EDITORIAL

International Symposium on Green Chemistry

The first *International Symposium on Green Chemistry* organised by the Royal Society of Chemistry and the Green Chemistry Network was held in Swansea, Wales in April 2001. The 'international' in the title was nicely reflected by the representation which included many delegates from the USA, Africa, Japan, Russia, India, Australia, Israel and Iran, as well as from Europe. The programme was put together with the intention of broadening the scope of the coverage from green chemistry to include green chemical engineering and technology, and educational issues—this worked very well. Thus while we were able to enjoy cutting edge research lectures from a number of distinguished chemists including Professor B. Trost (USA), Professor M. Poliakoff (UK), and Professor H. van Bekkum (The Netherlands), we also had presentations on energy analysis (J. Dewulf, Belgium), microreactors (K. F. Jenson, USA) and life cycle assessment (A. Azapagic, UK), as well as ones covering green chemistry education in Italy (A. Perosa, Italy) and teaching environmental chemistry in a sociotechnological context (V. Zoller, Israel).

The applied nature of green chemistry was illustrated by a number of very interesting presentations from industry. These included 'Biocatalysis from an Environmental Perspective' (A. Zaks, USA), 'Decolorable Printing Inks Suitable for Effective Paper Recycling' (S. Nachida, Japan) and 'Improving Routes to Improving Polymers' (P. Williams, UK).

The breadth of the conference and its participants was further illustrated by a presentation from Dr Warhurst of Friends of the Earth and Dr Anastas of the White House Office of Science and Technology Policy.

The final session in the symposium was dedicated to award-winning academics and industrialists. This started with a remarkable lecture from the 2001 Academic US Green Chemistry Presidential Challenge award winner Professor C.-H. Wong on 'Chemo-enzyme Approach to Carbohydrate-based Drug Discovery'. Three presentations by the first UK Green Chemistry Awards winner followed this: 'Novel Recyclable Catalyst for Atom Economic Aromatic Nitration' (C. Braddock) (*Green Chem.*, 2001, **3**, G26), 'Super-efficient Dyes for the Coloration of Cotton, the Procion XL+ Range' (W. J. Ebenezer) and 'Oxazolidine Diluents: Reacting for the Environment' (J. Peel) (*Green Chem.*, 2001, **3**, G40).

Where next? Green chemistry has come a long way since the first Gordon Conference 5 years ago and it is now prominent in many national and international conferences. However, we believe that there is a need for a major international conference series. I am delighted that preliminary discussions on this are now underway involving some of the major green chemistry organisations in the world and we can look forward to hearing their decision later this year.

James Clark
York, March 2001

Highlights

Duncan Macquarrie reviews the latest research in green chemistry

Selective nucleophilic substitution

The nucleophilic aromatic substitution of hydrogen (NASH) is a very important option in the synthesis of aromatic compounds. Nucleophilic aromatic substitution requires the formal elimination of X^- from the intermediate complex and, not surprisingly, halide and nitrite are favoured. This requires chlorination and nitration, to give the leaving group, processes which are rarely selective.

The elimination of hydride, while attractive from an environmental point of view, is not a realistic option. NASH allows the elimination of hydride, by oxidatively removing the hydrogen, avoiding the halogenation and nitration steps. The group led by Illuminada Gallardo from the Universitat Autonoma de Barcelona have studied a particularly interesting electrochemical oxidation system (*Chem., Eur. J.*, 2001, **7**, 1759). They have carried out some mechanistic work, which has helped to unravel the mechanism of these reactions, and which they have then applied to the cyanation of aromatics. Yields were good with a wide range of substrates, and selectivity excellent, with no other products being detected.
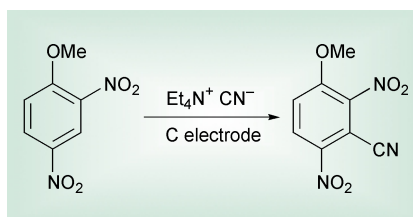

Oxidations

The clean oxidation of secondary alcohols continues to be a challenge. Bimal Banik and colleagues from the Anderson Cancer Center at the University of Texas have provided a novel method for this transformation, which uses oxygen as the stoichiometric oxidant (*J. Chem. Res (S),* 2001, 28). In their system, they employ iodine as catalyst, under microwave conditions. 20mol% iodine was enough to obtain yields, typically >75% in 6–8 minutes in air. The authors speculate on the mechanism, which is not entirely clear, but conclude that the iodine oxidised the alcohol, followed by

oxidation of the HI formed to iodine and water by oxygen.
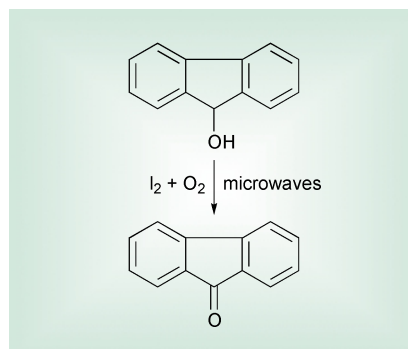
Sir John Meurig Thomas and Robert Raja of the Royal Institution and Cambridge University have published a Feature Article covering some of their work on the selective oxidation of a range of substrates using heterogeneous catalysts (*Chem. Commun.*, 2001, 675). They describe the design of porous oxide-based catalytic systems for the oxidation of hydrocarbons such as cyclohexane, hexane and alkylaromatics, as well as other work including supported ferrocene-based enantioselective catalysts.
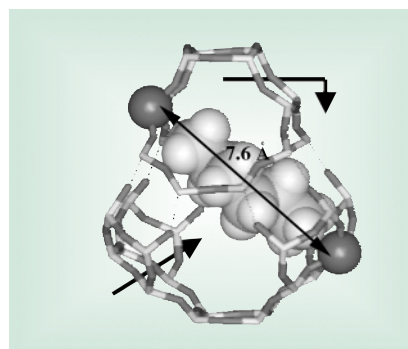

Transesterification

In the last *Highlights*, a paper on the use of metal alkoxides as transesterification catalysts was reported. Now the group led by B. P. Bandgar has reported the use of zinc dust as an efficient and general catalyst for the transesterification of β-ketoesters (*J. Chem. Res (S),* 2001, 16). *t*-Butyl esters can be prepared in reasonable yields, something which is generally difficult to achieve, primary

and secondary alcohols give yields of ≥88%, and allylic alcohols can also be used with reasonable efficiency. The zinc dust can be recovered by filtration, but no data relating to reuse was presented.
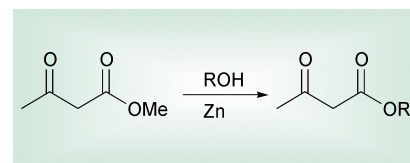
Selective electrophilic substitution

The functionalisation of aromatics by electrophilic substitution is one of the most studied reaction systems, with significant challenges remaining in the replacement of homogeneous acids such as aluminium chloride and HF with more benign catalysts, and attempts to control selectivity. One of the more fruitful areas has been the use of zeolites to promote *para*-selectivity in a range of articles (see for example *Green Chem.*, 1999, **1**, 35, 75, 83). However, the Friedel–Crafts reaction is generally considered to be worthless for the formation of *meta* isomers of aromatics, unless they are particularly electron-deficient. In a remarkable paper by Hendrikus van Herwijnen and Udo Brinker of the University of Vienna, just this sort of selectivity is found (*J. Org. Chem.*, 2001, **66**, 2874). They used a faujasite zeolite to dimerise benzyl chloride, with the logic being that the confinement in the pore structure of the zeolite would suppress the extensive polymerisation found in homogeneous systems. This was indeed the case, but the authors found that the isomer mixture obtained was surprisingly rich in *meta* isomer, with up to 65% of the product being *meta*. The authors ascribe this reversal of selectivity to the
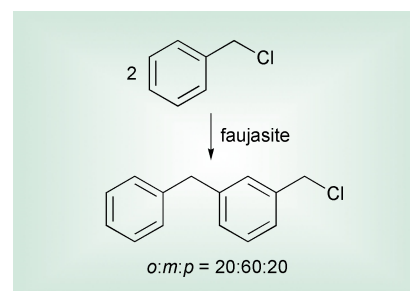
unusual "banana-shaped" cavities of this particular zeolite. How general this phenomenon is remains to be seen, but the changes from homogeneous phase are substantial.

Aryl amine synthesis

Clean methods for the preparation of aryl amines are being sought to replace the old tin-based methods, and improve on the more recent palladium-catalysed routes. Mayssam Ali and Stephen Buchwald of MIT have published their results concerning the Pd catalysed amination of aryl iodides (*J. Org. Chem.*, 2001, **66**, 2560). They found that the use of the biaryl ligand shown and NaO*t*-Bu as base is an excellent combination for many functional aryl iodides and aryl amines. Yields approach quantitative in most cases. In order to extend the reaction to include a wider range of functional groups, they also found that replacing the alkoxide base with cesium carbonate allowed a wider range of functionality to be incorporated, including esters, ketones and nitriles, with yields ranging from 62–91%.
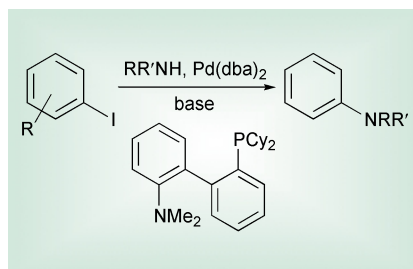

Solvents

The search for alternative solvents encompasses ionic liquids and supercritical fluids, but it is important not to lose sight of new "conventional" solvents. Diethoxymethane (DEM) is one such solvent, which has now been commercially available for a short period. It has a good liquid range (–66 °C to 88 °C) relatively low toxicity, and is immiscible with water. Some of its benefits have been reported in a paper by Neil Boaz and Bhaskar Venepalli of Eastman Chemical Company in Tennessee (*Org. Proc. R and D*, 2001, **5**, 127). They describe the solvent as being superior to THF and dichloromethane in organometallic reactions and phase transfer applications. The solvent is hydrophobic; it thus does not need to be dried, and can be very easily separated from water and recycled. It is stable to bases, does not form peroxides as easily

as some other ethers, and even has some stability towards mild aqueous acids.
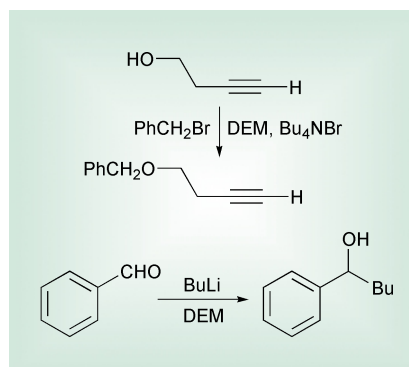
The addition of CO_2 to propylene glycol has been studied using ionic liquids as catalyst and solvent. Jiajian Peng and Youquan Deng of the Chinese Academy of Sciences in Langzhou have shown that the reaction is highly efficient and the solvent recyclable in a straightforward process (*New. J. Chem.*, 2001, **25**, 639). They showed that, using BMIM BF_4^- (BMIM = 1-*n*-butyl-3-methyl imidazolinium) as solvent and catalyst, CO_2 would add very efficiently to propylene oxide, giving the carbonate in high yield in an autoclave under modest CO_2 pressure. Release of the CO_2 followed by distillation gave the product and the solvent, which could be used directly for a further batch.
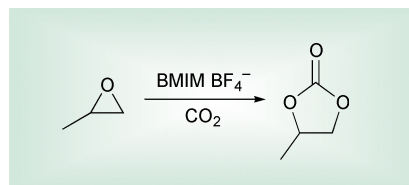

Asymmetric synthesis

The use of simple chiral ligands and auxiliaries was mentioned in the last *Highlights*, and the use of phase transitions to drive equilibria has also been described recently in *Green Chem.*, 2000, **2**, 49. Now a group of workers from DSM Research Life Sciences in Groningen, led by Quirinus Broxterman has published details of the asymmetric Strecker synthesis of amino acids using a combination of a simple chiral auxiliary and selective crystallisation to drive equilibria selectively to the desired product (*Org. Lett.*, 2001, **3**, 1121). They use (*R*)-phenylglycine amide, along with a ketone and HCN to produce the Strecker intermediate as a pair of diastereoisomers. Only one of these is

soluble in the reaction solvent (aqueous methanol or even water) and the other precipitates selectively. The soluble diastereomer re-equilibrates and the precipitation of one of the two drives the reaction to completion, and the formation of one diastereoisomer in >99% selectivity. This is then converted to novel amino acids using known methods.
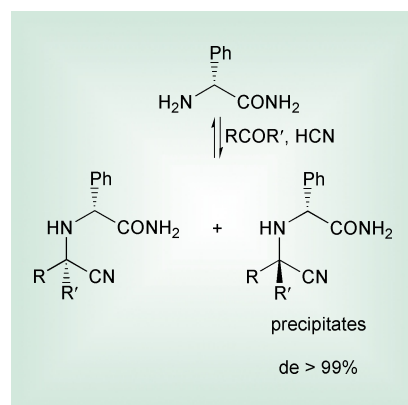
Hydroformylation

Hydroformylation is a relatively clean method for the production of aldehydes, and has been the subject of intense efforts recently. One of the latest describes research aimed at the functionalisation of acrylates, rather then the usual simple alkenes. Jianliang Xiao and co-workers at the Leverhulme Centre for Innovative Catalysis in Liverpool and at the University of Leicester have published details of the use of supercritical CO_2 in the hydroformylation of alkyl acrylates, highly functional compounds, useful as intermediates in organic chemistry (*Chem. Commun.,* 2001, 725). They show that, using rhodium catalysts coupled

NEWS & VIEWS
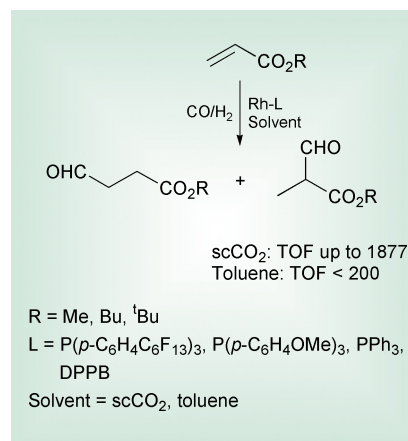
with fluorinated phosphine ligands, the hydroformylation proceeds in excellent selectivity, with turnovers an order of magnitude higher than in conventional solvent systems.

Materials chemistry

While the majority of chemistry reported as green relates to organic synthesis, materials chemistry is also an area where the same principles apply, and which is experiencing a time of remarkable and exciting growth (see, for example, *Green*

Chem., 1999, **1**, 169; 2000, **2**, 79; 2000, **2**, 93). Guanghou Wang and co-workers at Nanjing University have developed a remarkably simple and clean route to copper oxide nanorods, useful as sensors and in semiconductor applications (*Chem. Commun.*, 2001, 727). They found that copper chloride and sodium hydroxide could be simply ground together in the presence of PEG 400, following by washing and recovery of the PEG, resulting in copper oxide nanorods, without high temperatures or prolonged reaction periods. Typical dimensions of

the wires were 8 nm across and up to 400 nm long.

100 nm
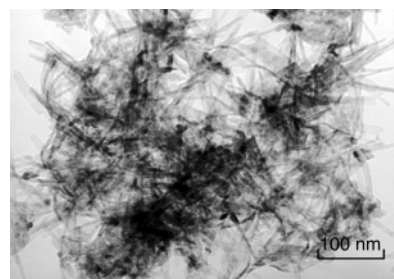
NEWS

Green Chemistry Network Symposium

The next Green Chemistry Network symposium will be held on 26 September 2001 at the University of Strathclyde in Glasgow, UK. The Keynote speaker will be Professor Stan Roberts from the Department of Chemistry, University of Liverpool whose presentation will be entitled 'Biotransformations using Natural and Non-natural Catalysts'.

If you would like to attend the symposium, please contact Dr Helen Coombs, Green Chemistry Network, University of York, Heslington, York YO10 5DD, UK. Tel/Fax: + 44 (0)1904 434550. Email: greennet@york.ac.uk

Emerging technologies—sustainable development

The 1st Binational RSC/SACI International Conference on Organic Chemistry was held at the University of Cape Town, South Africa (http://www.uct.ac.za) in January 2001. This outstanding meeting, chaired by Professor J. R. Bull, included a post-conference workshop on emerging technologies at which one presentation was by Professor Keith Smith, University of Wales Swansea, UK, on 'Sustainable Development.'

In particular, Professor Smith described work taking place in his laboratories on electrophilic aromatic substitution with zeolites:
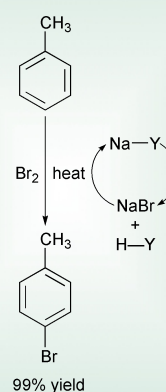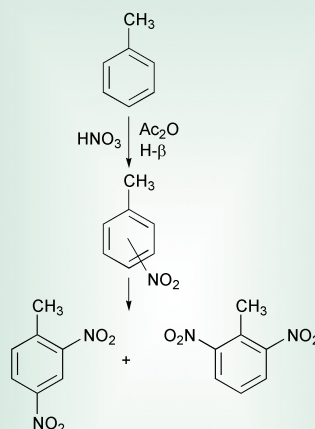
SELECTIVE DI-TERT-BUTYLATION OF NAPHTHALENE
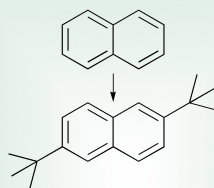
Catalyst	HM
naphthalene conversion (%)	96
DTBN (%)	61
2,6-BTBN (%)	60
2,6/2,7	50.6

(K. Smith and S. D. Roberts, *Catalysis Today*, 2000, **60**, 227)

DIRECT, NEAR-QUANTITATIVE DINITRATION OF TOLUENE

99% overall yield 70:1
ca. 3% of other isomers
isolated yield 90% with 99% purity
(K. Smith, T. Gibbins, R. W. Miller and R. Claridge, *J. Chem. Soc., Perkin Trans. 1*, 2000, 2753)

REGIOSELECTIVE BROMINATION OF AROMATICS

99% yield

HIGHLY REGIOSELECTIVE NITRATION OF AROMATICS
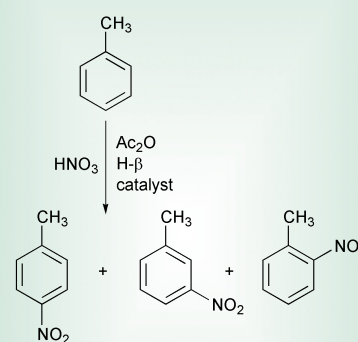
- Yield of *para* product ca. 80%
- Only byproduct (acetic acid) easily recovered
- H-β catalyst reused several times
- No washing required
- Distillation costs (fuel) reduced

A Powerpoint file of Professor Smith's slide presentation is available as Electronic Supplementary Information (ESI) at http://www.rsc.org/suppdata/gc/b1/b103992j/

Further details on Professor Smith's work can be found in *Green Chem*., 2001, **3**, G13.

Green Chemistry Stall

The Green Chemistry Stall at the Royal Society's summer exhibition 2001 will be a multifaceted view of the progress of Green Chemistry. The growing interest in Green Chemistry will be illustrated through the work of the Green Chemistry Network, both in the UK and abroad. A video will be screened throughout the day highlighting the chemical industry as it is now, current research and the future 'greener' chemical industry. The heterogeneous catalysis work carried out here at York in the Clean Technology Centre will be represented by video, posters and interactive models to demonstrate the nature of catalyst surfaces. The value of collaboration between chemistry and chemical engineering will be demonstrated through a working model of a novel catalytic reactor. We hope that the stall will have something to offer for visitors of all ages and of all backgrounds.

Reducing the use of organic solvents

US Department of Agriculture (USDA) Agricultural Research Service (ARS) scientists in Peoria, Illinois, USA, are coupling two environmentally friendly techniques to reduce or eliminate the use of toxic organic solvents in the processing of agricultural commodities. The U.S. Environmental Protection Agency has called for a reduction in the amount of toxic solvents released into the environment, which has impacted industrial manufacturers.

Solutions called ionic liquids, salt-like fluids at room temperature, are safer to use than organic solvents like hexane in research laboratories, according to ARS biochemist Joseph A. Laszlo at the National Center for Agricultural Utilization Research in Peoria. In the past, researchers had to use solvents to get enzymes to act as a catalyst for chemical reactions. Now, ionic liquids can be used in place of solvents.

Laszlo and ARS chemist David L. Compton made ionic liquids in their laboratory. They are the first researchers to perform enzymatic reactions in ionic liquids in combination with supercritical CO_2. They tested the liquids as a solvent for the enzyme chymotrypsin with a commonly used laboratory substrate. This enzyme may catalyze reactions needed to manufacture important chemical ingredients in drugs and skin care products.

Laszlo says that combining ionic liquids and supercritical CO_2 results in a superior processing method, which is better than either one alone. In the technique, CO_2 is heated and compressed to the point that it becomes both liquid and gas, which is the supercritical state.

Laszlo reported these findings at the 221st annual meeting of the American Chemical Society meeting in San Diego, April 1–5, 2001, where he participated in a 5-day symposium on the development of ionic liquids.

New Faraday for a greener chemical industry

A Government funded multi-partner initiative for a 'Greener Chemical Industry' has recently been established in the UK. The initiative is funded under the Faraday Partnership programme which provides funding for research, training, networking and technology translation.

The partnership, called CRYSTAL will be administered by the Institution of Chemical Engineers with the Royal Society of Chemistry and the Chemical Industries Association being the other hub partners. Other CRYSTAL partners include 18 academic institutions, 8 companies and 12 other networks and similar organisations representing most of the UK chemical industry. CRYSTAL's mission is to become the lead UK body, for the research, development, implementation and promotion of green chemical technology and practices, by leveraging and synergising the resources of all the partners for the benefit of the UK chemical industry.

CRYSTAL's major objectives are:

- *Technology transfer*: use CRYSTAL's experienced Technology Translators, TCS, and partner organisations to promote the widest uptake of existing, emerging and future technologies.

- *Strategic research*: develop step change green chemical technology and practices through industry identified core research programmes bringing together innovative chemistry and chemical engineering and other relevant disciplines (biotech, IT) in new collaborative partnerships.

- *Training*: develop and run both inter and intra company courses (including MRes and PhD) for postgraduate chemists and chemical engineers,
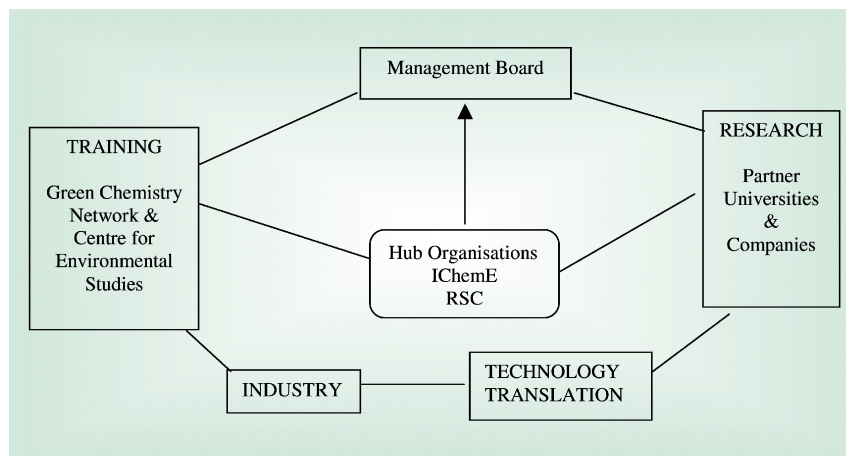
CRYSTAL structure

industry technologists and business managers. This will enable the culture change to allow future research and development work to be undertaken in a more eco-efficient and competitive way.

• *Awareness/Best Practice*: increase the awareness in industry, government and academia of opportunities for developing sustainable products and processes.

Initially the main focus of research will cover:

• *Metrics:* given the complexity of the concept, there is a recognised need for a set of metrics to underpin the paradigm shift implied by sustainable development by providing operational guidelines. The overall objective is to develop and test a comprehensive set of sustainable development metrics, from which specific sectors and companies can identify and use the metrics with most significance for their particular businesses.

• *Catalysis:* the prime route to chemical manufacturing processes with the required degree of selectivity, energy efficiency and atom economy is to develop new catalytic systems. This approach offers the best way to avoid stoichiometric reactions, use of protection for sensitive functionalities, and employing hazardous or toxic reagents. Significant emphasis will be placed on enhancing the ease of recovery and reuse of both homogeneous and heterogeneous catalytic systems of proven activity and selectivity

• *Eco-efficient solvents*: VOC's remain a key issue for most chemistry-based industries and eco-friendly solvent alternatives for many processes and product formulations are required. Many classical reactions still employ 'unfriendly' solvents such as dichloromethane, acetone or dimethylformamide and a 'toolkit' of alternatives is required which are cost effective, have ease of handling and are recyclable. This toolkit of solvents is likely to include supercritical fluids, biphasic systems, ionic liquids, bio-solvents as well as solvent free technologies. Each of these provides challenging scale-up, cost and supply issues which need to be overcome before they will be more widely adopted by industry.

• *Alternative feedstocks:* the potential for using crops as a chemical feedstock is huge, but largely untouched due to barriers such as cost, quality and availability. For example a recent IENICA report suggests that at least 12.5% of the EU solvents market (currently 4 million tpa) could be supplied from bio-based sources; the current figure is less than 1.5%. Initial processing can account for much of the costs, hence by developing innovative, clean extraction and separation technologies the cost of the raw chemical feedstocks can be significantly improved, facilitating wider use.

• *Energetic chemistry:* CRYSTAL will systematically explore alternative ways of introducing energy into catalytic chemical reactions in ways which use it most cleanly and effectively. In particular many of the problems associated with waste in chemicals manufacture could be avoided if electrons could be used to drive the processes. Small scale reactors, easily replicated for scale out of manufacturing, are available: the keys are (i) to find electrodes capable of enacting the desired chemistry and (ii) to expand the culture of synthetic and manufacturing chemists to include electrochemistry

• *Reaction engineering:* All the above areas require underpinning by innovations in reaction engineering. In particular significant environmental and cost benefit are to be realised from the redesign of conventional reactors to accommodate new and existing technologies. Through obtaining a more thorough understanding of reaction kinetics reactors can be designed to take advantage of the underlying chemistry leading to more efficient processes.

Much of the training will be provided by the Green Chemistry Network at York and the Centre for Environmental Studies at Surrey. Emphasis will be placed on meeting industry requirements and will include training on general aspects of Green Chemical Technology as well as specific technologies.

A particular important aspect of CRYSTAL is technology translation. Initially process types and industry sectors will be road-mapped to identify best practice and identify gaps. Technology translation will also be required to convert the outcomes of the research process into useful technology and to transfer this technology to a cross-section of industry.

Apology

We wish to offer our apologies to Dennis Curran and Zhiyong Luo for allowing the Feature article on 'Fluorous techniques for the synthesis and separation of organic molecules' (*Green. Chem.*, 2001, **3**, G3–G7) to be published without being being checked by the authors. We very much regret the embarrassment and inconvenience that this has caused the authors. Revised procedures should prevent any similar occurrence in the future.

A W A R D

Oxazolidine diluents: reacting for the environment

Neil G. Carter, Research & Development Manager, describes the work at Industrial Copolymers Ltd† which won the industrial category of the UK Green Chemistry Awards, 2000

Introduction

Over the last decade, there has been a considerable transformation in the solvent-borne industrial coatings market. Major developments have taken place in water-based coatings technology, which has now expanded from the consumer housepaint market into industrial sectors. Increasingly stringent volatile organic compounds (VOCs) regulations have led to the development of a more viable water-based alternative to solvent-borne technology. However, some limitations still exist, particularly with the key characteristics of chemical and abrasion resistance in coating performance.

Alongside the advances in water-based technology, has been the development of high-solids coatings. These are usually formulated with lower-molecular-weight components to achieve the lowest possible viscosity with the minimum use of solvent. However, there is a limit to molecular weight reduction, as this can lead to problems associated with loss of coating performance.

An example of a market that has seen the trends as described above is 2-pack polyurethane OEM coatings. Typically, these systems are comprised of an acrylic (or acrylic and polyester) polyol and an HDI-based polyisocyanate (usually biuret or trimer). These form polyurethanes possessing unique performance properties including excellent chemical resistance and weather exposure, as well as good abrasion resistance.

One possible solution to maintaining the coating benefits of solvented systems, whilst reducing the VOC, is to incorporate a reactive diluent. Incozol LV[1], a low viscosity bisoxazolidine reactive diluent, has been specifically designed to achieve high performance coatings compliant with even the strictest environmental legislation.

Incozol LV: reactive diluent

Incozol LV (**I**) is a low-viscosity bisoxazolidine designed as a co-reactant in polyurethane coatings to achieve low VOC levels. Incozol LV is comprised of two oxazolidine rings (five-membered heterocyclic rings containing nitrogen and oxygen) linked by a carbonato bridge, which affords low viscosity by restricting intermolecular hydrogen bonding.

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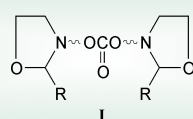
† Industrial Copolymers Limited, PO Box 347, Primrose Hill, London Road, Preston, UK PR1 4LT.

Incozol LV has the ability to reduce the viscosity of the polyol component of the 2-pack system in which it should be incorporated, in a similar way to solvent (Fig. 1).
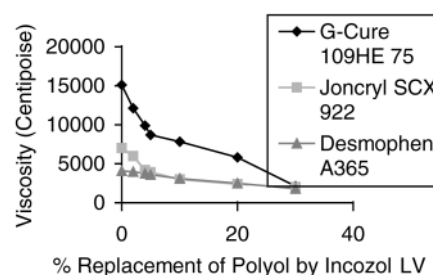

Fig. 1 Viscosity-reducing effect of Incozol LV.

Incozol LV possesses key properties demanded of a good reactive diluent,[2] namely:

- Good polyol and solvent compatibility
- Low intrinsic viscosity: 50 mPa at 20 °C
- Reasonably high equivalent weight: 90 (functionality of 4)
- Low colour (essential for clear lacquer finishing)
- Workable pot life and cure response
- No adverse effect on coating properties (including film hardness development and resistance, gloss and weathering properties)

Chemistry of oxazolidine diluents

Activation of oxazolidine reactivity with polyurethanes : ring opening hydrolysis reaction

The ability of Incozol LV to co-react into the polyurethane backbone of the coating is activated by the ring opening hydrolysis of the two oxazolidine rings, resulting from the reaction of water present as moisture contamination in both the solvent and polyol components. Moisture in the atmosphere during spraying application also aids the activation of the oxazolidine rings. Consequently, the inclusion of Incozol LV has the dual benefit of scavenging moisture, as well as lowering the VOC. Polyurethane coatings can be adversely affected by moisture, through the reaction of water with the polyisocyanate component, forming carbon dioxide gassing. This can often result in pinholing defects in the coating or hazing problems with clear lacquer finishes. Hence, pre-mixing Incozol LV with the polyol and solvent component to scavenge the moisture prior to polyisocyanate mixing is clearly an advantage towards improving the coating. Indeed, repeated opening of containers will serve to further activate the oxazolidine prior to hardener (polyisocyanate) mixing.

Activation of Incozol LV results from the hydrolytic ring opening of the oxazolidines yielding hydroxyl and amino

functionalities on each ring. Consequently, with Incozol LV, four sites (two hydroxyl and two amino) are available for reaction with polyisocyanate (Scheme 1).
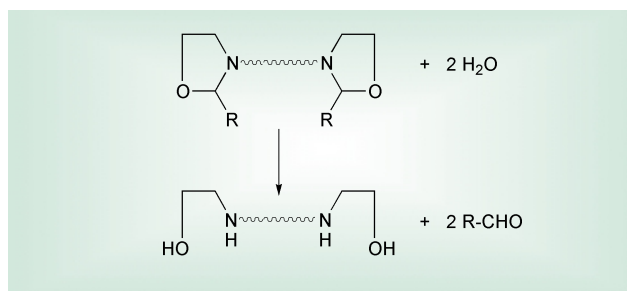
**Scheme 1** Hydrolysis reaction ring opening Incozol LV.

Recently, research has been conducted in conjunction with the University of Central Lancashire in Preston, UK[3], to determine quantitatively the hydrolysis reaction, both from the point of view of extent and rate of hydrolysis. Practically, this has been achieved by determining the concentration of residual Incozol LV (if any) detectable using gas chromatography, with respect to the amount of water added in different stoichiometric mixes of Incozol LV and water. Furthermore, the rate of hydrolysis has been studied by following the residual Incozol LV depletion with respect to mixing time.

The extent of hydrolysis (Fig. 2), indeed the driving force for reacting the diluent, indicates that Incozol LV is almost completely ring opened and available for reaction with isocyanate after only 30 minutes mixing; 15% residual Incozol LV is detected when a stoichiometric amount of water was mixed with the oxazolidine. At 0.5 moles of water, which would represent a more typical level of water present in polyol and solvent components, a majority (about 80%) of Incozol LV has been activated after six hours mixing. This indicates that some interaction with atmospheric moisture must also contribute to the oxazolidine ring opening.
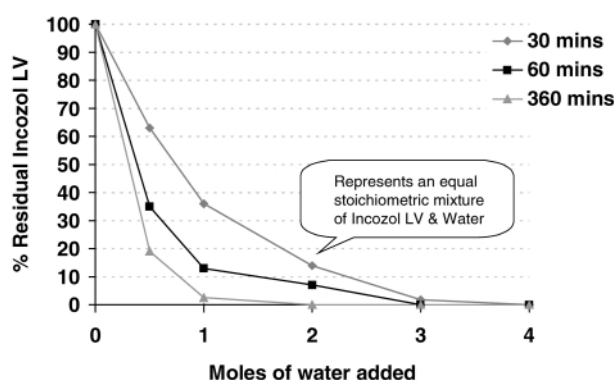
**Fig. 2** Extent of hydrolysis of Incozol LV.

The rate of hydrolysis (Fig. 3) for 0.5 moles of water showed a large proportion of oxazolidine activated by the water present initially in the mixture. The rate of hydrolysis then declined as Incozol LV was consumed by the atmospheric moisture. After 12 hours the oxazolidine ring has fully opened and the amino alcohol generated is fully available for reaction with polyisocyanate.
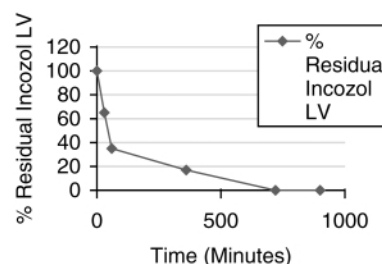
Fig. 3 Rate of hydrolysis for 0.5 moles of water.

Reaction of ring opened oxazolidine (aminoalcohol) with polyisocyanate

Once activation of Incozol LV has been completed, the aminoalcohol generated is then available for reaction into the polyurethane backbone. This takes place through the formation of urea couplings formed from isocyanate reaction with the secondary amine sites and urethane linkages *via* the terminal OH groups (Scheme 2).
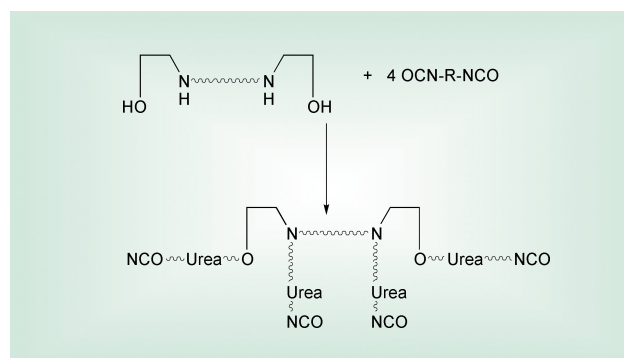
**Scheme 2** Reaction of Incozol LV with isocyanate.

A second study[4] by the University of Central Lancashire examined the interaction of the aminoalcohol with HDI polyisocyanates (Tolonate HDT™) using Fourier Transform infra-red spectrophotometry (FTIR). Incozol LV was added to a large excess of Tolonate HDT™ (20% w/w Incozol LV to 80% w/w Tolonate HDT™). Quantitative FTIR analysis in absorbance mode of the depleting NCO peak was performed for the following reaction combinations:

- Tolonate HDT™
- Tolonate HDT™ + water
- Tolonate HDT™ + Incozol LV
- (Incozol LV + water) + Tolonate HDT™

N.B. - Tolonate is a trademark of Rhodia Ltd.

Differences in NCO peak depletion, at different mixing times up to 150 minutes, with respect to the mix combinations, was compared to determine the influence of the ring opened Incozol LV (Fig. 4).

It was discovered that 40% of the available isocyanate was consumed immediately on addition of Incozol LV (Fig. 7). Addition of a small quantity of water did not greatly increase the extent of reaction with isocyanate. Since reaction mixtures were exposed to the atmosphere during mixing, the results suggest that water activates the oxazolidine ring opening, in preference to the reaction with isocyanate. This is a fair assumption, since no bubbling (resulting from the formation of CO_2 from the isocyanate–water reaction) was observed on incorporation of Incozol LV. The amount of Tolonate HDT™
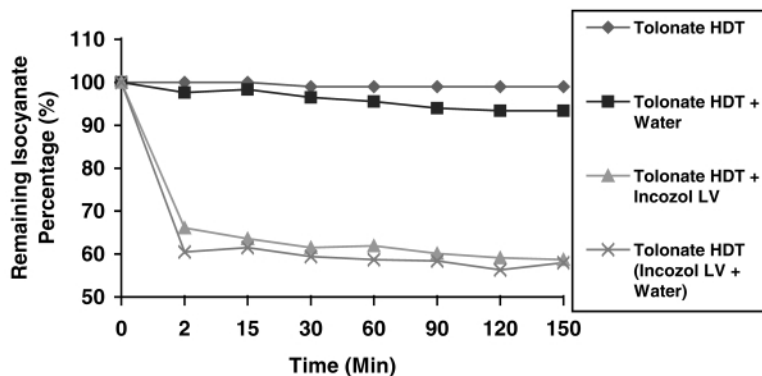
Fig. 4 Reduction in isocyanate percentage for 80:20 w/w Tolonate HDT: Incozol LV at ambient temperature. *Note 1* - Constant Mix Ratio Tolonate HDT: Incozol LV 80% : 20%. *Note 2* - Water content, where added, is equivalent to one quarter of the stoichiometric amount of Incozol LV

consumed represents the maximum concentration that can react with Incozol LV at the chosen mix ratio, with the residual Tolonate HDT™ being the reaction excess.

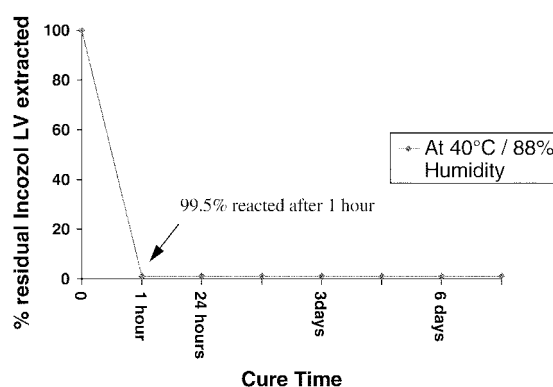## Incorporation of Incozol LV into 2-pack polyurethane coatings

Having demonstrated the reactivity of activated (ring-opened) oxazolidine with polyisocyanate, a further study[5] was conducted to determine the practical implications of isocyanate reactivity in 2-pack polyurethane lacquers. This involved investigating how much Incozol LV is reacted into a 2-pack acrylic/polyurethane lacquer formulation, Desmophen A365/Desmodur N3390, throughout the duration of film curing. The amount of unreacted Incozol LV was quantitatively determined by gas chromatography of a Soxhlet extract of the film. The amount of Incozol LV incorporated into the polyurethane backbone can be calculated by subtracting the result from the known concentration of Incozol LV in the formulation. Extraction of Incozol LV was performed on films cured for 0 hours (uncured), 24 hours, 48 hours, 72 hours and 1 week.

N.B. - Desmophen / Desmodur are trademarks of Bayer PLC.

At 22 ˚C/23% humidity (Fig. 5), almost complete reaction of Incozol LV into the lacquer was observed after 2 days curing the film. At a higher temperature (40 ˚C) and humidity, (88%) (Fig. 6) incorporation of the oxazolidine was a much faster process, with very little (0.5%) Incozol LV extracted from the film after only 1 hour.
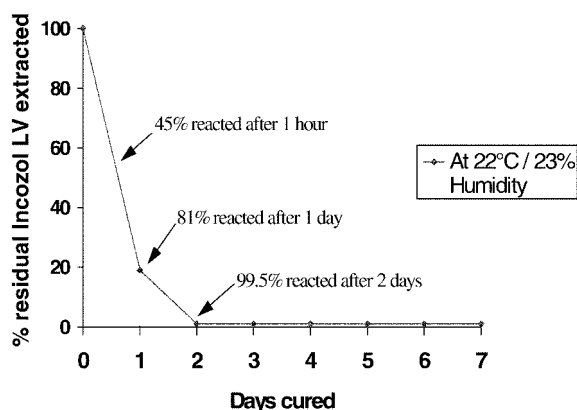

Fig. 5 Rate of incorporation of Incozol LV into 2K Polyurethane Lacquer.

Fig. 6 Rate of incorporation of Incozol LV into 2K polyurethane lacquer.

The studies described so far have shown that complete utilisation of Incozol LV is possible in the polyurethane lacquer, but how does the level of Incozol LV incorporated influence the VOC of the lacquer?

Fig. 7 shows the effect on VOC for clear lacquer formulations (Formulations 1 and 2) and primer paint (Formulation 3) (Table 1).
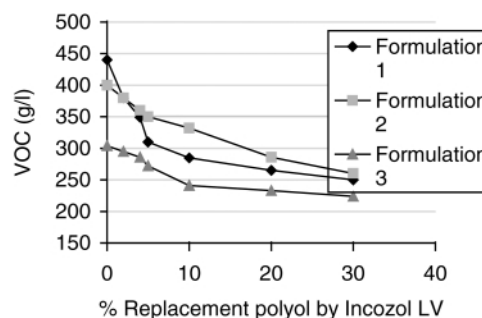
Fig. 7 VOC reduction for up to 30% w/w polyol replacement with Incozol LV. VOC limit for a topcoat clear lacquer 420 g/l. VOC limit for pre-coat / primer paint 250 g/l. (EC Directive April 1998.)

In each case, up to 30% polyol has been replaced by Incozol LV reactive diluent. At 30% Incozol LV, considerable reductions in VOC are possible, with VOC as low as 250 g/l achievable for a clear lacquer depending on selection of a suitable formulation. This is certainly a favourable figure when compared to the present European legislation demand for a top coat clear lacquer of 420 g/l. VOC regulation-compliant paints can also be achieved incorporating Incozol LV.

AWARD

Table 1 Formulations used in performance property studies.

Formulation	Composition
Formulation 1	A 2K acrylic/polyurethane lacquer - G-Cure 109 HE75 + up to 30% w/w replacement Incozol LV/Tolonate HDT90
Formulation 2	A 2K acrylic/polyurethane lacquer - Desmophen A365/Desmodur N3390
Formulation 3	A 2K acrylic/polyurethane paint - Joncryl SCX-922/Tolonate HDB75MX

N.B. G-Cure is a trademark of Henkel PLC and Joncryl is a trademark of S.C. Johnson & Sons B.V.

Effect of incorporating Incozol LV on 2-pack polyurethane clear lacquer film properties[6,7]

Film curing properties

Ideally, the true benefit of using a suitable reactive diluent is to achieve a reduction in VOC without adversely affecting the cure properties of the coating.

The influence on pot life (Fig. 8) and cure response (Fig. 9) is shown for the three formulations in Table 1. Pot life was measured as the time taken for the initial mix viscosity of the lacquer to double. Viscosity was measured at 20 °C using a Ford No 3 flow cup.

Cure response was determined using a Sheen Model B-K dry time recorder. In each of the formulations up to 30% w/w polyol has been replaced by Incozol LV without greatly influencing the cure properties.

Furthermore, for the two clear lacquer and the paint formulations, incorporating up to 30% w/w Incozol LV as polyol replacement did not significantly alter the Persoz film hardness development (Fig. 10).

Dry coating properties

Cured panels of the three formulation case studies were evaluated for chemical resistance using a variety of solvents including isopropyl alcohol, methyl ethyl ketone, petrol and skydrol (aviation brake fluid). The method used for measurement was a Satra rub fastness tester (Model STM 61), comprising of a felt pad which had been pre-soaked in the test reagent/solvent, and rotated for 100 revolutions under a constant applied force of 24.5 N. The effect on the film is
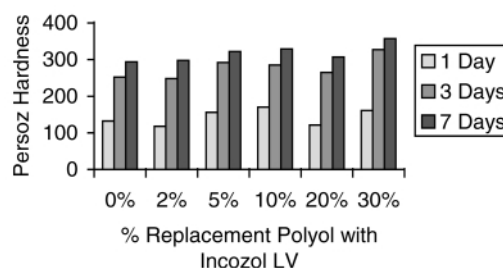
Fig. 10 Film hardness using ASTM D4366-95 Method B for formulation 1 (Table 1).
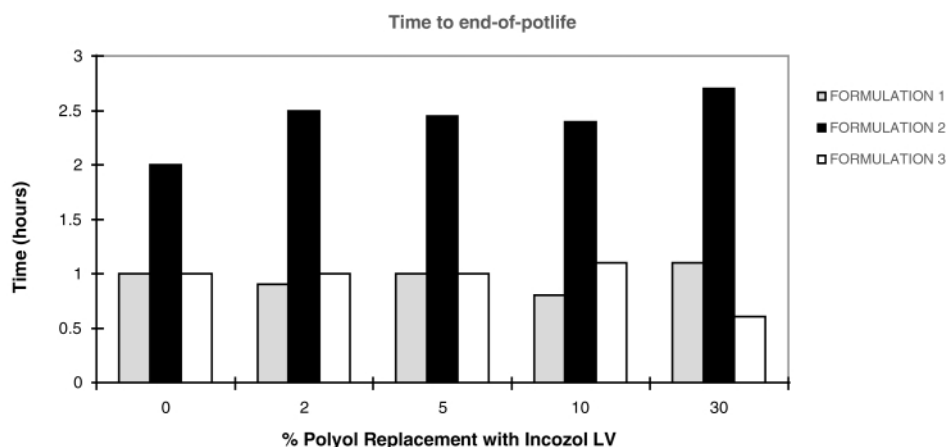
Fig. 8 Effect on pot life with incorporation of Incozol LV.
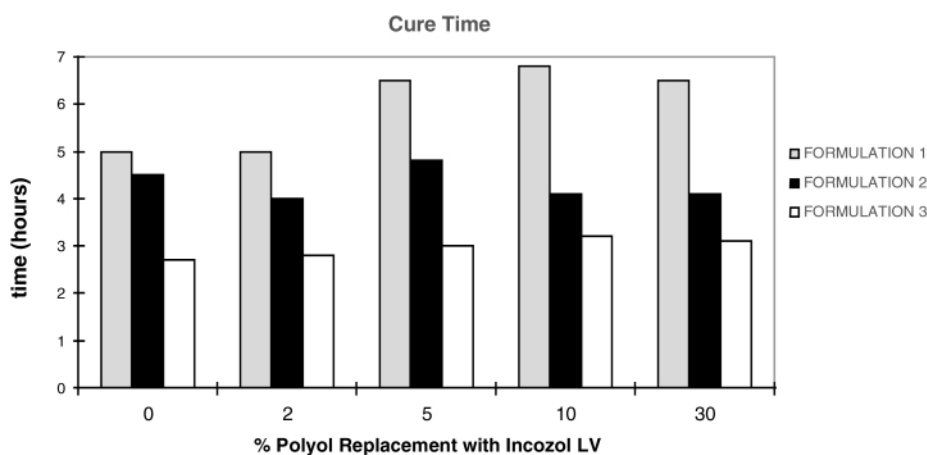
Fig. 9 Effect on cure response over time with incorporation of Incozol LV.

recorded as an observation and graded according to the scale defined with the results in Table 2.

Table 2 Effect on chemical resistance of a clear lacquer incorporating up to 20% w/w Incozol LV.

	Formulation 1			Formulation 2		
% Replacement with Incozol LV	**0**	**5**	**20**	**0**	**5**	**20**
Chemical Resistance to IPA	10	10	10	10	10	10
Chemical Resistance to MEK	10	9	10	10	10	9
Chemical Resistance to Petrol	10	9	9	10	10	10
Chemical Resistance to Skydrol	9	10	10	9	9	10

Key:- 0 = film fully removed, 4 = film softened, significantly marked, 8 = slight gloss reduction / marked, 9 = film very slightly marked, 10 = film unaffected.

Formulating with bisoxazolidine reactive diluent appears to have no significant influence on coating chemical resistance.

Table 3 shows the effect on the gloss retention of the clear lacquer formulations after weathering trials by QUV B after 500, 1000 and 3000 hours.

No significant influence on the level of gloss retention by incorporating up to 20% Incozol LV was observed.

Summary

Incozol LV is a low viscosity bisoxazolidine reactive diluent that is activated by moisture contamination present in both the polyurethane coating components (polyol and solvent) and in the atmosphere during application. The moisture triggered ring opening allows Incozol LV, *via* chemical reaction with polyisocyanate, to be successfully incorporated into the polyurethane coating.

Incozol LV offers the benefit of reducing the VOC of polyurethane coatings beyond the present legislative demands without adversely altering cure and coating properties.

Table 3 Incorporating Incozol LV results in high gloss retention after QUV B weathering. Method used to determine gloss was a sheen gloss meter at 20° using ASTM D523-89.

	Formulation 1			Formulation 2		
% Polyol Replacement with Incozol LV	**0**	**5**	**20**	**0**	**5**	**20**
% Gloss Retention after 500 hr QUV B	96	94	100	80	88	88
% Gloss Retention after 1000 hr QUV B	94	91	100	73	80	80
% Gloss Retention after 3000 hr QUV B	93	90	98	70	76	78

Acknowledgements

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4 A. Holden and R. Clarke. University of Central Lancashire Internal Report to Industrial Copolymers, April 1998.
5 A. J. Thrift and E. Whalley. Internal Report, Industrial Copolymers, April 1998.
6 D. P. Moore and N. G. Carter. *From Cars to Transport Bridges*, Proceedings of 4th Nürnberg Congress, April 1997.
7 D. P. Moore and N. G. Carter. *The Versatility of Oxazolidines as Reactive Diluents in Two-Component Polyurethanes*, Pitture & Vernici. *Paints and Varnishes*, **20**, September 1997.

Ethyl lactate: a green solvent for magnetic tape coating

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The hazardous air pollutants (MEK, MIBK and toluene) used in magnetic tape coatings are replaced with ethyl lactate, which is not a hazardous air pollutant and made from renewable resources. A magnetic dispersion, containing 50/50 ethyl lactate and tetrahydrofuran, has rheological properties similar to a conventional dispersion and gave tape samples with magnetic properties comparable to VHS tape. The materials cost of the formulation containing ethyl lactate was higher than the costs of the conventional formulations.

Introduction

Magnetic tape is the highest capacity, lowest cost removable storage medium and will continue to play a major role in information storage and distribution on the Internet in terms of electronic libraries and back-up storage for servers. The digital linear tape (DLT) and linear tape open (LTO) data cartridge formats offer a native storage capacity of 80–100 gigabytes at a cost of about $1 per gigabyte. The LTO format has a roadmap to increase this capacity to 800 gigabytes per cartridge by the end of this decade.

Video remains the highest volume magnetic tape application, with more than 2 billion T-120 video cassettes manufactured in 1994.[1] The near future will bring dramatic changes to the magnetic tape industry. High-definition television (HDTV) has begun broadcasting in the US. This new video format is digital, rendering the current VHS format obsolete, and will require a new format for video distribution. The new format may either be a new magnetic tape, digital video cassette (DVC) or a new optical disk, digital video disk (DVD). Historically, consumers have chosen the lower cost format, which has been magnetic tape.

Magnetic tape and floppy disks are manufactured by quite similar, continuous web coating processes. Polyester base film is coated with a fluid that contains a dispersion of the magnetic particles in a mixture of organic solvents. The solvents include butan-2-one (MEK), cyclohexanone, 4-methylpentan-2-one (MIBK), tetrahydrofuran (THF), and toluene. These solvents present an occupational hazard to the workers and emissions hazard to the environment. MEK, MIBK and toluene are on the US Environmental Protection Agency's Toxics Release Inventory.[2] They are hazardous air pollutants (HAPs) that cause photochemical smog and ground level ozone.[3–5] Furthermore, these solvents are derived from petroleum, a non-renewable resource.

In the US the Pollution Prevention Act and the Clean Air Act Amendments of 1990 apply pressure on the industry to seek alternative methods for magnetic media manufacture. The thrust of the Pollution Prevention Act is to reduce or prevent pollution at the source. This is to be done by encouraging industry to make changes in the production, operation, or use of raw materials in the manufacturing process. The US Congress and the Environmental Protection Agency believe that source reduction is more desirable than waste management and pollution control. The Clean Air Act amendments, Title III, lists 189 hazardous air pollutants, which includes MEK, MIBK, and toluene. The regulations for the magnetic tape industry have been published in the 1994 National Emissions Standards for Hazardous Air Pollutants.[6] In modern tape manufacturing plants the solvent vapors from the drier are recovered by use of a carbon bed adsorber. The carbon bed is stripped by steam, the steam is condensed or put through a distillation column. This allows recovery and reuse of the individual components. The coating operations are safe and the air emissions meet EPA standards. However, the three world-class magnetic tape manufacturing sites in the State of Alabama released *ca*. 10^6 lb of MEK and 4.0×10^5 lb of toluene in 1998.[2] Considerable capital equipment is required to contain and recycle the organic solvents. The steam stripping generates contaminated water that must be disposed properly. Furthermore, maintaining the emission prevention equipment adds complexity to the tape manufacturing process. With more stringent federal regulations on emission controls, tape manufacturers may be forced to install even more capital equipment to comply with the regulations. Alternatively, they may be forced to shut down their operations and move offshore. The US and Europe can not afford to lose manufacturing jobs, particularly in a high technology industry that plays an important role in the information superhighway.

Magnetic dispersions, or inks, contain magnetic particles dispersed in organic solvents. A poly(vinyl chloride) wetting binder is used as a dispersing aid, either MR-110 from Nippon Xenon or UCARMAG from Union Carbide. The binders contain carboxylate or sulfonate functional groups that chem-isorb to the particle surface. The adsorbed polymer layer provides a steric barrier that separates the particles, thereby stabilizing the dispersion. The dispersions also contain a thermoplastic polyurethane that gives the coating its requisite mechanical properties. Modern magnetic tape formulations use either Estane from BFGoorich or Morthane from Morton

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Green Context

The replacement of reagents and auxiliary materials such as solvents with more benign and renewable alternatives is a key area of green chemistry. This paper describes the use of ethyl lactate, a renewable solvent with low toxicity and minimal detrimental effects on air quality, as a solvent in the formation of magnetic tapes. This can replace much more volatile and toxic solvents such as hydrocarbons and low MW ketones, while producing a high quality tape. A cost analysis indicates an increased price for the product, which may be a barrier to use, at least in the short term. *DJM*

International. The binder is cross-linked with a polyisocyanate cross-linker, such as Mondur CB-701 from Bayer.

Our continuing interest in preventing air pollution in magnetic tape manufacture has led us to examine the possibility of using ethyl lactate as the solvent in the magnetic inks. We were inspired by a presentation by R. Datta entitled '*Lactate Esters for Green Solvents—Process Technology Advances*' at the *3rd Annual Green Chemistry and Engineering Conference*.[7] He stated that ethyl lactate is non-toxic, indeed it is a FDA approved food additive. If released to the environment it quickly biodegrades whilst, in addition, it is not an air pollutant. Recent process technology advances promise to lower the cost of ethyl lactate to \$0.85 lb^{-1} or \$1.90 kg^{-1}. Here we demonstrate the possibility of replacing the HAPs used in magnetic tape manufacture with ethyl lactate. We also consider the economics of using ethyl lactate in the coating process.

Experimental

Videotape grade cobalt modified γ-Fe$_2$O$_3$ particles (Pferrico 3570) were a gift from ISK Magnetics. MR-110 was a poly(vinyl chloride) wetting binder from Nippon Xenon. Morthane CA-271 was a thermoplastic polyurethane binder from Morton International. Tetrahydrofuran (THF) was HPLC grade from Fisher Scientific. Ethyl lactate was reagent grade from Aldrich.

MR-110 (2.50 g) was dissolved in 15.14 g THF and then the solution was diluted with 15.06 g ethyl lactate. Morthane CA-271 (2.51 g) was dissolved in 15.52 g THF with shaking overnight. The next day the solution was diluted with 15.03 g ethyl lactate. Both polymer solutions were homogeneous mixtures. The MR-110 solution was mixed with 20.01 g Pferrcio 3570. The heterogeneous mixture was poured in an Eiger 'Mini 50' bead mill. THF (7.53 g) and ethyl lactate (7.52 g) were added and the mixture was milled for an hour using glass beads as the milling media. After milling for 1 h, the Morthane solution was added and milling continued for another 30 min. The dispersion was then pumped into a glass jar. Magnetic coatings were cast onto polyester base film using a 6 mil Garner blade in a hand draw-down apparatus that passed the wet coating through a 2000 G orienting magnetic field. The coatings were dried overnight at 65 °C in a convection oven.

The rheolgical properties for the magnetic dispersions were measured on a Haake RS-100 controlled stress rheometer. The magnetic properties of the dried tape samples were determined by measuring hysteresis curves on a Digital Measurement Systems model 1660 vibrating sample magnetometer.

Results and discussion

The first consideration was to replace all the solvents with ethyl lactate, a 'fully green' solvent system. Unfortunately neither MR-110 nor Morthane CA-271 were soluble in ethyl lactate. However, both were soluble in a 50/50 (wt/wt) mixture of ethyl lactate and tetrahydrofuran. Tetrahydrofuran is not listed as a HAP and is commonly used in as a solvent in magnetic inks. Therefore we proceeded to prepare a 'partially green' formulation using the ingredients listed in Table 1.

Rheology is a tool to characterize the properties of the magnetic dispersions. Fig. 1 shows plots of elastic modulus (G') and viscous modulus (G'') as a function of frequency, for both dispersions, values of G' were greater than G''. The value of G' was relatively independent of frequency, suggesting the dispersions were behaving like cross-linked networks.[8] The dispersion also displayed a shear-thinning behavior, similar to that observed for conventional dispersions, Fig. 2. These results were consistent with the microstructural model for magnetic

dispersions and its effect on their rheological properties.[9] In magnetic dispersions the particles form bundles consisting of a few to tens of particles, held together by magnetic attraction. The bundles are held together by magnetic attraction forces, giving a sample-spanning network. This network gives the dispersion its high elasticity. Under high shear conditions the network structure is temporarily broken and the viscosity decreases exponentially. The rheological behavior indicates that dispersions containing ethyl lactate would have flow characteristics similar to conventional solvent-based dispersions and should not present a problem in coating operations.
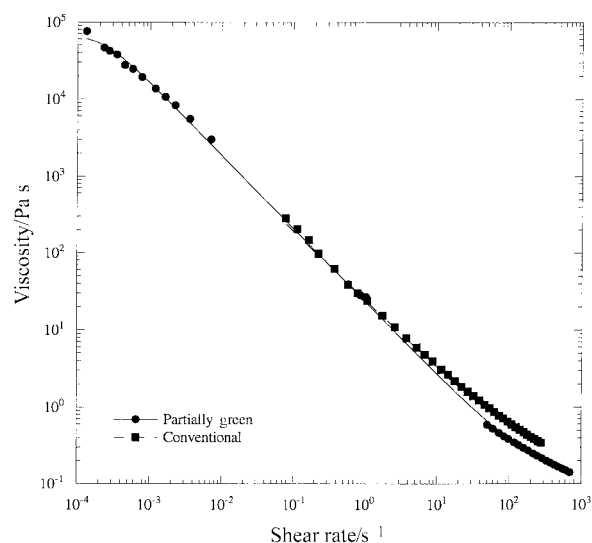
The magnetic properties of the dried tape sample were determined from magnetic hysteresis curves measured by

Table 1 Partially green formulation

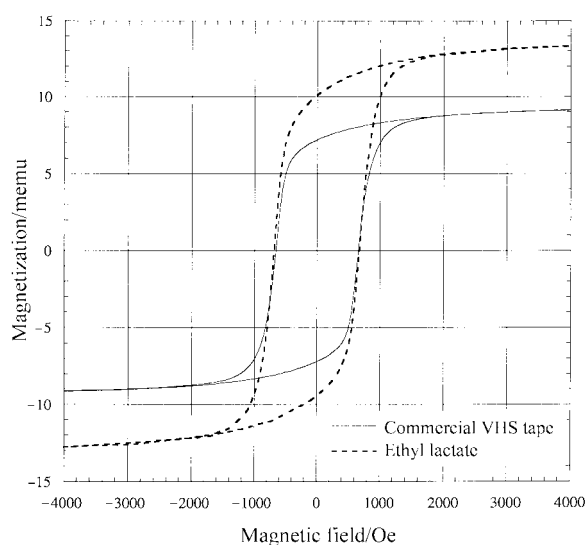| Ingredient	Amount/g
Pferrico 3570	20.01
MR-110	2.50
Morthane CA-271	2.51
Tetrahydrofuran	38.19
Ethyl lactate	37.61
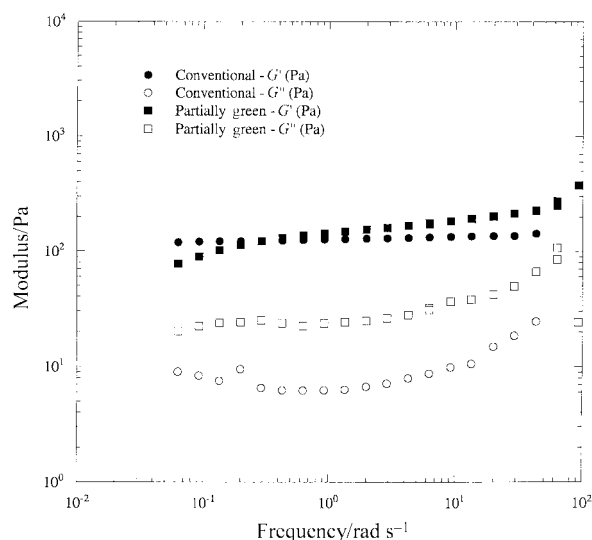
Fig. 1 Rheological properties of the magnetic dispersion containing ethyl lactate. Frequency dependence of the elastic modulus (G') and the viscous modulus, G''.

Fig. 2 Rheological properties of the magnetic dispersion containing ethyl lactate. Shear rate dependence of the viscosity.

vibrating sample magnetometry. Fig. 3 shows hysteresis curves for the tape sample made from the partially green formulations and for a commercial VHS tape. The curves were quite similar, except the magnetization for the partially green sample was higher, indicating that the magnetic coating was thicker. Values of coercivity and squareness, Table 2, were quite similar for each sample. The coercivity is the field required to switch the magnetic particles from one remanent state to a magnetization value of zero and is largely dependent on the identity of the particles. However, coatings made from better dispersions and having more highly oriented particles, give higher values of coercivity. Since the source of the particles used in the commercial tape are not known, no attempt will be made to interpret the higher coercivity value for the partially green tape. Values of squareness were obtained by dividing the remanent magnetization (M_r) by the saturation magnetization (M_s) where M_r is the magnetization at zero applied field, while M_s was the

magnetization at a saturating field of 8000 Oe. The squareness is a measure of the degree of orientation of the magnetic particles in the tape samples. For perfectly aligned particles, the squareness would have a value of 1. In practice the particles are not perfectly ordered, but have a distribution of orientations about an average, directed along the length of the tape. The value of squareness for the tape made from the partially green formulation was very close to the value of squareness for the VHS tape. Clearly, magnetic dispersions can be prepared with 50/50 THF–ethyl lactate and these dispersions give tape with adequate magnetic properties.

Although we have shown that the partially green formulation can give tape with good magnetic properties, there was a concern about the dynamics of drying and film formation. THF is more volatile than ethyl lactate and will leave the film more quickly during drying. Since ethyl lactate is a non-solvent for the binder polymers, the solvent quality in the film will decrease during drying. It is expected that this will effect the microstructure of the dried film, which would influence the mechanical properties of the coating. At worst it may give rise to coating stresses, that would case cupping which is a curling of the tape about its line axis. Cupping is deleterious to the transport of the tape through the drive system. The effect of drying dynamics has not been determined here and will be left for future studies. This would not be a concern if alternative binders could be identified that were soluble in ethyl lactate.

Economics

With the demonstration that magnetic tape can be cast from dispersions containing ethyl lactate, the next consideration becomes the economics of the process. We have reported a hourly materials consumption costs for a videotape coating line using conventional, solvent-based magnetic dispersion.[10] Table 3 shows a comparison of the hourly materials costs for a conventional coating process, a partially green coating process, and a fully green coating process. The raw materials prices were obtained from the vendors. The prices for MEK, MIBK and toluene were taken from the most recent issue of the Chemical Market Reporter.[11] The conventional process consumes $2240 of materials per hour. The partially green process, where the solvents are 50/50 THF and ethyl lactate, consumes $3222 of materials per hour, a 44% increase. The increase is largely due to the higher cost of THF, relative to MEK and toluene. The fully green process (only ethyl lactate), consumed $2646 of materials per hour, only an 18% increase over the conventional process. The tape industry runs on very tight margins. They would hesitate at using a process that increases costs. In order

Fig. 3 Magnetic hysteresis curve for a commercial VHS tape (——) and the tape sample cast from the dispersion containing ethyl lactate (– – –). The curves were measured in the direction parallel to the particle orientation.

Table 2 Magnetic properties of the tape samples

	VHS tape	Partially green tape
Coercivity/Oe	669	680
Squareness	0.78	0.76

Table 3 Comparison of the hourly materials consumption and materials costs

Material	Price/$ kg^{-1}	Conventional		Partially green		Fully green	
		Amount	Cost/$	Amount	Cost/$	Amount	Cost/$
Pferrico 3570	4.85	200.8	973.88	200.8	973.88	200.8	973.88
Carbon Black	3.40	4.01	13.63	4.01	13.63	4.01	13.63
Alumina	5.69	12.1	68.85	12.1	68.85	12.1	68.85
UCARMAG-536	4.41	22.6	99.67	22.6	99.67	22.6	99.67
Morthane CA-271	8.71	27.6	240.40	27.6	240.40	27.6	240.40
Mondur CB-701	5.18	5.03	26.06	5.03	26.06	5.03	26.06
Butyl stearate	1.30	2.51	3.26	2.51	3.26	2.51	3.26
Stearic acid	1.01	2.51	2.54	2.51	2.54	2.51	2.54
THF	3.70	129	477.30	320	1184.00		
MEK	1.00	258	258.00				
Toluene	0.30	254	76.20				
Ethyl lactate	1.90			321	609.90	641	1217.90
Total			2240		3222		2646

for the materials costs for the fully green process to match that of the conventional process, the price of ethyl lactate must be $1.26 kg^{-1} or $0.57 lb^{-1}.

This analysis does not account for solvent recycling. Most modern tape manufacturers recover, purify and reuse their solvents. Although we have not demonstrated recycling of ethyl lactate, we fully expect this can be accomplished. Indeed Argonne National Laboratory reported a demonstration that the ethyl lactate can be recovered and recycled in cleaning and degreasing operations.[12] We expect that the costs for recycling ethyl lactate will be similar to the cost for recycling the other solvents. Earlier we estimated the energy cost for solvent recovery and recycle to be about $14 h^{-1} for the conventional process.[10] This cost was insignificant relative to the cost of the solvents, Table 3. We might expect that the solvent recovery for the fully green process would be easier, therefore lower cost, because only a single solvent would be recovered and purified.

Another consideration is the hourly energy consumption. Table 4 compares the hourly energy consumption and costs for the three different cases. Values for the enthalpy of vaporization for THF, MEK and toluene were taken from the *CRC Handbook of Chemistry and Physics*.[13] The value for the enthalpy of vaporization for ethyl lactate was found in a Pilot Project Report from Argonne National Laboratory.[12] The enthalpy of vaporization for ethyl lactate is similar to that for the other solvents. Accordingly the energy required for drying in the fully green process is close to that for the other processes. The energy cost was calculated with the assumption that the drier was heated electrically and the electricity cost was 6.09¢ per kilowatt hour, a value obtained from Alabama Power. The energy costs are in the range of $4–5 h^{-1}, which is insignificant relative to the materials costs.

A cost that we have not determined is the cost of compliance. This would be the cost of maintaining records and filing reports with regulatory agencies. There would also be a hidden burden of worrying about compliance. Furthermore, MEK, MIBK and toluene would provide a worker exposure hazard that would be regulated under the Occupational Health and Safety Administration (OSHA). Assuming that if a tape coating operation used the fully green process, it would no longer be subject to EPA or OSHA regulations, there would be cost savings. The company would not have to keep records and not have to report to those agencies. We have not estimated the cost savings. We do not feel competent to deal with these issues. However, let us assume the company must assign a professional engineer to work full time on compliance issues. If the cost of an engineer (salary, benefits and overhead[14]) were $100 h^{-1}, this cost would significantly increase the cost of the conventional process and decrease the cost differential between the conventional coating process and the fully green process.

Table 4 Comparison of energy consumption and costs

Solvent	Amount/ kg h^{-1}	ΔH_{vap}/ kJ kg^{-1}	Energy use/MJ h^{-1}	Cost[a]/ $ h^{-1}
Conventional				
THF	129	480	61.9	1.05
MEK	258	473	122	2.06
Toluene	254	426	108	1.83
			292	4.94
Partially green				
THF	320	480	154	2.60
Ethyl lactate	321	419	135	2.28
			288	4.87
Fully green	641	419	269	4.54

[a] Assuming an energy cost of 6.09¢ per kW h.

Conclusions

Here we have demonstrated the magnetic dispersions can be prepared using a 50/50 mixture of ethyl lactate and tetrahydrofuran, a partially green formulation. The fluid rheology was similar that that for a conventional dispersion, suggesting the partially green formulation should have flow characteristics compatible with a conventional tape coating operation. The magnetic properties of hand drawn magnetic coatings made from the partially green process were quite similar to those of a commercial VHS tape. This demonstrates the possibility of manufacturing magnetic tape using the partially green formulation. However, we have not made real magnetic tape that could be used for recording. This is beyond our capability and a task better left to the industry.

The economic analysis assumes that the new process technology from Argonne National Laboratory will enable the price of ethyl lactate to be lowered to $0.85 lb^{-1} or $1.90 kg^{-1}. There is a cost penalty in using either the partially green or the fully green formulation. The cost of the partially green formulation was prohibitively large, due to the high cost of tetrahydrofuran. The cost penalty of the fully green process, where all the solvents where replaced with ethyl lactate, was not as great. If the price of ethyl lactate could be further lowered to $1.26 kg^{-1} or $0.57 lb^{-1}, then cost would not be an issue. Alternatively, if the cost of the petroleum-based MEK, MIBK and toluene increased by about 20%, then ethyl lactate at $1.90 kg^{-1} would be competitive. The cost of compliance with Federal, State and local regulations significantly add to the cost of the conventional process. However, we were not able to accurately quantify these costs.

We have not demonstrated a fully green formulation. The conventional binder polymers were not soluble in ethyl lactate. The next step would be to identify new binder polymers that are soluble in ethyl lactate. Recently we have prepared a series of acrylate and styrene copolymers as potential replacements for MR-110. Many of the these polymers were soluble in ethyl lactate. We will determine if they can be used as wetting binders in magnetic dispersions using ethyl lactate as the solvent.

Acknowledgments

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Clean and efficient syntheses of calix[4]arene modified polymer supports

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The syntheses of two polymer supported calix[4]arenes **8** and **9**, using TentaGel S NH_2[1] and aminomethyl polystyrene, have been significantly improved by the replacement of thionyl chloride and excessive amounts of solvents with carbodiimide coupling reagents. The new, environmentally friendly route reduces the number of synthetic steps from five to three and achieves a high loading of calix[4]arene, as shown by attenuated total reflectance infrared spectroscopy (ATR-IR), NMR and solid-state NMR. Furthermore, the extraction efficiencies of uranium and cadmium by these polymer supported calix[4]arenes demonstrate an additional green aspect to the work.

1. Introduction

Calixarenes are well documented in their ability to complex metal cations and extensive reviews may be found on the subject.[2] The extraction of metal cations with polymer supported calixarenes has been addressed by many authors and has been reviewed by Roundhill[3] and Yilmaz.[4] A variety of polymer supports have found use, for example polyethyleneimine supported calix[6]arenes have been used to extract uranium from seawater,[5] polyacryloyl chloride and chloromethyl polystyrene supported calix[4]arenes have been shown to extract iron[4,6] and lead[6] and methacrylate,[7] acrylonitrile and styrene[8] derived calix[4]arenes have been polymerised to make calixarene oligomers.

Recently, a lower rim functionalised calix[4]arene **1** was developed[9,10] which has shown excellent extraction of some
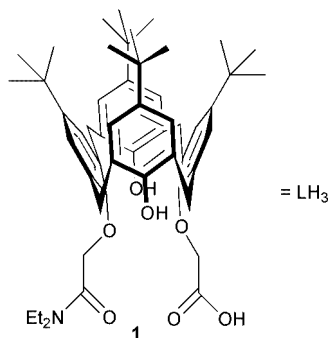
heavy metals, uranium and lanthanides, forming a neutral 2∶2 complex with the uranyl cation as shown by X-ray crystallography. This in turn stimulated our interest in the possibility of using these molecules to polish uranium and cadmium containing waste streams using polymer supported calixarenes. Both cadmium and uranium are known to cause acute toxicological effects in mammals, for example, the oral reference dose (RfD) for cadmium is 0.5 μg kg^{-1} of water (*i.e.*, 0.5 parts per billion) per day and for uranium it is 3 μg kg^{-1} of water (3 ppb) per day for rabbits,[11] therefore in order to discharge cadmium and uranium polluted water into the environment, methods of completely removing these metals is required. It is also interesting to note that cigarettes are reported to contain between 1000 and 3000 ppb of cadmium.

Preliminary experiments were performed[9] whereby the calixarene **1** was covalently bound to a commercially available resin, TentaGel S NH_2 (for a discussion about the properties of

polystyrene–poly(ethyleneglycol)-graft (PEG) copolymers or TentaGel resins, see Rapp[12]) as shown in Fig. 1 and quantitative extraction of uranium was obtained over the pH range 4–9.

Previous work[9,10] also demonstrated the reusability of the calixarene, because the calixarene may be protonated or
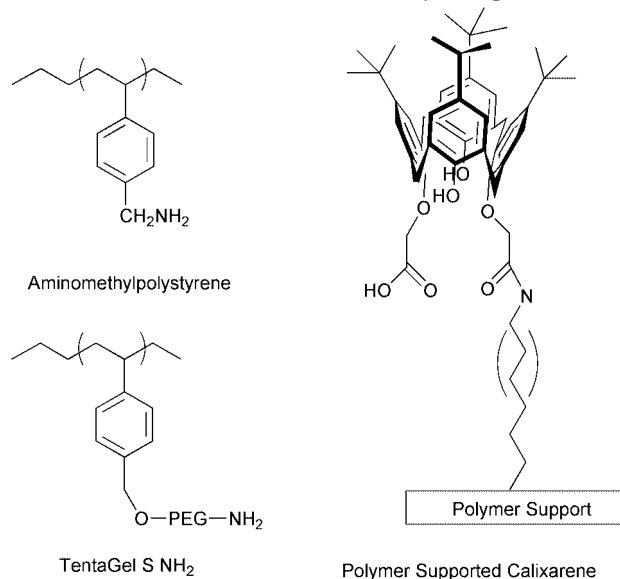

Fig. 1 Aminomethyl polystyrene, TentaGel S NH_2 and polymer supported calixarene.

Green Context

Clean synthesis is at the heart of Green Chemistry. It encompasses alternative routes, a reduction in the number of synthetic steps, and the use of less environmentally damaging or in other ways hazardous reagents, catalysts and solvents. In this paper we see how the reduction in the number of steps in a synthesis (from five to three) the replacement of thionyl chloride, and the reduction in the volume of solvents used makes a synthesis not only more environmentally acceptable but also more economically attractive and technically feasible. The principles are applied to the synthesis of polymer supported calix[4]arenes which are very effective at extracting uranium and cadmium **JHC**

deprotonated depending on the solution pH, according to Scheme 1, therefore, once the metal is bound to the calixarene, it may be released by reducing the pH of the solution.

In order to make the TentaGel bound calixarene more attractive for larger scale synthesis and extraction purposes, we have performed experiments to synthesise TentaGel–calixarene using fewer steps and to covalently attach the calixarene to another less expensive resin, aminomethyl polystyrene. The modified resins were characterised by NMR, solid state NMR and ATR-IR and assessed for their extraction performance against standard solutions of uranium, cadmium and real cadmium waste solutions.

2. Results and discussion

2.1. Synthesis

Firstly, in order to fully characterise the product **8** and prepare **9**, using the methodology previously developed,[9] the acid

chloride **5** was reacted with the amino functionalised supports, TentaGel S NH$_2$ and aminomethylpolystyrene giving the ester–amide derivatives **6** and **7**, then hydrolysed, as shown in Scheme 2, to give the acid amides **8** and **9**, our target extractant materials, with loadings of 10 and 27% respectively, according to the mass balances of the resins before and after reaction.

Next, in order to achieve the synthesis of **8** and **9** in as few synthetic steps as possible, we used various carbodiimides to effect the attachment of the calix[4]arene to the amine functionalised support using the three step route as shown in Scheme 3.
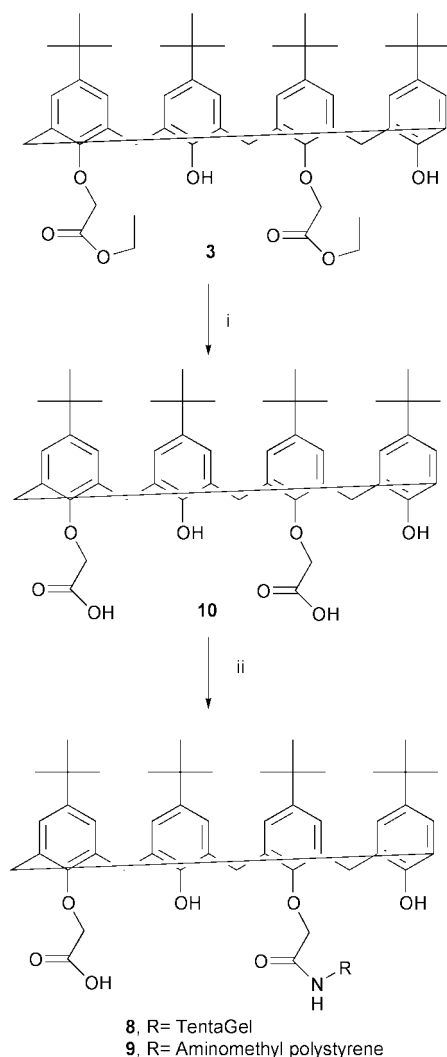
On inspection of the calixarene **10**, it was obvious that both the carboxylic acid functionalities had the ability to react with the amine in the presence of the coupling agent to give the diamide, however, we desired to retain the one carboxylic acid functionality and convert the other to a new amide link to the polymer support, in order to maintain the binding sites necessary for uranyl complexation. However, we found that using both one equivalent and two equivalents of **10** to one equivalent of amine on the resins gave the acid–amide product **8** and **9**, although superior loadings were obtained when two equivalents of **10** and diisopropylcarbodiimide were employed giving **8** with a loading of 10% and **9** with a loading of 27% by mass, which was the same as that obtained with the acid-chloride route. Interestingly, both dicyclohexylcarbodiimide (DCC) and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimde

$$M^{2+} + LH_3 \rightleftharpoons LMH + 2H^+$$

$$M^{3+} + LH_3 \rightleftharpoons LM + 3H^+$$

Scheme 1 LH$_3$ = **1**.

Scheme 2 *Reagents and conditions*; i, BrCH$_2$CO$_2$Et, K$_2$CO$_3$, acetone; ii, KOH–EtOH, reflux; iii, SOCl$_2$, DCM, reflux; iv, resin-NH$_2$, Et$_3$N, DCM; v, KOH–EtOH, reflux.

6 R= TentaGel
7 R= Aminomethyl polystyrene

8 R= TentaGel
9 R= Aminomethyl polystyrene

hydrochloride (EDCI) gave **8** with lower loadings of 8 and
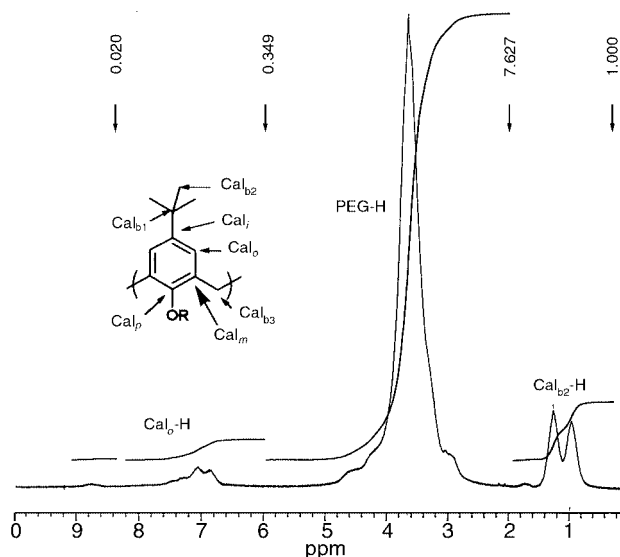<2% respectively by mass.

The extent of reaction, that is, the loading of the calix[4]arene
on TentaGel, was calculated two ways. It was known that
TentaGel and molecules immobilised on TentaGel swollen in
solvents gave rise to NMR spectra with line widths comparable
with free molecules in solution.[12] Therefore, by considering the
mass balances, a loading was deduced, as already described,
then this figure was compared to the solution-state proton NMR
spectrum of **8** swollen in chloroform. We were able to measure
the integral ratio of the polyethylene glycol hydrogen atoms to
that of the tertiary butyl hydrogen atoms of the calix[4]arene as
shown in Fig. 2. Thus, a 10% weight loading corresponded to a
ratio of 8:1.

The characterisation of the materials was done primarily by
solution-state NMR, attenuated total reflectance infrared (ATR-
IR) and solid-state NMR spectroscopy. We used solution-state
NMR to calculate the loadings and purity, then identified the
amide and carboxylic acid moieties by IR spectroscopy. The IR
spectra of **8** and **9** prepared according to Scheme 3 are shown in
Figs. 3 and 4, and the amide and carboxylic moieties at 1675 and
1744 cm^{-1} are clearly visible, attributable to the binding of the
calix[4]arene to the support (1675 cm^{-1}) and remaining acid
functionality (1744 cm^{-1}).

Solid-state NMR of TentaGel and **8** prepared in Scheme 2
was carried out and the solid-state cross-polarization magic
angle spinning (CPMAS) spectra, shown in Fig. 5(a) and (b)
respectively, clearly showed the binding of the calixarene to the
resin with an amide carbonyl peak at 169 ppm.

Fig. 2 Proton NMR of **8**.

Fig. 3 ATR-IR of **8**.

Aminomethyl polystyrene did not form solutions or gels with
chloroform, hence we also used solid-state NMR to aid
characterisation on **7** prepared in Scheme 2. A cross-polarisa-
tion magic-angle spinning (CPMAS) spectrum of **7** was
obtained, shown in Fig. 6(b) and if this is compared to the
spectrum of aminomethyl polystyrene in Fig. 6(a), it was clear
that the calix[4]arene has indeed been bound to the support.
Additionally, further confirmation that the calixarene was
bound to the polymer was obtained from a dipolar dephasing
spectrum of **7**, which clearly showed [Fig. 6(c)] the enhance-
ment of the peaks at 32 and 34 ppm (*tert*-butyl carbon atoms),
146 ppm (aromatic unprotonated carbon atoms) and 168 ppm
(carbonyl carbon atoms) which was entirely consistent with the
assignment of these signals to the resin bound calix[4]arene,
because the dipolar dephasing experiment enhances signals due
to quaternary and methyl carbon atoms.

3. Extraction results

The calixarene modified polymer supports **8** and **9** were then
tested for their extraction properties for uranium and cadmium.
Cadmium extraction was studied on a small (0.58 g of resin) and
large scale (180 g of resin) and uranium was studied on a small
scale (0.58 g of resin). In all the extraction experiments, the
concentration of cadmium and uranium were determined by
inductively coupled plasma atomic emission spectroscopy

8, R= TentaGel
9, R= Aminomethyl polystyrene

Scheme 3 *Reagents and conditions*; i, KOH–EtOH, reflux; ii, carbodii-
mide, TentaGel S NH$_2$ or aminomethyl polystyrene, DCM, RT.

(ICP-AES). The efficiency of the resin was measured using eqn. (1) where the distribution constant (K_d) measures the

$$K_d = [1 - (B/A)]V/M \qquad (1)$$

efficiency of the resin, B is the concentration of the element after contact with the resin, A is the concentration of the element before contact with the resin, V is the volume of solution in contact with the resin (cm^3) and M is the dry weight of the resin (g).

3.1. Uranium extraction with TentaGel supported calix[4]arene

Aliquots (10 cm^3) of a uranium solution (49 ppm at pH 7.0) were passed through a small column containing the resin **8** (0.58 g), at a flow rate of 1 cm^3 min^{-1}.

It was found that up to 90 cm^3 of the 49 ppm uranium solution (equivalent to 4420 μg) could be extracted with 100% efficiency. The extraction data is shown in Fig. 7.

Beyond this point, following the addition of further aliquots (10 cm^3) of uranium solution (95 ppm), the efficiency of the resin reached a peak at $K_d = 180$ (see Fig. 8) corresponding to an uptake of 7088 μg (0.03 mmol) of uranium (equivalent to 12.2 mg of uranium per gram of resin or 0.05 mmol g^{-1}). Working with a 10% mass loading of calixarene on the resin, this represented a total mass of calixarene of 0.06 g (0.07 mmol), which meant that approximately 43% of the cation binding sites on the resin were actually occupied with uranium. Further volumes of uranyl solution were passed, with the resin reaching a maximum uptake of 11033 μg (0.05 mmol) of uranium, which corresponded to an occupancy of 66% of the available calixarene sites.

3.2. Recovery of uranium from the column

Firstly, water (200 cm^3) was passed through the column and ICP-AES indicated that 688 μg of uranium was eluted which indicated that 5.5% of the extracted uranium was probably only held by physisorption of uranium solution on the resin. Next, a solution of nitric acid (1 M) was passed through the uranium saturated column and after the first 10 cm^3 aliquot, the total

uranium recovered was 10185 mg, representing a 92% recovery; 98% recovery was attained following washing with 70 cm^3 of acid, as shown in Fig. 9. Thus, the resin successfully extracted 10185 from a total 11033 mg uranium from a pretreatment volume of 270 cm^3, giving essentially 260 cm^3 of decontaminated water and 10 cm^3 of a concentrated uranium acid solution.

3.3. Extraction performance of aminomethyl polystyrene supported calixarene with uranium

A 25 ppm solution of uranium at pH 7 was passed through a column containing the polystyrene supported calix[4]arene **9**. Analysis of the uranium solution before and after the extractions was carried out and indicated zero extraction for **9**. This result was not surprising in view of the nature of the resin. During the extraction, we observed virtually no wetting of the resin, therefore we can attribute the lack of extraction to negligible physical contact between the calix[4]arene and the uranium solution. We may conclude from these results and by comparison with TentaGel and TentaGel bound calix[4]arenes, that hydrophobic resins such as aminomethyl polystyrene are poor supports for extractions, whereas the results for the readily wettable hydrophilic resin, TentaGel, indicate that good physical contact between the support and aqueous media contributes to extraction performance. Thus, it was clear that future development of a resin support must account for the hydrophobicity of the support, in addition to the loading of the calix[4]arene and the physical and mechanical properties of the resin.

3.4. Cadmium extraction with TentaGel supported calixarene

The resin **8** was preconditioned with aqueous lithium hydroxide (8 l at pH 9.1) in order to deprotonate the calix[4]arene in order to negate any pH drop as the calixarene bound the metal.

Next, 370 litres of the cadmium contaminated waste (169 ppb, equivalent to a total of 0.0625 g cadmium) at pH 9.1 was passed through a column packed with **8** (180 g, equivalent
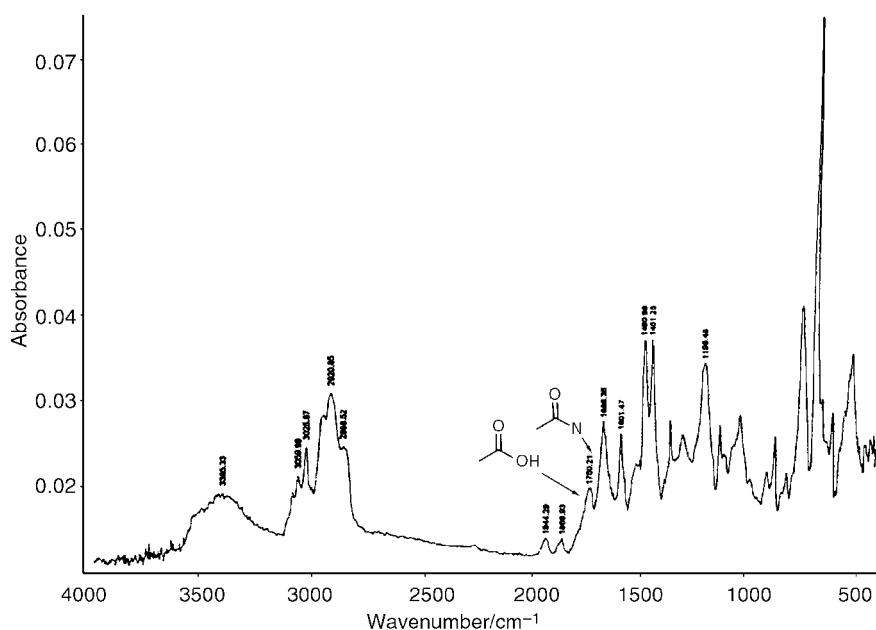

Fig. 4 ATR-IR of **9**.

to 22.0 mmol of calix[4]arene, based on a 10% weight loading of calixarene) at 100 cm^3 min^{-1}. The pH of the sample remained constant throughout the course of the experiment indicating that pretreatment had fully deprotonated the calixarene (see Scheme. 1). A list of interfering cations and anions in this waste is shown in Table 1.

The extent of decontamination was determined as a function of time as shown in Fig. 10. After one circulation, the cadmium concentration was reduced to below the required 150 ppb limit[13] and after 17 recirculations a 3 ppb limit was achieved. Thus, in less than 20 equivalent recirculations the resin **8** had removed 98.3% of the total cadmium.

In total, 0.5 mmol of cadmium was extracted which meant that only 2.3% of the available calixarene receptor sites were occupied with Cd^{2+}, although smaller scale studies performed at lower flow rates (see later) gave a 6.6% efficiency for cadmium.

Then, in order to demonstrate the reusability of the resin, a solution of nitric acid (1 M) was passed through the cadmium containing column. After 7 l, the total cadmium recovered was 51%, then after a further 9 l, this had increased to 53.6% as shown in Fig. 11.

3.5. Small-scale extraction of cadmium with TentaGel supported calixarene

Aliquots (10 cm^3) of a cadmium solution (46 ppm at pH 9.4) were passed through a small column containing the resin **8** (0.58 g), at a flow rate of 1 cm^3 min^{-1}.

The extraction profile shown in Fig. 12 indicated rapid initial extraction of cadmium, followed by a levelling off in efficiency, with a maximum uptake of 522 μg achieved. This represented
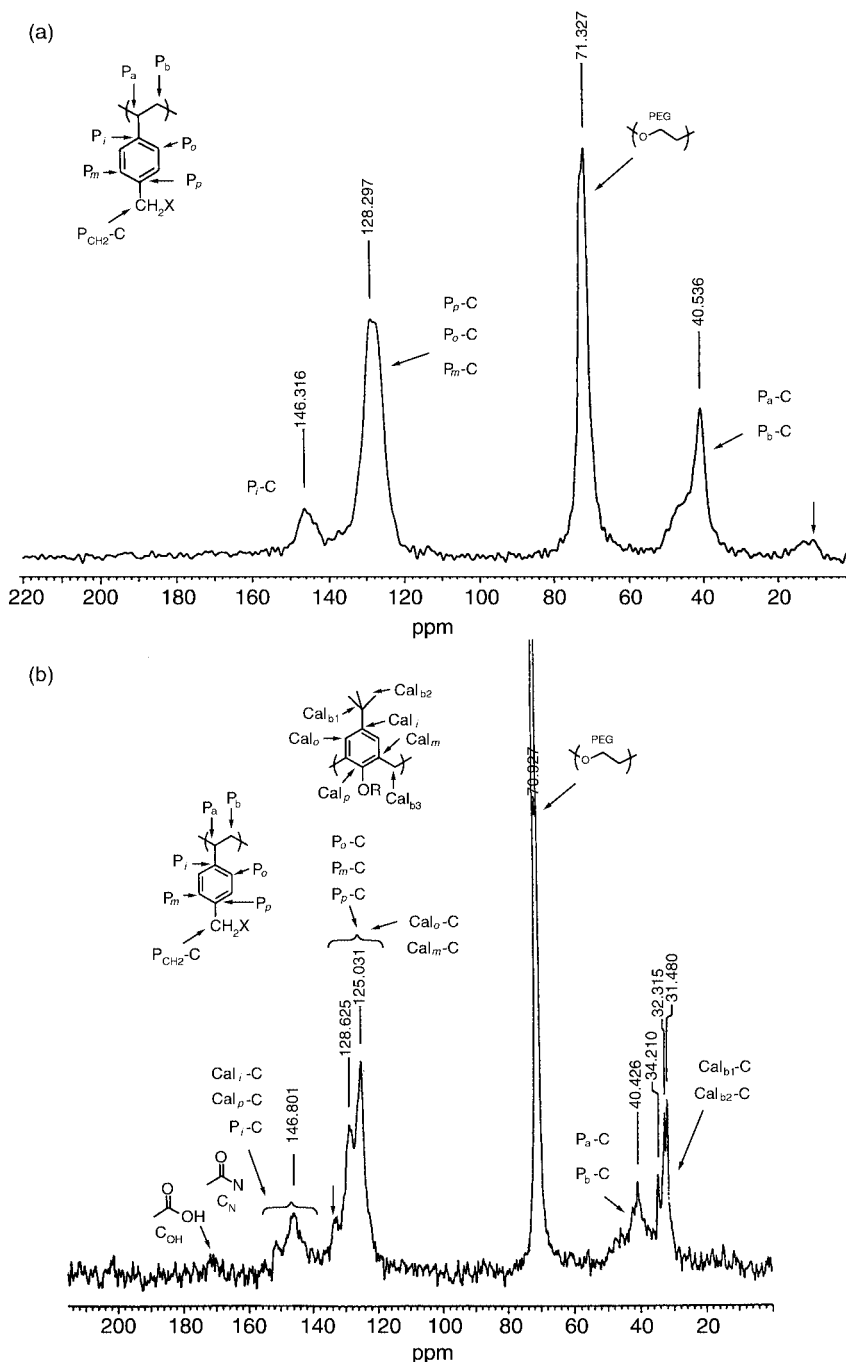

Fig. 5 (a) Solid-state CPMAS spectrum of TentaGel S NH$_2$ and (b) solid-state CPMAS spectrum of **8**.

an occupancy of calixarene receptor sites of 6.7%, which was considerably lower than the 66% achieved for uranium.

A profile of K_d *vs.* volume of cadmium passed was obtained, which gave a maximum K_d of 14.7. The cadmium extraction results also indicated that TentaGel alone was probably responsible for a significant proportion of the extraction.[14]
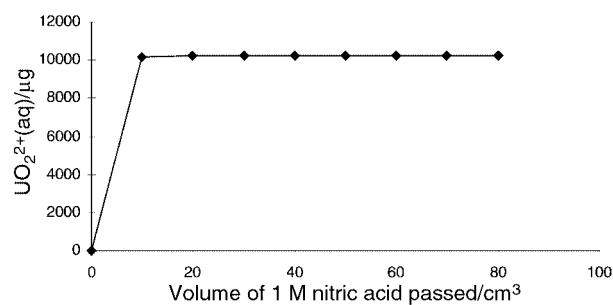

(a)

(b)

(c)
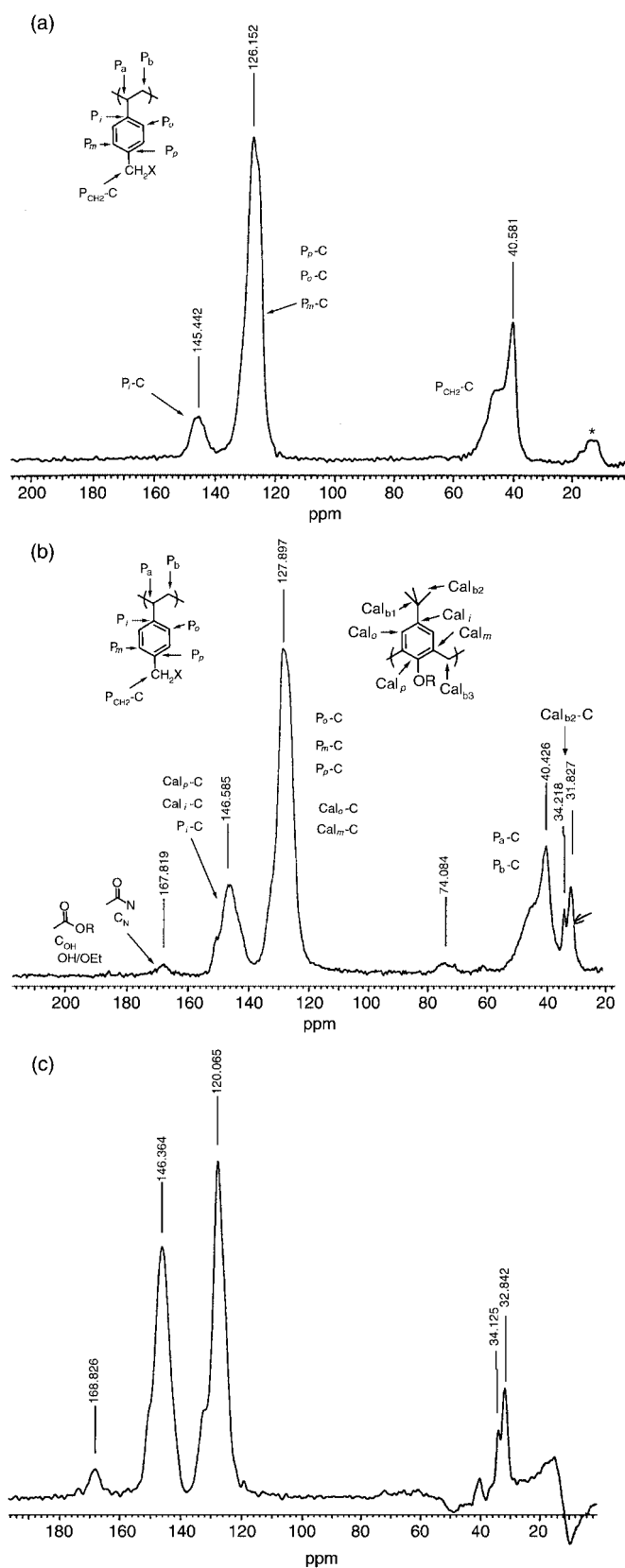
Fig. 6 (a) Solid-state CPMAS spectrum of aminomethyl polystyrene, (b) solid-state CPMAS spectrum of **7** and (c) solid-state dipolar dephasing spectrum of **7**.
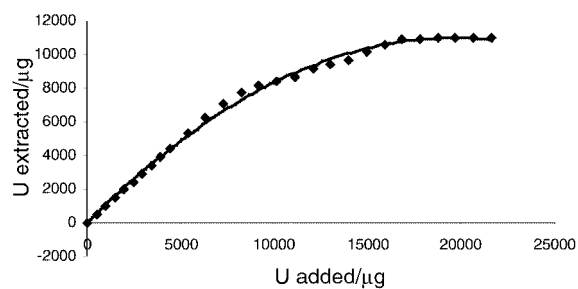
Fig. 7 Extraction of uranium with resin **8**.
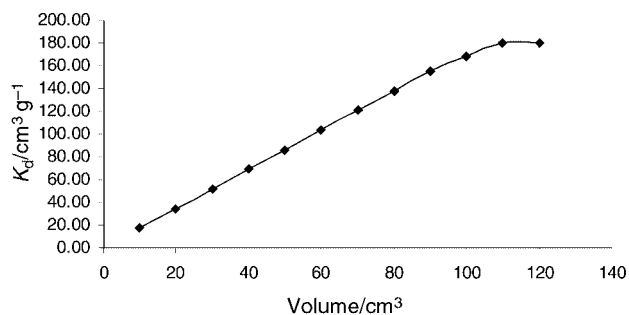
Fig.8 Plot of K_d *vs.* volume of uranyl passed.

Fig. 9 Recovery of uranium with nitric acid.

Table 1 Concentration of matrix cations and anions in the real cadmium

Cation	μg l^{-1}/ppb	Anion	μg l^{-1}/ppb
Cd^{2+}	169.3	CN^{-}	15 000
Ag^{+}	< 14 (LOD)	NO_3^{-}	30 000
Al^{3+}	< 68 (LOD)	SO_4^{2-}	56 000
Ca^{2+}	5 140	PO_4^{3-}	< 10 000
Fe^{3+}	14 131	Cl^{-}	74 000
K^{+}	11 600	F^{-}	3 000
Li^{+}	< 82 (LOD)		
Mg^{2+}	21 740		
Na^{+}	465 880		
Sr^{2+}	1 306		
Pb^{2+}	< 98 (LOD)		
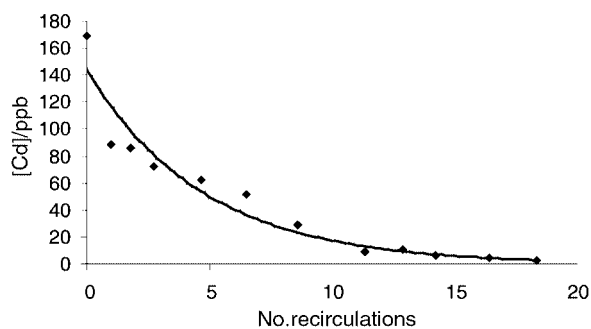
Fig. 10 Large scale cadmium extraction.

4. Chemical and radiolytic stability of the polymer supported calixarenes

Although exhaustive studies on the chemical stability of the materials was not carried out, solution state carbon and proton NMR measurements of the TentaGel supported calixarene were performed following laboratory tests with the material (a period of approximately 12 months). Neither the proton nor carbon spectra showed any loss of calixarene from the polymer by cleavage of the amide bond, which was the most likely degradation mechanism in strongly acidic solution.

It is known that the decay of radioisotopes will lead to chemical degradation of polymer supports during extraction experiments, however, for our purposes, only depleted uranium was used, which has a low activity[15] and therefore any damage as a result of irradiation was assumed to be negligible. Moreover, calixarenes are known to act as inhibitors of the thermo- and photo-oxidation of hydrocarbons and poly-olefins,[16] and therefore might act as inhibitors of radiolytic damage to the polymer.

5. Conclusions

The synthesis of the calixarene modified TentaGel resin has been significantly improved using two fewer steps than the established route and reduces the need for toxic reagents such as thionyl chloride and greatly reduces the volume of solvent required.

Small-scale experiments showed that the calixarene modified TentaGel resin offered excellent extraction for uranium and moderate extraction for cadmium, with uranium extraction found to be an order of magnitude superior to that of cadmium, thus reflecting the favourable binding properties of the calixarene for uranium over cadmium and highlighting the potential of using **8** as a selective uranium extractant for wastes polluted with common interfering cations such as calcium, sodium and potassium.

A large volume of real cadmium waste was purified with **8**, reducing the cadmium concentration from 150 to 3 ppb. This
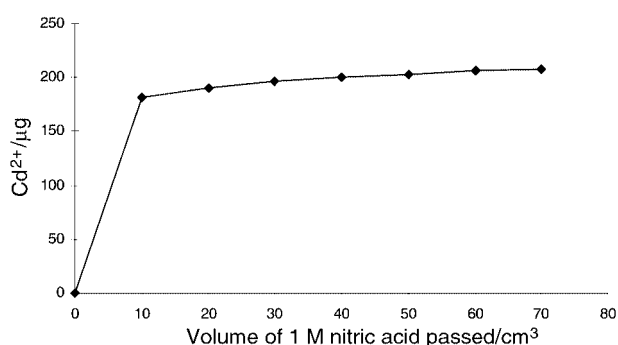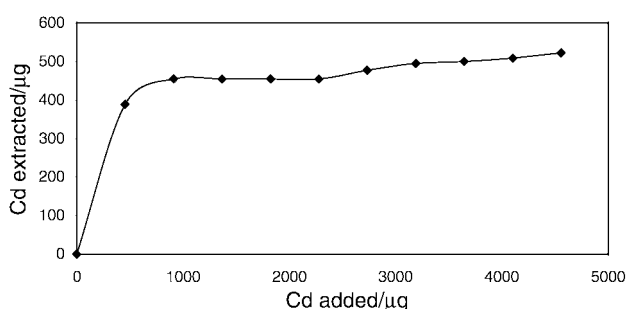
was a very promising result, showing how this research may be applied to solving waste clean-up.

Further work to improve the efficiency of extraction is in progress to attach the calixarene to polymer supports with enhanced hydrophilic properties, whilst exhibiting extraction under high flow rates and pressure.

Additionally, we are investigating the covalent attachment of polymers to modified versions of **1** containing receptor functionalities better suited to binding softer metals such as cadmium. Trials to assess the extraction performance of **8** for uranium in a mixture of metal cations, such as real waste, will also be addressed.

6. Experimental

Metal ion concentrations were determined from ICP measurements performed on either an ARL 3410+ ICP-AES for uranium or a Fisons VG PlasmaQuad ICP-MS for cadmium. ICP measurements were recorded with an error of two relative standard deviations . Matrix anions were determined by ion chromatography using a Dionex 2010i instrument and CN analysis was obtained using the pyridine pyrazalone method, using a HACH DR2000 spectrophotometer and values are quoted to within ±5%. Mass spectra were obtained with a Finnegan 4600 quadrupole mass spectrometer. NMR spectra were run on a JEOL spectrometer operating at 270 MHz with deuterated chloroform ($CDCl_3$) as the solvent and tetra-methylsilane (TMS) as the internal reference; J values are given in Hz. FTIR spectra were recorded on a Perkin-Elmer 1600 Series FT-IR spectrometer using KBr discs. ATR-IR spectra were recorded on a Mattesons Infinity FT-IR machine, equipped with a Harricks Split Pea Single Bounce ATR Cell and PAS-IR spectra were run on a Nicolet 460 Protege equipped with a MTech 100 PAS cell.

Solid-state NMR spectra were recorded using a Varian UNITY plus with Oxford instruments 7 T magnet. The operating frequencies were 75.4 MHz for carbon and 300 MHz for hydrogen. Doty Scientific probes were used for all the experiments. Silicon nitride rotors (5 mm o.d.) were used for all experiments. Kel-F endcaps were used throughout. Referencing was to an external sample of tetramethylsilane.

For large scale extractions, a portable unit was used consisting of a commercially supplied water purification system which was modified to house the resin. A Millipore Milli-Q RG system was used with a Q-PAK (containing four internal purification cartridges with dimensions 300 by 70 mm). The top 30 mm of the Q-PAK was cut off and the contents removed. Plastic liners were placed in the four tubes with two O-rings at the top and bottom. The top of the liners stood proud of the outer casing such that when the top was put on an effective seal was formed. The O-rings were lubricated with grease. The resin (180 g dry weight, 550 cm^3 wet volume) was slurry packed into the first tube so that the liquid flow was downwards and thus there was less pressure on the more leak prone top seal. Normal operational flow rates of 900 cm^3 min^{-1} were possible with this system but this was limited to 100–250 cm^3 min^{-1} to minimise leaks during 24 hour operation and to maximise extraction through longer contact time between resin and liquid.

For smaller scale experiments, small columns with dimensions 30 mm by 15 mm were used and fed with the aqueous solution at a flow rate of 1 cm^3 min^{-1}.

All chemicals were obtained from Aldrich except for TentaGel S NH_2 from Fluka. TentaGel S NH_2 with a bead size of 90 μm and a loading of 0.24 mmol g^{-1} of amine functionality and aminomethyl polystyrene cross linked with 1% div-inylbenzene, with a mesh size of 200–400 and a loading of 0.9 mmol g^{-1} of nitrogen were used. Depleted uranium (DU) was used throughout the experiments. The following abbreviations

Fig. 11 Recovery of cadmium with nitric acid.

Fig. 12 Extraction of cadmium with resin **8**.

were used: dichloromethane (DCM), 1,3-diisopropylcarbodiimide (DIC), 1,3-dicyclohexylcarbodiimide (DCC), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDCI) and 4-(dimethylamino)pyridine (DMAP).

Synthesis of 10

A mixture of 3^9 (3.0 g, 3.5 mmol), ethanol (225 cm³) was heated at reflux, with stirring, until all of **3** had dissolved, then potassium hydroxide (KOH) (30 cm³, 9.2 mmol of 0.307 M ethanol solution) was added and the mixture refluxed, with stirring for 2.5 h. Excess ethanol was removed under reduced pressure then the mixture was cooled and acidified with dilute hydrochloric acid. The mixture was filtered off and washed with water and recrystallised from acetone–water, followed by drying an a vacuum oven at 50 °C to give **10** by comparison with literature data[17] (2.3 g, 86%); ν_{max} 3440, 2960, 1744, 1483, 1362 cm⁻¹ (lit., 3430 and 1740 cm⁻¹); m/z (CI⁺) 765 (M + 1); λ_{max} 292 nm; δ_H 1.04 (18H, s, C(CH_3)₃), 1.27 (18H, s, C(CH_3)₃), 3.41 (4H, d, $^2J_{HH}$ 13.2, ArCH_2Ar), 4.15 (4H, d, $^2J_{HH}$ 13.2, ArCH_2Ar), 4.66 (4H, s, OCH_2CO), 6.93 (4H, s, ArH), 7.06 (4H, s, ArH) [lit., 1.03 (18H, s, C(CH_3)₃), 1.30 (18H, s, C(CH_3)₃), 3.38 (4H, d, $^2J_{HH}$ 13.8, ArCH_2Ar), 4.23 (4H, d, $^2J_{HH}$ 13.8, ArCH_2Ar), 4.70 (4H, s, OCH_2CO), 6.88 (4H, s, ArH), 7.08 (4H, s, ArH), 7.93 (4H, br s, OH and CO₂H)].

Synthesis of TentaGel bound amide-ester 6 *via* the acid-chloride route

A mixture of 4^9 (4.0 g, 5.0 mmol), thionyl chloride (3.0 cm³) and DCM (80 cm³) was stirred under nitrogen, at reflux for 18 h, then the DCM and thionyl chloride were removed under reduced pressure. The resultant solid was dissolved in DCM (30 cm³) and added to a mixture of TentaGel S NH₂ (11.0 g, 2.6 mmol of –NH₂), DCM (80 cm³) and triethylamine (0.70 cm³, 5.0 mmol), under nitrogen, with stirring at RT. After stirring for 19 h, the mixture was filtered off and washed with DCM and blown dry with nitrogen to give **6** (12.28 g, corresponding to a mass loading of 10% and an occupancy of amine sites of 61%). Found: C, 65.8; H, 8.9; N, 0.3%. ν_{max} 1750 and 1679 cm⁻¹, δ_H 0.98 (0.5H, s, C(CH_3)₃), 1.27 (0.5H, s, C(CH_3)₃), 3.63 (7.6 H, br s, –(OCH_2CH_2)$_n$–), 7.00 (0.35 H, br m, ArH); δ_C 30.7 (CH_3), 31.2 (CH_3), 31.7 (CH_3), 33.4 (CCH₃), 33.6 (CCH₃), 53.1 {(CH_2)$_n$}, 70.1 {(OCH_2CH_2O)$_n$}, 76.1 (OCH_2CO), 125.1, 125.7, 126.6 (*o-, p-*ArC), 131.9 (*m-*ArC_{calix}), 141.8 (ArCCCH₃), 147.6, 149.0, 149.7 (ArCOH), 168.3 (CONH, CO₂Et). The filtrate was evaporated to dryness giving a solid (2.9 g) which was shown to consist of triethylaminehydrochloride and **5** by considering the IR spectrum, ν_{max} 3446, 2962, 2677 (Et₃NH⁺Cl⁻), 1811 (COCl), 1758, 1483 cm⁻¹. This solid was then shaken with water (50 cm³), filtered off, washed with water and dried giving a solid (1.90 g, which corresponds to a mass loading of 16%) which was identified as **3** (>60%) and other unidentified products, by comparison of proton NMR and IR data with authentic samples and the filtrate was evaporated to dryness giving triethylamine hydrochloride (0.48 g), ν_{max} 2962, 2938, 2738, 2677, 2491, 1475, 1398, 1171, 1036 cm⁻¹ (lit.,[18] 3500, 2940, 2790, 2700, 2490, 1470, 1430, 1400, 1170, 1040 cm⁻¹).

Preparation of 8 from 6

TentaGel bound amide–ester **6** (24.0 g, 3.0 mmol NH₂), ethanol (100 cm³), water (12 cm³) and KOH–EtOH (25 cm³ of a 0.45 M solution, 11.0 mmol) was heated at reflux for 1.5 h. The mixture was cooled and acidified with dilute hydrochloric acid, then the mixture was filtered off, washed with ethanol, then DCM and

dried with nitrogen giving **10** (25.0 g). A sample of **10** was taken and dried in an oven to eliminate traces of water which would interfere with the analysis, Found: C, 65.1; H, 8.8; N, 0.1%. ν_{max} 1744 and 1675 cm⁻¹, δ_H 1.01 (0.5H, s, C(CH_3)₃), 1.26 (0.5H, s, C(CH_3)₃), 3.63 (7.7H, br s, –(OCH_2CH_2)$_n$–), 7.05 (0.37H, br m, ArH); solution state NMR, δ_C 30.6, 31.3, 31.5, 33.5, 33.6, 70.8, 76.3, 124.8, 124.9, 125.5, 126.6, 126.8, 132.0, 141.7, 147.2, 147.7, 149.0, 149.7, 168.7, 169.3; Solid-state NMR, δ_C 31.5 and 32.3 (s, CCH₃), 34.2 (s, CCH₃ and ArCH), 40.4 (br s, –(CH_2CHPh)$_n$), 70.9 (s, (OCH_2CH_2)$_n$), 125.0, 128.6 and 133.0 (3s, calixarene/polystyrene Ar), 146.1 and 151.6 (br s, calixarene/polystyrene Ar), 171.0 (br s, CNO, CO₂H).

Synthesis of 9 *via* acid-chloride route

A mixture of **4** (0.25 g, 0.32 mmol), DCM (10 cm³) and thionyl chloride (0.4 cm³) was stirred at reflux, under nitrogen, for 24 h. DCM and excess thionyl chloride were removed under reduced pressure, then the solid **5** was dissolved in DCM (10 cm³) and added to a mixture of aminomethyl polystyrene (0.35 g, 0.32 mmol), triethylamine (0.1 cm³) and DCM (20 cm³) and the mixture stirred at RT for 24 h. Filtering off the mixture and washing with DCM gave **7** (0.48 g), which corresponded to a loading of 27%; ν_{max} 1749 (CO₂H), 1684 (CONH) cm⁻¹; solid-state NMR, δ_C 31.9 (s, C(CH_3)₃), 34.2 (s, C(CH_3)₃ and ArCH_2), 40.4 (–(CH_2CHPh)$_n$), 127.9 (polystyrene and calixarene Ar), 146.6 (polystyrene and calixarene Ar), 167.8 (CNO, CO₂H).

The filtrate was evaporated to dryness giving a residue of **4** and triethylamine hydrochloride (0.07 g); ν_{max} 3442, 2961, 2677 (Et₃NHCl), 2492, 1759 (CO₂H, CO₂Et), 1482 cm⁻¹.

Water (10 cm³) and ethanol (30 cm³) and KOH (1.3 cm³ of 0.46 M ethanol solution, 0.6 mmol) were added to the resin, which was stirred for 2 h. Filtering off and washing with ethanol and DCM, then drying in a vacuum oven at 50 °C gave **9** (0.50 g); ν_{max} 1754 (CO₂H), 1686 cm⁻¹. This material was not characterised further.

General procedure for the synthesis of resin bound acid–amides 8 and 9 using carbodiimides

The coupling agent was added to a mixture of the bis-acid **10**, amino derivatised polymer, DMAP (optional) and DCM, at RT, under nitrogen, with stirring. After 3 d, the mixture was filtered and washed with a solvent gradient of DCM–MeOH–HCl (dilute)–MeOH–DCM. The resin was dried in a vacuum oven (45 °C) for 3 h, then the filtrate was extracted into DCM, dried (MgSO₄), evaporated to dryness and dried in a vacuum oven (45 °C).

Synthesis of 8

DIC (2 equiv.). DIC (0.37 cm³, 2.40 mmol), **10** (1.76 g, 2.30 mmol), TentaGel (5.00 g, 1.22 mmol) and DCM (150 cm³), after 3 d, gave **8** (5.54 g); δ_H 1.00 (0.5H, s, C(CH_3)₃), 1.27 (0.5H, s, C(CH_3)₃), 3.63 (8.1H, br s, –(OCH_2CH_2)$_n$–), 7.05 (0.4 H, br m, ArH); solution NMR, δ_C identical to acid-chloride route; ν_{max} 1736, 1677 cm⁻¹. The filtrate gave **10**, DIC and its urea (0.30 g).

DIC (1 equiv.). DIC (0.15 cm³, 0.96 mmol), **10** (0.75 g, 0.98 mmol), TentaGel (4.0 g, 0.96 mmol) and DCM (60 cm³), after 3 d, gave **8** (4.28 g); δ_H 1.00 (0.5H, s, C(CH_3)₃), 1.27 (0.5H, s, C(CH_3)₃), 3.63 (14.7 H, br s, –(OCH_2CH_2)$_n$–), 7.05 (0.2 H, br m, ArH; solution NMR, δ_C identical to that obtained with 2 equiv. of DIC; ν_{max} 1750, 1677 cm⁻¹. The filtrate gave **10** and DIC and its urea (0.54 g).

DIC–DMAP. DIC (0.05 cm³, 0.33 mmol), **10** (0.25 g, 0.33 mmol), TentaGel (1.40 g, 0.33 mmol), DMAP (0.043 g, 0.35 mmol) and DCM (20 cm³), after 3 d, gave **8** (1.30 g); ν_{max} 1750, 1676 cm^{-1} and proton NMR indicated a loading of <1%. The filtrate gave **10** and DIC and its urea (0.28 g).

DCC. DCC (0.33 cm³, 0.33 mmol of 1.0 M DCM solution), **10** (0.25 g, 0.33 mmol), TentaGel (1.32 g, 0.33 mmol) and DCM (20 cm³), after 4 d, gave a resin, which was shown to contain **8** and DCC and its urea. The filtrate gave **10** (0.1 g). A loading of 7% was estimated by NMR.

EDCI. EDCI (0.068 g, 0.33 mmol), **10** (0.25 g, 0.33 mmol), TentaGel (1.40 g) and DCM (20 cm³), after 3 d, gave **8** (1.40 g) with a loading of *ca.* 2% by NMR. The filtrate gave **10** (0.15 g).

EDCI–DMAP. EDCI (0.067 g, 0.33 mmol), **10** (0.26 g, 0.33 mmol), TentaGel (1.40 g), DMAP (0.043 g) and DCM (20 cm³), after 3 d, gave **8** (1.36 g) with a loading of *ca*. 1%. The filtrate gave **10** (0.24 g).

Synthesis of 9. DIC (0.15 cm³, 0.96 mmol), **10** (0.75 g, 0.98 mmol), aminomethyl polystyrene (1.10 g, 0.99 mmol) and DCM (60 cm³), after 3 d, gave **9** (1.52 g); ν_{max} 3385, 3026, 2921, 1747 (CO$_2$H), 1683 (CONH), 1601, 1492, 1451, 1194 cm^{-1} , which corresponds to a loading of 28%. The filtrate gave **10,** DIC and its urea (0.34 g).

Acknowledgements

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Solvent-free ruthenium-catalysed vinylcarbamate synthesis from phenylacetylene and diethylamine in 'supercritical' carbon dioxide

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The solvent-free synthesis of β-[(diethylcarbamoyl)oxy]styrene from phenylacetylene and diethylamine in supercritical carbon dioxide is greatly accelerated for a series of ruthenium catalysts compared to the same reactions in toluene.

Introduction

The discovery that metal vinylidene complexes are readily available *via* the reaction of late transition metal complexes with terminal alkynes spawned a new field of catalytic chemistry utilizing this functionality.[1] Among these transformations, the ruthenium-catalysed synthesis of vinylcarbamates from carbon dioxide, secondary amines and terminal acetylenes has proved particularly interesting (Scheme 1).[2] Vinylcarbamates are versatile synthetic intermediates used in the pharmaceutical and agrochemical industries.[3] In the past, all preparative routes to this class of compounds have involved the highly toxic chemical phosgene.[4]

In the late 1980's, Dixneuf and coworkers reported the homogeneous ruthenium(II)-catalysed synthesis of vinylcarbamates from secondary amines, a terminal alkyne and carbon dioxide in organic solvents, effectively replacing phosgene with non-toxic carbon dioxide.[5] The high natural abundance and ease of handling of carbon dioxide has prompted considerable interest in its utilization in chemical processes.[6–8] Recent developments in this field demonstrate that carbon dioxide is a useful reactant which can simultaneously be used as reaction medium.[9–11] In the present contribution we show that catalytic vinylcarbamate **1** synthesis (Scheme 1) may be conducted in the absence of any solvent in supercritical carbon dioxide (scCO$_2$), thus simplifying product/catalyst separation. In addition, we report that ruthenium(II) catalysts are more active under these conditions.

Results and discussion

A comparison of conversion and selectivity for [RuCl$_2$(C$_5$H$_5$N)$_4$] **4** and [RuCl$_2$(η^6-C$_6$H$_6$)(PMe$_3$)] **5** catalysed vinylcarbamate **1** synthesis in scCO$_2$ and toluene is presented in Fig. 1(a) and (b). In general, conversions are significantly higher in scCO$_2$ than in toluene (Fig. 1(a)), with RuCl$_3$·xH$_2$O **3** (not shown) and **4** results being similar, and **5** displaying the highest activity. The corresponding TOFs reflect this behaviour and are approximately three times higher in scCO$_2$ (92 h^{-1}) than in toluene (31 h^{-1}) as demonstrated for **5** at 90 °C and 90 bar. For catalysts **4** and **5** conversion increased significantly from 60 up to 120 °C at 90 bar, whereas selectivity reached a maximum at 90 °C. Highest conversion was reached at a total pressure of 90 bar and 120 °C. For **5**, at a constant temperature of 90 °C, selectivity increased whereas conversion was only slightly affected by increasing pressure. Favorable reaction conditions (90 °C, 90 bar) for selectivity in ruthenium-catalysed vinylcarbamate **1** synthesis are similar for the reaction in scCO$_2$ and toluene. Previously used solvents included toluene, THF and acetonitrile.[5] Toluene was selected here for comparison purposes based on the similarity of solvent properties with those of scCO$_2$. The positive influence of scCO$_2$ as reaction medium manifests itself as a considerable increase in conversion. For
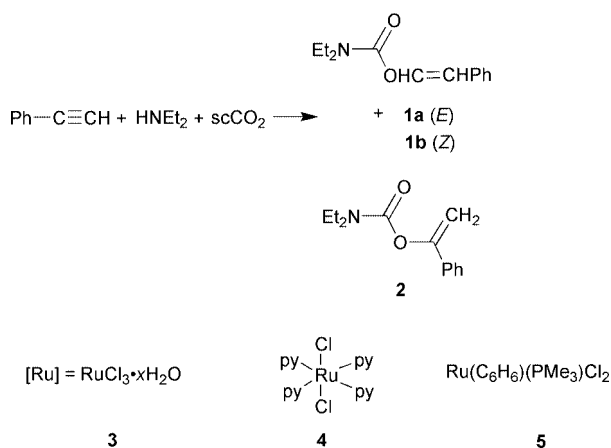
Scheme 1 Vinylcarbamate synthesis from phenylacetylene, diethylamine and scCO$_2$ with ruthenium catalysts [Ru].

Green Context

While the utilisation of carbon dioxide as a feedstock cannot be expected to result in a significant reduction in global emissions, its natural abundance and ease of handling do make it an attractive C$_1$ substrate. This is especially true for chemical syntheses that have traditionally involved toxic substrates notably phosgene. The synthesis of vinyl carbamate is a good example of this and here an environment-friendly route not only based on CO$_2$ as substrate but also using (supercritical) CO$_2$ as the solvent is described. The new method also gives enhanced reaction rates compared to organic solvent-based systems.

HVC

catalyst **5**, 95% conversion is achieved in just 3 h at 120 °C and 90 bar as opposed to 20 h required in earlier work.[5] The increased catalytic activity in $scCO_2$ is not unprecedented. A similar behaviour was observed in the ruthenium-catalysed syntheses of *N,N*-diethylformamide where TOFs were also much greater in $scCO_2$.[12]

The Markovnikov product **2** (Scheme 1) was formed in negligible amounts in agreement with Dixneuf's work.[5] *Z/E* ratios for vinylcarbamate **1** were in the range 3.8–8.3 : 1 with a mean of 6 : 1, compared with 4 : 1 reported previously.[5] Interestingly, at 90 °C and 90 bar the *Z/E* ratios were considerably different for **4** and **5**, being higher for the latter. The catalysts also showed opposite behaviours; for example, at 90 bar the *Z/E* ratio increased for **4** and decreased for **5** with increasing temperature. Therefore, it appears that although **4** is active for the catalytic synthesis of **1** the reaction may proceed by a slightly different pathway to that for **5**. In general, increasing the amount of base to *ca.* 100 mmol had no significant effect on *Z/E* ratios or conversion. Increasing the amount further led to reduced conversions, probably due to competitive attack of the base and reactants at the metal center. Under similar conditions, $RuCl_2(PPh_3)_3$ displayed significantly lower conversion and selectivity than **4** and **5**. This may be a consequence of the sterically more demanding phosphine substituents preventing approach of the reactant to the catalytically active center.
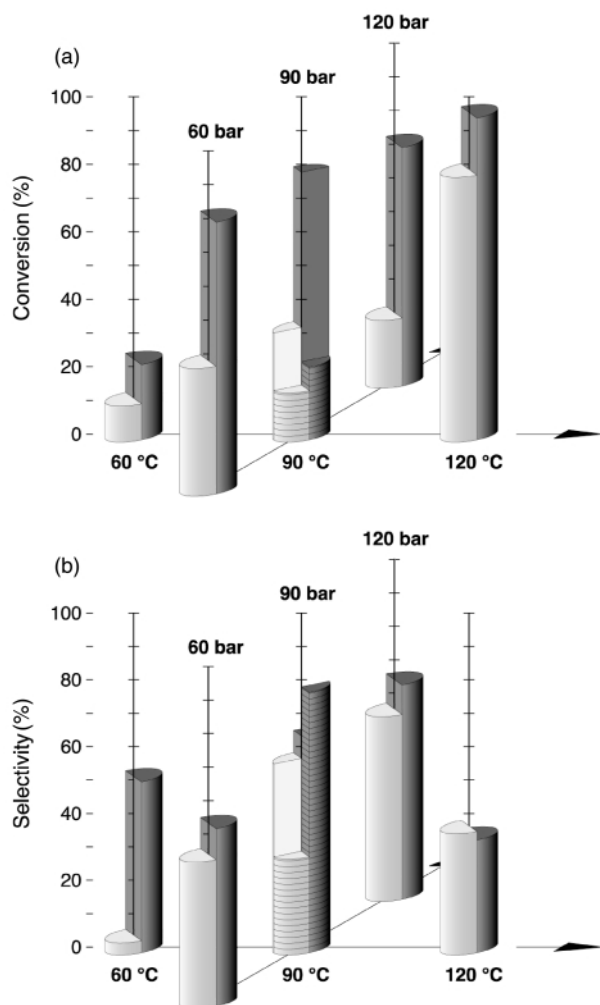
Vinylcarbamate synthesis and phenylacetylene polymerization share the same ruthenium–vinylidene intermediate. Therefore, selectivity to **1** depends at least partly on the relative rates of nucleophilic attack of the carbamate anion ($Et_2NCO_2^-$) and phenylacetylene incorporation at the α-carbon of the vinylidene intermediate.[2] Indeed, for catalysts **4** and **5** the selectivity was <10% to the acetylene insertion products 1,4-diphenylbut-3-en-1-yne and 1,1′-(1-butan-3-yne-1,4-diyl)bibenzene. Therefore, it seems likely that higher molecular weight polymers, which are not detected by gas chromatography, constituted the remaining byproducts as indicated by the formation of viscous reaction residues.

Examination of the reaction mixture using a purpose-built view-cell[13] combined with video imaging[14] revealed a complex phase behaviour. At the beginning of the reaction two phases were present; a small amount of a liquid phenylacetylene–diethylamine phase saturated in CO_2 at the reactor base and an upper 'supercritical' CO_2–rich phase (Fig. 2(a)). Note that here the term "supercritical" describes the dense CO_2-rich phase at temperatures beyond its critical point, irrespective of any other liquid phases present in the system. As the reaction proceeds (*ca.* 2 h), the liquid phase increases in volume at the bottom of the reactor (Fig. 2(b)). This increase can be traced to the lower volatility of the vinylcarbamate **1** leading to product condensation.

In conclusion, considerably higher rates of reaction are observed in the solvent-free $scCO_2$ system compared to toluene, even though the reaction conditions have not been optimized. Potential for further improvement of the reaction performance may lie in increasing the density of $scCO_2$, and consequently the solubility of reactants and catalyst in the latter, eventually leading to a 'supercritical' single-phase system. The present synthetic route to vinylcarbamates abandons the use of phosgene and any solvent, and thus may pave the way to a new environment-friendly catalytic process.

Experimental

Catalytic tests were run in a 250 ml stainless steel autoclave. The reactor was charged with phenylacetylene (10 mmol), diethylamine (80 mmol) and catalyst (0.036, 0.027 and 0.018 mmol for catalysts **3**, **4** and **5**, respectively). Carbon dioxide was introduced using a compressor. The catalysts $[RuCl_2(C_5H_5N)_4]$ **4**[15] and $[RuCl_2(\eta^6-C_6H_6)(PMe_3)]$ **5**[16] were prepared according to literature methods and $RuCl_3 \cdot xH_2O$ **3** was used as supplied by ABCR, Karlsruhe, Germany. β-[(diethylcarbamoyl)oxy]styr-

Fig. 1 Influence of temperature and pressure on phenylacetylene conversion (a) and selectivity (b) to vinylcarbamate **1**. Data for catalysts **4** and **5** are shown in light and dark grey, respectively. Experiments with toluene (50 ml) as solvent are depicted with striped bars, all other bars represent experiments in $scCO_2$. Conversions are defined as [mol phenylacetylene reacted/initial mol phenylacetylene] and selectivities as [mol vinylcarbamate **1**/mol phenylacetylene reacted]. The reaction duration was 3 h in all cases.
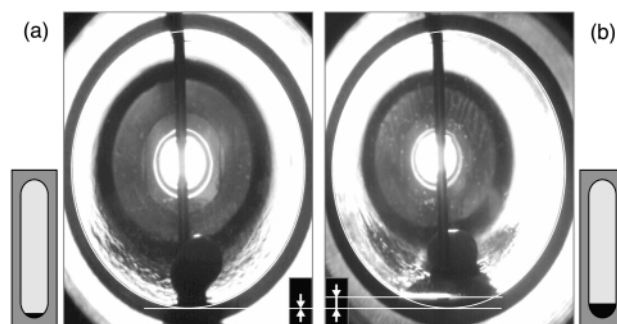
Fig. 2 Video images of the reaction mixture at the beginning (a) and after 2 h (b) of the vinylcarbamate **1** synthesis in $scCO_2$ (90 bar, 90 °C). The increase in volume of liquid phase is highlighted and represented schematically at the side. The illuminated sapphire window is visible as the bright round spot at the far end of the cell; the outer bright circle is caused by reflection of light at the outer flange of the sapphire window; the vertical thermocouple and magnetic stirrer at the bottom of the cell are also visible.

ene **1** was isolated and identified by comparison with available spectroscopic data.[5] After reaction, the autoclave was cooled to room temperature and vented. Reaction samples were dissolved in toluene with pentadecane added as standard. Analysis was performed on a HP 6890 gas chromatograph equipped with a FID detector and HP-5 column (length 30.0 m, diameter 320 µm, film thickness 0.25 µm). Turnover frequencies (TOFs) were calculated as [mol **1**/(mol catalyst × time)]. The phase behaviour of the reaction was studied in a computer-controlled high-pressure variable volume (23–63 ml) view-cell,[13] equipped with online digital video camera. The magnetically stirred cell comprised a horizontal cylinder fitted with a sapphire window covering the entire diameter, opposite a horizontally moving piston equipped with an illuminated sapphire window. The computer-based approach with video imaging has been described elsewhere.[14]

Acknowledgement

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A sonoelectrochemical Fenton process for efficient synthesis of tetramethyladipic acid from pivalic acid

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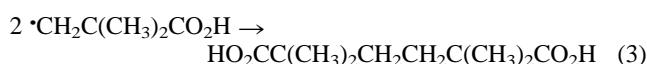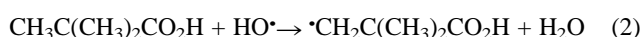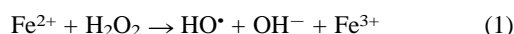[b] Department of Instrumentation and Analytical Science, UMIST, Manchester, UK M60 1QD

Tetramethyladipic acid (TMAA), a starting monomer for several technically important polymers (polyester resins and polyamide fibres) is synthesised by direct carbon–carbon bond formation between the saturated primary carbon atoms of pivalic acid (PA) using a sonoelectrochemical Fenton process. Through controlled electrochemical dissolution assisted by ultrasound radiation, Fe^{2+} ions are produced *in situ* from metallic iron in the reaction mixture. The effects of ultrasound with electrolysis, temperature, amount of substrate present, reagent concentration, solution acidity and quantity of electric charge have been examined. Under suitable conditions, the synthesis yield based on initial PA present, hydrogen peroxide used and amount of iron dissolved reached 34, 40 and 75%, respectively and less by-product was observed. These results show significant improvement in terms of direct cost savings by omission of separate preparation of a ferrous salt, fewer side reactions during the dimerisation process, less waste, easier purification; increased efficiency due to recycling of iron ions and improved reactivity of fresh Fe^{2+} ions. All of these advantages make this sonoelectrochemical approach a much more efficient and environmentally cleaner option.

Introduction

The dimerisation of pivalic acid through direct coupling of carbon centred radicals generated *via* traditional Fenton chemistry has been previously reported.[1] More recently, the effects of ultrasonic irradiation on this reaction were re-investigated[2] and may be represented overall by eqns. (1)–(3).

$$Fe^{2+} + H_2O_2 \rightarrow HO^{\bullet} + OH^- + Fe^{3+} \quad (1)$$

$$CH_3C(CH_3)_2CO_2H + HO^{\bullet} \rightarrow {}^{\bullet}CH_2C(CH_3)_2CO_2H + H_2O \quad (2)$$

$$2\ {}^{\bullet}CH_2C(CH_3)_2CO_2H \rightarrow \\ HO_2CC(CH_3)_2CH_2CH_2C(CH_3)_2CO_2H \quad (3)$$

The product, tetramethyladipic acid (TMAA), has the same main carbon chain as adipic acid, one of the major intermediates of polyester resins[3] and polyamide fibres.[4] However, the additional methyl groups in TMMA modify the intermolecular interaction of the polymer chains and hence physical aspects such as crystallinity and mechanical properties. Their close proximity to the carbonyl group may also exert significant effects on the amide moieties in the polymer and alter the chemical properties such as resistance to hydrolytic, thermal and photo-decomposition.[4]

Unlike radical chain reactions, in which the initiator radicals are used in trace quantity at the outset, radical dimerisation consumes hydroxyl radicals throughout, as required by the stoichiometry. Furthermore, in order for the bimolecular radical coupling reaction to proceed at a sufficient rate, the concentration of hydroxyl radicals has to be maintained at a relatively high level. Therefore, efficient generation of hydroxyl radicals in the synthesis is necessary. In previous studies of reaction,[1] the classic Fenton process[5,6] was used where simultaneous addition of H_2O_2 and an acidic ferrous sulfate solution is required. The Fenton process is attractive for small laboratory preparations but on an industrial scale is problematical due to the way in which Fe^{2+} ions are delivered. Constant addition and consumption (rather than recycling) in large quantity (1.5 kg of

$FeSO_4$ is required to react with 1 kg of PA) of a pure reagent separately prepared add significantly to process cost and waste.

Here, a strategy of controlled electrochemical dissolution of metallic iron is used to produce pristine ferrous ions [eqn. (4)].

$$Fe^0 \xrightarrow{\text{sonoelectrodissolution}} Fe^{2+} \quad (4)$$
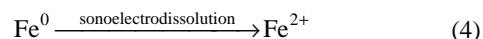
These ions now react in the usual Fenton process and are used to synthesise TMAA from pivalic acid. This sonoelectrochemical Fenton process, similar to that used for the electrochemical treatment of aqueous herbicide solutions with hydrogen peroxide[7] and the electrochemical regeneration of Fenton reagent in the hydroxylation of aromatic substrates[8] is expected to offer a number of advantages over the purely chemical approach. These include: (a) cost savings by omission of separate preparation of a ferrous salt; (b) fewer side-reactions during the

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Green Context

The Fenton reaction provides an almost unique method for the activation of certain molecules. In particular, the dimerisation of pivalic acid gives tetramethyladipic acid, useful as a property modifier in polyamides. Unfortunately, classical Fenton chemistry requires large quantities of iron(II) salts, which are consumed stoichiometrically. This paper highlights an apporaoch based on a combination of sonochemistry and electrochemistry, which delivers these iron species efficiently to the reaction, and which can be (partially) recycled to iron(II) after reaction, leading to a much more efficient process. The combination of the electrochemical dissolution of ions from bulk iron with the advantages of rapid mass transport caused by sonochemical irradiation, makes the approach an alternative to conventional Fenton methodology. *DJM*

dimerisation process; (c) less waste by minimising by-product formation; (d) easier separation and purification stages; (e) increased efficiency due to recycling of iron ions through the cathodic reaction $Fe^{3+} + e^- \rightarrow Fe^{2+}$ and the thermodynamically propitious equilibrium: $2Fe^{3+} + Fe \rightarrow 3Fe^{2+}$ (calculated $\Delta G^{\ominus} = -234$ kJ mol^{-1}); and (f) greater reactivity of pristine Fe^{2+} ions for simultaneous and more efficient HO$^\bullet$ generation.

Experimental

Typical initial composition of the reaction mixture: pivalic acid (25 g, 99% from Lancaster), H_2SO_4 (6 M, 45 ml), HCl (2 M, 10 ml), and H_2O_2 (*ca.* 27% by weight, 25 ml) and distilled water (500 ml). PA was dissolved/suspended in water by stirring with an overhead mechanical stirrer (operating at *ca.* 200–300 rpm). TMAA synthesis was initiated by supplying a dc current using a Model L30E stabilised power supply unit (from Farnell Instruments Ltd.). The two electrodes of iron strip (purity 99.9%, 20 mm wide, 1 mm thick), each with an immersed area of *ca.* 40 cm^2, were inserted in the same reaction vessel (*i.e.* an undivided electrolytic cell). Ultrasound radiation (20 kHz frequency) was supplied using a Sonics and Materials Model VC600 *via* a cup-horn water bath. The full power of the ultrasound generator (600 W electrical, 100 W ultrasonic) can be attenuated in 10 levels. The output can be continuous or pulsed with varying percentage of cycle duty from 10 to 100% (*i.e.* continuous). Mechanical stirring was maintained throughout the reaction. A schematic diagram of the experimental set-up used is shown in Fig. 1.

Preliminary rapid identification of the product in the reaction mixture was by thin layer chromatography (light petroleum (bp 60–80 °C)–ethyl acetate (1:3, v/v, universal indicator visualisation). The unreacted PA was readily removed and recovered by steam distillation. Separation of the product was carried out by extraction with ethyl acetate followed by vacuum evaporation of the solvent. The solid extract was then recrystallised from diethyl ether–light petroleum (bp 60–80 °C) to give white TMAA crystals, which were characterised by comparison with authentic samples prepared according to published methods.[2] Based on the semi-quantitative observation of TLC and mp, the purity of TMAA (*i.e.* percentage of TMAA in the mass recovered) was estimated to be > 95% under appropriate reaction conditions and the conversion rate is used approximately as the yield.

Results and discussion

The parameters investigated include: ultrasound with electrolysis, temperature, amount of substrate, reagent concentra-
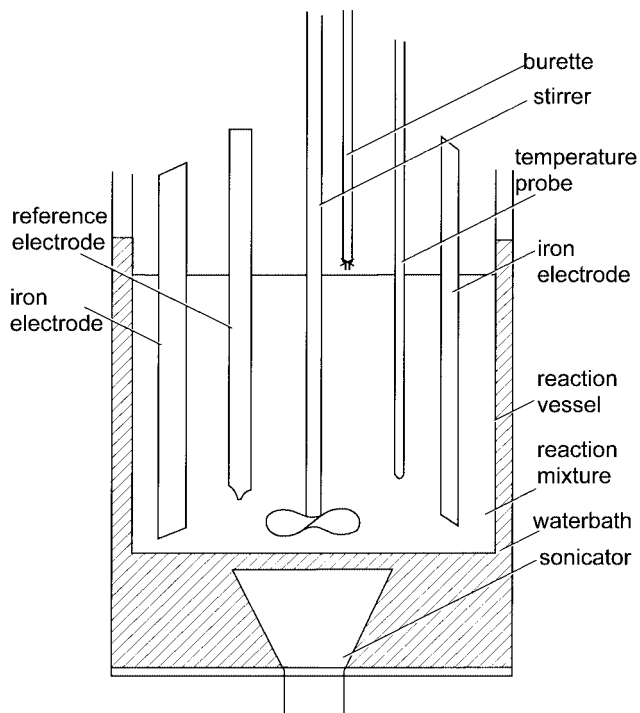

Fig. 1 Schematic diagram of the experimental set-up.

tions, solution acidity and quantity of electric charge. Table 1 lists TMAA yields achieved under various reaction conditions.

Ultrasound with electrolysis

Previous studies using the Fenton reaction in the classical chemical solution method[2] showed that ultrasonic radiation provided no additional benefits as measured by yield and purity of product. This is characteristic of reactions between species residing in the same phase where specific, as well as, relatively intense input of ultrasonic energy is generally required.[9] In contrast, reactions between species in solution and solid reagents or where electrode interfaces are involved can be markedly assisted by ultrasound in a number of ways.[10,11] One important effect of sonication arises from improved mass transport to and from solid surfaces. Significant rate increases in electrolysis have been shown[12] to result from an increase in momentum brought about as the solvent molecules absorb energy from the propagating sound wave. This acoustic streaming is a non-specific phenomenon that improves mass transport between the bulk of the liquid and an electrode surface. It is independent of cavitation effects at liquid/solid

Table 1 Yield and efficiency for TMAA synthesis under various conditions^a

No	Variable	Composition of starting mixture	T/°C	Time/min	Q/10^4 C	W_{TMAA}/g	Y_{PA}(%)	n_{Fe}/mmol	η_{Fe}(%)	Y_{Fe}(%)	Y_Q(%)
1	—	H_2SO_4 (0.5 M), HCl (35 mM) PA (sat., 10 g), H_2O_2 (0.35 M)	14	180	3.24	0.5	5	—	—	—	3
2	Temperature	As 1	24	150	2.70	3.1	31	50	36	61	22
3	[H_2O_2]	As 1, but H_2O_2 (0.14 M)	24	120	2.16	2.2	22	37	33	59	19
4	[H^+],[Cl^-]	As 1, but H_2SO_4 (1 M) no Cl^-	24	150	2.70	1.5	15	29	21	51	11
5	[PA]	As 1, but PA (sat., 15 g)	24	210	3.78	3.5	24	59	30	59	17
6	[PA]	As 1, but PA (sat., 25 g)	24	270	4.86	8.3	34^b	110	43	75	32
7	Time	As 6	24	120	2.16	4.8	19	68	61	70	42
8	[Cl^-]	As 6, but HCl (82 mM)	24	250	4.50	5.3	21	128	55	41	22
9	[Cl^-]	As 6, but HCl (210 mM)	24	360	6.48	5.1	21	180	54	28	15

^{a} Q/10^4 C is the quantity of electricity passed in coloumbs; W_{TMAA}/g is the number of watts used per gram of product; Y_{PA}(%) represents the yield of TMAA based on amount of pivalic acid at the beginning; n_{Fe}/mmol is amount of iron consumed; η_{Fe}(%) is the electrochemical efficiency of iron dissolving as Fe^{2+}; Y_{Fe}(%) is the yield of product based on the amount of iron consumed; and Y_Q(%) indicates the yield of TMAA relative to the current passed; a dash in the table indicates that the information is not available or not relevant. ^{b} 40% yield (based on H_2O_2).

interfaces frequently observed in the well known cleaning property of ultrasound of metal surfaces. It is likely that the cleaning and improved mass transport effects combine by increasing the number of active surface sites available and the overall rate of species transfer.[9,13]

Electrolysis without ultrasound lacks the acoustic streaming and cavitational cleaning effects to the extent that surface films on the electrodes rapidly inhibit reaction progress and negligible product forms. Consequently, electrolysis combined with ultrasound was indicated as a necessary condition. It was observed that the sonoelectrochemical interaction allowed both iron anode and cathode to be freed of inhibiting product or passivating reaction films. Each electrode showed surface iron removal with usually eight times more abstracted from the anode. Scrutiny of the electrode surfaces also showed pitting corrosion had aided surface cleaning and iron dissolution, particularly at the anode. Efficient sonoelectrochemical Fenton processing was found to proceed at a level of ultrasound that maintained active iron surfaces with the selected electrolysis current. In this study, electrolysis was carried out at a current of 3 A (*ca.* 75 mA cm^{-2}) and ultrasound combined efficiently at a fixed input at power level 8 (*ca.* 80% of the full power) and a 50% cycle duty. This current and input of ultrasound had been found to be appropriate in a model synthesis (phenol from benzene)[14] where electrolytic Fenton processing was considerably enhanced by ultrasonic assistance using the same apparatus. The weight loss from the electrodes signified the amount of iron (mol) that had dissolved during the electrolysis, η_{Fe}. From the amount of charge Q consumed, the electrochemical efficiency of iron dissolution in the form of Fe^{2+} can be calculated: $\eta_{Fe} = 2F\eta_{Fe}/Q$. The yield of the product can be calculated on the initial PA present and the synthesised TMAA recovered after the selected reaction time, to give Y_{PA} which is thus a function of reaction time (synthesis yield may also be based on H$_2$O$_2$ used). Alternatively, the yield can be calculated on the basis of quantity of electric charge consumed or on amount of iron dissolved. Thus, $Y_Q = 4Fn_{TMAA}/Q$, indicates the efficiency of the charge injected and $Y_{Fe} = 2n_{TMAA}\eta_{Fe}$ the efficiency of the utilisation of dissolved iron for the synthesis.

Temperature

From the data listed in Table 1, it is clear that reaction temperature T has a significant effect on the synthetic yields. A moderate increase in temperature from 14 to 24 °C (entry 2 compared with entry 1) resulted in an increase in the yield Y_{PA} from 5 to over 30% in spite of the reduction of reaction time (and thus electric charge used). The overall electrochemical efficiency increased from 3 to 22%. On the other hand, melting of PA (at 36 °C) creates a viscous and sticky mixture, which is detrimental to the synthesis and separation. Therefore, further increase in temperature was not attempted and all subsequent synthesis was carried out at 24 °C.

Hydrogen peroxide concentration

Comparison between entries 3 and 2 in Table 1 shows that as the concentration of hydrogen peroxide is increased from 14 to 35 mM, Y_{PA} is increased from 22 to 31%. Allowing for the difference in reaction time, this corresponds to a relative increase of 13%. Meanwhile, the overall electrochemical efficiency is increased from 19 to 22% and the efficiency of iron dissolution is increased from 33 to 36%. The observation is consistent with the case of phenol synthesis through direct hydroxylation of benzene[14] where an increase in hydrogen peroxide excess from 25 to 100% leads to a relative increase in the yield by 36%. However, hydrogen peroxide can react with hydroxyl radical: H$_2$O$_2$ + HO$^\bullet$ → HO$^\bullet_2$ + H$_2$O, potentially

reducing the yield of TMAA and placing an upper limit for H$_2$O$_2$:PA of about 2:1.

Solution acidity and chloride concentration

In a recent study from this laboratory of phenol synthesis through the *in situ* electrochemical Fenton process,[14] it was found that hydroxyl radicals are produced more effectively by the fresh-formed iron ions than by any electrochemical reduction of hydrogen peroxide on the metallic iron surface. Therefore, factors that influence the dissolution and passivation of iron are expected to have major effects on the synthetic yields of TMAA. Most prominent among these factors, which have been studied extensively in previous corrosion research,[15] are solution acidity and the presence of so-called 'aggressive' anions such as halides.[16,17] Therefore, the effects of proton concentration [H$^+$] and chloride concentration [Cl$^-$] were investigated.

When the initial [H$^+$] is low, (*ca.* 0.1 M), very little iron dissolves and TMAA synthesis is ineffective. TLC analysis shows that the concentration of TMAA in the mixture is virtually zero after 120 min reaction (recovery of product not attempted). An increase in [H$^+$] to 1.0 M leads to increased dissolution and thus an improved yield of Y_{PA} of 15% (entry 4) after 150 min reaction. However, this yield is still quite low, indicating that the sole effect of acid is not sufficient for effective dissolution of iron under the particular conditions. Chloride is known to have a dramatic enhancing effect on the dissolution of iron[15–17] owing mainly to its polarisibility. Therefore, addition of 35 mM chloride (entry 2 in comparison with 4) in the reaction mixture resulted in an increase in the efficiency of iron dissolution to 36 from 21%, in spite of the reduction in [H$_2$SO$_4$] from 1.0 to 0.5 M. Correspondingly, the yield based on dissolved iron Y_{Fe} is also increased to 61 from 51% and the synthesis yield Y_{PA} is doubled. This means that in the presence of chloride ions, not only is the iron electrode dissolved more easily but also an increased percentage of the dissolved iron is effective for the synthesis.

As expected, increasing [Cl$^-$] from 35 to 82 and 210 mM (entry 2 compared to entries 8 and 9) led to an increase in the dissolution efficiency from 36 to *ca.* 55%. The yield and efficiency of TMAA synthesis, however, are reduced significantly: Y_{PA} from 31 to 21% and Y_{Fe} from 61 to 28–41%, indicating that although iron dissolution is facilitated by a higher chloride concentration, synthesis of TMAA is hindered. This effect is attributed to the side reaction between chloride ions and the hydroxyl radicals producing molecular chlorine:[18] Cl$^-$ + HO$^\bullet$ → Cl$^\bullet$ + HO$^-$. At a moderate chloride concentration, the positive effect of facilitating iron dissolution and thus HO$^\bullet$ generation is predominant, whereas at high concentrations, a large proportion of HO$^\bullet$ radicals are converted to hydroxide and the negative effect becomes dominant. Therefore, the choice of chloride concentration has to be a compromise between the two conflicting effects, and [Cl$^-$] in the range 30–50 mM is appropriate.

Amount of pivalic acid used

Generally, an increase in the amount of PA present helps the desired reaction compete more effectively with side reactions, and thus enhances the yield and efficiency.[1] This is expected to be particularly true for the TMAA synthesis because of the low selectivity of hydroxyl radicals due to their high reactivity. Therefore, when the amount of PA is increased from 10 to 25 g (entry 2 compared with entry 6), the efficiency of iron utilisation increased from 61 to 75% and the overall electrochemical efficiency from 22 to 32%. In other words, at a higher initial amount of PA an increased proportion of the hydroxyl radicals

produced are utilised by TMAA synthesis rather than by side reactions. The limited solubility of PA in water means that even at the lowest amount of PA present (10 g), the reaction mixture is saturated. It is considered that abstraction of a hydrogen atom from PA by hydroxyl radical may take place at the interface between water and the PA (solid particles or liquid droplets) as well as in the homogeneous solution and the effects of increased amount of PA is attributed to an increased interfacial area. The unexpected decrease in the yield and efficiency in entry 5 compared with entry 2 was due to overreaction (*i.e.* excessive electrolysis) as discussed below.

Reaction time and quantity of charge

During the synthesis, a large fraction of the TMAA produced is removed from the solution through spontaneous deposition onto the contacting surfaces of the reaction vessel and electrodes or formation of a precipitate, but some remains dissolved in the solution (the solubility of TMAA not being known). The dissolved TMAA may undergo further reactions *via* a similar radical intermediate generated by HO• to give rise to trimers, tetramers and higher oligomers of PA.[2] (These reactions may also take place at the interface between the agglomerated TMAA and the solution at a slower rate.) As the synthesis of TMAA proceeds, the probability of HO• attacking the product instead of the substrate increases. Therefore, the efficiency of the reaction is expected to change with the stages of the reaction. To investigate such changes, the reaction time was extended or shortened in comparison with the 'normal' time of entry 6. The product was recovered using the extraction procedure described[2] and the yields and efficiencies evaluated.

Formation of trimers, tetramers and higher oligomers of PA over extended periods of electrolysis is manifested in foaming of the reaction mixture (due to structural similarities to the surfactant fatty acids) and more complex reaction mixtures (TLC). More serious overreaction leads to the formation of a brownish precipitate in large quantity (*e.g.* > 2 g of dry mass was separated), which decomposes, instead of melting, at 250–270 °C. Such overreaction explains the reduced yield and efficiency of entry 5 in Table 1 (compared with entry 2) in spite of the increase in amount of PA present. Therefore, the desire for a high yield *via* sustained supply of charge needs to be balanced against overreaction. (This type of degradation process under different conditions has been found to be highly effective, with environmental implications, particularly for waste-water remediation, and will form the basis of another and detailed study to be reported.)

In contrast, when the reaction was stopped at earlier stages (after 120 min, entry 7, or 44% of the full time of 270 min, entry 6) the efficiency of iron dissolution is appreciably higher (61% compared with 43%). Consequently, the overall electrochemical efficiency Y_Q also increased from 32 to 42%. The higher electrochemical efficiency at the early stages is not related to the changes in the amount of PA, which are insignificant compared with the large excess throughout. Instead, it is attributed to more favourable dissolution of iron owing to decreased adsorption and deposition of the product on the electrode surface brought about by the interfacial activity of the ultrasound.

Comparison with chemical synthesis

In the chemical synthesis of TMAA using a ferrous salt solution, the product mass recovered following the procedures of steam distillation, ethyl acetate extraction and vacuum evaporation is a brownish oil containing substantial proportions of trimers, tetramers and higher oligomers.[2] In order to obtain relatively pure TMAA, difficult separation *e.g.* using column chromatography must be carried out. In the sonoelectrochemical approach under suitable conditions, the product mass recovered following the same procedures consisted predominantly of crystalline TMAA with only a slight orange-brown tinge. Experiments show that pure product (giving the same mp as that purified by chromatography) can be obtained simply by filtration following re-crystallisation from diethyl ether–light petroleum (bp 60–80 °C). Occasionally, white crystalline TMAA precipitate was produced in the reaction media, which can be directly collected by filtration, thus greatly simplifying the recovery procedure.

Previous systematic optimisation of the chemical method lead to a best yield of *ca.* 30% calculated on the initial amount of PA used. This was achieved by using equivalent amounts of reagents (H_2O_2 and Fe^{2+}) and substrate (PA). In the sonoelectrochemical approach, $Y_{PA} = 34\%$ (40% for yield based on H_2O_2) is readily obtained under the selected conditions and it is considered room exists for further improvement. A survey of the Y_{Fe} column in Table 1 shows that the utilization efficiency of the iron dissolved is generally in the range 51–75%. This confirms that the pristine Fe^{2+} ions are more effective for HO• generation than those solvated in a solution prepared in advance.

In the chemical synthesis, a significant proportion of the substrate is converted to undesired products and relatively little PA can be recovered. In the sonoelectrochemical approach, undesired conversion of PA can be controlled conveniently and the unreacted substrate can be recovered easily. Such ready reuse means that even if the yield Y_{PA} of 34% is near to a natural limit that is impracticable to exceed, it should not constitute a serious difficulty for an industrial process.

The main problem of an electrochemical approach without ultrasound assistance relates to the adsorption and deposition of organic mass on the electrode surface, which hinders iron dissolution and suppresses reaction progress. The necessary inclusion of ultrasonic radiation directed across the electrode surfaces and through the reaction mixture so improves both yield and efficiency that the iron–solution interface for sonochemical synthesis is currently being studied.

Conclusions

The sonoelectrochemical Fenton process involving *in situ* generation of Fe^{2+} ions through controlled dissolution of metallic iron has proved successful for the synthesis of TMAA from pivalic acid *via* a route of direct carbon–carbon bond formation. Yield is improved by augmenting electrochemical energy with ultrasonic irradiation. Raising the reaction temperature within a certain range also delivers a higher yield. Increased solution acidity facilitates iron dissolution and hence the generation of hydroxyl radicals and ensuing reaction. The presence of a corrosive chloride serves the same purpose, but too high a concentration is detrimental owing to competition with the substrate for hydroxyl radicals. Increased H_2O_2 concentration is also beneficial to the yield up to a point where again competition for hydroxyl radicals becomes significant. The more efficient or proportionately higher yield at the early stages of synthesis, which is not an effect of amount of substrate present, demonstrates the possibilities for further gains in efficiency by limiting the reaction process to 60 min or less before removing the TMAA and recycling the residual PA. Compared with previous chemical synthesis using a ferrous salt solution prepared separately in advance, the sonoelectrochemical approach offers advantages of purer product, practical reuse of the unreacted substrate, and more efficient use of H_2O_2 and iron to reach a given yield. This work is of direct relevance to Green Chemistry because it illustrates clean synthesis, shows a

reduction in waste products allied to the use of water as the solvent. Additionally, the use of iron, instead of ferrous sulfate, is of great benefit in enhanced atom utilisation by replacement of stoichiometric reagents. These features mean a cleaner and more effective process for industrial production and may actually be more energy efficient overall.

Acknowledgements

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Tungstophosphoric acid catalyzed oxidation of aromatic amines to nitro compounds with sodium perborate in micellar media

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Several primary aromatic amines, substituted with electron-donating groups, were converted to their corresponding nitro compounds in good to excellent yields with sodium perborate tetrahydrate (SPB) in micellar media in the presence of a catalytic amount of tungstophosphoric acid ($H_3PW \cdot nH_2O$).

Introduction

Oxidation of anilines to their nitro compounds is an important chemical transformation. Oxidation of aromatic primary amines has attracted the attention of chemists in recent years.[1] The nature of the oxidation products formed depends on the type of the oxidant used and the reaction conditions, *i.e.* aqueous or non-aqueous media and the pH employed for the reaction. For this purpose methods are well documented. Various reagents, including metal compounds, organic peroxides and hydrogen peroxide, have been used to form oxygen-containing derivatives of anilines.[2] Some of the procedures described in the literature suffer from harsh reaction conditions, over-oxidation, low yields of the desired products, and unavailability of the reagents. The non-toxic, inexpensive and easily available peroxygen compound sodium perborate (SPB)($NaBO_3 \cdot nH_2O$, n = 1–4) is extensively used in the detergent industry as a bleaching and antiseptic agent as well as in organic synthesis. SPB is a good substitute for potentially hazardous concentrated H_2O_2. SPB has been extensively used for functional group oxidation in organic synthesis and has recently been reviewed.[3] McKillop has reported the use of a large excess of sodium perborate ($NaBO_3$) in acetic acid at 50–55 °C for the oxidation of anilines containing electron-withdrawing groups to the corresponding nitro arenes. In contrast, anilines with electron-donating groups were readily over-oxidized affording the crude nitro arenes[4] in only low yields and the method was recognized to be unsuitable for this type of oxidation. The use of water as a medium for promoting organic reactions (and also as the solvent in which the vast majority of biochemical processes take place) is very important and in recent years has received much attention.[5] Micelles, which are dynamic clusters of surfactant molecules which possess both hydrophilic and hydrophobic structures, may associate in aqueous media to form dynamic aggregates.[6] It is well established that, in many cases, the rates and pathways of many chemical reactions can be altered by performing the reactions in micellar media instead of pure bulk solvents. Micelles can concentrate the reactants within their small volumes; stabilize substrates, intermediates or products and orient substrates so that ionization potential and oxidation–reduction properties, dissociation constants, physical properties and reactivities are changed. Thus they can alter the reaction rate, mechanism, and regio- and stereo-chemistry.[7] Micellar solubilization has been exploited to speed up and sometimes change the product distribution of several types of reactions.[8] Tungstophosphoric acid salts have also been used as catalysts

for organic reactions and their properties and uses are extensively studied.[9]

Here we report that a variety of anilines are smoothly and efficiently oxidized to nitro compounds in the presence of a large excess of SPB in aqueous basic media (rather than acidic media in the absence of organic co-solvents). The reaction was conducted in the presence of cetyltrimethylammonium bromide (CTAB) as the micelle source and tungstophosphoric acid ($H_3PW_{12}O_{40} \cdot nH_2O$) as the catalyst.

Results and discussion

The use of sodium perborate (SPB) in water as the reaction medium, cetyltrimethylammonium bromide (10 cmc, 0.02 M) as a surfactant and tungstophosphoric acid ($H_3PW \cdot nH_2O$) as a catalyst (0.01–0.2 mmol) promote facile oxidation of aniline and anilines substituted with electron-donating groups.

In order to show the important effect of the micellar media upon the reactions in this investigation, oxidation of aniline in water by SPB in the absence of surfactants was studied. Detection by GC showed that even after 24 h at room temperature, nitrobenzene formation only reached 4%. Increasing the temperature to 55–60 °C affected the rate of the reaction

Green Context

The continued innovation in the detergent industries driven by demands for higher levels of cleaning, low temperature efficiency and minimal environmental harm caused by the discharge of enormous volumes of effluent has led to the development of a number of safe and environmentally benign oxidants. Such reagents are becoming increasingly attractive to the environmentally-conscious chemicals manufacturing industries. They are however water-soluble which would normally restrict their value in organic synthesis. Here we see how a micellar environment can be used to overcome the incompatibility of an aqueous oxidant and an aromatic substrate. The synthetically useful transformation of anilines to nitroaromatics can be achieved using an aqueous micellar catalytic system containing the major detergency oxidant, sodium perborate, as the source of oxygen.

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and nitrobenzene formation only reached 60% after 16 h. The effect of several surfactants; cetyltrimethylammonium bromide, CTAB (cationic), sodium dodecyl sulfate, SDS (anionic) and TritonX-100 (neutral) at their critical micellar concentration (cmc) in the presence of SPB in water, upon the rate of oxidation of aniline was also studied. The results show that CTAB at 10 cmc shows the best micellar activity and enhances the chemoselectivity (nitro compound only formed) of the reaction.

In order to avoid higher temperatures which causes generation of by-products, the catalytic effects of sodium tungstate and tungstophosphoric acid were studied. Our investigation showed that in the presence of tungstophosphoric acid the reaction rate almost doubled and the oxidation of aniline reached 97% (GC). Therefore, we applied this reaction condition for the oxidation of substituted anilines. The results showed that in contrast to the previously reported method,[4] our procedure is suitable for the high yield conversion of aniline and substituted anilines with electron-releasing groups. The results are presented in Table 1.

Table 1 Oxidation of anilines in the presence of CTAB and $H_3PW \cdot nH_2O$ by $NaBO_3 \cdot 4H_2O$ at 55–60 °C[a]

Entry	Ar	Yield[b] (%)
1	Ph	91
2	2-MeC_6H_4	89
3	3-MeC_6H_4	77
4	4-MeC_6H_4	88
5	2-MeOC_6H_4	81[c]
6	4-MeOC_6H_4	85[c]
7	$3,4\text{-(MeO)}_2C_6H_3$	68[d]
8	2-ClC_6H_4	45
9	4-ClC_6H_4	53
10	2-BrC_6H_4	48
11	4-BrC_6H_4	58

[a] All reactions performed for 12 h unless otherwise indicated. [b] Yields refer to isolated pure products which were characterized by their physical constants, IR, ¹H NMR and comparison with authentic samples. [c] 10 h. [d] 4 h.

Experimental

Typical procedures

1 Anilines substituted with electron-releasing groups. In a 50 ml round-bottomed flask, equipped with mechanical stirrer, were added tungstophosphoric acid (0.025 mmol) and CTAB [5 ml (10 cmc)]. The mixture was stirred at room temperature for 5 min, sodium perborate tetrahydrate (17.5 mmol) added and the temperature of the mixture raised to 55–60 °C. A warm solution of the cleaned aniline (2.5 mmol) in 5 ml of CTAB (10 cmc) was added slowly (1 h) to the mixture. The reaction mixture was stirred at 55–60 °C for the appropriate time (Table 1). The progress of the reaction was monitored by TLC or GC. The reaction mixture was cooled to room temperature and the organic layer extracted with Et_2O (3 × 25). The ethereal solution was separated, and washed with aqueous HCl (6 M, 2 × 10 ml), H_2O (2 × 25 ml), and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave the almost pure target nitro compounds. Further purification was performed by column chromatography on silica gel using ethyl acetate–light petroleum (bp 40–60 °C) (3 : 7) as eluent.

2 Anilines substituted with electron-deficient groups. In a 50 ml round-bottomed flask, equipped with mechanical stirrer, were added tungstophosphoric acid (0.25 mmol) and CTAB [10 ml (10 cmc)]. The mixture was stirred at room temperature for 5 min and then sodium perborate tetrahydrate (25 mmol) added and the temperature of the mixture raised to 55–60 °C. The aniline (2.5 mmol) added to the mixture. The reaction mixture stirred at 55–60 °C for the appropriate time (Table 1) and the work-up of the mixture was performed as above.

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Efficient conversion of 2′-hydroxychalcones into flavanones and flavanols in a water suspension medium

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Conversion of 2′-hydroxychalcones into flavanones and flavanols was found to proceed very efficiently in a water suspension medium.

Introduction

Flavanones **2** are important naturally occurring pharmacological compounds and are valuable precursors for the synthesis of flavanoids.[1] Preparation of flavanones **2** has been carried out by intramolecular cyclization of 2-hydroxychalcone **1** under various conditions using acids,[2] bases,[3] thermolysis,[4] electrolysis[5] and photolysis.[6] However, the yields of these reactions are often moderate (20–90% yield) and the reaction usually gives a mixture of **1** and **2**, the separation of which requires a lot of organic solvent such as benzene. We have now found that 2′-hydroxychalcones **1** are converted into flavanones **2** very efficiently in a water suspension medium and the products isolated simply by filtration. An efficient cyclization reaction of 2′-hydroxychalcones **1** to 2,3-dihydroflavanols **3** by using NaOH–H_2O_2 in a water suspension medium is also reported. These reactions require no organic solvent (except for product recrystallisation), and waste minimization, simple operation, and easier product work-up can be achieved.

Results and discussion

It has been reported that the intramolecular cyclization reaction of **1a** in MeOH using NaOH as base gives flavanone **2a** in only 20% yield at room temperature after 2–3 days.[3] Very interestingly, however, when the reaction was carried out in a water suspension medium in the presence of surfactants, flavanone **2a** was obtained in quantitative yield. For example, a suspension of a mixture of powdered 2′-hydroxychalcone **1a** (1.0 g, 4.5 mmol), NaOH (8 M, 0.1 ml) and sodium 1-dodecane sulfonic acid (0.01 g) in water (10 ml) was stirred at room temperature for 1 h. The crude product was collected by filtration, washed with water and dried in a desiccator to give flavanone **2a** (0.95 g, 95% yield). However, the reaction using no surfactant gave **2a** in only 13% yield. Similarly, tetrabutylammonium iodide, tetrabutylphosphonium bromide, hexadecyltrimethylammonium bromide, glycine, L-alanine, L-proline and L-leucine were also effective for the conversion of **1a** to **2a** in a water suspension medium (Table 1)

It is also found that piperidine catalysed intramolecular cyclization reaction of **1** into **2** proceeds very efficiently in a water suspension medium (Table 2). The preparation of flavanone **2a** is representative of the general procedure employed. For example, a suspension of powdered 2′-hydroxychalcone **1a** (1.0 g, 4.5 mmol) in water (10 ml) containing piperidine (0.01 g, 0.12 mmol) was stirred at room temperature for 1 h. The crude product was collected by filtration, washed with water and dried in a desiccator to give flavanone **2a** (0.98

g, 98% yield). Similarly, chalcones **1b**, **1c**, **1e**, **1f** and **1g** gave the corresponding flavanones **2b**, **2c**, **2e**, **2f** and **2g**, whilst **1d** yielded a 45∶55 mixture of **1d** and **2d** (Table 2).
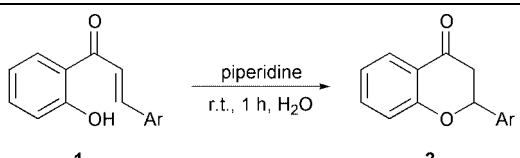
2,3-Dihydroxyflavonol **3a** has been reported to be formed in poor yield by treatment of 2′-hydroxychalcone **1a** with NaOH–H_2O_2 in organic solvents (Table 3).[7,8] We have found that the conversion of **1a** into **3a** proceeds more efficiently in a water suspension medium and the products are isolated simply by filtration. For example, a suspension of a mixture of powdered 2′-hydroxychalcone **1a** (0.10 g, 0.45 mmol), an aq. NaOH solution (8 M, 1.0 ml) and a 30% hydrogen peroxide solution (0.25 g) was stirred at room temperature for 2 h. The crude

Table 1 NaOH catalysed cyclization of 2′-hydroxychalcone **1a** to flavanone **2a**
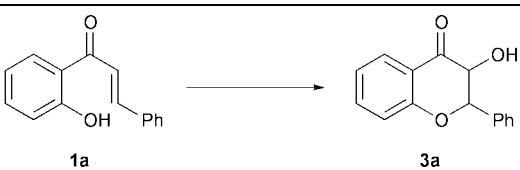

Additive	Yield (%)
None	13
$Bu^n_4N^+I^-$	82
$Bu^n_4P^+Br^-$	80
$C_{16}H_{33}N^+Me_3Br^-$ (CTAB)	92
$C_{12}H_{25}SO_3^-Na^+$ (SDS)	95
Glycine	96
L-Alanine	99
L-Proline	92
L-Leucine	93

Green Context

The simplicity of a chemical process often correlates well with its 'greenness'. Multistep or multi-component reactions almost invariably lead to waste if only as a result of demanding separation steps. Here we see some examples of relatively simple one-step reactions that do not use organic solvents either in the reaction or in the work-up. By running the reaction as a suspension in water, the organic product can be separated simply by filtration with no work-up required. Simple basic catalysts are used to ensure fast reactions under moderate conditions. In one case hydrogen peroxide is used as an in-situ oxidant—ideal as the by-product in the reaction medium, water. *JHC*

Table 2 Piperidine catalyzed cyclization reaction of 2′-hydroxychalcones **1** to flavanones **2** in a water suspension medium

Compound	Ar	Yield (%)
a	Ph	98
b	o-MeOC$_6$H$_4$	95
c	m-MeOC$_6$H$_4$	96
d	p-MeOC$_6$H$_4$	55
e	o-ClC$_6$H$_4$	93
f	m-ClC$_6$H$_4$	94
g	p-ClC$_6$H$_4$	97

Table 3 Conversion of 2′-hydroxychalcone **1a** to 2,3-dihydroflavonol **3a**

Reagent	Solvent	Temp.	Time/h	Yield (%)
NaOH–H$_2$O$_2$[a]	MeOH	rt	3	49
Et$_2$NH–H$_2$O$_2$[b]	dioxane	<5 °C	40	38
NaOH–H$_2$O$_2$	H$_2$O	rt	2	100

[a] Ref. 7. [b] Ref. 8.

product was collected by filtration, washed with water and dried in a desiccator to give flavanol **3a** (0.10 g, 100% yield).

Experimental

Typical procedure for the conversion of 2′-hydroxychalcones 1 into flavanones 2 in a water suspension medium

Crystals of **1a** were finely powdered by grinding with a pestle and mortar for a few minutes. A suspension of a powdered 2′-hydroxychalcone **1a** (1.0 g, 4.5 mmol) was stirred in water (10 ml) containing piperidine (0.01 g, 0.12 mmol) at room temperature for 1 h. The crystalline powder formed was filtered off, washed with water and dried in a desiccator to give flavanone **2a** (0.98 g, 98% yield). The crude crystals thus obtained were recrystallized from EtOH to give pure **2a** as colorless needles. Data for **2a**; mp 75–76 °C; ν(C=O) 1718 cm^{-1}; δ_H(300 MHz, CDCl$_3$, Me$_4$Si) 7.04–7.96 (9H, m), 5.50 (1H, dd, J 3.0, 13.2), 3.11 (1H, dd, J 13.2, 16.8), 2.90 (1H, dd, J 3.0, 16.8).

Typical procedure for the conversion of 2′-hydroxychalcones 1 into flavanols 3 in a water suspension medium

Crystals of **1a** were finely powdered by grinding with a pestle and mortar for a few minutes. A suspension of a mixture of powdered 2′-hydroxychalcone **1a** (0.10 g, 0.45 mmol), an aq. NaOH solution (8 M, 1.0 ml) and a 30% hydrogen peroxide solution (0.25 g) was stirred at room temperature for 2 h. The crude product was filtered off, washed with water and dried in a desiccator to give flavanol **3a** (0.10 g, 100% yield). Recrystallization of the crude product from MeOH gave pure **3a** as colorless needles. Data for **3a**; mp 178–180 °C; ν(OH) 3675 (OH), ν(C=O) 1718 cm^{-1}; δ_H(300 MHz, CDCl$_3$, Me$_4$Si) 7.04–7.94 (9H, m), 5.14 (1H, d, J 12.0), 4.64 (1H, d, J 12).

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Darzens condensation reaction in water

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Darzens condensation of benzaldehyde with phenacyl chloride proceeded very efficiently in a water suspension medium and the products were isolated simply by filtration.

Introduction

The Darzens condensation reaction is an important C–C bond forming reaction[1] and is usually carried out in organic solvents under dry conditions.[2] We have now found that Darzens condensation reactions of benzaldehydes **1** with phenacyl chloride **2** proceeds very efficiently in a water suspension medium and that 2,3-epoxy-1,3-diphenyl-1-propanone derivatives **3** are obtained simply by filtration. Enantioselective Darzens condensation reaction in the presence of a chiral chinchonidinium salt is also reported.

Results and discussion

An equimolar mixture of benzaldehyde **1a** , phenacyl chloride **2** and NaOH in a small amount of water was stirred at room temperature for 2 h. The crude product was collected by filtration, washed with water and dried in a desiccator to give 2,3-epoxy-1,3-diphenyl-1-propanone **3a** in 94% yield. When the reaction was carried out using KOH, LiOH or Ca(OH)$_2$ as base, **3a** was obtained in 93, 92 and 93% yield, respectively. However, reaction with relatively weaker bases, Ba(OH)$_2$ and K$_2$CO$_3$ gave **3a** in lower yields (Table 1).

Similarly, Darzens condensation reactions of **1b–i** with **2** in the presence of NaOH proceeded very efficiently and the products **3b–i** were obtained in good yields as shown in Table 2. In comparison, conventional method for preparation of **3a** in aqueous dioxan requires a longer reaction time (12 h) at lower temperature (0 °C).[3] This completely organic solvent-free procedure is valuable since waste minimization, simple operation and easier product work-up can be achieved.

It has been reported that enantioselective Darzens reaction of **1** with **2a** in the presence of chiral phase-transfer catalyst **5** affords a 90:10 mixture of *trans*-**3a** (3.9% ee) and *cis*-**4a** in 81% yield under phase-transfer conditions.[4] We have found that Darzens reaction in the presence of *N*-benzylcinchonidinium chloride **6** proceeded more selectively in a water suspension medium and only *trans*-**3a** (12% ee) was obtained in 90% yield.

Table 1 Darzens condensation of benzaldehyde **1a** with phenacyl chloride **2** in water

Entry	Base	Yield (%)
1	NaOH	94
2	KOH	93
3	LiOH	92
4	Ca(OH)$_2$	93
5	Ba(OH)$_2$	77
6	K$_2$CO$_3$	46
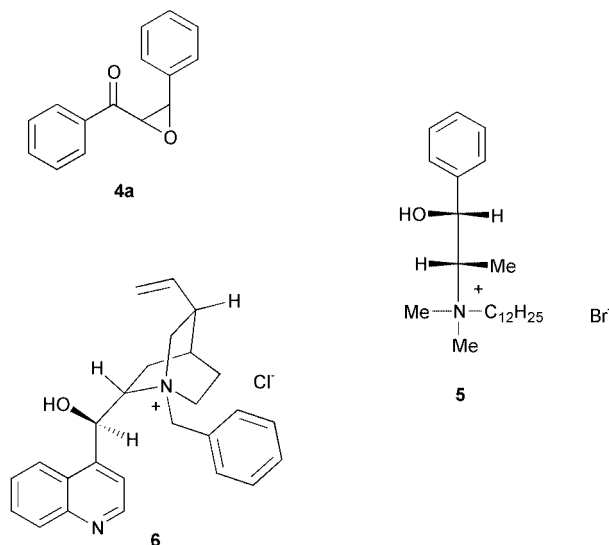
Green Context

The avoidance of volatile organic solvents in chemical processing is an important goal for green chemistry. The use of water as a solvent is somewhat controversial: while it is safe to handle and use, separation of the organics at the end of the reaction and subsequent clean-up of the dirty water can be major difficulties. Here these problems are at least partly overcome since the reaction is close to 100% atom efficient and the product can be easily separated by filtration. The reaction described is an important C–C bond forming reaction and the survival of the epoxy function and the effectiveness of the method in an enantioselective synthesis are added attractions of this aqueous solvent-based procedure. *JHC*

Table 2 Darzens condensation of aldehydes **1a**–**i** with phenacyl chloride **2** in water

Compound 1	Ar	Time/h	Yield (%)	Mp/°C
a	Ph	2	94	82–85[3]
b	C_6H_4Me-4	2	91	60–70[5]
c	C_6H_4Cl-4	2	98	47–50[5]
d	C_6H_4Br-4	3	95	55–58[6]
e	C_6H_4OMe-4	2	89	69–73[6]
f	C_6H_4Ph-4	4	93	57–59
g	C_6H_4Cl-3	3	98	56–59
h	$C_6H_3Cl_2$-3,4	3	91	103–106
i	C_6H_3Br-3-OMe-4	3	86	59–62

Experimental

Typical procedure for Darzens condensation reaction in a water suspension medium

A suspension of a mixture of benzaldehyde **1a** (0.21 g, 1.94 mmol), phenacyl chloride **2** (0.30 g, 1.94 mmol) and NaOH (0.08 g, 2 mmol) was stirred in water (3 ml) at room temperature for 2 h. The crystalline powder formed was collected by filtration, washed with water and dried in a desiccator to give 2,3-epoxy-1,3-diphenyl-1-propanone **3a** (0.41 g, 94% yield).

The crude crystals thus obtained were recrystallized from EtOH to give pure **3a** (mp 82–85 °C) as colorless prisms.

Typical procedure for enantioselective Darzens condensation reaction in a water suspension medium

A suspension of a mixture of benzaldehyde **1a** (0.21 g, 1.94 mmol), phenacyl chloride **2** (0.30 g, 1.94 mmol), N-benzylcin-chonidinium chrolide **6** (0.82 g, 1.94 mmol) and NaOH (0.08 g, 2 mmol) was stirred in water (3 ml) at room temperature for 2 h. The crystalline powder formed was collected by filtration, washed with water and dried in a desiccator to give 2,3-epoxy-1,3-diphenyl-1-propanone **3a** (0.39 g, $[\alpha]_D$ −26° (c 0.13, CH_2Cl_2), 12% ee) in 90% yield. The optical purity of (−)-**3a** was determined by HPLC analysis using a DAICEL CHIR-ALCEL OJ column (hexane–2-Pr^iOH 9:1, 0.3 ml min^{-1}, 254 nm).

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Respective conversion of *n*-butylamine to methyl *N-n*-butylcarbamate and oxalbutyline in supercritical carbon dioxide

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O_2 and the solvent (MeOH–supercritical carbon dioxide) can control the chemoselectivity of the palladium-catalyzed carbonylation of amines; methyl *N-n*-butylcarbamate or oxalbutyline could be obtained in high yields upon varying the conditions.

Considerable studies have focused on palladium-catalyzed carbonylation of amines to give carbamate esters, oxamate esters, ureas and α-keto amines.[1–5] In the 1980s, Alper *et al.*[6] reported that the carbonylation reaction of primary amines in alcohols gave carbamate esters in the presence of hydrochloric acid, $PdCl_2$, $CuCl_2$ and O_2. The reaction of secondary amines yielded a mixture of carbamate esters and oxamate esters. Recently, we found that in the absence of hydrochloric acid the carbonylation of amines yielded carbamate esters in 80–99% in the presence of $PdCl_2$, $CuCl_2$ and O_2 in alcohols.[7] (Scheme 1).

$$RNH_2 \ + \ CO \ \xrightarrow[\text{R'OH}]{PdCl_2} \ RNHCO_2R'$$
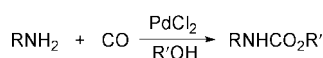
Scheme 1

Our interest stems from a continued research for reactions catalyzed by transition-metal catalysts in supercritical carbon dioxide ($scCO_2$). For environmental reasons $scCO_2$ is a preferred reaction medium. In addition, the advantages of reactions in $scCO_2$ include the high solubility of gaseous reactants, rapid diffusion of solutes, and possible weakening of the solvation around the reactants. Such properties can provide substantial chemoselectivity, stereoselectivity, and rate enhancement.[8] Herein we describe our recent results of carbonylation reactions of *n*-butylamine catalyzed by $PdCl_2$ in $scCO_2$.

Table 1 shows the results of the carbonylation reactions in $scCO_2$. In ordinary solvents, it is necessary to add O_2, otherwise the reaction is not clean and some by-products are obtained. In $scCO_2$, preliminary results showed that the reaction was clean in the absence of O_2 and oxalbutyline (1,1'-oxalyldibutylamine) was obtained primarily (entry 1 in Table 1). Using $PdCl_2$ (5 mmol%), $CuCl_2$ (2 mmol), $BuNH_2$ (5 mmol) and MeOH (10 mmol) and performing the reaction under CO (1.0 MPa) in $scCO_2$, the product was obtained in 98% yield and the ratio of oxalbutyline : methyl *N-n*-butylcarbamate was 96 : 4. This result encouraged us to screen other reaction conditions. We first investigated the effect of the amount of $CuCl_2$ and found that this played an important role in the reaction (entries 1–3 in Table 1). Oxalbutyline was obtained in high yield when 2 mmol of $CuCl_2$ was added. The yield decreased in the absence of $CuCl_2$ or in the presence of 3 mmol of $CuCl_2$. We then examined the effect of solvent (MeOH–$scCO_2$) by varying the amount of MeOH and found that the chemoselectivity and yields of the reaction changed according to different levels of MeOH (entries 1, 4, and 5). When 0.4 mL of MeOH was added, oxalbutyline was obtained as the major product (entry 1)

whereas when 1.0 mL of MeOH was added, oxalbutyline become the minor product (entry 5). Only oxalbutyline, in 60% yield, was obtained in the absence of MeOH (entry 4).

In our previous report,[7] suitable adjustment of the $CO : O_2$ ratio ($CO : O_2 = 2 : 1$, CO: 1.0 MPa, O_2: 0.5 MPa) and the

Table 1 $PdCl_2$-catalysed carbonylation of N-*n*-butylamine in $scCO_2$[a]

$$Bu^nNH_2 \ + \ CO \ \xrightarrow[\substack{MeOH \\ \text{in } scCO_2}]{PdCl_2, \ CuCl_2} \ \begin{array}{l} \nearrow \ Bu^nNHCOCONHBu^n \quad \textbf{2} \\ \searrow_{O_2} \ Bu^nNHCO_2Me \quad \textbf{3} \end{array}$$

Entry	MeOH/mL	CO_2/MPa	$CuCl_2$/mmol	O_2/MPa	yield (%)[b] 2:3
1	0.4	10	2	0	98 (96:4)
2[c]	0.4	10	0	0	9 (97:3)
3[c]	0.4	10	3	0	71 (95:5)
4	0	10	2	0	60 (100:0)
5	1.0	10	2	0	99 (36:64)
6[c]	0.4	0	2	0	Trace
7[d]	0.4	10	2	0	—
8[e]	0.4	10	0	0	—
9	0.2	10	2	0.5	78 (37:63)
10	0.4	10	2	0.5	98 (13:87)
11	1.0	10	2	0.5	100 (0:100)
12	1.0	0	2	0.5	Trace
13[c]	1.0	10	0	0.5	17 (1:99)
14[d]	1.0	10	2	0.5	—
15[e]	1.0	10	0	0.5	—

[a] Reaction conditions: **1** (5 mmol) and $PdCl_2$ (5 mmol%) under CO (1.0 MPa) overnight at 40 °C. *[b]* Isolated yields. Ratios of **2** : **3** were determined by GC analyses using an internal standard. *[c]* An unidentified by-product was formed. *[d]* In the absence of CO. *[e]* In the absence of $PdCl_2$.

Green Context

The carbonylation of amines is an atom economic route to building functional molecules such as carbamates and oxamides. This article focusses on the use of supercritical fluids (CO_2 and methanol) to effect carbonylation of amines with and without oxygen, under Pd catalysis. The authors show that carbonylation occurs readily using these benign and recyclable solvent systems, the nature of the products being primarily determined by the presence or absence of oxygen. This aspect of the work makes use of the far higher miscibility of gases in supercritical media than in typical sub-critical solvents. *DJM*

amount of MeOH (5.0 mL) made the reaction proceed smoothly and methyl N-n-butylcarbamate was obtained as the sole product. In scCO$_2$, the reaction could also be carried out smoothly under the same pressure ratio of CO$:$O$_2$ (CO$:$O$_2$ = 2$:$1, CO: 1.0 MPa, O$_2$: 0.5 MPa), but the chemoselectivity of the reaction changed and a mixture of oxalbutyline **2** and methyl N-n-butylcarbamate **3** were obtained. Results of entries 9–11 indicated that the effect of solvent (MeOH–scCO$_2$) also affected the chemoselectivity of the reaction. The yield of **3** was enhanced with an increase in the amount of MeOH (entries 9–11 in Table 1) and methyl N-n-butylcarbamate was obtained as the sole product when 1.0 mL of MeOH was added (entry 11). The results also showed that the amount of CuCl$_2$ affected the yield to some extent (entries 11 and 13). Unidentified by-products were formed with trace only of products in the absence of CO$_2$ (entries 6, 12). No products were obtained in the absence of the catalyst or CO (entries 7, 8, 14 and 15).

As can be seen from the results of the carbonylation reactions summaried in Table 1, the following conclusions can be drawn. (1) O$_2$ plays a very important role in the chemoselectivity of the carbonylation of amines. In the absence of O$_2$, oxalbutyline was obtained primarily in high yields *via* the double carbonylation of BuNH$_2$. In the presence of O$_2$, oxidative carbonylation occurred and methyl N-n-butylcarbamate was obtained primarily. (2) The effect of the solvent (MeOH–scCO$_2$) could also affect the chemoselectivity of the carbonylation of amines to some extent. It has been reported that some organic or inorganic compounds, so-called 'modifiers', can be added to supercritical fluids to increase the solvent power.[8–10] Our results indeed show that the addition of MeOH affected the yields and the chemoselectivity of the reaction. In MeOH, only methyl N-n-butylcarbamate was obtained in the presence of O$_2$ while in MeOH/scCO$_2$, methyl N-n-butylcarbamate and oxalbutyline were obtained and the ratio of methyl N-n-butylcarbamate to oxalbutyline could be regulated with the amount of MeOH. (3) For the carbonylation reaction to proceed smoothly a fixed amount of copper(II) chloride (2 mmol) should be used. The yields decreased in the absence of CuCl$_2$ or in the presence of 3 mmol of CuCl$_2$.

Based on the above results, a possible mechanism of the reaction is outlined in Scheme 2.[1–6] After the intermediate **4** is formed by the reaction of BuNH$_2$ and PdCl$_2$, CO insertion can occur to afford **5**. The reaction might then proceed in two ways under different conditions. In pathway A complexation of a second molecule of BuNH$_2$ and carbonylation would give **6** which can decompose to provide **2** and Pd(0)L$_2$, without adding O$_2$. In the presence of O$_2$, pathway B oxidative carbonylation of BuNH$_2$ and MeOH would occur to give **3**. In the process, the amount of Cl$^-$ (4.1 mmol) present is not enough to fully complex with H$^+$ (10 mmol), so [HPdH] might be produced.[11] Oxygen might play a role in the oxidation of [HPdH] to produce H$_2$O and regenerate the catalyst.
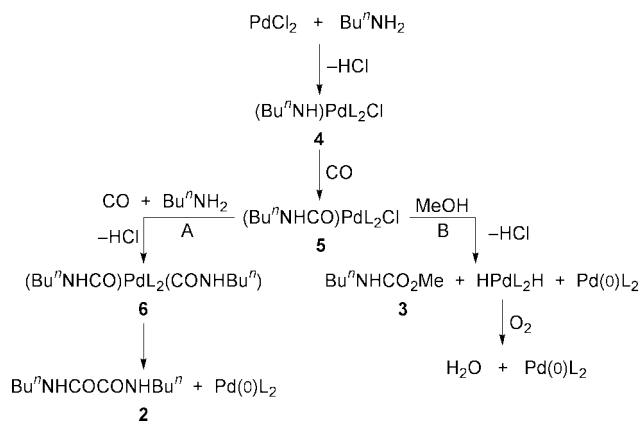
In the pesence of MeOH, competition between pathways A and B occur; the addition of MeOH would favor the latter.

In conclusion, we have presented the first example of selective carbonylation of amines in scCO$_2$. We observed that O$_2$ and the effect of solvent (MeOH–scCO$_2$) can affect the chemoselectivity of the carbonylation reaction. Methyl N-n-butylcarbamate on oxalbutyline can be synthesized in high yield in scCO$_2$ upon variation of the conditions. Of particular note, this carbonylation reaction of amines is superior to earlier reports in terms of being environmentally friendly and providing a new route to synthesize oxamates. Further study is currently under investigation in our laboratory.

Experimental

Oxalbutyline 2

δ_H (CDCl$_3$, 400 MHz) 0.883–0.919 (t, 3H, J = 7.2 Hz), 1.315–1.388 (m, 2H, J = 7.2 Hz), 1.490–1.524 (m, 2H, J = 6.8 Hz), 3.169–3.202 (t, 2H, J = 6.6 Hz), 5.553 (s, 1H, N–H, br s); δ_c (CDCl$_3$, 400 MHz) 13.7, 19.9, 31.6, 41.0, 159.4; IR (neat): v cm^{-1} 3425, 1711, 1556; MS: m/z (%), 200 (M$^+$, 2), 172 (4), 157 (4), 143 (4), 129 (4), 100 (46), 72 (25), 57 (100), 41 (42), 30 (67).

Methyl N-n-butylcarbamate 3

δ_H (CDCl$_3$, 400 MHz) 0.864–0.903 (t, 3H, J = 7.8 Hz), 1.277–1.352 (m, 2H, J = 7.3 Hz), 1.405–1.476 (m, 2H, J = 7.3 Hz), 3.116–3.162 (t, 2H, J = 7.3 Hz), 3.621 (s, 1H), 4.677 (s, 1H, N–H, br s); δ_c(CDCl$_3$, 400 MHz) 13.5, 19.7, 31.9, 40.6, 51.7, 157.0; IR (neat): v/cm^{-1}, 3334, 1704, 1540; MS: m/z (%), 131(M$^+$, 9), 116 (3), 100 (3), 88 (100), 59 (16), 44 (38).

Typical procedure

Bu^{n}NH$_2$ (5 mmol) was added to a mixture of PdCl$_2$ (5 mmol%), CuCl$_2$ (2 mmol) and MeOH in an HF-10 autoclave. CO (and sometimes O$_2$) and liquid CO$_2$ was then transferred into the autoclave to the desired pressure. The reaction mixture was stirred at 40 °C overnight (*ca*. 15 h). After completion of the reaction, the gas was vented and the residue was extracted and purified. The ratios of the products were determined by GC analyses using an internal standard.

Caution: Care should be taken when working at high pressure.

PdCl$_2$ + Bu^{n}NH$_2$
↓ –HCl
(Bu^{n}NH)PdL$_2$Cl
4
↓ CO

CO + Bu^{n}NH$_2$ —A, –HCl→ (Bu^{n}NHCO)PdL$_2$Cl —B, MeOH, –HCl→
5

(Bu^{n}NHCO)PdL$_2$(CONHBu^n)
6

Bu^{n}NHCO$_2$Me + HPdL$_2$H + Pd(0)L$_2$
3
↓ O$_2$
H$_2$O + Pd(0)L$_2$

Bu^{n}NHCOCONHBu^n + Pd(0)L$_2$
2

Scheme 2

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Efficient solvent-free *O*-silylation of alcohols with R₃SiCl

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Solvent-free *O*-silylation of liquid or crystalline alcohols with liquid or crystalline silyl chlorides proceeds efficiently to give silyl ethers in good yield. *O*-Silylation of sterically hindered alcohols which cannot be performed in solution is also accomplished efficiently under solvent-free conditions.

Introduction

From the viewpoint of sustainable and green chemistry,[1] solvent-free reactions have received considerable attention in recent years.[2] The solvent-free synthetic method is valuable not only for ecological and economical reasons but also for simplicity in procedures and the high yields of its products. We now report a solvent-free *O*-silylation method for alcohols. This method is applicable to all silylation reactions of liquid or crystalline alcohols with liquid or crystalline silyl chlorides. Furthermore, this method is very effective for the silylation of sterically hindered alcohols which cannot be silylated in solution [eqn. (1)].

$$R'\!-\!OH \xrightarrow[\text{no solvent}]{R_3SiCl} R'\!-\!OSiR_3 \qquad (1)$$

primary, secondary, tertiary
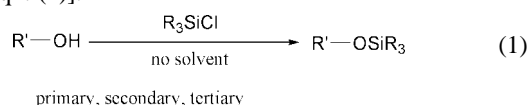
Results and discussion

When a mixture of powdered L-menthol **1**, *tert*-butyldimethylsilyl chloride **2** and imidazole **3** was kept at 60 °C for 5 h, *O-tert*-butyldimethylsilyl L-menthol **4** was obtained in 97% yield (Scheme 1). Similar treatments of **1** with the liquid silyl chlorides, trimethyl- **5a** and triethylsilyl chloride **5b** gave the corresponding *O*-silylation products, **6a** and **6b**, respectively (Scheme 1), in the yields indicated in Table 1. However, *O*-silylation of **1** with triisopropyl- **5c** and triphenylsilyl chloride **5d** proceeded with difficultly even at 120 °C and gave **6c** and **6d**, respectively in relatively low yields (Table 1). Nevertheless, when the solvent-free silylation reactions at 120 °C were carried

out using two equivalents of **5c** and **5d**, **6c** and **6d** were obtained, respectively, in relatively high yields (Table 1).

It is well known that *O*-silylation of alcohols in solution using silyl chlorides bearing sterically bulky substituents proceeds only with great difficulty.[3] For example, neither the reaction of **1** with **5c** nor **5d** in DMF at 120 °C for 5 h gave the *O*-silyl ether in practically significant yields. Since silyl triflate is more reactive than silyl chloride, the former is more useful when the substituent is sterically bulky. However, the silyl chloride is cheaper and easier to handle. Finally, the solvent-free *O*-silylation method with silyl chlorides has some advantages.

The solvent-free *O*-silylation can also be applied to liquid alcohols. Treatment of liquid alcohols **7**–**11** with various silyl chlorides at 60 °C for 5 h gave the corresponding *O*-silyl ethers in good yields (Table 2). In this case, the steric bulkiness of the

Table 1 Solvent-free *O*-silylation of L-menthol **1**

Silyl chloride	Mol ratio of silyl chloride to **1**	*T*/°C	Yield (%) of silyl ether
2	1	60	97
5a	1	60	89
5b	1	60	89
5c	1	120	57[a]
5c	2	120	77[a]
5d	1	120	70[a]
5d	2	120	99[a]

[a] After purification by column chromatography on silica gel.
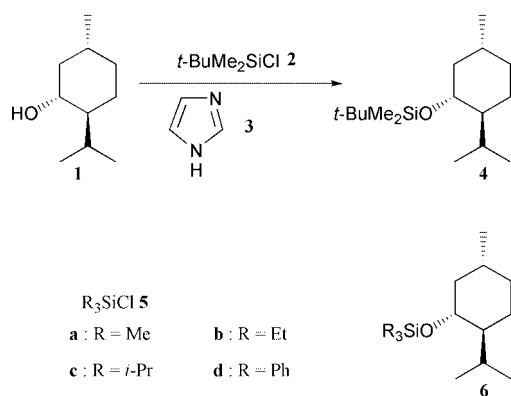
Green Context

The avoidance of volatile organic solvents or other environmentally unacceptable solvents in chemical processes is one of the most important general goals in green chemistry. While environmentally benign alternative solvents such as supercritical carbon dioxide or water can be attractive options in many cases it should be generally preferable to try to avoid solvent altogether. Solventless reactions make the process simpler and less expensive, and avoid all concerns over solvent emissions and toxicity. Here the authors describe the direct reaction of alcohols with chlorosilanes for the important *O*-silylation reaction. Solid–solid and liquid–liquid reactions work very well. An additional and perhaps unexpected benefit is that, unlike with conventional solution reactions, sterically hindered alcohols react very efficiently under solvent free conditions. *JHC*

Scheme 1
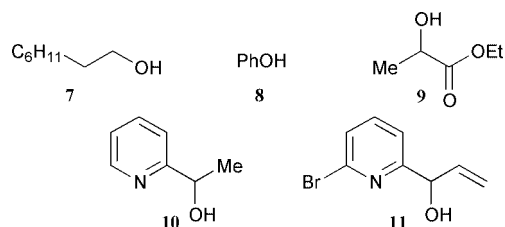
alcohol and reagent do not present any significant problem, except in the case of tertiary alcohols.

Table 2 Solvent-free *O*-silylation of liquid alcohols[a]

Alcohol	Silyl chloride	Yield (%) of silyl ether
7	**2**	88
8	**2**	78
9	**2**	80
9	**5b**	86
9	**5c**	78
10	**2**	78
11	**2**	84

[a] A mixture of alcohol (1 mmol), silyl chloride (1 mmol) and **3** (2 mmol) was heated at 60 °C for 5 h.

Although the *O*-silylation reaction of the tertiary alcohol, 1,1-dimethyl-2-phenylethanol **12** with **2** required a reaction temperature of 120 °C and use of two equivalents of **2**, the *O*-silyl ether **13** was still obtained in 86% yield by the simple solvent-free procedure (Scheme 2). By contrast, the sterically hindered hydroxy group of **12** was not silylated at all by heating with **2** in DMF at 120 °C for 5 h.

The solvent-free *O*-silylation reaction can also be accomplished selectively. For example, when 1-methyl-1-phenylethane-1,2-diol **14** was treated with **2** at 60 °C for 5 h, its primary hydroxy group was silylated to give **15** in 70% yield. Reaction of **14** with three mol equivalents of **2** at 120 °C for 5 h gave the fully *O*-silylated product **16** in 85% yield.

In summary the solvent-free *O*-silylation method is useful owing to its simplicity and effectiveness as well as cleanness and economy.
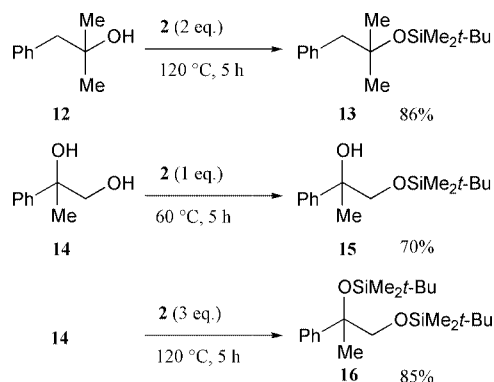
Scheme 2 Solvent-free *O*-silylation of tertiary alcohols.

Experimental

General procedure for solvent-free *O*-silylation of alcohols

A mixture of alcohol (30.0 mmol), silyl chloride (30.0 mmol) and imidazole (60.0 mmol) was stirred at 60 °C for 5 h and the reaction mixture was filtered to give the silyl ether in the pure state. For **6c**, **6d**, **13**, **15** and **16**, the silyl ether was separated

from the reaction mixture by filtration and purified by column chromatography on silica gel.

Reaction of L-menthol 1 with triisopropylsilyl chloride 5c in DMF

To a solution of **1** (469 mg, 3.0 mmol) and imidazole (817 mg, 12.0 mmol) in DMF (20 mL) was added **5c** (1.3 mL, 6.0 mmol) at room temperature and the reaction mixture was stirred at 120 °C for 24 h. However, no reaction occurred and **1** was recovered unchanged. Similar results were obtained for **6d** and **12** in DMF.

Registry number for silyl ethers

76358-81-1 (**4**); 6808-39-7 (**6a**); 17676-41-4 (**6b**); 92976-53-9 (*tert*-butyldimethylsilyl ether of **7**); 18052-27-2 (*tert*-butyldimethylsilyl ether of **8**); 106513-42-2 (*tert*-butyldimethylsilyl silyl ether of **9**); 109170-82-3 (triethylsilyl ether of **9**); 143429-13-4 (triisopropylsilyl ether of **9**); 162085-25-8 (*tert*-butyldimethylsilyl ether of **10**); 213909-43-4 (*tert*-butyldimethylsilyl ether of **11**).

Spectroscopic data

Tris(1-methylethyl)[{(1R, 2S, 5R)-5-methyl-2-(1-methylethyl)cyclohexyl}oxy]silane 6c. IR (neat) 2956, 2867, 1463, 1385, 1113, 1085, 1067, 1054, 882, 789, 676 cm^{-1}; $[\alpha]$ = -42.1; δ_H(300 MHz, CDCl$_3$) 3.58–3.49 (m, 1H), 2.35–2.32 (m, 1 H), 1.97–1.93 (m, 1 H), 1.64–1.56 (m, 2 H), 1.38–1.13 (m, 4 H), 1.07 (d, 18 H, *J* 3.9 Hz), 1.04–0.95 (m, 3 H), 0.90 (d, 6 H, *J* 6.3 Hz), 0.86–0.80 (m, 1H), 0.75 (d, 3 H, *J* 6.9 Hz); δ_C(75 MHz, CDCl$_3$) 72.9, 50.8, 45.8, 34.7, 31.8, 25.0, 22.8, 22.5, 21.5, 18.4, 16.0, 13.2. Anal. Calc. for C$_{19}$H$_{40}$OSi: C, 73.00; H, 12.90. Found: C, 72.54; H, 12.74%.

Triphenyl[{(1R, 2S, 5R)-5-methyl-2-(1-methylethyl)cyclohexyl}oxy]silane 6d. IR (neat) 3068, 2955, 2921, 2869, 1428 1115, 1082, 1066, 1051, 710, 700 cm^{-1}; $[\alpha]$ = -48.0; δ_H(300 MHz, CDCl$_3$) 7.84–7.491 (m, 15 H), 3.81–3.75 (m, 1H), 2.63–2.58 (m, 1 H), 2.15–2.08 (m, 1 H), 1.75–1.71 (m, 2 H), 1.58–1.51 (m, 1 H), 1.39–1.32 (m, 2 H), 1.08 (d, 3 H, *J* 7.2 Hz), 1.03–1.00 (m, 2 H), 0.97 (d, 3 H, *J* 6.0 Hz), 0.60 (d, 3 H, *J* 6.9 Hz); δ_C(75 MHz, CDCl$_3$) 135.6, 135.2, 129.7, 127.9, 73.9, 50.2, 45.3, 34.4, 31.6, 25.3, 22.6, 22.2, 21.3, 15.3. Anal. Calc. for C$_{28}$H$_{34}$OSi: C, 81.10; H, 8.26. Found: C, 81,00; H, 8.43%.

2-(1,1-Dimethylethyl)dimethyl(2-methyl-3-phenylpropoxy)silane 13. IR (neat) 2957, 2930, 2857, 1472, 1462, 1381, 1364, 1252, 1217, 1155, 1127, 1039, 835, 772, 700 cm^{-1}; δ_H(300 MHz, CDCl$_3$) 7.31–7.30 (m, 5 H), 2.81 (s, 1H), 1.29 (s, 6 H), 0.96 (s, 9 H), 0.10 (s, 6 H); δ_C(75 MHz, CDCl$_3$) 138.8, 130.8, 127.5, 126.0, 73.9, 51.5, 29.6, 26.0, 18.1, -2.00. Anal. Calc. for C$_{16}$H$_{28}$OSi: C, 72.66; H, 10.67. Found: C, 72.67; H, 10.77%.

α-[{(1,1-Dimethylethyl)dimethylsilyl}oxy]methyl-α-methylbenzenemethanol 15. IR (neat) 3564, 2955, 2930, 2858, 1463, 1256, 1095, 837, 778, 699 cm^{-1}; δ_H(300 MHz, CDCl$_3$) 7.52–7.29 (m, 5 H), 3.71 (d, 2 H, *J* 2.7 Hz) 3.12 (s, 1H), 1.57 (s, 3 H), 0.92 (s, 9 H), 0.07 (s, 3 H), 0.02 (s, 3 H); δ_C(75 MHz, CDCl$_3$) 145.3, 128.0, 126.7, 125.1, 74.2, 71.6, 25.8, 18.2, -5.5; Anal. Calc. for C$_{15}$H$_{26}$OSi: C, 67.61; H, 9.84. Found: C, 68.00; H, 9.77%.

[[1,2-Bis{(1,1-dimethylethyl)dimethylsilyl}oxy]-1-methylethyl]benzene 16. IR (neat) 1460, 1248, 1085, 835, 770, 700 cm^{-1}; δ_H(300 MHz, CDCl$_3$) 7.50–7.24 (m, 5 H), 3.58 (q, 2 H,

J 17.2 Hz) 1.64 (s, 3 H), 0.98 (s, 9 H), 0.86 (s, 9 H), 0.12 (s, 3 H), 0.00 (s, 3 H), −0.05 (s, 3H), −0.10 (s, 3 H); δ_C(75 MHz, CDCl$_3$) 146.8, 127.5, 126.6, 126.0, 77.6, 73.0, 26.1, 25.9, 25.0, 18.5, 18.3, −2.0, −2.4, −5.6, −5.7. Anal. Calc. for C$_{21}$H$_{40}$O$_2$Si$_2$: C, 66.25; H, 10.59. Found: C, 66.45; H, 10.33%.

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Metal(IV) phosphates as solid acid catalysts for selective cyclodehydration of 1,n-diols

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Metal(IV) phosphates of tin, zirconium and titanium are applied, for the first time, as catalysts for selective cyclodehydration of butane-1,4-diol to tetrahydrofuran in high yields. Tin(IV) phosphate showed highest activity among the three, and was used as a catalyst for cyclodehydration of various 1,n-diols. Cyclodehydration of butane-1,4-diol, pentane-1,5-diol, hexane-1,6-diol and diethanolamine gave tetrahydrofuran, tetrahydropyran, oxapane and morpholine, respectively. Cyclodehydration of diethylene glycol, triethylene glycol, diethylene glycol monomethyl ether, polyethylene glycol 200 and polyethylene glycol 300 gave 1,4-dioxane.

Introduction

There is a strong interest in the use of solid acid catalysts as replacements to conventional homogeneous catalysts such as mineral and organic acids, due to environmental concerns. Though the conventional catalysts are very effective, they produce highly corrosive media and chemically reactive waste streams, whose treatment can be both difficult and hazardous. By contrast, solid acid catalysts are easier to handle and general operation of a large chemical process is safer and ecofriendly.

Cyclodehydration of butane-1,4-diol to tetrahydrofuran and diethylene glycol to 1,4-dioxane are industrially important reactions. These reactions are usually carried out by use of mineral and organic acids,[1] solid acid catalysts such as clays,[2] group(IV) metal halides,[3] metallocenes,[3] sulfated zirconia,[4] zeolite[5] and calcium phosphate.[6] Tetravalent metal phosphates, to our knowledge, have not been used as catalysts for this reaction. Tetravalent metal acid (tma) salts have the general formula $M^{IV}(HXO_4)_2 \cdot nH_2O$ where M^{IV} = Sn, Ti, Zr, Ce, Th, etc. and X = P, As, W, Mo, etc. These materials contain structural hydroxyl groups with labile protons and therefore are potential candidates as solid acid catalysts. These compounds can be prepared in both amorphous and crystalline forms. The amorphous forms possess a greater number of acid sites as compared to the crystalline materials[7] and thus are catalytically more active. These materials have been used as catalysts in a variety of reactions such as dehydration of alcohols,[7] double bond isomerization of alkenes,[8] Friedel–Crafts reactions,[9] and reverse Prins reaction.[10] The present paper reports, for the first time, application of amorphous tma salts—tin phosphate (SnP), zirconium phosphate (ZrP) and titanium phosphate (TiP)—as solid acid catalysts for cyclodehydration of 1,n-diols to the corresponding cyclic ethers in high yields and selectivity.

Experimental

Catalyst preparation

The metal(IV) phosphates were prepared by modification of an earlier reported procedure.[9,10] A 0.1 M aqueous solution of disodium hydrogen phosphate was added dropwise to an equimolar, equivolume, stirred aqueous solution of metal ion (tetrachloride for Sn and Ti and oxychloride for Zr) maintained at 50 °C. The resulting gel was stirred at 50 °C for 2 h and at room temperature for 24 h. It was then filtered off and dried at room temperature. The dried material was powdered and converted to the hydrogen form by treatment with 1 M HNO_3 for 3 h, the acid being intermittently replaced with a fresh batch. It was then washed several times with conductivity water to remove hydrogen ions and dried at room temperature.

Characterization of the metal(IV) phosphates

The metal(IV) phosphates were analyzed gravimetrically for metal ions by the cupferron method[11,12] and for phosphorus as magnesium pyrophosphate.[12] Analysis showed a metal to phosphorus ratio of 1. The materials were assessed for chemical stability and were found to be stable in mineral acids such as conc. H_2SO_4, conc. HNO_3, HCl (4 M); aqueous bases like KOH and NaOH up to ca. 0.5 M concentrations and organic solvents such as alcohols, terahydrofuran and acetic acid. IR spectra were recorded on a Brüker 113V FT-IR spectrometer. The spectra of the metal phosphates showed a broad band around 3600 cm^{-1} which is attributed to symmetric and asymmetric OH stretching. A medium band around 1620 cm^{-1} is assigned to HOH bending. A band at 1150 cm^{-1} is due to HPO_4^{2-}. Surface area and pore volume determination were carried out on a Carlo Erba Sorptomatic Series 1800 instrument at −196 °C using the BET method. TPD studies were performed using a heating rate of 10 °C min^{-1}. A series of 0.5 ml NH_3 pulses were supplied until no more uptake of NH_3 was observed. Helium

Green Context

The cyclodehydration of butane-1,4-diol to tetrahydrofuran, diethylene glycol to 1,4-dioxane and diethanolamine to morpholine are industrially valuable reactions. Current processes rely on liquid or soluble acids which present handling and corrosion problems as well as leading to waste on separation. This article describes the use of non-corrosive solid acids for such important reactions. The catalysts are also easily separated from the reaction mixture. *JHC*

was then passed over the sample at a flow rate of 30 ml min^{-1} and the heating started in a programmed manner. The desorbed NH_3 was detected by a thermal conductivity detector and the TPD profiles were recorded (Fig. 1). The properties of the catalysts are summarized in Table 1.

### Procedure for cyclodehydration reactions and analysis

In a typical reaction, a mixture of butane-1,4-diol (100 mmol) and SnP catalyst (1.54 mmol) was taken in a round bottom flask fitted with a microdistillation unit. The mixture was stirred magnetically and heated in an oil bath. When the temperature reached 175 °C terahydrofuran (THF) and water began distilling out. Stirring and heating at this temperature was continued until the distillation stopped. The reactions with various 1,n-diols were performed in bulb-to-bulb distillation unit (Aldrich Kugelrohr) at atmospheric pressure.

Identification of the products were done by gas chromatographic comparison with authentic samples and also by ^{1}H NMR spectra. GC analyses were performed on Datalab GC 900 series gas chormatograph with flame ionization detector. A 15 m long capillary column AT-wax was used. Injector and detector temperature were 220 and 250 °C, respectively. The oven was kept at 100 °C. Nitrogen was used as the carrier gas. ^{1}H NMR spectra were recorded on a JEOL FX 100 spectrometer in CDCl$_3$ using TMS as internal standard.

Results and discussion

Cyclodehydration of butane-1,4-diol to THF was chosen as the model reaction to compare the activity of the metal phosphate catalysts. The results are shown in Table 2.

Cyclodehydration of butane-1,4-diol with SnP catalyst gave THF selectively in excellent yields (entry 1). A decrease in the amount of catalyst used resulted in a lower yield of THF and required longer reaction times (entry 2). Therefore, a substrate
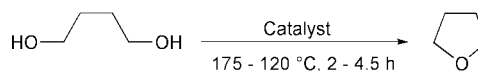
to catalyst mole ratio of 65:1 was used for all other reactions. The TiP catalyst at 175 °C gave poor yield of THF (entry 3). However, when the temperature of the bath was raised to 210 °C, THF started distilling out and was obtained in 66% yield in 4.5 h (entry 4). Similarly, the ZrP catalyst gave THF in high yield at 210 °C (entry 5). In these experiments, THF was obtained as the only product, and so attests the highly selective nature of the catalysts for this reaction. In the absence of catalyst, no reaction occurred in 5 h at 210 °C.

Amongst the three catalysts, tin phosphate showed substantially higher activity than the corresponding titanium and zirconium analogues. The latter required higher temperature and longer reaction times. These observations can be easily explained on the basis of acidity of the three materials (Table 1). SnP has the highest number of acid sites per gram of the material while TiP has the least. This is also evident from the ammonia desorption profile of the three materials (Fig. 1). In the case of ZrP and TiP a temperature maxima is observed at *ca.* 350 °C which can be attributed to weak acid sites. After this temperature, total desorption takes place indicating absence of any strong acid sites. For SnP a small peak present at *ca.* 270 °C is due to weak acid sites; no significant desorption takes place until 540 °C which indicates the presence of strong acid sites. This also accounts for the higher activity of SnP. A significantly higher surface area of SnP as compared to those of ZrP and TiP is also in accord with the difference in their catalytic activities (Table 1). The recycling ability of the catalyst was assessed by reusing the catalyst from the reaction in entry 1. Thus, a fresh amount of butane-1,4-diol was added to the residual catalyst at the end of the reaction in entry 1 and the mixture was stirred and heated at 175 °C. THF was again obtained in a high yield of 95%, however, this required 2.5 h, as compared to 2 h in the previous run.

Since SnP was found to be the best catalyst for cyclodehydration of butane-1,4-diol, it was chosen for cyclodehydration of other substrates to evaluate the scope of the reaction. The results of these reactions are given in Table 3. The reactions were performed in bulb-to-bulb distillation unit (Aldrich Kugelrohr), as it was more convenient and efficient than the simple distillation assembly. Thus, cyclodehydration of butane-1,4-diol gave 95% yield of THF in 1.5 h (entry 1) as compared to 2 h required for the same yield in the distillation unit (see entry 1 in Table 2). Pentane-1,5-diol gave tetrahydropyran in nearly quantitative yield at slightly higher temperature (entry 2). Cyclodehydration of hexane-1,6-diol required an even higher temperature to yield oxapane but in lower yield (entry 3). A significantly lower yield of cyclic ether from hexane-1,6-diol as compared to those from butane-1,4-diol and pentane-1,5-diol has previously been observed with other catalyst systems.[3,4] It is interesting that SnP catalyzed cyclodehydration of hexane-1,6-diol gave oxapane selectively whereas sulfated zirconia catalyzed reaction led to a mixture of products.[5] Cyclodehydration of diethylene glycol gave 1,4-dioxane in 28% yield (entry
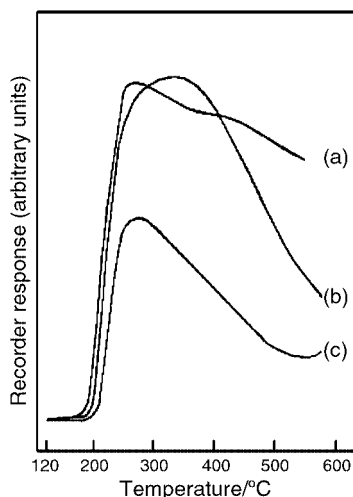
Fig. 1 Temperature programmed desorption profiles of (a) SnP, (b) ZrP and (c) TiP.

Table 1 Properties of the metal phosphate catalysts

| Catalyst	Surface area/ m^2 g^{-1}	Pore volume/ cm^3 g^{-1}	Acidity^a/mol g^{-1}
SnP	141	0.18	6.08×10^{-4}
ZrP	68	0.19	5.61×10^{-4}
TiP	59	0.23	2.98×10^{-4}

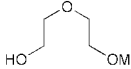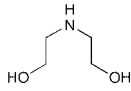^{a} Determined by NH$_3$ desorption method.
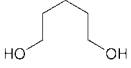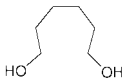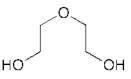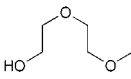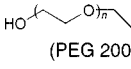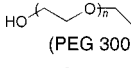
Table 2 Cyclodehydration of butane-1,4-diol by metal phosphate catalysts

Entry	Catalyst	Mole ratio substrate:catalyst	T/°C	t/h	THF yield^a (%)
1	SnP	65:1	175	2.0	95
2	SnP	130:1	175	3.5	75
3	TiP	65:1	175	2.5	7
4	TiP	65:1	210	4.5	66
5	ZrP	65:1	210	4.0	71

^{a} Yields are based on butane-1,4-diol. Selectivity to THF is 100%.

Table 3 Cyclodehydration of 1,*n*-diols catalyzed by tin phosphate

Entry	Substrate	T/°C	t/h	Product	Yield[a](%)
1	HO—⌣—OH	175	1.5	(tetrahydrofuran)	95
2	(pentanediol)	200	1.25	(tetrahydropyran)	97
3	(hexanediol)	230	1.5	(oxepane)	32
4	(diethylene glycol)	230	1.5	(1,4-dioxane)	28
5	(triethylene glycol)	230	1.5	(1,4-dioxane)	25
6	HO(O)nOH (PEG 200)	230	4.5	(1,4-dioxane)	17
7	HO(O)nOH (PEG 300)	230	4.5	(1,4-dioxane)	11
8	HO...OMe (DEG monomethyl ether)	230	1	(1,4-dioxane)	97
9	HO...NH...OH (diethanolamine)	230	2	(morpholine)	11

a Yields are based on substrate taken.

4). Triethylene glycol under these conditions also gave 1,4-dioxane albeit in slightly lower yields. Similarly, polyethylene glycols 200 and 300 gave 1,4-dioxane in low yields (entries 6 and 7). In reactions with triethylene and polyethylene glycols the residue after 1,4-dioxane distillation was more viscous indicating polymerization to higher molecular weight ethers. The yield of 1,4-dioxane decreased with increase in molecular weight on going from diethylene glycol to polyethylene glycol 300 (entries 4–7). Cyclodehydration of 100 mmol triethylene glycol gave 25 mmol of 1,4-dioxane and 10 mmol of water in the distillate (entry 5). Ethylene glycol, a possible by-product, was absent in the distillate and also in the residue. Ethylene glycol did not undergo cyclodehydration with the SnP catalyst under these conditions.

Cyclodehydration of diethylene glycol monomethyl ether was facile as compared to DEG giving selectively 1,4-dioxane in excellent yield in 1 h (entry 8). Although the reaction was performed above the boiling point of the substrate, only 1,4-dioxane and water distilled out. The present catalyst is superior to HZSM-5 for this reaction as the latter is reported[5] to give 92% conversion and 78% selectivity to 1,4-dioxane. Cyclodehydration of diethanolamine gave morpholine in low

yield (entry 9). Water was formed in nearly three times the molar quantity of morpholine and the residue became thick indicating polymerization of the substrate. Reaction with butan-1-ol was performed with SnP catalyst at 210 °C for 7 h in a Parr autoclave. There was no formation of dibutyl ether and the substrate was recovered. This shows that the catalyst is selective for intramolecular cyclodehydration of diols.

Conclusion

The tetravalent metal acid salts described herein are novel and selective heterogeneous catalysts for cyclodehydration of 1,*n*-diols to the corresponding cyclic ethers. They also catalyze conversion of polyethylene glycols to 1,4-dioxane. The selectivities exhibited by these catalysts are even better than some of the reported catalysts systems for similar cyclodehydration reactions. Therefore, these catalysts hold promise as solid acid catalysts for further development.

Acknowledgments

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Microwave-accelerated Suzuki cross-coupling reaction in polyethylene glycol (PEG)

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Polyethylene glycol (PEG) is found to be an inexpensive and non-toxic reaction medium for the microwave-assisted Suzuki cross-coupling of arylboronic acids with aryl halides. This environmentally friendly microwave protocol offers ease of operation and enables recyclability of catalyst and synthesis of a variety of substituted biaryls employing palladium chloride as catalyst and potassium fluoride as the base.

Introduction

Carbon–carbon bond formation *via* the reaction of organometallics with organic electrophiles is one of the most important reactions in modern synthetic chemistry.[1] Most of these organometallic reagents are air- and moisture-sensitive, and fail to accommodate diverse sets of functional groups in molecules and hence limit their application. The palladium catalyzed carbon–carbon coupling reaction of organoboron compounds with aromatic halides (Suzuki reaction), in the presence of a base provides a mild method for the synthesis of various substituted biaryls.[2] The Suzuki reaction has gained prominence in recent years because of the availability of functionally substituted boronic acids which are environmentally safer than most other organometallics[3] and the importance of biaryls as pharmacophores in a variety of biologically active molecules.[4] The reaction is usually conducted in ethereal solvents such as tetrahydrofuran in the presence of a host of complex palladium catalysts.[5] Most of these palladium reagents tend to be expensive and difficult to recover and recycle. Consequently, improved conditions have been developed for the Suzuki reaction such as supported catalysts on mineral surfaces[6] or using water[7a] or ionic liquids.[7b] Recently, the cross-coupling of PEG-bound esters of bromo-, iodo- and triflate-*para*-substituted benzoates with aryl boronic acids in water have been reported.[7] PEG and its monomethyl ethers are known to be inexpensive, thermally stable, recoverable, and non-toxic media for phase-transfer catalysts.[8] In view of our general interest in microwave-assisted organic reactions[9] and cleaner chemical processes,[10] we examined the Suzuki reaction in PEG. In the present study the results are described for the preparation of various substituted biaryls from substituted aromatic bromides/iodides and aromatic boronic acids in PEG-400 as reaction medium. The deployment of PEG eliminates the use of volatile organic solvents and provides a high yielding route to Suzuki coupling using relatively inexpensive forms of palladium salts, such as palladium chloride, in contrast to expensive ligands.

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† V.V.N. is a postgraduate research participant at the National Risk Management Laboratory administered by the Oak Ridge Institute for Science and Education through an interagency agreement between the U. S. Department of Energy and the U. S. Environmental Protection Agency.
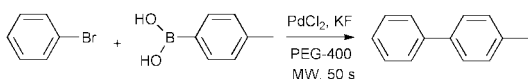
Results and discussion

In an unmodified household microwave (MW) oven it is not possible to vary the MW power. The reduction in power level simply entails that it operates at its full power but for a reduced period of time. In the present study we have used a recently introduced household MW oven (Panasonic) equipped with inverter technology[11] that provides a realistic control of the microwave power to a desirable level. The presence of a base is necessary for the reaction and among a variety of bases investigated, we find the use of potassium fluoride (KF) to be the most convenient (Table 1). The use of other bases requires water as co-solvent for their dissolution which not only reduces the solubility of the aromatic halides but increases the self condensation of boronic acids. Consequently, KF is selected as the base for this study wherein varied amounts of base and catalyst concentration are explored (Table 1). The reaction involves mixing the reactants and catalyst with PEG on a vortex mixer for 30 s to obtain a uniform mixture. The base, KF, is added at this stage and mixed thoroughly for another 30 s and then the reaction mixture is subjected to microwave irradiation. The subsequent addition of KF affords better yields. With lower amounts of PEG, the mixing is inefficient, which results in lower yields. Similarly, at higher concentrations of PEG, yields are inadequate. The optimum amount of PEG is found to be 2 g (mmol substrate)$^{-1}$ for higher yields. Among the aromatic halides, iodo and bromo compounds were found to be more reactive than the corresponding chloride (Table 2). The formation of a small amount ($<5\%$) of symmetrical biaryl occurs due to the self-coupling of boronic acids.[12] The aliphatic halide, 1-butyl iodide, did not undergo reaction under these

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Green Context

In view of its importance in organic synthesis, the Suzuki reaction has been extensively investigated in a variety of reaction media including solvent-free conditions and ionic liquids. This paper describes an improved protocol using inexpensive and non-toxic poly(ethylene glycol), PEG, that couples readily with microwaves and can be recycled. Unlike other protocols, self-coupling of the reactants has been eliminated or reduced to provide high yields. *DJM*

Table 1 Influence of bases and palladium chloride on MW-assisted Suzuki coupling[a]

No.	PdCl$_2$/mmol	Base	Quantity/ mmol	Water/mL	Irradiation time/s	Isolated yield (%)
1	0.282	KF	0.67	0	50	81
2	0.282	Na$_2$CO$_3$	0.67	0	50	40
3	0.282	NaOH	0.67	0	50	35
4	0.282	Na$_2$CO$_3$	0.67	0.5	20+15+15+15	76
5	0.282	NaOH	0.67	0.5	20+15+15+15	74
6	0.282	KF	0.67	0.5	20+15+15+15	78
7[b]	0.282	KF	0.33	0	50	58
8[b]	0.282	KF	0.5	0	50	73
9	0.338	KF	0.67	0	50	81
10[b]	0.225	KF	0.67	0	50	76
11[b]	0.169	KF	0.67	0	50	67
12[b]	0.113	KF	0.67	0	50	55
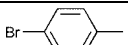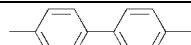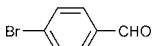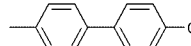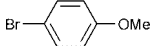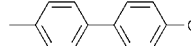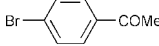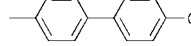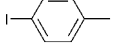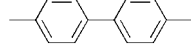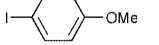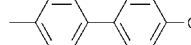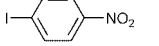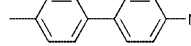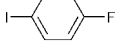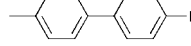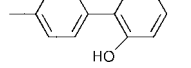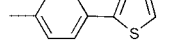
[a] 4-Methylphenyl (1.1 mmol), bromobenzene (1 mmol) and MW power = 240 W. [b] Formation of symmetrical biaryl due to self-coupling of boronic acid was observed.

Table 2 Reactivity trends of aromatic halides in Suzuki coupling[a]
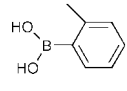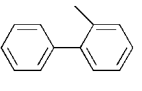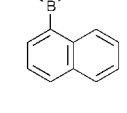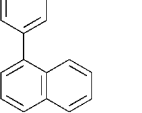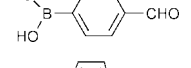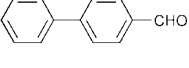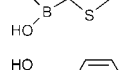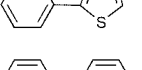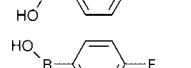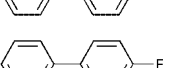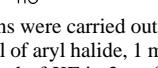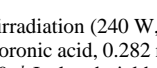
No.	Halide (1 mmol)	PEG/g	MW/s	Isolated yield (%)
1	Iodobenzene	2	50	85
2	Bromobenzene	2	50	81
3	Chlorobenzene	2	50	15
4	1-Butyl iodide	2	50	< 5
5[b]	Bromobenzene	1	50	70
6	Bromobenzene	2	60	81
7	Bromobenzene	3	50	72

[a] Reaction with 4-methylphenylboronic acid under the influence of microwaves (240 W). [b] Formation of the symmetrical biaryl is relatively higher.

Table 3 Effect of functional groups on the reactivity of aryl halides with 4-methylphenyl boronic acid under microwave irradiation

No.	RX (1 mmol)	Product	Isolated yield (%)
1			76
2			87
3			80
4			87
5			78
6			82
7			92
8			84
9			79
10			74

Table 4 Reactivity of various boronic acids with bromobenzene[a]

No	Boronic acid	Product	Yield[b] (%)
1			76
2			66
3			90
4			76
5			85
6			84

[a] Reactions were carried out by MW irradiation (240 W, 50 s) on a mixture of 1 mmol of aryl halide, 1 mmol of boronic acid, 0.282 mmol of PdCl$_2$ and 0.671 mmol of KF in 2 g of PEG-400. [b] Isolated yield.

conditions. The reaction can be conducted in 15 min using an alternative heating medium (oil-bath at 100 °C) with similar yields. However, we find the use of microwave oven is very convenient and clean. Further, the approach is adaptable for the parallel synthesis to generate a library of compounds.[13]

The reactions of 4-tolylboronic acid with a variety of aryl halides containing both electron-donating and electron-with-drawing substituents are examined. The results, summarized in Table 3, clearly show that the iodo compounds afford products in higher yield than the corresponding bromides. Among the aromatic halides the yields are higher for substrates bearing electron-withdrawing groups on the aromatic ring when compared to electron-donating groups. Finally, the reactivity pattern of bromobenzene with a variety of substituted boronic acids is examined (Table 4) which indicates that the electron-withdrawing substituents increase the yield of the reactions. If the recycling option is not undertaken, water is added to the reaction mixture and the unreacted aryl halide and the products

can be extracted with diethyl ether. In the recycling study, the reaction between 4-tolylboronic acid and bromobenzene could be repeated three times without reduction of the yield (80 ± 2%).

Experimental

Boronic acids were purchased from Matrix Chemical Co. Palladium chloride, KF, PEG-400, NaOH, Na_2CO_3 and aryl halides were purchased from Aldrich Chemical Co. and were used as such. The synthesis of 4-methylbiphenyl is representative of the general reaction protocol: PEG 400 (2 g), palladium chloride (0.050 g, 0.282 mmol), *p*-methylphenylboronic acid (0.150 g, 1.10 mmol) and bromobenzene (0.156 g, 1 mmol) were placed in a 25 ml round bottomed flask and mixed well on a Fisher Scientific touch mixer (Model 231). Potassium fluoride (0.390 g) was added to the reaction mixture, mixed well and the contents were then heated in an unmodified household microwave oven (Panasonic NN-S740WA, 1200 W)[11] at 240 W for 50 s. The reaction mixture turned from red to brown–black and the bulk temperature was found to be between 100 and 105 °C. After cooling, the product was extracted into diethyl ether (2 mL × 3) by vortexing and was purified by flash chromatography to afford 4-methylbiphenyl (84%); mp 44.0–45.0 °C; δ_H(CDCl$_3$) 7.40 (m, 9H), 2.37 (s, 3H). The recycling study was carried out by adding the reactants to the spent reaction medium, removing the residual diethyl ether on the rotary evaporator and subjecting the reaction to microwave irradiation.

Conclusions

Polyethylene glycol offers a convenient, non-toxic, thermally stable, inexpensive and recyclable reaction medium for Suzuki coupling, thus substituting for volatile organic solvents. The microwave heating offers a rapid and clean alternative at high solid concentrations and reduces the reaction times from hours to minutes. Further, the deployment of inexpensive forms of palladium (palladium chloride) as the catalyst and tolerance of a variety of functional groups bodes well for the general utility of the reaction. The recyclability of the catalyst makes the reaction economically and potentially viable for commercial applications.

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