Baby chewing PVC teething ring containing phthalates

Phthalate esters in children's toys—calls for product substitution

Becky Allen examines a current public safety controversy

Introduction

In 1997, Greenpeace opened up a new front in its campaign against polyvinyl chloride (PVC), raising concerns about the safety of phthalate esters in children's toys. Despite the defeat—by one vote—in the European Commission of a measure to ban phthalates in certain children's toys in 1998, many toy retailers and manufacturers are eliminating phthalates and PVC from their products.

Although eclipsed by media coverage of genetically modified foods, the debate over phthalates in toys has all the hallmarks of a classic scientific controversy: conflicting accounts of scientific 'facts' fought out in public by a plethora of experts. Superficially about science, most controversies are less concerned with scientific facts and more about politics and the democracy of decision-making.

The current phthalate controversy in Europe began in Denmark. In April 1997 Danish authorities approached the European Commission with concerns about the levels of phthalates being released from teething rings made in China for a company called Chicco-Artsana. Although the manufacturer withdrew the products from sale in Europe, the issue revealed the absence of a validated method for testing phthalate migration. As a result—and in response to lobbying by Greenpeace and the toy industry—the Commission asked its Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE) to evaluate the evidence.

CSTEE evaluation

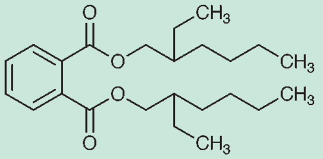
The CSTEE met five times during 1998, examining the amount of phthalate esters in toys, data on leaching from toys, exposure to phthalates from other sources as well as their toxicity. In its review of the literature, the CSTEE found that DEHP causes liver cancer in rats and mice, but *via* a pathway that is less relevant in humans. It also noted that DEHP caused reproductive effects, including testicular atrophy, embryo toxicity and teratogenicity. Other phthalate esters produce a similar pattern of effects, and there is some evidence that BBP has oestrogenic effects *in vitro*.[1]

In April 1998 the CSTEE concluded that for two phthalate esters—DINP and DEHP—estimated safety margins were below 100, and the safety margin of 8.8 for DINP 'gave cause for concern'. However, when the CSTEE met again in November 1998, results were available from Dutch and Austrian tests on the release of DINP and DEHP into saliva in human volunteers, plus results from tests by the US Consumer Product Safety Commission (CPSC) laboratory. These data gave a more reassuring picture of the amount of phthalates leached from toys when sucked, but the CSTEE said: 'The revised margin of safety (MOS) values are 75 for DINP and 19 for DEHP, respectively. The MOS for DINP raises some concern as it is less than the previously recommended safety margin of at least 100. The MOS for DEHP raises clear concern.'[2] Its November 1998 opinion concluded: 'The CSTEE recommends that an interlaboratory comparison exercise be carried out in order to document the reproducibility of

Phthalate esters

Phthalate esters have been widely used since the 1940s, especially as plasticisers in vinyl products to make them soft and flexible. Examples include the following:

- **butyl benzyl phthalate (BBP)**
- **diisononyl phthalate (DINP)**
- **dibutyl phthalate (DBP)**
- **di-2-ethyl hexyl phthalate (DEHP)**



Di(2-ethylhexyl) phthalate (DEHP)

- **di-*n*-octyl phthalate (DNOP)**
- **diiso-decyl phthalate (DIDP)**

The phthalate esters causing the most concern as regards toxicity are DEHP and DINP.

the Dutch laboratory method to measure phthalate release from PVC toys. Studies performed in order to shed light on the issue of buccal absorption of phthalates should be carried out. The CSTEE further recommends that additional studies be carried out in order gain more insight as to the total time children are mouthing PVC toys.'

Calls for a ban

Despite the narrow defeat in the European Commission of measures to ban phthalates in toys in 1998, several member states—as well as toy manufacturers and retailers—have taken action, and in December 1998 the US CPSC asked industry to find substitutes for phthalates in products for children under three. Although not recommending a ban, the CPSC said there were 'several areas of uncertainty where additional scientific research is needed'. As a precaution while more scientific work is done, the CPSC requested industry to remove phthalates from soft rattles and teethers. By early 1999, companies including Hasbro, Mattel and Toys-R-Us stopped using phthalates in teethers and rattles or removed phthalate-containing products from their shelves.

Although Greenpeace has presented such moves as another victory in its war against PVC, industry bodies including the US Chemical Manufacturers' Association (CMA) Phthalate Esters Panel say that adverse effects in animals exposed to phthalates only occur at 'extremely high doses' and that DEHP, about which the CSTEE expressed most concern, is rarely used in children's toys. 'Countries that are banning phthalates are not acting in accordance with the scientific evidence,' says the CMA.

Product substitution

Amid the heat and light of the debate over phthalate toxicity, less is being said about alternatives to phthalates in PVC, or alternatives to PVC itself in children's toys. According to Maurits Bruggink of the Toy Industries of Europe: 'An unfortunate consequence has been the announcement by some companies that they will use alternative raw materials, not because their products are unsafe but simply because of pressure. In the end it will be the consumer who will suffer, not only from lack of choice, but also because many raw materials are far less well understood.'

Manufacturers that decide to address consumer concerns about the safety of phthalates have several choices. They could attempt to make phthalates in PVC more immobile, switch to plasticisers other than phthalate esters, or replace PVC altogether. Although recent Indian work suggests that surface-modification techniques using sodium sulfide might prevent phthalate migration,[3] previous attempts to lock phthalates into PVC have resulted in loss of flexibility. Alternative plasticisers include adipates and citrates, although less is known about their toxicity and mobility in PVC. The third option is replacing PVC with other materials such as polyolefins.

Soft plastic toys often end up in children's mouths

'A Greenpeace report concludes that the toy industry should abandon plastics based on petrochemicals'

Metallocene polyolefins, thermoplastic elastomers and ethylene vinyl acetate are identified as interim substitutes for PVC in toys in a report commissioned from the University of Massachusetts by Greenpeace.[4] But despite being safer and cost-competitive, industry currently lacks the will to change, the report says. 'Rather than spending resources on only assessing the risks of phthalate plasticiser in PVC toys, attention should focus on which alternatives can be developed and selected to replace PVC in toys,' says the report. It also points to new technologies such as thin wall injection moulding and gas assisted injection moulding as a way forward. However, in the long term the report says the toy industry should abandon plastics based on petrochemicals altogether. The report concludes: 'Advancements in biodegradable plastics hold hope for the future production of toys that are more sustainable through their life cycle.'

Recent developments

Dutch migration test validated[5]

On 31 May 1999 it was announced that the so-called 'Dutch Migration Test', which can be used to measure the

Phthalates on the Web

For further information on phthalates, especially in PVC toys, see the following websites:

- **http://www.greenpeace.org/-comms/pvctoys/**
- **http://www.vinyltoys.com**
- **http://www.phthalates.com**
- **http://www.vinylinfor.org**
- **http://www.ecpi.org and links therefrom.**

migration of the phthalate plasticiser DNIP from toys *etc.* has been successfully validated in trials organised by the TNO Nutrition and Food Research Institute in the Netherlands, and carried out in 6 laboratories in Germany, the Netherlands and the UK; it was expected that the test could be also validated for other phthalates. The test could be used to ensure that toys and childcare items, intended to be put in the mouths of children under 3 years old, conform to the migration limits suggested by CSTEE. Whether EU Member States, including the Netherlands, adopt the Dutch test method still has to be decided. Any EU-wide agreement may have to follow collaborative trials being conducted by the EU Joint Research Centre (JRC) at Ispra in Italy. The JRC is believed to be looking at a number of methods, including one similar to that of the Dutch that has been developed by the Laboratory of the Government Chemist in the UK and which is also currently undergoing interlaboratory testing.

Danish regulation of phthalates

On the 1 April 1999 the Danish ban on phthalates in toys and baby articles for children under 3 years of age came into force, making it the second European country to enforce such a ban, following Austria which banned them in January 1999.

> 'The Danish goal is to reduce the use of phthalates by 50% by the year 2010'

In June 1999 the Danish Government announced a new plan to regulate the use of PVC and phthalates by introducing taxes on both of them—2 Danish Kroner per kg of PVC and 7 Danish Kroner per kg phthalates. In addition the Danish plan covers a range of initiatives which, if fully implemented, would keep PVC away from incineration plants. In recent years Denmark has taken the lead in the regulation of PVC and phthalates, and has found that voluntary agreements between its government and the PVC industry have not worked—hence the proposed legislation. The Danish goal is to reduce the use of phthalates by 50% by the year 2010.

US panel confirms safety of phthalates[6]

An independent expert panel convened by the American Council on Science and Health (ACSH) announced on 22 June its conclusion that phthalates are safe for use in toys and medical devices. The 17-member panel, chaired by the former US Surgeon General Dr C. Everett Koop, reviewed a wide variety of published and unpublished scientific literature from the US, Canada and Europe to evaluate potential health risks from DEHP and DINP. The conclusions were that DEHP and DINP are not carcinogenic nor do they have other harmful effects at levels to which people are exposed, casting doubt on the extrapolations which have been made in the past from animal studies to human health. On toys, the panel recommends further studies to expand knowledge of children's exposure, but states clearly its view that 'DNIP in toys is not harmful for children who use these toys normally.'

> 'A US panel states that DNIP in toys is not harmful for children who use these toys normally'

The controversy goes on

The conclusions of the ACSH report have been welcomed by the European Council for Plasticisers and Intermediates. But Greenpeace and other organisations do not accept the panel's findings and claim that there is sufficient doubt about the risks involved to ban the controversial materials. They will therefore continue their campaign to ban PVC and phthalates.

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Lead at the roadside

Kam Kit Lam, Gerry Ottewill, Brian Plunkett and Frank Walsh at the University of Portsmouth describe the change to roadside vegetation in southern England resulting from the switch from leaded to unleaded fuel *

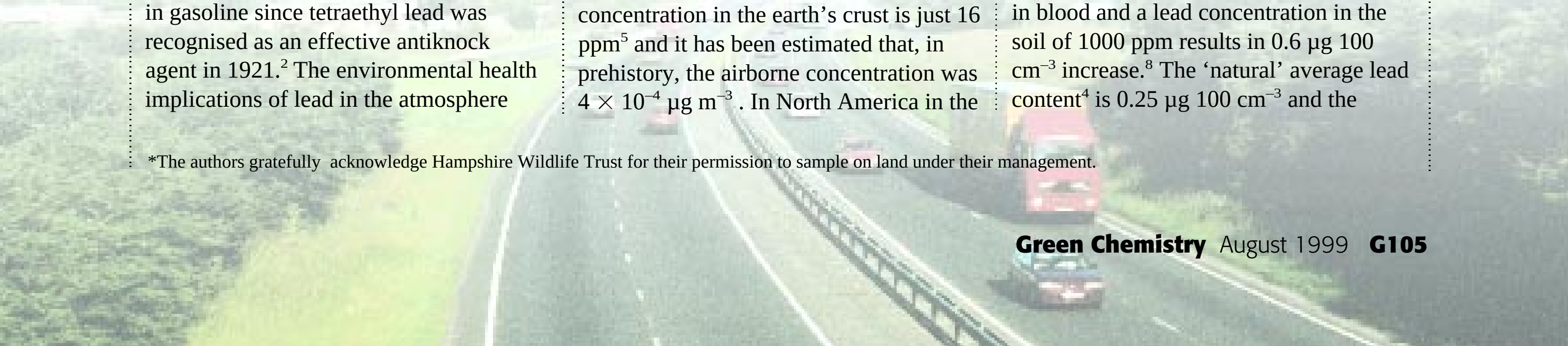
Lead usually enters the environment by one of four routes—primary or secondary smelting, fabrication processes or paint manufacture, disposal or discarding of unwanted lead-containing materials and combustion of coal and other fuels, especially leaded gasoline. Lead emission from industrial processing is subject to stringent regulation of acceptable emission levels and safe working practice and industrial emission is usually centred on a specific locality and so largely confined to relatively small geographical regions.

Lead from automobile exhaust

In the mid-1980s approximately 85% of all lead discharged into the atmosphere originated from automobile exhaust.[1] Alkyl lead compounds, especially tetramethyl and tetraethyl lead, have been accepted as antiknock agents in gasoline since tetraethyl lead was recognised as an effective antiknock agent in 1921.[2] The environmental health implications of lead in the atmosphere were brought into question[3] as early as 1922 but, from 1923, when it first went on sale, consumption of leaded fuel soared.

A low-level background concentration of lead, arising through mobilisation from lead ores, is naturally present in the environment but anthropogenic lead emission has raised atmospheric lead levels significantly since leaded fuel became widely used. Comparison of the Northern Hemisphere air lead levels with those of the Southern Hemisphere (where there is a substantially lower anthropogenic contribution) shows that the Northern Hemisphere has up to 10 times as much airborne lead as the Southern—0.05–0.20 μg Pb m^{-3} compared with 0.02 μg m^{-3}. The *natural* atmospheric concentration of lead arising through airborne particulates and gaseous diffusion should, it is calculated,[4] be as low as 5×10^{-4} μg m^{-3}. The mean lead concentration in the earth's crust is just 16 ppm[5] and it has been estimated that, in prehistory, the airborne concentration was 4×10^{-4} μg m^{-3}. In North America in the mid 1980s levels in even the most remote areas were around 10×10^{-4} μg m^{-3} and up to 10 μg m^{-3} in urban areas. Although substantially higher than natural background levels this represented a decrease from the levels of the 1960s and 1970s when leaded gasoline consumption was higher. In 1967, atmospheric lead levels in large US cities averaged 10–35 μg m^{-3}—an isolated case of *ca.* 70 μg m^{-3} was measured near Hollywood, California.[6] In dust collected in Birmingham, England from 1972–75 lead was found at a concentration of *ca.* 970 ppm.[7] The particle size strongly influences environmental lead burdens—the smallest particles contain the greatest lead concentrations.

The physiological effects of lead pollution are well documented. An atmospheric lead concentration of 1 μg m^{-3} can produce a rise of 1.0 μg 100 cm^{-3} in blood and a lead concentration in the soil of 1000 ppm results in 0.6 μg 100 cm^{-3} increase.[8] The 'natural' average lead content[4] is 0.25 μg 100 cm^{-3} and the



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*The authors gratefully acknowledge Hampshire Wildlife Trust for their permission to sample on land under their management.

'acceptable' blood lead level,[8] 70–80 µg 100 cm^{-3} in adults. For children[1] 25 µg 100 cm^{-3} is considered the upper limit 'normal'. Over the period 1976–1980, as use of leaded fuel fell, mean blood levels began to decrease.[5]

Consumption of leaded gasoline began to decline only when legislation was passed in the US enforcing the reduction of exhaust emissions—50 years after we started to use it! The capital cost to the US refineries to produce 100% lead free petrol was almost 15 000 million U.S. dollars,[9] but by 1985, unleaded fuel had the major market share, 78% of the total compared with only 25% in 1977.

We have looked at lead distribution on the vegetation alongside a length of the A27 major roadway in three different years, 1978, 1984 and 1994, measuring the lead concentrations and examining their variation over time, distance from the road and vegetation type.†

Lead in grass samples

Figure 1 shows the lead content of grass samples as a function of distance from the roadside. The lead content in unwashed grass samples collected in 1978 is shown in Figure 1(a). It ranged from 77 µg Pb g^{-1} to 45 µg Pb g^{-1} at distances of 37 m and 50 m, respectively, with distinct maxima and minima at distances of approximately 20 and 50 m. The distance profile for the 1984 samples [Figure 1(b)] shows a more linear pattern falling from 160 µg Pb g^{-1} at 10 m to 15 µg Pb g^{-1} at a distance of 60 m. Results for the 1994 analyses, illustrated in Figure 1(c) are reported for both washed and unwashed samples. The lead in unwashed grass had a concentration range from 5.22 (±1.05) µg Pb g^{-1} to 35.0 (±0.9) µg Pb g^{-1} at distances of 0 m and 80 m, respectively, from the roadside. Lead content in washed samples averaged 55% of that in the unwashed, ranging from 2.31 (±0.38) to 16.8 (±0.1) µg Pb g^{-1} at 0 m and 80 m distances, respectively. The distance profiles for washed and unwashed samples both fall from a maximum at the road edge to a shallow minimum at 20 m. A second maximum occurs at about 40 m where the concentration is almost as high as at the roadside. From 40 m to 80 m overall the lead content drops. The unwashed sample profile has a much

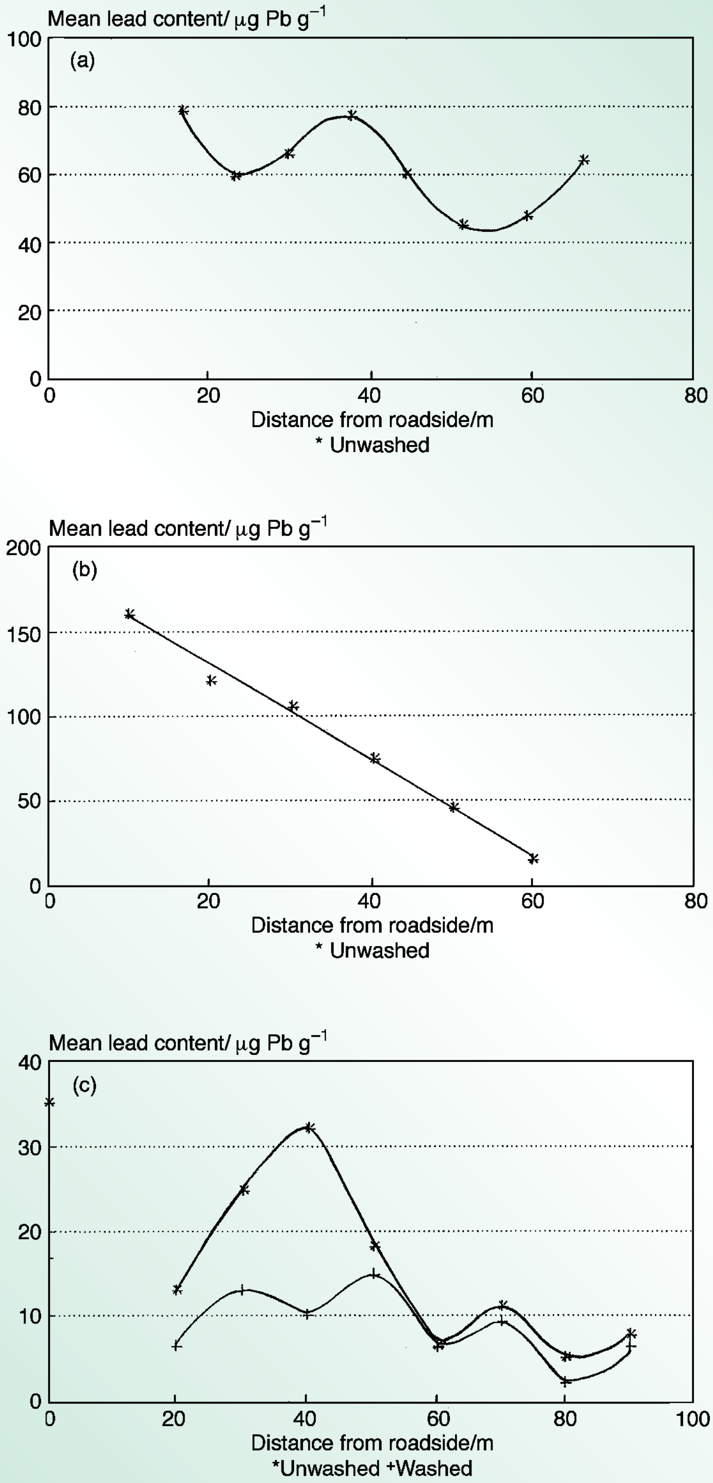


Figure 1. Lead content of grass samples as a function of distance from the side of the A27 roadway: (a) 1978 data; (b) 1984 data; (c) 1994 data.

† The sampling sites lay beside a busy section of the A27 trunk road running through the Farlington Marshes Nature Reserve, Hampshire, England. A series of posts, 1.5 m in height, was erected in a line perpendicular to the carriageway. The posts were placed at 10 m intervals up to a total distance of 90 m from the roadside. Vegetation samples consisted of grass, weed and moss. The species of grass were, primarily, False-brome (*Brachypodium sylvaticum*), foxtail (*Alopecurus geniculatus*) and Yorkshire fog (*Holcus lanatus*). Weed samples were silverweed (*Potentilla anserina)*; the moss was *Sphagnum acubifolium* aggregate.[10]

All samples were air-dried and then oven-dried for 36 h at 110 ºC. The dried material was ground into a powder and portions of the powdered vegetation (0.5–1.5 g) were digested for 2 h in a 4:1 v/v mixture of aqueous Analar nitric and perchloric acids (25 cm^{3}). The digest was filtered and diluted twofold using 1% nitric acid. Samples were analysed, in triplicate, using flame atomic absorption spectroscopy. The lower detection limit was 0.02 µg Pb cm^{-3} with a concentration range linear up to 20 µg Pb cm^{-3}.

shallower maxima and minima, particularly evident around 40 m. The decrease in the lead content at 40 m is around 70% with washing. At 60 m the reduction due to washing is much less—only about 2%.

Lead in silverweed samples

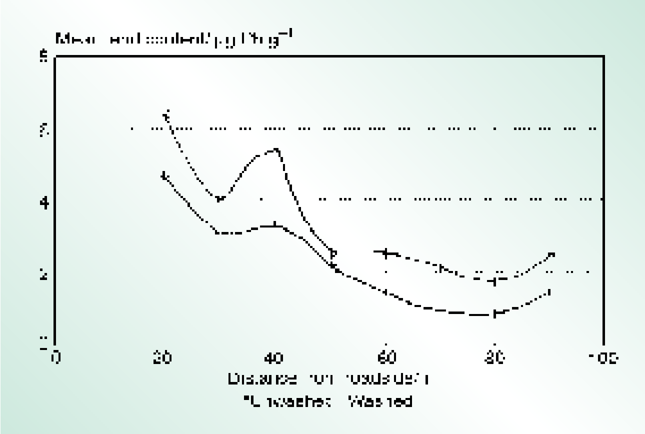
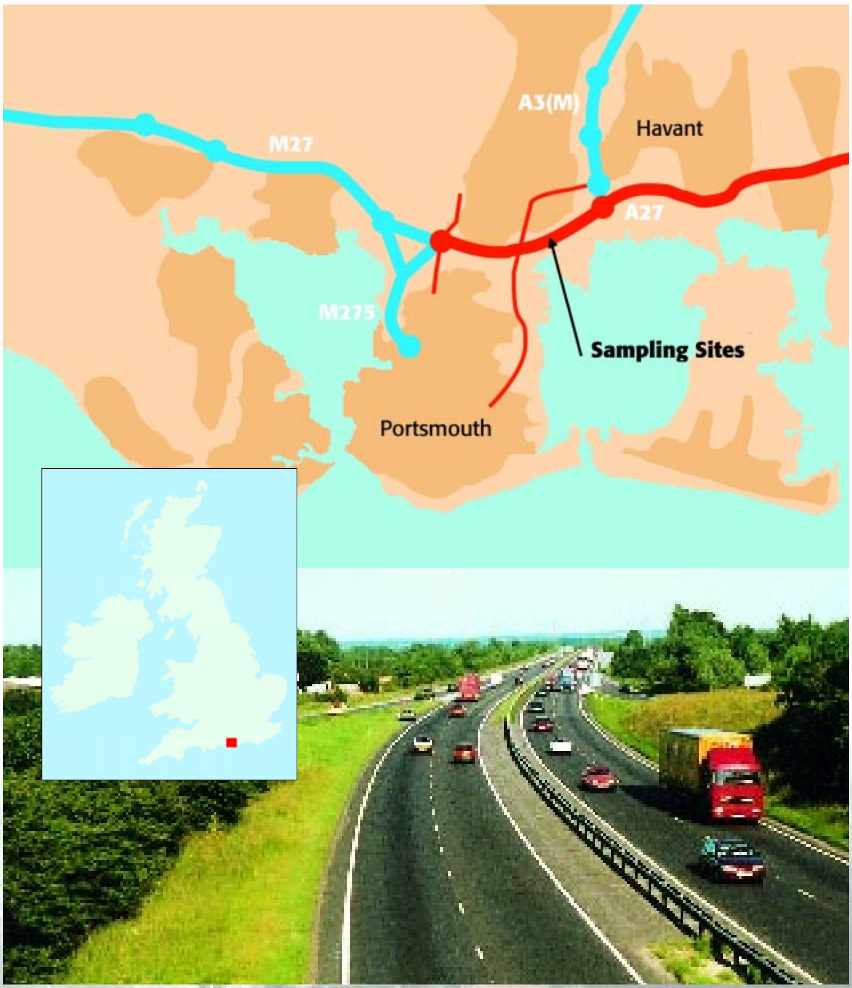


Figure 2. Lead content of weed samples as a function of distance from the side of the A27 roadway (1994 data).

Figure 2 shows distance profiles for washed and unwashed samples of silverweed collected in 1994. Concentrations ranged from 1.7 (±1.1) µg Pb g^{-1} at a 20 m distance to 6.4 (±2.0) µg Pb g^{-1} at 80 m in unwashed silverweed and from 0.83 (±0.21) µg Pb g^{-1} to 4.7 (±1.3) µg Pb g^{-1} at corresponding distances in washed silverweed samples. As for grass, washing produced a reduction in lead content but a much smaller reduction than in the silverweed. Washed samples of silver weed were found to contain approximately 70% of the lead content of unwashed ones, a higher percentage than the 55% that remained in the washed grass samples. Washing, which removes particulate lead effectively, appears to have a much greater effect on grass than on silverweed. A multiple *t* test (8 degrees of freedom; 95% confidence level) confirms a statistically significant difference in lead content between washed and unwashed samples of grass (t_{expt} = 7.96; t_{crit} = 2.31). A similar statistical test (7 degrees of freedom; 95% confidence level), on results from silverweed samples, indicates *no* statistically significant difference between washed and unwashed specimens (t_{expt} = 0.68; t_{crit} = 2.37). Profiles for washed and unwashed samples follow similar overall shapes falling from a maximum at the roadside to an overall minimum at *ca*. 80 m. Within this, a smaller maximum appears at 40 m. As for grass samples, the greatest difference between washed and unwashed sample lead content (2.1 µg Pb g^{-1}, 39%) occurs at 40 m. At a distance of 70 m from the road no difference at all is discernible.

At the sampling site hedgerows lined the roadside. The shelter provided by these explains the reduction in grass lead content that occurs in the initial 20 m from the road. Interestingly, the drop in weed lead concentration is delayed, occurring between 20 and 30 m, probably due to shielding by higher grasses in the open field. The maxima at around 40 m are due to the dispersion pattern of automobile exhaust. Sunlight and traffic heat the air immediately above the road surface. The warmed air rises carrying automobile exhaust emission which is dispersed along a line between the vertical and horizontal planes. Thermal currents, wind speed and direction also influence the dispersion and the fact that the road here is approximately 5 m above the surrounding field is probably a contributory factor.

The degree of lead removal is closely related to the surface texture of the leaves. A rougher surface, such as that of the silverweed, can retain particulate material better than the smooth surface of the blades of grass and the rougher leaf holds the deposited material more tenaciously when washed. The relationship we observed between lead retention and leaf texture agrees with results found by other authors.[11] It was shown,[11] using radioactively labelled petrol, that rough or hairy leaves such as white poplar retain up to 8 times as much lead as smooth ones like laurel. Hazel, oak, birch and ash trees were examined at distances up to 50 m from the edge of the M25. The lead concentration decreased exponentially for hairy, retentive hazel leaves but smoother oak leaves had lower surface lead levels that varied differently with distance. Leaves closest to the motorway showed lower levels than those more remote, possibly due to exposure to the adverse weather as



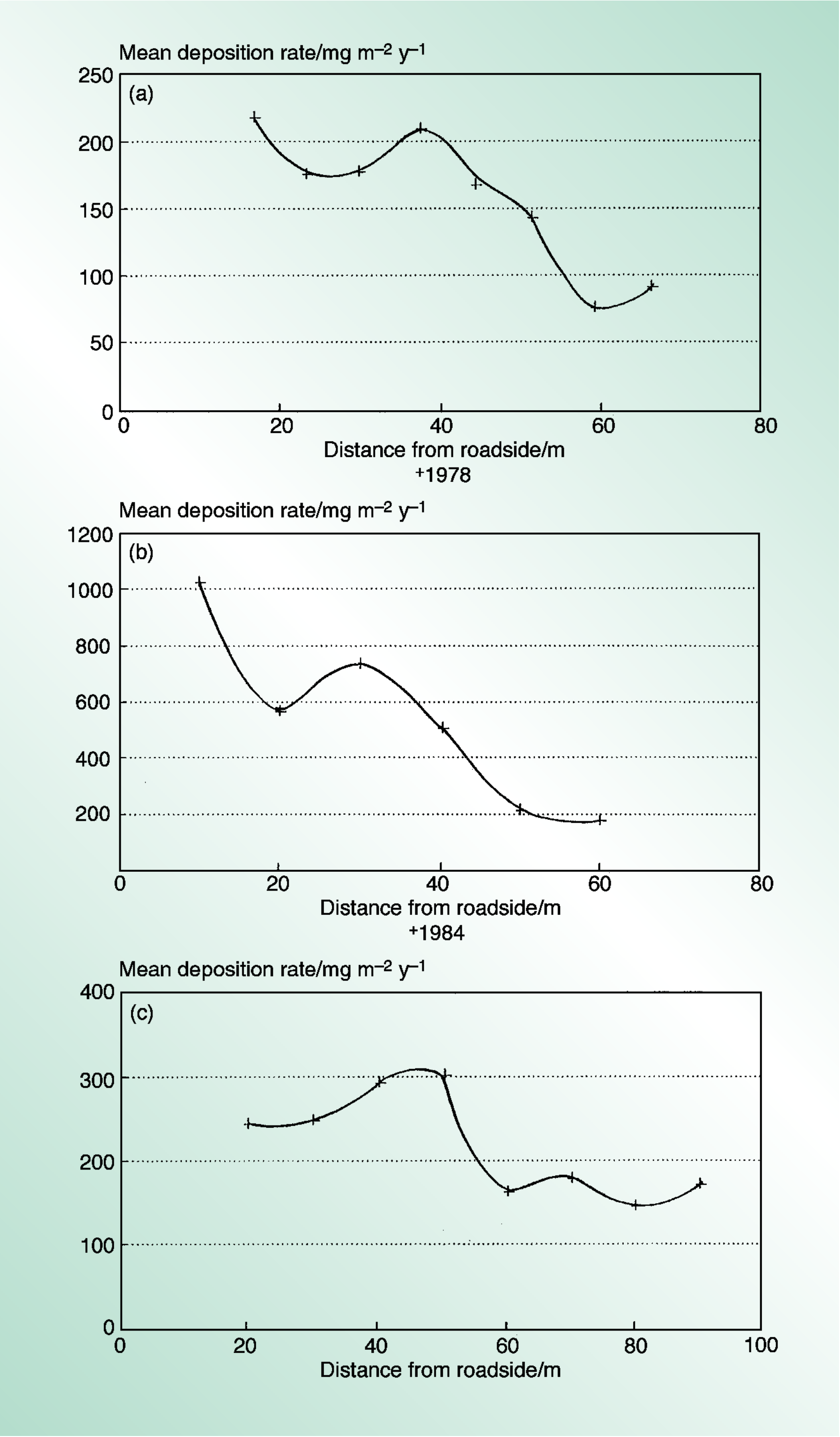


Figure 3. Lead deposition rate on moss samples as a function of distance from the side of the A27 roadway: (a) 1978 data; (b) 1984 data; (c) 1994 data.

well as to their lower retentive capacity.

Our results indicate that, on average, the grass at a given distance from the road has a greater deposited lead content than silverweed at an equivalent distance. The relative concentrations in grass and silverweed result from a combination of two conflicting effects, surface texture and duration of exposure to exhaust emission. The rougher texture of the silverweed leaf allows adhesion of particulates and so tends to raise the lead levels in silverweed relative to those in grass, but the grass is present *throughout* the year. Its persistent exposure to the automobile emissions compared with the seasonal exposure of the silverweed results, overall, in accumulation of more lead particulates, *i.e.* the length of exposure outweighs the differences due to surface roughness. The balance of these two effects needs close monitoring, allowing for seasonal trends in automobile use and emission dispersion and seasonal plant growth patterns with analysis of foliage at different stages of development.

The age of foliage influences the degree of metal retention.[12,13] Marked seasonal variation in retained lead has been observed,[14] with a maximum in autumn when leaves have been exposed for the longest time. The longer exposure clearly outweighs the growth dilution effect. Other factors also influence lead uptake by vegetation. Different portions of a plant show very different levels of lead retention. In coniferous forest,[15] twigs retain more lead (approximately 28 $\mathrm{mg\ kg^{-1}}$) than tree bark (23 $\mathrm{mg\ kg^{-1}}$) which, in turn, retains more than the foliage (3 $\mathrm{mg\ kg^{-1}}$) and the highest concentration has been found in tree roots.[16] Metals uptake by plants also depends on the nature of the soil and the height of the growth site. Lead concentrations in clouds and fog are usually higher than concentrations in rain and so, since high elevation areas usually have more precipitation and high rates of interception of cloud water, lead deposition may increase at high elevations.

Lead in moss

Virtually all particulate matter suspended in the air has a diameter of less than 20 µm. Metals suspended in this way can be deposited on the ground surface by rain out or wash out or simply settling under gravity. Alternatively, they may be intercepted by vegetation, by soil or by a water surface. *Sphagnum* moss obtains mineral nutrients from the air and can, therefore, be used to monitor airborne metal levels. A study of heavy metal retention in moss[17] showed that lead and copper are retained more strongly than Ni, Co, Zn or Mn, a characteristic that means moss bags can be exploited as a natural field gauge to measure the deposition of lead to ground vegetation.

We studied the relationship between lead deposition rate and distance from the roadside using bags of *sphagnum* moss placed at regular intervals over a 90 m length by the A27 in Hampshire. Figures 3(a), (b) and (c) show plots of mean lead deposition rate on moss [mean lead content ($\mathrm{mg\ Pb\ y^{-1}}$) divided by the exposure area ($\mathrm{m^2}$)] as a function of distance. The 1978 data [Figure 3(a)] show an overall decrease from 217 to 75 $\mathrm{mg\ Pb\ m^{-2}\ y^{-1}}$ with a local minimum at 23 m where the rate falls to 175 $\mathrm{mg\ Pb\ m^{-2}\ y^{-1}}$, and a local maximum of 209 $\mathrm{mg\ Pb\ m^{-2}\ y^{-1}}$ at 37 m.

1984 samples [Figure 3(b)] show a similar pattern ranging from 1025 mg Pb m^{-2} y^{-1} to 175 mg Pb m^{-2} y^{-1} with a local maximum of *ca.* 560 mg Pb m^{-2} y^{-1} and maximum of *ca.* 735 mg Pb m^{-2} y^{-1} at 20 and 35 m, respectively. In the 1994 analyses [Figure 3(c)] the deposition rate initially rises with distance reaching a broad maximum at a distance range of 30–50 m. The extremes of lead deposition rate are at distances of 50 m (a maximum) 300±70 mg Pb m^{-2} y^{-1} and 80 m (a minimum) ±25 mg Pb m^{-2} y^{-1}. Beyond 50 m the deposition rate falls rapidly remaining approximately steady at 165±15 mg Pb m^{-2} y^{-1} by about 60 m.

> ‘Reduction in lead emissions will reduce environmental damage—but lead already in the environment will cause continuing damage’

In other investigations[18–20] the lead deposition rate in air decreased exponentially with distance, distinctly different from the rising and falling concentration we observed. We believe this is a consequence of the environment of the sampling site. A steep slope runs from the road surface down to the sampling posts so that vegetative growth on the slope and the boundary fence offer some screening. The second important factor is the upward dispersal of pollutants. Airborne lead concentration will be underestimated unless deposition rates take into account the small proportion of emitted lead that deposits in the immediate vicinity of the roadway.

Conclusions

Our results show, as expected, that vegetation lead levels decrease with distance from the roadside. At a distance greater than 20–30 m deposition falls approximately to background level. The 1978 and 1984 studies, made in the same area, showed as expected, that the lead content in the roadside grass increased with traffic density. The traffic volume has expanded considerably recently following upgrading of the road to an 8 lane highway but, over the same period, the use of unleaded fuel has increased and so a compensation effect was anticipated.

Lead deposition is strongly dependent on the species of vegetation owing to differences in surface texture and to seasonality of growth and its interrelationship with the seasonal patterns in road traffic. Reduction in lead emissions will undoubtedly result in less environmental damage in future years but the *continuing* damage resulting from the lead that has already entered the environment is often underestimated, especially in terms of the lead entering the soil. The distribution of lead in the roadside soil has been studied and will be reported in another paper. Future monitoring of the site is also planned.

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Environmental monitoring using X-ray fluorescence analysis

Chemical Industry Swap Shop

A Chemical Industry Swap Shop with the theme Waste Minimisation and Monitoring took place in May 1999. The event was jointly organised by the Environmental Business Network, RIS—Yorkshire & Humber Chemical Sector, ETBPP (Environmental Technology Best Practice Programme) and the Green Chemistry Network. The day centred around a series of presentations covering legislation, industry examples of waste minimisation and developments in monitoring systems followed by a series of surgeries covering everything from Green Chemistry to Environmental Compliance to support available from ETBPP. Throughout the day there was the opportunity for delegates to visit various stands and to take a look at the latest monitoring equipment on the market.

The day started with an overview, given by Peter Calow who is Director of the EBN (European Business Network) and Chair of the Government Advisory Panel on Hazardous Substances, of the implications for the chemical industry of legislation.

Legislation can broadly be placed in two categories:

- that concerned with Direct Toxicity Assessment *i.e.* it is the environmental consequences that are measured, not the nature or concentration of chemicals.
- that concerned with answering the question: Are critical concentrations likely to be exceeded?

As monitoring equipment becomes more sophisticated then there is an increasing trend to measure and therefore limit allowable concentrations to lower and lower levels—the only answer therefore is to prevent waste being produced in the first place.

George Smith from Hickson & Welch gave an overview of what industry can achieve in terms of minimising energy, water, gas and nitrogen use as well as effluent production. Through taking a critical look at their activities and targeting process development Hickson's have achieved savings of over £1.3 million pa at a cost of £300 000.

The afternoon surgeries took the form of general discussion groups. The two Green Chemistry surgeries were well attended and attracted interest from large and small chemical companies, environmental specialists and research institutions. It was obvious that there is a lot of interest in what Green Chemistry can offer and we all enjoyed a lively debate.

It is worth noting that the EBN are running a TIDE Programme until June 2001. This programme provides financial assistance for SME's (Small to Medium Sized Enterprises) (from the Yorkshire & Humber region) to buy in specialist expertise for the development of environmentally friendly products and processes. Topics covered include clean technology, monitoring and clean-up technologies. Further information can be obtained from Fiona Raynor, EBN, 5 Palmerston Road, Sheffield, S10 2TE, UK.

COST Chemistry Action: Symposium on 'Towards Environmentally Benign Chemical Processes'

Chambery in France was the location for the recent COST Meeting which brought together sonochemists, collaborating through the COST Chemistry Action D10/0008/98, with green chemists. The objective of the meeting which was organised by Professor Jean Louis Luche, was to examine the possible contribution of sonochemistry to green chemistry. The lectures covered the strategic use of sonochemistry in synthetic organic

What is COST?

COST is the acronym for the French equivalent of 'European Cooperation in the Field of Scientific and Technical Research'. It takes the form of 'concerted actions' coordinating nationally funded pre-competitive research. It is complementary to, and does not compete with, the EUREKA initiative and the EU's Framework Programmes. There are 28 COST member countries: the 15 EU member states plus Iceland, Norway, Switzerland, the Czech Republic, Slovakia, Hungary, Poland, Turkey, Slovenia, Croatia, Malta, Estonia and Romania—plus the European Commission.

chemistry (Professor Ando), efficient oxidation processes assisted by ultrasound (Professor Sae Melo), sonochemical studies on cycloaddition reactions and related cyclisations (Professor Cintas), new processes for the use of agricultural resources as raw materials: the case for sucrose (Professor Queneau), ultrasound effects on photochemical and SET reactions (Professor Toma), sono-photodegradation of 2-chlorophenol (Professor Ragainin), sonolysis of organic compounds in water (Professor Petrier), sonolytic degradation of 1,2-dichloroethane and related compounds in natural ground water (Professor Peters) and scaling up sonochemistry: prospects and reality. Additionally Professors Clark and Sheldon gave talks on environmentally friendly organic synthesis and Professor Brunel described new mesoporous hybrid organic–inorganic materials as catalysts in fine chemistry. (http://www.cordis.lu/cost/home.html).

Embassy commercial officers learn about green chemistry

Over twenty commercial officers from UK embassies and high commissions throughout the world have recently spent two weeks in the UK on an industry-briefing course organised by ENTEC environmental consultants.

The main responsibility of the commercial officers is to promote UK industry and expertise abroad; this course, aimed at demonstrating expertise within the UK environmental technology industry, included lectures, seminars and site visits —the highlight of which was a visit to the Millennium Dome.

The Green Chemistry Network were invited to give a general talk on clean production, areas of UK expertise and technology. It was evident from the great enthusiasm and follow up questions that there is a real opportunity for both industry and consultants to exploit their know-how through collaboration, licensing *etc*. As expected the major areas of opportunity lie in the countries developing their chemical industry with places like China and India increasingly demanding that new chemical plants employ the latest clean, environmentally friendly technologies. The requirement for clean technology is truly universal: even highly developed countries such as Japan see a need for improved technology in the area of waste incineration, for example, where dioxin production is still a major concern.

Interuniversity Consortium
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European Commission - DG XII

TMR - Programme

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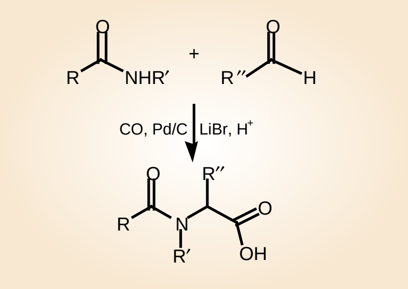
Perspectives

Palladium-catalysed reactions

Over the past 20 years or so, the use of palladium as a highly efficient catalyst for a range of reactions has provided many vitally important methods for the production of chemicals. The following examples represent valuable green additions to palladium's repertoire.

Non-natural amino acid production

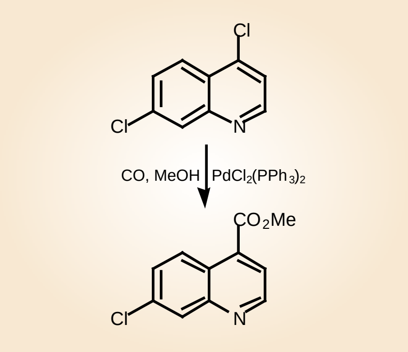
The first comes from Matthias Beller's group at the University of Rostock, and follows on from earlier work on homogeneous Pd catalysts (*Angew. Chem. Int. Ed. Engl.*, 1997, **36,** 1494). Beller has developed a novel heterogenous catalyst system which is capable of the addition of three components—an amide, carbon monoxide and an aldehyde—to give an amidocarboxylic acid (*Tetrahedron Lett.* 1999, **40**, 4523):



The products from the reaction are non-natural amino acids, and find uses as structural units in peptoids, and in a range of other applications. Current methodology involves the Strecker reaction (aldehyde + cyanide, followed by hydrolysis) followed by acylation, and generates considerable amounts of salt. The new method uses Pd/C as the catalyst with small amounts of LiBr, and either *N*-methylpyrrolidone or acetonitrile as solvent. Phosphines are not required. The amide product can be secondary or tertiary, with aryl or alkyl substituents being possible. Yields are high and turnover numbers are good (54 to 144). Most impressively, the tertiary products are produced in much higher yield and with far better turnover numbers than can be achieved with the homogeneous palladium bromide–triphenylphosphine system. The authors claim that the catalyst is more thermally robust and more easily recovered than the homogeneous versions.

Carbonylation of chloroquinones

A second, related piece of work is the Pd catalysed carbonylation of chloroquinones, as described by Carpentier, Castanet and co-workers from the CNRS in Lille (*Tetrahedron Lett*, 1999, **40**, 3719). Their target class of compounds are potentially valuable as anti-malarials. They found that the desired esters could be produced by insertion of carbon monoxide into the C–Cl bond of the substrate selectively at the 4-position (selectivity up to 99%). Trapping of the product with ethanol or methanol gave the desired ester cleanly:

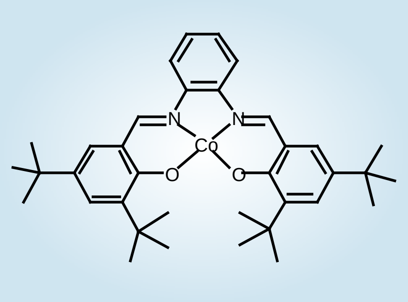


Attempts to extend this selectivity to dichloropyridines were less successful, although good selectivity could be achieved in some cases.

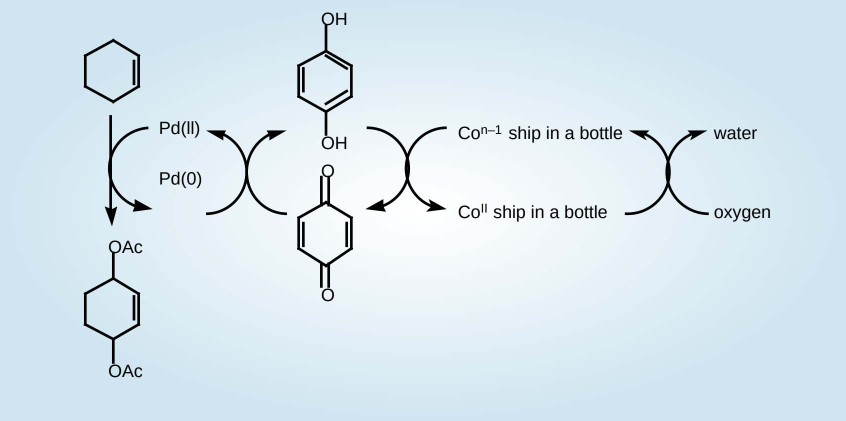
1,4-Oxidation of dienes

Palladium often works in tandem with other metals to effect selective catalytic reactions, examples being the Wacker and the Sonagashira reactions (Pd and Cu). Jan-E Bäckvall and Jens Woltinger of the University of Uppsala and Agnes Zsigmond of Jozsef Attila University in Szeged, Hungary, have combined forces to develop a powerful technique for the Pd–Co catalysed 1,4-oxidation of dienes (*Eur. J. Chem.*, 1999, **5**, 1460).

One of the most elegant parts of this work is the combination of a heterogeneous cobalt catalyst with a homogeneous palladium species. This allows for ready separation of the metals after reaction, as well as slowing down the degradation of the cobalt catalyst, a salophen catalyst with oxidisable π-electron periphery, and a propensity to form non-catalytically active bridged dimers. The approach taken to immobilise the Co–salophen catalyst was 'ship-in-bottle' encapsulation in a zeolite:



The oxidative cycle involves aerobic activation of the cobalt by oxygen, and subsequent oxidation of hydroquinone by the activated complex, liberating water. The Pd cycles from oxidation state 0 to oxidation state +2 by reaction with the quinone, with the Pd(II) finally converting the diene to a 1,4-diacetate. The combination of immobilised Co and homogeneous Pd was found to be more active than the wholly homogeneous version of the system.

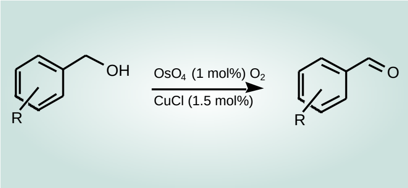


Aerobic oxidations

Some more aerobic oxidations have been described in two other papers.

Alcohols to aldehydes

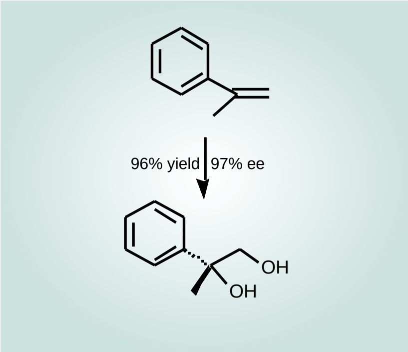
The first comes from John Osborn's group in Strasbourg (*Tetrahedron Lett.*, 1999, **40**, 3723) who have developed a method for the catalytic oxidation of alcohols to aldehydes using catalytic amounts of osmium tetroxide and copper(I) chloride:



While copper was not absolutely necessary, its use did result in improvements to the system. Benzylic alcohols were oxidised most efficiently, with allylic and aliphatic alcohols being relatively less prone to oxidation (selectivity was very high in all cases though). Turnover numbers of several hundred were reported, meaning that very small amounts of osmium are required.

Asymmetric dihydroxylation

A second osmium-mediated aerobic oxidation was reported by Kriel *et al.* (*Tetrahedron Lett.*, 1999, **40**, 4189). This paper describes the asymmetric dihydroxylation of α-methylstyrene by air, using a combination of cinchona-derived ligands, a selenium species and light. The latter two serve to reoxidise the osmium from VI to VIII, and replace the large amounts of potassium ferricyanide normally used for this purpose:

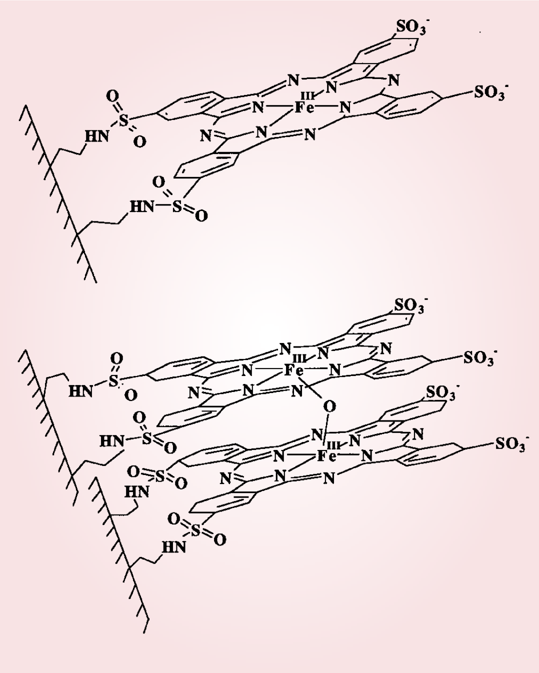


The oxidations proceed at 12 °C, and after 24 hours, the product, the chiral diol is isolated. Yields are excellent (87–93%) and ee's are equally impressive (93–97%). Thus, this method represents a significant step towards a green asymmetric dihydroxylation.

Mesoporous catalysts

Vitamin K3

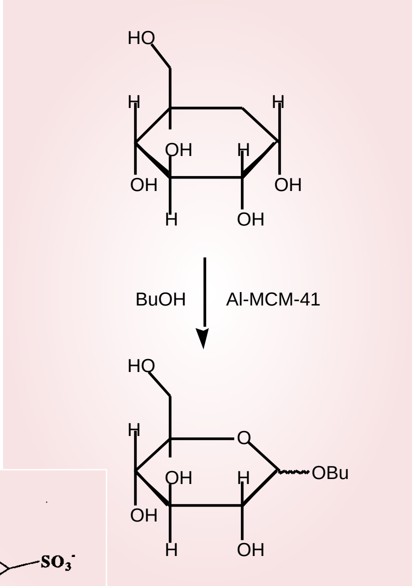
Mesoporous catalysts have found uses in oxidation chemistry too. Sorokin and Tuel have recently published details of their studies on immobilising metallophthalocyanines on silicas or MCMs (*New J. Chem.*, 1999, **23**, 473). This work is aimed at new methods for the clean production of vitamin K3. Current technology is still based on stoichiometric Cr(VI), but methods to carry out hydroxylation of 2-methylnaphthalene are slowly improving. Sorokin and Tuel prepared immobilised iron(III) phthalocyanines and used them to catalyse the hydroxylation of 2-methylnaphthalene with *tert*-butyl hydroperoxide.



Their results indicate that the selective oxidation of the methyl-substituted ring is possible with a 4:1 ratio of 1,4-hydroxylation to 5,8-hydroxylation. These results are promising from the point of view of developing a further, more selective catalytic system, but also for some of the details about the catalysts. Unusually, the μ-oxo bridged dimer form of the catalyst is significantly more active than the monomeric species—in such species the dimeric form is normally considered to be inactive.

Alkyl glucosides

A further example of the use of MCM-41 materials comes from the group led by Avelino Corma in Valencia (*J. Catal.*, 1999, **183**, 76). This work describes the use of Al-MCM-41 as a mild acid catalyst for the preparation of alkyl glucosides—useful as surfactants and derived from renewable resources (*Green Chem.*, 1999, **1**, 38).

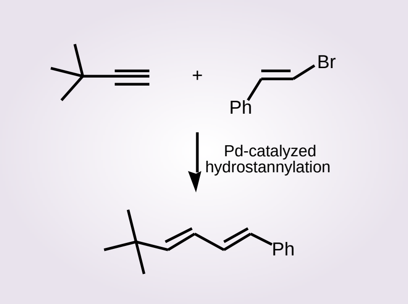


The authors have carefully examined a number of factors relating to catalyst performance, and shown that pore size and hydrophobicity (controlled by the Si/Al ratio) play important roles in determining the activity of the catalysts. Reuse was shown to be possible after washing the catalyst with methanol, and then water. This was successful, although slight loss of activity was seen after a few cycles—this was attributed to slow degradation of the catalyst structure.

Making tin catalytic

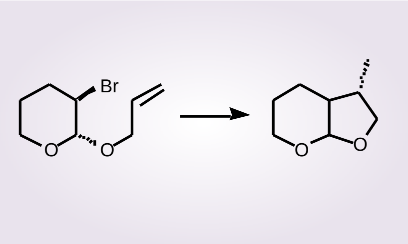
Organotin reagents are amongst the most versatile in organic chemistry. Unfortunately, they are also difficult to separate from products, and are toxic. They are also typically used in stoichiometrically quantities. Recently, various research groups have begun to find solutions to this problem. The problem of separation has been tackled successfully by McCluskey (*Green Chem.*, 1999, **1**(3), 167) by the development of an aqueous reaction system, where the tin by-products separate easily owing to solubility differences.

Maleczka and Terstiege (*J. Org. Chem.*, 1998, **63,** 9622) have developed a one-pot Pd-catalysed Stille coupling of acetylenes with bromoalkenes, which is catalytic in tin. The overall scheme is depicted below, and revolves round the *in situ* generation of tributyltin hydride from the oxide and a reducing agent, poly(methylhydrosiloxane) (PMHS). The tin hydride then adds to the acetylene, under Pd catalysis, to form a vinylstannane. This is then coupled with the bromoalkene *via* Pd(0) catalysis, generating the tin bromide. Aqueous sodium carbonate and PMHS is sufficient to regenerate the tin hydride.

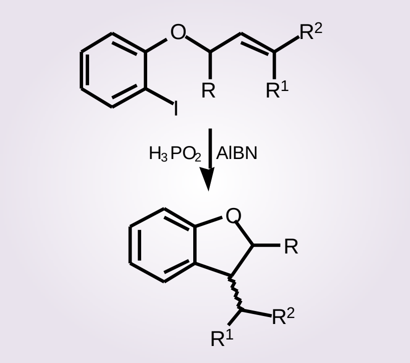


This procedure is remarkable in that it surmounts a variety of difficulties: *e.g.* the requirements for the two Pd catalysed steps are opposing, strong σ-donor ligands are necessary for the first step, weak donors for the second, and the complexity of the catalytic sequence requires compatibility of a range of different reagents. Yields are comparable with step-wise reactions, and although the turnover numbers are relatively modest, a reduction in the amount of tin required of up to 80% is achievable.

Another paper by the same group (*J. Org. Chem.*, 1999, **64**, 342) describes a similar procedure based on the combination of PHMS and KF, with the active species possibly being a hypervalent Si–F centre. This method was applied to both dehalogenations, and to C–C bond forming reactions. Turnover rates indicate that the tin centre can be used between 2 and 10 times.



An alternative approach can be found in *Tetrahedron*, 1999, **40**, 2415, where John Murphy's group at Strathclyde University have shown that hypophosphorous acid and its salts are capable of carrying out some transformations associated with tributyltin hydride, thus avoiding the difficulties associated with tin waste.



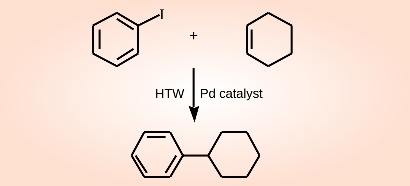
The methodology works in both organic and aqueous environments. Stephen Graham, the student who carried out the work, recently won two prizes at the Pfizer National Poster Symposium in London for this work.

Reactions in water

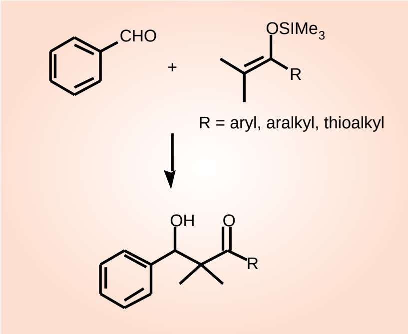
High-temperature water

The Heck reaction is a versatile and popular synthetic procedure. Typical solvents include dipolar aprotics and acetonitrile. In an attempt to move towards more environmentally friendly methodology Liz Gron and Amanda Tinsley of Hendrix College, Arkansas, have developed a novel version of the Heck reaction which uses high temperature water (HTW) as solvent (*Tetrahedron Lett.*, 1999, **40**, 227). HTW is becoming a popular choice of solvent for organic transformations—it is much less aggressive than supercritical water, but is still much less polar than 'normal' water, making it more able to interact with organics.

Reactions studied involved iodobenzene and cycloalkenes. The observed reactivity trend—faster rates as ring size increases—differs from that seen in organic systems. For example, reactions run in dimethyl formamide give relative reactivity of cyclopentene > cyclooctene > cycloheptene > cyclohexene. The different trend may be due to differing hydrophobicity. Reactions are also much faster in HTW, being complete in minutes, as opposed to several days for conventional systems (*Green Chem.*, 1999, **1**, 65).



In another study, Manabe and Kobayashi have shown that certain combinations of scandium salts and surfactants can enhance the activity of simple Brønsted acids (*Tetrahedron Lett.*, 1999, **40**, 3773). They studied the Mukaiyama aldol reaction in water at room temperature, and found that the combination of surfactant and Brønsted acid (tosic acid or HCl) resulted in large rate enhancements, with little hydrolysis of the silyl thioketone acetals.

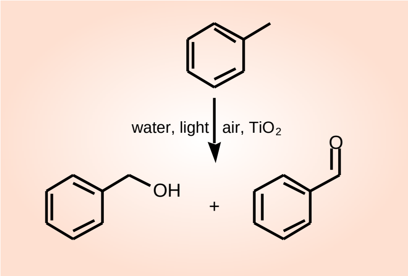


(See this issue for a further paper by Kobayashi on scandium salts and surfactant combinations.)

Selective photooxygenations of alkanes in water

The ability to functionalise alkanes is an important target, and one which has received a great deal of attention. The oxidation of many alkylaromatics takes place at high temperature and uses corrosive mixtures of metals, bromide and carboxylic acids. Such conditions are harsh, and novel chemistry is needed to produce the many important products accessed *via* this method.

Water as a reaction medium, coupled with air as oxidant, and light as a catalyst is a particularly green combination, which has been put to good use by a group led by Michael Gonzalez from the USA (*J. Catal*., 1999, **183**, 159). They have managed to oxidise toluene and ethylbenzene to the corresponding alcohols and aldehyde/ketone products in moderate yields and selectivity. Reactions run at room temperature in water and the photocatalyst is provided by a combination of a quartz lamp and titanium dioxide.



While the results are preliminary, this technique does represent a potentially valuable and clean route to useful products.

Conference Diary

SEPTEMBER 1999

The 2nd Post-Graduate Summer School on Green Chemistry
September 6–12
Venice, Italy.
(http://hydra.unive.it/inca/summer/index2.htm)

Biotrans '99
September 26 –October 1
Giardini Naxos-Taormini, Sicily, Italy
(http://dept.chem.polimi.it/biotrans)

One-day Symposium on Green Chemistry for Young Chemists
September 28
University of York, UK
(greennet@york.ac.uk)

OCTOBER 1999

Catalysis Technology Car Boot Sale
October 7
Weston Building, Manchester
Conference Centre, Manchester, UK
(http://www.chemsoc.org/bootsales/home.htm)

3rd European Biofuels Forum
October 11–13
Palais des Congres, Brussels, Belgium
(http://www.europoint-bv.com)

NOVEMBER 1999

Sustainability 2000 (S2K): The online global conference for sustainable development
November 1–12
World Wide Web, organised by
Institution of Chemical Engineers
(http://www.sustainability2000.org)

GRIF'99 (Gateway to Renewable Industrial Feedstocks)
November 2–3
John Innes Centre, Norwich, UK
(http://www.actin.co.uk)

Environment China '99
November 2–5
Guangzhou, China
(environment@gima.de)

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)

APRIL 2000

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

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)

MAY 2000

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)

JULY 2000

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

AUGUST 2000

ACS 220th National Meeting including a symposium on Environmental Issues
August 20–24
Washington, DC, USA
(http://www.acs.org/meetings/future/washdcacp.htm)

Green Chemistry

Editorial

The week starting June 28, 1999 marked an important and enjoyable annual event in the Green Chemistry world: the presentation of the Presidential Green Chemistry Challenge Awards at the National Academy of Sciences in Washington DC, USA. Following the award presentations, the 3rd Annual Green Chemistry and Engineering Conference provided a forum for award winners and other scientists and engineers to report their results and engage in state-of-the-art discussions. As usual, **Paul Anastas, Tracy Williamson,** and **Joe Breen** were responsible for much of the organization of this event, which is sponsored by the US Environmental Protection Agency, American Chemical Society, American Institute of Chemical Engineers, Chemical Manufacturers Association, Council for Chemical Research, Green Chemistry Institute, National Institute of Standards and Technology, National Research Council, National Science Foundation, US Department of Energy, and the Organization for Economic Cooperation and Development. I offer congratulations to the award winners, the organizers, sponsors and conference participants.

This year's Presidential Awardees are briefly listed here, and I look forward to a series of articles in *Green Chemistry* from the various scientists and engineers who contributed to and administered these programs:

- **Professor Terry Collins** of Carnegie Mellon University won in the academic category for his iron-based peroxide activators that have broad applications to oxidations in the pulp and paper industry, water disinfection, and laundry bleaching. Terry has a background in coordination chemistry and catalysis, and has become a major force in the development of green oxidants.

Biofine Inc.'s plant converting paper mill sludge into levulinic acid received a 1999 Presidential Green Chemistry Award

- The Small Business Award went to **Biofine, Incorporated** for a process that converts cellulosic biomass into levulinic acid, a useful building block for many chemical products. The biomass feedstocks for this process include paper mill sludge, unrecyclable paper waste, waste wood and certain agricultural residues. An industry–government consortium has conducted the work on high value-added derivatives of levulinic acid. It was a pleasure to see that my old friend and former colleague Joe Bozell was one of the lead scientists on this program.

- The Alternative Synthetic Pathways Award went to **Eli Lilly and Company** for designing a green synthesis of a compound currently under testing for a variety of central nervous system diseases. Key aspects of this work included replacing a CrO_3 oxidation with an air oxidation, and the use of a biocatalytic transformation using specially identified yeast. I had the pleasure of chairing the conference session where **Dr. Benjamin Anderson** described the work done by the Lilly group.

- **Nalco Chemical Company** received the Alternative Reaction Conditions Award for developing a new water-based process for the manufacture of liquid polymers. Applied to the preparation of acrylamide polymers that are important for waste-water treatment, this method avoids the exposure hazards and energy costs associated with dry (powder) polyacrylamide samples, and also avoids the use of organic solvents and surfactants associated with the alternative ‘water-in-oil’ preparations of these materials.

- **Dow AgroSciences** received the award for Designing Safer Chemicals for the development of Spinosad, a selective, low-risk insecticide (registered by EPA as a reduced risk pesticide). A fermentation process using a naturally occurring microorganism isolated from a Caribbean soil sample produces Spinosad. Spinosad has demonstrated remarkable selectivity in targeting pests that attack cotton, trees, turf, fruits, vegetables and ornamental plants without harming 70–90% of beneficial insects and predatory wasps. Spinosad presents little risk to the environment since it does not leach, bioaccumulate, volatilize or persist in the environment. These properties make it a valuable tool for pest management. For a fuller discussion of this award see the short article by Anastas *et al.* on page G88 of this issue of *Green Chemistry*.

At the same awards ceremony, the Kenneth G. Hancock Memorial Scholarship in green chemistry was presented to **W. Clayton Bunyard** of the University of North Carolina, Chapel Hill. Bunyard’s research centers on environmentally benign syntheses of perfluoropolyethers (PFPEs) and new uses for these materials. One such synthesis uses carbon dioxide instead of ozone-depleting CFCs as the solvent. New uses of PFPEs include so-called ‘fouling-release coatings’ for ocean-going ships. These coatings prevent marine organisms from adhering to ships, in contrast to traditional antifouling coatings (*i.e.* alkyltin reagents) that are toxic and that accumulate in water and marine life.

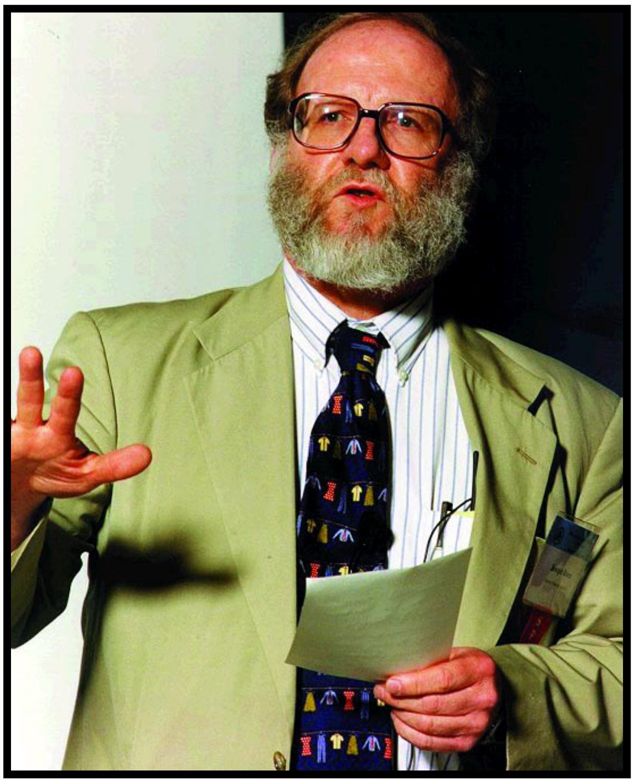
One theme that has been common for many of the awards and conference presentations is the following: green chemistry does not hurt the simple economic bottom line while it helps the environment. Instead, many green processes provide considerable economic advantages even before the savings in environmental costs have been computed. How can this be? In public debates in the US, environmentally benign industrial practices are often automatically associated with higher costs to industry. This false, inverse relationship between public good and industrial benefit was certainly in evidence during early debates over automobile emissions and safety, with sides being chosen on political rather than economic grounds. It is important to spread the news that, time and again, green innovation goes hand-in-hand with economic benefits—lower raw materials costs, less wasted material, more energy-efficient processes, more efficient synthetic chemical routes, fewer separation steps.

I believe that most industrial processes are the brainchildren of earlier eras. They used *then* state-of-the-art chemistry to prepare the products. Any reason for a complete, modern technical re-evaluation should lead to processes that offer greatly enhanced environmental and economic attributes. This certainly is true for ‘old’ chemistry such as that sometimes found in commodity chemicals production, but also occurs for pharmaceutical chemistry, where companies can become locked into a particular synthetic route because of the need for the entire route to be subject to regulatory approval. We heard a wonderful talk in Washington by Sam L. Nguyen of Roche Colorado Corporation, who along with my old friend Chris Roberts and other team members, developed a green and economically beneficial synthesis of Cytovene®, an important drug against cytomegalovirus (CMV). CMV plagues AIDS and transplant patients. Reducing the number of chemical processing and isolation steps from 6 to 2 and cutting the number of reagents and intermediates from 22 to 11 were just some of the ways that the costs (economic and environmental) were reduced, allowing sustainable and cost-effective scale-up to meet increasing patient need.

Of course, often there are capital expenditures that are necessary to capture the economic and environmental benefits of new processes, and large capital spending does entail risk. Therefore, the companies that move forward with new green processes are to be congratulated, and should enjoy considerable economic benefit just as our global ecosystem benefits from the greening of their industry. Green processes that can be retrofitted into existing plants may allow the faster route to capturing value. Conferences such as the 3rd Annual Green Chemistry and Engineering Conference and the 1999 Gordon Conference on Green Chemistry allow industrial, academic and government scientists and policymakers to interact and cross-fertilize each other’s efforts.

James K. Bashkin, St. Louis, MO, USA, July 1999.

Joe Breen—heart and soul of Green Chemistry



It is with great sadness that we have to report the death on 19 July 1999 of Joe Breen—one of the Editorial Board members of *Green Chemistry*.

Only a short time ago, on the evening of 28 June 1999, in the Great Hall of the National Academy of Sciences, Joe was presented with the Distinguished Service to Green Chemistry Award from the President of the American Chemical Society. For the hundreds of people in attendance that evening, many of whom participate in the Green Chemistry research, education or industrial applications, the award was welcome and deserved recognition for a driving force in the development of Green Chemistry. As inscribed on the award itself, Joe Breen was recognised for his 'extraordinary leadership and tireless efforts in the advancement of Green Chemistry globally through research, education and outreach'.

Joe Breen was the executive director of the Green Chemistry Institute and served as the Chair of the Committee on Environmental Improvement of the American Chemical Society. In both of these roles Joe promoted green chemistry as a new and innovative approach to environmental protection.

The decade of the 1990s has seen green chemistry develop from its inception and infancy into a growing recognised area with activities around the world. In these years Joe Breen was a leading ambassador for the expansion of green chemistry. He was a founding member of the editorial advisory boards of the journal, *Green Chemistry*. As a co-chair of the Green Chemistry and Engineering Conference, Joe guided the conference to demonstrate the broad applicability of green chemistry throughout academia, industry and government. Joe's interests consistently centred on breaking down barriers through the use of green chemistry. Green chemistry knows no borders was a centrepiece of Joe's approach as evidenced by his almost evangelical tours which spread the word of green chemistry across national boundaries. One could just as easily find Joe addressing a group of industrial chemists in Oakash (Wisconsin) or Eire (Pennsylvania) as addressing researchers and students in Hefei (China), Venice (Italy) or St. Petersburg (Russia).

Joe Breen's twenty years in the U.S. Environmental Protection Agency (EPA) helped to inform him on exactly how important and urgent Green Chemistry is at this stage of the environmental movement. During his time at EPA, Joe was involved in the many regulatory aspects of the Toxic Substances Control Act including playing a major part in the EPA's Lead Program. He won the Agency's highest honour, the EPA Gold Medal, for designing and implementing the 'Test Our Kids for Lead' Program and was co-editor of the book 'Lead Poisoning: Exposure, Abatement and Regulation'. But while valuing the impacts and necessity of regulatory command-and-control approaches to cleaning up the waste of the past, Joe Breen was more interested in looking forward to the future.

With the passage of the Pollution Prevention Act of 1990, Joe focussed his efforts on the prevention of waste before it is ever generated by the proper design of the process in the first place. In 1993, the book 'Pollution Prevention in Industrial Processes: The Role of Process Analytical Chemistry' by Breen and Dellarco illustrated how process analytical chemistry can prevent the formation of undesirable by-products and parasites before they accumulate.

In 1995, Joe Breen organised the Design-for-Environment symposium at the American Chemical Society Meeting in Washington D.C. with over 140 speakers on Green Chemistry and related topics. It would be the first of many symposia that Joe organised and/or participated in.

Because of his strong desires to support educational activities, Joe devoted considerable time and effort to teaching green chemistry at such diverse locations as Trinity College (Washington D.C.), Hood College (Maryland) and the Venice Summer School on Green Chemistry in Italy. A major project that Joe was recently involved in is the incorporation of Green Chemistry principles into the popular ACS chemistry textbook Chemistry in Context.

The importance of green chemistry to achieve the goals of industrial ecology was a central theme of Joe Breen's work. One of the illustrative examples that Joe played a major role in promoting is the use of supercritical and liquid CO_2 in the area of garment care. From funding of basic research (during his time both at EPA and as Executive Director of GCI) to promoting and catalyzing industrial and academic interactions in this area, Joe served as a conduit in bringing this industrial ecology technology from the lab bench to commercial fruition.

Joe will be sadly missed by his friends and colleagues within Green Chemistry and beyond. In 1998, he published a paper in the Journal of Cleaner Production entitled "Green Chemistry and Design for Environment: The Heart and Soul of Industrial Ecology". From the contributions that Joe Breen has made to Green Chemistry it is easy to see why his colleagues often refer to him as "the heart and soul of green chemistry".

Paul T. Anastas, *Chief, Industrial Chemistry Branch, Office of Pollution Prevention and Toxics, US EPA, Washington, USA.*

SPINOSAD - a new natural product for insect control

Paul Anastas, Mary Kirchchoff and Tracy Williamson of the USA EPA present the first in a series of short profiles on this year's Green Chemistry Award winners

Controlling insect pests is essential to maintaining high agricultural productivity and minimising monetary losses. Synthetic organic pesticides, from a relatively small number of chemical classes, play a leading role in pest control today. The development of new and improved pesticides is necessitated by increased pest resistance to existing products, along with stricter environmental and toxicological regulations. To meet this need, Dow AgroSciences has designed spinosad, a highly selective, environmentally-friendly insecticide.

Discovery

During the 1980s, Lilly Research Laboratories (Indianapolis, USA) operated a program directed at finding new natural products that possessed utility in the pharmaceutical and agrochemical industries. Soil samples from all over the world were collected, fermented, extracted, and screened in a variety of assay systems. Wherever possible, the soil samples were collected from unusual habitats, to improve the chances of finding new microorganisms.

During the course of this fermentation screening program, extracts from the fermentation broth of a soil sample, collected in 1982 on a Caribbean island, were found to be active in a mosquito larvicide assay and against the southern army worm (*Spodoptera eridania*). The microorganism was identified as *Saccharopolyspora spinosa*, and it produced a family of new macrolides (molecules containing a macrocyclic lactone), now called spinosyns, of which the primary components are spinosyn A and spinosyn D. An extract of the fermentation broth that contains this naturally occurring mixture is called spinosad. Products such as Tracer® Naturalyte® Insect Control and Precise® contain spinosad as the active ingredient.

Mode of action

Spinosad demonstrates both rapid contact and ingestion activity in insects, which is unusual for a biological product. The mode of action of spinosad (although not fully elucidated) is characterized by excitation of the insect nervous system, leading to involuntary muscle contractions, prostration with tremors, and paralysis. These effects are consistent with the activation of nicotinic acetylcholine receptors and prolongation of acetylcholine responses through a novel mechanism.

Insect spectrum

Spinosad has been tested extensively on a global basis since 1990 and found to provide effective control of pests in the insect orders Lepidoptera, especially the tobacco bollworm (*Heliothis virescens*), the cotton bollworm (*Helicoverpa zea*), American bollworm (*H. armigera*) and armyworms (*Spodoptera spp.*).

Environmental fate

Spinosad presents a favourable environmental profile. It does not leach, bioaccumulate, volatilize, or persist in the environment. Spinosad will degrade photochemically when exposed to light after application. Because spinosad strongly adsorbs to soils, it does not leach through soil to groundwater when used properly and no buffer zones are required by the United States Environmental Protection Agency.

Nontarget toxicology

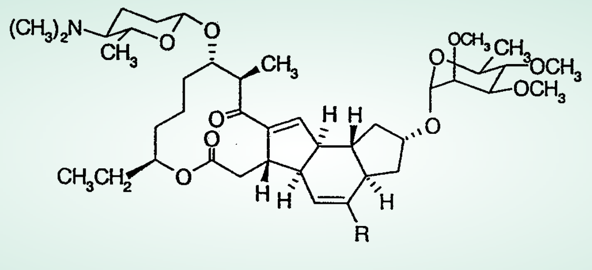
Spinosad is relatively low in toxicity to mammals and birds, and, although moderately toxic to fish, this toxicity represents a reduced risk to fish when compared with many synthetic insecticides in use. In addition, 70-90% of beneficial insects and predatory wasps are left unharmed by spinosad.

Conclusion

The unique mode of action of spinosad, coupled with a high degree of activity on targeted pests, low toxicity to non-target organisms (including many beneficial arthropods), and resistance management properties make spinosad an excellent new tool for integrated pest management.

Further reading

Thompson, G.; Hutchins, S. (1999) Spinosad - a new class of fermentation-derived insect control agents. *Pesticide Outlook* **10**(2), 78-81.



Spinosad is a mixture of spinosyn A and spinosyn D

Cleaner fuels

The search for cleaner fuels is a major element of the drive to reduce the environmental impact of transport. Many approaches are being taken to reduce the pollution from vehicles.

Gas-to-liquids technology

...Chevron and Sasol in gas-to-liquids joint venture

Chevron and Sasol have signed an agreement to create a new global joint venture founded on gas to liquids (GTL) technology, one of the most promising prospects for clean fuel development in the 21st century. The application of GTL technology to the enormous gas reserves located throughout the world could become the preferred method to commercialize such natural gas resources, many of which are remote and cannot easily be made commercial. A proposal was announced in April 1998, in which Chevron and Sasol outlined plans to build a GTL products plant in Nigeria. Design and engineering continue on the GTL facility, which will be capable of converting natural gas into synthetic crude oil for further processing into commercial products, principally high quality diesel and naphtha. The initial feasibility study has recently been expanded to increase target production from 20000 to 30000 barrels per day. The plant is expected to come on stream in 2003. The global joint venture would build on the foundation laid by Sasol, based on their Fischer–Tropsch technology and would utilize proprietary technologies of both companies—Chevron's ISOCRACKING and Sasol's Slurry Phase Distillate Process (http://www.chevron.com).

...Rentech agreement with Texaco agreement

Texaco and Rentech announced the signing of a Technical Services Agreement to research the integration of Rentech's Fischer–Tropsch technology with Texaco's gasification process. The goal is to produce a clean burning, sulfur- and aromatic-free diesel fuel. The new Agreement calls for technical and developmental work to be carried out at the Rentech research and development facilities in Denver. The companies will work to maximize the hydrocarbon yield from synthesis gas produced by the Texaco gasification process. Rentech Inc. has also completed an agreement with Republic Financial Corp by which Rentech and Republic will jointly develop projects utilizing Rentech's proprietary Fischer–Tropsch technology. The agreement represents a milestone for Rentech in its efforts to commercialize this technology (http://www.gastoliquids.com).

New US sulfur specifications for gasoline

On 1 May 1999, President Bill Clinton personally announced newly proposed federal standards for sulfur levels in gasoline that promise to allow automobiles to run 80% cleaner. The tough new specifications call for 30 ppm sulfur in gasoline, down from the current average of 340 ppm. The US Environmental Protection Agency estimates that this would take 3 million tonnes of pollution out of the air. The oil industry estimates that meeting the new sulfur targets using existing technology will require more than $6 bn in new US refinery investment. Refiners argue that the cost may be too high to meet the new sulfur standards.

Biotechnological route to desulfurisation of fuels

Energy BioSystems Corp is currently developing its $3 M biocatalytic technology to desulfurize gasoline at a target cost of 1 cent/gallon to 2 cents/gallon of gasoline. Energy BioSystems has already licensed its first unit for diesel fuel biodesulfurization to Petro Star Inc., a subsidiary of Arctic Slope Regional Corp, for their Valdez, AL, refinery. Energy BioSystems Corp of Houston is developing and commercializing biotechnology based processes for the petroleum refining and production industries. The company's focus to date has been on developing biocatalytic desulfurization, a proprietary process involving the use of enzymes to remove sulfur from petroleum, including gasoline, diesel, and heavy and crude oils, while operating at mild temperature and pressure. The company is also pursuing opportunities to apply the principles of biocatalysis to the chemical industry, initially by developing a line of organosulfur products that are derived from its biodesulfurization process (http://www.energybiosystems.com).

Shell Pura Diesel

According to Shell, its Pura Diesel meets tough European emissions regulations six years early. A positive response from a London-based trial meant that the national launch was brought forward. Shell claims that Pura Diesel, with its unique formulation, helps meet growing demands from both the public and the government for cleaner fuels, and does so without compromising performance. The good news for the environment is that it contains 90% less sulfur than standard diesel, which means smoke and particulate pollution from exhaust pipes is greatly reduced. Further benefits for motorists arise because its additive package helps prevent carbon deposits building up in the engine, and gives improved combustion and protection against corrosion. Additionally, Pura Diesel is claimed to improve the fuel economy of a vehicle by up to 5–6% (http://www.shell.co.uk).

Ultra-low-sulfur diesel

Total Oil GB (Watford, Herts) is the producer of Ultra Low Sulfur Diesel (ULSD), which is being produced at its Lindsey Oil Refinery (LOR). Total Oil GB was the first oil company in the UK to introduce the modern cleaner diesel fuel when they introduced 'City Diesel' to tackle urban pollution, smoke and particulates (sooty particles) *etc.* ULSD was defined in the 1998 UK budget and Total Oil GB now produces it at LOR. It offers all the advantages of City Diesel, specifically in the following areas: 90% reduction in sulfur emissions, virtual elimination of black smoke, airborne particulate reduction greater than 30% and reduction of carbon dioxide and carbon monoxide emissions. Total ULSD is designed to be compatible with the latest catalyst equipped vehicles and those which qualify for the reduction in Vehicle Excise Duty. Bus company London United, an existing Total Oil GB customer, has recently announced that it is expanding its use of ULSD by switching its Kingston buses from conventional diesel to the new, green fuel.

Low sulfur diesel in India

The Indian Oil Corporation has just become the first in India to produce low-sulfur diesel *via* a hydrodesulfurization process. The capacity is 1.2 million tonnes per year and the refinery at Gujarat cost $127M. There are plans to set up further hydrodesulfurization units at three other refineries.

Replacing MTBE

Great West Energy and Exploration Inc. of Dallas, TX has entered into an agreement with Millennium Fuels USA that conveys the exclusive right to capitalize and participate in the only plants capable of producing one of the premier alternative replacements for the current refining industry standard additive, methyl-*tert*-butyl ether (MTBE). MTBE and other ether-type additives, utilized each day by the refining industry as octane enhancers and/or oxygenates, have come under attack due to their ground water contamination, harmful emissions and more importantly their possible effects on the human body. In March 1999, California became the first state in the US to ban the use of MTBE owing to its significant environmental risks. It is predicted that other states such as Massachusetts, New Hampshire, Connecticut, New York and New Jersey among others, will follow suit to ban the use of MTBE by 2000. The additive is produced from various natural hydrocarbons and raw ethanol through a patented process that produces an environmentally friendly octane additive/enhancer and oxygenate.

New Fuels

E85 from Ford

The Twin Cities of Minneapolis/St Paul and Chicago will become test beds for efforts aimed at building sustainable ethanol (E85) infrastructure, and will also be part of a Ford coupon programme aimed at promoting the use of ethanol in flexible fuel vehicles (FFVs). FFVs allow drivers to run their vehicles on any combination of E85 and unleaded gasoline in the same tank. Ford Motor Co. plans to spend at least $1 M on developing retail alternative fuel infrastructure to help increase the use of these environmentally friendlier fuels. Ford is in partnership with the US Department of Energy to develop infrastructure in two pilot areas. In these test cities, Ford will provide eight $5 coupons to every purchaser of a 3 litre Ford Ranger pickup, which has FFV capability, targeting owners living within 15 miles of an E85 outlet. The E85 coupon programme is designed to encourage drivers of the Ranger FFV to visit the 10 E85 refuelling stations opening in Chicago and the up to 30 E85 stations planned for the Twin Cities area. By providing drivers with incentives to purchase E85 rather than gasoline, the Ford Motor Co. hopes to stimulate the use of E85 as an alternative to gasoline (http://www.ford.com).

Ethanol blends

...in the US

Ethanol currently accounts for less than 1% of US gasoline volume. Gasoline blending provides a market for 1.4 bn lbs/y of ethanol capacity and generates ethanol sales of $1.3 bn/y. The target of 10% ethanol content in gasoline by 1990 has never been approached owing to the price of ethanol and logistical constraints. Its use in hot weather is limited, and there are special requirements for storage and delivery of ethanol-containing gasoline which have led to marketing problems. The ethanol lobby portrays it as the long-term solution for reformulated gasoline, but gasoline producers and analysts do not agree. However, they do see a role for ethanol as a discretionary octane improving additive, and as an oxygenate in some markets. If the US subsidy on ethanol were removed it would probably not be used at all. It also receives additional subsidies in some US states.

...and in Brazil

Brazil was one of the pioneers of the ethanol car, using ethanol derived from the sugar cane industry. In the 1970s and 1980s there were hundreds of thousands of ethanol-powered cars in the country; nowadays there are only a couple of thousand. However, the price of sugar-cane ethanol in Brazil is very low at the moment, and pollution fears combined with the risk of substantial job losses in the sugar industry have led the government to persuade General Motors and Ford to restart production of alcohol cars. Fiat and Volkswagen are already producing them in Brazil. The government has announced that it will increase the amount of alcohol added to petrol from 24% to 26% and that taxi drivers will no longer enjoy tax breaks on petrol-fuelled cars, but will continue to do so if they use ethanol as a fuel.

Fuel cell taxi cab (London) from Zevco

First generation fuel cell transit bus from Ballard Power Systems

Fuel cells

Fuel cells for Canada

Petro-Canada, Ballard Power Systems and Methanex have announced the signing of a Memorandum of Understanding under which the three companies will work together to prepare for the establishment of a commercially viable fuel distribution network to meet the expected market demand for fuel cell vehicles. Petro-Canada, Ballard and Methanex will collaborate in laying the groundwork for a pilot project involving the supply and distribution of appropriate fuel, starting with methanol to facilitate the introduction of fuel cell vehicles (http://www.petro-canada.ca).

Shell Hydrogen

Shell is the first of the major oil companies to state its commitment to bringing fuel cells to market, with its formation of Shell Hydrogen. Shell has reached an agreement with a subsidiary of Daimler Benz involving co-operative research into fuel cell power for motor vehicles (http://www.shell.co.uk).

Delphi and BMW announce fuel cell developments

Delphi Automotive Systems (Troy, Michigan, USA) and BMW have signed a development agreement to produce vehicles that use a solid oxide fuel cell as an auxiliary power unit and that have the potential of being clean, high power generation vehicles. Under the development agreement, BMW and Delphi are jointly developing a fuel cell system that will be used as an auxiliary power unit for gasoline engines. This will allow BMW to offer more features more efficiently with the potential to reduce the emissions of an internal combustion engine. Delphi will develop the fuel cell system and BMW will integrate the unit into a vehicle. The solid oxide fuel cell unit will provide more energy into the vehicle to enhance the electrical systems. Delphi and BMW plan to produce the solid oxide fuel cell unit in the near future. The solid oxide fuel cell unit has the ability to increase the electric power within a vehicle to offer more features in the most efficient way. Additionally, it provides tremendous potential to reduce the emissions of the internal combustion engine (http://www.delphiauto.com).

Hydrogen fuel cell vehicles

Zevco, a British manufacturer of hydrogen fuel cell powered vehicles, has announced that it will become listed on the Easdaq and Nasdaq stock exchanges this year. This will allow the company to meet the expected increase in demand. The company is negotiating a contract to supply some vans to the UK Royal Mail, and has recently introduced the first zero-emission taxi to New York following its launch of the zero emission London Millennium Taxi. Other tests for short journey vehicles (*e.g.* taxis to and from airports) are being held, and the company expects to start manufacturing in the US soon.

More on cars

Automatic shut-off

Honda has announced that it will market a scooter, the Giorno Crea DeLuxe, which automatically shuts off when stopping. The price will be around £1000. The scooter emits about half the levels of pollution allowed in Japan, and is also claimed to be more fuel-efficient than similar scooters.

Germany stalls car recycling

The European Union has been working on a plan to make car producers bear the cost of recycling old cars. However, the European Automobile Manufacturers Association (ACEA) have been lobbying strongly against this proposed law. The law has finally been defeated amidst accusations of Germany buckling under pressure from its powerful car lobby. ‘It is quite clear that the way the German presidency handled the end-of-life car directive was nothing less than a disgrace,’ Peter Jorgensen, spokesman for Environment Commissioner Ritt Bjerregaard, told a news briefing. The legislation would only have added 0.5% to the price of a new car, Jorgensen added.

German Chancellor Gerhard Schroeder said recently that an appeal from Volkswagen AG had prompted his country to think again. Schroeder is a former member of VW’s supervisory board. Britain and Spain, both with significant car manufacturing capacity, said they were sympathetic to the

German position. It will now be up to the next EU president, Finland, an enthusiastic supporter of the proposals, to find a compromise. Environment ministers next meet in October, though Finland has said it would consider dealing with the proposal before then.

CO_2 deal between EU and Korea, but not yet with Japan

The European Commission has struck a deal with Korea to reduce pollution from cars in a voluntary scheme. This would mean that average fuel consumption would be reduced from the current average of 7.7 litres/100 km to around 6. The European Commission has said that it is seeking to achieve this by 2008, the Koreans by 2009. Japan has not yet agreed, claiming that it has a different balance of the large and small car markets to the other countries, and that the target will affect it differently. The European Union has threatened to impose restrictions if a voluntary agreement is not reached soon.

New products

Coalescent solvent for specialist coatings

Chemoxy International plc, of Middlesbrough, UK, has launched a new coalescent solvent which has been formulated to assist the film formation properties of speciality wood coatings, finishes, varnishes and lacquers. The low VOC (volatile organic chemical) content, low odour solvent is also well suited for use in decorative paints and coatings, adhesives, screen printing inks and leather coatings. Called Estasol BG, the coalescent solvent is the latest addition to Chemoxy's rapidly expanding range of low toxicity solvents. The new high purity solvent is biodegradable, colourless and has a high flash point of 75°C. Compatible with a wide range of resins including polyvinylacetate, nitrocellulose and polyvinylbutyrate, Estasol BG is ideal for formulators looking to produce the 'next generation' of quick evaporation, environmentally friendly coating products.

Forming and stamping fluids

Solutia Inc., St Louis, USA, is introducing a new series of water-based forming and stamping fluids, the Glacier 5000 series, as new members of its metalworking fluid family. These unique products provide the benefits of oil in a water-based fluid, and serve as an alternative to the oil-based forming that currently dominates the market. Developed from breakthrough protein technology, Glacier 5000 is designed for both ferrous and non-ferrous metals. The bright and clear amber liquid uses water-based chemistry and does not contain oil. As a result, it can be easily cleaned or washed off parts using water or traditional cleaning systems. Glacier 5000 works in a wide range of applications with a broad array of applicators. It also helps parts and dies stay cooler. In addition, Glacier 5000 promotes a cleaner, safer work environment. Glacier 5000, and all Glacier fluids, are thoroughly tested for health effects. Glacier 5000 holds the safest rating for toxicity, and has a low odour. In addition, the fluid is biodegradable and recyclable, and contains no hazardous waste constituents (http://www.solutia.com).

High-temperature carbon dioxide-absorbing ceramics

Toshiba, Japan, has developed a ceramic material that can absorb carbon dioxide at 450–700°C through a chemical reaction after contact. This material is made from lithium zirconate which can absorb 400 times its volume of carbon dioxide—10 times better than conventional materials. Thus, it is possible to absorb carbon dioxide from high-temperature high-pressure gases, applicable for example in coal-burning power generation plants, manufacturing sites and cars. The recovered carbon dioxide can also be utilized. Research is underway to lower the production cost and widen the applications.

New processes

Copper sulfate by nitric acid-catalyzed air oxidation

A process for making copper sulfate has been developed by a group from the Northwest University, China, that does not evolve sulfur dioxide during the process to pollute the environment. Waste copper wire or other copper waste is heated with water, sulfuric acid and a catalytic amount of nitric oxide at 85°C and 8 kPa, with four air inlets to give an even and ample oxygen supply. The crystalline product is collected by filtration, and the mother liquor is recycled for another run of the production.

A water-based process for manufacturing optical brighteners

Optical brighteners have been traditionally manufactured by dissolving cyanuric chloride in a volatile solvent such as acetone and reacting this with a sulfonated amine. Ultimately the solvent which is required to effectively get the water-insoluble cyanuric chloride in an active form, is recycled but it can be avoided altogether in some cases through the use of surfactants. Hickson and Welch have recently extended the cleaner technologies to the manufacture of optical brighteners for the detergent industry. The major reasons for this are removing solvent costs, avoiding handling flammable solvents, avoiding VOC containment costs and adding value through the exploitation of more environmentally friendly technologies. Hickson and Welch now operate a water-based manufacturing process which eliminates the use of some 3000 tonnes/year of solvent (*Environmental Business Magazine*, May 1999).

Awards

ICI wins environmental award

ICI's newly formed Synetix business has won the Queen's Award for Environmental Achievement for Hydecat, its unique process for treating sodium hypochlorite produced from waste chlorine streams. The Hydecat process, as it is known, converts sodium hypochlorite (bleach) from a potentially harmful mixture to a benign common salt solution and oxygen. Hydecat technology is essentially automatic and guaranteed for at least three years. ICI's first commercial units were installed in 1993 and since then further improvements have been made both to the process and to the catalyst. More than 20 customers in 9 countries have successfully applied the Hydecat technology. Customer savings are impressive: one customer has reduced the cost of destruction of hypochlorite from £300000/y to £30000/y.

Dexter recognized with five 1999 patent awards

Dexter Electronic Materials (Industry, California, USA) received five 1999 patent awards for patents issued in 1998. The patent for stabilized nitric acid compositions claims a stabilizer that reduces the decomposition of acid when used to strip tin or tin/lead solder from printed circuit boards. Benefits to Dexter customers include dramatically extended bath life and ease of waste treatment relative to competitive processes. The patent for propargyl ether-containing compositions useful for underfill applications claims the use of aromatic propargyl ethers as an underfill resin chemistry. The described resins can be cured to produce hydrophobic, high glass transition thermosets with no evolution of volatiles. The patent for perfluorinated hydrocarbon polymer-filled adhesive formulations and uses claims the use of perfluorinated hydrocarbon filler in die attach adhesives. Products based on this technology provide customer value in the form of reduced potential for radio frequency cross talk and ease of application. The patent for maleimide-containing formulations and uses claims the use of hydrophobic resin combinations useful in the preparation of high temperature, blister resistant laminates for printed wiring boards. The patent for bleed resistant cyanate ester-containing compositions claims the use of novel bleed reduction additives in cyanate ester-based attach adhesives. Products based on this technology provide improved reliability and productivity.

Catalysts

Second-generation titanium dioxide photocatalyst

A titanium dioxide photocatalyst which can operate at wavelengths higher than 420 nm and in the visible light region has been successfully developed by EcoDevice Company, Japan. With this material, most of the available energy from the sun can be utilized (compared with only 3% available at ultra-violet bands in the <400 nm region when using older photocatalysts). The company has already signed a contract with a manufacturing company, and expects to increase the production capacity to several kilograms per month soon. It is hopeful that the price will fall in due course (presently at more than Yen 20000/g). The photocatalyst can also be applied in solar cells to decompose water to generate clean hydrogen fuel.

Reagent catalysts

Contract Chemicals is developing a second generation of its Envirocats supported reagent catalysts. These can replace traditional catalysts associated with unacceptable levels of waste and by-products. They can be used instead of Friedel–Crafts and Brønsted acid and oxidation catalysts. They are non-toxic, non-corrosive and inert relative to homogeneous catalysts like aluminium trichloride. Contract recently commissioned a £5 M fine chemical plant expansion at Knowsley, UK.

Catalytic synthesis of tributyl citrate

Tributyl citrate (TBC) is a non-toxic plasticizer, with superior compatibility and plasticization properties to impact, cold, light and water resistance. Since phthalate plasticizers are well regulated because of their undesirable environmental impact, TBC has become the material of choice. Conventionally, TBC is made with concentrated sulfuric acid as catalyst for esterification. However, due to the low yield, corrosion to equipment and environmental pollution caused by the use of sulfuric acid, newer catalysts have been developed. A homemade activated carbon-supported heteropoly acid catalyst has been prepared by a team from the Fujian Institute of Research on Structure of Matter, China. When reacting citric acid and butanol in the presence of 22.5% of the catalyst at 145°C, up to 98% pure TBC is obtainable (see article by Becky Allen on phthalates in toys in this issue of *Green Chemistry*).

Biotechnological processes

The recent patents are Merck's for a microbial conversion of glycerol to dihydroxyacetone and Genencor's for the microbial synthesis of quinic acid from glucose. DuPont and Genencor have jointly developed, using recombinant DNA technology, a process to create a single microbe that converts sugar from corn starch into the monomer propane-1,3-diol using a biotransformation process. The new technology will enable production of propane-1,3-diol at a cost approaching that of ethylene glycol, the monomer for production of poly(ethylene terephthalate). The company is taking this further with the biological processing of propane-1,3-diol to the polyester poly(trimethylene terephthalate) (PTT). DuPont claims the PTT has enhanced properties compared with conventional polyester. The technology will be commercially available by 2004 and DuPont plans to build a 20000 tonnes/y plant. Recently, Shell of Holland has been developing PTT for use in the textile and carpet industries. Other research groups in various European countries and in China are also studying such production technology.

DuPont builds new fluoropolymer plant for supercritical carbon dioxide process

DuPont Co. (Wilmington, Delaware, USA) has begun construction of a $40 million, 2.5 million lb/year development and manufacturing facility to make melt-processable fluoropolymers using a process based on supercritical carbon dioxide. It is planned that $275 million will be spent over the next seven years if the trials are successful.

The company has already been testing the technology at a $2-million pilot plant it brought on stream in 1999 at the DuPont Experimental Station in Wilmington. It expects the new unit to open in late 2000 and produce fluorinated ethylene propylene (FEP) and perfluoroalkoxy resin (PFA). The company plans to demonstrate the technology for two to three years before building a larger plant.

The technology gives DuPont the ability to make new grades of polymer which have specialized properties. It also promises to be more efficient, more flexible, and less costly than existing processes.

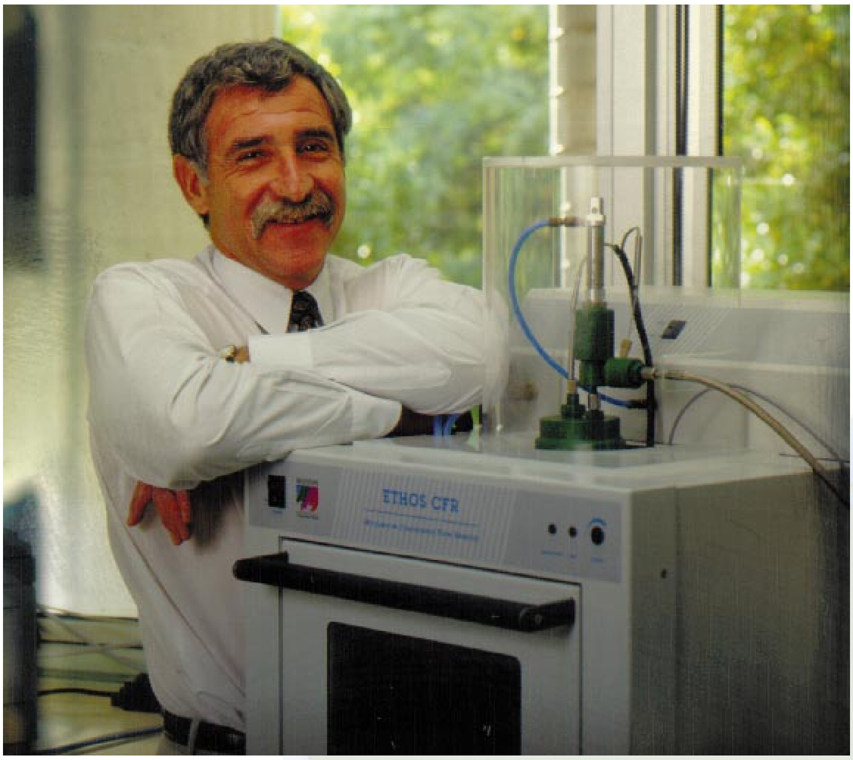
The process came about from a partnership between DuPont and Joseph DeSimone, William R. Kenan, Jr. Distinguished Professor of Chemistry and Chemical Engineering at both the University of North Carolina at Chapel Hill and North Carolina State University in Raleigh, N.C. He is a pioneer in polymer synthesis using supercritical fluids. DuPont has supported his research since 1990.

DuPont's Teflon FEP is widely used for plenum cable insulation because of its excellent insulating properties, fire resistance, and light weight, which makes it easier to string over long distances. A new production technology based on supercritical carbon dioxide promises more specialized grades and improved process economics.

DeSimone's group reported the first successful homogeneous free radical polymerization in an inert supercritical fluid (SCF) in 1992 (*Science*, 1992, **257**, 945). Since then, he has expanded synthesis technology to include dispersion, cationic, ring-opening metathesis, step-growth, and additional heterogeneous polymerizations.

Award for microwave chemistry

Susan Cumming from Howard Florey Institute describes the achievements of Chris Strauss from the CSIRO who has received the Royal Australian Chemical Institute (RACI) Inaugural Green Chemistry Challenge Award



Chris Strauss of CSIRO with his continuous microwave reactor.

There were fewer than five papers on microwave-assisted organic synthesis when Dr Chris Strauss entered the field in 1988. The state-of-the-art equipment consisted of rudimentary domestic microwave ovens and relatively primitive reaction vessels susceptible to explosions. There was little fundamental knowledge about the effects of microwave energy on organic molecules and it was difficult to obtain a uniform energy distribution and to control and measure temperature. In short, the technique had shown promise, but was dangerous.

Chris thought that if equipment could be developed to allow the organic chemist to carry out reactions safely and controllably, microwave technology could become a valuable tool for cleaner chemical processing.

The continuous microwave reactor

He was the principal inventor of the continuous microwave reactor (CMR) which operates by pumping organic solvents and reactants through a microwave-transparent vessel held in a microwave zone.[1] The monitoring and controlling operations are performed outside the microwave zone and allow organic reactions to be performed rapidly and continuously at elevated pressures and temperatures. With this unit, several difficult reactions, including preparations of highly reactive monomers and the iron-chelating drug deferiprone, have been carried out cleanly and easily in his laboratory.

Chris was instrumental in the technology transfer and CSIRO's commercial partner, Milestone MLS (Germany and Italy), is now manufacturing and distributing units globally under licence.

Microwave batch reactor for chemical synthesis

Chris was also the principal inventor of the microwave batch reactor (MBR), a system that can be operated at pressures up to 100 atmospheres and temperatures up to 265 °C under rigorously controlled and monitored conditions in the laboratory.[2] The vessels are fabricated from inert materials. Reactions are monitored from within the microwave zone and the computer-driven system has the capability for stirring, sample withdrawal and reagent introduction, as well as for rapid post-reaction cooling. Microwave power input can be carefully controlled and is continuously variable. This reactor is expected to become important for organic synthesis, particularly through the application of new techniques such as differential heating and concurrent heating and cooling.

Summary of Chris Strauss' role in microwave chemistry

Chris Strauss' work has helped transform microwave chemistry from a laboratory curiosity into an important field, for which dedicated international conferences are now held regularly. His group is the only one to have designed, built and demonstrated microwave reactors for liquid phase organic synthesis at elevated temperature and pressure. Until these innovations, the equipment for carrying out preparative organic reactions had changed little over decades.

Through the MBR and CMR, Chris has anticipated emerging requirements of industrial chemical reactors. His systems can be easily cleaned, an important consideration in lowering waste output. They also are portable, multi-purpose, self-contained and do not require an external boiler. Capabilities for just-in-time processing and the materials of construction promote short turnaround times. The systems provide for remote, programmable operation and have the potential for tandem procedures including distillative reactions and coupling with catalytic membranes.

The number of published refereed papers on microwave-assisted organic synthesis now exceeds 500. Chris is regarded not only as a pioneer in microwave-assisted organic chemistry, but as an authority in the field. By invitation, he has reviewed his work[3] and presented plenary lectures at international microwave conferences in USA (1995), Canada (1997) and the Czech Republic (1998).

Water as solvent

Chris Strauss was first to recognise that high temperature water has properties that can be exploited for organic synthesis and product isolation. In a broad investigation facilitated by his microwave equipment, relatively modest differences in temperature afforded substantial variations in product distributions.[4,5] High-temperature aqueous conditions had advantages over established synthetic procedures and were an attractive alternative to acidic or basic catalysts in organic solvents at lower temperatures. When addition of acid or base was necessary, less agent was usually required than for processes at and below 100 °C and the reactions often were selective. In some cases, the requirement was orders of magnitude lower.

Significantly, inorganic salts account for the bulk of industrial chemical wastes. They contaminate soil and ground water and can lower the pH of atmospheric moisture and contribute to acid dew or acid rain. For cleaner production their minimisation is essential. Chris's work represents a major advance in this context.

The preparation of the important synthetic building block, 3-methylcyclopent-2-enone, is a good example.[6] Earlier workers had used strong base in high concentration for the moderately yielding preparation and generated substantial amounts of salt in their work-up. His method employed up to 400 times more dilute base. Competing reactions were suppressed, salt formation was lowered and the product was obtained in the highest yield so far reported. The industrial viability of the process was established using a heat-jacketed autoclave and a continuous microwave reactor.

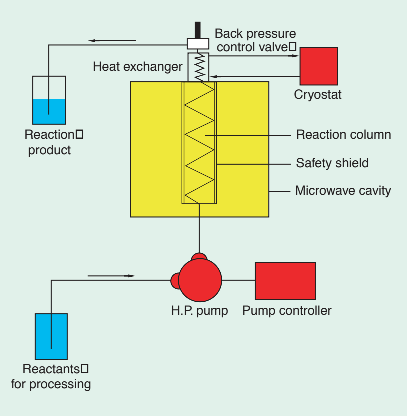


Figure 2. Flow diagram of the operation of the continuous microwave reactor.

Resin-based isolation methods

Chris was also first to develop resin adsorption and ion-exchange techniques for isolation and purification of products synthesised under aqueous conditions.[6] Advantages of such non-extractive processes for clean processing include ease of use, high throughput and low waste. The resin can be readily recycled, as can the solvent used for desorption.

The preparation of 3-methylcyclopent-2-enone exemplified his strategy for cleaner production.[6] Microwave technology, high-temperature aqueous media and resin-based isolation procedures were combined to overcome difficulties with established methods and to obtain products in high yield.

Catalytic membranes

Chris has also recognised that catalytic methods can avoid the use of stoichiometric inorganic reagents. He has developed methods for retaining catalytic metals on porous glass tubing and investigated these novel materials as catalysts for Heck-type couplings.[7]

Advantages of palladium on porous glass included resistance to aerial oxidation, ease of manufacture, mechanical strength and thermal stability, recyclability, negligible loss of palladium into the reaction mixture and obviation of air- and temperature-sensitive ligands. He has used palladium on porous glass in conjunction with microwave heating to catalyse reactions. High turnover numbers were obtained in some cases and he also discovered a new tandem coupling–oxidation process.

New and improved reactions

Uncatalysed hydrogen transfer

Chris also discovered that aldehydes and ketones can be reduced to the corresponding alcohols by transfer hydrogenation at high temperature with ethanol, *n*-propanol or isopropanol as hydrogen donors in the absence of catalysts and base.[8] The potential environmental benefits include inexpensive, renewable reagents, minimal waste and that no inorganic salts are introduced or formed.

Catalytic etherification

Most methods for etherification use either strongly acidic or basic conditions and

RACI—and its Green Chemistry Awards

The Royal Australian Chemical Institute, founded in 1917, is both the qualifying body in Australia for professional chemists and a learned society promoting the science and practice of chemistry. The Institute has 9000 members and was granted a Royal Charter in 1932. It is concerned with the teaching and practice of chemistry and with the application of chemistry in industry, academia and government authorities. Thus, it represents and caters for the professional needs of all chemists, providing various activities and services that encompass the profession of chemistry in Australia. For example, it holds an annual National Chemistry Week, a National Convention every 5 years, and publishes a monthly magazine, *Chemistry in Australia.*

In 2001 RACI will host the World Chemistry Congress (incorporating the 39th IUPAC Congress, 9th Asian Chemical Congress and the AIMECS meeting) at which Green Chemistry is one of the 5 major themes.

This year RACI has inaugurated Green Chemistry Challenge Awards to recognise and promote fundamental and innovative chemical methods in Australia that accomplish pollution prevention through source reduction and that have broad applicability in industry, and to recognise contributions to education in Green Chemistry. The Green Chemistry Challenge Awards are open to all individuals, groups and organisations, both nonprofit and for profit, including academia, government, and industry.

The nominated green chemistry technology must have reached a significant milestone within the past 5 years in Australia (*e.g.* been researched, demonstrated, implemented, applied, patented, *etc.*) and should be an example of one or more of the following 3 focus areas:

- **the use of alternative synthetic pathways**
- **the use of alternative reaction conditions**
- **the design of alternative chemicals**

For more information about RACI see http://www.raci.org.au

have well documented disadvantages. The nearly 150 year old Williamson synthesis is still the most common procedure. It involves substitution of an alkyl halide (RX) by a strongly basic alkoxide or phenoxide (*e.g.* KOR or NaOR) and so is unsuitable if base catalysed elimination of HX from RX can compete. A stoichiometric amount of waste salt (KX or NaX) is also produced.

Chris has invented a catalytic etherification that produces little organic waste and that can be carried out without the addition of acid or base.[9]

For a symmetrical ether, an excess of alcohol (ROH) and a catalytic amount of RX are heated (see Scheme 1). A solvolytic displacement reaction between RX and ROH affords R_2O along with HX or its elements (hereafter referred to as HX; equation 1). The liberated HX reacts with another molecule of ROH to form water and to regenerate RX (equation 2). If the rates of these forward reactions are comparable, the concentration of HX will be low throughout and that of RX will remain relatively constant. Although HX and RX are stoichiometric reactants or products in equations 1 and 2, they do not appear in the sum, equation 3. The nett process involves condensation of two molecules of ROH to give R_2O plus water. It requires participation by the counterion X^- and utilises ostensibly neutral conditions. For efficient operation, X^- should be a good leaving group (to satisfy equation 1), an effective nucleophile (to accommodate equation 2) and a weak base to minimise competing elimination reactions. Bromide and iodide possess these properties. It appears that a critical participatory role for the counterion of the acid has not previously been envisaged or recognised.

CSIRO—where Chris Strauss works

CSIRO (Commonwealth Scientific and Industrial Research Organisation) is the largest R&D organisation in Australia, employing over 7000 staff in areas such as agriculture, minerals and energy, manufacturing, communications, construction, health and the environment. Chris Strauss works within the Molecular Science Division of CSIRO that employs over 300 staff in Melbourne and Sydney. Its research programs are designed to assist the development of industries related to the medical, pharmaceutical, chemicals, polymers, water treatment and waste management sectors of the Australian economy. For further information on CSIRO in general see http://www.csiro.au and on the Molecular Science Division in particular see http://www.molsci.csiro.au

$$\mathrm{RX + ROH \rightleftharpoons R_2O + HX} \tag{1}$$

$$\mathrm{HX + ROH \rightleftharpoons RX + H_2O} \tag{2}$$

$$\mathrm{2\ ROH \rightleftharpoons R_2O + H_2O} \tag{3}$$

Scheme 1. Pathway for catalytic ether synthesis

The potential for commercial exploitation of the reaction is currently under consideration.

New tandem arylamidation

Chris has also developed a single-pot synthesis for *N*-aryl amides which can be conducted as a domino reaction or a tandem sequence.[10] Before this reaction, there were few, if any, useful literature methods for obtaining, in a single step, *N*-aryl amides from aromatic compounds which do not possess an amino function. The new method greatly simplifies the Hoechst–Celanese process for the manufacture of paracetamol. The opportunities for clean processing include atom economy, obviation of isolation and purification of intermediates, savings in time, raw materials and solvent consumption and avoidance of multiple work-up and cleaning operations.

Avoidance of heat transfer oils

A key step in the preparation of quinolone antibacterial agents involves the formation of an amino ketone ring system by intramolecular cyclisation of a diethyl *N*-(aryl)aminomethylene malonate derivative at temperatures near 250 °C. To obviate intermolecular reactions, the condensations are usually carried out in high dilution using heat transfer oils consisting of diphenyl ether or a eutectic mixture of diphenyl ether and diphenyl. However, such oils are unacceptable for clean chemical processing.

Chris developed a thermal method for carrying out such Jacobs–Gould reactions in high conversion, rapidly, predictably and controllably, without a diluting heat transfer oil.[11] He established a continuous process and demonstrated it on a laboratory scale. This was the first example of a Jacobs–Gould reaction having been performed in such a manner. The procedure accommodates high throughput, is energy efficient, is low polluting and offers easy work-up.

Indole transformations

Direct, preparative methods utilising high-temperature aqueous media, were developed for indole and indole-2-carboxylic acid from ethyl indole-2-carboxylate.[12] Yields were excellent for these reactions, which were carried out in 1 hour or less, at temperatures up to 270 °C, in the microwave batch reactor. Avoidance of undesirable copper salts, high boiling organic bases and heat transfer oils made the methods environmentally benign.

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Professor Anthony Barrett

In the first of a new series of reports looking at some of the leading workers in the field of green chemistry and clean technology, Mike Lancaster describes some of the work of Tony Barrett's group at Imperial College of Science, Technology and Medicine, London.

Tony Barrett's group at Imperial College of Science, Technology and Medicine

Tony Barrett is Glaxo Professor of Chemistry and Director of the Wolfson Centre for Organic Chemistry in Medical Science at Imperial. Following his Ph.D. at Imperial under the tutorship of Professor Sir Derek Barton, Professor Barrett was immediately appointed to a lectureship at the College. In 1983 he moved to the USA for 10 years taking in Professorships at Northwestern University and Colorado State before returning to Imperial as Head of Organic Chemistry.

Barrett's research interests cover a wide range of organic chemistry ranging from identification of effective fungicidal agents to olefin metathesis, and optical and imaging materials. This article will focus on Barrett's work with lanthanide triflates as clean catalysts of potential use to the fine chemicals industry. Tony Barrett's interest in clean technology started following Kobayashi's work in the early nineties describing lanthanide triflates as water tolerant Lewis acids. Barrett is also a keen advocate of Trost's atom economy concepts and much of his work on clean technology has combined these two areas.

Nitration

One of Professor Barrett's leading co-workers is Dr Chris Braddock who worked in the group as postdoctoral fellow until his recent appointment to a Lectureship at Imperial in October 1998. On arriving in the group in January 1996 he was challenged to nitrate toluene without using more than one mole equivalent of nitric acid, and without the use of sulfuric acid. Nitroaromatics are key chemical feedstocks for dyes, pharmaceuticals and plastics, but, their synthesis historically uses mixtures of fuming nitric acid and sulfuric acid leading to significant amounts of waste. More recently nitration has been carried out with nitric acid in the presence of Lewis acids such as BF_3 but this approach is equally 'unclean' since stoichiometric amounts of 'catalyst' are required resulting in copious quantities of acidic waste. Rising to this challenge, Braddock's application of lanthanide triflates to the nitration of toluene was highly successful, with greater than 95% conversion achieved using a single equivalent of nitric acid and a catalytic quantity (10 mol%) of ytterbium triflate. The real benefit of this work was that the only side-product was water, and that the catalyst could be recovered and reused—most unusual for a Lewis acid.

EPSRC and Air Products sponsored further work in the area aimed at scoping the reaction and studying the mechanism. On screening the entire series of lanthanide(III) triflates for catalytic activity (for nitration) it became evident that there was a clear relationship between the extent of nitration and the ionic radius of the lanthanide ion with activity increasing as the radius decreased. This led Barrett and Braddock to postulate that the ever-increasing electrostatic interaction between the lanthanide ion, and nitric acid was responsible for the increase in activity. Further mechanistic study led to the belief that nitric acid was displacing water in the inner co-ordination sphere of the lanthanide ion, this resulted in the reversible elimination of a proton, as shown. It is this proton that leads to the accentuation of the Brønsted acidity of the nitric acid through formation of a nitronium ion.

$$[Ln(OH_2)_9]^{3+} \leftrightarrow [Ln(OH_2)_y(HNO_3)]^{3+}$$

$$[Ln(OH_2)_y(HNO_3)]^{3+} \leftrightarrow [Ln(OH_2)_y(NO_3)]^{2+} + H^+$$

$$H^+ + HNO_3 \leftrightarrow NO_2^+ + H_2O$$

Although this work has not yet been commercialised, Professor Barrett is currently patenting extensions to this technology for which he sees many commercial applications. The rare earth metals are not actually that rare and neither availability nor cost would preclude their use as commercial catalysts. With the current system the recycling technology is different to that available on most industrial plants, Barrett believes however that new plants, designed to use lanthanide catalysts, would be cost effective. A significant advantage for industry would be heterogeneous versions of the catalyst which may be just around the corner.

'Barrett believes that new plants, designed to use lanthanide catalysts, would be cost effective'

Esterification with lanthanide(III) triflates

Esterification is another reaction that finds widespread use in the chemical industry. At first sight this is green chemistry at its best, the only by-product being water, for example:

$$\mathrm{ROH + AcOH \rightarrow ROAc + H_2O}$$

Chemistry is rarely that simple however; the reaction is reversible and typically a significant excess of either acid or alcohol as well as a strong mineral acid are required to drive the reaction forward. Azeotropic removal of water also drives the reaction but this sometimes requires complex and expensive distillation towers and produces significant amounts of acid waste. Although Lewis acids do catalyse the reaction they offer no benefit in terms of clean technology. Since the lanthanide triflates are stable in water they seemed an obvious choice to Barrett and Braddock. They found that both scandium (III) and lanthanide(III) triflates catalysed the acylation of a range of primary, secondary and tertiary alcohols with acetic acid. Quantitative yields were obtained with primary alcohols such as phenethyl alcohol at room temperature using just 5 mol% Sc(OTf)$_3$, and even the extremely bulky tertiary alcohol 1-adamantanol could be acetylated to 80% conversion within minutes at reflux.

The Green Chemistry Movement

Within the UK Tony Barrett believes that one of the most important factors in pushing forward clean technology was the establishing of the Institute of Applied Catalysis (*i*Ac) which came out of the Government's Foresight panel of which he was a member. *i*Ac has been responsible for encouraging and supporting catalyst research in the UK that is at the heart of much clean technology. Indeed Barrett believes more money should be put into the *i*Ac programmes to underpin clean technology themes. One weakness of the current funding programme in the UK is that it is not always related to the needs of society, programmes often being funded for political rather than social need.

> 'Barrett believes that clean technology in the UK was pushed forward by the establishing of the Institute of Applied Catalysis'

Two of the most important aspects, in Barrett's view, to drive new clean technology into industry are the forging of close links between academia and industry at an early stage and the establishment of close working relationships between chemists and chemical engineers so that the process is developed alongside the chemistry. To this end Barrett and Braddock are currently working on establishing a MSci course in 'Chemistry with Fine Chemicals Processing' in conjunction with the Department of Chemical Engineering at Imperial. Professor Barrett also attributes much of the success of his long collaboration with Air Products to the significant involvement of engineers. Imperial saw the need to involve industry at an early stage in academic research several years ago. A full-time post, the Director of Strategic Alliances, was created to enable the research work to be marketed and to identify potential industrial partners. This has been of invaluable help to the work of the Barrett group.

> 'the key drivers which Barrett thinks will force industry to become more green are financial and legislative'

At the end of the day the key drivers which Barrett thinks will force industry to become more green are financial and legislative. He is starting to see both of these come together in the pharmaceutical industry. There is now much more competition in this area forcing prices down and as the cost of waste rises so new technology is needed. As outsourcing becomes widespread so does the opportunity for new, competitive clean technology.

Barrett is however scathing of people and technology jumping on the green bandwagon. As an example he cites biotransformations, generally perceived as being green, but many examples suffer from extremely low turnovers producing huge volumes of waste. One problem we have is defining what 'green' is, especially when comparing processes. Professor Barrett is a keen supporter of the atom economy concept but at the end of the day chemical instinct is usually a good measure.

In terms of chemistry education Tony Barrett is a traditionalist, he firmly believes in teaching fundamental core chemistry and that undergraduate courses should not be modified too much to include latest green chemistry methodology.

> 'Barrett would like to see aromatic transformations revolutionised with clean technology'

If he could revolutionise one area of chemistry with clean technology Barrett would choose aromatic transformations—which are at the centre of the fine and speciality chemicals industry.

Meanwhile as Chris Braddock starts on an independent career in the area of clean technology he is looking to use metal free asymmetric catalysts (MFAC) such as recyclable carbocations to overcome the problematic issue of toxic metal residues in pharmaceutical products. I'm sure we will be hearing much more about MFAC in the coming few years.

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The Hazards Forum

Terry Farthing describes an interdisciplinary forum for engineers concerned with the mitigation of both natural and man-made disasters

Historical perspective

The Hazards Forum, a registered Charity, was founded in 1989 by the Institutions of Chemical, Civil, Electrical and Mechanical Engineers to provide an interdisciplinary focus for:

- the study of disasters and the promulgation of lessons drawn from them
- the promotion of risk reduction strategies
- raising awareness in the professional community of the responsibility of the individual to improve safety

Disasters arising from both natural and man-made hazards were within the remit although it was British examples of the latter that were the primary drivers for the initiative by the Institutions. The first Mission Statement stated 'The Hazards Forum exists to provide a focal point in which engineering features in the mitigation and reduction of both man-made and natural hazards and disasters'.

Forum membership was initially restricted to the engineering institutions and associated bodies but in recent years membership has been extended beyond engineering. Other institutions and societies, including the Royal Society of Chemistry, the Geological Society, the Institute of Physics, Institute of Occupational Safety and Health, Institute of Hydrology, are Associate Members. A range of companies, distinguished persons and others with an interest in hazards and risk are also included in the membership.

The Forum, under the successive Executive chairmanship of Sir Frederick Warner, Sir Bernard Crossland and Professor Phillip Bennett, has pursued its aims and objectives via regular meetings, special keynote events and the publication of a Newsletter and books. The aim has been to provide a service to members and to bring important issues to a wider audience.

Constitution and membership

The Forum is constituted with an Executive Committee and an Activities Committee, both supported by a Secretariat based at the Institution of Civil Engineers. Membership of both committees is not limited to Engineers, but is by invitation only, with the minimum requirements of chartered status in their own field, and formal approval of the Executive.

Stuart Luxon was the RSC-Environment, Health and Safety representative on the Forum until he resigned from the EHSC a few years ago. I was nominated as his successor (partly due to my background as Chief Chemist and Company Environmental Health Chemist with Rolls-Royce plc.), then was invited to join the Activities Committee the following year. When Darrol Stinton, a former test-pilot, and now Engineering consultant in Aero and Marine, stepped down from the chairmanship due to overseas commitments in December 1998, I was offered and accepted the chair.

Following the resignation of Professor Bennett, also due to overseas commitments, Stuart Mustow, a distinguished Fellow of the Royal Academy of Engineering, accepted the Executive Chairmanship in January 1999.

Both committees have a balanced representation from engineering, science, technology, safety and emergency planning.

Recent issues addressed by The Hazards Forum

Seminars and meetings have included:

- The Successful Management of Safety
- Safety of Ships
- Flood Hazards in Bangladesh
- An Engineer's Response and Tasks in Disaster Preparedness
- Blowing the Whistle for Safety
- Risks to the Public–The Rules, The Rulers and The Ruled
- Gas-Rich Volcanic Lakes–A Major Natural Hazard

Strategy for the Future

The Forum was initially conceived to ensure that lessons of the past learned from major disasters both natural and man-made should not be forgotten. It has been recognized that with its multidisciplinary composition, the Forum is ideally suited to address the whole spectrum of issues of Hazard and Risk. In order to address this spectrum however, a much greater degree of cooperation will be sought with other Institutions and major companies in organizing attractive meetings that will offer a balanced perspective.

> 'The Forum exists as a focal point for engineers involved in mitigating hazards and disasters'

The British National Committee for the UN International Decade for Natural Disaster Reduction (IDNDR) is established under the auspices of the Royal Society and the Royal Academy of Engineering to co-ordinate British initiatives in support of the decade. It is interdisciplinary and reflects the involvement of many British nationals; consultancies and NGOs in natural disaster-related work worldwide. The decade ends in December 1999 and the Committee will be disbanded, but there is an opportunity for the Hazards Forum to provide an on-going focus for the work and in particular to incorporate consideration of risks arising from British natural hazards.

The next seminar will be a half-day

one with the title, The Montreal Protocol–Twelve Years On. Chaired by Sir John Krebs, Chief Executive of the National Environmental Research Council, with speakers from The Meteorological Office, Rolls-Royce plc, ICI, Environmental Investigation Agency and the Health and Safety Executive (see details in box).

The Montreal Protocol... 12 years on

Half-Day Seminar on October 13 1999, at the Institution of Civil Engineers, 1 Great George Street, London, UK

In 1987, the developed nations signed an agreement in Montreal, Canada to limit production of, and ultimately ban the general production and use of Halons, chlorofluorocarbons [CFCs], carbon tetrachloride, and certain other solvents which had been shown to have a damaging effect upon the Global Ozone Layer. This agreement, to which some 130 nations are now committed, was termed the Montreal Protocol.

The Seminar has been arranged to hear the extent to which the Protocol has been successful in damage limitation in respect of the Ozone Layer, the lessons learnt by industry, the current availability of alternative substances and the problems experienced in identifying CFC smuggling from countries which are not signatories to the protocol.

Chairman: Sir John Krebs, currently Chief Executive of the National Environmental Research Council.
Presenters: John Austin (The Meteorological Office),
Ian Liddle (Rolls-Royce plc),
Michael Walker (ICI),
Steve Trent (The Environmental Investigation Agency),
Bernard Robinson (The Health and Safety Executive).

Tickets (£56 for Members of the Hazards Forum and Affiliates; £70 for Non-Members) are available from The Hazards Forum Secretariat, 1 Great George Street, London SW1P 3AA
Tel. 0171 665 2158,
Fax 0171 233 1806,
E-mail torey_d@ice.org.uk)

Responsible Care

Chemical Industries Association Re-launch Responsible Care

Responsible Care is the Chemical Industries Association (CIA) commitment to continual improvement in health, safety and environmental performance and openness in communication about its activities. The CIA organised a meeting in May 1999 to both celebrate 10 years of commitment to Responsible Care and take a critical look at what is needed for the next 10 years.

The highlight of the day was a speech by Michael Meacher—UK Minister of State for the Environment. Mr Meacher announced that a New Chemicals Strategy would be launched within the next few months. It is likely that this will contain measures to ensure that industry pursues a more sustainable approach in the production and use of chemicals. The strategy is also likely to emphasise the requirement for improved information on the environmental risk of all chemicals with the likely phase out of the most toxic and persistent chemicals. Mr Meacher did however make it clear that industry competitiveness will be maintained. Although somewhat critical of the current state of the Responsible Care programme, he did offer some praise for what had been achieved; it was clear however that he expected industry to become much more open and pro-active in obtaining SHE (safety, health & environmental) information and making this available to the public. Meacher also announced that his department had commissioned a full life cycle assessment and economic analysis of PVC and alternatives to it (such as wood for window frames). The work will be carried out by ENTEC and Ecobalance UK and will take a year to complete.

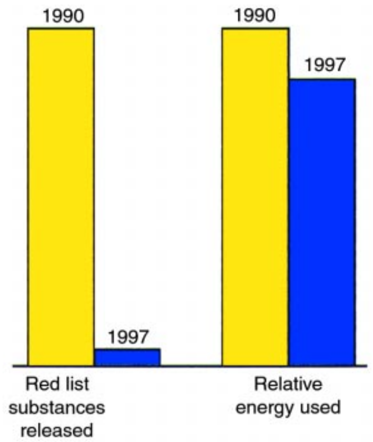
The theme of improved openness on both product and process information recurred several times throughout the day. It was particularly encouraging to hear this message coming from Paula Gough (CIA Young Person of the Year) who was speaking on behalf of younger chemists and engineers in the industry. She believed that industry must accept, indeed encourage, greater transparency of data. At the same time industry should produce cost benefit analysis studies to show that being eco-friendly can also have a positive effect on the bottom line.

There were also several speakers calling for industry to accept benchmarking, sharing of best practice and independent auditing in all areas of responsible care. These calls were particularly strong from the Environment Agency and the Health and Safety Executive. CIA members recognised these areas of concern and were self-critical over the industry's obsessive concern for confidentiality. With over 150 senior managers attending the event, we will hopefully see industry taking notice of these concerns.

Responsible Care is now an undoubted success story but took a long time to gain acceptance since its launch in Canada in 1986. As a direct result of the programme CIA members have made significant improvements to both toxic release and energy efficiency through process development and uses of alternative materials. The histogram below shows the improvements made in release of red list substances (now only 20 tonnes per annum) and energy efficiency since the CIA's launch 10 years ago.

In re-launching the programme Dr Joe Blaker, CIA President, highlighted two important new statements that CEOs of member companies will be required to sign up to.

- ‘We will work to conserve resources and reduce waste in all our activities’
- ‘In addition to ensuring our activities



> meet relevant statutory obligations, we will share experience with our industry colleagues and seek to learn from and incorporate best practice into our own activities'

Industry is taking steps to become greener and cleaner; the conference achieved an appropriate balance of self-congratulation, critical assessment and suggestions for improvement. This is indeed good news for green chemists in all walks of life.

European Responsible Care questionnaire

A questionnaire was sent to member companies of CEFIC (European Chemical Industry Council) which aimed to illustrate how Responsible Care is being implemented in Europe. Those responding to this questionnaire also had the opportunity to submit a case history which demonstrated some aspect of Responsible Care implementation. For example, Celanese has opened a 100000 tonnes/y butyraldehyde facility based on unique high-pressure rhodium technology, which enables improved use of raw materials and has lower production costs. The new process is more environmentally acceptable than the previous cobalt-based technology because it uses less energy and no waste water accumulates. Complete conversion of raw materials results in a considerable reduction in the number of side products generated. Other companies providing case studies include Borealis, BP Amoco, Henkel, Lyondell, and Shell Chemicals.

Sweden implements OSPAR policy

Sweden has become the first country to implement the policy set out at last year's meeting of the OSPAR Commission[1] at which North Atlantic nations agreed to eliminate emissions of hazardous chemicals that accumulate in biological systems or are environmentally persistent, as well as carcinogens and hormone disrupters. It had been thought that the Swedish policy would be even tougher after an Environment Ministry report recommended immediate prohibition.

1999 Queen's Awards

The 1999 Queen's Awards included 5 awards for technological achievement. Among those honoured were Zeneca Metal Extraction Products in Manchester for a novel magnesium-based process to manufacture a chemical for extracting copper from waste ore. There is a corresponding reduction in effluent from the process of some 85%. Synetix in Billingham won an award for the Hydecat process which is a fixed-bed catalytic process for the treatment of waste sodium hypochlorite liquor which is created whenever chlorine is produced or used. The hypochlorite is converted into oxygen and salt solution.

Sustainable Technologies Initiative

A new Sustainable Technologies Initiative (STI) has a total of £7.8m over 3 years available in funding to help businesses reduce their impact on the environment. The funding will support the development of technologies to help businesses produce less waste and pollution, use resources more efficiently and achieve greater social equity in their operations and products. Details of the initiative are still being finalised but it is likely that it will act as an umbrella for a range of activities focussed largely on R&D programmes and projects. The common theme of these will be the integration of sustainability into processes and products from the design stage. Sectoral and cross-sectoral topics will be addressed. It may be possible for some of the funding to be used to support small projects to investigate scope for creating a stimulated interest in sustainable technologies. Further information is available from the Department of Trade and Industry in London (tel. 0171 215 2988).

Royal Society of Chemistry Green Chemistry Network

The GCN has now been active for around 6 months. During this time we have published a number of general articles promoting the Green Chemistry movement; these have been met with a great deal of interest and resulted in invitations to give various presentations. This snowballing effect has resulted in growing membership and requests for information.

Our web site is now up and running (http://www.chemsoc.org/gcn); we will be continuously improving and updating this. Additional programming is required before the members' area goes live but this should be available within a few weeks. Please send us any ideas or materials for inclusion.

We recently held the first meeting of the Technical Advisory Panel; consisting of representatives of government departments, regulatory authorities, trade associations, research funding bodies and professional associations (see web site for full list of members). Topics discussed included the best ways of providing educational material for schools and universities and how best to involve industry in technology transfer and sharing of best practice. We are going to establish sub-panels on education and industry to work out the details of how to move forward—if anyone wishes to be involved please let us know.

The official launch of the GCN will be held at the British Association Festival of Science Week on 16 September in Sheffield. We are still working out the full details of the event but if anyone would like to attend please let us know.

Also in September (28th) we will be holding our first Green Chemistry seminar in York. The aim of the one-day seminar is to get young people discussing their work and to learn about the wider aspects of Green Chemistry outside their immediate research area; as such the majority of speakers will be postdocs from 'local' universities. We are fortunate in getting Ken Seddon from Belfast to give the Keynote lecture on ionic liquids, one of the fields that offer so much promise for future Green processes. Please let us know if you would like to attend. Still on the conference theme a note for your diaries; for April 2001, we are starting to plan the first RSC Green Chemistry conference to be held in Swansea. All aspects of Green Chemistry will be covered but we will be again be focussing on the work of younger chemists and engineers as well as highlighting what is happening in industry.

Mike Lancaster,
GCN Manager (greennet@york.ac.uk)

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[1] The OSPAR Commission came into force on 25 March 1998, replacing the **OS**lo and **PAR**is Conventions. For further information see http://www.ospar.org/eng/html/welcome.html

Zeolite mediated protection of carbonyl groups

Appaswami Lalitha,[a] Kasi Pitchumani*[b] and Chockalingam Srinivasan*[a]

[a] Department of Materials Science and [b] School of Chemistry, Madurai Kamaraj University, Madurai - 625 021, India

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Summary

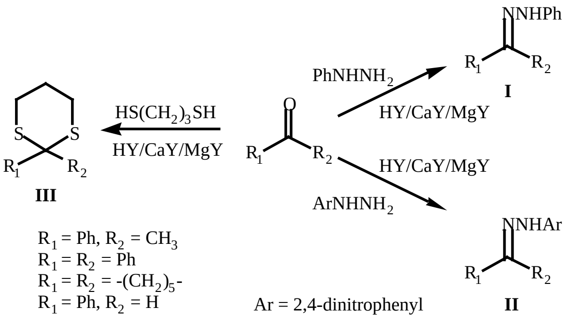
Faujasites such as HY, CaY and MgY are employed as solid acid catalysts for the clean and less hazardous preparation of phenylhydrazone, 2,4-dinitrophenylhydrazone as well as 1,3-dithiane derivatives of carbonyl compounds. The reactions proceed very smoothly and the yields of the derivatives are excellent.

Introduction

Zeolites are microporous, crystalline aluminosilicates made up of corner-sharing SiO_4 and AlO_4 tetrahedra. By virtue of their structure, crystallinity and variable stoichiometry, zeolite catalysts have well defined pore size distributions, high and adjustable acidity, very high surface area and good thermal stability.[1] The range of available pore dimensions permits chemists to choose suitable zeolites which can match the size of organic molecules enabling one to successfully include these molecules within the cavities and carry out selective transformations. Due to the presence of high and tunable acidity,[2–5] zeolites can potentially replace conventional corrosive liquid acids in many of their applications.[6]

Protection of carbonyl groups is often a necessary requirement in reactions involving substrates with multifunctional groups. Usually the carbonyl groups are protected as 1,3-dithianes while their oximes, phenylhydrazones and 2,4-dinitrophenylhydrazones are other useful derivatives. The formation of these derivatives involves Brønsted as well as Lewis acid catalysis.[7] As the conventional acids used in the preparation of these derivatives are highly corrosive, they pose severe environmental hazards. Solid acids like zeolites[8] and clays[9] with high and adjustable acidity can overcome this problem. They enjoy advantages over conventional liquid acid catalysts by giving good and higher yields, easier separation of products, reusability, milder reaction conditions, *etc.*

Herein we report a smooth and facile conversion of carbonyl compounds to phenylhydrazones, 2,4-dinitrophenylhydrazones and 1,3-dithianes (Scheme 1) in the presence of acidic zeolites as catalysts. The reaction involves the addition of an acidic zeolite to a solution of a carbonyl compound and the reagent used for derivatization and refluxing for a short period. The reaction is general and has been successfully demonstrated with a representative example of each of an alkyl aryl ketone (acetophenone), a diaryl ketone (benzophenone), a cyclic ketone (cyclohexanone) and also with an aromatic aldehyde (benzaldehyde). To the best of our knowledge, this is the first report in which divalent cation-exchanged zeolites are used for derivatisation.



Scheme 1

Results and discussion

When the nonacidic zeolite NaY is employed as the catalyst in the carbonyl protection reactions no derivative is isolated. This rules out any significant role of the basic zeolite framework in derivatization and indicates the need for generation of acidic sites in the framework. However, when acidic zeolites such as HY, CaY and MgY are used, the formation of derivatives of carbonyl compounds is clean, smooth and excellent (Table 1). The acidic sites present in the zeolites are primarily responsible for the formation of the derivatives.

Replacement of Na^+ by H^+ in NaY leads to the formation of acidic HY zeolites. Acidity in CaY and MgY can be explained by the dissociation of coordinatively bound water molecules under the action of the electrostatic field associated with the divalent cations. It is known that CaY and MgY activated at 500 °C under aerated conditions possess a large number of Brønsted acidic sites,[10] which are employed[11,12] in generating carbocationic intermediates.

Thus the present work highlights the utility of HY and divalent cation exchanged acidic zeolites in protecting the carbonyl groups in a simple, clean and efficient way. The experimental methods are easier and superior compared to conventional

Green Context

The adage that the best protecting group is no protecting group is very true. However, there is still a need to protect reactive functional groups as a method of improving selectivity, and it is therefore imperative that the protection and deprotection steps generate as little waste as possible. This contribution describes the efficient formation of dithianes as protecting groups for carbonyl compounds using zeolite catalysis. Several other derivatives can also be prepared using such catalytic systems. Yields are excellent under mild conditions. The development of a similarly clean deprotection system will complete the cycle of protection/deprotection nicely. ***DJM***

Table 1 Zeolite catalysed derivatisation of carbonyl compounds[a,b]

Carbonyl compound	Zeolite	**I**[c] (% yield)	**II**[c] (% yield)	**III**[d] (% yield)
Acetophenone	HY	93 (105)	87 (249)	92 (97)
	CaY	91	85	90
	MgY	80	82	83
Benzophenone	HY	92 (137)	95 (238)	90 (136)
	CaY	92	91	90
	MgY	85	87	86
Cyclohexanone	HY	87 (77)	89 (162)	87 (145)*
	CaY	83	85	89
	MgY	85	82	80
Benzaldehyde	HY	90 (158)	92 (237)	96 (69)
	CaY	87	92	91
	MgY	81	83	86

[a] Numbers in the parentheses are the melting points/boiling points* of the derivatives in °C. [b] For structures **I** to **III** refer to Scheme 1. [c] Warmed for 10 min. [d] Refluxed for 1 h. [e] Yields refer to isolated pure products.

methods. Also this method is advantageous as it employs heterogeneous catalysts which can be reused (zeolites after washing thrice with dichloromethane are activated again at 500 °C before reuse. The catalytic efficiency is essentially retained; however, the yield decreases significantly after using the zeolites four or five times) and are attractive alternatives to hazardous reagents such as strong corrosive liquid acid catalysts. Also while earlier studies employing conventional acid catalysts have been carried out in polar solvents,[6] derivatisation with acidic zeolites can be performed in nonpolar solvents. Absence of any tetrahydrocarbazole formation from the phenylhydrazone of cyclohexanone indicates that the reaction is also selective and does not proceed beyond derivatization.

Experimental

Acidic zeolites CaY and MgY were obtained by exchanging NaY (Aldrich) powder by stirring with the respective nitrate solution (10%) at 70 °C for about 12 h. The exchange was repeated at least four times. After each exchange, the zeolite powder was washed repeatedly with distilled water and then dried. The procedure is essentially the same as that employed previously by one of the authors.[11] All these zeolites were activated at 500 °C for about 10h prior to use.

To a solution of carbonyl compound with the respective reagent in hexane/methanol as solvent, activated acidic zeolites were added. The reaction mixture was refluxed with stirring for a specified time. The zeolite was filtered off and the filtrate was evaporated to give the products which were identified by GC analysis (Netel Chromatographs with OV1GC column packed with 10% phenyl methyl silicone and using an FID detector) and also by their melting points. The derivatization was also confirmed by coinjecting with the derivatives prepared by conventional methods.

Formation of phenylhydrazones and 2,4-dinitrophenylhydrazones

For the preparation of phenylhydrazones and 2,4-dinitrophenylhydrazones, the carbonyl compound (0.3 g) and the reagent (0.5 g) were dissolved in methanol to which zeolites (0.3 g) were added and warmed for 10 min over a water bath. The zeolite was filtered off and the derivative separated out from the filtrate.

Formation of 1,3-dithianes

To a solution of carbonyl compound (0.6 g) and 1,3-propanedithiol (0.6 g) in hexane, activated acidic zeolite (0.6 g) was added and refluxed with stirring for 1 h. The zeolite was filtered and the filtrate was extracted with an aqueous solution of NaOH to remove excess thiol and the organic solvent was evaporated to give the pure 1,3-dithiane derivative. The yields are quantitative.

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Paper 9/02533B

Catalytic asymmetric aldol reactions in water

using a chiral Lewis acid–surfactant-combined catalyst

Shū Kobayashi,* Yuichiro Mori, Satoshi Nagayama and Kei Manabe
Graduate School of Pharmaceutical Sciences, The University of Tokyo, CREST, Japan Science and Technology Corporation (JST), Hongo, Bunkyo-ku, Tokyo 113-0033, Japan.
E-mail: skobayas@mol.f.u-tokyo.ac.jp

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Summary

Catalytic asymmetric aldol reactions in water without the use of organic solvents have been carried out by using a combination of copper bis(dodecyl sulfate), a chiral bis(oxazoline) ligand, and a carboxylic acid to afford the desired products in high yields with good enantiomeric excesses.

Introduction

The use of water as a solvent in organic synthesis is of great current interest in relation to environmental consciousness.[1,2] In such reactions, tedious procedures to remove water from the substrates (water of crystallization, *etc.*) and solvents are not necessary and, moreover, the use of harmful organic solvents can be avoided. While Lewis acid-catalyzed aldol reactions of aldehydes with silyl enolates (Mukaiyama aldol reaction)[3–5] are powerful tools for carbon–carbon bond formation in modern organic synthesis to produce diverse β-hydroxy carbonyl compounds, strictly anhydrous conditions are needed when typical Lewis acids such as $TiCl_4$ and $BF_3{\cdot}Et_2O$ are used. On the other hand, we have found that metal triflates such as $Sc(OTf)_3$ and $Cu(OTf)_2$[6–10] can be used as water-stable Lewis acids for organic reactions in water-containing solvents (water–THF, *etc.*).[11] Furthermore, we have recently developed a new reaction system in which $Sc(OTf)_3$ catalyzes the aldol reactions in water without using organic solvents in the presence of a small amount of a surfactant such as sodium dodecyl sulfate (SDS).[12] More recently, a new type of Lewis acid, scandium tris(dodecyl sulfate), has been introduced.[13,14] This ‘Lewis acid–surfactant-combined catalyst (LASC)’ forms stable colloidal dispersion systems with organic substrates in water and efficiently catalyzes the aldol reactions.

In the course of our investigations on stereoselective reactions in aqueous media, chiral copper(II)-catalyzed asymmetric aldol reactions have been successfully carried out in a water–EtOH solution.[15] These reactions have great advantages over the previously reported catalytic asymmetric aldol reactions[16–18] because our system does not require strictly anhydrous conditions and extremely low temperature such as –78 °C. In order to develop this system further, we planned to use LASCs for asymmetric aldol reactions in water without using any organic solvents. Here we report that a combination of copper bis(dodecyl sulfate) $[Cu(DS)_2]$[19,20] and chiral bis(oxazoline) ligands[21] has achieved the catalytic asymmetric aldol reactions in water with the aid of catalytic amounts of carboxylic acids as additives.

Results and discussion

We chose the reaction of benzaldehyde with 3-trimethylsiloxypent-2-ene ($E:Z = 6:94$) in water as a model. After several trials, a combination of $Cu(DS)_2$ as a LASC and bis(oxazoline) **1**[22–26] as a chiral ligand was found to give the corresponding aldol adduct in 23% yield with 58% enantiomeric excess (ee) (Table 1, run 1).

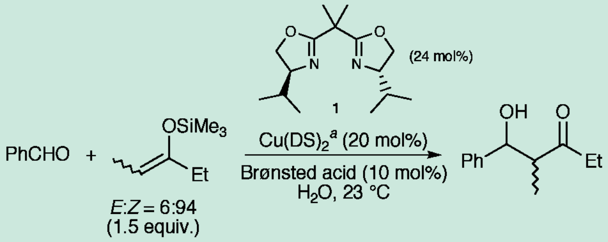
Quite recently, we have reported that addition of a small amount of a Brønsted acid, especially HCl, dramatically accelerated LASC-mediated aldol reactions in water.[27] To improve the low chemical yield, therefore, we tested various Brønsted acids as additives for the present asymmetric aldol reactions. Although HCl slightly increased the yield of the product (Table 1, run 2), benzoic acid gave the product in better yields (runs 3, 4 and 5). It should be noted that not only the yield but also the enantioselectivity of the major diastereomer was improved by addition of the acid. Neither a stronger Brønsted acid, camphorsulfonic acid (run 6), nor a weaker one, phenol (run 7), was better than benzoic acid. Among the carboxylic acids tested, lauric acid gave the best result as far as both the yield and the ee of the *syn* isomer were concerned (run 11). As for the substituents of the bis(oxazoline) ligand, isopropyl groups were found to give better results than isobutyl, *tert*-butyl, phenyl or benzyl groups.

Green Context

The use of water as a solvent has a range of obvious advantages as a replacement for traditional organic solvents. Work is being carried out on two main fronts, ‘normal’ conditional (see for example A. McCluskey, *Green Chemistry*, 1999, 1, 167) and supercritical/close to critical (‘hot’ water see *e.g.* M. Poliakoff, *Green Chemistry*, 1999, 1, 65). Despite the intuitive keep-water-out feeling that most of us have about organic reactions, a surprising number of organic reactions run very well in water. This article describes the early stages in the development of a useful procedure for the asymmetric aldol reaction in water, using a combined Lewis acid-surfactant catalyst system. This paper demonstrates that it is possible to obtain good enantioselectivity in such a system, although for this to be genuinely useful will require some further development.

DJM

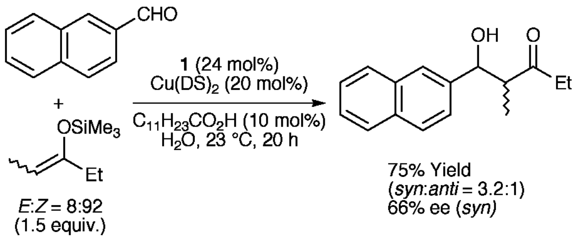
Table 1 Effect of Brønsted acids on asymmetric aldol reactions in water



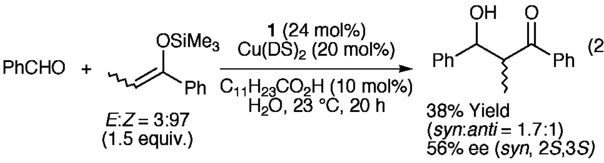
Run	Brønsted acid	t/h	Yield(%)	*syn*:*anti*	ee (*syn*)[b]
1	—	20	23	3.2 : 1	58
2	HCl	12	31	2.7 : 1	61
3	$PhCO_2H$	12	48	2.7 : 1	65
4	$PhCO_2H$	20	76	2.7 : 1	63
5	$PhCO_2H$[c]	20	70	2.8 : 1	66
6	(+)-camphorsulfonic acid	20	34	3.0 : 1	63
7	PhOH	20	15	2.7 : 1	60
8	p-$O_2NC_6H_4CO_2H$	20	63	2.4 : 1	64
9	p-$MeOC_6H_4CO_2H$	20	73	3.0 : 1	61
10	$C_5H_{11}CO_2H$	20	72	3.3 : 1	58
11	$C_{11}H_{23}CO_2H$	20	76	2.8 : 1	69
12	$C_{17}H_{35}CO_2H$	20	68	2.8 : 1	63

[a] DS = dodecyl sulfate ($O_3SOC_{12}H_{25}$). [b] Determined by HPLC analysis using DAICEL CHIRALPAK AS. [c] 5 mol%.

The present reaction conditions could be applied to other substrates affording the products with the comparable enantioselectivities (eqns. 1 and 2). Although the yields and the selectivities are still not yet optimized, it is noted that these enantioselectivities have been attained at ambient temperature in water.



(1)



(2)

The precise mechanism of the effects of the Brønsted acids on the yields and the enantioselectivities is not clear at this moment. We assume that the Brønsted acids raise the Lewis acidity of the Cu cation, producing a more active catalytic species. It is noteworthy that the hydrophobic and hydrophilic structure as well as the acidity of the Brønsted acids affects the results of the reactions.[28]

A general experimental procedure is as follows. $Cu(DS)_2$ (0.10 mmol) and **1** (0.12 mmol) were added to water (1.5 mL) at 23 °C. A Brønsted acid (0.05 mmol), an aldehyde (0.50 mmol) and then a silyl enolate (0.75 mmol) were successively added. After stirring the reaction mixture for 20 h at 23 °C, satd. aq. $NaHCO_3$ and brine were added. The mixture was extracted with ethyl acetate three times, and concentrated. This was dissolved in 1 M aq. HCl–THF (1 : 20) at 0 °C, and the whole was stirred for 1 h. After evaporation of the solvents, saturated aq. $NaHCO_3$ and brine were added. The mixture was extracted with ethyl acetate three times, dried over Na_2SO_4, concentrated, and purified by silica gel chromatography to give the desired product. The diastereoselectivity was determined by ^1H NMR, and the enantioselectivity was determined by HPLC analysis.

Conclusion

Catalytic asymmetric aldol reactions of aldehydes with silyl enolates in water have been achieved by using a combined catalytic system of the Cu^{II}-based LASC, chiral ligand **1** and a carboxylic acid. This is the first example of Lewis acid-catalyzed asymmetric aldol reactions in water without using organic solvents.[29] It is noted that this reaction system does not need strictly anhydrous conditions and low temperature in contrast with the conventional examples of chiral Lewis acid-catalyzed asymmetric aldol reactions in organic solvents. In addition, the present reaction system may be applied to precise enzymatic reactions in flasks in terms of asymmetric reactions occurring at a hydrophobic reaction site created in water. Further investigations to improve the yield and the selectivity and to clarify the detailed reaction mechanism in these reactions are now in progress.

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Paper 9/04439F

Friedel–Crafts reaction in fluorous fluids

Hirofumi Nakano and Tomoya Kitazume*

Department of Bioengineering, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku Yokohama 226-8501, Japan. E-mail: tkitazum@bio.titech.ac.jp

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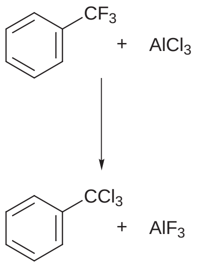
Summary

The scope and utility of fluorous (perfluorinated) fluids as reaction media for Lewis acid catalyzed Friedel–Crafts reaction are described.

Introduction

The Friedel–Crafts reaction is one of the most important synthetic reactions, especially in industrial production.[1] Usually, this reaction is carried out in toxic and/or harmful organic reaction media like CH_2Cl_2, CS_2, *etc.*[2] Ogawa and Curran reported that benzotrifluoride (BTF) is a useful alternative solvent to CH_2Cl_2 and can be used in Friedel–Crafts acylation.[3] However, BTF reacts with $AlCl_3$ which is typically used in Friedel–Crafts reactions (Scheme 1).[4] In addition, BTF is sensitive to some reducing conditions and hydrolyzed by aqueous acid at high temperature.[5] These reactivities clearly limit its utility as a reaction medium. Recent studies of fluorous (perfluorinated) fluids as new alternative reaction media are having an important impact on organic reactions.[6] These fluids all have very unusual properties, such as high density and high stability, low solvent strength, and extremely low solublity in water and organic materials.[6] However, the scope and limitations of the utility of fluorous media are still unclear. In our previous paper,[7] we reported the ease of handling and re-use of fluorous fluids. In this paper, we describe the utility of fluorous fluids as the reaction medium for Friedel–Crafts reactions.



Scheme 1

Results and discussion

As shown in Table 1, acetylation proceeds smoothly in every fluorous reaction medium tested as well as in CH_2Cl_2, and negligible differences in solvent effect were observed. The catalyzed acetylation of benzene and *p*-xylene using an equimolar amount of $AlCl_3$ was performed at room temperature by employing perfluorotriethylamine as the solvent, resulting in 89 and/or 55% yields, respectively; however the reaction in hexane did not proceed. We have reported that fluorous solvents can be more than 90% recovered by three phase extraction,[7] and it is possible to reuse them in the same reaction system. These results show that fluorous liquids possess the possibility to be good reaction media, especially for Friedel–Crafts reaction.

Common problems in the use of stoichiometric amounts of $AlCl_3$ are its instability and the disposal of the stoichiometric amount of $Al(OH)_3$ after aqueous work-up. In view of 'Atom Economy',[8] catalytic reactions are preferable. Hence, catalytic acylation with $ZnCl_2$ was next investigated (Table 2). This benzoylation was performed at reflux temperature in highly toxic *sym*-tetrachloroethane (entry 11).[9] The same reaction was carried out in perfluoro-2-butyltetrahydrofuran under the same conditions (entry 12) and the benzoylated product was isolated in comparable yield. In entry 13, the same reaction was successfully carried out in perfluorotriethylamine at a lower reflux temperature. These results show that fluorous media with lower reflux temperatures and non-flammability are good substitutes in Friedel–Crafts acylation for conventional organic liquids.

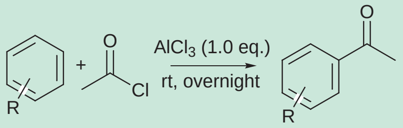
For economical and environmental reasons, recycling of catalysts is favorable. Thus far, the use of catalysts bearing perfluorinated ligands and their recovery after reaction using a fluorous biphase system[6] has been of great concern to chemists. However, such 'fluorous catalysts' are not commercially available and their synthesis often requires tedious steps and expensive starting materials. Therefore, before pursuing perfluorinated catalysts, we

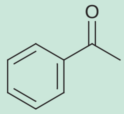
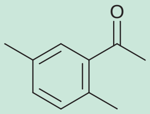
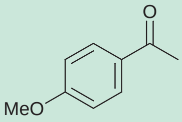
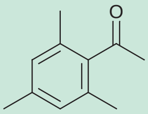
Green Context

One of the main issues in green chemistry is the choice of solvent. Many solvents such as benzene and carbon tetrachloride are now considered as unusable due to toxicity problems, and others such as hydrocarbons are problematic due to difficulties with flammability and volatility. Ionic liquids and supercritical fluids are some of the newer choices available to the chemist (see *e.g. Green Chemistry*, 1999, 1 23, 65 and 91). A third class of solvents which may be of some benefit are the fluorous materials—highly fluorinated molecules with exceptional stability. The work in this paper describes the use of these solvents in the Friedel–Crafts reaction, a particularly aggressive reaction medium, involving strong Lewis acids such as aluminium chloride, and also a very important reaction industrially.

DJM

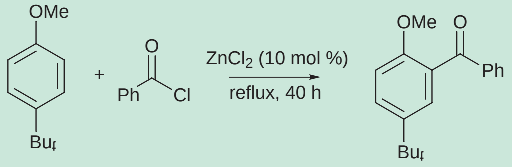
Table 1 Acetylation reactions using different solvents



Entry	Arene	Solvent	Product	Yield (%)[a]
1	Benzene	Perfluorotriethylamine		89
2		Perfluorotri-*n*-butylamine		81
3		Perfluoro-2-butyltetrahydrofuran		87
4	*p*-Xylene	Perfluorotriethylamine		55
5		Perfluorotri-*n*-butylamine		57
6		Perfluoro-2-butyltetrahydrofuran		46
7		Perfluoro-*n*-hexane		63
8		CH_2Cl_2		78
9	Anisole	Perfluorotriethylamine		89[b]
10	Mesitylene			Quantitative

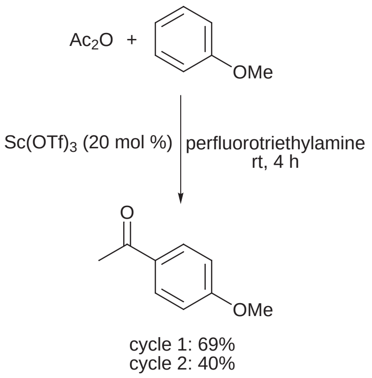
[a] Isolated yield.[b] Only *p*-adduct was obtained.

Table 2 Catalytic acylation with $ZnCl_2$



Entry	Solvent	Reflux temp./°C[a]	Yield (%)[b]
11	*sym*-Tetrachloroethane	138	66[c]
12	Perfluoro-2-butyltetrahydrofuran	99–107	62
13	Perfluorotriethylamine	70	64

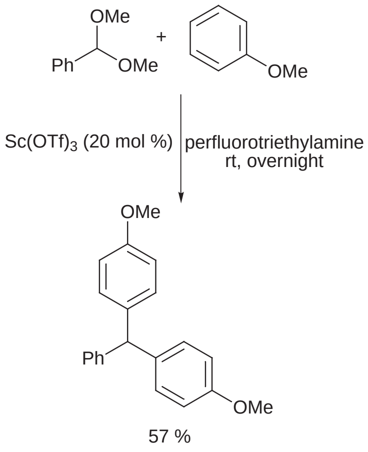
[a] Bath temperature. [b] Isolated yield. [c] Ref. 9.



Scheme 2

tried to utilize commercially available catalysts which can be recycled easily. $Sc(OTf)_3$ has been shown to be a good Friedel–Crafts catalyst and can be recovered quantitatively after extractive work-up in an aqueous phase separated from the organic products.[10] As shown in Scheme 2, $Sc(OTf)_3$ effectively catalyzes the acetylation of anisole in perfluorinated solvents and only the *p*-adduct was obtained in 69%, 3 times the average isolated yield. Moreover, benzaldehyde dimethylacetal was also reacted with anisole to produce a disubstituted material in 57% yield (Scheme 3). Further, $Sc(OTf)_3$ can be recovered free from organic products by simple extractive work-up. Successive reuse of the recovered $Sc(OTf)_3$ and solvent in the same reaction without further purification yielded the product in 40% yield (Fig. 1).

In conclusion, we have shown that perfluorinated liquids are good alternative reaction media for use in the Lewis acid catalyzed Friedel–Crafts reaction.



Scheme 3

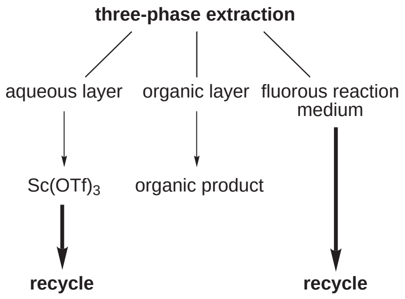


Fig. 1

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11 Typical procedure is as follows. To a solution of acetyl chloride (0.356 ml, 5 mmol), aluminium chloride (667 mg, 5 mmol) and perfluorotriethylamine (3 ml) at 0 °C, benzene (0.444 ml, 4 mmol) was added. After completion of the addition, the ice bath was removed and the reaction mixture was stirred overnight at room temperature. The reaction was quenched with 4 ml of water, and stirred for a few minutes. Then, the fluorous solvent was recovered by three phase extraction, and the organic layer was extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by silica gel chromatography afforded the product.

Paper 9/03544C

Utilization of an industrial feedstock without separation

Ruthenium-catalysed hydrocarboxylation of propadiene and propyne

Christian Bruneau,* Muriel Neveux-Duflos and Pierre H. Dixneuf*

UMR 6509: CNRS - Université de Rennes, Organométalliques et Catalyse : Chimie et Electrochimie Moléculaires, Campus de Beaulieu, 35042 Rennes, France

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Summary

The reaction of carboxylic acids with propadiene or propyne catalysed by $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ affords isopropenyl esters *via* regioselective addition of the carboxylate to the central carbon atom of the allene.

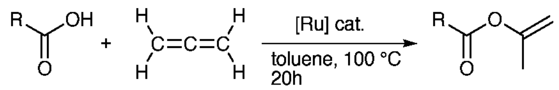
Introduction

The C3 mixture resulting from cracking of hydrocarbon feedstocks mainly contains propene and propane, together with propyne and propadiene. The possibility of direct utilization of this C3 mixture without separation of its constituents to produce high added-value compounds *via* a clean and selective catalytic transformation would increase the synthetic value of this hydrocarbon fraction and be of major interest from an economical point of view.

The ability of ruthenium complexes to activate terminal alkynes in a stoichoimetric manner is well documented[1] and new ruthenium-catalysed transformations of alkynes with high regio- and stereoselectivity and atom economy have been developed.[2–4] By contrast, the analogous catalytic activation of allenes by ruthenium catalysts has not been performed yet.

Isopropenyl esters[5] and diisopropenyl diesters,[6] respectively prepared from carboxylic acids and oxalic acid, and ruthenium-activated propyne have been shown to be useful acylating and 1,2-diacylating reagents under very mild and neutral conditions releasing only acetone as by-product. The presence of allene together with propyne in the industrial hydrocarbon C3 mixture provided impetus to study the addition of carboxylic acids to allene in the presence of a ruthenium catalyst, as we had previously shown that the addition of acids to alkenes did not take place under these catalytic conditions. The palladium-catalysed additions of carbonucleophiles,[7] amines,[8] tosylhydrazine[9] and carboxylic acids[10] to unactivated allenes have recently been reported, all of them afford allylic derivatives resulting from an intermediate allylpalladium species generated *via* insertion of the terminal double bond of the allene into a Pd–H bond.

We report here that ruthenium catalysis offers the first example of metal-catalysed activation of propadiene towards the addition of carboxylic acids to selectively produce isopropenyl esters *via* addition of the carboxylate to the central C-2 carbon atom (Scheme 1).



1–4

$[Ru] = [Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$

Scheme 1

Results and discussion

In the presence of (p-cymene)$RuCl_2(PPh_3)$ as catalyst, which is known to give the Markovnikov addition of carboxylic acids to terminal alkynes,[3–5] the addition of benzoic acid to propyne at 100 °C for 20 h led to 87% of esters containing 91% of isopropenyl benzoate **1** (R = Ph). Under similar conditions, the activation of allene itself in the presence of (p-cymene)$RuCl_2(PPh_3)$ was less efficient as only 44% of the acid was converted after 20 h at 100 °C and the total conversion required 40 h of heating. $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$[11] appeared to be a much better catalyst and the treatment of 20 mmol of propadiene with 10 mmol of benzoic acid in 10 mL of toluene at 100 °C for 15 h in the presence of 0.5 mol% of $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ as catalyst precursor led to the complete conversion of the carboxylic acid into propenyl benzoates. An overall yield of 81% of ester was isolated by distillation under reduced pressure, which contained 90% of isopropenyl benzoate **1** and 10% of the two stereoisomers of prop-1-en-1-yl benzoate $PhCO_2CH{=}CHMe$. Moreover, when a 1 : 1 mixture of propyne and allene was reacted with benzoic acid at 100 °C for 20 h in the presence of the same catalyst, complete conversion was observed and after distillation 86% of benzoates were collected containing isopropenyl benzoate as the major

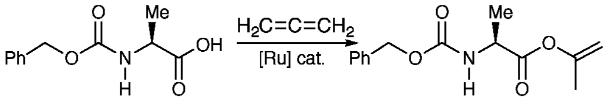
Green Context

The conversion of small hydrocarbon feedstocks to more functional materials is of vital importance to the chemical industry. The ability to carry out such transformations without the need for pre-separation of components in a complex mixed feedstock is an additional benefit, as it reduces the complexity of the process and eliminates wasteful and energy-intensive separations. This article describes the conversion of a C3 feedstock containing a range of compounds (including propadiene and propyne) to isopropenyl esters. Reaction involves catalytic hydrocarboxylation of both propyne and propadiene with high regioselectivity to C-2. The products are excellent acylating agents. ***DJM***

compound (>90%) with a small amount of prop-1-en-1-yl benzoate. Isopropenyl benzoate has a boiling point of 80 °C under 2 mm Hg and is easily separated from the gaseous starting C3 reactants.

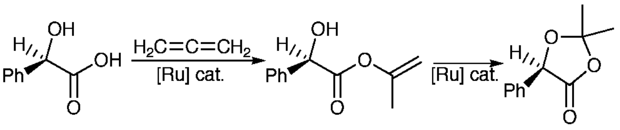
These first results clearly showed that in the presence of the binuclear ruthenium complex as catalyst, the regioselective addition of the carboxylate to the central carbon atom of both the allene and propyne leading to isopropenyl ester could be achieved. Among the C3 components, as only allene and propyne—and not propene and propane—are activated towards the addition of carboxylic acids in the presence of a ruthenium catalyst and as the reaction is complete, this catalytic transformation followed by a classical distillation allows an easy separation of the enol esters from the other hydrocarbons. From another viewpoint, this catalytic reaction actually makes possible the elimination of allene and propyne from the C3 mixture.

The ruthenium-catalysed addition to allene was extended to other carboxylic acids. *p*-Chlorobenzoic acid led to the corresponding isopropenyl aromatic ester **2** (R = *p*-ClC_6H_4) in 80% yield and more than 90% regioselectivity after reaction for 20 h at 100 °C in toluene in the presence of $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ as catalyst. Under the above conditions, the addition of *N*-protected Z-alanine gave the optically pure isopropenyl amino ester **3** in 86% yield with a high regioselectivity of 90% (Scheme 2).



Scheme 2

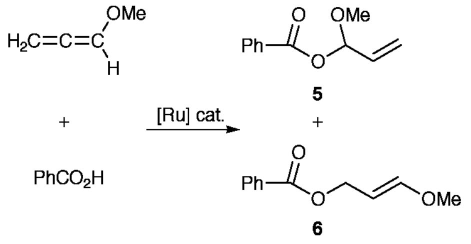
Similarly, mandelic acid led to 77% of the dioxolanone **5** in the presence of $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$. We have shown[11] that the dioxolanone **5** resulted from the formation of the intermediate isopropenyl mandelate **4** without racemization, and that the ruthenium catalyst promoted as well the intramolecular addition of the OH group to the activated C=C bond of **4** to produce **5** with a high stereoselectivity (Scheme 3).



4 **5** (77%)

Scheme 3

It must be noted that the presence of a ruthenium catalyst precursor had no influence on the reaction of carboxylic acid with an activated allene such as methoxyallene. Indeed, the addition of benzoic acid to methoxyallene at 100 °C for 20 h with or without catalyst led to a mixture of the allylic esters **5** and (*E*)-**6** in the ratio 57:43 (84% total yield) resulting from the addition of the carboxylate to both C-1 and C-3 carbons of the allene (Scheme 4).



Scheme 4

The results in Table 1 show that the reactivity of allene in the presence of $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ which provides the most efficient catalytic system is very similar to that of propyne.

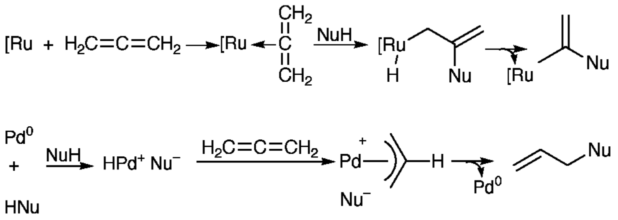
Table 1 Ruthenium-catalysed formation of isopropenyl esters from propyne and propadiene[a]

Acid	Ester	Yield from Me–C≡CH cat. $[Ru]_1$ (%)	Yield from H_2C=C=CH_2 cat. $[Ru]_2$ (%)
Benzoic acid	1	87[3]	90
p-Chlorobenzoic acid	2	58[3]	80
Z-Alanine	3	72[3]	76
(*R*)-Mandelic acid	5	70[11]	77

[a] Allene or propyne (30 mmol), carboxylic acid (20 mmol), toluene, 100 °C, 20 h. Z = $PhCH_2OCO$; $[Ru]_1$ = (*p*-cymene)$RuCl_2(PPh_3)$; $[Ru]_2$ = $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$.

The addition of carboxylic acids to propadiene takes place with the same regioselectivity as the addition of thiols to allenes in the presence of $Pd(OAc)_2$[12] but dramatically contrasts with the Pd^0-catalysed addition of other pronucleophiles which leads to allylic derivatives *via* (π-allyl)Pd species resulting from hydro- or carbopalladation of the allene.[7–10]

The reactivity of ruthenium catalysts corresponds to an electrophilic activation of one C=C double bond of the allene, whereas protonation of the precursor to give an allylruthenium intermediate is not favoured as is the insertion of allenes into a Pd–H bond (Scheme 5).



Scheme 5

In conclusion, we have shown that the catalytic activation of propadiene towards the addition of carboxylic acids to form isopropenyl esters is very efficient in the presence of the binuclear ruthenium catalyst $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$. As propyne and propadiene present the same reactivity towards carboxylic acids under similar catalytic conditions, the above results have potential for the direct utilization of the industrial C3 mixture without previous separation of its constituents for the catalytic preparation of isopropenyl esters. The use of a recoverable and reusable ruthenium catalyst such as $[Ru(O_2CH)(CO)_2(Ph_2P(CH_2CH_2)_nCH_2CH_3)]_2$ which is also very efficient in this type of catalytic addition[13] might present advantages from economical, industrial and environmental viewpoints. The overall process requires the catalytic transformation followed by a simple distillation and can be achieved on the spot where C3 is produced, thus avoiding inflammable products transportation.

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Paper 9/03452H

Henry reactions catalysed by modified Mg–Al hydrotalcite:

an efficient reusable solid base for selective synthesis of β-nitroalkanols†

B. M. Choudary,*[a] M. Lakshmi Kantam,*[a] Ch. Venkat Reddy,[a] K. Koteswara Rao[a] and F. Figueras[b]

[a] *Indian Institute of Chemical Technology, Hyderabad-500007, India. E-mail: choudary@iict.ap.nic.in*

[b] *Institut de Recherches sur la Catalyse, 2, Avenue Albert Einstein, 69626 Villeurbanne cedex, France*

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Summary

Henry reactions have been performed for the first time with suitably activated Mg–Al hydrotalcite as catalyst in quantitative yields in the liquid phase under mild reaction conditions and with low reaction times. Exclusive synthesis of β-nitroalkanols (**3**) is realised by the compatible basic Brönsted hydroxy sites of the modified hydrotalcite. Reusability with consistent activity and selectivity for a number of cycles is established indicating that the hydrated hydrotalcite employed here is a potentially eco-friendly catalyst which can replace soluble bases in commercial synthesis.

Introduction

The design and development of environment-friendly solid base catalysts to replace soluble bases for C–C bond formation in organic transformations widely employed in the bulk and fine chemical industries in order to achieve atomic selectivity of the desired product and reduce the salts formed as a result of neutralisation of soluble bases is of intense research activity.[1–3] 2-Nitroalkanols, the products of the Henry reaction and important representatives of C–C bond formation, are ubiquitous materials extensively used in many important syntheses.[4] The greatest challenge in the selective synthesis of 2-nitroalkanols among the multiple product options such as polymerization, aldol olefins and Cannizzaro products, is the selection of the appropriate base to achieve the most sensitive operation in the organic synthesis. Further, 2-nitroalkanols formed from aryl aldehydes tend to eliminate water to form nitroalkenes[5] which readily polymerise. The classical methods for this important transformation involving the use of bases such as alkali metal hydroxides, carbonates, bicarbonates, alkoxides, barium and calcium hydroxide, magnesium and aluminium ethoxides, a rhodium complex, potassium exchanged zirconium phosphate and also organic bases such as primary, secondary and tertiary amines predominantly give dehydrated products.[4] Thus, careful control of the basicity of the reaction medium is crucial to achieve better yields of β-nitroalcohols. Such efforts require longer reaction times but only give moderate yields.[6,7]

Heterogeneous catalysis induced by solid catalysts such as basic alumina,[8] alumina-KF,[9] amberlyst[6] and phase transfer catalysis with surfactants[10] are the two divergent approaches applied in an attempt to obtain improved selectivity. The former approach requires longer reaction times and in some cases affords condensed olefins.[5,11] Although good selectivity has been achieved in phase transfer reactions, the reaction still requires a soluble base, which tends to give salts upon neutralisation at the end of the reaction.[10] With this background, we envisaged the use of solid bases in the form of layered double hydroxides (LDHs) or hydrotalcite like compounds (HTLCs) in view of their potential usefulness as adsorbents, anion-exchangers and most importantly as basic catalysts.[3,12] LDHs upon thermal decomposition at *ca.* 450 °C give highly active homogeneous mixed oxides, which are potential basic catalysts used for a variety of organic transformations.[13–17] Recently, we reported a modified method[2] for the activation of a hydrotalcite catalyst the basicity of which was tuned for base catalysed aldol, Knoevenagel and Michael reactions[18,19] in the liquid phase under very mild reaction conditions. The significance of 2-nitroalkanols in organic synthesis[4] and our continued interest involving hydrotalcites prompted us to explore the Henry reaction.

Green Context

The Henry reaction is an important class of C–C bond forming reaction. It operates under base catalysis conditions to give β-nitro alkanols, important intermediates for a variety of useful compounds such as amino alcohols. Difficulties which lead to poor selectivity and thus waste include dehydration (and possible subsequent reaction of the nitroalkene formed) and Cannizzaro reaction of the aldehydic component. This paper describes the application of Mg–Al hydrotalcites to the Henry reaction. Hydrotalcites are mixed oxides, in some ways similar to clays, but basic rather than acidic, and have found uses as medium strength base catalysts in recent years. They are readily prepared, and catalyse several reactions selectively. In the cases described here, they produce a selective and clean reaction under mild conditions. Catalyst reuse is also demonstrated. A fully optimised procedure would require further optimisation of the solvent used to wash the catalyst, and recovery and recycling of the excess nitroalkane. ***DJM***

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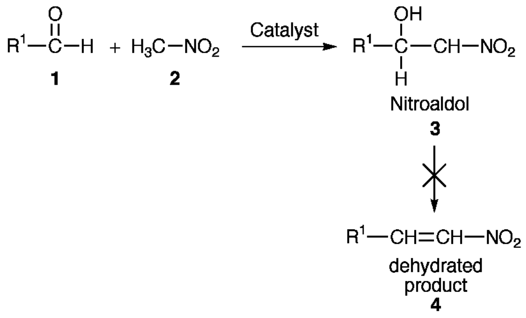
† IICT Communication no. 4021.

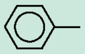
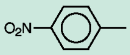
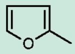
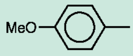
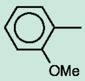
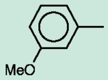
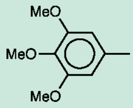
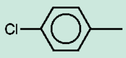
Experimental

Here, we report a convenient and selective synthesis of 2-nitroalkanols *via* the Henry reaction,[20] Scheme 1, affording 100% selectivity to β-nitroalcohols (**3**) in quantitative yields using modified Mg–Al hydrotalcite.[18] Modified Mg–Al hydrotalcite (Mg/Al ratio = 2.5) was synthesized as follows: an aqueous solution (0.221 l) containing $Mg(NO_3)_2\cdot6H_2O$ (0.2213 mol) (Aldrich) and $Al(NO_3)_3\cdot9H_2O$ (0.0885 mol) (Aldrich) was added slowly to a second solution (0.221 l) containing NaOH (0.7162 mol) and Na_2CO_3 (0.2084 mol) in a 1.0 l round-bottom flask under vigorous stirring. The addition took nearly 3 h. Then the contents were heated to 338 K for 16 h. The precipitate formed was filtered off and washed with hot distilled water until the pH of the filtrate was 7. The precipitate was dried in an oven at 353 K for 15 h. The XRD pattern shows the presence of pure hydrotalcite, with lattice parameters corresponding to those reported in the literature.[3]



Scheme 1 Henry reactions between nitromethane and various substituted aromatic and aliphatic aldehydes.

Table 1 Henry reactions of various substituted aromatic and aliphatic aldehydes with nitromethane catalysed by MHT

Entry	R^1	Time/h	Yield (%)[a]
1		0.5	95[b]
2		0.5	100
3		1.0	92
4		1.5	54
5		1.0	98 (97)[c]
6		1.5	93
7		2.0	88
8		1.0	95
9	Et	1.0	100
10	Me_2CHCH_2	1.0	100

[a] Determined by ^1H NMR,based on starting aldehyde. [b] Isolated pure product. [c] Yield after fifth cycle.

The synthesised Mg–Al hydrotalcite catalyst was first activated by calcination at to 723 K in a flow of air. The temperature was raised at a rate of 10 K min^{-1} to 723 K and maintained at this temperature for 8 h. The solid was then cooled in dry nitrogen and rehydrated at room temperature under a flow of nitrogen gas (6 l h^{-1}) saturated with water vapour for *ca.* 6 h before use in reactions.

Results and discussion

Results of Henry aldol product synthesis are compiled in Table 1 with modified hydrotalcites showing the best catalytic performance. No dehydrated product (**4**) was observed even after continuing the reaction for prolonged periods when we deliberately chose aryl aldehydes as one of the reactants. The reused catalyst exhibited consistent activity and selectivity.

Taking the Henry reaction of benzaldehyde with nitromethane as a model reaction we compared the activity and selectivity of the modified Mg–Al hydrotalcite catalyst with a variety of soluble and solid bases such as sodium hydroxide, neutral aluminium oxide, magnesium oxide and diamino-functionalised MCM-41[21] under similar reaction conditions (Table 2). The reaction of benzaldehyde with nitromethane using magnesium oxide or neutral aluminium oxide catalyst required longer reaction times and gave poor yields, while the reaction with diamino-functionalised MCM-41 yields the nitroalkene as the sole reaction product. The Henry reaction was slightly sluggish under phase transfer conditions[10] using sodium hydroxide as a soluble base. In summary, the results show that the modified Mg–Al hydrotalcite catalyst is more active and selective than the other catalysts.

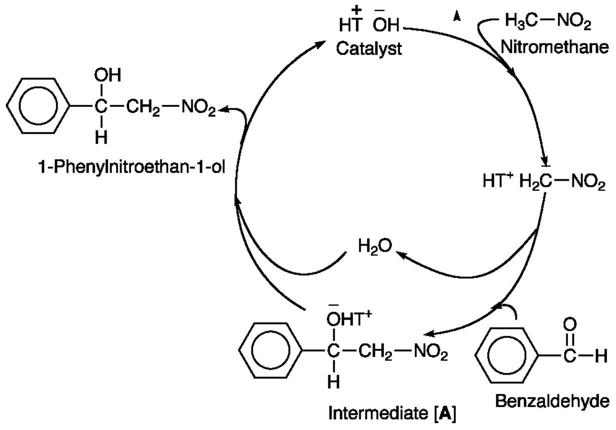
Table 2 Henry reaction between benzaldehyde and nitromethane using various base catalysts

Entry	Catalyst	*t*/h	Yield (%)[a]
1	Modified Mg–Al hydrotalcite	0.5	95[b]
2	Aluminium oxide	12.0	37
3	Magnesium oxide	8.0	51
4	Sodium hydroxide with PTC	2.0	70[c]
5	Diamino-functionalised MCM-41	3.0	97[d]

[a] Determined by ^1H NMR, based on starting aldehyde, unless otherwise stated. [b] Isolated pure product. [c] Isolated yield, using sodium hydroxide with surfactant.[10] [d] Using diamino-functionalised MCM-41, nitroalkene is the sole product.[21]

The Henry reaction usually requires Brönsted hydroxy sites to abstract a proton from an active methylene group of the nitro compound. X-Ray diffraction studies of the activated hydrotalcite show that the layered structure is removed upon calcination but is restored by rehydration and a meixnerite-like structure is formed in which OH^- are the compensating anions. These anions are mobile and therefore basic and catalyse several reactions proceeding through basic mechanisms such as aldolisation,[2,22,23] Knoevenagel[18] or Michael reactions.[19] From their catalytic properties it is usually accepted that LDH has a pK_b of *ca.* 11.4–12 and therefore is a base of moderate strength comparable to piperidine.[23] The lack of activity of calcined hydrotalcites reiterates that the reaction of Henry requires Brönsted bases of mild strength.

The classical mechanism of the Henry reaction[6] can therefore be applied here. The abstraction of a proton from the active methylene group of the nitro compound gives a carbanion which can be stabilised by the cationic charge of aluminium in the lattice of hydrotalcite as suggested in Scheme 2. In this scheme it is sug-



Scheme 2 A plausible mechanism for the Henry reaction between nitromethane and benzaldehyde catalysed by modified Mg–Al hydrotalcite.

gested that this carbanion further adds to the carbonyl compound to form an intermediate **A** which, in turn, removes a proton from water to give the final nitro aldol product. It is of interest that this aldolisation reaction is very specific towards the nature of the Brönsted base.[2,23] In spite of the large number of basic sites determined by calorimetric adsorption of CO_2, decarbonated hydrotalcites are not active, as they do not have any Brönsted hydroxy groups.

Conclusion

Compatible Brönsted basic hydroxy sites present in the modified hydrotalcite give rise to selective nitroaldol reactions in excellent yields over short times more efficiently than methodologies described earlier. The following advantages are: (a) high catalytic activity under very mild liquid phase conditions, (b) easy separation of the catalyst by simple filtration, (c) excellent yields and 100% selectivity of β-nitroalkanols at high rates of reaction, (d) use of non-toxic and inexpensive materials, (e) recycling of the catalyst and (f) zero emission of pollutants. The present catalytic system is thus a potential alternative to soluble bases.

Acknowledgements

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19 B. M. Choudary, M. Lakshmi Kantam, Ch. Venkat Reddy, K. Koteswara Rao and F. Figueras, *J. Mol. Catal.*, in press.
20 *Representative procedure*: To a mixture of nitromethane (10 mmol) and benzaldehyde (2 mmol), 0.2 g of catalyst was added at room temperature and stirring was continued until completion of the reaction, as monitored by TLC. The catalyst was filtered off, washed with dichloromethane (10 ml × 3) and the filtrate concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, 60–120 mesh; hexane–ethyl acetate 98 : 2 v/v) to give $PhCH(OH)CH_2NO_2$ (0.317 g, 95% yield). The product was characterised by comparison of its NMR and IR spectra with those reported in the literature.[10]
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Paper 9/04075G

An easy synthesis of 4,4′-diaminodiphenylmethanes

on natural kaolinites

Damodaran Bahulayan, Rugmini Sukumar, Kuzhunellil Raghavanpillai Sabu and Malathy Lalithambika*

Regional Research Laboratory [CSIR], Thiruvananthapuram - 695 019, India.

E-mail:lali@csrrltrd.ren.nic.in

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Summary

Adsorbed on kaolinite, aromatic amines are readily condensed with formaldehyde to give the corresponding diaminodiphenylmethanes. The methodology is novel in its simplicity, selectivity and ecofriendly nature.

Introduction

Diaminodiphenylmethanes find use in a variety of applications including curing agents and chain extenders in polymers.[1] The conventional preparation is cumbersome involving specific use of mineral acids and alkalis at various stages. Polymerization is unavoidable resulting in poor selectivity.[2]

Heterogeneous catalysis on clays under solvent conditions with ultrasound irradiation and also in dry media under microwave conditions have been extensively studied compared to catalysis over clays in aqueous media.[3–14] Here we report the synthesis of 4,4′-diaminodiphenylmethanes employing natural kaolinite as catalyst in aqueous media for the first time. It is known that kaolinites intercalate with molecules as polar as water, formamide, *N*,*N*-dimethylformamide, dimethyl sulfoxide and dimethylselenoxide within their layers.[15] Nevertheless, the catalytic activity of kaolinitic clays have been seldom exploited contrary to their smectite counterparts. Commercial catalysts like K10, KSF, Filtrol, *etc.* are derived from the latter variety.

Results and discussion

The experimental procedure involves the following steps: (*a*) mixing of catalyst and water; (*b*) addition of amine to the agitated slurry, and (*c*) dropwise addition of formaldehyde to the catalyst–water–amine mixture and continuing stirring for the completion of the reaction. Work-up involves simple filtration followed by dissolution of the product in hot alcohol from which it is recrystallised. The method employed is simple, efficient, reproducible and avoids the use of hydrocarbons, acid, alkali *etc.* unlike the conventional procedure.[2] It is noteworthy that no conversion takes place when the reaction is performed on commercial silica or alumina (chromatographic grade). Moreover, the catalyst employed is regenerable by washing with hot acetone. The catalytic performance studied up to 5 cycles of the same reaction is found to be steady. Results are presented in Table 1.

The condensation of aniline with formaldehyde is typical for the general procedure.

In a typical experiment, the catalyst (1 g) was stirred with 200 ml of water. Aniline (9.3 g, 0.1 mol) was added to this solution under stirring. To this formaldehyde solution (37%, 4.5 ml, 0.05 mol) was added slowly and stirring was continued. The precipitated 4,4′-diaminodiphenylmethane was extracted into hot alcohol from which it is recrystallised: mp 98 °C [lit, mp 96–98 °C].[2]

Conclusion

To summarise, we have developed an efficient method of synthesis of 4,4′-diaminodiphenylmethane catalyzed by an ecofriendly catalyst, kaolinitic clay, which is abundantly available. The conversion is significantly high with product selectivity in the range 68–98%. Besides, the operational ease makes the process attractive and cost effective.

Acknowledgements

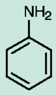
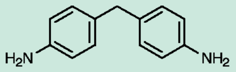
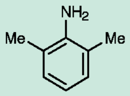
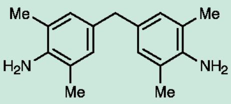
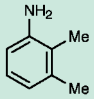
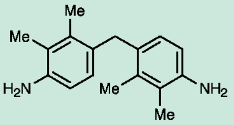
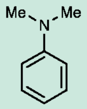
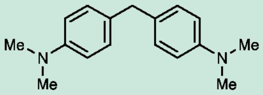
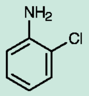
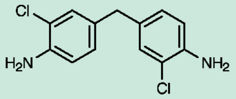
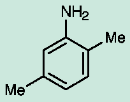
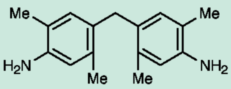
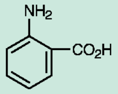
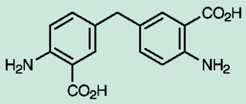
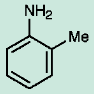
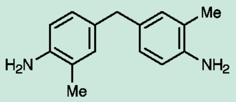
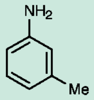
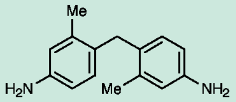
We thank Dr Vijay Nair, Director, RRL, Trivandrum, for his wholehearted cooperation during the progress of this work. Fellowships to D. B. and K. R. S. by the CSIR, Government of India is also acknowledged.

Green Context

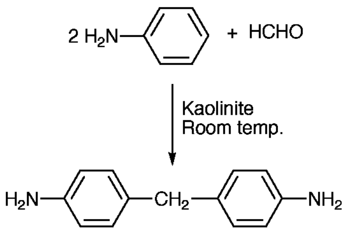
The polymer industry requires large quantities of 4,4′-diaminodiphenylmethanes. These compounds find use in various applications as polymer additives. Current synthetic methods involve the condensation of anilines with formaldehyde under acidic conditions. As is common for such reactions, a substantial amount of waste acid needs to be neutralised, generating substantial aqueous salt waste which is likely to be contaminated with residual anilines and/or formaldehyde, both compounds of considerable toxicity. While a completely green solution to this problem might involve the replacement of this chemistry with an inherently less toxic combination of reagents, the replacement of the current homogeneous catalysts with a heterogeneous catalyst might ease the problems of a waste aqueous phase. Such a catalyst switch might improve the situation by allowing the easy separation of catalyst from product, without the need for neutralisation. Thus, the aqueous waste stream can be avoided, and the catalyst can be recovered. This article demonstrates a feasible process for this chemistry, using a readily available and reusable clay catalyst. Yields of a range of diamines are excellent, and the method avoids the use of problematic solvents.

DJM

Table 1 Condensation of aromatic amines with formaldehyde, formation of 4,4′-diaminodiphenylmethanes

Entry	Amine	Product	Reaction time/min	Isolated yield (%)
1			60	96
2			60	99
3			60	68
4			60	98
5			30	100
6			60	79
7			60	97
8			60	78
9			60	71

[a] Amine : formaldehyde = 2 : 1, ambient temperature.



Notes and references

The catalyst used is natural kaolinitic clay. SiO_2 = 47.05%, Al_2O_3 = 36.98%, Fe_2O_3 = 0.34%, TiO_2 = 0.34%, Na_2O = 0.12%, K_2O = 0.08%, Loss on ignition = 14.34%, BET surface area = 13.0 $m^2\ g^{-1}$, Hammett acidity function, $H_o = -3.0$ (0.03 mmol g^{-1}). The 4,4′-diaminodiphenylmethanes obtained were characterized on the basis of ^1H NMR (300 MHz), HPLC, GC-MS and elemental analysis. Selected data for 4,4′-diaminodiphenymethane: Anal. Calc. for $C_{13}H_{14}N_2$: C 78.78, H 7.07, N 14.14%. Found: C 78.64, H 7.11, N 14.08%. ^1H NMR ($CDCl_3$, 300 MHz): δ 3.4 (s, 2H, $-CH_2-$), 3.7 (s, 4H, $2NH_2$), 6.4–6.8 (m, 8H, Ar). HPLC: CLC-NH_2 (M) column, 1 ml min^{-1} CH_3CN, R_t 3.07 min. GC-MS : OV-101, m/z 298 ($M^{\cdot+}$).

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Paper 9/06165G

Organically modified hexagonal mesoporous silicas

Clean synthesis of catalysts and the effect of high loading and non-catalytic second groups on catalytic activity of amine-derivatised materials

Duncan J. Macquarrie

Department of Chemistry, University of York, Heslington, York, UK YO10 5DD.

E-mail:djm13@york.ac.uk

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Summary

The versatility of the one-pot synthesis of organically modified silicas is shown by the preparation of materials with very high loadings (up to 4.85 mmol g^{-1}) and by the synthesis of bifunctional catalysts. The synthesis of these materials is shown to be very atom efficient, with all the Si species being incorporated into the product, and 98% of the template being recovered, and successfully reused. Catalytic activity is excellent, and the new catalysts outperform both the traditional silica-based catalyst, and the initial versions of these materials. The incorporation of non-polar phenyl groups has a particularly pronounced positive effect on the rate of reaction, the yield and the catalyst lifetime.

Introduction

The development of a simple one-pot method for the preparation of organically modified hexagonal mesoporous silicas (HMS)[1–3] has made available a range of different hybrid materials. These materials exhibit pore sizes which are in the mesoporous range and have a very narrow pore size distribution, making them excellent potential candidates for catalytic applications. We have published initial evaluations of the catalytic activity of two different amino-substituted HMSs. 3-Aminopropyl-HMS is an effective catalyst for the Knoevenagel reaction, giving good yields and excellent selectivity,[2] whereas 3-*N*,*N*-dimethylaminopropyl-HMS is active in the Michael reaction.[3] One of the great strengths of the one-pot preparative method is that the loadings achieved can be much higher than those achieved by other routes. We have found that 2.5 mmol g^{-1} loaded materials are, not surprisingly, more active than the corresponding 1.1 mmol g^{-1} systems in both the Knoevenagel and Michael systems. Loadings > 2.5 mmol g^{-1} have been prepared for certain materials,[4] and are effective in oxidation reactions, but do not exhibit the highly uniform pore system of the true HMSs.

We present here results relating to the clean preparation of these materials, to the use of high loading materials in the Knoevenagel reaction, and to the development of highly active surface modified materials which display further advantages of activity, yield and lifetime in this reaction.

Results and discussion

2.1 Preparation of the catalysts

Detailed results on the preparation of the catalysts have already been published.[1,5] To summarise, a solution of long chain amine (in this case, *n*-dodecylamine) is prepared in aqueous ethanol (46 ml ethanol–53 ml water). To this is added tetraethoxysilane (TEOS) and 3-aminopropyl(trimethoxy)silane (AMP-silane); the triethoxy derivative can also be used. After reaction is complete, the solid product is filtered off, and the template extracted with hot ethanol. One of the prerequisites for the incorporation of organic groups into the synthesis gel is that the template can be removed without damaging the incorporated groups. Thus, the use of quaternary ammonium templates, as described in the preparation of the MCMs,[6] is not suitable for a one-step process as their removal requires the use of high temperatures. Neutral templates can be easily and completely removed by washing with *e.g.* ethanol. One of the key goals for us was to develop a synthetic method for the preparation of the catalysts which itself generated minimal quantities of waste. In order to do this, it is necessary to recover and reuse the template. This is in fact very easily achieved. After the reaction is complete, and the solid filtered off, one is left with a solid containing template, and a solution containing ethanol, water and amine—if the trimethoxy silane is used, then a small amount of methanol is also found in solution. Extraction of the solid recovers the remaining template, leaving a solution of amine in ethanol. Combination of both solutions gives a solution resembling the original templating solution. This contains a larger quantity of ethanol than necessary. Complete evaporation of this solution gave a 98% recovery of the

Green Context

Important organic transformations, including the Knoevenagel and Michael reactions, proceed under base catalysed conditions, and there is continuing interest in heterogeneous, reusable catalysts for these systems. This report describes the use of hexagonal mesoporous silicas modified with organic amine groups as base catalysts. The catalysts themselves are prepared in a highly atom-efficient manner, and with effective recovery of the templating agent, to ensure that the environmental impact of catalyst manufacture AND the organic synthesis are minimised.

Stewart J. Tavener, University of York

template of a comparable purity to the original amine. No silicon-containing material was found in the recovered amine, indicating complete copolymerisation during the formation of the catalyst. Re-dissolution of the amine in the templating solvents, and repeated reaction gave product with essentially identical physical and catalytic characteristics.

Thus, a completely atom efficient synthesis can be achieved—all the silicon species are incorporated into the catalyst, and all the template can be recovered and reused. The only losses are potential solvent losses during solvent recovery. It should be possible to develop a procedure where the appropriate amount of ethanol is removed from the recovered combined solution and this should reduce processing losses even more. This has not yet been tested, since the relatively small scale makes it difficult to produce the exact ethanol–water ratio required for synthesis. Nonetheless, the process as it stands is a remarkably clean route to these catalysts.

2.2 Preparation and evaluation of high loading catalysts

The preparation of the high loading peracids by Elings *et al.*[4] has shown that materials with organic contents up to *ca.* 4.0 mmol g^{-1} can be prepared by this route. This contrasts with post-modified silicas, where *ca.* 1.0 mmol g^{-1} is achievable for amine containing materials, and typically < 0.5 mmol g^{-1} is the maximum possible for other silanes. We have therefore prepared a series of catalysts varying the ratio of TEOS to AMP-silane from 9:1 to 1:1. The results are shown in Table 1.

Table 1 Properties of catalysts investigated

	Composition/mmol g^{-1}				
Catalyst	AMP	Ph	Me	(S^a/) $m^2\ g^{-1}$	Pore size/nm
1	1.2	0	0	756	3.6
2[b]	1.2	0	0	748	3.7
3	2.7	0	0	745	3.7
4	4.0	0	0	132	10 (broad)
5	4.85	0	0	249	10 (broad)
6	1.15	1.15	0	947	2.0
7	1.1	0	1.1	790	2.1
8[c]	1.1	0	0	715	1.9
9	1.0 AMP-silica			254	8.0 (broad)

[a] Specific surface area. [b] Repeat preparation of **1**. [c] Prepared with *n*-octylamine template.

As can be seen, the materials prepared are structured up to 2.7 mmol g^{-1}; at higher loadings than this, the materials are amorphous, but still display respectable surface areas, with the highest loading being 4.85 mmol g^{-1}. Higher loadings have not yet been investigated, owing to the results obtained in the catalytic reactions, but no drop in yield was seen in the range tried.

Catalytic activity was evaluated in the Knoevenagel reaction of ethyl cyanoacetate and cyclohexanone. This reaction was chosen as a reasonably challenging example of the Knoevenagel reaction. The usual ethyl cyanoacetate–benzaldehyde test reaction is much more facile with most base catalysts, but is anomalously slow with aminopropyl-HMS materials.[2,7] Results for this reaction (in toluene at reflux, with continuous removal of water) with aminopropyl-HMS of different loading are presented in Table 2.

As can be seen, the activity increases with loading up to *ca.* 4.0 mmol g^{-1} and then drops off somewhat. The reasons for this behaviour are likely to be a complex interplay of many factors, such as the physical nature of the catalysts (pore size distribution, surface area, pore shape), the relative polarity of the catalyst surface (which is expected to drop with increasing organic content) and the proportion of amine groups which are available to react. Indeed, in the higher loading, amorphous materials, it is likely that many aminopropyl groups are embedded within the bulk structure and cannot take part in catalysis, making the effective catalyst loading lower than the total nitrogen content would predict.

Table 2 Knoevenagel reaction (**10** + **13**)[a] catalysed by AMP-HMS materials with different loadings of amine

Catalyst	Loading/mmol g^{-1}	Yield (%)	*t*/h
1	1.2	92	2
3	2.7	94	1.5
4	4.0	96	1.0
5	4.85	94	1.5

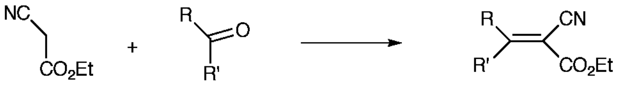
[a] **10** = Cyclohexanone; **13** = ethyl cyanoacetate.

2.3 Catalysts containing two functional groups

Since one of the most important criteria controlling the rates of heterogeneously catalysed reactions is sorption of substrates/products to and from the surface, the ability to control the nature of the surface is important. Corma *et al.*[8] have recently published details of improvements which are made possible by increasing the hydrophobicity of catalyst surfaces by post-treatment with trimethylsilylating agents. Mann *et al.*[9] have recently reported the direct formation of organically modified MCMs containing two different groups. We have prepared and evaluated the catalytic activity of materials containing the aminopropyl catalytic centre, and a second catalytically inert group, designed to modify the polarity of the catalyst surface. This approach is extremely simple, and involves a synthesis mixture consisting of TEOS, the AMP-silane and a third alkyl or aryl substituted silane.

The aminopropyl/phenyl and the aminopropyl/methyl materials **6** and **7** were tested in the Knoevenagel reaction and compared to two simple aminopropyl-HMSs **1** and **8**. The physical characteristics of the catalysts are summarised in Table 1. The first of these (**1**) is a 3.6 nm pore diameter material with a surface area of 756 $m^2\ g^{-1}$, and has been used as an efficient catalyst for the Knoevenagel reaction.[2] The second (**8**) has smaller pore size (1.9 nm) but similar surface area. Results are given in Table 3.

Comparison is hindered somewhat by the differences in pore size between **1**, **6**, **7** and **8**, but the relative rates of **1** and **8** indicate that initial rates of reaction are essentially independent of pore size for the reactants under investigation. The only significant difference between the two is that the lower pore sized material becomes poisoned much more rapidly.[2] As can be seen, the methyl-substituted material displayed the same activity as the simple aminopropyl system **1**. The phenyl containing material was, however, substantially more active than the simple materials. For example, the reaction between ethyl cyanoacetate **13** and cyclohexanone **10** took 2 h to go to completion with **1** (loading 1.2 mmol g^{-1}), and 1.5 h with 2.7 mmol g^{-1} **3**; with **6** (1.15 mmol g^{-1} aminopropyl and 1.15 mmol g^{-1} Ph) the same reaction



10 R+R' = $(CH_2)_5$; **11** R = Me, R' = Ph; **12** R = R' = Et

Table 3 Knoevenagel reactions of various aminopropyl–containing catalysts

	Composition							
Catalyst	AMP	Ph	Me	Reaction	Yield (%)	*t*/h	Solvent	TON
1	1.2	0	0	**10** + **13**	92	2	Toluene	2400
3	2.5	0	0	**10** + **13**	94	1.5	Toluene	2550
6	1.15	1.2	0	**10** + **13**	98	0.5	Toluene	5900
7	1.1	0	1.1	**10** + **13**	93	2	Toluene	2520
8	1.1[a]	0	0	**10** + **13**	49	2	Toluene	
9	1.0	AMP-silica[b]		**10** + **13**	98	1	Cyclohexane	650
1	1.2	0	0	**11**[c] + **13**	49	72	Toluene	55
3	2.5	0	0	**11** + **13**	48	36	Toluene	47
6	1.15	1.2	0	**11** + **13**	86	24	Toluene	215
9	1.0	AMP-silica[b]		**11** + **13**	68	72	Cyclohexane	250
1	1.2	0	0	**12**[d] + **13**	95	18	Toluene	1127
3	2.5	0	0	**12** + **13**	97	4	Toluene	305
6	1.15	1.1	0	**12** + **13**	96	2.5	Toluene	3600
9	1.0	AMP-silica[b]		**12** + **13**	97	2	Cyclohexane	265

[a] 1.9 nm pore size catalyst: rate to *ca*. 40% conversion was identical to that from the larger pore catalysts X. [b] Cyclohexane was found to be the optimum solvent for AMP-silica; toluene the best for AMP-HMS catalysts. [c] **11** = Acetophenone. [d] **12** = Pentan-3-one.

was complete in 30 min. Thus, reaction rates are much faster with **4** than with a catalyst with a higher loading of catalytic sites. (All reactions were carried out with the same mass of catalyst.) Little effect was seen with the methyl-substituted material, presumably due to the methyl groups being too small to exert any significant effect on the reaction space.

Similar results were obtained with ethyl cyanoacetate and pentan-3-one, where **6** again outperformed even the 2.5 mmol g^{-1} aminopropyl catalyst **3**. The very challenging substrate acetophenone is also converted to the corresponding Knoevenagel product in 86% yield within 24 h, significantly better than the results obtained with the simple aminopropyl catalysts. These results are consistent with the polarity of the surface being a major determining factor in the activity of the catalysts.

A particularly important finding is that the turnover number (TON) is also substantially increased by having phenyl groups present. Increases in TON lie in the range of 2.5–4 compared to the larger pore materials, and by an order of magnitude compared to the silica-based catalyst **9**. TONs were not measured for the 1.9 nm pore size material **8**, since it became deactivated very rapidly. However, it can be estimated that TONs for the new catalyst **1** compared to **8** are higher by a factor of *ca*. 25–40 for most substrates. This represents a second major advantage of these catalysts over the simple materials. While we are not yet sure of the deactivation mechanism of the HMS catalysts, it does appear to be related to the preferential adsorption of the ketone component to the exclusion of the carbon acid.[10] Such a mechanism should be very dependent on the surface chemistry of the catalyst, and the results here are again consistent with altered adsorption characteristics owing to the presence of the phenyl groups.

Experimental

All chemicals were obtained from Aldrich and were used as received. Porosimetry was carried out on a Coulter SA2100 porosimeter using dinitrogen as adsorbate. IR spectra were measured on a Bruker Equinox spectrometer fitted with an Environmental Chamber diffuse reflectance unit.

3.1 Preparation and recycling of template

To a solution of *n*-dodecylamine (5.08 g, 27.5 mmol) in water–ethanol (53 ml water, 46 ml ethanol) were added, at room temperature, separately but simultaneously, TEOS (18.8 g, 0.09 mol) and AMP-silane (1.79 g, 0.01 mol). The mixture was initially clear, but became increasingly cloudy, and after 18 h was a thick white paste. Filtration of the mixture gave a white solid (catalyst + template) and filtrate (water + ethanol + template). The solid was then extracted with ethanol using a Soxhlet extractor (8 h). The solid was collected and dried at 110 °C. The yield of solid was 10.6 g.

The template can be recovered by combination of the filtrate and the extract solutions and removal of solvent by evaporation. The resultant material is *n*-dodecylamine, pure by IR, NMR and melting point. Yield of recovered template, 4.99 g, 98%. Reuse of the template resulted in an identical reaction with the same yield (10.4 g) and physical characteristics (See Table 1, entries **1** and **2**).

3.2 Preparation of high-loading materials

Higher loading materials were prepared by the above procedure, but using ratios of TEOS : AMP-silane of 4 : 1, 2 : 1 and 1 : 1. Total molar quantities of Si remained 0.1 mol. Yields were 9.86 g, 10.32 g and 9.95 g, respectively. Physical characteristics are given in Table 1.

3.3 Preparation of bifunctional materials

Organically modified HMSs containing two organic groups were easily prepared by an extension of the original method.[3] Tetraethoxysilane (TEOS; 16.8 g, 0.08 mol), 3-aminopropyl (trimethoxy)silane (AMPS, 1.79 g, 0.01 mol) and phenyl(triethoxy)silane (2.40 g, 0.01 mol) were added separately but simultaneously and rapidly to a solution of *n*-dodecylamine (5.09 g) in a water–ethanol mixture (53 ml–46 ml) at 20 °C. The clear solution initially became turbid, then milky (after a few minutes), and finally solid began to appear (*ca*. 30 min). The suspension was allowed to age for 18 h. The solid was filtered off, and washed with ethanol. The amine template was then removed by Soxhlet extraction with ethanol (15 h). The resultant material was then dried overnight at 110 °C, to yield 8.95 g of a fine white powder **6**. Elemental analysis indicated a loading of aminopropyl groups of 1.15 mmol g^{-1}, but phenyl loading could not be calculated from elemental analysis due to residual RO groups in the material. However, analysis of the liquid from the reaction indicated that no silicon-containing species were present, and thus the loading of phenyl groups is likely to be similar to that of aminopropyl groups.

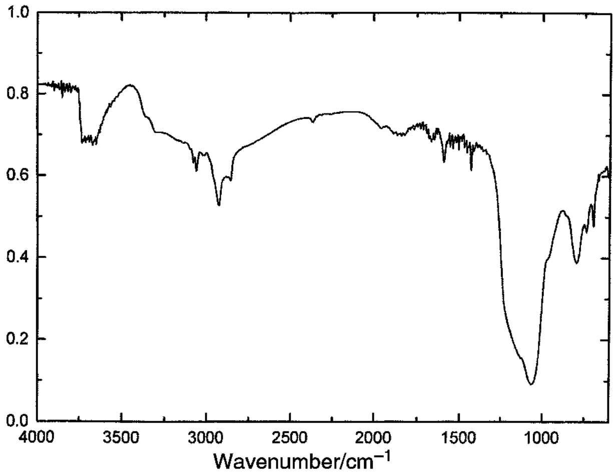


Fig. 1

The diffuse reflectance IR spectrum of the phenyl/aminopropyl spectrum is shown in Fig. 1. As expected, v(C–H) bands from the phenyl groups can be clearly seen at 3060 cm^{-1}, as well as v(C–H) vibrations from the aliphatic chains of the aminopropyl groups. A vibration at 1600 cm^{-1} is also present and the invariance of this band with temperature (150–325 °C) suggests that it is due to N–H deformations rather than surface water.

Aminopropyl/methyl HMS **7** was prepared in the same way, using methyl(triethoxy)silane in place of phenyl(triethoxy)silane. Again, aminopropyl loading was approximately the expected value of 1.1 mmol g^{-1}.

Pore size distributions and surface areas were measured for both the phenyl and the methyl containing materials. In both cases the materials displayed isotherms characteristic of HMS materials with small pores and high surface areas (2.0 nm and 947 m^2 g^{-1} for **6**; 2.1 nm and 790 m^2 g^{-1} for **7**).

3.4 Reaction studies

All reactions were carried out as described in ref. 4. A typical experiment involved the reaction of ethyl cyanoacetate (20 mmol) with the ketone (20 mmol) in the presence of 0.25 g catalyst in 25 ml of toluene at reflux. Water was separated by a Dean and Stark trap. Turnover numbers were calculated by reaction, decantation of supernatant, and addition of further substrate, until no more conversion was achieved. The reactions did not proceed with the reagents alone, nor did they proceed with unfunctionalised HMS or with phenyl-HMS.

Conclusion

High loading and bifunctional organically modified hexagonal mesoporous silicas can be easily prepared by a simple extension of the existing methodology. The materials prepared display significant advantages over the simple mono-functional materials in terms of rate, yield and catalyst lifetime. It is thought that the reasons for both these improvements lie in the more advantageous sorption of material to and from the surface.

Acknowledgement

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Synthesis of 2,4-D ester herbicides

New routes using inorganic solid supports

Laura Lami,[b] Blanca Casal,[a] Luis Cuadra,[c] Jesús Merino,[a] Amauri Alvarez[b] and Eduardo Ruiz-Hitzky*[a]

[a] *Instituto de Ciencia de Materiales de Madrid, CSIC, Cantoblanco, E-28049 Madrid, Spain. E-mail: eduardo@icmm.csic.es*

[b] *Instituto Cubano de Investigaciones de los Derivados de la Caña de Azúcar, ICIDCA Cuba*

[c] *Centro de Ciencias Medioambientales, CSIC, c/ Serrano 115 dpdo., E-28006 Madrid, Spain*

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Summary

A clean method for the rapid and solventless preparation of herbicides based on 2,4-dichlorophenoxyacetic acid (2,4-D esters) is reported. Micro-particulate inorganic materials such as silica, clays and zeolites are able to act as supports for the 2,4-D esterification reactions under mild conditions in the absence of organic solvents. The synthesis takes place with elevated yield and the conversion rate of the process is strongly enhanced when the reaction is microwave-assisted. Not only can well-defined supports be used, but soil can also be used for this synthesis, except when iron oxides are present which lead to extensive oxidation under microwave irradiation. The 2,4-D ester remains adsorbed on the solid support as a bioactive product. Therefore the resulting powder is a partially formulated compound that can be directly applied in the field avoiding the use of solvents and with minimal hazardous and pollutant effects.

Introduction

2,4-Dichlorophenoxy acetic acid (2,4-D) esters are extensively used around the globe as effective hormonal herbicides with high selectivity receiving wide application to *e.g.* cereals, grazing land and sugar cane plantations.[1] These herbicides are also used in domestic gardening in Western Europe and in the USA. Unfortunately, as is well known, the manufacture and use of pesticides often results in environmental damage. Besides, more than 40 years of experience in the continuous and increasing use of such herbicides shows that their usage provokes only minor changes in the soil when they are employed with caution. There is thus the opportunity to study strategies to mitigate their harmful environmental impact in their use and preparation.

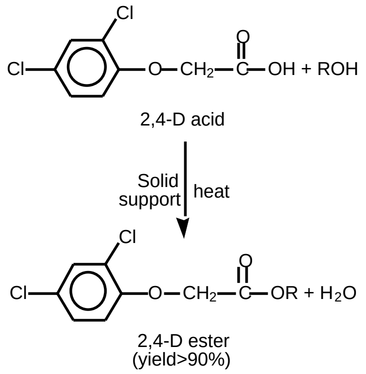
New approaches to 2,4-D ester preparation and use have been developed with the aim to make these herbicides more ecologically acceptable. Thus, bioactive polymers based on 2,4-D and cross-linked acrylamide gels have been recently prepared in order to obtain controlled-release formulations enhancing the efficacy of the herbicide and reducing any environmental problems.[2]

The conventional esterification of 2,4-D and related compounds following standard methods consists in the treatment of these acids with the corresponding alcohol, the mixture being refluxed in benzene for long periods of time (in general more than 10 hours) in the presence of an acid catalyst (*e.g.* H_2SO_4) and using the 2,4-D in excess with respect to the alcohol.[3] It is necessary to control the amount of alcohol present in the reaction media as the esterification progresses. Thus, a progressive addition of alcohol is needed, the reaction yield being critically determined by the quantity of water produced in the reaction. Alternative procedures for 2,4-D esters synthesis are based either on (i) direct reaction of the 2,4-D in the acid chloride form with the appropriate alcohol,[4] or (ii) use of polymer-supported reagents involving the preparation of intermediate Amberlist 2,4-dichlorophenoxy acetate resins.[5] Although this last method appears a laborious procedure, it produces under mild experimental conditions (2–9 h at room temperature), different 2,4-D esters in high yield (85–97%). However, all these routes involve the use of large quantities of chemicals and generate a significant volume of waste.

This paper reports the synthesis of 2-4-D esters using micro-particulate inorganic solids such as silica, clays and zeolites as reaction media, without organic solvents, *i.e.* in so-called dry media conditions,[6–10] either by conventional heating or using microwaves.[8,11,15] In the last case, the esters of 2,4-D are obtained in high yield in short reaction times (Scheme 1). In addition, the resulting product can be directly applied to the field because they are semi-formulated compounds which could find application in controlled release processes.

Green Context

The use of microwaves on a solid support has led to many very useful synthetic methods. Rapid reaction times and high conversions and selectivities are some of the benefits of this approach (see *e.g.* R. S. Varma, *Green Chemistry*, 1999, 1, 43. This paper deals with the preparation of a herbicide, and the authors have shown that the solid support can actually be a soil. This could allow the possibility of a preparative method for a soil–pesticide composite which could be applied to the land with fewer handling difficulties than traditional methods. *DJM*



Scheme 1

Results and discussion

The preparation of the 2,4-D ester in dry media conditions consisted of heating the 2,4-D and the alcohol in almost equi-molecular quantities (1 : 1 molar ratio) with both co-adsorbed on an inorganic powder. Heating can be either conventional (100–150 °C, 2–6 h) or, better, by microwave (MW) irradiation (150–350 W, 3–10 min). The 2,4-D esterification yield, using different alcohols, in experiments carried out on silica under microwave irradiation (3–5 min) always occurs with high conversion rates (Table 1).

Table 1 2,4-D esterifications on silica gel using MW irradiation

Alcohol:acid	Alcohol	Reaction time/min	Yield of ester (%)
1.5:1	ethyl	3	98
1.5:1	isopropyl	3	99
1.5:1	*n*-octyl	3	98
1.5:1	isooctyl	3	99
1:1	ethyl	5	98[a]
1:1	isopropyl	5	95[a]
1:1	*n*-octyl	5	96[a]
1:1	isooctyl	5	97[a]
1:1	isopropyl	5	96[b]

[a] 50% of full power MW irradiation. [b] 75% of full power MW irradiation.

Fig. 1 shows, as an example, the IR spectra of the reaction products after MW heating of the 2,4-D and isooctanol mixture co-adsorbed on a silica support. The intense band around 1725 cm^{-1} is clearly observed and is assigned to the ν(C=O) stretching vibrations of the ester functional group, whereas the 342 cm^{-1} band associated to the 2,4-D acid is absent, confirming that the esterification reaction is almost quantitative. Typical ν(O–H) bands of possible residual alcohol or acid reagents is overlapped by the broad intense ν(O–H) absorption band of silanol groups of the silica support (3300–3700 cm^{-1}). The bands observed in the 1500–1650 and 750–1000 cm^{-1} regions correspond to the characteristic vibrations of the 1,2,4-substituted aromatic ring, and the stretching vibrations corresponding to the C–H groups, appears in the 2800–3100 cm^{-1} region. The organic reaction products are easily extracted by an organic solvent such as methanol or acetone, and analysed by GC-MS and GC-FTIR. The mass spectra (MS) of the resulting products show typical fragmentation of the 2,4-D esters. As an example, the MS of the reaction product with isooctanol shows the main fragments corresponding to the 2,4-D isooctyl ester at (*m/z*): 332 [M$^+$], 220 [M$^+$ —isooctyl (2,4-D acid)], 164 [M$^+$—acetate (2,4-dichlorophenol)], 145, 111 and 71 [2,4-dichlorophenol fragmentation].

High conversion rates (>90%) were also observed when other solids were used as the support, (Table 2). In particular, silicates of relatively high S_o specific surface area (S_o > 100 m^2 g^{-1}) (zeolites, sepiolite and saponite), and therefore solids with high adsorptive capacity, were particularly efficient reaction supports. By contrast, the kaolinite aluminosilicate of low specific surface area S_o = 8.5 m^2 g^{-1}, gives much lower reaction yield (<50%) than the other silicates used, in experiments carried out under similar experimental conditions (Table 2).

The water content of the supports must also be considered in order to explain the effectiveness of the microwave activation. In fact, the kaolinite is practically water-free because only its external surface contains physically adsorbed water molecules (<1% *w/w*). In contrast, zeolites and saponites are tecto- and layered-silicates respectively, containing water molecules (5–10% *w/w*) that belong to the hydration shell of the exchangeable cations which are located either on the external surfaces and/or in the intracrystalline region of these silicates. Sepiolite is a hydrated magnesium silicate of large specific surface area (>300 m^2 g^{-1}) containing about 15% (*w/w*) water. As is well known, the MW action in heating materials is directly related to their dielectric polarisation capacity and, therefore, with the presence of associ-

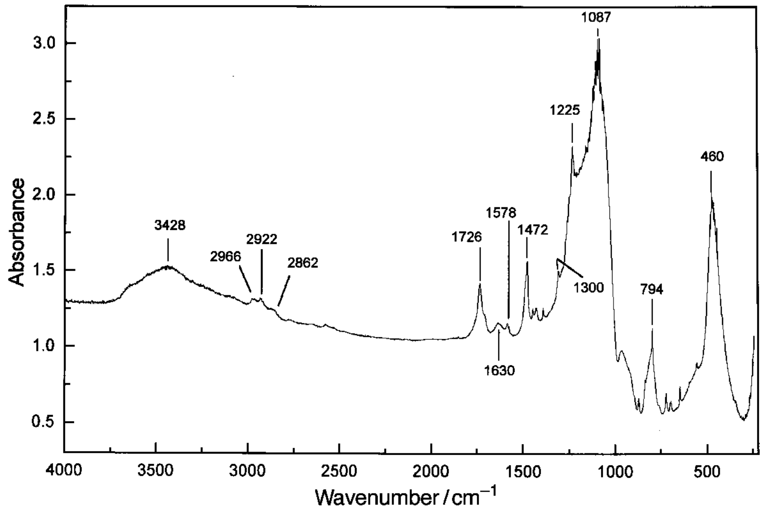


Fig. 1 Infrared spectra of the 2,4-D isooctyl ester synthesised on silica gel (5 min of MW irradiation).

Table 2 2,4-D isooctanol esterification using silicates as supports in dry media microwave-assisted synthesis

Inorganic support	Alcohol : acid molar ratio (support : reagents *w/w*, %)	Power (%)	Irradiation time/min	Yield of ester (%)
Na–Y zeolite	1:1 (50)	50	10	90
Na–Y zeolite	1.5:1 (55)	50	5	92
Zeolite (natural)[a]	1:1 (33)	50	5	93
Zeolite (natural)[b]	1:1 (50)	50	5	97
Kaolinite	1:1 (50)	75	5	47
Saponite	1.5:1 (55)	100	10	100
Sepiolite	1.5:1 (55)	50	10	97
Sepiolite	1:1 (50)	50	15	93
Sepiolite (*Pangel*)	1:1 (50)	50	7	100

[a] From San Ignacio. [b] From La Pita.

ated water molecules with the solids. Thus, the action of the alternating electromagnetic field on the water molecules produces rotational energy which is transferred to the surrounding environment, activating the supported reactions.[15] The temperatures reached by the solids supports after 2–5 min of MW irradiation are in the 150–180 °C range, using sample amounts and MW powers as employed in this work.

The use of metal oxides, such as alumina and iron(III) oxides, produces a strong decrease in the reaction yield (<5% for the 2,4-D isooctyl ester synthesis) (Table 3). Alumina has been largely used as an efficient support for dry media synthesis.[16] Nevertheless, in this case it is probable that the carboxylic acid remains chemisorbed on the alumina surface preventing further reaction between the CO_2H and the OH group of the alcohol. Such explanation implies the existence of symmetric bi-anchored carboxylate anions (Fig. 2), as reported elsewhere.[17] The incorporation of an additional amount of water to those systems increases the conversion rate. In this way, the addition of 5% (*w/w*) of water to the alcohol increases the ester yield from 5 to about 15% (Table 3). In agreement with other authors[17] this behaviour is probably due to the enhancement of reactivity produced by the presence of water on the alumina surface inducing the capture of protons. Besides this effect, the role of the MW–water interactions increasing the heating of the system should be considered although it is necessary to take into account the fact that the presence of water could disfavour the esterification reaction (Scheme 1). At present, it is difficult to ascertain a balance between these factors.

When the experiments were carried out using α-Fe_2O_3 as support, the reaction yield drops practically to zero due to the oxidative degradation of the adsorbed organic compounds (Table 3).

As occurs in general for MW-assisted organic phases,[9,10,13] the activation by MW irradiation compared to conventional heating (oven) is always more efficient in producing strong acceleration of reactions. In the case of 2,4-D esterification, some representative results are shown in Table 4, showing the potential interest in the use of such a procedure as a promising clean method.

The potential advantages of using clay minerals are well known because the herbicide interacting with such micro-particulate solids could be slowly released resulting in a sustainable activity. Large amounts of clay minerals are used as pesticide carriers (around 200 000 tons per year both in the USA and in Western Europe). This means that 2,4-D supported esters can be directly used as obtained in the procedure involving the use of natural silicates operating in dry media conditions. In this way we have carried out bioassays consisting in the application of such compounds as aqueous dispersions containing the same amount of the herbicide as in conventional formulations, revealing good activity towards young plants of the *Amaranthaceae* family (*Amaranthus albus*). Such bioactivity assayed in the greenhouse (30 °C at daylight and 5 °C at night), corresponds to herbicide amounts that could be extrapolated to around 600 g a.i. ha^{-1}, *i.e.* almost the same quantity that is currently used in field application. The observed pre-emergent activity in soils afforded by the silicate/2,4-D isooctyl ester is also a novelty because the activity of 2,4-D esters has been always described to have a post-emergent character.

It is also noteworthy, that in place of the more or less pure silicates described above, it is possible to use soil to prepare the 2,4-D esters. Thus, we have selected two agricultural soils (calcium Luvisol from Toledo, Spain, and ortic ferralsol from Havana, Cuba). Both were finely sieved and used under the same conditions as the silicates (Table 5). Thermal treatment in the same

Table 3 2,4-D isooctanol esterification using Al_2O_3 and α-Fe_2O_3 metal oxides as supports in dry media microwave-assisted synthesis

Inorganic support	Alcohol : acid molar ratio (support : reagents *w/w* %)	Power (%)	Irradiation time/min	Yield of ester (%)
Al_2O_3	1 : 1 (50)	100	10	<5
Al_2O_3[a]	1 : 1 (50)	75	5	14
α-Fe_2O_3	1 : 1 (50)	50	2	0
α-Fe_2O_3	1 : 1 (50)	50	5	0
α-Fe_2O_3	1 : 1 (50)	50	10	0

[a] Experiments carried out adding 5% (*w/w*) of water with respect to the alcohol.

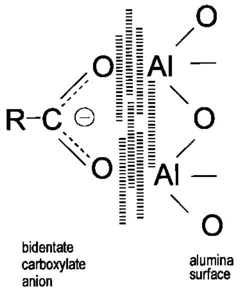


Fig. 2 Schematic representation of carboxylate anions adsorbed onto alumina.

way as pure silicates in a conventional oven gives the supported esters which also exhibit good activity in the corresponding bioassays. The only negative result detected was with ferralsols when the activation of the esterification reaction was carried out using MW irradiation. In this case, the iron content (identified by X-ray diffraction as α-Fe_2O_3) of the soil used as reaction support induces organic decomposition which can be explained in terms of oxidation enhancement imposed by the electromagnetic field interacting with the strongly paramagnetic iron oxide particles. The addition of small amounts of α-Fe_2O_3 (*i.e.* 5% *w/w*) to the Toledo soil, or to a selected clay mineral, also reduces the reaction yield (Table 5) corroborating the role of such oxide.

Finally, Fig. 3 resumes the steps needed in the use of soil minerals to obtain semi-formulated 2,4-D ester compounds. We have reported here a profitable approach to a selected herbicide which could be extended to other pesticide formulations. It should also be noted that this approach could lead to a lower dosage based on the slow release of the bio-active agents associated with the inorganic materials that have been used as supports in the preparation.

Experimental

Reagents

2,4-Dichlorophenoxyacetic acid (2,4-D) as well as ethyl, isopropyl, n-octyl and isooctyl alcohol (*i.e.* 2-ethylhexanol) were purchased from Fluka (reactive quality) and were used without further purification.

Mineral substrates and metal oxides

Sepiolite

This mineral is a hydrated magnesium silicate, $Si_{12}O_{30}Mg_8(OH,F)_4(H_2O)_{4x}\cdot 8H_2O$, which is structurally formed by the alternation of blocks and tunnels along the *c*-axis.[18] Sepiolite from Yunclillos (Toledo, Spain) (<200 mesh), purchased from TOLSA S.A., with 99% pure mineral, was used. The specific surface area (N_2, B.E.T.) is 340 $m^2\ g^{-1}$ and the cationic exchange capacity is close to 0.15 meq g^{-1}. Micronised sepiolite purchased from TOLSA S.A. with the trade name of *Pangel* was also used as a reaction support. Other characteristics of sepiolite and *Pangel* are described in ref. 19.

Saponite

This clay mineral belongs to the layered 2 : 1 charged silicates, with its octahedral sites mainly occupied by magnesium ions and the electrical charge located in the tetrahedral layers (Si/Al substitutions). The mineral used here, also purchased from TOLSA S.A., is from Vicálvaro (Madrid, Spain) deposits, that contains about 15% of sepiolite. The hydrated exchangeable cations located in the interlayer space are mainly Mg^{2+} and Ca^{2+}. Other characteristics are described elsewhere.[20]

Kaolin

From Asturias (Spain), with a high content in pure kaolinite mineral (>90%). The chemical composition (%) of this 1 : 1 layer aluminosilicate is: SiO_2 = 48.68; Al_2O_3 = 38.40; Fe_2O_3 = 0.15; CaO = 0.012; MgO = 0.049; TiO_2 = 1.05; K_2O = 1.08; Na_2O = 0.011. Specific surface area (BET, N_2): 8.5 $m^2\ g^{-1}$. Quartz content: <5%.

Zeolites

Synthetic (Y-zeolite) in its Na^+ form, was purchased from Union Carbide. Chemical composition (%): SiO_2 = 67.9; Al_2O_3 = 20.6; Na_2O = 8.49. Two natural zeolites: from San Ignacio (zeolite-1) and from La Pita (zeolite-2), Cuba, were also used, and consisted of a mixture of minerals: zeolite-1 (heulandite-clinoptilolite 56%; mordenite 30%; quartz and montmorillonite <5%) and zeolite-2 (heulandite-clinoptilolite 26%; mordenite 10%; montmorillonite 22%; calcite 5,4%).

Oxides

Silica : silica gel 60 (Merck), for column chromatography (220–440 mesh). Alumina (Fluka) for chromatography, type 507 C neutral (100–125 mesh). Iron oxide identified as hematite (α-Fe_2O_3).

Soils

The raw mineral fraction (<200 mesh) of the two soils used was (i) from Toledo (Spain), a calcium luvisol containing 67.5% of sand, 20.1% of slime, 12.4% of clays, and (ii) from Havana (Cuba), an ortic ferralsol containing 18.9% of sand, 22.0% of slime and a 59.1% fraction of clays and iron oxide which is mainly α-Fe_2O_3 hematite representing about 38% of this fraction.

Synthesis of 2,4-D esters

The standard procedure consists in the preparation, as the first step, of a homogeneous mixture of the reagents, *i.e.* 2,4-D and the

Table 4 Comparison between conventional thermal treatment and microwave-assisted synthesis of 2,4-D esters on inorganic solid supports (dry media conditions)

Inorganic support	Alcohol : acid ratio (support : reagent, %)	Conventional heating (*T*/°C)	MW irradiation (power) (%)	Time of treatment	Yield of ester (%)
Silica gel	1 : 1 (50)	—	100	3 min	97
Silica gel	1.5 : 1 (50)	—	100	5 min	93
Silica gel	1.5 : 1 (50)	150	—	4 h	94
Silica gel	1 : 1 (50)	100	—	6 h	90
Zeolite[a]	1 : 1 (50)	—	50	5 min	97
Zeolite[a]	1 : 1 (50)	100	—	4 h	93

[a] Natural zeolite (from San Ignacio, Cuba).

Table 5 Esterification of 2,4-D with isooctyl alcohol using soil as reaction support (1 : 1 alcohol : 2,4-D acid molar ratio and 50% *w/w* soil : reagents)

Soil	Heating method	Yield (2,4-D isooctyl ester) (%)
Luvisol (Toledo)	Conventional heating, 125 °C, 2 h	98
Luvisol (Toledo)	MW irradiation, 7 min	97
Ferralsol (Havana)	Conventional heating, 125 °C, 2 h	95
Ferralsol (Havana)	MW irradiation 5–10 min	<5
Luvisol + 5% Fe_2O_3	MW irradiation 2–10 min	<50

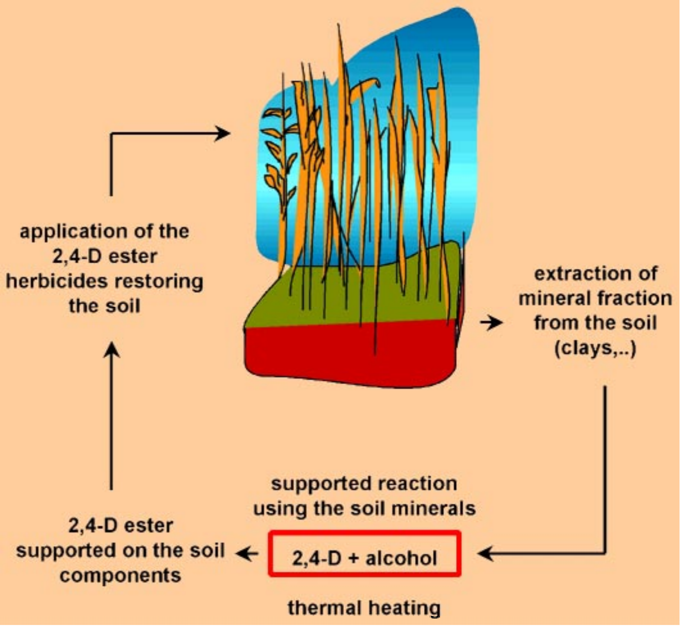


Fig. 3 Methodology proposed for 2,4-D ester synthesis using soil as reaction support.

alcohol (in general isooctanol was used, *i.e.* 2-ethylhexanol), with the inorganic solid as support (support/reagent: 50% *w/w*; typical experiments involve the use of 1 g of solid support). This operation could also be carried out with the assistance of an organic solvent common for both the acid and the alcohol which after impregnation is completely removed in a rotary evaporator. The reaction mixture is heated over variable periods of time (2–6 h) in an oven (100–150 °C). Alternatively, the heating could be carried out by MW irradiation (150–350 W, 3–10 min). The resulting products that remain impregnated on the solid support are extracted with a solvent (methanol, acetone, *etc.*), filtered over microporous alumina and analysed by GC-MS and FTIR. The yields (%) are deduced from the amount of unreacted material remaining adsorbed on the inorganic support.

Apparatus

The experiments using MW irradiation (2450 MHz) were carried out in a domestic Moulinex FM 460 oven. Characterisation of the extracted phases (2,4-D esters) was carried out by GC-MS using a Hewlett Packard 5890 series II spectrometer coupled to a selective mass detector series 5971 equipped with a capillary column (25 m length and 0.20 mm internal diameter), with a stationary phase thickness (methylsilicone) of 0.33 mm. FTIR Nicolet 20SXC spectrophotometer was used (Nujol dispersion or KBr pellets).

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Paper 9/02531F

Photoinduced decarboxylation reactions

Radical chemistry in water

Axel G. Griesbeck,* Wolfgang Kramer and Michael Oelgemöller

Institute of Organic Chemistry, University of Cologne, Greinstr. 4, D-50939 Köln, Germany.

E-mail: griesbeck@uni-koeln.de

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Summary

Intramolecular photodecarboxylation reactions of potassium ω-phthalimido carboxylates in water or mixtures of water and organic solvents (acetone, acetonitrile) were investigated using an incoherent XeCl excimer radiation source emitting at 308 nm. Electron transfer induced *intermolecular* addition of alkyl carboxylates to phthalimides likewise proceeded efficiently under these conditions. The reactions can be performed in multigram (*i.e.* 10–30 g product) quantities using easily available substrates such as glutamic acid (for the synthesis of **3**), leucine (for **8**, **9**) or simple alkyl carboxylates (for **11**). The advantages of this methodology are: clean and high-yielding reactions, solvent and waste minimization, water-based processes and efficient utilization of photons of defined energy.

Introduction

Photons are the environmentally most friendly reagents in chemistry. They can be tuned in order to selectively excite one part of a molecule or a bimolecular entity either by wavelength adaptation or by intensity variation (one- *versus* two-photon chemistry). Another aspect which makes photochemistry attractive is that solar radiation is the source of life on earth and still is the most powerful and productive way to produce organic molecules. Thus, use of this natural energy reservoir to perform chemical reactions would be highly desirable in order to approach the noble goals of sustainable chemistry.

Many photochemical reactions, however, suffer from their very special reaction conditions, *i.e.* the use of a limited number of organic solvents which are photostable during the reaction, low concentrations of substrates, sophisticated substrate and/or product structures, complex product mixtures, special prerequisites for the performance of the reactions (wavelength and filters), *etc*. It is therefore highly desirable to develop photochemical processes which come nearer to 'natural' photochemistry, *i.e.* aqueous media, oxygen tolerable and long-wavelength irradiation. Not all conditions will be reached immediately but a stepwise modification of efficient photochemistry might lead to these goals.

We have investigated in the last decade the photochemistry of N- and C-activated α-amino acids. The motivation for this project was the search for new and efficient amino acid transformations which might be useful additions to known organometallic or electrochemical methods. Concerning the nature of the chromophoric group, one has to take into account that any oligopeptide with *n* amino acid residues has at least $(n - 1)$ chromophoric groups which can be electronically excited under short-wavelength excitation beside the terminal carboxylate. Thus, light must be concentrated and collected into a selective molecular trap, either directly linked to the amino acid (or the peptide) or by energy or electron transfer using external sensitizing agents. Covalently linked chromophores which show highly selective photochemistry include aromatic ketones (C-terminal),[1] pyruvamides (N-terminal)[2] and especially the phthalimide group.[3] The advantages of all these chromophores were as follows: absorption in the 310–350 nm region, rapid intersystem crossing (ISC) to give relatively long-lived triplet excited states, selective activation of proximate C–H bonds (for aromatic ketones or pyruvamides) or photoinduced electron-transfer activity (for phthalimides).

An especially attractive photochemical reaction was discovered when C-unprotected ω-phthalimido carboxylic acids were irradiated. Applied as the free acids, only α-phthalimido carboxylic acids were prone to decarboxylation in a variety of solvents giving rise to the corresponding *N*-alkyl phthalimides.[4] This reaction was successfully applied by Mariano and Yoon for the generation of 1,3-dipoles which were trapped with dipolarophiles.[5] Remote carboxy groups, however, were unreactive under these reaction conditions. A major improvement came with the use of potassium salts of the carboxylates.[6]

Results and discussion

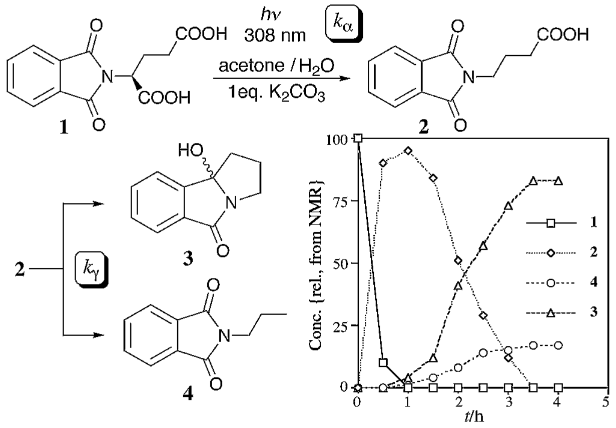
In earlier experiments we used acetone solutions with small amounts of water added in order to improve the solubility of the potassium salt. Actually, higher water concentrations diminished the chemoselectivity, *i.e.* more 'simple' decarboxylation products were formed.[7] Another step forward was made when we found that preparing the potassium salts prior to photolysis made the reaction more selective and even higher water concen-

Green Context

Aqueous photochemistry represents a potentially very interesting technique for the selective and clean transformation of organic chemicals. This contribution outlines the use of photochemistry in water for the highly selective and high-yielding decarboxylation of carboxylic acids, leading to polycyclic compounds. it also contributes to the growing body of organic reactions which can be advantageously carried out using water as solvent (see *e.g. Green Chemistry*, 1999, 1, 167). *DJM*

trations could now be tolerated.[8] The reaction principle is shown in Scheme 1 with *N*-phthaloyl glutamic acid as a model substrate.

NMR spectroscopic investigation of the reaction progress revealed that k_α/k_γ must be higher than 10. This reaction was performed using solely water as solvent in which the bis-potassium salt of the starting material **1** as well as the product mixture was soluble in concentrations up to 0.1 M. In order to optimize also the light source and the geometry of the reactor, we investigated a new setup for photodecarboxylation in aqueous media. As the light source we used a 3 kW XeCl excimer lamp[9] in a falling film apparatus with a 2–5 liter reservoir. This incoherent excimer radiation source emits a narrow line centered at 308 nm and can be used also in an immersion well configuration. About 10% of the electric power is converted into light emission. There is only little heat release and water cooling is sufficient.[10] For conversion of 50 mmol of substrate **1** *ca*. 10 kW h are necessary. The excimer radiation setup is shown in Fig. 1.



Scheme 1

The use of aqueous solvent mixtures or pure water as solvent is advantageous also in the sense that pH measurement could be used as an analytical tool to follow the reaction progress. As shown in Scheme 2 the decarboxylative photocyclization of a 0.05 M solution of the bis-potassium salt **1-K$_2$** in water can be monitored by pH which starts at 6.4 and levels off at 7.45.

Two other photocyclization reactions which involve the formation of CO_2 were also investigated under the reaction conditions described above: the macrocyclization of substrate **5** to give the twelve-membered annulated amide **6**[7] (Scheme 3) and the cyclization of the anthranilic acid derivative **7** to give the isoindolo benzodiazepine **8**.[11] Both reactions proceeded smoothly when performed with mercury low pressure lamps (phosphor coated with an emission maximum at 300 nm) in acetone solutions. Relatively long irradiation times were needed to run the reaction to complete conversion (*ca*. 20 h for 5 mmol conversion using 800 W mercury low pressure lamps).

In contrast to this, 3 kW XeCl excimer irradiation gave complete conversion of 50 mmol of **5** in 2 liter of water after only 4.5 h. In a first experiment, 200 ml of acetonitrile were added in order to solubilize the substrate; however, the product precipitated during photolysis. In order to circumvent the use of organic solvents, we irradiated a suspension of **5-K** in water and produced a suspension of **6** in water. Workup of the reaction mixture was extremely easy: after evaporation of 75% of the solvent, the product precipitated and was isolated by filtration in 82% yield. The purity of **6** was even higher than that from 'traditional' irradiation.[7]

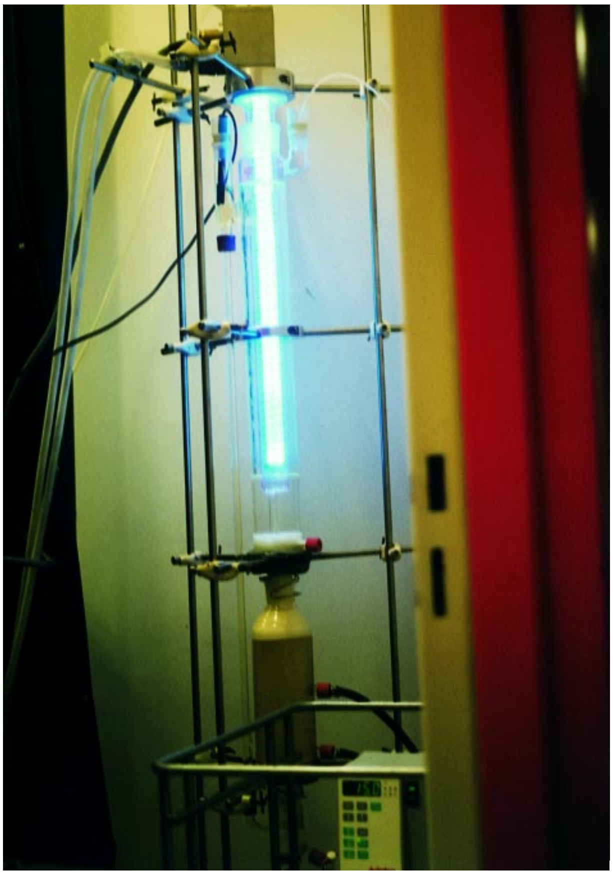
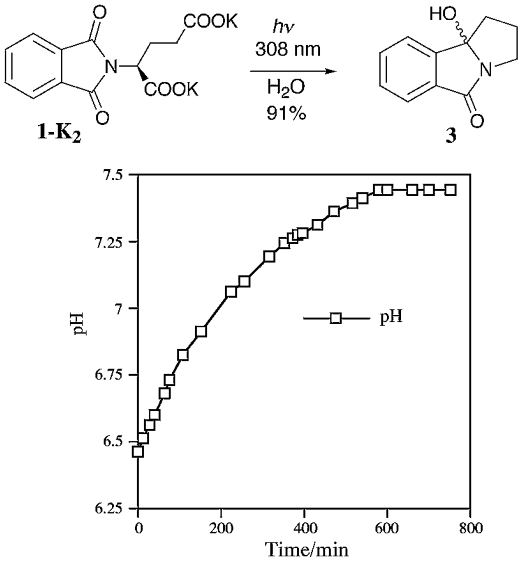
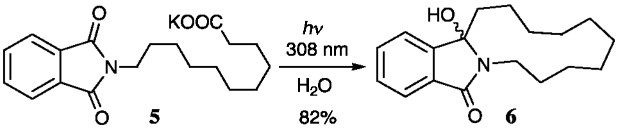


Fig. 1 Excimer radiation reactor: falling-film configuration with pH control (left) and N_2/Ar inlet

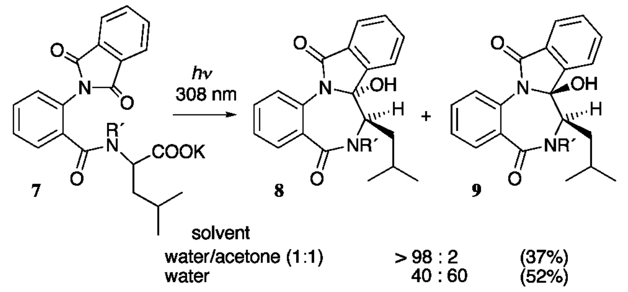


Scheme 2



Scheme 3

A highly surprising result was obtained with the anthranilic acid-based substrate **7**: when irradiated in water–acetone mixtures selectively the *trans*-diastereoisomeric cyclization product **8** was formed from **7-K**, whereas irradiation in pure water led to a 60 : 40 mixture of *trans*- and *cis*-isomers **8** and **9** (Scheme 4).



Scheme 4

Obviously, an increase in solvent polarity and protic conditions favor less tight donor–acceptor structures which lead to less stereoselective C–C coupling reactions. The yield was strongly enhanced from 37% to 52% when switching from solvent mixtures to purely aqueous conditions.

Also intermolecular addition reactions could be performed in aqueous media, *e.g.* the photodecarboxylative addition of potassium isobutyrate to *N*-methylphthalimide **10** (Scheme 5).[12] This reaction proceeded smoothly in a 3 : 1 (vol%) water–acetone mixture using 6 equivalents of alkyl carboxylate and a 0.02 M solution of **10**. The reaction progress was monitored by continuous pH control and gas chromatographic determination of the substrate/product ratio. The pH change for this reaction was similar to that for the intramolecular photodecarboxylations described above: the initial pH value was 6.66 and the final value 8.02. Until *ca.* 80% conversion of **10** the reaction progress was linear which indicates a pseudo-first order reaction with the alkyl carboxylate as an excess component (which seems not be consumed other than by radical addition). On the other hand, the pH/time correlation showed sigmoidal behaviour in contrast to the intramolecular reactions. This unusual behaviour can be rationalized by assuming a competition between radical addition and catalytic decarboxylation with the formation of Kolbe products which has been already shown for 1-adamatane carboxylic acid.[12]

In summary, intra- and intermolecular photodecarboxylation is a versatile method for radical addition reactions and proceeds efficiently in water by using XeCl excimer based technology. These processes minimize the use of toxic solvents and of organic waste materials.

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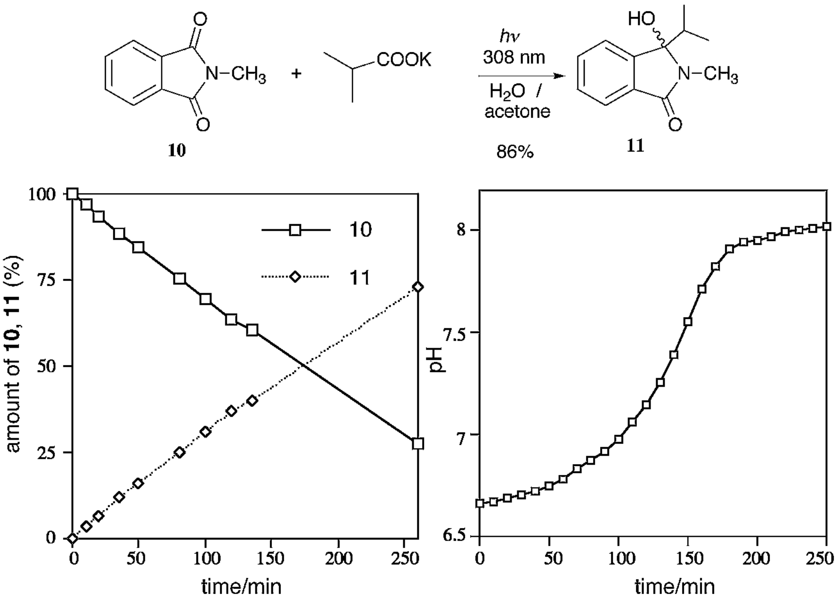

Scheme 5

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