodium D-gluconate seems to be reached under these conditions. The strongly complexing 1,2 unit will also adsorb well onto the Ca at the surface of a $CaCO_3$ crystallization nucleus, thus inhibiting growth.

A decrease of the concentration of NaOH in solution led to a decrease of the Ca-sequestering capacity of sodium D-gluconate. At a concentration of NaOH = 1 wt.%, the molar ratio of sodium D-gluconate/Ca ions added was about 2 (2.19). The Ca ion is probably coordinated to two molecules of sodium D-gluconate with partial 2-OH ionization.

On the other hand, a further increase of the concentration of NaOH beyond 3 wt.% led also to a decrease of the Ca-sequestering capacity of sodium D-gluconate. The molar ratio of sodium D-gluconate/Ca ions added up to turbidity reached a value of 2 at a concentration of NaOH = 5 wt.%. A dimer complex of sodium D-gluconate with Ca ion again seemed to be formed. Under these highly alkaline conditions the hydroxy groups of sodium D-gluconate are partly ionized and become strong Ca ion coordinating sites. The Ca ion might be coordinated to a diol system of two molecules of sodium D-gluconate. Formation of such a dimer complex with sodium D-gluconate under highly alkaline conditions in the presence of Fe or Cu ions was reported previously.[20]

Sodium D-galactonate exhibited the same behavior as sodium D-gluconate toward the coordination of Ca ion in highly alkaline solutions, however the measured Ca-sequestering values are smaller. This is probably due to the low solubility of Ca D-galactonate in water, which makes it difficult to measure its true Ca-sequestering capacity by the turbidity method.

The effect of the concentration of NaOH on the Ca-sequestering capacity of an equimolar mixture of sodium D-gluconate/sodium D-galactonate was also studied. The Ca-sequestering values are roughly equal to the averaged sum of the Ca-sequestering values of the components. Here too, a maximum is observed at 3 wt.% NaOH (pH = 13).

The dependence of the Ca-sequestering behaviour of disodium D-glucarate, disodium galactarate and an equimolar mixture thereof on the concentration of NaOH in solution is presented in Fig. 6. Disodium D-glucarate and disodium galactarate exhibit a Ca-sequestering optimum value at 3–4 wt.% NaOH in solution. The sequestering agent/Ca ions added molar ratio is about 0.5, meaning that two Ca ions are coordinated to each molecule of the sequestering agent. The two carboxylate groups of the aldaric acid and the *ionized* α-hydroxy groups are assumed to serve as the coordination sites for the two Ca ions, by analogy to the proposed high pH coordination site for sodium D-gluconate.

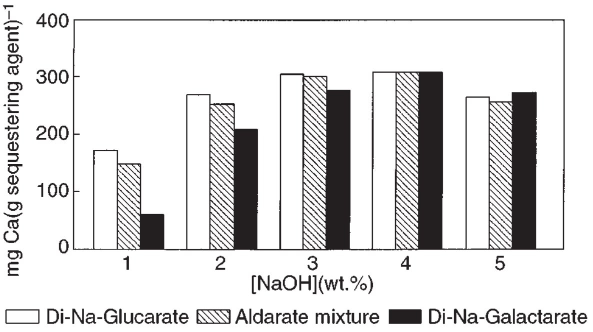

Fig. 6 Effect of the concentration of NaOH on the Ca-sequestering capacity of disodium D-glucarate, disodium galactarate and the equimolar mixture thereof.

Increasing the concentration of NaOH beyond 4 wt.% led to a slight decrease of the Ca-sequestering capacity of the sequestering agents studied. Under these highly alkaline conditions, the hydroxy groups are ionized and form new and strong Ca ion coordination sites. A part of the Ca ions present in solution may become coordinated to a diol system of two molecules of the sequestering agent and hence a decrease of the Ca-sequestering capacity takes place.

Conclusion

The aldonates and aldarates studied, as well as the equimolar mixtures thereof, exhibit a relatively low Ca-sequestering capacity at 25 °C, pH = 10 (NH_3 buffer) and $\mu = 0.045$ (KCl) compared to other sequestering agents. Upon the addition of boric acid, the Ca-sequestering values increase substantially, especially those of the polyhydroxycarboxylic acids derived from D-glucose (*i.e* D-gluconate and D-glucarate).

Under highly alkaline conditions, sodium D-gluconate, disodium D-glucarate, disodium galactarate and the equimolar mixture of aldaric acids show a high Ca-sequestering value at a concentration of NaOH = 3–4 wt.%. As for sodium D-galactonate, the effect of the concentration of NaOH on its Ca-sequestering capacity was difficult to quantify because of the low solubility of this aldonic acid under our experimental conditions.

Experimental

Materials

Boric acid, calcium acetate, calcium chloride, ammonium chloride, ammonia (25% in water) and potassium chloride, all of analytical grade, D-glucose and D-galactose were purchased from Acros Organics. The 5% Bi/5% Pd/C catalyst was obtained from Degussa AG.

Preparation of aldonic and aldaric acids

Aldonic acids

D-Gluconic acid, D-galactonic acid and the equimolar mixture thereof were prepared by heterogeneous selective catalytic oxidation of the corresponding aldose (mixture) as previously reported in the literature.[21,22] The oxidation reaction was performed at 50 °C, under pH control (pH = 9 constant) in water using bismuth-modified palladium as the catalyst. The complete conversion of the aldose (mixture) was achieved within 3–4 hours with a selectivity toward aldonic acid >99%. The aldonic acids were obtained as crystalline material suspended in water. Details of the oxidation procedure and equipment were reported elsewhere.[23]

Aldaric acids

For the preparation of D-glucaric acid (D-saccharic acid), galactaric acid (mucic acid) and the mixture thereof, we opted for the oxidation of the corresponding aldose (mixture) with nitric acid according to the procedure reported in the literature.[24] The platinum-catalyzed oxidation of aldose to aldaric acid also provides moderate yield and the isolation of the product is more laborious.[25] The purity of the aldaric acids obtained was >98% as confirmed by HPLC (for details related to the analysis procedure see ref. 26).

Ca-Sequestering capacity measurements

The Ca ion selective electrode measures the activity of free, hydrated calcium ions in solution. Once calibrated in standardizing solutions of known calcium ion activity the electrode responds directly to sample calcium ion activity.

The Ca-sequestering capacity of the polyhydroxycarboxylic acids studied was measured using a Unicam IS-Ca ion selective electrode and a Unicam RE15 double junction reference electrode (Unicam Analytical Systems, Cambridge, UK). Before carrying out the measurement, the Ca ion selective electrode was first calibrated in the range 10^{-1}–10^{-6} M $CaCl_2$ at 25 °C, pH = 10 (NH_3 buffer) and at an ionic strength $\mu = 0.045$ (KCl).

The Ca-sequestering capacity of a given sequestering agent is defined as the amount of calcium to be added to a solution containing 1 g of this sequestering agent, under the conditions applied to the calibration of the Ca ion selective electrode (25 °C, pH = 10, NH_3 buffer, $\mu = 0.045$), to reach a concentration in solution of [Ca] = 10^{-5}M (or 0.4 mg L^{-1}). This value is considered as the upper limit for the calcium concentration during the washing process.[27] In practice, 100 mL of doubly distilled water containing 0.1 g of the sequestering agent, at pH = 10 (NH_3 buffer) and at an ionic strength $\mu = 0.045$, is titrated with a solution of known concentration of $CaCl_2$ until [Ca] = 10^{-5}M. In our studies a 10^{-3} M $CaCl_2$ solution was used to carry out the titration of the sequestering agent solution.

i. Effect of the addition of boric acid on the Ca-sequestering capacity

The influence of the addition of boric acid on the Ca-sequestering capacity of a given sequestering agent was also investigated by using a Ca ion selective electrode. The measurements were performed at 25 °C, pH = 10 (NH_3 buffer) and at an ionic strength $\mu = 0.045$ (KCl).

ii. Effect of the concentration of NaOH on the Ca-sequestering capacity

The effect of the NaOH concentration on the Ca-sequestering capacity was evaluated by titration of a solution of known concentration of a given sequestering agent with 0.1 M calcium acetate. The NaOH concentration was varied in the range 1–5 wt.%. Under these highly alkaline conditions D-gluconate is used to prevent the formation of insoluble soap films in cleaning glassware and food processing equipment. In practice, 0.1 g sequestering agent was dissolved in 10 mL of a solution of 1% Na_2CO_3 and a desired amount of NaOH. This solution was titrated against 0.1 M aqueous calcium acetate while the concentration of Na_2CO_3 and NaOH was maintained constant. The end point of the titration was indicated by the appearance of the first persisting turbidity.

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Selective carbomethoxylation of aromatic diamines

with mixed carbonic acid diesters in the presence of phosphorous acids

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Summary

The reactivity of industrially relevant amines, 4,4′-methylenedianiline (MDA) and 2,4-diaminotoluene (TDA), towards methylphenylcarbonate (MPC), in the presence of $Ph_2P(O)OH$, has been investigated. Both MDA and TDA are catalytically and selectively converted into mono- and di-methylcarbamate esters. Under the relatively mild working conditions used, the formation of ureas and/or *N*-methyl derivatives is totally repressed. The full spectroscopic characterization of the compounds formed upon interaction of amines with $Ph_2P(O)OH$ is also reported. The methodology here described also holds for other mono- and di-amines, both aliphatic and aromatic.

Introduction

The substitution of phosgene with less noxious starting materials in synthetic chemistry represents a major target of ‘green chemistry’ for the future.[1] As a matter of fact, much effort is currently being aimed at setting up new alternative clean synthetic methodologies avoiding phosgene which, in spite of its very high toxicity,[2] is still largely used as the ‘active carbonyl’ species in chemical industry for the synthesis of a number of chemicals such as carbamates, ureas, isocyanates and organic carbonates.[3]

In previous studies we have shown that carbon dioxide itself can be employed as an effective replacement for phosgene in the synthesis of organic carbamates.[1,4] These chemicals, widely used as agrochemicals, pharmaceuticals and dyestuffs, can also play a key role in synthetic chemistry as suitable intermediates for the synthesis of ureas, isocyanates and organic carbonates.[1,5]

Aminolysis of organic carbonates [eqn. (1)][6] is another attractive synthetic route to carbamates[7] since non-phosgene routes to carbonic acid diesters are now available. In fact, dimethylcarbonate (DMC) is currently produced on a large scale by oxidative carbonylation of methanol [eqn. (2)].[8] Moreover, organic carbonates of high-boiling alcohols[9] or phenols [eqn. (3) and (4)][8] can be easily obtained by transesterification of DMC or diethylcarbonate.

$$RR'NH + R''OC(O)OR'' \rightarrow RR'NC(O)OR'' + R''OH$$
$$R,R' = H, \text{alkyl or aryl}; R'' = \text{alkyl or aryl} \quad (1)$$

Green Context

Aromatic diamines are key intermediates in a range of plastics applications (for a green synthesis of some of these materials see Lalithambika *et al.* in *Green Chemistry* Issue 4, page 191. Important derivatives of some of these compounds include carbamates. Such derivatives are typically produced *via* routes involving phosgene, a particularly difficult chemical due to handling, toxicity and pollution difficulties—1 kg of phosgene gives 1.17 kg of salt waste. Thus, the development of routes not involving phosgene is an important task in this area of chemistry. In addition to the prior work described in the text, Ube industries have commercialised a non-phosgene route to dimethylcarbonate [*Belg. Pat.*, 1979, 870 268] This route involves palladium catalysed reaction of CO with methanol, and involves an elegant catalytic re-oxidation of Pd. Further work has extended this to diphenylcarbonate [see *e.g.* J. E. Hallgren and G. M. Lucas, *J. Organomet. Chem.*, 1981, 212, 135], again not involving phosgene, and generating little waste. The authors of this paper have discovered an acid catalysed route where two industrially relevant carbamates can be formed selectively from mixed carbonates. The chemistry involves the use of a phosphorus centred acid as catalyst, which allows the reaction to proceed at relatively low temperatures. This is important, since the carbamates are capable of reacting further to give ureas, and the carbonates can also, not surprisingly, function as good methylating agents under harsher conditions. Conversions are still quite low in the work described here, making very high selectivity vital. With the high selectivity demonstrated here, it should be possible to develop reactor technology which will provide a selective reaction and recycling of both unreacted diamine and phenol. Thus, the concept demonstrated here represents a partial solution, but nonetheless a significant step towards a green process.

DJM

$$2\ \mathrm{MeOH} + \mathrm{CO} + 1/2\ \mathrm{O_2} \xrightarrow{\mathrm{Cu(I)/Cu(II)}} \mathrm{(MeO)_2C{=}O} + \mathrm{H_2O} \quad (2)$$

$$\mathrm{(MeO)_2C{=}O} + \mathrm{PhOH} \xrightarrow{\mathrm{Ti(OPh)_4}} \mathrm{PhOC(O)OMe} + \mathrm{MeOH} \quad (3)$$

$$2\mathrm{PhOC(O)OMe} \xrightarrow{\mathrm{Ti(IV)}} \mathrm{(PhO)_2C{=}O} + \mathrm{(MeO)_2C{=}O} \quad (4)$$

Basic amines smoothly react with diphenylcarbonate (DPC)[10] or other organic carbonates having fairly good leaving groups (4-nitro-, 2 nitro-, 2,4-dinitro-, 2,3,5 trichloro-, 2,4,6-trichloro-, pentachloro-, 4-acetylphenoxy; $H_2C{=}C(Me)O$-; $H_2C{=}C(OMe)O$-).[6c,11] However, carboalkoxylation of aliphatic amines by unactivated carbonic acid diesters usually requires a suitable catalyst in order to observe good conversion rate and selectivity. Lewis acids, such as $AlCl_3$, $SnCl_2$, $ZnCl_2$, $Zn(O_2CCH_3)\cdot 2H_2O$, $FeCl_3$, or metal (Rh, Ru) complexes, can catalytically promote the carboethoxylation of *n*-propylamine with diethylcarbonate.[12] Recently, we have shown that CO_2 itself is an effective catalyst for the synthesis of *N*-alkylmethylcarbamates from aliphatic amines and DMC.[13] This methodology cannot be extended to the carbomethoxylation of aromatic amines, most probably because of both their lower basicity and nucleophilicity towards carbon dioxide.

Carboalkoxylation of anilines, and more generally of aromatic amines, is usually achieved using metal catalysts (Zn, Co, Sn, Al, or Ti derivatives),[14] as well as strong bases (Group 1 alkoxides).[15] The reaction conditions are usually severe and the side-formation of *N*-alkylation products and/or ureas represents a major drawback of these synthetic procedures. Efficient carboalkoxylation and carboaryloxylation of amines (including a few aromatic ones) has been achieved by Tamura and coworkers using asymmetric α-methoxyvinylcarbonates, $H_2C{=}C(OMe)O{-}C(O)OR$ or $H_2C{=}C(OMe)O{-}C(O)OAr$.[11] Unfortunately, this synthetic approach does not seem to be suitable for industrial exploitation, as the starting carbonates [$H_2C{=}C(OMe)O{-}C(O)OR$ or $H_2C{=}C(OMe)O{-}C(O)OAr$] are prepared from bis(carbomethoxy)methylmercury and alkyl- or aryl-chloroformates, or in other cases using phosgene.

Recently, we have reported the formation of carbamate esters by reaction of aromatic monoamines with unactivated carbonic acid diesters, such as DMC or DPC, in the presence of organophosphorus acids [$Ph_2P(O)OH$, $(PhO)_2P(O)OH$, $(BuO)_2P(O)OH$, $(BuO)P(O)(OH)_2$].[10] The best catalytic activity was shown by diphenylphosphinic acid. The formation of carbamate is very selective and excellent yields have been obtained using DPC. DMC, however, reacts much more slowly as a result of its poorer reactivity. The mechanism of this reaction (Scheme 1) shows intriguing analogies with the mechanism of formation of carbamate anion in living systems from ammonia and hydrogencarbonate catalyzed by carbamylphosphate synthase (CPS) enzyme (Scheme 2).[16]

$$\mathrm{X_2P(O)OH} + \mathrm{ArNH_2} \rightleftharpoons \mathrm{X_2P(O)O^-}\ {}^{+}\mathrm{H_3NAr} \quad (5)$$

$$\mathrm{X_2P(O)O^-}\ {}^{+}\mathrm{H_3NAr} + \mathrm{(RO)_2C{=}O} \rightarrow \mathrm{X_2P(O)OC(O)OR} + \mathrm{ROH} + \mathrm{ArNH_2} \quad (6)$$

$$\mathrm{X_2P(O)OC(O)OR} + \mathrm{ArNH_2} \rightarrow \mathrm{ArNHC(O)OPh} + \mathrm{X_2P(O)OH} \quad \mathrm{X = Ph, PhO, BuO;\ R = methyl, phenyl} \quad (7)$$

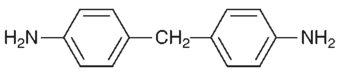
Scheme 1

$$\mathrm{ATP} + \mathrm{HCO_3^-} \xrightarrow{\mathrm{CPS}} \mathrm{ADP} + \mathrm{HOC(O)OPO_3^{2-}} \quad (8)$$

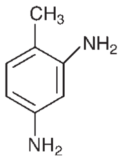
$$\mathrm{HOC(O)OPO_3^{2-}} + \mathrm{NH_3} \xrightarrow{\mathrm{CPS}} \mathrm{H_2NCO_2^-} + \text{‘phosphate’} \quad (9)$$

Scheme 2

We have now extended this study to 4,4′-methylenedianiline (MDA, **1a**) and 2,4-diaminotoluene (TDA, **1b**). Both the considered aromatic diamines are important from the industrial point of view as their carbamate derivatives are used to generate isocyanates, precursors of polymers. The reactivity of both **1a** and **1b** towards DPC in the presence of the ‘P’-acids mentioned above has been described elsewhere.[17] In this paper, we describe their reactivity towards methylphenylcarbonate (MPC) in the presence of $Ph_2P(O)OH$ and report the first example of *selective carboalkoxylation of aromatic diamines* by an unactivated mixed alkylarylcarbonate promoted by a *non-metal catalyst*.



1a



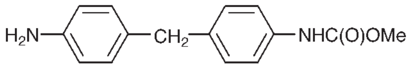
1b

Results and discussion

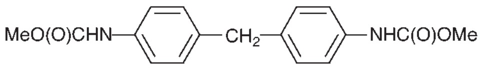
Reactivity of MDA and TDA towards MPC in the presence of $Ph_2P(O)OH$

The utilization of MPC as a carbomethoxylating agent permits one to carry out, under the proper experimental conditions, the carbamation of both **1a** and **1b** in a very selective way.

At 363 K, **1a** (0.35695 g, 1.80 mmol), MPC (0.600 g, 3.94 mmol) and $Ph_2P(O)OH$ (0.03825 g, 0.175 mmol) react in THF (5 mL) to give **3a** and **4a** with 43 and 9% HPLC yields, respectively, after 12 h.[18] The carbamation reaction is very selective: no formation of *N*-methyl derivatives or ureas is observed. A progressive deactivation of the catalyst has been observed.



3a



4a

Fig. 1 illustrates the effect of further addition of the catalyst after a reaction time of 16 h, which results in a significant increase of the yield of both **3a** and **4a**. The overall conversion yield of the diamine is 90% after 22 h.

Analogously, at 363 K, in THF (10 mL), **1b** (0.422 g, 3.46 mmol) reacts with MPC (1.052 g, 6.92 mmol) in the presence of $Ph_2P(O)OH$ (0.07335 g, 0.336 mmol) to give selectively **3b**, as the major product (38% HPLC yield, after 15 h), and **4b**.[19] Under the above experimental conditions carbamate **3b′** is formed only in very small amounts, most probably because carbamation of the 2-NH_2 group suffers from the steric hindrance due to the vicinal methyl group. This fact also explains why the formation of dicarbamate **4b** (2–3% HPLC yield, after 15 h) takes place much more slowly than that of **3b**. In any case the carbamation is very selective

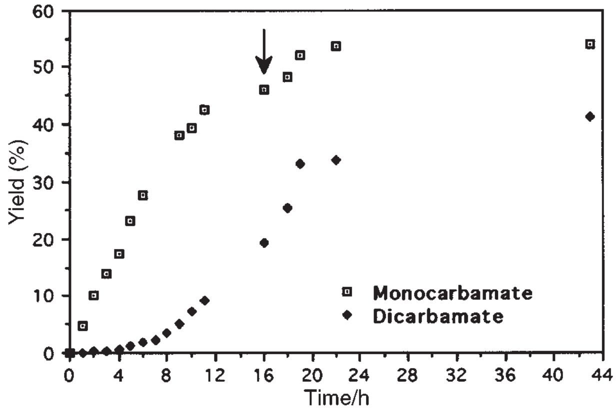
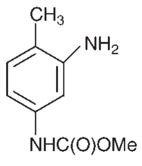
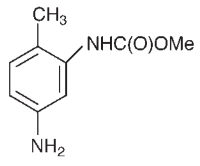


Fig. 1 Kinetics of formation of **3a** and **4a**. This reaction was carried out as described in the Experimental section (Kinetic measurements) using the following amounts of reactants: **1a** (0.31565 g, 1.59 mmol), MPC (0.500 g, 3.29 mmol) and $Ph_2P(O)OH$ (0.03455 g, 0.158 mmol). Solvent: THF (5 mL). Temperature: 363 K. Internal standard: naphthalene (0.08075 g, 0.63 mmol). After 16 h 0.03485 g (0.160 mmol) of $Ph_2P(O)OH$ were added.

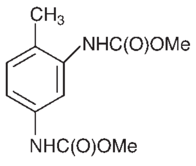
as the methylated products of the starting amine **1b** were detectable only after 33 h. At this time, the rate of carbomethoxylation process is extremely low, probably because of progressive deactivation of the catalyst. Nevertheless, also in this case, further addition of the catalyst markedly increases the carbamate yield (see the Experimental section).



3b



3b'



4b

We have investigated the reaction mechanism to find the pathway responsible for the deactivation of the catalyst. Under the working conditions, $Ph_2P(O)OH$ reacts promptly with TDA and MDA to afford $(TDAH)O_2PPh_2$ and $(MDAH_2)(O_2PPh_2)_2$, respectively. The above mentioned phosphinate salts are not soluble in the reaction medium at room temperature. They can be isolated and characterized (see the Experimental section). These salts appear to be the precursors of the catalytically active species. As a matter of fact, their suspension in THF added with MPC and the corresponding diamine (**1b** or **1a**, respectively), promptly promotes the carbamation reaction at 363 K. The 'active species' $Ph_2P(O)OC(O)OMe$[10] [eqn. (10a–a′) and (10b)] may be deactivated according to reaction (11).[10,17] Accordingly, the GC-MS of the reaction solution shows the presence of diphenylphosphinic acid methyl ester, $Ph_2P(O)OMe$ (*m/z* = 232), in the reaction mixture.

$$(MDAH_2)(O_2PPh_2)_2 + MPC \rightarrow Ph_2P(O)OC(O)OMe + PhOH + (MDAH)O_2PPh_2 \qquad (10a)$$

$$(MDAH)O_2PPh_2 + MPC \rightarrow Ph_2P(O)OC(O)OMe + PhOH + MDA \qquad (10a')$$

$$(TDAH)O_2PPh_2 + MPC \rightarrow Ph_2P(O)OC(O)OMe + PhOH + TDA \qquad (10b)$$

$$Ph_2P(O)OC(O)OMe \rightarrow Ph_2P(O)OMe + CO_2 \qquad (11)$$

The carbomethoxylation reaction is very selective and we have never observed the formation of mono- or di-phenyl carbamate esters.[17] This result finds an easy rationale in the reaction mechanism (see Scheme 1) and in the fact that the phenoxo is a better leaving group than the methoxo group. These facts are also of help in explaining both the higher reactivity and, at least partly, the better selectivity of MPC with respect to DMC as carboxymethylating agent.[20] Nevertheless, the different selectivity of the carbamation process in the two cases (DMC and MPC) emphasizes the fact that DMC is a better methylating agent than MPC. In fact, the methylation reaction involves a nucleophilic attack by the amine on the electrophilic methyl carbon atom of the organic carbonate. In the case of DMC, this process could be facilitated by the less bulky leaving group (methylcarbonate *vs.* phenylcarbonate).

Carbamates **3a**, **4a**, **3b** and **4b** have been isolated and characterized by elemental analysis and spectroscopic methods (Experimental section). Interestingly, in no case did the isolated products show contamination by phosphorus derivatives. The total yield of highly purified mono- and di-carbamate ranges around 70–80% (the overall yield is close to 90%). Both the catalyst and unreacted amine can be recovered in almost quantitative yield using conventional methods (filtration, extraction, chromatography).

Conclusions

In the presence of $Ph_2P(O)OH$, aromatic diamines **1a** and **1b** react with methylphenylcarbonate to give the corresponding mono- and di-methylcarbamate esters under mild conditions. The carbamation reaction is very selective as both methylation of the starting amines and formation of ureas are practically repressed or not observed under the described working conditions. To the best of our knowledge the above reactions represent the first example of *selective carboalkoxylation of aromatic diamines by an unactivated alkylarylcarbonate promoted by a non-metal catalyst.*

Experimental

Unless otherwise specified, all reactions and manipulations were carried out under a dinitrogen atmosphere with rigorous exclusion of both air and atmospheric moisture, by using vacuum line techniques. All solvents were dried as described in the literature[21] and stored under dinitrogen. Amines **1a**,**b** and DMC were a gift from EniChem Synthesis. MPC was prepared as described in the literature.[22] $Ph_2P(O)OH$ was from Aldrich.

IR spectra were obtained with a Perkin Elmer 883 spectrophotometer. ^1H, ^{31}P and ^{13}C NMR spectra were recorded with a Bruker AM 500 or Varian XL-200. Proton and carbon chemical shifts are in ppm *vs.* TMS and have been referenced to the solvent peak, while ^{31}P resonances were calibrated with respect to 85% H_3PO_4. GC-MS analyses were carried out with a HP 5890 gas chromatograph linked to a HP 5970 selective mass detector (capillary column: 30 m SE-30, 0.25 mm film thickness). GC analyses were made with a DANI HR 3800 gas chromatograph equipped with a SE-30 packed column. HPLC analyses were performed with a Perkin Elmer Series 4 LC connected with a LC 290 UV/Vis spectrophotometer detector.

Kinetic measurements.

The reaction vessel was a 25 mL tube sealed with a two-way valve that allowed sampling without exposure to air using a chromatography syringe. The reaction mixture containing the reactants (DPC and **1a** or **1b**), the acid catalyst (if used) and the internal standard was heated up to the working temperature (±1 K). At fixed times the reaction mixture was cooled to room temperature (293 K) and the liquid phase analyzed by HPLC. The following HPLC analysis conditions were used:

– reactions involving MPC or DMC and **1a:** naphthalene (internal standard); Supelcosil LC-DP, 5 μm, 250 × 4.6 mm (column); acetonitrile–water 35 : 65 v/v (mobile phase); 2 mL min^{-1} (flow);

– reactions involving MPC or DMC and **1b**: benzene (internal standard); Supelcosil LC8, 5 μm, 250 × 4.6 mm (column); acetonitrile–water 30 : 70 v/v (mobile phase); 2 mL min^{-1} (flow).

Reaction of MDA with MPC in the presence of $Ph_2P(O)OH$. Synthesis, isolation and characterization of MDA mono- (**3a**) and di-carbamate (**4a**)

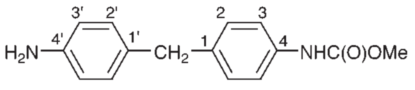
A mixture of MPC (1.160 g, 7.61 mmol), MDA (0.75305 g, 3.80 mmol) and $Ph_2P(O)OH$ (0.08375 g, 0.384 mmol) in THF (6 mL) was stirred at 363 K for 16 h. After cooling to room temperature, 0.08115 g of $Ph_2P(O)OH$ (0.410 mmol) were added and the reaction mixture was left to react at 363 K for a further 7 h. The reaction mixture was cooled to 293 K and the solid precipitated was isolated by filtration, washed with THF, dried *in vacuo* and identified as $(MDAH_2)(O_2PPh_2)_2$ (0.138 g; for characterization, see below). The gross yield of conversion of the amine into mono- and di-carbamates estimated by HPLC is 95%.

The mother liquor and the washing solutions, collected together, were concentrated *in vacuo* and fractionated on a silica gel column (1.5 cm × 120 cm) using, as eluent, diethyl ether–toluene (3 : 1 v/v). After evaporation of the solvent, 0.143 g (0.56 mmol) of pure **3a** [anal. calc. for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.92. Found: C, 70.71; H, 6.34; N, 10.61%] were recovered in addition to **4a** slightly contaminated by traces of PhOH and MPC. By recrystallization of this fraction from diethyl ether–hexane, 0.264 g of pure **4a** (0.84 mmol) were isolated [anal. calc. for $C_{17}H_{18}N_2O_4$: C, 64.96; H, 5.77; N, 8.90. Found: C, 65.26; H, 5.74; N, 8.69%].

The mixed fractions **3a**/**4a** and **3a**/**1a** were collected and, after solubilization in 2 mL of THF, fractionated once more on a silica gel column (1.5 cm × 120 cm) using, as eluent diethyl ether–toluene (1 : 1 v/v) and then diethyl ether–toluene (3 : 1 v/v). In this way, 0.124 g (0.39 mmol) of **4a** [anal. calc. for $C_{17}H_{18}N_2O_4$: C, 64.96; H, 5.77; N, 8.90. Found: C, 64.96; H, 5.78; N, 8.30%] and 0.220 g (0.86 mmol) of **3a** [anal. calc. for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.92. Found: C, 70.57; H, 6.47; N, 10.98%] were recovered in an analytically pure form. Overall yield for **3a**: 1.32 mmol, 35%. Overall yield for **4a** : 1.23 mmol, 32%. Total yield of highly purified mono- and di-carbamates: 67%.

Characterization of 3a

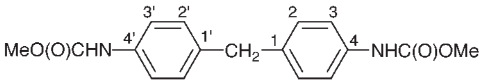
ν(Nujol)/cm^{-1}: 3405 (ms), 3315 (m), 3220 (mw, br), 3170 (w, br), 3095 (w, br), 3030 (mw), 3005 (mw), 1707 (vs, ν_{CO}), 1615 (ms), 1600 (ms), 1544 (s), 1510 (s), 1432 (ms), 1410 (ms), 1309 (ms), 1278 (m), 1245 (vs), 1205 (mw), 1185 (mw), 1175 (mw), 1115 (w), 1076 (s), 1013 (mw), 951 (w), 935 (vw), 912 (mw), 855 (mw), 833 (m), 811 (m), 768 (ms), 720 (ms), 602 (mw), 530 (m), 510 (m), 496 (mw). δ_H (acetone-d$_6$, 500.138 MHz, 293 K): 3.66 (s, 3 H, CH$_3$), 3.74 (s, 2 H, CH$_2$), 4.41 (br, 2H, NH$_2$), 6.57 (dm, 2 H, H2′ or H3′), 6.88 (dm, 2 H, H2′ or H3′), 7.10 (d, ^3J = 8.44 Hz, 2 H, H2 or H3), 7.42 (d, 2 H, H2 or H3), 8.51 (s, br, 1 H, NH). δ_C (acetone-d$_6$, 50.3 MHz, 293 K): 154.67 (C(O)O), 147.07 (C4′), 137.71 and 137.43 (C1 and C4), 130.21 (C1′), 129.87 and 129.50 (C2 and C2′), 118.93 (C3), 115.04 (C3′), 51.75 (OCH$_3$), 40.73 (CH$_2$).



3a

Characterization of 4a

ν(Nujol)/cm^{-1}: 3330 (s, br), 3190 (w, br), 3120 (mw, br), 1704 (vs, ν_{CO}), 1610 (m), 1595 (ms), 1527 (vs), 1438 (ms), 1410 (ms), 1320 (ms), 1275 (m), 1236 (vs), 1204 (m), 1190 (m), 1180 (mw), 1170 (mw), 1105 (w), 1070 (s), 1020 (w), 1013 (w), 955 (w), 945 (w), 935 (vw), 910 (mw), 855 (mw), 845 (m), 830 (mw), 815 (m), 775 (m), 765 (m), 730 (m), 722 (m), 700 (w), 675 (m), 635 (m), 600 (m), 570 (w), 510 (ms). δ_H (acetone-d$_6$, 500.138 MHz, 293 K): 3.66 (s, 6 H, CH$_3$), 3.86 (s, 2 H, CH$_2$), 7.13 (d, ^3J = 8.35 Hz, 4 H, H2 or H3), 7.45 (d, 2 H, H2 or H3), 8.54 (s, br, 2 H, NH). δ_C (acetone-d$_6$, 125.760 MHz, 293 K): 154.78 (C(O)O), 138.09 and 136.66 (C1 and C4), 129.75 (C2), 119.11 (C3), 51.88 (OCH$_3$), 40.91 (CH$_2$).



4a

Characterization of $(MDAH_2)(O_2PPh_2)_2$

Anal. calc. for $C_{37}H_{36}P_2N_2O_4$: C, 70.02; H, 5.71; N, 4.41. Found: C, 69.24; H, 5.44; N, 4.32%. ν(Nujol)/cm^{-1}: 3070 and 3040 (mw), 2700–2100 (vbr), 1625 (m), 1605 (m), 1580 (m), 1505 (ms), 1433 (m), 1305 (w), 1220 (w), 1165 (s), 1125 (s), 1115 (s), 1065 (ms), 1035 (s), 1015 (s), 995 (ms), 915 (mw), 855 (w), 810 (mw), 760 (m), 748 (ms), 725 (s), 695 (s), 638 (mw), 560 (s), 540 (s), 500 (mw), 475 (m), 435 (mw). δ_H(DMSO-d$_6$, 500.138 MHz, 293 K): 3.54 (s, 2 H, CH$_2$), 3.87 (vbr, NH), 6.46 (d, ^3J = 8.31 Hz, 4 H, H2 or H3), 6.80 (d, 4 H, H2 or H3), 7.45 (m, 8 H, H$_{PPh}$), 7.50 (m, 4 H, H$_{para,PPh}$), 7.71 (m, 8 H, H$_{PPh}$). δ_C(DMSO-d$_6$, 50.3 MHz, 293 K): 144.72 (C4), 135.51 (d, $^1J_{C-P}$ = 134.3 Hz, C$_{ipso,PPh}$), 131.09 (d, $^4J_{C-P}$ = 2.8 Hz, C$_{para,PPh}$), 130.83 (d, $^2J_{C-P}$ = 10.0 Hz, C$_{ortho,PPh}$), 130.42 (C1), 128.92 (C2), 128.23 (d, $^3J_{C-P}$ = 12.6 Hz, C$_{meta,PPh}$), 114.74 (C3), 15.81 (CH$_2$). The assignment was supported by an APT experiment. δ_P(DMSO-d$_6$, 81 MHz, 293 K): 23.42.

Reaction of TDA with MPC in the presence of $Ph_2P(O)OH$. Synthesis, isolation and characterization of TDA mono- (**3b**) and di-carbamate (**4b**)

Procedure A

A mixture of MPC (1.050 g, 6.90 mmol), TDA (0.42175 g, 3.45 mmol) and $Ph_2P(O)OH$ (0.07565 g, 0.347 mmol) in THF (10 mL) was stirred at 363 K for 10 h, then cooled to room temperature (293 K) and analyzed by HPLC. The quantitative analysis (by HPLC) of the reaction mixture (benzene as internal standard) showed the selective formation of monocarbamate **3b** in 32% yield. The reaction mixture was evaporated *in vacuo* until complete removal of the solvent and the residue re-dissolved in CH$_2$Cl$_2$. The dichloromethane solution was extracted several times with water in order to remove the unreacted amine, dried over MgSO$_4$, and evaporated *in vacuo*. Recrystallization of the residue from diethyl ether–hexane afforded pure monocarbamate **3b** which was isolated by filtration, washed with hexane and dried *in vacuo*. Yield: 0.170 g, 28%. Anal. calc. for $C_9H_{12}N_2O_2$: C, 59.99; H, 6.71; N, 15.53. Found: C, 60.09; H, 6.88; N, 15.46%. ν(Nujol)/cm^{-1}: 3470 (ms), 3377 (ms), 3230 (w, br), 1706 (vs, ν_{CO}), 1631 (ms), 1611 (s), 1591 (m), 1530 (s), 1515 (ms), 1485 (ms), 1452 (ms), 1411 (m), 1324 (ms), 1302 (m, br), 1231 (vs), 1196 (mw), 1143 (mw), 1093 (m), 1050 (m), 1001 (m), 966 (mw), 937 (w), 843 (ms), 804 (ms), 785 (w), 769 (m), 721 (m), 579 (m), 569 (m), 465 (mw). δ_H ($CDCl_3$, 500.138 MHz, 293 K): 2.08 (s, 3 H, CH_3), 3.72 (s, 3 H, OCH_3), 3.86 (s, br, 2 H, NH_2), 6.58 (dd, ^3J = 8.04 Hz, ^4J = 2.0 Hz, 1 H, H5), 6.74 (s, br, 1 H, NH), 6.90 (partially overlapped with the signal due to H6, 1 H, H3), 6.91 (d, ^3J = 8.04 Hz, 1 H, H6). δ_C ($CDCl_3$, 125.760 MHz, 293 K): 154.08 (C(O)O), 144.49 (C2), 136.72 (C4), 130.60 (C6), 117.77 (C1), 109.16 (C5), 105.61 (C3), 52.12 (OCH_3), 16.62 (CH_3).

Procedure B

A mixture of MPC (1.570 g, 10.3 mmol), TDA (0.63130 g, 5.17 mmol) and $Ph_2P(O)OH$ (0.11305 g, 0.518 mmol) in THF (10 mL) was stirred at 363 K for 10 h. After cooling to room temperature, 0.10315 g of $Ph_2P(O)OH$ (0.473 mmol) were added and the reaction mixture was left to react at 363 K for 15 h longer. The total conversion of the amine into the mono- and di-carbamates estimated by HPLC was 75%. Upon cooling the reaction mixture to 293 K, a brown solid precipitated, that was isolated by filtration, washed with diethyl ether, dried *in vacuo* and identified as $(TDAH)O_2PPh_2$ (0.180 g; for characterization, see below).

The mother liquor and the washing solutions, collected together, were dried *in vacuo*. The residue, dissolved in THF (4 mL), was fractionated on a silica gel column (1.5 cm × 120 cm) using, as eluent, diethyl ether–hexane (1:1 v/v) until elution of **4b** and, then, diethyl ether–hexane (4:1 v/v). After evaporation of the solvent, 0.47535 g (2.64 mmol) of pure **3b** were recovered. Yield: 51%. Anal. calc. for $C_9H_{12}N_2O_2$: C, 59.99; H, 6.71; N, 15.53. Found: C, 60.60; H, 6.93; N, 15.53%. No attempt was made to recover minor amounts of **3b** from mixed fractions containing **3b**/**4b** or **3b**/**1b**.

The fractions containing **4b**, pure or contaminated by residues of phenol and/or MPC, were collected and evaporated *in vacuo*. The residue (0.090 g) was recrystallized from diethyl ether–hexane to give 0.07355 g (0.31 mmol) of pure dicarbamate **4b**. Yield: 6%. Anal. calc. for $C_{11}H_{14}N_2O_4$: C, 55.46; H, 5.92; N, 11.75. Found: C, 55.57; H, 5.81; N, 11.42%. ν(Nujol)/cm^{-1}: 3260 (s, br), 3130 (m, br), 3070 (m), 1710 and 1685 (vs, ν_{CO}), 1605 (s), 1545 (vs), 1535 (vs), 1495 (ms), 1440 (ms), 1420 (m), 1312 (m), 1280 (s), 1245 (vs), 1203 (s), 1195 (ms), 1130 (mw), 1065 (s), 995 (mw), 985 (mw), 955 (w), 945 (w), 875 (m), 815 (ms), 770 (ms), 740 (m), 725 (s), 638 (m), 628 (m) 585 (w), 569 (m), 452 (m), 395 (m). δ_H ($CDCl_3$, 500.138 MHz, 293 K): 2.17 (s, 3 H, CH_3), 3.74 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 6.39 (s, br, 1 H), 6.61 (s, br, 1 H), 7.06 (d, ^3J = 7.25 Hz, 1 H, H6), 7.24 (br, 1 H, partially overlapped with the signal due to the solvent), 7.73 (s, br, 1 H). δ_C ($CDCl_3$, 125.760 MHz, 293 K): 154.10 and 154.01 (C(O)O), 136.62 and 136.17 (C2 and C4), 130.81 (C6), 121.96 (C1), 114.34 and 111.11 (C3 and C5), 52.47 and 52.32 (OCH_3), 16.96 (CH_3).

***Characterization of* $(TDAH)O_2PPh_2$**

Anal. calc. for $C_{19}H_{21}PN_2O_2$: C, 67.04; H, 6.22; N, 8.22. Found: C, 67.22; H, 5.98; N, 8.04%. ν(Nujol)/cm^{-1}: 3470 (m), 3390 (m), 3070 and 3050 (mw), 2700–2100 (vbr), 1615 (ms), 1575 (m), 1550 (mw), 1505 (m), 1433 (m), 1320 (w), 1305 (mw), 1287 (mw), 1200 (w), 1155 (s), 1125 (s), 1065 (m), 1035 (ms), 1012 (ms), 995 (ms), 945 (mw), 835 (mw), 810 (mw), 785 (mw), 755 (m), 745 (m), 715 (s), 695 (ms), 560 (s), 540 (s), 500 (w), 468 (mw), 450 (mw). δ_H (THF-d_8, 500.138 MHz, 293 K): 2.02 (s, 3 H, CH_3), 6.14 (d, slightly broad, J = 6.62 Hz, 1 H, H5), 6.27 (s, 1 H, H3), 6.42 (vbr, NH), 6.70 (d, ^3J = 7.78 Hz, 1 H, H6), 7.25 (tr, J = 7.1 Hz, 4 H, H_{PPh}), 7.30 (tr, ^3J = 7.14 Hz, 2 H, $H_{para,PPh}$), 7.72 (m, 4 H, H_{PPh}). δ_C (DMSO-d_6, 50.3 MHz, 293 K): 146.00 and 143.11 (C2 and C4), 136.80 (d, $^1J_{C-P}$ = 133.1 Hz, $C_{ipso,PPh}$), 130.86 (d, $^2J_{C-P}$ = 9.7 Hz, $C_{ortho,PPh}$), 130.59 (d, $^4J_{C-P}$ = 2.6 Hz, $C_{para,PPh}$), 130.23 (C6), 128.02 (d, $^3J_{C-P}$ = 12.3 Hz, $C_{meta,PPh}$), 112.32 (C1), 105.32 and 102.52 (C3 and C5), 16.59 (CH_3). The assignment was supported by an APT experiment. δ_P (DMSO-d_6, 81 MHz, 293 K): 21.28.

Acknowledgements

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18 As a comparison, neither **3a** nor **4a** were formed when a mixture of **1a** (0.0305 g, 0.154 mmol) and MPC (0.047 g, 0.308 mmol) in THF (0.5 mL) were heated at 363 K for 24 h, in the absence of any catalyst. Only methylated amines were formed under the above conditions.

19 It is worth noting that heating a THF (1 mL) solution of **1b** (0.0405 g, 0.332 mmol) and MPC (0.100 g, 0.664 mmol) at 363 K for 6 h, in the absence of any catalyst, affords **3b** in 0.2% yield, whereas no dicarbamate **4b** was found to form under these conditions.

20 The reaction of **1a** (1.005 g, 5.05 mmol) with DMC (10 mL) in the presence of $Ph_2P(O)OH$ (0.13600 g, 0.624 mmol) at 363 K did not afford either **3a** or **4a**, but, after 63 h, (4-methylaminophenyl)-4-aminophenylmethane (m/z = 212) and dimethylation products (m/z = 226) were found (by GC-MS) as the unique reaction products. When a DMC (10 mL) solution of **1b** (1.003 g, 8.20 mmol) and $Ph_2P(O)OH$ (0.17850 g, 0.820 mmol) was heated at 363 K for 64 hours, both monocarbamates **3b** (the most abundant) and **3b′** were formed, but with very low selectivity as considerable amounts of mono- (m/z = 136) and di-methylated amine (m/z = 150) were found as by-products. Higher temperature, or the use of solvents other than DMC (THF, for example), did not improve the yield or selectivity of the carbomethoxylation reaction, but favoured the methylation process.

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Solvent-free one-pot rapid synthesis of 3-carboxycoumarins

using focused microwaves

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Summary

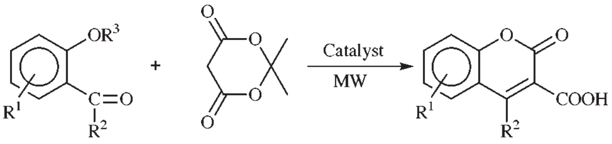
Reaction of 2-hydroxy- or 2-methoxy-substituted benzaldehydes or acetophenones with Meldrum's acid in the presence of environmentally-friendly catalysts, like natural kaolinitic clays, EPZ10 and EPZG, without solvent using focused microwaves afforded 3-carboxycoumarins in excellent yields.

Introduction

Coumarins are very well known natural products which exhibit a broad range of biological activities.[1] Many synthetic coumarins have shown interesting properties such as anticoagulants[2] and triplet sensitizers.[3] This has stimulated the search for new and more convenient methods for the preparation of coumarins, and several procedures have been reported.[4] 3-Carboxycoumarins may be synthesized in two steps from 2-methoxybenzaldehydes and Meldrum's acid.[5] 2-Methoxybenzaldehydes were first condensed with Meldrum's acid in the presence of DMF, which plays the dual role of a base as well as a solvent, resulting in a benzylidene derivative which was subsequently cyclized in the presence of sulfuric acid to afford 3-carboxycoumarins.[5]

Heterogenous organic reactions have proven useful to chemists in the laboratory as well as in industry. 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. In recent years there has been considerable growth in interest in the catalysis of organic reactions by natural clay[6] or inorganic reagents supported on high surface area inorganic materials.[7] Envirocats® are a new family of supported reagents which constitute a significant breakthrough in environmentally friendly chemistry. These supported reagents are non-toxic powders which can be filtered easily from the process and may be reused. Envirocats EPZG, EPZ10 and natural kaolinitic clay are solid catalysts which exhibit both Brønsted and Lewis acid characteristics.[6–8] A related development that had a profound impact on these heterogenous reactions is the use of microwave (MW) irradiation techniques for the acceleration of organic reactions.[9]

We report herein the use of a combination of natural kaolinitic clay or Envirocats (EPZG, EPZ10) and focused microwaves for the rapid one-pot synthesis of 3-carboxycoumarins from 2-hydroxy- or 2-methoxy-substituted benzaldehydes or acetophenones and Meldrum's acid under solvent-free conditions (Scheme 1).



Scheme 1 R^1 = H, Cl, OMe, OH; R^2 = H, Me; R^3 = H, Me

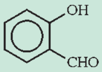
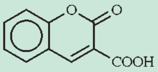
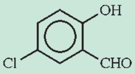
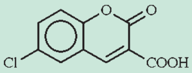
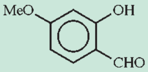
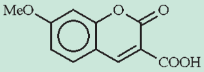
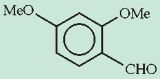
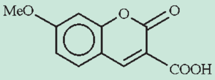
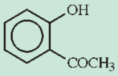
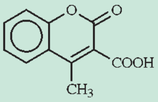
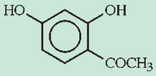
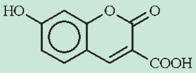
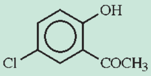
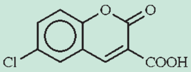
Results and discussion

Using focused microwaves 2-hydroxy- or 2-methoxy-substituted benzaldehydes or acetophenones with Meldrum's acid underwent Knoevenagel condensation due to the Lewis acid characteristics[10] of the Envirocats to yield the corresponding benzylidene derivatives which were cyclised spontaneously due to the Brønsted acid characteristics[5] of EPZG and EPZ10. The acidity of natural kaolinitic clay is not sufficient to bring about this conversion, therefore a drop of conc. H_2SO_4 should be added only when natural kaolinitic clay is used as the catalyst (conc. H_2SO_4 alone cannot bring about this transformation). Thus 3-carboxycoumarins were obtained in a one-pot reaction under solvent-free conditions. This one-pot procedure to obtain 3-carboxycoumarins (Table 1) is rapid compared with the reported two-

Green Context

The clean synthesis of heterocyclic compounds is an area of great interest, with many compounds showing significant biological activity. Rapid, simple methodology is a major benefit in their preparation. The acid-catalysed condensation and subsequent cyclisation of Meldrum's acid and carbonyl compounds is an important route to 3-substituted coumarins. Although this involves the loss of acetone, and is therefore not 100% atom efficient, it is an effective route to these compounds. The combination of microwaves and solid acid catalysts allows the rapid and high-yielding synthesis of several examples of these compounds. The paper describes a work-up which involves separation of catalyst and product by extraction with solvents, thus making the overall process, rather than the reaction, not solvent free. This drawback is often seen in such reactions. In order to really benefit from the very fast reaction times, and otherwise excellent performance of these reaction systems, work should be carried out to improve isolation, or to provide low-environmental-impact methods for the presentation of the product in the next reaction system and the recovery of the catalyst. *DJM*

Table 1 Synthesis of 3-carboxycoumarins using focused microwaves

	Carbonyl compound	Catalyst	Product	Reaction time/min	mp /°C	Yield[a,b] (%)
1		EPZ10		4	191	82
		EPZG		3	192	84
		Natural clay		5	191	71
2		EPZ10		6	120	76
		EPZG		4	121	97
		Natural clay		5	120	90
3		EPZ10		5	192	55
		Natural clay		7	192	84
4		EPZG		5	192	60
		Natural clay		7	192	93
5		EPZ10		3	154	68
		EPZG		5	154	74
		Natural clay		1	150	73
6		EPZG		2	126	66
		Natural clay		2	126	75
7		EPZ10		6	152	64

[a] Yields are of pure isolated products. [b] Products were characterised by their physical constants, IR and ^1H NMR spectra and comparison with authentic samples.

step method.[5] This cyclization reaction is possible only when the 2-methoxy or 2-hydroxy group acts as a nucleophile on the closer carbonyl function.

In conclusion, we describe herein a rapid, one-pot synthesis of 3-carboxycoumarins from 2-hydroxy- or 2-methoxy-benzaldehydes or acetophenones and Meldrum's acid with EPZ10, EPZG or natural kaolinitic clay under solvent-free conditions using focused microwaves.

Experimental

All reactions were carried out in oven dried flasks. Solvent (diethyl ether) was distilled before used. All chemicals were of analytical grade. Envirocats EPZG and EPZ10 were procured from Contract Chemicals, England whereas natural kaolinitic clay was obtained from the Padappakara mine of Quilon District, Kerala, India and it was purified and supplied by Dr Lalithambika, RRL, Trivandrum. IR spectra (results not cited here) were recorded on Bomem MB 104 FTIR spectrometer.

Preparation of 3-carboxycoumarins

A mixture of the carbonyl compound (5 mmol) and Meldrum's acid (5 mmol) was placed in a beaker containing EPZG/EPZ10 (100 mg) or natural clay (100 mg, with a drop of conc. H_2SO_4) and exposed to pulsed microwave irradiation for 2 s using an unmodified microwave oven (Kelvinator, T-37 model, India, 760 W, 2450 MHz) operating at 100% power. The reaction mixture was then removed from the microwave oven and allowed to cool to room temperature (1 min) and irradiated again for 2 s. After completion of the reaction (TLC), the reaction mixture was filtered and the catalyst was washed with diethyl ether (4 × 10 ml). The solvent was removed under reduced pressure to obtain crude 3-carboxycoumarin which was purified by column chromatography (Silica gel G, S.D. Fine, Mumbia, India) using ethyl acetate–light petroleum (1:9) as eluent.

Acknowledgement

We thank Contract Chemicals, England and Dr Lalithambika, Regional Research Laboratory, Trivandrum for generous gifts of EPZG, EPZ10 and natural kaolinitic clay respectively. Financial assistance from U.G.C., New Delhi is gratefully acknowledged.

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Paper 9/05811G

Synthesis of allylbenzenes

by cross-coupling of allyl bromide with arylboronic acids using a palladium chloride and tetraphenylphosphonium bromide intercalated clay catalyst

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Summary

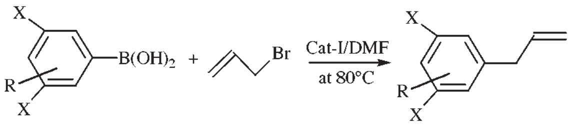
A facile route for the synthesis of allylbenzenes is described from easily accessible allyl bromide and arylboronic acids using a new reusable catalyst system, palladium chloride and tetraphenylphosphonium bromide intercalated clay.

Introduction

Among the C–C bond forming reactions, the Suzuki type coupling of aryl halides with arylboronic acids or esters has found widespread applicability in organic chemistry.[1–4] The easier handling, high stability and low toxicity of boronic acids have made them among the most popular intermediates for cross-coupling reactions with a wide variety of substrates. There are several reports on cross-coupling reactions of arylboronic acids using nickel[5,6] or palladium[7] complexes and the extension of such reactions to sulfonium salts[8] has been described. The mild coupling conditions and flexibility are some of the main advantages which render boronic acids as ideal reagents for combinatorial chemistry applications.[9,10] Recently, the coupling reaction of arylboronic acids catalyzed by pre-formed palladium and palladium–nickel clusters[11] has been reported in phosphine-free reaction with arenediazonium fluoroborates[12,13] and synthesis of neoflavones by arylation of coumarin-4-triflates.[14] In these examples, the isolation of regenerated catalyst is difficult and further steps are necessary for any subsequent reaction. Consequently, the enhancement of catalyst efficiency and reusability and, especially in the industrial context, the development of new catalytic materials is desired. Clays, their cation-exchanged forms, clay-supported reagents and pillared clays play extensive roles in organic synthesis under mild reaction conditions.[15–20] These modified clay materials, unlike other conventional catalysts, have considerable advantages such as low cost, recyclability, ease of handling and easier modulation of acidity levels by suitable exchange of cations. Our interest in modified clay materials and their application in organic synthesis[20] prompted us to explore the preparation of allylbenzenes using a new catalyst system, palladium chloride and tetraphenylphosphonium bromide intercalated clay (Cat-I).

Results and discussion

In a typical experiment, an equimolar amount (1 mmol) of allyl bromide and arylboronic acid was continuously stirred with a mixture of catalyst and potassium carbonate in refluxing dimethylformamide (Scheme 1) for a specified time period as shown in Table 1.



R = H, 2-Ph, 4-Ph, 4-SMe and 4-Bu^t
X = H, F and Cl

Scheme 1

Our results for the synthesis of various allylbenzenes are summarized in Table 1. The boronic acids bearing an electron withdrawing substituent in the aryl moiety undergo the reaction at a faster rate as compared to the boronic acids with electron releasing substituents. In the case of *ortho*-substituted arylboronic acids, the rate of the reaction is slow when compared to the *para*-substituted analogue presumably due to the large steric hindrance. The rate of the reaction with this heterogeneous catalyst is much faster, even at these very low catalyst concentrations, when compared to homogeneous reaction conditions.

Conclusions

We have demonstrated that a system consisting of palladium chloride and tetraphenylphosphonium bromide intercalated clay is a very efficient catalyst for the rapid assembly of allylbenzenes. Some of the main advantages of this method over homogeneous conditions are the ease of handling of the reaction, and the separa-

Green Context

The Suzuki coupling of halides and arylboronic acids requires the use of Pd catalysts and base. The isolation and reuse of the expensive Pd catalyst is difficult and generates waste, as well as having economic implications. Tetraarylphosphonium intercalated clays are known, as are a variety of similar materials. They can be easily prepared and their isolation after reaction is straightforward. This paper describes the extension of this method to make tetraphenylphosphonium intercalated clays containing Pd as easily isolable and reusable catalysts for the Suzuki reaction of allyl halides and arylboronic acids. ***DJM***

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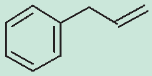
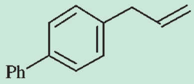
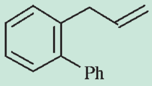
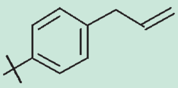
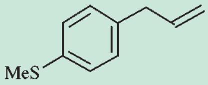
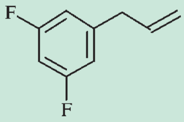
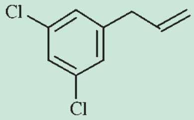
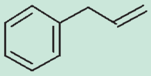
† *Current address*: U.S. Environmental Protection Agency, National Risk Management Research Laboratory, 26 West Martin Luther King Drive, MS 443 Cincinnati, Ohio 45268. USA. E-mail: rajender@epamail.epa.gov

Table 1 Product distribution in the coupling reaction of allyl bromide and arylboronic acids catalyzed by palladium chloride and tetraphenylphosphonium bromide intercalated clay[a]

Entry	Product	Time/h	Products (%)		
			I	**II**	**III**
1		1.5	70	10	20
2		1	90	5	5
3		2	55	10	35
4		4	75	7	18
5		1.5	69	10	21
6		1	60	27	13
7		1	60	20	20
8		1.5	68	12	20

[a] The relative amounts of product formation were determined by GC-MS analysis; **I** is the cross-coupling product; **II** is the self-coupling product from boronic acid and **III** is the starting materials; the results in entry 8 are obtained by using recycled catalyst.

tion of the catalyst by simple filtration. The subsequent reuse (Table 1, entry 8) of the catalyst (recycled twice) without any loss in activity makes this an ideal protocol and a useful and attractive alternative to the currently available methods.

Experimental

To a warmed solution of 300 mg $PdCl_2$ and 1.5 g tetraphenylphosphonium bromide in 50 ml water, 6 g of sodium-exchanged clay[20a,21] was added and the mixture was refluxed with stirring for 48 h. The clay material was then filtered off, washed thoroughly with water and dried overnight in an oven at 100–110 °C.

General procedure for the synthesis of allylbenzenes

In a typical example, the clay-based catalyst (20 mg) and K_2CO_3 (276 mg, 2 mmol) were intimately mixed using a pestle and mortar and placed in a round bottomed flask. To this, equimolar amounts (1 mmol) of the starting materials (arylboronic acid and allyl bromide) were added followed by dimethylformamide (2 cm^3) and the mixture refluxed with continuous stirring for the time specified in Table 1. After completion of the reaction, as indicated by TLC examination, the mixture was quenched with water and the product was extracted into ethyl acetate. The organic layer was washed with an excess of water in order to remove any residual dimethylformamide. The product composition was determined by GC-MS analysis (Hewlett-Packard model 5890 gas chromatograph with a mass spectrometer) and the identities of the products were confirmed by spectral data. The clay material was retrieved from the aqueous layer by filtration, washed with organic solvent and dried overnight at 110 °C for further reuse (recycled twice) without any loss in catalytic activity (Table 1, entry 8).

Acknowledgement

We thank Professor T. J. Pinnavaia for help in the preliminary characterization of intercalated clay materials and the Texas Research Institute for Environmental Studies (TRIES) for the financial support.

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and K. P. Naicker, *Tetrahedron Lett.*, 1999, **40,** 439; (*g*) R. S. Varma, D. Kumar and P. J. Liesen, *J. Chem. Soc., Perkin Trans 1*, 1998, 4093; (*h*) A. Vass, J. Dudas and R. S. Varma, *Tetrahedron Lett.*, 1999, **40,** 4951; (i) R. S. Varma and D. Kumar, *Tetrahedron Lett.*, 1999, in press.
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Paper 9/05846J

Synthesis of allylbenzenes

by cross-coupling of allyl bromide with arylboronic acids using a palladium chloride and tetraphenylphosphonium bromide intercalated clay catalyst

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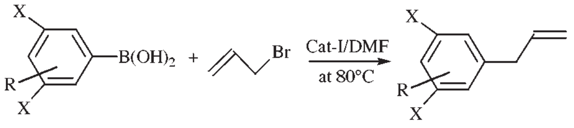

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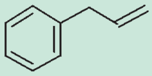
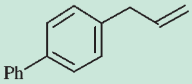
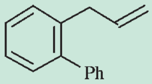
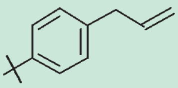
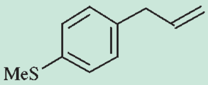
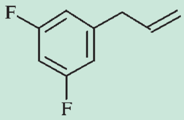
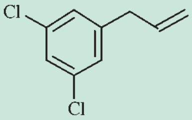
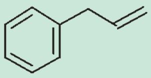
1		1.5	70	10	20
2		1	90	5	5
3		2	55	10	35
4		4	75	7	18
5		1.5	69	10	21
6		1	60	27	13
7		1	60	20	20
8		1.5	68	12	20

[a] The relative amounts of product formation were determined by GC-MS analysis; **I** is the cross-coupling product; **II** is the self-coupling product from boronic acid and **III** is the starting materials; the results in entry 8 are obtained by using recycled catalyst.

tion of the catalyst by simple filtration. The subsequent reuse (Table 1, entry 8) of the catalyst (recycled twice) without any loss in activity makes this an ideal protocol and a useful and attractive alternative to the currently available methods.

Experimental

To a warmed solution of 300 mg $PdCl_2$ and 1.5 g tetraphenylphosphonium bromide in 50 ml water, 6 g of sodium-exchanged clay[20a,21] was added and the mixture was refluxed with stirring for 48 h. The clay material was then filtered off, washed thoroughly with water and dried overnight in an oven at 100–110 °C.

General procedure for the synthesis of allylbenzenes

In a typical example, the clay-based catalyst (20 mg) and K_2CO_3 (276 mg, 2 mmol) were intimately mixed using a pestle and mortar and placed in a round bottomed flask. To this, equimolar amounts (1 mmol) of the starting materials (arylboronic acid and allyl bromide) were added followed by dimethylformamide (2 cm^3) and the mixture refluxed with continuous stirring for the time specified in Table 1. After completion of the reaction, as indicated by TLC examination, the mixture was quenched with water and the product was extracted into ethyl acetate. The organic layer was washed with an excess of water in order to remove any residual dimethylformamide. The product composition was determined by GC-MS analysis (Hewlett-Packard model 5890 gas chromatograph with a mass spectrometer) and the identities of the products were confirmed by spectral data. The clay material was retrieved from the aqueous layer by filtration, washed with organic solvent and dried overnight at 110 °C for further reuse (recycled twice) without any loss in catalytic activity (Table 1, entry 8).

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Microwave promoted synthesis of β-aminoalcohols in dry media†

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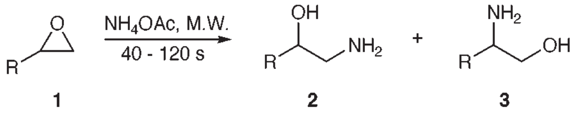
Summary

Aminolysis of epoxides with ammonium acetate has been achieved for the first time under microwave irradiation conditions. This reaction is regioselective and affords β-aminoalcohols in good yields.

Introduction

vic-Aminoalcohols are important intermediates[1] in natural product synthesis and are also used as building blocks for the synthesis of pharmaceuticals,[2] as insecticidal agents,[3] and as chiral ligands for asymmetric catalysis.[4] As a consequence, several approaches towards their preparation have been reported in the literature.[5] Even though aminolysis of expoxides is an attractive route to aminoalcohols, this reaction is slow and affords aminoalcohols in low yields along with the recovered starting materials.[6] Attempts to effect the aminolysis of epoxides by subjecting them to microwave irradiation with ammonium acetate afforded good yields of β-aminoalcohols with high regioselectivity.

In continuation of our interest to develop environmentally safe methods,[7] herein we wish to report a regioselective ring opening of epoxides **1** with ammonium acetate by microwave irradiation under solvent free conditions (in dry media). This method is clean, rapid and completely regioselective, affording the corresponding β-aminoalcohols **2** with a trace of the other isomer **3** (Scheme 1). The regioselectivity of this reaction can be explained by the nucleophilic attack on the less hindered carbon atom of the oxirane ring.



Scheme 1

Results and discussion

The epoxides used in this study were prepared by a known literature[6] method. The reaction was performed by irradiating a mixture of epoxide (10 mmol) and NH_4OAc (15 mmol) in a domestic microwave oven with an output of 600 watts.[7] A minor quantity of N-acetylated product was also isolated in several cases (Table 1, entries a, b, d, and i). In order to determine the rate enhancement under microwave irradiation, we conducted the same reaction by refluxing the epoxide (10 mmol) and ammonium acetate (15 mmol) in THF (15 mL) for 8 h, affording β-aminoalcohols in low yield along with recovered starting material, which confirms the role of microwave irradiation in this transformation. This reaction rate and yield were dramatically increased by the addition of catalytic amount of Lewis acids ($BF_3 \cdot OEt_2$ or $FeCl_3$).

Conclusion

We have described a simple and convenient method for the synthesis of β-aminoalcohols by regioselective ring opening of epoxides under microwave irradiation in solvent free conditions, thus it is an attractive addition to the existing methods.

Experimental

In a typical procedure, the epoxide **1a** (1.5 g, 10 mmol) and ammonium acetate (1.15 g, 15 mmol) were admixed in a Pyrex test tube and subjected to microwave irradiation for 40 s. After complete conversion, as indicated by TLC, the reaction mass was diluted with water (20 mL) and extracted with ethyl acetate (2 × 25 mL), washed with brine (20 mL) and dried over Na_2SO_4. The organic extract was concentrated *in vacuo* to obtain the crude product, which was purified by column chromatography on silica gel (Aldrich 100–200 mesh, hexane–ethyl acetate, 7:3) affording **2a** (1.25 g, 75% yield) as an oily liquid.

Acknowledgement

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Green Context

The preparation of aminoalcohols is often a key step in synthetic sequences. Selectivity and reaction time are issues, particularly if catalysts are to be avoided. This article describes initial experiments designed at using microwave irradiation to accelerate the transformation in the absence of solvent and catalyst. Rates are very fast, with complete conversion being achieved in seconds. Selectivity to the secondary alcohol was generally very good. The paper describes a work-up which involves extraction with solvents, thus making the overall process, rather than the reaction, not solvent free. This is a generic difficulty with such solvent free reactions, which may be overcome if the crude product is sufficiently pure to be used directly in a further step. Otherwise, effort must be expended to provide a generally useful methodology for the isolation of products from this type of reaction without the use of solvents. ***DJM***

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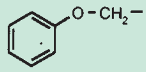
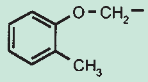
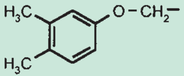
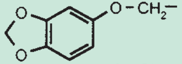
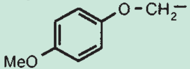
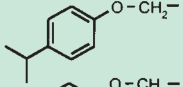
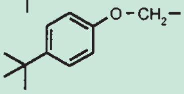
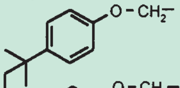
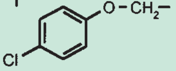
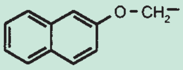
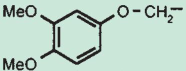
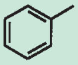
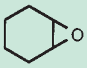
† IICT Communication No. 4236.

Table 1 Conversion of epoxides to β-aminoalcohols under microwave irradiation

Entry	Epoxide (R)	Reaction time^a/s	Yield (%)^b	Regio-selec-tivity (**2**:**3**)^c
a.		40	75	100 : 0
b.		45	77	80 : 20
c.		50	83	90 : 10
d.		120	78	97 : 3
e.		60	82	100 : 0
f.		90	76	98 : 2
g.		120	74	100 : 0
h.		80	70	98 : 2
i.		90	65	75 : 25
j.		60	85	95 : 5
k.		120	80	95 : 5
l.		60	68	100 : 0
m.		60	82	– –
n.		120	70	94 : 6
o.		120	72	92 : 8

^{a} All reactions were carried out in a domestic microwave oven (BPL, BMO) at an output of 600 watts. ^{b} Isolated after column chromatography. ^{c} Ratio of **2**:**3** was determined by ^{1}H NMR and GLC analysis.

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